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The study of newer methods for the oxidation of organic compounds

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THE STUDY OF NEWER METHODS FOR THE OXIDATION OF ORGANIC COMPOUNDS

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Supervisor: Dr.J.B.Lee

A thesis

submitted for the degree of

Doctor of Philosophy

of

Loughborough University of Technology

October, 1968

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Many a tale hath been told in many a way;
but for any one to coin new fancies and
submit them to the touchstone of assay
is perilous indeed.

"The Odes of Pindar"
(Pindar; ca. 518-438 B.C.)

SUMMARY

Methods for the oxidation of aralkyl compounds have been examined with special reference to the oxidation of toluene and o-toluenesulphonamide. Catalytic aerial oxidations have been investigated as possible procedures with an industrial application. The stability of o-toluenesulphonamide towards oxidation is accounted for and the mechanism of oxidation of toluene by both homolytic and heterolytic bond fission is discussed. The preparation of saccharin by oxidation of o-toluenesulphonamide with manganese dioxide in acid solution is reported.

A study of the reactions of the silver II oxidation state with a variety of functional groups has been ~~examined~~ reported. A comparison of the potential uses of argentic picolinate and silver II oxide as preparative reagents for organic oxidations is made and the yields of product and type of reaction occurring with each oxidant is reported. Good yields of aldehydo-compounds have been obtained from the oxidation of primary alcohols and α-amino acids with argentic picolinate. The possible mechanisms of oxidation of these compounds and of other reactions with the reagents are discussed. The factors governing the rate of oxidation of compounds by argentic picolinate have been measured and can be accounted for in terms of steric and electronic considerations and choice of solvent. The kinetics of alcohol oxidation in aqueous media have been investigated by ultraviolet spectroscopy and the data are presented. The proton magnetic resonance spectra of carbonyl 2,4-dinitrophenylhydrazones have been analysed and data for configurational isomerism about the C=N bond have been calculated and are discussed.

ACKNOWLEDGEMENTS

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GENERAL INTRODUCTION

GENERAL INTRODUCTION.

Stewart (1) has recently defined oxidation in the following terms, "An oxidation or reduction has occurred in a chemical reaction if the product differs from the reactants in a way that cannot be accounted for simply by an exchange of protons, hydroxyl ions, halide ions, alkali metal ions, ammonium ions, amide ions, etc., or what is equivalent, by an exchange of water, hydrogen halide, ammonia, etc." For the purposes of oxidation reactions involving organic compounds, the definition is probably the most appropriate as other definitions tend to be difficult to visualise in terms of organic systems.

Historically, the term oxidation was applied by Lavoisier, to the reaction of a metal with oxygen to give the metal oxide. Conversely, the term reduction implied removal of oxygen from an oxide (usually with hydrogen) to yield the metal. Therefore oxidation and reduction are complementary. Nearly two centuries have lapsed and still the most popular concept of oxidation and reduction is addition or removal of oxygen and hydrogen. Since the time of Lavoisier, scientists have tended to generalise the term oxidation, and dehydrogenation or the transfer of electrons from an element or a compound are also oxidation reactions. Consequently, the following equations are all representative of oxidation reactions, although this may not be immediately apparent : -

$$2\,Cu + O_2 = 2\,CuO \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots 1$$

$$Cu^{+} + Ag^{+} = Cu^{2+} + Ag \quad \ldots\ldots\ldots\ldots\ldots\ldots 2$$

$$CH_4 + Cl_2 = CH_3Cl + HCl \quad \ldots\ldots\ldots\ldots\ldots\ldots 3$$

$$CH_3CH_2CHO + H_2O_2 = CH_3CH_2COOH + H_2O \quad \ldots\ldots 4$$

and $$Fe^{2+} = Fe^{3+} + e^{-} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots 5$$

Equation 1 is representative of Lavoisier's definition of oxidation, whilst equations 2 and 5 support the later definition (i.e. the transfer of electrons). Hence in equation 1, copper is oxidised to its oxide whilst oxygen is reduced and in equation 5, ferrous ions are oxidised to ferric ions by loss of an electron.

With reference to inorganic oxidation processes, the transfer or removal of electrons is an easily recognisable and usually reversible reaction e.g., equation 5 which for completeness should be rewritten :-

$$Fe^{2+} \underset{\text{REDUCTION}}{\overset{\text{OXIDATION}}{\rightleftharpoons}} Fe^{3+} + e^{-} \quad \ldots\ldots\ldots\ldots\ldots 6$$

However, when this concept is applied to the oxidation of organic compounds, the analogy is not so clear because (a) the atoms compounding a molecule are not "seen" to lose electrons except in an artificial manner and (b) organic oxidation reactions are rarely reversible except for enzyme oxidation reactions in biological systems. Hence, for equation 7, it is difficult to assert that electrons have been removed from methanol to yield formaldehyde because no atom has been deprived of its valence electrons.

$$CH_3OH + [O] \longrightarrow H.CHO + H_2O \quad \ldots\ldots\ldots\ldots 7$$

But on closer examination, equation 8, it can be seen that whereas methanol has 14 valence electrons (10 involved in bond formation), the product has only 12 (8 involved in bond formation). Hence two electrons have been removed along with two hydrogen atoms.

$$\begin{array}{l} \quad H \\ H : \ddot{C} : \ddot{O} : H \\ \quad H \\ \quad 14e^- \end{array} \longrightarrow \begin{array}{l} \quad H \\ H : \ddot{C} : : \ddot{O} : + 2H^{\cdot} \\ \quad\quad 12e^- \end{array} \quad \ldots 8$$

Classification of oxidation processes.

Organic compounds are essentially covalent compounds and hence reaction is unlikely to occur by direct electron transfer on collision of an oxidant molecule with the substrate as valence electrons are relatively inaccessible. Therefore for oxidation to occur, covalent bond fission is essential. Because of the low polarisability of carbon to carbon (C-C) bonds, fission of carbon to hydrogen (C-H) bonds is likely to initiate oxidation and C-C ruptures will occur because of attack at another site on the molecule. Bond fission of C-H linkages can occur by (a) homolytic or (b) heterolytic means.

Homolytic fission is the symmetrical breaking of the bond to yield a hydrogen radical i.e. a single electron transfer process (e.g. equation 9)

$$CH_3 - H + Cl - Cl \longrightarrow CH_3^{\cdot} + HCl \quad \ldots\ldots 9$$

The methyl radical so formed has an unpaired electron and must therefore undergo some further reaction to gain stability.

The radical can react with another molecule of chlorine to give a chlorine radical or it can react with another methyl radical to yield ethane; and each is possible. Homolytic bond fission can be initiated by traces of free-radicals, exposure to radiant energy or single-electron transfer to an inorganic ion of the transition element series where an incomplete d-orbital is available.

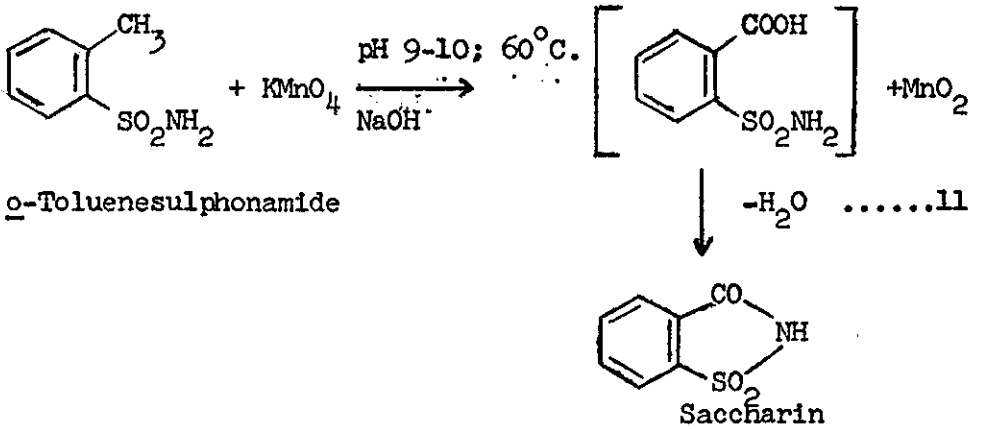
Heterolytic oxidation is brought about by transfer of electron-pairs from one to the other of the atoms involved in the bond, and hence the heterolytic fission can be by two processes (a) proton abstraction and (b) hydride abstraction. Hydride abstraction always leads to oxidation but proton loss only leads to oxidation when some subsequent change occurs in the molecule.

SECTION I

A study of the oxidation of aralkyl compounds.

INTRODUCTION.

The oxidation of the alkyl side chains of aralkyl compounds is of particular interest industrially and one example is the preparation of saccharin (o-benzoylsulphonimide) from o-toluenesulphonamide. Since the turn of the century this oxidation has been undertaken, in Britain, by the use of an alkaline solution of potassium permanganate (2). The oxidation is carried out as a batch process with a very close control of temperature and pH in order to prevent the hydrolysis of the imide and the build-up of a component having a very bitter taste. This bitter material is thought to be formed by the condensation of saccharin and o-toluenesulphonamide. The mechanism of the oxidation has not been closely studied and the conditions used have been optimised by a process of trial and error. At pH values less than 9, the bitter principle becomes more evident and at elevated temperatures and pH greater than 10, the cyclic imide undergoes hydrolysis to form o-sulphonamidobenzoic acid. The reaction as presently employed, can be summarised by the following equation :-



o-Toluenesulphonamide

Saccharin

There is an extensive literature concerned with the oxidation of alkyl-aromatic compounds, both from an academic

standpoint and from an industrial application. Examination of the literature shows that a variety of methods have been studied among which may be mentioned:- oxidations by sulphur and/or sulphur dioxide; oxidations catalysed by metal ions (aerial oxidations); oxidations effected by oxidising acids and those accomplished by a variety of other reagents.

In general reactions carried out with sulphur and with sulphur dioxide are heavy industrial processes, employing extremes of temperature and pressure and usually involve either water or alkaline solutions as the reaction media. High yields of m- and p-toluic acids have been obtained (3,4) by the reaction of the respective xylenes with sulphur and aqueous sodium hydroxide at high temperature and pressure. Also by this process, p-sulphobenzoic acid has been prepared in good yield from the toluene sulphonic acid. It has also been found (5,6) that sulphur and water will bring about the oxidation of toluene to benzoic acid at elevated temperature and pressure; but at extended reaction times the reaction was found to be reversible, giving rise to poor yields of the acid. However, the addition of sulphur dioxide to the reaction vessel increases the conversion to benzoic acid. Sulphur dioxide has been found to oxidise toluene (7). In this process the toluene and sulphur dioxide were passed over a vanadium pentoxide catalyst at 410°C. for a contact time of 3 seconds. Benzoic acid was formed in high yield and a good conversion was recorded. Similar reactions have been carried out (8-14) using the oxides of the heavy metals, vanadium, niobium and tantalum with sulphur dioxide; all reported satisfactory

yields of the intended product.

By far the most important development, over the past two decades, has been the introduction of metal ion catalysts for the liquid phase, aerial oxidation of aromatic compounds. On an industrial scale, such catalytic processes are very attractive because of their cheapness. Cobalt naphthenate (15) has been proposed for an industrial oxidation of toluene, by air, on a continuous basis. The parameters have been established and are extremely mild by industrial standards i.e. temperature, 140°C.; pressure, 6 atmospheres. Under these conditions an 81% conversion to benzoic acid has been recorded on the continuous process. Other processes involving cobaltous ions have been developed, in which the general reaction is the same with only minor modifications being employed to improve yields. Hence cobaltous acetate, acetic acid and p-methyl benzaldehyde (16); cobaltous acetate, acetic acid and hydrogen bromide (17, 18); cobalt naphthenate and cumene (19); cobalt oxide (20); cobaltous acetate, manganese bromide and o-dichlorobenzene (21, 22); manganese acetate, acetic anhydride and traces of butyl peroxide (23); cobaltous acetate or benzoate (24, 25) and the mixed oxides of cobalt and zirconium with acetic acid (26) have all been employed for the aerial oxidation of toluene in particular, and of aralkyl compounds in general. Other metal ion catalysts have been used to promote the required oxidation but mainly in the vapour phase (27-29).

