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Enabling the rearrangement of unactivated allenes to 1,3-dienes by use of a Pd⁰ / boric acid system

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Abstract: A redox neutral rearrangement of an allene to a 1,3-diene by means of a unique palladium hydride complex is reported. The palladium hydride complex is generated from a simple Pd⁰ source and boric acid (B(OH)₃), which is typically identified as a waste by-product of the Suzuki-Miyaura reaction. A mechanism for this transformation, using this novel palladium hydride complex is presented; and using direct sample loop and flow injection ESI-HR-MS analysis we have detected and identified key π -allylpalladium complexes, that support the addition of the palladium hydride complex to the allene.

Key words Allene, 1,3-diene, palladium, boric acid, palladium-hydride

INTRODUCTION

1,3-Dienes are prominent and ubiquitous motifs in natural products, biosynthetic metabolites, potential drug targets and functional molecules.¹ It is core within polyketide antibiotics such as callistatin A (**1**),^{2a} the EPA oxidation anti-inflammatory metabolite resolvin E1 (**3**),^{2b} as well as anticancer agents such as maytansine (**2**)^{2c} which is currently used within antibody drug conjugates ado-trastuzumab emtansine marketed by Genetech and ImmunoGen under the name Herceptin® (figure 1).

Figure 1. Representative natural products, metabolites and marketed drugs that contain 1,3-dienes.

Importantly, they have proven value as flexible intermediates in complex target synthesis.³ The success of staple reactions such as [4+2]-cycloadditions (e.g. Diels Alder reaction,^{1b} ¹O₂ addition,⁴ etc.) are predicated on convenient routes to suitably functionalized 1,3-dienes. Additionally, a number of high profile transition metal transformations using 1,3-diene have been

recently reported that also highlight the need to access these substrates.⁵

The isomerization of an unactivated allene (**4**) to a 1,3-diene (**5**) represents a redox neutral, atom efficient process, where the overall oxidation state of the starting material and product remain unchanged (scheme 1). Similarly, the rearrangement of an unactivated alkyne (**6**) to a 1,3-diene (**5**) also can be seen as a redox neutral process. Yet, although unactivated alkynes have been shown to undergo this arrangement,⁶ often facilitated by a transition metal, synthetically useful examples of unactivated allenes undergoing this transformation are far scarcer within the literature.

allene - 1,3-diene - alkyne relationship

Scheme 1. Rearrangement of unactivated alkynes and allenes to 1,3-dienes.

To date this rearrangement has been accomplished under thermal, acidic and metal mediated reaction conditions. In the 1960s and 70s cyclopropyl derived allenes were shown to experience thermal rearrangement; while in the late 1980s, allenic system were shown to give cyclopentyl dienes under high temperature.⁷ Acidic conditions, using both mineral acids and organic Brønsted acids, have also been employed; however, the substrate scope for these processes has been limited and often biased toward more electron rich allenyl substrates.⁸

More recently, metal mediated processes, using complexes of palladium and gold, have found prominence (scheme 2).⁹ Following on from initial reports by Tsuji in the 1980s, Yamamoto in 1998 described the use of a palladium hydride complex derived from Pd⁰ and acetic acid, H-Pd^{II}-OAc, to affect this rearrangement, although yields were modest, substrate scope limited and the reaction was complicated by a competing hydroalkoxylation pathway.¹⁰ In 2012 Liu successfully developed a Au^I / PhNO system to efficiently transform a range of allenyl substrates to their 1,3-diene products; while Widenhoefer in 2014 was able to crystallize a Au^I- π -1,3-diene complex derived from the reaction of an allene and a Au^I complex.¹¹

Scheme 2. Rearrangement of un-activated alkynes and allenes to 1,3-dienes.

