Metal-promoted [3+2] and [4+2] cycloaddition reactions

Metal Promoted [3+2] and [4+2] Cycloaddition Reactions

by

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Abstract

Dicobalt complexes have been extensively used in synthetic chemistry to protect triple bonds, to form new carbon/carbon bonds using the Nicholas reaction and to form polycyclic molecules using the Pauson-Khand reaction. Using these dicobalt complexes, the formation of new carbon-heteroatom bonds was developed through [3+2] and [4+2] cycloaddition reactions *via* a stabilised dipole intermediate. Initial work carried out makes use of cyclopropanes substituted with a metal-alkyne complex towards the synthesis of tetrahydrofurans and pyrrolidines in good yields and with acceptable diastereoselectivity. The initial aim of the work described hereafter was to improve and expand the previous work carried out within the group. An alternative route using dihydrofurans as a cyclopropane surrogate was explored as well as other methods to form the cyclopropane in α-position to the alkyne. To extend the scope of the methodology, [4+2] cycloaddition reactions have been explored, using Nicholas carbocation. Various precursors have been prepared using a Knoevenagel condensation or an ene reaction. For the first time in synthetic chemistry, a novel [4+2] dipolar cycloaddition reaction from a cyclobutane has been developed. This reaction has opened a new way for the synthesis of six-membered heterocycles in a totally diastereoselective fashion using cyclobutane cores as precursors. A wide range of aldehydes was used as trapping reagents to form tetrahydropyrans in good yields up to 95% and with a good to total diastereoselectivity proven by nOe and X-Ray analyses. The use of other reagents such as ketones, imines and alkenes has been investigated towards the formation of new six-membered rings as an extension of the methodology.

Keywords:

Alkyne, cobalt, cycloaddition, cyclobutane, cyclopropane, Nicholas, Pauson-Khand.

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Contents

Abbreviations

Ac	=	acetyl
acac	=	acetylacetonate
bp	=	boiling point
Bn	=	benzyl group
^{t}Bu	=	tert-butyl
^{n}BuLi or BuLi	=	butyllithium
°C	=	degrees Celcius
CAN	=	ceric ammonium nitrate
cat	=	catalytic
CSA	=	camphor sulfonic acid
cm^{-1}	=	wave number
δ	=	chemical shift
d	=	doublet
1,2-DCE	=	1,2-dichloroethane
DCM	=	dichloromethane
dd	=	doublet of doublet
d.e.	=	diastereoisomeric excess
DME	=	1,2-dimethoxyethane
DMF	=	*N*,*N*-dimethylformamide
DMS	=	dimethylsulfide
d.r.	=	diastereoisomeric ratio
e^-	=	electron
e.e.	=	enantiomeric excess
EI	=	electron ionisation
eq	=	equivalent(s)
Et	=	ethyl
EtOH	=	ethanol
FAB	=	fast atom bombardment
g	=	gram
h	=	hour
^{n}hexyl	=	hexyl
Hz	=	Hertz

IR	=	infra-red
LDA	=	lithium diisopropylamine
$LiBH_4$	=	lithium borohydride
$LiAlH_4$	=	lithium aluminium hydride
m	=	multiplet
Me	=	methyl
MeCN	=	acetonitrile
MeOH	=	methanol
MHz	=	megahertz
min	=	minute
mL	=	millilitre
mmol	=	millimole
mp	=	melting point
ms	=	4 Å molecular sieves
Ms	=	mesyl
MS	=	mass spectrometry
m/z	=	mass to charge ratio
NBS	=	*N*-bromosuccinimide
NMO	=	*N*-methylmorpholine-*N*-oxide
NMR	=	Nuclear Magnetic Resonance
nOe	=	nuclear Overhauser effect
Nu	=	nucleophile
o-	=	ortho-substituted
OTf	=	trifluoromethanesulfonate
P	=	protecting goup
p-	=	para-substituted
Ph	=	phenyl
PKR	=	Pauson-Khand reaction
ppm	=	parts per million
^iPr	=	iso-propyl
RCM	=	ring closure metathesis
r.t.	=	room temperature
s	=	singlet
SM	=	starting material

t	=	triplet or time
T	=	temperature
TBAF	=	tetrabutylammonium fluoride
TBDMS	=	tert-butyldimethylsilyl
TBDPS	=	tert-butyldiphenylsilyl
Tf	=	trifluoromethanesulfonyl
THF	=	tetrahydrofuran
TLC	=	thin layer chromatography
TMANO	=	trimethylamine-*N*-oxide
TMS	=	trimethylsilyl
μL	=	microlitre

1. INTRODUCTION

1.1. Outline of alkyne/dicobalt hexacarbonyl complexes

Organocobalt chemistry is particularly diverse since all the oxidation states from −1 to +3 show quite extensive organometallic chemistry.[1] Cobalt is in group nine in the periodic table with a [Ar] $4s^2\ 3d^7$ electronic configuration. Since cobalt has an odd number of electrons, it has to form a dimer ($Co_2(CO)_8$) to complete the 18-electron configuration for a CO complex. Each Co atom donates an electron to create a Co–Co bond.[2a] X-Ray crystallographic studies of $Co_2(CO)_8$ established that two carbon monoxide ligands are bridging between the two cobalt atoms (Figure 1).[2b,c] Each one of these bridging ligands donates only one electron to each cobalt centre. This conformation prevents the Co–Co bonding orbitals from being collinear. Instead, the Co–Co bond is bent and each of the cobalt atoms is sp^3d^2 hybridised and is at the centre of an octahedral environment.

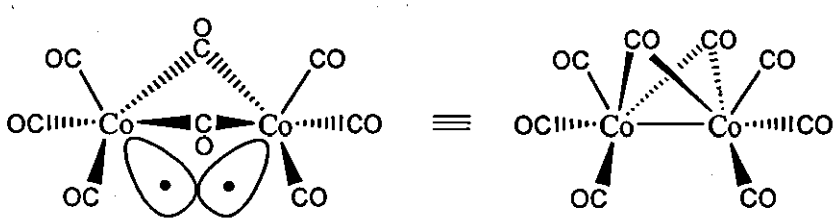
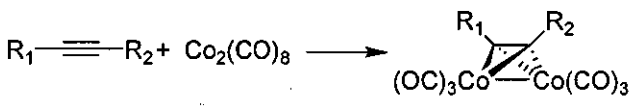


Figure 1

Sternberg *et al.* reported in 1954 that acetylene and substituted acetylenes readily displace the two bridging ligands in $Co_2(CO)_8$ to yield a new organometallic compound in which the alkyne acts as a four-electron donor ligand.[3a,b] In this new organometallic complex, the C–C bond originally C≡C is perpendicular to the Co–Co bond (Scheme 1).



Scheme 1

These alkyne/dicobalt hexacarbonyl complexes are some of the most stable complexes amongst the transition metal complexes with a low oxidation state.[1] They are air stable and their complexation is easy to perform, simply by means of addition of dicobalt octacarbonyl to a solution of alkyne in a non-polar solvent. The new bimetallic complex is rapidly formed with the loss of two carbon monoxide ligands.

The complexation of triple bonds with cobalt complexes modifies the geometry of the substrate.[4a,b] The linear geometry of the *sp* acetylenic carbon atoms changes towards the geometry of a *"pseudo* sp^3*"* hybridisation which results in a modification of the angle between acetylenic carbons and the substituents. If only the carbon chain is considered, a distortion is observed which brings the structure closer to that of an olefin. The substrate changes from a linear geometry to a complex in which the valence angles of the initially sp carbon atoms are approximately 140°. The new complex formed is then closer to a *Z*-substituted alkene (Figure 2).[4a]

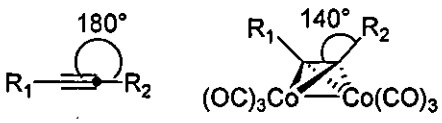
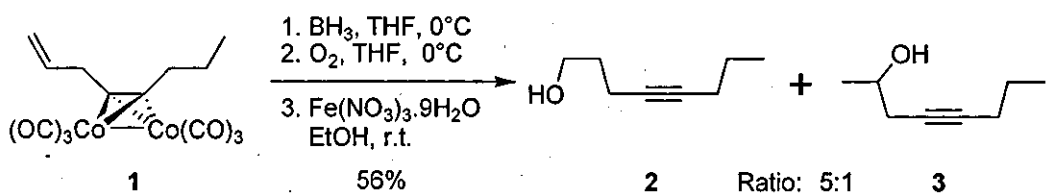


Figure 2

1.2. Protection of alkynes

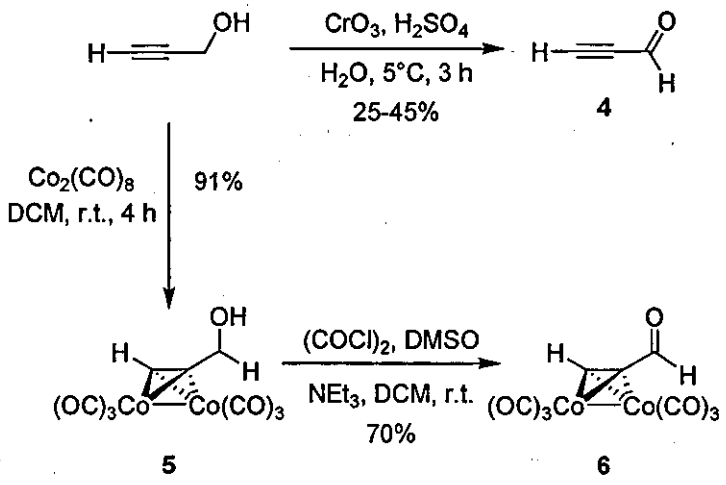
The dicobalt complexes may be used in synthetic reactions as a regioselective-protecting group for triple bonds. In the example hereafter, Nicholas and Pettit protected the triple bond from hydroboration.[5] The complex **1** was treated with BH_3 and oxidised under an O_2 atmosphere. The dicobalt complex was then removed by oxidation with iron (III) affording the two alcohols **2** and **3** in 56% yield in a 5:1 ratio (Scheme 2).



1 56% **2** Ratio: 5:1 **3**

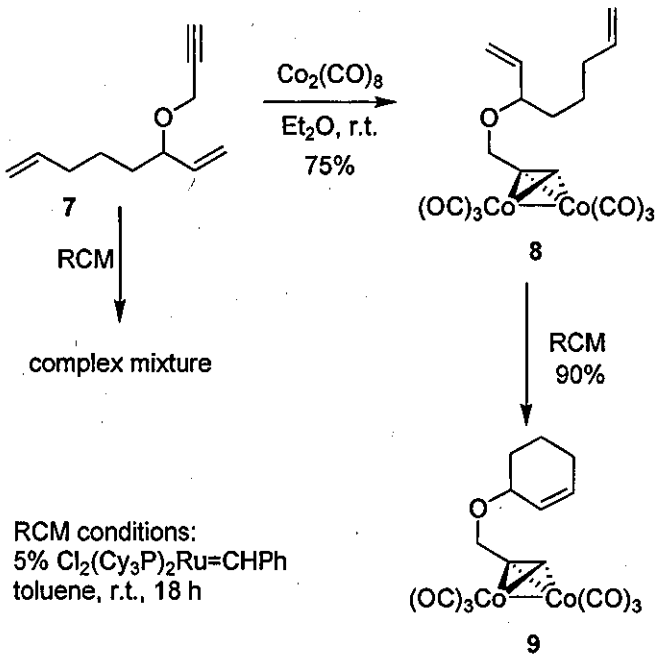
Scheme 2

Such a protection of the triple bond has also been used for the preparation of acetylenic aldehydes, which are generally obtained by oxidation of the corresponding propargylic alcohol using Jones oxidation with yields not exceeding 45%.[6a-c] Moreover, propargylic aldehydes such as propiolaldehyde **4** are very toxic, lachrymatory and volatile. After complexing the triple bond, the complexed propargyl alcohol **5** can be easily oxidised in a good yield using the Swern oxidation.[7a-c] This process lowers the toxicity of the reaction by avoiding the use of chromium based reagents such as Collins or Jones reagent. This method also increases the yield to 70% (Scheme 3).



Scheme 3

The protection of the triple bond with dicobalt complexes has also been used in the literature to avoid the triple bond from participating in the ring closure metathesis.[8a-c] In the example below, Pérez-Castells obtained a complex mixture of at least 3 metathesis products when the alkyne derivative 7 was not protected. On the other hand, using the complexed derivative **8**, only one product of RCM **9** was isolated in 90% yield.[8a]

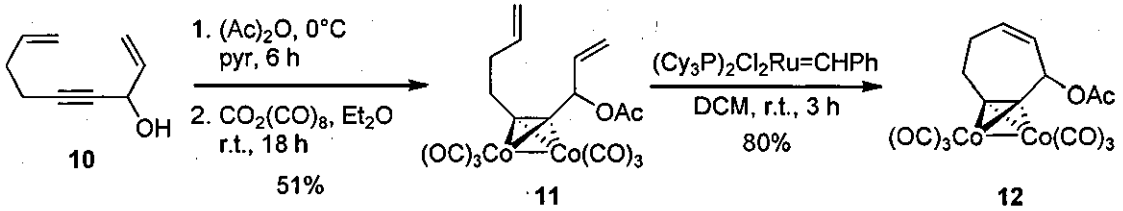


Scheme 4

1.3. Use of dicobalt complexes towards the synthesis of medium rings

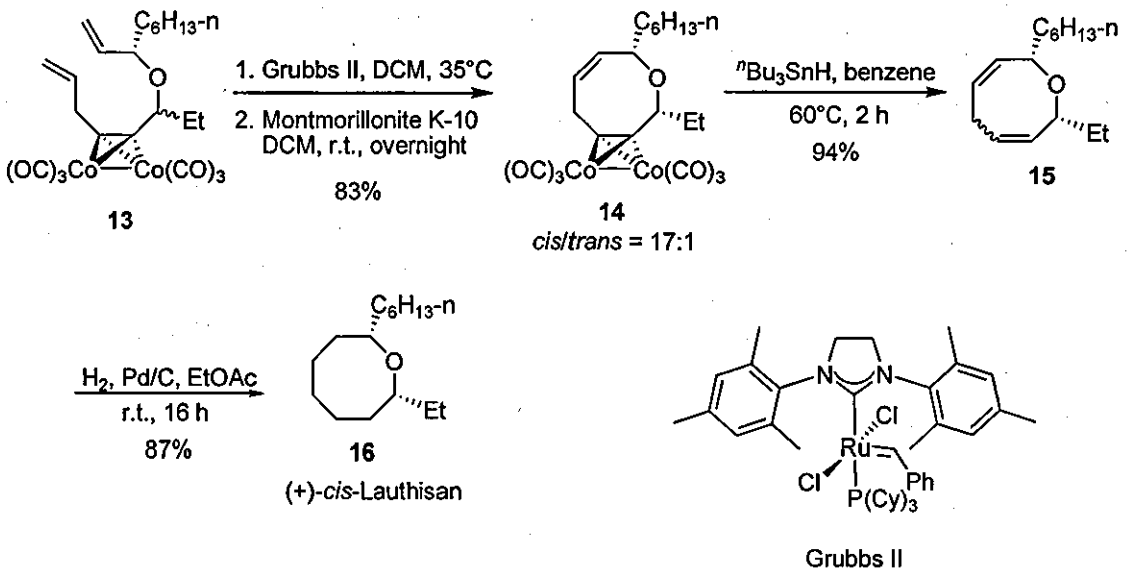
1.3.1. Ring closing metathesis

The change in the geometry of the linear alkyne to a homo-bimetallic cluster allowed the synthesis of medium rings and macrocycles using dicobalt complexes while the same ring closures with a free alkyne would not have been possible.[9a-d] In the example below, Green *et al.* prepared the nona-1,8-dien-4-yn-3-yl acetate complex **11** by complexation of the corresponding free alkyne **10**.[9a] A ring closing metathesis using Grubbs' I catalyst afforded the desired seven-membered ring **12** in 80% yield (Scheme 5).



Scheme 5

Martín also used the same methodology towards the synthesis of (+)-*cis*-Lauthisan.[9c] A ring closing metathesis of the complex **13** afforded the two diastereoisomers of the corresponding eight-membered ring **14** in 83%. The isomerisation to the *cis*-isomer using montmorillonite K-10 quantitatively led to a good 17:1 *cis*:*trans* ratio. Reduction of the alkyne/dicobalt hexacarbonyl complex using $^{n}Bu_3SnH$ afforded the corresponding diene **15** in 94% yield. A final reduction of the diene using Pd/C under a hydrogen atmosphere yielded the desired (+)-*cis*-lauthisan **16** in 87% (Scheme 6).



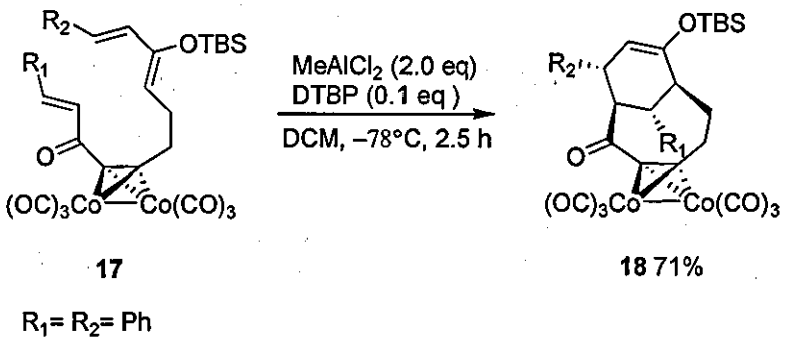
Scheme 6

In this synthesis, the use of an alkene instead of an alkyne would have led to a mixture of different products of ring closing metathesis. Using an alkyne/dicobalt hexacarbonyl complex was therefore important to protect this position and also to allow a distortion of the C–C bond allowing the ring closure to occur. The use of the dicobalt complex was also important for the isomerisation to the *cis*-isomer **14** using the Nicholas reaction. If an oxidising agent had been used instead of $^{n}Bu_3SnH$, the strain-energy produced by the generation of the free alkyne would probably have induced a ring opening.

1.3.2. [4+2] cycloaddition reaction

Iwasawa *et al.* also utilised this change in the geometry of the complexed alkyne. They predicted that the complexation of an alkyne bearing a diene and a dienophile unit on

opposite ends with dicobalt octacarbonyl would bring the diene and the dienophile closer to each other initiating an intramolecular Diels-Alder reaction (Scheme 7).[10]



17

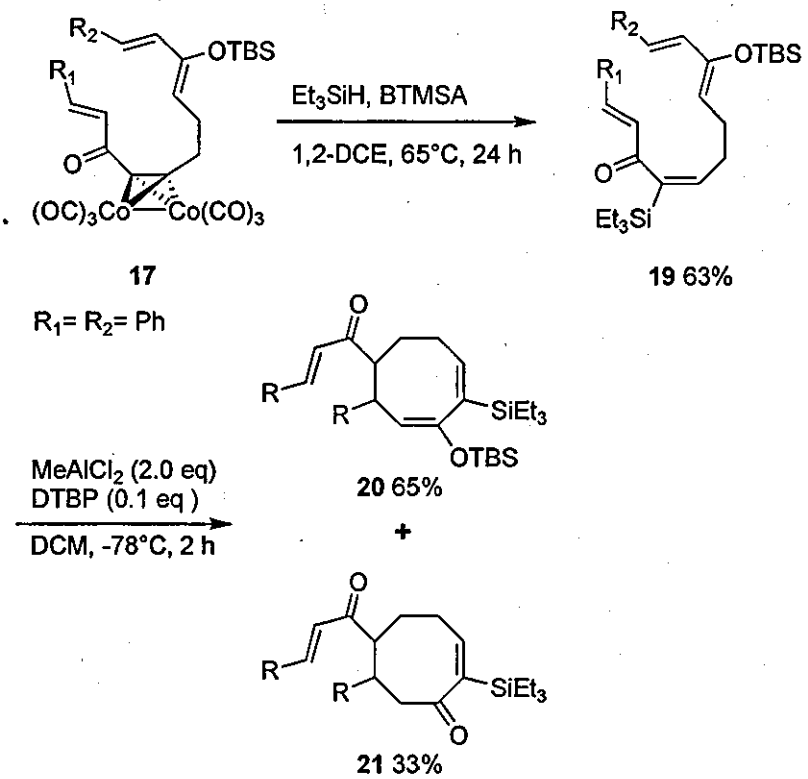
$R_1 = R_2 = Ph$

18 71%

Scheme 7

When compound **17** was dissolved in DCM in the presence of a Lewis acid and subsequently treated with 2,6-di-*tert*-butylpyridine (DTBP) at –78°C, the cycloadduct **18** was obtained in 71% yield after 2.5 h as a single stereoisomer. DTBP acted as a proton scavenger to prevent hydrolysis of the silyl group. Diels-Alder reactions on this type of substrate are known, usually leading to a fused-type cycloadduct and rarely to a bridged bicyclic molecule. Iwasawa *et al.* concluded that the mechanism involved in this reaction was not a concerted Diels-Alder reaction but rather a stepwise, double Michael type reaction leading to bridged-type [4+2]-cycloadducts.

In order to confirm the importance of the alkyne/dicobalt hexacarbonyl moiety, the corresponding olefinic substrate **19** was prepared from **17** by reduction of the dicobalt complex using triethylsilane (Scheme 8).



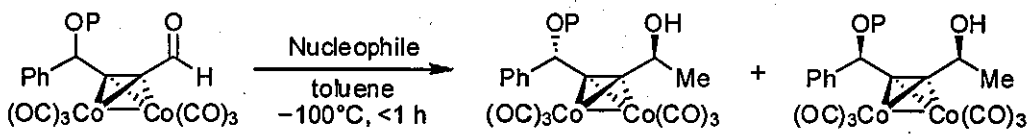
Scheme 8

The alkene derivative **19** under the same conditions did not afford the bridged-type cycloadduct but instead the monocyclic Michael addition products **20** and **21** in 65 and 33% yield respectively.

Iwasawa *et al.* also suggested that the distortion of the alkyne when complexed, released the steric strain of the transition state allowing the formation of the bridged-type cycloadduct. In the case of the olefin derivative **19**, the sp^2 carbons must not release enough strain in the transition state and only one Michael addition occurs.

1.4. 1,4-Asymmetric induction using Cobalt Alkyne Complexes

Hayashi *et al.* recently reported the use of alkyne/dicobalt complexes towards the diastereoselective synthesis of propargyl alcohol by nucleophilic attack of corresponding aldehydes (Scheme 9).[11]



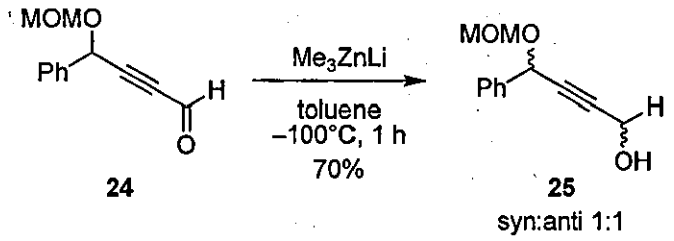
22_{a-c} *anti* **23_{a-c}** *syn*

SM	P	Nucleophile	Yield (%)	*anti*:*syn*
22_a	H	MeMgI	69	2 : 1
22_a	H	Me_3ZnLi	76	1 : 1
22_b	Bn	MeLi	41	2.3 : 1
22_b	Bn	MeMgI	33	1 : 1
22_b	Bn	Me_3ZnLi	0	n/a
22_c	MOM	MeLi	44	5.1 : 1
22_c	MOM	MeMgI	81	1.2 : 1
22_c	MOM	Me_3ZnLi	90	16 : 1

Scheme 9

The poor diastereoselectivity with a free complexed propargylic alcohol (22_a) was improved when the alcohol was protected. When using 22_b, the benzyl protecting group afforded poor yields and only a slight increase in diastereoselectivity was observed. The choice of the nucleophile was also important to prevent side reactions from occurring. A Nicholas type reaction could have occurred if the nucleophile used had Lewis acid properties and nucleophiles could have attacked the CO ligands on the cobalt, inducing decomplexation. The best results were achieved with 22_c when MOM was utilised as the protecting group and Me_3ZnLi was used as the nucleophile. These conditions improved the reaction with yields up to 90% and an excellent 16:1 *anti*:*syn* diastereoselectivity.

In their studies, Hayashi *et al.* noted that cobalt complexation was essential for the excellent diastereoselectivity, since no selectivity was observed in **25** when the uncomplexed alkynyl aldehyde **24** was used with identical conditions (Scheme 10).



24 **25**
syn:anti 1:1

Scheme 10

The angle of the triple bond of the alkyne is 180° whereas that of an alkyne complex is about 140°. Upon formation of the complex, the stereogenic and pre-stereogenic centres are forced closer together and therefore metal chelation is likely to occur. This then allows asymmetric induction of the substrate/metal *via* a 1,4-chelation (Figure 3).

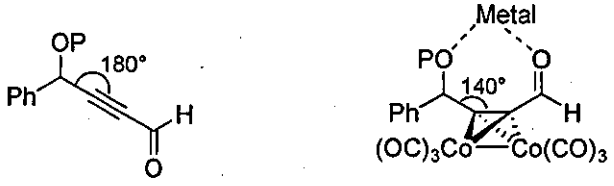
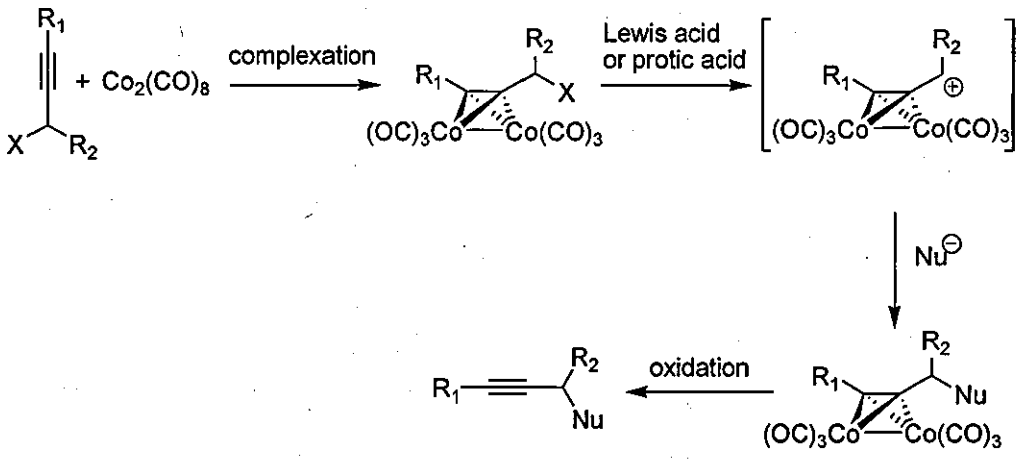


Figure 3

1.5. The Nicholas reaction

1.5.1. Outline of the Nicholas Reaction

The Nicholas reaction[12a] uses complexation to activate the "*pseudo*" propargylic position. The dicobalt complex stabilises a positive charge in the α-position to the triple bond thanks to the electrons in the d orbital. The stabilised carbocation can be trapped with various nucleophilic reagents avoiding the formation of allenic derivatives. The alkyne can then be decomplexed by oxidation with iron (III) or with ceric ammonium nitrate to release the free alkyne (Scheme 11). The Nicholas carbocation can be formed from various precursors, especially propargyl alcohols upon treatment with a Lewis or a protic acid.

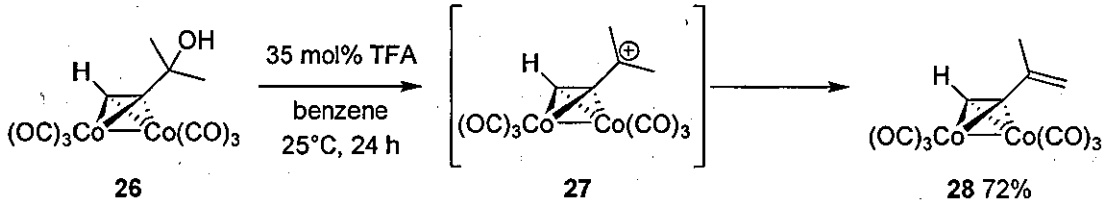


Scheme 11

Just a few examples are outlined hereafter but several comprehensive reviews are available, covering most of the work carried out on this reaction.[12a-c]

1.5.2. Reaction discovery

Propargylic alcohols and ethers can be easily activated using dicobalt complexes. Nicholas and Pettit were the first to report the formation of such propargylic ions in 1972.[13] They discovered that the tertiary propargyl alcohol complexes, such as compound **26**, readily undergo an acid-catalysed dehydration to yield the corresponding enyne complexes affording in this case the vinyl cobalt complex **28** in 72% yield in 24 h (Scheme 12).

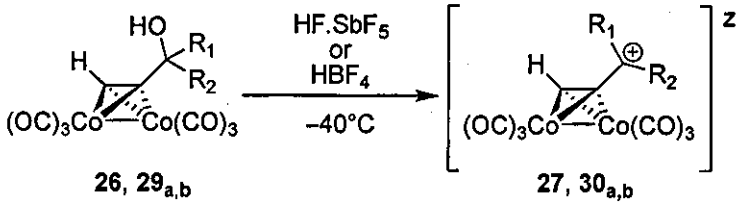


26 **27** **28** 72%

Scheme 12

Under identical reaction conditions, the uncomplexed carbinols were unchanged. As dehydration of the corresponding free tertiary propargyl alcohols required considerably higher temperatures (80-200°C), Nicholas and Pettit suggested that the dicobalt cluster interfered in the reaction process, allowing the formation of propargylium intermediate **27**.

Further evidence of this propargylic cation intermediate was demonstrated by ^{1}H NMR spectroscopy at 10°C after treatment of the propargyl alcohols with deuterated-TFA at 0°C. Further investigations allowed the preparation of the salts **27** and $\mathbf{30_{a,b}}$ by treatment of complexed propargyl alcohols **26** and $\mathbf{29_{a,b}}$ with HBF_4 or $HF.SbF_5$ in diethyl ether at –40°C (Scheme 13).[14]



26, $\mathbf{29_{a,b}}$ **27**, $\mathbf{30_{a,b}}$

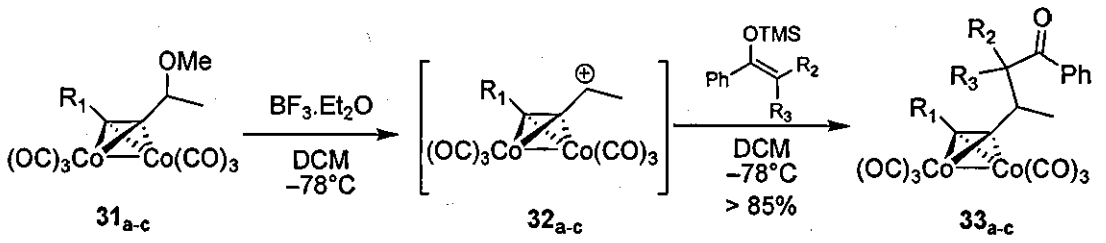
SM	R_1	R_2	Acid	Z	Product
26	Me	Me	$HF.SbF_5$	$\ominus SbF_6$	**27**
$\mathbf{29_a}$	H	H	HBF_4	$\ominus BF_4$	$\mathbf{30_a}$
$\mathbf{29_b}$	Me	H	HBF_4	$\ominus BF_4$	$\mathbf{30_b}$

Scheme 13

Evidence was established that dicobalt hexacarbonyl complexes induce a S_N1 heterolysis of propargyl alcohols revealing a "pseudo" propargylic carbocation, which was since referred to as the Nicholas carbocation. The generation of such a carbocation in this position is also possible without complexation although a rearrangement to the corresponding allene is likely.

1.5.3. Generation of Nicholas carbocation

Since its discovery, several methods have been developed to produce these carbocations. The most frequently used is the activation of a propargylic alcohol *via* treatment with a Lewis or a protic acid. Schreiber investigated a Lewis acid mediated version of this reaction on dicobalt complexed propargylic ethers. The carbonium intermediates $\mathbf{32_{a-c}}$ were generated by treatment of the corresponding propargyl ethers $\mathbf{31_{a-c}}$ with a Lewis acid. Then the intermediates were trapped using the enolate of the trimethylsilyl enol ether generated *in situ* using $BF_3.Et_2O$ a second time to yield compounds $\mathbf{33_{a-c}}$ (Scheme 14).[15]



31_{a-c} 32_{a-c} 33_{a-c}

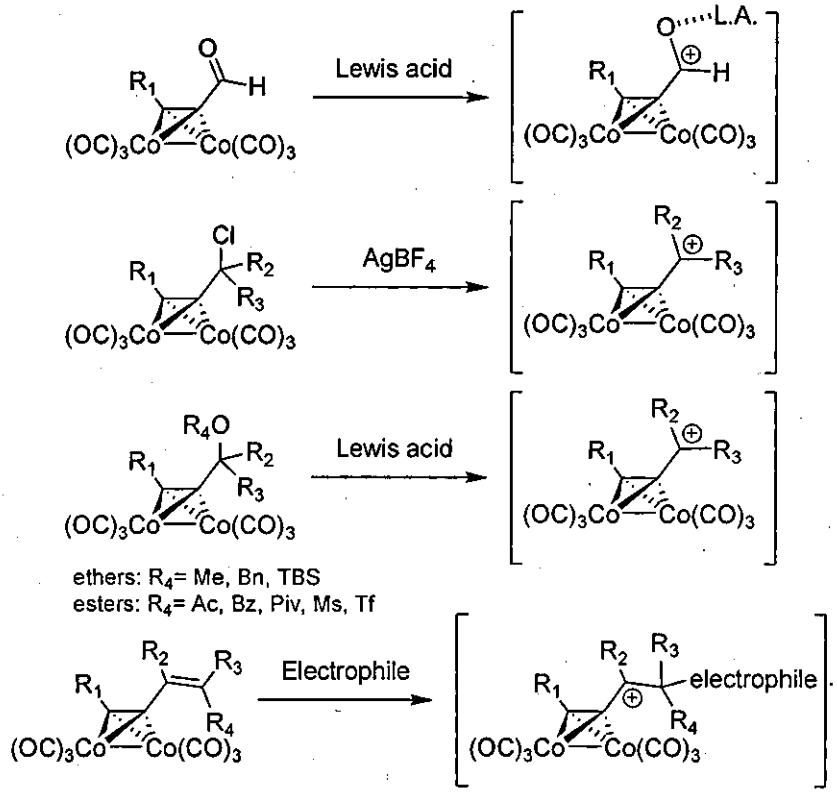
31_a R_1 = TMS; R_2 = Me; R_3 = H

31_b R_1 = Me; R_2 = Me; R_3 = H

31_c R_1 = Me; R_2 = H; R_3 = Me

Scheme 14

Several other methods summarised in Scheme 15 can be used to generate the Nicholas carbocation. Stabilised carbocations can be generated starting from various precursors such as propargyl aldehydes or chlorides,[16] different ethers including alkyl, benzyl and silyl derivatives,[17] various esters including mesylates and triflates,[18,19] and by electrophilic addition to 1,3-enyne complexes.[20]

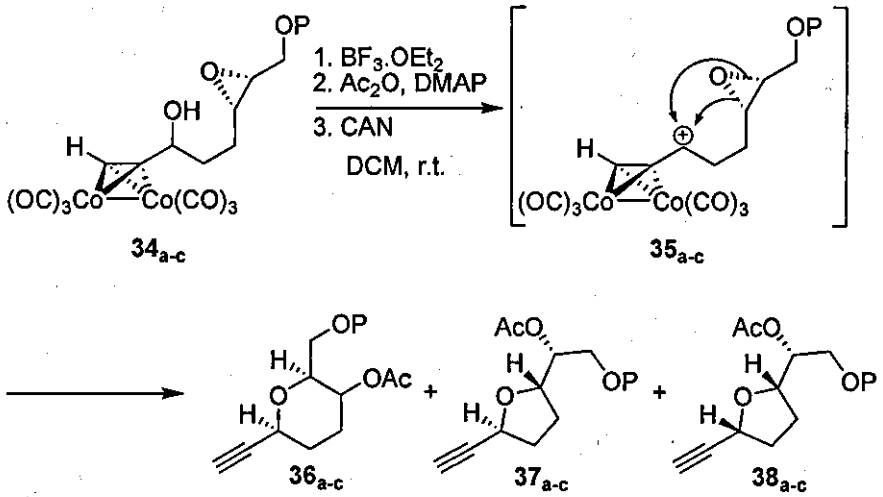


Scheme 15

1.5.4. Nucleophilicity towards Nicholas carbocation

1.5.4.1. Reaction with heteroatoms

Martín developed an application of this reaction. He used the Nicholas reaction to prepare poly-substituted tetrahydropyrans and oxepanes using epoxides as nucleophiles for the first time (Scheme 16).[21]

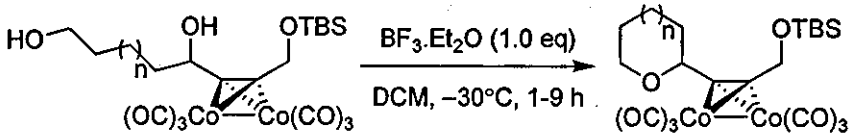


SM	P	t (h)	T (°C)	Yield (%)	36_{a-c} : 37_{a-c} : 38_{a-c}
34_a	Ac	24	r.t.	91	80 : 11 : 9
34_b	Boc	4	–20	70	100 : 0 : 0
34_c	TBDPS	24	r.t.	25	0 : 100 : 0

Scheme 16

The cyclisation was carried out using $BF_3.Et_2O$ as the Lewis acid affording the corresponding complexed oxacycles. The products obtained differed depending on the group used to protect the primary alcohol. The *endo*-tetrahydropyran diacetate $\mathbf{36_a}$ was obtained as the main product when $\mathbf{34_a}$ was submitted to the cyclisation conditions at room temperature for 24 h. However, the *exo*-tetrahydrofurans $\mathbf{37_a}$ and $\mathbf{38_a}$ could also be observed in substantial amounts. Under identical conditions, the use of a TBDPS group as the protecting group exclusively led to the formation of the *exo*-cyclisation product $\mathbf{37_c}$. The best selectivity was achieved when the carbonate $\mathbf{34_b}$ was submitted to similar conditions at –20°C. This afforded compound $\mathbf{36_b}$ in 70% yield. Martín also used primary and secondary

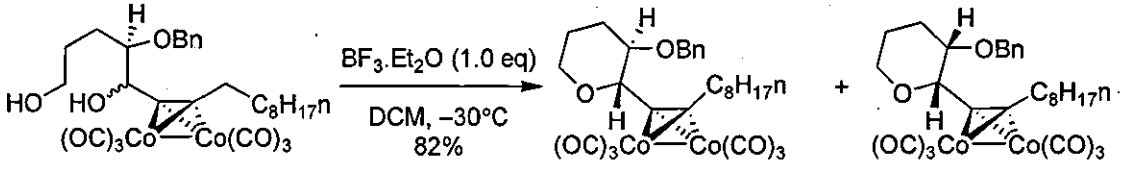
alcohols towards the synthesis of cyclic ethers *via* an intra-molecular Nicholas reaction (Scheme 17).[22a-d] Their initial studies focused on the attack of a hydroxyl group in a suitable saturated chain onto a Nicholas carbocation generated by acid treatment of the corresponding complexed propargylic alcohol.[22a] As the carbon chain was extended to prepare larger rings, the yields decreased substantially, particularly once the chain extended past three additional carbon atoms.



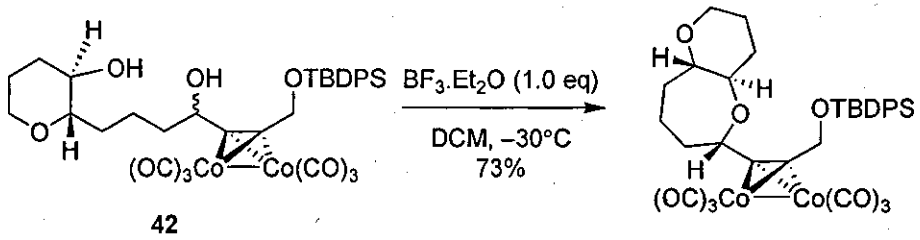
a: n= 1; 85%
b: n= 2; 78%
c: n= 3; 72%
d: n= 4; 55%

Scheme 17

An important feature of their methodology is the intramolecular stereocontrol (Scheme 19). When the acid-mediated cyclisation of **39** was performed, the two isomers **40** and **41** were obtained in a 1:3 *cis*:*trans* ratio. Improved stereocontrol was observed with cyclic secondary alcohols. In the case of the precursor **42**, only the diastereoisomer **43** was seen after cyclisation.[22a]



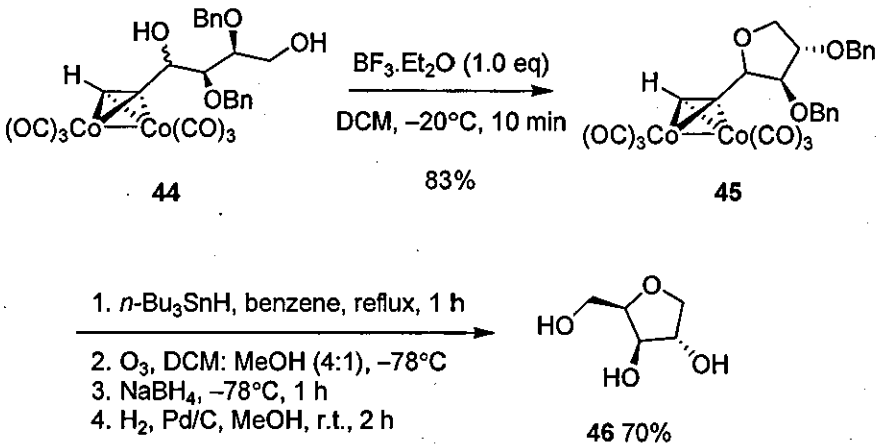
39 **40** **41**



42 **43**

Scheme 18

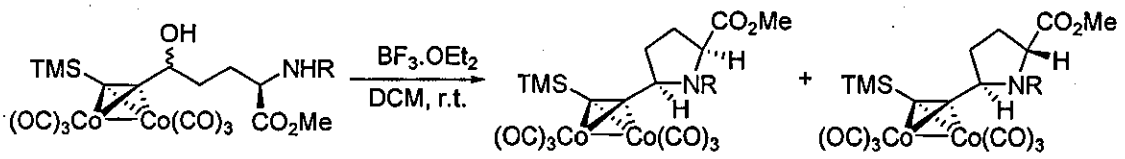
In order to show the potential synthetic applications of this methodology, Martín achieved the synthesis of 1,4-anhydro-L-arabitinol in a good yield (Scheme 19).[23] The tetrahydrofuran derivative **45** was formed using the Nicholas carbocation by intramolecular cyclisation. The reduction of the bimetallic cluster to the corresponding alkene using tri-*n*-butyltin hydride followed by ozonolysis of the double bond afforded the aldehyde derivative. The aldehyde was then reduced to the corresponding alcohol using sodium borohydride and subsequent deprotection of the alcohols afforded the desired natural product **46** in 58% overall yield.



44 **45** **46** 70%

Scheme 19

Given the similar chemical reactivity of nitrogen based nucleophiles and alcohols, Nicholas reactions have also been reported using tosyl-amines.[24] Recently, Martín *et al.* have developed the stereoselective synthesis of 5-alkynylprolines using the Nicholas carbocation (Scheme 20).[25] A suitable choice of the *N*-protecting group (tosyl or benzoyl derivative) allowed the control of the stereochemistry during the ring formation.



$47_{a,b}$ $48_{a,b}$ $49_{a,b}$

SM	R	t	Yield (%)	*cis*:*trans* ratio
47_a	Ts	15 min	88	>99:1
47_b	Bz	2 h	86	1:10

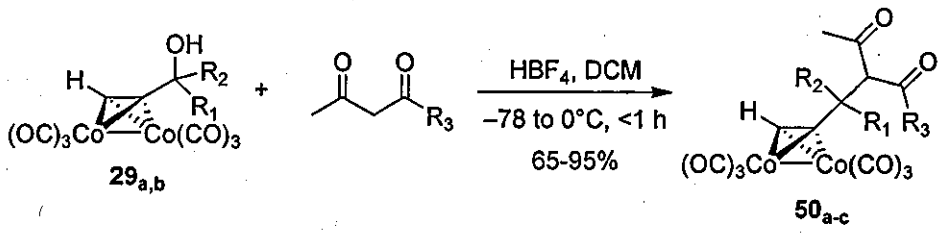
Scheme 20

When a tosyl protecting group was used, the cyclisation afforded the *cis* five-membered ring 48_a only, in 88% yield after 15 min. The stereoselectivity of the reaction could be reversed when a benzoyl group was used as the *N*-protecting group affording a mix of the pyrrolidines 48_b and 49_b in 86% yield after 2 h as a 1:10 ratio respectively.

1.5.4.2. Coupling to carbon centred nucleophiles

1.5.4.2.1. Enolate as nucleophile

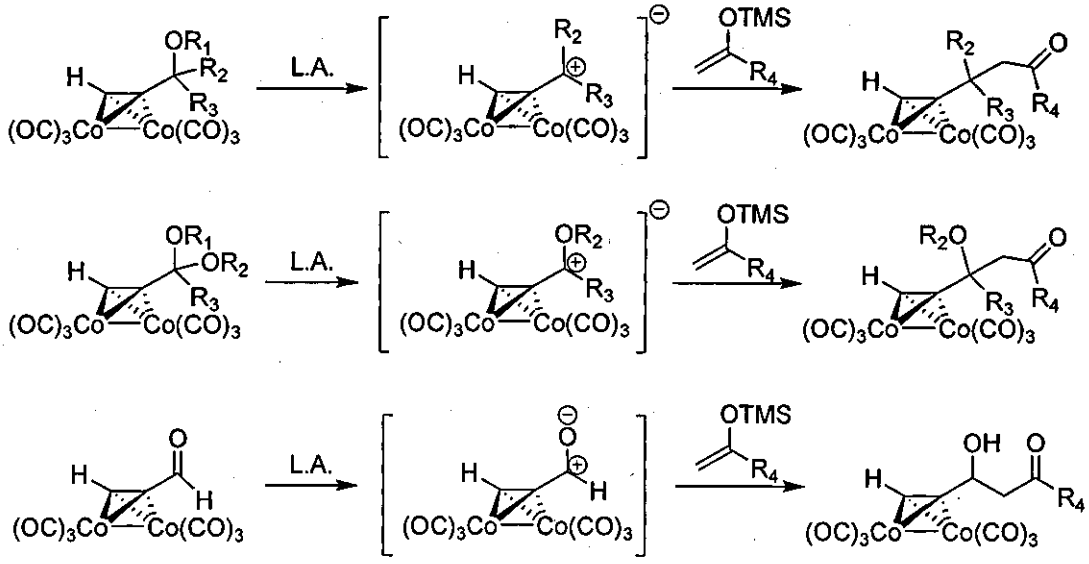
The formation of carbon-carbon bonds using the Nicholas carbocation is well reported in the literature. Nicholas and Hodes reported the first addition of an enolate to a Nicholas carbocation in 1978.[26a] The Nicholas carbocation was generated *in situ* by the treatment of the secondary alcohols $29_{a,b}$ with HBF_4 at −78°C (Scheme 21). The reaction of acetylacetone or benzoylacetone with the newly formed propargylic cations afforded the alkylated product 50_{a-c} as its dicarbonyl tautomer in good to high yields (>95% by NMR spectroscopy).



SM	R_1	R_2	R_3	Product	Yield (%)
29_a	H	H	Me	50_a	95
29_a	H	H	Ph	50_b	90
29_b	Me	H	Me	50_c	65

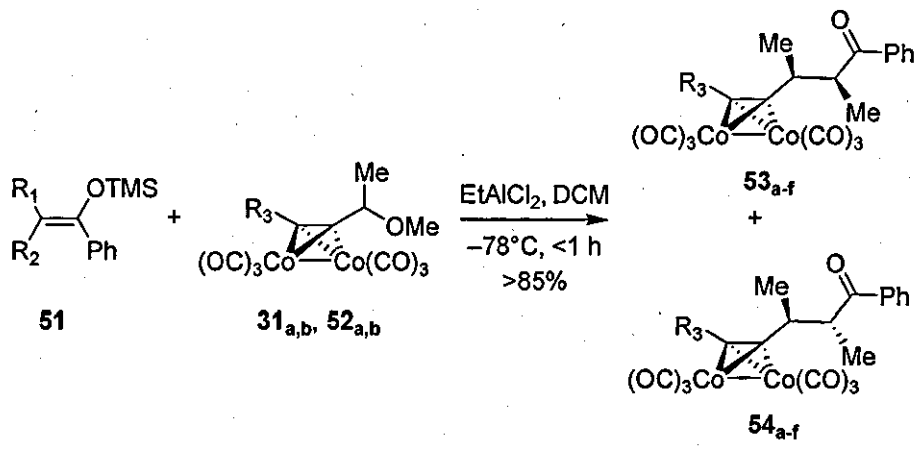
Scheme 21

Silyl enol ethers have been used in Nicholas type reactions with a wide range of propargyl ethers,[27a-b] acetals[28a-d] and aldehydes[29a-c] (Scheme 22).



Scheme 22

Schreiber *et al.* also developed a selective Lewis acid mediated enolate addition of silyl enol ethers onto propargyl ethers (Scheme 23).[27a]



Reactant	R_1	R_2	R_3	Lewis acid	Products		*syn:anti*
31_a	Me	H	Me_3Si	$BF_3.Et_2O$	**53_a**	**54_a**	15:1
52_a	Me	H	Ph	$EtAlCl_2$	**53_b**	**54_b**	18:1
52_a	H	Me	Ph	$EtAlCl_2$	**53_c**	**54_c**	9:1
31_b	Me	H	Me	$BF_3.Et_2O$	**53_d**	**54_d**	6.8:1
31_b	H	Me	Me	$BF_3.Et_2O$	**53_e**	**54_e**	3.5:1
52_b	Me	H	H	$EtAlCl_2$	**53_f**	**54_f**	1.6:1

Scheme 23

The addition of both (*Z*) and (*E*)-trimethylsilyl enol ethers of propiophenone resulted in the synthesis of predominantly the *syn* diastereoisomers **53_{a-f}**. However it was found that the (*Z*)-enol provided a better diastereoselectivity than the (*E*) isomer. The R_3 group on the cobalt complex also influenced the reaction as bulkier groups provided better stereoselectivity increasing the *syn:anti* ratio from 1.6:1 for an atom of hydrogen (product **53_f** and **54_f**) to 18:1 for when a phenyl group was used (product **53_b** and **54_b**). Schreiber suggested that the rational for this stereoselectivity was based on the existence of a transition state with a synclinal alignment of the two π-systems obtained by isomerisation, thus resulting in *syn*-alkylation (Figure 4).

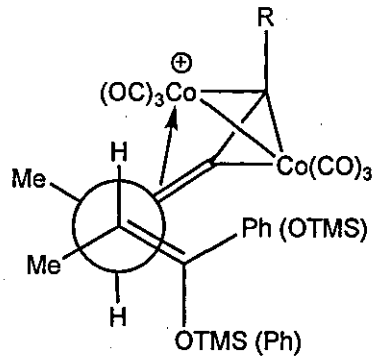
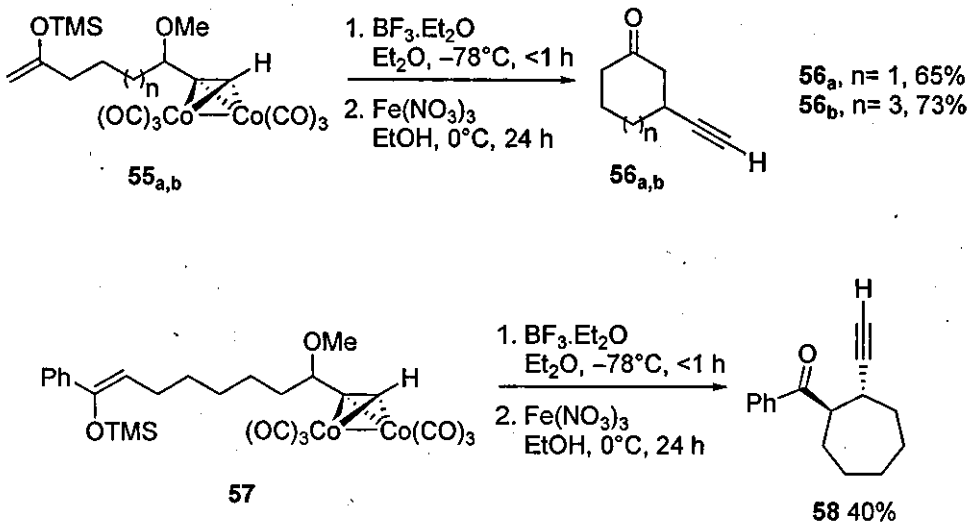


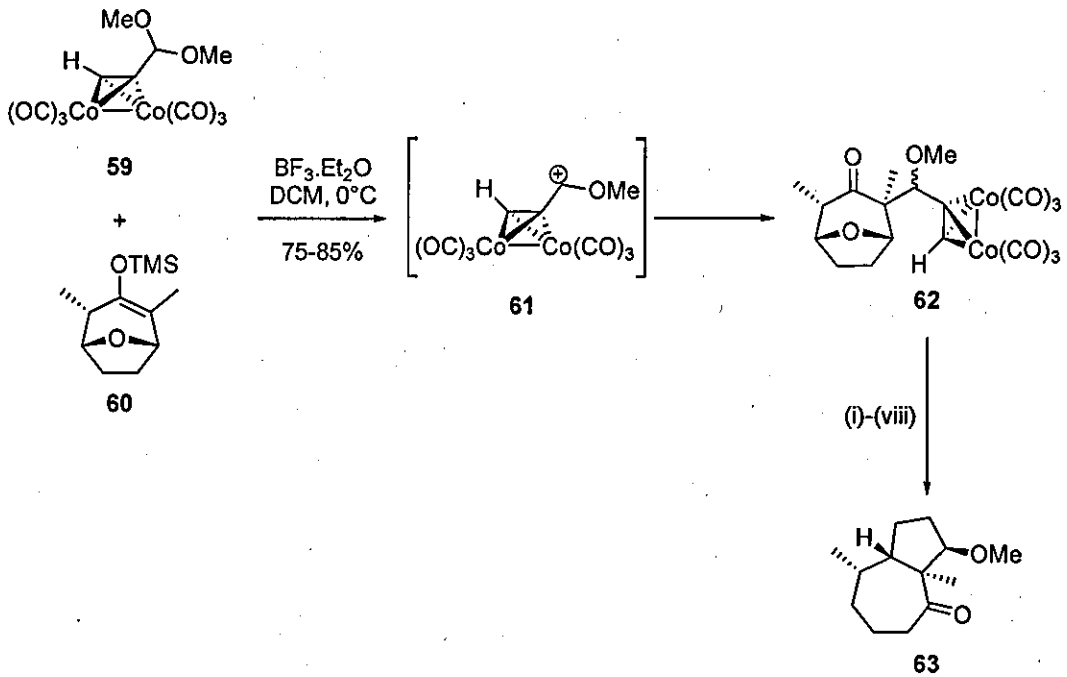
Figure 4

An intramolecular version of this reaction was developed by Tyrrell *et al.* while investigating the synthesis of cyclic β-alkynyl ketones.[30] The resulting keto product can be either *endo* $\mathbf{56_{a,b}}$ or *exo*-cyclic **58** and this depends on the enol ether used (Scheme 24).



Scheme 24

In a similar way, Montaña *et al.* utilised acetals to generate the Nicholas carbocation and he used silyl enol ethers as nucleophilic trapping reagents.[28a-d] A good example of the methodology that he developed used the Nicholas reaction towards the synthesis of *trans*-fused bicyclo[5.3.0]decane ring **63** (Scheme 25).[31a,b]



(i) CAN, Et_3N, acetone, 0°C, 95%; (ii) Hg^{II} *p*-toluensulfamidate, EtOH/H_2O (85/15) reflux, 82%; (iii) KOH, EtOH, r.t., 72%; (iv) $SOCl_2$, Py, –24°C, 94%; (v) $HSCH_2CH_2SH$, $BF_3.Et_2O$, 0°C, 95%; (vi) Raney-Ni, EtOH, reflux, 85%; (vii) H_2, Pd/C(10%), MeOH, r.t., chromatographic separation, 90%; (viii) PCC, DCM, r.t., 95%.

Scheme 25

The Nicholas carbocation was generated by treatment of the acetal **59** with a Lewis acid to form the desired intermediate **61**. A subsequent nucleophilic attack of the silyl enol ether **60** onto the Nicholas carbocation afforded the complex **62** which was then transformed into the *trans*-fused bicyclo[5.3.0]decane ring **63**. The diastereoselective attack of the silyl enol ether onto the Nicholas carbocation was induced by the hindrance of the bicyclic core of the silyl enol derivative (Figure 5). The large size of the cobalt group ensured that the attack was directed exclusively onto the *exo* face of the silyl enol ether, resulting in the formation of only one isomer.

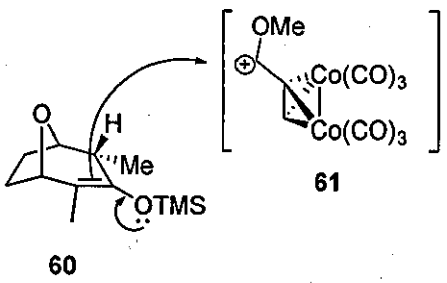
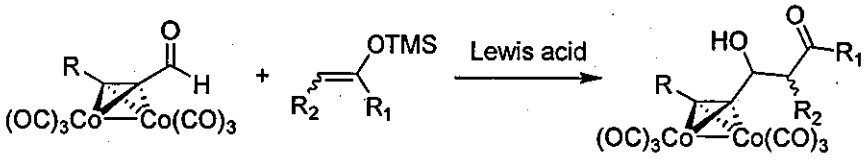


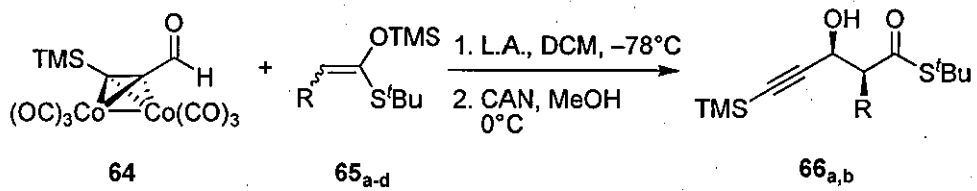
Figure 5

Hanaoka[32] and other groups[33] researched into the use of propargylic aldehydes to perform aldol type reactions with silyl enol ethers (Scheme 26).



Scheme 26

During their investigations, they focused on the aldol reaction between the cobalt complexed propynal **64** and *O*-silyl ketene *O*,*S*-acetals **65**$_{a-d}$.[34a] They found that the use of these type of acetal systems provided a high *syn*-selectivity independently of the stereochemistry of the alkene (Scheme 27).



64 **65**$_{a-d}$ **66**$_{a,b}$

SM	R	Alkene	Lewis acid	Product	Yield (%)	*syn:anti*
65$_a$	Me	*E*	$TiCl_4$	**66**$_a$	90	98:2
65$_b$	Me	*Z*	$TiCl_4$	**66**$_a$	84	98:2
65$_c$	Et	*E*	$BF_3.Et_2O$	**66**$_b$	89	98:2
65$_d$	Et	*Z*	$TiCl_4$	**66**$_b$	93	98:2

Scheme 27

Complex **64** was allowed to react in dry DCM with *O,S*-acetals $\mathbf{65_{a-d}}$ in the presence of $TiCl_4$ or $BF_3.Et_2O$ to afford the aldol products with the cobalt moiety, which were then decomplexed by oxidation with cerium (IV) ammonium nitrate in methanol at 0°C. The result was the exclusive formation of the *syn*-isomers $\mathbf{66_{a,b}}$ in excellent yields, whilst the degree of *syn*-selectivity was found not to be dependent on the geometry of the alkene.

These results can also be explained with Schreiber's intermediate. The *O,S*-acetal synclinally approaches the Nicholas carbocation intermediate where the hydrogen atom is in the most hindered position of the cobalt complex thus minimising Van der Vaals interactions with the bulky cobalt moiety. This positions the oxygen atom and the R group in an antiperiplanar fashion in relation to the π-systems (Figure 6).

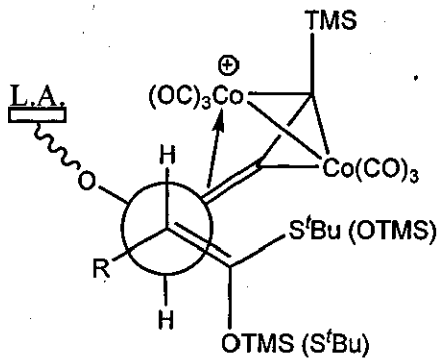
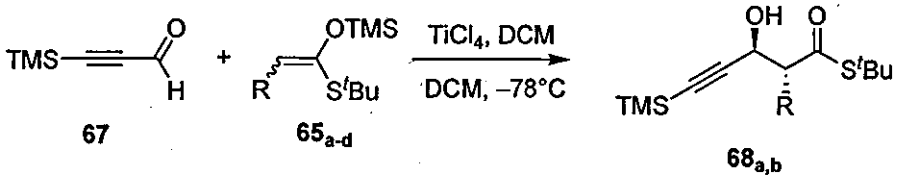


Figure 6

The aldol reaction with propargylic aldehyde is well documented in the literature and can be easily performed without the cobalt complex. Hanaoka *et al.* further investigated the use of the same *O,S*-acetals $\mathbf{65_{a-d}}$ and observed that the aldol reaction with the uncomplexed propynal **67** with similar conditions yielded the *anti*-isomers $\mathbf{68_{a,b}}$ in a highly stereoselective manner regardless of the geometry of the silyl enol ethers (Scheme 28).



SM	R	Alkene	Product	Yield (%)	*syn:anti*
65_a	Me	*E*	68_a	87	5:95
65_b	Me	*Z*	68_a	86	4:96
65_c	Et	*E*	68_b	74	2:98
65_d	Et	*Z*	68_b	92	2:98

Scheme 28

Hanaoka proposed that the high-*trans*-selectivity observed with the uncomplexed propargylic aldehyde was due to the interaction between the R group on the double bond of the *O,S*-ketal and the Lewis acid co-ordinated with the aldehyde oxygen. The interactions involved force the oxygen atom into being *trans* to the R group (Figure 7).

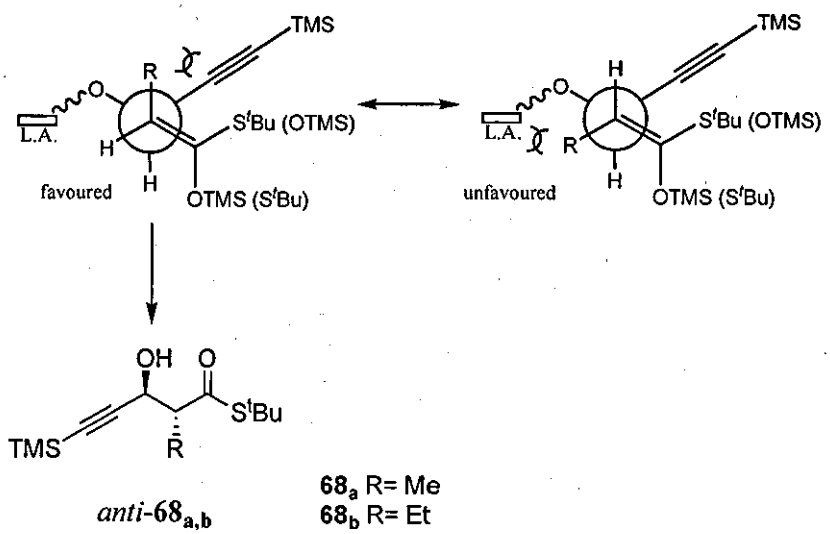
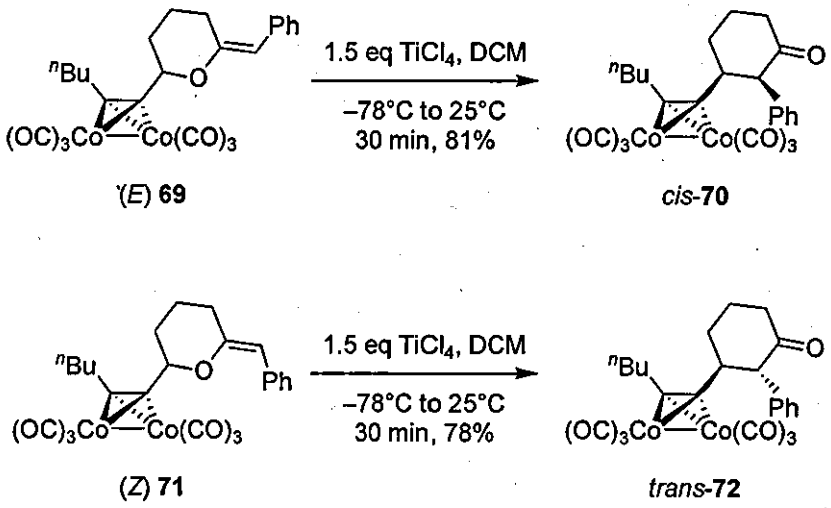


Figure 7

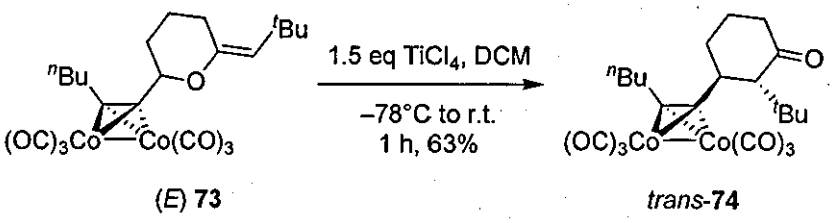
1.5.4.2.2. Dipolar rearrangement

Harrity *et al.* investigated an intramolecular rearrangement of enol ethers to α-alkyl β-alkynyl cyclohexanone.[35] They found that under Lewis acid conditions, propargylic enol ethers rearrange to yield cyclohexanones in a diastereoselective manner (Scheme 29).[36a,b]



Scheme 29

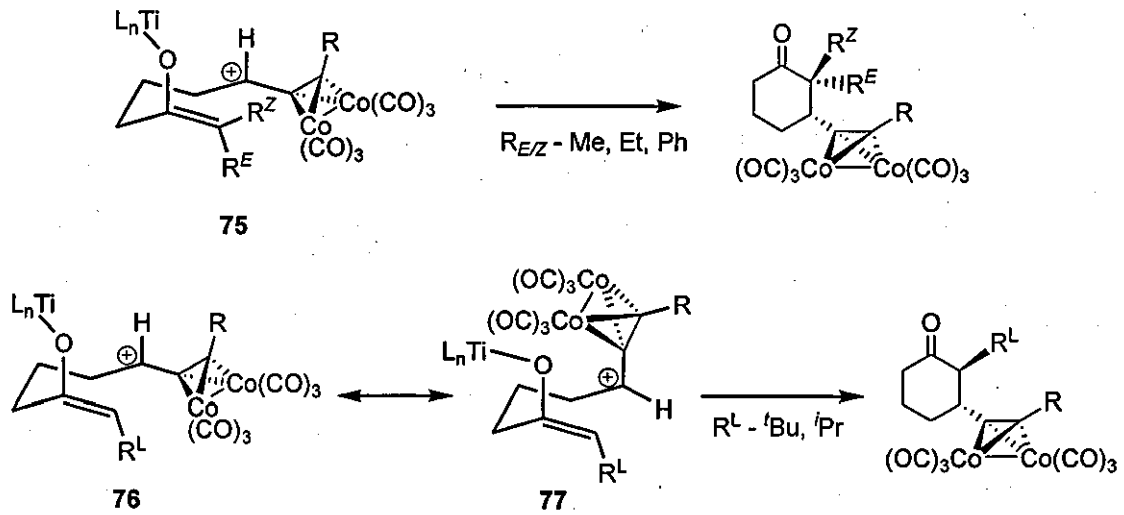
The (*E*)-enol ether **69** was easily converted into the corresponding *cis*-disubstituted ketone **70**, while the *Z*-isomer **71** yielded the *trans*-disubtituted ketone **72**.[36a] Surprisingly, these results were found to be dependant on the size of the group borne by the enolate: when a ^{t}butyl group (**73**) replaced the phenyl group, the stereoselectivity of the reaction was reversed affording the cyclohexanone **74** (Scheme 30).[37]



Scheme 30

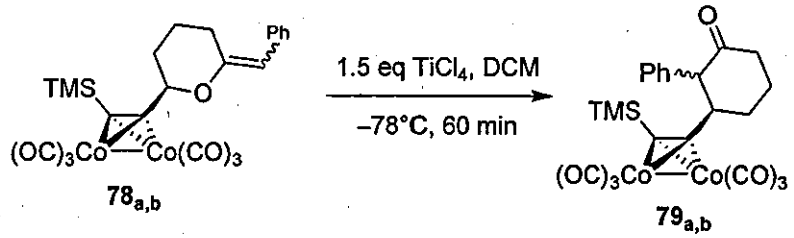
A chair conformation type intermediate could explain the stereoselectivity of the reaction; reactions with enol ethers bearing small groups such as Me, Et or Ph proceed *via* an

intermediate **75** in which the oxygen is in an axial position (Scheme 31). The stereoselectivity then depends on the geometry of the alkene. In the case of a sterically larger groups, such as ^{t}Bu or ^{i}Pr substituted substrates, the different stereochemical outcome suggest a different intermediate since a similar chair transition state **76** with the dicobalt cluster in equatorial position would provoke greater unfavourable steric interactions. Rotation of 180° around the propargylic carbon would lead to the intermediate **77** in which the steric interactions are limited (Scheme 31). Therefore, the latter transition state is more likely to result.



Scheme 31

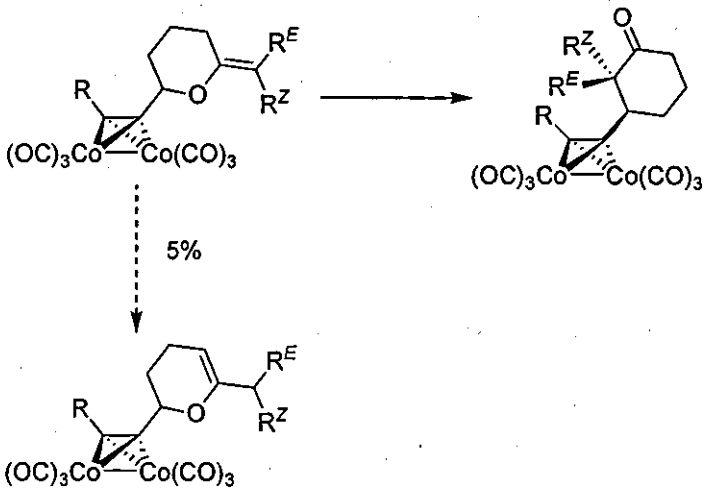
Optically pure *E*/*Z*-isomers of the enol ether **77** were used to measure the enantioselectivity of the reaction (Scheme 32).[38] Yields were not affected by the geometry of the alkene but the use of the *Z*-olefin improved the enantioselectivity from 77% for $\mathbf{79_b}$ to 87% for $\mathbf{79_a}$.



SM	Product	Yield (%)	ee (%)
Z-**78**$_a$	*trans*-**79**$_a$	84	87
E-**78**$_b$	*cis*-**79**$_b$	84	77

Scheme 32

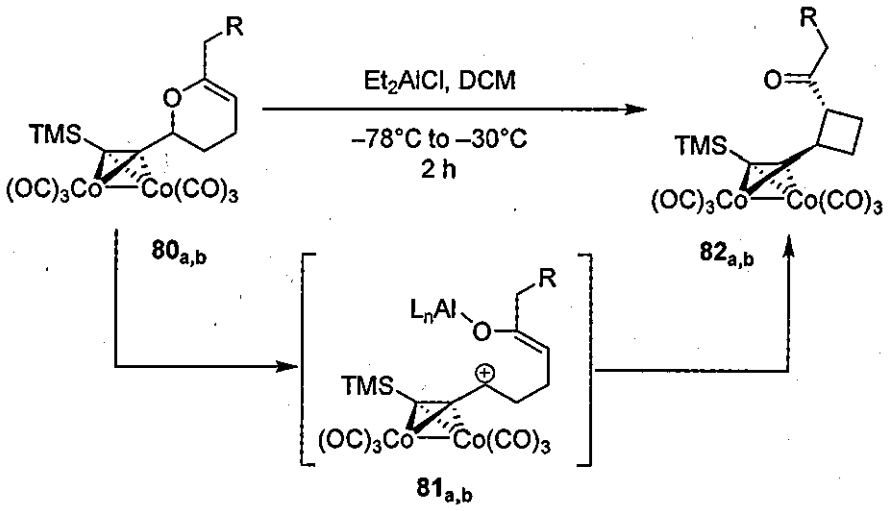
During their investigations, Harrity *et al.* inadvertently discovered that the starting material could isomerise during purification on silica gel affording a dihydropyran by-product in 5% yield (Scheme 33).[39]



Scheme 33

They used this by-product and found that upon treatment with a Lewis acid, the dihydropyrans **80**$_{a,b}$ led to the unexpected cyclobutanes **82**$_{a,b}$ *via* the formation the intermediates **81**$_{a,b}$ in good yields and with excellent diastereoselectivity (Scheme 34). However, when optically pure starting material was used, the stereochemistry could not be retained. The reasons for the poor enantiocontrol in the ring contraction could reside in the elevated temperature required to form the cyclohexanone (–78°C to –30°C) while other

similar enantioselective Co-mediated O→C rearrangement reactions were carried out at lower temperatures (–90°C to –78°C).[38]

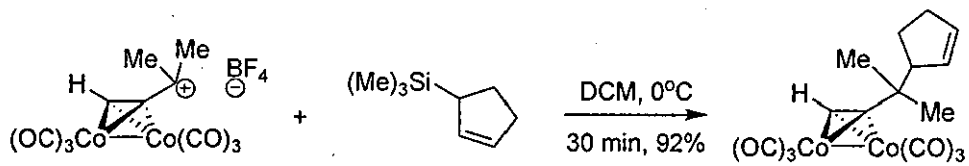


SM	R	Product	Yield (%)
80_a	Ph	82_a	81%
80_b	^{t}Bu	82_b	54%

Scheme 34

1.5.4.2.3. Alkene as nucleophile

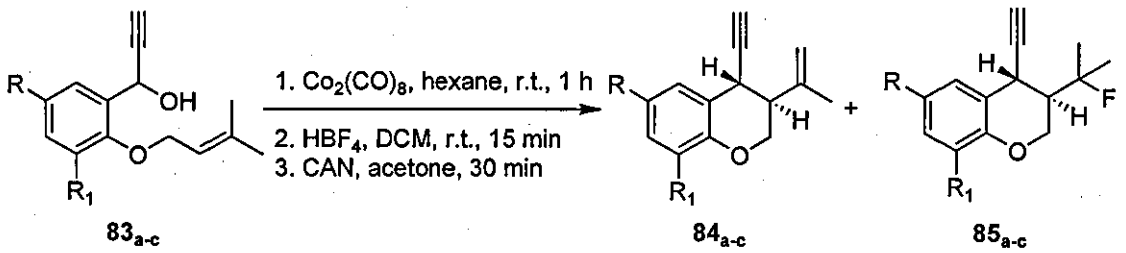
Nicholas was the first to report the formation of 1,5-ene-ynes *via* the coupling of propargyl cations with allyl silanes.[40] He noted that the ene-ynes were prepared in good yields and quaternary centers were produced without competing elimination (Scheme 35).



Scheme 35

Tyrell *et al.* have investigated a series of intramolecular cyclisation reactions in which the key cyclisation step involved the attack of a dicobalt hexacarbonyl complexed propargyl cation with a trisubstituted alkene.[41a-e] The treatment of 83_{a-c} with dicobalt octacarbonyl led

to quantitative conversion to the dicobalt hexacarbonyl complexes. This was then cyclised, by reaction with tetrafluoroboric acid, and subsequent treatment with ceric ammonium nitrate to decomplex the cobalt. This novel procedure led to the synthesis of the *trans* benzopyrans $\mathbf{84_a}$ and $\mathbf{85_a}$, as a 1:1 ratio, in 35% yield (Scheme 36).[41a]



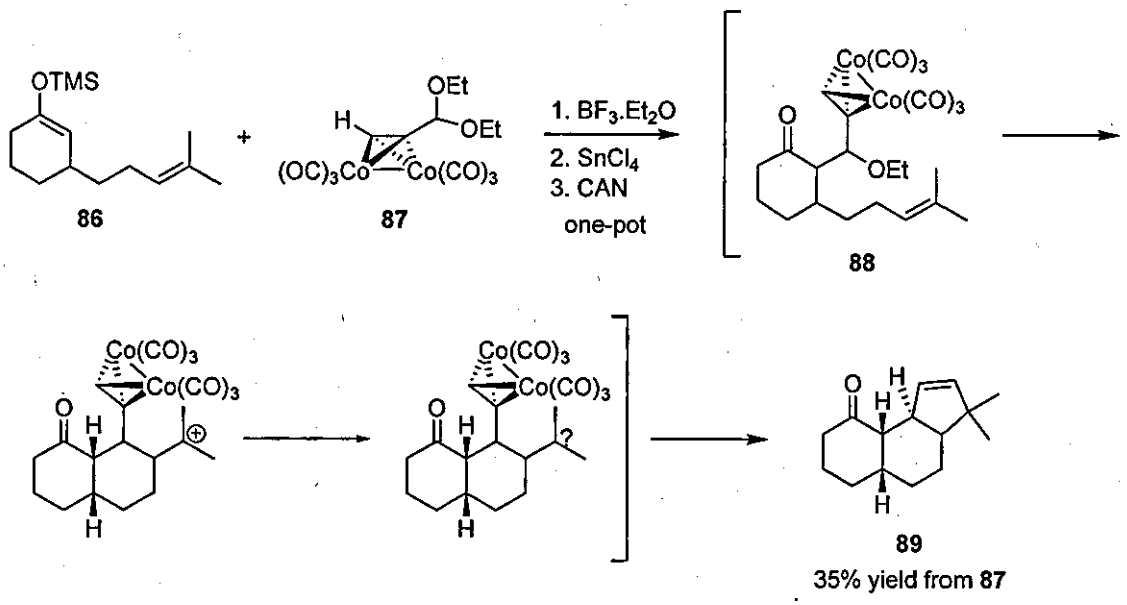
$\mathbf{83_{a-c}}$ $\mathbf{84_{a-c}}$ $\mathbf{85_{a-c}}$

SM	R	R_1	Yield (%)	84:85 ratio
$\mathbf{83_a}$	H	H	35%	1 : 1
$\mathbf{83_b}$	NO_2	H	65%	0 : 1
$\mathbf{83_c}$	Cl	Cl	55%	0 : 1

Scheme 36

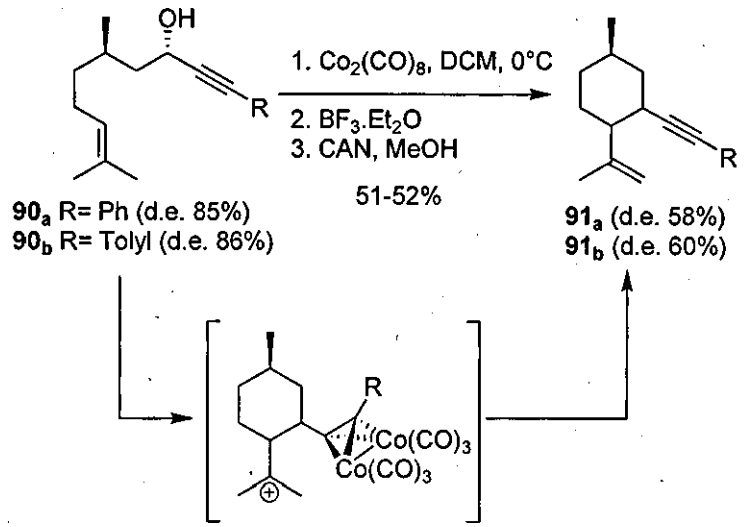
As the cobalt clusters are highly coloured, they are readily visualised by thin layer chromatography. This feature, coupled with the significant R_f differences between complexed precursors and the decomplexed products, facilitates a one-pot protocol. In an effort to improve yields, Tyrell *et al.* developed a one-pot procedure which afforded exclusively $\mathbf{85_b}$ in 65% yield from $\mathbf{83_b}$. Using the same procedure, $\mathbf{83_c}$ cyclised to produce $\mathbf{89_c}$ in 55% yield and none of the corresponding isopropenyl derivatives $\mathbf{84_b}$ and $\mathbf{84_c}$ were observed. Both newly synthesised compound $\mathbf{85_{b,c}}$ exhibited a *trans*-stereochemistry.

A deviation of this one-pot procedure was then applied to other reagents such as non-aromatic substrates. However, instead of producing the desired decalin products, the reaction resulted in the formation of a tricyclic product. An example is shown in Scheme 37, where the tricyclic naphthalene derivative **89** was prepared in 35% yield starting from **87** *via* an *in situ* formation of the complex **88**.[41c] Not all reaction conditions were reported and on a mechanistic point of view, the nature of the latest intermediate to afford **89** has yet to be elucidated.



Scheme 37

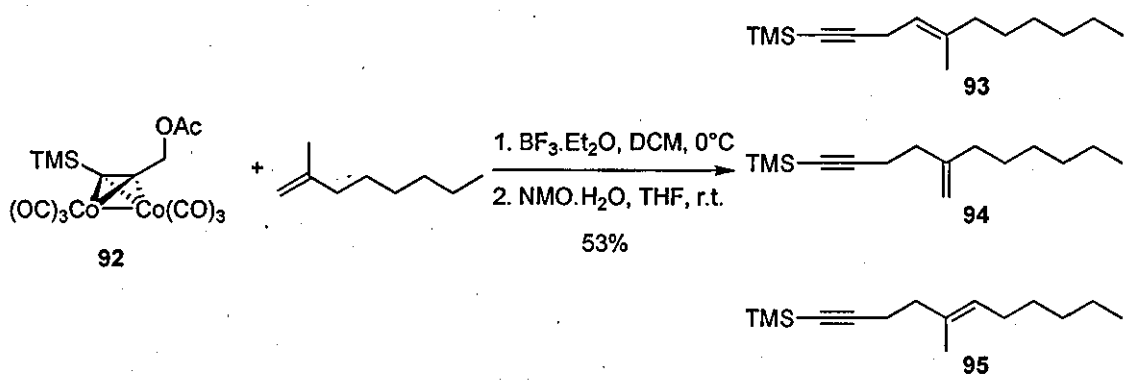
More recently, this strategy was employed towards the synthesis of the monoterpenoid derivatives $\mathbf{91_{a,b}}$ starting from the alkyne derivative $\mathbf{90_{a,b}}$ in moderate yields, with diastereoisomeric excesses not exceeding 60% (Scheme 38).[41e]



Scheme 38

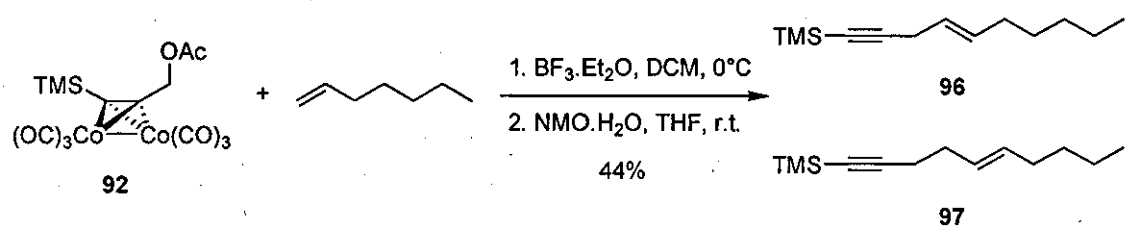
Tyrell *et al.* found that the nature of the double bond had a strong influence upon the reaction as attempts to cyclise terminal alkenes failed. These results were consistent with those obtained by Krafft[42] while investigating the electrophilic addition of the Nicholas

carbocation to unfunctionalised terminal alkenes. They found that the treatment of the complex **92** with a Lewis acid permits reactions with non-activated alkenes such as 2-methyl-1-octene to give a mixture of the alkene regioisomers **93**, **94** and **95** in 53% yield (Scheme 39).



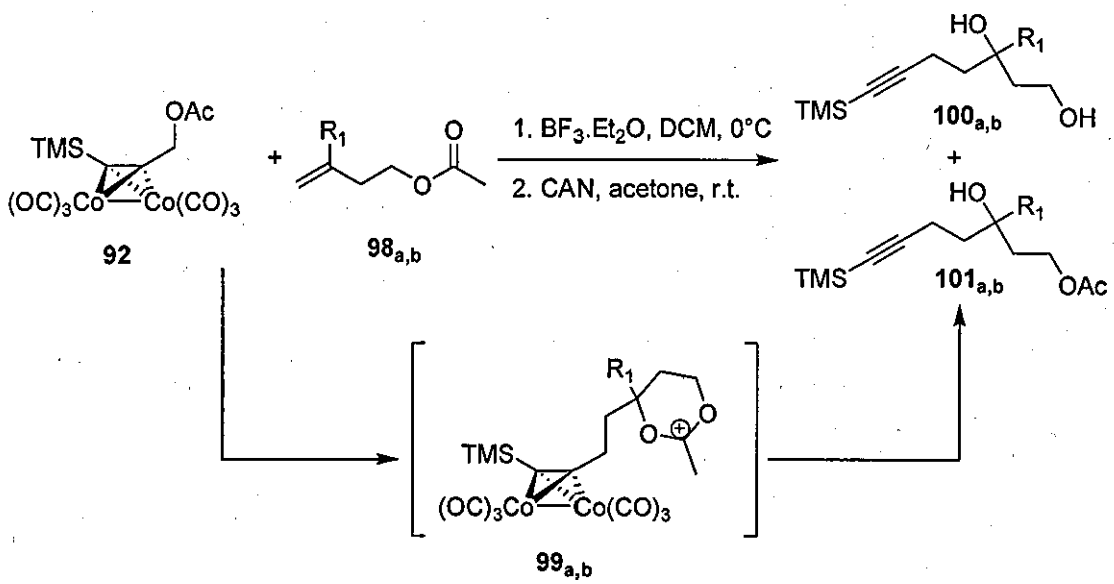
Scheme 39

Unsubstituted 1-heptene gave similar results, affording the two possible regioisomers **96** and **97** with a 44% yield with a ratio of approximately 1:1 (Scheme 40).



Scheme 40

Other examples showed that unsubstituted alkenes do not favour the addition. This might be due to the formation of a secondary carbocation intermediate, while a more stable tertiary carbocation is formed with a disubstituted alkene. In the example below, Krafft utilised terminal alkenes (**98**$_{a,b}$) bearing an oxygen moiety oriented in such a way that it could trap the carbocation in an intramolecular fashion along with the formation of the intermediate **103**$_{a,b}$, which was then hydrolysed by an aqueous work up to afford **100**$_{a,b}$ and **101**$_{a,b}$ (Scheme 41).

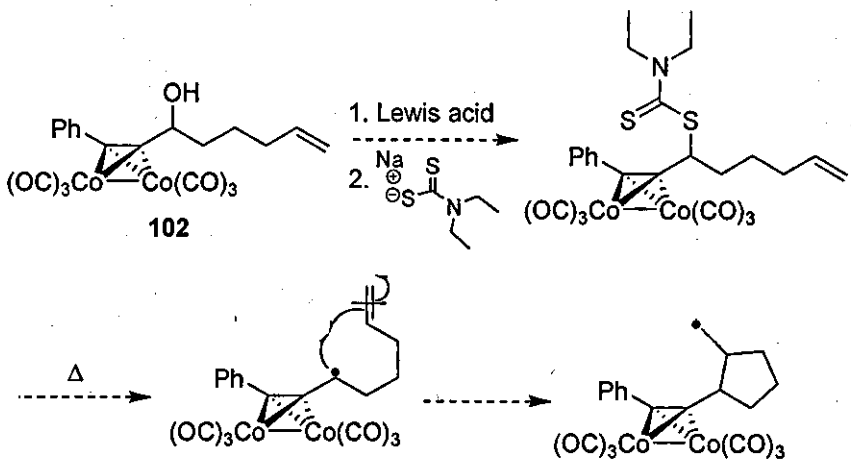


Reactant	R_1	Yield (%)	Ratio 100:101
98_a	Me	54	1.16:1
98_b	H	7	1:0

Scheme 41

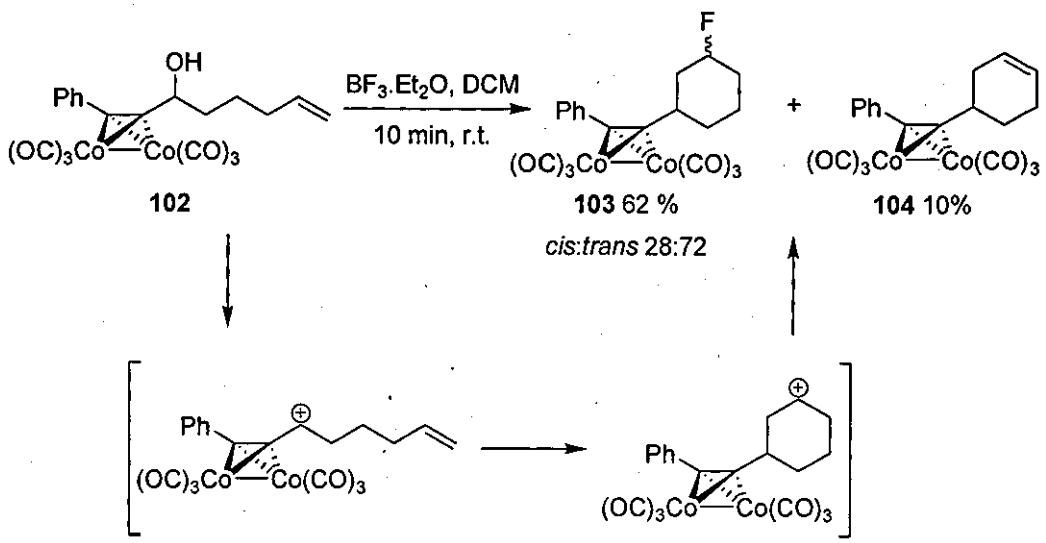
In the case of the homoallylic acetate 98_b the reaction proceeded in very poor yield which was attributed to the intermediate carbocation being secondary.

Bertrand *et al.* fortuitously discovered the addition of unactivated alkenes onto propargylic alcohols[43] while investigating the use of the propargyl alcohol **104** as a potential radical precursor to perform 5-*exo* ring closure since the C–S bond is known for performing a homolytic cleavage under thermal conditions.



Scheme 42

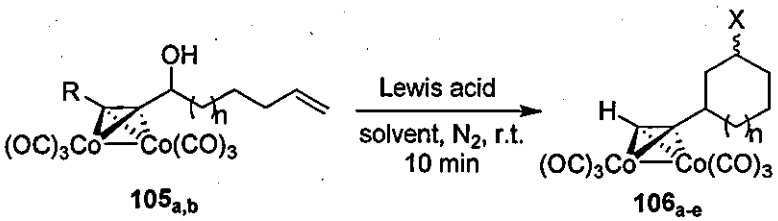
Unexpectedly, a 6-*endo* cyclisation proceeded under the Lewis acid treatment affording the cyclohexane derivative **103** in 62% yield with a 28:62 *cis:trans* ratio along with the cyclohexene **104** in 10% yield (Scheme 43). It was the first reported successful cyclisation reaction of Nicholas carbocations onto unactivated terminal alkenes.



Scheme 43

Bertrand *et al.* extended the methodology in synthesising a range of substituted cyclohexanes by 6-*endo* cyclisations (Scheme 44) and cycloheptanes by 7-*endo* cyclisations starting from the corresponding propargylic alcohols in good yields with moderate to

excellent diastereoselectivity. However attempts to perform 5-*endo* ring closure were not successful.