Industrial scale oxidations involving mineral acids have been reported for aralkyl compounds (30-38). Thus, 15% aqueous nitric acid, at temperatures between 165-220°C. and pressures

between 15-25 atmospheres, will convert p-nitrotoluene to the corresponding acid (30); whilst p-cymene has been oxidised to terephthalic acid by 50% nitric acid at 195°C. and 30 Kg./cm.^{2} pressure (31). Para-toluenesulphonic acid has been oxidised to p-sulphobenzoic acid by aqueous nitric acid at 145°C., in a pressure vessel, although some 2-nitro-4-sulphobenzoic acid was also formed (32). Crude p-cymene has been oxidised to pure terephthalic acid and o-chlorotoluene to the o-chloro-acid using a process (33) in which a thermosiphon was used to heat the pressure vessel. A vertical, cylindrical vessel was used for the oxidation of p-nitrotoluene to p-nitrobenzoic acid by 30% aqueous nitric acid at 210°C and 40 atmospheres pressure (34). Other oxidation processes involving aqueous nitric acid have been established (35-37) for the oxidation of toluene, and substituted toluenes, to the expected carboxylic acids. One major drawback to the use of nitric acid is the heterogeneous nature of the phases; a patent has been published (38) in which the passage of nitrogen dioxide through the organic phase, eliminates stratification of the materials involved. Thus, aralkyl compounds have been reported to be oxidised in better yields than with aqueous nitric acid.

The oxidising power of sulphuric acid alone does not appear to have been made use of, although oxidations involving the acid have been reported (39-47). However, these reactions involve other chemicals such as potassium dichromate or manganese dioxide. Mixtures of sulphuric acid and potassium dichromate have been considered (39) to be a very powerful and useful

oxidising agent for alkyl-aromatic compounds. The reaction conditions, for the oxidation of toluene, appeared to be largely dependent on the concentration of sulphuric acid employed, as were the type of products and the ratio in which they were formed. Under optimised conditions, toluene gave benzoic acid in moderate yield. It is noteworthy that when sulphuric acid was absent, the side-chain oxidised terminally. Thus, at 275°C. and with one equivalent of sodium dichromate for one hour reaction time (40); toluene was converted to benzoic acid in 96% yield whilst ethylbenzene gave a 96% yield of phenylacetic acid. The use of pyrolusite and sulphuric acid to oxidise toluene to benzoic acid has been established (41-45) as an industrial process; and its use has been extended to substituted aromatic compounds (46,47). Para-nitrotoluene, 2,4-dinitrotoluene and 2-chloro-4-nitrotoluene all gave the expected acid in moderately high yield.

A number of other processes are worthy of note: hydrogen sulphide and alkali-metal bisulphites at 500-800°F. and a pressure of 1000-3000 p.s.i. have been employed (48); whilst oxygen, or a compound such as selenium dioxide, and bromine (49) brought about the desired reactions. Recently, a new method for promoting base-catalysed oxidations has been reported (50); in which use is made of molecular oxygen at room temperature to yield the carboxylic acid. Also, oxygen and nitrogen have been passed through molten m-toluic acid at 442°C. to yield iso-phthalic acid.(51). Even a fermentation process has been developed (52).

With regard to the oxidation of o-toluenesulphonamide; this is carried out industrially in Britain using alkaline

potassium permanganate (2). Remsen and Falberg (53) prepared saccharin, originally, using neutral permanganate at lower temperatures; but Pamfilor (54) showed that better reaction occurred using alkaline potassium permanganate. Only a few variations on this method have been reported (55-59). Good yields of saccharin have been reported (55, 56) using potassium dichromate and sulphuric acid at 40-55°C. Chromium trioxide in acetic anhydride at -5 to 30°C. has brought about the oxidation (57) but four products were formed; one of these products was identified as N-acetyl saccharin. Chromium trioxide in 20N. sulphuric acid has been reported (58) to give good yields of saccharin; and also peroxy-sulphuric acid with manganese sulphate and silver nitrate, as catalysts, gave a high yield of pure saccharin (59).

Electrochemical studies of the oxidation have led to a number of publications (60-69). High yields of saccharin can be obtained by careful choice of electrode materials and the process becomes industrially viable where cheap electricity is available, e.g. Japan.

This section describes some attempts to apply the methods mentioned above to saccharin formation. In addition, since manganese dioxide is a by-product of the present process (2), the possible use of this material for oxidation was examined.

DISCUSSION AND RESULTS

The oxidation of o-toluenesulphonamide by alkaline potassium permanganate has been known for a long time (2,54); but the mechanism of the reaction has not been closely studied. However, the mechanism of oxidation of toluene with the reagent has been thoroughly investigated by Cullis and Ladbury (70), although the medium was aqueous acetic acid. Study of the kinetics led them to the conclusion that hydroxyl radicals and Mn^{3+} ions were the most likely oxidising species in the reaction; but that all manganese ions from oxidation 3 to 7 may be of some importance. Hence they suggested that the reaction, equation 12, led to the formation of the principal oxidant.

$$Mn^{3+} + H_2O \rightleftharpoons Mn^{2+} + HO^{\bullet} + H^{+} \quad \ldots\ldots\ldots\ldots 12$$

Manganous ions and permanganate react rapidly to give intermediate ions (71); therefore the addition of manganous ions should increase the rate of oxidation and this was shown to be the case. Waters (72) has suggested that permanganate does not exchange oxygen with water but that in strong alkali, it decomposes to give manganate ions and oxygen (equation 13).

$$4\,MnO_4^{-} + 4OH^{-} \longrightarrow 4\,MnO_4^{2-} + O_2 + 2H_2O \quad \ldots\ldots 13$$

However, Symons (73) has shown by use of $H_2O,^{18}$ that in alkaline solution all of the oxygen comes from water and therefore equation 14 is more probable.

$$MnO_4^{-} + OH^{-} \rightleftharpoons MnO_4^{2-} + HO^{\bullet} \quad \ldots\ldots\ldots\ldots 14$$

The oxidation of toluene by alkaline potassium permanganate solution is most probably initiated by the abstraction of a hydrogen radical to form the stabilised benzyl radical, equation 15.

The radical so formed, stabilised by delocalisation of the charge around the aromatic nucleus, is then involved in further reaction with either (a) water or (b) a hydroxyl radical to give benzyl alcohol, equations 16.

$$C_6H_5.CH_3 + HO^{\cdot} \longrightarrow C_6H_5CH_2^{\cdot} + H_2O \quad \ldots\ldots\ldots 15$$

$$C_6H_5CH_2^{\cdot} + H_2O \rightleftharpoons C_6H_5.CH_2OH + H^{\cdot} \quad \ldots\ldots\ldots 16(a)$$

$$C_6H_5CH_2^{\cdot} + HO^{\cdot} \longrightarrow C_6H_5CH_2OH \quad \ldots\ldots\ldots 16(b)$$

In alkaline solution, the benzyl alcohol will be rapidly converted to the aldehyde probably by the initial attack of hydroxyl ion, equation 17, followed by hydride ion transfer to permanganate to give the Mn^{V} ion, equation 18. The final step of the oxidation to yield benzoic acid is again fast and is probably initiated by either the attack of a hydroxyl ion on benzaldehyde, followed by hydride loss to permanganate ion, equation 19 (a), or the attack of the permanganate ion to yield an ester, followed by base abstraction of the aldehyde proton, equation 19 (b).

$$C_6H_5.CH_2OH + HO^{-} \overset{\text{Rapid}}{\rightleftharpoons} C_6H_5.CH_2O^{-} + H_2O \quad \ldots\ldots\ldots 17$$

$$C_6H_5CH_2O^{-} + MnO_4^{-} \xrightarrow{\text{Slow}} C_6H_5CHO + HMnO_4^{2-} \quad \ldots\ldots\ldots 18$$

$$C_6H_5\underset{H}{\overset{O}{C}} + HO^{-} \rightleftharpoons C_6H_5\overset{OH}{\underset{H}{C}}{-}O^{-} \xrightarrow{MnO_4^{-}} C_6H_5\overset{O}{\underset{OH}{C}} + HMnO_4^{2-} \quad \ldots 19(a)$$

$$C_6H_5\underset{H}{\overset{O}{C}} + MnO_4^{-} + H_2O \rightleftharpoons C_6H_5.\overset{OH}{\underset{H}{C}}{-}O{-}MnO_3 + HO^{-} \qquad 19(b)$$

$$\xrightarrow[OH]{H} \quad \downarrow$$

$$C_6H_5\overset{O}{\underset{OH}{C}} + MnO_3^{-} + H_2O.$$

The oxidation of o-toluenesulphonamide by an alkaline solution of permanganate is likely to be by the same mechanism; the difference however, will be in the rate of the reaction. Strongly electron-withdrawing substituents, such as the sulphonamido-group situated ortho on the aromatic nucleus, will slow the initial abstraction of a hydrogen radical because its effect will tend to enhance the heterolytic fission of the C-H bond to give a proton. Hence the production of o-sulphonamido-benzyl alcohol will be slower than the production of the unsubstituted alcohol (at the same temperature). However, the electron-withdrawing nature of the ortho-substituent will now aid the oxidation of the alcohol and the aldehyde (especially in basic solution) to the acid.

Ball, Goodwin and Morton (74) first showed that neutral manganese dioxide could bring about the oxidation of primary and secondary alcohols to the corresponding carbonyl compounds. Later, Attenburrow and co-workers (75) showed the oxidant to be specific for the conversion of allylic alcohols to allylic aldehydes and ketones; but since that time this specificity of action has been challenged (76,77). Hence, it is now generally known that manganese dioxide can be employed for a variety of oxidation procedures, some of which are novel rearrangement reactions (78, 79).

Gritter and Wallace (80) and Evans (81) have prepared manganese dioxide by a variety of methods and compared the reactivity of each sample in the oxidation of a variety of materials under comparable conditions; and Gritter, Wallace and

Dupre (82) have examined the effect of different solvents on the oxidation of benzyl alcohol to benzaldehyde. They showed that the physical nature of the surface was very important and that the solvent used can have a marked effect on the activity of the dioxide. Reactions carried out in benzene were found to be slower than those in carbon tetrachloride which in turn were slower than those using petroleum ether as the solvent and hence, the interaction of the solvent with the surface of the oxidant, inhibits the reaction of the benzyl alcohol with the reagent. It was apparent that centres of low electron-density were present on the surface of the manganese dioxide and it was these centres that could attract the electron-rich oxygen of the alcohol. The reaction sequence proposed by Gritter, Wallace and Dupre is as shown in Figure 1 for the oxidation of benzyl alcohol.

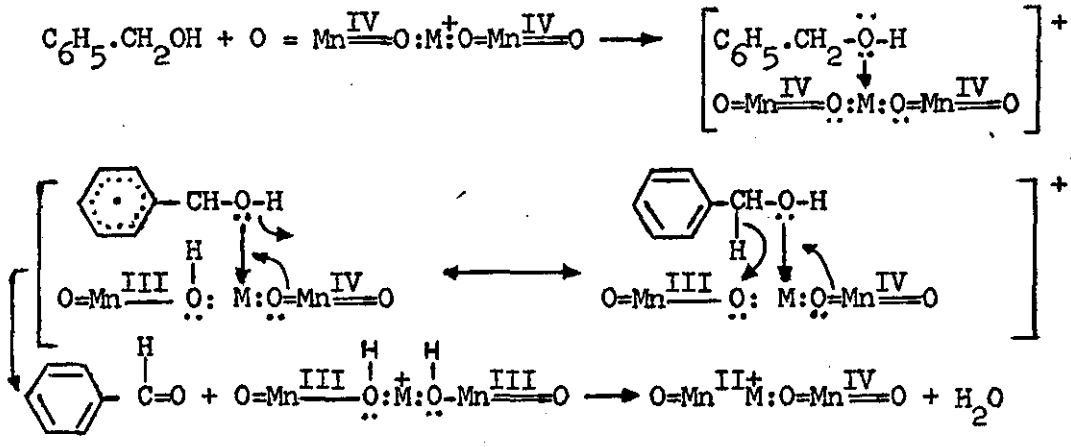


Fig.1.