Recently, the authors herein, described a direct conversion of propargyl alcohols and aryl/heteroarylboronic acids into 1,3-dienes.¹² This process was expedited by way of a distinctive, and as yet unreported, palladium hydride complex ($\text{H-Pd}^{\text{II}}\text{-OB(OH)}_2$) that derives from Pd^0 and the by-product of the base free Suzuki-Miyaura reaction, boric acid (B(OH)_3). Boric acid is rarely considered as a functional element within catalytic reactions, and there is surprisingly little within the literature describing the use of boric acid as a reagent. This is remarkable given it is ubiquitous as a by-product in many classical metal catalysed process, such as the Suzuki-Miyaura reaction. An exception to this is the work of Watson and co-workers who identified boric acid's key role within the Cham-Lam amination reaction.¹³

Therefore, herein, we describe the direct conversion of an allene to its 1,3-diene (scheme 2, **11** to **12**) using this unique palladium hydride complex ($\text{H-Pd}^{\text{II}}\text{-OB(OH)}_2$). Furthermore, we provide ESI-HR-MS evidence, utilising a direct sample loop and flow injection system, that supports the proposed mechanism of this rearrangement and formation of the palladium hydride complex.

RESULTS AND DISCUSSION

The Rearrangement

Mechanistic work on the propargyl alcohol to 1,3-diene transformation had established the pivotal role of boric acid.¹² Therefore, using this as a starting point we treated allene **13a** with 10 mol% of $\text{Pd(PPh}_3)_4$ in the presence of 200 mol% of boric acid in 1,4-dioxane at 75°C for 8h, and this gave the expected 1,3-diene product **14a** in a respectable 66% conversion (table 1, entry 1). Increasing the reaction time to 24h increased this conversion of **13a** to **14a** to 90%, and an isolated yield of 70% was also achieved (entry 2). When the rearrangement was conducted at room temperature it proved detrimental, with the conversion to **14a** dropping to 55% (entry 3); and an increase in temperature to 90°C, resulted in the conversion to **14a** slightly rising to 60%, but we did observe degradation of the product via polymerisation (entry 4). When the amount of boric acid was

reduced by 100 mol% the conversion to **14a** fell to 35% and a minor product, **15**, was also observed (entry 5). This product **15** was also detected when B(OH)_3 was replaced with BzOH ,¹⁴ however, in this case, minimal 1,3-diene was observed.

Scheme 3 and table 1. The rearrangement of allene **13a** to 1,3-diene **14a**.^a

Entry	Temp (°C)	Time (h)	Observed product	
			14a	15
1	75	8	66	-
2	75	24	90 [70] ^b	-
3	RT	24	55	-
4	90	24	60 ^c	-
5 ^d	75	24	35	45
6 ^e	75	4.5	>5	40

^aReactions were performed under an N_2 or argon atmosphere with the allene (1 equiv), $\text{Pd(PPh}_3)_4$ (10 mol%), B(OH)_3 (200 mol%) in 1,4-dioxane unless otherwise stated. ^bIsolated yields. ^cDegradation. ^d100 mol% B(OH)_3 . ^e BzOH (100 mol %) instead of B(OH)_3 .

With rearrangement conditions established we examined the scope of the rearrangement with a number of allenyl substrates (scheme 4a). All the allenes in this study were synthesised using known methods and full details can be found within the supporting information.¹⁵ The cyclohexyl aryl allenes **13a-c** could be cleanly converted to their 1,3-dienyl products **14a-c**; an exception was the naphthyl allene **13d**, which failed to deliver the expected 1,3-diene **14d**. Yields for the 1,3-diene **14e** were variable due to the instability of the allene; additionally, attempts to synthesise a pyridyl substituted allene for the rearrangement proved difficult. The cyclopentyl (**13f**), cycloheptyl (**13g**) and cyclooctyl allenes (**13h**) all cleanly gave their respective 1,3-diene products **14f-h** in good to excellent isolated yields. As can be seen in these examples, there is no prerequisite in having an activated allene, for example the 3-methyl aryl allenes (**13c**, **f** and **g**) all underwent conversion, as do **13b** and **13f**. The 1,1-dimethyl-3-aryl-allene series (**14i-n**) also performed adequately in this rearrangement giving the desired 1,3-dienes in high isolated yields; of note is the performance of relatively electron poor allene **13n** that gave the anticipated 1,3-diene **14n** in 98% yield. This later result suggests to the both electron-rich and electron-deficient aryl allenes perform well in this rearrangement in contrast to the acid mediated processes previously reported.⁸