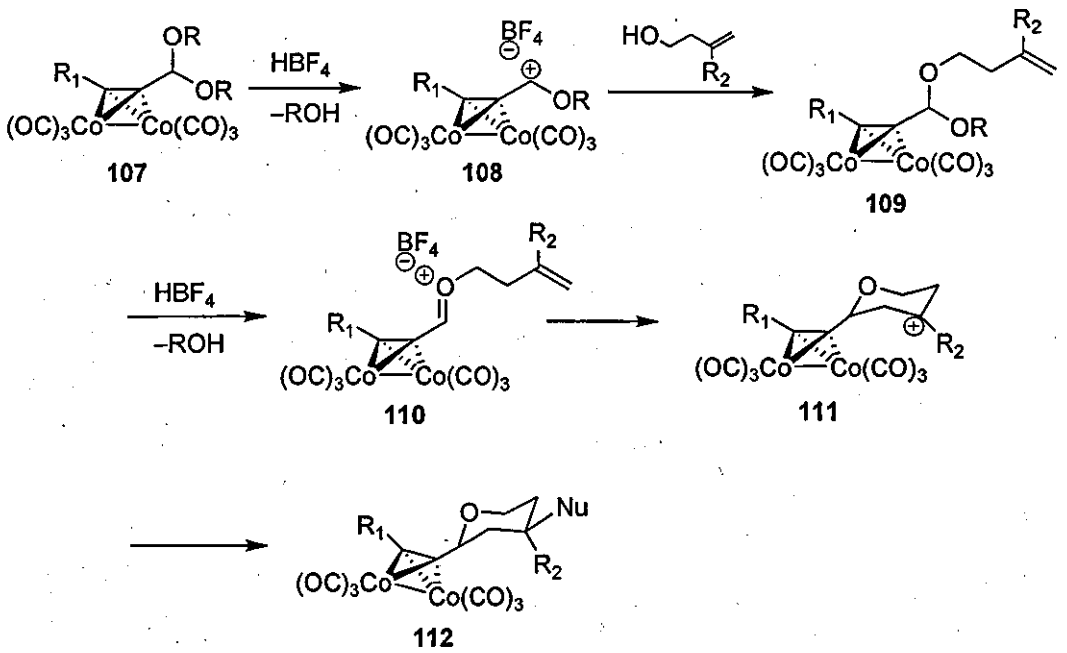
105$_{a,b}$ **106$_{a-e}$**

SM	R	n	Lewis acid	Solvent	X	Product	Yield (%)	*cis:trans*
105$_a$	H	1	HBF_4	DCM	F	**106$_a$**	67	49:51
105$_a$	H	1	$BF_3.Et_2O$	DCM	F	**106$_a$**	56	46:54
105$_a$	H	1	TfOH	MeCN	HNCOMe	**106$_b$**	99	100:0
105$_b$	H	2	HBF_4	DCM	F	**106$_c$**	34[1]	n/a
105$_c$	Ph	1	HBF_4	MeCN	HNCOMe	**106$_d$**	66[1]	n/a
105$_d$	Ph	2	$TiCl_4$	DCM	Cl	**106$_e$**	50[1]	n/a

[1] Single isomer, stereochemistry not assigned

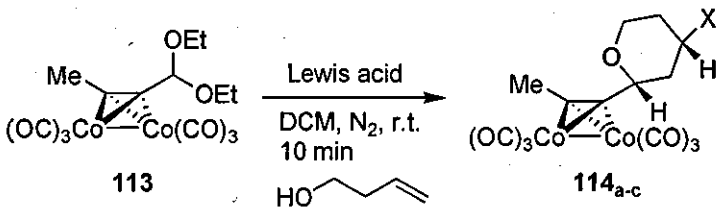
Scheme 44

Bertrand *et al.* also investigated the use of propargylic acetals towards the formation of tetrahydropyrans *via* a Nicholas-Prins cyclisation (Scheme 45).[44] They found that propargylic acetals undergo the cyclisation when reacted with homoallylic alcohols. As depicted in Scheme 45, the mechanism of the Prins cyclisation developed proceeded *via* the formation of the "doubly stabilised" Nicholas carbocation **108** which was obtained by treatment of the acetal **107** with a Lewis acid. A subsequent attack to this intermediate by a homoallylic alcohol led to the formation of a new acetal **109**, which was converted into the oxocarbonium ion **110**. The latter was then trapped intramolecularly by the terminal alkene affording the carbocation **111**, which was then trapped by an external nucleophile providing the tetrahydropyrans **112**.



Scheme 45

Using this methodology, Bertrand *et al.* prepared a range of pyrans using homoallylic alcohol in moderate to good yields. The best result was obtained when TMS-Tf was used as the Lewis acid, which afforded **114$_c$** in 99% yield with a 99:1 *cis:trans* ratio (Scheme 46).



Lewis acid	X	Product	Yield (%)	*cis:trans*
$TiCl_4$	Cl	**114$_a$**	58	64:36
$BF_3.Et_2O$	F	**114$_b$**	52	83:17
TMSOTf	OTf	**114$_c$**	99	99:1
HBF_4	F	**114$_b$**	63	93:7

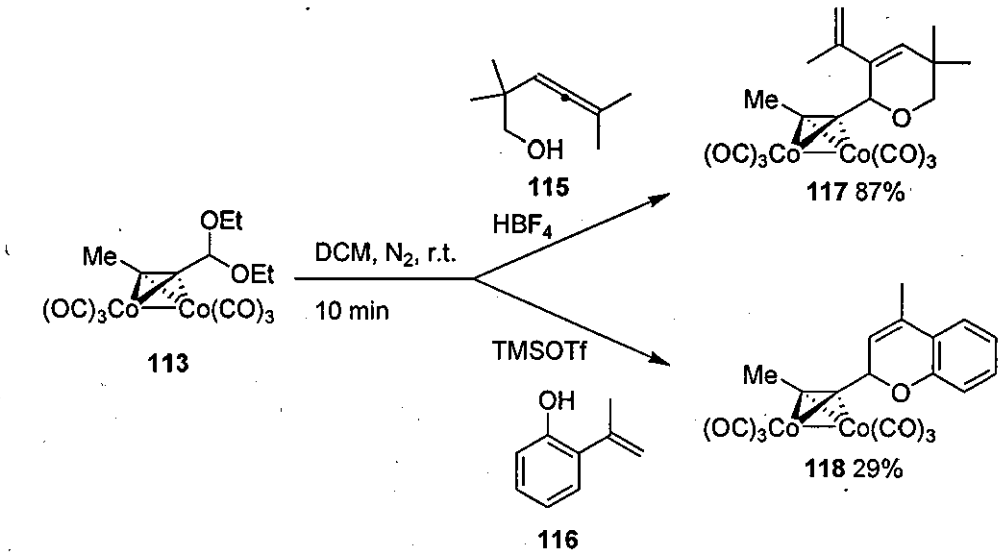
Scheme 46

When the alkyne was not complexed, the Prins cyclisation occurred, however the corresponding pyrans were formed in lower yields and diastereoselectivities. This might be

due to a possible rearrangement followed by degradation after formation of the propargylic carbocation.

The complexation prevents allenic derivatives from being formed and the bulky dicobalt hexacarbonyl complex may also affect the stereoselectivity of the reaction in orienting the nucleophilic attack on the equatorial position affording a more stable cycloadduct.

Other alcohols were used to perform the cyclisation but the reaction occurred in lower yields (Scheme 47). Regarding the use of allenes as internal traps, only the homoallenic alcohol **115** underwent the Prins cyclisation affording the cycloadduct **117** in a good **87%** yield after loss of a proton. The reaction with *O*-vinylphenol **116** led to rather disappointing results affording the desired dihydropyran **118** in only 29% yield. This could be due to electronic factors. Other *O*-vinylphenols did not allow the Prins cyclisation to occur.

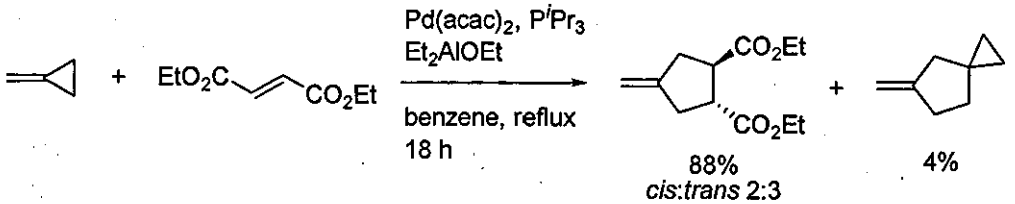


Scheme 47

1.6. [3+2] cycloaddition reactions

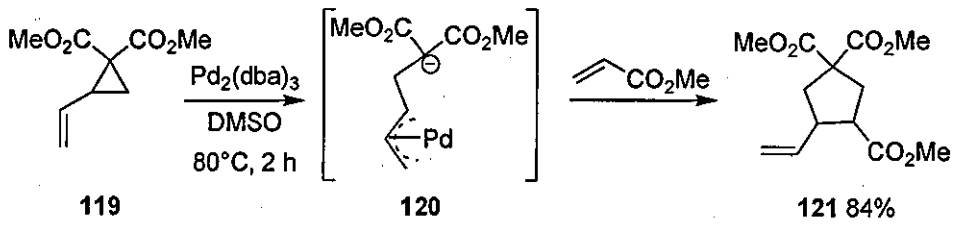
1.6.1. Discovery and application

Dipolar cycloadditions involving the use of a cyclopropane was discovered by Schuchardt, Trost and Tsuji in the early 1980's.[45a-d] Their methodology involved the use of Pd^0 to stabilise a carbocation which was formed during the ring opening. The use of electron deficient olefins allowed the dipolar intermediate to be trapped affording new five-membered ring cycloadducts as shown in Scheme 48.



Scheme 48

Two major factors can affect the reactivity of cyclopropanes towards the ionic ring opening: the ability of the electron-withdrawing group to stabilise an adjacent negative charge and the ability of the electron-donating group to stabilise the positive charge. Suitable π-donors such as aromatics and alkenes are particularly effective in stabilising a developing positive charge. Tsuji and Yamamato improved the reaction and performed cycloaddition reactions using a vinyl cyclopropane **119** which was suitably substituted with two ester groups (Scheme 49).[46a-e] Upon treatment with Pd^0, the cyclopropane ring opens to reveal a zwitterionic η^3 (π-allyl)palladium complex **120**. The malonyl moiety stabilises the carbanion while the carbocation formed is stabilised by the π-allylpalladium complex. This dipolar intermediate is then trapped by α,β-unsaturated esters or ketones to form the corresponding vinylcyclopentane in good yields as the example shown in the Scheme 49.

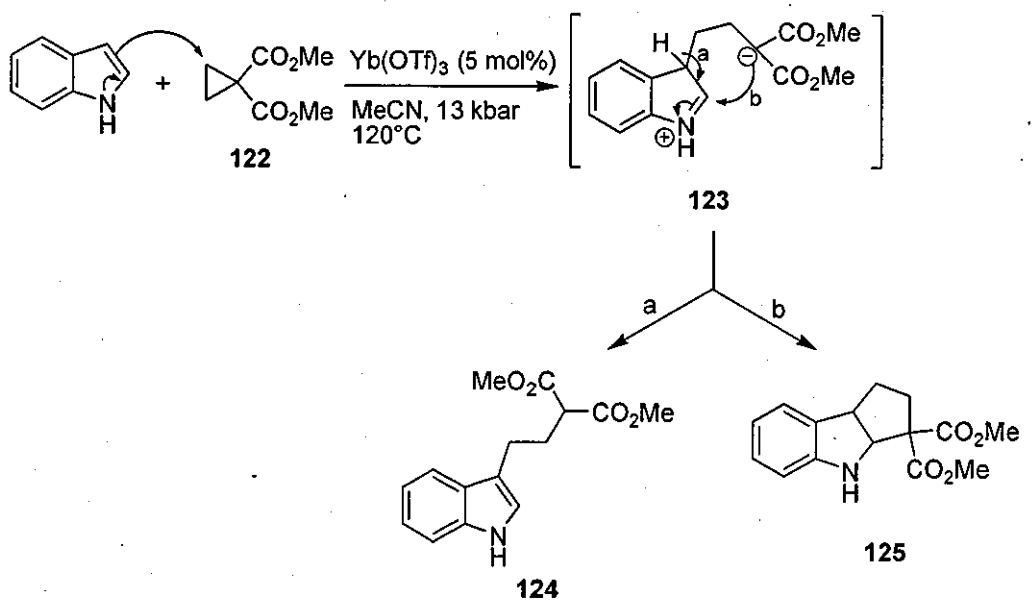


Scheme 49

The cyclopentane cycloadduct **121** could be isolated as a 1:1 mixture of diastereoisomers in 84% yield after 2 h of reaction at 80°C.

1.6.2. Dipolar cycloaddition reactions

Kerr *et al.* discovered that activated cyclopropanes could undergo a [3+2] cyclisation with indoles while investigating the homo-Michael addition of indoles onto cyclopropanes.[47a-c] They found that yields of the expected products were dramatically lowered when no substituent was present on the indole nitrogen and the unexpected formation of the by-product **125** was observed (Scheme 50).[47a] Full details of the reaction were not reported. However, it appeared that the formation of both compounds **124** and **125** was in competition and the electrophilic iminium ion formed after the homo-Michael addition could be trapped *via* a tandem attack of the malonic enolate affording the tricyclic pyrolidine derivative **125**.



Scheme 50

Kerr *et al.* were the first to report the successful homo [3+2] dipolar cycloaddition using a cyclopropane diester moiety with nitrones.[48a-c] They discovered that the cyclopropane ring behaved very much like an α,β-unsaturated carbonyl compound in its ability to react with nucleophiles. The mechanism of the cycloaddition reaction is not fully understood, however the co-ordination of a Lewis acid to one or more of the ester moieties and the increased reaction rates with a π-system vicinal to the diester functionality can be used to consider the nature in which the cyclopropane undergoes a significant degree of charge separation. Kerr *et al.* suggested that the strained carbon–carbon bonds in the 1,1-diester cyclopropane have a significant π-character that could induce a certain polarisation of the weakest carbon–carbon bond upon treatment with a Lewis acid (Figure 8). Such a charge separation would also be enhanced by the presence of stabilising groups (R_1, R_2) on the cyclopropane unit.

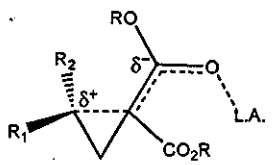
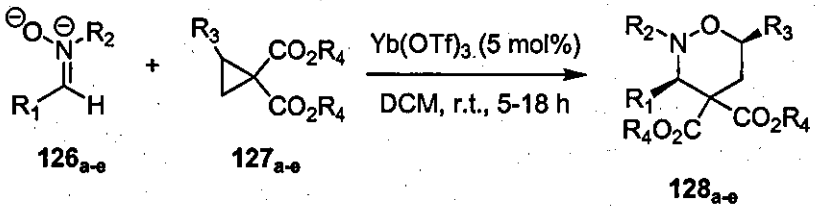


Figure 8

Using this polarisation of the cyclopropane under Lewis acid conditions, Kerr *et al.* performed [3+2] cycloaddition between nitrones and substituted cyclopropanes affording tetrahydro-1,2-oxazines **128**$_{a-e}$ in a 3,6-*cis* configuration (Scheme 51). They developed their methodology using different nitrones and found that better results were obtained using a nitrone bearing a *p*-tolyl on the nitrogen.[48a] The presence of phenyl, styryl or vinyl substituent vicinal to the diester moiety on the cyclopropane ring greatly reduced the reaction time and in the case of the styryl and the phenyl, improved significantly the yields as shown in the table below. The tetrahydro-1,2-oxazines were prepared with a *cis* stereochemistry only.

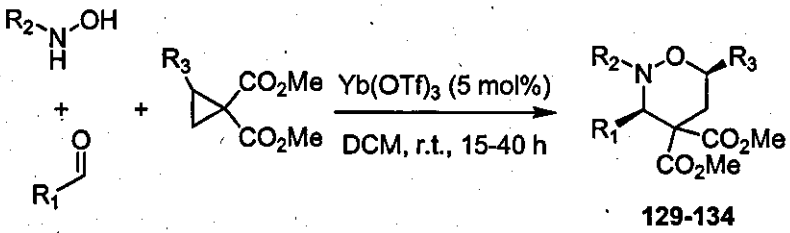


126_{a-e} 127_{a-e} 128_{a-e}

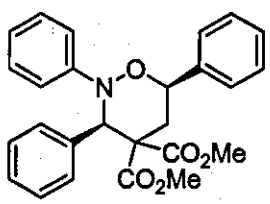
R_1	R_2	R_3	R_4	t (h)	Product	Yield (%)
Ph	*p*-tolyl	H	Et	18	128_a	77
Ph	*p*-tolyl	Ph	Me	18	128_b	94
Ph	*p*-tolyl	styryl	Me	5	128_c	95
Ph	*p*-tolyl	vinyl	Et	42	128_d	73
Ph	Me	Ph	Et	42	128_e	84

Scheme 51

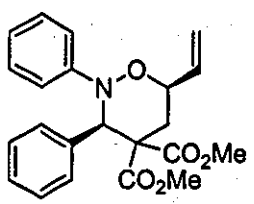
As some nitrones were difficult to prepare, they developed a one-pot protocol, preparing the reactant *in situ* prior to the addition of the cyclopropane, avoiding the isolation of the unstable nitrones.[48b]



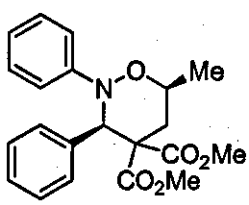
129-134



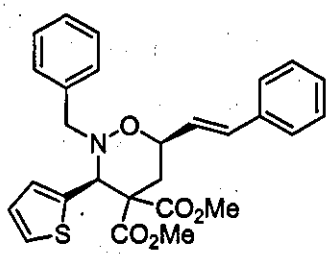
129 92% 15 h



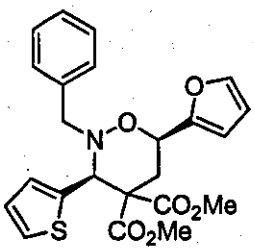
130 87% 17 h



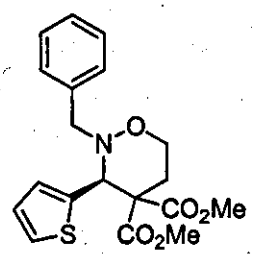
131 80% 20 h



132 93% 15 h



133 93% 15 h

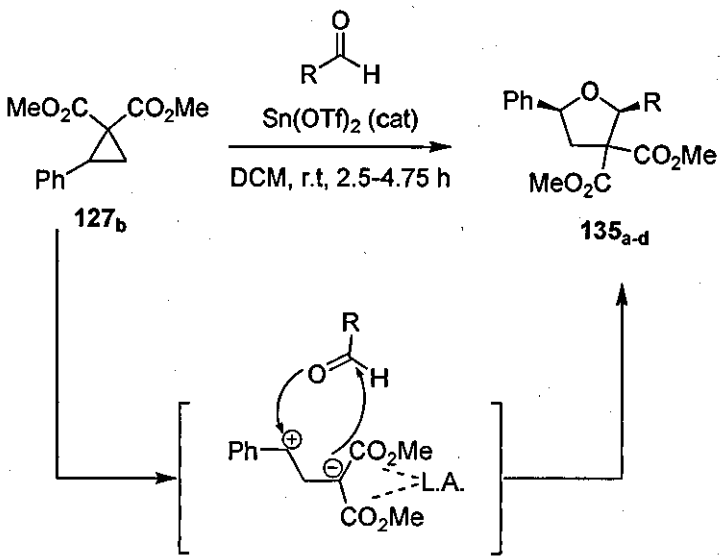


134 70% 40 h

Scheme 52

The use of cyclopropanes bearing a π-electron donor group such as vinyl or styryl or an aromatic group on the cyclopropane allowed the synthesis of the oxazines **130** and **132** in 87% and 93% yield respectively, as well as compounds **129** and **133** in 92 and 93% yield respectively. Lower yields were obtained with a methyl-substituted or unsubstituted diester-cyclopropane which afforded **131** and **134** in 80% after 20 h and in 70% after 40 h, respectively.

Substituted furans can also be synthesised using the same strategy *via* a [3+2] dipolar cycloaddition. Johnson *et al.* reported the synthesis of 2,5-disubstituted furans from donor-acceptor cyclopropanes and aldehydes using a catalytic amount of tin triflate (Scheme 53).[49]

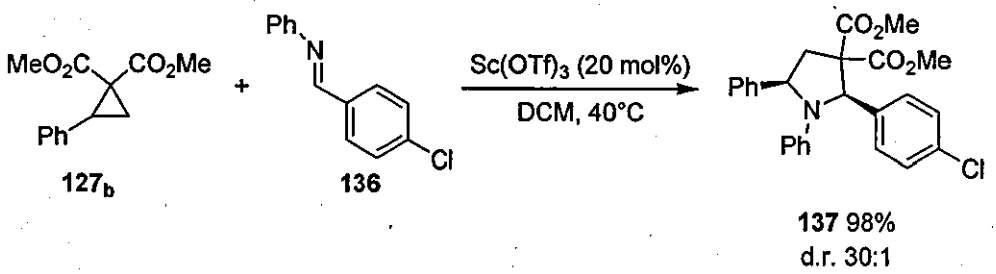


R	t (h)	Product	Yield (%)	d.r.
Ph	2.5	**135a**	100	100:1
4-ClPh	4.75	**135b**	96	80:1
4-OMePh	3.5	**135c**	98	86:1
4-NO_2Ph	15	**135d**	89	19:1

Scheme 53

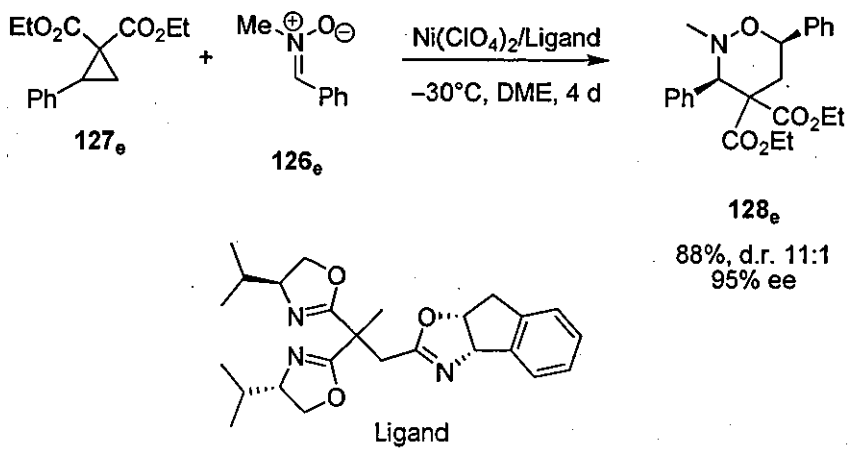
Tang *et al.* described the synthesis of poly-substituted pyrrolidines[50a] using the same methodology (Scheme 54). The tandem ring-opening-cyclisation reaction of the cyclopropane **127b** with the imine **136** in the presence of a catalytic amount of scandium

triflate afforded the pyrrolidine **137** in a very good yield with a 30:1 *cis*:*trans* ratio (Scheme 54).



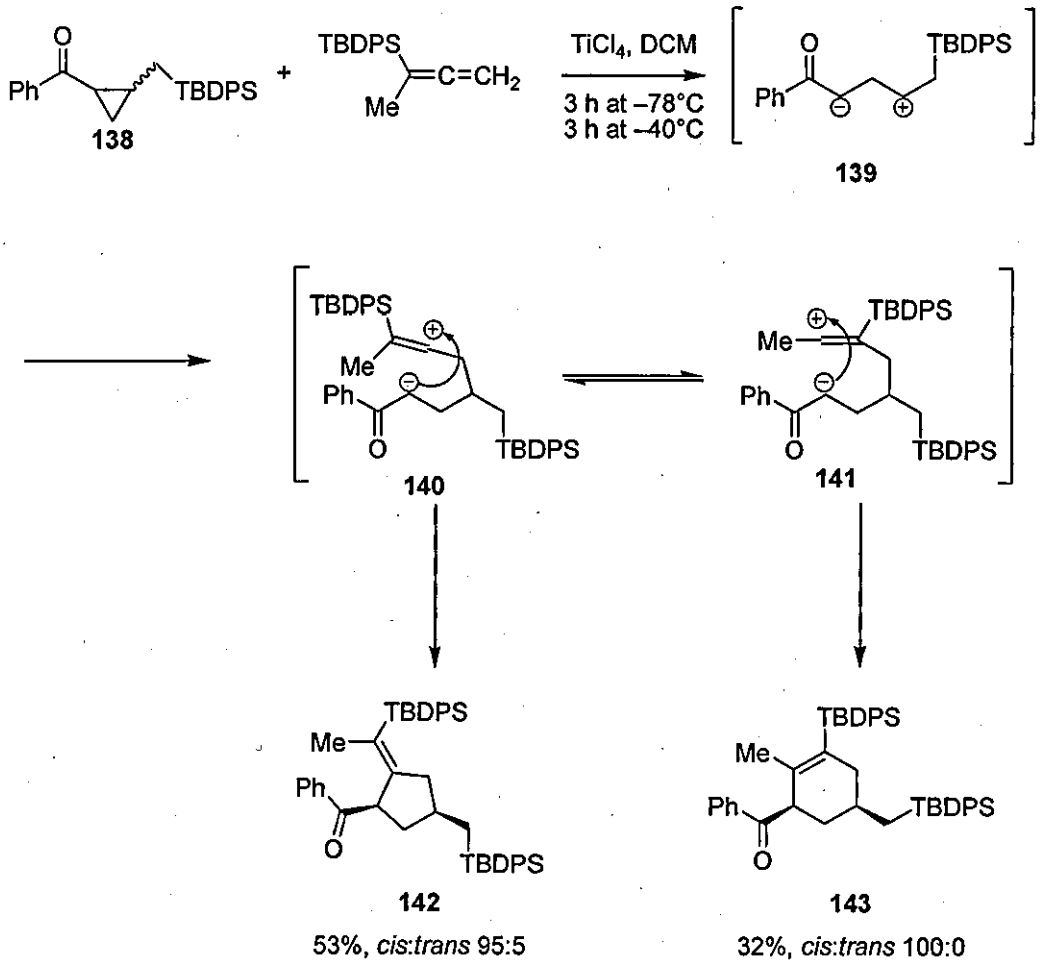
Scheme 54

Using the method developed by Sibi and Goti,[51] Tang *et al.* used trisoxazolines as chiral ligands to achieve a highly diastereo and enantioselective version of the cycloaddition using nickel as the catalyst. In this way the tetrahydro-1,2-oxazine **128$_e$** was synthesised in 88% yield with excellent diastereo and enantioselectivity (Scheme 55).[50b]



Scheme 55

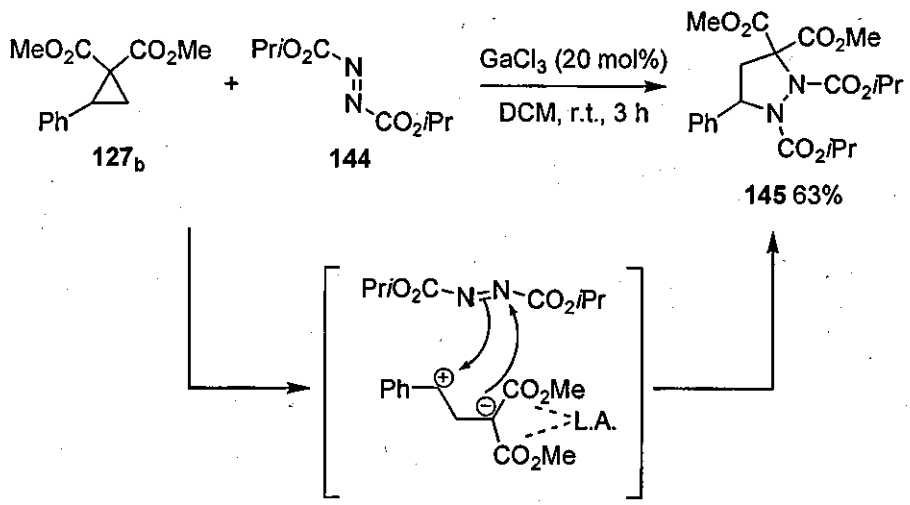
In a similar way, Yadav *et al.* described the synthesis of tri-substituted cyclopentanes and cyclohexenes (Scheme 56).[52] A donor-acceptor substituted cyclopropane **138** was treated with a Lewis acid to reveal a 1,3-dipolar synthon **139**. This intermediate could subsequently be trapped using allenylsilanes affording [3+2] and [3+3] cycloadducts with high regio and stereocontrol as shown in the Scheme 56.



Scheme 56

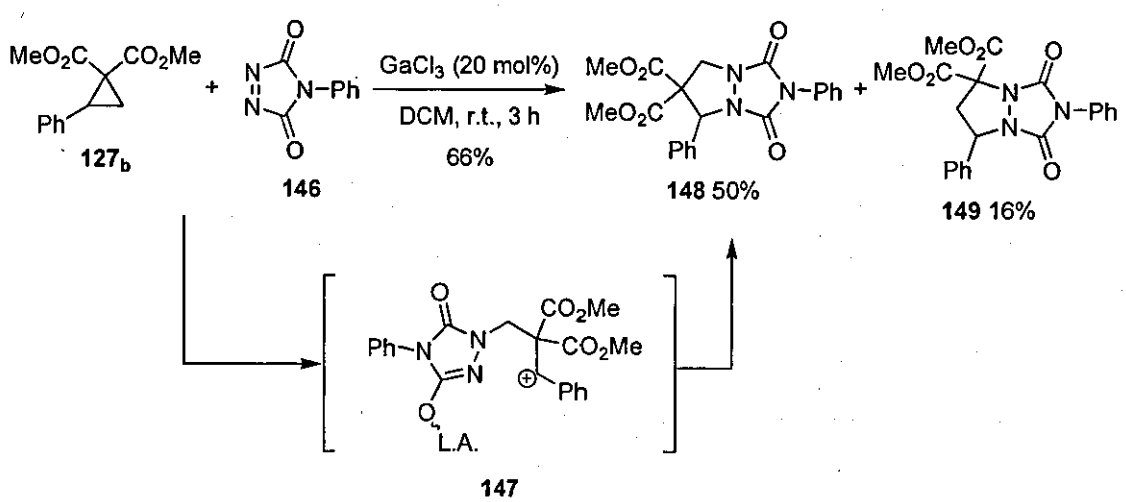
Once the cyclopropane opened, the addition of a polarised silane allene derivative led to the formation of a new intermediate **140**, which was converted into the five-membered ring adduct **142**. The formation of the six-membered ring product **143** resulted in an intramolecular rearrangement of the vinyl cation **140** to the vinyl cation **141** entailing a 1,2-migration of the TBDPS group.

Recently, De Meijere *et al.* found that diester cyclopropane could undergo the same type of cycloaddition with diazene derivatives giving rise to new pyrazolidines in a complete regioselective fashion (Scheme 57).[53] When the cyclopropane $\mathbf{127_b}$ was reacted with the *trans* diazene **144** in the presence of a catalytic amount of gallium chloride, only one regioisomer of the pyrazolidines **145** was obtained in 63% yield showing that a conventional mechanism must occur in this case.



Scheme 57

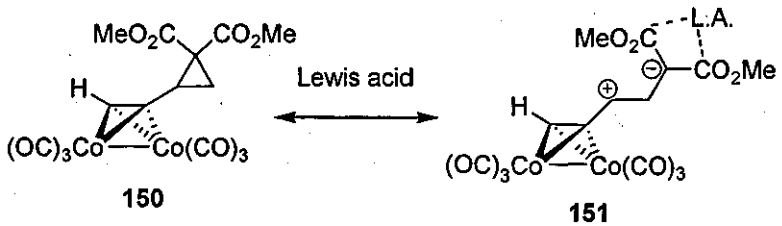
When the *cis* diazene **146** was used in the same conditions, the major product obtained was unexpectedly the other regioisomer **148**. In this case another mechanism may occur in which a new intermediate **147** is formed, competing with the conventional intermediate which affords compound **149**.



Scheme 58

1.6.3. The use of the Nicholas carbocation in the [3+2] dipolar cycloaddition

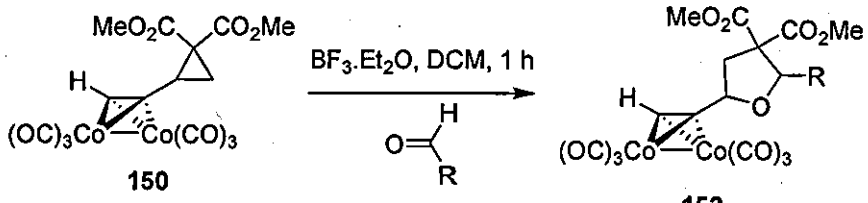
Dipolar cycloaddition reactions can be used with a dicobalt complex to stabilise the positive charge formed during the ring opening. This variation of the Nicholas reaction has previously been used within the research group.[54,55] A diester cyclopropane **150** has been prepared exhibiting an alkyne/dicobalt hexacarbonyl complex (Figure 9). When treated with a Lewis acid, the three-membered ring opens to reveal a dipole **151** in which the malonate motif stabilises the carbanion and the metal/alkyne complex stabilises the Nicholas carbocation.



150 **151**

Figure 9

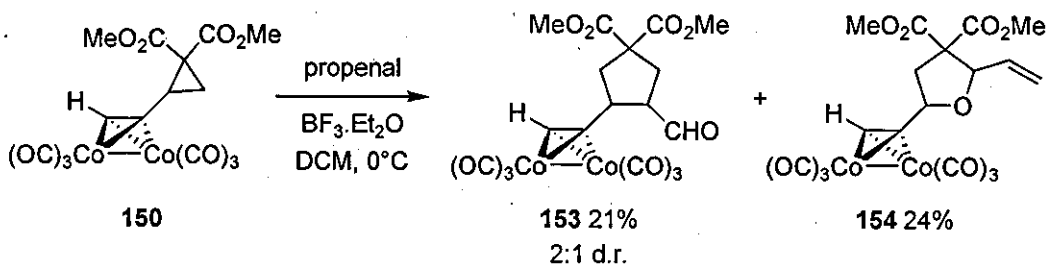
The initial work carried out in the group made use of this activated cyclopropane towards the formation of tetrahydropyrans by cycloaddition with aldehydes (Scheme 59).[55a] The cycloaddition reaction only afforded the corresponding tetrahydrofurans when an electron deficient aldehyde was used. The *cis* and the *trans* diastereoisomers were isolated in a 1:1 mixture in most of the reactions. A maximum diastereoisomeric ratio of 1:2 was obtained using *p*-nitrobenzaldehyde as the trapping reagent affording the tetrahydrofuran **152$_b$** in 77% yield.



R	T (°C)	Product	Yield (%)	*cis:trans*
Ph	40	$\mathbf{152_a}$	83	1:1
4-MeOPh	0; 40	**n/a**	0	n/a
4-NO_2Ph	40	$\mathbf{152_b}$	77	1:2
CO_2Et	40	$\mathbf{152_c}$	86	1:1.6
4-FPh	0	$\mathbf{152_d}$	85	1:1

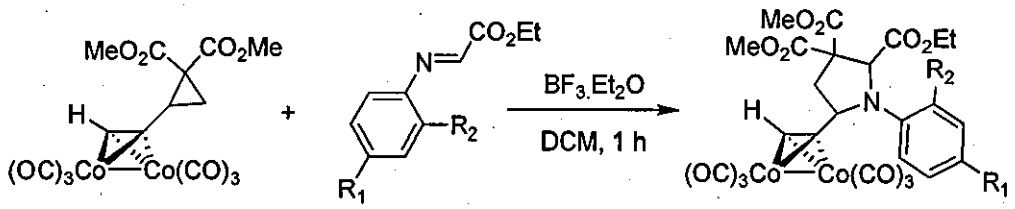
Scheme 59

When propenal was used, the cycloaddition afforded the expected tetrahydrofuran in 24% yield and the corresponding cyclopentane in 21% yield (Scheme 60). No diastereoselectivity was apparent on reaction with the carbonyl but a 2:1 d.r. was identified by ^{1}H NMR for the cyclopentane, signifying a presence of attack most likely by reducing steric interactions with the metal complex. The cycloaddition could be performed for the first time onto an alkene but propenal was found to be the only reactant to afford the corresponding cyclopentane **153** along with the formation of tetrahydrofuran **154**.



Scheme 60

Using identical conditions, imines were used to form pyrrolidines.[55b] Excellent yields were generally achieved when the nitrogen was substituted with an electron-donating group and the carbon of the imine bond was substituted with an electron-withdrawing group (Scheme 61).



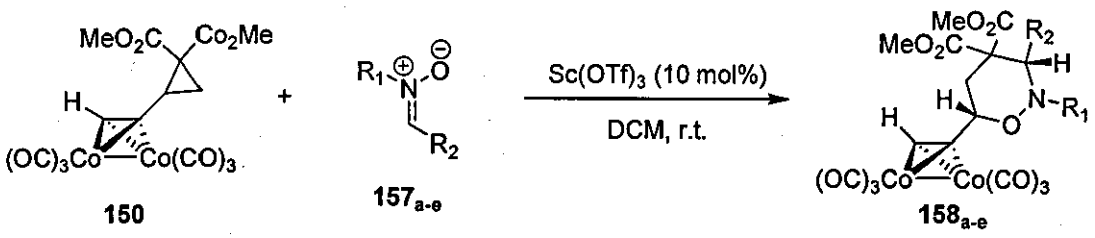
150 **155_{a-d}** **156_{a-d}**

Reactant	R_1	R_2	T (°C)	Product	Yield (%)	*cis:trans*
155_a	MeO	H	0	156_a	91	1:1
155_b	MeO	MeO	0	156_b	85	2:1
155_c	H	CN	25	156_c	72	3:1
155_d	NO_2	H	40	156_d	30	1:2

Scheme 61

The use of the imine 155_a, obtained from *p*-methoxyaniline and ethyl glyoxylate, afforded the pyrrolidine 156_a in an excellent 91% yield. However no selectivity could be observed. On increasing steric hindrance in the *ortho*-position, diastereoselectivity was achieved, affording 156_b in 85% yield with a 2:1 *cis:trans* d.r. and compound 156_c in 72% with a 3:1 *cis:trans* ratio. When the aromatic group on the amine was substituted with an electron-withdrawing group, such as in 155_d, yields dramatically decreased with a surprising inversion of diastereoselectivity affording the pyrrolidine 156_d in only 30% with a 1:2 *cis:trans* ratio.

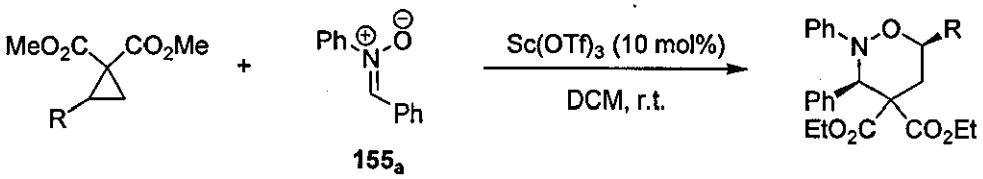
Kerr *et al.* also used the Nicholas carbocation to perform [3+2] dipolar cycloadditions with nitrones.[56] They screened a range of Lewis acids and found that only ytterbium triflate and scandium triflate were suitable to promote the reaction, however scandium triflate was the preferred catalyst affording the oxazines in better yields (Scheme 62).



R_1	R_2	t (h)	Product	Yield (%)
Ph	Ph	3	**158_a**	90
Ph	4-NO_2Ph	2	**158_c**	67
Ph	4-MeOPh	5	**158_d**	73

Scheme 62

In their studies they compared the different groups which are susceptible of stabilising the positive charge during the ring opening (Scheme 63).



Cyclopropane	R	t	Product	Yield (%)
122	H	25 h	**160**	46
127_b	Ph	15 min	**130**	95
159	≡—	19 h	**161**	7
150	(OC)3Co—Co(CO)3	3 h	**158_a**	90

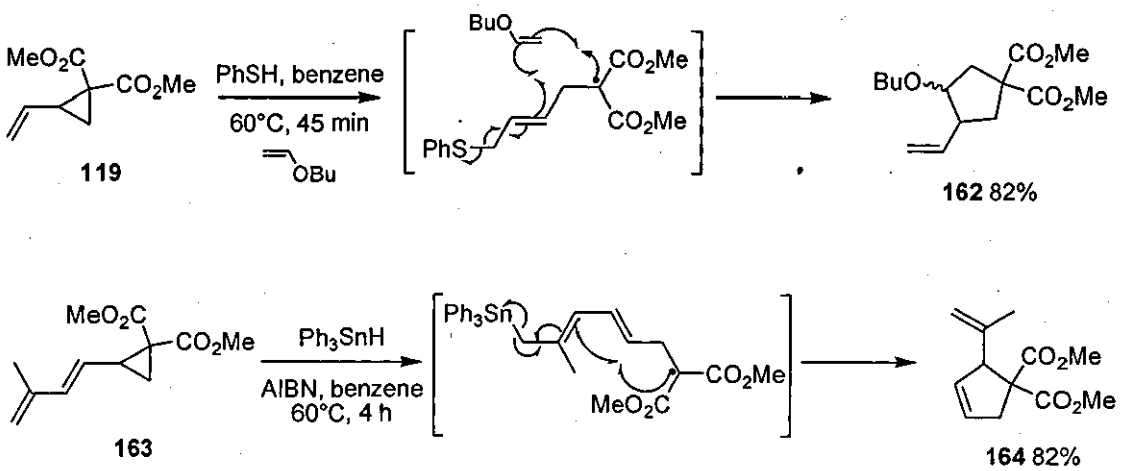
Scheme 63

The phenyl-substituted cyclopropane **127_b** was found to be the most reactive affording the oxazine **134** in 95% yield after 15 min. Dimethyl cyclopropane-1,1-dicarboxylate **122** surprisingly led to the cycloadduct **160** in 46% yield while not exhibiting any π-electron stabilisation. The uncomplexed alkynyl cyclopropane **159** gave only a small amount of the desired adduct. The poor yield could be attributed to the decomposition of the zwitterionic intermediate through the formation of an allene. In contrast with the complexed

cyclopropane **150**, the oxazine **158**$_a$ could be prepared in a good 90% yield although its reactivity was expected to be higher than that of the phenyl-substituted cyclopropane **127**$_b$.

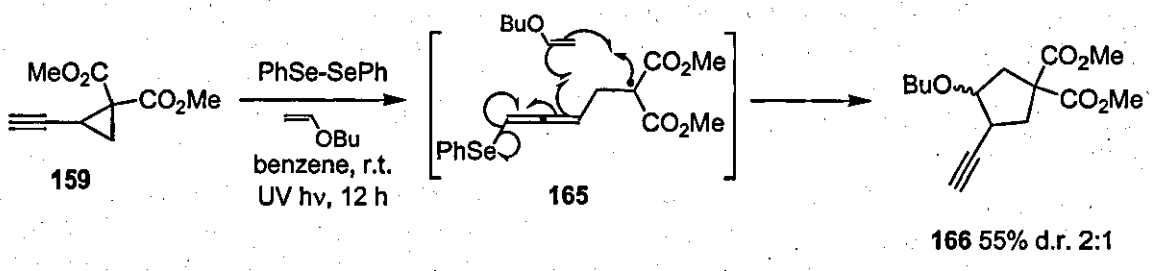
1.6.4. Radical cycloaddition reactions

A similar radical mediated reaction has been reported by Oshima *et al.* using triphenyl tin hydride or benzenethiol as radical precursors. Using vinyl cyclopropane **119**, the preparation of vinylcyclopentanes was easily achieved *via* the radical cyclisation with alkenes. They noted that electron rich olefins such as butyl vinyl ether provided the cyclopentanes in good yields and that alkenes containing electron-withdrawing substituents, such as acrylonitrile and methyl acrylate gave poor yields.[57a] In the case of the use of homoallylic cyclopropanes, an internal cyclisation could occur affording the corresponding cyclopentenes in good yields.[57b] In the example below, both cyclopentane **162** and cyclopentene **164** were prepared in 82% yield.



Scheme 64

Recently, Byers *et al.* used the same methodology to perform radical additions of propargylic cyclopropanes to electron- rich olefins using 1,2-diphenyldiselane as the radical precursor through the formation of an phenylselenoallene intermediate **165**.[58] In the example shown in Scheme 65, the cyclopentane **166** was isolated in 55% yield with a 2:1 diastereoisomeric ratio.

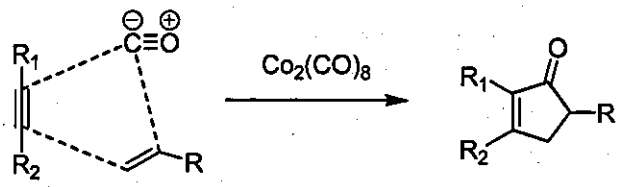


Scheme 65

1.7. The Pauson-Khand reaction

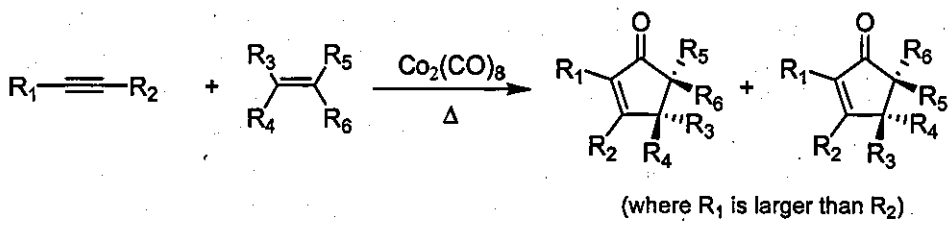
1.7.1. Reaction Discovery

Another application of alkyne/dicobalt complexes is the Pauson-Khand reaction, which formally represents a [2+2+1] cycloaddition (Scheme 66). This reaction involves the cyclisation of one alkyne, one alkene and a cobalt carbonyl (as a carbon monoxide source) to yield cyclopentenones with the formation of 3 new C–C bonds in only one step. Just a brief description is outlined hereafter but comprehensive reviews covering all aspects of the PKR are available.[59]



Scheme 66

The reaction was discovered accidentally in the 1970s during investigations towards the preparation of various dicobalt alkyne complexes by Pauson, Khand and co-workers.[60] They discovered that cyclopentenones could be synthesised under thermal conditions in moderate yields (Scheme 67).

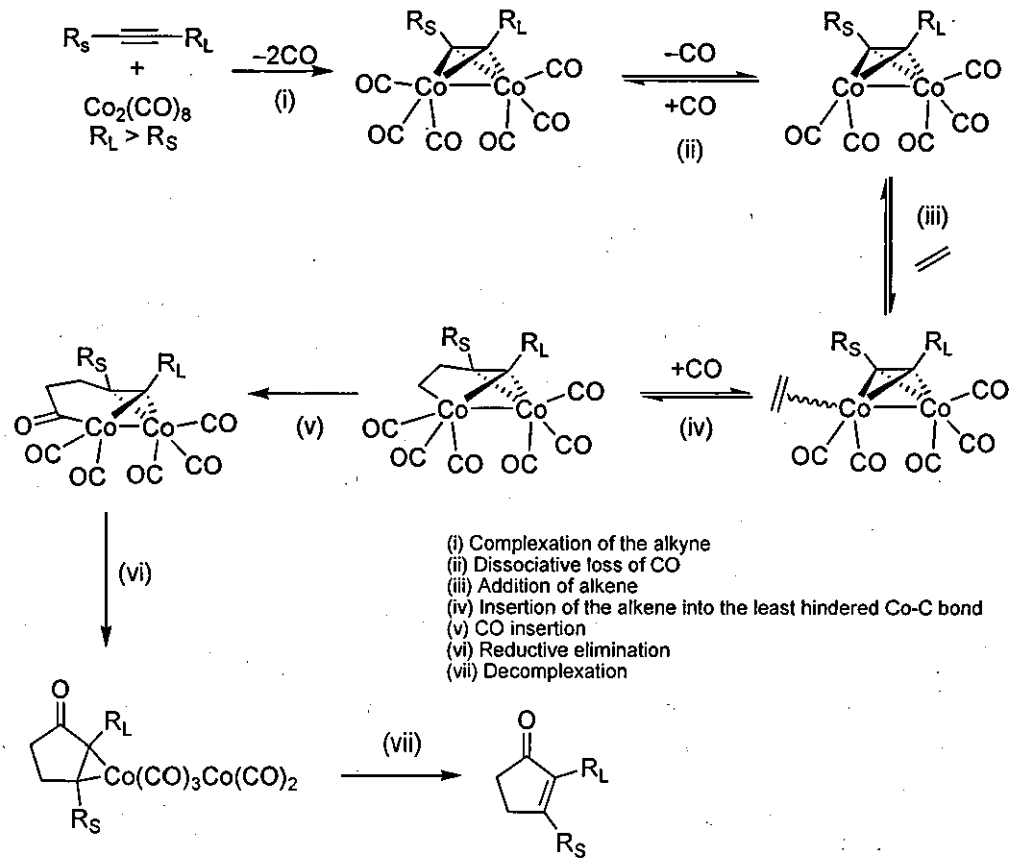


(where R_1 is larger than R_2)

Scheme 67

1.7.2. Reaction mechanism

Since its discovery, the PKR has become a key synthetic route among transition metal promoted cycloaddition reactions. Magnus was the first to propose a full mechanism which is generally accepted, although it remains unproven (Scheme 68).[61] The dicobalt complex is prepared by reaction of the alkyne with dicobalt octacarbonyl. The next step is the loss of a carbon monoxide ligand from one of the prochiral cobalt atoms. This step is reversible and thought to be rate limiting. The unsaturated cobalt atom has only 16 e^- thus allowing an alkene to coordinate to the vacancy (step 3). Insertion of the alkene along with the gain of a carbon monoxide ligand (step 4), allows a carbon monoxide insertion leading to the formation of a cobaltacycle intermediate (step 5). A reductive elimination (step 6) followed by a decomplexation (step 7) leads to the cyclopentenones.



Scheme 68

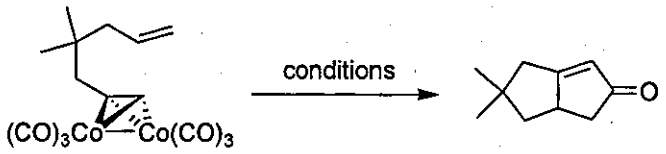
The PKR consists of olefin insertion, CO insertion, and reductive elimination steps. The olefin insertion step was found to be an irreversible step that determines the stereo- and regiochemistry of the overall reaction.[62] The following steps are low activation energy processes and reversible. The bond-forming events occur only on one of the two metal atoms, while the second metal atom not only acts as an anchor that fixes the metal cluster to the organic substrate but also exerts electronic influences on the reaction at the first atom.

Theoretical studies have shown that the dissociative loss of a carbon monoxide ligand from the alkyne dicobalt cluster (step 2) is the most energetic and hence limiting step.[62] This dissociative loss of carbon monoxide can be promoted using a range of hard bases, *N*-oxides or sulfides. These theorical and experimental evidences implement the possible mechanism described by Magnus.

1.7.3. Reaction promoters

The PKR was developed initially using a thermal activation to promote the necessary loss of a carbon monoxide ligand to instigate the olefin insertion. Some substrates readily undergo the cyclisation affording their cycloadduct; however, long reaction time and poor yields often limit the scope of the reaction.

The PKR process has been improved since the 1980's with the use of different promoters allowing milder conditions to be employed such as amines,[63] *N*-oxides,[64] sulfides.[65] Smit and Caple were the first to report a solid state promoted PKR by adsorption of the substrate onto silica gel (Scheme 69).[66] They prepared the compound **168** starting from the allyl ether **167** using the SiO_2 promoted PKR protocol they developed. They improved the yield to reach 76% in 30 min at 45°C, while using the initial thermal PKR, the desired fused cycloadduct **168** was isolated in only 29% yield after 24 h at 60°C.[67]

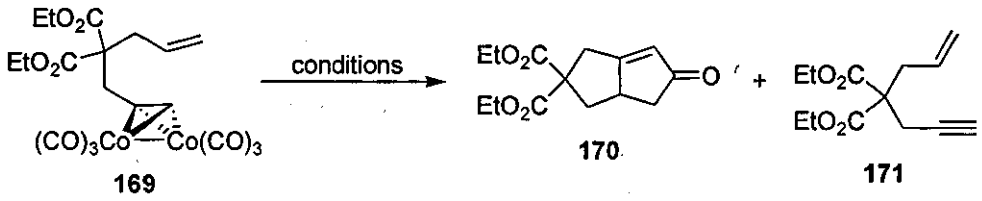


167 168

Conditions	t	T (°C)	Yield (%)
isooctane, CO atm.	24 h	60	29
pentane, SiO_2	30 min	45	76

Scheme 69

Amine-*N*-oxides were known to induce cleavage of the carbon monoxide ligand from the metal cluster *via* oxidation to carbon dioxide.[68] Schreiber reasoned that they could therefore induce the PKR and found that *N*-methylmorpholine-*N*-oxide (NMO) was able to promote the intramolecular reaction with improving the stereoselectivity in some cases.[69] Following this statement, Jeong *et al.* investigated further in the use of oxidants as promoters (Scheme 70).[70]



169 170 171

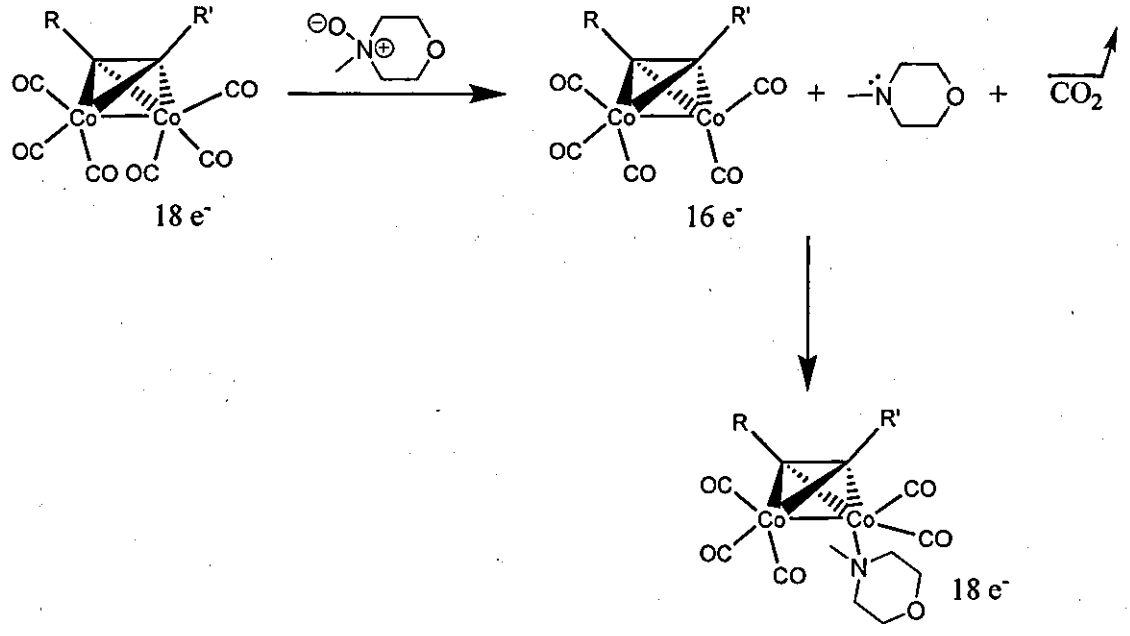
Conditions	Yield 170 (%)	Yield 171 (%)
TMANO, O_2, DCM, 3 h, r.t.	90	0
CAN (3 eq.), DCM, 16 h, r.t.	32	45
CAN (3 eq.), acetone, 3 h, r.t.	0	80
NMO (3 eq.), DCM, 8 h, r.t.	87	0

Scheme 70

Cerium ammonium nitrate, which was known to decomplex the dicobalt moiety from the alkyne, could also be used in DCM to perform the PKR. However the yield remained minimal and products of simple decomplexation of the starting material accompanied the formation of the cycloadduct. When the compound **169** was treated with CAN in acetone,

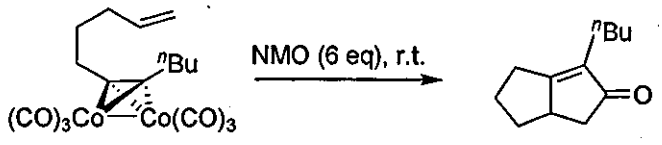
only the decomplexed starting material **171** was isolated at the end of the reaction. *N*-oxides such as TMANO and NMO afforded the desired cycloadduct **170** in good yields with reaction time reduced to 3 hours with TMANO.

Schreiber *et al.* early studies suggested that once the CO ligand was lost as a carbon dioxide, the remaining tertiary amine could act as a ligand, co-ordinating to the vacant site and stabilising the reaction intermediate (Scheme 71).[69]



Scheme 71

This work prompted research into the use of hard Lewis bases as reaction promoters. Krafft developed the use co-ordinating solvents as catalysts for the NMO mediated reaction (Scheme 72).[71]



172 173

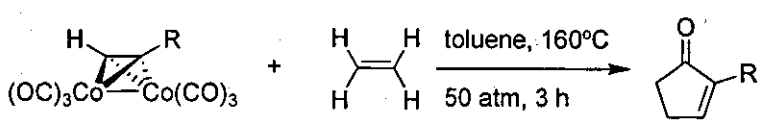
Solvent	t	Yield 173 (%)
MeCN	4 min	88
EtOAc	8 min	63
THF	10 min	72
acetone	10 min	78
THF/DCM (1:1)	25 min	61
DCM	30 min	70
Et_2O	8 h	50
DMSO	14 h	71

Scheme 72

The best result was obtained using acetonitrile as the solvent affording the cyclopentenones **173** in 88% yield after only 4 min. The results demonstrated that co-ordinating solvents not only catalysed the reaction but also increased the yields. However, DMSO, which was initially expected to catalyse the reaction, gave surprisingly opposite results by retarding the reaction.

1.7.4. Limitation of the reaction

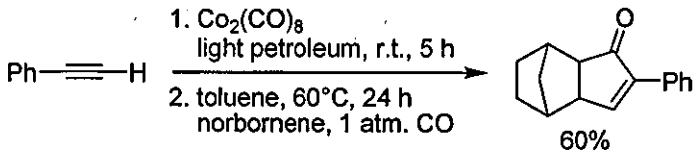
The Pauson-Khand reaction has developed into a very general method of forming cyclopentenones and its process has been improved since its discovery allowing the reaction on sensitive substrates. However, stoichiometric conditions, thermal initiation and long reaction time are often required and thus limit the scope of the reaction (Scheme 73).[72]



Scheme 73

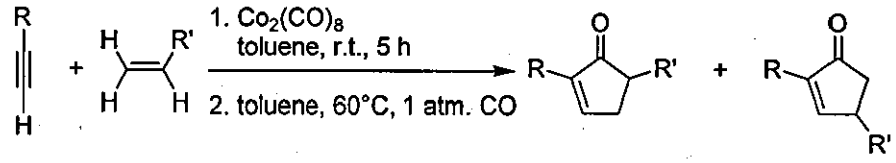
Most simple alkenes seem to be suitable substrates for the PKR owing to a low steric hindrance. It was found that increasing the substitution at the double bond lowered the

reactivity. However, strained cyclic alkenes such as norbornene or norbornadiene tend to provide better yields than internal alkenes under milder conditions, presumably due to the relief of strain (Scheme 74).[73]



Scheme 74

The scope of the reaction is also limited by the regioselectivity as two regiosiomers are likely to be obtained in the final product (Scheme 75).[74a-c] The ratio of regiosiomers can be controlled by the size of groups R and R' remote from the double bond, although the use of a highly substituted alkene or an alkyne is problematic as the reaction will not occur.

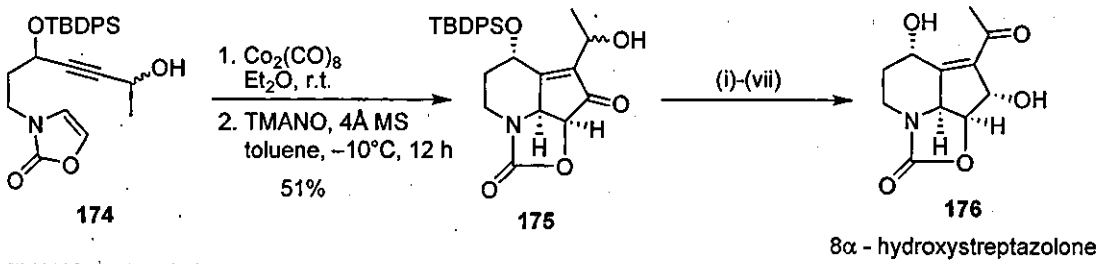


Scheme 75

Intramolecular PKR are well documented (for reviews, see note 59). They have the advantage to solve problems related to the regioselectivity of the reaction. Strained alkenes are not required to achieve the reaction in good yields and bicyclic products are then easily prepared starting from linear reactants.

1.7.5. Use of the PKR towards the synthesis of natural products

Mukai *et al.* used the Pauson-Khand reaction towards the formation of a tricyclic molecule starting from a monocyclic precursor.[75] They synthesized (±)-8α-hydroxystreptazolone **176** using an intramolecular Pauson-Khand reaction carried out on a 2-oxazolone derivative **174** (Scheme 76).

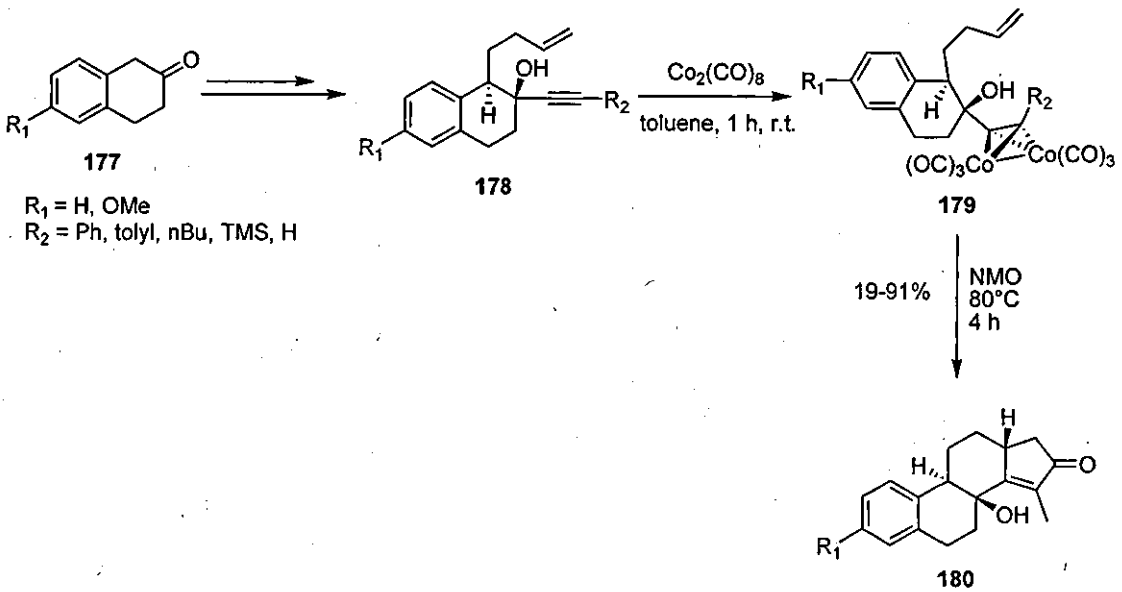


TMANO = trimethylamine-N-oxide

(i) MOMCl, iPr_2NEt, DCM, reflux; (ii) $NaBH_4$, $CeCl_3$, MeOH, 0°C (90%); (iii) p-$NO_2C_6H_4CO_2H$, PPh_3, DEAD, benzene 60°C; (iv) HCl_{conc}, THF, 60°C; (v) Dess-Martin periodinane, DCM, r.t. (65%); (vi) K_2CO_3, MeOH, r.t.; (vii) TBAF, THF, r.t. (82%)

Scheme 76

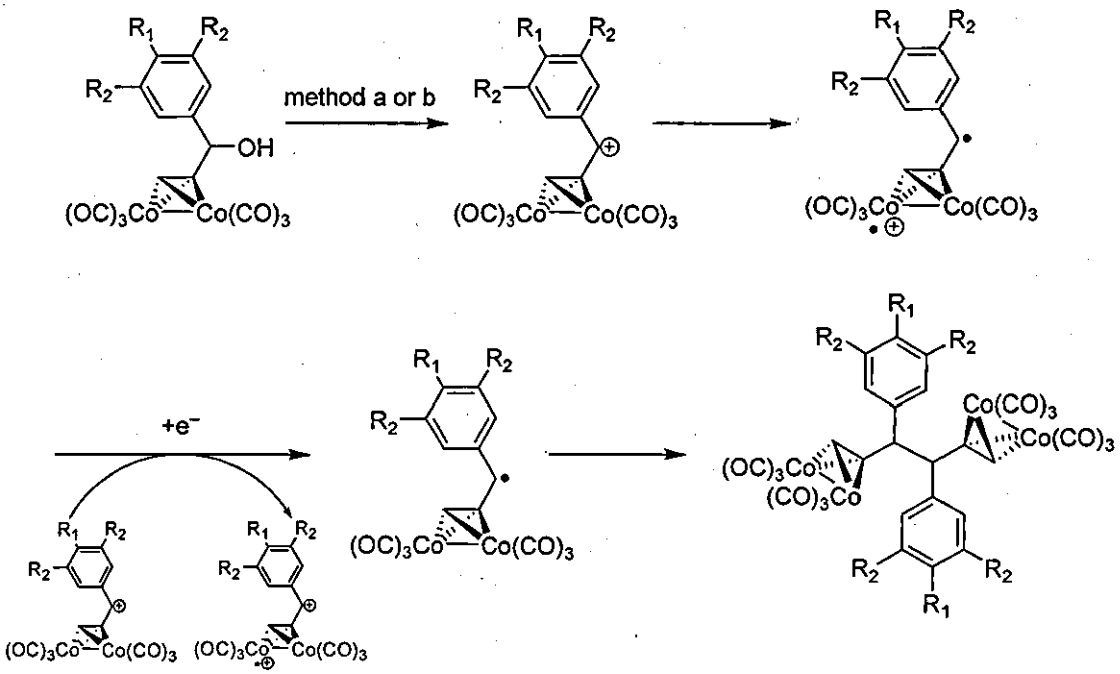
Recently, Chung *et al.* have used the Pauson-Khand reaction towards the synthesis of steroids.[76] They developed a high-yield synthesis of steroid-type molecules (**180**) under mild reaction conditions in two steps involving the nucleophilic addition of alkynyl cerium reagent to an easily enolizable carbonyl compound **177** (β-tetralone), followed by an intramolecular Pauson-Khand reaction (Scheme 77).



Scheme 77

1.8. Alkyne/dicobalt hexacarbonyl complexes in radical chemistry

While cobalt-stabilised cations have been extensively exploited for synthetic purposes, the corresponding radical chemistry has been less developed. Just a few examples of alkyne/dicolbalt complexes inducing radicals have been described in the literature. Melikyan *et al.* and Mc Glinchey *et al.* worked on the stereoselective coupling of two alkyne/dicobalt hexacarbonyl complexes. A dimer was obtained using triflic anhydride or HBF_4 (Scheme 78).[77]



Method a: HBF_4, DCM, 20°C
Method b: Tf_2O, DCM, 20°C

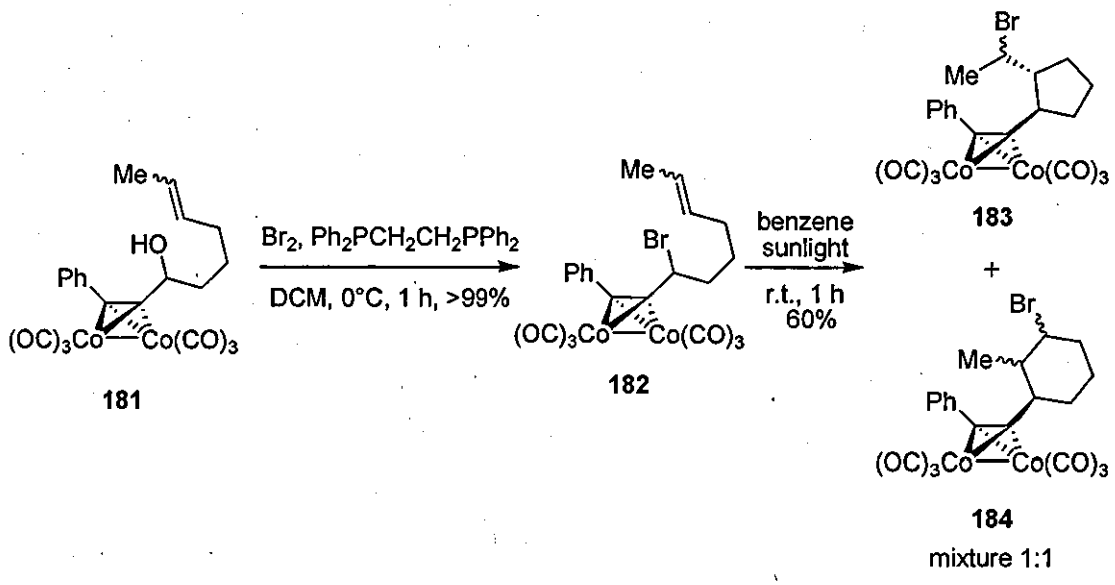
Method	R_1	R_2	Yield (%)	t (h)	d.e. (%)
a	H	H	80	9	88
a	MeO	H	80	13	94
b	H	H	42	23	84
b	MeO	H	68	23	98

Scheme 78

Melikyan *et al.* suggested that after heterolysis of the C–O bond, the radical was formed *via* electron transfer from the bimetallic complex towards the carbocation. Then the metal is

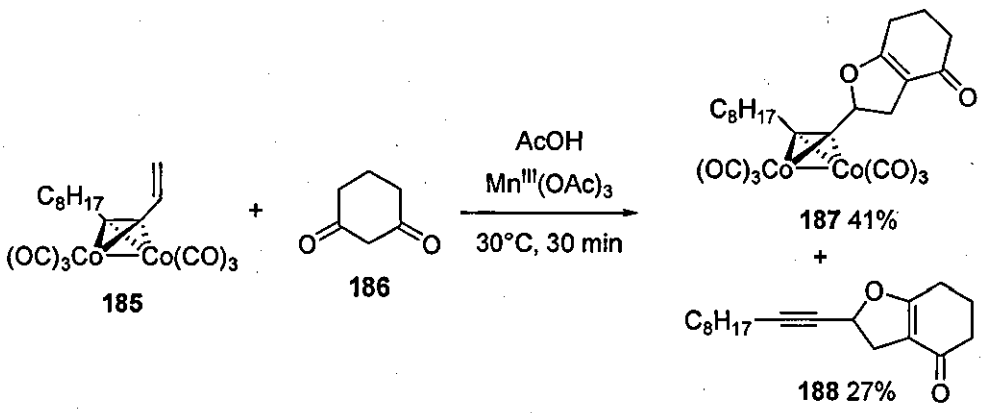
reduced *via* an external electron transfer from another bimetallic complex. They noted that when the R_1 group in "*para*" position to the alkyne complexed chain was an electron donating group such as a methoxy group, the delocalisation of the electrons through the aromatic ring delayed the generation of the radical.

Nicholas *et al.* also discovered fortuitously that propargylic radicals could be spontaneously formed in sunlight *via* the homolytic cleavage of the C–Br bond.[78] A subsequent atom transfer afforded the five- and the six-membered rings **183** and **184** in good yield as a 1:1 mixture (Scheme 79).



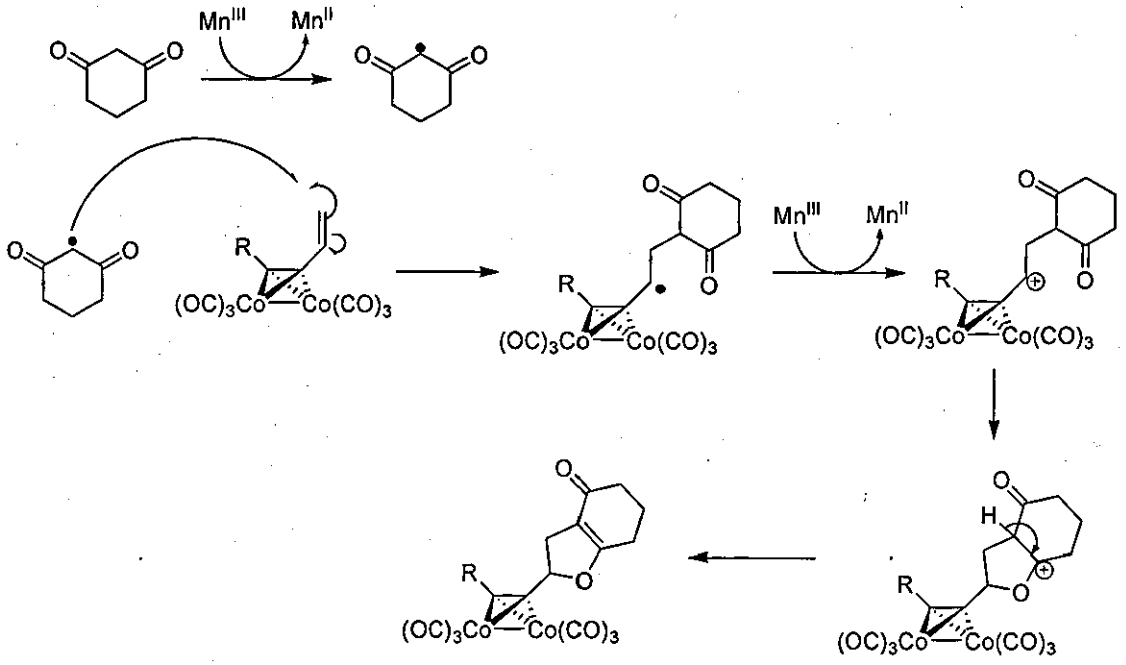
Scheme 79

Melikyan also used dicobalt complexes in conjunction with Mn^{III} to form dihydrofurans (Scheme 80). In the following example the complexed 1-dodecen-3-yne **185** was treated with Mn^{III} and cyclohexan-1,3-dione **186** affording the complexed hydrobenzofuranone **187** and its decomplexed analogue **188** in 41% and 27% yield respectively.[79]



Scheme 80

The mechanism is believed to proceed as follows: the Mn^{III} is initially reduced to Mn^{II} while the β-dicarbonyl is oxidised into a radical. The latter adds onto the dicobalt hexacarbonyl activated alkene. The radical formed in the propargylic position is oxidised again by Mn^{III} to form a Nicholas carbocation, which is then trapped by a carbonyl, closing a five-membered oxonium ring. A subsequent loss of a proton affords the dihydrofuran (Scheme 81).



Scheme 81

Copper^{II} acetate dihydrate had to be used as a co-oxidant when the enyne was not complexed. It appeared that the Mn^{III} could not oxidise the propargylic radical into the indispensable carbocation resulting in a gross polymerisation. On the other hand, when the substrate was complexed with dicobalt octacarbonyl, the combination Mn^{III}/Cu^{II} was not required to allow the formation of the furan rings. Melikyan suggested that the cobalt complex lowers the oxidation potential of the propargylic radical.

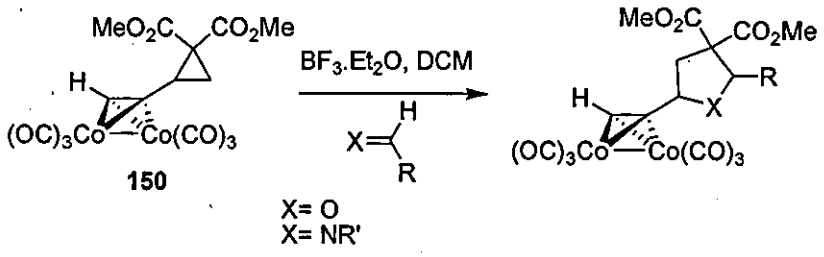
The initial aim of the work described hereafter was to improve and expand the previous work done within the group,[54,55] directed towards the synthesis of furan and pyrrolidine rings *via* [3+2] cycloadditions. To expand the methodology, the formation of the corresponding six-membered rings in α-position to the complexed alkyne *via* a [4+2] dipolar cycloaddition was also investigated.

2. Results and Discussion

2.1. Dicobalt hexacarbonyl mediated [3+2] cycloaddition reaction

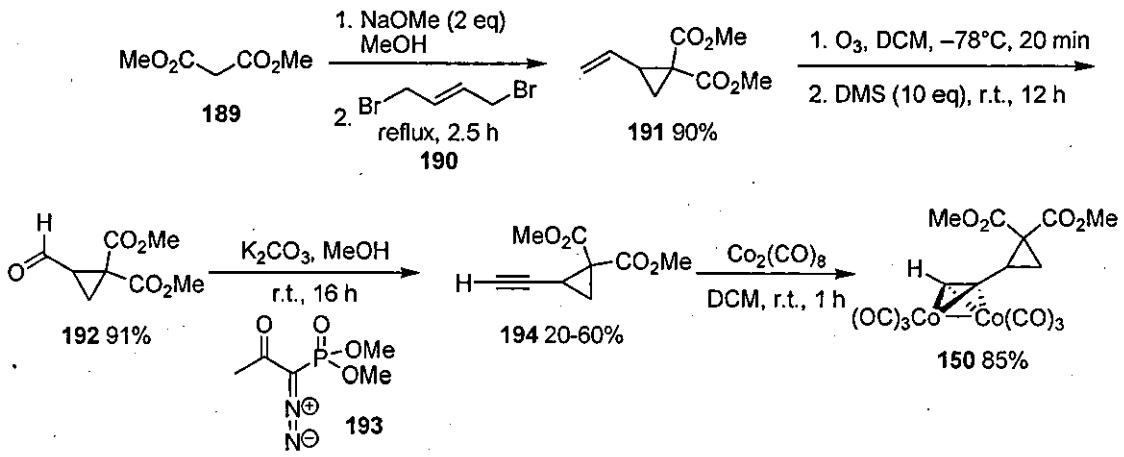
2.1.1. Background

The work within the group has extended the methodology developed in the 80's by Tsuji, Yamamato and Trost[45,46] *via* the reaction of a homobimetallic alkynyl diester cyclopropane with a range of aldehydes and imines to provide highly functionalised tetrahydrofurans and pyrrolidines respectively in good yield but poor diastereoselectivity (Scheme 82).



Scheme 82

Cyclopropane **150** was synthesised using a four-step methodology involving the Bestmann reaction to form the desired alkyne (Scheme 83).[54,55]

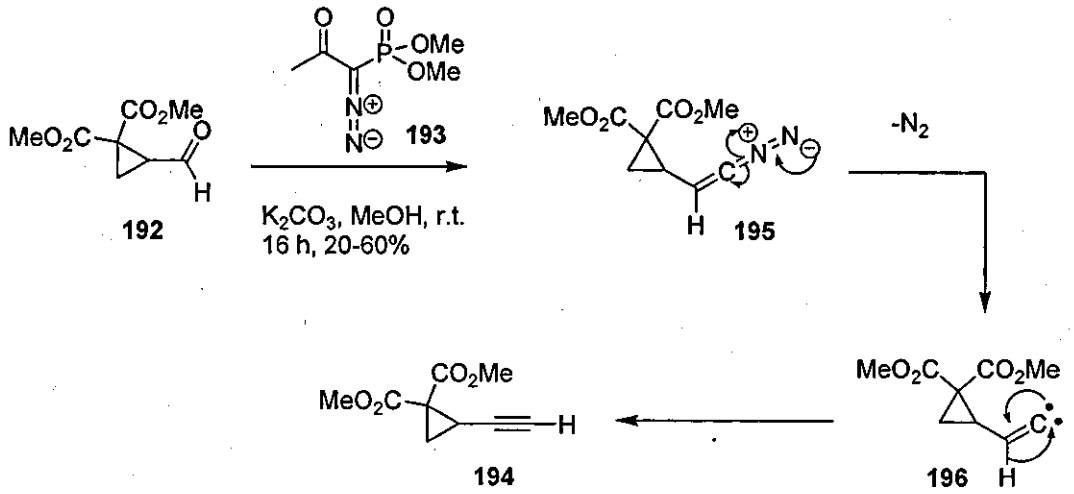


Scheme 83

Deprotonation of dimethylmalonate **189** with sodium methoxide and subsequent alkylation with *trans*-1,4-dibromobutene **190** afforded the vinyl cyclopropane **191** in 90% yield. The alkene was oxidised *via* ozonolysis, at –78°C, to afford the aldehyde derivative

cyclopropane **192** in 91% yield after treatment of the ozonide with DMS. The latter was then allowed to react with Bestmann's reagent **193** in methanol in presence of potassium carbonate to generate the desired alkyne cyclopropane in a variable 20-60% yield after purification. Subsequent complexation with dicobalt octacarbonyl yielded the complexed cyclopropane **150** in 85%.

Reaction of the Bestmann's reagent with aldehydes gives terminal alkynes often in very high yield.[80] However, the limiting step of the strategy described in Scheme 83 was the formation of the alkyne using this procedure. The Bestmann reaction is a derivation of the Seyferth-Gilbert homologation[81] allowing the use of the milder potassium carbonate to make the procedure more compatible with a wide variety of functional groups. The mechanism of the Bestmann reaction is shown in the Scheme 84.



Scheme 84

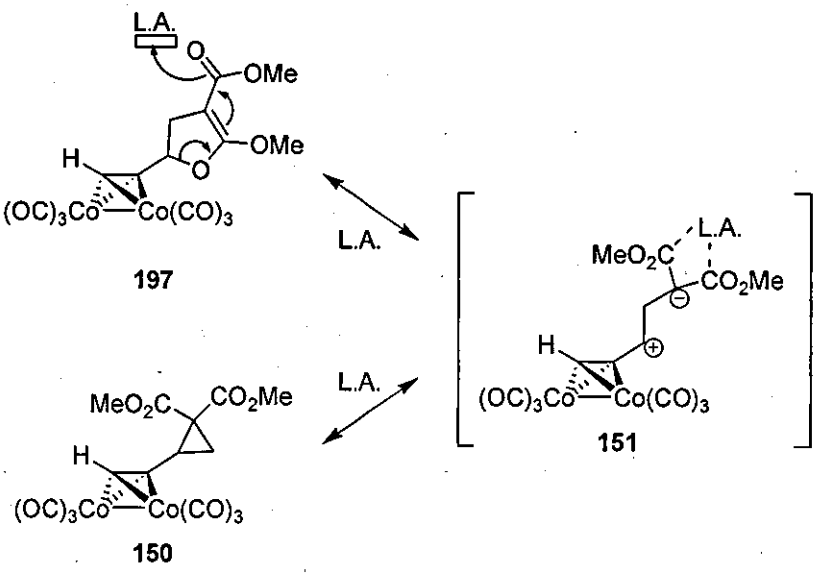
The route above shows the synthesis of the alkynyl cyclopropane **194** using the Bestmann reagent that was used within the group. The synthesis of **194** is achieved *via* the olefination of the aldehyde derivative **192** to form the diazo compound **195**. After nitrogen elimination, a [1,2]-rearrangement of the vinyl carbene gives the alkyne. It is believe that the generation of methanoate *in situ* may be responsible for the low yield of the reaction as it may open the activated cyclopropane *via* a nucleophilic attack.

In an effort to improve the methodology developed within the group, the research focused on two areas:

- The use of dihydrofurans as cyclopropanes surrogates.
- Alternative routes to the complexed alkynyl cyclopropane, circumventing the capricious and poor yielding Bestmann reaction and allowing possible transfer to chiral systems.

2.1.2. Dihydrofuran as cyclopropane surrogates

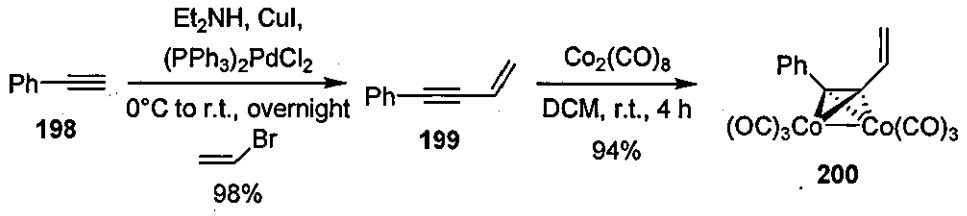
As described in the introduction, it is possible to form dihydrofurans in α-position to an alkyne using the strategy developed by Melikian *et al.* (Scheme 80).[79] The formation of a dihydrofuran with groups **197** could open a new way to perform a dipolar [3+2] cycloaddition reaction upon treatment with a Lewis acid, using the dihydrofuran ring as a synthetic equivalent to the cyclopropane ring, hence avoiding the low yielding Bestmann step (Scheme 85). We thought that under Lewis acid activation, the dihydrofuran **197** would form an intermediate **151** similar to that proposed for the ring opened cyclopropane.



Scheme 85

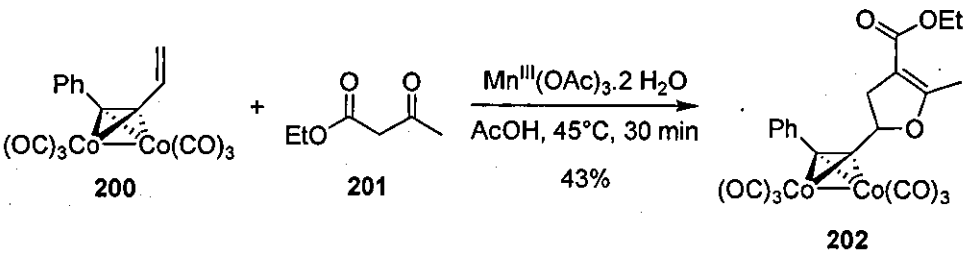
2.1.2.1. First attempt – starting from phenyl acetylene

The first step involved in the strategy was the synthesis of the enyne **199** starting from phenyl acetylene **198** *via* a Sonogashira coupling with vinyl bromide using Et_2NH as solvent. After complexation, the enyne **200** was obtained in 92% yield over two steps (Scheme 86).



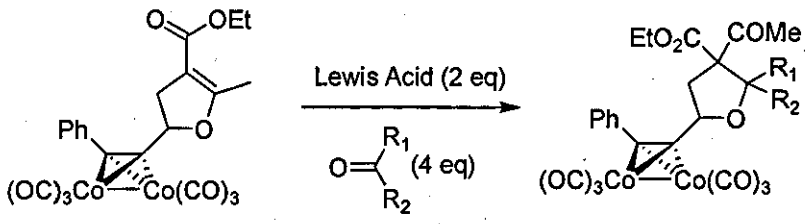
Scheme 86

In a first attempt to form the dihydrofuran, ethyl acetoacetate was used as the β-dicarbonyl as it was reported to be easily prepared by Melikian. The addition of ethyl glyoxylate to the double bond using Mn^{III} acetate in acetic acid, at 45°C for 30 min, afforded the dihydrofuran **202** in 43% yield (Scheme 87).



Scheme 87

Previous investigations within the research group established that the cobalt mediated [3+2] dipolar cycloaddition was more efficient using electron deficient trap reagents such as ethyl glyoxylate or *p*-nitrobenzaldehyde.[54,55] Therefore, dihydrofuran **202** was initially reacted with several electron poor aldehydes or ketones under Lewis acid activation in an attempt to form substituted tetrahydrofurans **203** using 2 eq of Lewis acid and 4 eq of the trapping reagent. The results are shown in Table 1.



202 **203**

Scheme 88

Entry	Lewis acid	Reagent (4 eq)	T (°C)	t (h)	R_1	R_2	Yield (203)
1	$BF_3.Et_2O$	diethylketomalonate	45	19	CO_2Et	CO_2Et	SM
2	$ZnBr_2$	acetaldehyde	r.t.	17	Me	H	complex mixture
3	$BF_3.Et_2O$	acetaldehyde	r.t.	5	Me	H	31%
4	$ZnBr_2$	ethyl glyoxylate	45	17	CO_2Et	H	50%
5	$ZnBr_2$	ethyl glyoxylate	–15	2	CO_2Et	H	39%

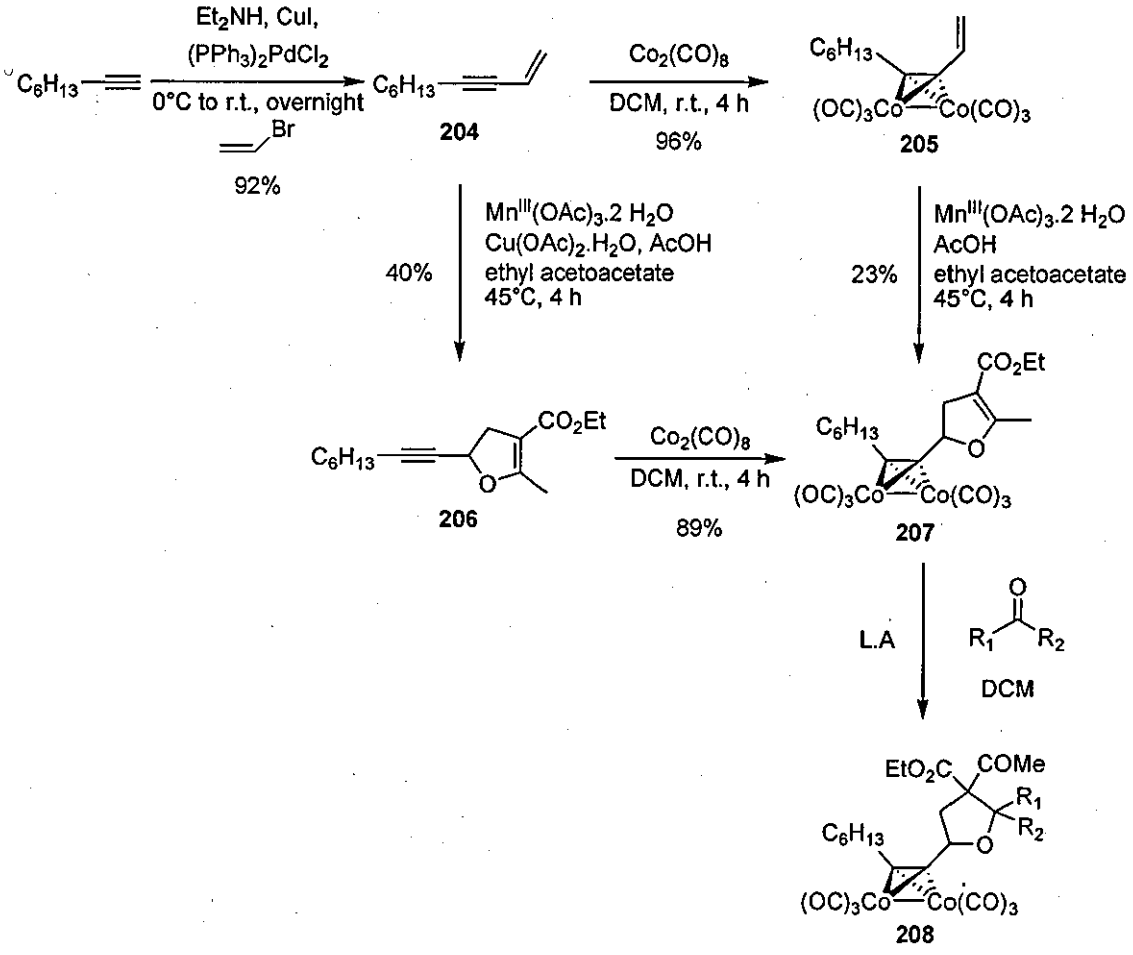
Table 1

The best yield was obtained using ethyl glyoxylate as the trapping reagent (entry 4). With 3 stereocenters in the final product **203**, 4 diastereoisomers were possibly visible by NMR. Unfortunately this led to a spectrum too complex to elucidate, however mass spectrometry showed the existence of the desired product. The stereoselectivity could not even be thermally controlled as the use of ethyl glyoxylate at –15°C afforded the same complex mixture of diastereoisomers (entry 5). No stereoselectivity could be obtained, also using acetaldehyde (entry 2). The use of zinc bromide and acetaldehyde for this reaction just gave decomposition (entry 3). In an effort to reduce the number of stereocenters, diethylketomalonate was used to form the substituted furan. However only starting material was recovered from the reaction (entry 1).

Previous research within the group suggested that the phenyl substituent could affect the reaction of the complex hence this was replaced for a ^{n}hexyl group.[7c]

2.1.2.2. Second attempt – starting from 1-octyne

To avoid any possible problem with the aromatic ring, the enyne **204** was prepared using the same methodology, involving a Sonogashira coupling between 1-octyne and vinyl bromide. A radical addition of ethyl acetoacetate initiated by Mn^{III} in presence of a co-oxidant and followed by complexation with dicobalt octacarbonyl gave the dihydrofuran **207** in 33% yield over 3 steps (Scheme 89). When the Mn^{III} reaction was performed on the pre-complexed enyne **205**, the product was obtained in only 20% yield over 3 steps thus the first route was preferred.



Scheme 89

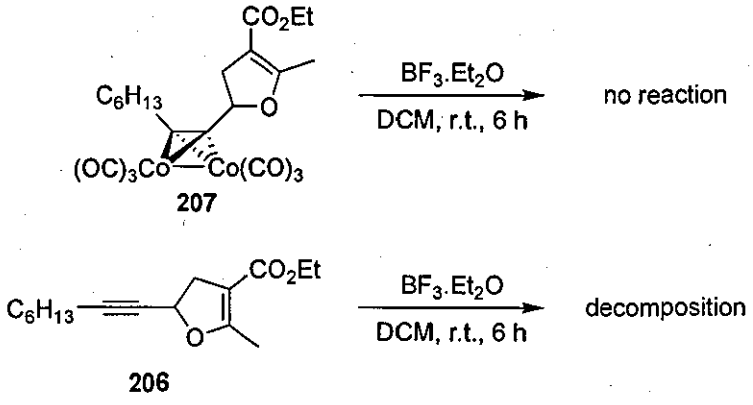
Subsequent cycloadditions were attempted onto the dihydrofuran **207**, using ethyl glyoxylate and dimethylketomalonate (Table 2). Unfortunately, the same results as previously were

observed, leading mostly to complex mixtures. In an effort to control the diastereoselectivity, the cycloaddition onto ethyl glyoxylate was performed in DCM at different temperatures without any improvement (entries 1, 2 and 3).

Entry	Lewis acid (4 eq)	Reagent (3 eq)	T (°C)	T	R_1	R_2	Yield (208)
1	$BF_3.Et_2O$	ethyl glyoxylate	r.t.	10 min	H	CO_2Et	complex mixture
2	$BF_3.Et_2O$	ethyl glyoxylate	45	10 min	H	CO_2Et	complex mixture
3	$BF_3.Et_2O$	ethyl glyoxylate	–15	2 h	H	CO_2Et	complex mixture
4	$BF_3.Et_2O$	dimethylketomalonate	r.t.	10 h	CO_2Et	CO_2Et	complex mixture

Table 2

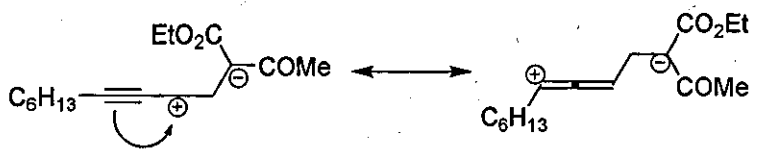
To assess the effect of the use of the dicobalt moiety, the dihydrofuran **207** was allowed to react with $BF_3.Et_2O$ without any trapping reagent (Scheme 90). This reaction returned the starting material and no product of degradation was observed.



Scheme 90

On the other hand, when the same conditions were applied to the uncomplexed dihydrofuran **206**, the reaction led to decomposition of the starting material. This may be due to a

rearrangement of the alkyne into the corresponding allene during the ring opening (Scheme 91).