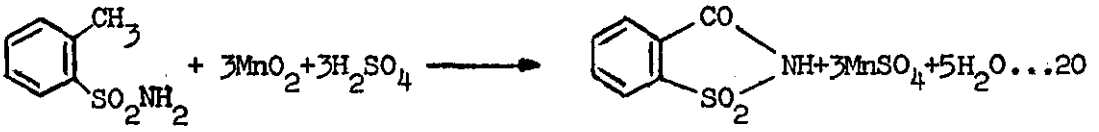
No oxidation products were isolated when manganese dioxide was reacted with o-toluenesulphonamide under a variety of conditions. Manganese dioxide and o-toluenesulphonamide were reacted together at different temperatures in different solvents for long periods of time (Table 2); but even when air was passed

through the mixtures, no oxidation was found to occur. The reactions were carried out with three types of material namely residual manganese dioxide from the saccharin-plant, material prepared by acid treatment of saccharin-plant dioxide and material prepared by the method of Attenburrow et al.(75). Infra red spectra recorded on the organic material separated from the reaction mixtures, showed no bands typical of those expected for products of oxidation.

Although no oxidation was recorded in the reactions examined, the activity of the acid-washed plant material was established by the reaction of small amounts of the dioxide with acetone, di-isopropylidene glycerol and ethanol. Vigorous reactions occurred on addition of small portions of the organic materials (di-isopropylidene glycerol spontaneously ignited) but this did not occur when larger amounts of organic material were added. Both the dioxide prepared in the laboratory and that direct from the saccharin plant showed no such activity, even when large amounts of the dioxide were present. The lack of activity was probably due to occluded ions of manganese and potassium in the first case and sodium and potassium in the latter. Tenaciously held o-toluene-sulphonamide was found to be present to 26% (by weight) in the plant dioxide. The presence of the starting material may well deactivate the surface of the oxidant by forming a strong complex which could not undergo ele ctron change due to the presence of the sulphonamide group.

Manganese dioxide in acid media was examined as a reagent for the oxidation of o-toluenesulphonamide to saccharin. Reactions

were carried out in glacial acetic acid, hydrochloric and sulphuric acid; the results indicate that in glacial acetic acid and hydrochloric acid, manganese dioxide is unsuitable for the oxidation desired. In all cases examined in these two media, no oxidation product was found and no indication that reaction had occurred was noted. However, with sulphuric acid as the medium, some oxidation occurred to form saccharin and hence equation 20 holds in part (see Table 2).



Pyrolusite in sulphuric acid has been reported (46) to oxidise toluene and toluene derivatives to the respective benzoic acids; and some of the compounds oxidised had de-activating substituents on the aromatic nucleus e.g., 2-chloro-4-nitrotoluene to 2-chloro-4-nitrobenzoic acid in high yield. It was suggested that a reason for the high yields with manganese dioxide (in comparison to potassium dichromate), is that only 1 atom of oxygen is formed per molecule of oxidant and hence less over-oxidation occurs.

Experiments carried out in the laboratory showed that acid-washed manganese dioxide in 50% sulphuric acid, oxidised toluene to benzaldehyde and benzoic acid, while reactions involving o-toluenesulphonamide and different concentrations of sulphuric acid showed that, up to 50% concentration, no appreciable hydrolysis of the sulphonamide group resulted. It was also found that 50% sulphuric acid was necessary to bring

about the oxidation, whereas 98% sulphuric acid charred the material and lower than 50% concentration resulted in no oxidation occurring. Hence, optimum conditions for maximum oxidation with least hydrolysis product were found to be 50% sulphuric acid under reflux.

During the early stages of each reaction carried out with 50% sulphuric acid, a purple material was formed. This was found to occur even when no organic material was present and therefore must be considered to be due to an intermediate ion of manganese. An examination of the formation of the purple colour when o-toluenesulphonamide was present, showed that the colour had to be dispersed before any oxidation product was formed (approximately 60 minutes at 90°C. with 50% sulphuric acid present. This fact would support the formation of an intermediate manganese ion of high oxidation state.

Under conditions where manganese dioxide reacted with o-toluenesulphonamide (3:1 molar ratio) to form saccharin, four other components were found in the mixture (see Plate 1) in addition to starting material. Examination of the reaction product by thin layer chromatography (t.l.c.) indicated the presence of saccharin and a more polar component (possibly a sulphonic acid derivative) but showed that o-sulphonamido-benzoic acid had not been formed. Hence, none of the saccharin formed had been hydrolysed.

The catalytic use of manganese dioxide for aerial oxidation of the molten sulphonamide material was examined, but results indicated that no oxidation had occurred even when benzoyl peroxide was added to the melt as a co-catalyst (promotor).

T.L.C. examination of product from reaction of

o-toluenesulphonamide, MnO_2 and 50% H_2SO_4.

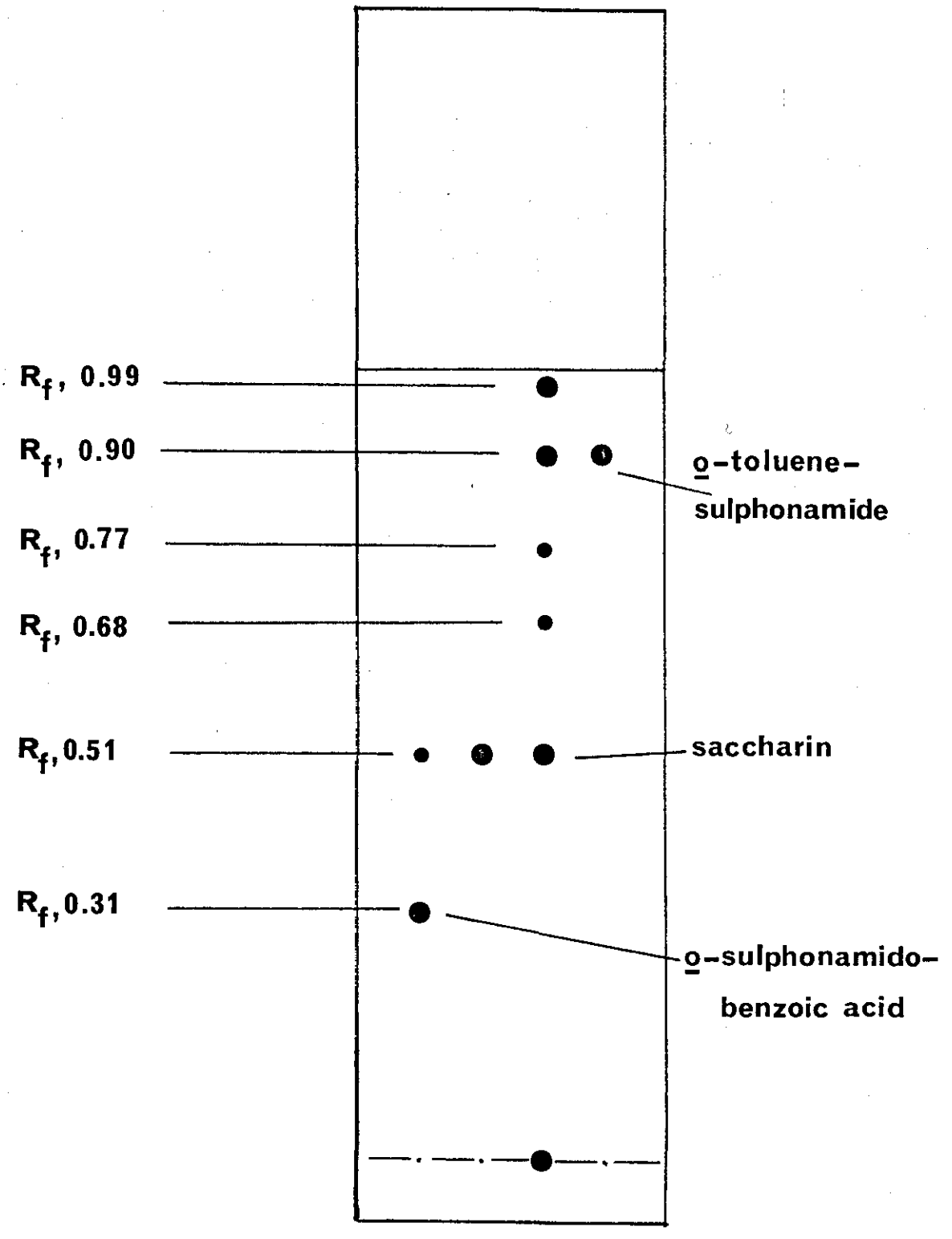
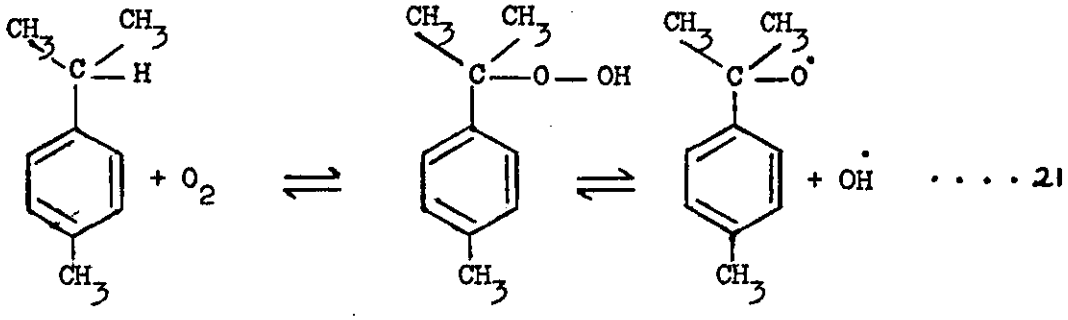


Plate 1

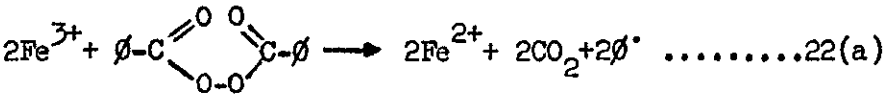
Other aerial oxidation methods were examined, but no oxidised material was found. Hence, molten o-toluenesulphonamide was not attacked by air and catalytic amounts of potassium permanganate; and use of p-cymene to promote aerial oxidation by a free-radical mechanism, failed. Toluene was reported (83) to be oxidised, catalytically to benzoic acid by potassium permanganate and a trace of acetone. However, this reaction could not be carried out in the laboratory because high pressure apparatus was not available. The parallel reaction with o-toluenesulphonamide was not attempted.

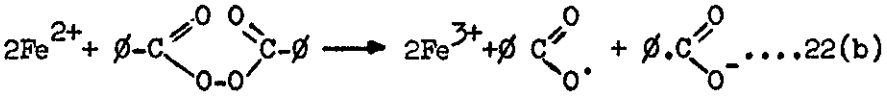
Manganese or ferric stearate and benzoyl peroxide have been used catalytically (84-86) for the aerial oxidation of aralkyl compounds but when reactions of this type were undertaken with toluene and toluenesulphonamide in the laboratory, neither compound was oxidised.

Reactions with p-cymene are facilitated due to the formation of a hydroperoxide with molecular oxygen, equation 21. The hydroperoxide can undergo homolytic fission to give a hydroxyl radical, which can then promote free-radical oxidation. Similarly, oxidations with multivalent metal ions and benzoyl peroxide are initiated by attack of the metal ion on the peroxide to yield a radical e.g., equation 22 (a) and 22 (b).



. . . . 21





One possible reason for the failure to oxidise o-toluenesulphonamide in these experiments is the difficulty with which the homolytic fission of the benzylic C-H bond takes place. The presence of the electron-withdrawing group in the ortho-position will tend to facilitate the heterolytic fission of the bond to yield the carbanion and a proton. Hence, o-toluenesulphonamide will be more stable to radical attack than toluene; and this type of reaction is only likely to occur under more severe conditions, if it occurs at all.

The oxidation of toluene to benzoic acid has been reported (50) to occur using a base catalysed method. Essentially, hexamethylphosphoramide was used as a solvent and potassium t-butoxide assisted molecular oxygen to react with the material at room temperature. The strong base brought about ionisation of the benzylic C-H bond, followed by transfer of an electron to oxygen to form a benzyl radical which then underwent autoxidation. Reactions of this type were carried out with o-toluenesulphonamide; but no definite product of oxidation was found. It would seem unlikely that the o-sulphonamidobenzyl carbanion would lose an electron readily to oxygen at room temperature due to the presence of the substituent on the aromatic nucleus.