A 1,3-diaryl allene, **13o**, was rearranged (scheme 4b) to give its 1,3-diene (**14o**) as indicated by crude ^1H nmr, but its isolation proved very problematic, as it readily polymerised upon standing. The 1,1-dimethyl diaryl allene **13p** could also be rearranged under these conditions, giving its 1,3-diene **14p** as a

Scheme 4. (a) Rearrangement of unactivated allenes to 1,3-dienes; (b) Formation of 1,3-diaryl-1,3-diene; (c) Rearrangement of tetrasubstituted allenes; (d) product distribution observed from the rearrangement of allene **16**.

1:1 mixture of *E/Z* geometric isomers and in an isolated yield of 67% (scheme 4c).

1-Aryl-3-methyl-1,2-pentadiene **16** was exposed to the rearrangement conditions (scheme 4d). Again, this allenyl-substrates performed very well, but gave a mixture of 1,3-diene products (**17a–c**) in good isolated yields. The thermodynamically stable *E,E*-1,3-diene **17a** proved to be the predominant product, together with small amount of its *Z,E*-isomer **17c**; however, the *exo*-1,3-diene **17b** was also detected and subsequently isolated.

Mechanism

The mechanism of this transformation can be adequately described in scheme 5a. Following formation of the hydridopalladium species $\text{H-Pd}^{\text{II}}\text{-OB(OH)}_2$ (**18**),¹² hydropalladation of **19** can occur to give the π -allylpalladium complex **20**. Of the two plausible structures, **21** is the only one that can undergo syn- β -hydride elimination to give the thermodynamic 1,3-diene product **22**. This mechanism is, in part, supported by the hydroalkoxylation of alkynes described by Yamamoto,¹⁴ but importantly in the case shown in scheme 5a the absence of an external nucleophile adding to the π -

Scheme 5. (a) Plausible mechanism for $\text{Pd}^0/\text{B}(\text{OH})_3$ mediated allene to 1,3-diene rearrangements; (b) the detected palladium complexes by direct sample loop and flow injection ESI-HR-MS analysis.

allylpalladium complex **21** leads to the formation **22**. Furthermore, unlike benzoic acid, which also can also lead to 1,3-diene formation¹⁵ boric acid does not undergo reductive coupling, possibly due to the significant difference in pK_a .¹⁶ It is entirely plausible that the by-product observed in entries 5 and 6 in table 1 derives from intermediate **21**.

To give further support to this mechanistic hypothesis, and particularly the formation of the key π -allylpalladium complex **20**, we utilised the ESI-FTMS approach of Guo and Ma.¹⁷ We selected two arylallenes (**13a** and **13i**) as substrates for this study; where the substitution on the aryl ring on each allene was selected to ensure adequate ionization, *via* the use of a protonatable group. However, to reduce the electron donating ability of each allene, and to impede any adventitious protonation, a *meta* substitution pattern was also selected. Firstly, the rearrangement of allene **13a** was monitored by direct sample loop and flow injection analysis by ESI-HR-MS. After 10 minutes, we were able to intercept, detect and characterize a number of significant palladium complexes. Two distinct complexes can be observed¹⁸ which correspond well to the π -allylpalladium complex (**20**) described in scheme 5a; complex **23a** where one phosphine is attached to the Pd centre (m/z 585.1378; calcd. for $[\text{C}_{33}\text{H}_{34}\text{OPd}]^+$: m/z 585.1386) and complex **23b** (m/z 323.0467; calcd. for $[\text{C}_{15}\text{H}_{19}\text{OPd}]^+$: m/z 323.0470) where there are no phosphines attached to the Pd centre (scheme 5b). To further support the formation of the π -allylpalladium complex **20** shown in scheme 5a, allene **13i** was also analysed where an ion corresponding to complex **24** where one phosphine is attached to the Pd centre (m/z 545.1072; calcd. for $\text{C}_{30}\text{H}_{30}\text{OPd}^+$: m/z 545.1072) was observed (scheme 5b).¹⁸