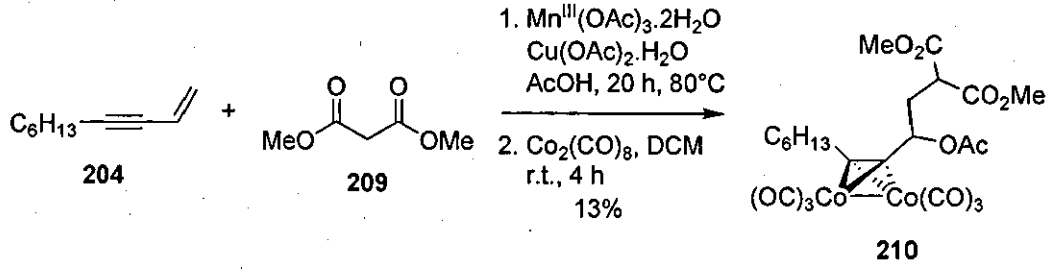


Scheme 91

2.1.2.3. Third attempt – use of symmetric β-dicarbonyls

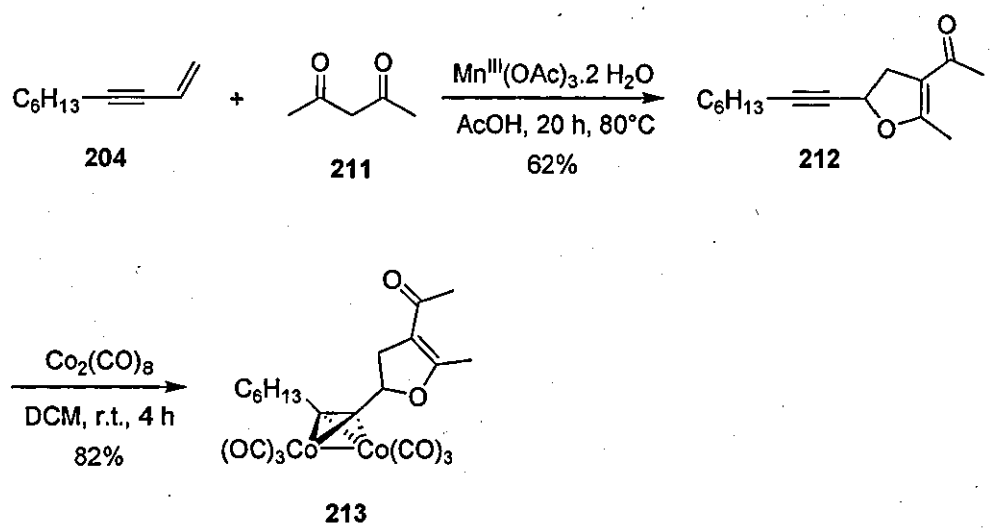
Due to the presence of 3 stereocenters in the final products **203** and **208**, 8 possible diastereoisomers were likely to form during the cycloaddition resulting in complex mixtures with difficult purification and characterisation. To reduce the number of possible diastereoismers, symmetric β-dicarbonyls were used to form the dihydrofuran.

Addition of dimethyl malonate **209** was attempted without any success on the two enynes **204** and **205**. The dihydrofuran formed during this step appeared to decompose on silica so it was complexed prior to purification. Unfortunately only the dicobalt complex derivative **210** could be observed, bearing an acetate group which must have come from acetic acid (Scheme 92).



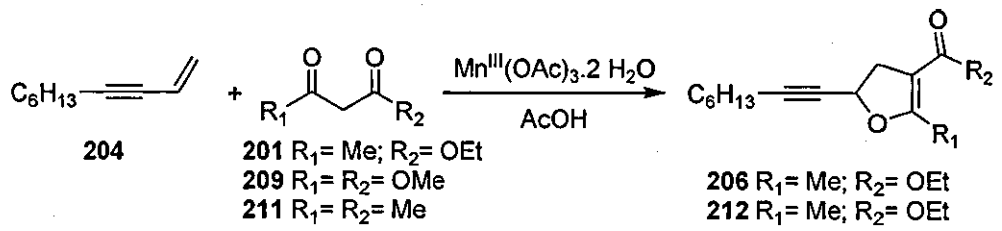
Scheme 92

The manganese acetate reaction was attempted with acetylacetone **211**. The desired dihydrofuran **212** was obtained in a 62% yield. The complexation with dicobalt octacarbonyl in DCM at room temperature afforded the corresponding complexed dihydrofuran **213** in 51% yield over 2 steps (Scheme 93).



Scheme 93

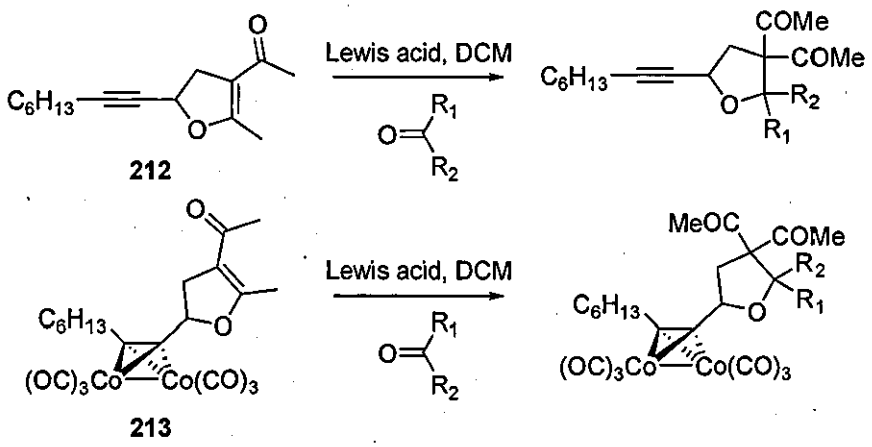
During these investigations, we noted that the formation the dihydrofuran using the manganese reaction was dependent on the pKa of the β-dicarbonyl used. Yields decreased when the pKa increased (Table 3).



Entry	β-dicarbonyl	pKa of β-dicarbonyl	dihydrofuran	Yield (%)
1	acetylacetone **211**	9	**212**	62
2	ethylacetoacetate **201**	11	**206**	40
3	dimethylmalonate **209**	13	n/a	0

Table 3

The cycloaddition reaction was then attempted onto dihydrofurans **212** (Table 4) and **213** (Table 5) with a range of trapping reagents (Scheme 94). In addition, variations of Lewis acid and temperature were attempted.



Scheme 94

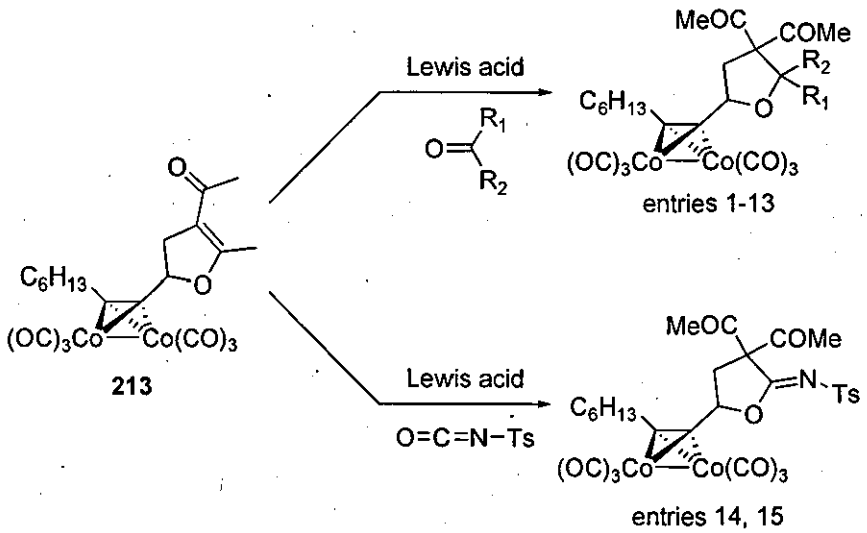
Using the conditions developed previously within the research group, the use of the uncomplexed dihydrofuran **212** returned the starting material (Table 4). When dihydrofuran **212** was reacted at r.t. with dimethylketomalonate or ethyl glyoxylate and $BF_3.Et_2O$ as the Lewis acid, no reaction occurred as expected (Table 4, entry 1 and 2). In addition, in an effort to further activate the dihydrofuran ring, the reaction mixtures were also heated to reflux although it returned the starting material. In an attempt to use the conditions described by Kerr *et al.*,[48a] $Yb(OTf)_3$ was also used as the Lewis acid without any success (Table 4, entry 3). These results were consistent with the assumptions that dicobalt complexes were required to open the dihydrofuran.

Entry	Substrate	Lewis acid	Reagent (3 eq)	T (°C)	T	Yield
1	**212**	$BF_3.Et_2O$ (4 eq)	dimethylketomalonate	r.t. 40	5 h 8 h	no reaction
2	**212**	$BF_3.Et_2O$ (4 eq)	ethyl glyoxylate	r.t. 40	13 h 8 h	no reaction
3	**212**	$Yb(OTf)_3$ (2.5 eq)	ethyl glyoxylate	40	36 h	no reaction

Table 4

Using the dihydrofuran **213**, the cycloaddition reaction was first attempted using $BF_3.Et_2O$ as the Lewis acid, in DCM in presence of ethyl glyoxylate (Scheme 95 and Table 5). At

room temperature, the reaction returned the starting material while when heated to reflux only decomposition was observed (entry 1). The use of stronger Lewis acid, such as $TiCl_4$ at room temperature or at –78°C, also led to decomposition of the starting material (entry 2). The only conditions found to afford the desired cycloadduct were $Yb(OTf)_3$ in DCM with ethyl glyoxylate as the trapping reagent. Using 5 eq of $Yb(OTf)_3$ and 1.5 eq of ethyl glyoxylate, the desired substituted furan **214** was prepared in 60% yield with a 1:3 *cis*:*trans* ratio (entry 3). The yield was unchanged by reducing the amount of Lewis acid or ethyl glyoxylate. However the diastereoselectivity was affected when the amount of $Yb(OTf)_3$ was reduced to 2.5 eq, affording the tetrahydrofuran **214** in 57% in a 3:4 *cis*:*trans* ratio (entry 4). Using a catalytic amount of Lewis acid, only the starting material was recovered (entry 5 and 10). Using the suitable conditions established using ethyl glyoxylate, similar electron deficient trap reagents were utilised in attempts to perform the cycloaddition. The use of diethylketomalonate, *p*-nitrobenzaldehyde in DCM with 2.5 eq of $Yb(OTf)_3$ returned the starting material (entries 6, 7 and 8). In an attempt to use the conditions reported by Johnson *et al.*,[49] $Sn(OTf)_3$ with *p*-nitrobenzaldehyde was used without success (entry 9). To verify that, as reported earlier with the cyclopropane,[54,55] the reaction occurs preferably with electron deficient trapping reagents, acetaldehyde, heptanal, benzaldehyde and *p*-anisaldehyde were also submitted to the cycloaddition reaction conditions. Unfortunately no reaction was observed (entries 10-13). Tosyl isocyanate was also used for its highly electron deficient carbonyl. When it was submitted to the reaction conditions, with $BF_3.Et_2O$ (entry 14) or $Yb(OTf)_3$ (entry 15) no product of cycloaddition was observed (Scheme 95).



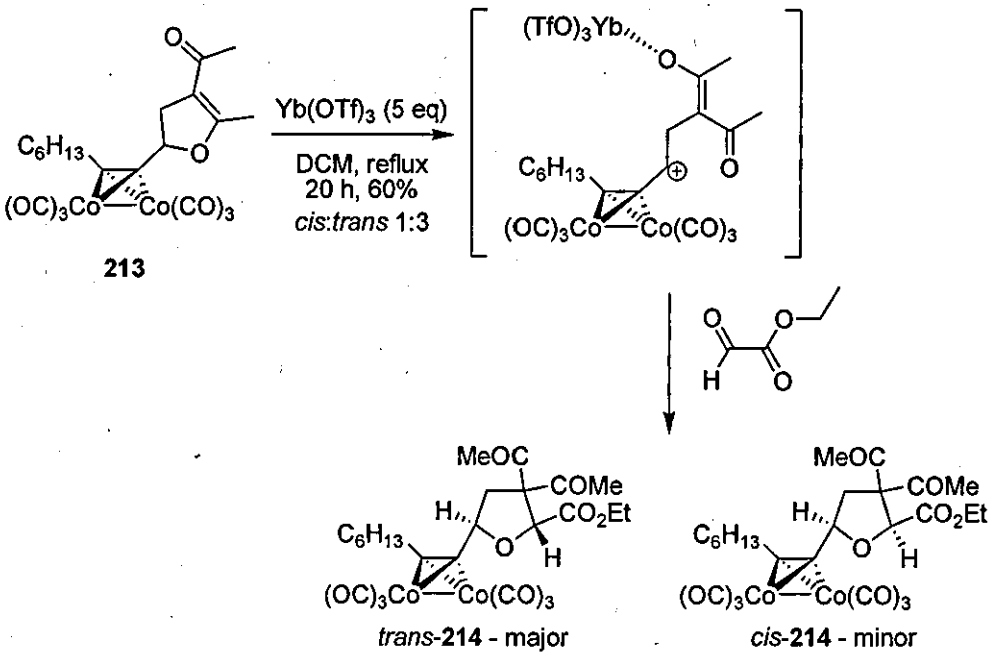
Scheme 95

Entry	Solvent	Lewis acid	Reagent	T (°C)	T	Yield*
1	DCM	$BF_3.Et_2O$ (4 eq)	ethyl glyoxylate (3 eq)	R.T 40	12 h 20 h	SM complex mixture
2	DCM	$TiCl_4$ (2.5 eq)	ethyl glyoxylate (2.5 eq)	40 –78	16 h	complex mixture
3	DCM	$Yb(OTf)_3$ (5 eq)	ethyl glyoxylate (1.5 eq)	40	20 h	**214** 60% (1:3 *cis*:*trans*)
4	DCM	$Yb(OTf)_3$ (2.5 eq)	ethyl glyoxylate (3 eq)	40	20 h	**214** 57% (3:4 *cis*:*trans*)
5	DCM	$Yb(OTf)_3$ (10 mol%)	ethyl glyoxylate (3 eq)	40	20 h	SM
6	DCM	$Yb(OTf)_3$ (2.5 eq)	diethylketomalonate (2 eq)	40	36 h	SM
7	DCM	$Yb(OTf)_3$ (2.5 eq)	*p*-nitrobenzaldehyde (3 eq)	40	36 h	SM
8	1,2-DCE	$Yb(OTf)_3$ (2.5 eq)	*p*-nitrobenzaldehyde (3 eq)	84	20 h	complex mixture
9	DCM	$Sn(OTf)_3$ (10 mol%)	*p*-nitrobenzaldehyde (3 eq)	40	20 h	complex mixture
10	DCM	$Yb(OTf)_3$ (2.5 eq)	acetaldehyde (3 eq)	40	8 h	SM
11	DCM	$Yb(OTf)_3$ (2.5 eq)	pentanal (3 eq)	40	4 d	SM
12	DCM	$Yb(OTf)_3$ (2.5 eq)	benzaldehyde (3eq)	40	20 h	SM
13	DCM	$Yb(OTf)_3$ (2.5 eq)	anisaldehyde (3 eq)	40	20 h	SM
14	DCM	$BF_3.Et_2O$ (4 eq)	tosyl isocyanate (1.5 eq)	r.t. 40	2 h 3 h	SM complex mixture
15	DCM	$Yb(OTf)_3$ (2.5 eq)	tosyl isocyanate (1.5 eq)	40	3 d	SM

* starting from **213**

Table 5

Ethyl glyoxylate was then the only trapping reagent to allow the cycloaddition reaction with **213** when used in conjunction with $Yb(OTf)_3$ affording **214** with a *trans* diastereoselectivity (Scheme 96). Ethyl glyoxylate is known for being an excellent trapping reagent owing to its high electrophilic properties. The tetrahydrofuran **214** formed during the reaction was found to be unstable even at low temperature and rapidly decomposed. The different diastereoisomer ratios obtained were deducted from ^1H NMR spectrum and confirmed by nOe analysis.



Scheme 96

The relative stereochemistry of the tetrahydrofuran **214** can also be assigned from the shifts of the CH_2 protons on the furan ring, with the *cis*- or *trans*-arrangement of the adjacent proton. A smaller difference of 0.45 ppm is seen for the doublets in the *trans*-isomer and a larger 0.71 ppm difference for the *cis*-isomer (Figure 10). This confirmed previous results obtained within the group using the dicobalt cluster.[54]

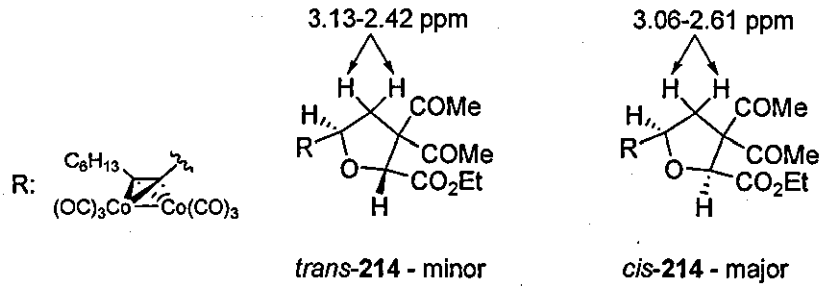


Figure 10

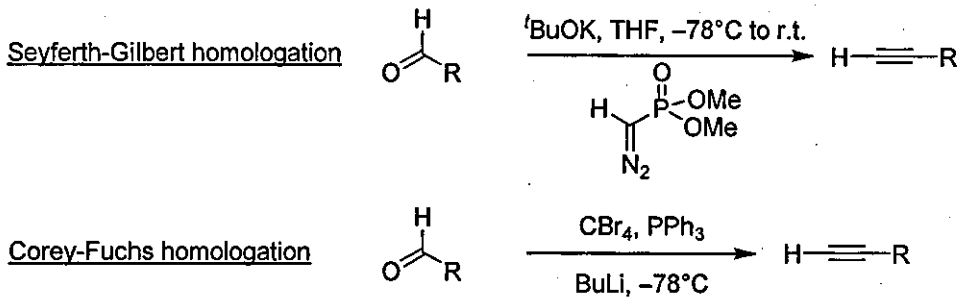
These observations are correct for dihydrofuran substituted with an alkyne/cobalt complex as opposite results were seen with dihydrofurans substituted with phenyl or diene groups.[49,82]

2.1.3. Synthesis of alkynyl cyclopropane

The main concern with the methodology used previously to synthesise the cyclopropane **150** was the formation of the alkyne, *via* the poor yielding Bestmann reaction. We first considered altering the previous methodology preparing the required alkynyl cyclopropane **150** from the aldehyde derivative **192** (Scheme 97). Other methods to prepare the alkyne starting from an aldehyde, after the formation of the cyclopropane moiety were then envisaged (Scheme 97):

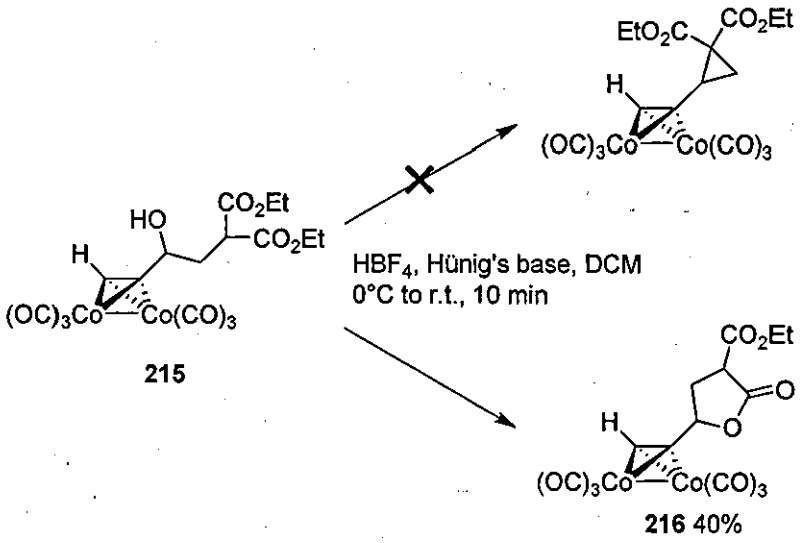
- The Seyferth-Gilbert homologation from which the Bestmann reaction has been developed makes use of potassium tert-butoxide which is a stronger base than potassium carbonate but with a less nucleophilic character than potassium methanoate.[81] However, this reaction is known for being incompatible with a wide range of functional groups.

- The Corey Fuchs reaction could also be envisaged but the use of strong ^{n}BuLi could also open the cyclopropane ring by nucleophilic attack.[83]



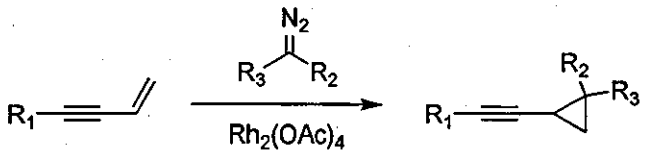
Scheme 97

Another route involving a propargylic alcohol **215** and a rather ambitious use of Nicholas chemistry has been investigated previously within the group.[84] However, the reaction failed to produce the desired cyclopropane. Instead, the substituted γ-butyrolactone **216** was isolated in 40% yield after 10 min (Scheme 98).



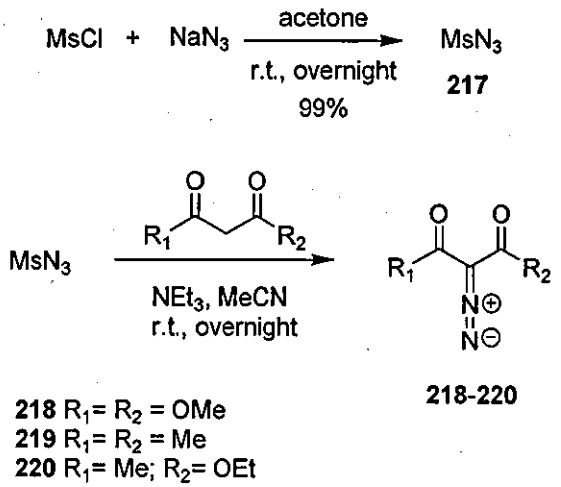
Scheme 98

Another strategy we envisaged involved the formation of the cyclopropane after that of the alkyne. Cyclopropanation of olefins has been reported using diazo-compounds using rhodium acetate dimer as a catalyst.[85,86] We thought that it would be possible to form the desired cyclopropane moiety in the α-position to the triple bond by cyclopropanation of the double bond of an enyne (Scheme 99).



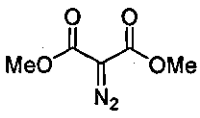
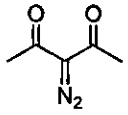
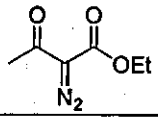
Scheme 99

The synthesis started from methanesulfonyl chloride which was converted into mesyl azide using sodium azide **217**.[87] Mesyl azide was then reacted with ethyl acetoacetate, dimethyl malonate and acetylacetone in acetonitrile and in the presence of Et_3N to give the corresponding diazo compounds **218-220** (Scheme 100).



Scheme 100

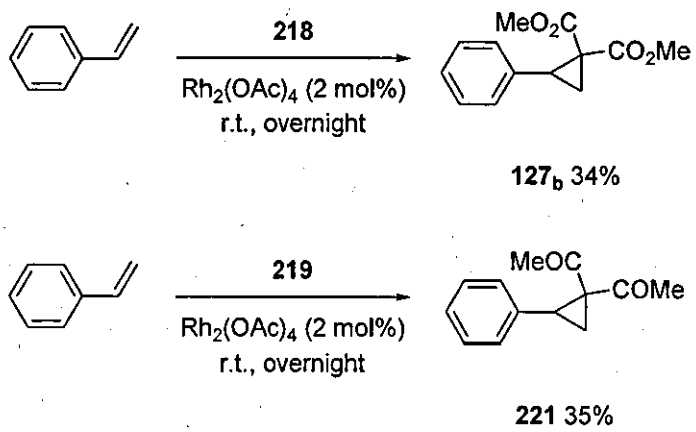
Dimethyl diazomalonate **218**, acetyldiazoacetone **219** were prepared in 98% yield and ethyl acetodiazoacetate **220** in a 71% yield (Table 6).

β-dicarbonyl	Product		Yield (%)*
dimethylmalonate **209**		**218**	98
acetylacetone **211**		**219**	98
ethylacetoacetate **201**		**220**	71

* reaction conducted in acetonitrile, overnight and at r.t.

Table 6

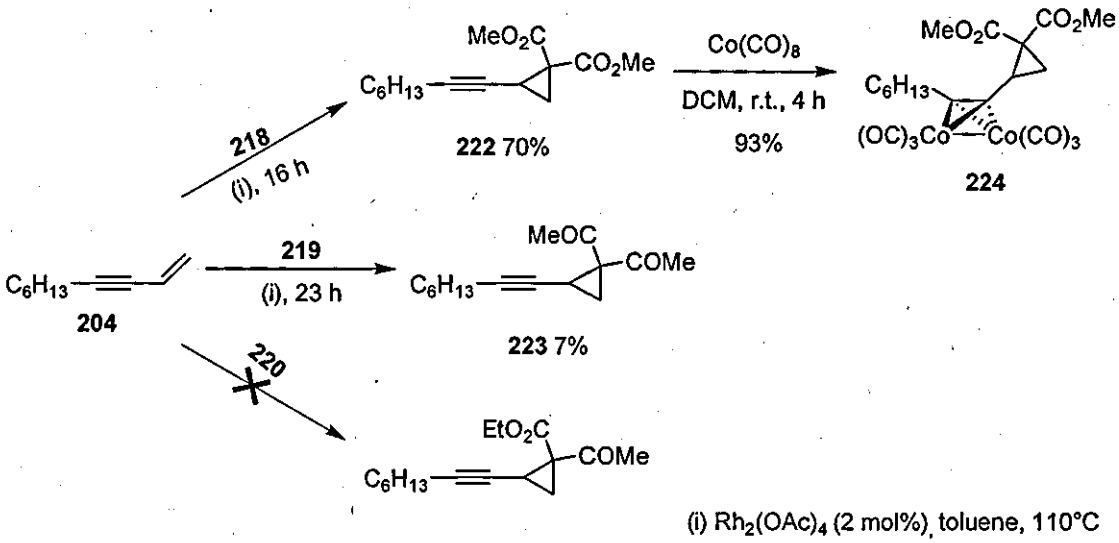
Initial attempts at cyclopropanation of the complexed enyne **205** were unsuccessful. In order to find out whether the cyclopropanation failed because of the substrate, catalyst or the solvent, the reaction was performed using styrene and dimethyl diazomalonate **218** in the presence of 2 mol% of rhodium acetate dimer which afforded the corresponding cyclopropane derivative **127$_b$** in 34% yield (based on diazo-compounds). The same reaction with acetyl diazoacetone **219** provided the cyclopropane **221** in 35% yield (Scheme 101). In both cases, styrene was used as reagent and as solvent.



Scheme 101

When dimethyl diazomalonate was reacted with the uncomplexed enyne **204** heating to reflux in toluene and in presence of a catalytic amount of rhodium acetate dimer, the desired

cyclopropane **222** was prepared in 70% yield. Further complexation of cyclopropane **222** afforded the corresponding cobalt complex **224** in 93% (Scheme 102). In the case of acetyldiazoacetone, using the same conditions, the cyclopropanation afforded the cyclopropane **223** in only 7% yield. Hence, the use of this substrate was not pursued further. The cyclopropanation with ethyl acetodiazoacetate **220** was completely unsuccessful under the same conditions.



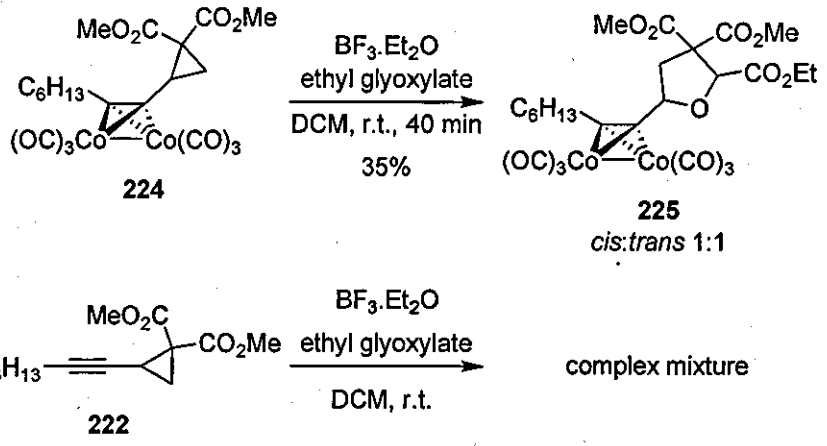
Scheme 102

2.1.3.1. Cycloaddition reaction

Using the reaction conditions developed previously within the group,[54,55] cycloaddition reactions have been attempted utilising the complexed cyclopropane **224** and a range of aldehydes and imines towards the synthesis of dihydrofurans and pyrrolidines.

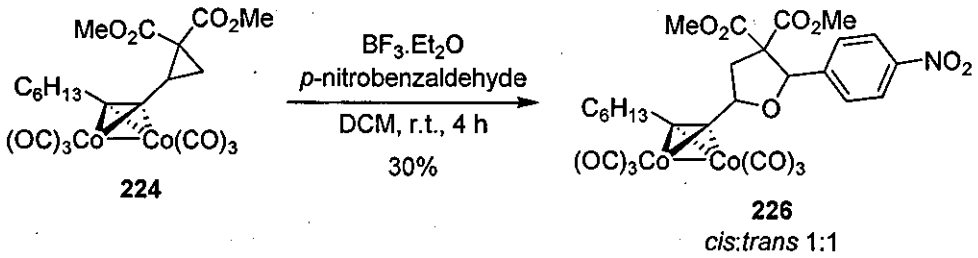
2.1.3.1.1. Cycloaddition with aldehydes

The cycloaddition reaction was first attempted with ethyl glyoxylate. When the complexed cyclopropane **224** was allowed to react with ethyl glyoxylate at r.t. in DCM with 3 eq of $BF_3.Et_2O$, the starting material was entirely converted after 40 min. However, as observed previously with the furan **214**, because of instability the cycloadduct **225** was isolated in only 35% yield and no evidence of diastereoselectivity was detected by ^1H NMR (Scheme 103).



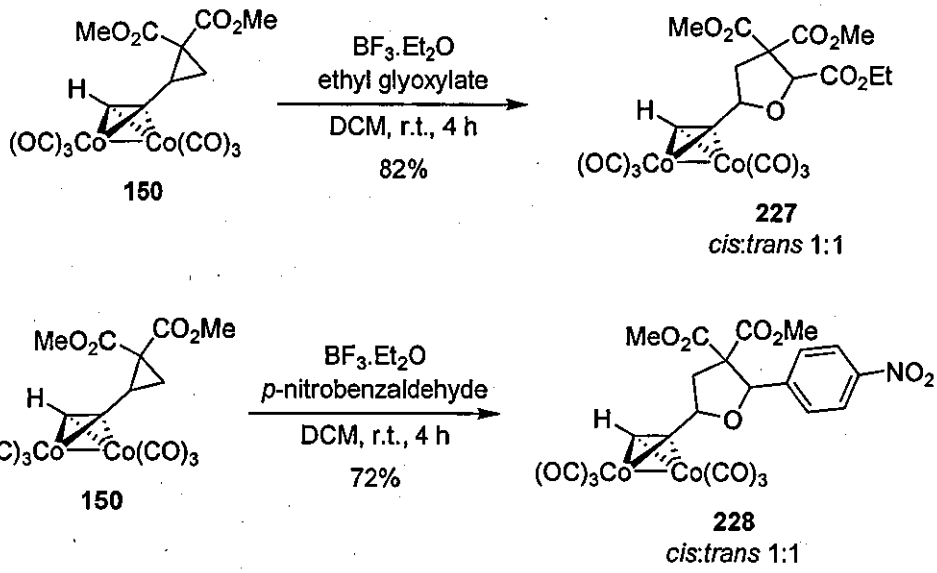
Scheme 103

When the same conditions were applied to the uncomplexed alkyne cyclopropane **222**, only degradation of the starting material was observed. Again, a rearrangement of the alkyne into the corresponding allene after the ring opening may be the origin of the decomposition. Using 2 eq of $BF_3.Et_2O$ and 1.5 eq of *p*-nitrobenzaldehyde furan **226** was isolated in only 30% yield and no diastereoselectivity was observed (Scheme 104).



Scheme 104

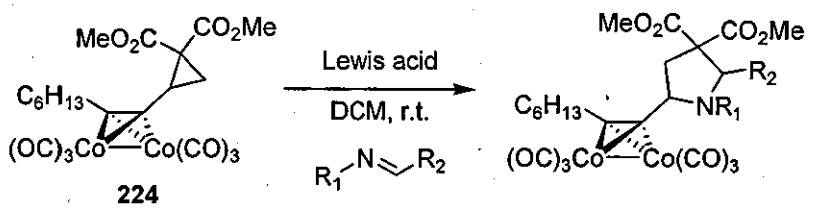
These 2 examples proved that the cycloaddition reaction developed previously can be used utilising the cyclopropane **224**. However, the long aliphatic chain substituting the alkyne complex possibly had an influence on yields as similar tetrahydrofurans **227** and **228** were previously prepared in 86 and 77% yield respectively, starting from cyclopropane **150**, using the same conditions (Scheme 105).[54,55]



Scheme 105

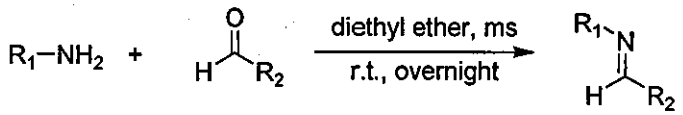
2.1.3.1.2. Cycloaddition with imines

Imines can be added to cyclopropanes using the same Lewis acid mediated [3+2] dipolar cycloaddition reaction (Scheme 106).[48c,54]



Scheme 106

To extend the work carried out within the research group on the [3+2] dipolar cycloaddition reaction, several imines were prepared including some designed with a later Pauson-Khand reaction in mind and some designed to investigate the possibility of controlling the diastereoselectivity. Imines were prepared in very high yield from the corresponding amines and aldehydes in diethyl ether at r.t. in presence of 4 Å molecular sieves (Scheme 107).



Scheme 107

Ethyl 2-(4-nitrophenylimino)acetate **229** was prepared from *p*-methoxybenzenamine and ethyl glyoxylate in 99% yield (table 7). (S)-*N*-(4-Nitrobenzylidene)-1-phenylethanamine **230** was synthesised from (S)-1-phenylethanamine and *p*-nitrobenzaldehyde in 99% yield. (R)-*N*-(4-Nitrobenzylidene)-3-methylbutan-2-amine **231** was prepared from (R)-3-methylbutan-2-amine and *p*-nitrobenzaldehyde in 99% yield, ethyl 2-(4-nitrophenylimino)acetate **232** from allylamine and benzaldehyde in 97% yield, *N*-(4-nitrobenzylidene)prop-2-en-1-amine **233** from allylamine and *p*-nitrobenzaldehyde in 99%, ethyl 2-(allylimino)acetate **234** from allyl amine and ethyl glyoxylate in 98% yield and finally *N*-(4-methoxybenzylidene)prop-2-en-1-amine **235** from allylamine and benzaldehyde in 99% yield (Table 7).

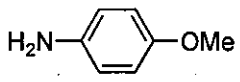
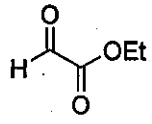
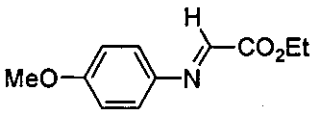
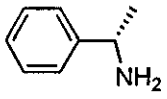
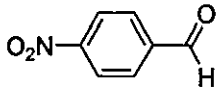
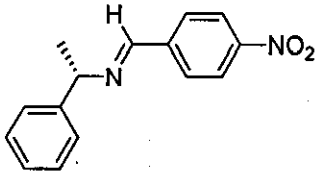
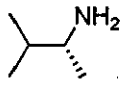
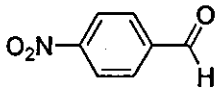
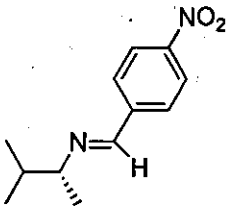
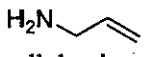
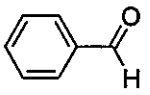
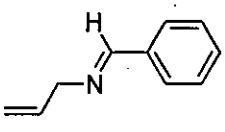
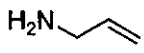
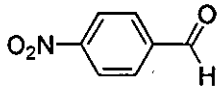
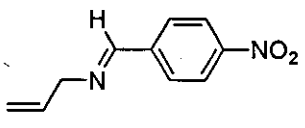
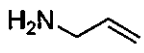
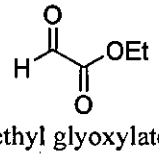
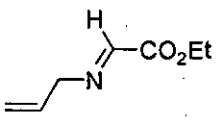
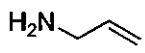
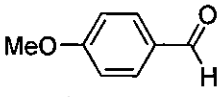
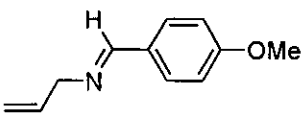
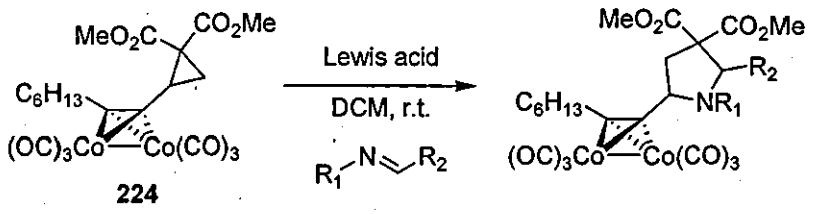
Amine	Aldehyde	Imine		Yield (%)
 4-methoxybenzenamine	 ethyl glyoxylate		**229**	99
 (*S*)-1-phenylethanamine	 *p*-nitrobenzaldehyde		**230**	99
 (*R*)-3-methylbutan-2-amine	 *p*-nitrobenzaldehyde		**231**	99
 allylamine	 benzaldehyde		**232**	97
 allylamine	 *p*-nitrobenzaldehyde		**233**	99
 allylamine	 ethyl glyoxylate		**234**	98
 allylamine	 anisaldehyde		**235**	99

Table 7

The imines prepared previously were then reacted with to the cyclopropane **224**. All of the reactions were carried out in DCM, at room temperature, under a nitrogen atmosphere. Results are shown in Table 8.

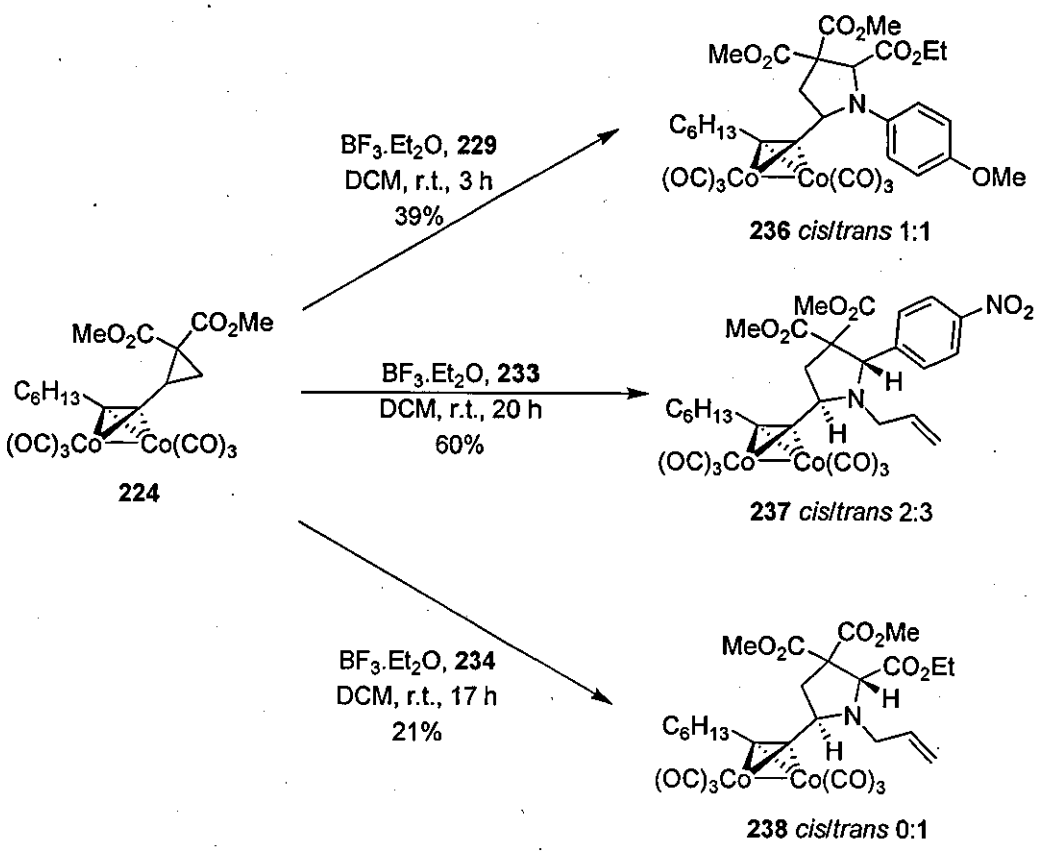


Entry	Imine	t (h)	Lewis acid	Product	Yield (%)	*cis:trans*
1	**229** (2 eq)	3	$BF_3.Et_2O$ (3 eq)	**236**	39	1:1
2	**230** (2 eq)	20	$BF_3.Et_2O$ (3 eq)	complex mixture	n/a	n/a
3	**231** (2 eq)	20	$BF_3.Et_2O$ (3 eq)	complex mixture	n/a	n/a
4	**232** (1.1 eq)	20	$BF_3.Et_2O$ (3 eq) $ZnBr_2$ (3 eq)	complex mixture **224** (SM)	n/a >99	n/a n/a
5	**233** (8 eq)	20	$BF_3.Et_2O$ (3 eq) $Yb(OTf)_3$ (0.5 eq)	**237** complex mixture	60 n/a	2:3 n/a
6	**234** (8 eq)	17	$BF_3.Et_2O$ (3 eq)	**238**	21	0:1
7	**235** (8 eq)	20	$BF_3.Et_2O$ (3 eq)	complex mixture	n/a	n/a

Table 8

The cycloaddition was attempted first using the imine **229** with 3 eq of $BF_3.Et_2O$. The corresponding pyrrolidine **236** was isolated in 39% yield after 3 h and no diastereoselectivity was observed (Table 8 entry 1 and Scheme 108). In an attempt to control the diastereoselectivity, the chiral imine **230** and **231** were used, under the same reaction conditions (Table 8 entries 2 and 3). However, only decomposition of the starting material was observed after 20 h. When the allyl amine **232** was allowed to react in the same conditions, only decomposition of the starting material was also observed after 20 h and the use of $ZnBr_2$ returned the starting material (Table 8 entry 4). Using the more electron-withdrawing substituted imine **233**, the cycloaddition using $BF_3.Et_2O$ afforded the desired pyrrolidine **237** in 60% yield after 30 hours in a 2:3 *cis:trans* ratio (Table 8 entry 5 and Scheme 108). When $Yb(OTf)_3$ was used, no reaction occurred and the reaction returned to

the staring material **224**. Using the imine **234**, exhibiting a similar high electron-deficient character on the C=N bond, the pyrrolidines **238** was prepared in a poor 21% yield although with high diastereoselectivity as only the *trans* isomer was isolated after 17 h (Table 8 entry 6 and Scheme 108). To confirm that as seen previously, the cycloaddition onto cyclopropane has an affinity for electron poor reagents, the imine **235** was submitted to the standard conditions with $BF_3.Et_2O$. Only decomposition of the starting material was observed after 20 h (Table 8 entry 7).

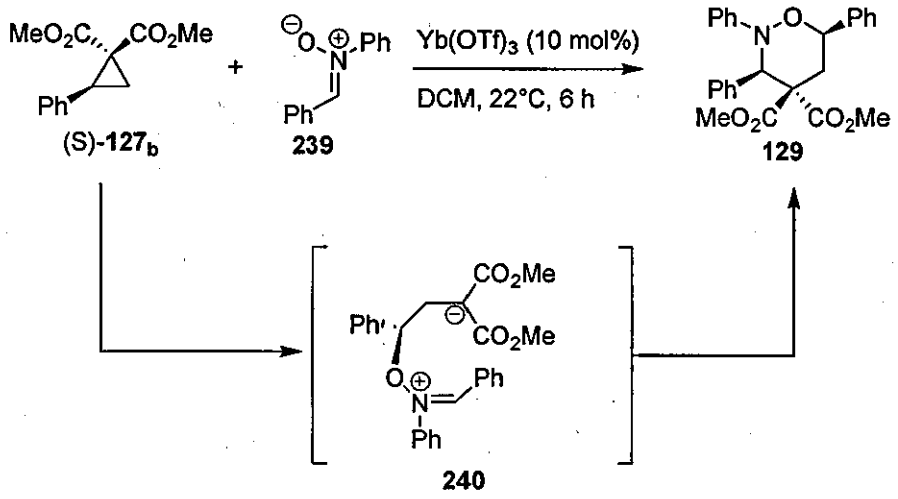


Scheme 108

As it was observed in early results, the alkyne/dicobalt mediated [3+2] cycloaddition reaction tended to provide a *trans* stereoselectivity[54,55] while *cis* selectivities were reported for other stabilising systems.[46-53]

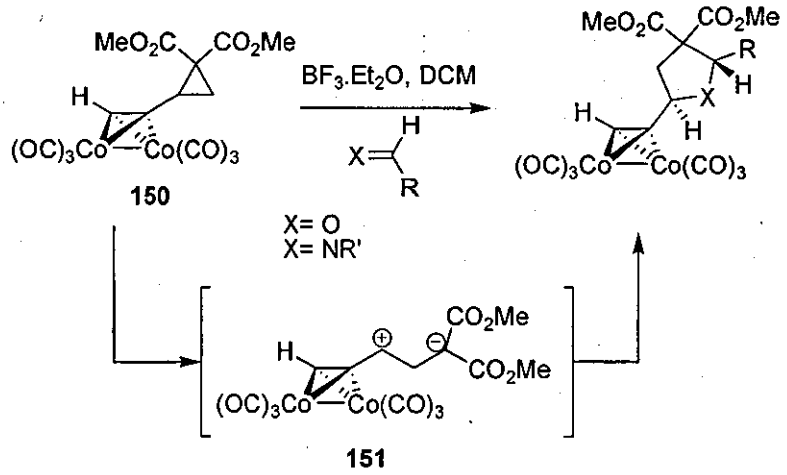
Recently, Kerr *et al.* reported a cycloaddition reaction of nitrones with homochiral cyclopropanes.[88] Their results suggested that the reaction mechanism was probably a stepwise annulative process instead of a concerted mechanism, involving an initial S_N2

displacement of the malonate ion, followed by a ring closure of the resulting iminium species. The use of their enantiomerically pure cyclopropane (S)-**127**$_b$ and the nitrone **239** afforded the enantiomerically enriched oxazine **129** in a *cis* configuration without using a chiral Lewis acid (Scheme 109).



Scheme 109

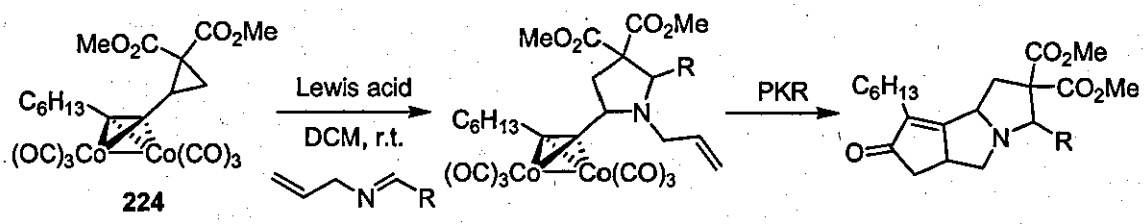
A Nicholas carbocation is more stable than a benzylic carbocation and another mechanism in which the generation of the zwitterionic intermediate **151** might occur, involving racemisation. This intermediate would then be trapped by a concerted mechanism, affording the *trans* diastereoselectivity (Scheme 110).



Scheme 110

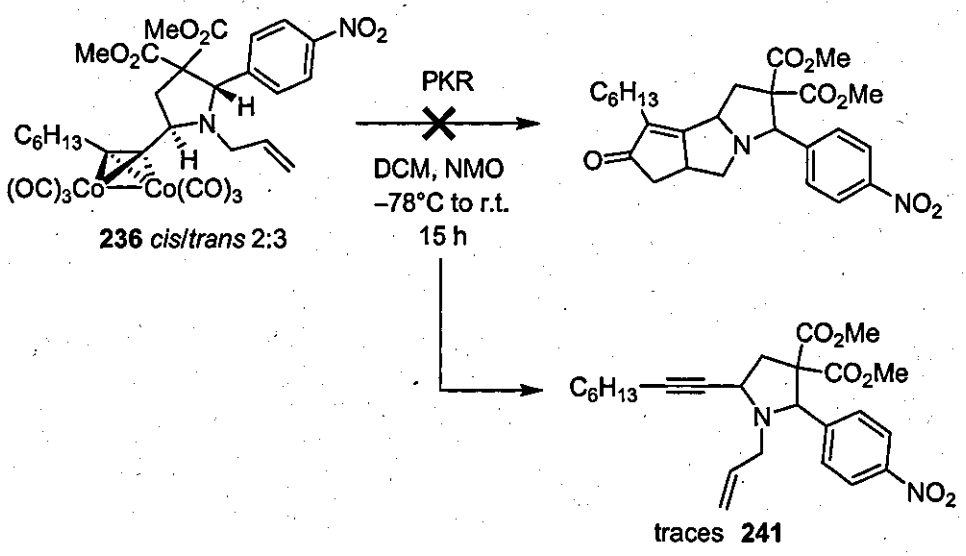
2.1.3.2. Pauson-Khand reaction

The use of imines bearing an allyl group could allow a later Pauson Khand reaction. Such a tandem Nicholas reaction/Pauson-Khand reaction would form 5 new carbon-carbon/nitrogen bonds (Scheme 111).



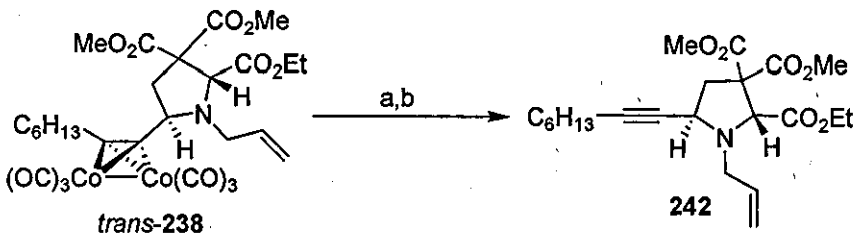
Scheme 111

The first attempt was performed using pyrrolidine **237** according to the protocol described by Pericàs and Riera.[89] The pyrrolidine was dissolved in dry DCM and the reaction mixture was cooled down to –78°C before 6 eq of *N*-methylmorpholine-*N*-oxide (NMO) were added. After an hour, the reaction mixture was warmed up slowly to room temperature. The reaction was monitored by TLC. After 15 hours only trace amounts of the decomplexed starting material **241** were observed on the crude NMR spectrum (Scheme 112).



Scheme 112

Same results were obtained using the protocol developed by Smit and Caple,[66] in adsorbing the allyl substituted pyrrolidine *trans*-**238** on silica gel at 40°C for 20 min (Scheme 113, conditions a) or using the odourless protocol developed by Kerr *et al.*,[90] with dodecyl methyl sulphide, heated to reflux in 1,2-DCE for 30 min (conditions b).

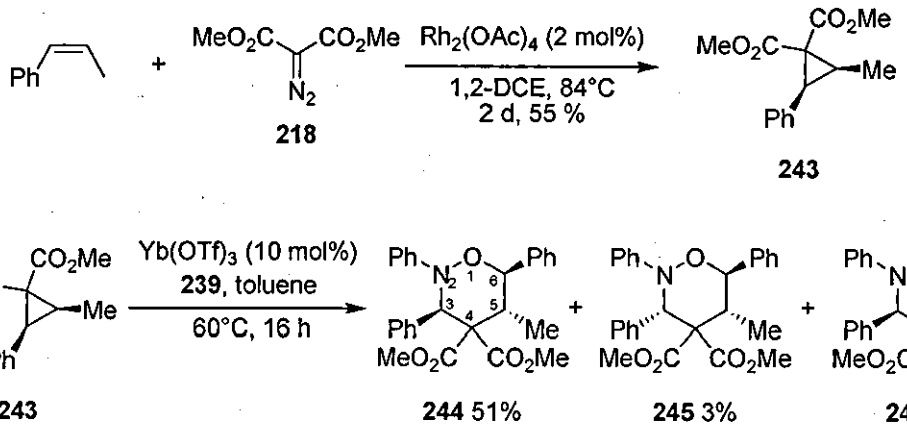


a: silica gel 40°C, 20 min, 60%
b: DodSMe, 1,2-DCE, 83°C, 30 min, 57%

Scheme 113

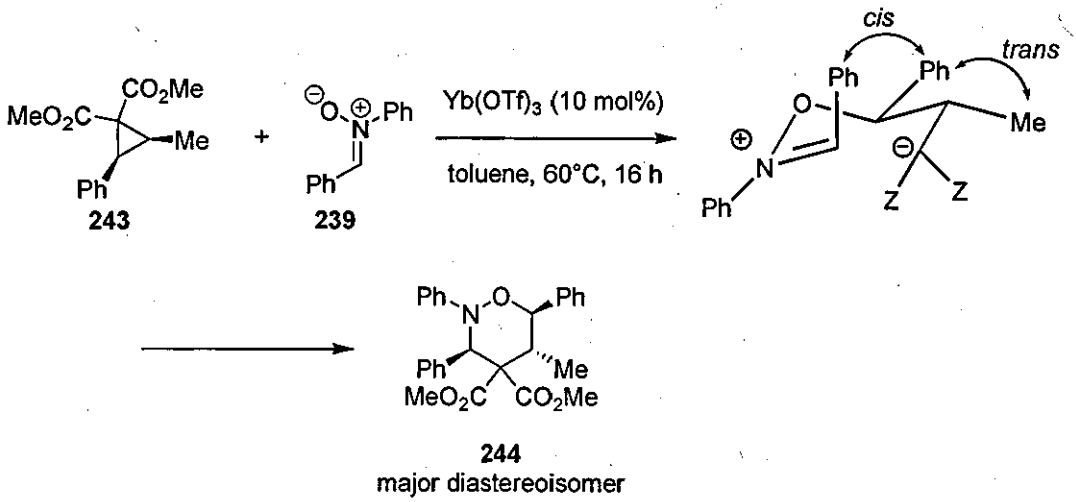
2.1.4. Synthesis of 2,3-disubstituted 1,1-diester cyclopropane

Another research interest focused on increasing the degree of substitution on cyclopropanes in attempts to improve the diastereoselectivity. This work has recently been reported by Kerr *et al.* using a 2-phenyl, 3-methyl substituted 1,1 diester cyclopropane **243** (Scheme 114).[91a]



Scheme 114

The disubstituted cyclopropane **243** was prepared in 55% *via* insertion of the carbenoid of diazomalonate **218** onto *cis*-β-methylstyrene using rhodium acetate. When Kerr *et al.* performed the cycloaddition reaction with the nitrone **239**, 3 different products were obtained, all exhibiting a *trans* relationship between groups in positions 5 and 6 (see numbering on **244**). These results clearly demonstrated that the ring opening of the cyclopropane had occurred with inversion of configuration. As suggested previously (Scheme 109), the cycloaddition with phenyl substituted cyclopropanes must go through a stepwise process instead of a concerted mechanism, involving an initial S_N2 displacement of the malonate ion. Hence, this first step is accompanied with an inversion of configuration which establishes the *trans* geometry between groups in position 5 and 6 on the tetrahydro-1,2-oxazines. The *cis*-relationship observed between substituents in position 3 and 6 is then set during the annulation step (Scheme 115).



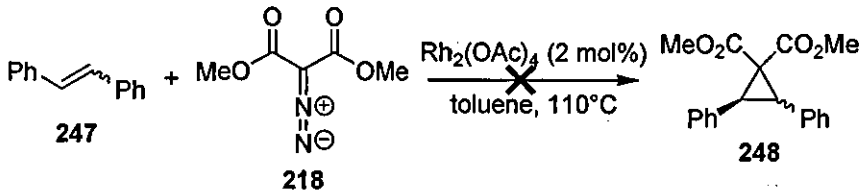
244
major diastereoisomer

Scheme 115

The synthesis of enantionerically pure cyclopropanes substituted with a dicobalt cluster could also help confirm the reaction mechanism suggested in Scheme 110 as the formation of the intermediate **151** will be accompanied with racemisation of the initial chiral center in the final five-membered ring. This could also explain the *trans* diastereochemistry outcome obtained using our methology

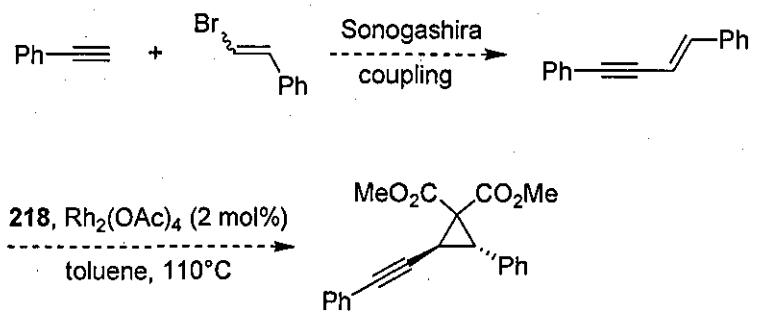
As the cycloaddition reaction was previously reported with a phenyl group to stabilise the carbocation formed during the cyclopropane opening, we initially tried to prepare a similar

2,3-diphenyl-1,1-diester cyclopropane **248** using the cyclopropanation of *cis* and *trans*-stilbene **247** with dimethyl diazomalonate **218** and a catalytic amount of rhodium acetate dimer refluxing in toluene. Unfortunately, this reaction returned the starting material (Scheme 116).



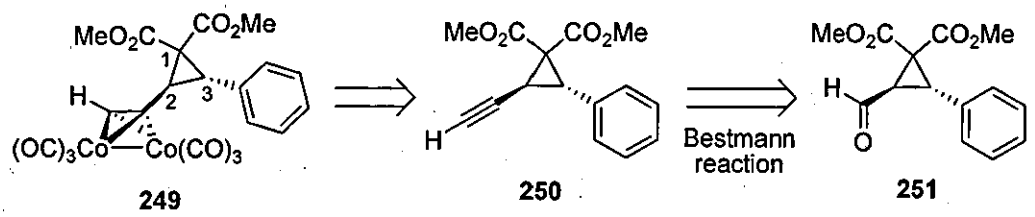
Scheme 116

Currently, the reactivity of stilbenes towards the cyclopropanation using other catalysts and other diazo compounds is being investigated in the research group.[92] To achieve our goal, a 1,1-diester cyclopropane substituted with an alkyne/dicobalt hexacarbonyl and a phenyl group in position 2 and 3 respectively was required. Alkenes substituted with conjugated π-systems such as stilbenes seemed to be unreactive to the cyclopropanation with rhodium acetate thus the route using a Sonogashira coupling between an acetylene and β-bromostyrene followed by a cyclopropanation with dimethyl diazomalonate **218** was believed to be inadequate (Scheme 117).



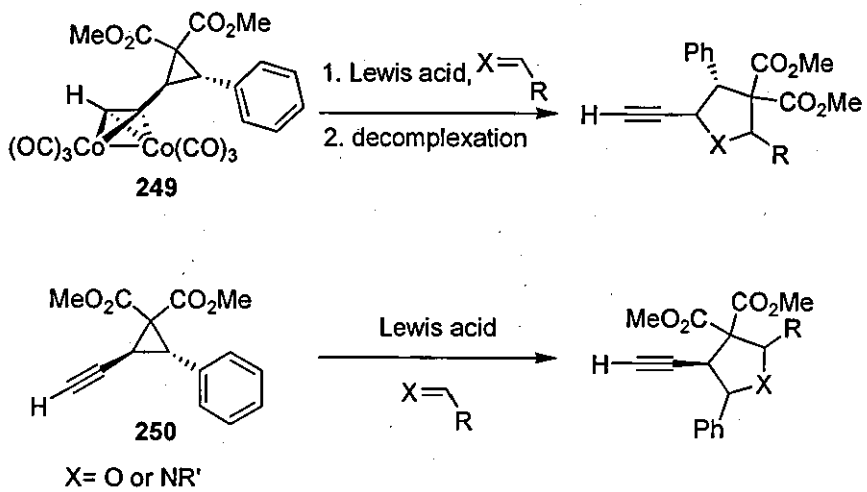
Scheme 117

Instead, another route was considered. Again, our retro synthesis returned to a cyclopropane substituted with an aldehyde. This route involved the Bestmann reaction to form the alkynyl cyclopropane **250** from the aldehyde derivative **251** (Scheme 118).



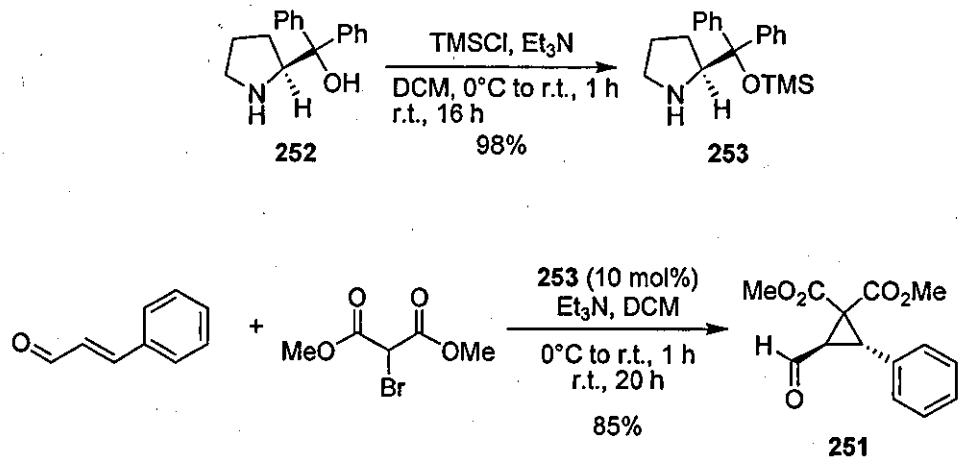
Scheme 118

This 2,3-disubstituted cyclopropane system would have synthetic interest for the potential control of the diastereo- and enantioselectivity and this would help to elucidate the mechanism of the reaction. Also, 2 regioisomers could potentially be synthesised depending on the complexation of the alkyne as the cyclopropane could eventually be opened on both sides (Scheme 119).



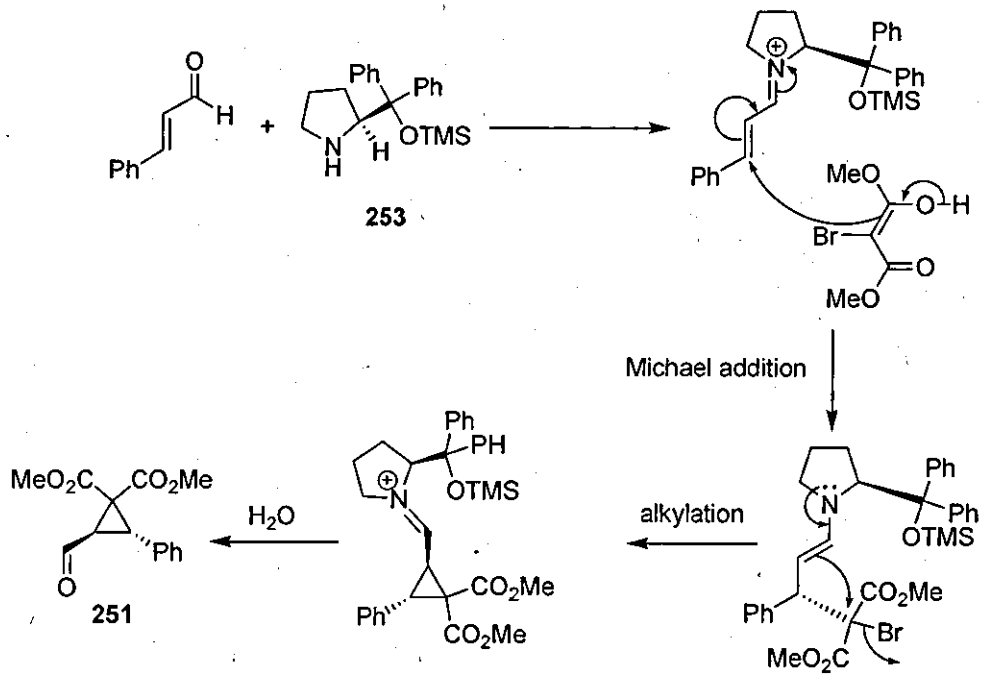
Scheme 119

The synthesis of cyclopropane **251** has recently been reported in good yield by Wang *et al.* using an organocatalytic asymmetric cascade Michael-alkylation reaction.[93] The α,β-unsaturated *trans*-cinnamaldehyde was reacted with dimethyl bromomalonate using diphenylprolinol TMS ether **253** as the catalyst (Scheme 120). The cyclopropane **251** was then prepared using this protocol in 85% yield after 20 h. The catalyst **253** was prepared in 98% yield by reaction of TMSCl on the parent alcohol **252** in DCM at r.t. in presence of Et_3N.[93]



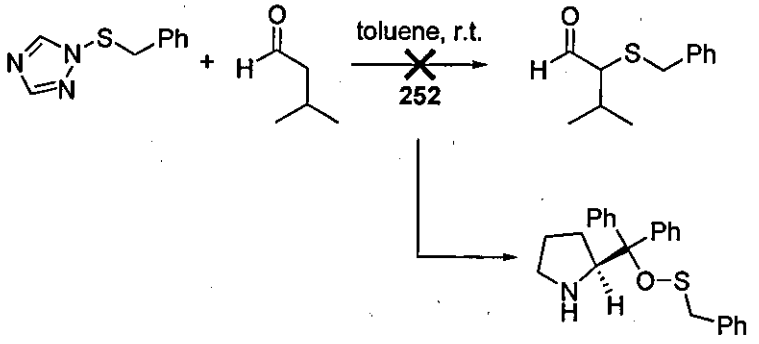
Scheme 120

It was expected that the initial enantioselective Michael addition reaction, controlled by the chiral diphenylprolinol TMS ether **253** would lead to a highly enantiomeric enriched nucleophilic enamine which would be intramolecularly trapped by the resulting electrophile alkyl bromide to form the cyclic three-membered ring (Scheme 121). Unfortunately, the enantiomeric excess could not be determined at the time of the experiment. However, the data collected to characterise **251** were consistent with those reported by Wang *et al.* using identical conditions.[93]



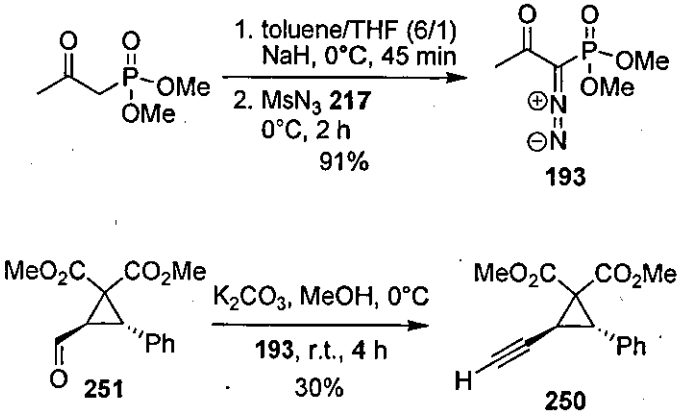
Scheme 121

It is worth noting that all attempts to use the parent diphenylprolinol **252** as the catalyst failed to allow the cascade Michael-alkylation to occur. Wang suggested that the bulky TMS group on **253** may prevent the *N*-alkylation of the pyrrolidine ring with dimethyl bromomalonate.[93] Using the same catalyst, Jørgensen observed the same results while investigating the enantioselective organocatalysed α-sulfenylation of aldehydes.[94] He suggested that no reaction occurred with the prolinol **252** as a result of the reaction between the free hydroxyl group and the sulfenylation reagent (Scheme 122).



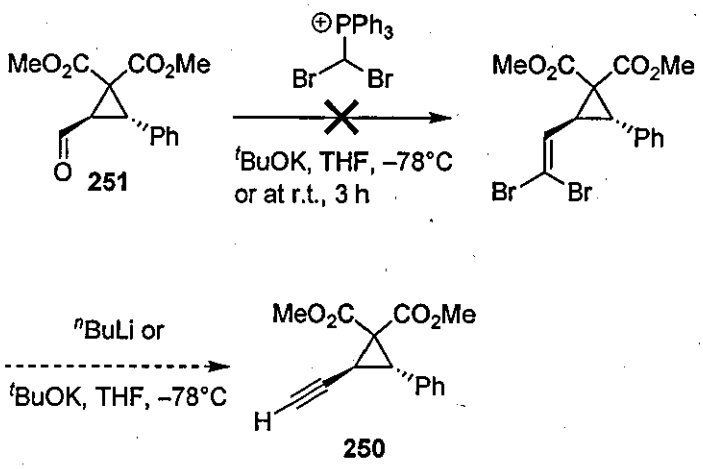
Scheme 122

A subsequent conversion of the aldehyde **251** into an alkyne using the Bestmann reagent **193**, afforded the desired alkynyl cyclopropane **250** in 30% yield (Scheme 123). The Bestmann reagent **193** was by prepared reacting dimethyl 2-oxopropylphosphonate and mesyl azide **217** in the presence of sodium hydride in 91% yield.[80]



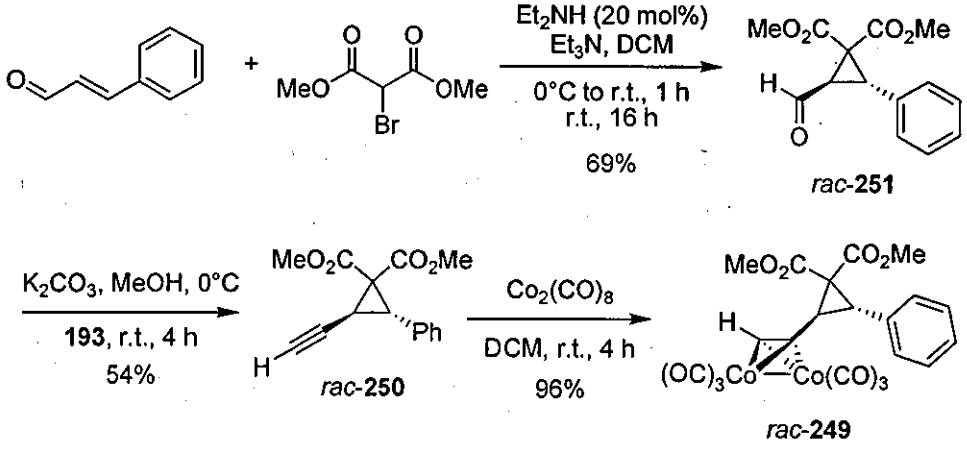
Scheme 123

In an attempt to improve yields, the Corey-Fuchs reaction conditions reported by Rassat *et al.* were used.[95] However the addition of the phosphorus ylide onto the aldehyde failed to occur, returning the starting material, presumably due to steric hindrance (Scheme 124).



Scheme 124

To synthesise the racemic equivalent of cyclopropane **250**, the diphenylprolinol TMS ether **252** was replaced with a catalytic amount of diethyl amine (20 mol%). After the formation of the alkyne using the Bestmann reaction followed by complexation with dicobalt octacarbonyl, *rac*-**249** was isolated in 36% yield over 3 steps (Scheme 125).



Scheme 125

The cyclopropane derivative *rac*-**249** was found to be crystalline and an X-Ray structure could be recorded (Figure 11 and Appendix I). To our knowledge, it was the first X-Rray of a cyclopropane moiety bearing a dicobalt cluster.[96]

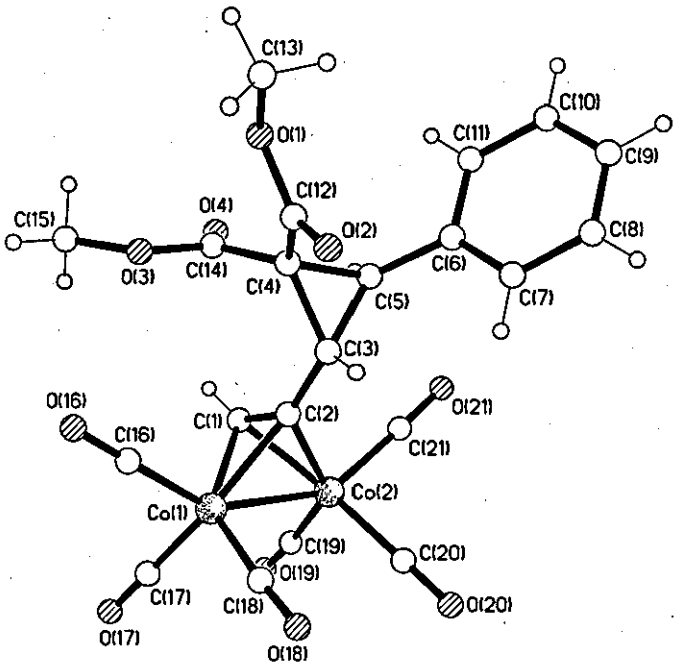
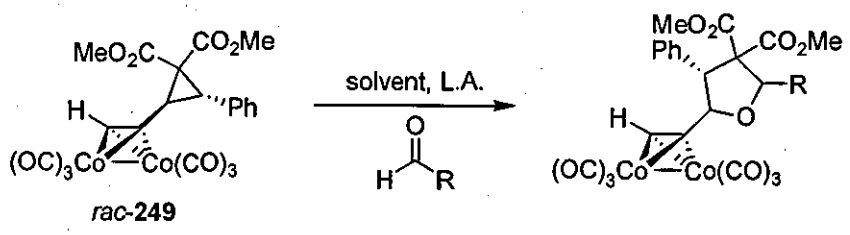


Figure 11

2.1.4.1. Cycloaddition reactions

Attempts to perform a cycloaddition were first considered using *rac*-**249** to assess the feasibility of the reaction (Scheme 126). A range of aldehydes and Lewis acids were used, though none of the conditions attempted were found suitable to perform the cycloaddition. Only complex mixtures and starting material were observed at the end of the reactions. Results are summarised in Table 9.



rac-**249**

Scheme 126

Entry	Reagent	Solvent	Lewis acid	T (°C)	T	Yield*
1	ethyl glyoxylate	DCM	$BF_3.Et_2O$ (3 eq) $Sc(OTf)_3$ (5 mol%)	40 40	3 h 20 h	complex mixture SM
2	*p*-nitrobenzaldehyde	DCM	$BF_3.Et_2O$ (3 eq)	r.t. 40	3 h	complex mixture
3	*p*-nitrobenzaldehyde	DCM	$ZnBr_2$ (3 eq) $Sc(OTf)_3$ (5 mol%)	r.t.	20 h	SM
4†	*p*-nitrobenzaldehyde	1,2-DCE	$Sc(OTf)_3$ (5 mol%)	40	20 min	complex mixture
5	anisaldehyde	DCM	$BF_3.Et_2O$ (3 eq) $Sc(OTf)_3$ (5 mol%)	r.t.	20 h	SM
6	cinnamaldehyde	DCM	$BF_3.Et_2O$ (3 eq) $Sc(OTf)_3$ (5 mol%)	r.t.	20 h	SM

* Reactions performed on *rac*-**249**, under an atmosphere of nitrogen (Scheme 126).

† performed under microwave conditions

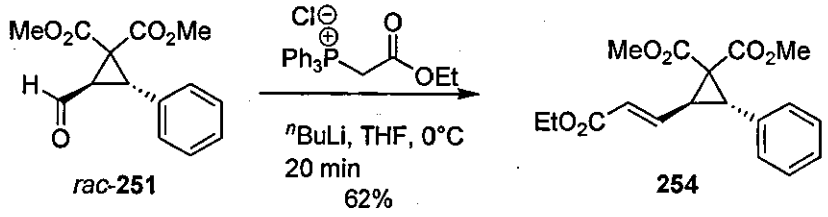
Table 9

The cycloaddition reaction was first attempted using ethyl glyoxylate for its high reactivity, refluxing in DCM. The use of $BF_3.Et_2O$ as the Lewis acid afforded a complex mixture after only 3 h while the use of a catalytic amount of scandium triflate returned the starting material after 20 h (Table 9 ,entry 1). *p*-Nitrobenzaldehyde in conjunction with $BF_3.Et_2O$ unfortunately afforded a complex mixture after 3 h of reaction, both at r.t. and refluxing in DCM (Table 9, entry 2). Using $ZnBr_2$, $Sc(OTf)_3$ or $In(OTf)_3$ at r.t., only the starting material could be recovered after 20 h of reaction. When *p*-nitrobenzaldehyde was reacted with the

cyclopropane *rac*-**249** in 1,2-DCE under microwave conditions, only products of decomposition were observed after 20 min of reaction (Table 9 ,entry 4). The use of *p*-anisaldehyde (Table 9, entry 5) and cinnamaldehyde (Table 9 ,entry 6) also did not afford the desired cycloadducts when reacted with *rac*-**249** .in DCM with a catalytic amount of $Sc(OTf)_3$ or with $BF_3.Et_2O$. Instead the starting material was recovered. The reactivity of 2,3-disubstituted diester cyclopropanes **249** and **250** is currently being investigated within the research group using nitrones.[92]

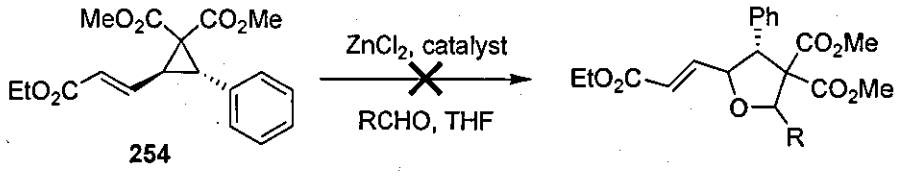
2.1.4.2. Use of vinylcyclopropane

Following the failure to perform the cycloaddition onto *rac*-**249**, we further investigated the cycloaddition reaction using Pd^0 chemistry and vinylcyclopropane[97] as the vinylcyclopropane **254** was readily available starting from *rac*-**251** *via* a Wittig homologation. The cyclopropane *rac*-**251** was then reacted with (ethoxycarbonylmethyl)triphenyl phosphonium chloride and butyl lithium in THF at 0°C for 20 min affording the vinyl cyclopropane **254** in 62% yield.[98]



Scheme 127

Standard conditions developed previously within the group[99] to perform cycloaddition reaction with vinyl cyclopropane were then used in attempts to prepare substituted vinyl tetrahydrofurans (Scheme 128). Results are summarised in Table 10.



Scheme 128

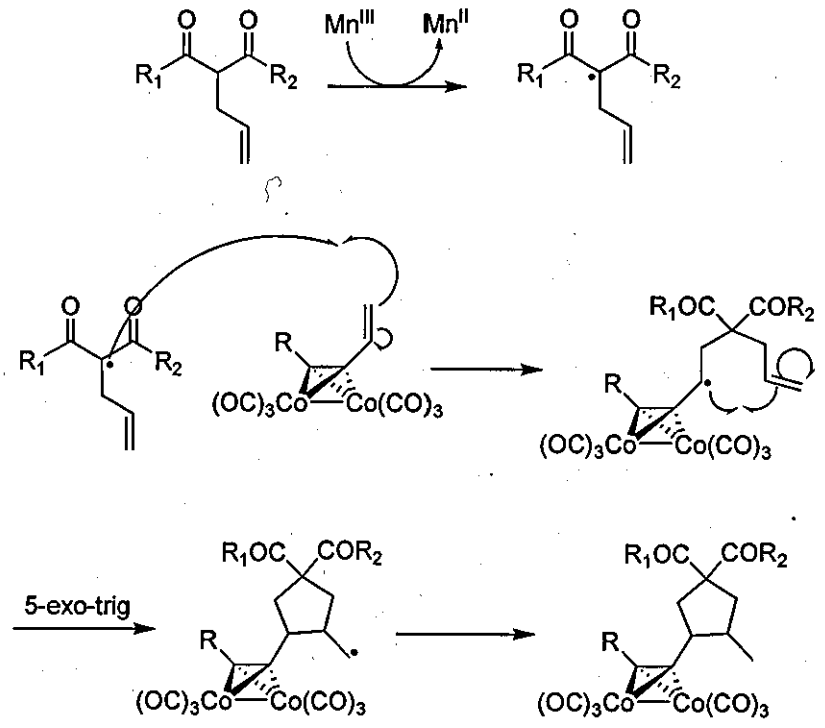
Entry	Reagent	Catalyst (10 mol%)	T (°C)	T	Yield
1	ethyl glyoxylate	$Pd(PPh_3)_4$	r.t. 66	2 d 20 h	complex mixture
2	*p*-nitrobenzaldehyde	$PdCl_2 + PPh_3$ (20 mol%)	r.t. 66	1 d 1 d	complex mixture

Table 10

As seen previously using the cobalt complexed cyclopropane *rac*-**249**, only products of degradation were observed after the reaction. The use of ethyl glyoxylate or *p*-nitrobenzaldehyde has been unsuccessful, at r.t. or refluxing in THF, whatever Pd source was used. Unfortunately, due to time restriction, this Pd catalysed intermolecular [3+2] cycloaddition could not be investigated further.

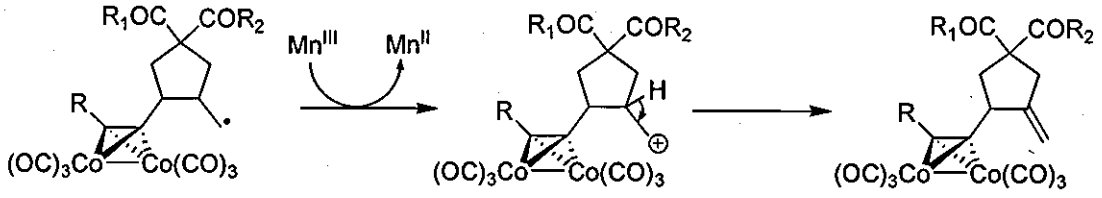
2.1.5. Radical addition of allyl β-dicarbonyls

The manganese reaction reported by Melikyan *et al.*[77] was initiated owing to the reduction of Mn^{III} into Mn^{II} and accompanied with the formation of a radical. In using a β-dicarbonyl bearing an allyl group, it was believed that a five-membered ring could be formed by a radical 5-*exo* cyclisation onto an enyne (Scheme 129). This exo-radical would eventually be quenched by abstraction of an hydrogen from another allyl β-dicarbonyl or from acetic acid. As during this pericyclic radical process, two π-bonds would be lost and two σ-bonds would be gained, this addition can be classified as a radical [3+2] cycloaddition.



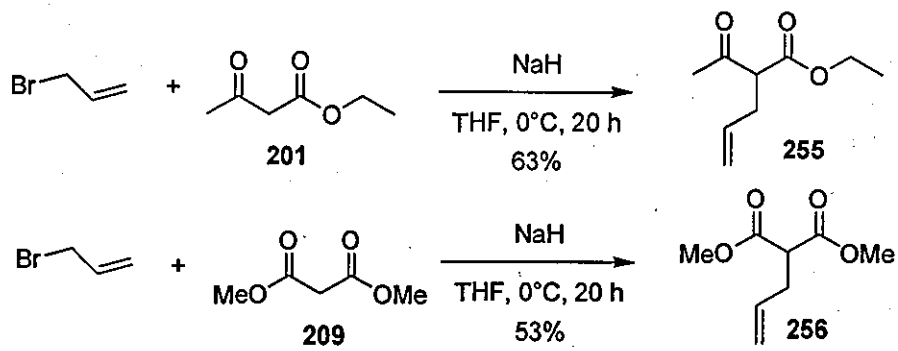
Scheme 129

The *exo*-radical formed after the first addition could also be oxidised again by Mn^{III} as in Melikian's proposed mechanism.[79] This reaction could potentially afford an alkyne/dicobalt substituted methylenecyclopentane (Scheme 130).



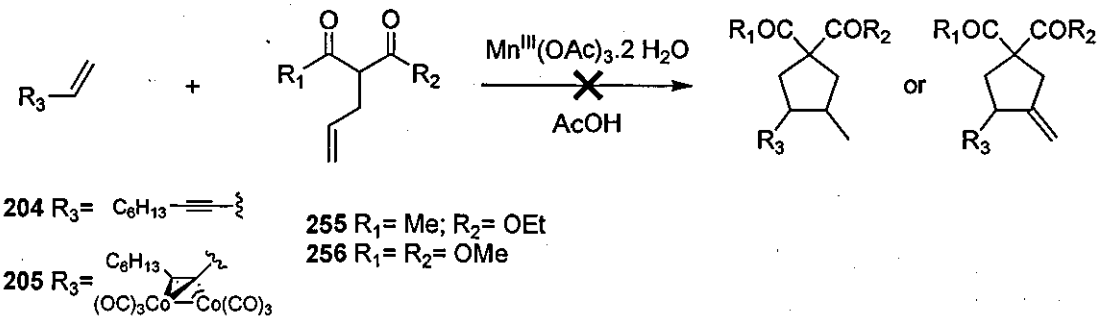
Scheme 130

To apply this strategy, allylic acetoacetate **255** was prepared in 63% yield from allyl bromide and ethyl acetoacetate in THF at 0°C, by addition of small portions of sodium hydride to avoid the formation of the di-alkylated ethyl acetoacetate. Using the same protocol, the allyl malonate **256** was prepared from dimethylmalonate in 53% yield (Scheme 131).



Scheme 131

These two allylic derivatives were then used to try to form the corresponding cyclopentanes as illustrated in Scheme 132. The enynes **204** and **205** were submitted to the conditions previously used to form dihydrofurans **212** and **213**, with 3 eq of the allyl derivative in presence of 4 eq of manganese acetate and 1 eq of copper acetate in solution in acetic acid (Table 11). Unfortunately, this time the Mn^{III} promoted addition was not successful using the same conditions (Scheme 132).



Scheme 132

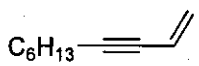
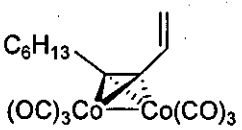
Entry	Enyne	Allylic β-dicarbonyl (3 eq)	T (°C)	T (h)	Yield
1	 **204**	**255**	118	17	complex mixture
		256	118	10	
2	 **205**	**255**	35	15	complex mixture
		256	35	17	

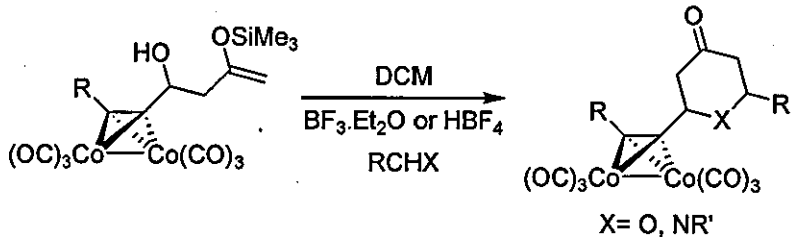
Table 11

2.2. Dicobalt hexacarbonyl mediated [4+2] cycloaddition reaction

2.2.1. Use of a ene reaction in the synthesis of six-membered rings

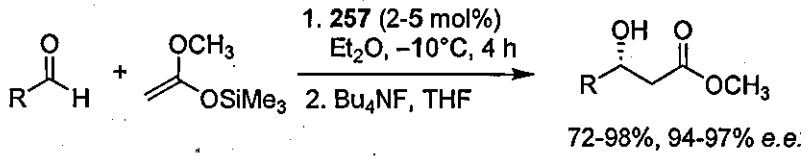
2.2.1.1. Background and strategy

We have investigated the use of silyl enol ethers coupled to the use of Nicholas chemistry towards cycloaddition reactions (Scheme 133).

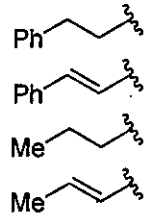


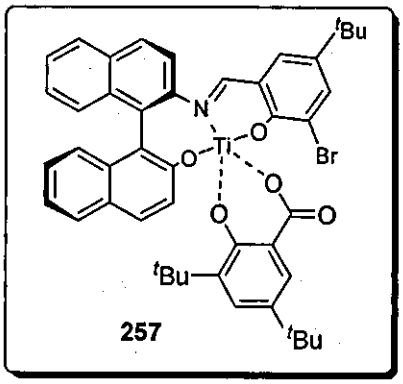
Scheme 133

A litterature search provided us with protocols to prepare silyl enol ether/alcohols using aldol or ene reactions. Carreira *et al*[100a,b] and Denmark *et al.*[100c] have reported a catalytic aldol addition with alkyl acetate *O*-silyl enolates using the Ti^{IV} based catalyst **257** prepared with a chiral tridentate ligand (Scheme 134). Starting from aldehydes and *O*-TMS *O*-methyl ketene acetal, they prepared the corresponding aldol products in high yields and with excellent *e.e.*'s. The silylated adducts were then hydrolysed using Bu_4NF affording the corresponding ester/alcohols.



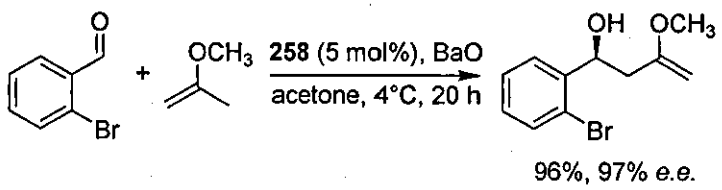
R: C_6H_{11}, C_6H_5,

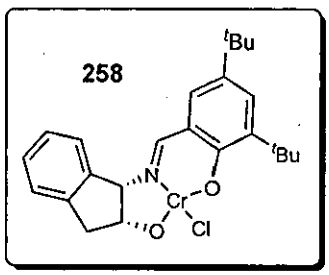




Scheme 134

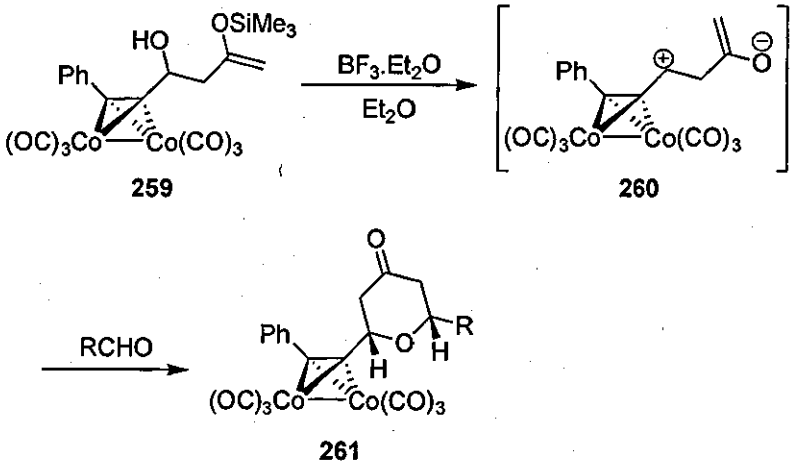
A ene reaction involving a similar chemistry was also developed by Jacobsen *et al.* using another catalyst **258** based on Cr^{III} which was chelated to a Schiff base (Scheme 135).[101] An excellent enantiocontrol was also observed owing to the chiral tridentate ligand. They also found during their investigations that yields and reaction rates could be improved in presence of desiccants such as barium oxide. Using 2-bromo benzaldehyde and 2-methoxyprop-1-ene, the corresponding enol was synthesised in 96% yield and with a 97% *e.e.* (Scheme 135).





Scheme 135

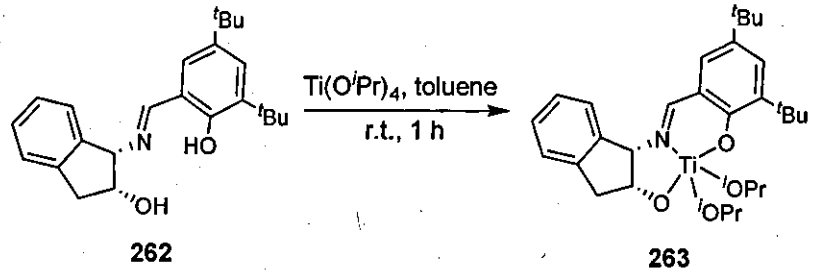
Our interest in this methodology was to form the silylated product **259** resulting from the ene reaction between a propargyl aldehyde and a silyl enol ether. We though that upon treatment with HBF_4 or $BF_3.Et_2O$ to hydrolyse the silyl enol ether, we would also form the Nicholas carbocation by de-hydroxylation. A zwitterionic intermediate **260** would be formed. The latter could be eventually trapped *in situ* with aldehydes affording tetrahydropyran-4-ones **261** (Scheme 136).