Toluene was oxidised to benzyl alcohol by addition of argentic picolinate in aqueous dimethyl sulphoxide at 70°C. Benzyl alcohol was then oxidised to benzaldehyde and then further to the carboxylic acid. Each step in the oxidation was controlled by the molar ratio of oxidant to toluene employed. Hence with a molar ratio of oxidant to toluene (2:1), benzyl alcohol was formed whereas with a molar ratio (6:1), benzoic acid was produced in good yield. The parallel reaction with o-toluenesulphonamide was attempted but no oxidation product was recorded although the oxidant was reduced. The discussion of these reactions is included in Section II.

Summary of results of reactions with toluene

	Reaction	Result
1.	MnO_2 and 50% H_2SO_4	ØCHO and ØCOOH
2.	Catalytic aerial oxidation reactions:-	
(a)	$KMnO_4$ and trace CH_3COCH_3	No reaction
(b)	Mn^{II} stearate and Fe^{III} stearate	No reaction
3.	Oxidations with argentic picolinate in aqueous dimethyl sulphoxide.	
(a)	$ØCH_3$	$ØCH_2OH$.
(b)	$ØCH_2OH$	ØCHO
(c)	ØCHO	ØCOOH

TABLE 1

Summary of results with o-toluenesulphonamide

1.	MnO_2 in neutral media:-	
(a)	Plant material	No oxidation
(b)	Acid-washed plant material (88)	No oxidation
(c)	Prepared material (75)	No oxidation
2.	MnO_2(88) in acidic media:-	
(a)	Glacial acetic acid	No oxidation
(b)	Hydrochloric acid	No oxidation
(c)	Sulphuric acid	Saccharin with 50% H_2SO_4
3.	Catalytic aerial oxidation reactions:-	
(a)	Manganese dioxide	No oxidation
(b)	MnO_2 and benzoyl peroxide	No oxidation
(c)	$KMnO_4$	No oxidation
(d)	p-Cymene	No oxidation
(e)	Mn^{II} and Fe^{III} stearates + benzoyl peroxide	No oxidation
(f)	K t-butoxide in hexamethylphosphoramide	No oxidation confirmed
4.	Oxidation reaction with argentic picolinate in aqueous medium	No oxidation product but silver complex reduced.

TABLE 2

EXPERIMENTAL

Infra-red spectra were recorded on Perkin-Elmer Spectrophotometers 237 and 257. The abbreviations used in the spectra quoted are as follows :- s = strong, m = medium, w = weak, sh = shoulder and b = broad. The values quoted have the wavenumber ($cm.^{-1}$) as units and have been corrected.

Proton magnetic resonance spectra were recorded on a Perkin-Elmer R.10, 60 Mc./s. spectrometer. The chemical shifts are quoted with reference to tetramethylsilane as standard and the tau -values recorded for any multiplet are at the mid-point of that multiplet and may not be at its centre of gravity. The abbreviations m = multiplet, s =singlet, d = doublet and t =triplet are used throughout.

Thin layer chromatography was carried out using two solvent systems :- (A) 20%. diethylether/petroleum ether ($40-60^{\circ}$) used with plates prepared by dipping in a Kieselgel-GF/chloroform slurry; and (B) chloroform/methanol/ ammonia (s.g.= 0.88 g/ml.)=100/50/11.8 used with plates (20x5cm.) prepared by spreading Kieselgel-GF_{254} to a thickness of 0.4 mm. and activating at $150^{\circ}C.$ for three hours (87). Spots were located by their adsorption of iodine vapour or by use of a Mineralight UVS-11, ultra-violet lamp. Analytical gas-liquid chromatography (g.l.c.) was carried out on Pye series 104 chromatographs with flame ionisation detectors. Nitrogen, as carrier gas, at 60 ml./min. was used with the following columns:- 10% silicon oil (SE-30) on firebrick and 5%

dinonyl phthalate (DNP) on chromosorb-W. Both columns were 1.5m. in length and of 4 mm. bore.

Preparation of Active Manganese Dioxide (75).

A solution of manganese sulphate (tetrahydrate, 89.16g.; 0.4M.) in water (120 ml.) and a solution of sodium hydroxide (40%; 95 ml.) were added simultaneously during 1 hr. to a hot stirred solution of potassium permanganate (76.8g.; 0.46M.) in water (480 ml.). Manganese dioxide was precipitated soon after the start of the reaction as a fine brown solid. Stirring was continued for a further hour and the solid was separated by centrifugation and washed with water until the washings were colorless. The solid was dried at 120°C. and ground to a fine powder before use. Yield; 73g.

Preparation of active Manganese dioxide from saccharin-plant material. (88).

Manganese dioxide from the saccharin plant (100g.) was washed free from tenaciously held alkali with several portions of hot distilled water (5 x 250 ml.), followed by sulphuric acid ($^{N}/_{1}$; 250 ml.) and finally with hot distilled water (5x250ml.). The material was dried at the pump and then in an oven at 120°C. The material was ground to a fine powder before use. Yield; 74g.

The activity of the prepared material was shown by careful addition of small quantities of a few oxidisable organic liquids. Hence for manganese dioxide (1g.) and organic liquid (0.1g.); the following occurred:-

(a) Iso-propylidene glycerol was converted to iso-propylidene glyceraldehyde with spontaneous ignition occurring in one case.

(b) Dry ethanol was converted to acetaldehyde accompanied by a temperature rise from 21 to 107°C.

(c) Dry toluene was converted to benzaldehyde accompanied by a temperature rise from 20 to 80°C.

Preparation of o-sulphonamidobenzoic acid. (89)

Saccharin (40 g.; 0.22 M.), sodium hydroxide (20 g., 0.5M.) and water (250 ml.) were heated together under reflux for 3 hr. The mixture was cooled and acidified to pH2 with dilute hydrochloric acid (2N) and set aside overnight. The white crystalline material was separated and washed free from chloride ions with distilled water. The damp material was dried at 70°C. to constant weight (26g.). Yield, 59.6%. The material melted at 151-153°C. (Lit.(89) m.p.154°C.).

Preparation of hexamethylphosphoramide.(90)

Petroleum ether (40-60°; 500 ml.) was cooled to approximately -40°C. using an acetone/dry ice mixture. Dimethylamine (200 ml.) was added and the flask was fitted with a mechanical stirrer, a reflux condenser and a dropping funnel containing phosphorus oxychloride (50 ml.) and petroleum ether (40-60°; 100 ml.). The phosphorus oxychloride was added slowly to the stirred solution whilst the temperature was maintained at -40°C. When all of the mixture had reacted, the temperature was allowed to reach ambient. The solid amine hydrochloride was separated and the petroleum ether was removed from the filtrate by rotary evaporation. The residue was distilled and the fraction boiling at 73°C./1mm. was collected. Yield; 50g. n_D1.4552 (Lit.(93) n_D^{25} 1.4570).

Attempted aerial oxidations with manganese dioxide.

The general procedures described below were carried out with three different types of manganese dioxide i.e. manganese dioxide obtained from the saccharin plant, acid-washed manganese dioxide (obtained from the saccharin plant) (88) and active manganese dioxide prepared in the laboratory.(75)

(a) Dry manganese dioxide (13g.; 0.15M.) and o-toluenesulphonamide (5g.; 0.03M.) were mixed with dry benzene in a 250ml. flask fitted with a reflux condenser. The mixture was heated under reflux and agitated by a mechanical stirrer for a period of 83 hr. During this time, aliquots (5ml.) were taken from the reaction vessel at various intervals. The manganese dioxide was removed by centrifugation and each aliquot was examined by thin layer chromatography (solvent system A). All showed a single spot at 0.95, equivalent to starting material.

(b) Dry manganese dioxide (13g.; 0.15M.) and o-toluenesulphonamide (5g.; 0.03M.) were mixed with dry petroleum ether (100-120°; 150 ml.). The mixture was heated and stirred under reflux for 44.5 hr. The reaction mixture was filtered whilst hot and the residual manganese dioxide was washed with hot alcohol. The filtrate and washings were examined by thin layer chromatography (solvent system A) and showed a single spot at R_f=0.96which was concurrent with o-toluenesulphonamide. The solvent was removed and the residue was shown to be unchanged starting material, m.p. 153°C. (lit. (93) m.p. 153-156°C.).

(c) Dry manganese dioxide (13g.; 0.15M.) and o-toluenesulphonamide (5g.; 0.03M.) were heated together under reflux with petroleum ether (100-120°; 200 ml.). During the reaction, air at a

pressure of 0.5 p.s.i. was passed through the mixture. The reaction was continued for 24 hr. It was found necessary to use a very efficient condenser system to prevent the loss of solvent. The mixture was filtered whilst hot; the residual manganese dioxide was washed with hot alcohol and the filtrate and washings were examined by thin layer chromatography (solvent system A). A single spot equivalent to starting material was recorded at R_f=0.91. The solvent was removed and the residue material examined, m.p. 154°C. (Lit.(93) m.p. 153-6°C.).

Reactions of o-toluenesulphonamide with manganese dioxide in acidic media.

Reactions in acidic media were carried out using manganese dioxide prepared by acid-wash of material obtained from the saccharin plant.

1. Glacial acetic acid.

(a) o-Toluenesulphonamide (5g.; 0.03M.) and dry manganese dioxide (13g.; 0.15M.) in glacial acetic acid (150 ml.) were kept at room temperature with stirring for 72.5 hr. Four aliquots (5 ml.) were removed from the reaction vessel at suitable intervals and the solid manganese dioxide was removed by centrifugation. The aliquots were examined by thin layer chromatography (solvent system A) and showed a single spot at R_f=0.98 identical with starting material.

(b) Dry manganese dioxide (13g.; 0.15M.) and o-toluene-sulphonamide (5g.; 0.03M.) were stirred together in glacial acetic acid (150 ml.) under reflux for 82.5 hr., during which time 6 aliquots (5 ml.) were removed, filtered and the filtrates

examined by thin layer chromatography (solvent system A). Each aliquot showed a single spot at R_f=0.99 equivalent to o-toluenesulphonamide.

2. Hydrochloric acid.

Manganese dioxide (5.2g.; 0.06M.) and o-toluenesulphonamide (5.0g,; 0.03M.) were mixed together in a 150ml. flask fitted with a reflux condenser. After the initial, vigorous, reaction had subsided, the mixture was heated under reflux for 3.5 hr. in a fume hood; chlorine was liberated during the reaction. The reaction mixture was cooled and filtered, the filtrate was neutralised with sodium hydrogen carbonate solution and then the solution was evaporated to dryness. The solid residue was extracted with boiling alcohol and examined by thin layer chromatography. A single spot was shown at R_f=0.91 (starting material).

3. Sulphuric acid.

(a) o-Toluenesulphonamide (5g.; 0.03M.) and dry manganese dioxide (5.2g.; 0.06M.) were mixed thoroughly in a 100 ml.flask fitted with a reflux condenser. To this mixture, sulphuric acid (98% $^{w}/_{w}$; 50 ml.) was added in small portions (5 ml.). After the vigorous reaction had subsided, the mixture was heated under reflux for 30 min. The mixture was cooled and the charred and blackened mass was discarded.

(b) Dry manganese dioxide (5.2g.; 0.06M.) and o-toluene-sulphonamide (5.0g.; 0.03M.) were intimately mixed and placed in a 100ml. flask fitted with a reflux condenser. Sulphuric acid (50% $^{v}/_{v}$; 60 ml.) was added in small portions (5ml.) and

after the initially vigorous reaction had subsided, the mixture was heated under reflux for 45 min. The mixture was cooled and filtered under vacuum, leaving a buff-coloured residue which was washed with hot alcohol. The yellow filtrate was brought to pH6 by addition of sodium hydrogen carbonate solution. The filtrate was then evaporated to dryness by rotary evaporation. The resulting material was ground to a fine powder and extracted with boiling chloroform from which extract, a yellow syrup was obtained on evaporation. The infra-red spectrum of this material showed absorptions at the following $\nu_{max.}$:- 3600-2550 (b,s), 3420 (w), 3200 (w), 2630(w), 1720 (s), 1665(m), 1650 (sh), 1610 (m), 1570 (m), 1330 (w), 1300 (w), 1265(m), 1185 (m), 1150 (s), 1130 (m), 1120 (w), 1090 (sh), 1055(w), 1040 (w), 960(w), 940 (w), 900 (m), 855(m), 810 (sh), 770 (sh), 760 (m), 715 (m), 670 (m).