These MS results firmly support the formation of the Pd^{II} -hydride complex, as the key π -allylpalladium complex can only result from addition of the Pd^{II} to the allene as described by Yamamoto.¹⁵ However, unlike Yamamoto's report the poor nucleophilicity of boric acid results in β -hydride elimination instead of undergoing reductive elimination to give the addition product.

CONCLUSIONS

In summary, we have demonstrated that a palladium hydride complex derived from simple $\text{Pd}(\text{PPh}_3)_4$ and boric acid ($\text{B}(\text{OH})_3$) can rearrange allenes to their respective 1,3-dienes in good isolated yields. The mechanism of this rearrangement has been supported by the identification of key π -allylpalladium complexes *via* direct sample loop and flow injection analysis by ESI-HR-MS. Importantly, this rearrangement demonstrates that

boric acid can play a significant role within an established palladium catalysed reactions.

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All reagent chemicals were purchased from Sigma-Aldrich Chemical Company Ltd. and Lancaster Chemical Synthesis Ltd. Commercially available reagents were used and without further purification. Palladium reagents were obtained from Sigma-Aldrich Chemical Company Ltd and were handled under argon. All solvents were directly used commercially except tetrahydrofuran (THF) was distilled from sodium and benzophenone prior to use. Petroleum ether refers to the fractions with a boiling point between 40–60°C. Air-sensitive reactions were carried out using oven-dried glassware under nitrogen atmosphere. Proton magnetic resonance spectra (^1H NMR) and carbon magnetic resonance spectra (^{13}C NMR) were recorded at 400MHz and 100MHz respectively using a Bruker Avance 400MHz spectrometer as solutions in CDCl_3 . Coupling constants are measured in hertz (Hz) and chemical shifts are quoted as parts per million (ppm) Thin layer chromatography (TLC) analysis was carried out on aluminium backed silica plates, and plates were visualized by Ultra Violet light (254nm) or vanillin stain.

General procedure for allene to 1,3-diene isomerization.

To a solution of of allene (1.00 mmol) in 1,4-dioxane (5.00 mL) was added boric acid (123 mg, 2.00 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (116 mg, 0.10 mmol, 10 mol%) in one portion. The resultant reaction mixture was stirred and heated to 75°C under a N_2 or argon atmosphere for 24h. After this period the reaction was cooled, diluted with Et_2O (50 mL) and transferred to a separating funnel and washed with NaHCO_3 (50 mL). The aqueous layer was then extracted with Et_2O (50 mL), and the combined organic layers washed with brine (50 mL), dried with MgSO_4 , filtered and the solvent removed under reduced pressure. The crude residue was then purified by column chromatography giving the following compounds.

1-[(E)-2-(Cyclohex-1-en-1-yl)ethenyl]-3-methoxybenzene (**14a**).¹²

Obtained as a colourless oil in 76% (162 mg) yield (R_f = 0.54, 1:10 ethyl acetate / petroleum ether).

IR (neat): 3010, 2931, 1651, 1157, 771 cm^{-1} .

^1H NMR (CDCl_3 , 400 MHz): δ = 7.23 (t, J = 8.0 Hz, 1H), 6.99 (d, J = 16.0 Hz, 1H), 6.93 (s, 1H), 6.79–6.71 (m, 2H), 6.39 (d, J = 16.0 Hz, 1H), 5.91 (t, J = 4.4 Hz, 1H), 3.81 (s, 3H), 2.26–2.24 (m, 2H), 2.19–2.18 (m, 2H), 1.72–1.70 (m, 2H), 1.64–1.61 (m, 2H).