Scheme 136

2.2.1.2. Tandem ene reaction/cycloaddition

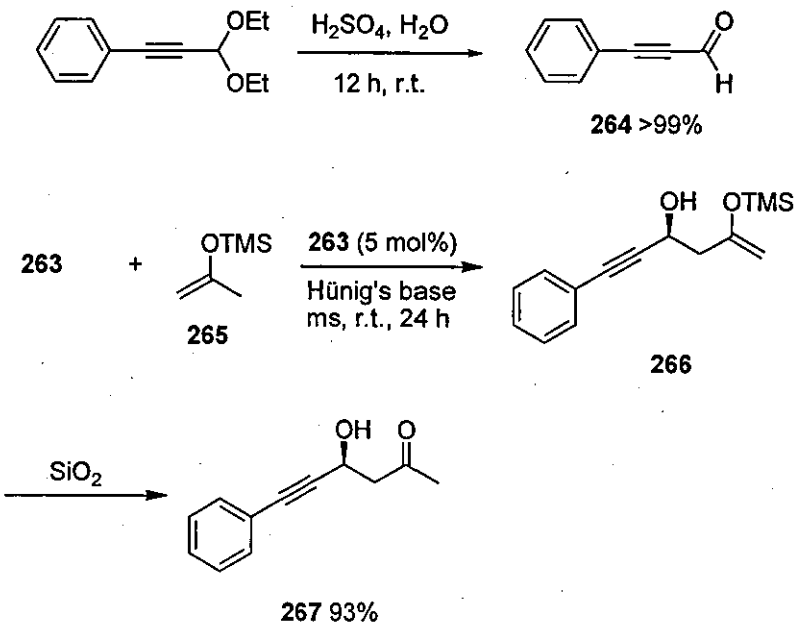
The ene reaction was performed using phenyl propargyl aldehyde **264** and the silyl enol ether **264** (Scheme 138). The propargylic C–OH bond formed during the ene reaction was supposed to be cleaved using a Lewis acid, then the *e.e.* of the ene reaction product was not an issue considering that the formation of Nicholas carbocation will induce racemisation. Jacobsen and Carreira reported that the ene reaction was unsuccessful without ligands.[100,101] The easiest way to perform the ene reaction has been developed combining the 2 protocols described by Jacobsen and Carreira. Hence, the ene reaction was carried out using the catalyst obtained from the readily available $Ti(O^iPr)_4$ used by Carreira and the Schiff base used by Jacobsen as the ligand (Scheme 137). The catalyst **263** was freshly prepared prior to the reaction by adding 1.2 eq of $Ti(O^iPr)_4$ to a solution of the Schiff base **262** in toluene at room temperature. After an hour, an orange solid was formed and the solvent was removed. The catalyst was then used without any purification.



262 **263**

Scheme 137

Once the catalyst formed, it was used in the subsequent ene reaction of acetone trimethyl silyl enol ether **265** and phenylpropargyl aldehyde **264** in the presence of Hünig's base and powdered 4 Å molecular sieves (Scheme 138). Phenylpropargyl aldehyde **264** was freshly prepared prior to the reaction by deprotection of the corresponding commercially available diethyl acetal.

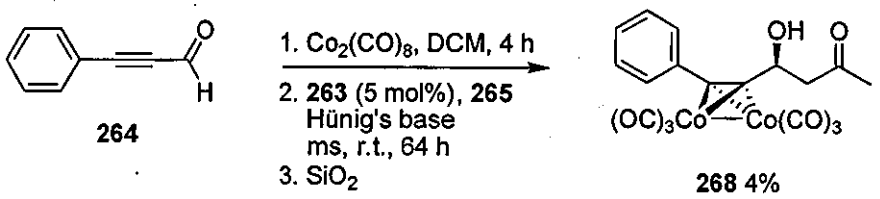


Scheme 138

This solvent free reaction was monitored by TLC and the starting material was entirely converted into the aldol product **266** after 24 h. The crude ^{1}H NMR spectrum exhibited a peak at 0.07 ppm showing the presence of a TMS group on the oxygen. In an attempt to purify the crude product, the corresponding ketol **267** was isolated in 93% yield after cleavage of the Si–O bond during purification by flash chromatography. The enantiomeric

excess was not determined at the time of this experiment as it was not required for the rest of our investigations. However, a similar $[\alpha]_D^{22}$ of +31.2 (c = 0.10 g/mL) to that reported by Carreira ($[\alpha]_D^{19}$= +37.2, c = 0.10 g/mL) suggested that our catalyst provided a similar enantioselectivity.

The same conditions as above were used to form the cobalt complex analogue **268**. The propargylic aldehyde was complexed *in situ*, in DCM and at r.t. prior to perform the ene reaction. Unfortunately, the complexed ketol **268** was isolated in only 4% yield after purification by flash chromatography presumably due to hindrance caused by the bulky homobimetallic system (Scheme 139).



264 **268** 4%

Scheme 139

Carreira *et al.* described the mechanism which is likely to proceed *via* an intermediate in which the titanium was bonded to the alcohol. In our case, the bulky dicobalt cluster could prevent the approach of the catalyst by interference with the ligand (Figure 12).

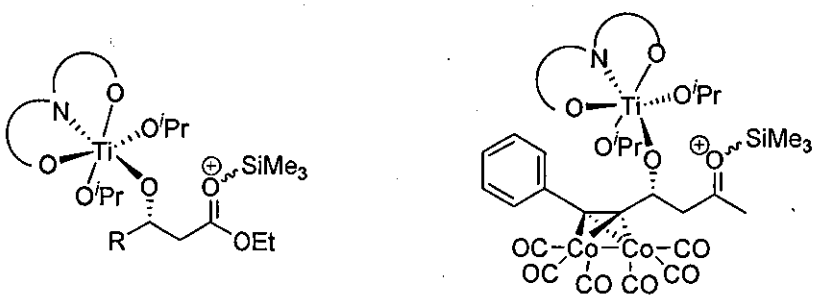
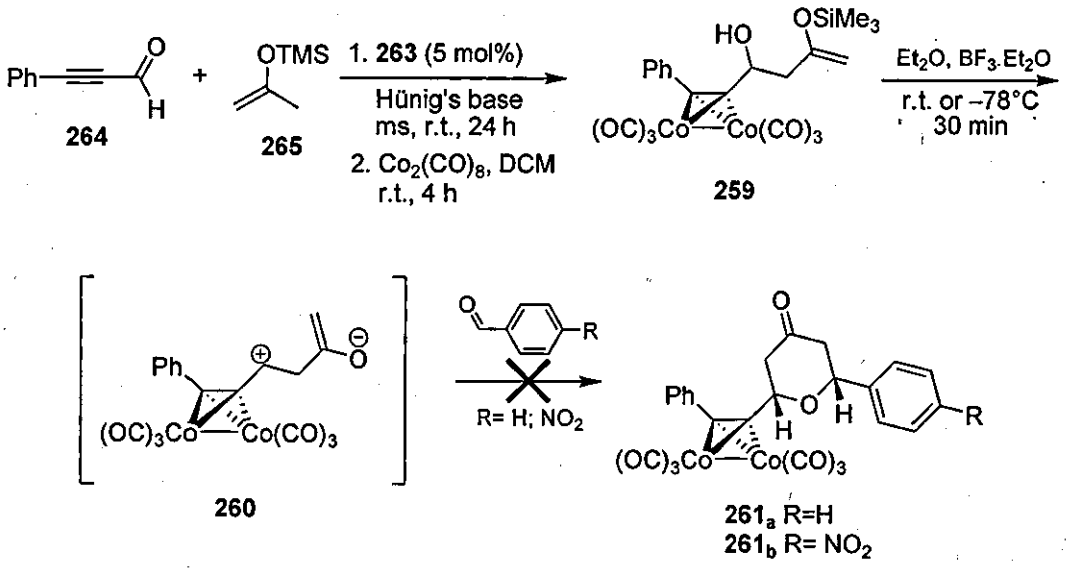


Figure 12

The next step of the strategy was to carry out cyclisation reaction using the silyl ether/alcohol formed during the ene reaction and the electron donating property of the dicobalt system. Jacobsen *et al.* mentioned that the material isolated after the ene reaction could be used in subsequent reactions without deleterious effect although it was

contaminated with the catalyst.[101] Thus the crude β-hydroxy silylenol **266** formed during the ene reaction was subsequently dissolved in DCM and complexed *in situ* without prior purification to avoid the heterolysis of the silicon/oxygen bond (Scheme 140). This led to the formation of complex **259**. Benzaldehyde or *p*-nitro benzaldehyde and boron trifluoride were then added and the reaction mixture was allowed to stir at r.t. or at –78°C. After 30 min, the starting material had completely disappeared but none of the desired products could be isolated after several attempts. Unfortunately, the addition of $BF_3.Et_2O$ only led to a complex mixture.

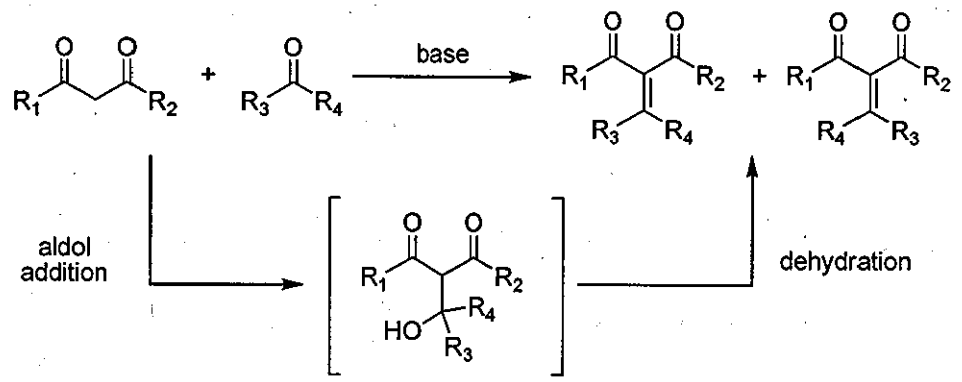


Scheme 140

2.2.2. Cobalt mediated condensation/Nicholas reaction

2.2.2.1. Knoevenagel condensation

The Knoevenagel condensation involves an aldehyde or a ketone with no α-hydrogens and a substrate with an α-carbon flanked by two electron withdrawing groups (Scheme 141). As in the aldol reaction, the addition of the enolate to the carbonyl compound is followed by a dehydration affording an alkene.

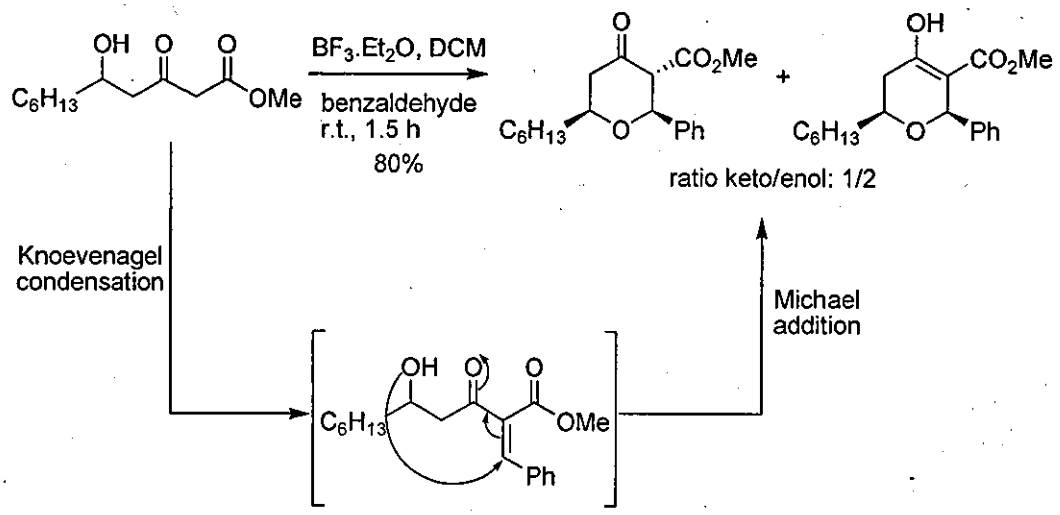


Scheme 141

The Knoevenagel reaction is usually catalysed by bases, such as amines, ammonia, or sodium ethoxide in organic solvents.[102] Lewis acids,[103a,b] zeolites,[104] and heterogeneous catalysts[105] have also been employed to catalyse the reactions.

2.2.2.2. Synthesis of tetrahydropyran-4-ones

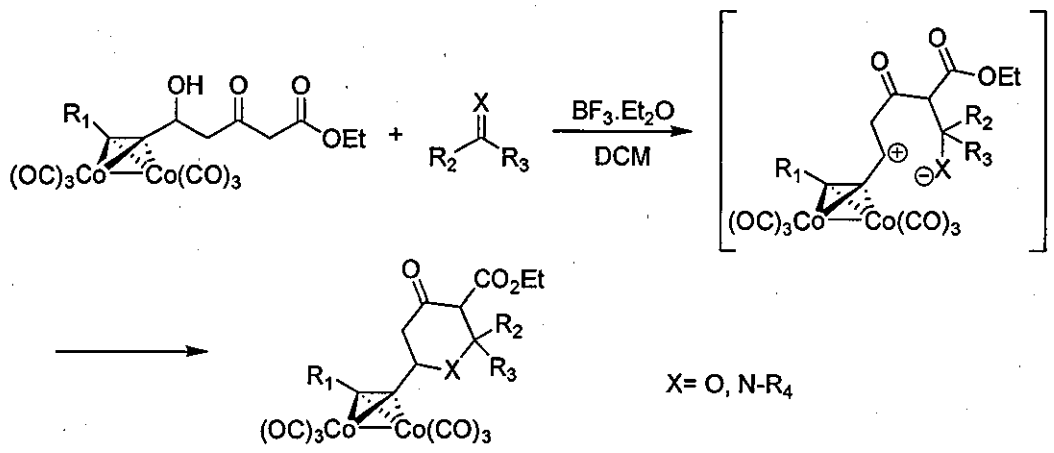
A strategy using a γ-hydroxy β-ketoester has been developed by Clarke *et al.* to form tetrahydropyran-4-ones.[106a,b] Their methodology included a Knoevenagel condensation followed by an oxy-Michael addition as shown in Scheme 142.



Scheme 142

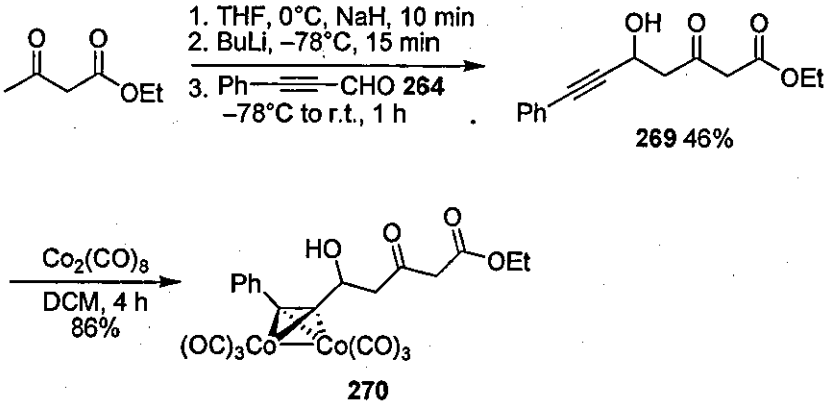
Each step of their methodology was promoted using a Lewis acid by simply adding the aldehyde to a solution of the ketoester in DCM in the presence of $BF_3.Et_2O$. The two tautomers of the cycloadduct could be separated by flash chromatography. Nonetheless the enol tautomer slowly converted to the keto tautomer upon standing in chloroform.

We believed that this strategy could be adapted to the formation of tetrahydropyran-4-ones in α-position to an alkyne/dicobalt complex. The use of $BF_3.Et_2O$ could allow the formation of the Nicholas carbocation and also initiate the Knoevenagel condensation. However, it was expected that the intermediate formed during the condensation (Scheme 141) would trap the Nicholas carbocation (Scheme 143).



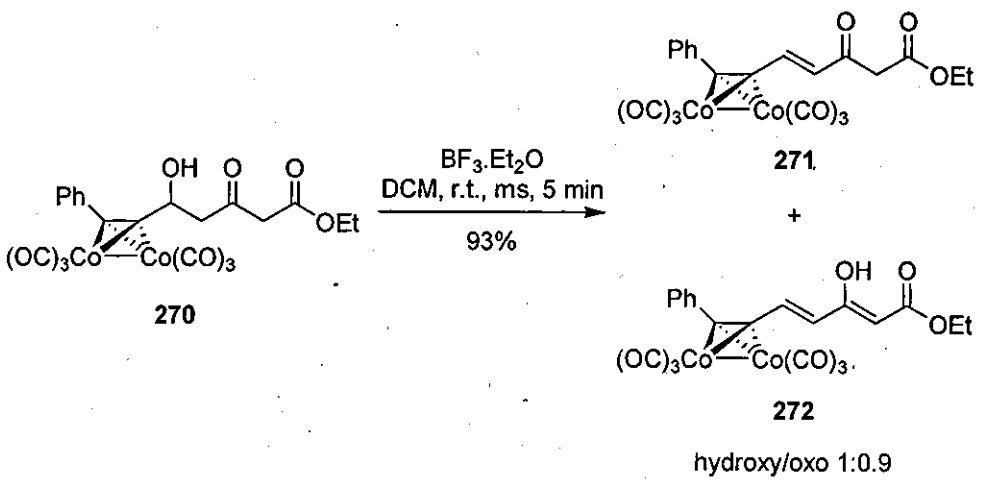
Scheme 143

In this reaction, the mechanism would proceed in a different way compared to that described by Clarke. The Knoevenagel final adduct would not be formed. Instead, the condensation intermediate would play a key role in the ring closure in trapping Nicholas carbocation. Thus the Michael addition would not occur. The precursor **269** was synthesised starting from phenylpropargyl aldehyde **264**. Ethyl acetoacetate was treated with NaH in THF at 0°C and ^{n}BuLi at −78°C. The resulting dianion was then reacted with 1.0 eq of phenylpropargyl aldehyde at −78°C, slowly warming up to room temperature over a period of an hour. The aldol product **269** was isolated after purification by flash chromatography in 46% yield (Scheme 144). It was then complexed with $Co_2(CO)_8$ in DCM at r.t. affording the homo bimetallic complex **270** in 86% yield.



Scheme 144

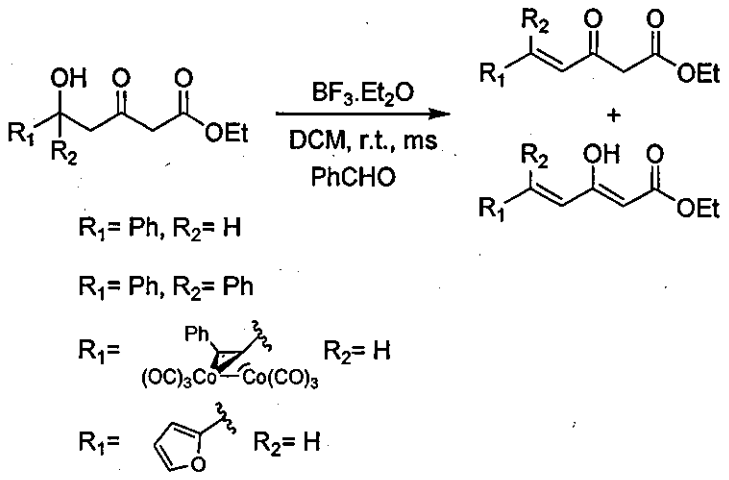
The products **269** and **270** were then used to attempt the condensation/Nicholas reaction described in Scheme 143, using 1.5 eq of $BF_3.Et_2O$ and various reagents. Using the conditions described by Clarke,[106a] the uncomplexed alkyne **269** was surprisingly found to be unreactive and the starting material could be entirely recovered when it was reacted with benzaldehyde. When the alkyne was complexed with dicobalt hexacarbonyl, the use of $BF_3.Et_2O$ spontaneously led to the formation of the dehydroxylated derivatives **271** and **272** and no Knoevenagel reaction products were observed (Scheme 145).



Scheme 145

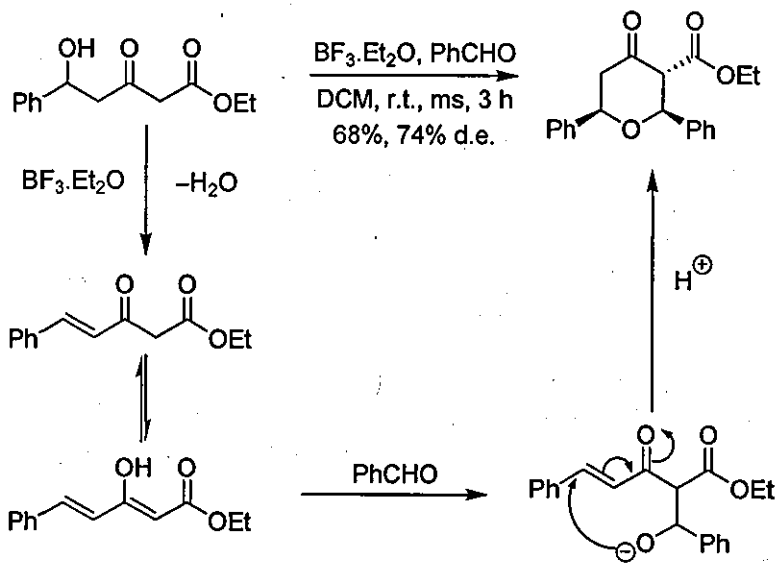
Clarke *et al.* also isolated this type of dehydrated degradation products while attempting to purify their γ-hydroxy β-ketoesters by column chromatography.[106b] The same results were also observed by a MSc student with other starting materials, as shown in the Scheme

146.[107] When stabilising groups such as phenyl, diphenyl, furan or an alkyne dicobalt complex were used, the addition of $BF_3.Et_2O$ at r.t. spontaneously afforded the enone derivative product as shown in the Scheme 146. The presence of an aldehyde did not improve the results, only affording the dehydrated products.



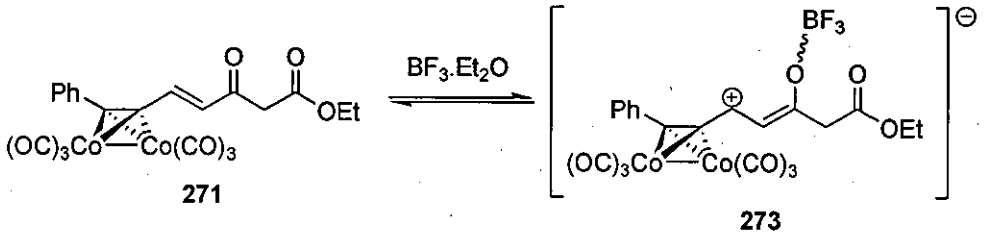
Scheme 146

These results could also suggest that the mechanism proposed by Clarke may proceed in a different way when an electron donating group is situated in α-position to the hydroxyl group as the addition of $BF_3.Et_2O$ spontaneously initiated dehydration. Instead of forming the first Knoevenagel product, its intermediate would cyclise through a Michael addition onto the newly formed α,β-unsaturated ketone as shown in the Scheme 147.



Scheme 147

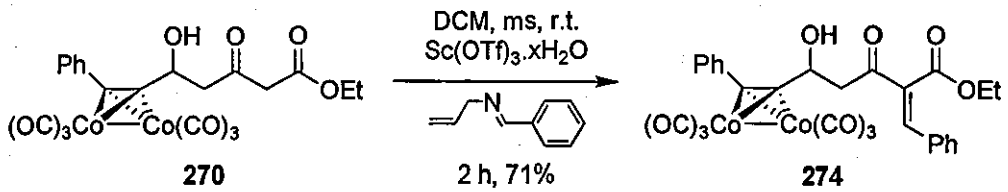
However, this does not explain why this tandem condensation-Michael addition does not occur with the cobalt complex **271**. One possible reason might reside in the excellent electron donating property of the dicobalt complex. If $BF_3.Et_2O$ is added to the complex **271**, the double bond formed by dehydration could migrate in generating Nicholas carbocation. The formation of Nicholas carbocation **273** would then prevent the Knoevenagel condensation from proceeding (Scheme 148).



Scheme 148

Following the failure to form the tetrahydropyran-4-ones using $BF_3.Et_2O$, the Knoevenagel condensation was attempted using a catalytic amount of $Sc(OTf)_3$ at r.t. in DCM (Table 12). When benzaldehyde was used, no reaction occurred (entry 1). The same reaction conditions were also applied using the allyl amine substituted imine **232** (entry 2). Surprisingly, the Knoevenagel reaction product **274** was obtained after 2 hours of reaction in 71% yield

(Scheme 149). This might have resulted from hydrolysis of the imine into allyl amine and benzaldehyde as the catalyst contains trace amounts of water.



270 **274**

Scheme 149

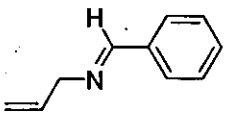
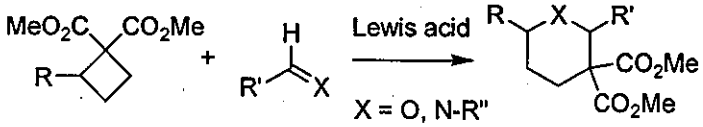
Entry	Reagents	Lewis acid	T (h)	Product	Yield (%)
1	benzaldehyde	$Sc(OTf)_3$	16	**270**	n/a
2	 **232**	$Sc(OTf)_3$	2	**274**	71
3	benzaldehyde + triethylamine	$Sc(OTf)_3$	2	**274**	68

Table 12

In an effort to understand why the condensation did not occur with benzaldehyde only, the Knoevenagel reaction has been attempted using scandium triflate, benzaldehyde and a catalytic amount of triethylamine (entry 3). Compound **274** was again isolated in 68% yield after 2 h of reaction. This last result suggested that the condensation that occurred in Scheme 148 was not catalysed by $Sc(OTf)_3$. Instead, the amine formed after hydrolysis of the imine initiated the condensation of the β-dicarbonyl with benzaldehyde. Hence, the condensation that occured in this case returned to a conventional Knoevenagel condensation using a base and not a Lewis acid.

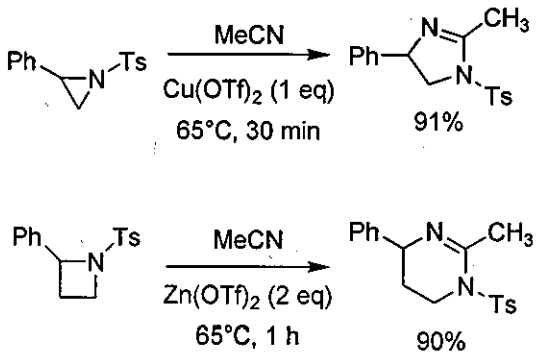
2.2.3. Use of cyclobutanes towards [4 + 2] dipolar cycloaddition reactions

Cycloaddition reactions onto three-membered rings have been extensively used in organic chemistry to synthesise pyridines and tetrahydrofurans.[47-56] As seen previously, the preparation of tetrahydrofurans and pyrrolidines *via* cycloaddition reaction onto cyclopropyl moiety has been used and described in the literature. However, the formation of the corresponding six-membered rings using the same method has not been reported. To extend the methodology developed within the group, we investigated the use of cyclobutane rings, towards the preparation of tetrahydropyrans and piperidines using a [4 + 2] cycloaddition reaction (Scheme 150).



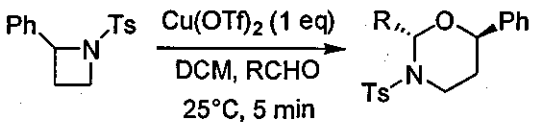
Scheme 150

To our knowledge the dipolar cycloaddition onto a cyclobutane has not yet been reported in the literature. However, Ghorai *et al* recently reported related reactions for the synthesis of substituted imidazoline mediated by copper triflate[108] and the synthesis of γ-iodoamines and tetrahydropyrimidines promoted by zinc triflate[109] (Scheme 151).



Scheme 151

They also reported similar cycloaddition reactions of *N*-tosylazetidines with aldehydes. Using this methodology, they could prepare 1,3-oxazines (Scheme 152).[110]



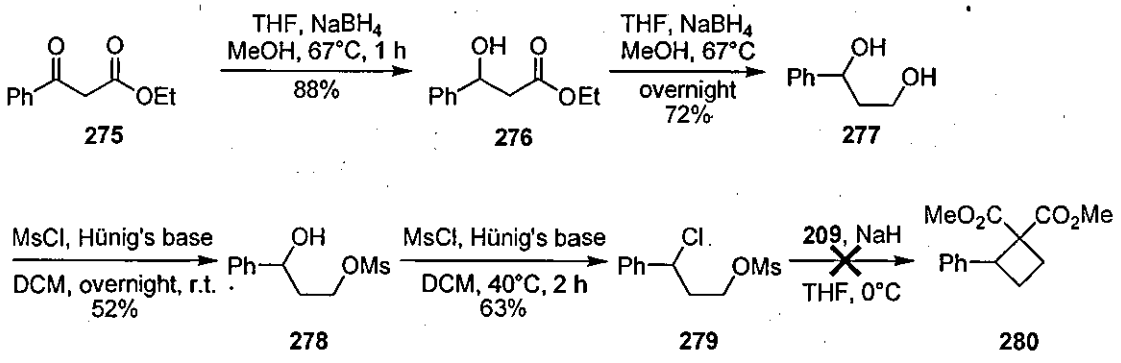
up to 99% d.e.
up to 93% yield

R= Et, ^{n}Pr, Bn, Ph, -CH=CH-Ph, furyl

Scheme 152

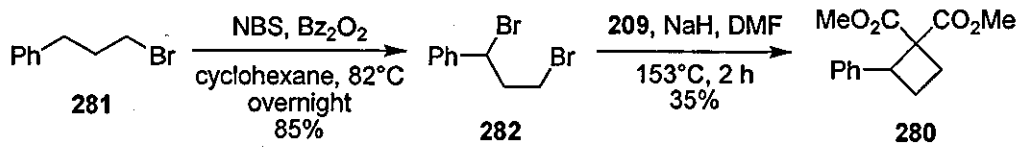
2.2.3.1. Phenyl substituted cyclobutane

The first attempt to synthesise the required cyclobutane started from ethyl 3-oxo-3-phenylpropanoate **275** (Scheme 153). The reduction of the ketone by $NaBH_4$ refluxing in THF over an hour afforded the alcohol derivative **276** in 88% yield.[111] The latter was converted into the corresponding diol **277** in 72% yield using again $NaBH_4$ refluxing overnight in THF.[112] The diol **277** was not stable therefore it was used in subsequent reactions straight after purification. When $LiAlH_4$ was used instead of $NaBH_4$, the reduction of the ester afforded the allylic alcohol derivative. The mesylation of the diol **277** using 3 eq of mesyl chloride refluxing in DCM surprisingly afforded only the mono-mesylated derivative **278**. In an effort to convert the remaining secondary alcohol into a OMs leaving group, the reaction mixture was heated to reflux. Instead of the di-mesylated product, the chloride derivative **279** was isolated in 63% yield. However, this chloride derivative was found to be interesting on a synthetic point of view and subsequent attempts to form the four-membered ring in displacing the chloride atom and the OMs group by dimethylmalonate using NaH unfortunately led to a complex mixture.



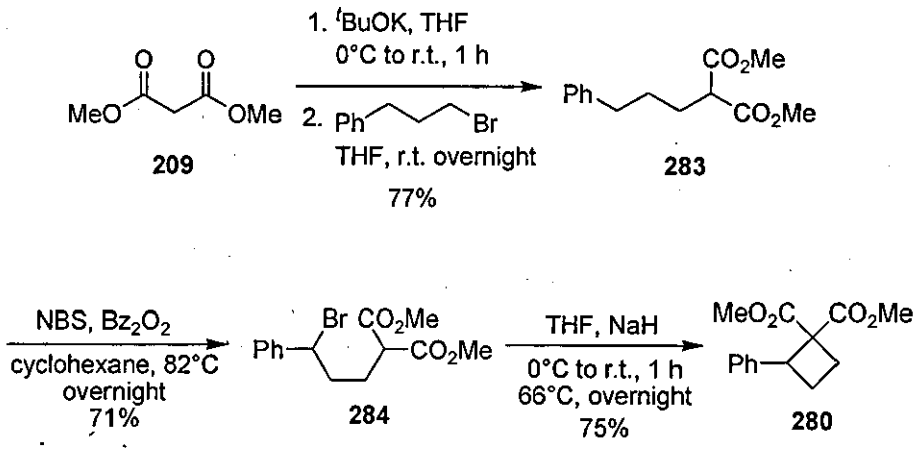
Scheme 153

The route above was inadequate for the preparation of the phenyl substituted cyclobutane **280**. After further literature search, the synthesis described by Cativiela *et al.* starting from 1-(3-bromopropyl)benzene **281** was found to be more suitable (Scheme 154).[113] Benzylic bromination using *N*-bromosuccinimide and benzoyl peroxide afforded the desired dibromide **282**.[114] Displacement of the two bromines by dimethyl malonate in THF using sodium hydride afforded the desired cyclobutane **280** in 30% overall yield.



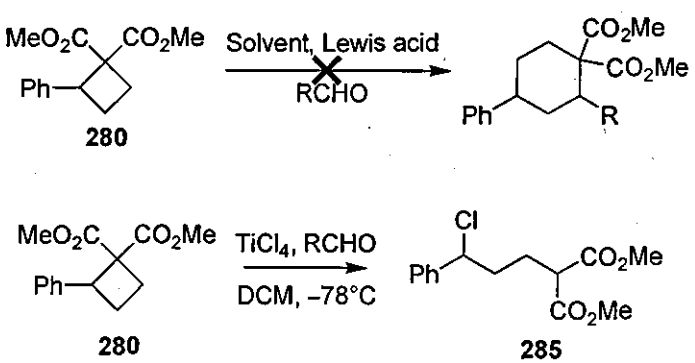
Scheme 154

In an attempt to improve the overall yield, another strategy was employed to synthesise the cyclobutane **280** (Scheme 155). The bromide atom on 1-(3-bromopropyl)benzene **281** was displaced by dimethyl malonate using potassium tert-butoxide. A benzylic bromination using *N*-bromosuccinimide and benzoyl peroxide refluxing overnight in cyclohexane afforded the bromobenzyl derivative **284** in 71% yield. Further ring closure using sodium hydride in DMF afforded the cyclobutane **280** in 41% yield over 3 steps. When **284** was subjected to the next step without purification, the desired cyclobutane **280** was isolated after purification in 63% yield from **283** (48% yield from **209**).



Scheme 155

Cycloaddition reactions were then attempted on cyclobutane **280** with a range of Lewis acids and aldehydes as summarised in Table 13. Unfortunately, none of the conditions used resulted in the formation of the cycloadducts. Instead, in most cases the starting material was entirely recovered. The cycloaddition reaction was first attempted using ethyl glyoxylate and $BF_3.Et_2O$ heated to reflux in DCM (entry 1). This returned the starting material. Thus the reaction was attempted using $Yb(OTf)_3$ and *p*-nitrobenzaldehyde in the same conditions without success (entry 2). $Sc(OTf)_3$, was also used, refluxing in 1,2-DCE in presence of *p*-nitrobenzaldehyde (entry 3). However this returned no result. When *p*-anisaldehyde was allowed to react with the cyclobutane **280** in presence of $Sc(OTf)_3$ the reaction also returned the starting material (entry 11). When $ZnBr_2$ was used as the catalyst in presence of benzaldehyde, the reaction returned the starting material (entry 4) unless it was allowed to reflux in toluene. However this afforded a complex mixture (entry 5). The same result was obtained when it was allowed to reflux in DMF in presence of *p*-nitrobenzaldehyde (entry 6). In order to increase the strength of the Lewis acid, zinc triflate was used as an alternative of zinc bromide (entry 7). However this returned the cyclobutane **280**. The use of $TiCl_4$ led to decomposition of the starting material (entry 8) unless cyclobutane **280** was treated at low temperature (entries 9 and 10). Nevertheless this only afforded the chloride derivative **285** (Scheme 156).

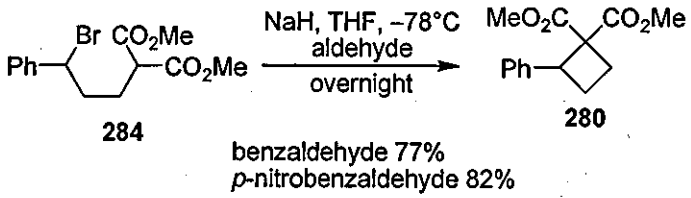


Scheme 156

Entry	Lewis acid	Reagent	Solvent	T(°C)	Product
1	$BF_3.Et_2O$ (2.5 eq)	ethyl glyoxylate (1.1 eq)	DCM	40	SM **280**
2	$Yb(OTf)_3$ (20 mol%)	*p*-nitrobenzaldehyde (3 eq)	DCM	40	SM **280**
3	$Sc(OTf)_3$ (20 mol%)	*p*-nitrobenzaldehyde (1.5 eq)	1,2-DCE	84	SM **280**
4	$ZnBr_2$ (2.5 eq)	benzaldehyde (1.5 eq)	DCM	40	SM **280**
5	$ZnBr_2$ (2.5 eq)	benzaldehyde (1.5 eq)	Toluene	110	complex mixture
6	$ZnBr_2$ (2.5 eq)	*p*-nitrobenzaldehyde (1.5 eq)	DMF	153	complex mixture
7	$Zn(OTf)_2$ (1 eq)	benzaldehyde (3 eq)	DCM	40	SM **280**
8	$TiCl_4$ (2 eq)	benzaldehyde (5 eq)	DCM	40	complex mixture
9	$TiCl_4$ (2 eq)	benzaldehyde (5 eq)	DCM	−78	**285** (77%)
10	$TiCl_4$ (2 eq)	*p*-nitrobenzaldehyde (3 eq)	DCM	−78	**285** (82%)
11	$Sc(OTf)_3$ (5 mol%)	*p*-anisaldehyde (1.5 eq)	DCM	r.t.	SM **280**
12	$ZnBr_2$ (2 eq)	MeCN	MeCN	82	SM **280**

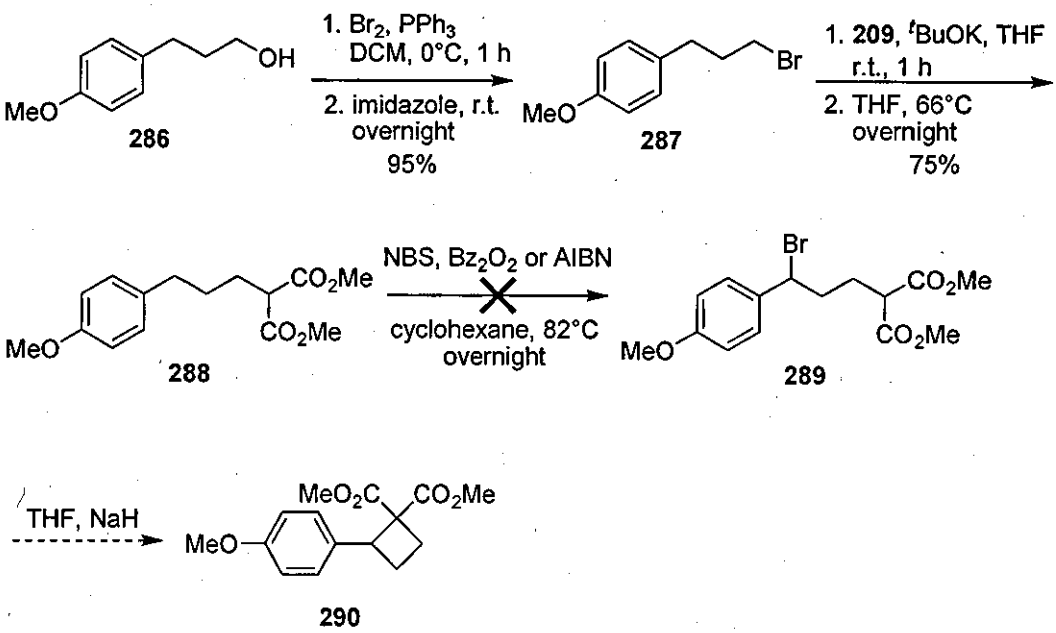
Table 13

In an attempt to cyclise aldehydes onto the open bromo butane derivative **284**, NaH was added to a mixture of **284** in THF in presence of benzaldehyde or *p*-nitrobenzaldehyde. Unfortunately, instead of the six-membered ring cycloadduct, the cyclobutane **280** was isolated at the end of the reaction in 77 and 82% yield respectively (Scheme 157).



Scheme 157

Results summarised in Table 13 using the phenyl substituted diester cyclobutane **280** suggested that the phenyl group could not activate the cyclobutane enough to allow a ring opening and hence to allow the cycloaddition reaction. To further activate the aromatic ring, we investigated the synthesis of *p*-methoxy substituted phenyl cyclopropane **290** (Scheme 158). The synthesis started from the propanol **286** which was converted into the corresponding bromide **287** in 95% yield using the protocol described by Diederich *et al.* [115] with bromine, triphenyl phosphine and imidazole. Displacement of the bromine by dimethyl malonate **209** using potassium tert-butoxide in THF afforded the diester **288** in 75% yield. Unfortunately subsequent attempts to perform the benzylic bromination using *N*-bromosuccinimide in conjunction with benzoyl peroxide failed to produce the desired bromide substituted diester butane **289**.



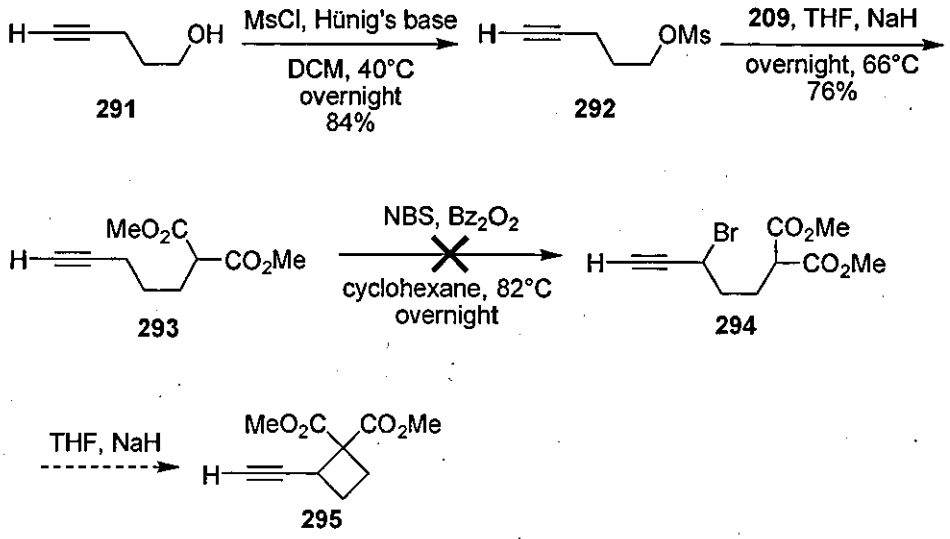
Scheme 158

2.2.3.2. Alkyne/dicobalt hexacarbonyl substituted diester cyclobutane

2.2.3.2.1. Preparation

Following the failure to perform cycloaddition reaction using phenyl substituted diester cyclobutanes, the use of more stabilising alkyne/dicobalt hexacarbonyl group in α-position to the cyclobutane was investigated. The cyclobutane **295** was thought to be ideal as a free alkyne could also be used before/after the cycloaddition reaction in other reactions e.g. Sonogashira coupling. This was thought to be important on a synthetic point of view as highly substituted building blocks could then be prepared.

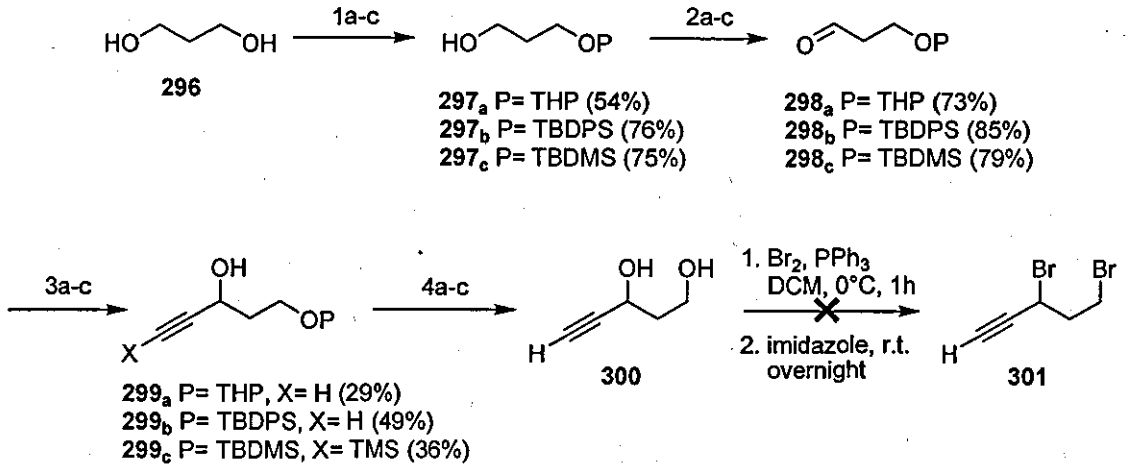
The synthesis of the cyclobutane **295** was attempted starting from pent-4-yn-1-ol **291** (Scheme 159). The mesylation of the primary alcohol followed by displacement of the mesylate formed by dimethyl malonate using sodium hydride afforded the diester hexyne derivative **293** in 59% yield over 2 steps. Attempts to perform a propargylic bromination using *N*-bromosuccinimide and benzoyl peroxide failed to produce the desired product **294**. Hence, this route was not pursued further.



Scheme 159

To bypass the generation of the required propargylic bromide **294** using an inadequate propargylic bromination with NBS and Bz_2O_2, another route was investigated with, as utilised in the synthesis of the phenyl substituted cyclobutane **280**, the preparation of a 1,3-diol followed by a conversion of the alcohols into bromides (Scheme 160). Further literature

search provided us with a protocol for the synthesis of the protected alcohol derivatives 299_a and 299_c (Scheme 160).[116]



1a) DHP, Amberlyst® N°15, THF/DCM (1/1) r.t., overnight, 54%; 2a) PCC, DCM, r.t., overnight, 73%; 3a) ethynyl MgBr, THF, –78°C, 1 h, 29%; 4a) CSA, MeOH, r.t., overnight, 55%.

1b) (i) NaH, THF, r.t., 1 h; (ii) TBDPSCl, r.t., overnight, 76%; 2b) PCC, DCM, r.t., overnight, 85%; 3b) ethynyl MgBr, THF, –78°C, 30 min, 49%; 4b) TBAF, THF, r.t., 5 min, 9%.

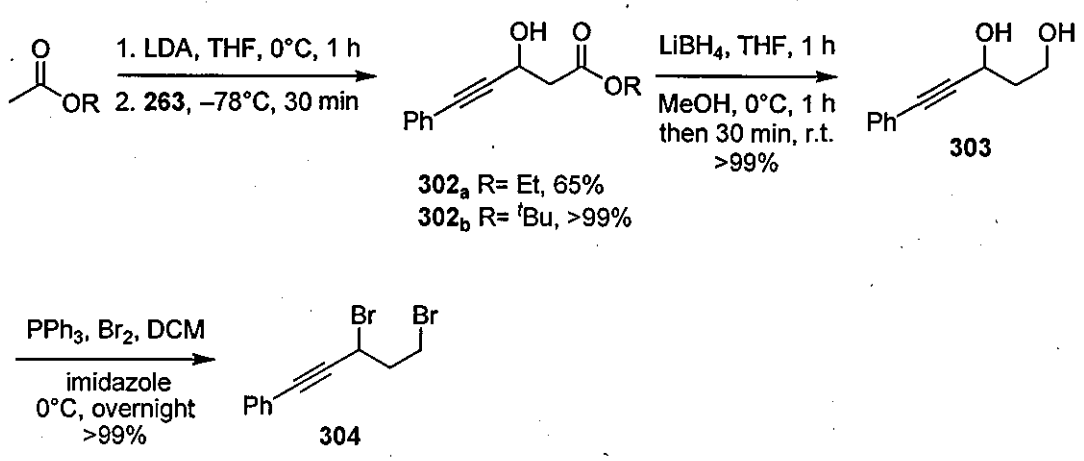
1c) (i) NaH, THF, r.t., 1 h; (ii) TBDMSCl, r.t., overnight, 75%; 2c) PCC, DCM, r.t., overnight, 79%; 3c) lithium (trimethylsilyl)acetylide, THF, –78°C, 30 min, 36%; 4c) TBAF, THF, r.t., 5 min, 36%.

Scheme 160

Our synthesis started from 1,3-propandiol which was monoprotected with a THP group in 54% yield. An oxidation of the remaining primary alcohol using PCC in DCM afforded the desired aldehyde derivative 298_a in 73% yield. A nucleophilic attack of the aldehyde using ethynyl magnesium bromide in THF at –78°C afforded the propargylic alcohol derivative 299_a in only 29% yield. Subsequent deprotection of the primary alcohol using camphor sulfonic acid in methanol afforded the desired 1,3-diol **300** in 55% yield. In an attempt to improve yields, **1**,3-propandiol **296** was monoprotected using TBDPSCl or TBDMSCl in THF using sodium hydride in THF affording 297_b and 297_c in 76 and 75% yield respectively.[117] Oxidation of the alcohols using PCC afforded the corresponding aldehydes 298_b and 298_c in 85 and 79% respectively. Nucleophilic attack of the aldehyde 298_b using ethynyl magnesium bromide followed by treatment with TBAF in THF afforded the 1,3 diol **300** in 4% yield over 2 steps. When 298_c was treated with lithium (trimethylsilyl)acetylide, the propargylic alcohol derivative 299_c was isolated in 49% yield. A subsequent treatment with TBAF in THF afforded the 1,3-diol **300** in 36% yield. Subsequent attempts to form the

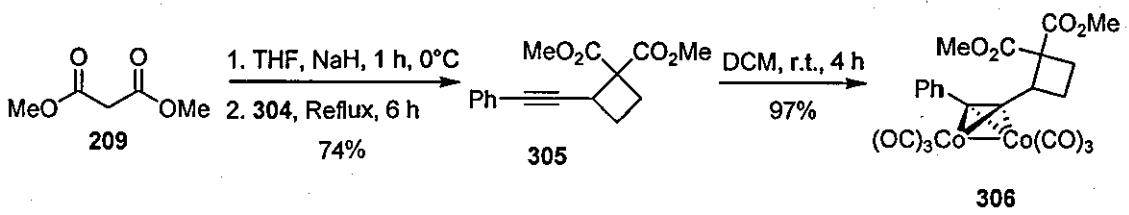
dibromide derivative **301** using bromine, triphenylphosphine and imidazole failed to produce the desired product, affording mostly decomposition material, presumably due to reaction with the acetylenic position.

The alkyne was then substituted with a phenyl group to avoid side reactions with the acetylenic position. The synthesis began with the addition of ^{t}butyl acetate to phenyl propargyl aldehyde using LDA, which was prepared *in situ* on reaction of diisopropyl amine with ^{n}BuLi at –78°C (Scheme 161).[118] The resulting ester $\mathbf{302_b}$ was isolated in a quantitative yield. When ethyl acetate was used, the aldol product $\mathbf{302_a}$ was isolated in only 65% yield using the same conditions. Both esters $\mathbf{302_a}$ and $\mathbf{302_b}$ were then reduced into the 1,3-diol **303** using $LiBH_4$ in a quantitative yield. When $LiAlH_4$ was used as the reducing agent, an allylic alcohol derivative was obtained instead of the desired diol. The diol **303** was then converted into the dibromide **304** using bromine and triphenylphosphine at 0°C in a quantitative yield, after several recrystallisations of the triphenylphosphine oxide in cold petrol (Scheme 3).



Scheme 161

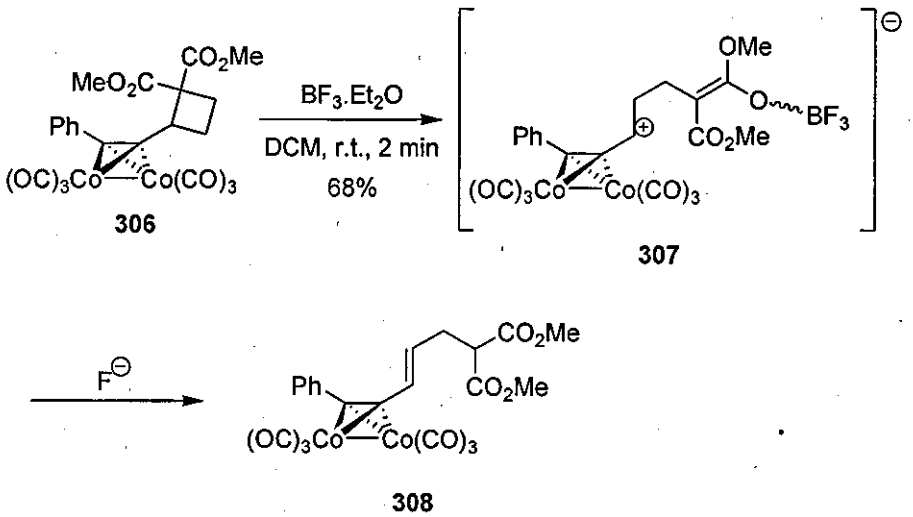
The sequence of reactions described above starting from ^{t}butyl acetate was "chromatography-free" as each step was quantitative and crude products were clean. Dibromide **304** was subsequently used to prepare the required cyclobutane **305**, using dimethyl malonate and sodium hydride, heated to reflux in THF for 6 h. Cyclobutane **305** was isolated in 74% yield after further purification by flash chromatography. Further complexation of the alkyne with dicobalt hexacarbonyl afforded the desired dicobalt complex **306** in an excellent 72% over 5 steps.



Scheme 162

2.2.3.2.2. [4 + 2] dipolar cycloaddition reactions with aldehydes

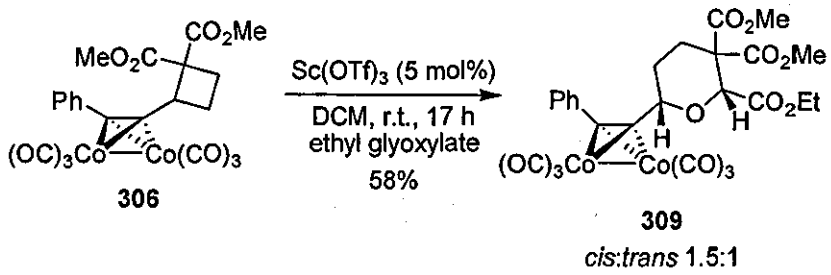
The cycloaddition was first attempted using the conditions developed previously within the research group, with 3 eq of $BF_3.Et_2O$ and 2 eq of electron deficient aldehydes. When *p*-nitrobenzaldehyde was reacted with the cyclobutane **306** in DCM at room temperature with $BF_3.Et_2O$, the cycloaddition did not occur leading mainly to decomposition of the starting material. However, trace amounts of the olefinic derivative **308** were observed in the crude product. This was the evidence that, unlike the phenyl substituted cyclobutane **280**, the cyclobutane **306** could be open using dicobalt complexes resulting in the formation of an intermediate **307**. The same observation was made using 2 eq of *p*-nitrobenzaldehyde, *p*-anisaldehyde. When the cyclobutane **306** was reacted with only using $BF_3.Et_2O$ without any trapping reagent, the alkene derivative **308** was isolated in 68% yield after only 2 min of reaction (Scheme 163).



Scheme 163

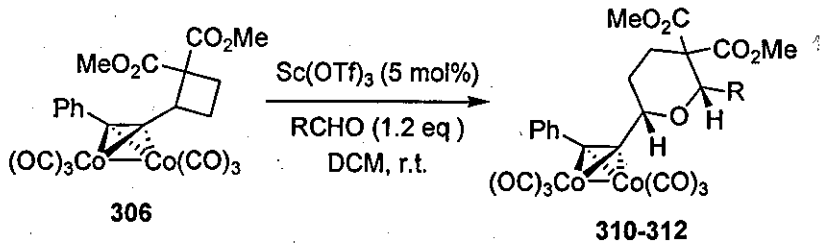
The double bond may be formed due to amounts of fluorine in the $BF_3.Et_2O$ solution. Free fluoride in the reaction mixture could trap the acidic proton in the α-position to the Nicholas carbocation allowing the formation of the alkene.

Following the failure of the use of $BF_3.Et_2O$, the cycloaddition reaction was attempted using the conditions described by Kerr *et al.*[56] in DCM, with a catalytic amount of scandium triflate (5 mol%) as the Lewis acid. Expecting the cyclobutane core to have the same reactivity as the cyclopropane we used earlier in the group, we first attempted to perform the reaction using ethyl glyoxylate as it is highly electron deficient. The two separable diastereoisomers of the corresponding tetrahydropyran adduct **309** were isolated in 58% yield after 17 h with in a 1.5:1 *cis*:*trans* ratio (Scheme 164 and Table 14 entry 1).



Scheme 164

Following this success, a range of aldehydes were used in attempts to form the corresponding tetrahydropyrans. All experiments were carried out in dry DCM, at r.t. with a catalytic amount of scandium triflate and in the presence of 4Å molecular sieves (Table 14). *p*-Nitrobenzaldehyde was used as it had similar reactivity as ethyl glyoxylate when it was reacted with three-membered rings. Unfortunately only the starting material was recovered after 2 days (entry 2). To assess the reactivity of the four-membered ring, cyclobutane **306** was reacted with benzaldehyde. The corresponding tetrahydropyran **311** was isolated in 38% yield after 24 h in a *cis* configuration only. Surprisingly, unlike the three-membered ring, the cyclobutane **306** was found to react quickly with electron rich aldehydes such as *p*-anisaldehyde. The tetrahydropyran **312** was isolated in 58% yield after only 10 min as a single *cis* diastereoisomer (entry 4). The stereochemistry of the final products was identified by nOe experiments. Aliphatic aldehydes such as hexanal and trimethyl acetaldehyde unfortunately were found to be unreactive (entries 5 and 6).



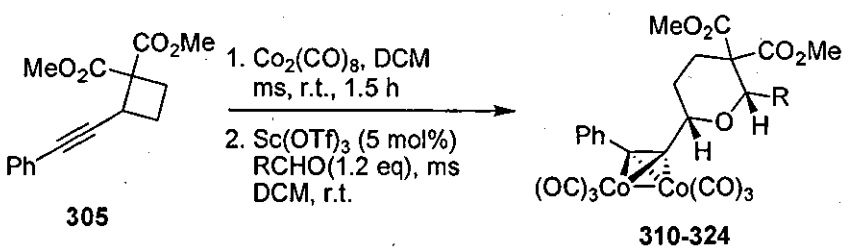
Scheme 165

Entry	Aldehyde	R	Product	t	Yield (%)	*cis*:*trans* ratio
1	ethyl glyoxylate	CO_2Et	**310**	17 h	58	1.5:1
2	*p*-nitrobenzaldehyde	*p*-NO_2Ph	**306***	2 d	n/a	n/a
3	benzaldehyde	Ph	**311**	24 h	38	*cis*
4	anisaldehyde	*p*-MeOPh	**312**	10 min	58	*cis*
5	hexanal	C_5H_{11}	**306***	2 d	n/a	n/a
6	trimethyl acetaldehyde	$(CH_3)_3C$	**306***	4 d	n/a	n/a

* Determined by H^1-NMR analysis on crude mixtures.

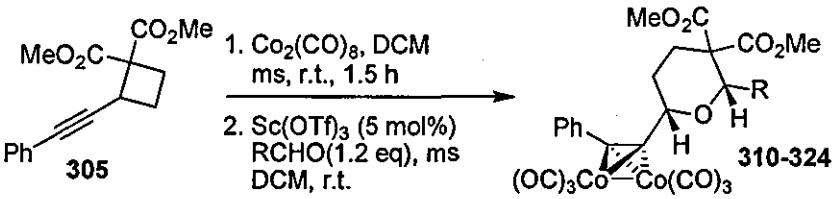
Table 14

In an attempt to improve the yields, the cyclobutane **305** was complexed *in situ* with dicobalt octacarbonyl before adding successively the aldehyde and the Lewis acid. Cycloaddition reactions were then performed in DCM at room temperature using $Sc(OTf)_3$ (5 mol%) as the Lewis acid. The presence of 4 Å molecular sieves was also found to be useful as yields could sensibly be improved when the reaction was performed under dry conditions (Scheme 166). A number of aldehydes were utilised as summarised in Table 15.



Scheme 166

Using these conditions, no improvement was observed when ethyl glyoxylate was reacted with the complexed cyclobutane (entry 1). When *p*-nitrobenzaldehyde was used, again, no reaction occurred and most of the complex **306** was recovered at the end of the reaction (entry 2). Same result was observed with the electron deficient aldehyde *p*-chlorobenzaldehyde (entry 3). To extend the scope of the reaction to aliphatic substrates, acetaldehyde, hexanal, heptanal and 2,2-dimethylpent-4-enal were subjected to the cycloaddition reaction (entries 4-7). However, only acetaldehyde afforded the corresponding cycloadduct in 73% yield after 30 min in a 1.6:1 *cis*:*trans* ratio (entry 4). Benzaldehyde was allowed to react under these conditions and the formation of **311** could be improved from 38 to 64% yield with an exclusive *cis* configuration (entry 8). Steric hindrance affects yields as the use of *p*-tolualdehyde afforded the corresponding tetrahydropyran **314** in 64% yield while *o*-tolualdehyde gave **315** in 47% yield. Conjugated aldehydes such cinnamaldehyde, α-methyl-*trans*-cinnanaldehyde, (*E*)-but-2-enal and (2*E*,4*E*)-hexa-2,4-dienal afforded the *cis* diastereoisomer of their corresponding tetrahydropyran **316**, **317**, **318** and **319** in 82, 84, 82 and 51% yield respectively (entries 11-14). When *p*-anisaldehyde was reacted with the cyclobutane using these conditions, its corresponding tetrahydropyran cycloadduct **312** was isolated in 85% yield. Yields were impoved as aldehydes were more electron rich. The two dimethoxybenzaldehydes (entries 22 and 23) afforded their corresponding tetrahydropyrans **323** and **324** in 92% yield in a *cis* configuration exclusively. However the use of the equivalent 2,4-dihydroxybenzaldehyde (entry 21) returned to the complexed starting material **306**. Heterocyclic aldehydes such as furaldehyde and thiophenecarbaldehyde also afforded their corresponding six-membered ring cycloadduct **321** and **322** in 95 and 73% yield respectively with a *cis* configuration. However the use of the similar pyrrolecarboxaldehyde and *N*-methyl-pyrrolecarboxaldehyde failed to produce the desired tetrahydropyran. Diastereoselectivities were confirmed by nOe experiments and X-Rray structure of **313**, **314**, **321** and **322** were recorded as the tetrahydropyran **314** showed in Figure 13 (X-Rray structures attached in appendices).



Entry	Aldehyde	R	Product	t	Yield (%)	*d.e.*(%)
1	ethyl glyoxylate	CO_2Et	**310**	17 h	58	20
2	*p*-nitrobenzaldehyde	*p*-NO_2Ph	**306***	1 d	n/a	n/a
3	*p*-chlorobenzaldehyde	*p*-ClPh	**306***	1 d	n/a	n/a
4	acetaldehyde	Me	**313**	30 min	73	23
5	hexanal	C_5H_{11}	**306***	1 d	n/a	n/a
6	heptanal	C_6H_{13}	**306***	1 d	n/a	n/a
7	2,2-dimethylpent-4-enal	$(CH_3)_2CCH=CH_2$	**306***	1 d	n/a	n/a
8	benzaldehyde	Ph	**311**	1 d	64	*cis*
9	*p*-tolualdehyde	*p*-CH_3Ph	**314**	10 min	64	*cis*
10	*o*-tolualdehyde	*o*-CH_3Ph	**315**	1 h	47	*cis*
11	*trans*-cinnalmaldehyde	PhCH=CH	**316**	1 h	82	*cis*
12	α-methyl-*trans*-cinnanaldehyde	$PhCH=CCH_3$	**317**	25 min	84	*cis*
13	(E)-but-2-enal	MeCH=CH	**318**	1 h	82	*cis*
14	(2*E*,4*E*)-hexa-2,4-dienal	$CH_3CH=CHCH=CH$	**319**	1 h	51	*cis*
15	*p*-anisaldehyde	*p*-MeOPh	**312**	10 min	85	*cis*
16	*p*-phenoxybenzaldehyde	*p*-PhOPh	**320**	2 h	65	*cis*
17	furaldehyde	2-C_4H_3O	**321**	10 min	95	*cis*
18	2-thiophenecarbaldehyde	2-C_4H_3S	**322**	15 min	73	*cis*
19	2-pyrrolecarboxaldehyde	2-C_4H_3N	**306***	1 d	n/a	n/a
20	*N*-methyl-2-pyrrolecarboxaldehyde	2-C_4H_3N-Me	**306***	1 d	n/a	n/a
21	2,4-dihydroxybenzaldehyde	2,4-(OH)Ph	**306***	1 d	n/a	n/a
22	2,4-dimethoxybenzaldehyde	2,4-$(CH_3O)_2Ph$	**323**	10 min	92	*cis*
23	3,4-dimethoxybenzaldehdye	3,4-$(CH_3O)_2Ph$	**324**	10 min	92	*cis*

* Determined by H^1-NMR analysis on crude mixtures.

Table 15

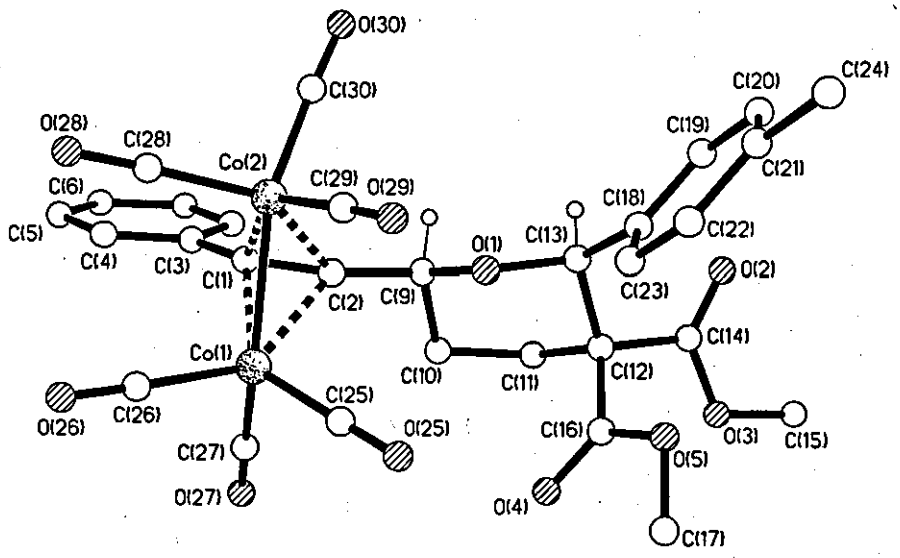
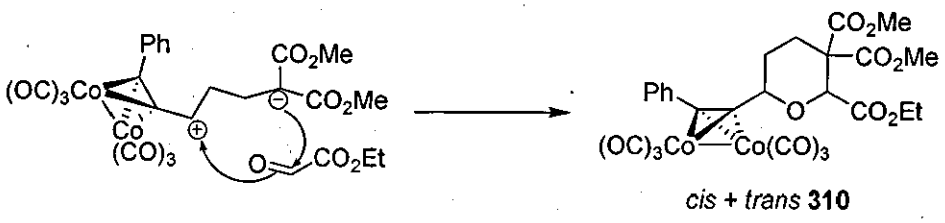


Figure 13

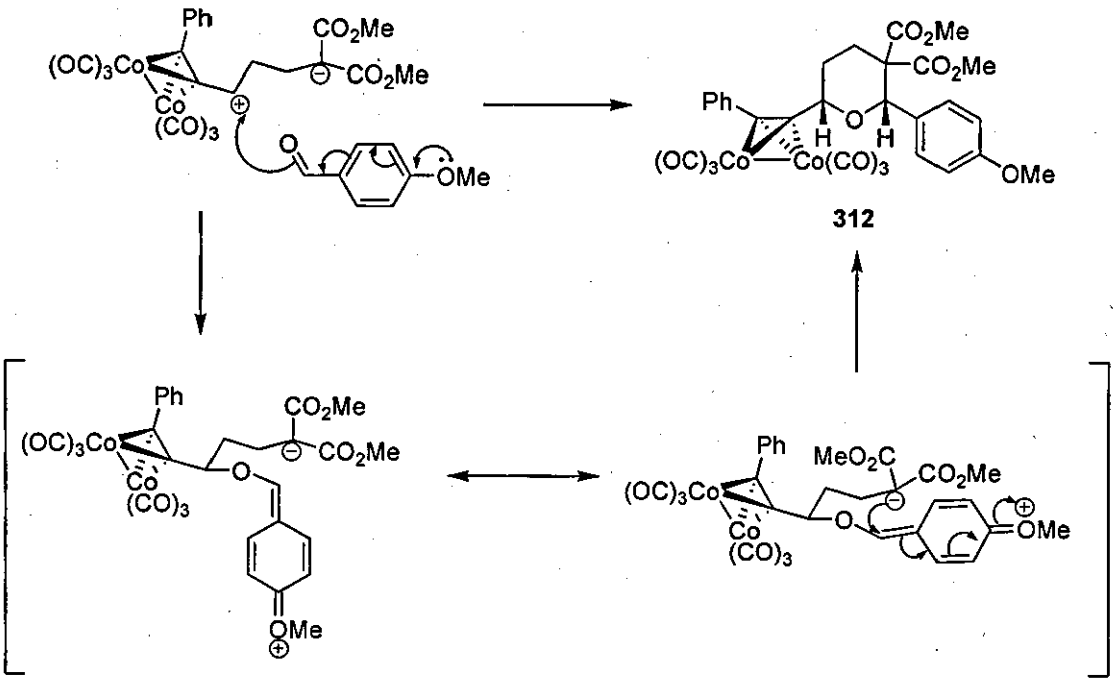
The mechanism of the reaction is not solved yet, however the results described above suggest that two different mechanisms are likely to occur whether the aldehyde is electron rich or poor. If the aldehyde is electron poor the reaction is very slow or does not proceed at all e.g. *p*-nitrobenzaldehyde unless the aldehyde is highly electron deficient e.g. ethyl glyoxylate. The highly electron deficient carbonyl would be attacked by the carbanion in first place. In the case of a concerted mechanism, the two diastereoisomers can be formed depending on the initial position of the aldehyde (Scheme 167).



cis + *trans* **310**

Scheme 167

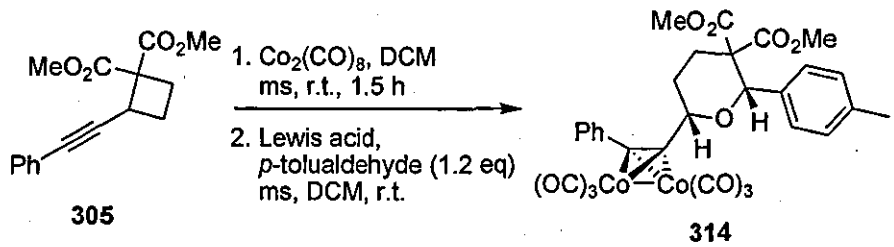
When electron rich or conjugated aldehydes are used, the oxygen of the carbonyl may attack the Nicholas carbocation first through delocalization of π-electrons. If the mechanism is not concerted, the carbon-oxygen bond can rotate to obtain the most stable conformation before trapping the carbanion. Only the *cis* isomer is obtained (Scheme 168).



Scheme 168

2.2.3.2.3. Choice of the catalyst

Using *p*-tolualdehyde, we also carried out more experiments to assess the efficiency of the catalyst. We varied the Lewis acid as summarized in Table 16, to verify whether or not the yield could be significantly improved. As previously found, cyclobutane **305** was complexed *in situ* before adding the catalyst and the aldehyde. Experiments were carried at r.t. in DCM and in the presence of 4 Å molecular sieves (Scheme 169). Results are summarised in Table 16.



Scheme 169

Entry	Lewis acid	t	Product (Yield %)
1	$BF_3.Et_2O$ (3 eq)	5 min	complex mixture
2	$ZnBr_2$ (2eq)	3 d	**314** (22)
3	$Yb(OTf)_3$ (5 mol%)	1 d	**306***
4	$Cu(OTf)_3$ (5 mol%)	1 d	**306***
5	$Sn(OTf)_3$ (5 mol%)	1 d	**306***
6	$Zn(OTf)_3$ (2 eq)	1 d	**306***
7	$AlCl_3$ (3 eq)	5 min	**314** (30)
8	$Sc(OTf)_3$ (5 mol%)	10 min	**314** (64)

* Determined by H^1-NMR analysis on crude mixtures.

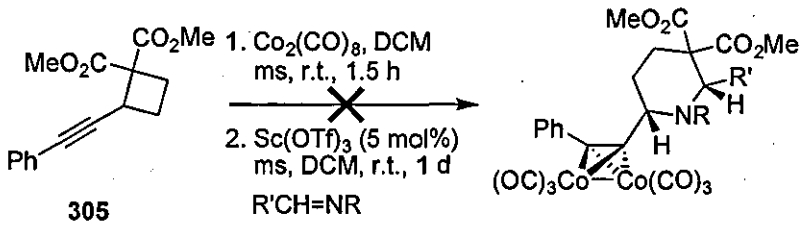
Table 16

The use of $BF_3.Et_2O$ only produced decomposition of the starting material while $ZnBr_2$ allowed the slow formation of the desired cycloadduct **314** in 22% yield after 3 days. When $Yb(OTf)_3$, $Cu(OTf)_3$, $Sn(OTf)_3$, or $Zn(OTf)_3$ were utilised, the complexed starting material **306** could only be isolated after a few hours in a nearly quantitative yield. Finally $AlCl_3$ used in 3 eq afforded **314** in a modest 30% yield after 5 min. However the product began to decompose quickly when the reaction was left stirring at room temperature for a further few minutes. The best catalyst was found to be scandium triflate, which afforded **314** in 64% yield after 10 min of reaction (entry 8).

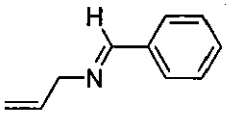
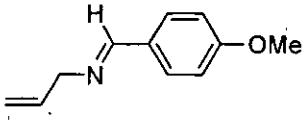
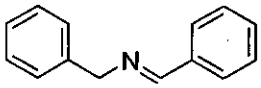
2.2.3.2.4. Extension of the methodology

2.2.3.2.4.1. Cycloaddition with imines and nitrones

To extend the methodology, the cycloaddition reaction was attempted with imines using the reaction conditions developed previously with aldehydes. However when imines **232, 235** and **325** were allowed to react using these conditions, the reactions returned only the complexed starting material **306** (Scheme 170 and Table 17).



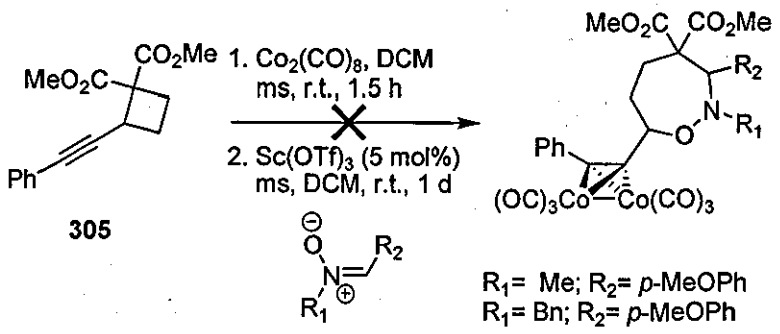
Scheme 170

Entry	Imine	Product
1	 **232**	**306***
2	 **235**	**306***
3	 **325**	**306***

* Determined by H^1-NMR analysis on crude mixtures.

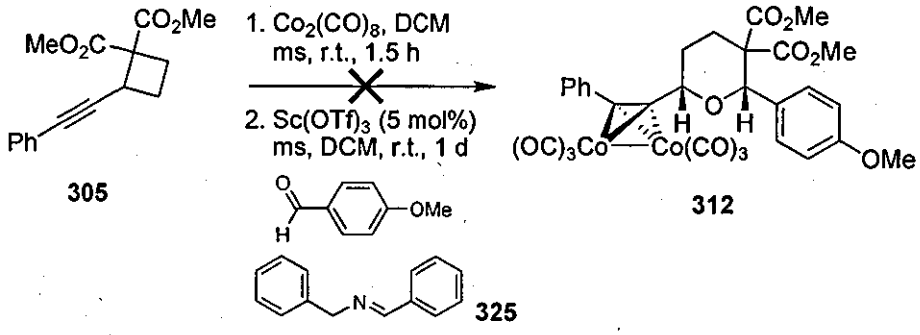
Table 17

Similar work has been carried by a member of the research group with nitrones in attempts to prepare substituted 1,2-oxazepanes.[119] Unfortunately these experiments gave similar results, affording only the complexed cyclobutane **306.**



Scheme 171

The results suggested that the reaction was inactivated by the presence of imines or nitrones. To investigate the reasons of the failure of the cycloaddition reaction with nitrogen based reagents, the highly successful reaction of *p*-anisaldehyde with the complexed cyclobutane **306** was performed again using the same conditions, in DCM, at r.t. and with $Sc(OTf)_3$ as the catalyst, but spiked with an equal amount of the imine **325** (Scheme 171). It was found that the presence of a nitrogen based reagent prevented the reaction from proceeding. The same results were observed in the research group when the reaction was spiked with nitrones (Scheme 172).[119]

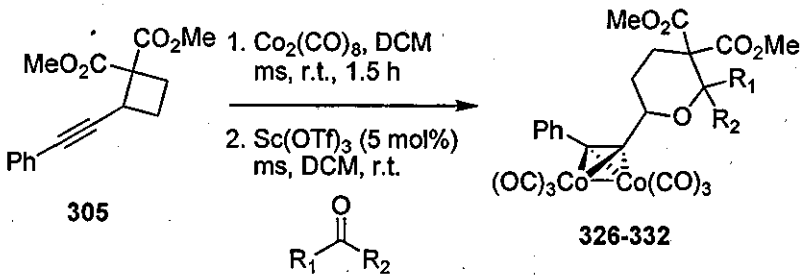


Scheme 172

This probably also explains why 2-pyrrolecarboxaldehyde and *N*-methyl-2-pyrrolecarboxaldehyde were the only 2 aromatic aldehydes which did not afford the corresponding tetrahydropyrans when subjected to the cycloaddition reaction conditions with **306** (Table 15, entries 18 and 19).

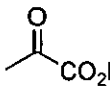
2.2.3.2.4.2. Cycloaddition with ketones and lactones

The cycloaddition reaction onto the cyclobutane **306** seemed to be oxophilic only. As an extension to this work, it was hoped that [4+2] cycloaddition with ketones would produce more heavily substituted tetrahydropyrans (Scheme 173). A range of different ketones has been utilised within the group and results are shown in Table 18 and Table 19.



Scheme 173

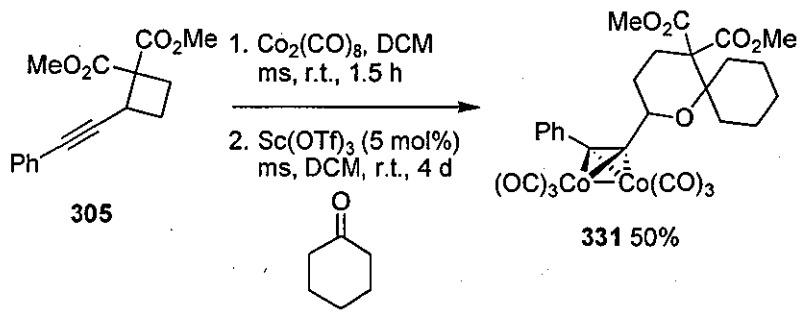
First, the cycloaddition reaction was attempted using ketones resembling to the aldehydes that previously afforded tetrahydropyrans. When acetone was used, the corresponding tetrahydrofuran **326** was isolated in a decent 41% yield after 17 h (Table 18, entry 1). Following this success, acetophenone was allowed to react with the cyclobutane in the same conditions. However, the reaction returned to the complexed cyclobutane **306** (Table 18, entry 2). The same result was also observed using the ethyl glyoxylate analogue, ethyl 2-oxopropanoate (Table 18, entry 3).

Entry	Ketone	R_1	R_2	Product	t	Yield (%)
1	 acetone	Me	Me	**326**	17 h	41
2	 acetophenone	Me	Ph	**306***	2 d	n/a
3	 ethyl 2-oxopropanoate	Me	CO_2Et	**306***	1 d	n/a

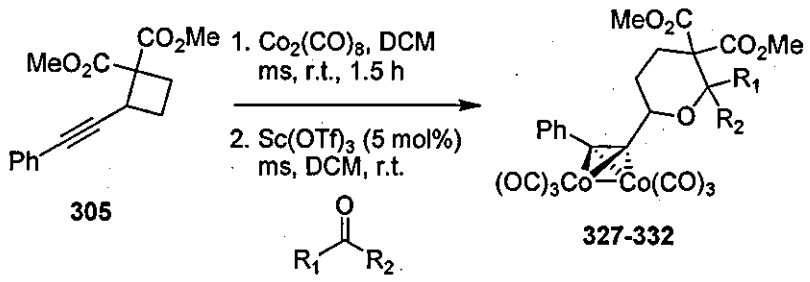
* Determined by H^1-NMR analysis on crude mixtures.

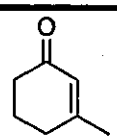
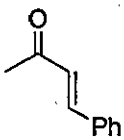
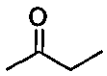
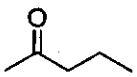
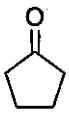
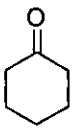
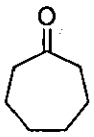
Table 18

Other ketones have also been successfully used by a member of the research group, including aliphatic and cyclic ketones (Table 19).[119] Yadav and Gupta investigated the formation of tetrahydrofurans *via* [3+2] cycloaddition reactions of ketones with silylmethyl-substituted cyclopropanes.[120] They suggested that ketones possessing electron-donating susbtituents were more effective than those with electron-withdrawing substituents, when reacted with a silylmethyl-subsituted cyclopropane. Cycloaddition was therefore attempted using cyclic α,β-unsaturated ketones. Unfortunately the use of 3-methylcyclohex-2-enone returned to the complexed cyclobutane **306** (Table 19, entry 1). A further attempt was made using the acyclic (*E*)-4-phenylbut-3-en-2-one (Table 19, entry 2). The reaction was surprisingly poor yielding, affording the tetrahydropyran **327** in only 4% yield after 4 days as a single diastereoisomer. However, the geometry could not be determined by nOe analysis. The aliphatic butan-2-one was also reacted with the complexed cyclobutane **306**, affording its corresponding tetrahydropyran **328** in 19% yield after 4 days (Table 19, entry 3). When the aliphatic chain was extended, the yield was reduced. The use of pentan-2-one afforded the six-membered cycloadduct **329** in only 6% yield after 3 days of reaction (Table 19, entry 4). In attempt to form spiro systems, the cycloaddition reaction was attempted with cyclic ketones. Cyclopentanone afforded the tetrahydropyran **330** in 23% yield after 36 hours (Table 19, entry 5). The best yield was obtained when cyclohexanone was used. The tetrahydropyran **331** was isolated in 50% after 4 days of reaction (Table 19, entry 6 and Scheme 174). Finally when the size of the ring was extended to seven-members, the yield was dramatically reduced, affording **332** in only 12% yield after 48 h (Table 19, entry 7).



Scheme 174



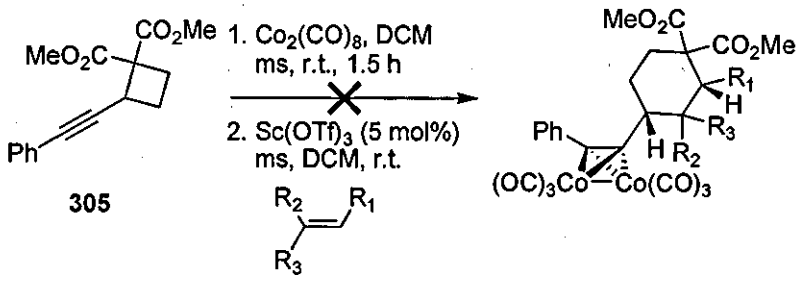
Entry	Ketone	R_1	R_2	Product	t	Yield (%)
1	 3-methylcyclohex-2-enone	$-CH_2-(CH_2)_2-(CH_3)C=CH-$		**306***	5 d	n/a
2	 (*E*)-4-phenylbut-3-en-2-one	Me	CH=CH-Ph	**327**	4 d	4
3	 butan-2-one	Me	CH_2-CH_3	**328**	4 d	19
4	 pentan-2-one	Me	$CH_2-CH_2-CH_3$	**329**	3 d	6
5	 cyclopentanone	$-CH_2-(CH_2)_2-CH_2-$		**330**	1.5 d	23
6	 cyclohexanone	$-CH_2-(CH_2)_3-CH_2-$		**331**	4 d	50
7	 cycloheptanone	$-CH_2-(CH_2)_4-CH_2-$		**332**	2 d	12

* Determined by H^1-NMR analysis on crude mixtures.

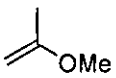
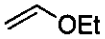
Table 19

2.2.3.2.4.3. Cycloaddition with alkenes

Cycloaddition reactions between the cyclopropane **150** and the alkene on propenal has been performed previously within the group (Scheme 60). The cycloaddition afforded a mixture of the expected tetrahydrofuran **153** and the corresponding cyclopentane **154** in 24 and 21% yield respectively (Scheme 60). The cyclopropyl moiety was also found to be more reactive with electron deficient reagents while the cyclobutane **306** provided better results for the [4+2] cycloaddition reaction when electron donating reagents were used. Therefore, we thought that we could prepare polysubstituted cyclohexanes by cycloaddition reactions between the cyclobutane **306** and electron-rich alkenes (Scheme 175). Results are summarised in Table 20.



Scheme 175

Entry	Reagent	t (h)	Product	Yield (%)
1		24	**306***	n/a
2		24	**306***	n/a
		24	**306***	n/a
3		2	**333**	90
4		2	**334**	92

* Determined by H^1-NMR analysis on crude mixtures.

Table 20

The first alkene used was allyltrimethylsilane as the silyl group vicinal to the alkene can polarise the double bond. The ability of organosilicon compounds to stabilise a cation in a β-position, is called β-effect of silicon. The basis of the β-effect is thought to be the α–π hyperconjugation (Figure 14).[121a] Another form, the *p–d* homoconjugation is also discussed in the literature.[121b]

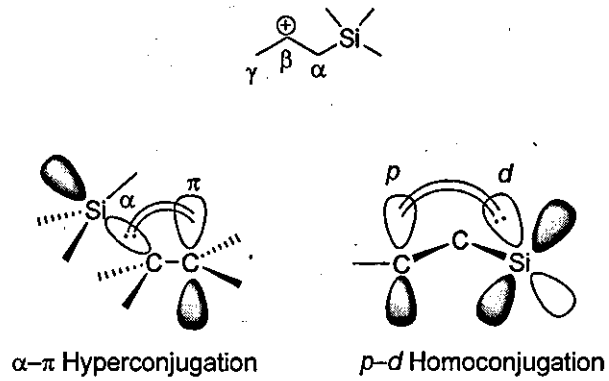
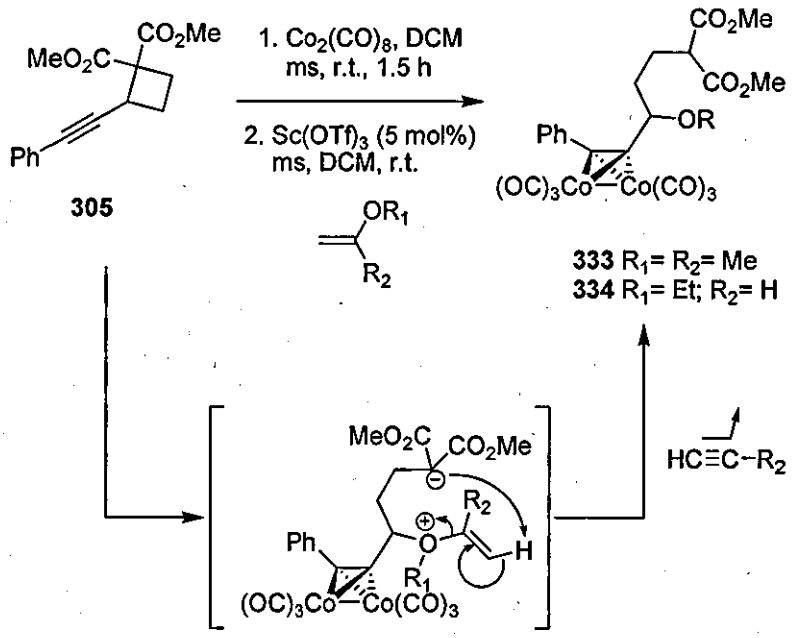


Figure 14

Unfortunately, the use of allyltrimethylsilane returned no results as only the complexed cyclobutane **306** was observed after 24 h of reaction (Table 20, entry 1). Same results were obtained when furan or dihydropyran were utilised (Table 20, entries 2 and 3). Surprisingly, when 2-methoxypropene was used, the corresponding six-membered ring was not formed but instead the cobalt complex **333** was isolated in 90% yield after 1 hour of reaction (Table 20, entry 4 and Scheme 176). A similar product **334** was isolated in 92% yield when ethyl vinyl ether was allowed to react with the dicobalt cyclobutane **306** in the same conditions (Table 20, entry 5 and Scheme 176). The formation of these two ethers can be attributed to the loss of acetylene as shown in Scheme 176.



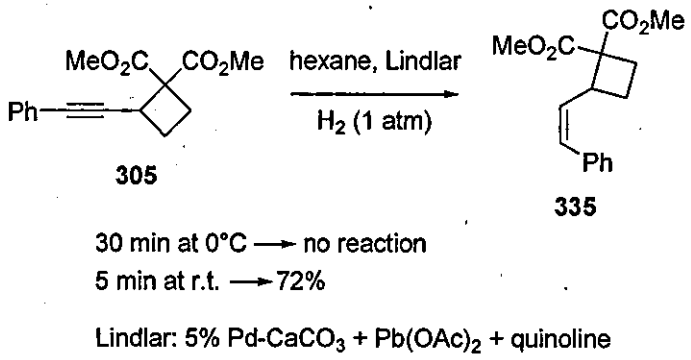
Scheme 176

Ethanol was also used in an attempt to form the ether derivative **333**. Surprisingly, when it was allowed to react with the cyclobutane **306** in the same conditions no reaction occurred and most of the starting material was recovered.

2.2.3.3. Vinyl substituted cyclobutane

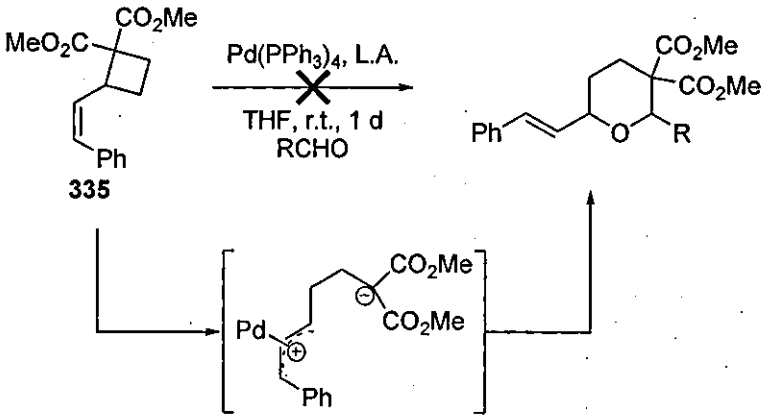
Palladium chemistry coupled to vinylcyclopropanes has been used within the research group to extend the methodology initially described by Tsuji and Yamamato (Scheme 49).[46] Substituted tetrahydrofurans and pyrrolidines were prepared in good yield. We thought that it would be possible to extend the methodology to the use of vinylcyclobutanes towards the synthesis of the corresponding six-membered rings.

Due to time restriction we could not prepare the free alkenyl cyclobutane. Instead, the *Z*-subtituted vinyl cyclobutane **335** was produced starting from our available alkynyl cyclopropane **305** (Scheme 177). The alkyne was easily reduced into the corresponding alkene using Lindlar's catalyst in hexane at room temperature and under a H_2 atmosphere. The vinylcyclobutane **335** was isolated in 72% yield after only 5 min of reaction. When the reaction was performed at 0°C, no reaction occurred and the starting material was entirely recovered after 30 min of reaction.



Scheme 177

Cycloaddition reactions were then attempted with aldehydes using the conditions previously developed within the group (Scheme 178).[99] Experiments were then first attempted in THF at r.t. and with $ZnCl_2$ as the Lewis acid. When cyclobutane **335** was allowed to react with *p*-nitrobenzaldehyde or with *p*-anisaldehyde, the reaction only returned the starting material (Table 21, entries 1 and 2). As we noted previously using the dicobalt complex **306**, the cyclobutane had a certain affinity for $Sc(OTf)_3$ as it was found to be the best catalyst for our [4+2] cycloaddition reaction with aldehyde. Thus $Sc(OTf)_3$ was used in attempts to perform the cycloaddition onto **335**. Unfortunately, the experiments using *p*-nitrobenzaldehyde or *p*-anisaldehyde again returned no results (Table 21, entries 3 and 4).



Scheme 178

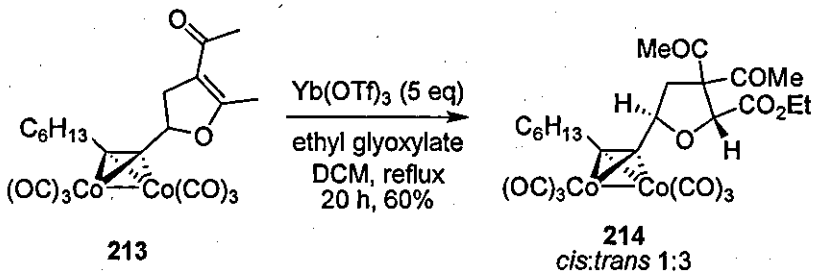
Entry	Lewis acid	R	Product	Yield (%)
1	$ZnCl_2$	4-NO_2Ph	**SM 335***	n/a
2	$ZnCl_2$	4-MeOPh	**SM 335***	n/a
3	$Sc(OTf)_3$	4-NO_2Ph	**SM 335***	n/a
4	$Sc(OTf)_3$	4-MeOPh	**SM 335***	n/a

* Determined by H^1-NMR analysis on crude mixtures.