(c) Dry manganese dioxide (2.6g.; 0.0 M.) and o-toluene-sulphonamide (2.5g.; 0.015M.) were mixed thoroughly and treated with sulphuric acid (50% v/v; 20 ml.) in small portions (4ml.). The mixture was cooled throughout the addition of the sulphuric acid. A purple colouration was noted during the addition of the acid, this being dispersed, when the reaction mixture was gently heated, to yield a yellow solution and a buff-coloured precipitate. The precipitate was separated by filtration and the organic material was removed by exhaustive extraction with chloroform to give, on evaporation of the solvent, an orange oil. Neutralisation of the aqueous layer with sodium hydrogen carbonate and

subsequent extraction with chloroform, yielded no more material. Examination of the oil by thin layer chromatography (solvent system A) showed four spots to be present at the following values:-R_f=1.0; R_f=0.82; R_f=0.65 and R_f=0. Starting material run concurrently travelled with the solvent front.

(d) Investigation of the purple colouration.

Nine boiling tubes were each charged with dry manganese dioxide (0.1g.), o-toluenesulphonamide (0.1g.) and cold sulphuric acid (50% $^{v}/_{v}$; 5 ml.). The tubes were placed in a thermostatted water-bath at 90°C. and the first tube was removed as soon as the temperature of the contents had reached 90°C. Tubes were removed from the bath at increasing intervals of time up to 4.5 hr. and all were cooled in iced-water upon removal. The first four tubes were found to contain a purple material, the fifth a clear solution whilst the last four tubes contained a yellow solution. Each sample was diluted with water, whereupon the purple colour was dispersed from the first four to yield manganese dioxide. The solutions were extracted with ether and examined by thin layer chromatography (solvent system A). The first four samples showed a single spot at R_f=0.96; whilst the remainder showed two spots:- R_f=0.96 and a baseline spot. o-Toluenesulphonamide run concurrently showed a spot at R_f=0.96.

(e) Dry manganese dioxide (15.2g.; 0.17M.) and o-toluenesulphonamide (10g.; 0.06M.) were intimately mixed in a 250 ml. flask fitted with a reflux condenser and a dropping funnel. Sulphuric acid (50% $^{v}/_{v}$; 100 ml.) was added dropwise until the vigorous reaction had subsided and then rapidly until all had been added. The

reaction mixture was warmed under reflux for 1 hr. further. The mixture was cooled and filtered under vacuum to remove the buff precipitate from the yellow solution. The residue was washed thoroughly with hot alcohol and the combined washings and filtrate were reduced in volume by evaporation of water and alcohol. The solution was neutralised with sodium hydrogen carbonate solution, evaporated to dryness and extracted with boiling alcohol. Removal of the solvent left a brown solid which contained the following six components as shown on thin layer chromatography (solvent system B.):- R_f=0.99; R_f=0.90; R_f=0.77; R_f=0.68; R_f=0.51 and a baseline spot. Authentic samples of o-toluenesulphonamide R_f=0.90; saccharin, R_f=0.51 and o-sulphonamidobenzoic acid, R_f=0.31 were run concurrently (see Plate 1). The spots were only developed with difficulty as they would not char with concentrated sulphuric acid, nor would they react with phosphomolybdic acid.

(f) Dry manganese dioxide (1.52g.; 0.017M.) and o-toluenesulphonamide (1.0g.; 0.006M.) were mixed thoroughly in a 100ml. flask fitted with a reflux condenser. Sulphuric acid (25%$^{v}/_{v}$, 25 ml.) was added and the mixture was heated under reflux for 90 min. to give a clear pink solution. The reaction mixture was cooled and filtered and the residue was washed with alcohol. The filtrate and washings were neutralised with aqueous sodium hydrogen carbonate and filtered to remove more precipitated manganese sulphate. The filtrate was evaporated to dryness and extracted with hot alcohol. Examination by thin layer chromatography (solvent system B) showed the following

three spots :- R_f=0.85 (o-toluenesulphonamide ran concurrently); R_f=0.11 and a baseline spot. The major spot was that at R_f=0.85.

(g) Dry manganese dioxide (7.7 g.; 0.085M.) and o-toluenesulphonamide were mixed thoroughly and sulphuric acid (10% v/v, 50 ml.) was added. The mixture was refluxed for 60 min., cooled and the unreacted manganese dioxide was filtered from the mixture. The solid was washed with alcohol and the combined washings and filtrate were neutralised with sodium hydrogen carbonate solution. The solution was evaporated to dryness and the residue was extracted with boiling acetone. The material was found to contain only starting material by thin layer chromatography (solvent system A).

Oxidation of Toluene.

Dry manganese dioxide (5g.; 0.058 M.) and dry toluene (5g.; excess) were added to a 250 ml. flask fitted with a reflux condenser and dropping funnel. Sulphuric acid (50% v/v; 50 ml.) was added slowly until the vigorous reaction subsided; the remainder of the acid was added and the mixture was heated to reflux for 2 hr. The mixture was cooled, the manganese sulphate was separated from the solution by filtration and washed with chloroform. The filtrate was diluted with water and extracted with chloroform. The combined chloroform layers were dried and examined by gas-liquid chromatography on a silicon oil (S.E.-30) column at 150°C. Two peaks were recorded with retention times of 2.55 min. and 3.3 min. (major peak) respectively. (Benzaldehyde, retention time 2.55 min. and benzyl alcohol, 3.83 min.). On a dinonyl phthalate column at 100°C., the mixture showed peaks after 14.1 min. and 22.2 min. (major peak);

benzaldehyde, 14.19 min.; and benzyl alcohol, 36.3 min. The chloroform layer was shaken with aqueous sodium hydrogen carbonate. Acidification yielded a white solid, m.p. 117-119°C, (Lit. (93) m.p. 122°C.+ benzoic acid).

Attempted catalytic oxidation reactions with toluene and o-toluenesulphonamide.

(a) Dry manganese dioxide (0.1g.), o-toluenesulphonamide (1.0g.) and fusion mixture (50% sodium carbonate, 50% potassium carbonate; 0.1g.) were melted together at 180°C. in a small flask suspended in an oil-bath. The bath was maintained at that temperature for 2 hr. and then cooled to room temperature. The mixture was removed and ground to a fine powder, extracted with hot alcohol and examined by thin layer chromatography (solvent system A). A single spot was shown at the solvent front; starting material ran concurrently.

(b) Reaction (a) was repeated using o-toluenesulphonamide (10g.) and air, which was slowly metered through the molten mixture. After cooling and subsequent separation, only o-toluenesulphonamide was shown to be present by thin layer chromatography (solvent system A).

(c) Reaction (b) was repeated employing benzoyl peroxide (0.1g.) as a free-radical initiator. As before, only o-toluenesulphonamide was identified by thin layer chromatography (solvent system A).

(d) Potassium permanganate (0.05g.) and o-toluenesulphonamide (5g.) were heated together in a glycerol-bath at 180°C. for

2.5 hr. Air was slowly metered through the molten mixture throughout the duration of the reaction. On cooling, the mixture was ground to a fine powder and extracted with boiling chloroform. Examination by thin layer chromatography (solvent system A) showed a single spot at R_f=0.92; equivalent to starting material.

(e) The glass container of a Cookes rocking hydrogenator apparatus was charged with o-toluenesulphonamide(5g.) and p-cymene (100ml.). The container was placed in the hydrogenator and the temperature was set and maintained at 70°C. The expansion cylinder was filled with compressed-air to a pressure of 15 p.s.i. and the mixture was shaken for 14 hr. during which time, the pressure dropped to 1 p.s.i. The mixture was removed from the apparatus, cooled and the solvent distilled by rotary evaporation. The solid residue was o-toluenesulphonamide (infra-red spectrum);m.p.=154°C. (Lit.(92) m.p.=153 - 156°C.)

(f) Dry toluene (100 ml.) was placed in the glass container of the Cookes hydrogenator with potassium permanganate (0.1g.) and acetone (1 ml.). The mixture was shaken at 60°C. for 17.5 hr. with an atmosphere of oxygen at a pressure of 15 p.s.i. No uptake of oxygen was recorded and vapour chromatography showed that only toluene was present.

(g) Manganese stearate (1g.) was dissolved in dry toluene (100ml.) and placed in the Cookes hydrogenator. The mixture was shaken for 44 hr. at room temperature under an atmosphere of oxygen at a pressure of 15 p.s.i. During the reaction, a

pressure drop of 5 p.s.i. was recorded. The mixture was examined by gas-liquid chromatography and shown to contain only toluene.

(h) Ferric stearate (1g.) and dry toluene (100 ml.) were treated as for procedure (g). The reaction was continued for 47.5 hr. in which time a drop in pressure of 5 p.s.i. was recorded. Only toluene was found by g.l.c.

(i) Manganese stearate (0.1g.), benzoyl peroxide (0.1g.), o-toluenesulphonamide (1g.) and water (150 ml.) were placed in the Cookes hydrogenator. The mixture was shaken at room temperature for 48 hr. under an atmosphere of oxygen at 15 p.s.i. pressure. During the reaction, no drop in pressure was recorded and upon subsequent examination by thin layer chromatography (solvent system A), only o-toluenesulphonamide was found; R_f=0.91.

(j) Ferric stearate (0.1g.), benzoyl peroxide (0.1g), o-toluenesulphonamide (1g.) and water (150 ml.) were reacted as for procedure (i). The reaction was continued for 48 hr. in which time no drop in pressure was recorded. Examination of the mixture by thin layer chromatography (solvent system A) showed a single spot at R_f=0.93 concurrent with starting material.

(k) Attempted anionic base catalysed reaction.

Hexamethylphosphoramide (100 ml.) was placed in a 250ml. conical flask with o-toluenesulphonamide (4.3g.; 0.025M.) and freshly prepared potassium t-butoxide (7.9g.; 0.07M.) (94). The flask was stoppered with an inlet device which

allowed an atmosphere of oxygen to be maintained above the solution. (The oxygen was metered by a constant head reservoir system). The mixture was stirred magnetically and maintained at 70°C. throughout the experiment which lasted for 1 week. The mixture was distilled to remove hexamethylphosphoramide and t-butanol, leaving a yellow oil which showed the following spots on examination by thin layer chromatography (solvent system A):- R_f=0.92; R_f=0.2 and a baseline spot. The major spot was due to starting material, R_f=0.92.

Reaction of toluene with silver II picolinate.

(a) Toluene (0.92g.; 0.01M.), argentic picolinate (7.0g.; 0.02M.) and aqueous dimethyl sulphoxide (50% $^{v}/_{v}$; 20 ml.) were warmed at 70°C., under reflux, for 60 min. The mixture was acidified with hydrochloric acid (2N) and the residual silver material was removed by filtration. The filtrate was diluted with water (50 ml.) and extracted with chloroform. Examination of the extract by gas-liquid chromatography showed only benzyl alcohol to be present.

(b) Benzyl alcohol (1.1g.; 0.01M.), argentic picolinate (7.0g.; 0.02M.) and aqueous dimethyl sulphoxide (50% $^{v}/_{v}$; 20ml.) were warmed under reflux at 65°C. for 15 min. The mixture was acidified with hydrochloric acid (2N), cooled and argentous material was separated by filtration. The filtrate was diluted with water (50ml.) and extracted with chloroform. Examination of the extract by g.l.c. showed only benzaldehyde to be present.

(c) Benzaldehyde (1.1g.; 0.01M.), silver II picolinate (7.0g.; 0.02M.) and aqueous dimethyl sulphoxide (50%$^{v}/_{v}$; 2 ml.) were heated under reflux at 70°C. for 45 min. The mixture was acidified with hydrochloric acid (2N), cooled and the solid was separated by filtration. The filtrate was diluted with water (50 ml.) and extracted with chloroform. The extract was washed thoroughly with aqueous sodium hydrogen carbonate and separated. The aqueous layer was acidified with hydrochloric acid (2N) and the precipitate was extracted with chloroform to yield a white solid, m.p.=119°C. A mixture of this material with authentic benzoic acid, m.p.=119-120°C. (Lit.(93) m.p.=122°C.).