^{13}C NMR (CDCl_3 , 100 MHz): δ = 159.9, 139.6, 135.9, 133.0, 131.2, 129.5, 124.6, 119.0, 112.6, 111.4, 55.3, 26.2, 24.6, 22.6, 22.6.

HRMS (ESI): m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{15}\text{H}_{18}\text{O}$: 215.1430, found: 215.1436.

1-[(E)-2-(Cyclohex-1-en-1-yl)ethenyl]-3-methylbenzene (**14b**).¹²

Obtained as a colourless oil in 73% (145 mg) yield (R_f = 0.45, 100% petroleum ether).

IR (neat) 3045, 2965, 1640, 732 cm^{-1} .

^1H NMR (CDCl_3 , 400 MHz): δ = 7.20–7.16 (m, 3H), 7.00 (d, J = 4.8 Hz, 1H), 6.77 (d, J = 16.0 Hz, 1H), 6.42 (d, J = 16.0 Hz, 1H), 5.88 (t, J = 4.0 Hz,

1H), 2.33 (s, 3H), 2.30 - 2.21 (m, 2H), 2.21 - 2.13 (m, 2H), 1.78 - 1.68 (m, 2H), 1.65 - 1.61 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz): δ = 138.4, 136.0, 132.5, 130.7, 128.7, 127.6, 127.0, 124.8, 123.1, 25.7, 24.8, 22.8, 21.5.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₅H₁₈: 199.1418, found: 199.1421.

1-[(E)-2-(Cyclohex-1-en-1-yl)ethenyl]-benzene (14c).^{11a}

Obtained as a colourless oil in 72% (133 mg) yield (*R*_f = 0.29, 100% petroleum ether).

IR (neat) 3082, 2933, 1641, 1493, 739 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.40 - 7.38 (m, 2H), 7.31 - 7.24 (m, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 16.0 Hz, 1H), 6.45 (d, *J* = 16.0 Hz, 1H), 5.89 (t, *J* = 4.0 Hz, 1H), 2.27 - 2.25 (m, 2H), 2.19 - 2.18 (m, 2H), 1.78 - 1.69 (m, 2H), 1.69 - 1.60 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz): δ = 137.7, 135.6, 132.7, 131.2, 128.6, 127.2, 126.2, 124.5, 26.5, 24.5, 22.6.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₄H₁₆: 185.1325, found: 185.1321

2-[(E)-2-(Cyclohex-1-en-1-yl)ethenyl]-furan (14e).¹²

Obtained as a colourless oil in 62% (106 mg) yield (*R*_f = 0.85, 10% ethyl acetate in petroleum ether).

¹H NMR (CDCl₃, 400 MHz): δ = 7.30 (d, *J* = 16.0 Hz, 1H), 6.79 (d, *J* = 16.0 Hz, 1H), 6.45-6.43 (m, 1H), 6.21-6.18 (m, 1H), 6.20-6.17 (m, 1H), 5.88 (t, *J* = 3.2 Hz, 1H), 2.16-2.12 (m, 4H), 1.70-1.60 (m, 2H), 1.60-1.54 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz): δ = 154.0, 141.4, 135.5, 131.2, 131.0, 113.0, 111.4, 106.9, 26.2, 24.2, 22.6, 22.1.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₂H₁₄O: 173.0961, found: 173.0981.

1-[(E)-2-(Cyclopent-1-en-1-yl)ethenyl]-benzene (14f).^{19a}

Obtained as a colourless oil in 98% (166 mg) yield (*R*_f = 0.29, 100% petroleum ether).

IR (neat) 3054, 2986, 1598, 1420, 738 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.42 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 5.6 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.02 (d, *J* = 16.0 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 5.86 - 5.84 (m, 1H), 2.58 - 2.54 (m, 2H), 2.50 - 2.46 (m, 2H), 2.05 - 1.94 (m, 2H).

¹³C NMR (CDCl₃, 100 MHz): δ = 142.9, 137.9, 132.2, 128.8, 128.7, 127.2, 126.3, 125.9, 33.2, 31.3, 23.3.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₃H₁₄: 171.1174, found: 171.1168.