Table 21

3. CONCLUSION

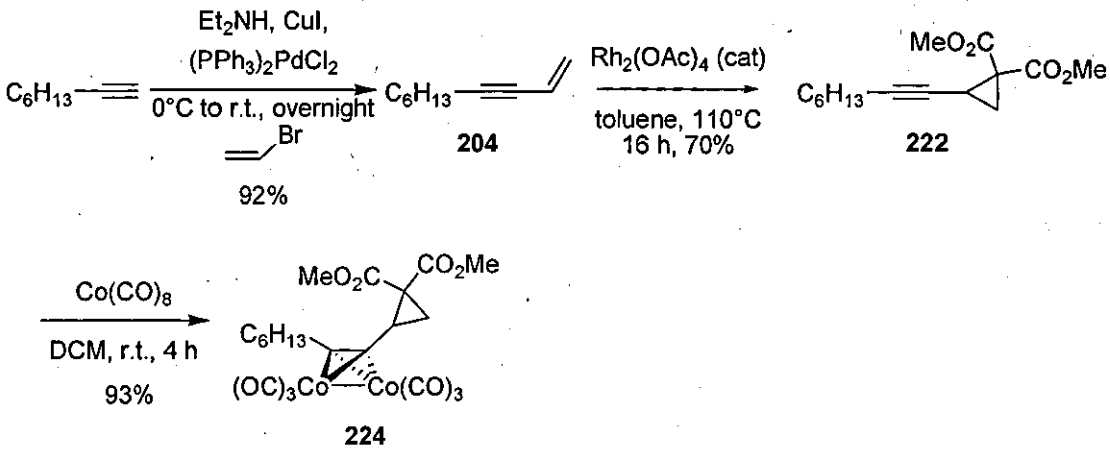
The use of dihydrofurans as cyclopropane surrogates has been shown to work in principle, however extreme substrate specificity means that this route is not a viable synthetic procedure (Scheme 179).



213 **214** *cis*:*trans* 1:3

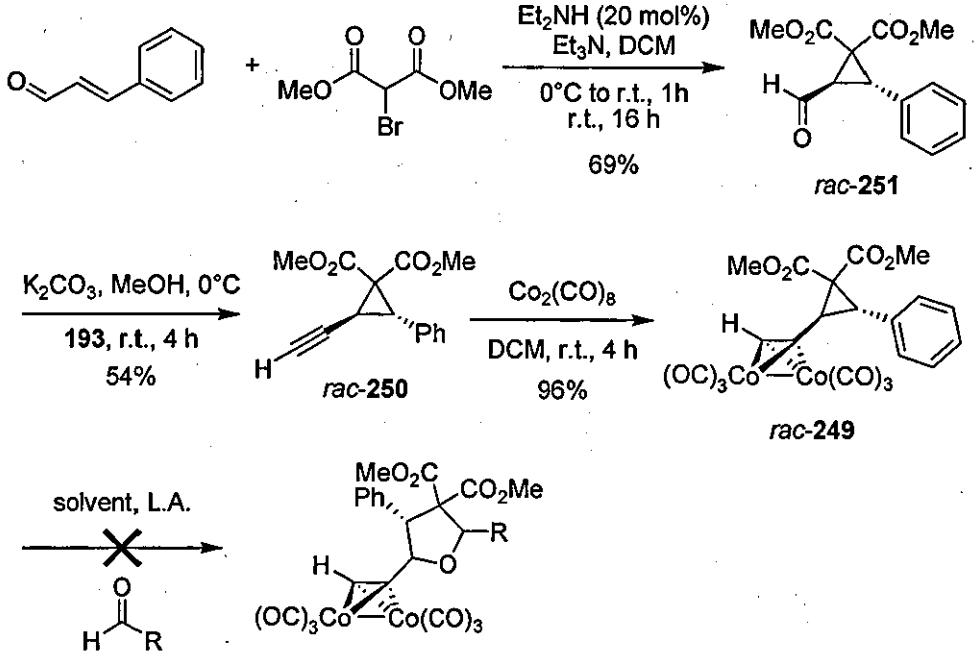
Scheme 179

The cyclopropane synthesis starting from enyne using $Rh_2(OAc)_4$ has been successful. The complexed cyclopropane **224** has been prepared *via* a 3 step methodology in 60% overall yield (Scheme 180). Subsequent [3+2] cycloaddition reactions with aldedydes and imines have also been performed to show the viability of the methodology. However, attempts to perform cascade Nicholas/Pauson-Khand reactions to form tri-cyclic molecules have been unsuccessful.



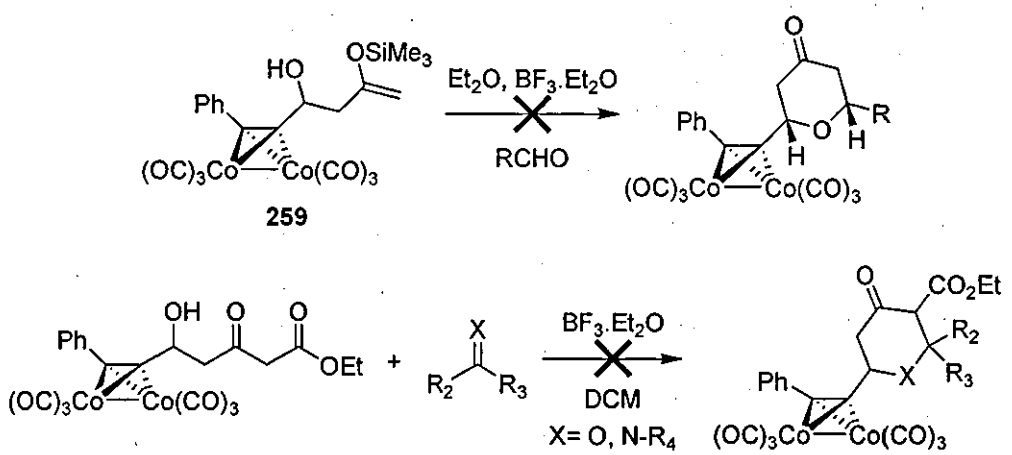
Scheme 180

A 2,3-disubtituted diester cyclopropane bearing an alkynyl group has been prepared in good yield (Scheme 181). Nevertheless attempts of subsequent cycloaddition reactions have been vain.



Scheme 181

Tetrahydropyran-4 ones could not be prepared *via* an ene reaction or *via* Knoevenagel-Michael addition tandem reaction. The use of dicobalt complexes in both strategies stops the reactions described in the literature without the bimetallic system (Scheme 182).



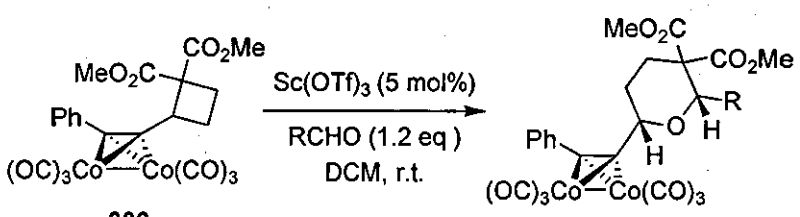
Scheme 182

To extend the scope of the methodology developed in the group with cyclopropane rings, a novel and efficient [4+2] cycloaddition reaction has been developed using cyclobutane cores. The first attempt to perform [4+2] cycloaddition reaction was carried out using a phenyl group to stabilize the carbocation formed during the ring opening. A suitably substituted cyclobutyl **280** was synthesized using the protocol described by Cativiela.[113] We attempted to perform the cycloaddition reaction using a range of Lewis acids and aldehydes, however only the starting material was recovered, regardless of conditions (Scheme 183).

280

Scheme 183

It appeared that the phenyl group was not stabilizing enough and the ring opening could not proceed. We then decided to explore the use of dicobalt complexes in this reaction as they have a higher stabilising property. We have synthesised a cyclobutane in the propargylic position in 74% yield over 4 steps. This cyclobutane was then used towards [4+2] dipolar cycloaddition reactions with aldehydes to form new tetrahydropyrans in good yield with excellent diastereoselectivity (Scheme 184).



306

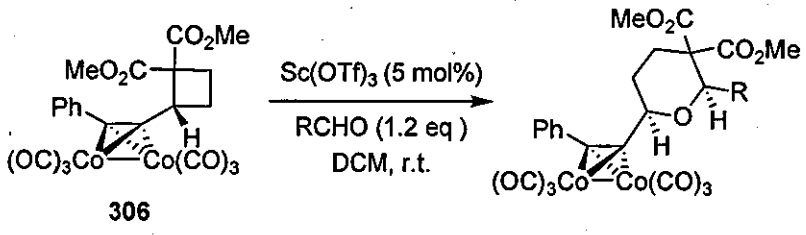
310-312

up to 95%, up to 99% *d.e.*

Scheme 184

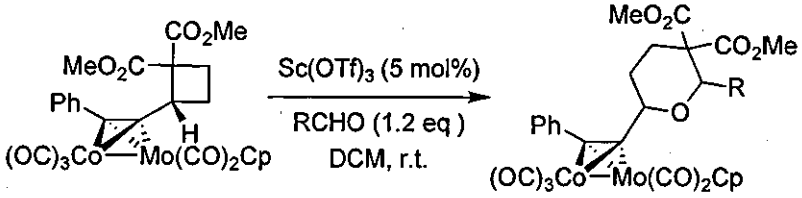
We report for the first time a catalytic [4+2] type cycloaddition reaction using a cyclobutyl as precursor, opening a new way for the synthesis of six-membered heterocycles in a totally diastereoselective fashion. The limits of the methodology have been met with electron poor and aliphatic aldehydes. A wide range of aldehydes were used as trapping reagents to form

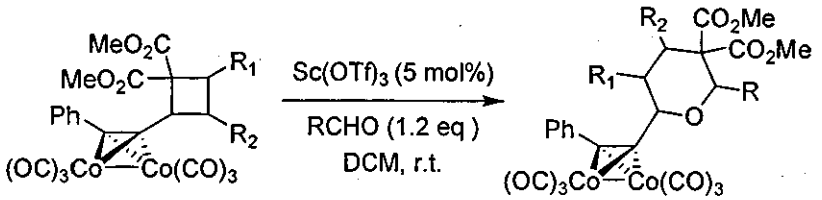
tetrahydropyrans in good yields (up to 95%) and with good to total diastereoselectivies. However, the mechanism of the reaction stays unproven, the use of enantiomerically pure cyclobutane could help understanding it. An inversion of configuration of the propargylic carbon would show that the cycloaddition goes through a stepwise process instead of a concerted mechanism, involving an initial S_N2 displacement of the malonate ion.



Scheme 185

A transfer of the methodology to heterobimetallic complexes could possibly lead to another diastereoselectivity if the mechanism pathway goes through another process. It could also be interesting to prepare more heavily substituted cyclobutanes to assess their reactivity and possible control of the diastereoselectivity (Scheme 186).





Scheme 186

4. EXPERIMENTAL

General information

All reactions herein were carried out in one of the following solvents, which were dried and purified, or purchased by the following procedures.

Acetone	Stirred over anhydrous potassium carbonate, followed by distillation over anhydrous calcium sulfate.
Acetonitrile	Purchased from Aldrich (99.8%), Sure/seal™ anhydrous quality.
Chloroform	Purchased from Aldrich (99+%) and used without further purification.
Dichloromethane	For general use, DCM was distilled over boiling chips or CaH_2 for anhydrous reactions.
Diethyl ether	Purchased from Fischer Scientific (99+%) used without purification for general use or distilled over sodium and benzophenone for anhydrous reactions.
Ethyl acetate	Distilled over $CaCl_2$ for general use.
Light petroleum	Distilled over boiling chips for general use, collecting the fraction distilling below 60°C.
Tetrahydrofuran	Distilled over sodium and benzophenone.

$Co_2(CO)_8$ was purchased from Strem (stabilised by 1-5% hexane) and used without any further purification.

Anhydrous reactions were carried out in oven-dried glassware and under an atmosphere of nitrogen. All metal carbonyl complexes were stored under a nitrogen atmosphere and kept at –18°C in a freezer.

Analysis of the compounds created herein was made using a number of the following instruments and procedures.

High-resolution mass spectroscopy was carried out on a Jeol SX 102 machine, used for both electron ionisation (EI) and fast atom bombardment (FAB) ionisation techniques. For FAB

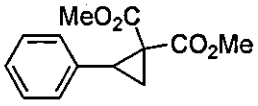
spectroscopy a matrix of 1,3-nitrobenzylalcohol was used to dissolve the compounds under investigation prior to ionisation.

Nuclear magnetic resonance spectroscopy was carried out using a Brucker DPX 400 instrument. The spectra were calibrated where possible to the signals of tetramethylsilane or the small quantity of $CHCl_3$ present in $CDCl_3$. Where possible, coupling constants (*J*) are shown denoting the multiplicity as a singlet (s), doublet (d), triplet (t), quarter (q), multiplet (m), or broad signal (br). The size of the coupling constant is given in Hertz (Hz).

Fourrier transformation Infra Red spectroscopy was recorded using a Paragon 1000 Perkin Elmer FT-IR spectrophotometer in the range of 600-3800 cm^{-1} following a standard background correction.

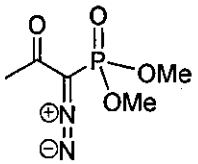
Flash silica column chromatography was used as a standard purification procedure using Fluka Kiesel gel 60, 0.04-0.063 mm particle size. Thin layer chromatography was used where possible as a standard procedure for monitoring the course and rate of a given reaction. TLC plates used were Merck aluminium backed sheets with Kiesel gel 60 F_{254} silica coating.

Dimethyl 2-phenylcyclopropane-1,1-dicarboxylate (127_b)[49a,b]



To a solution of dimethyl diazomalonate (800 mg, 5.1 mmol) in styrene (15 mL) was added a catalytic amount of rhodium acetate dimer (45 mg, 2 mol%) and the reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The mixture was then filtered through a pad of celite and silica and the crude mixture was purified by flash chromatography on silica gel (15% EtOAc/petrol) to give the *title compound* as a colourless viscous oil in 34% yield (400 mg, 1.7 mmol); ν_{max} (film)/cm^{-1} 1275 (C–O), 1740 (C=O), 2951 (sp^3 C–H) and 3028 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 1.75 (1H, dd, *J* 5.2, 9.4 Hz, CHC*H*HC), 2.20 (1H, dd, *J* 5.2, 8.0 Hz, CHC*H*HC), 3.23 (1H, t, *J* 8.0 Hz, C*H*CH_2), 3.36 (3H, s, CO_2CH_3), 3.79 (3H, s, CO_2CH_3), 7.15-7.22 (2H, m, ArC*H*) and 7.23-7.25 (3H, m, ArC*H*); δ_C (100 MHz; $CDCl_3$) 19.1 (CH*C*H_2C), 32.6 (*C*HCH_2C), 37.2 (*C*$(CO_2Me)_2$), 52.2 (CO_2CH_3), 52.8 (CO_2CH_3), 127.4 (Ar*C*H), 128.2 (2 Ar*C*H), 128.4 (2 Ar*C*H), 134.6 (ArC), 167.0 (*C*OCH_3) and 170.2 (*C*OCH_3). HRMS (EI) (M^+), found 234.0892, $C_{13}H_{14}O_4$ requires 234.0892 (±0.0 ppm); m/*z* 234 (2%), 202 (32), 121 (74) and 115 (100).

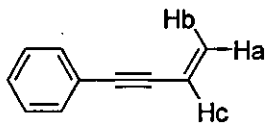
Dimethyl (1-diazo-2oxopropyl)phosphonate (193)[122]



To a cold suspension (0-5°C) of sodium hydride (1.64 g, 40.9 mmol, 60% in mineral oil, 1.1 eq) in toluene (70 mL) and THF (11 mL) was added dimethyl 2-oxopropylphosphonate (6.17 g, 37.2 mmol). The resulting suspension was stirred for 45 min and mesyl azide (2.12 g, 37.2 mmol) was added. The reaction mixture was allowed to stir for 2 h and was then filtered through a pad of celite. The filtrate was concentrated *in vacuo* and the residue was purified by trituration of the crude oil affording the *title compound* as a red/orange oil (91%, 6.50 g, 33.8 mmol); ν_{max} (film)/cm^{-1} 2125 (C=N_2), 1652 (C=O) and 1668 (C=O); δ_H(400

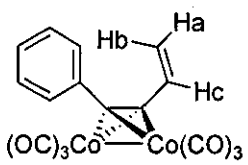
MHz; $CDCl_3$) 2.28 (3H; s, CCH_3), 3.85-3.88 (6H, s, OCH_3); δ_C(100 MHz; $CDCl_3$) 27.4 (CCH_3), 53.9 (OCH_3), 54.0 (OCH_3) and 190.2, 190.3 (*C*=O and *C*=N).

1-(But-3-en-1-ynyl)benzene (199)[123]



In an oven dried Schlenk tube under a dry nitrogen atmosphere, diethylamine (30 mL) was degassed using 3 freeze-pump-thaw cycles. Phenylacetylene (2.04 g, 20.0 mmol), copper iodide (200 mg, 1.1 mmol, 5 mol%) and palladium bistriphenylphosphine dichloride (140 mg, 0.2 mmol, 1 mol%) were then successively added at 0°C under a nitrogen atmosphere. Vinyl bromide (1M solution in THF, 20.0 mL, 20.0 mmol) was added slowly over 5 min. The resulting mixture was allowed to warm up slowly to r.t. and was then stirred overnight under a nitrogen atmosphere. The diethylamine was removed *in vacuo* and the residue was dissolved in diethyl ether (25 mL). The ethereal extract was washed with water (2×25 mL) and dried over magnesium sulfate. Subsequent purification by flash chromatography (petrol) afforded the desired 1-(3-ene-1-ynyl)benzene as a yellow oil in 98% yield (2.47 g, 19.6 mmol); ν_{max} (film)/cm^{-1} 1605 (C=C), 2216 (C≡C), 3008 (ArC–H), 3054 (ArC–H) and 3079 (ArC–H); δ_H (400 MHz; $CDCl_3$) 5.52 (1H, dd, *J* 2.1, 11.2 Hz, H_a), 5.72 (1H, dd, *J* 2.1, 17.6 Hz, H_b), 6.01 (1H, dd, *J* 11.2, 17.6 Hz, H_c), 7.28-7.31 (3H, m, ArC*H*) and 7.42-7.45 (2H, m, ArC*H*); δ_C (100 MHz; $CDCl_3$) 88.1 (C≡*C*), 90.0 (*C*≡C), 117.3 (*C*H), 123.1 (Ar*C*), 126.9 (Ar*C*H), 128.2 (CH_2), 128.3 (2Ar*C*H) and 131.6 (2Ar*C*H).

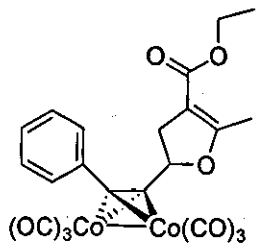
Dicobalt hexacarbonyl-1-(but-3-en-1-ynyl)benzene (200)[123a]



To a solution of dicobalt octacarbonyl (7.05 g, 20.6 mmol, 1.1 eq) in DCM (140 mL) was added *via* a cannula a solution of 1-(3-ene-1-ynyl)benzene (2.40 g, 18.8 mmol) in DCM (20

mL). The resulting reaction mixture was allowed to stir at r.t., under a nitrogen atmosphere for 4 h. The solvent was then removed *in vacuo* and the residue was purified by flash chromatography on silica gel (petrol) affording 6.55 g (15.9 mmol, 84%) of the desired dicobalt hexacarbonyl complex as a dark red oil; ν_{max} (film)/cm^{-1} 1630 (C=C), 2046 (C≡O), 2088 (C≡O), 3026 (ArC–H) and 3076 (ArC–H); δ_H (400 MHz; $CDCl_3$) 5.59 (1H, d, *J* 10.2 Hz, H_a), 5.72 (1H, d, *J* 16.4 Hz, H_b), 7.08 (1H, dd, *J* 10.2, 16.4 Hz, H_c), 7.09-7.35 (3H, m, ArC*H*) and 7.40-7.60 (2H, m, ArC*H*); δ_C (100 MHz; $CDCl_3$) 91.2 (*C*–C), 92.4 (C–*C*), 120.4 (CH_2), 128.0 (Ar*C*H), 128.9 (2Ar*C*H), 129.2 (2Ar*C*H), 134.0 (*C*H), 138.2 (Ar*C*) and 199.2 ($CO_{complex}$); HRMS (FAB) (M^+–CO), found 385.9040, $C_{15}H_8Co_2O_5$ requires 385.9036 (+1.2 ppm); m/z 386 (13%), 358 (25%), 330 (17%), 302 (8%) and 274 (8%).

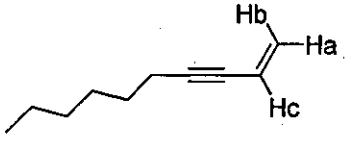
Dicobalt hexacarbonyl ethyl 4,5-Dihydro-2-methyl-5-(2-phenylethynyl)furan-3-carboxylate (202)



A suspension of $Mn(OAc)_3.2H_2O$ (5.18 g, 19.3 mmol, 4.0 eq) in glacial acetic acid (200 mL) was degassed under dry nitrogen flow for 10 min in a 500 mL flame dried round-bottom flask. The mixture was then warmed up to 45°C and was allowed to stir for 30 minutes. A solution of 1-(but-3-en-ynyl)benzene hexacarbonyl (2.00 g, 4.8 mmol) and ethyl acetoacetate (4.9 mL, 5.03 g, 38.6 mmol, 8.0 eq) in glacial acetic acid (20 mL) was then added in one portion. The reaction mixture was allowed to stir for 4 h at 45°C (TLC monitoring) under an inert atmosphere and was diluted with water (60 mL). The resulting aqueous solution was extracted with diethyl ether (3×35 mL). The combined ethereal extracts were neutralised with a saturated solution of sodium carbonate, washed with water (3×30 mL) and dried over magnesium sulfate. The crude product was purified by flash chromatography on silica gel (8% EtOAc/petrol) to give 1.12 g (2.1 mmol, 43%) of the desired complexed dihydrofuran as a dark red oil; ν_{max} (film)/cm^{-1} 1442 (C=C), 1700 (C=O), 1734 (C=O), 2055 (C≡O), 2092 (C≡O), 2871 (sp^3 C–H), 2931 (sp^3 C–H), 2980 (sp^3 C–H), 3058 (ArC–H) and 3075 (ArC–H); δ_H (400 MHz; $CDCl_3$) 1.26 (3H, t, *J* 7.0 Hz,

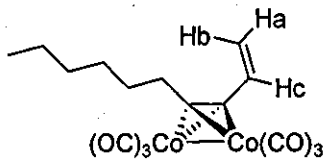
$COCH_2CH_3$), 2.26 (3H, s, $OCCH_3$), 2.84 (1H, dd, *J* 5.9, 14.6 Hz, C*H*HCHO), 3.44-3.51 (1H, dd, *J* 10.6, 14.6 Hz, C*H*HCHO), 4.18 (2H, q, *J* 7.0 Hz $CO_2CH_2CH_3$), 5.98 (1H, dd, *J* 5.9, 10.6 Hz, CH_2CHO), 7.31-7.40 (3H, m, ArC*H*) and 7.50-7.55 (2H, m, ArC*H*); δ_C (100 MHz; $CDCl_3$) 13.8 ($OCCH_3$), 14.4 ($CO_2CH_2CH_3$), 38.0 (CH_2CHO), 61.4 ($CO_2CH_2CH_3$), 82.0 (CH_2CHO), 90.6 (*C*≡C), 95.9 (C≡*C*), 101.9 (CH_2CCO_2Et), 128.2 (Ar*C*H), 128.8 (2Ar*C*H), 129.6 (2Ar*C*H), 137.3 (Ar*C*), 165.7 ($CO_2CH_2CH_3$), 167.4 (CH_3CO), and 199.0 ($CO_{complex}$); HRMS (FAB) (M^+–CO), found 513.9517, $C_{22}H_{16}Co_2O_9$ requires 513.9509 (+1.5 ppm); m/z 514 (5%), 486 (5%), 458 (22%), 430 (100%), 402 (27%) and 374 (20%).

Dec-1-en-3-yne (204)[124]



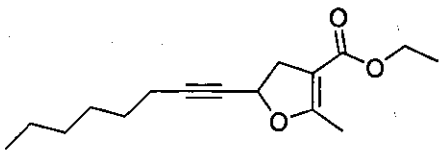
In an oven dried Schlenk tube under a dry nitrogen atmosphere, diethylamine (120 mL) was degassed using 3 freeze-pump-thaw cycles. 1-Octyne (13.4 mL, 10.00 g, 99.9 mmol), copper iodide (860 mg, 4.5 mmol, 5 mol%) and palladium bis triphenylphosphine dichloride (450 mg, 0.6 mmol, 0.07 mol%) were then successively added at 0°C under a nitrogen atmosphere. Vinyl bromide (100 g Sure-Pac™ cylinder) was flushed through the reaction mixture until a persistent red colour appeared. The resulting mixture was allowed to warm up slowly to room temperature and the mixture was stirred overnight under a nitrogen atmosphere. The diethyl amine was then removed *in vacuo* and the residue was dissolved in diethyl ether (60 mL). The ethereal mixture was washed with water (2×40 mL) and dried over magnesium sulfate. Subsequent purification by flash chromatography (petrol) afforded the desired dec-1-en-3-yne as a yellow oil (11.40 g, 84.0 mmol, 92%); ν_{max} (film)/cm^{-1} 1607 (C=C), 2226 (C≡C), 2857 (sp^3 C–H), 2930 (sp^3 C–H), 2955 (sp^3 C–H), 3008 (sp^2 C–H) and 3097 (sp^2 C–H); δ_H (400 MHz; $CDCl_3$) 0.89 (3H, t, *J* 6.8 Hz, CH_3), 1.22-1.46 (6H, m, $3CH_2$), 1.28-1.58 (2H, m, CH_3CH_2), 2.28 (2H, dt, *J* 7.2, 2.1 Hz, CH_2CH_2C), 5.37 (1H, dd, *J* 2.3, 11.1 Hz, H_a), 5.53 (1H, dd, *J* 2.3, 17.5 Hz, H_b) and 6.05 (1H, ddt, *J* 11.1, 17.5, 2.1 Hz, H_c); δ_C (100 MHz; $CDCl_3$) 14.0 (CH_3CH_2), 19.3 (CH_2CH_2C≡C), 22.6 (CH_3CH_2), 28.6 ($2CH_2$), 31.4 (CH_2), 79.3 (*C*≡C), 91.3 (C≡*C*), 117.6 ($CHCH_2$) and 125.4 ($CHCH_2$); HRMS (EI) (M^+H) found 137.1329, $C_{10}H_{17}$ requires 137.1330 (–0.6 ppm); m/z 121 (9%), 107 (30%), 93 (30%), 79 (72%), 60 (51%), 55 (49%), 43 (90) and 41 (100%).

Dec-1en-3yne-dicobalt hexacarbonyl (205)



To a solution of dicobalt octacarbonyl (9.61 g, 28.1 mmol, 1.2 eq) in DCM (175 mL) was added *via* a cannula a solution of dec-1-en-3-yne (3.19 g, 23.4 mmol) in DCM (25 mL). The resulting reaction mixture was allowed to stir at r.t., under a nitrogen atmosphere for 4 h. The solvent was then removed *in vacuo* and the residue was purified by flash chromatography on silica gel (petrol) affording the desired *title complex* in 96% yield (9.53 g, 22.6 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1632 (C=C), 2011 (C≡O), 2088 (C≡O), 2857 (sp^3 C–H), 2929 (sp^3 C–H), 2930 (sp^3 C–H) and 3092 (sp^2 C–H); δ_H (400 MHz; $CDCl_3$) 0.91 (3H, t, *J* 6.9 Hz, C*H*$_3$CH$_2$), 1.21-1.52 (6H, m, 3C*H*$_2$), 1.55-1.76 (2H, m, C*H*$_2$), 2.89 (2H, t, *J* 8.0 Hz, C*H*$_2$C–C), 5.45 (1H, dd, *J* 1.5, 10.1 Hz, *H*$_b$), 5.55 (1H, dd, *J* 1.5, 16.4 Hz, *H*$_a$) and 6.84 (1H, dd, *J* 10.1, 16.3 Hz, *H*$_c$); δ_C (100 MHz; $CDCl_3$) 14.0 (*C*H$_3$CH$_2$), 22.6 (CH$_2$*C*H$_2$C–C), 29.2 (CH$_3$*C*H$_2$), 31.6 (2*C*H$_2$), 34.4 (*C*H$_2$), 90.8 (*C*–C), 101.3 (C–*C*), 119.4 (*C*HCH$_2$), 133.8 (CH*C*H$_2$) and 199.9 (*C*O$_{complex}$); HRMS (FAB) (M$^+$–CO), found 393.9667, $C_{15}H_{16}Co_2O_5$ requires 393.9662 (+1.5 ppm); m/z 394 (42%), 366 (87%), 338 (30%), 310 (61%) and 282 (19%).

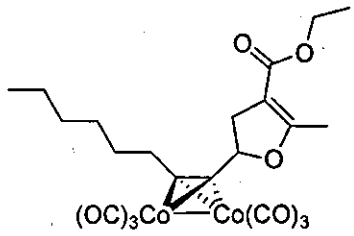
Ethyl 4,5-dihydro-2-methyl-5-(oct-1-ynyl)furan-3-carboxylate (206)



A suspension of Mn(OAc)$_3$.2H$_2$O (1.97 g, 7.3 mmol, 4.0 eq) in glacial acetic acid (35 mL) was degassed under dry nitrogen flow for 10 min in a 250 mL flame dried round-bottom flask. The mixture was then warmed up to 45°C and was allowed to stir for 30 minutes. A solution of dec-1-en-3-yne (250 mg, 1.8 mmol), ethyl acetoacetate (1.91 g, 14.7 mmol, 8.0 eq) and copper acetate dihydrate (730 mg, 3.7 mmol, 2.0 eq) in glacial acetic acid (20 mL) was then added in one portion. The reaction mixture was allowed to stir for 4 h at 45°C

(TLC monitoring) under an inert atmosphere and was diluted with water (30 mL). The resulting aqueous solution was extracted with diethyl ether (3×35 mL). The combined ethereal extracts were neutralised with a saturated solution of sodium carbonate, washed with water (3×15 mL) and dried over magnesium sulfate. The crude product was purified by flash chromatography on silica gel (5% EtOAc/petrol) to give 190 mg (0.7 mmol, 40%) of the desired ethyl 4,5-dihydro-2-methyl-5-(oct-1-ynyl)furan-3-carboxylate as a yellow oil; ν_{max} (film)/cm^{-1} 1082 (C–O), 1220 (C–O), 1382 (C–O), 1653 (C=C), 1700 (C=O), 2239 (C=C), 2858 (sp^3 C–H) and 2929 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 0.88 (3H, t, *J* 6.8 Hz, $CH_3CH_2CH_2$), 1.27 (3H, t, *J* 7.2 Hz, $CO_2CH_2CH_3$), 1.30-1.41 (6H, m, $3CH_2$), 1.46-1.56 (2H, m, $CH_3CH_2CH_2$), 2.19 (3H, t, *J* 1.6 Hz, $COCH_3$), 2.22 (2H, dt, *J* 7.2, 2.0 Hz, $CH_2C{\equiv}C$), 2.91 (1H, ddq, *J* 8.4, 14.4, 1.6 Hz, CHHCHO), 3.14 (1H, ddq, *J* 10.4, 14.4, 1.6 Hz, CHHCHO), 4.16 (2H, q, *J* 7.2 Hz, $CO_2CH_2CH_3$) and 5.16 (1H, ddt, *J* 8.4, 10.4, 2.0 Hz, CH_2CHO); δ_C (100 MHz; $CDCl_3$) 14.0 (CH_3CH_2), 14.1 ($OCCH_3$), 14.5 ($CO_2CH_2CH_3$), 18.8 ($CH_2CH_2C{\equiv}C$), 22.5 (CH_3CH_2), 28.3 (CH_2), 28.5 (CH_2), 31.3 (CH_2), 37.8 (CH_2CHO), 59.6 ($CO_2CH_2CH_3$), 71.2 (CH_2CHO), 78.2 ($C{\equiv}C$), 87.8 ($C{\equiv}C$), 101.8 (CH_2CCO_2Et), 165.8 ($CO_2CH_2CH_3$) and 167.0 ($OCCH_3$); Mass ion could not be observed.

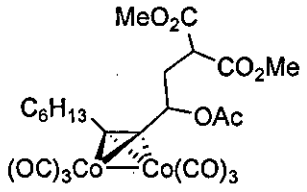
Dicobalt hexacarbonyl ethyl 4,5-dihydro-2-methyl-5-(oct-1-ynyl)furan-3-carboxylate (207)



A suspension of $Mn(OAc)_3.2H_2O$ (5.08 g, 18.9 mmol, 4.0 eq) in glacial acetic acid (65 mL) was degassed under dry nitrogen flow for 10 min in a 250 mL flame dried round-bottom flask. The mixture was then warmed up to 45°C and was allowed to stir for 30 minutes. A solution of dec-1-en-3-yne dicobalt hexacarbonyl (2.00 g, 4.7 mmol) and ethyl acetoacetate (1.84 g, 14.2 mmol, 4.0 eq) and copper acetate dihydrate (730 mg, 3.7 mmol, 2.0 eq) in glacial acetic acid (25 mL) was then added in one portion. The reaction mixture was allowed to stir for 4 h at 45°C (TLC monitoring) under an inert atmosphere and was diluted with water (60 mL). The resulting aqueous solution was extracted with diethyl ether (3×35 mL).

The combined ethereal extracts were neutralised with a saturated solution of sodium carbonate, washed with water (3×20 mL) and dried over magnesium sulfate. The crude product was purified by flash chromatography on silica gel (8% EtOAc/petrol) to give 590 mg (1.1 mmol, 23%) of the desired ethyl 4,5-dihydro-2-methyl-5-(oct-1-ynyl)furan-3-carboxylate dicobalt hexacarbonyl as a dark red oil; ν_{max} (film)/cm^{-1} 1082 (C–O), 1221 (C–O), 1382 (C–O), 1653 (C=C), 1700 (C=O), 2024 (C≡O), 2049 (C≡O), 2090 (C≡O), 2858 (sp^3 C–H) and 2956 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 0.86 (3H, t, *J* 6.8 Hz, $CH_3CH_2CH_2$), 1.21 (3H, t, *J* 7.2 Hz, $CO_2CH_2CH_3$), 1.22-1.45 (6H, m, $3CH_2$), 1.46-1.48 (2H, m, $CH_3CH_2CH_2$), 2.15 (3H, s, $COCH_3$), 2.65 (1H, dd, *J* 2.0, 6.0 Hz, CHHCHO), 2.76 (2H, dd, *J* 6.4, 9.2 Hz, CH_2C–C), 3.27 (1H, dd, *J* 2.0, 10.8 Hz, CHHCHO), 4.12 (2H, t, *J* 7.2 Hz, $CO_2CH_2CH_3$) and 5.68 (1H, dd, *J* 6.0, 10.8 Hz, CH_2CHO); δ_C (100 MHz; $CDCl_3$) 13.8 (CH_3CH_2), 14.1 ($CO_2CH_2CH_3$), 14.4 ($OCCH_3$), 22.5 (CH_3CH_2), 29.2 (CH_2), 31.6 (CH_2), 31.8 (CH_2), 33.9 (CH_2C–C), 37.7 (CH_2CHO), 59.6 ($CO_2CH_2CH_3$), 81.8 (CH_2CHO), 96.1 (C–C), 99.4 (C–C), 101.5 (CH_2CCO_2Et), 165.8 (CO_2Et), 167.4 ($OCCH_3$) and 199.6 ($CO_{complex}$); HRMS (FAB) (M^+–CO), found 522.0126, $C_{21}H_{24}Co_2O_8$ requires 522.0135 (–1.6 ppm); m/z 522 (3%), 494 (8%), 466 (31%), 438 (31%), 410 (25%) and 382 (16%).

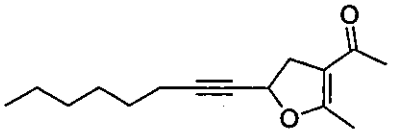
Dicobalt hexacarbonyl dimethyl 2-acetoxy-tetrahydro-5-(oct-1-ynyl)furan-2,3-dicarboxylate (210)



A suspension of $Mn(OAc)_3.2H_2O$ (1.18 g, 4.4 mmol, 4.0 eq) in glacial acetic acid (15 mL) was degassed under dry nitrogen flow for 10 min in a 50 mL flame dried round-bottom flask. The mixture was then warmed up to 45°C and was allowed to stir for 30 minutes. A solution of dec-1-en-3-yne (150 mg, 1.1 mmol), dimethyl malonate (400 µL, 440 mg, 3.3 mmol, 3.0 eq) and copper acetate dihydrate (220 mg, 1.1 mmol) in glacial acetic acid (5 mL) was then added in one portion. The reaction mixture was allowed to stir for 19 h at 45°C (TLC monitoring) under an inert atmosphere and was then diluted with water (60 mL). The resulting aqueous solution was extracted with diethyl ether (3×15 mL). The combined

ethereal extracts were neutralised with a saturated solution of sodium carbonate, washed with water (3×20 mL) and dried over magnesium sulfate. The crude product was then taken up in DCM (10 mL) and was allowed to react with dicobalt octacarbonyl (410 mg, 1.2 mmol, 1.1 eq) for 4 h. Solvent was then removed *in vacuo*, and the crude product was purified by flash chromatography on silica gel (8-10% EtOAc/petrol) to give 80 mg (0.1 mmol, 13%) of the desired *title compound* as dark red oil; ν_{max} (film)/cm^{-1} 1224 (C–O), 1742 (C=O), 2028 (C≡O), 2048 (C≡O), 2091 (C≡O), 2858 (sp^3 C–H), 2831 (sp^3 C–H) and 2956 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.2 Hz, CH_3CH_2), 1.30-1.41 (4H, m, CH_2), 1.41-1.52 (2H, m, CH_2), 1.58-1.69 (2H, m, CH_2), 2.10 (3H, s, $OCOCH_3$), 2.30 (1H, ddd, *J* 5.2, 10.4, 14 Hz, CHC*H*HCHO), 2.50 (1H, ddd, *J* 2.8, 9.2, 14 Hz, CHC*H*HCHO), 2.75-2.2.81 (2H, m, CH_2C–C), 3.55 (1H, dd, *J* 5.2, 9.2 Hz, $CHCH_2CHO$), 3.77 (3H, s, OCH_3), 3.78 (3H, s, OCH_3) and 6.10 (1H, dd, *J* 2.8, 10.4 Hz Hz, $CHCH_2CHO$); δ_C (100 MHz; $CDCl_3$) 14.0 (CH_3CH_2), 20.5 ($OCOCH_3$), 22.6 (CH_3CH_2), 29.3 (CH_2), 31.6 (CH_2), 31.9 (CH_2), 33.4 (CH_2), 35.5 (CH_2), 48.5 ($COCH_3$), 52.8 (CO_2CH_3), 52.9 ($CHCH_2CHO$) 71.5 ($CHCH_2CHO$), 94.6 (C–C), 99.2 (C–C),168.8, (CO_2CH_3) 169.0 (CO_2CH_3), 170.2 ($OCOCH_3$) and 199.8 ($CO_{complex}$).

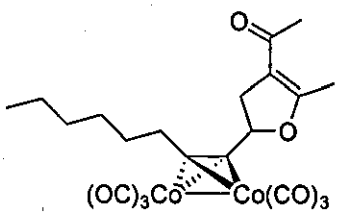
1-(4,5-Dihydro-2-methyl-5-(oct-1-ynyl)furan-3-yl)ethanone (212)



A suspension of $Mn(OAc)_3.2H_2O$ (7.88 g, 29.4 mmol, 4.0 eq) in glacial acetic acid (100mL) was degassed under dry nitrogen flow for 10 min in a 250 mL flame dried round-bottom flask. The mixture was then warmed up to 45°C and was allowed to stir for 30 minutes. A solution of dec-1-en-3-yne (1.00 g, 7.3 mmol), acetylacetone (5.3 mL, 5.15 g, 51.5 mmol, 7.0 eq) and copper acetate dihydrate (1.47 g, 7.3 mmol) in glacial acetic acid (25 mL) was then added in one portion. The reaction mixture was allowed to stir for 4 h at 45°C (TLC monitoring) under an inert atmosphere and was diluted with water (60 mL). The resulting aqueous solution was extracted with diethyl ether (3×35 mL). The combined ethereal extracts were neutralised with a saturated solution of sodium carbonate, washed with water (3×20 mL) and dried over magnesium sulfate. The crude product was purified by flash

chromatography on silica gel (5% EtOAc/petrol) to give 1.08 g (4.6 mmol, 63%) of the desired *title compound* as a yellow oil; ν_{max} (film)/cm^{-1} 1222 (C–O), 1603 (C=C), 1675 (C=O), 2238 (C≡C), 2856 (sp^3 C–H) and 2928 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 0.89 (3H, t, *J* 6.8 Hz, C*H*$_3$CH$_2$), 1.22-1.42 (6H, m, 3C*H*$_2$), 1.47-1.58 (2H, m, CH$_3$C*H*$_2$), 2.21 (3H, s, OCC*H*$_3$), 2.23 (3H, s, COC*H*$_3$), 2.18-2.27 (2H, m, C*H*$_2$C≡C), 2.99 (1H, ddd, *J* 1.6, 8.4, 15.6 Hz, C*H*HCHO), 3.21 (1H, ddd, *J* 1.6, 10.4, 14.0 Hz, C*H*HCHO) and 5.18 (1H, ddt, *J* 8.4, 10.4, 2.0 Hz, CH$_2$C*H*O); δ_C (100 MHz; $CDCl_3$) 13.9 (*C*H$_3$CH$_2$), 14.8 (O–C*C*H$_3$), 18.7 (*C*H$_2$C≡C), 22.5 (CH$_3$*C*H$_2$), 28.2 (*C*H$_2$), 28.4 (*C*H$_2$), 29.3 (CH2CCO*C*H3), 31.2 (*C*H$_2$), 38.8 (*C*H$_2$CHO), 71.1 (CH$_2$*C*HO), 78.0 (*C*≡C), 87.9 (C≡*C*), 111.8 (CH$_2$*C*COCH$_3$), 166.6 (O–*C*CH$_3$) and 193.9 (CH$_2$*C*COCH$_3$); no mass ion could be observed; m/z 207 (48%), 182 (100%), 179 (70%), 137 (83%), 85 (40%) and 57 (65%).

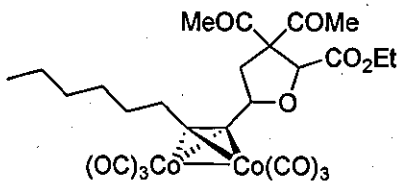
Dicobalt hexacarbonyl-1-(4,5-dihydro-2-methyl-5-(oct-1-ynyl)furan-3-yl)ethanone (213)



To a solution of dicobalt octacarbonyl (880 mg, 2.6 mmol, 1.2 eq) in DCM (5 mL) was added *via* syringe a solution of 1-(4,5-dihydro-2-methyl-5-(oct-1-ynyl)furan-3-yl)ethanone (490 mg, 2.1 mmol) in DCM (5 mL). The resulting reaction mixture was allowed to stir at r.t., under a nitrogen atmosphere for 4 h. The solvent was then removed *in vacuo* and the residue was purified by flash chromatography on silica gel (5% EtOAc/petrol) affording the desired *title complex* in 82% yield (900 mg, 1.7 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1221 (C–O), 1620 (C=C), 1651 (C=C), 1697 (C=O), 2016 (C≡O), 2047 (C≡O), 2090 (C≡O), 2857 (sp^3 C–H) and 2929 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 0.92 (3H, t, *J* 6.8 Hz, C*H*$_3$CH$_2$), 1.30-1.51 (6H, m, 3C*H*$_2$), 1.59-1.69 (2H, m, C*H*$_2$), 2.22 (3H, s, CH$_2$CCOC*H*$_3$), 2.25 (3H, t, *J* 1.6 Hz, OCC*H*$_3$), 2.78 (1H, ddd, *J* 1.6, 5.6, 14.4 Hz, C*H*HCHO), 2.81-2.87 (2H, m, C*H*$_2$C–C), 3.45 (1H, ddd, *J* 1.6, 10.8, 14.4 Hz, C*H*HCHO) and 5.77 (1H, dd, *J* 5.6, 10.8 Hz, CH$_2$C*H*O); δ_C (100 MHz; $CDCl_3$) 13.0 (*C*H$_3$CH$_2$), 14.7 (O–C*C*H$_3$), 22.6 (*C*H$_2$C–C), 29.2 (CH$_3$*C*H$_2$), 29.4 (CH$_2$COC*H*$_3$), 31.6 (*C*H$_2$), 31.8 (*C*H$_2$), 33.9 (*C*H$_2$), 38.4 (*C*H$_2$CHO), 81.9

(CH_2CHO), 95.9 (*C*–C), 99.5 (C–*C*), 111.7 (CH_2CCOCH_3), 167.0 ($CCCH_3$), 194.0 ($COCH_3$) and 199.7 ($CO_{complex}$); HRMS (FAB) (M^+), found 521.0051, $C_{21}H_{22}Co_2O_8$ requires 521.0059 (–1.0 ppm); m/z 521 (11%), 492 (3%), 465 (48%), 436 (100%), 409 (39%), 408 (47%) and 410 (25%).

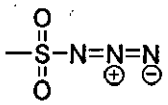
Dicobalt hexacarbonyl ethyl 3,3-diacetyl-tetrahydro-5-(oct-1-ynyl)furan-2-carboxylate (214)



To a solution of dicobalt hexacarbonyl 1-(4,5-dihydro-2-methyl-5-(oct-1-ynyl)furan-3-yl)ethanone (50 mg, 0.10 mmol) in DCM (10 mL) was added ytterbium triflate hydrate (300 mg, 0.48 mmol, 5.0 eq) and the resulting mixture was allowed to stir for 10 min at r.t. under a nitrogen atmosphere. Ethyl glyoxylate (30 µl, 0.14 mmol, 1.5 eq, 50% in toluene) was then added and the reaction mixture was heated to reflux for 20 h. The crude mixture was washed with water (2×20 mL) and dried over magnesium sulfate. After filtration, the product was concentrated *in vacuo* and purified on silica gel (5% EtOAc/petrol) to give the *title compound* in 60% yield (40 mg, 0.06 mmol) as a mixture of the two inseparable diastereoisomers in a 1:3 *cis:trans* ratio as a dark red oil; ν_{max} (film)/cm^{-1} 1217 (C–O), 1705 (C=O), 1734 (C=O), 2021 (C≡O), 2049 (C≡O), 2090 (C≡O), 2856 (sp^3 C–H), 2929 (sp^3 C–H); assigned from combined spectrum, (i) minor diastereoisomer *cis*, δ_H (400 MHz; $CDCl_3$) 0.91 (3H, t, *J* 6.8 Hz, CH_3CH_2), 1.27 (3H, t, *J* 7.2Hz, $CO_2CH_2CH_3$), 1.30-1.37 (8H, m, $4CH_2$), 2.20 (3H, s, $COCH_3$), 2.30 (3H, s, $COCH_3$), 2.42 (1H, dd, *J* 7.6, 12.8 Hz, CHHCHO), 2.80 (2H, m, CH_2C–C), 3.13 (1H, dd, *J* 7.6, 12.8 Hz, CHHCHO), 4.22 (2H, q, *J* 7.2 Hz, $CO_2CH_2CH_3$), 5.25 (1H, s, $OCHCO_2Et$) and 5.51 (1H, t, *J* 7.6 Hz, CH_2CHO); δ_C (100 MHz; $CDCl_3$) 13.9 (CH_3CH_2), 14.0 ($CO_2CH_2CH_3$), 22.3 (CH_3CH_2), 26.4 ($COCH_3$), 28.5 ($COCH_3$), 29.7 (CH_2), 31.6 (CH_2), 31.7 (CH_2), 33.9 (CH_2C–C), 38.2 (CH_2CHO), 61.5 ($CO_2CH_2CH_3$), 79.3 ($C(COMe)_2$), 80.1 (CH_2CHO), 80.8 ($OCHCO_2Et$), 93.4 (*C*–C), 100.0 (C–*C*), 169.0 (CO_2Et), 200.0 ($CO_{complex}$), 201.2 ($COCH_3$) and 201.4 ($COCH_3$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 5.25 ppm and the proton at 5.51 ppm; (ii) major diastereoisomer *trans*, δ_H (400

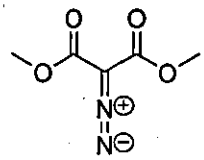
MHz; $CDCl_3$) 0.91 (3H, t, *J* 6.8 Hz, CH_3CH_2), 1.27 (3H, t, *J* 7.2Hz, $CO_2CH_2CH_3$), 1.30-1.37 (8H, m, $4CH_2$), 2.18 (3H, s, $COCH_3$), 2.37 (3H, s, $COCH_3$), 2.61 (1H, dd, *J* 10.8, 12.0 Hz, CHHCHO), 2.80 (2H, m, CH_2C–C), 3.06 (1H, dd, *J* 5.2, 12.0 Hz, CHHCHO), 4.17 (2H, q, *J* 7.2 Hz, $CO_2CH_2CH_3$), 5.05 (1H, dd, *J* 5.2, 10.8 Hz, CH_2CHO) and 5.26 (1H, s, $OCHCO_2Et$); δ_C (100 MHz; $CDCl_3$) 13.9 (CH_3CH_2), 14.0 ($CO_2CH_2CH_3$), 22.6 (CH_3CH_2), 26.5 ($COCH_3$), 28.2 ($COCH_3$), 29.3 (CH_2), 31.6 (CH_2), 31.7 (CH_2), 33.8 (CH_2C–C), 38.3 (CH_2CHO), 61.6 ($CO_2CH_2CH_3$), 79.2 ($C(COCH_3)_2$), 80.1 (CH_2CHO), 80.8 ($OCHCO_2Et$), 93.4 (C–C), 100.0 (C–C), 168.9 (CO_2Et), 200.0 ($CO_{complex}$), 201.2 ($COCH_3$) and 201.4 ($COCH_3$); no apparent coupling was observed by nOe analysis between the proton at 5.05 ppm and the proton at 5.26 ppm suggesting a trans stereochemistry; HRMS (FAB) (M^+–2CO), found 566.0394, $C_{23}H_{28}Co_2O_9$ requires 566.0397 (+0.5 ppm); m/z 566 (13%), 538 (39%), 510 (100%), 482 (32%) and 454 (47%).

Mesyl azide (217)[125]



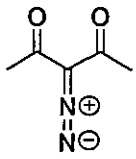
Sodium azide (4.25 g, 65.5 mmol, 1.5 eq) was slowly added by small portions to a solution of mesyl chloride (3.4 mL, 5.00 g, 43.7 mmol) in acetone (20 mL) and the resulting mixture was allowed to stir at r.t. under a nitrogen atmosphere for 4 hours. The solvent was then evaporated *in vacuo* and the residue taken up in diethyl ether (20 mL). The ethereal solution was washed with water (30 mL) and the aqueous layer was extracted with diethyl ether (2×25 mL). The ethereal extracts were combined and dried on magnesium sulfate. After solvent removal, the desired mesyl azide was isolated in 99% yield (5.27 g, 43.5 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 2138 (C=N_3) and 2935 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 3.27 (3H, s, CH_3); δ_C (100 MHz; $CDCl_3$) 42.8 (CH_3).

Dimethyl diazomalonate (218)[126]



To a solution of dimethyl malonate (4.3 mL, 4.96 g, 37.6 mmol) in acetonitrile (60 mL) under a nitrogen atmosphere was added mesyl azide (5.00 g, 41.4 mmol, 1.1 eq) and the resulting mixture was cooled down to 0°C with an ice bath. Triethylamine (11.5 mL, 8.35 g, 82.6 mmol, 2.0 eq) was then added dropwise *via* a syringe and the reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The solution was concentrated *in vacuo* and the residue was taken up in 30 mL of a 1:1 petrol/chloroform solution. The solids were filtrated on a Büchner funnel and the filtrate was concentrated *in vacuo* affording the dimethyldiazomalonate as a yellow oil in 98% yield (5.82 g, 36.8 mmol); ν_{max} (film)/cm^{-1} 1695 (C=O), 1761 (C=O), 2137 (C=N); δ_H (400 MHz; $CDCl_3$) 3.77 (6H, s, CO_2CH_3); δ_C (100 MHz; $CDCl_3$) 52.4 ($2CO_2CH_3$), 65.5 (C=N) and 161.3 ($2CO_2CH_3$).

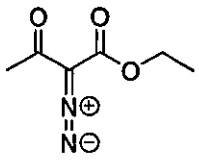
Acetyl diazoacetone (219)[127]



To a solution of pentan-2,4-dione (1.7 mL, 1.67 g, 16.5 mmol) in acetonitrile (15 mL) under a nitrogen atmosphere was added mesyl azide (2.00 g, 16.5 mmol) and the resulting mixture was cooled down to 0°C with an ice bath. Triethyl amine (4.6 mL, 3.34 g, 33.1 mmol, 2.0 eq) was then added dropwise *via* a syringe and the reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The solution was concentrated *in vacuo* and the residue was taken up in 20 mL of a 50:50 petrol/chloroform solution. The solids were filtrated on a Büchner funnel and the filtrate was concentrated *in vacuo* affording the acetyl diazoacetone as a yellow oil in 95% yield (1.98 g, 15.7 mmol); ν_{max} (film)/cm^{-1} 1667 (C=O), 2127 (C=N) and 3005 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 2.39 (6H, s, $COCH_3$); δ_C (100

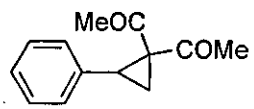
MHz; $CDCl_3$) 28.4 ($2COCH_3$), 84.6 (C=N) and 188.2 ($2CO$); HRMS (EI^+) (M^+), found 127.0501, $C_5H_7N_2$ requires 127.0507 (+1.4 ppm); m/z 127 (76%) and 102 (100%).

Ethyl acetodiazoacetate (220)[127]



To a solution of ethyl acetoacetate (1.07 g, 8.3 mmol) in acetonitrile (10 mL) under a nitrogen atmosphere was added mesyl azide (1.00 g, 8.3 mmol) and the resulting mixture was cooled down to 0°C with an ice bath. Triethylamine (2.3 mL, 1.67 g, 16.5 mmol, 2.0 eq) was then added dropwise *via* a syringe under a nitrogen atmosphere. The reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The solution was concentrated *in vacuo* and the residue was taken up in 10 mL of a 50/50 petrol/chloroform solution. The solids were filtrated on a Büchner funnel and the filtrate was concentrated *in vacuo* affording the ethyl acetodiazoacetate as a yellow oil 71% yield (910 mg, 5.8 mmol); ν_{max} (film)/cm^{-1} 1716 (C=O), 2138 (C=N) and 2984 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 1.29 (3H, t, J 6.8 Hz, $CO_2CH_2CH_3$), 2.4 (3H, s, $COCH_3$) and 4.26 (2H, q, J 6.8Hz, $CO_2CH_2CH_3$); δ_C (100 MHz; $CDCl_3$) 14.3 ($CO_2CH_2CH_3$), 28.2 ($COCH_3$), 61.4 ($CO_2CH_2CH_3$), 76.4 (C=N), 161.3 ($CO_2CH_2CH_3$) and 190.1 ($COCH_3$).

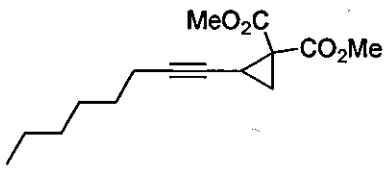
1,1-Diacetyl-2-phenyl cyclopropane (221)[128]



To a solution of diazo acetylacetone (200 mg, 1.6 mmol) in styrene (15 mL) was added a catalytic amount of rhodium acetate dimer (14 mg, 2 mol%) and the reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The mixture was filtered through a pad of celite and silica and the crude product was purified by flash chromatography on silica gel (15% EtOAc/petrol) to give the *title compound* as a yellow oil in 35% yield (110 mg, 0.5 mmol); ν_{max} (film)/cm^{-1} 1684 (C=O), 2860 (sp^3 C–H), 3028 (sp^2

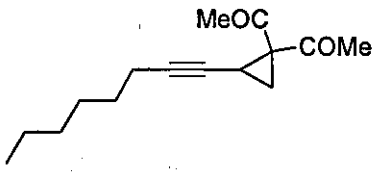
ArC–H); δ_H(400 MHz; $CDCl_3$) 1.58 (1H, dd, *J* 5.2, 8.6 Hz, CHC*H*HC), 1.73 (3H, s, COCH_3), 2.18 (1H, dd, *J* 5.2, 8.6 Hz, CHC*H*HC), 2.19 (3H, s, COCH_3), 3.21 (1H, t, *J* 8.6 Hz, C*H*CH_2C), 7.02-7.09 (2H, m, ArC*H*) and 7.12-7.24 (3H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 18.0 (CH*C*H_2C), 26.6 (CO*C*H_3), 29.4 (CO*C*H_3), 32.6 (*C*HCH_2C), 51.7 (*C*(COCH_3)$_2$), 127.6 (Ar*C*H), 128.4 (2Ar*C*H), 128.6 (2Ar*C*H), 134.2 (Ar*C*), 201.2 (*C*OCH_3) and 201.8 (*C*OCH_3); HRMS (EI) (M^+), found 202.0995, $C_{13}H_{14}O_2$ requires 202.0994 (+0.6 ppm); m/z 202 (100%), 187 (26%), 183 (39%), 159 (43%), 141 (57%), 115 (69%) and 105 (52%).

1,1-Dimethyl dicarboxylate-2-(oct-1-ynyl)cyclopropane (222)



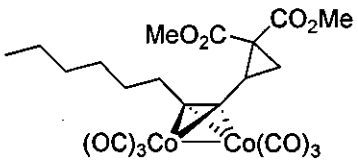
Dimethyl diazomalonate (5.02 g, 31.8 mmol, 1.7 eq) was added to a solution of dec-1-en-3-yne (2.59 g, 19.1 mmol) in toluene (25 mL). A catalytic amount of rhodium acetate dimer (170 mg, 2 mol%) was then added and the reaction mixture was allowed to stir, heated to reflux under a nitrogen atmosphere for 16 h. The crude product was filtered through a pad of celite and silica and the crude mixture was purified by flash chromatography on silica gel (7% EtOAc/petrol) to give 3.58 g (13.4 mmol, 70%) of 1,1-diacetyl-2-(oct-1-ynyl)cyclopropane as a yellow oil. ν_{max} (film)/cm^{-1} 1279 (C–O), 1730 (C=O), 2143 (C≡C), 2930 (sp^3 C–H) and 2952 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 0.81 (3 H, t, *J* 6.8 Hz, C$H_3$$CH_2$), 1.11-1.30 (6H, m, 3C$H_2$), 1.31-1.40 (2H, m, C$H_2$), 1.48 (1H, dd, *J* 4.4, 9.2 Hz, CHC*H*HC), 1.71 (1H, dd, *J* 4.4, 7.2 Hz, CHC*H*HC), 2.03 (2H, dt, *J* 6.8, 2.0 Hz, CH_2C≡C), 2.37 (1H, ddt, *J* 7.2, 9.2, 2.0 Hz, C*H*CH_2C), 3.67 (3H, s, CO_2CH_3) and 3.72 (3H, s, CO_2CH_3); δ_C (100 MHz; $CDCl_3$) 13.1 (*C*$H_3$$CH_2$), 16.5 (*C*H$CH_2$C), 17.6 (*C*$H_2$C≡C), 21.3 (CH*C*$H_2$C), 21.5 (*C*$H_2$), 27.4 ($CH_3$*C*$H_2$), 27.7 (*C*$H_2$), 30.3 (*C*$H_2$), 34.9 (*C*(C$O_2CH_3$)$_2$) 51.7 ($CO_2$*C*$H_3$), 51.8 ($CO_2$*C*$H_3$), 74.4 ($CH_2$*C*≡C), 80.2 (*C*H$CH_2$C), 166.0 (*C*$O_2CH_3$) and 168.3 (*C*$O_2CH_3$); mass ion could not be observed.

1,1-Diacetyl-2-(oct-1-ynyl)cyclopropane (223)



Diazo acetylacetone (185 mg, 1.47 mmol, 2.0 eq) was added to a solution of dec-1-en-3-yne (100 mg, 0.73 mmol) in toluene (10 mL). A catalytic amount of rhodium acetate dimer (7 mg, 2 mol%) was then added and the reaction mixture was allowed to stir, heated to reflux under a nitrogen atmosphere for 23 h. The crude product was filtered through a pad of celite and silica before being purified by flash chromatography on silica gel (5% EtOAc/petrol) to give 13 mg (0.05 mmol, 7%) of the *title compound* as a yellow oil; ν_{max} (film)/cm^{-1} 2928 (sp^2 CH), 1696 (C=O), 2180 (C≡C), 2952 (sp^3 C–H) and 3025 (sp^3 C–H); δ_H (400 MHz; $CDCl_3$) 1.81 (3H, t, *J* 7.2 Hz, CH_3CH_2), 1.11-1.38 (6H, m, $3CH_2$), 1.39-1.41 (2H, m, CH_3CH_2), 1.44 (1H, dd, *J* 4.4, 9.2 Hz, CHHCHC), 1.71 (1H, dd, *J* 4.4, 7.2 Hz, CHHCHC), 2.03 (2H, dt, *J* 6.8, 2.0 Hz, $CH_2C{\equiv}C$), 2.15 (3H, s, $COCH_3$), 2.29 (3H, s, $COCH_3$) and 2.37 (1H, ddt, *J* 7.2, 9.2, 2.0 Hz, CH_2CHC); δ_C (100 MHz; $CDCl_3$) 11.9 (CH_3CH_2), 15.5 (CH_2CHC), 16.4 (CH_2CHC), 20.3 ($CH_2C{\equiv}C$), 20.6 (CH_3CH_2), 25.8 ($COCH_3$), 26.3 (CH_2), 26.4 (CH_2), 27.7 ($COCH_3$), 29.1 (CH_2), 47.6 ($C(COCH_3)_2$), 73.3 ($C{\equiv}C$), 80.0 ($C{\equiv}C$), 199.8 ($COCH_3$) and 200.0 ($COCH_3$); HRMS (FAB) (M^+), found 235.1694, $C_{15}H_{23}O_2$ requires 235.1698 (–1.6 ppm); m/z 207 (29%), 176 (34%), 154 (54%), 136 (74%), 107 (34%), 91 (64%), 69 (60%) and 55 (100%).

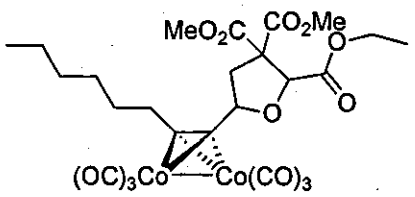
Dicobalt hexacarbonyl-1,1-diacetyl-2-(oct-1-ynyl)cyclopropane (224)



To a solution of dicobalt octacarbonyl (860 mg, 2.5 mmol, 1.2 eq) in dry DCM (20 mL), 1,1-diacetyl-2-(oct-1-ynyl)cyclopropane (560 mg, 2.1 mmol) was added and the reaction mixture was allowed to stir for 5 h at r.t. and under a nitrogen atmosphere. The crude product was then concentrated *in vacuo* and purified by flash chromatography on silica gel

(10% EtOAc/petrol) to give 1.07 g (1.9 mmol, 93%) of the *title compound* as a dark red oil; ν_{max} (film)/cm^{-1} 1221 (C–O), 1698 (C=O), 1743 (C=O), 2048 (C≡C) and 2933 (sp^3 CH); δ_H (400 MHz; $CDCl_3$) 0.84 (3H, t, *J* 7.2 Hz, CH_3CH_2), 1.16-1.59 (8H, m, CH_3CH_2), 1.75 (1H, dd, *J* 4.8, 8.0 Hz, C*H*HCHC), 2.84 (1H, dd, *J* 4.8, 9.2 Hz, C*H*HCHC), 2.45-2.63 (2H, m, CH_2C–C), 3.21 (1H, dd, *J* 8.0, 9.2 Hz, CH_2CHC), 3.71 (3H, s, CO_2CH_3) and 3.72 (3H, s, CO_2CH_3); δ_C (100 MHz; $CDCl_3$) 14.1 (CH_3CH_2), 22.6 (CH_2C–C), 25.3 (CH_3CH_2), 29.3 (CH_2), 31.6 (CH_2), 32.0 (CH_2), 32.4 (CH_2CHC), 33.7 (CH_2CHC), 39.7 ($C(CO_2CH_3)_2$), 53.1 ($2OCH_3$), 90.9 (C–C), 105.9 (C–C), 167.4 (CO_2CH_3), 169.5 (CO_2CH_3) and 199.7 ($CO_{complex}$); HRMS (FAB) (M^+–2CO), found 495.9971, $C_{19}H_{22}Co_2O_8$ requires 495.9979 (–1.4 ppm); m/z 496 (38%), 468 (16%), 440 (100%), 412 (43%) and 384 (16%).

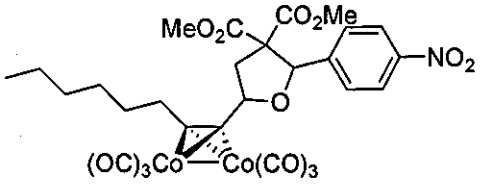
Dimethyl dihydro-2-(ethyl formate)-5-(oct-1-ynyl)furan-3,3(2H)-dicarboxylate dicobalt hexacarbonyl (225)



To a solution of 1,1-diacetyl-2-(oct-1-ynyl)cyclopropane dicobalthexacarbonyl (100 mg, 0.18 mmol) in DCM (5 mL) were added successively $BF_3.Et_2O$ (70 μL, 0.54 mmol, 3.0 eq) and ethyl glyoxylate (140 μL, 0.72 mmol, 50% in toluene, 4.0 eq) and the resulting mixture was allowed to stir for 40 min at r.t. under a nitrogen atmosphere. The crude mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel (8% EtOAc/petrol) to give 42 mg (0.06 mmol, 35%) of the *title compound* as a mixture of the 2 inseparable diastereoisomers in a 1:1 *cis:trans* ratio as a dark red oil; ν_{max} (film)/cm^{-1} 1219 (C–O), 1735 (C=O), 1744 (C=O), 2054 (C≡O) and 2927 (sp^3 CH); δ_C (100 MHz; $CDCl_3$) 13.9 ($CO_2CH_2CH_3$), 14.0 (CH_3CH_2), 22.6 (CH_3CH_2), 31.6 (CH_2), 31.8 (CH_2), 31.9 (CH_2), 33.8 (CH_2C–C), 40.9 (CH_2CHO), 41.9 (CH_2CHO), 49.4 ($C(CO_2Me)_2$), 53.1 (CO_2CH_3), 53.3 (CO_2CH_3), 53.5 (CO_2CH_3), 53.7 (CO_2CH_3), 61.5 ($CO_2CH_2CH_3$), 79.9 (CH_2CHO), 80.0 (CH_2CHO), 81.2 ($OCCO_2Et$), 81.4 ($OCCO_2Et$), 93.4 (C–C), 100.0 (C–C), 167.9 ($CO_2CH_2CH_3$), 168.4 (CO_2CH_3), 169.2 (CO_2CH_3), 169.3 (CO_2CH_3), 169.7 (CO_2CH_3) and 199.6 ($CO_{complex}$); assigned from combined spectrum, (i) *cis* diastereoisomer, δ_H (400 MHz;

$CDCl_3$) 0.83 (3H, t, *J* 6.8 Hz, CH_3CH_2), 1.22 (3H, t, *J* 7.2Hz, $CO_2CH_2CH_3$), 1.23-1.30 (4H, m, $2CH_2$), 1.32-1.44 (2H, m, CH_2), 1.49-1.60 (2H, m, CH_2), 2.30 (1H, dd, *J* 8.0, 13.2 Hz, CHHCHC), 2.71-2.78 (2H, m, CH_2C–C), 3.23 (1H, dd, *J* 7.6, 13.2 Hz, CHHCHC), 3.66 (3H, s, CO_2CH_3), 3.80 (3H, s, CO_2CH_3), 4.06-4.16 (2H, m, $CO_2CH_2CH_3$), 5.15 (1H, s, OCHCO$_2$Et) and 5.53 (1H, t, *J* 7.6 Hz, CH_2CHO); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 5.15 ppm and the proton at 5.53 ppm; assigned from combined spectrum, (ii) *trans* diastereoisomer, δ_H (400 MHz; $CDCl_3$) 0.83 (3H, t, *J* 6.8 Hz, CH_3CH_2), 1.18 (3H, t, *J* 7.2Hz, $CO_2CH_2CH_3$), 1.23-1.30 (4H, m, $2CH_2$), 1.32-1.44 (2H, m, CH_2), 1.49-1.60 (2H, m, CH_2), 2.69 (1H, dd, *J* 10.4, 12.8 Hz, CHHCHC), 2.71-2.78 (2H, m, CH_2C–C), 2.79 (1H, dd, *J* 5.6, 12.8 Hz, CHHCHC), 3.69 (3H, s, CO_2CH_3), 3.75 (3H, s, CO_2CH_3), 4.16 (2H, q, *J* 7.2 Hz, $CO_2CH_2CH_3$), 5.03 (1H, s, OCHCO$_2$Et) and 5.10 (1H, dd, *J* 10.4, 5.6 Hz, CH_2CHO); no apparent coupling was observed by nOe analysis between the proton at 5.03 ppm and the proton at 5.10 ppm suggesting a trans stereochemistry; no mass ion could be observed.

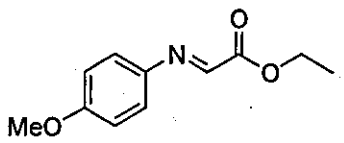
Dicobalt hexacarbonyl dimethyl dihydro-2-(4-nitrophenyl)-5-(oct-1-ynyl)furan-3,3(2H)-dicarboxylate (226)



To a solution of 1,1-diacetyl-2-(oct-1-ynyl)cyclopropane dicobalthexacarbonyl (50 mg, 0.09 mmol) in DCM (3 mL), $BF_3.Et_2O$ (25 μL, 0.18 mmol, 2.0 eq) and *p*-nitrobenzaldehyde (20 mg, 0.13 mmol, 1.5 eq) were successively added and the resulting mixture was allowed to stir for 4 h at r.t. under a nitrogen atmosphere. The crude mixture was then concentrated *in vacuo* and purified by flash chromatography (8% EtOAc/petrol) to give 42 mg (0.02 mmol, 30%) of the *title compound* as a mixture of the 2 inseparable diastereoisomers in a 1:1 *cis:trans* ratio as a dark red oil; ν_{max} (film)/cm^{-1} 1271 (C–O), 1700 (C=O), 1718 (C=O), 2139 (C≡O) and 2983 (sp^3 CH); assigned from combined spectrum, 1st eluted diastereoisomer, δ_H (400 MHz; $CDCl_3$) 0.89 (3H, t, *J* 6.8 Hz, CH_3), 1.25-1.75 (8H, m, $4CH_2$), 2.26 (1H, dd, *J* 8.4, 12.8 Hz, CHHCHO), 2.76-2.90 (3H, m, CH_2C–C), 3.24 (3H, s, CO_2CH_3), 3.29 (1H, dd, *J* 6.4, 12.8 Hz, CHHCHO), 3.81 (3H, s, CO_2CH_3), 5.75-5.85 (2H,

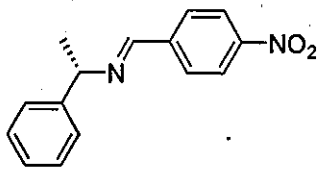
m, OC*H*–Ar + CH_2CHO), 7.65-7.73 (2H, m, ArC*H*) and 8.15-8.20 (2H, m, ArC*H)*; assigned from combined spectrum, 2nd eluted diastereoisomer, δ_H (400 MHz; $CDCl_3$) 0.89 (3H, t, *J* 6.8 Hz), 1.25-1.75 (8H, m, $4CH_2$), 2.76-2.90 (4H, m, CH_2C–C + CH_2CHO), 3.07 (3H, s, CO_2CH_3), 3.79 (3H, s, CO_2CH_3), 5.14 (1H, dd, *J* 6.4, 10.0 Hz, CH_2CHO), 5.70 (1H, s, OC*H*–Ar), 7.57-7.65 (2H, m, ArC*H*) and 8.04-8.14 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 14.0 (CH_3CH_2), 22.6 (CH_2CC), 29.3 (CH_3CH_2), 31.6 (CH_2), 31.9 (CH_2), 33.9 (CH_2), 42.3 ($CHCH_2C$), 52.5 ($COCH_3$), 53.3 ($COCH_3$), 66.4 ($C(CO_2CH_3)_2$), 78.6 (CCCH), 83.3 (CH_2CCH), 91.5 (*C*–C), 96.3 (*C*–C), 123.0 (2ArCH), 127.7 (2ArCH), 159.0 (CO_2CH_3), 164.5 (CO_2CH_3) and 205.5 ($CO_{complex}$); due to fast decomposition, Mass Spectrometry analysis could not be carried out.

Ethyl 2-(4-methoxyphenylimino)acetate (229)[129]



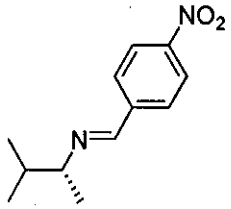
Ethyl glyoxylate (850 µL, 420 mg, 4.1 mmol, 50% in toluene) and 4Å molecular sieves (10.0 g) were added to a solution of *p*-anisidine (500 mg, 4.1 mmol) in diethyl ether (30 mL) and the reaction mixture was stirred at ambient temperature for 18 h under an atmosphere of nitrogen. The mixture was then filtered through a plug of celite and the solvent was removed *in vacuo* to yield the *title compound* as a brown oil (710 mg, 3.4 mmol, 84%); ν_{max} (film)/cm^{-1} 1745 (C=O), 1753 (C=O), 1624 (C=N), 2838 (sp^3 C–H), 2905 (sp^3 C–H), 2937 (sp^3 C–H) and 2980 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.42 (3H, t, *J* 7.1 Hz, $CO_2CH_2CH_3$), 3.85 (3H, s, OCH_3), 4.43 (2H, q, *J* 7.1 Hz, $CO_2CH_2CH_3$), 6.93-6.97 (2H, m, 2ArC*H*), 7.36-7.40 (2H, m, 2ArC*H*) and 7.95 (1H, s, N=C*H*); δ_C(100 MHz; $CDCl_3$) 14.2 ($CO_2CH_2CH_3$), 55.5 (OCH_3), 61.9 ($CO_2CH_2CH_3$), 114.5 (2ArCH), 123.7 (2ArCH), 141.3 (Ar*C*), 148 (N=*C*H), 160.5 (Ar*C*) and 163.6 ($CO_2CH_2CH_3$).

(S)-*N*-(4-Nitrobenzylidene)-1-phenylethanamine (230)



(R)-(+)-1-Phenylethylamine (1.00 g, 8.3 mmol) was added to a solution of *p*-nitrobenzaldehyde (1.26 g, 8.3 mmol) in diethyl ether (30 mL) and 4Å molecular sieves (10.0 g) were added. The reaction mixture was allowed to stir at r.t. for 18 h under a nitrogen atmosphere and was then filtered through a pad of celite and silica. The filtrate was concentrated *in vacuo* to give the *title compound* in 87% yield (1.82 g, 7.2 mmol) as a colourless oil; ν_{max} (film)/cm^{-1} 1651 (C=N), 2839 (sp^3 C–H), 2953 (sp^3 C–H) and 3003 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.53 (3H, d, *J* 6.6 Hz, CHC*H*$_3$), 4.53 (1H, q, *J* 6.6 Hz, C*H*CH$_3$), 7.17-7.21 (1H, m, ArC*H*), 7.26-7.31 (2H, m, ArC*H*), 7.33-7.36 (2H, m, ArC*H*), 7.84-7.88 (2H, m, ArC*H*), 8.16-8.19 (2H, m, ArC*H*) and 8.36 (1H, s, N=C*H*); δ_C(100 MHz; $CDCl_3$) 24.8 (CHCH$_3$), 70.1 (*C*HCH$_3$), 123.8 (2ArCH), 126.6 (2ArCH), 127.2 (ArCH), 128.6 (2ArCH), 129.0 (2ArCH), 141.9 (Ar*C*), 144.4 (Ar*C*), 149.0 (Ar*C*) and 157.1 (N=*C*H).

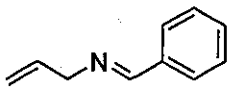
(R)-*N*-(4-Nitrobenzylidene)-3-methylbutan-2-amine (231)



(R)-(–)-3-Methylbutan-2-amine (660 μL, 500 mg, 5.7 mmol) was added to a solution of *p*-nitrobenzaldehyde (870 mg, 5.7 mmol) in diethyl ether (25 mL). 4Å molecular sieves were added (10.0 g) and the reaction mixture was allowed to stir overnight under a nitrogen atmosphere. The mixture was then filtered through a pad of celite and silica. The filtrate was concentrated *in vacuo* affording the *title compound* in 99% yield (1.26 g, 5.7 mmol) as a viscous yellow oil; ν_{max} (film)/cm^{-1} 1345 (C–NO_2), 1517 (C–NO_2), 1525 (C–NO_2), 1646 (C=N) and 2870 (sp^3 C–H), 2930 (sp^3 C–H) and 2965 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 0.79

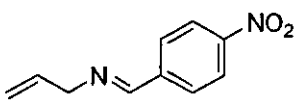
(3H, d, *J* 6.7 Hz, $CH(CH_3)_2$), 0.85 (3H, d, *J* 6.4 Hz, $CH(CH_3)_2$), 1.13 (3H, d, *J* 6.4 Hz, $CH(CH_3)$), 1.63-1.68 (1H, m, $CH(CH_3)_2$), 3.01 (1H, quint, *J* 6.4 Hz, $CH(CH_3)$), 7.81 (2H, d, *J* 8.8 Hz, ArCH), 8.15 (2H, d, *J* 8.8 Hz, ArCH) and 8.23 (1H, s, N=CH); δ_C(100 MHz; $CDCl_3$) 19.1 ($CH(CH_3)_2$), 19.2 ($CH(CH_3)_2$), 19.7 ($CH(CH_3)$), 34.4 ($(CH_3)_2CH$), 72.7 ($CH(CH_3)$), 123.7 (2ArCH), 128.7 (2ArCH), 142.1 (ArC), 148.8 (ArC) and 156.3 (N=CH).

(E)-*N*-Benzylideneprop-2-en-1-amine (232)[130]



Allyamine (2.2 mL, 1.70 g, 29.4 mmol) was added to a solution of benzaldehyde (3.0 mL, 3.12 g, 29.4 mmol) in diethyl ether (30 mL) and 4Å molecular sieves (10.0 g) were added. The reaction mixture was allowed to stir at r.t. for 18 h under a nitrogen atmosphere and was filtered through a pad of celite and silica. The filtrate was concentrated *in vacuo* to give the *title compound* in 97% (4.13 g, 28.5 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1620 (C=C), 1657 (C=N), 2980 (sp^3 C–H), 3024 (sp^2 C–H) and 3061 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 4.24-4.31 (2H, m, CH_2N), 5.19 (1H, m, CHH=CH), 5.28 (1H, dq, *J* 1.6, 16.8 Hz, CHH=CH), 6.05-6.17 (1H, m, CH_2=CH), 7.38-7.47 (3H, m, ArCH), 7.74-7.83 (2H, m, ArCH) and 8.29 (1H, s, N=CH); δ_C(100 MHz; $CDCl_3$) 63.8 (CH_2N), 116.0 (CH_2=CH), 127.9 (2ArCH), 129.0 (2ArCH), 130.7 (ArCH), 136.0 (CH_2=CH), 136.2 (ArC) and 162.0 (NCH).

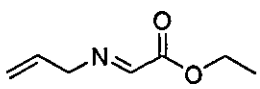
***N*-(4-Nitrobenzylidene)prop-2-en-1-amine (233)**



Allyamine (2.0 mL, 1.51 g, 26.5 mmol) was added to a solution of *p*-nitrobenzaldehyde (4.00 g, 26.5 mmol) in diethyl ether (80 mL) and 4Å molecular sieves (10.0 g) were added. The reaction mixture was allowed to stir at r.t. for 18 h under a nitrogen atmosphere and was then filtered through a pad of celite and silica. The filtrate was concentrated *in vacuo* to give the *title compound* in 98% yield (4.93 g, 25.9 mmol) as a yellow solid; mp 64-67°C; ν_{max}

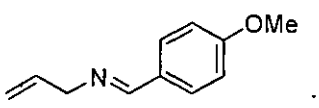
(film)/cm^{-1} 1342 (NO_2), 1370 (NO_2), 1647 (C=N), 2871 (sp^3 C–H), 2934 (sp^3 C–H), 2971 (sp^3 C–H) and 3078 (sp^2 CH); δ_H(400 MHz; $CDCl_3$) 4.24-4.31 (2H, m, CH_2N), 5.19 (1H, dq, *J* 1.6, 10.4 Hz, C*H*H=CH), 5.24 (1H, dq, *J* 1.6, 17.2 Hz, C*H*H=CH), 5.99-6.10 (1H, m, CH_2=C*H*), 7.85-7.91 (2H, m, ArC*H*), 8.20-8.25 (2H, m, ArC*H*) and 8.36 (1H, s, NC*H*); δ_C(100 MHz; $CDCl_3$) 63.4 (*C*H_2N), 115.9 (CH*C*H_2), 123.3 (2 Ar*C*H), 128.6 (2 Ar *C*H), 135.5 (CH_2*C*H), 141.6 (Ar*C*CH), 148.8 (Ar*C*NO_2) and 162.0 (NCH); HRMS (EI) (M^+), found 190.0745, $C_{10}H_{10}N_2O_2$ requires 190.0742 (+0.4 ppm); m/z 190 (56%), 173 (100%), 149 (32%) and 68 (15%).

Ethyl 2-(allylimino)acetate (234)



Allyamine (2.5 mL, 1.91 g, 33.4 mmol) was added to a solution of ethyl glyoxylate (6.6 mL, 33.4 mmol, 50% in toluene) in diethyl ether (100 mL) and 4Å molecular sieves (20.0 g) were added. The reaction mixture was allowed to stir at r.t. for 18 h under a nitrogen atmosphere and was then filtered through a pad of celite and silica. The filtrate was concentrated *in vacuo* to give the *title compound* in 98% yield (4.60 g, 32.7 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1645 (C=N), 1725 (C=O) and 3025 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.31 (3H, t, *J* 7.2 Hz, $CO_2CH_2CH_3$), 4.23-4.28 (2H, m, CH_2N), 4.30 (2H, q, *J* 7.2 Hz, $CO_2CH_2CH_3$), 5.14-5.16 (1H, m, C*H*H=CH), 5.16-5.22 (1H, m, C*H*H=CH), 5.90-6.04 (1H, m, CH_2=C*H*) and 7.65-7.70 (1H, m, N=C*H*); δ_C(100 MHz; $CDCl_3$) 14.1 (CH_3), 53.3 (*C*H_2N), 61.8 ($CO_2CH_2CH_3$), 117.9 (*C*H_2=CH), 133.6 (CH_2=*C*H), 154.2 (N=*C*H) and 168.6 (*C*O).

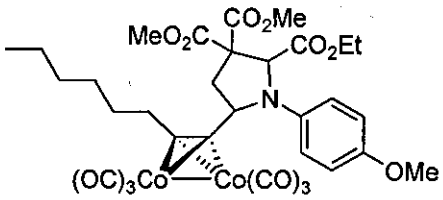
***N*-(4-Methoxybenzylidene)prop-2-en-1-amine (235)**[130,131]



Allyamine (2.2 mL, 1.67 g, 29.3 mmol) was added to a solution of *p*-anisaldehyde (3.6 mL, 3.99 g, 29.3 mmol) in diethyl ether (100 mL) and 4Å molecular sieves (20.0 g) were added.

The reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere and the resulting mixture was filtered through a pad of celite and silica. The filtrate was concentrated *in vacuo* to give the *title compound* in 99% yield (5.09 g, 29.0 mmol); ν_{max} (film)/cm^{-1} 1644 (C=N), 2835 (sp^3 C–H), 2958 (sp^3 C–H), 3007 (sp^2 C–H) and 3075 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 3.74 (3H, s, OCH_3), 4.15-4.20 (2H, m, CH_2N), 5.11 (1H, dq, *J* 1.6, 10.4 Hz, C*H*H=CH), 5.20 (1H, dq, *J* 1.6, 17.2 Hz, C*H*H=CH), 5.97-6.10 (1H, m, CH_2=C*H*), 6.83-6.90 (2H, m, ArC*H*), 7.68-7.73 (2H, m, ArC*H*) and 8.15 (1H, s, N=C*H*); δ_C(100 MHz; $CDCl_3$) 55.5 (OCH_3), 63.5 (CH_2N), 113.9 (2Ar*C*H), 115.8 (CH_2=CH), 129.1 (Ar*C*), 129.5 (2Ar*C*H), 136.2 (CH_2=*C*H), 161.3 (N=*C*H) and 161.7 ($COCH_3$); HRMS (EI) (M^+), found 175.0999, $C_{11}H_{13}NO$ requires 175.0997 (+0.3 ppm); m/z 175 (63%), 174 (100%), 121 (32%) and 41 (34%).

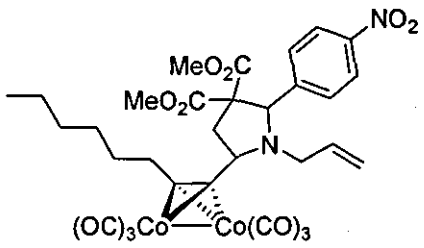
2-Ethyl 3,3-dimethyl 1-(4-nitrophenyl)pyrrolidine-2,3,3-tricarboxylate-5-oct-8-yne (236)



Ethyl 2-(4-methoxyphenylimino)acetate (53 mg, 0.25 mmol, 2.0 eq) was added to a solution of dicobalt hexacarbonyl-1,1-diacetyl-2-(oct-1-ynyl)cyclopropane (40 mg, 0.13 mmol) in dry DCM (3 mL) with molecular sieves. $BF_3.Et_2O$ (50 μL, 54 mg, 0.38 mmol, 3.0 eq) was added and the reaction mixture was allowed to stir at r.t. under a nitrogen atmosphere for 3 h. The resulting mixture was then filtered through a pad of celite and silica. The solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (6% EtOAc/petrol) affording the 2 inseparable diastereoisomers of the *title compound* in 39% yield (37 mg, 0.05 mmol) as a dark red oil with a 1:1 *cis:trans* ratio; ν_{max} (film)/cm^{-1} 1736 (C=O), 1744 (C=O), 1750 (C=O) and 2054 (C≡O); assigned from combined spectrum, 1st eluted diastereoisomer, δ_H(400 MHz; $CDCl_3$) 0.81 (3H, t, *J* 7.2 Hz, $CH_2CH_2CH_3$), 1.05-1.58 (11H, m, $4CH_2$ + $CO_2CH_2CH_3$), 2.44-2.59 (2H, m, CH_2C–C), 2.64 (1H, dd, *J* 4.8, 14.0 Hz, C*H*HCH), 3.49 (1H, dd, *J* 9.4, 14.0 Hz C*H*HCH), 3.66 (3H, s, CO_2CH_3), 3.67 (3H, s, CO_2CH_3), 3.78 (3H, s, $ArOCH_3$), 4.11-4.20 (2H, m, $COCH_2CH_3$), 5.03 (1H, s, NC*H*CO_2Et)

5.38 (1H, dd, *J* 4.8, 9.4 Hz, CH_2CHN); assigned from combined spectrum, 2nd eluted diastereoisomer, δ_H(400 MHz; $CDCl_3$) 0.81 (3H, t, *J* 7.2 Hz, $CH_2CH_2CH_3$), 1.05-1.58 (11H, m, $4CH_2+CO_2CH_2CH_3$), 2.44-2.59 (2H, m, CH_2C–C), 2.87 (1H, dd, *J* 6.0, 12.8 Hz, CHHCH), 3.09 (1H, dd, *J* 10.4, 12.8 Hz, CHHCH), 3.66 (3H, s, CO_2CH_3), 3.67 (3H, s, CO_2CH_3), 3.78 (3H, s, $ArOCH_3$), 4.11-4.20 (2H, m, $COCH_2CH_3$), 4.58 (1H, s, $NCHCO_2Et$), 4.96-5.04 (1H, m, CH_2CHN), 6.74-6.78 (2H, m, ArCH), 6.88-6.92 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 13.0 ($2CH_3CH_2$), 13.6 ($2CO_2CH_2CH_3$), 21.5 ($2CH_3CH_2$), 28.7 ($2CH_2$), 30.5 ($2CH_2$), 31.2 ($2CH_2$), 33.4 ($2CH_2C$–C), 40.3 (CH_2CHN), 43.0 (CH_2CHN), 51.9 ($2CO_2CH_3$), 52.5 ($2CO_2CH_3$), 60.4 ($2ArOCH_3$), 60.8 ($2CO_2CH_2CH_3$), 65.4 ($2C(CO_2Me)_2$), 70.3 (CH_2CHN), 70.7 (CH_2CHN), 78.5 ($NCHCO_2Et$), 78.7 ($NCHCO_2Et$), 96.3 (2C–C), 100.5 (2C–C), 113.2 (4ArCH), 116.9 (4ArCH), 141.2 (2NCAr), 153.1 ($2ArCOCH_3$), 169.8 ($2CO_2CH_3$), 170.0 ($2CO_2CH_3$), 171.2 ($2CO_2CH_2CH_3$) and 199.9 ($CO_{complex}$); HRMS (FAB) (M^+–2CO), found 703.0854, $C_{30}H_{35}Co_2NO_{11}$ requires 703.0874 (–0.4 ppm); m/z 703 (3%), 675 (21%), 647 (100%), 619 (41%) and 591 (36%).

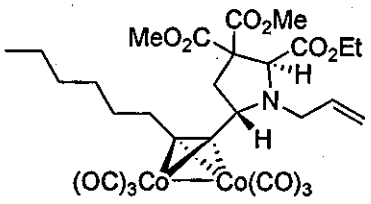
Dimethyl 1-allyl-2-(4-nitrophenyl)-5-(oct-1-ynyl)pyrrolidine-3,3-dicarboxylate dicobalt hexacarbonyl (237)



N-(4-Nitrobenzylidene)prop-2-en-1-amine (410 mg, 2.2 mmol, 8.0 eq) was added to a solution of dicobalt hexacarbonyl-1,1-diacetyl-2-(oct-1-ynyl)cyclopropane (150 mg, 0.3 mmol) in dry DCM (2.5 mL) with molecular sieves. $BF_3.Et_2O$ (100 µL, 170 mg, 1.2 mmol, 3.0 eq) was added and the reaction mixture was allowed to stir at r.t. under a nitrogen atmosphere for 20 h. The resulting mixture was then filtered through a pad of celite and silica and the solvent was removed *in vacuo*. The residue was taken up in methanol (15 mL) and a solution of sodium borohydride (170 mg, 4.4 mmol, 16.0 eq) in cold water (3 mL) was added. The resulting mixture was allowed to stir for one hour at r.t. and ethyl acetate (10 mL) was slowly added. The two resulting layers were separated and the aqueous layer was

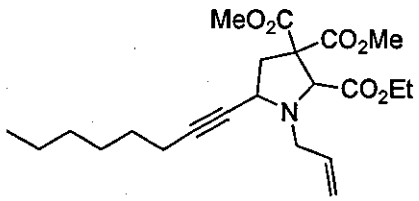
extracted with ethyl acetate (2×20 mL). The organic extracts were combined and dried over magnesium sulfate. The solvent was removed *in vacuo* and the residue was purified by flash chromatography (6% EtOAc/petrol) affording the 2 diastereoisomers of the *title compound* as a dark red oil in 60% yield (120 mg, 0.2 mmol) with a 2/3 *cis:trans* ratio; ν_{max} (film)/cm^{-1} 1277 (C–N), 1734 (C=O), 2020 (C≡O), 2047 (C≡O), 2088 (C≡O), 2656 (sp^3 C–H), 2930 (sp^3 C–H) and 2954 (sp^3 C–H); assigned from combined spectrum, (i) major *trans* diastereoisomer, δ_H(400 MHz; $CDCl_3$) 0.83 (3H, *J* 7.2 Hz, C*H*$_3$CH$_2$), 2.12-2.30 (4H, m, 2CH$_2$), 1.31-1.44 (2H, m, CH$_2$), 1.52-1.66 (2H, m, CH$_2$), 2.48 (1H, dd, *J* 6.0, 13.2 Hz, C*H*HCHN), 2.76-2.84 (2H, m, C*H*$_2$C–C), 2.87 (1H, dd, *J* 10.8, 13.2 Hz, C*H*HCHN), 3.07 (3H, s, CO$_2$C*H*$_3$), 3.31 (2H, dd, *J* 7.2, 13.6 Hz, NC*H*$_2$), 3.76 (3H, s, CO$_2$C*H*$_3$), 4.01 (1H, dd, *J* 6.0, 10.8 Hz, CH$_2$C*H*N), 4.92-5.03 (2H, m, CH$_2$CH=C*H*$_2$), 5.55-5.66 (1H, m, CH$_2$C*H*=CH$_2$), 5.76 (1H, s, NC*H*–Ar), 7.45-7.49 (1H, m, ArCH), 7.60-7.64 (1H, m, ArCH) and 8.04-8.13 (2H, m, 2ArCH); no apparent coupling was observed by nOe analysis between the proton at 4.01 ppm and the proton at 5.76 ppm suggesting a *trans* stereochemistry; assigned from combined spectrum, (ii) minor *cis* diastereoisomer, δ_H(400 MHz; $CDCl_3$) 0.83 (3H, *J* 7.2 Hz, C*H*$_3$CH$_2$), 2.12-2.30 (4H, m, 2CH$_2$), 1.31-1.44 (2H, m, CH$_2$), 1.52-1.66 (2H, m, CH$_2$), 2.18 (1H, dd, *J* 8.4, 13.2 Hz, C*H*HCHN), 2.76-2.84 (2H, m, C*H*$_2$C–C), 3.18 (3H, s, CO$_2$C*H*$_3$), 3.23 (1H, dd, *J* 6.8, 13.2 Hz, C*H*HCHN), 3.31 (2H, dd, *J* 7.2, 13.6 Hz, NC*H*$_2$), 3.74 (3H, s, CO$_2$C*H*$_3$), 4.92-5.03 (2H, m, CH$_2$CH=C*H*$_2$), 5.55-5.66 (1H, m, CH$_2$C*H*=CH$_2$), 5.70 (1H, s, NC*H*–Ar), 5.75 (1H, dd, *J* 6.8, 8.4 Hz, CH$_2$C*H*N), 7.45-7.49 (1H, m, ArC*H*), 7.60-7.64 (1H, m, ArC*H*) and 8.04-8.13 (2H, m, 2ArC*H*); a weak coupling between the proton at 5.70 ppm and the proton at 5.75 ppm was observed by nOe analysis suggesting a *cis* stereochemistry; δ_C(100 MHz; $CDCl_3$) 14.0 (2*C*H$_3$CH$_2$), 22.6 (2CH$_3$*C*H$_2$), 29.3 (2*C*H$_2$), 31.6 (*C*H$_2$), 31.7 (*C*H$_2$), 32.0 (2*C*H$_2$), 34.4 (2*C*H$_2$C–C), 40.7 ((i)*C*H$_2$CHN), 43.0 ((ii)*C*H$_2$CHN), 52.3 (CO$_2$*C*H$_3$), 52.4 (CO$_2$*C*H$_3$), 53.3 (CO$_2$*C*H$_3$), 53.4 (CO$_2$*C*H$_3$), 53.6 (2N*C*H$_2$), 61.6 ((i)CH$_2$*C*HN), 66.0 (*C*(CO$_2$Me)$_2$), 66.4 (*C*(CO$_2$Me)$_2$), 79.4 ((ii)CH$_2$*C*HN), 82.4 ((i)N*C*HCAr), 83.2 ((ii)N*C*HCAr), 97.0 (2*C*–C), 100.9 (2*C*–C), 119 (2CH$_2$CH=*C*H$_2$), 123.0 (4Ar*C*H), 129.7 (4Ar*C*H), 132.0 (2CH$_2$*C*H=CH$_2$), 168.4 (*C*O$_2$Me), 169.5 (*C*O$_2$Me), 170.9 (*C*O$_2$Me), 171.6 (*C*O$_2$Me) and 199.9 (C≡O complex); HRMS (FAB) (M$^+$–4CO), found 630.0727, $C_{28}H_{32}N_2O_9Co_2$ requires 630.0721 (+0.9 ppm); m/z 630 (59%), 602 (30%), 574 (18%), 496 (26%) and 440 (100%).