Reaction of o-toluenesulphonamide with silver II picolinate.

Argentic picolinate (14 g.; 0.04M.), o-toluenesulphonamide (1.2g.; 0.007M.) and water (300 ml.) were heated at 70°C. for 3 hr. (The mixture was stirred continually throughout the reaction. The mixture was acidified with hydrochloric acid (2N), cooled and the precipitate was separated by filtration. The filtrate was evaporated and the residue was extracted with hot chloroform. Removal of the solvent showed only starting material to be present (infra-red spectrum).

Spectral Data.

o-Toluenesulphonamide.

I.R.spectrum showed absorption at the following $\nu_{max.}$ (cm^{-1}):- 3405 (s), 3280 (s), 3110(m), 3070 (w), 2600 (w), 1995 (w), 1910 (w), 1830 (w), 1600 (w), 1565 (w), 1470 (m), 1455 (sh), 1415 (w), 1385 (w), 1315 (s), 1290 (m), 1280 (w),

1200 (w), 1165 (m), 1155 (s), 1135 (m), 1070 (m), 1050 (w), 955 (w), 920 (m), 875 (w), 805 (w), 770 (s), 760 (m), 710 (m) and 695 (m).

P.m.r. spectrum measured in hexa-deuteroacetone showed signals at the following tau values:- 2.1 (m), 1 proton; 2.6 (m), 3 protons; 3.5 (broad (s.), 2 protons; 7.35 (s), 3 protons.

Saccharin.

I.R. spectrum showed absorption at the following $\nu_{max.}$ (cm^{-1}) 3425 (w), 3110 (s,b), 3000 (s,b), 2700 (m,b), 1990 (w), 1825 (w), 1730 (s,b), 1595 (m), 1465 (m), 1460 (w), 1400(m), 1350 (s,b), 1320 (sh), 1295 (m), 1260 (s), 1180 (s), 1165 (w), 1140 (s), 1120 (s), 1055 (m), 1015 (m), 1005 (m), 970 (m), 900 (s), 795 (m), 775 (m), 760 (s), 705 (s) and 630 (m).

P.m.r. spectrum recorded in dimethyl sulphoxide showed signals at the following tau values :- -3.05 (s), 1 proton; 1.98 (m), 4 protons.

o-Sulphonamidobenzoic acid.

I.R.spectrum showed absorption at the following $\nu_{max.}$ (cm^{-1}):- 3550 (sh), 3380 (m), 3275 (m), 3120 (w), 2635 (w), 2490 (w), 1965 (w), 1835 (w), 1715 (s,b), 1650 (sh), 1590 (m), 1580 (m), 1545 (m), 1475 (m), 1440 (m), 1395 (s), 1340 (s), 1330 (s), 1300 (w), 1270 (w), 1250 (s), 1160 (s), 1120 (m), 1065 (m), 1050 (w), 970 (w), 910 (m), 895 (w), 865 (w), 810 (m), 800 (m), 760 (s), 720 (m), 690 (w) and 650 (s).

P.m.r. spectrum recorded in hexadeuteroacetone showed signals at the following tau values :- o (broad s), 1 proton;

1.9 (m), 2 protons; 2.2 (m), 2 protons; 3.4 (broad s), 2 protons.

Hexamethylphosphoramide.

I.R. spectrum showed absorption at the following $\nu_{max.}$ (cm^{-1}):- 3010 (w), 2930 (sh), 2890 (s,b), 2850 (w), 2810 (m), 1510 (sh), 1485 (w), 1460 (s), 1355 (w), 1300 (s), 1210 (s), 1170 (sh), 1150 (w), 1135 (sh), 1110 (w), 1070 (m), 980 (s,b), 925 (w), 805 (w), 745 (s) and 690 (w).

P. m.r. spectrum recorded in carbon tetrachloride showed a signal at the following tau value :- 7.36 (d, J=10 c.p.s.) 18 protons.

SECTION II

A study of the reactions of the silver II oxidation state with organic compounds.

INTRODUCTION.

The role of silver as an oxidising agent for use in organic chemistry has been appreciated for some considerable time (95); but within the last few years silver, along with most other transition metal ions, has been examined in more detail. The monovalent (argentous) ion has been used in the form of the oxide (96) and as the nitrate in ammoniacal solution (97), to bring about mild oxidation reactions. However, attention of late has been focused on the silver II and silver III oxidation states which are potentially more powerful reagents.

Marshall (98) in 1891 noted the effect of catalytic amounts of Ag^{+} ions in aqueous solutions of potassium persulphate. He found that a small amount of the argentous ion enhanced the powerful oxidising nature of the persulphate solution and increased its potential as a reagent markedly. The solution chemistry becomes complex but the simplified equations 23-25, probably summarise the mode of action. Hence sulphate radical-ions and

$$S_2O_8^{2-} + Ag^{+} \longrightarrow SO_4^{\cdot -} + SO_4^{2-} + Ag^{2+} \quad \ldots\ldots\ldots 23 .$$

$$SO_4^{\cdot -} + Ag^{+} \longrightarrow SO_4^{2-} + Ag^{2+} \quad \ldots\ldots\ldots\ldots\ldots\ldots 24$$

$$SO_4^{\cdot -} + H_2O \longrightarrow SO_4^{2-} + HO^{\cdot} + H^{+} \quad \ldots\ldots\ldots\ldots\ldots 25$$

hydroxyl radicals are produced and the increased efficiency of the mixture can be attributed to the production of argentic ions which are probably the main oxidising species. Studies

of this system have been applied to inorganic reactions (99) and extensively to organic chemistry (100-106). Recently Bacon has studied the reactions of Ag^{+}/persulphate ion mixtures with primary and secondary amines and α-amino acids (106) to yield carbonyl compounds, and the oxidative decarboxylation of acids (100,101). In all of these reactions, he reports the reagent to be efficient.

The powerful oxidising nature of Ag^{II}, which must be attributed to its $4d^{9}$ electronic configuration, can also be employed in catalytic amounts by setting up a silver electrode system (107) in alkaline solution; the argentic state being produced transiently at the electrode. Measurement of the electrode potential in 4M. $HClO_4$ at 25°C.(108), indicates the power of silver II as an oxidant (equation 26).

$$Ag^{+} \rightleftharpoons Ag^{2+} + e^{-}, \quad E^{\circ} = -2.00 \text{ V.}(25^{\circ}\text{C.}) \ldots\ldots 26$$

To study the potentialities and the mechanism of reaction of the silver II state, it is necessary to study the effect of the ion without interference from persulphate ions or other species of oxidising ability. Hence it is convenient to stabilise the higher oxidation state by complex formation, although this must have some effect on its redox potential. Bases, such as pyridine and the picolines (109), have been used to give complexes of the type $[Ag.Py_4]^{2+}$; in the presence of α-picolinic acid however, a red-orange complex is formed. This complex has been prepared (110) by the action of potassium persulphate on aqueous solutions of argentous picolinate, when the argentic compound separates. The complex

has been shown to have a square-planar structure (Fig.2) by X-ray crystallography (111) and its stability in aqueous suspension, acid media and cold ammonia solution has been studied (112). With cold aqueous ammonia, a vigorous reaction ensued in which nitrogen was evolved (see equation 27); however only approximately 14% of the theoretical quantity of ammonia is oxidised and therefore equation 28 is probably more representative of the overall reaction. Reaction of the complex with hydrogen peroxide, benzidine, antimony trichloride and methanol (113) and amines (112, 114) show it to be a powerful oxidising agent.

$$6Ag^{2+} + 2NH_3 \longrightarrow 6Ag^{+} + N_2 + 6H^{+} \quad \ldots\ldots\ldots\ldots\ldots\ldots 27$$

$$6Ag^{2+} + 14NH_3 \longrightarrow 6[Ag(NH_3)_2]^{+} + 6H^{+} \quad \ldots\ldots\ldots\ldots\ldots 28$$

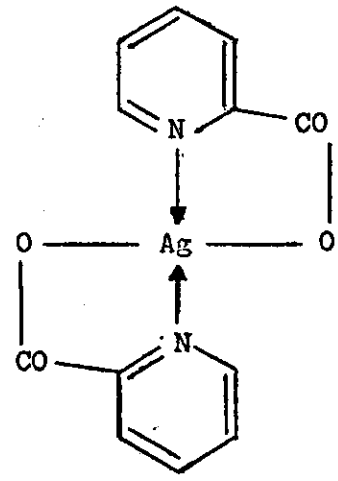


Fig.2.

Oxidation by argentic picolinate will depend on the ability of the material, under investigation, to displace α-picolinic acid as the ligand in the complex (115); and on the fact that

the material may complex with the Ag^{I} formed, thus prohibiting further reaction. It has also been suggested that the type of solvent influences the yield of the product and reactions involving the complex in aqueous solution and polar organic solvents have been examined (112).

The higher oxidation state(s) of silver can also be stabilised by formation of silver oxide (116). It was originally considered that this compound was a mixture of the Ag^{I} and Ag^{III} oxides which analysed as AgO; but Scatturin, et al. (117) have shown by neutron diffraction, that it has a monoclinic lattice structure involving both silver I and silver III bonded to oxygen. This oxide, referred to throughout this section as silver II oxide, has been shown by Lingane and Davis (118) to be a powerful reagent for the oxidimetric determination of Mn^{2+}, Ce^{2+} and Cr^{3+} ions in solution. Dirkse (119) has measured the standard potential of the $AgO/Ag_2O/OH^-$ electrode system against a hydrogen electrode and finds the value to be 0.599 ± 0.001 V. at $25^{\circ}C$. However, little work has been carried out using silver II oxide for organic oxidation reactions, although a preliminary report of its use in acidic media has recently appeared (120).

Experiments have been designed to show the potential value of argentic picolinate and silver II oxide in neutral (aqueous) solution, as oxidising reagents for use in preparative organic chemistry. The results of these experiments are discussed in this section.

RESULTS AND DISCUSSION.

The reactions reported and discussed in this section were carried out to establish the use of the silver II oxidation state as a preparative reagent for use in organic chemistry. Reactions were examined with various functional groups in an attempt to show the types of product formed and their yields. In addition, some relative rates of reaction are reported together with a simple kinetic investigation, but the thesis does not set out to discuss precise mechanisms of oxidation or the absolute kinetics and therefore sophisticated physico-chemical measurements were not made.

A.1. THE REACTION OF ARGENTIC PICOLINATE WITH ALCOHOLS.

The procedure developed for the oxidation of alcohols by argentic picolinate is a simple one. The alcohol (1 mole) and the oxidant (2 moles) were stirred together in the form of an aqueous suspension at an optimised temperature of 70°C. A stream of nitrogen was passed slowly through the reaction mixture and any volatile material was swept over into a trap containing 2,4-dinitrophenylhydrazine (2,4-D.N.P.) reagent. The products were isolated and examined as their 2,4-D.N.P. derivatives. The non-volatile products were isolated by treating the cooled reaction mixture with dilute acid, removal of the inorganic salts and then extraction with an organic solvent. The reaction can be conveniently followed by the colour change red-orange to white which accompanies the reduction of the silver from the argentic to the argentous state.

The results of the reactions carried out at 70°C. in water with many alcohols are recorded in tables 3 and 4.

Primary aliphatic alcohols were oxidised to the corresponding aldehyde, secondary alcohols to the ketone and substituted benzyl alcohols to the equivalent benzaldehyde; all alcohols were oxidised to give good to excellent yields of the carbonyl compound. The reaction was found to proceed smoothly at 70°C. and the time for reaction was generally one to two hours. The results show that the yields of the low molecular weight aldehydes and ketones were very high and may well be quantitative if the method of isolation of the product is optimised. With increase in chain length of the alcohol progressively lower yields of the product were obtained and this might be accounted for by further oxidation to the carboxylic acid in the case of primary alcohols. The removal of the aldehyde from the mixture as it was formed would tend to eliminate the possibility of "over-oxidation" but as the products became less volatile with increase in molecular weight this is not very easy to achieve. Benzyl alcohols were converted to the expected benzaldehyde in high yields even though the products were not removed from the reaction mixture, but it is well accepted that aromatic aldehydes are more stable to further oxidation than those of the aliphatic series. Hence, the general reaction between an alcohol and argentic picolinate may be written as in equation 29

$$2\ Ag\ (pic.)_2 + R_2CH.OH \longrightarrow R_2C{=}O + 2\ Ag\ (pic.) + 2\ pic.{-}H \quad ...29$$

where pic. = picolinate

THE OXIDATION OF ALCOHOLS BY ARGENTIC PICOLINATE AT 70°C IN WATER.