1-[(E)-2-(Cyclohept-1-en-1-yl)ethenyl]-3-methylbenzene (14g).

Obtained as a colourless oil in 98% (206 mg) yield (*R*_f = 0.46, 100% petroleum ether).

IR (neat) 3028, 2921, 1603, 1444, 1264 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.21 - 7.17 (m, 3H), 7.00 - 6.98 (m, 1H), 6.74 (d, *J* = 16.0 Hz, 1H), 6.44 (d, *J* = 16.0 Hz, 1H), 6.04 - 6.01 (m, 1H), 2.44 - 2.41 (m, 2H), 2.33 (s, 3H), 2.30 - 2.23 (m, 2H), 1.83 - 1.76 (m, 2H), 1.57 - 1.50 (m, 4H).

¹³C NMR (CDCl₃, 100 MHz): δ = 143.3, 138.1, 135.4, 133.2, 128.5, 127.7, 127.0, 124.9, 123.4, 32.4, 28.8, 27.3, 26.9, 26.4, 21.5.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₆H₂₀: 213.1643, found: 2213.1640.

1-[(E)-2-(Cycloocta-1-en-1-yl)ethenyl]-3-methylbenzene (14h).

Obtained as colourless oil in 89% (200 mg) yield (*R*_f = 0.46, 100% petroleum ether).

IR (neat) 3024, 2919, 1702, 1601, 1444 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.23 - 7.17 (m, 3H), 7.01 - 6.99 (m, 1H), 6.74 (d, *J* = 16.4 Hz, 1H), 6.47 - 6.43 (d, *J* = 16.0 Hz, 1H), 5.86 (t, *J* = 8.8 Hz, 1H), 2.52 - 2.49 (m, 2H), 2.33 (s, 3H), 2.26 - 2.23 (m, 2H), 1.62 - 1.47 (m, 8H).

¹³C NMR (CDCl₃, 100 MHz): δ = 139.5, 138.1, 138.1, 133.7, 132.1, 128.5, 128.0, 127.0, 125.3, 123.1, 30.6, 28.5, 27.5, 27.1, 26.4, 24.4, 21.5.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₇H₂₂: 227.1800, found: 227.1788.

[(1E)-3-Methylbuta-1,3-dien-1-yl]-3-methoxybenzene (14i).

Obtained as a colourless oil in 51% (88 mg) yield (*R*_f = 0.55, 5% ethyl acetate in petroleum ether).

IR (neat) 2939, 1603, 1464, 1156 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.25 - 7.21 (m, 1H), 7.04 - 7.02 (m, 1H), 6.96 - 6.94 (m, 1H), 6.85 (d, *J* = 16.4 Hz, 1H), 6.78 - 6.76 (m, 1H), 6.49 (d, *J* = 16.4 Hz, 1H), 5.11 (s, 1H), 5.07 (s, 1H), 3.81 (s, 3H), 1.96 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 159.9, 142.1, 138.9, 132.1, 129.6, 128.7, 119.3, 117.6, 113.3, 111.7, 55.3, 18.7.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₂H₁₄O: 175.1123, found: 175.1114.

[(1E)-3-Methylbuta-1,3-dien-1-yl]-3,5-dimethylbenzene (14j).

Obtained as a colourless oil in 84% (144 mg) yield (*R*_f = 0.56, 100% petroleum ether).

IR (neat) 2916, 1598, 1445, 1162, 840 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.05 (s, 2H), 6.88 (s, 1H), 6.85 (d, *J* = 16.0 Hz, 2H), 6.48 (d, *J* = 16.0 Hz, 1H), 5.10 (s, 1H), 5.04 (s, 1H), 2.30 (s, 6H), 1.95 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 142.3, 138.1, 137.4, 131.4, 129.3, 128.9, 124.6, 124.5, 117.1, 21.4, 20.4, 18.7.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₃H₁₆: 173.1330, found: 173.1328.