***trans*-2-Ethyl 3,3-dimethyl 1-allyl-5-(oct-1-ynyl)pyrrolidine-2,3,3-tricarboxylate dicobalt hexacarbonyl (238)**



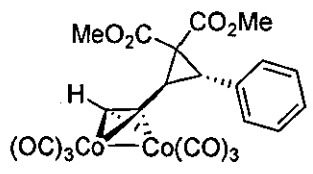
Ethyl 2-(allylimino)acetate (450 mg, 3.2 mmol, 8.0 eq) was added to a solution of dicobalt hexacarbonyl-1,1-diacetyl-2-(oct-1-ynyl)cyclopropane (220 mg, 0.4 mmol) in dry DCM (3 mL) with molecular sieves (500 mg). $BF_3.Et_2O$ (150 µL, 170 mg, 1.2 mmol, 3.0 eq) was then added and the reaction mixture was allowed to stir at r.t. under a nitrogen atmosphere for 17 h. The resulting mixture was then filtered through a pad of celite and silica. The solvent was removed *in vacuo* and the residue was purified by flash chromatography on silica gel (6% EtOAc/petrol) affording the *trans* diastereosimer only of the *title compound* in 21% yield (60 mg, 0.1 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1738 (C=O), 2018 (C≡O), 2046 (C≡O), 2087 (C≡O) and 2930 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 0.84 (3H, *J* 6.8 Hz, CH_3CH_2), 1.69 (3H, t, *J* 7.2 Hz, $CO_2CH_2CH_3$), 2.22-2.30 (4H, m, $2CH_2$), 1.31-1.42 (2H, m, CH_2), 1.50-1.62 (2H, m, CH_2), 2.63 (1H, dd, *J* 5.6, 12.8 Hz, CHHCHN), 2.76 (2H, t, *J* 8.0 Hz,CH_2C–C), 2.81 (1H, dd, *J* 11.2, 12.8 Hz, CHHCHN), 3.49-3.57 (1H, dd, *J* 8.8, 14.0 Hz, NCHH), 3.49-3.57 (1H, m, NCHH), 3.61 (3H, s CO_2CH_3), 3.75 (3H, s, CO_2CH_3), 3.94-4.14 (3H, m, CH_2CHN + $CO_2CH_2CH_3$), 4.25 (1H, s, $NCHCO_2Et$), 5.09 (1H, br d, *J* 10.0 Hz, CH_2CH=CHH), 5.19 (1H, br d, *J* 16.8 Hz, CH2CH=CHH) and 5.76-5.91 (1H, m, CH_2CH=CH_2); δ_C(100 MHz; $CDCl_3$) 14.0 ($2CH_3$), 22.6 (CH_3CH_2), 29.3 (CH_2), 31.6 (CH_2), 31.9 (CH_2), 34.0 (CH_2C–C), 40.7 (CH_2CHN), 52.8 (CO_2CH_3), 53.5 (CO_2CH_3), 57.4 (NCH_2), 60.9 ($CO_2CH_2CH_3$), 64.2 (CH_2CHN), 66.4 ($C(CO_2Me)_2$), 69.0 ($NCHCO_2Et$), 98.8(C–C), 100.6 (C–C), 118.0 (CH_2CH=CH_2), 134.9 (CH_2CH=CH_2), 168.4 (CO_2Et), 170.6 (CO_2Me), 171.3 (CO_2Me) and 200.0 ($CO_{complex}$); no apparent coupling was observed by nOe analysis between the proton (CH_2CHN) present in the multiplet 3.94-4.14 ppm and the proton at 4.25 ppm, suggesting a probable *trans* stereochemistry; no mass ion could not be observed.

2-Ethyl 3,3-dimethyl 1-allyl-5-(oct-1-ynyl)pyrrolidine-2,3,3-tricarboxylate (242)



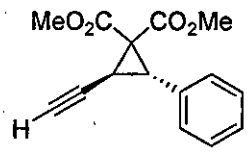
In a 50 mL round-bottom flask, dicobalt hexacarbonyl-2-ethyl 3,3-dimethyl 1-allyl-5-(oct-1-ynyl)pyrrolidine-2,3,3-tricarboxylate (35 mg, 0.05 mmol) was adsorbed on silica gel (2.5 g) and the reaction flask was allowed to agitate on a rotary evaporator at 40°C at atmospheric pressure. When the dark red colour disappeared (20 min), the silica was washed on a sinter funnel with ethyl acetate (20 mL). The filtrate was concentrated *in vacuo* affording the *trans* isomer of the *title compound* in 60% yield (13 mg, 0.03 mmol); ν_{max} (film)/cm^{-1} 1210 (C–N), 1742 (C=O), 2934 (sp^3 C–H), 2955, (sp^3 C–H) and 3082 (sp^2 CH); δ_H(400 MHz; $CDCl_3$) 0.81 (3H, t, *J* 6.8 Hz, CH_3CH_2), 1.12-1.34 (9H, m, $CO_2CH_2CH_3$ + $3CH_2$), 1.36-1.47 (2H, m, $CH_2C{\equiv}C$), 2.10 (2H, dt, *J* 2.0, 6.8Hz, CH_3CH_2), 2.51 (1H, dd, *J* 6.4, 13.2 Hz, CHHCHN), 2.71 (1H, dd, 10.8, 13.2 Hz, CHHCHN), 3.61 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 4.02-4.12 (4H, m, $CO_2CH_2CH_3$ + CH_2CHN + $NCHCO_2Et$), 5.06-5.12 (1H, m, CH=CHH), 5.13-5.21 (1H, m, CH=CHH) and 5.76-5.90 (1H, m $CH_2CH{=}CH_2$); δ_C(100 MHz; $CDCl_3$) 14.0 (CH_3CH_2), 14.1 ($CO_2CH_2CH_3$), 18.8 ($CH_2C{\equiv}C$), 22.5 (CH_3CH_2), 28.5 (CH_2), 28.6 (CH_2), 29.7 (CH_2), 31.3 (CH_2), 39.8 (CH_2CHN), 52.9 (CH_2CHN), 53.3 (OCH_3), 53.5 (OCH_3), 61.2 ($CO_2CH_2CH_3$), 68.1 ($NCHCO_2Et$), 118.3 ($CH_2CH{=}CH_2$) and 133.4 ($CH{=}CH_2$); due to the weakness of the sample, quaternaries, acetylenics and carbonyls are missing; no mass ion could be observed.

(2R,3S) and (2S,3R)-Dicobalt hexacarbonyl dimethyl 2-ethynyl-3-phenylcyclopropane-1,1-dicarboxylate (*rac*-249)



Dicobalt octacarbonyl (1.40 g, 4.1 mmol, 1.1 eq) was added to a solution of (2R,3S) and (2S,3R)-dimethyl 2-ethynyl-3-phenylcyclopropane-1,1-dicarboxylate (960 mg, 3.7 mmol) in dry DCM (10 mL). The resulting mixture was stirred at r.t. under a nitrogen atmosphere for 4 h and the solvent was evaporated *in vacuo*. The residue was purified by flash chromatography on silica gel (5% EtOAc/Petrol) to give the *title compound* in 96% yield (1.95 g, 3.6 mmol) as dark red crystals; mp 68-70°C; ν_{max} (film)/cm^{-1} 1121 (C–O), 1295 (C–O), 1435 (C–O), 1736 (C=O), 2094 (C≡O) and 2955 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 3.39 (3H, s, OC*H*$_3$), 3.40 (1H, d, *J* 8.0 Hz, C*H*–Ar), 3.73 (3H, s, OC*H*$_3$), 3.80 (1H, d, *J* 8.0 Hz, C–CC*H*) and 7.12-7.28 (5H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 34.5 (HC–*C*CH), 42.3 (*C*H–Ar), 49.2 (*C*(CO$_2$CH$_3$)$_2$), 52.7 (OCH$_3$), 53.1 (OCH$_3$), 69.8 (H*C*–C), 89.6 (HC–*C*), 127.8 (Ar*C*H), 128.1 (2Ar*C*H), 128.5 (2Ar*C*H), 133.8 (Ar*C*), 166.1 (*C*O$_2$CH$_3$), 167.2 (*C*O$_2$CH$_3$) and 199.3 (*C*O$_{complex}$); HRMS (FAB) (M$^+$–2CO), found 487.9361, $C_{19}H_{14}Co_2O_8$ requires 487.9352 (+1.8 ppm); m/z 488 (96%), 460 (10%), 432 (30%), 404 (100%) and 376 (21%); $[\alpha]_D^{22}$= 0.0 (*c* = 0.10 g/mL in $CHCl_3$).

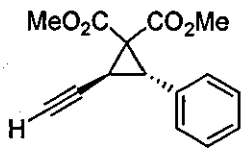
(2R,3S)-Dimethyl 2-ethynyl-3-phenylcyclopropane-1,1-dicarboxylate (250)



Dimethyl-1diazo-2oxopropylphosphonate (290 mg, 1.5 mmol, 2.0 eq) and potassium carbonate (200 mg, 1.5 mmol, 2.0 eq) were successively added to a solution of (2R,3S)-dimethyl 2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (200 mg, 0.7 mmol) in dry methanol (3 mL) at 0°C. The resulting mixture was allowed to stir for 4 h at r.t. (TLC monitoring) and was then filtered through a pad of celite. The solvent was concentrated *in vacuo* and the crude product was purified by flash chromatography on silica gel to give the *title compound* in 30% yield (60 mg, 0.2 mmol) as a yellow oil; $[\alpha]_D^{22}$= –41.6 (*c* = 0.10 g/mL in $CHCl_3$); ν_{max} (film)/cm^{-1} 1121 (C–O), 1297 (C–O), 1437 (C–O), 1731 (C=O), 1736 (C=O), 2952 (sp^3 C–H), 3031 (sp^2 ArC–H) and 3288 (sp C–H); δ_H(400 MHz; $CDCl_3$) 2.08 (1H, d, *J* 2.4 Hz, *H*C≡C), 3.04 (1H, dd, *J* 2.4, 7.6 Hz, HC≡CC*H*), 3.44 (3H, s, OC*H*$_3$), 3.51 (1H, d, *J* 7.6 Hz, C*H*–Ar), 3.86 (3H, s, OC*H*$_3$), 7.18-7.72 (5H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 19.3 (HC≡*C*CH), 37.3 (*C*H–Ar), 44.0 (*C*(CO$_2$CH$_3$)$_2$), 52.7 (OCH$_3$), 53.1 (OCH$_3$),

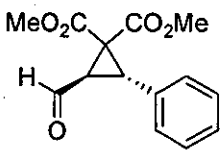
69.4 (HC≡C), 79.0 (HC≡*C*), 127.8 (Ar*C*H), 128.3 (2Ar*C*H), 128.4 (2Ar*C*H), 133.0 (Ar*C*), 165.7 (*C*O_2CH_3) and 166.7 (*C*O_2CH_3); HRMS (FAB) ($M+H^+$), found 259.0970, $C_{15}H_{15}O_4$ requires 259.0970 (±0.0 ppm); m/z 259 (100%), 227 (43%), 195 (42%), 167 (27%) and 154 (20%).

Racemic-Dimethyl 2-ethynyl-3-phenylcyclopropane-1,1-dicarboxylate (*rac*-250)



Dimethyl-1diazo-2oxopropylphosphonate (2.70 g, 14.1 mmol, 2.0 eq) and potassium carbonate (1.94 g, 14.1 mmol, 2.0 eq) were successively added to a solution of racemic-dimethyl 2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (1.84 g, 7.0 mmol) in dry methanol (30 mL) at 0°C. The resulting mixture was allowed to stir for 4 h at r.t. (TLC monitoring) and was then filtered through a pad of celite. The solvent was concentrated *in vacuo* and the crude product was purified by flash chromatography on silica gel to give the *title compound* in 54% yield (980 mg, 3.8 mmol) as a yellow oil; for data see (2R,3S)-dimethyl 2-ethynyl-3-phenylcyclopropane-1,1-dicarboxylate; $[\alpha]_D^{22}$= 0.0 (*c* = 0.10 g/mL in $CHCl_3$).

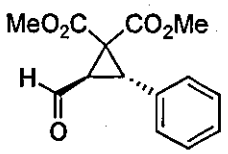
(2R,3S)-Dimethyl 2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (251)[93]



To a mixture of dimethyl bromomalonate (450 µL, 650 mg, 2.8 mmol), triethylamine (470 µL, 340 mg, 3.4 mmol, 1.5 eq) and trimethylsilyldiphenyl((S)-pyrrolidin-2-yl)methanol (100 mg, 0.3 mmol, 10 mol%) in DCM (8 mL) at 0°C was added *trans*-cinnamaldehyde (470 µL, 490 mg, 3.7 mmol, 1.3 eq). The resulting orange mixture was allowed to stir for an hour at 0°C whilst a precipitate formed. The reaction mixture was slowly warmed up to r.t. and was allowed to stir for a further 20 h until completion of the reaction (TLC monitoring). The

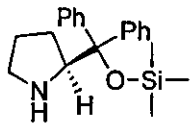
crude mixture was washed with water (10 mL), extracted with DCM (2×15 mL) and finally dried over magnesium sulfate. The solvent was removed *in vacuo* and the crude product was purified by flash chromatography on silica gel (5% EtOAc/Petrol) to give the *title compound* in 85% yield (610 mg, 2.3 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1292 (C–O), 1736 (C=O), 2848 (sp^3 C–H) and 2954 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 3.32 (1H, dd, *J* 4.4, 7.6 Hz, C*H*CHO), 3.39 (3H, s, OC*H*$_3$), 3.84 (4H, m, OC*H*$_3$ + C*H*–Ar), 7.22-7.31 (5H, m, ArCH) and 9.42 (1H, d, *J* 4.4 Hz, C*H*O); δ_C(100 MHz; $CDCl_3$) 35.7 (*C*H–Ar), 38.2 (CHO*C*H), 44.6 (*C*(CO$_2$CH$_3$)$_2$), 52.9 (O*C*H$_3$), 53.4 (O*C*H$_3$), 128.0 (Ar*C*H), 128.2 (2Ar*C*H), 128.5 (2Ar*C*H), 132.1 (Ar*C*), 165.0 (*C*O$_2$CH$_3$), 166.5 (*C*O$_2$CH$_3$) and 196.1 *C*HO); $[\alpha]_D^{22}$= –50.0 (*c* = 0.10 g/mL in $CHCl_3$) (*lit.* $[\alpha]_D^{22}$= –15.1 (*c* = 0.10 g/mL in $CHCl_3$)).

Racemic-dimethyl 2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (*rac*-251)[93]



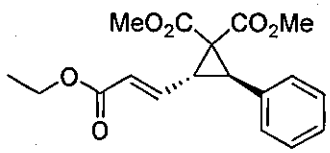
To a mixture of dimethyl bromomalonate (1.1 mL, 1.60 mg, 7.6 mmol), triethylamine (1.2 mL, 840 mg, 8.3 mmol, 1.1 eq) and diethylamine (160 µL, 110 mg, 1.5 mmol, 20 mol%) in DCM (20 mL) at 0°C was added *trans*-cinnamaldehyde (1.2 mL, 1.20 g, 9.1 mmol, 1.2 eq). The resulting orange mixture was allowed to stir for an hour at 0°C whilst a precipitate formed. The reaction mixture was slowly warmed up to r.t. and was allowed to stir for a further 20 h until completion of the reaction (TLC monitoring). The crude mixture was washed with water (20 mL), extracted with DCM (2×20 mL) and finally dried over magnesium sulfate. The solvent was removed *in vacuo* and the crude product was purified by flash chromatography on siligal gel (5% EtOAc/Petrol) to give the *title compound* in 69% yield (1.37 g, 5.2 mmol) as a yellow oil; for characterisation, see (2R,3S)-dimethyl 2-formyl-3-phenylcyclopropane-1,1-dicarboxylate; $[\alpha]_D^{22}$ = 0.0 (*c* = 0.10 g/mL in $CHCl_3$).

Trimethylsilyldiphenyl((S)-pyrrolidin-2-yl)methanol (253)[132]



Trimethylsilyl chloride (130 μL, 110 mg, 1.0 mmol, 1.3 eq) was added to a solution of (S)-(–)-α,α-diphenyl-2-pyrrolidinemethanol (200 mg, 0.8 mmol) and triethylamine (330 μL, 240 mg, 2.4 mmol, 3.0 eq) in DCM (4 mL) at 0°C. The resulting mixture was allowed to stir for 16 h (TLC monitoring) at r.t. whilst a white precipitate formed. The reaction was quenched with water (5 mL) and washed with a saturated solution of sodium bicarbonate (10 mL). The aqueous layer was extracted with DCM (3×5 mL) and the combined organic extracts were dried over magnesium sulfate. Solvent removal afforded the *title compound* in 98% yield (250 mg, 0.8 mmol) as a colourless oil; ν_{max} (film)/cm^{-1} 2945 (sp^3 C–H), 2980 (sp^3 C–H), 3330 (C–NH); δ_H(400 MHz; $CDCl_3$) 0.09 (9H, s, Si(C*H*$_3$)$_3$), 1.32-1.44 (1H, m, C*H*H), 1.51-1.64 (3H, m, C*H*H + C*H*$_2$), 2.74-2.90 (2H, m, C*H*$_2$NH), 4.04 (1H, t, *J* 7.2 Hz, C*H*CH$_2$), 7.16-7.31 (6H, m, ArC*H*), 7.32 (2H, m, ArC*H*) and 7.44-7.49 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 0.0 (Si(*C*H$_3$)$_3$), 22.8 (*C*H$_2$), 25.3 (*C*H$_2$), 45.0 (*C*H$_2$NH), 63.2 (*C*HCH$_2$), 80.9 (*C*OSi(CH$_3$)$_3$), 124.5 (2Ar*C*H), 124.7 (2Ar*C*H), 125.4 (4Ar*C*H), 125.4 (2Ar*C*H), 126.2 (2Ar*C*H), 140.0 (Ar*C*) and (Ar*C*); $[\alpha]_D^{22}$= –12.8 (*c* = 0.10 g/mL in $CHCl_3$) (*lit.* $[\alpha]_D^{22}$= –8.7 (*c* = 0.10 g/mL in $CHCl_3$)).

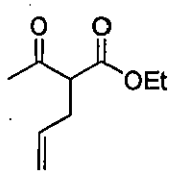
(2S,3R) and (2R,3S)-Dimethyl 2-((E)-2-(ethoxycarbonyl)vinyl)-3-phenylcyclopropane-1,1-dicarboxylate (254)



Buthyl lithium (3.0 mL, 7.6 mmol, 2.5 M in THF), was added dropwise to a solution of (ethoxycarbonylmethyl)triphenylphosphonium chloride (2.93 g, 7.6 mmol) in THF (30 mL) at 0°C and the reaction mixture was allowed to stir for 30 min. Racemic dimethyl 2-formyl-3-phenylcyclopropane-1,1-dicarboxylate (2.00 g, 7.6 mmol) in THF (20 mL) was then added

and the resulting mixture was stirred for a further 20 min. The reaction was then quenched with water (5 mL) and brine (20 mL). The crude mixture was extracted with ethyl acetate (3×20 mL) and dried over magnesium sulfate. Subsequent purification by flash chromatography afforded the *title compound* in 62% yield (1.56 g, 4.7 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1294(C–O), 1434 (C–O), 1730 (C=O), 1736 (C=O), 2982 (sp^3 C–H) and 2953 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.29 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 3.25 (1H, dd, *J* 8.0, 9.6 Hz, CH=CHC*H*), 3.44 (3H, s, OCH_3), 3.49 (1H, d, *J* 8.0 Hz, CH–Ar), 3.81 (3H, s, OCH_3), 4.19 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 6.20 (1H, d, *J* 15.6 Hz, C*H*=CHCH), 6.69 (1H, dd, *J* 9.6, 15.6 Hz, CH=C*H*CH) and 7.17-7.33 (5H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 14.3 (OCH_2CH_3), 32.6 (CH=CHCH), 37.2 (*C*H–Ar), 44.7 ($C(CO_2CH_3)_2$), 52.7 (OCH_3), 53.2 (OCH_3), 60.5 (OCH_2CH_3), 124.9 (*C*H=CHCH), 127.7 (Ar*C*H), 128.4 (2Ar*C*H), 128.6 (2Ar*C*H), 133.5 (Ar*C*), 142.2 (CH=*C*HCH), 165.7 (CO_2CH_3), 166.3 (CO_2CH_3) and 167.2 ($CO_2CH_2CH_3$) and 199.3 ($CO_{complex}$); m/z 333 (MH^+ 6%), 281 (15%), 227 (11%), 207 (21%), 197 (10%) and 147 (40%); $[\alpha]_D^{22} = 0.0$ (*c* = 0.10 g/mL in $CHCl_3$).

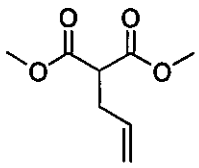
Ethyl 2-acetylpent-4-enoate (255)



Sodium hydride (1.34 g, 33.4 mmol, 60% in mineral oil, 1.5 eq) was slowly added by small portions to a solution of ethyl acetoacetate (3.1 mL, 3.00 g, 23.0 mmol) in THF (100 mL) at 0°C. The reaction mixture was allowed to stir for an hour and allyl bromide (2.2 mL, 3.10 g, 25.3 mmol, 1.1 eq) was added. The resulting mixture was allowed to stir for 20 h and was then quenched with methanol (10 mL). The crude mixture was washed successively with a saturated solution of ammonium chloride (40 mL) and brine (40 mL). The aqueous layers were combined and extracted with diethyl ether (2×25 mL). The combined organic fractions were dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified on silica gel (15% DCM/petrol) to give 2.26 g (14.5 mmol, 63%) of ethyl 2-acetylpent-4-enoate as a yellow oil; ν_{max} (film)/cm^{-1} 1642 (C=C), 1717 (C=O), 1742 (C=O), 2962 (sp^3 C–H) and 3079 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 1.20 (3H, t, *J* 7.2 Hz, $CO_2CH_2CH_3$), 2.17 (3H, s, $COCH_3$), 2.59 (2H, dd, *J* 6.9, 7.4 Hz, $CHCH_2CH{=}CH_2$), 3.52 (1H, t, *J* 7.4 Hz,

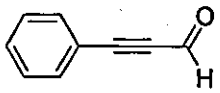
C*H*C*H*$_2$CH=CH$_2$), 4.20 (2H, q, *J* 7.2 Hz, CO$_2$C*H*$_2$CH$_3$), 5.01-5.09 (1H, m, CH=C*H*H), 5.11-5.15 (1H, m, CH=C*H*H) and5.78 (1H, ddt, *J* 6.9, 10.2, 17.1 Hz, CH$_2$C*H*=CH$_2$); δ_C(100 MHz; $CDCl_3$) 14.1 (CO$_2$CH$_2$*C*H$_3$), 29.1 (CO*C*H$_3$), 32.2 (CH*C*H$_2$CH=CH$_2$), 59.2 (*C*HCH$_2$CH=CH$_2$), 60.4 (CO$_2$*C*H$_2$CH$_3$), 117.4 (CH$_2$CH=*C*H$_2$), 134.2 (CH$_2$*C*H=CH$_2$), 169.2 (*C*O$_2$CH$_2$CH$_3$), 202.5 (*C*OCH$_3$); HRMS (EI) (M–H$^+$), found 169.0861, $C_9H_{14}O_3$ requires 169.0865 (–1.9 ppm); m/z 169 (26%), 152 (72%), 151 (48%), 131 (26%), 119 (29%), 69 (65%) and 60 (100%).

Dimethyl 2-allylmalonate (256)



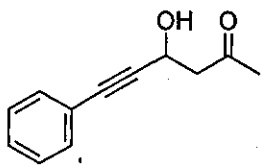
Sodium hydride (1.51 g, 37.9 mmol, 60% in mineral oil) was slowly added by small portions to a solution of dimethyl malonate (5.8 mL, 5.00 g, 37.9 mmol) in THF (60 mL) at 0°C. The reaction mixture was allowed to stir at 0°C for an hour and allyl bromide (3.6 mL, 5.00 g, 41.7 mmol, 1.1 eq) was added. The resulting mixture was allowed to stir for 20 h and was then quenched with methanol (10 mL). The crude mixture was washed successively with a saturated solution of ammonium chloride (40 mL) and brine (40 mL). The aqueous layers were combined and extracted with diethyl ether (2×25 mL). The combined organic fractions were dried over magnesium sulfate and concentrated *in vacuo*. The residue was purified on silica gel (15% DCM/petrol) to give 3.46 g (20.1 mmol, 53%) of the *title compound* as a yellow oil; ν_{max} (film)/cm^{-1} 1745 (C=O), 2954 (sp^3 C–H) and 3079 (sp^2 CH); δ_H(400 MHz; $CDCl_3$) 2.62-2.68 (2H, m, CHC*H*$_2$CH=CH$_2$), 3.47 (1H, t, *J* 7.6 Hz, C*H*CH$_2$CH=CH$_2$), 3.74 (6H, s, OC*H*$_3$), 5.04-5.09 (1H, m, CHC*H*HCH=CH$_2$), 5.12 (1H, ddd, *J* 1.2, 3.2, 17.2 Hz, CHC*H*HCH=CH$_2$) and 5.77 (1H, ddt, *J* 6.8, 10.2, 17.2 Hz, CHCH$_2$C*H*=CH$_2$); δ_C(100 MHz; $CDCl_3$) 32.8 (CH*C*H$_2$CH=CH$_2$), 51.3 (*C*HCH$_2$CH=CH$_2$), 52.5 (2O*C*H$_3$), 117.6 (CHCH$_2$CH=*C*H$_2$), 133.9 (CHCH$_2$*C*H=CH$_2$) and 169.3 (2*C*=O); HRMS (EI) (M$^+$), found 172.0731, $C_8H_{12}O_4$ requires 172.0735 (–2.6 ppm); m/z 172 (3%), 141 (11), 113 (83), 112 (100), 81 (95), 59 (45) and 53 (36).

3-phenylpropiolaldehyde (264)[133]



To a stirred solution of sulfuric acid (5.2 mL, 97.9 mmol, 4.0 eq) in water (60 mL) was added a solution of phenylpropargyl diethyl acetal (5.0 mL, 24.5 mmol) and the resulting mixture was stirred at room temperature for 12 h. The mixture was extracted with diethyl ether (2×20 mL). The organic fractions were combined and dried over magnesium sulfate. After filtration, the solvent was removed *in vacuo*. Subsequent purification on silica gel, eluting with 5% EtOAc in light petroleum afforded the desired aldehyde in a quantitative yield (>99%, 3.56 g, 27.4 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1662 (C=O), 2189 (C≡C), 2238 (C≡C), 2854 (ArC–H), 2976 (ArC–H) and 3058 (ArC–H); δ_H(400 MHz; $CDCl_3$) 7.39-7.43 (2H, m, ArC*H*), 7.60-7.62 (2H, m, ArC*H*) and 9.43 (1H, s, C*H*O); δ_C(100 MHz; $CDCl_3$) 84.4 (*C*≡C), 95.2 (*C*≡C), 119.4 (Ar*C*), 129.1 (2Ar*C*H), 133.3 (Ar*C*H) and 133.3 (2Ar*C*H).

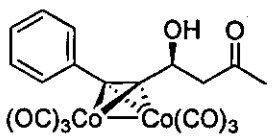
4-Hydroxy-6-phenylhex-5-yn-2-one (267)[100b]



(1S, 2R)-1-[(3,5-Di-tert-butyl-2-hydroxybenzilidene)amino]-2-indanol (20 mg, 0.05 mmol, 5 mol%) was added to a solution of $Ti(O^iPr)_4$ (25 μL, 25 mg, 0.08 mmol, 8 mol%) in toluene (20 mL). The resulting solution was allowed to stir for 1 hour at r.t. and the solvent was removed *in vacuo* to leave an orange solid which was transferred into a sample vial. Activated 4Å molecular sieves (400 mg) were smashed in a mortar and added to the reaction vial. Phenylpropargyl aldehyde (130 mg, 1.0 mmol), diisopropylethylamine (25 μL, 2 mg, 0.01 mol%) and acetone trimethylsilyl enol ether (560 μL, 370 mg, 2.9 mmol, 2.9 eq) were successively added. The reaction mixture was allowed to stir at r.t. for 24 h under a nitrogen atmosphere. The powdered molecular sieves were then removed by filtration through a pad of celite and washed with DCM (15 mL). The filtrate was concentrated *in vacuo* and the

crude product was purified by flash chromatography (15% EtOAc/petrol) affording the desired compound in 93% yield (175 mg, 0.9 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1713 (C=O), 2194 (C≡C), 2919 (sp^3 C–H), 2960 (sp^3 C–H) and 3418 (OH); δ_H(400 MHz; $CDCl_3$) 2.24 (3H, s, C*H*$_3$), 2.94 (1H, dd, *J* 4.0-17.6 Hz, C*H*H), 3.03 (1H, dd, *J* 8.0, 17.6 Hz, C*H*H), 3.13 (1H, d, *J* 5.2 Hz, CHO*H*), 5.03 (1H, ddd, *J* 4.0, 5.2, 8.0 Hz, C*H*OH), 7.27-7.37 (3H, m, ArC*H*) and 7.39-7.49 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 30.7 (*C*H$_3$), 50.1 (*C*H$_2$), 58.9 (*C*H), 83.0 (*C*≡C), 89.5 (*C*≡C), 128.3 (2Ar*C*H), 128.6 (Ar*C*H), 131.7 (2Ar*C*H), 136.7 (Ar*C*) and 202.5 (*C*=O); (EI) m/z 187 (M$^+$–H, 11%), 171 (15%), 154 (100%) and 136 (96%); $[\alpha]_D^{22}$= +31.2 (*c* = 0.10 g/mL in $CHCl_3$).

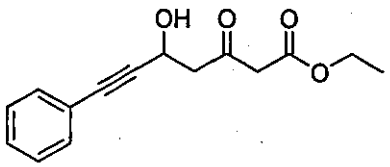
4-Hydroxy-6-phenylhex-5-yn-2-one dicobalt hexacarbonyl (268)



Phenylpropargyl aldehyde (65 mg, 0.50 mmol) was added to a solution of dicobalt octacarbonyl (190 mg, 0.55 mmol, 1.1 eq) in DCM (3 mL) and the reaction mixture was allowed to stir for 1 h at r.t. under a nitrogen atmosphere. (1S, 2R)-1-[(3,5-di-tert-butyl-2hydroxybenzilidene)amino]-2-indanol (10 mg, 0.02 mmol, 5 mol%) was added to a solution of Ti(O^{i}Pr)$_4$ (12 μL, 12 mg, 0.01 mmol, 8 mol%) in toluene (10 mL). The resulting solution was allowed to stir for 1 hour at r.t. and the solvent was removed *in vacuo* to leave an orange solid which was transferred into a sample vial. Activated 4Å molecular sieves (200 mg) were smashed in a mortar and added to the reaction vial. The complexed phenyl propargyl aldehyde, diisopropylethylamine (4 μL, 3 mg, 0.05 mol%) and acetone trimethylsilyl enol ether (290 μL, 200 mg, 1.50 mmol, 3.0 eq) were successively added to the vial containing the catalyst. The reaction mixture was allowed to stir at r.t. for 64 h under a nitrogen atmosphere. The powdered molecular sieves were then removed by filtration through a pad of celite and washed with DCM (15 mL). The filtrate was concentrated *in vacuo* and the crude product was purified by flash chromatography (15% EtOAc/petrol) affording the desired *title* compound in 4% yield (8 mg, 0.02 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1710 (C=O), 1748 (C=O), 2019 (C≡O), 2050 (C≡O), 2090 (C≡O) and 3446 (O–H); δ_H(400 MHz; $CDCl_3$) 2.25 (3H, s, C*H*$_3$), 2.89 (1H, dd, *J* 9.2, 17.6 Hz, C*H*$_2$), 3.01

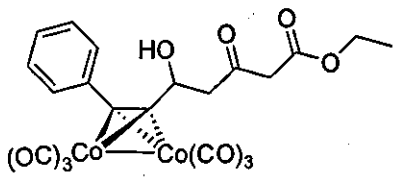
(1H, dd, *J* 2.8, 18.0 Hz, CH_2), 3.62 (1H, d, *J* 3.8 Hz, CHO*H*), 5.52 (1H, ddd, *J* 2.6, 3.8, 9.2 Hz, C*H*OH), 7.27-7.42 (3H, m, ArC*H*) and 7.51-7.65 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 30.7 (*C*H_3), 51.3 (*C*H_2), 68.4 (*C*H), 90.7 (*C*–C), 98.3 (*C*–C), 128.0 (Ar*C*H), 129.0 (2Ar*C*H), 129.6 (2Ar*C*H), 137.5 (Ar*C*) and 199.6 ($CO_{complex}$), 202.9 (*C*=O); no mass ion could be observed; (FAB) m/z 307 (13%), 289 (100%), 176 (31%), 154 (100%) and 136 (72%); $[\alpha]_D^{22}$ = +28.6 (*c* = 0.10 g/mL in $CHCl_3$).

Ethyl 5-hydroxy-3-oxo-7-phenylhept-6-ynoate (269)



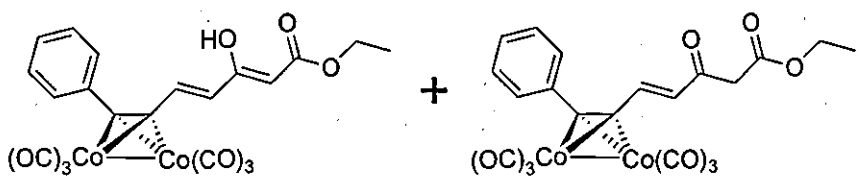
Ethyl acetoacetate (290 μL, 300 mg, 2.3 mmol) was added dropwise to a solution of sodium hydride (140 mg, 3.4 mmol, 60% in mineral oil, 1.5 eq) in dry THF (6 mL) at –78°C under a nitrogen atmosphere. The reaction mixture was allowed to stir for 10 minutes and butyl lithium (1.0 ml, 2.5 mmol, 1.1 eq, 2.5 M solution in THF) was added dropwise. The resulting solution was stirred for a further 15 min and 3-phenylpropiolaldehyde (300 mg, 2.3 mmol) was added dropwise. The reaction mixture was allowed to warm up slowly to r.t. over 1 h and was then quenched with methanol (10 mL) at 0°C. The resulting mixture was successively washed with a saturated solution of ammonium chloride (20 mL) and brine (20 mL). The aqueous washings were combined and extracted with diethyl ether (2×20 mL). The combined ethereal extracts were dried over magnesium sulfate and filtered through a pad of silica affording the desired ethyl 5-hydroxy-3-oxo-7-phenylhept-6-ynoate in 46% yield (270 mg, 1.1 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1712 (C=O), 1737 (C=O), 2230 (C≡C), 2981 (sp^3 C–H) and 3444 (O–H); δ_H(400 MHz; $CDCl_3$) 1.20 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 2.96 (1H, dd, *J* 4.0, 17.2 Hz, $CHCH_2CO$), 3.08 (1H, dd, *J* 8.0, 17.2 Hz, $CHCH_2CO$), 3.12 (1H, br d, *J* 4.4 Hz, O*H*), 3.46 (2H, s, $COCH_2CO$), 4.13 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 4.99 (1H, ddd, *J* 4.0, 4.4, 8.0 Hz, C*H*-OH), 7.18-7.27 (3H, m, ArC*H*) and 7.31-7.38 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 14.1 (*C*H_3), 49.8 ($CHCH_2$), 49.9 ($COCH_2CO$), 58.6 (*C*HOH), 61.7 ($COCH_2CH_3$), 85.5 (*C*≡C), 88.5 (*C*≡C), 122.3 (Ar*C*), 128.3 (2Ar*C*H), 128.7 (Ar*C*H), 131.7 (2Ar*C*H) 166.8 (CO_2Et) and 201.6 (CH_2COCH_2); no mass ion could be observed.

Dicobalt hexacarbonyl ethyl 5-hydroxy-3-oxo-7-phenylhept-6-ynoate (270)



Dicobalt octacarbonyl (100 mg, 0.30 mmol, 1.1 eq) was added to a solution of ethyl 5-hydroxy-3-oxo-7-phenylhept-6-ynoate (70 mg, 0.27 mmol) in dry DCM (5 mL). The resulting mixture was allowed to stir for 4 h at r.t. under a nitrogen atmosphere. The solvent was then removed *in vacuo* and the crude product was purified by flash chromatography (15% EtOAc/petrol) to give the desired *titled compound* in 86% yield (130 mg, 0.23 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1712 (C=O), 1737 (C=O), 2020 (C≡O), 2050 (C≡O), 2090 (C≡O), 3498 (O–H); δ_H(400 MHz; $CDCl_3$) 1.26 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 2.99 (1H, dd, *J* 9.6, 17.6 Hz, $CHCH_2CO$), 3.12 (1H, dd, *J* 2.4, 17.6 Hz, $CHCH_2CO$), 3.42 (1H, d, *J* 4.0 Hz, O*H*), 3.54 (2H, d, *J* 1.2 Hz $COCH_2CO$), 4.20 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 4.99 (1H, ddd, *J* 2.4, 3.6, 9.6 Hz, C*H*-OH), 7.29-7.40 (3H, m, ArC*H*) and 7.53-7.60 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 13.0 (CH_3), 48.8 ($CHCH_2$), 49.9 ($COCH_2CO$), 60.7 ($COCH_2CH_3$), 67.3 (*C*HOH), 89.5 (*C*–C), 97.1 (*C*–C), 127.3 (1Ar*C*H), 128.0 (2Ar*C*H), 128.6 (2Ar*C*H), 136.3 (Ar*C*), 165.7 (CO_2Et), 198.2 ($CO_{complex}$) and 201.5 (CH_2COCH_2); HRMS (FAB) (M^+–3CO), found 461.9565, $C_{18}H_{16}Co_2O_7$ requires 461.9560 (+1.2 ppm); m/*z* 462 (5%), 434 (12%), 406 (3%), 136 (75%) and 73 (100%).

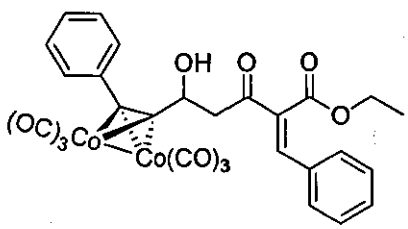
Dicobalt hexacarbonyl (E)-ethyl 3-oxo-7-phenylhept-4-en-6-ynoate (271) and dicobalt hexacarbonyl (2*Z*,4*E*)-ethyl 3-hydroxy-7-phenylhepta-2,4-dien-6-ynoate (272)



Dicobalt octacarbonyl (75 mg, 0.21 mmol, 1.1 eq) was added to a solution of ethyl 5-hydroxy-3-oxo-7-phenylhept-6-ynoate (50 mg, 0.19 mmol) in dry DCM (5 mL) and the reaction mixture was allowed to stir for 2 h at r.t. under an atmosphere of nitrogen. $BF_3.Et_2O$

(55 mg, 0.40 mmol, 2.0 eq) was then added and the mixture was stirred for a further 5 minutes. The solution was then filtered through a pad of celite and silica. Purification by flash chromatography (45% EtOAc/petrol) afforded the two inseparable tautomers in 92% yield (95 mg, 0.17 mmol) in a 1:0.9 hydroxy/oxo ratio as a dark red oil; ν_{max} (film)/cm^{-1} 1526 (C=C), 1640 (C=C), 1737 (C=O), 2025 (C≡O), 2054 (C≡O), 2091 (C≡O), 2069 (sp^2 C–H) and 3443 (C–OH); δ_H(400 MHz; $CDCl_3$) 1.27 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 1.28 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 3.61 (2H, s, $COCH_2CO$), 4.22 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 4.24 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 5.13 (1H, s, $CHCO_2Et$), 6.32 (1H, dd, *J* 1.6, 14.8 Hz, CCH=CHCOH), 6.66 (1H, dd, *J* 1.6, 14.8 Hz, CCH=CHCO), 7.29-7.40 (6H, m, ArCH), 7.43-7.56 (4H, m, ArCH), 7.82 (1H, d, *J* 14.8 Hz, CCH=CHCOH), 8.10 (1H, d, *J* 14.8 Hz, CCH=CHCO) and 11.92 (1H, d, *J* 1.6 Hz, OH); δ_C(100 MHz; $CDCl_3$) 13.2 ($2CH_2CH_3$), 47.2 ($COCH_2CO$), 59.3 (OCH_2CH_3), 59.9 (OCH_2CH_3), 85.4 (2C–C), 86.6 (2C–C), 91.3 (OHC=CHCO), 127.0 (CCH=CH), 127.0 (2ArC), 127.2 (4ArCH), 127.9 (2ArCH), 128.1 (4ArCH), 129.9 (CCH=CH), 135.6 (C=CHCO), 144.1 (C=CHCOH), 166.7 (CO_2Et), 167.1 (CO_2Et), 190.0 (CH_2CO), 171.8 (COH) and 197.6 ($CO_{complex}$); accurate mass could not be observed; ; m/*z* 482 (1%), 460 (3%), 338 (1%) and 329 (100%).

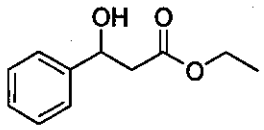
Dicobalt hexacarbonyl (*Z*)-ethyl 2-benzylidene-5-hydroxy-3-oxo-7-phenylhept-6-ynoate (274)



Scandium triflate (4 mg, 0.01 mmol, 5 mol%) and (E)-*N*-benzylideneprop-2-en-1-amine (32 mg, 0.21 mmol, 1.2 eq) were successively added to a solution of dicobalt hexacarbonyl ethyl 5-hydroxy-3-oxo-7-phenylhept-6-ynoate (100 mg, 0.18 mmol) in dry DCM (3 mL). The reaction mixture was allowed to stir at r.t. under a nitrogen atmosphere for 2 h. The solvent was evaporated *in vacuo* and the residue was taken up in ethyl acetate (5 mL). The crude product was washed with water (15 mL) and the aqueous layer was extracted with ethyl acetate (2×10 mL). The organic extracts were combined and dried over magnesium sulfate. Purification by flash chromatography afforded the *title compound* in 71% yield (83 mg, 0.13

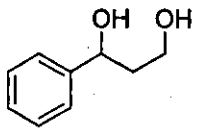
mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1702 (C=O), 1721 (C=O), 2020 (C≡O), 2051 (C≡O), 2090 (C≡O) and 3490 (OH); δ_H(400 MHz; $CDCl_3$) 1.26 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 2.99 (1H, dd, *J* 10.0, 18.0 Hz, CHC*H*HCO), 3.02 (1H, dd, *J* 2.0, 18.0 Hz, CHC*H*HCO), 3.58 (1H, d, *J* 3.2 Hz, O*H*), 4.25 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 5.52 (1H, ddd, *J* 2.0, 3.2, 10.0 Hz, C*H*-OH), 7.17-7.25 (6H, m, ArC*H*), 7.31-7.42 (4H, m, ArC*H*) and 7.74 (1H, s, C=C*H*); δ_C(100 MHz; $CDCl_3$) 13.1 (CH_3), 50.6 ($CHCH_2CO$), 60.8 (OCH_2CH_3), 67.5 (*C*HOH), 89.1 (*C*–C), 97.3 (*C*–C), 126.9 (Ar*C*H), 127.9 (2Ar*C*H), 128.1 (2Ar*C*H), 128.6 (2Ar*C*H), 128.7 (2Ar*C*H), 129.9 (Ar*C*H), 131.6 (Ar*C*), 132.0 (Ar*C*), 136.4 (*C*=CH), 141.2 (C=*C*H), 163.2 (CO_2Et), 198.2 ($CO_{complex}$) and 204.0 (CH_2CO); no mass ion could be observed.

Ethyl 3-hydroxy-3-phenylpropanoate (276)[100c,111,134]



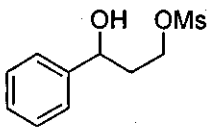
Methanol (16.0 mL) was added dropwise over an hour *via* a syringe pump to a refluxing mixture of ethyl 3-oxo-3-phenylpropanoate (3.84 g, 20.0 mmol) and sodium borohydride (1.90 g, 50.0 mmol, 2.5 eq) in THF (40 mL). The resulting mixture was then cooled down to r.t. and 10 mL of water were slowly added. A 3N hydrochloric acid solution (5 mL) was then added to the reaction mixture to obtain a pH 4 solution. Most of the organic solvents were evaporated *in vacuo* and the remaining aqueous residue was extracted with ethyl acetate (3×10 mL). The organic extracts were combined and dried over magnesium sulfate. The crude product was concentrated *in vacuo* and subsequent purification by flash chromatography (45% EtOAc/petrol) afforded the *title compound* in 88% yield (3.41 g, 17.6 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1038 (C–O), 1732 (C=O), 2980 (sp^3 C–H), 3029 (sp^2 ArC–H), 3061 (sp^2 ArC–H) and 3444 (OH); δ_H(400 MHz; $CDCl_3$) 1.18 (1H, t, *J* 7.2 Hz, CH_3), 2.62 (1H, dd, *J* 4.0, 16.4 Hz, CHC*H*HC), 2.68 (1H, dd, *J* 9.2, 16.4 Hz, CHC*H*HC), 3.27 (1H, d, *J* 1.6 Hz, O*H*), 4.10 (2H, q, *J* 7.2 Hz, OCH_2), 5.05 (1H, ddd, *J* 1.6, 4.0, 9.2 Hz, C*H*OH), 7.15-7.27 (3H, m, ArC*H*) and 7.28-7.38 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 14.2 (CH_3), 43.4 ($CHCH_2$), 68.9 (OCH_2CH_3), 70.3 (*C*HOH), 125.7 (2Ar*C*H), 127.8 (Ar*C*H), 128.6 (2Ar*C*H), 142.5 (Ar*C*) and 172.4 (*C*=O).

1-Phenylpropane-1,3-diol (277)[113]



Sodium borohydride (2.27 g, 60.0 mmol, 3.0 eq) was added slowly to a solution of ethyl 3-oxo-3-phenylpropanoate (3.84 g, 20.0 mmol) in THF (20 mL) and the resulting reaction was allowed to stir, heating to reflux for an hour. Methanol (16 mL) was then slowly added *via* a syringe pump over 1 hour and the reaction mixture was heated to reflux overnight. After cooling to r.t. water (10 mL) was added and the mixture was acidified with a 3N hydrochloric acid solution (5 mL). Most of the organic solvents were evaporated *in vacuo* and the remaining aqueous residue was extracted with ethyl acetate (3×10 mL). The organic extracts were combined and dried over magnesium sulfate. After evaporation of the solvent, the crude product was purified by flash chromatography (65% EtOAc/petrol) to yield the 1-phenylpropane-1,3-diol in 72% (14.4 mmol, 2.19 g) as a yellow oil; ν_{max} (film)/cm^{-1} 1048 (C-O), 1485 (ArC=C), 1602 (ArC=C), 2950 (sp^3 C–H), 3029 (sp^2 C–H), 3060 (sp^2 C–H), 3084 (sp^2 C–H) and 3376 (OH); δ_H(400 MHz; DMSO) 3.38-3.56 (2H, m, CHC*H*$_2$), 3.88 (1H, m, C*H*HOH), 4.03 (1H, m, C*H*HOH), 4.43 (1H, t, *J* 4.8 Hz, CHHO*H*), 4.64 (1H, dt, *J* 4.0, 8.0 Hz, C*H*OH), 5.14 (1H, d, *J* 4.0 Hz, CHO*H*) and 7.12-7.45 (5H, m, ArC*H*); ^{13}C NMR data and mass ion could not be recorded because of the instability of the diol.

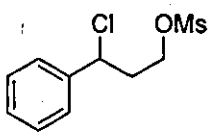
3-Hydroxy-3-phenylpropyl methanesulfonate (278)



Diisopropylethyl amine (3.4 mL, 2.55g, 19.7 mmol, 3.0 eq) and mesyl chloride (1.5 mL, 2.26 g, 19.7 mmol, 3.0 eq) were successively added to a solution of 1-phenylpropane-1,3-diol (1.00 g, 6.6 mmol) in DCM (20 mL) at −78°C. The reaction mixture was allowed to stir overnight at r.t. and was then quenched with water (30 mL). The aqueous residue was extracted with diethyl ether (2×25 mL). The ethereal extracts were combined and dried over magnesium sulfate. The crude product was then purified by flash chromatography (50-60%

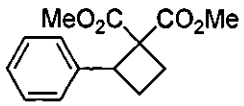
EtOAc/petrol) to give 0.79 g (3.5 mmol, 52%) of the *title compound* as a yellow oil. ν_{max} (film)/cm^{-1} 1348 (S=O), 2936 (sp^3 C–H), 3028 (sp^2 C–H) and 3519 (OH); δ_H(400 MHz; $CDCl_3$) 1.95 (1H, d, *J* 3.6 Hz, CHO*H*), 1.99-2.10 (2H, m, CHCH_2), 2.93 (3H, s, OSO_2CH_3), 4.15-4.25 (1H, m, C*H*HOMs), 4.35-4.45 (1H, m, C*H*HOMs), 4.80 (1H, t, *J* 6.4 Hz, C*H*OH) and 7.16-7.35 (5H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 37.2 (*C*H3), 38.2 (CH*C*H_2), 67.3 (*C*H_2OMs), 70.2 (*C*HOH), 126.0 (2Ar*C*H), 128.7 (Ar*C*H), 128.9 (2Ar*C*H) and 143.5 (Ar*C*); HRMS (EI) (M^+–H), found 229.0539, $C_{10}H_{13}SO_4$ requires 229.0535 (+1.8 ppm); m/*z* 229 (4%), 213 (10%), 154 (22%), 137 (22%) and 117 (100%).

3-Chloro-3-phenylpropyl methanesulfonate (279)



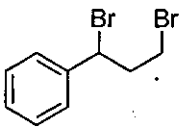
Diisopropylethyl amine (0.8 mL, 560 mg, 4.4 mmol, 1.5 eq) and mesyl chloride (0.3 mL, 500 mg, 4.4 mmol, 1.5 eq) were successively added to a solution of 3-hydroxy-3-phenylpropyl methanesulfonate (670 mg, 2.9 mmol) in DCM (15 mL). The resulting reaction mixture was allowed to stir for 2 h, heating to reflux under a nitrogen atmosphere and was then quenched with water (30 mL). Most of the organic solvents were evaporated *in vacuo* and the remaining aqueous layer was extracted with diethyl ether (2×25 mL). The combined organic layers were dried over magnesium sulfate and filtered through a pad of celite and silica. The crude product was purified by flash chromatography (25% EtOAc/petrol) to give the chloromesyl derivative in 63% yield (460 mg, 1.8 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 699 (C–Cl), 763 (C–Cl), 1172 (C–O), 1359 (S=O), 2937 (sp^3 C–H), 2967 (sp^3 C–H), 3030 (sp^2 ArC–H) and 3061 (sp^2 ArC–H); δ_H(400 MHz; $CDCl_3$) 2.40-2.55 (2H, m, CHCH_2), 3.03 (3H, s, OSO_2CH_3), 4.27-4.38 (1H, m, C*H*HOMs), 4.41-4.52 (1H, m, C*H*HOMs), 5.06 (1H, dd, *J* 6.0, 8.4 Hz, C*H*Cl); 7.20-7.38 (5H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 37.3 (*C*H_3), 39.1 (CH*C*H_2), 59.0 (*C*HOH), 67.0 (*C*H_2OMs) 126.9 (2Ar*C*H), 128.8 (Ar*C*H), 128.9 (2Ar*C*H) and 140.3 (Ar*C*).

Dimethyl 2-phenylcyclobutane-1,1-dicarboxylate (280)[113]



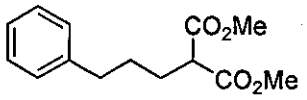
N-Bromosuccinimide (3.68 g, 20.7 mmol, 1.1 eq) and benzoyl peroxide (230 mg, 0.9 mmol, 5 mol%) were successively added to a solution of dimethyl 2-(3-phenylpropyl)malonate (4.70 g, 18.8 mmol) in anhydrous DCM (160 mL) and the reaction mixture was allowed to stir overnight, heating to reflux under a nitrogen atmosphere. The crude mixture was filtered through a Büchner funnel and the solids were washed with DCM (25 mL). The extracts were combined, dried over magnesium sulfate and evaporated to leave a residue which was taken up in DMF (10 mL). The resulting solution was added dropwise to a suspension of sodium hydride (1.50 g, 37.6 mmol, 60% in mineral oil, 2.0 eq) in DMF (40 mL) at 0°C. The reaction mixture was then heated to reflux for 4 h under an atmosphere of nitrogen. The solvent was then evaporated and the residue was taken up in diethyl ether (30 mL) and treated with cold water (15 mL). The organic layer was dried over magnesium sulfate and the solvent was evaporated *in vacuo*. Purification by flash chromatography (10% EtOAc/petrol) afforded the *title compound* in 63% yield (2.94 g, 11.8 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1730 (C=O), 2951 (sp^3 ArC–H), 2998 (sp^3 ArC–H), 3028 (sp^2 ArC–H), 3059 (sp^2 ArC–H) and 3084 (sp^3 ArC–H); δ_H(400 MHz; $CDCl_3$) 2.15-2.25 (1H, m, C*H*HC), 2.26-2.36 (1H, m, C*H*HC), 2.58-2.68 (1H, m, CHC*H*H), 2.69-2.77 (1H, m, CHC*H*H), 3.26 (3H, s, OCH_3), 3.81 (3H, s, OCH_3), 4.39 (1H, t, *J* 9.4 Hz, C*H*CH$_2$), 7.17-7.27 (3H, m, ArC*H*) and 7.28-7.39 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 20.7 (CH*C*H$_2$), 25.6 (*C*H$_2$C), 45.1 (*C*HCH$_2$), 51.9 (O*C*H$_3$), 52.5 (O*C*H$_3$), 59.7 (*C*(CO$_2$Me)$_2$), 127.0 (Ar*C*H), 127.5 (2Ar*C*H), 128.0 (2Ar*C*H), 139.0 (Ar*C*), 169.8 (*C*=O) and 172.2 (*C*=O).

1-(1,3-Dibromopropyl)benzene (282)[113,114]



N-Bromosuccinimide (1.87 g, 10.5 mmol, 1.1 eq) and benzoyl peroxide (120 mg, 0.5 mmol, 5 mol%) were successively added to a solution of 1-bromo-3-phenylpropane (1.5 mL, 1.99 g, 10.0 mmol) in cyclohexane (15 mL) and the reaction mixture was allowed to stir overnight, heating to reflux under a nitrogen atmosphere. Cyclohexane was then evaporated *in vacuo* and the residue was taken up in ethyl acetate (10 mL). The crude mixture was washed with water (30 mL). The aqueous layer was extracted with ethyl acetate (2×10 mL). The organic layers were combined and dried over magnesium sulfate. Subsequent purification by flash chromatography (petrol) afforded the desired dibromide derivative in 85% yield (2.36 g, 8.5 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 696 (C–Br), 755 (C–Br), 2917 (sp^3 ArC–H), 3028 (sp^2 ArC–H), 3061 (sp^2 ArC–H); δ_H(400 MHz; $CDCl_3$) 2.53-2.66 (1H, m, CHC*H*H), 2.75-2.89 (1H, m, CHC*H*H) 3.40-3.51 (1H, m, CH_2Br), 3.54-3.64 (1H, m, CH_2Br), 5.24 (1H, dd, *J* 5.4, 8.4 Hz, C*H*Br) and 7.18-7.55 (5H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 31.1 (*C*HCH_2), 42.1 (*C*H_2Br), 52.6 (*C*HBr), 127.2 (2Ar*C*H), 128.8 (Ar*C*H), 129.0 (2Ar*C*H) and 140.8 (Ar*C*).

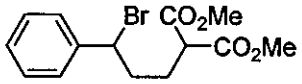
Dimethyl 2-(3-phenylpropyl)malonate (283)[113]



Dimethyl malonate (1.2 mL, 530 mg, 4.0 mmol) was added dropwise to a solution of potassium *t*-butoxide (490 mg, 4.4 mmol, 1.1 eq) in THF (30 mL) at 0°C under a nitrogen atmosphere. After addition, the reaction mixture was allowed to warm up slowly to r.t. over 1 hour. 3-Bromopropylbenzene (600 µL, 800 mg, 4.0 mmol) in THF (10 mL) was then added dropwise to the solution and the resulting mixture was allowed to stir overnight. The solvent was then evaporated *in vacuo* and the residue was taken up in ethyl acetate (15 mL). The crude mixture was washed with water (20 mL) and the aqueous layer was extracted with diethyl ether (2×10 mL). The combined ethereal extracts were dried over magnesium sulfate. Purification by flash chromatography (5% EtOAc/petrol) afforded the desired *title compound* in 77% yield (770 mg, 3.1 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1734 (C=O), 2952 (sp^3 C–H) and 3024 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 1.52-1.64 (2H, m, $CH_2CH_2CH_2$), 1.82-1.93 (2H, m, CH_2CH), 2.57 (2H, t, *J* 7.6 Hz, Ar-CH_2), 3.31 (1H, t, *J* 7.6 Hz, CH_2CH), 3.65 (6H, s, CH_3), 7.12-7.05 (3H, m ArC*H*) and 7.24-7.13 (2H, m, ArC*H*); δ_C(100 MHz;

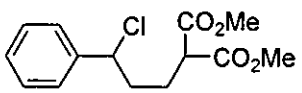
$CDCl_3$) 28.5 (CH_2CH), 29.1 ($CH_2CH_2CH_2$), 35.5 (Ar-CH_2), 51.6 (CH), 52.5 ($2CH_3$), 125.9 (ArCH), 128.4 (2ArCH), 128.5 (2ArCH), 141.6 (ArC), 169.8 ($2CO$).

Dimethyl 2-(3-bromo-3-phenylpropyl)malonate (284)[113]



N-Bromosuccinimide (390 mg, 2.2 mmol, 1.1 eq) and benzoyl peroxide (30 mg, 0.1 mmol, 5 mol%) were successively added to a solution of dimethyl 2-(3-phenylpropyl)malonate (500 mg, 2.0 mmol) in anhydrous cyclohexane (16 mL) and the reaction mixture was allowed to stir overnight, heating to reflux under a nitrogen atmosphere. The reaction mixture was cooled down to r.t. and filtered through a Büchner funnel. The solids were washed with DCM (2×15 mL). The organic washings were combined and evaporated *in vacuo*. The crude residue was purified by flash chromatography (5% EtOAc/petrol) affording the *title compound* in 71% yield (470 mg, 1.4 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 696 (C–Br), 1732 (C=O), 2844 (sp^3 C–H), 2952 (sp^3 C–H), 3003 (sp^2 ArC–H) and 3062 (sp^2 ArC–H); δ_H(400 MHz; $CDCl_3$) 1.83-1.96 (1H, m, C*H*HCH(CO_2Me)$_2$), 2.08-2.38 (3H, m, Ar-CHCH_2 + C*H*HCH(CO_2Me)$_2$), 3.40 (1H, t, *J* 7.2 Hz, CH_2CH(CO_2Me)$_2$), 3.73 (3H, s, CH_3), 3.75 (3H, s, CH_3), 4.93 (1H, dd, *J* 6.4, 8.0 Hz, C*H*Br) and 7.44-7.27 (5H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 27.5 (CH_2CH(CO_2Me)$_2$), 37.4 (Ar-$CHCH_2$), 50.8 (CH(CO_2Me)$_2$), 52.6 ($2CH_3$), 54.2 (CHBr), 127.2 (2ArCH), 128.5 (ArCH), 128.8 (2ArCH), 141.5 (ArC), 169.3 ($2CO$); HRMS (EI) (M^++H), found 329.0381, $C_{14}H_{18}O_4Br$ requires 329.0388 (–2.2 ppm); m/*z* 329 (9%), 327 (6%), 249 (72%), 248 (13%), 185 (13%), 154 (13%), 137 (13%) and 117 (100%).

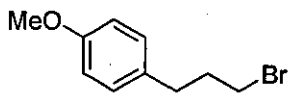
Dimethyl 2-(3-chloro-3-phenylpropyl)malonate (285)



Titanium tetrachloride (0.3 mL, 460 mg, 2.4 mmol, 2.0 eq) and benzaldehyde (100 μL, 130 mg, 1.2 mmol) were successively added to a solution of dimethyl 2-phenylcyclobutane-1,1-dicarboxylate (300 mg, 1.2 mmol) in DCM (10 mL) at −78°C. The resulting mixture was allowed to stir for 10 minutes under an atmosphere of nitrogen and the reaction was

quenched with water (5 mL). Most of the organic solvents were removed *in vacuo* and the aqueous residue was taken up in ethyl acetate (10 mL) and washed with water (20 mL). The aqueous layer was extracted with ethyl acetate (2×10 mL). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The crude product was purified by flash chromatography (5% EtOAc/petrol) to yield the dimethyl 2-(3-chloro-3-phenylpropyl)malonate in 77% (270 mg, 0.9 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 699 (C–Cl), 762 (C–Cl), 1732 (C=O), 2844 (sp^3 C–H), 2952 (sp^3 C–H), 3029 (sp^2 ArC–H) and 3062 (sp^2 ArC–H); δ_H(400 MHz; $CDCl_3$) 1.86-1.98 (1H, m, C*H*HCH$(CO_2Me)_2$), 2.03-2.21 (3H, m, Ar-CHC*H*$_2$ + C*H*HCH$(CO_2Me)_2$), 3.39 (1H, t, *J* 7.2 Hz, $CH_2CH(CO_2Me)_2$), 3.73 (3H, s, C*H*$_3$), 3.74 (3H, s, C*H*$_3$), 4.85 (1H, dd, *J* 8.0, 6.0 Hz, C*H*Cl) and 7.27-7.44 (5H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 26.4 (CH_2*C*H$(CO_2Me)_2$), 37.4 (Ar-CH*C*H$_2$), 50.9 (*C*H$(CO_2Me)_2$), 52.6 (2*C*H$_3$), 62.8 (*C*HCl), 126.8 (2Ar*C*H), 128.4 (Ar*C*H), 128.7 (2Ar*C*H), 141.1 (Ar*C*), 169.4 (2*C*O); HRMS (EI) (M^++H), found 285.0899, $C_{14}H_{18}O_4Cl$ requires 285.0894 (+2.0 ppm); m/*z* 285 (10%), 249 (65%), 185 (14%), 154 (13%), 137 (18%), 136 (13%), 129 (13%) and 117 (100%).

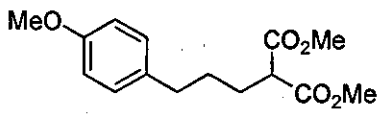
1-(3-Bromopropyl)-4-methoxybenzene (287)



Bromine (1.0 mL, 3.31 g, 21.7 mmol, 1.1 eq) was added to a solution of triphenylphosphine (5.69 g, 21.7 mmol, 1.1 eq) in DCM (40 mL) at 0°C and the resulting mixture was stirred for 10 min under a nitrogen atmosphere. A solution of imidazole (1.61 g, 23.7 mmol, 1.2 eq) in DCM (60 mL) was added to the bromine solution *via* a cannula and the reaction mixture was allowed to stir overnight at ambient temperature. Solvents were then removed *in vacuo* and the crude residue was taken up with ethyl acetate (25 mL). The resulting organic solution was washed with water (35 mL). The aqueous layer was then extracted with ethyl acetate (3×25 mL). The organic extracts were combined and dried over magnesium sulfate and concentrated *in vacuo*. Subsequent purification by flash chromatography on silica gel afforded the *title compound* in 95% yield (4.29 g, 18.7 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 699 (C–Br), 1036 (C–O), 1248 (C–O), 1512 (ArC=C), 2832 (sp^3 C–H), 2934 (sp^3 C–H), 3000 (sp^2 ArC–H) and 3028 (sp^2 ArC–H); δ_H(400 MHz; $CDCl_3$) 2.09-2.18 (2H, m,

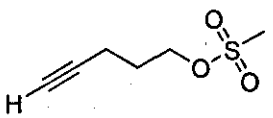
$CH_2CH_2CH_2$), 2.71 (2H, t, *J* 7.4 Hz, Ar-CH_2), 3.39 (2H, t, *J* 6.4 Hz, CH_2Br), 3.79 (3H, s, OCH_3), 6.84 (2H, d, *J* 8.8 Hz, 2ArC*H*) and 7.12 (2H, d, *J* 8.8 Hz, 2ArC*H*); δ_C(100 MHz; $CDCl_3$) 33.1 ($CH_2CH_2CH_2$), 33.3 (CH_2Br), 34.5 (Ar–CH_2), 55.3 (CH_3O), 114.0 (2ArCH), 129.6 (2ArCH), 132.6 (ArC) and 158.1 (MeOC).

Dimethyl 2-(3-(4-methoxyphenyl)propyl)malonate (288)



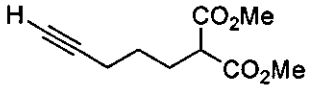
Dimethyl malonate (2.1 mL, 2.43 g, 18.4 mmol, 1.0 eq) was added to a suspension of potassium *t*-butoxide (2.07 g, 18.4 mmol, 1.0 eq) in THF (50 mL) and the reaction mixture was stirred at r.t. under a nitrogen atmosphere for an hour. A solution of 1-(3-bromopropyl)-4-methoxybenzene (4.12 g, 18.0 mmol) in THF (20 mL) was then added *via* a cannula and the resulting mixture was allowed to stir overnight, heated to reflux. The reaction was then quenched with methanol (20 mL) and the crude product was filtered through a plug of celite. Solvents were evaporated *in vacuo* and subsequent purifiaction by flash chromatography on silica gel (10% EtOAc/petrol) afforded the *title compound* in 76% yield (3.83g, 13.69 mmol); ν_{max} (film)/cm^{-1} 1245 (C–O), 1513 (ArC=C), 1731 (C=O), 2953 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.55-1.68 (2H, m, $CH_2CH_2CH_2$), 1.88-1.93 (2H, m, CH_2CH_2CH), 2.58 (2H, t, *J* 7.6 Hz, $ArCH_2CH_2$), 3.38 (1H, t, *J* 7.6 Hz, CH_2CH), 3.73 (6H, s, $HC(CO_2CH_3)_2$), 3.78 (3H, s, CH_3Oar), 6.82 (2H, d, *J* 8.8 Hz, 2ArC*H*), 7.08 (2H, d, *J* 8.8 Hz, 2ArC*H*); δ_C(100 MHz; $CDCl_3$) 28.4 ($CH_2CH_2CH_2$), 29.3 (CH_2CH), 34.5 (Ar–CH_2), 51.6 (CO_2CH_3), 51.6 (CO_2CH_3), 55.3 (CH_3O–Ar), 113.8 (2ArCH), 129.7 (2ArCH), 133.7 (ArC), 157.8 (MeOC–Ar) and 169.8 ($2CO_2Me$).

Pent-4-ynyl methanesulfonate (292)



Pent-4-yn-1-ol (1.6 mL, 1.50 g, 17.8 mmol) and diisopropyl ethyl amine (4.6 mL, 3.46 g, 26.7 mmol, 1.5 eq) were dissolved in anhydrous DCM (60 mL) and the resulting mixture was cooled to −20°C followed by the addition of mesyl chloride (2.0 mL, 2.90 g, 25.3 mmol, 1.4 eq). The reaction mixture was allowed to warm up to r.t. over an hour and was then stirred overnight heating to reflux under a nitrogen atmosphere. The solvent was evaporated and the residue was taken up in ethyl acetate (15 mL). The crude solution was washed with water (20 mL). The aqueous layer was extracted with ethyl acetate (2×10 mL). The combined organic extracts were dried over magnesium sulfate and the crude product was purified by flash chromatography (10% EtOAc/petrol) affording the desired mesylate derivative as a yellow oil in 84% yield (2.44 g, 15.0 mmol); ν_{max} (film)/cm^{-1} 1196 (C–O), 2118 (C≡C) and 3292 (sp C–H); δ_H(400 MHz; $CDCl_3$) 1.92-2.01 (2H, m, $CH_2CH_2CH_2$), 2.03 (1H, t, *J* 2.8 Hz, *H*C≡C), 2.37 (2H, dt, *J* 2.8, 6.8 Hz, HC≡C*CH*$_2$), 3.04 (3H, s, *CH*$_3$) and 4.36 (2H, t, *J* 6.4 Hz, *CH*$_2$OMs); δ_C(100 MHz; $CDCl_3$) 14.7 (HC≡*C*CH$_2$), 27.8 ($CH_2CH_2CH_2$), 37.2 (*C*H$_3$), 68.3 (*C*H$_2$O), 69.8 (*HC*≡C) and 82.1 (HC≡*C*); HRMS (FAB) (M^++H), found 163.0430, $C_6H_{11}O_3S$ requires 163.0428 (+1.6 ppm); m/*z* 163 (34%), 155 (28%), 154 (100%), 138 (39%), 137 (82%), 136 (81%) and 107 (35%).

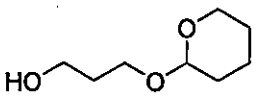
Dimethyl 2-(pent-4-ynyl)malonate (293)



Dimethyl malonate (1.8 mL, 2.05 g, 15.5 mmol, 1.1 eq) was added to a solution of sodium hydride (710 mg, 17.8 mmol, 60% in mineral oil, 1.2 eq) in THF (30 mL) at 0°C. The reaction mixture was allowed to stir for 1 hour and a solution of pent-4-ynyl methanesulfonate (2.40 g, 14.8 mmol) in THF (20 mL) was added *via* a syringe pump over an hour. The resulting mixture was then allowed to warm up slowly to r.t. and was stirred for a further 60 min. The reaction mixture was then heated to reflux overnight under an nitrogen atmosphere. The crude mixture was successively quenched with methanol (10 mL) and water (5 mL). Most of the organic solvents were evaporated *in vacuo*. The aqueous residue was taken up with ethyl acetate (20 mL) and washed with water. The aqueous layer was extracted with ethyl acetate (2×10 mL). The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. The crude product was purified by flash

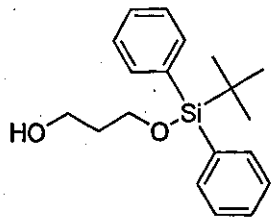
chromatography (10% EtOAc/petrol) affording the desired *title compound* in 70% yield (2.05 g, 10.4 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1197 (C–O), 1653 (C=O), 2115 (C≡C), and 3287 (sp C–H); δ_H(400 MHz; $CDCl_3$) 1.51-1.62 (2H, m, $CH_2CH_2CH_2$), 1.97 (1H, t, *J* 2.8 Hz, *H*C≡C), 1.99-2.08 (2H, m, CH_2CH), 2.23 (2H, dt, *J* 2.8, 6.8 Hz, HC≡CCH_2), 3.40 (1H, t, *J* 7.6 Hz, CH_2CH) and 3.75 (6H, s, CH_3); δ_C(100 MHz; $CDCl_3$) 18.1 (HC≡CCH_2), 26.1 ($CH_2CH_2CH_2$), 27.8 (CH_2CH), 51.2 (CH_2CH), 52.6 ($2CH_3$), 69.0 (*H*C≡C), 83.4 (HC≡*C*) and 169.6 (2*C*=O); HRMS (FAB) (M^++H), found 199.0972, $C_{10}H_{15}O_4$ requires 199.0970 (+0.9 ppm); m/*z* 199 (100%), 167 (21%), 139 (26%), 137 (24%), 135 (23%), 132 (34%), 107 (37%) and 79 (47%).

3-(Tetrahydro-2H-pyran-2-yloxy)propan-1-ol (297_a)[116]



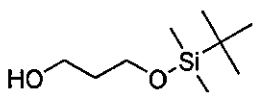
Dihydropyran (5.4 mL, 5.00 g, 59.4 mmol) was added to a solution of propanediol (15.0 mL, 15.83 g, 208.0 mmol, 3.5 eq) and Amberlyst N°15 (780 mg) in THF/DCM (1:1, 300 mL) and the resulting mixture was allowed to stir overnight at room temperture. The resine was then removed by filtration through a plug of celite. The filtrate was concentrated on a rotary evaporator and the resulting residue was taken up with DCM (50 mL). The crude product was washed with water (2×50 mL) and dried over magnesium sulfate. Solvent removal *in vacuo* followed by purification by flash chromatography on silica gel afforded the desired mono-protected diol in 54% yield (5.08 g, 31.9 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} ν_{max} (film)/cm^{-1} 2890 (sp^3 C–H), 2936 (sp^3 C–H), 2951 (sp^3 C–H) and 3620 (O–H); δ_H(400 MHz; $CDCl_3$) 1.38-1.58 (4H, m, $2CH_2$), 1.62-1.85 (4H, m, $2CH_2$), 2.52 (O*H*), 3.39-3.49 (1H, m, C*H*H), 3.50 (1H, m, C*H*H) 3.65-3.71 (2H, m, CH_2), 3.73-3.91 (2H, m, CH_2) and 4.52 (1H, dd, *J* 4.4, 7.0 Hz, C*H*CH_2); δ_C(100 MHz; $CDCl_3$) 19.6 (CH_2), 25.4 (CH_2), 30.6 (CH_2), 32.0 (CH_2), 61.4 (CH_2), 62.5 (CH_2), 66.2 (CH_2) and 99.1 (*C*H).

***O*-('Butyldiphenylsilyl)-propane-1,3-diol (297_b)**



Propane-1,3-diol (2.6 mL, 2.77 g, 36.4 mmol) was slowly added *via* a syringe pump over 45 min to a suspension of sodium hydride (1.45 g, 36.4 mmol, 60% in mineral oil) in dry THF (60 mL). The resulting mixture was stirred for an hour at r.t. and under a nitrogen atmosphere until a white precipitate appeared. *t*-Butyldiphenylsilyl chloride (9.5 mL, 10.00 g, 36.4 mmol) was then added and the reaction mixture was allowed to stir overnight. Diethyl ether (100 mL) was then added and the resulting mixture was washed successively with a solution of potassium carbonate (10% w/w) and brine. The ethereal layer was dried over magnesium sulfate and concentrated *in vacuo*. Subsequent purification by flash chromatography on silica gel (15% EtOAC/petrol) afforded the desired mono-protected diol in 76% yield (8.84 g, 27.8 mmol); ν_{max} (film)/cm^{-1} 2912 (sp^3 C–H), 2982 (sp^3 C–H), 2988 (sp^3 C–H) and 3588 (O–H); δ_H(400 MHz; $CDCl_3$) 1.08 (9H, s, C(C*H*$_3$)$_3$), 1.78-1.87 (2H, m, $CH_2CH_2CH_2$), 2.47 (1H, br s, O*H*), 3.83-3.89 (4H, m, O$CH_2CH_2CH_2$O), 7.37-7.49 (6H, m, ArC*H*) and 7.67-7.74 (4H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 19.1 (*C*(CH$_3$)$_3$), 34.3 (C(*C*H$_3$)$_3$), 34.2 ($CH_2CH_2CH_2$), 61.9 (*C*H$_2$OH), 63.3 (*C*H$_2$OSi), 127.8 (4Ar*C*H), 129.6 (2Ar*C*H), 133.3 (2Ar*C*) and 135.4 (4Ar*C*H); HRMS (FAB) (MH$^+$), found 315.1784, $C_{19}H_{27}O_2Si$ requires 314.1702 (+1.1 ppm); *m/z* 315 (22%), 257 (25%), 237 (14%), 200 (18%), 199 (100%), 197 (39%), 179 (71%) and 167 (17%).

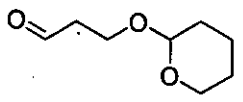
***O*-('Butyldimethylsilyl)-propane-1,3-diol (297_c)**[116]



Propane-1,3-diol (4.8 mL, 5.05 g, 66.3 mmol) was slowly added *via* a syringe pump over 30 min to a suspension of sodium hydride (2.65 g, 66.3 mmol, 60% in mineral oil) in dry THF

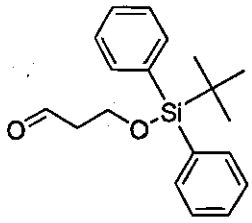
(100 mL). The resulting mixture was stirred for an hour at r.t. under a nitrogen atmosphere until a white precipitate appeared. *t*-Butyldimethylsilyl chloride (10.00 g, 66.3 mmol) was then added and the reaction mixture was allowed to stir overnight. The reaction was then quenched with methanol (20 mL) and with a saturated solution of sodium carbonate (15 mL). Most of the organic solvents were removed on a rotary evaporator and diethyl ether was added (100 mL). The crude product was washed with water (2×30 mL) and the organic layer was dried over magnesium sulfate. Subsequent purification by flash chromatography on silica gel (15% EtOAc/petrol) afforded the desired mono-protected diol in 75% yield (9.48 g, 49.8 mmol); ν_{max} (film)/cm^{-1} 2910 (sp^3 C–H), 2976 (sp^3 C–H), 2980 (sp^3 C–H) and 3590 (O–H); δ_H(400 MHz; $CDCl_3$) 0.07 (6H, s, Si(C*H*$_3$)$_2$), 0.89 (9H, s, C(C*H*$_3$)$_3$), 1.73-1.80 (2H, m, $CH_2CH_2CH_2$), 2.64 (1H, br s, O*H*) and 3.77-3.85 (4H, m, OC*H*$_2$CH$_2$C*H*$_2$O); δ_C(100 MHz; $CDCl_3$) –5.5 (Si(*C*H$_3$)$_2$), 18.2 (*C*(CH$_3$)$_3$), 25.8 (C(*C*H$_3$)$_3$), 34.2 ($CH_2CH_2CH_2$), 62.4 (*C*H$_2$OH) and 62.9 (*C*H$_2$OSi); HRMS (EI) (MH^+), found 191.1473, $C_9H_{23}O_2Si$ requires 191.1474 (+2.9 ppm); *m/z* 191 (3%), 175 (2%), 133 (54%), 105 (63%) and 75 (100%).

3-(Tetrahydro-2H-pyran-2-yloxy)propanal (298$_a$)[116,135]



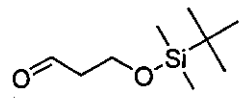
To a suspension of pyridinium chlorochromate (3.03 g, 14.1 mmol, 1.5 eq) in DCM (20 mL) was added a solution of 3-(tetrahydro-2H-pyran-2-yloxy)propan-1-ol (1.50 g, 9.4 mmol) in DCM (15 mL). The resulting mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The crude mixture was then filtered through a pad of celite and silica and the filtrate was concentrated *in vacuo* affording the *title compound* in 73% yield (1.09 g, 68.9 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1035 (C–O), 1201 (C–O), 1737 (C=O) and 2944 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.39-1.56 (4H, m, 2C*H*$_2$), 1.57-1.76 (2H, m, C*H*$_2$), 2.63 (2H, dt, *J* 6.0, 7.6 Hz, CHOC*H*$_2$), 3.41-3.50 (1H, m, C*H*H), 3.65 (1H, m, C*H*H), 3.74-3.83 (1H, m, C*H*H), 3.97-4.07 (1H, m, C*H*H), 4.53-4.59 (1H, m, C*H*CH$_2$) and 9.75 (1H, s, C*H*O); δ_C(100 MHz; $CDCl_3$) 19.1 (*C*H$_2$), 25.3 (*C*H$_2$), 30.5 (*C*H$_2$), 43.8 (*C*H$_2$), 61.1 (*C*H$_2$), 62.2 (*C*H$_2$), 98.9 (*C*HCH$_2$) and 201.4 (*C*HO).

***O*-(*t*Butyldiphenylsilyl)-3-hydroxypropanal (298$_b$)**



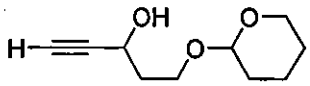
Pyridium chlorochromate (4.11 g, 19.1 mmol, 1.5 eq) was added at 0°C to a solution of *o*-(*t*-butyldiphenylsilyl)-propane-1,3-diol (2.50 g, 13.1 mmol) in DCM (30 mL) and the reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The crude mixture was then filtered through a plug of celite and the filtrate was concentrated *in vacuo* affording the *title compound* in 85% yield (3.37 g, 10.8 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1732 (C=O), 2910 (sp^3 C–H) and 2981 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.04 (9H, s, C(C*H*$_3$)$_3$), 2.60 (2H, dt, *J* 2.0, 6.0 Hz, CHOC*H*$_2$), 4.02 (2H, t, *J* 6.0 Hz, C*H*$_2$OSi), 7.37-7.50 (6H, m, ArC*H*) and 7.66-7.74 (4H, m, ArC*H*) and 9.82 (1H, t, *J* 2.0 Hz, C*H*O); δ_C(100 MHz; $CDCl_3$) 19.1 (*C*(CH$_3$)$_3$), 26.7 (C(*C*H$_3$)$_3$), 46.4 (*C*H$_2$OSi), 58.3 (CH*C*H$_2$), 127.8 (4Ar*C*H), 129.9 (2Ar*C*H), 133.2 (2Ar*C*), 135.5 (4Ar*C*H) and 202.0 (*C*HO).

***O*-(*t*Butyldimethylsilyl)-3-hydroxypropanal (298$_c$)**[116]



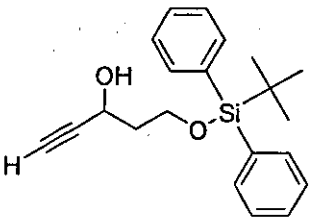
Pyridium dichromate (7.41 g, 19.7 mmol, 1.5 eq) was added to a solution of *o*-(*t*-butyldimethylsilyl)-propane-1,3-diol (2.50 g, 13.1 mmol) in DCM (50 mL) at 0°C and the reaction mixture was allowed to stir overnight at r.t. under a nitrogen atmosphere. The crude mixture was then filtered through a pad of celite affording the *title compound* in 79% yield (1.96 g, 10.4 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1726 (C=O), 2910 (sp^3 C–H) and 2978 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 0.06 (6H, s, Si(C*H*$_3$)$_2$), 0.88 (9H, s, C(C*H*$_3$)$_3$), 2:59 (2H, dt, *J* 2.0, 6.0 Hz, CHOC*H*$_2$), 3.98 (2H, t, *J* 6.0 Hz, C*H*$_2$OSi) and 9.79 (1H, t, *J* 2.0 Hz, C*H*O); δ_C(100 MHz; $CDCl_3$) –5.5 (Si(*C*H$_3$)$_2$), 18.3 (*C*(CH$_3$)$_3$), 25.9 (C(*C*H$_3$)$_3$), 46.5 (*C*H$_2$OSi), 57.4 (CH*C*H$_2$) and 202.1 (*C*HO).

5-(Tetrahydro-2H-pyran-2-yloxy)pent-1-yn-3-ol (299_a)[116]



Ethynyl magnesium bromide (15.2 mL, 7.6 mmol, 0.5 M in THF, 1.2 eq) was added dropwise over an hour *via* a syringe pump to a solution of 3-(tetrahydro-2H-pyran-2-yloxy)propanal (1.20 g, 7.6 mmol) in THF (40 mL) at –78°C under a nitrogen atmosphere. The crude mixture was quenched with a saturated solution of ammonium chloride (10 mL). The crude product was washed with water (20 mL) and the aqueous layer was extracted with diethyl ether (2×20 mL). The crude product was dried over magnesium sulfate and concentrated *in vacuo*. Purification by flash chromatography on silica gel afforded the two inseparable diastereoismers of the *title compound* in 29% yield (400 mg, 2.2 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1035 (C–O), 1201 (C–O), 2897 (sp^3 C–H), 2939 (sp^3 C–H), 3302 (sp C–H) and 3620 (O–H); δ_H(400 MHz; $CDCl_3$) 1.39-1.56 (2H, m, C*H*$_2$), 1.57-1.88 (2H, m, C*H*$_2$), 1.90-2.19 (2H, m, C*H*$_2$), 2.47 (1H, s, *H*C≡C), 3.14 (1H, br s, O*H*), 3.41-3.57 (1H, m, C*H*OH), 3.58-3.66 (1H, m, C*H*H), 3.70-4.05 (4H, m, 2C*H*$_2$), 4.07-4.19 (1H, m, C*H*H) and 4.55-4.71 (1H, m C*H*CH$_2$); δ_C(100 MHz; $CDCl_3$) 19.5 (*C*H$_2$), 25.3 (*C*H$_2$), 30.5 (*C*H$_2$), 36.6 (*C*H$_2$), 61.0 (*C*H), 61.3 (*C*H), 62.2 (*C*H$_2$), 62.4 (*C*H$_2$), 64.5 (*C*H$_2$), 64.7 (*C*H$_2$), 72.9 (H*C*≡C), 73.0 (H*C*≡C), 84.3 (HC≡*C*), 98.9 (*C*HCH$_2$) and (*C*HCH$_2$).

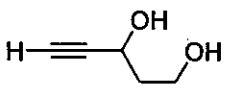
5-((Trimethylsilyl)diphenylmethoxy)pent-1-yn-3-ol (299_b)



Ethynyl magnesium bromide (29.3 mL, 14.6 mmol, 0.5 M in THF,) was added dropwise over an hour *via* a syringe pump to a solution of *O*-(*t*-butyldiphenylsilyl)-3-hydroxypropanal (2.28 g, 7.3 mmol) in THF (40 mL) at –78°C under a nitrogen atmosphere. The crude mixture was allowed to stir for 30 min and was quenched with a saturated solution of potassium carbonate (10 mL). The crude product was washed with water (20 mL) and the

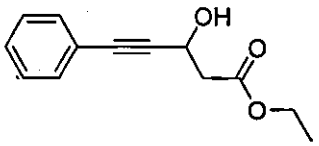
aqueous layer was extracted with diethyl ether (2×20 mL). The crude product was dried over magnesium sulfate and concentrated *in vacuo*. Purification by flash chromatography on silica gel (10% EtOAc/petrol) afforded the *title compound* in 49% yield (1.22 mg, 3.6 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 2171 (C≡C), 2957 (sp^3 C–H) and 3414 (O–H); δ_H(400 MHz; $CDCl_3$) 1.03 (9H, s, C(C*H*$_3$)$_3$), 1.88-1.98 (1H, m, CHC*H*HCH$_2$), 2.02-2.12 (1H, m, CHC*H*HCH$_2$), 2.49 (1H, d, *J* 2.4 Hz, *H*C≡C), 3.45 (1H, br s, O*H*), 3.82-3.91 (1H, m, C*H*HOSi), 4.03-4.12 (1H, m, C*H*HOSi), 4.70-4.76 (1H, m, C*H*OH), 7.37 (6H, m, ArC*H*) and 7.66-7.76 (4H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 19.1 (*C*(CH$_3$)$_3$), 26.8 (C(*C*H$_3$)$_3$), 38.6 (CH*C*H$_2$CH$_2$), 61.5 (*C*HOH), 61.7 (*C*H$_2$OSi), 73.0 (H*C*≡C), 84.5 (HC≡*C*), 127.7 (2Ar*C*H), 129.9 (2Ar*C*H), 132.9 (2Ar*C*) and 135.6 (2Ar*C*H).

Pent-4-yne-1,3-diol (300)[136]



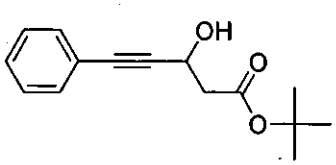
Protocol 4a: Camphor sulfonic acid (45 mg, 0.19 mmol, 10 mol%) was added to a solution of 5-(tetrahydro-2H-pyran-2-yloxy)pent-1-yn-3-ol (360 mg, 1.95 mmol) in methanol (10 mL) at r.t. and the resulting mixture was allowed to stir overnight. Water was added (15 mL) and the crude mixture was extracted with diethyl ether (2×10 mL). Solvents were concentrated *in vacuo* to give the *title compound* in 55% yield (110 mg, 1.07 mmol); Protocole 4c: Tetra-*n*-butylammonium fluoride tri-hydrate (880 mg, 2.80 mmol, 1.6 eq) was added dropwise to a solution of 5-(2-(trimethylsilyl)propan-2-yloxy)-1-(trimethylsilyl)pent-1-yn-3-ol (500 mg, 1.75 mmol) in THF (15 mL) at room temperature. The reaction mixture was stirred for 5 min (TLC monitoring) and quenched with water (10 mL). The crude mixture was extracted with diethyl ether (2×15mL) and dried over magnesium sulfate. Solvent removal followed by purification by flash chromatography on silica gel (EtOAc) afforded the unexpected *title compound* in 36% yield (64 mg, 0.64 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 2171 (C≡C), 2957 (sp^3 C–H), 3387 (OH) and 3418 (O–H); δ_H(400 MHz; $CDCl_3$) 1.82-2.12 (2H, m, CHC*H*$_2$CH$_2$), 2.45 (1H, d, J Hz, *H*C≡C), 2.63 (1H, br s, O*H*), 3.48 (1H, br s, O*H*), 3.77-3.88 (1H, m, C*H*HOH), 3.89-4.03 (1H, m, C*H*HOH) and 4.55-4.61 (1H, m, C*H*OH); δ_C(100 MHz; $CDCl_3$) 38.6 (CH*C*H$_2$CH$_2$), 60.2 (*C*H$_2$O), 61.4 (*C*HOH), 73.4 (H*C*≡C) and 84.2 (HC≡*C*); no mass ion could be observed.

Ethyl 3-hydroxy-5-phenylpent-4-ynoate (302_a)[118]



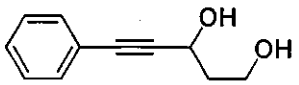
Butyl lithium (39.4 mL, 98.5 mmol, 2.5 M in THF) was added dropwise to a solution of diisopropyl amine (13.8 mL, 9.96 g, 98.5 mmol) in THF (140 mL) at 0°C. The reaction mixture was allowed to stir for 30 minutes and was then cooled down to −78°C. Ethyl acetate (9.6 mL, 8.67 g, 98.5 mmol) was added dropwise and the reaction mixture was allowed to stir for one more hour. A solution of 3-phenylpropiolaldehyde (12.81 g, 98.5 mmol) in THF (20 mL) was slowly added and the reaction mixture was allowed to stir for 30 min. The reaction was then quenched with a saturated solution of ammonium chloride (25 mL). Most of the organic solvents were concentrated on a rotary evaporator and the aqueous residue was taken up in ethyl acetate (30 mL). The crude product was washed with water (30 mL). The aqueous layer was extracted with ethyl acetate (2×15 mL). The combined organic extracts were dried over magnesium sulfate and concentrated *in vacuo*. Subsequent purification by flash chromatography (10% EtOAc/petrol) afforded the *title compound* in 65% yield (13.99 g, 64.2 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1726 (C=O), 2870 (sp^3 C–H), 2831 (sp^3 C–H), 2979 (sp^3 C–H), 3058 (sp^2 ArC–H), 3079 (sp^2 ArC–H) and 3416 (OH); δ_H(400 MHz; $CDCl_3$) 1.30 (3H, t, *J* 7.2 Hz, CH_3), 2.84 (2H, d, *J* 5.6 Hz, $CHCH_2$), 3.18 (1H, d, *J* 6.4 Hz, O*H*), 4.22 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 5.00 (1H, dt, *J* 5.6, 6.4 Hz, C*H*OH), 7.27-7.34 (3H, m, ArC*H*) and 7.39-7.51 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 14.2 (CH_3), 42.0 ($CHCH_2$), 59.3 (*C*H), 61.1 (OCH_2), 81.2 (*C*≡C), 88.3 (*C*≡C), 122.4 (Ar*C*), 128.3 (2Ar*C*H), 128.6 (Ar*C*H), 131.8 (2Ar*C*H) and 173.1 (*C*=O).