ALCOHOL	YIELD(%)	PRODUCT
Methanol	80	Formaldehyde
Ethanol	77	Acetaldehyde
n-Propanol	71	Propionaldehyde
iso-Propanol	79	Acetone
n-Butanol	76	n-Butyraldehyde
iso-Butanol	57	iso-Butyraldehyde
sec-Butanol	68	Methylethyl ketone
n-Pentanol	74	n-Pentanaldehyde
iso-Pentanol	61	iso-Pentanaldehyde
neo-Pentanol	70	Pivalaldehyde
n-Hexanol	69	n-Hexanaldehyde
Cyclohexanol	66	Cyclohexanone
2-Ethyl-n-hexanol	52	2-Ethyl-n-hexanaldehyde
n-Heptanol	54	n-Heptanaldehyde
n-Decanol	68	n-Decanaldehyde
DL-1-Phenylethanol	73	Acetophenone
DL-2-Phenylethanol	61	Phenylacetaldehyde
Benzhydrol	80	Benzophenone
Borneol	79	Camphor
iso-Borneol	53	Camphor
2-Ethoxyethanol	53	2-Ethoxyacetaldehyde
Tetrahydrofurfuryl alcohol	62	Tetrahydrofurfuraldehyde

Table 3.

THE OXIDATION OF SUBSTITUTED-BENZYL ALCOHOLS BY ARGENTIC PICOLINATE AT 70°C. IN WATER.

ALCOHOL	TIME (Hours)	PRODUCT	YIELD (%)
p-Nitrobenzyl alcohol	2.5	p-Nitrobenzaldehyde	84
Benzyl alcohol	1.1	Benzaldehyde	79
p-Methoxybenzyl alcohol	0.42	Anisaldehyde	87
3,4-Dimethoxybenzyl alcohol	0.08	Veratraldehyde	83
Piperonyl alcohol	0.12	Piperonaldehyde	77

Table 4.

Measurement of the electrode potential of the systems H^+,pic.$^-$/Ag^{I}(pic.)$_{(s)}$,Ag and H^+,pic.$^-$/Ag^{II}(pic.)$_{2(s)}$,Ag at 25°C. and pH.5, gave values of 0.694 V. and 0.720 V. respectively (121). These values are not the oxidation potentials of the systems but they are a measure of the change in free energy of the systems under conditions of reversible equilibrium. Organic reactions are mostly non-reversible in the sense implied above therefore the values quoted are only an indication of the oxidising power of silver II picolinate. In the introduction to this section a value of E°= -2.00 V. (25°C.) was quoted for the $Ag^+ \rightleftharpoons Ag^{2+} + e^-$ equilibrium. This value is so high that silver II compounds are rarely stable; immediate oxidation of the anion by the silver II cation often occurring; however, complex formation with ligands such as picolinic acid lowers the oxidation potential considerably. Although silver II picolinate can be considered to be a powerful oxidising agent, it does not follow that it is a non-selective oxidant. The Ag^{2+} ion has the outer-orbital electronic configuration of $4d^9$ which suggests that to gain the stability of the complete ($4d^{10}$)orbital, it will participate in any one-electron transfer process. Completion of the 4d-orbital partially stabilises the silver moiety, especially when complexed to a ligand such as picolinate and reduction of the argentous ion to elemental silver and hence further oxidation of any organic material becomes less likely.

The results shown in tables 3 and 4 indicate the wide application of the reagent and emphasises the limitations of other methods available for the preparation of aldehydes from primary alcohols. Aldehydes are very valuable intermediates in organic syntheses but because of their reactivity, they are often difficult to prepare. They occupy a central position in the series of oxidation levels for organic compounds and hence they readily undergo oxidation to the corresponding carboxylic acid. Other methods for the oxidation of primary alcohols to aldehydes suffer the disadvantages of either low yields of product or difficulty in the isolation of the product. Hence chromic acid oxidations (72) may give good yields of the aldehyde, but employs severe acid conditions, and leads to the formation of esters unless the product is removed from the mixture continuously (122). The use of chromium trioxide or t-butyl chromate in pyridine (123) is more successful but can prove hazardous; whilst the strongly basic conditions of the Oppenauer oxidation give rise to condensation and polymerisation of the product (124). Benzylic and allylic alcohols have been oxidised by manganese dioxide (81) and the oxidation of aliphatic primary alcohols can be brought about if a large excess of the oxidant is employed (80, 125); see also section I. Many other oxidants have been used including ruthenium tetraoxide (126), lead tetra-acetate (127, 128), mercuric acetate (128), thallic acetate (128), nickel peroxide (129), selenium dioxide (130), nitrogen tetraoxide (131), ceric ammonium nitrate (132), potassium

hypochlorite in methanol (133), iodosobenzene (134) and N-bromosuccinimide in carbon tetrachloride (135); but with the exception of iodosobenzene (134) they are often only useful for the oxidation of benzylic alcohols. Consequently, the reaction of argentic picolinate with aliphatic alcohols is of considerable importance for the synthesis of aliphatic aldehydes (136).

Tables 5 and 6 record the results of the reactions of alcohols with argentic picolinate at 40°C. in aqueous dimethyl sulphoxide (DMSO). These results list the time of reaction; in these particular experiments products were never isolated. Comparison of the reaction times, for ethanol for example, given in table 5 and table 6 shows the effect of stirring the mixture. It can be seen that the time of reaction was shortened by 6.5 hours when the reaction mixture was shaken such that the oxidant and alcohol were kept continually mobile. The effect of adding DMSO to the reaction mixture is also to shorten the reaction time, presumably by increasing the homogeneity of the mixture. However, it was found that at 70°C., the reactions proceeded very satisfactorily with water only as solvent and the isolation of the products is simplified; therefore the use of DMSO as co-solvent was discontinued.

THE RATE OF REACTION OF ARGENTIC PICOLINATE WITH ALCOHOLS AT 40°C. IN AQUEOUS DMSO.

ALCOHOL	TIME (Hours).
Cyclohexanol	8
Ethanol	16.5
4-Methylcyclohexanol	22.5
3,5-Dimethylcyclohexanol	24
2,5-Dimethylcyclohexanol	25.5
2,3-Dimethylbutan-2-ol	50
3-Methylcyclohexanol	50
2-Methylcyclohexanol	Partially after 96
3-Methylbutan-1-ol	" " "
2,2-Dimethylbutan-3-ol	" " "

Table 5.

THE RATE OF REACTION OF ARGENTIC PICOLINATE SHAKEN WITH ALCOHOLS AT 40°C. IN AQUEOUS DMSO.

ALCOHOL	TIME (Hours).
Benzyl alcohol	8
Ethanol	10
n-Propanol	12
iso-Propanol	14
2-Butoxyethanol	14
Tetrahydropyran-2-carbinol	17
n-Butanol	22
iso-Butanol	23
n-Pentanol	24
iso-Pentanol	26
sec-Butanol	30.5
2-Acetoxyethanol	32
t-Butanol	No reaction after 50.

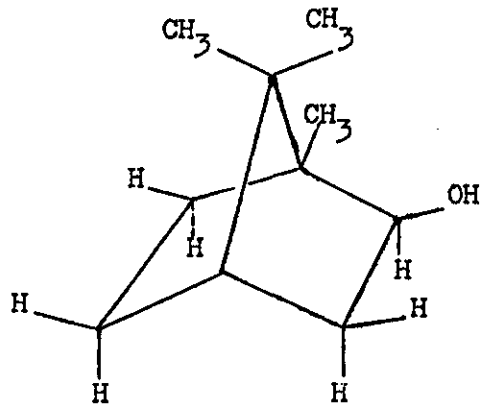
Table 6.

From the results in table 5, the effect of substitution of cyclohexanols on the rate of the reaction with argentic picolinate can be appreciated. The rate of reaction of 4-methylcyclohexanol was markedly reduced (by comparison with cyclohexanol) and this alcohol was the least sterically hindered

of the series examined. Table 7 shows the relative rates of oxidation of substituted cyclohexanols and it can be seen that as the site of oxidation (i.e. the hydroxyl group) becomes more crowded with substituent groups, the rate of reaction decreases. Little more can be said about these reactions as the alcohols examined were mixtures of the cis and trans isomers.

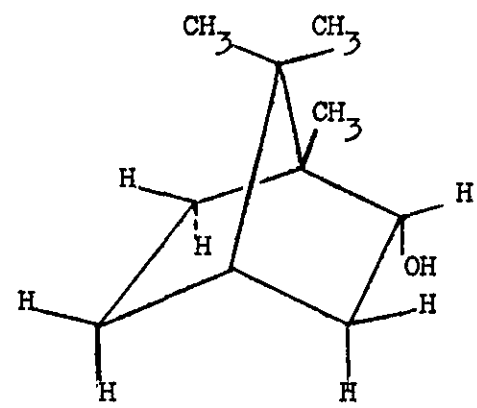
The results of reactions carried out at 40°C. showed clearly the effect of chain length and chain-branching on the rate of reaction; at 70°C. in water the rates were so fast that these effects could not be observed easily. The relative rates of some alcohol oxidations (with ethanol = 100, as standard) have been calculated and are presented in table 8. These results show that the rate of reaction decreases with the increase in carbon number for aliphatic alcohols and that secondary alcohols react more slowly than primary alcohols of equivalent size. Tertiary alcohols react very much more slowly than secondary alcohols and this decrease in reactivity from primary to secondary alcohols can be explained by the increase in steric hindrance at the hydroxyl group carbon atom. In the case of tertiary alcohols oxidation requires breakage of C-C bonds. The effect of steric hindrance on the rate of reaction is very clearly shown by the relative rates of oxidation of borneol and iso-borneol (table 8). By reference to fig.3, the stereo-chemistry of the compounds can be seen to be such that oxidation of iso-borneol would be expected to be slower than borneol because of the greater steric hindrance at the

hydroxyl group. This was shown to be the case, borneol was



iso-borneol

(exo-isomer)



borneol

(endo-isomer)

Fig.3

oxidised at quadruple the rate of iso-borneol. The relative rates of reaction of some alcohols containing a β-alkoxy- or β-acyloxy group are recorded in table 9 (relative to ethanol=100) and it can be seen that the rate of oxidation of 2-ethoxyethanol was twice that of n-pentanol (table 8) which is about equivalent in molecular size, whereas 2-acetoxyethanol was oxidised more slowly.

THE RELATIVE RATES OF REACTION OF SUBSTITUTED CYCLOHEXANOLS WITH ARGENTIC PICOLINATE.

ALCOHOL	RELATIVE RATE *
Cyclohexanol	100
4-Methylcyclohexanol	35
3,5-Dimethylcyclohexanol	33
2,5-Dimethylcyclohexanol	31

* Rate relative to cyclohexanol=100; at 40°C. in aqueous DMSO.

Table 7.

THE RELATIVE RATE OF OXIDATION OF ALCOHOLS BY ARGENTIC PICOLINATE.

ALCOHOL.	RELATIVE RATE*
Ethanol	100
n-Propanol	84
iso-Propanol	72
2-Butoxyethanol	72
Borneol	47
n-Butanol	46
n-Pentanol	44
iso-Pentanol	42
sec-Butanol	38
iso-Borneol	12
t-Butanol	-

*Rate relative to ethanol = 100.

Table 8.

THE RELATIVE RATE OF OXIDATION OF β-ALKOXY-ALCOHOLS WITH ARGENTIC PICOLINATE.

ALCOHOL.	RELATIVE RATE*
Ethanol	100
2-Ethoxyethanol	80
Tetrahydrofuran-2-carbinol	76
2-Butoxyethanol	71
Tetrahydropyran-2-carbinol	59
2-Acetoxyethanol	31

*Rate relative to ethanol = 100.

Table 9.