[(1E)-3-Methylbuta-1,3-dien-1-yl]-4-methylbenzene (14k).^{19b}

Obtained as a colourless oil in 98% (155 mg) yield (*R*_f = 0.56, 100% petroleum ether).

IR (neat) 2986, 1603, 1513, 1265, 908 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.34 (d, *J* = 3.6 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 16.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.10 (s, 1H), 5.05 (s, 1H), 2.34 (s, 3H), 1.98 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 142.3, 137.2, 134.9, 131.0, 129.4, 128.7, 126.1, 116.7, 21.3, 18.7.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₂H₁₄: 159.1174, found: 159.1163.

[(1E)-3-Methylbuta-1,3-dien-1-yl]-4-methoxybenzene (14l)

Obtained as a colourless oil in 55% (96 mg) yield (*R*_f = 0.55, 5% ethyl acetate in petroleum ether).

IR (neat) 2959, 1604, 1509, 1172, 827 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.39 - 7.37 (d, *J* = 8.0 Hz, 2H), 6.85 (d, *J* = 8.0 Hz, 2H), 6.78 (d, *J* = 16.0 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 5.09 - 5.05 (m, 2H), 3.81 (s, 3H), 1.98 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 159.2, 142.6, 130.2, 129.7, 128.2, 127.7, 116.3, 114.1, 55.3, 18.7.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₂H₁₄O: 175.1123 found: 175.1119.

[(1E)-3-Methylbuta-1,3-dien-1-yl]-3-methylbenzene (14m).

Obtained as a colourless oil in 88% (138 mg) yield (*R*_f = 0.56, 100% petroleum ether).

IR (neat) 3022, 2919, 1605, 1449, 1264 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.26 - 7.21 (m, 3H), 7.06 - 7.05 (m, 1H), 6.87 (d, *J* = 16.0 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 5.11 (s, 1H), 5.06 (s, 1H), 2.33 (s, 3H), 1.99 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 202.4, 138.1, 136.1, 128.3, 124.4, 105.3, 94.5, 27.3, 21.4, 19.0, 12.4.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₂H₁₄: 159.1174, found: 159.1171.

Methyl-[(1E)-3-methylbuta-1,3-dien-1-yl]-4-carboxybenzene (14n).

Obtained as a colourless solid in 98% (198 mg) yield (M.P. = 94.5 - 95.5°C, *R*_f = 0.61, 5% ethyl acetate in petroleum ether).

IR (neat) 2947, 1708, 1600, 1455, 1275 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.98 (d, *J* = 6.4 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 16.0 Hz, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 5.18 (s, 1H), 5.12 (s, 1H), 3.89 (s, 3H), 1.97 (s, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 167.0, 142.0, 141.84, 134.2, 130.0, 128.8, 127.7, 126.4, 119.1, 52.2, 18.6.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₃H₁₄O₂: 203.1072, found: 203.1065.

(3-Methylbuta-1,3-dien-1-yl)-1-phenyl-1-(4-methylbenzene) (14p).

Obtained as a colourless oil in 67% (156 mg) yield and as an approx. 1:1 of *E/Z* isomers (*R*_f = 0.37 100% petroleum ether).

IR (neat) 3021, 2914, 1599, 1489, 1180, 883 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.42 - 7.01 (m, 9H), 6.67 (s, 1H), 5.04 - 4.98 (m, 2H), 2.44 (s, 3H), 2.36 (d, *J* = 14 Hz, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 141.7, 141.4, 138.3, 131.0, 130.4, 128.6, 128.2, 128.1, 128.0, 127.8, 127.2, 124.8, 124.3, 119.1, 22.1, 21.6.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₈H₁₈: 235.1487, found: 235.1486.

Isomerisation of (3-methyl-1,2-pentadien-1-yl)-3-methylbenzene (16).

This compound (**16**) was isomerized using the general procedure giving a mixture of three compounds **17a**:**17b**:**17c** in a ratio of 4:2:1; **17a** could be isolated, however, **17b** and **17c** were isolated and subsequently characterized as a mixture:

[(2E, 4E)-3-Methylpenta-2,4-dien-1-yl]-3-methylbenzene (17a).