^{t}Butyl-3-hydroxy-5-phenylpent-4-ynoate (302_b)



Butyl lithium (26.1 mL, 2.5 M solution, 65.2 mmol, 1.1 eq) was added dropwise to a solution of diisopropyl amine (9.1 mL, 6.56 g, 65.2 mmol, 1.1 eq) in THF (90 mL) at 0°C. The reaction mixture was stirred for 30 minutes and ^{t}butyl acetate (9.6 mL, 8.26 g, 71.1 mmol) was added at −78°C. The reaction mixture was stirred one more hour and a solution of 3-phenylpropiolaldehyde (7.62 g, 58.6 mmol) in THF (20 mL) was slowly added. After 30 minutes, the reaction was quenched with a solution of saturated ammonium chloride (25 mL). Most of the organic solvents were evaporated *in vacuo*. The residue was taken up in ethyl acetate (30 mL) and washed with water (30 mL). The aqueous layer was extracted with ethyl acetate (2×15 mL). The organic extracts were combined and dried over magnesium sulfate. Evaporation of the solvent afforded the desired compound in 99% yield (14.42 g, 58.5 mmol) as a yellow oil; Rf (15% EtOAc/petrol) 0.42; ν_{max} (film)/cm^{-1} 1733 (C=O), 2234 (C≡C), 2931 (ArC–H), 2978 (ArC–H) and 3444 (OH); δ_H(400 MHz; $CDCl_3$) 1.49 (9H, s, C*H*$_3$), 2.61 (1H, d, *J* 6.4 Hz, CHC*H*H), 2.76 (1H, d, *J* 5.2 Hz, CHC*H*H), 3.35 (1H, d, *J* 6.4 Hz, O*H*), 4.93 (1H, dt, *J* 5.2, 6.4 Hz, C*H*OH), 7.27-7.34 (3H, m, ArC*H*) and 7.40-7.45 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 29 (3*C*H$_3$), 42.9 (CH*C*H$_2$), 59.5 (*C*H), 81.5 (O*C*(CH$_3$)$_3$), 84.8 (*C*≡C), 88.2 (C≡*C*), 122.4 (Ar*C*), 128.3 (2Ar*C*H), 128.5 (2Ar*C*H) and 131.7 (1Ar*C*H) and 170.8 (*C*=O); HRMS (EI) (M^+), found 247.1339, $C_{15}H_{19}O_3$ requires 247.1334 (+1.9 ppm); *m/z* 247 (10%), 191 (29%), 173 (100%), 131 (44%) and 57 (59%).

5-Phenylpent-4-yne-1,3-diol (303)[133]



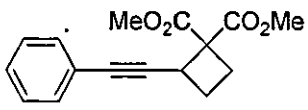
Lithium borohydride (71.0 mL, 142.0 mmol, 2.0 M solution, 2.5 eq) was added over an hour to a solution of ^{t}butyl-3-hydroxy-5-phenylpent-4-ynoate (14.09 g, 57.2 mmol) in THF (200 mL). Methanol (46.3 mL, 1.1 mol, 20 eq) was then added *via* a syringe pump over an hour at 0°C. The reaction mixture was allowed to stir at room temperature for a further 30 min. Ice cold water (10 mL) was added and the resulting mixture was extracted from ethyl acetate (3×30 mL). The combined organic layers were dried over magnesium sulfate to give the *title compound* in 99% yield (10.04 g, 57.0 mmol) as a yellow oil; Rf (15% EtOAc/petrol) 0.13; ν_{max} (film)/cm^{-1} 1049 (C–O), 2230 (C≡C), 2886 (ArC–H), 2953 (ArC–H) and 3341 (OH); δ_H(400 MHz; $CDCl_3$) 1.92-2.09 (2H, m, CHC*H*$_2$), 2.33 (1H, broad s, OH), 2.99 (1H, broad

s, OH), 3.85 (1H, ddd, *J* 4.0, 6.4, 10.8 Hz, C*H*HOH), 4.00 (1H, ddd, *J* 4.0, 7.6, 10.8 Hz, C*H*HOH), 4.81 (1H, dd, *J* 4.4, 6.4 Hz C*H*OH), 7.16-7.29 (3H, ArC*H*) and 7.31-7.42 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 38.9 (CH*C*H_2), 60.7 (*C*H_2OH), 62.3 (*C*HOH), 85.4 (*C*≡C), 89.2 (C≡*C*), 122.4 (Ar*C*), 128.3 (2Ar*C*H), 128.5 (Ar*C*H) and 131.8 (2Ar*C*H); no mass ion could be observed.

1-(3,5-Dibromopent-1-ynyl)benzene (304)

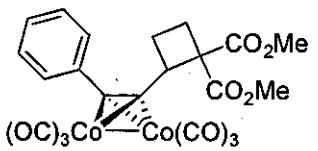
Bromine (5.6 mL, 17.52 g, 114.7 mmol, 2.4 eq) was added dropwise to a solution of triphenylphosphine (31.33 g, 119.5 mmol, 2.5 eq) in DCM (250 mL) at 0°C. The resulting mixture was allowed to stir until the phosphonium salt precipitated (approximately 20 min). A solution of diol **303** (8.42 g, 47.8 mmol) and imidazole (8.13 g, 119.5 mmol, 2.5 eq) in DCM (150 mL) was slowly added *via* a cannula to the phosphonium salt at 0°C and the resulting reaction mixture was allowed to stir overnight at room temperature. The reaction mixture was quenched with ice-cold water (30 mL) and extracted from ethyl acetate (3×15 mL). The combined organic extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Triphenylphosphine oxide and triphenylphosphine were recrystallised thrice from cold petrol using DCM and filtered off. The filtrates were combined and the solvents were removed *in vacuo* affording the *title compound* in 99% (14.41 g, 47.8 mmol) as an orange oil; Rf (petrol) 0.24; ν_{max} (film)/cm^{-1} 755 (C–Br), 689 (C–Br), 2224 (C≡C), 2965 (ArC–H) and 3054 (ArC–H); δ_H(400 MHz; $CDCl_3$) 2.61 (2H, dt, *J* 6.4, 6.8 Hz, CHCH_2); 3.62 (2H, t, *J* 6.4 Hz, CH_2Br), 4.97 (1H, t, *J* 6.8 Hz, C*H*Br), 7.24-7.37 (3H, m, ArC*H*) and 7.40-7.47 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 30.0 (CH*C*H_2), 35.4 (*C*HBr), 41.9 (*C*H_2Br), 86.6 (C≡*C*), 87.7 (*C*≡C), 121.8 (Ar*C*), 128.4 (2Ar*C*H), 129.1 (Ar*C*H) and 131.9 (2Ar*C*H); no mass ion could be observed.

Dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (305)



Dimethyl malonate (0.9 mL, 1.08 g, 7.7 mmol, 1.1 eq) was added to a suspension of sodium hydride (620 mg, 15.4 mmol, 60% in mineral oil, 2.2 eq) in THF (140 mL) at 0°C under a nitrogen atmosphere. A solution of 1-(3,5-dibromopent-1-ynyl)benzene (2.11 g, 7.0 mmol) in THF (60 mL) was added *via* a cannula over 5 min and the resulting mixture was allowed to stir at room temperature for 2 hours. The reaction mixture was heated to reflux for 6 hours. Most of the solvent was evaporated *in vacuo* and the residue was taken up in diethyl ether (20 mL). The organic crude solution was washed with water (25 mL), dried over magnesium sulfate and concentrated *in vacuo*. The crude cyclobutane was purified by flash chromatography (5% ethyl acetate/petrol) affording the *title compound* as a yellow oil in 74% yield (1.41 g, 5.2 mmol); Rf (15% EtOAc/petrol) 0.92; ν_{max} (film)/cm^{-1} 1754 (C=O), 1737 (C=O), 2227 (C≡C), 2953 (ArC–H) and 3001 (ArC–H); δ_H(400 MHz; $CDCl_3$) 2.09-2.33 (3H, m, 1H $CHCH_2CHH$ + 2H $CHCH_2CH_2$), 2.73-2.82 (1H, m, $CHCH_2CHH$), 3.71 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 3.95 (1H, t, *J* 8.8 Hz, *CH*), 7.17-7.24 (3H, m, Ar*CH*) and 7.26-7.41 (2H, m, Ar*CH*); δ_C(100 MHz; $CDCl_3$) 24.4 ($CHCH_2$), 26.1 ($CHCH_2CH_2$), 31.5 (*CH*), 52.7 (CO_2CH_3), 52.8 (CO_2CH_3), 57.7 ($C(CO_2CH_3)_2$), 84.4 (C≡*C*), 88.0 (*C*≡C), 123.1 (Ar*C*), 128.0 (Ar*CH*), 128.2 (2Ar*CH*), 131.6 (2Ar*CH*), 169.6 (*C*=O) and 171.1 (*C*=O); HRMS (EI) (M^+), found 273.1127, $C_{16}H_{16}O_4$ requires 273.1121 (+0.8 ppm); *m/z* 273 (24%), 213 (20%), 145 (100%), 141 (37%) and 113 (61%).

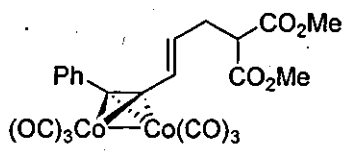
Dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate dicobalt hexacarbonyl (306)



Dicobalt octacarbonyl (1.81 g, 5.3 mmol, 1.2 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (1.20 g, 4.4 mmol) in DCM (60 mL). The reaction mixture was allowed to stir for 4 hours at room temperature under a nitrogen atmosphere. The solvent was evaporated and the residue was taken up in ethyl acetate (20 mL). The resulting solution was washed with water (25 mL). The aqueous layer was

extracted with ethyl acetate (2×10 mL). The combined organic layers were dried over magnesium sulfate, filtered through celite and concentrated *in vacuo*. The crude product was purified by flash chromatography (15 % ethyl acetate/petrol) affording the desired dicobalt hexacarbonyl complex in 97% yield (2.38 g, 4.3 mmol) as a dark red oil; Rf (15% ethyl acetate/petrol) 0.83; ν_{max} (film)/cm^{-1} 1731 (C=O), 2018 (C≡O), 2048 (C≡O), 2088 (C≡O) and 2993 (ArC–H); δ_H(400 MHz; $CDCl_3$) 2.15-2.26 (1H, m, $CHCH_2CHH$), 2.35-2.52 (2H, m, $CHCH_2CH_2$), 2.60-2.69 (1H, m, $CHCH_2CHH$), 2.97 (3H, s, OCH_3), 3.65 (3H, s, OCH_3), 4.47 (1H, dd, *J* 9.2, 10.4 Hz, CH_2CH), 7.17-7.28 (3H, m, ArCH) and 7.36-7.46 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 26.7 ($CHCH_2$), 28.8 ($CHCH_2CH_2$), 46.5 ($CHCH_2$), 52.3 (CO_2CH_3), 52.6 (CO_2CH_3), 58.6 ($C(CO_2CH_3)_2$), 81.9 (C–C), 93.4 (C–C), 127.6 (ArCH), 128.6 (2ArCH), 129.7 (2ArCH), 131.8 (ArC), 169.5 (C=O), 171.2 (C=O) and 199.4 ($CO_{complex}$); HRMS (FAB) (M^+–3CO), found 473.9574, $C_{19}H_{16}Co_2O_7$ requires 473.9560 (+2.6 ppm); *m/z* 503 (5%), 475 (4%), 447 (26%), 419 (14%), 391 (21%), 390 (80%), 331 (21%) and 273 (15%).

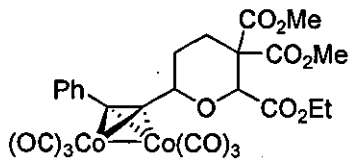
Dicobalt hexacarbonyl 2-(5-phenyl-pent-2-en-4-ynyl)-molnic acid dimethyl ester (308)



$BF_3.Et_2O$ (170 µL, 1.2 mmol, 3.0 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate dicobalt hexacarbonyl (250 mg, 0.4 mmol) in DCM (15 mL) at room temperature and the reaction mixture was allowed to stir under a nitrogen atmosphere for 2 min. The solvent was evaporated *in vacuo* and the residue was taken up in ethyl acetate (10 mL). The resulting solution was washed with water (20 mL) and the aqueous layer was extracted with ethyl acetate (2×10 mL). The organic extracts were combined and dried over magnesium sulfate. After filtration and solvent removal *in vacuo*, the crude product was purified by flash chromatography (15 % ethyl acetate/petrol) affording the *title compound* in 68% yield (170 g, 0.3 mmol) as a dark red oil; Rf (15% ethyl acetate/petrol) 0.72; ν_{max} (film)/cm^{-1} 1735 (C=O), 2019 (C≡O), 2049 (C≡O), 2088 (C≡O) and 2953 (ArC–H); δ_H(400 MHz; $CDCl_3$) 2.76 (2H, t, *J* 7.5 Hz, CH_2), 3.48 (1H, t, *J* 7.6 Hz, $CHC(CO_2Me)_2$), 3.68 (6H, s, CH_3), 6.06 (1H, q, J 7.4 Hz, CH), 6.79 (1H, d, *J* 14.8 Hz,

C–CCH), 7.25-7.31 (3H, m, ArC*H*) and 7.43-7.45 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 32.2 (*C*H_2), 51.3 (CO_2CH_3), 52.6 (CO_2CH_3), 52.7 ($C(CO_2CH_3)_2$), 91.3 (*C*–C), 92.6 (C–*C*), 128.0 (Ar*C*H), 128.9 (2Ar*C*H), 129.2 (2Ar*C*H), 129.9 (*C*H=CH), 132.7 (*C*H=CH), 138.0 (Ar*C*), 169.1 (CO_2CH_3), 169.2 (CO_2CH_3) and 199.6 ($CO_{complex}$).

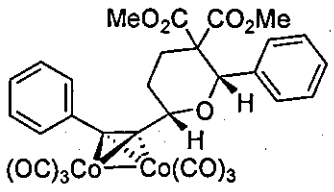
Dicobalt hexacarbonyl 2-ethyl 3,3-dimethyl dihydro-6-(2-phenylethynyl)-2H-pyran-2,3,3(4H)-tricarboxylate (309)



Dicobalt octacarbonyl (140 mg, 0.41 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (100 mg, 0.36 mmol) in DCM (10 ml) and activated 4 Å molecular sieves were added (200 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Ethyl glyoxylate (70 µL, 0.43 mmol, 1.2 eq) and scandium triflate (9 mg, 5 mol%) were successively added. The resulting mixture was allowed to stir at room temperature for 17 h under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 58% (140 mg, 0.21 mmol) in a 1.42/1 *cis*:*trans*; (i) first eluted *trans* isomer Rf (15% EtOAc/petrol) 0.52; ν_{max} (film)/cm^{-1} 1069 (C–O), 1737 (C=O), 2021 (C≡O), 2053 (C≡O), 2057 (C≡O), and 2991 (ArC–H); δ_H(400 MHz; CDCl3) 1.23 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 1.50-1.68 (1H, m, CHC*H*H), 1.93-2.06 (1H, m, CHC*H*H), 2.24-2.35 (1H, m, $CHCH_2CHH$), 2.57-2.66 (1H, m, $CHCH_2CHH$), 3.68 (3H, s, OCH_3), 3.72 (3H, s, OCH_3), 4.18 (2H, q, *J* 7.2 Hz, OCH_2CH_3), 4.83 (1H, dd, *J* 2.4, 11.2 Hz, CH_2CHO), 5.42 (1H, s, $OCHCO_2Et$), 7.21-7.30 (3H, m, ArCH) and 7.50-7.56 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 13.0 (OCH_2CH_3), 24.0 ($CHCH_2$), 28.9 ($CHCH_2CH_2$), 51.9 (OCH_3), 52.2 (OCH_3), 54.3 ($C(CO_2CH_3)_2$), 60.6 (OCH_2CH_3), 72.1 (CH_2CHO), 75.3 ($OCHCO_2Et$), 89.0 (*C*–C), 94.9 (*C*–C), 126.8 (Ar*C*H), 127.7 (2Ar*C*H), 128.9 (2Ar*C*H), 136.6 (Ar*C*), 167.3 (CO_2CH_3), 167.6 (CO_2CH_3), 168.6 (CO_2Et) and 198.2 ($CO_{complex}$); HRMS (FAB) (M^+–2CO), found 603.9815, $C_{24}H_{22}Co_2O_{11}$ requires 603.9826 (–1.8 ppm); m/z 576 (17%), 548 (100%), 520 (12%) and 492 (52%); no apparent coupling was observed by nOe analysis between the

proton at 4.83 ppm and the proton at 5.42 ppm suggesting a *trans* stereochemistry (ii) second eluted *Cis* isomer Rf (15% EtOAc/petrol) 0.34; ν_{max}.(film)/cm^{-1} 1116 (C–O), 1732 (C=O), 2021 (C≡O), 2053 (C≡O), 2091 (C≡O), 2959 (ArC–H); δ_H(400 MHz; $CDCl_3$) 1.18 (3H, t, *J* 7.2 Hz, OCH_2CH_3), 1.53-1.66 (1H, m, CHC*H*H), 1.98-2.07 (1H, m, CHC*H*H), 2.21-.2.31 (1H, m, $CHCH_2CHH$), 2.68 (1H, ddd, *J* 2.8, 4.0, 13.6 Hz, $CHCH_2CHH$) 4.13-4.23 (2H, m, OCH_2CH_3), 4.63 (1H, s, $OCHCO_2Et$), 4.80 (1H, dd, *J* 2.5, 11.2 Hz, CH_2CHO), 7.18-7.29 (3H, m, ArC*H*) and 7.52-7.58 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 12.9 (OCH_2CH_3), 28.8 ($CHCH_2$), 30.5 ($CHCH_2CH_2$), 51.6 (OCH_3), 52.0 (OCH_3), 56.5 ($C(CO_2CH_3)_2$), 60.2 (OCH_2CH_3), 77.3 (CH_2CHO), 78.0 ($OCHCO_2Et$), 89.3 (*C*–C), 94.1 (*C*–C), 126.8 (ArCH), 127.7 (2ArCH), 128.9 (2ArCH), 136.6 (Ar*C*), 167.4 (CO_2CH_3), 167.7 (CO_2CH_3), 169.4 ($CO_2CH_2CH_3$) and 198.1 ($CO_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.63 ppm and the proton at 4.80 ppm; HRMS (FAB) (M^+–3CO), found 575.9890, $C_{23}H_{22}Co_2O_{10}$ requires 575.9877 (+2.2 ppm); *m/z* 548 (100%), 520 (5%) and 492 (92%).

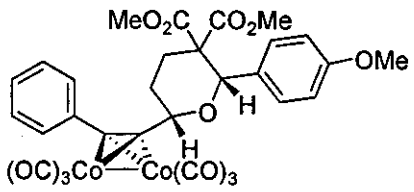
(2R,6R) and (2S,6S) Dicobalt hexacarbonyl dimethyl dihydro-2-phenyl-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (311)



Dicobalt octacarbonyl (100 mg, 0.29 mmol) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (80 mg, 0.29 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Benzaldehyde (35 µL, 0.34 mmol, 1.2 eq) and scandium triflate (6 mg, 5 mol%) were successively added. The resulting mixture was allowed to stir at room temperature for 24 h under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 64% (120 mg, 0.18 mmol) as dark red crystals; Rf (15%

EtOAc/petrol) 0.68; mp 114-115°C; ν_{max} (film)/cm^{-1} 1083 (C–O), 1262 (C–O), 1731 (C=O), 1736 (C=O), 2020 (C≡O), 2051 (C≡O), 2091 (C≡O), 2848 (ArC–H) and 2913 (ArC–H); δ_H(400 MHz; $CDCl_3$) 2.09-2.18 (2H, m, $CHCH_2$), 2.36-2.46 (1H, m, $CHCH_2CHH$), 2.72 (1H, dt, *J* 3.6, 13.6 Hz, $CHCH_2CHH$), 3.54, (3H, s, CO_2CH_3), 3.69 (3H, s, CO_2CH_3), 4.99-5.05 (1H, m, CH_2CHO), 5.27 (1H, s, $OCHAr$), 7.23-7.32 (6H, m, ArCH), 7.40-7.45 (2H, m, ArCH) and 7.55-7.60 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 30.0 ($CHCH_2$), 32.7 ($CHCH_2CH_2$), 51.7 (CO_2CH_3), 52.6 (CO_2CH_3), 59.1 ($C(CO_2CH_3)_2$), 79.2 (OCHAr), 82.8 (CH_2CHO), 89.9 (CoCCCo), 96.0 (CoCCCo), 126.0 (2ArCH), 126.4 (2ArCH), 126.5 (ArCH), 126.8 (ArCH), 127.7 (2ArCH), 128.8 (2ArCH), 137.6 (ArC), 138.9 (ArC), 169.0 (CO_2CH_3), 171.2 (CO_2CH_3) and 198.2 ($CO_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 5.05 ppm and the proton at 5.27 ppm; HRMS (FAB) (M^+–2CO), found 607.9940, $C_{27}H_{22}Co_2O_9$ requires 607.9928 (+2.1 ppm); *m/z* 580 (90%), 552 (43%), 524 (100%) and 496 (48%).

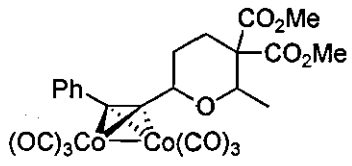
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-2-(4-methoxyphenyl)-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (312)



Dicobalt octacarbonyl (135 mg, 0.39 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (100 mg, 0.36 mmol) in DCM (10 ml) and activated 4 Å molecular sieves were added (200 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. *p*-Anisaldehyde (50 µL, 0.43 mmol, 1.2 eq) and scandium triflate (9 mg, 5 mol%) were successively added. The resulting mixture was allowed to stir at room temperature for 15 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 85% (210 mg, 0.30 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.61; ν_{max} (film)/cm^{-1} 1085 (C–O), 1251 (C–O), 1731 (C=O), 1736 (C=O),

2021 (C≡O), 2090 (C≡O) and 2954 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 2.01-2.11 (2H, m, $CHCH_2$), 2.28-2.38 (1H, m, $CHCH_2CHH$), 2.64 (1H, dt, *J* 3.2, 13.2 Hz, $CHCH_2CHH$), 3.49 (3H, s, CO_2CH_3), 3.61 (3H, s, CO_2CH_3), 3.72 (3H, s, $ArOCH_3$), 4.91-4.97 (1H, m, CH_2CHO), 5.14 (1H, s, OCHAr), 6.70-6.75 (2H, m, ArCH), 7.17-7.25 (3H, m, ArCH), 7.26-7.31 (2H, m, ArCH) and 7.48-7.53 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 29.0 ($CHCH_2$), 31.6 ($CHCH_2CH_2$), 50.7 (CO_2CH_3), 51.5 (CO_2CH_3), 54.0 ($ArOCH_3$), 58.0 ($C(CO_2CH_3)_2$), 78.2 (OCHAr), 81.6 (CH_2CHO), 88.9 (C–C), 95.1 (C–C), 111.4 (2ArCH), 126.7 (ArCH), 127.6 (2ArCH), 127.8 (2ArCH), 128.8 (2ArCH), 130.1 (ArC), 136.6 (ArC), 157.8 (ArC), 168.0 (CO_2CH_3), 170.2 (CO_2CH_3) and 198.4 ($CO_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton presenting the multiplet at 4.91-4.97 ppm and the proton at 5.14 ppm; HRMS (FAB) (M^+–2CO), found 638.0047, $C_{28}H_{24}Co_2O_{10}$ requires 638.0033 (+2.2 ppm); *m/z* 610 (77%), 582 (75%), 554 (100%) and 526 (26%).

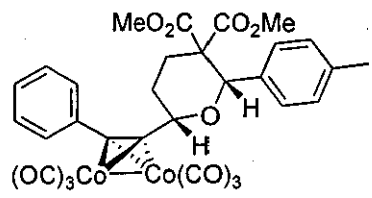
(2S,6R) and (2R,6S)-Dicobalt hexacarbonyl dimethyl dihydro-2-methyl-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate isolated (313)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Acetaldehyde (70 µL, 0.78 mmol, 5.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 30 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 73% (113 mg, 0.19 mmol) in a 1.6/1 d.r.; (i) first eluted, *cis* isomer as dark red crystals, Rf (15% EtOAc/petrol) 0.76; mp 111.8-112.4°C; ν_{max} (film)/cm^{-1} 1264, (C–O), 1730 (C=O), 2022 (C≡O), 2050 (C≡O), 2090 (C≡O) and 2953 (ArC–H);

δ_H(400 MHz; $CDCl_3$) 1.39 (3H, d, *J* 6.4 Hz, $CHCH_3$), 1.91-2.08 (3H, m, 2H $CHCH_2$ + 1H $CHCH_2CHH$), 2.50-2.58 (1H, m, $CHCH_2CHH$), 3.68 (3H, s, CO_2CH_3), 3.70 (3H, s, CO_2CH_3), 4.13 (1H, q, *J* 6.4 Hz, $OCHCH_3$), 4.73 (1H, dd, *J* 3.2, 10.0 Hz, CH_2CHO), 7.21-7.30 (3H, m, ArC*H*) and 7.46-7.51 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 18.2 ($CHCH_3$), 29.8 ($CHCH_2$), 32.0 ($CHCH_2CH_2$), 52.0 (CO_2CH_3), 52.6 (CO_2CH_3), 56.7 ($C(CO_2CH_3)_2$), 77.4 ($OCHCH_3$), 77.9 (CH_2CHO), 89.6 (*C*–C), 96.9 (*C*–C), 127.7 (ArCH), 128.7 (2ArCH), 129.8 (2ArCH), 137.8 (Ar*C*), 169.4 (CO_2CH_3), 171.4 (CO_2CH_3) and 199.4 ($CO_{complex}$); HRMS (FAB) (M^+–2CO), found 545.9782, $C_{22}H_{20}Co_2O_9$ requires 545.9771 (+2.1 ppm); *m/z* 518 (5%), 490 (100%), 462 (5%) and 434 (18%); mp 112-113°C; the stereochemistry was confirmed by X-Rray crystallography (Appendix II) (ii) second eluted minor isomer as a dark red oil, Rf (15% EtOAc/petrol) 0.71; ν_{max} (film)/cm^{-1} 1262 (C–O), 1730 (C=O), 2028 (C≡O), 2050 (C≡O), 2089 (C≡O) and 2957 (ArC–H); δ_H(400 MHz; $CDCl_3$) 1.29 (3H, d, *J* 6.9 Hz, $CHCH_3$), 1.44-1.57 (1H, m, CHC*H*H), 1.92-2.01 (1H, m, CHC*H*H), 2.25-2.35 (1H, m, $CHCH_2CHH$), 2.39-2.47 (1H, m, $CHCH_2CHH$), 3.66 (3H, s, CO_2CH_3), 3.71 (3H, s, CO_2CH_3), 4.85 (1H, dd, *J* 2.8, 11.2 Hz, CH_2CHO), 4.97 (1H, q, *J* 6.8 Hz, $OCHCH_3$), 7.21-7.30 (3H, m, ArC*H*) and 7.46-7.52 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 14.7 ($CHCH_3$), 23.7 ($CHCH_2$), 30.2 ($CHCH_2CH_2$), 52.8 (CO_2CH_3), 52.9 (CO_2CH_3), 57.0 ($C(CO_2CH_3)_2$), 68.6 (CH_2CHO), 71.2 ($OCHCH_3$), 90.0 (C–C), 97.8 (C–C), 126.9 (ArCH), 128.7 (2ArCH), 129.9 (2ArCH), 137.8 (Ar*C*), 169.5 (CO_2CH_3), 170.0 (CO_2CH_3) and 199.4 ($CO_{complex}$); HRMS (FAB) (M^+–2CO), found 545.9780, $C_{22}H_{20}Co_2O_9$ requires 545.9771 (+1.7 ppm); *m/z* 518 (20%), 490 (100%) and 434 (48%).

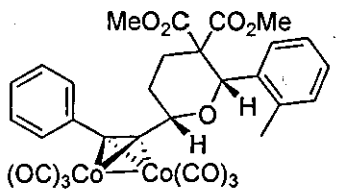
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-6-(2-phenylethynyl)-2-p-tolyl-2H-pyran-3,3(4H)-dicarboxylate isolated (314)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to

stir at room temperature under a nitrogen atmosphere for 1.5 hour. *p*-Tolualdehyde (90 μL, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 10 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 64% (112 mg, 0.16 mmol) as dark red crystals; Rf (15% EtOAc/petrol) 0.75; mp 114.1-114.8°C; ν_{max} (film)/cm^{-1} 1083, 1262 (C–O), 1731, (C=O) and 2090 (C≡O), 2051 (C≡O), 2023 (C≡O) and 2952 (ArCH); δ_H(400 MHz; $CDCl_3$) 2.08-2.18 (2H, m, CHC*H*$_2$), 2.33 (3H, s, ArC*H*$_3$), 2.37-2.49 (1H, m, CHCH$_2$C*H*H), 2.72 (1H, dt, *J* 3.6, 13.2 Hz, CHCH$_2$C*H*H), 3.57 (3H, s, CO_2CH_3), 3.69 (3H, s, CO_2CH_3), 4.94 (1H, dd, *J* 6.0, 8.2 Hz, CH$_2$C*H*O), 5.24 (1H, s, OC*H*Ar), 7.27-7.36 (5H, m, ArC*H*), 7.32-7.37 (2H, m, ArC*H*) and 7.56-7.63 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 21.2 (Ar*C*H$_3$), 30.1 (CH*C*H$_2$), 32.7 (CHCH$_2$*C*H$_2$), 51.7 (CO_2CH_3), 53.3 (CO_2CH_3), 60.4 (*C*(CO_2CH_3)$_2$), 79.2 (CH$_2$*C*HO), 82.9 (O*C*HAr), 89.9 (C–*C*), 96.1 (*C*–C), 127.3 (1Ar*C*H), 127.9 (4Ar*C*H), 128.8 (2Ar*C*H), 129.9 (2Ar*C*H), 136.0 (Ar*C*), 137.0 (Ar*C*), 137.7 (Ar*C*), 169.0 (*C*O_2CH_3), 171.2 (*C*O_2CH_3) and 199.3 (*C*$O_{complex}$); the stereochemistry was confirmed by X-Rray crystallography (Appendix III); HRMS (FAB) (M^+–2CO), found 622.0096, $C_{28}H_{24}Co_2O_9$ requires 622.0084 (+1.9 ppm); *m/z* 594 (100%), 566 (79%), 538 (96%) and 510 (57%).

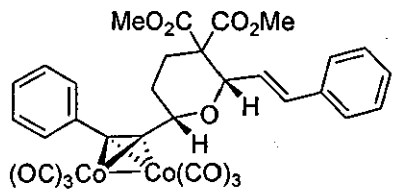
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-6-(2-phenylethynyl)-2-o-tolyl-2H-pyran-3,3(4H)-dicarboxylate (315)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. *m*-Tolualdehyde (90 μL, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The

resulting mixture was allowed to stir at room temperature for 1 h under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 47% (83 mg, 0.12 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.77; ν_{max} (film)/cm^{-1} 1261 (C–O), 1083 (C–O), 1732, (C=O), 2090 (C≡O), 2051 (C≡O), 2022 (C≡O), 2958 (ArC–H) and 3002 (ArC–H); δ_H(400 MHz; $CDCl_3$) 2.01-2.08 (1H, m, CHC*H*H), 2.09-2.21 (1H, m, CHC*H*H), 2.27-2.39 (4H, m, 1H, $CHCH_2CHH$ + $ArCH_3$), 2.64 (1H, dt, *J* 4.4, 13.6 Hz, $CHCH_2CHH$), 3.49 (3H, s, CO_2CH_3), 3.57 (3H, s, CO_2CH_3), 4.99 (1H, dd, *J* 3.6, 10.4 Hz, CH_2CHO), 5.34 (1H, s, OC*H*Ar), 6.99-7.12 (3H, m, ArC*H*), 7.16-7.24 (4H, m, ArC*H*) and 7.44-7.52 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 20.0 ($ArCH_3$), 29.7 ($CHCH_2$), 31.9 ($CHCH_2CH_2$), 51.9 (CO_2CH_3), 52.6 (CO_2CH_3), 57.8 ($C(CO_2CH_3)_2$), 78.3 (CH_2CHO), 79.3 (OCHAr), 90.1 (*C*–C), 96.3 (*C*–C), 124.8 (ArCH), 127.7 (ArCH), 127.8 (ArCH), 128.7 (2ArCH), 129.0 (ArCH), 129.8 (ArCH), 129.9 (2ArCH), 135.8 (ArC), 136.5 (ArC), 137.7 (ArC), 169.4 (CO_2CH_3), 171.0 (CO_2CH_3) and 199.3 ($CO_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.99 ppm and the proton at 5.34 ppm; HRMS (FAB) (M^+–2CO), found 622.0071, $C_{28}H_{24}Co_2O_9$ requires 622.0084 (–2.0 ppm); *m/z* 594 (76%), 566 (72%), 538 (100%) and 510 (65%); mp 114-115°C.

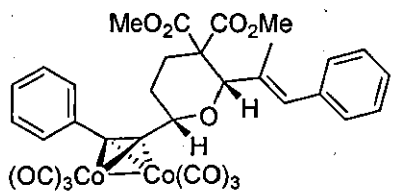
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-6-(2-phenylethynyl)-2-styryl-2H-pyran-3,3(4H)-dicarboxylate (316)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Cynnamaldehyde (100 µL, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The

resulting mixture was allowed to stir at room temperature for 1 h under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 82% (146 mg, 0.21 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.69; ν_{max} (film)/cm^{-1} 1084 (C–O), 1264 (C–O), 1731 (C=O), 2021 (C≡O), 2050 (C≡O), 2088(C≡O), 2953 (ArC–H), 3025 (sp^2 C–H) and 3058 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 1.97-2.20 (2H, m, CHC*H*$_2$), 2.64-2.55 (2H, m, CHCH$_2$C*H*$_2$), 3.62 (3H, s, CO_2CH_3), 3.66 (3H, s, CO_2CH_3), 4.72 (1H, d, *J* 5.2 Hz, OC*H*CH=CH), 4.84-4.90 (1H, m, CH$_2$C*H*O), 6.49 (1H, dd, *J* 5.2, 16.4 Hz, C*H*=CHPh), 6.60 (1H, d, *J* 16.4 Hz, CH=C*H*Ph), 7.11-7.30 (8H, m, ArC*H*) and 7.48-7.54 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 28.8 (CH*C*H$_2$), 30.7 (CHCH$_2$*C*H$_2$), 51.1 (CO_2CH_3), 51.7 (CO_2CH_3), 56.9 (*C*(CO$_2$CH$_3$)$_2$), 77.2 (CH$_2$*C*HO), 80.3 (O*C*HCH), 88.9 (*C*–C), 95.5 (*C*–C), 125.5 (2Ar*C*H), 125.9 (*C*H=CHPh), 126.4 (Ar*C*H), 126.8 (Ar*C*H), 127.4 (2Ar*C*H), 127.8 (2Ar*C*H), 129.2 (CH=*C*HPh), 129.8 (2Ar*C*H), 136.2 (Ar*C*), 136.7 (Ar*C*), 168.0 (*C*O$_2$CH$_3$), 170.0 (*C*O$_2$CH$_3$) and 198.3 (*C*O$_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.72 ppm and the proton presenting a multiplet at 4.84-4.90 ppm; HRMS (FAB) (M$^+$–3CO), found 606.0144, $C_{26}H_{24}Co_2O_8$ requires 606.0135 (+1.5 ppm); *m/z* 578 (80%), 550 (4%) and 522 (100%).

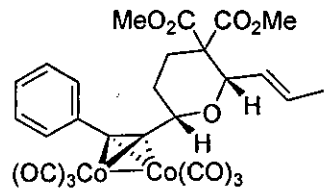
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-6-(2-phenylethynyl)-2-((*E*)-1-phenylprop-1-en-2-yl)-2H-pyran-3,3(4H)-dicarboxylate (317)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. (E)-2-methyl-3-phenylacrylaldehyde (110 µL, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%)

were added successively. The resulting mixture was allowed to stir at room temperature for 25 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 84% (153 mg, 0.22 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.75; ν_{max} (film)/cm^{-1} 1075 (C–O), 1259 (C–O), 1731 (C=O), 1736 (C=O), 2021 (C≡O), 2050 (C≡O), 2089 (C≡O), 2952 (sp^3 C–H), 2997 (sp^2 C–H), 3027 (sp^2 C–H) and 3057 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 1.89 (3H, s, CHCC*H*$_3$), 2.03-2.14 (2H, m, CHC*H*$_2$) , 2.25-2.41 (1H, m, CHCH$_2$C*H*H), 2.66 (1H, dt, *J* 3.6, 13.2 Hz, CHCH$_2$C*H*H), 3.71 (3H, s, CO_2CH_3), 3.74 (3H, s, CO_2CH_3), 4.82 (1H, s, OC*H*C=), 4.94-5.00 (1H, m, CH$_2$C*H*O), 6.66 (1H, s, C=C*H*Ph), 7.16-7.26 (2H, m, ArCH), 7.27-7.38 (6H, m, ArC*H*) and 7.57-7.63 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 15.7 (CHC*C*H$_3$), 29.9 (CH*C*H$_2$), 32.8 (CHCH$_2$*C*H$_2$), 52.0 (CO_2CH_3), 52.6 (CO_2CH_3), 58.4 (*C*(CO$_2$CH$_3$)$_2$), 79.8 (CH$_2$*C*HO), 84.9 (O*C*HCCH$_3$), 90.1 (*C*–C), 96.2 (*C*–C), 126.3 (Ar*C*H), 127.2 (Ar*C*H), 127.9 (=*C*HPh), 128.0 (2Ar*C*H), 128.8 (2Ar*C*H), 129.1 (2Ar*C*H), 129.9 (2Ar*C*H), 135.9 (CH*C*CH$_3$), 137.7 (Ar*C*), 137.9 (Ar*C*), 169.7 (*C*O$_2$CH$_3$), 171.6 (*C*O$_2$CH$_3$) and 199.3 (*C*O$_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.82 ppm and the proton presenting a multiplet at 4.94-5.00 ppm; HRMS (FAB) (M^+–2CO), found 648.0250, $C_{30}H_{26}Co_2O_9$ requires 648.0241 (+1.3 ppm); *m/z* 620 (20%), 592 (100%) and 536 (27%).

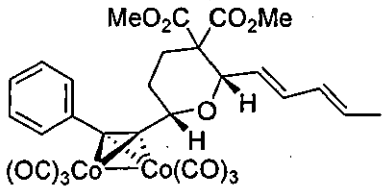
(2R,6R) and (2S,6S)-Dicolabt octacarbonyl dimethyl dihydro-6-(2-phenylethynyl)-2-((E)-prop-1-enyl)-2H-pyran-3,3(4H)-dicarboxylate (318)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. (E)-But-2-enal (65 µL,

0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 1 h under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 82% (133 mg, 0.21 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.77; ν_{max} (film)/cm^{-1} 1082 (C–O), 1266 (C–O), 1726 (C=O), 1731 (C=O), 2021 (C≡O), 2051 (C≡O), 2090 (C≡O), 2954 (ArC–H) and 3058 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 1.62 (3H, d, *J* 6.4 Hz, $CHCH_3$), 1.79-2.02 (2H, m, $CHCH_2$), 2.13 (1H, dt, *J* 4.8, 13.2 Hz, $CHCH_2CHH$), 2.55 (1H, ddd *J* 2.8, 4.0, 13.2 Hz, $CHCH_2CHH$), 3.64 (3H, s, CO_2CH_3), 3.67 (3H, s, CO_2CH_3), 4.41 (1H, d, *J* 6.4 Hz, $OCHCH$), 4.78 (1H, dd, *J* 3.2, 11.2 Hz, CH_2CHO), 5.64 (1H, ddd, *J* 0.8, 6.4, 15.2 Hz, $CH=CHCH_3$), 5.83 (1H, ddd, *J* 1.6, 6.4, 15.2 Hz, $CH=CHCH_3$), 7.19-7.29 (3H, m, ArCH) and 7.46-7.53 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 16.9 ($CHCH_3$), 28.8 ($CHCH_2$), 30.8 ($CHCH_2CH_2$), 51.0 (CO_2CH_3), 51.8 (CO_2CH_3), 57.2 ($C(CO_2CH_3)_2$), 77.0 (CH_2CHO), 81.3 ($OCHCH$), 88.9 (*C*–C), 95.5 (*C*–C), 126.7 (ArCH), 126.9 ($CH=CHCH_3$), 127.3 ($CH=CHCH_3$), 127.7 (2ArCH), 128.9 (2ArCH), 136.8 (ArC), 168.2 (CO_2CH_3), 170.0 (CO_2CH_3) and 198.3 ($CO_{Complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.41 ppm and the proton at 4.78 ppm; HRMS (FAB) (M^+–2CO), found 571.9915, $C_{26}H_{24}Co_2O_8$ requires 571.99278 (–1.4 ppm); *m/z* 629 (4%), 572 (19%), 545 (14%), 517 (65%), 516 (100%), 488 (15%) and 460 (30%).

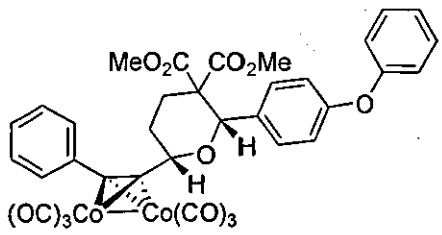
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-2-((1E,3E)-penta-1,3-dienyl)-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (319)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to

stir at room temperature under a nitrogen atmosphere for 1.5 hour. (E)-penta-2,4-dienal (85 μL, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 1 h under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 51% (86 mg, 0.13 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.78; ν_{max} (film)/cm^{-1} 1083 C–O), 1262 (C–O), 1731 (C=O), 2020, 2089 (C≡O), 2953 (sp^3 C–H), 3019 (sp^2 C–H), 3057 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 1.75 (3H, d, *J* 6.8 Hz, C*H*$_3$), 1.98-2.10 (2H, m, CHC*H*$_2$), 2.19 (1H, dt, *J* 5.2, 13.2 Hz, CHCH$_2$C*H*H), 2.63 (1H, ddd, *J* 2.8, 4.0, 13.2 Hz, CHCH$_2$C*H*H), 3.72 (6H, s, OC*H*$_3$), 4.59 (1H, d, *J* 6.0 Hz, OC*H*CH), 4.87 (1H, dd, *J* 4.0, 10.8 Hz, CH$_2$C*H*O), 5.62 (1H, dd, *J* 6.8, 14.9 Hz, CH$_3$C*H*=CH), 5.92 (1H, dd, *J* 6.0, 15.6 Hz, OCHC*H*), 6.03-6.14 (1H, m, CH$_3$CH=C*H*), 6.24 (1H, dd, *J* 10.4, 15.6 Hz, CH$_3$CH=CHC*H*), 7.27-7.36 (3H, m, ArC*H*) and 7.52-7.59 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 18.2 (CHC*H*$_3$), 29.8 (CHC*H*$_2$), 31.7 (CHCH$_2$C*H*$_2$), 52.1 (CO$_2$C*H*$_3$), 52.6 (CO$_2$C*H*$_3$), 58.1 (*C*(CO$_2$CH$_3$)$_2$), 78.2 (CH$_2$*C*HO), 81.7 (O*C*HCH), 89.9 (*C*–C), 96.5 (*C*–C), 127.4 (OCHC*H*), 127.8 (ArC*H*), 128.8 (2ArC*H*), 129.7 (CH$_3$C*H*), 129.8 (2ArC*H*), 131.2 (CH$_3$CH=C*H*), 131.5 (CH$_3$CH=CHC*H*), 137.8 (Ar*C*), 169.1 (*C*O$_2$CH$_3$), 180.0 (*C*O$_2$CH$_3$) and 199.4 (*C*O$_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.59 ppm and the proton at 4.87 ppm; HRMS (FAB) (M$^+$–2CO), found 598.0071, $C_{26}H_{24}Co_2O_9$ requires 598.0084 (–2.1 ppm); *m/z* 570 (37%), 542 (100%), 514 (11%) and 486 (89%).

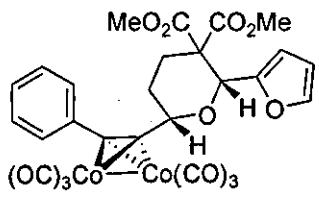
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-2-(4-phenoxyphenyl)-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (320)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and

activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. 4-Phenoxybenzaldehyde (150 mg, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 2 h under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 65% (126 mg, 0.17 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.66; ν_{max} (film)/cm^{-1} 1072 (C–O), 1240 (C–O), 1263 (C–O), 1730 (C=O), 2021 (C≡O), 2050 (C≡O), 2089 (C≡O), 2952 (sp^3 C–H) and 3059 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 2.09-2.21 (2H, m, $CHCH_2$), 2.33-2.45 (1H, m, $CHCH_2CHH$), 2.72 (1H, dt, *J* 3.2, 13.6 Hz, $CHCH_2CHH$), 3.57, (3H, s, CO_2CH_3), 3.70 (3H, s, CO_2CH_3), 4.94 (1H, dd, *J* 4.0, 10.0 Hz, CH_2CHO), 5.18 (1H, s, OCHAr), 6.79-6.86 (2H, ArCH), 6.90-6.96 (2H, ArCH), 6.97-7.06 (1H, m, ArCH), 7.18-7.36 (7H, m, ArCH) and 7.47-7.54 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 30.0 ($CHCH_2$), 32.7 ($CHCH_2CH_2$), 51.7 (CO_2CH_3), 52.6 (CO_2CH_3), 59.0 ($C(CO_2CH_3)_2$), 72.3 (OCHAr), 82.5 (CH_2CHO), 90.0 (*C*–C), 96.0 (*C*–C), 117.3 (2ArCH), 119.1 (2ArCH), 123.2 (ArCH), 127.9 (ArCH), 128.8 (2ArCH), 128.9 (2ArCH), 129.7 (2ArCH), 129.9 (2ArCH), 133.8 (ArC), 137.7 (ArC), 156.6 (ArC), 157.2 (ArC), 168.9 (CO_2CH_3), 171.2 (CO_2CH_3) and 199.4 ($CO_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.94 ppm and the proton at 5.18 ppm; HRMS (FAB) (M^+–3CO), found 672.0253, $C_{32}H_{26}Co_2O_9$ requires 672.0241 (+1.8 ppm); *m/z* 672 (21%), 644 (11%), 616 (3%) and 588 (100%).

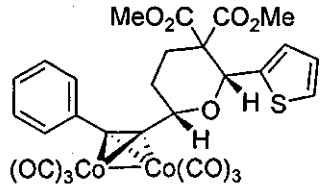
(2R,6S) and (2S,6R)-Dicobalt hexacarbonyl dimethyl 2-(furan-2-yl)-dihydro-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (321)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and

activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Furan-2-carbaldehyde (65 μL, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 10 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 95% (160 mg, 0.24 mmol) as dark red crystals; Rf (15% EtOAc/petrol) 0.62; mp 119-120.°C; ν_{max} (film)/cm^{-1} 1080 (C–O), 1263 (C–O), 1734 (C=O), 2022 (C≡O), 2052 (C≡O), 2091 (C≡O) and 2953 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.94-2.06 (1H, m, CHC*H*H), 2.07-2.17 (1H, m, CHC*H*H), 2.34 (1H, dt, *J* 4.4, 13.2 Hz, $CHCH_2CHH$), 2.73 (1H, ddd, *J* 2.8, 4.0, 13.2 Hz, $CHCH_2CHH$), 3.59 (3H, s, CO_2CH_3), 3.80 (3H, s, CO_2CH_3), 5.03 (1H, dd, *J* 2.8, 11.2 Hz, CH_2CHO), 5.34 (1H, s, OC*H*Ar), 6.33 (2H, d, *J* 1.2 Hz, ArC*H*), 7.27-7.36 (4H, m, ArC*H*) and 7.55-7.60 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 29.9 ($CHCH_2$), 31.8 ($CHCH_2CH_2$), 52.1 (CO_2CH_3), 52.9 (CO_2CH_3), 57.6 ($C(CO_2CH_3)_2$), 78.0 (O*C*HAr), 78.9 (CH_2CHO), 89.9 (*C*–C), 95.6 (*C*–C), 106.5 (Ar*C*H), 110.3 (Ar*C*H), 127.9 (Ar*C*H), 128.8 (2Ar*C*H), 129.8 (2Ar*C*H), 137.7 (Ar*C*), 140.9 (Ar*C*H), 152.2 (Ar*C*), 168.5 (CO_2CH_3), 170.8 (CO_2CH_3) and 199.3 ($CO_{complex}$); the stereochemistry was confirmed by X-Rray crystallography (Appendix IV); HRMS (FAB) (M^+–2CO), found 597.9734, $C_{25}H_{20}Co_2O_{10}$ requires 597.9720 (+2.2 ppm); *m/z* 570 (22%), 540 (100%) and 486 (42%).

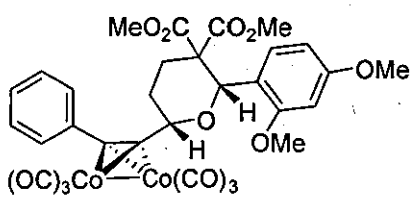
(2R,6S) and (2S,6R)-Dicobalt hexacarbonyl dimethyl dihydro-6-(2-phenylethynyl)-2-(thiophen-2-yl)-2H-pyran-3,3(4H)-dicarboxylate (322)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Thiophene-2-

carbaldehyde (70 μL, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 15 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 89% (154 mg, 0.23 mmol) as dark red crystals; Rf (15% EtOAc/petrol) 0.66; mp 122-123°C; ν_{max} (film)/cm^{-1} 1077 (C–O), 1265 (C–O), 1728 (C=O), 2024, 2052 (C≡O), 2091 (C≡O) and 2952 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.98-2.19 (2H, m, CHC*H*$_2$), 2.20-2.32 (1H, dt, *J* 4.0, 12.8 Hz, CHCH$_2$C*H*H), 2.60-2.70 (1H, broad d, *J* 12.8 Hz, CHCH$_2$C*H*H), 3.49 (3H, s, CO_2CH_3), 3.70 (3H, s, CO_2CH_3), 4.96 (1H, broad d, *J* 9.8 Hz, CH$_2$C*H*O), 5.50 (1H, s, OC*H*Ar), 6.83-6.98 (2H, m, ArC*H*), 7.12-7.31 (4H, m, ArC*H*) and 7.47-7.57 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 29.9 (CH*C*H$_2$), 32.3 (CHCH$_2$*C*H$_2$), 52.0 (CO_2CH_3), 52.7 (CO_2CH_3), 59.2 (*C*(CO$_2$CH$_3$)$_2$), 79.4 (O*C*HAr), 79.8 (CH$_2$*C*HO), 90.2 (CoC*C*Co), 95.5 (Co*C*CCo), 124.6 (Ar*C*H), 124.8 (Ar*C*H), 125.8 (Ar*C*H), 127.9 (Ar*C*H), 128.8 (2Ar*C*H), 129.9 (2Ar*C*H), 137.6 (Ar*C*), 142.0 (Ar*C*), 168.6 (*C*O$_2$CH$_3$), 171.1 (*C*O$_2$CH$_3$) and 199.3 (*C*O$_{complex}$); the stereochemistry was confirmed by X-Rray crystallography (Appendix V); HRMS (FAB$^+$) (M−2CO), found 613.9482, $C_{25}H_{20}Co_2O_9S$ requires 613.9492 (−1.6 ppm); *m/z* 614 (5%), 586 (77%), 558 (100%), 530 (9%) and 502 (27%).

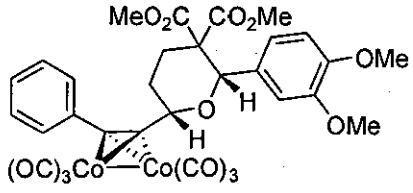
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-2-(2,4-dimethoxyphenyl)-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (323)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. 2,4-dimethoxybenzaldehyde (85 mg, 0.51 mmol, 2.0 eq) and scandium triflate (6 mg, 5 mol%)

were added successively. The resulting mixture was allowed to stir at room temperature for 15 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 92% (170 mg, 0.24 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.30; ν_{max} (film)/cm^{-1} 1045 (C–O), 1085 (C–O), 1158 (C–O), 1208 (C–O), 1255 (C–O), 1732 (C=O), 1736 (C=O), 2019 (C≡O), 2050 (C≡O), 2089 (C≡O), 2952 (sp^{3}C–H), 3000 (sp^{3}C–H); δ_H(400 MHz; $CDCl_3$) 1.58-1.71 (1H, m, CHC*H*H), 2.01-2.12 (1H, m, CHC*H*H), 2.52-2.68 (2H, m, $CHCH_2C\mathit{H}_2$), 3.48 (3H, s, $OC\mathit{H}_3$), 3.58 (3H, s, $OC\mathit{H}_3$), 3.67 (3H, s, $OC\mathit{H}_3$), 3.73 (3H, s, $OC\mathit{H}_3$), 4.88 (1H, dd, *J* 2.6, 11.2 Hz, $CH_2C\mathit{H}O$), 5.13 (1H, s, OC*H*Ar), 6.27 (1H, d, *J* 2.4 Hz, ArCH), 6.42 (1H, dd, *J* 2.0, 8.4 Hz, ArC*H*), 7.20-7.28 (3H, m, ArC*H*), 7.51-7.57 (2H, m, ArC*H*) and 7.72 (1H, d, *J* 8.4 Hz, ArC*H*); δ_C(100 MHz; $CDCl_3$) 29.6 ($CHC\mathit{H}_2$), 30.9 ($CHCH_2C\mathit{H}_2$), 50.9 ($OC\mathit{H}_3$), 51.2 ($OC\mathit{H}_3$), 54.0 ($CO_2C\mathit{H}_3$), 54.2 ($CO_2C\mathit{H}_3$), 57.3 ($\mathit{C}(CO_2CH_3)_2$), 76.4 ($CH_2\mathit{C}HO$), 78.5 (O*C*HAr), 89.0 (*C*–C), 95.0 (*C*–C), 95.4 (Ar*C*H), 102.3 (Ar*C*H), 118.3 (Ar*C*), 126.7 (Ar*C*H), 127.7 (2Ar*C*H), 128.9 (2Ar*C*H), 130.5 (Ar*C*H), 136.7 (Ar*C*), 155.7 (ArOMe), 159.0 (ArOMe), 168.3 ($\mathit{C}O_2CH_3$), 168.6 ($\mathit{C}O_2CH_3$) and 198.4 ($\mathit{C}O_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.88 ppm and the proton at 5.13 ppm; HRMS (FAB) (M^+–3CO), found 640.0177, $C_{28}H_{26}Co_2O_{10}$ requires 640.0189 (–2.0 ppm); *m/z* 612(100%), 584 (13%) and 556 (12%).

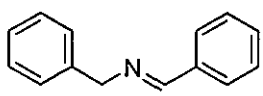
(2R,6R) and (2S,6S)-Dicobalt hexacarbonyl dimethyl dihydro-2-(3,4-dimethoxyphenyl)-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (324)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. 3,4-

dimethoxybenzaldehyde (85 mg, 0.51 mmol, 2.0 eq) and scandium triflate (6 mg, 5 mol%) were added successively. The resulting mixture was allowed to stir at room temperature for 15 min under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% ethyl acetate/petrol) to yield the *title compound* in 92% (171 mg, 0.24 mmol) as a dark red oil; Rf (15% EtOAc/petrol) 0.19; ν_{max} (film)/cm^{-1} 1029 (C–O), 1074 (C–O), 1234 (C–O), 1264 (C–O), 1731 (C=O), 2022 (C≡O), 2050 (C≡O), 2090 (C≡O), 2953 (sp^3 C–H), 3002 (sp^2 C–H) and 3075 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 2.03-2.11 (2H, m, $CHCH_2$), 2.28-2.37 (1H, m, $CHCH_2CHH$), 2.64 (1H, dd, *J* 3.2, 13.2 Hz, $CHCH_2CHH$), 3.49 (3H, s, OCH_3), 3.62 (3H, s, OCH_3), 3.66 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 4.95 (1H, dd, *J* 6.0, 8.0 Hz, CH_2CHO), 5.17 (1H, s, OCHAr), 6.68 (1H, d, *J* 8.4 Hz, ArCH), 6.83 (1H, dd, *J* 2.0, 8.4 Hz, ArCH), 7.03 (1H, d, *J* 2.0 Hz, ArCH), 7.19-7.27 (3H, m, ArCH) and 7.48-7.55 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 29.0 ($CHCH_2$), 37.7 ($CHCH_2CH_2$), 50.7 (CO_2CH_3), 51.6 (CO_2CH_3), 54.4 ($ArOCH_3$), 54.6 ($ArOCH_3$), 58.2 ($C(CO_2CH_3)_2$), 78.3 (OCHAr), 81.6 (CH_2CHO), 89.0 (CoCCCo), 95.1 (CoCCCo), 108.4 (ArCH), 109.3 (ArCH), 118.4 (ArCH), 126.9 (ArCH), 127.8 (2ArCH), 128.7 (2ArCH), 130.5 (ArC), 136.6 (ArC), 146.8 (ArCOMe), 147.1 (ArCOMe), 168.1 (CO_2CH_3), 170.2 (CO_2CH_3) and 198.2 ($CO_{complex}$); the stereochemistry was confirmed by nOe analysis showing a strong coupling between the proton at 4.95 ppm and the proton at 5.17 ppm; HRMS (FAB) (M^+–3CO), found 640.0178, $C_{28}H_{26}Co_2O_{10}$ requires 640.0189 (–1.8 ppm); *m/z*, 612(43%), 584 (100%) and 556 (60%).

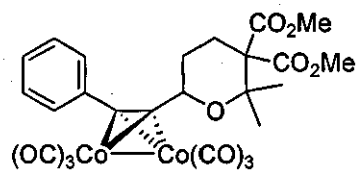
<u>*N*-benzylidene(phenyl)methanamine (325)</u>



Benzylamine (3.2 mL, 3.16 g, 29.5 mmol) was added to a solution of benzaldehyde (3.0 mL, 3.13 g, 29.5 mmol) in diethyl ether (70 mL) and 4Å molecular sieves (15.0 g) were added. The reaction mixture was allowed to stir overnight at room temperature under a nitrogen atmosphere and the resulting mixture was filtered through a pad of celite and silica. The filtrate was concentrated *in vacuo* to give the *title compound* in 92% yield (5.32 g, 27.2 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} 1622 (C=N), 2981 (sp^3 C–H), 3016 (sp^2 C–H), 3024

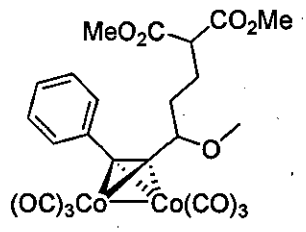
(sp^2 C–H), 3071 (sp^2 C–H) and 3091 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 4.94 (2H, d, *J* 13.6 Hz, C*H*$_2$), 7.35-7.42 (1H, m, ArC*H*), 7.44-7.49 (4H, m, ArC*H*), 7.50-7.58 (3H,m, ArC*H*), 7.88-7.95 (2H, m ArC*H*) and 8.47 (1H, d, *J* 13.6 Hz, N=CH); δ_C(100 MHz; $CDCl_3$) 65.2 (*C*H$_2$), 127.1 (Ar*C*H), 128.2 (2Ar*C*H), 128.4 (2Ar*C*H), 128.6 (2Ar*C*H), 128.7 (2Ar*C*H), 130.9 (Ar*C*H), 136.3 (Ar*C*), 139.5 (Ar*C*) and 162.1 (N=*C*H).

Dicobalt hexacarbonyl dimethyl dihydro-2,2-dimethyl-6-(2-phenylethynyl)-2H-pyran-3,3(4H)-dicarboxylate (326)



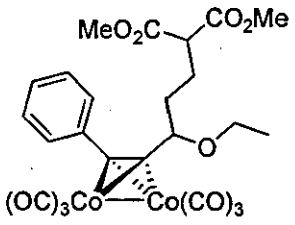
Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Acetone (40 µL, 0.51 mmol, 2.0 eq) and scandium triflate (6 mg, 5 mol%) were successively added. The resulting mixture was allowed to stir overnight at room temperature under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% EtOAc/petrol) to yield the *title compound* in 41% (65 mg, 0.10 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1078 (C–O), 1264 (C–O), 1736 (C=O), 2024 (C≡O), 2050 (C≡O), 2090 (C≡O) and 2952 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.35 (3H, CC*H*$_3$), 1.53 (3H, CC*H*$_3$), 1.85-1.96 (2H, m, CHC*H*$_2$), 2.21-2.30 (1H, m, CHCH$_2$C*H*H), 2.37-2.49 (1H, m, CHCH$_2$C*H*H), 3.66 (3H, s, OC*H*$_3$), 3.68 (3H, s, OC*H*$_3$), 4.83-4.90 (1H, m, CH$_2$C*H*O), 7.20-7.31 (3H, m, ArC*H*) and 7.50-7.56 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 22.9 (C*C*H$_3$), 26.7 (C*C*H$_3$), 27.5 (CH*C*H$_2$), 29.0 (CHCH$_2$*C*H$_2$), 52.0 (CO$_2$*C*H$_3$), 52.5 (CO$_2$*C*H$_3$), 58.7 (*C*(CO$_2$CH$_3$)$_2$), 70.1 (CH$_2$*C*HO), 89.6 (*C*–C), 98.5 (*C*–C), 127.7 (Ar*C*H), 128.6 (2Ar*C*H), 129.9 (2Ar*C*H), 138.0 (Ar*C*), 170.1 (*C*O$_2$CH$_3$), 170.8 (*C*O$_2$CH$_3$) and 199.6 (*C*O$_{complex}$); HRMS (FAB) (M^+–2CO), found 559.9919, $C_{23}H_{22}Co_2O_9$ requires 559.9928 (–1.6 ppm); *m/z* 559 (9%), 531 (9%), 503 (21%), 475 (31%) and 447 (7%).

Dicobalt hexacarbonyl dimethyl 2-(3-methoxy-5-phenylpent-4-ynyl)malonate (333)



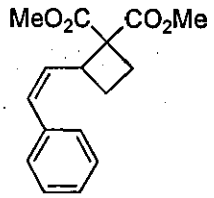
Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. 2-Methoxyprop-1-ene (75 μL, 55 mg, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were successively added. The resulting mixture was allowed to stir for 2 h at room temperature under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% EtOAc/petrol) to yield the unexpected *title compound* in 90% (131 mg, 0.23 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1078 (C–O), 1189 (C–O), 1265 (C–O), 1736 (C=O), 2028 (C≡O), 2047 (C≡O), 2090 (C≡O) and 2955 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.69-1.82 (2H, m, $CHCH_2$), 1.98-2.27 (2H, m, $CHCH_2CH_2$), 3.36 (1H, t, *J* 7.2 Hz, $CH(CO_2CH_3)$), 3.48 (3H, s, $CHOCH_3$), 3.62 (3H, s, CO_2CH_3), 3.65 (3H, s, CO_2CH_3), 4.45-4.51 (1H, m, CH_2CHO), 7.20-7.31 (3H, m, ArCH) and 7.37-7.44 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 24.8 ($CHCH_2$), 34.6 ($CHCH_2CH_2$), 50.2 (CO_2CH_3), 51.5 (CO_2CH_3), 58.1 ($CHOCH_3$) 70.1 (CH_2CHO), 80.5 ($CHOCH_3$), 90.6 (C–C), 96.5 (C–C), 126.7 (ArCH), 127.8 (2ArCH), 128.4 (2ArCH), 136.7 (ArC), 168.5 (CO_2CH_3), 168.7 (CO_2CH_3) and 198.3 ($CO_{complex}$); no mass ion could be observed.

Dicobalt hexacarbonyl dimethyl 2-(3-ethoxy-5-phenylpent-4-ynyl)malonate (334)



Dicobalt octacarbonyl (100 mg, 0.28 mmol, 1.1 eq) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (70 mg, 0.26 mmol) in DCM (5 ml) and activated 4 Å molecular sieves were added (150 mg). The reaction mixture was allowed to stir at room temperature under a nitrogen atmosphere for 1.5 hour. Ethyl vinyl ether (75 μL, 55 mg, 0.77 mmol, 3.0 eq) and scandium triflate (6 mg, 5 mol%) were successively added. The resulting mixture was allowed to stir for 2 h at room temperature under a nitrogen atmosphere (TLC monitoring). Once the reaction was completed, the crude reaction mixture was filtered through a pad of celite and silica and the solvent was evaporated *in vacuo*. The crude product was purified by flash chromatography on silica gel (5% EtOAc/petrol) to yield the unexpected *title compound* in 92% (134 mg, 0.23 mmol) as a dark red oil; ν_{max} (film)/cm^{-1} 1093 (C–O), 1156 (C–O), 1248 (C–O), 1736 (C=O), 2020 (C≡O), 2090 (C≡O) and 2955 (sp^3 C–H); δ_H(400 MHz; $CDCl_3$) 1.14 (3H, t, *J* 6.8 Hz, OCH_2CH_3), 1.69-1.79 (2H, m, $CHCH_2$), 1.96-2.24 (2H, m, $CHCH_2CH_2$), 3.36 (1H, dd, *J* 7.2, 8.4 Hz, $CH(CO_2CH_3)_2$), 3.59-3.57 (1H, m, $OCHHCH_3$), 3.61 (3H, s, OCH_3), 3.65 (3H, s, OCH_3), 3.66-3.74 (1H, m, $OCHHCH_3$), 4.54-4.60 (1H, m, CH_2CHO), 7.20-7.31 (3H, m, ArCH) and 7.37-7.44 (2H, m, ArCH); δ_C(100 MHz; $CDCl_3$) 14.0 (CH_3), 24.8 ($CHCH_2$), 34.7 ($CHCH_2CH_2$), 50.2 (CO_2CH_3), 51.5 (CO_2CH_3), 51.5 ($CHOCH_3$), 65.7 (OCH_2CH_3), 78.6 (CH_2CHO), 78.6 ($CHOCH_3$), 90.5 (C–C), 97.3 (C–C), 126.7 (ArCH), 127.8 (2ArCH), 128.4 (2ArCH), 136.7 (ArC), 168.6 (CO_2CH_3), 168.7 (CO_2CH_3) and 198.4 ($CO_{complex}$); HRMS (FAB) (M^+–2CO), found 547.9936, $C_{22}H_{22}Co_2O_9$ requires 547.9927 (+1.6 ppm); *m/z* 548 (4%), 520 (75%), 492 (100%) and 464 (30%).

Dimethyl 2-(*E*)-styrylcyclobutane-1,1-dicarboxylate (335)



Lindlar catalyst (15 mg, 15% weight) was added to a solution of dimethyl 2-(2-phenylethynyl)cyclobutane-1,1-dicarboxylate (100 mg, 0.37 mmol) in hexane (5 mL). The resulting mixture was flushed with nitrogen for 5 min and then with hydrogen for 5 min. The reaction mixture was then allowed to stir at room temperature for 30 min under a nitrogn atmosphere (TLC monitoring). The crude mixture was then filtered through a plug of celite and concentrated *in vacuo*. Subsequent purification by flash chromatography on silica gel (5% EtOAc/petrol) affoded the *title compound* in 72% yield (73 mg, 0.27 mmol) as a yellow oil; ν_{max} (film)/cm^{-1} ν_{max} (film)/cm^{-1} 1270 (C–O), 1434 (C–O), 1732 (C=O), 2951 (sp^3 C–H), 3001 (sp^2 C–H) and 3056 (sp^2 C–H); δ_H(400 MHz; $CDCl_3$) 1.80-1.90 (1H, m, CHC*H*HCH$_2$), 2.08-2.18 (2H, m, CHC*H*HCH$_2$ + CHCH$_2$C*H*H), 2.63-2.74 (1H, m, CHCH$_2$C*H*H), 3.66 (3H, s, OC*H*$_3$), 3.68 (3H, s, OC*H*$_3$), 4.09 (1H, dd, *J* 10.0, 17.2 Hz, C*H*CH$_2$CH$_2$), 5.54 (1H, dd, *J* 10.0, 11.6 Hz, CH=C*H*–CH), 6.41 (1H, d, *J* 11.6 Hz, C*H*=CH–CH)), 7.17-7.27 (3H, m, ArC*H*) and 7.28-7.39 (2H, m, ArC*H*); δ_C(100 MHz; $CDCl_3$) 24.6 (CH*C*H$_2$CH$_2$), 25.9 (CHCH$_2$*C*H$_2$), 32.9 (*C*HCH$_2$CH$_2$), 52.5 (O*C*H$_3$), 52.6 (O*C*H$_3$), 57.3 (*C*(CO$_2$Me)$_2$), 127.4 (ArC*H*), 128.3 (2ArC*H*), 128.8 (2ArC*H*), 130.4 (*C*H=CH–CH), 131.6 (CH=*C*H–CH), 170.4 (*C*O$_2$CH$_3$) and 171.8 (*C*O$_2$CH$_3$).

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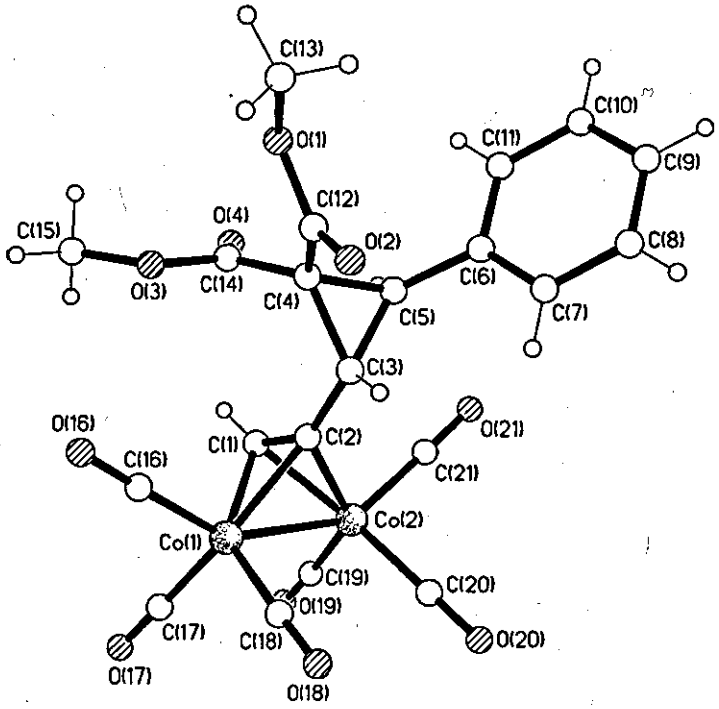
6. APPENDICES

Appendix I. X-Ray crystallographic data for *rac*-**249**



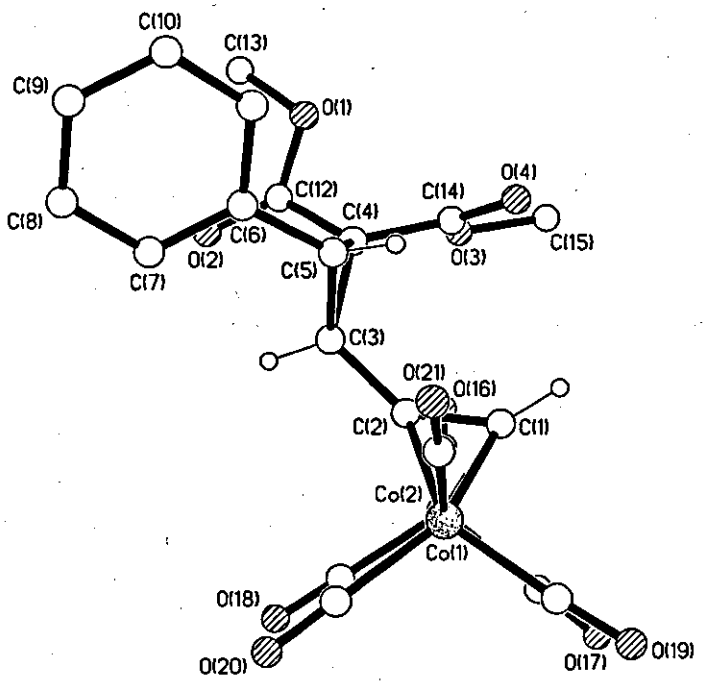


Table 1. Crystal data and structure refinement for sdrc19.

Identification code	sdrc19	
Chemical formula	$C_{21}H_{14}Co_2O_{10}$	
Formula weight	544.18	
Temperature	150(2) K	
Radiation, wavelength	MoK□, 0.71073 Å	
Crystal system, space group	monoclinic, C2/c	
Unit cell parameters	a = 26.3979(8) Å	□ = 90°
	b = 8.0016(2) Å	□ = 104.0254(4)°
	c = 22.5530(7) Å	□ = 90°
Cell volume	4621.8(2) $Å^3$	
Z	8	
Calculated density	1.564 g/cm^3	
Absorption coefficient □	1.488 mm^{-1}	
F(000)	2192	
Crystal colour and size	red, 0.33 × 0.29 × 0.27 mm^3	
Reflections for cell refinement	8753 (□ range 2.67 to 30.18°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	□ rotation with narrow frames	
□ range for data collection	1.86 to 31.95°	
Index ranges	h −39 to 38, k −11 to 11, l −33 to 32	

Completeness to □ = 29.00°	99.8 %
Intensity decay	0%
Reflections collected	27289
Independent reflections	7459 (R_{int} = 0.0302)
Reflections with F^2>2□	5923
Absorption correction	semi-empirical from equivalents
Min. and max. transmission	0.621 and 0.669
Structure solution	direct methods
Refinement method	Full-matrix least-squares on F^2
Weighting parameters a, b	0.0451, 0.9788
Data / restraints / parameters	7459 / 0 / 309
Final R indices [F^2>2□]	R1 = 0.0319, wR2 = 0.0810
R indices (all data)	R1 = 0.0439, wR2 = 0.0866
Goodness-of-fit on F^2	1.055
Largest and mean shift/su	0.001 and 0.000
Largest diff. peak and hole	0.409 and –0.515 e $Å^{-3}$

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for sdrc19. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Co(1)	0.144418(8)	0.68566(3)	0.417129(8)	0.02813(6)
Co(2)	0.053442(8)	0.73861(3)	0.422358(9)	0.03249(7)
C(1)	0.10099(6)	0.5622(2)	0.46096(6)	0.0320(3)
C(2)	0.11592(6)	0.70693(18)	0.48949(6)	0.0260(3)
C(3)	0.13398(5)	0.78024(17)	0.55076(6)	0.0237(3)
C(4)	0.16117(5)	0.67032(16)	0.60496(6)	0.0235(2)
C(5)	0.10638(6)	0.73892(17)	0.60003(6)	0.0253(3)
C(6)	0.09612(5)	0.86174(18)	0.64571(6)	0.0259(3)
C(7)	0.10082(6)	1.03262(19)	0.64019(7)	0.0311(3)
C(8)	0.09071(7)	1.1393(2)	0.68478(8)	0.0393(4)
C(9)	0.07549(7)	1.0749(3)	0.73465(8)	0.0453(4)
C(10)	0.07071(8)	0.9040(3)	0.74037(8)	0.0517(5)
C(11)	0.08101(7)	0.7977(2)	0.69635(7)	0.0399(4)
C(12)	0.20498(6)	0.74895(17)	0.65136(6)	0.0246(3)
O(1)	0.22255(5)	0.64493(14)	0.69770(5)	0.0391(3)
C(13)	0.26494(10)	0.7090(2)	0.74614(9)	0.0614(7)
O(2)	0.22093(4)	0.88850(13)	0.64839(5)	0.0327(2)
C(14)	0.16464(6)	0.48573(17)	0.59428(6)	0.0276(3)
O(3)	0.21175(5)	0.44583(13)	0.58707(6)	0.0373(3)
C(15)	0.21908(8)	0.2711(2)	0.57433(10)	0.0473(4)
O(4)	0.12961(5)	0.38815(14)	0.59031(6)	0.0423(3)
C(16)	0.20863(6)	0.60951(19)	0.45255(7)	0.0318(3)
O(16)	0.24898(5)	0.56100(15)	0.47571(5)	0.0397(3)
C(17)	0.13342(8)	0.5735(3)	0.34492(8)	0.0491(4)
O(17)	0.12663(8)	0.5023(2)	0.30050(7)	0.0835(6)
C(18)	0.15992(6)	0.8982(2)	0.40041(8)	0.0396(4)
O(18)	0.16796(6)	1.03420(19)	0.39091(8)	0.0678(5)
C(19)	0.01940(7)	0.6232(3)	0.35510(8)	0.0498(5)
O(19)	−0.00043(6)	0.5434(2)	0.31482(7)	0.0753(5)
C(20)	0.04887(7)	0.9588(3)	0.40203(8)	0.0423(4)
O(20)	0.04693(6)	1.09613(19)	0.38985(7)	0.0615(4)
C(21)	0.00554(7)	0.7370(3)	0.46695(8)	0.0461(4)
O(21)	−0.02310(6)	0.7370(2)	0.49689(7)	0.0710(5)

Table 3. Bond lengths [Å] and angles [°] for sdrc19.

Co(1)–C(16)	1.7963(16)	Co(1)–C(18)	1.8104(18)
Co(1)–C(17)	1.8200(17)	Co(1)–C(1)	1.9535(15)
Co(1)–C(2)	1.9629(14)	Co(1)–Co(2)	2.4695(3)
Co(2)–C(21)	1.7962(19)	Co(2)–C(19)	1.8167(18)
Co(2)–C(20)	1.817(2)	Co(2)–C(1)	1.9483(17)
Co(2)–C(2)	1.9664(14)	C(1)–C(2)	1.337(2)
C(2)–C(3)	1.4702(19)	C(3)–C(5)	1.5058(19)
C(3)–C(4)	1.5354(18)	C(4)–C(12)	1.4971(19)
C(4)–C(14)	1.5028(19)	C(4)–C(5)	1.526(2)
C(5)–C(6)	1.4953(19)	C(6)–C(7)	1.381(2)
C(6)–C(11)	1.395(2)	C(7)–C(8)	1.393(2)
C(8)–C(9)	1.382(3)	C(9)–C(10)	1.382(3)
C(10)–C(11)	1.383(2)	C(12)–O(2)	1.2010(17)
C(12)–O(1)	1.3287(16)	O(1)–C(13)	1.455(2)
C(14)–O(4)	1.1969(18)	C(14)–O(3)	1.3315(18)
O(3)–C(15)	1.4499(18)	C(16)–O(16)	1.1350(19)
C(17)–O(17)	1.128(2)	C(18)–O(18)	1.139(2)
C(19)–O(19)	1.130(2)	C(20)–O(20)	1.131(2)
C(21)–O(21)	1.129(2)		

C(16)–Co(1)–C(18)	100.06(7)	C(16)–Co(1)–C(17)	99.17(8)
C(18)–Co(1)–C(17)	105.78(9)	C(16)–Co(1)–C(1)	102.11(7)
C(18)–Co(1)–C(1)	140.39(7)	C(17)–Co(1)–C(1)	102.57(8)
C(16)–Co(1)–C(2)	99.80(6)	C(18)–Co(1)–C(2)	104.08(7)
C(17)–Co(1)–C(2)	140.94(8)	C(1)–Co(1)–C(2)	39.92(6)
C(16)–Co(1)–Co(2)	149.41(5)	C(18)–Co(1)–Co(2)	96.91(5)
C(17)–Co(1)–Co(2)	100.44(6)	C(1)–Co(1)–Co(2)	50.64(5)
C(2)–Co(1)–Co(2)	51.12(4)	C(21)–Co(2)–C(19)	101.01(8)
C(21)–Co(2)–C(20)	97.79(9)	C(19)–Co(2)–C(20)	107.04(9)
C(21)–Co(2)–C(1)	102.08(8)	C(19)–Co(2)–C(1)	98.02(8)
C(20)–Co(2)–C(1)	144.22(7)	C(21)–Co(2)–C(2)	98.10(7)
C(19)–Co(2)–C(2)	136.90(8)	C(20)–Co(2)–C(2)	108.13(7)
C(1)–Co(2)–C(2)	39.93(6)	C(21)–Co(2)–Co(1)	148.23(6)
C(19)–Co(2)–Co(1)	99.37(6)	C(20)–Co(2)–Co(1)	99.22(6)
C(1)–Co(2)–Co(1)	50.83(5)	C(2)–Co(2)–Co(1)	51.00(4)
C(2)–C(1)–Co(2)	70.76(10)	C(2)–C(1)–Co(1)	70.42(9)
Co(2)–C(1)–Co(1)	78.53(6)	C(1)–C(2)–C(3)	142.06(13)
C(1)–C(2)–Co(1)	69.66(9)	C(3)–C(2)–Co(1)	135.54(10)
C(1)–C(2)–Co(2)	69.30(9)	C(3)–C(2)–Co(2)	133.84(10)
Co(1)–C(2)–Co(2)	77.88(5)	C(2)–C(3)–C(5)	120.09(12)
C(2)–C(3)–C(4)	120.15(12)	C(5)–C(3)–C(4)	60.22(9)
C(12)–C(4)–C(14)	117.27(12)	C(12)–C(4)–C(5)	117.24(11)
C(14)–C(4)–C(5)	115.81(12)	C(12)–C(4)–C(3)	116.65(11)
C(14)–C(4)–C(3)	118.06(11)	C(5)–C(4)–C(3)	58.93(9)
C(6)–C(5)–C(3)	124.40(12)	C(6)–C(5)–C(4)	120.87(11)
C(3)–C(5)–C(4)	60.85(9)	C(7)–C(6)–C(11)	119.15(14)
C(7)–C(6)–C(5)	123.59(12)	C(11)–C(6)–C(5)	117.26(13)
C(6)–C(7)–C(8)	120.29(14)	C(9)–C(8)–C(7)	120.21(17)

C(10)–C(9)–C(8)	119.72(16)	C(9)–C(10)–C(11)	120.21(16)
C(10)–C(11)–C(6)	120.42(16)	O(2)–C(12)–O(1)	124.46(13)
O(2)–C(12)–C(4)	125.00(12)	O(1)–C(12)–C(4)	110.48(12)
C(12)–O(1)–C(13)	115.37(13)	O(4)–C(14)–O(3)	124.18(14)
O(4)–C(14)–C(4)	125.26(14)	O(3)–C(14)–C(4)	110.50(12)
C(14)–O(3)–C(15)	115.40(13)	O(16)–C(16)–Co(1)	178.98(14)
O(17)–C(17)–Co(1)	179.2(2)	O(18)–C(18)–Co(1)	177.07(18)
O(19)–C(19)–Co(2)	176.1(2)	O(20)–C(20)–Co(2)	178.80(19)
O(21)–C(21)–Co(2)	177.41(17)		

Table 4. Hydrogen coordinates and isotropic displacement parameters ($Å^2$) for sdrc19.

	x	y	z	U
H(1)	0.0964(7)	0.446(2)	0.4685(8)	0.038
H(3)	0.1479(6)	0.890(2)	0.5526(7)	0.028
H(5)	0.0829(7)	0.647(2)	0.5901(8)	0.030
H(7)	0.1110	1.0776	0.6058	0.037
H(8)	0.0943	1.2567	0.6809	0.047
H(9)	0.0684	1.1478	0.7649	0.054
H(10)	0.0603	0.8594	0.7746	0.062
H(11)	0.0778	0.6803	0.7006	0.048
H(13A)	0.2939	0.7438	0.7288	0.092
H(13B)	0.2769	0.6212	0.7766	0.092
H(13C)	0.2526	0.8050	0.7656	0.092
H(15A)	0.2120	0.2021	0.6073	0.071
H(15B)	0.2551	0.2530	0.5715	0.071
H(15C)	0.1950	0.2399	0.5356	0.071

Table 5. Torsion angles [°] for sdrc19.

C(16)–Co(1)–Co(2)–C(21)	5.29(16)	C(18)–Co(1)–Co(2)–C(21)	−118.13(14)
C(17)–Co(1)–Co(2)–C(21)	134.36(15)	C(1)–Co(1)–Co(2)–C(21)	36.60(14)
C(2)–Co(1)–Co(2)–C(21)	−15.60(14)	C(16)–Co(1)–Co(2)–C(19)	−124.06(12)
C(18)–Co(1)–Co(2)–C(19)	112.52(9)	C(17)–Co(1)–Co(2)–C(19)	5.00(10)
C(1)–Co(1)–Co(2)–C(19)	−92.75(9)	C(2)–Co(1)–Co(2)–C(19)	−144.95(9)
C(16)–Co(1)–Co(2)–C(20)	126.81(11)	C(18)–Co(1)–Co(2)–C(20)	3.39(8)
C(17)–Co(1)–Co(2)–C(20)	−104.13(9)	C(1)–Co(1)–Co(2)–C(20)	158.12(8)
C(2)–Co(1)–Co(2)–C(20)	105.92(8)	C(16)–Co(1)–Co(2)–C(1)	−31.31(11)
C(18)–Co(1)–Co(2)–C(1)	−154.73(8)	C(17)–Co(1)–Co(2)–C(1)	97.76(9)
C(2)–Co(1)–Co(2)–C(1)	−52.20(8)	C(16)–Co(1)–Co(2)–C(2)	20.89(11)
C(18)–Co(1)–Co(2)–C(2)	−102.53(8)	C(17)–Co(1)–Co(2)–C(2)	149.95(9)
C(1)–Co(1)–Co(2)–C(2)	52.20(8)	C(21)–Co(2)–C(1)–C(2)	−88.21(10)
C(19)–Co(2)–C(1)–C(2)	168.65(10)	C(20)–Co(2)–C(1)–C(2)	34.07(15)
Co(1)–Co(2)–C(1)–C(2)	73.06(8)	C(21)–Co(2)–C(1)–Co(1)	−161.27(7)
C(19)–Co(2)–C(1)–Co(1)	95.58(7)	C(20)–Co(2)–C(1)–Co(1)	−38.99(13)
C(2)–Co(2)–C(1)–Co(1)	−73.06(8)	C(16)–Co(1)–C(1)–C(2)	90.85(10)
C(18)–Co(1)–C(1)–C(2)	−31.81(15)	C(17)–Co(1)–C(1)–C(2)	−166.75(10)
Co(2)–Co(1)–C(1)–C(2)	−73.46(9)	C(16)–Co(1)–C(1)–Co(2)	164.31(5)
C(18)–Co(1)–C(1)–Co(2)	41.66(12)	C(17)–Co(1)–C(1)–Co(2)	−93.29(8)
C(2)–Co(1)–C(1)–Co(2)	73.46(9)	Co(2)–C(1)–C(2)–C(3)	136.0(2)
Co(1)–C(1)–C(2)–C(3)	−139.7(2)	Co(2)–C(1)–C(2)–Co(1)	−84.29(4)
Co(1)–C(1)–C(2)–Co(2)	84.29(4)	C(16)–Co(1)–C(2)–C(1)	−97.20(10)
C(18)–Co(1)–C(2)–C(1)	159.73(10)	C(17)–Co(1)–C(2)–C(1)	20.79(16)
Co(2)–Co(1)–C(2)–C(1)	72.19(9)	C(16)–Co(1)–C(2)–C(3)	48.19(15)
C(18)–Co(1)–C(2)–C(3)	−54.88(16)	C(17)–Co(1)–C(2)–C(3)	166.18(15)
C(1)–Co(1)–C(2)–C(3)	145.4(2)	Co(2)–Co(1)–C(2)–C(3)	−142.42(17)
C(16)–Co(1)–C(2)–Co(2)	−169.39(6)	C(18)–Co(1)–C(2)–Co(2)	87.54(6)
C(17)–Co(1)–C(2)–Co(2)	−51.40(13)	C(1)–Co(1)–C(2)–Co(2)	−72.19(9)
C(21)–Co(2)–C(2)–C(1)	99.17(11)	C(19)–Co(2)–C(2)–C(1)	−16.58(15)
C(20)–Co(2)–C(2)–C(1)	−159.84(10)	Co(1)–Co(2)–C(2)–C(1)	−72.61(9)
C(21)–Co(2)–C(2)–C(3)	−44.54(15)	C(19)–Co(2)–C(2)–C(3)	−160.28(14)
C(20)–Co(2)–C(2)–C(3)	56.45(15)	C(1)–Co(2)–C(2)–C(3)	−143.71(18)
Co(1)–Co(2)–C(2)–C(3)	143.69(16)	C(21)–Co(2)–C(2)–Co(1)	171.78(7)
C(19)–Co(2)–C(2)–Co(1)	56.03(11)	C(20)–Co(2)–C(2)–Co(1)	−87.23(7)
C(1)–Co(2)–C(2)–Co(1)	72.61(9)	C(1)–C(2)–C(3)–C(5)	−46.1(3)
Co(1)–C(2)–C(3)–C(5)	−166.04(11)	Co(2)–C(2)–C(3)–C(5)	69.72(18)
C(1)–C(2)–C(3)–C(4)	24.8(3)	Co(1)–C(2)–C(3)–C(4)	−95.15(16)
Co(2)–C(2)–C(3)–C(4)	140.61(12)	C(2)–C(3)–C(4)–C(12)	143.21(13)
C(5)–C(3)–C(4)–C(12)	−107.18(13)	C(2)–C(3)–C(4)–C(14)	−4.84(19)
C(5)–C(3)–C(4)–C(14)	104.76(14)	C(2)–C(3)–C(4)–C(5)	−109.61(14)
C(2)–C(3)–C(5)–C(6)	−141.02(14)	C(4)–C(3)–C(5)–C(6)	109.28(15)
C(2)–C(3)–C(5)–C(4)	109.70(14)	C(12)–C(4)–C(5)–C(6)	−8.66(18)
C(14)–C(4)–C(5)–C(6)	136.57(13)	C(3)–C(4)–C(5)–C(6)	−114.86(14)
C(12)–C(4)–C(5)–C(3)	106.19(13)	C(14)–C(4)–C(5)–C(3)	−108.58(13)

C(3)–C(5)–C(6)–C(7)	14.1(2)	C(4)–C(5)–C(6)–C(7)	87.96(17)
C(3)–C(5)–C(6)–C(11)	–165.88(14)	C(4)–C(5)–C(6)–C(11)	–92.05(17)
C(11)–C(6)–C(7)–C(8)	0.2(2)	C(5)–C(6)–C(7)–C(8)	–179.84(14)
C(6)–C(7)–C(8)–C(9)	–0.5(2)	C(7)–C(8)–C(9)–C(10)	0.5(3)
C(8)–C(9)–C(10)–C(11)	–0.1(3)	C(9)–C(10)–C(11)–C(6)	–0.2(3)
C(7)–C(6)–C(11)–C(10)	0.2(3)	C(5)–C(6)–C(11)–C(10)	–179.79(17)
C(14)–C(4)–C(12)–O(2)	146.37(14)	C(5)–C(4)–C(12)–O(2)	–68.91(18)
C(3)–C(4)–C(12)–O(2)	–1.9(2)	C(14)–C(4)–C(12)–O(1)	–36.05(17)
C(5)–C(4)–C(12)–O(1)	108.67(14)	C(3)–C(4)–C(12)–O(1)	175.65(12)
O(2)–C(12)–O(1)–C(13)	–1.7(2)	C(4)–C(12)–O(1)–C(13)	–179.31(16)
C(12)–C(4)–C(14)–O(4)	135.06(15)	C(5)–C(4)–C(14)–O(4)	–10.2(2)
C(3)–C(4)–C(14)–O(4)	–77.08(18)	C(12)–C(4)–C(14)–O(3)	–47.71(16)
C(5)–C(4)–C(14)–O(3)	167.08(11)	C(3)–C(4)–C(14)–O(3)	100.15(14)
O(4)–C(14)–O(3)–C(15)	–0.7(2)	C(4)–C(14)–O(3)–C(15)	–177.96(13)

Appendix II. X-Ray crystallographic data for **313**

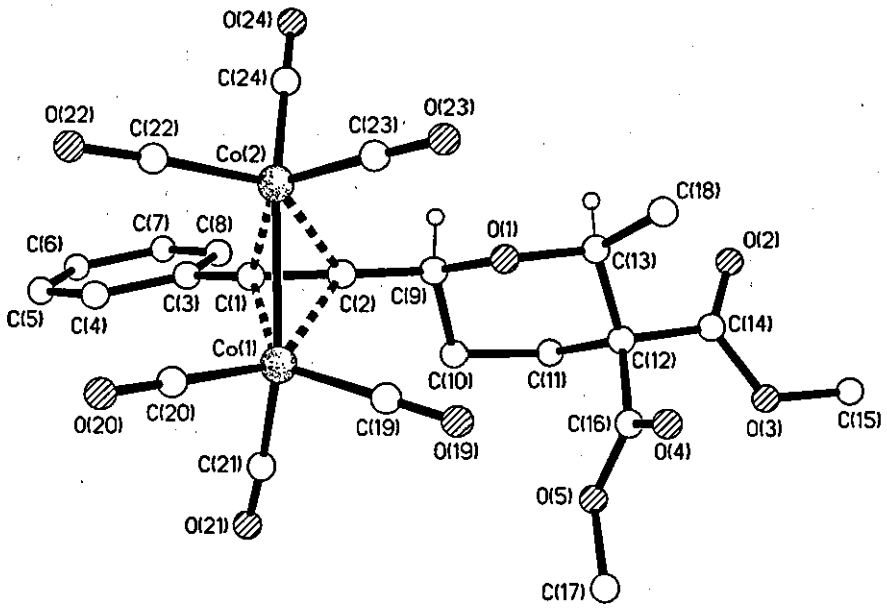


Table 1. Crystal data and structure refinement for sdrc14.

Identification code	sdrc14	
Chemical formula	$C_{24}H_{20}Co_2O_{11}$	
Formula weight	602.26	
Temperature	150(2) K	
Radiation, wavelength	MoK□, 0.71073 Å	
Crystal system, space group	monoclinic, C2/c	
Unit cell parameters	a = 30.4100(16) Å	□ = 90°
	b = 8.0633(4) Å	□ = 109.382(2)°
	c = 22.1301(12) Å	□ = 90°
Cell volume	5118.9(5) $Å^3$	
Z	8	
Calculated density	1.563 g/cm^3	
Absorption coefficient □	1.354 mm^{-1}	
F(000)	2448	
Crystal colour and size	red, 0.34 × 0.34 × 0.08 mm^3	
Reflections for cell refinement	4882 (□ range 2.62 to 24.73°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	□ rotation with narrow frames	
□ range for data collection	1.95 to 28.32°	
Index ranges	h –40 to 40, k –10 to 10, l –29 to 29	
Completeness to □ = 27.50°	100.0 %	
Intensity decay	0%	
Reflections collected	25700	
Independent reflections	6367 (R_{int} = 0.0430)	
Reflections with F^2>2□	4643	
Absorption correction	numerical	
Min. and max. transmission	0.656 and 0.899	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0389, 2.1101	
Data / restraints / parameters	6367 / 0 / 337	
Final R indices [F^2>2□]	R1 = 0.0360, wR2 = 0.0791	
R indices (all data)	R1 = 0.0574, wR2 = 0.0877	
Goodness-of-fit on F^2	1.024	
Largest and mean shift/su	0.000 and 0.000	
Largest diff. peak and hole	0.451 and –0.372 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for sdrc14. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Co(1)	0.084426(10)	0.23321(4)	0.374468(13)	0.03433(9)
Co(2)	0.049931(10)	0.49915(4)	0.392093(14)	0.03389(9)
C(1)	0.09004(7)	0.3451(3)	0.45562(9)	0.0269(4)
C(2)	0.11480(7)	0.4265(3)	0.42534(9)	0.0271(4)
C(3)	0.09058(7)	0.2930(3)	0.51926(9)	0.0261(4)
C(4)	0.05855(8)	0.1804(3)	0.52691(11)	0.0375(5)
C(5)	0.05870(8)	0.1360(3)	0.58731(11)	0.0428(6)
C(6)	0.09051(9)	0.2054(3)	0.64081(11)	0.0418(6)
C(7)	0.12281(9)	0.3178(3)	0.63391(11)	0.0462(6)
C(8)	0.12320(8)	0.3610(3)	0.57351(10)	0.0379(5)
C(9)	0.15916(7)	0.5161(3)	0.43384(9)	0.0247(4)
C(10)	0.20215(7)	0.4062(3)	0.45782(9)	0.0257(4)
C(11)	0.24561(7)	0.4973(2)	0.45524(9)	0.0246(4)
C(12)	0.23767(7)	0.5726(2)	0.38795(9)	0.0217(4)
C(13)	0.19411(7)	0.6843(3)	0.37333(9)	0.0249(4)
O(1)	0.15499(5)	0.58485(17)	0.37227(6)	0.0255(3)
C(14)	0.27987(7)	0.6793(3)	0.39193(9)	0.0258(4)
O(2)	0.28773(5)	0.81114(19)	0.41914(7)	0.0360(4)
O(3)	0.30682(5)	0.61068(18)	0.36254(8)	0.0353(4)
C(15)	0.34792(8)	0.7046(3)	0.36385(13)	0.0454(6)
C(16)	0.23148(7)	0.4406(2)	0.33576(10)	0.0253(4)
O(4)	0.21408(6)	0.46467(18)	0.27942(7)	0.0353(4)
O(5)	0.24918(5)	0.29438(17)	0.36069(7)	0.0316(3)
C(17)	0.24812(9)	0.1674(3)	0.31378(12)	0.0443(6)
C(18)	0.17925(8)	0.7799(3)	0.31081(10)	0.0334(5)
C(19)	0.10159(9)	0.2715(4)	0.30400(12)	0.0554(8)
O(19)	0.11292(8)	0.2938(4)	0.26116(10)	0.0906(9)
C(20)	0.02980(9)	0.1254(3)	0.34176(11)	0.0434(6)
O(20)	−0.00503(7)	0.0581(3)	0.31996(8)	0.0605(5)
C(21)	0.12020(9)	0.0621(4)	0.41317(13)	0.0466(6)
O(21)	0.14187(7)	−0.0455(3)	0.44088(11)	0.0696(6)
C(22)	−0.00877(9)	0.4299(3)	0.38305(12)	0.0460(6)
O(22)	−0.04414(7)	0.3788(3)	0.38126(11)	0.0721(6)
C(23)	0.05033(9)	0.6077(4)	0.32014(13)	0.0597(8)
O(23)	0.05296(7)	0.6764(4)	0.27652(10)	0.0967(9)
C(24)	0.05350(8)	0.6718(3)	0.44419(13)	0.0444(6)
O(24)	0.05754(7)	0.7777(3)	0.47935(12)	0.0709(6)

Table 3. Bond lengths [Å] and angles [°] for sdrc14.

Co(1)–C(21)	1.790(3)	Co(1)–C(20)	1.801(2)
Co(1)–C(19)	1.828(3)	Co(1)–C(2)	1.964(2)
Co(1)–C(1)	1.966(2)	Co(1)–Co(2)	2.4743(5)
Co(2)–C(24)	1.788(3)	Co(2)–C(22)	1.817(3)
Co(2)–C(23)	1.821(3)	Co(2)–C(2)	1.953(2)
Co(2)–C(1)	1.967(2)	C(1)–C(2)	1.335(3)
C(1)–C(3)	1.465(3)	C(2)–C(9)	1.486(3)
C(3)–C(4)	1.383(3)	C(3)–C(8)	1.391(3)
C(4)–C(5)	1.382(3)	C(5)–C(6)	1.375(3)
C(6)–C(7)	1.382(4)	C(7)–C(8)	1.385(3)
C(9)–O(1)	1.437(2)	C(9)–C(10)	1.522(3)
C(10)–C(11)	1.529(3)	C(11)–C(12)	1.551(3)
C(12)–C(14)	1.524(3)	C(12)–C(16)	1.535(3)
C(12)–C(13)	1.545(3)	C(13)–O(1)	1.428(2)
C(13)–C(18)	1.516(3)	C(14)–O(2)	1.206(2)
C(14)–O(3)	1.325(2)	O(3)–C(15)	1.453(2)
C(16)–O(4)	1.198(2)	C(16)–O(5)	1.337(2)
O(5)–C(17)	1.451(3)	C(19)–O(19)	1.125(3)
C(20)–O(20)	1.144(3)	C(21)–O(21)	1.138(3)
C(22)–O(22)	1.140(3)	C(23)–O(23)	1.138(3)
C(24)–O(24)	1.134(3)		

C(21)–Co(1)–C(20)	98.81(12)	C(21)–Co(1)–C(19)	103.77(13)
C(20)–Co(1)–C(19)	103.01(11)	C(21)–Co(1)–C(2)	103.99(10)
C(20)–Co(1)–C(2)	144.02(10)	C(19)–Co(1)–C(2)	98.17(10)
C(21)–Co(1)–C(1)	93.55(10)	C(20)–Co(1)–C(1)	112.20(9)
C(19)–Co(1)–C(1)	137.67(11)	C(2)–Co(1)–C(1)	39.70(8)
C(21)–Co(1)–Co(2)	144.59(8)	C(20)–Co(1)–Co(2)	95.69(9)
C(19)–Co(1)–Co(2)	104.14(10)	C(2)–Co(1)–Co(2)	50.62(6)
C(1)–Co(1)–Co(2)	51.03(6)	C(24)–Co(2)–C(22)	99.07(11)
C(24)–Co(2)–C(23)	99.95(14)	C(22)–Co(2)–C(23)	110.06(11)
C(24)–Co(2)–C(2)	98.82(10)	C(22)–Co(2)–C(2)	141.43(11)
C(23)–Co(2)–C(2)	100.07(10)	C(24)–Co(2)–C(1)	98.07(10)
C(22)–Co(2)–C(1)	103.77(10)	C(23)–Co(2)–C(1)	138.26(10)
C(2)–Co(2)–C(1)	39.81(8)	C(24)–Co(2)–Co(1)	146.97(8)
C(22)–Co(2)–Co(1)	99.70(9)	C(23)–Co(2)–Co(1)	98.78(11)
C(2)–Co(2)–Co(1)	51.03(6)	C(1)–Co(2)–Co(1)	51.00(6)
C(2)–C(1)–C(3)	142.73(19)	C(2)–C(1)–Co(1)	70.08(12)
C(3)–C(1)–Co(1)	135.77(16)	C(2)–C(1)–Co(2)	69.52(12)
C(3)–C(1)–Co(2)	132.45(14)	Co(1)–C(1)–Co(2)	77.97(7)
C(1)–C(2)–C(9)	144.59(19)	C(1)–C(2)–Co(2)	70.67(12)
C(9)–C(2)–Co(2)	131.51(15)	C(1)–C(2)–Co(1)	70.22(13)
C(9)–C(2)–Co(1)	133.84(14)	Co(2)–C(2)–Co(1)	78.35(7)
C(4)–C(3)–C(8)	118.86(19)	C(4)–C(3)–C(1)	121.51(19)
C(8)–C(3)–C(1)	119.61(19)	C(5)–C(4)–C(3)	120.8(2)
C(6)–C(5)–C(4)	120.2(2)	C(5)–C(6)–C(7)	119.6(2)
C(6)–C(7)–C(8)	120.4(2)	C(7)–C(8)–C(3)	120.1(2)
O(1)–C(9)–C(2)	106.08(15)	O(1)–C(9)–C(10)	110.52(15)

C(2)–C(9)–C(10)	113.57(17)	C(9)–C(10)–C(11)	111.13(16)
C(10)–C(11)–C(12)	111.27(15)	C(14)–C(12)–C(16)	109.02(15)
C(14)–C(12)–C(13)	109.25(16)	C(16)–C(12)–C(13)	111.35(16)
C(14)–C(12)–C(11)	107.81(15)	C(16)–C(12)–C(11)	113.10(16)
C(13)–C(12)–C(11)	106.18(15)	O(1)–C(13)–C(18)	106.03(16)
O(1)–C(13)–C(12)	109.12(16)	C(18)–C(13)–C(12)	117.57(16)
C(13)–O(1)–C(9)	112.97(14)	O(2)–C(14)–O(3)	124.15(19)
O(2)–C(14)–C(12)	123.40(18)	O(3)–C(14)–C(12)	112.45(17)
C(14)–O(3)–C(15)	116.13(17)	O(4)–C(16)–O(5)	123.42(19)
O(4)–C(16)–C(12)	124.92(19)	O(5)–C(16)–C(12)	111.63(16)
C(16)–O(5)–C(17)	114.62(16)	O(19)–C(19)–Co(1)	178.8(3)
O(20)–C(20)–Co(1)	178.8(2)	O(21)–C(21)–Co(1)	175.7(2)
O(22)–C(22)–Co(2)	174.8(3)	O(23)–C(23)–Co(2)	176.5(2)
O(24)–C(24)–Co(2)	176.7(2)		

Table 4. Hydrogen coordinates and isotropic displacement parameters ($Å^2$) for sdrc14.

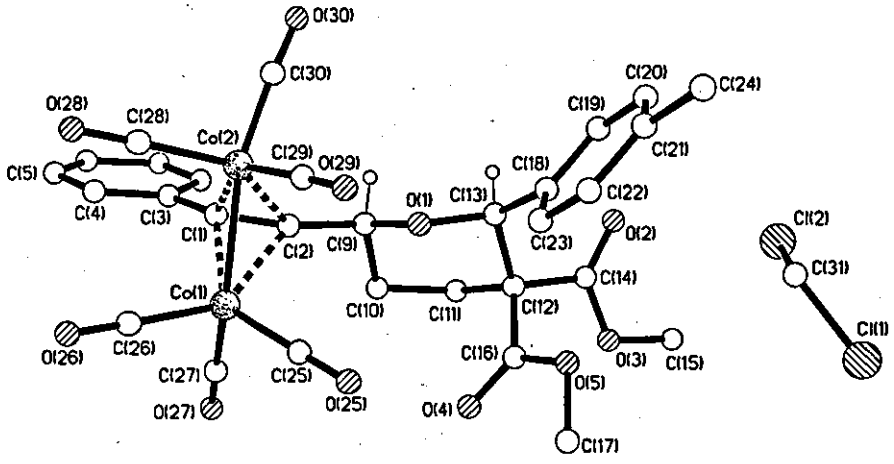
	x	y	z	U
H(4)	0.0362	0.1329	0.4902	0.045
H(5)	0.0367	0.0574	0.5919	0.051
H(6)	0.0903	0.1761	0.6823	0.050
H(7)	0.1449	0.3658	0.6708	0.055
H(8)	0.1458	0.4371	0.5691	0.045
H(9)	0.1622	0.6088	0.4650	0.030
H(10A)	0.1973	0.3049	0.4311	0.031
H(10B)	0.2068	0.3720	0.5025	0.031
H(11A)	0.2722	0.4190	0.4658	0.030
H(11B)	0.2536	0.5870	0.4876	0.030
H(13)	0.1998	0.7661	0.4091	0.030
H(15A)	0.3383	0.8078	0.3397	0.068
H(15B)	0.3668	0.6386	0.3444	0.068
H(15C)	0.3664	0.7307	0.4083	0.068
H(17A)	0.2158	0.1474	0.2867	0.066
H(17B)	0.2616	0.0646	0.3359	0.066
H(17C)	0.2663	0.2045	0.2871	0.066
H(18A)	0.1642	0.7041	0.2753	0.050
H(18B)	0.2067	0.8301	0.3043	0.050
H(18C)	0.1572	0.8672	0.3124	0.050

Table 5. Torsion angles [°] for sdrc14.

C(21)–Co(1)–Co(2)–C(24)	24.0(2)	C(20)–Co(1)–Co(2)–C(24)	137.96(17)
C(19)–Co(1)–Co(2)–C(24)	−117.07(17)	C(2)–Co(1)–Co(2)–C(24)	−28.06(17)
C(1)–Co(1)–Co(2)–C(24)	23.89(17)	C(21)–Co(1)–Co(2)–C(22)	−99.80(17)
C(20)–Co(1)–Co(2)–C(22)	14.14(11)	C(19)–Co(1)–Co(2)–C(22)	119.12(12)
C(2)–Co(1)–Co(2)–C(22)	−151.87(11)	C(1)–Co(1)–Co(2)–C(22)	−99.92(11)
C(21)–Co(1)–Co(2)–C(23)	147.96(17)	C(20)–Co(1)–Co(2)–C(23)	−98.10(11)
C(19)–Co(1)–Co(2)–C(23)	6.88(12)	C(2)–Co(1)–Co(2)–C(23)	95.89(11)
C(1)–Co(1)–Co(2)–C(23)	147.84(11)	C(21)–Co(1)–Co(2)–C(2)	52.07(16)
C(20)–Co(1)–Co(2)–C(2)	166.02(10)	C(19)–Co(1)–Co(2)–C(2)	−89.01(11)
C(1)–Co(1)–Co(2)–C(2)	51.95(10)	C(21)–Co(1)–Co(2)–C(1)	0.12(16)
C(20)–Co(1)–Co(2)–C(1)	114.07(11)	C(19)–Co(1)–Co(2)–C(1)	−140.96(11)
C(2)–Co(1)–Co(2)–C(1)	−51.95(10)	C(21)–Co(1)–C(1)–C(2)	107.73(14)
C(20)–Co(1)–C(1)–C(2)	−151.25(14)	C(19)–Co(1)–C(1)–C(2)	−7.3(2)
Co(2)–Co(1)–C(1)–C(2)	−72.34(12)	C(21)–Co(1)–C(1)–C(3)	−39.5(2)
C(20)–Co(1)–C(1)–C(3)	61.5(2)	C(19)–Co(1)–C(1)–C(3)	−154.5(2)
C(2)–Co(1)–C(1)–C(3)	−147.3(3)	Co(2)–Co(1)–C(1)–C(3)	140.4(2)
C(21)–Co(1)–C(1)–Co(2)	−179.93(9)	C(20)–Co(1)–C(1)–Co(2)	−78.91(11)
C(19)–Co(1)–C(1)–Co(2)	65.09(18)	C(2)–Co(1)–C(1)–Co(2)	72.34(12)
C(24)–Co(2)–C(1)–C(2)	−94.11(14)	C(22)–Co(2)–C(1)–C(2)	164.43(14)
C(23)–Co(2)–C(1)–C(2)	20.8(2)	Co(1)–Co(2)–C(1)–C(2)	73.01(12)
C(24)–Co(2)–C(1)–C(3)	49.9(2)	C(22)–Co(2)–C(1)–C(3)	−51.5(2)
C(23)–Co(2)–C(1)–C(3)	164.8(2)	C(2)–Co(2)–C(1)–C(3)	144.1(3)
Co(1)–Co(2)–C(1)–C(3)	−142.9(2)	C(24)–Co(2)–C(1)–Co(1)	−167.12(9)
C(22)–Co(2)–C(1)–Co(1)	91.42(10)	C(23)–Co(2)–C(1)–Co(1)	−52.21(19)
C(2)–Co(2)–C(1)–Co(1)	−73.01(12)	C(3)–C(1)–C(2)–C(9)	1.6(6)
Co(1)–C(1)–C(2)–C(9)	−139.9(3)	Co(2)–C(1)–C(2)–C(9)	135.9(3)
C(3)–C(1)–C(2)–Co(2)	−134.3(3)	Co(1)–C(1)–C(2)–Co(2)	84.19(6)
C(3)–C(1)–C(2)–Co(1)	141.5(3)	Co(2)–C(1)–C(2)–Co(1)	−84.19(6)
C(24)–Co(2)–C(2)–C(1)	92.05(14)	C(22)–Co(2)–C(2)–C(1)	−24.7(2)
C(23)–Co(2)–C(2)–C(1)	−166.11(16)	Co(1)–Co(2)–C(2)–C(1)	−72.91(12)
C(24)–Co(2)–C(2)–C(9)	−55.4(2)	C(22)–Co(2)–C(2)–C(9)	−172.18(18)
C(23)–Co(2)–C(2)–C(9)	46.4(2)	C(1)–Co(2)–C(2)–C(9)	−147.5(2)
Co(1)–Co(2)–C(2)–C(9)	139.6(2)	C(24)–Co(2)–C(2)–Co(1)	164.96(9)
C(22)–Co(2)–C(2)–Co(1)	48.19(17)	C(23)–Co(2)–C(2)–Co(1)	−93.20(12)
C(1)–Co(2)–C(2)–Co(1)	72.91(12)	C(21)–Co(1)–C(2)–C(1)	−78.45(15)
C(20)–Co(1)–C(2)–C(1)	49.3(2)	C(19)–Co(1)–C(2)–C(1)	175.07(15)
Co(2)–Co(1)–C(2)–C(1)	73.44(12)	C(21)–Co(1)–C(2)–C(9)	70.4(2)
C(20)–Co(1)–C(2)–C(9)	−161.90(19)	C(19)–Co(1)–C(2)–C(9)	−36.1(2)
C(1)–Co(1)–C(2)–C(9)	148.8(3)	Co(2)–Co(1)–C(2)–C(9)	−137.7(2)
C(21)–Co(1)–C(2)–Co(2)	−151.90(9)	C(20)–Co(1)–C(2)–Co(2)	−24.16(18)
C(19)–Co(1)–C(2)–Co(2)	101.63(11)	C(1)–Co(1)–C(2)–Co(2)	−73.44(12)
C(2)–C(1)–C(3)–C(4)	−168.6(3)	Co(1)–C(1)–C(3)–C(4)	−45.7(3)
Co(2)–C(1)–C(3)–C(4)	76.6(3)	C(2)–C(1)–C(3)–C(8)	13.1(4)

Co(1)–C(1)–C(3)–C(8)	136.0(2)	Co(2)–C(1)–C(3)–C(8)	–101.7(2)
C(8)–C(3)–C(4)–C(5)	0.2(3)	C(1)–C(3)–C(4)–C(5)	–178.1(2)
C(3)–C(4)–C(5)–C(6)	0.8(4)	C(4)–C(5)–C(6)–C(7)	–1.0(4)
C(5)–C(6)–C(7)–C(8)	0.1(4)	C(6)–C(7)–C(8)–C(3)	0.9(4)
C(4)–C(3)–C(8)–C(7)	–1.0(3)	C(1)–C(3)–C(8)–C(7)	177.3(2)
C(1)–C(2)–C(9)–O(1)	–173.4(3)	Co(2)–C(2)–C(9)–O(1)	–54.6(2)
Co(1)–C(2)–C(9)–O(1)	63.8(2)	C(1)–C(2)–C(9)–C(10)	65.0(4)
Co(2)–C(2)–C(9)–C(10)	–176.19(14)	Co(1)–C(2)–C(9)–C(10)	–57.8(2)
O(1)–C(9)–C(10)–C(11)	51.7(2)	C(2)–C(9)–C(10)–C(11)	170.74(16)
C(9)–C(10)–C(11)–C(12)	–52.0(2)	C(10)–C(11)–C(12)–C(14)	172.67(16)
C(10)–C(11)–C(12)–C(16)	–66.7(2)	C(10)–C(11)–C(12)–C(13)	55.7(2)
C(14)–C(12)–C(13)–O(1)	–177.61(14)	C(16)–C(12)–C(13)–O(1)	61.92(19)
C(11)–C(12)–C(13)–O(1)	–61.58(19)	C(14)–C(12)–C(13)–C(18)	61.7(2)
C(16)–C(12)–C(13)–C(18)	–58.8(2)	C(11)–C(12)–C(13)–C(18)	177.71(17)
C(18)–C(13)–O(1)–C(9)	–166.27(16)	C(12)–C(13)–O(1)–C(9)	66.20(19)
C(2)–C(9)–O(1)–C(13)	176.41(15)	C(10)–C(9)–O(1)–C(13)	–60.1(2)
C(16)–C(12)–C(14)–O(2)	164.82(19)	C(13)–C(12)–C(14)–O(2)	42.9(2)
C(11)–C(12)–C(14)–O(2)	–72.0(2)	C(16)–C(12)–C(14)–O(3)	–15.5(2)
C(13)–C(12)–C(14)–O(3)	–137.38(17)	C(11)–C(12)–C(14)–O(3)	107.64(18)
O(2)–C(14)–O(3)–C(15)	–0.5(3)	C(12)–C(14)–O(3)–C(15)	179.86(18)
C(14)–C(12)–C(16)–O(4)	–79.2(2)	C(13)–C(12)–C(16)–O(4)	41.4(3)
C(11)–C(12)–C(16)–O(4)	160.88(19)	C(14)–C(12)–C(16)–O(5)	99.07(18)
C(13)–C(12)–C(16)–O(5)	–140.32(16)	C(11)–C(12)–C(16)–O(5)	–20.9(2)
O(4)–C(16)–O(5)–C(17)	3.3(3)	C(12)–C(16)–O(5)–C(17)	
–175.00(17)			

Appendix III. X-Ray crystallographic data for **314**



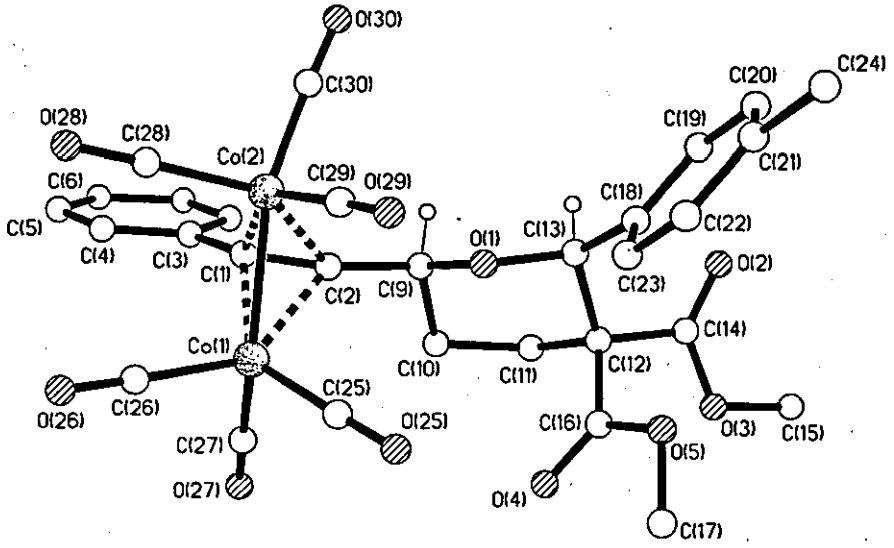


Table 1. Crystal data and structure refinement for sdrc13.

Identification code	sdrc13	
Chemical formula	$C_{31}H_{26}Cl_2Co_2O_{11}$	
Formula weight	763.28	
Temperature	150(2) K	
Radiation, wavelength	MoK□, 0.71073 Å	
Crystal system, space group	triclinic, P $\bar{1}$	
Unit cell parameters	a = 9.2516(12) Å	□ = 109.653(2)°
	b = 13.8248(19) Å	□ = 91.954(2)°
	c = 14.0220(19) Å	□ = 104.885(2)°
Cell volume	1617.9(4) $Å^3$	
Z	2	
Calculated density	1.567 g/cm^3	
Absorption coefficient □	1.249 mm^{-1}	
F(000)	776	
Crystal colour and size	red, 0.61 × 0.18 × 0.13 mm^3	
Reflections for cell refinement	3436 (□ range 2.41 to 27.02°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	□ rotation with narrow frames	
□ range for data collection	1.63 to 25.00°	
Index ranges	h −10 to 10, k −16 to 16, l −16 to 16	
Completeness to □ = 25.00°	99.8 %	
Intensity decay	0%	
Reflections collected	12711	
Independent reflections	5678 (R_{int} = 0.0322)	
Reflections with F^2>2□	4097	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.516 and 0.854	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.1371, 6.2845	
Data / restraints / parameters	5678 / 104 / 464	
Final R indices [F^2>2□]	R1 = 0.0774, wR2 = 0.2160	
R indices (all data)	R1 = 0.1044, wR2 = 0.2425	
Goodness-of-fit on F^2	1.054	
Largest and mean shift/su	0.000 and 0.000	
Largest diff. peak and hole	1.322 and −1.730 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for sdrc13. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Co(1)	0.18838(9)	0.67549(7)	0.18591(6)	0.0320(3)
Co(2)	−0.01537(9)	0.61398(8)	0.27873(7)	0.0341(3)
C(1)	0.1720(7)	0.7313(6)	0.3327(5)	0.0360(15)
C(2)	0.2006(7)	0.6364(6)	0.3071(5)	0.0324(14)
C(3)	0.2122(7)	0.8389(6)	0.4118(5)	0.0369(16)
C(4)	0.1548(16)	0.9171(9)	0.4070(9)	0.116(6)
C(5)	0.1924(18)	1.0176(10)	0.4841(9)	0.120(6)
C(6)	0.2885(10)	1.0420(7)	0.5657(7)	0.060(2)
C(7)	0.3465(15)	0.9628(8)	0.5739(9)	0.095(4)
C(8)	0.3099(13)	0.8620(8)	0.4981(7)	0.075(3)
C(9)	0.2894(7)	0.5765(6)	0.3428(5)	0.0348(15)
C(10)	0.4569(7)	0.6137(7)	0.3345(6)	0.0470(19)
C(11)	0.5384(8)	0.5363(7)	0.3534(6)	0.050(2)
C(12)	0.4590(8)	0.4175(7)	0.2933(5)	0.0440(19)
C(13)	0.2905(7)	0.3964(6)	0.3159(5)	0.0369(16)
O(1)	0.2260(5)	0.4656(4)	0.2820(3)	0.0346(10)
C(14)	0.5415(8)	0.3548(7)	0.3354(5)	0.0455(19)
O(2)	0.5056(6)	0.3219(5)	0.4030(4)	0.0518(14)
O(3)	0.6663(6)	0.3498(6)	0.2939(5)	0.0672(19)
C(15)	0.7610(12)	0.2957(11)	0.3297(9)	0.088(4)
C(16)	0.4732(10)	0.3927(8)	0.1831(6)	0.073(2)
O(4)	0.5356(16)	0.4637(11)	0.1516(9)	0.075(4)
O(5)	0.413(2)	0.2920(12)	0.1231(12)	0.085(4)
C(17)	0.4429(18)	0.2758(16)	0.0190(10)	0.088(6)
O(4X)	0.449(3)	0.2933(17)	0.139(2)	0.059(5)
O(5X)	0.487(3)	0.448(2)	0.1242(15)	0.079(5)
C(17X)	0.477(3)	0.381(2)	0.0171(14)	0.055(6)
C(18)	0.1831(8)	0.2854(6)	0.2698(5)	0.0382(16)
C(19)	0.1453(9)	0.2225(7)	0.3298(6)	0.0505(19)
C(20)	0.0388(10)	0.1250(7)	0.2921(7)	0.059(2)
C(21)	−0.0358(9)	0.0850(6)	0.1938(7)	0.053(2)
C(22)	0.0013(8)	0.1477(7)	0.1336(6)	0.0480(19)
C(23)	0.1082(8)	0.2468(7)	0.1716(6)	0.0454(18)
C(24)	−0.1564(12)	−0.0242(7)	0.1510(9)	0.074(3)
C(25)	0.1911(8)	0.5493(6)	0.0887(5)	0.0376(16)
O(25)	0.1931(7)	0.4706(5)	0.0299(4)	0.0537(14)
C(26)	0.0848(8)	0.7361(6)	0.1205(6)	0.0440(17)
O(26)	0.0160(7)	0.7702(5)	0.0796(5)	0.0659(17)
C(27)	0.3747(8)	0.7601(6)	0.1951(5)	0.0370(15)
O(27)	0.4944(6)	0.8140(5)	0.2050(4)	0.0530(14)
C(28)	−0.1497(8)	0.6819(7)	0.2557(6)	0.0470(19)
O(28)	−0.2303(6)	0.7269(6)	0.2411(6)	0.0698(18)
C(29)	−0.0860(7)	0.4785(6)	0.1870(5)	0.0386(16)
O(29)	−0.1274(6)	0.3945(5)	0.1273(4)	0.0512(13)
C(30)	−0.0631(7)	0.5901(7)	0.3927(6)	0.0439(18)

O(30)	−0.0860(6)	0.5746(6)	0.4663(4)	0.0621(17)
Cl(1)	0.3630(7)	−0.1032(5)	0.0165(6)	0.185(2)
C(31)	0.2705(17)	−0.0307(10)	0.1105(11)	0.128(6)
Cl(2)	0.3813(9)	0.0393(6)	0.2356(8)	0.198(5)
C(31X)	0.359(3)	0.0255(13)	0.106(2)	0.132(8)
Cl(2X)	0.5575(11)	0.0974(8)	0.1475(12)	0.131(5)

Table 3. Bond lengths [Å] and angles [°] for sdrc13.

Co(1)–C(27)	1.790(8)	Co(1)–C(25)	1.824(7)
Co(1)–C(26)	1.825(8)	Co(1)–C(2)	1.957(7)
Co(1)–C(1)	1.966(7)	Co(1)–Co(2)	2.4614(13)
Co(2)–C(30)	1.784(8)	Co(2)–C(29)	1.812(8)
Co(2)–C(28)	1.819(8)	Co(2)–C(2)	1.947(6)
Co(2)–C(1)	1.962(7)	C(1)–C(2)	1.338(10)
C(1)–C(3)	1.469(10)	C(2)–C(9)	1.487(9)
C(3)–C(4)	1.340(12)	C(3)–C(8)	1.378(11)
C(4)–C(5)	1.392(14)	C(5)–C(6)	1.316(14)
C(6)–C(7)	1.373(14)	C(7)–C(8)	1.387(14)
C(9)–O(1)	1.430(8)	C(9)–C(10)	1.525(9)
C(10)–C(11)	1.541(10)	C(11)–C(12)	1.535(12)
C(12)–C(16)	1.485(10)	C(12)–C(14)	1.528(10)
C(12)–C(13)	1.574(9)	C(13)–O(1)	1.442(8)
C(13)–C(18)	1.505(11)	C(14)–O(2)	1.204(9)
C(14)–O(3)	1.318(8)	O(3)–C(15)	1.462(9)
C(16)–O(4)	1.229(14)	C(16)–O(4X)	1.256(18)
C(16)–O(5X)	1.290(17)	C(16)–O(5)	1.318(16)
O(5)–C(17)	1.448(17)	O(5X)–C(17X)	1.459(19)
C(18)–C(23)	1.383(10)	C(18)–C(19)	1.393(11)
C(19)–C(20)	1.368(12)	C(20)–C(21)	1.381(12)
C(21)–C(22)	1.393(12)	C(21)–C(24)	1.538(12)
C(22)–C(23)	1.385(11)	C(25)–O(25)	1.128(8)
C(26)–O(26)	1.126(9)	C(27)–O(27)	1.139(8)
C(28)–O(28)	1.140(9)	C(29)–O(29)	1.136(9)
C(30)–O(30)	1.139(9)	Cl(1)–C(31)	1.761(13)
Cl(1)–C(31X)	1.807(18)	Cl(1)–Cl(2X')	2.459(17)
C(31)–Cl(2)	1.814(13)	C(31X)–Cl(2X)	1.816(18)
Cl(2X)–Cl(1')	2.459(17)		

C(27)–Co(1)–C(25)	102.7(3)	C(27)–Co(1)–C(26)	98.6(3)
C(25)–Co(1)–C(26)	105.1(3)	C(27)–Co(1)–C(2)	102.5(3)
C(25)–Co(1)–C(2)	99.1(3)	C(26)–Co(1)–C(2)	143.3(3)
C(27)–Co(1)–C(1)	95.7(3)	C(25)–Co(1)–C(1)	138.3(3)
C(26)–Co(1)–C(1)	108.7(3)	C(2)–Co(1)–C(1)	39.9(3)
C(27)–Co(1)–Co(2)	146.6(2)	C(25)–Co(1)–Co(2)	101.5(2)
C(26)–Co(1)–Co(2)	97.0(2)	C(2)–Co(1)–Co(2)	50.74(17)
C(1)–Co(1)–Co(2)	51.1(2)	C(30)–Co(2)–C(29)	99.5(3)
C(30)–Co(2)–C(28)	103.4(3)	C(29)–Co(2)–C(28)	104.6(3)
C(30)–Co(2)–C(2)	96.1(3)	C(29)–Co(2)–C(2)	104.8(3)
C(28)–Co(2)–C(2)	141.1(3)	C(30)–Co(2)–C(1)	100.4(3)
C(29)–Co(2)–C(1)	141.1(3)	C(28)–Co(2)–C(1)	102.8(3)
C(2)–Co(2)–C(1)	40.0(3)	C(30)–Co(2)–Co(1)	146.4(2)
C(29)–Co(2)–Co(1)	96.4(2)	C(28)–Co(2)–Co(1)	100.8(2)
C(2)–Co(2)–Co(1)	51.1(2)	C(1)–Co(2)–Co(1)	51.28(19)
C(2)–C(1)–C(3)	142.7(6)	C(2)–C(1)–Co(2)	69.4(4)
C(3)–C(1)–Co(2)	134.5(5)	C(2)–C(1)–Co(1)	69.7(4)
C(3)–C(1)–Co(1)	134.4(5)	Co(2)–C(1)–Co(1)	77.6(3)

C(1)–C(2)–C(9)	142.8(6)	C(1)–C(2)–Co(2)	70.6(4)
C(9)–C(2)–Co(2)	132.5(5)	C(1)–C(2)–Co(1)	70.5(4)
C(9)–C(2)–Co(1)	134.6(5)	Co(2)–C(2)–Co(1)	78.2(2)
C(4)–C(3)–C(8)	116.8(8)	C(4)–C(3)–C(1)	123.5(7)
C(8)–C(3)–C(1)	119.7(7)	C(3)–C(4)–C(5)	122.3(9)
C(6)–C(5)–C(4)	121.7(10)	C(5)–C(6)–C(7)	117.3(9)
C(6)–C(7)–C(8)	121.8(9)	C(3)–C(8)–C(7)	120.1(9)
O(1)–C(9)–C(2)	106.7(5)	O(1)–C(9)–C(10)	111.0(6)
C(2)–C(9)–C(10)	112.5(6)	C(9)–C(10)–C(11)	110.3(6)
C(12)–C(11)–C(10)	114.2(6)	C(16)–C(12)–C(14)	109.7(6)
C(16)–C(12)–C(11)	109.9(7)	C(14)–C(12)–C(11)	105.9(6)
C(16)–C(12)–C(13)	113.2(6)	C(14)–C(12)–C(13)	111.1(6)
C(11)–C(12)–C(13)	106.8(6)	O(1)–C(13)–C(18)	106.8(5)
O(1)–C(13)–C(12)	107.2(5)	C(18)–C(13)–C(12)	119.9(6)
C(9)–O(1)–C(13)	112.8(5)	O(2)–C(14)–O(3)	123.9(7)
O(2)–C(14)–C(12)	125.3(6)	O(3)–C(14)–C(12)	110.5(6)
C(14)–O(3)–C(15)	116.9(7)	O(4)–C(16)–O(4X)	127.5(17)
O(4)–C(16)–O(5X)	24.2(12)	O(4X)–C(16)–O(5X)	116.1(15)
O(4)–C(16)–O(5)	123.4(12)	O(4X)–C(16)–O(5)	17.3(17)
O(5X)–C(16)–O(5)	106.0(16)	O(4)–C(16)–C(12)	120.6(11)
O(4X)–C(16)–C(12)	109.5(15)	O(5X)–C(16)–C(12)	133.9(13)
O(5)–C(16)–C(12)	115.9(11)	C(16)–O(5)–C(17)	111.0(15)
C(16)–O(5X)–C(17X)	112.1(18)	C(23)–C(18)–C(19)	117.9(8)
C(23)–C(18)–C(13)	121.9(7)	C(19)–C(18)–C(13)	119.9(7)
C(20)–C(19)–C(18)	121.0(8)	C(19)–C(20)–C(21)	121.7(8)
C(20)–C(21)–C(22)	117.6(8)	C(20)–C(21)–C(24)	122.0(8)
C(22)–C(21)–C(24)	120.3(8)	C(23)–C(22)–C(21)	120.9(8)
C(18)–C(23)–C(22)	120.9(8)	O(25)–C(25)–Co(1)	178.7(6)
O(26)–C(26)–Co(1)	177.3(8)	O(27)–C(27)–Co(1)	177.1(6)
O(28)–C(28)–Co(2)	177.9(7)	O(29)–C(29)–Co(2)	177.7(7)
O(30)–C(30)–Co(2)	176.3(6)	C(31)–Cl(1)–C(31X)	32.4(10)
C(31)–Cl(1)–Cl(2X')	136.0(7)	C(31X)–Cl(1)–Cl(2X')	113.7(12)
Cl(1)–C(31)–Cl(2)	114.8(8)	Cl(1)–C(31X)–Cl(2X)	103.4(13)
C(31X)–Cl(2X)–Cl(1')	99.5(14)		

Symmetry operations for equivalent atoms
' −x+1,−y,−z

Table 4. Hydrogen coordinates and isotropic displacement parameters ($Å^2$) for sdrc13.

	x	y	z	U
H(4)	0.0862	0.9034	0.3489	0.139
H(5)	0.1474	1.0700	0.4776	0.144
H(6)	0.3166	1.1116	0.6168	0.072
H(7)	0.4136	0.9774	0.6331	0.114
H(8)	0.3522	0.8088	0.5056	0.090
H(9)	0.2769	0.5868	0.4158	0.042
H(10A)	0.5020	0.6867	0.3854	0.056
H(10B)	0.4697	0.6166	0.2656	0.056
H(11A)	0.6417	0.5540	0.3349	0.061
H(11B)	0.5475	0.5480	0.4273	0.061
H(13)	0.2923	0.4196	0.3917	0.044
H(15A)	0.8063	0.3388	0.4005	0.132
H(15B)	0.8410	0.2868	0.2863	0.132
H(15C)	0.6991	0.2252	0.3264	0.132
H(17A)	0.3945	0.2010	−0.0244	0.132
H(17B)	0.5520	0.2924	0.0169	0.132
H(17C)	0.4024	0.3230	−0.0060	0.132
H(17D)	0.4925	0.4270	−0.0245	0.083
H(17E)	0.3765	0.3294	−0.0054	0.083
H(17F)	0.5540	0.3435	0.0091	0.083
H(19)	0.1942	0.2477	0.3978	0.061
H(20)	0.0155	0.0836	0.3346	0.071
H(22)	−0.0475	0.1220	0.0654	0.058
H(23)	0.1304	0.2888	0.1297	0.054
H(24A)	−0.2536	−0.0138	0.1340	0.111
H(24B)	−0.1655	−0.0584	0.2023	0.111
H(24C)	−0.1269	−0.0701	0.0893	0.111
H(31A)	0.1769	−0.0810	0.1170	0.154
H(31B)	0.2408	0.0222	0.0870	0.154
H(31C)	0.3061	0.0174	0.1639	0.158
H(31D)	0.3089	0.0627	0.0717	0.158

Appendix IV. X-Ray crystallographic data for **321**

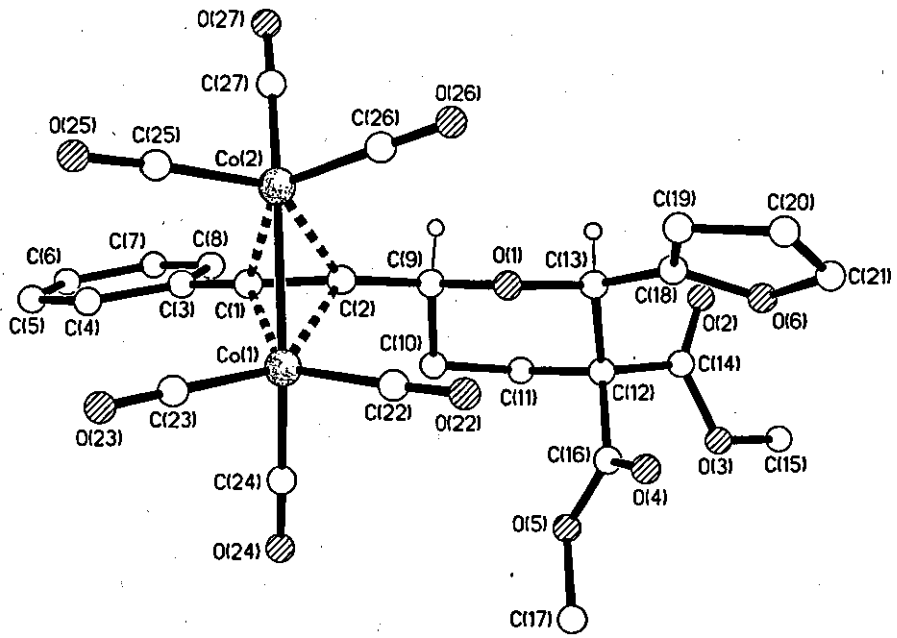


Table 1. Crystal data and structure refinement for sdrc15.

Identification code	sdrc15	
Chemical formula	$C_{27}H_{20}Co_2O_{12}$	
Formula weight	654.29	
Temperature	150(2) K	
Radiation, wavelength	MoK□, 0.71073 Å	
Crystal system, space group	triclinic, P $\bar{1}$	
Unit cell parameters	a = 8.0886(5) Å	□ = 106.534(2)°
	b = 11.7239(7) Å	□ = 102.796(2)°
	c = 15.7788(9) Å	□ = 91.966(2)°
Cell volume	1391.20(14) $Å^3$	
Z	2	
Calculated density	1.562 g/cm^3	
Absorption coefficient □	1.255 mm^{-1}	
F(000)	664	
Crystal colour and size	red, 0.53 × 0.34 × 0.15 mm^3	
Reflections for cell refinement	6766 (□ range 2.60 to 31.37°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	□ rotation with narrow frames	
□ range for data collection	1.82 to 31.85°	
Index ranges	h –11 to 11, k –16 to 16, l –22 to 22	
Completeness to □ = 27.50°	99.3 %	
Intensity decay	0%	
Reflections collected	16756	
Independent reflections	8572 (R_{int} = 0.0176)	
Reflections with F^2>2□	6949	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.556 and 0.834	
Structure solution	Patterson synthesis	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0377, 0.3533	
Data / restraints / parameters	8572 / 0 / 372	
Final R indices [F^2>2□]	R1 = 0.0313, wR2 = 0.0756	
R indices (all data)	R1 = 0.0426, wR2 = 0.0807	
Goodness-of-fit on F^2	1.041	
Largest and mean shift/su	0.001 and 0.000	
Largest diff. peak and hole	0.434 and –0.274 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for sdrc15. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Co(1)	0.17853(3)	0.613819(18)	0.359208(13)	0.02330(5)
Co(2)	0.47441(3)	0.711231(18)	0.412678(13)	0.02359(6)
C(1)	0.27912(18)	0.74700(13)	0.32769(10)	0.0222(3)
C(2)	0.33603(18)	0.64378(13)	0.28790(9)	0.0211(3)
C(3)	0.22940(19)	0.85987(13)	0.31261(10)	0.0249(3)
C(4)	0.1552(2)	0.93972(15)	0.37349(12)	0.0340(4)
C(5)	0.1116(3)	1.04751(16)	0.35829(15)	0.0484(5)
C(6)	0.1408(3)	1.07552(16)	0.28356(16)	0.0524(6)
C(7)	0.2156(3)	0.99785(17)	0.22349(15)	0.0461(5)
C(8)	0.2603(2)	0.89034(15)	0.23765(12)	0.0337(4)
C(9)	0.36664(18)	0.57198(12)	0.19950(9)	0.0203(3)
C(10)	0.20920(19)	0.55464(13)	0.12172(9)	0.0234(3)
C(11)	0.23765(18)	0.47094(13)	0.03367(9)	0.0215(3)
C(12)	0.29395(17)	0.35137(12)	0.04776(9)	0.0181(2)
C(13)	0.45313(17)	0.38334(12)	0.12891(9)	0.0188(2)
O(1)	0.41297(13)	0.45811(9)	0.20874(6)	0.02058(19)
C(14)	0.34120(17)	0.28497(12)	−0.04011(9)	0.0193(2)
O(2)	0.47038(14)	0.31016(10)	−0.05948(7)	0.0272(2)
O(3)	0.21763(14)	0.20272(10)	−0.09536(7)	0.0285(2)
C(15)	0.2406(2)	0.15080(16)	−0.18663(11)	0.0358(4)
C(16)	0.15326(18)	0.27764(14)	0.06620(10)	0.0228(3)
O(4)	0.17719(15)	0.20783(13)	0.10882(10)	0.0408(3)
O(5)	−0.00167(13)	0.30159(11)	0.02895(8)	0.0304(2)
C(17)	−0.1414(2)	0.2318(2)	0.04042(14)	0.0427(5)
C(18)	0.52692(18)	0.27966(13)	0.15444(9)	0.0211(3)
C(19)	0.6048(2)	0.26480(15)	0.23472(11)	0.0338(4)
C(20)	0.6509(2)	0.14538(16)	0.21504(11)	0.0349(4)
C(21)	0.5991(2)	0.09598(14)	0.12444(11)	0.0286(3)
O(6)	0.52275(13)	0.17734(9)	0.08480(7)	0.0236(2)
C(22)	0.2214(2)	0.46000(15)	0.35496(11)	0.0330(3)
O(22)	0.2525(2)	0.36643(11)	0.35316(10)	0.0510(4)
C(23)	0.1114(2)	0.66901(16)	0.46465(13)	0.0356(4)
O(23)	0.0693(2)	0.70113(14)	0.53089(10)	0.0553(4)
C(24)	−0.0278(2)	0.58860(16)	0.28227(13)	0.0363(4)
O(24)	−0.15888(18)	0.57394(15)	0.23409(11)	0.0564(4)
C(25)	0.4580(2)	0.80327(17)	0.52444(11)	0.0354(4)
O(25)	0.4394(2)	0.86360(16)	0.59099(9)	0.0583(4)
C(26)	0.5931(2)	0.58608(17)	0.42687(11)	0.0378(4)
O(26)	0.6674(2)	0.50741(14)	0.43219(10)	0.0596(5)
C(27)	0.6379(2)	0.80649(17)	0.39916(11)	0.0348(4)
O(27)	0.7388(2)	0.86880(16)	0.39044(10)	0.0602(4)

Table 3. Bond lengths [Å] and angles [°] for sdrc15.

Co(1)–C(24)	1.7919(19)	Co(1)–C(23)	1.8145(17)
Co(1)–C(22)	1.8333(17)	Co(1)–C(2)	1.9599(14)
Co(1)–C(1)	1.9701(14)	Co(1)–Co(2)	2.4725(3)
Co(2)–C(27)	1.7892(19)	Co(2)–C(26)	1.8203(18)
Co(2)–C(25)	1.8226(17)	Co(2)–C(2)	1.9574(14)
Co(2)–C(1)	1.9740(14)	C(1)–C(2)	1.343(2)
C(1)–C(3)	1.464(2)	C(2)–C(9)	1.4881(19)
C(3)–C(4)	1.393(2)	C(3)–C(8)	1.398(2)
C(4)–C(5)	1.394(2)	C(5)–C(6)	1.375(3)
C(6)–C(7)	1.377(3)	C(7)–C(8)	1.388(2)
C(9)–O(1)	1.4369(16)	C(9)–C(10)	1.5222(19)
C(10)–C(11)	1.5256(19)	C(11)–C(12)	1.5487(19)
C(12)–C(14)	1.5216(18)	C(12)–C(16)	1.5327(19)
C(12)–C(13)	1.5495(18)	C(13)–O(1)	1.4259(16)
C(13)–C(18)	1.4893(19)	C(14)–O(2)	1.2017(17)
C(14)–O(3)	1.3260(17)	O(3)–C(15)	1.4512(19)
C(16)–O(4)	1.1942(18)	C(16)–O(5)	1.3367(17)
O(5)–C(17)	1.4457(19)	C(18)–C(19)	1.346(2)
C(18)–O(6)	1.3704(17)	C(19)–C(20)	1.427(2)
C(20)–C(21)	1.342(2)	C(21)–O(6)	1.3753(18)
C(22)–O(22)	1.128(2)	C(23)–O(23)	1.137(2)
C(24)–O(24)	1.135(2)	C(25)–O(25)	1.131(2)
C(26)–O(26)	1.131(2)	C(27)–O(27)	1.133(2)

C(24)–Co(1)–C(23)	97.80(8)	C(24)–Co(1)–C(22)	100.95(8)
C(23)–Co(1)–C(22)	103.51(8)	C(24)–Co(1)–C(2)	104.47(7)
C(23)–Co(1)–C(2)	145.23(7)	C(22)–Co(1)–C(2)	98.11(7)
C(24)–Co(1)–C(1)	99.55(7)	C(23)–Co(1)–C(1)	110.55(7)
C(22)–Co(1)–C(1)	137.05(7)	C(2)–Co(1)–C(1)	39.97(6)
C(24)–Co(1)–Co(2)	150.22(6)	C(23)–Co(1)–Co(2)	98.52(6)
C(22)–Co(1)–Co(2)	99.22(6)	C(2)–Co(1)–Co(2)	50.82(4)
C(1)–Co(1)–Co(2)	51.25(4)	C(27)–Co(2)–C(26)	100.03(9)
C(27)–Co(2)–C(25)	97.18(8)	C(26)–Co(2)–C(25)	108.61(8)
C(27)–Co(2)–C(2)	102.59(7)	C(26)–Co(2)–C(2)	101.05(7)
C(25)–Co(2)–C(2)	140.64(7)	C(27)–Co(2)–C(1)	98.52(7)
C(26)–Co(2)–C(1)	139.91(7)	C(25)–Co(2)–C(1)	103.89(7)
C(2)–Co(2)–C(1)	39.95(6)	C(27)–Co(2)–Co(1)	148.81(6)
C(26)–Co(2)–Co(1)	101.22(6)	C(25)–Co(2)–Co(1)	97.37(6)
C(2)–Co(2)–Co(1)	50.91(4)	C(1)–Co(2)–Co(1)	51.11(4)
C(2)–C(1)–C(3)	142.12(14)	C(2)–C(1)–Co(1)	69.61(9)
C(3)–C(1)–Co(1)	137.71(11)	C(2)–C(1)–Co(2)	69.36(8)
C(3)–C(1)–Co(2)	131.57(10)	Co(1)–C(1)–Co(2)	77.64(5)
C(1)–C(2)–C(9)	142.12(13)	C(1)–C(2)–Co(2)	70.69(9)
C(9)–C(2)–Co(2)	135.73(10)	C(1)–C(2)–Co(1)	70.42(9)
C(9)–C(2)–Co(1)	131.91(10)	Co(2)–C(2)–Co(1)	78.27(5)
C(4)–C(3)–C(8)	119.03(15)	C(4)–C(3)–C(1)	120.90(14)
C(8)–C(3)–C(1)	120.05(14)	C(3)–C(4)–C(5)	119.72(18)
C(6)–C(5)–C(4)	120.57(19)	C(5)–C(6)–C(7)	120.20(17)

C(6)–C(7)–C(8)	120.03(19)	C(7)–C(8)–C(3)	120.45(18)
O(1)–C(9)–C(2)	107.64(10)	O(1)–C(9)–C(10)	110.20(11)
C(2)–C(9)–C(10)	111.54(11)	C(9)–C(10)–C(11)	110.62(11)
C(10)–C(11)–C(12)	110.68(11)	C(14)–C(12)–C(16)	110.98(11)
C(14)–C(12)–C(11)	104.87(10)	C(16)–C(12)–C(11)	112.66(11)
C(14)–C(12)–C(13)	110.53(10)	C(16)–C(12)–C(13)	110.72(11)
C(11)–C(12)–C(13)	106.87(11)	O(1)–C(13)–C(18)	106.01(10)
O(1)–C(13)–C(12)	110.33(10)	C(18)–C(13)–C(12)	115.42(11)
C(13)–O(1)–C(9)	112.57(10)	O(2)–C(14)–O(3)	124.15(13)
O(2)–C(14)–C(12)	123.63(12)	O(3)–C(14)–C(12)	112.03(11)
C(14)–O(3)–C(15)	114.99(12)	O(4)–C(16)–O(5)	123.60(13)
O(4)–C(16)–C(12)	124.89(13)	O(5)–C(16)–C(12)	111.50(12)
C(16)–O(5)–C(17)	114.70(13)	C(19)–C(18)–O(6)	110.23(13)
C(19)–C(18)–C(13)	132.82(13)	O(6)–C(18)–C(13)	116.92(11)
C(18)–C(19)–C(20)	106.52(14)	C(21)–C(20)–C(19)	106.81(14)
C(20)–C(21)–O(6)	110.07(14)	C(18)–O(6)–C(21)	106.36(11)
O(22)–C(22)–Co(1)	178.08(18)	O(23)–C(23)–Co(1)	178.50(17)
O(24)–C(24)–Co(1)	179.2(2)	O(25)–C(25)–Co(2)	175.51(17)
O(26)–C(26)–Co(2)	177.24(16)	O(27)–C(27)–Co(2)	178.36(19)

Table 4. Hydrogen coordinates and isotropic displacement parameters ($Å^2$) for sdrc15.

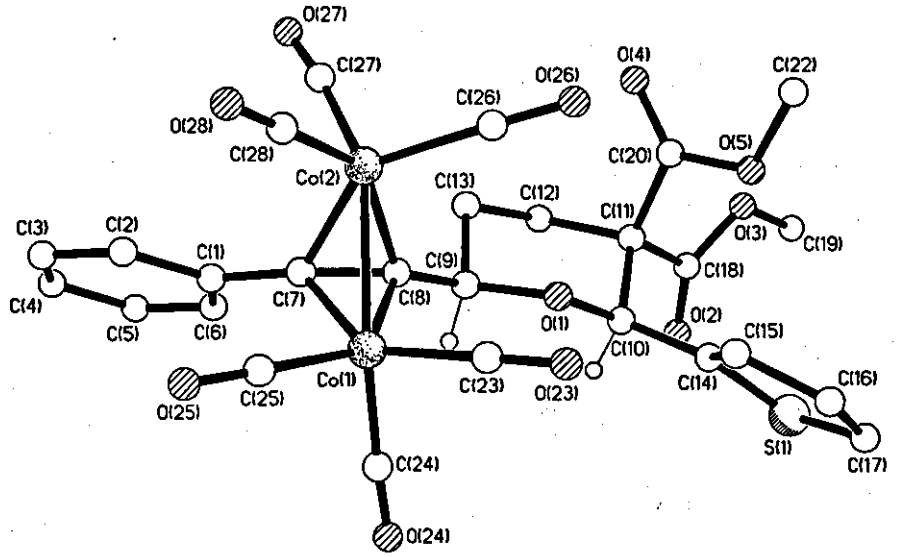
	x	y	z	U
H(4)	0.1344	0.9208	0.4251	0.041
H(5)	0.0614	1.1021	0.3999	0.058
H(6)	0.1091	1.1487	0.2734	0.063
H(7)	0.2367	1.0179	0.1723	0.055
H(8)	0.3122	0.8371	0.1961	0.040
H(9)	0.4633	0.6139	0.1863	0.024
H(10A)	0.1835	0.6331	0.1130	0.028
H(10B)	0.1102	0.5206	0.1372	0.028
H(11A)	0.3264	0.5098	0.0138	0.026
H(11B)	0.1308	0.4549	−0.0147	0.026
H(13)	0.5433	0.4286	0.1133	0.023
H(15A)	0.2379	0.2128	−0.2174	0.054
H(15B)	0.1487	0.0869	−0.2211	0.054
H(15C)	0.3506	0.1177	−0.1831	0.054
H(17A)	−0.1324	0.1465	0.0141	0.064
H(17B)	−0.2497	0.2528	0.0095	0.064
H(17C)	−0.1367	0.2489	0.1055	0.064
H(19)	0.6250	0.3225	0.2930	0.041
H(20)	0.7075	0.1080	0.2578	0.042
H(21)	0.6131	0.0164	0.0924	0.034

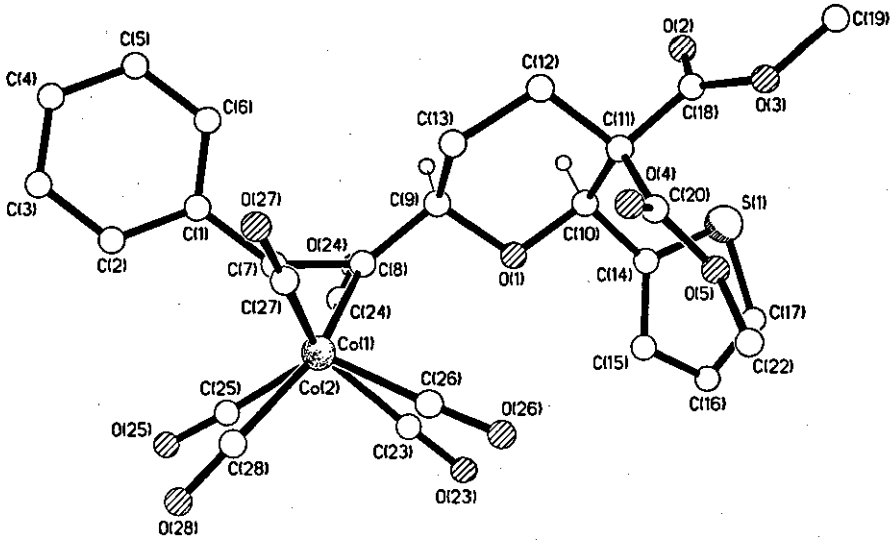
Table 5. Torsion angles [°] for sdrc15.

C(24)–Co(1)–Co(2)–C(27)	–2.28(17)	C(23)–Co(1)–Co(2)–C(27)	–124.83(13)
C(22)–Co(1)–Co(2)–C(27)	129.88(12)	C(2)–Co(1)–Co(2)–C(27)	36.89(12)
C(1)–Co(1)–Co(2)–C(27)	–15.26(12)	C(24)–Co(1)–Co(2)–C(26)	–134.38(13)
C(23)–Co(1)–Co(2)–C(26)	103.07(8)	C(22)–Co(1)–Co(2)–C(26)	–2.22(7)
C(2)–Co(1)–Co(2)–C(26)	–95.21(8)	C(1)–Co(1)–Co(2)–C(26)	–147.36(8)
C(24)–Co(1)–Co(2)–C(25)	114.92(13)	C(23)–Co(1)–Co(2)–C(25)	–7.64(8)
C(22)–Co(1)–Co(2)–C(25)	–112.93(8)	C(2)–Co(1)–Co(2)–C(25)	154.09(8)
C(1)–Co(1)–Co(2)–C(25)	101.93(8)	C(24)–Co(1)–Co(2)–C(2)	–39.17(13)
C(23)–Co(1)–Co(2)–C(2)	–161.72(8)	C(22)–Co(1)–Co(2)–C(2)	92.99(7)
C(1)–Co(1)–Co(2)–C(2)	–52.15(7)	C(24)–Co(1)–Co(2)–C(1)	12.98(13)
C(23)–Co(1)–Co(2)–C(1)	–109.57(8)	C(22)–Co(1)–Co(2)–C(1)	145.14(7)
C(2)–Co(1)–Co(2)–C(1)	52.15(7)	C(24)–Co(1)–C(1)–C(2)	–101.18(10)
C(23)–Co(1)–C(1)–C(2)	156.70(10)	C(22)–Co(1)–C(1)–C(2)	16.43(14)
Co(2)–Co(1)–C(1)–C(2)	72.33(8)	C(24)–Co(1)–C(1)–C(3)	46.26(17)
C(23)–Co(1)–C(1)–C(3)	–55.87(17)	C(22)–Co(1)–C(1)–C(3)	163.86(14)
C(2)–Co(1)–C(1)–C(3)	147.4(2)	Co(2)–Co(1)–C(1)–C(3)	–140.24(17)
C(24)–Co(1)–C(1)–Co(2)	–173.50(7)	C(23)–Co(1)–C(1)–Co(2)	84.37(8)
C(22)–Co(1)–C(1)–Co(2)	–55.90(11)	C(2)–Co(1)–C(1)–Co(2)	–72.33(8)
C(27)–Co(2)–C(1)–C(2)	99.46(10)	C(26)–Co(2)–C(1)–C(2)	–17.38(15)
C(25)–Co(2)–C(1)–C(2)	–160.91(10)	Co(1)–Co(2)–C(1)–C(2)	–72.62(8)
C(27)–Co(2)–C(1)–C(3)	–43.04(15)	C(26)–Co(2)–C(1)–C(3)	–159.88(15)
C(25)–Co(2)–C(1)–C(3)	56.60(16)	C(2)–Co(2)–C(1)–C(3)	–142.49(19)
Co(1)–Co(2)–C(1)–C(3)	144.88(16)	C(27)–Co(2)–C(1)–Co(1)	172.08(6)
C(26)–Co(2)–C(1)–Co(1)	55.24(12)	C(25)–Co(2)–C(1)–Co(1)	–88.29(7)
C(2)–Co(2)–C(1)–Co(1)	72.62(8)	C(3)–C(1)–C(2)–C(9)	–9.6(4)
Co(1)–C(1)–C(2)–C(9)	134.2(2)	Co(2)–C(1)–C(2)–C(9)	–141.7(2)
C(3)–C(1)–C(2)–Co(2)	132.1(2)	Co(1)–C(1)–C(2)–Co(2)	–84.03(4)
C(3)–C(1)–C(2)–Co(1)	–143.9(2)	Co(2)–C(1)–C(2)–Co(1)	84.03(4)
C(27)–Co(2)–C(2)–C(1)	–88.27(10)	C(26)–Co(2)–C(2)–C(1)	168.69(10)
C(25)–Co(2)–C(2)–C(1)	30.04(15)	Co(1)–Co(2)–C(2)–C(1)	73.15(8)
C(27)–Co(2)–C(2)–C(9)	58.72(16)	C(26)–Co(2)–C(2)–C(9)	–44.31(16)
C(25)–Co(2)–C(2)–C(9)	177.04(14)	C(1)–Co(2)–C(2)–C(9)	147.00(19)
Co(1)–Co(2)–C(2)–C(9)	–139.85(17)	C(27)–Co(2)–C(2)–Co(1)	–161.42(7)
C(26)–Co(2)–C(2)–Co(1)	95.54(7)	C(25)–Co(2)–C(2)–Co(1)	–43.11(12)
C(1)–Co(2)–C(2)–Co(1)	–73.15(8)	C(24)–Co(1)–C(2)–C(1)	87.64(10)
C(23)–Co(1)–C(2)–C(1)	–40.51(16)	C(22)–Co(1)–C(2)–C(1)	–168.77(10)
Co(2)–Co(1)–C(2)–C(1)	–73.46(8)	C(24)–Co(1)–C(2)–C(9)	–56.12(14)
C(23)–Co(1)–C(2)–C(9)	175.74(13)	C(22)–Co(1)–C(2)–C(9)	47.47(14)
C(1)–Co(1)–C(2)–C(9)	–143.75(17)	Co(2)–Co(1)–C(2)–C(9)	142.79(15)
C(24)–Co(1)–C(2)–Co(2)	161.10(7)	C(23)–Co(1)–C(2)–Co(2)	32.95(14)
C(22)–Co(1)–C(2)–Co(2)	–95.31(7)	C(1)–Co(1)–C(2)–Co(2)	73.46(8)
C(2)–C(1)–C(3)–C(4)	172.05(19)	Co(1)–C(1)–C(3)–C(4)	47.3(2)
Co(2)–C(1)–C(3)–C(4)	–76.07(19)	C(2)–C(1)–C(3)–C(8)	–9.7(3)
Co(1)–C(1)–C(3)–C(8)	–134.41(15)	Co(2)–C(1)–C(3)–C(8)	102.22(17)

C(8)–C(3)–C(4)–C(5)	0.6(2)	C(1)–C(3)–C(4)–C(5)	178.95(15)
C(3)–C(4)–C(5)–C(6)	0.2(3)	C(4)–C(5)–C(6)–C(7)	–0.9(3)
C(5)–C(6)–C(7)–C(8)	0.7(3)	C(6)–C(7)–C(8)–C(3)	0.2(3)
C(4)–C(3)–C(8)–C(7)	–0.8(2)	C(1)–C(3)–C(8)–C(7)	–179.15(15)
C(1)–C(2)–C(9)–O(1)	–172.76(19)	Co(2)–C(2)–C(9)–O(1)	64.08(17)
Co(1)–C(2)–C(9)–O(1)	–57.89(16)	C(1)–C(2)–C(9)–C(10)	–51.8(3)
Co(2)–C(2)–C(9)–C(10)	–174.92(11)	Co(1)–C(2)–C(9)–C(10)	63.11(16)
O(1)–C(9)–C(10)–C(11)	–55.01(15)	C(2)–C(9)–C(10)–C(11)	–174.51(12)
C(9)–C(10)–C(11)–C(12)	54.14(15)	C(10)–C(11)–C(12)–C(14)	
–172.32(11)			
C(10)–C(11)–C(12)–C(16)	66.87(15)	C(10)–C(11)–C(12)–C(13)	
–54.95(14)			
C(14)–C(12)–C(13)–O(1)	172.84(10)	C(16)–C(12)–C(13)–O(1)	–63.77(14)
C(11)–C(12)–C(13)–O(1)	59.26(13)	C(14)–C(12)–C(13)–C(18)	
–67.04(14)			
C(16)–C(12)–C(13)–C(18)	56.36(15)	C(11)–C(12)–C(13)–C(18)	179.39(11)
C(18)–C(13)–O(1)–C(9)	170.30(11)	C(12)–C(13)–O(1)–C(9)	–64.07(14)
C(2)–C(9)–O(1)–C(13)	–177.31(11)	C(10)–C(9)–O(1)–C(13)	60.85(14)
C(16)–C(12)–C(14)–O(2)	–163.02(13)	C(11)–C(12)–C(14)–O(2)	75.06(16)
C(13)–C(12)–C(14)–O(2)	–39.78(18)	C(16)–C(12)–C(14)–O(3)	21.83(15)
C(11)–C(12)–C(14)–O(3)	–100.09(13)	C(13)–C(12)–C(14)–O(3)	145.07(12)
O(2)–C(14)–O(3)–C(15)	–5.6(2)	C(12)–C(14)–O(3)–C(15)	169.49(12)
C(14)–C(12)–C(16)–O(4)	90.20(18)	C(11)–C(12)–C(16)–O(4)	
–152.55(16)			
C(13)–C(12)–C(16)–O(4)	–32.9(2)	C(14)–C(12)–C(16)–O(5)	–90.23(14)
C(11)–C(12)–C(16)–O(5)	27.02(16)	C(13)–C(12)–C(16)–O(5)	146.63(12)
O(4)–C(16)–O(5)–C(17)	–2.8(2)	C(12)–C(16)–O(5)–C(17)	177.67(14)
O(1)–C(13)–C(18)–C(19)	–23.7(2)	C(12)–C(13)–C(18)–C(19)	
–146.12(17)			
O(1)–C(13)–C(18)–O(6)	158.54(11)	C(12)–C(13)–C(18)–O(6)	36.08(17)
O(6)–C(18)–C(19)–C(20)	–0.7(2)	C(13)–C(18)–C(19)–C(20)	
–178.65(15)			
C(18)–C(19)–C(20)–C(21)	0.3(2)	C(19)–C(20)–C(21)–O(6)	0.2(2)
C(19)–C(18)–O(6)–C(21)	0.89(17)	C(13)–C(18)–O(6)–C(21)	179.17(12)
C(20)–C(21)–O(6)–C(18)	–0.69(18)		

Appendix V. X-Ray crystallographic data for **322**





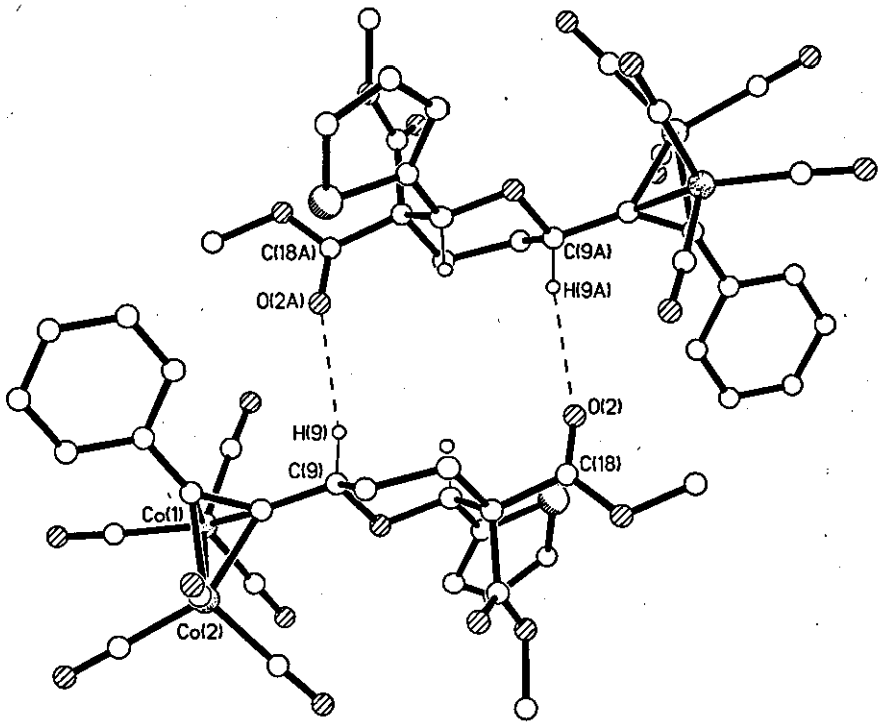

C(18A)
O(2A)
C(9A)
H(9A)
O(2)
H(9)
C(9)
C(18)
Co(1)
Co(2)

Table 1. Crystal data and structure refinement for sdrc17.

Identification code	sdrc17	
Chemical formula	$C_{27}H_{20}Co_2O_{11}S$	
Formula weight	670.35	
Temperature	150(2) K	
Radiation, wavelength	MoK□, 0.71073 Å	
Crystal system, space group	triclinic, P $\bar{1}$	
Unit cell parameters	a = 8.6480(5) Å	□ = 107.2871(9)°
	b = 12.0683(7) Å	□ = 93.7267(9)°
	c = 14.2184(9) Å	□ = 91.7003(9)°
Cell volume	1412.03(15) $Å^3$	
Z	2	
Calculated density	1.577 g/cm^3	
Absorption coefficient □	1.308 mm^{-1}	
F(000)	680	
Crystal colour and size	red, 0.30 × 0.19 × 0.13 mm^3	
Reflections for cell refinement	6351 (□ range 2.64 to 30.44°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	□ rotation with narrow frames	
□ range for data collection	1.77 to 30.55°	
Index ranges	h –12 to 12, k –17 to 17, l –20 to 20	
Completeness to □ = 30.55°	98.0 %	
Intensity decay	0%	
Reflections collected	17036	
Independent reflections	8495 (R_{int} = 0.0202)	
Reflections with F^2>2□	7011	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.695 and 0.848	
Structure solution	Patterson synthesis	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0420, 0.3069	
Data / restraints / parameters	8495 / 0 / 372	
Final R indices [F^2>2□]	R1 = 0.0323, wR2 = 0.0795	
R indices (all data)	R1 = 0.0421, wR2 = 0.0844	
Goodness-of-fit on F^2	1.033	
Largest and mean shift/su	0.001 and 0.000	
Largest diff. peak and hole	0.486 and –0.335 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters ($Å^2$) for sdrc17. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Co(1)	0.16466(2)	0.234436(18)	0.118997(16)	0.02303(6)
Co(2)	0.41626(2)	0.345909(18)	0.142359(15)	0.02164(6)
C(1)	0.41163(17)	0.16957(12)	0.26733(11)	0.0200(3)
C(2)	0.5085(2)	0.08543(14)	0.21633(13)	0.0278(3)
C(3)	0.5828(2)	0.01388(15)	0.26315(14)	0.0325(4)
C(4)	0.5613(2)	0.02538(16)	0.36107(14)	0.0317(4)
C(5)	0.4648(2)	0.10772(15)	0.41215(13)	0.0300(3)
C(6)	0.38942(19)	0.17957(14)	0.36588(12)	0.0251(3)
C(7)	0.33753(17)	0.24833(13)	0.21946(11)	0.0206(3)
C(8)	0.26303(17)	0.34775(13)	0.23819(11)	0.0201(3)
C(9)	0.20046(17)	0.43849(13)	0.31996(11)	0.0200(3)
O(1)	0.10272(12)	0.50731(9)	0.27644(8)	0.0195(2)
C(10)	0.02053(17)	0.58645(12)	0.34897(11)	0.0188(3)
C(11)	0.13943(17)	0.68063(13)	0.41789(11)	0.0195(3)
C(12)	0.25630(19)	0.61570(13)	0.46705(11)	0.0236(3)
C(13)	0.32727(18)	0.51655(13)	0.39051(12)	0.0239(3)
C(14)	−0.10810(17)	0.62837(13)	0.29409(11)	0.0205(3)
C(15)	−0.12427(18)	0.61106(15)	0.19367(12)	0.0261(3)
C(16)	−0.2629(2)	0.65932(17)	0.16595(14)	0.0336(4)
C(17)	−0.34678(19)	0.70965(15)	0.24306(14)	0.0307(4)
S(1)	−0.26108(5)	0.70033(4)	0.35192(3)	0.02860(9)
C(18)	0.05428(18)	0.75948(13)	0.50096(11)	0.0225(3)
O(2)	−0.03925(16)	0.72306(11)	0.54469(9)	0.0338(3)
O(3)	0.09905(14)	0.87098(9)	0.52055(8)	0.0269(2)
C(19)	0.0246(2)	0.95077(15)	0.60021(13)	0.0349(4)
C(20)	0.22509(18)	0.74970(13)	0.36085(11)	0.0212(3)
O(4)	0.36367(13)	0.76081(11)	0.36274(9)	0.0307(3)
O(5)	0.12680(13)	0.79480(10)	0.30762(9)	0.0255(2)
C(22)	0.1955(2)	0.85074(16)	0.24223(13)	0.0318(4)
C(23)	0.0562(2)	0.31838(17)	0.05260(13)	0.0324(4)
O(23)	−0.01282(19)	0.37067(15)	0.01249(12)	0.0515(4)
C(24)	0.0033(2)	0.19288(18)	0.17604(14)	0.0363(4)
O(24)	−0.10024(19)	0.17162(18)	0.21355(13)	0.0619(5)
C(25)	0.2060(2)	0.09870(19)	0.02972(17)	0.0465(5)
O(25)	0.2355(2)	0.01209(17)	−0.02219(17)	0.0857(7)
C(26)	0.3652(2)	0.47921(15)	0.11388(13)	0.0296(3)
O(26)	0.33059(18)	0.56177(12)	0.09795(12)	0.0451(4)
C(27)	0.5929(2)	0.38544(15)	0.22150(14)	0.0311(4)
O(27)	0.70039(17)	0.40095(13)	0.27442(13)	0.0490(4)
C(28)	0.4991(2)	0.25532(16)	0.03364(14)	0.0332(4)
O(28)	0.5497(2)	0.19772(14)	−0.03455(12)	0.0554(4)

Table 3. Bond lengths [Å] and angles [°] for sdrc17.

Co(1)–C(24)	1.790(2)	Co(1)–C(25)	1.811(2)
Co(1)–C(23)	1.8185(18)	Co(1)–C(8)	1.9575(15)
Co(1)–C(7)	1.9669(15)	Co(1)–Co(2)	2.4741(3)
Co(2)–C(27)	1.8008(19)	Co(2)–C(28)	1.8121(18)
Co(2)–C(26)	1.8312(17)	Co(2)–C(8)	1.9574(15)
Co(2)–C(7)	1.9670(15)	C(1)–C(2)	1.396(2)
C(1)–C(6)	1.397(2)	C(1)–C(7)	1.463(2)
C(2)–C(3)	1.386(2)	C(3)–C(4)	1.383(3)
C(4)–C(5)	1.382(3)	C(5)–C(6)	1.388(2)
C(7)–C(8)	1.343(2)	C(8)–C(9)	1.485(2)
C(9)–O(1)	1.4375(17)	C(9)–C(13)	1.527(2)
O(1)–C(10)	1.4252(16)	C(10)–C(14)	1.503(2)
C(10)–C(11)	1.564(2)	C(11)–C(18)	1.526(2)
C(11)–C(20)	1.531(2)	C(11)–C(12)	1.551(2)
C(12)–C(13)	1.533(2)	C(14)–C(15)	1.377(2)
C(14)–S(1)	1.7221(15)	C(15)–C(16)	1.431(2)
C(16)–C(17)	1.353(2)	C(17)–S(1)	1.7079(18)
C(18)–O(2)	1.200(2)	C(18)–O(3)	1.3306(19)
O(3)–C(19)	1.4520(19)	C(20)–O(4)	1.1997(19)
C(20)–O(5)	1.3342(19)	O(5)–C(22)	1.4472(19)
C(23)–O(23)	1.128(2)	C(24)–O(24)	1.132(2)
C(25)–O(25)	1.133(3)	C(26)–O(26)	1.130(2)
C(27)–O(27)	1.131(2)	C(28)–O(28)	1.135(2)

C(24)–Co(1)–C(25)	102.43(10)	C(24)–Co(1)–C(23)	96.31(8)
C(25)–Co(1)–C(23)	107.41(10)	C(24)–Co(1)–C(8)	96.51(8)
C(25)–Co(1)–C(8)	139.32(8)	C(23)–Co(1)–C(8)	105.83(7)
C(24)–Co(1)–C(7)	102.46(7)	C(25)–Co(1)–C(7)	100.25(8)
C(23)–Co(1)–C(7)	142.18(7)	C(8)–Co(1)–C(7)	40.03(6)
C(24)–Co(1)–Co(2)	146.97(6)	C(25)–Co(1)–Co(2)	101.79(7)
C(23)–Co(1)–Co(2)	97.51(6)	C(8)–Co(1)–Co(2)	50.80(4)
C(7)–Co(1)–Co(2)	51.03(4)	C(27)–Co(2)–C(28)	97.77(9)
C(27)–Co(2)–C(26)	104.72(8)	C(28)–Co(2)–C(26)	106.02(8)
C(27)–Co(2)–C(8)	101.49(7)	C(28)–Co(2)–C(8)	143.93(8)
C(26)–Co(2)–C(8)	98.20(7)	C(27)–Co(2)–C(7)	92.04(7)
C(28)–Co(2)–C(7)	109.61(7)	C(26)–Co(2)–C(7)	137.91(7)
C(8)–Co(2)–C(7)	40.03(6)	C(27)–Co(2)–Co(1)	143.03(6)
C(28)–Co(2)–Co(1)	96.99(6)	C(26)–Co(2)–Co(1)	103.43(6)
C(8)–Co(2)–Co(1)	50.81(4)	C(7)–Co(2)–Co(1)	51.03(4)
C(2)–C(1)–C(6)	118.97(14)	C(2)–C(1)–C(7)	120.75(14)
C(6)–C(1)–C(7)	120.25(14)	C(3)–C(2)–C(1)	120.50(16)
C(4)–C(3)–C(2)	120.03(16)	C(5)–C(4)–C(3)	120.03(16)
C(4)–C(5)–C(6)	120.39(16)	C(5)–C(6)–C(1)	120.07(15)
C(8)–C(7)–C(1)	142.69(14)	C(8)–C(7)–Co(1)	69.61(9)
C(1)–C(7)–Co(1)	135.53(11)	C(8)–C(7)–Co(2)	69.60(9)
C(1)–C(7)–Co(2)	133.04(11)	Co(1)–C(7)–Co(2)	77.94(6)
C(7)–C(8)–C(9)	141.90(14)	C(7)–C(8)–Co(2)	70.37(9)
C(9)–C(8)–Co(2)	135.31(11)	C(7)–C(8)–Co(1)	70.36(9)

C(9)–C(8)–Co(1)	132.77(11)	Co(2)–C(8)–Co(1)	78.39(6)
O(1)–C(9)–C(8)	107.59(12)	O(1)–C(9)–C(13)	109.81(12)
C(8)–C(9)–C(13)	112.97(12)	C(10)–O(1)–C(9)	111.36(11)
O(1)–C(10)–C(14)	106.72(11)	O(1)–C(10)–C(11)	108.57(11)
C(14)–C(10)–C(11)	117.13(12)	C(18)–C(11)–C(20)	111.91(12)
C(18)–C(11)–C(12)	106.61(12)	C(20)–C(11)–C(12)	110.24(12)
C(18)–C(11)–C(10)	108.80(12)	C(20)–C(11)–C(10)	112.13(12)
C(12)–C(11)–C(10)	106.87(12)	C(13)–C(12)–C(11)	111.88(12)
C(9)–C(13)–C(12)	110.65(13)	C(15)–C(14)–C(10)	125.96(13)
C(15)–C(14)–S(1)	111.54(11)	C(10)–C(14)–S(1)	122.44(11)
C(14)–C(15)–C(16)	111.16(15)	C(17)–C(16)–C(15)	113.54(16)
C(16)–C(17)–S(1)	111.66(13)	C(17)–S(1)–C(14)	92.09(8)
O(2)–C(18)–O(3)	124.62(14)	O(2)–C(18)–C(11)	122.91(14)
O(3)–C(18)–C(11)	112.44(13)	C(18)–O(3)–C(19)	115.35(13)
O(4)–C(20)–O(5)	124.03(15)	O(4)–C(20)–C(11)	124.21(15)
O(5)–C(20)–C(11)	111.75(13)	C(20)–O(5)–C(22)	116.23(13)
O(23)–C(23)–Co(1)	178.88(17)	O(24)–C(24)–Co(1)	177.0(2)
O(25)–C(25)–Co(1)	176.4(2)	O(26)–C(26)–Co(2)	178.18(17)
O(27)–C(27)–Co(2)	173.07(16)	O(28)–C(28)–Co(2)	179.26(19)

Table 4. Hydrogen coordinates and isotropic displacement parameters ($Å^2$) for sdrc17.

	x	y	z	U
H(2)	0.5235	0.0772	0.1490	0.033
H(3)	0.6486	–0.0431	0.2280	0.039
H(4)	0.6128	–0.0233	0.3932	0.038
H(5)	0.4499	0.1152	0.4793	0.036
H(6)	0.3227	0.2356	0.4013	0.030
H(9)	0.1359	0.3998	0.3582	0.024
H(10)	–0.0274	0.5423	0.3900	0.023
H(12A)	0.3403	0.6714	0.5056	0.028
H(12B)	0.2026	0.5837	0.5134	0.028
H(13A)	0.3982	0.5493	0.3525	0.029
H(13B)	0.3885	0.4700	0.4247	0.029
H(15)	–0.0527	0.5722	0.1487	0.031
H(16)	–0.2932	0.6563	0.0998	0.040
H(17)	–0.4416	0.7457	0.2374	0.037
H(19A)	–0.0880	0.9435	0.5847	0.052
H(19B)	0.0623	1.0306	0.6078	0.052
H(19C)	0.0492	0.9321	0.6619	0.052
H(22A)	0.2617	0.9181	0.2813	0.048
H(22B)	0.1132	0.8764	0.2040	0.048
H(22C)	0.2581	0.7956	0.1971	0.048

Table 5. Torsion angles [°] for sdrc17.

C(24)–Co(1)–Co(2)–C(27)	39.38(16)	C(25)–Co(1)–Co(2)–C(27)	–97.02(13)
C(23)–Co(1)–Co(2)–C(27)	153.36(11)	C(8)–Co(1)–Co(2)–C(27)	49.03(11)
C(7)–Co(1)–Co(2)–C(27)	–3.29(11)	C(24)–Co(1)–Co(2)–C(28)	152.29(13)
C(25)–Co(1)–Co(2)–C(28)	15.89(10)	C(23)–Co(1)–Co(2)–C(28)	–93.73(8)
C(8)–Co(1)–Co(2)–C(28)	161.94(8)	C(7)–Co(1)–Co(2)–C(28)	109.62(8)
C(24)–Co(1)–Co(2)–C(26)	–99.33(13)	C(25)–Co(1)–Co(2)–C(26)	124.26(10)
C(23)–Co(1)–Co(2)–C(26)	14.64(8)	C(8)–Co(1)–Co(2)–C(26)	–89.69(8)
C(7)–Co(1)–Co(2)–C(26)	–142.01(8)	C(24)–Co(1)–Co(2)–C(8)	–9.65(13)
C(25)–Co(1)–Co(2)–C(8)	–146.05(10)	C(23)–Co(1)–Co(2)–C(8)	104.33(8)
C(7)–Co(1)–Co(2)–C(8)	–52.32(8)	C(24)–Co(1)–Co(2)–C(7)	42.68(13)
C(25)–Co(1)–Co(2)–C(7)	–93.73(10)	C(23)–Co(1)–Co(2)–C(7)	156.65(8)
C(8)–Co(1)–Co(2)–C(7)	52.32(8)	C(6)–C(1)–C(2)–C(3)	–0.8(3)
C(7)–C(1)–C(2)–C(3)	177.64(16)	C(1)–C(2)–C(3)–C(4)	0.1(3)
C(2)–C(3)–C(4)–C(5)	0.4(3)	C(3)–C(4)–C(5)–C(6)	–0.2(3)
C(4)–C(5)–C(6)–C(1)	–0.5(3)	C(2)–C(1)–C(6)–C(5)	0.9(2)
C(7)–C(1)–C(6)–C(5)	–177.46(15)	C(2)–C(1)–C(7)–C(8)	–164.9(2)
C(6)–C(1)–C(7)–C(8)	13.4(3)	C(2)–C(1)–C(7)–Co(1)	74.0(2)
C(6)–C(1)–C(7)–Co(1)	–107.62(17)	C(2)–C(1)–C(7)–Co(2)	–48.9(2)
C(6)–C(1)–C(7)–Co(2)	129.47(15)	C(24)–Co(1)–C(7)–C(8)	–85.27(11)
C(25)–Co(1)–C(7)–C(8)	169.43(12)	C(23)–Co(1)–C(7)–C(8)	32.64(16)
Co(2)–Co(1)–C(7)–C(8)	72.49(9)	C(24)–Co(1)–C(7)–C(1)	61.10(17)
C(25)–Co(1)–C(7)–C(1)	–44.21(18)	C(23)–Co(1)–C(7)–C(1)	179.01(14)
C(8)–Co(1)–C(7)–C(1)	146.4(2)	Co(2)–Co(1)–C(7)–C(1)	–141.14(18)
C(24)–Co(1)–C(7)–Co(2)	–157.77(7)	C(25)–Co(1)–C(7)–Co(2)	96.93(9)
C(23)–Co(1)–C(7)–Co(2)	–39.85(13)	C(8)–Co(1)–C(7)–Co(2)	–72.49(9)
C(27)–Co(2)–C(7)–C(8)	105.52(10)	C(28)–Co(2)–C(7)–C(8)	–155.49(10)
C(26)–Co(2)–C(7)–C(8)	–9.24(14)	Co(1)–Co(2)–C(7)–C(8)	–72.50(9)
C(27)–Co(2)–C(7)–C(1)	–38.96(16)	C(28)–Co(2)–C(7)–C(1)	60.04(16)
C(26)–Co(2)–C(7)–C(1)	–153.71(14)	C(8)–Co(2)–C(7)–C(1)	–144.47(19)
Co(1)–Co(2)–C(7)–C(1)	143.03(17)	C(27)–Co(2)–C(7)–Co(1)	178.02(7)
C(28)–Co(2)–C(7)–Co(1)	–82.99(8)	C(26)–Co(2)–C(7)–Co(1)	63.26(11)
C(8)–Co(2)–C(7)–Co(1)	72.50(9)	C(1)–C(7)–C(8)–C(9)	–4.7(4)
Co(1)–C(7)–C(8)–C(9)	135.5(2)	Co(2)–C(7)–C(8)–C(9)	–140.2(2)
C(1)–C(7)–C(8)–Co(2)	135.5(2)	Co(1)–C(7)–C(8)–Co(2)	–84.28(5)
C(1)–C(7)–C(8)–Co(1)	–140.2(2)	Co(2)–C(7)–C(8)–Co(1)	84.28(5)
C(27)–Co(2)–C(8)–C(7)	–79.31(10)	C(28)–Co(2)–C(8)–C(7)	41.58(16)
C(26)–Co(2)–C(8)–C(7)	173.76(10)	Co(1)–Co(2)–C(8)–C(7)	73.08(9)
C(27)–Co(2)–C(8)–C(9)	66.53(16)	C(28)–Co(2)–C(8)–C(9)	–172.58(14)
C(26)–Co(2)–C(8)–C(9)	–40.41(16)	C(7)–Co(2)–C(8)–C(9)	145.8(2)
Co(1)–Co(2)–C(8)–C(9)	–141.08(17)	C(27)–Co(2)–C(8)–Co(1)	–152.39(6)
C(28)–Co(2)–C(8)–Co(1)	–31.51(14)	C(26)–Co(2)–C(8)–Co(1)	100.67(7)
C(7)–Co(2)–C(8)–Co(1)	–73.08(9)	C(24)–Co(1)–C(8)–C(7)	101.63(11)
C(25)–Co(1)–C(8)–C(7)	–16.08(18)	C(23)–Co(1)–C(8)–C(7)	–159.89(10)
Co(2)–Co(1)–C(8)–C(7)	–73.09(9)	C(24)–Co(1)–C(8)–C(9)	–42.28(16)
C(25)–Co(1)–C(8)–C(9)	–159.99(17)	C(23)–Co(1)–C(8)–C(9)	56.20(16)

C(7)–Co(1)–C(8)–C(9)	−143.91(19)	Co(2)–Co(1)–C(8)–C(9)	143.00(17)
C(24)–Co(1)–C(8)–Co(2)	174.73(7)	C(25)–Co(1)–C(8)–Co(2)	57.01(15)
C(23)–Co(1)–C(8)–Co(2)	−86.80(7)	C(7)–Co(1)–C(8)–Co(2)	73.09(9)
C(7)–C(8)–C(9)–O(1)	−167.11(19)	Co(2)–C(8)–C(9)–O(1)	71.89(18)
Co(1)–C(8)–C(9)–O(1)	−51.15(18)	C(7)–C(8)–C(9)–C(13)	71.5(3)
Co(2)–C(8)–C(9)–C(13)	−49.5(2)	Co(1)–C(8)–C(9)–C(13)	−172.52(11)
C(8)–C(9)–O(1)–C(10)	171.88(12)	C(13)–C(9)–O(1)–C(10)	−64.80(15)
C(9)–O(1)–C(10)–C(14)	−164.37(11)	C(9)–O(1)–C(10)–C(11)	68.53(14)
O(1)–C(10)–C(11)–C(18)	−175.20(11)	C(14)–C(10)–C(11)–C(18)	63.92(16)
O(1)–C(10)–C(11)–C(20)	60.46(15)	C(14)–C(10)–C(11)–C(20)	−60.41(16)
O(1)–C(10)–C(11)–C(12)	−60.45(14)	C(14)–C(10)–C(11)–C(12)	178.68(12)
C(18)–C(11)–C(12)–C(13)	168.95(13)	C(20)–C(11)–C(12)–C(13)	−69.38(16)
C(10)–C(11)–C(12)–C(13)	52.73(16)	O(1)–C(9)–C(13)–C(12)	54.22(16)
C(8)–C(9)–C(13)–C(12)	174.32(13)	C(11)–C(12)–C(13)–C(9)	−50.70(17)
O(1)–C(10)–C(14)–C(15)	−11.3(2)	C(11)–C(10)–C(14)–C(15)	110.55(17)
O(1)–C(10)–C(14)–S(1)	165.65(10)	C(11)–C(10)–C(14)–S(1)	−72.50(16)
C(10)–C(14)–C(15)–C(16)	178.02(15)	S(1)–C(14)–C(15)–C(16)	0.80(19)
C(14)–C(15)–C(16)–C(17)	−0.5(2)	C(15)–C(16)–C(17)–S(1)	−0.1(2)
C(16)–C(17)–S(1)–C(14)	0.44(15)	C(15)–C(14)–S(1)–C(17)	−0.72(13)
C(10)–C(14)–S(1)–C(17)	−178.06(13)	C(20)–C(11)–C(18)–O(2)	167.97(15)
C(12)–C(11)–C(18)–O(2)	−71.43(19)	C(10)–C(11)–C(18)–O(2)	43.5(2)
C(20)–C(11)–C(18)–O(3)	−13.90(18)	C(12)–C(11)–C(18)–O(3)	106.70(14)
C(10)–C(11)–C(18)–O(3)	−138.37(13)	O(2)–C(18)–O(3)–C(19)	−0.8(2)
C(11)–C(18)–O(3)–C(19)	−178.93(13)	C(18)–C(11)–C(20)–O(4)	111.52(17)
C(12)–C(11)–C(20)–O(4)	−6.9(2)	C(10)–C(11)–C(20)–O(4)	−125.89(16)
C(18)–C(11)–C(20)–O(5)	−69.34(16)	C(12)–C(11)–C(20)–O(5)	172.20(12)
C(10)–C(11)–C(20)–O(5)	53.25(16)	O(4)–C(20)–O(5)–C(22)	5.9(2)
C(11)–C(20)–O(5)–C(22)	−173.29(13)		