Obtained as a colourless oil in 58% (100 mg) yield (*R*_f = 0.39, 100% petroleum ether).

IR (neat) 3025, 2980, 1640, 1442, 732 cm⁻¹.

¹H NMR (CDCl₃, 400 MHz): δ = 7.24 - 7.18 (m, 3H), 7.01 (d, *J* = 6 Hz, 1H), 6.81 (d, *J* = 16.4 Hz, 1H), 6.43 (d, *J* = 16.0 Hz, 1H), 5.71 (m, 1H), 2.35 (s, 3H), 1.85 (s, 3H), 1.78 (d, *J* = 6.0 Hz, 3H).

¹³C NMR (CDCl₃, 100 MHz): δ = 138.0, 138.0, 133.8, 128.3, 128.0, 127.8, 127.0, 125.0, 123.0, 21.8, 14.0, 12.0.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₃H₁₇: 173.1325, found: 173.1323.

[(1E)-3-Ethylbuta-1,3-dien-1-yl]-3-methylbenzene (17b) and [(2Z, 4E)-3-methylpenta-2,4-dien-1-yl]-3-methylbenzene (17c).

17b and **17c** were isolated as an inseparable mixture in 35% (60 mg) yield.

IR (neat) 3025, 2980, 1640, 1442, 732 cm⁻¹.

17b: ¹H NMR (CDCl₃, 400 MHz): δ = 7.26-7.19 (m, 3H), 7.03 (d, *J* = 8 Hz, 1H), 6.82 (d, *J* = 16.0 Hz, 1H), 6.56 (d, *J* = 16 Hz, 1H), 5.10 (d, *J* = 2 Hz, 2H), 2.36 (m, *J* = 6.8 Hz, 2H), 2.38 (s, 3H), 1.16 (m, 3H).

17b: ¹³C NMR (CDCl₃, 100 MHz): δ = 147.8, 139.9, 128.5, 128.1, 127.1, 125.9, 123.6, 115.0, 24.8, 21.5, 18.8 ppm.

17c: ¹H NMR (CDCl₃, 400 MHz): δ = 7.26 - 7.19 (m, 3H), 7.03 (d, *J* = 8 Hz, 1H), (d, *J* = 8 Hz, 1H), 6.52 (d, *J* = 12 Hz, 1H), 5.54 (m, 1H), 2.36 (s, 3H), 1.91 (s, 3H), 1.84 (d, *J* = 6.8 Hz, 3H).

17c: ¹³C NMR (CDCl₃, 100 MHz): δ = 138.2, 133.0, 131.2, 128.1, 127.1, 125.6, 123.6, 22.7, 13.3.

HRMS (ESI): *m/z* [M+H]⁺ calcd for C₁₃H₁₇: 173.1325, found: 173.1322.

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Supporting Information

Supporting information for this article is available online at <http://>

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	Marc C. Kimber studied at the University of Adelaide and received his Ph. D. (1998) on the synthesis of <i>in vivo</i> Zn(II) fluorophores. After postdoctoral positions with Prof. Margaret M. Harding (Uni. of Syd.) and Prof. Dennis K. Taylor (Uni. of Adel.) he moved in 2002 to the UK to take up a postdoctoral position with Prof. J. Stephen Clark (Uni. of Nottingham) working on the total synthesis of gambieric acid A. In 2004 he moved into industry (2004) as a Senior Scientist at Evotec; but returned to academia in 2006 to work on the total synthesis of nosiheptide in the group of Prof. Christopher J. Moody (Uni. of Nottingham). In 2008 he took up a Lectureship in Organic Chemistry at Loughborough University where he was promoted to Senior Lecturer in 2015. His current research interests centre on the use of singlet oxygen ($^1O_2$) in natural product synthesis, and novel innovative synthetic transformations of allenes (and their derivatives!).