The oxidation of substituted benzyl alcohols by argentic picolinate at 70°C. in water is recorded in table 4 and the relative rates of these reactions are recorded in table 10. It can be seen that the rate of reaction is increased by the presence of an electron-donating substituent and decreased by an electron-withdrawing substituent on the

aromatic nucleus. Hence the rate of oxidation of the benzyl alcohols was progressively increased with the increase in electron-donating power of the substituents on the ring; whilst p-nitrobenzyl alcohol (electron-withdrawing group present) was oxidised at the slowest rate.

THE RELATIVE RATE OF OXIDATION OF SUBSTITUTED BENZYL ALCOHOLS BY ARGENTIC PICOLINATE.

ALCOHOL.	RELATIVE RATE*
p-Nitrobenzyl alcohol	43
Benzyl alcohol	100
p-Methoxybenzyl alcohol	262
3,4-Methylenedioxybenzyl alcohol	918
3,4-Dimethoxybenzyl alcohol	1505

*Rate relative to benzyl alcohol = 100; in water at 70°C.

Table 10.

An investigation of the kinetics of alcohol oxidation at 30°C.

The ultra-violet spectrum of argentic picolinate in water showed absorptions at 217 (ϵ = 5,985), 263 (ϵ =6,110) and 325 mμ (ϵ =1,660). The absorption peak at 325 mμ was found to be due to the presence of the argentic oxidation state. (Argentous picolinate showed only absorptions at 217 and 263 mμ ; but on addition of a small quantity of potassium persulphate, the solution became yellow and the weak absorption at 325 mμ appeared). A measurement of the disappearance of this absorption against time would be a measurement of the reduction of silver II to silver I and would indicate the order of reaction with respect to silver ions.

The rate of disappearance of a compound can be expressed

as $-dc/dt$, where c = concentration and t = time. Hence an expression can be derived (equation 36) which will apply to the kinetics if the reaction is governed by a first order rate law.

$$\text{Rate} = -dc/dt = k.c.$$

or $$-dc/dt = k.c. \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 30.$$

where k = rate constant.

$$\therefore -dc/c = k.dt \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 31$$

Integration of equation 31 and imposing the condition that $c = c_o$ at t = o gives rise to equation 35.

$$-\int dc/c = \int k.dt \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 32$$

$$\therefore -\log_e c = kt + a' \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots 33$$

where a' = constant of integration

when t = o and $c = c_o$ equation 33 becomes:-

$$-\log_e c_o = a' \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots 34$$

$$\therefore -\log_e c = kt - \log_c c_o \quad \ldots\ldots\ldots\ldots\ldots 35$$

$$\text{or } \log_e co/c = kt \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots 36$$

Hence for a first order rate law, the concentration c at any time t varies as $c_o e^{-kt}$.

For a first order rate law, it is often convenient to measure the change in concentration of the reactant by measuring the change in a function dependent upon the concentration. Hence, a measurement of the decrease in size of the 325 mμ absorption band will be a direct measurement of the change in concentration of silver II ion present in the reaction mixture. The reaction of a series of alcohols with argentic picolinate was examined

at 30°C. by measuring the decrease in size of the absorption at 325 mμ . The reactions were carried out in water with reactant concentrations in the molar ratio of 1:2, alcohol to oxidant. The rate of hydrolysis of the oxidant was also examined.

For the rate of disappearance of Ag^{II} to be governed by a first order rate law, a plot of $\log_{10} {}^{c_o}/_{c}$ vs. time (t) should give a straight line with a slope equal to ${}^{k}/_{2.303}$. It was found that a plot of $\log_{10}(A-A_{\infty})$ vs. time (t) gave straight lines for the reactions examined when A = absorbance at time t and A_{∞} = absorbance at infinite time, i.e. when all Ag^{II} had been reduced to Ag^{I}. When the values of absorbance against time where used with a second order rate equation, a curve was formed and not a straight line; hence it was considered that the reduction of silver II obeyed a first order rate equation.

THE KINETICS OF ALCOHOL OXIDATION AT 30°C.*

ALCOHOL	SLOPE	k (1st order rate constant)
Ethanol	0.385	0.98
n-Butanol	0.341	0.79
Cyclohexanol	0.313	0.72
Benzyl alcohol	0.300	0.69
iso-Pentanol	0.239	0.55
sec-Butanol	0.177	0.41
2-Pentanol	0.165	0.38
Water**	0.042	0.099 (0.1)

* See experimental section and Plates 2, 3 and 4.

** Hydrolysis constant for argentic picolinate, included for comparison.

Table 11.

The Kinetics Of Alcohol Oxidation at 30°C.

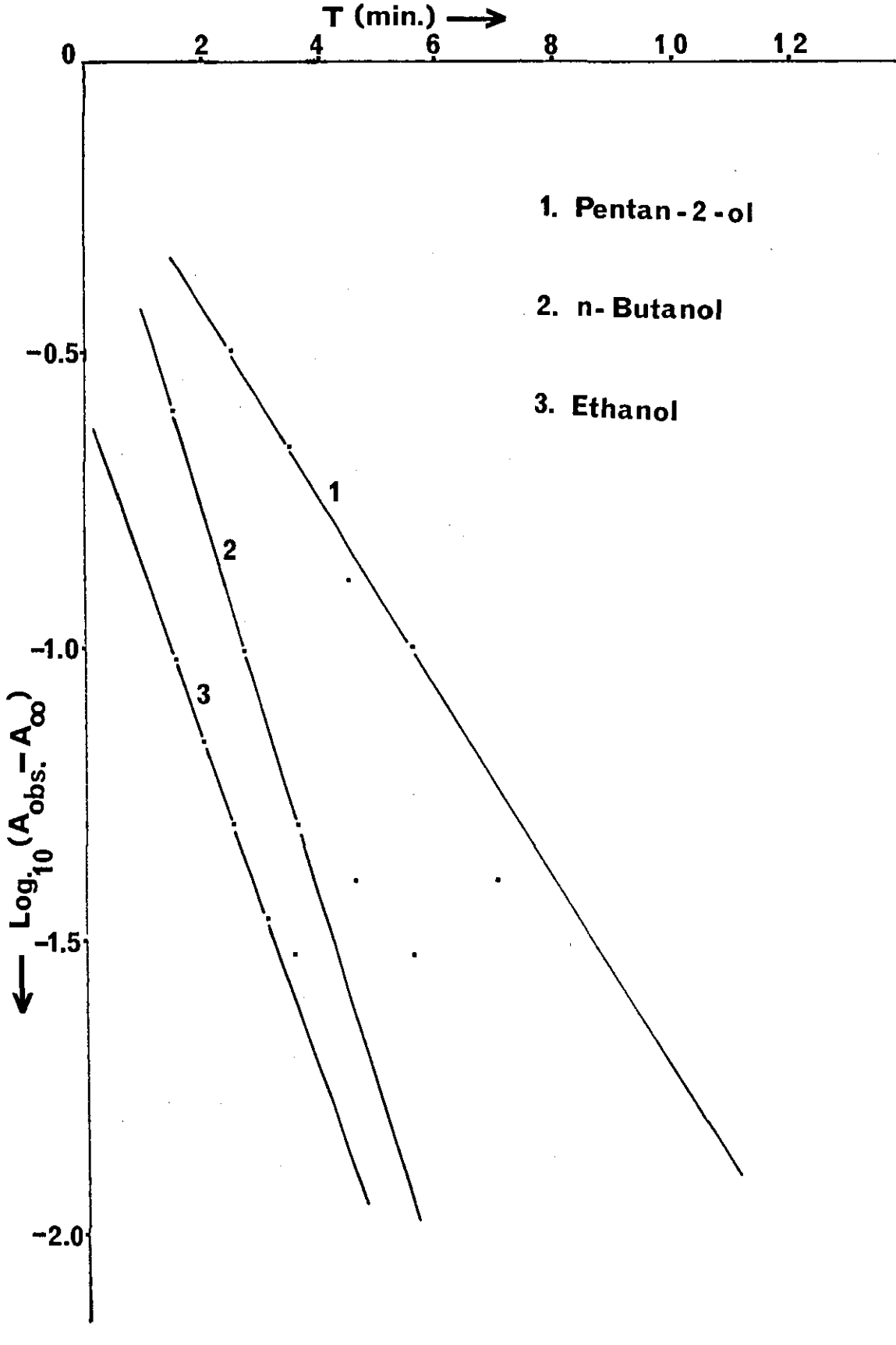


Plate 2

The Kinetics Of Alcohol Oxidation at 30°C.

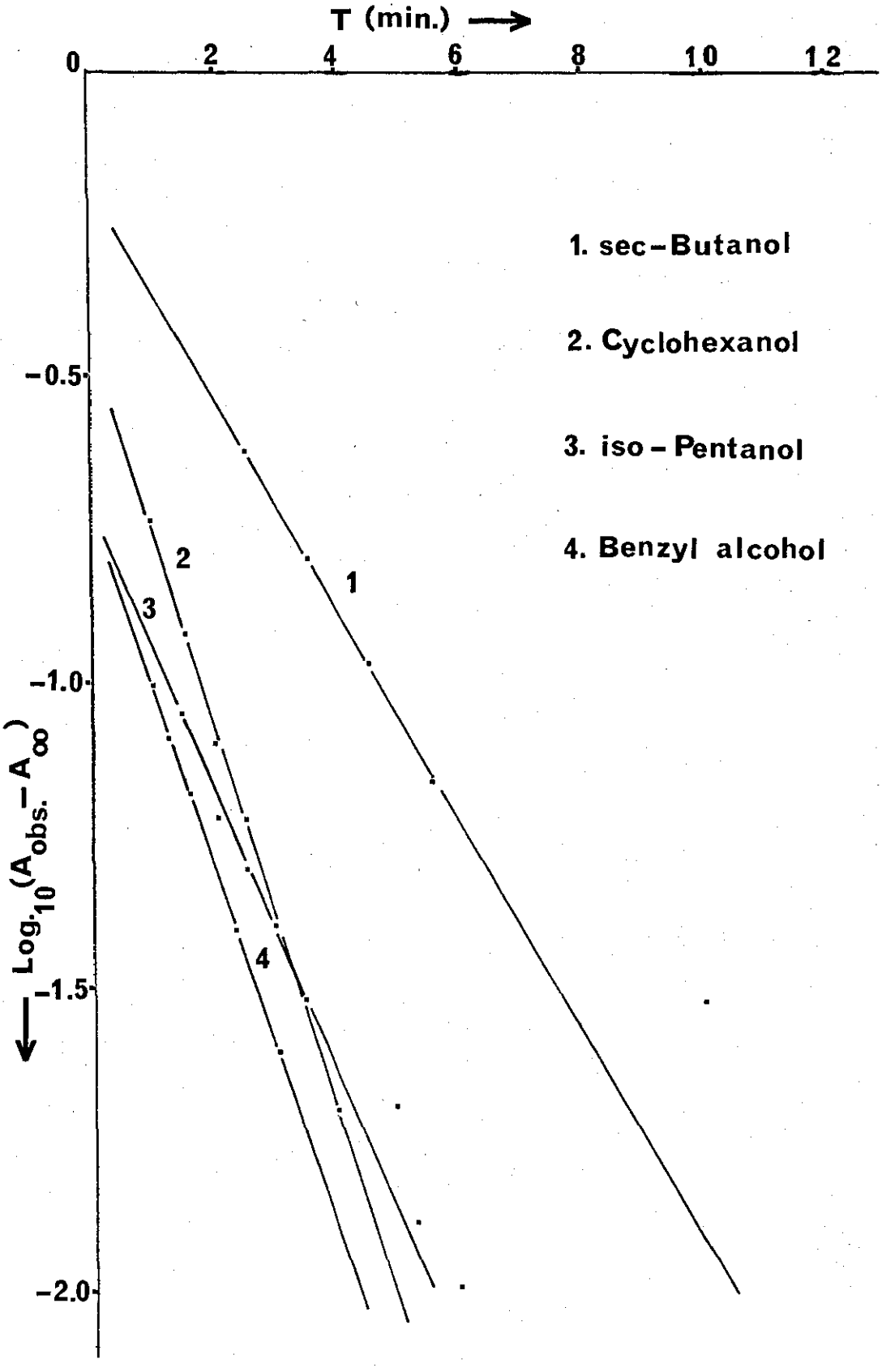


Plate 3

The Hydrolysis of Argentic Picolinate at 30°C.

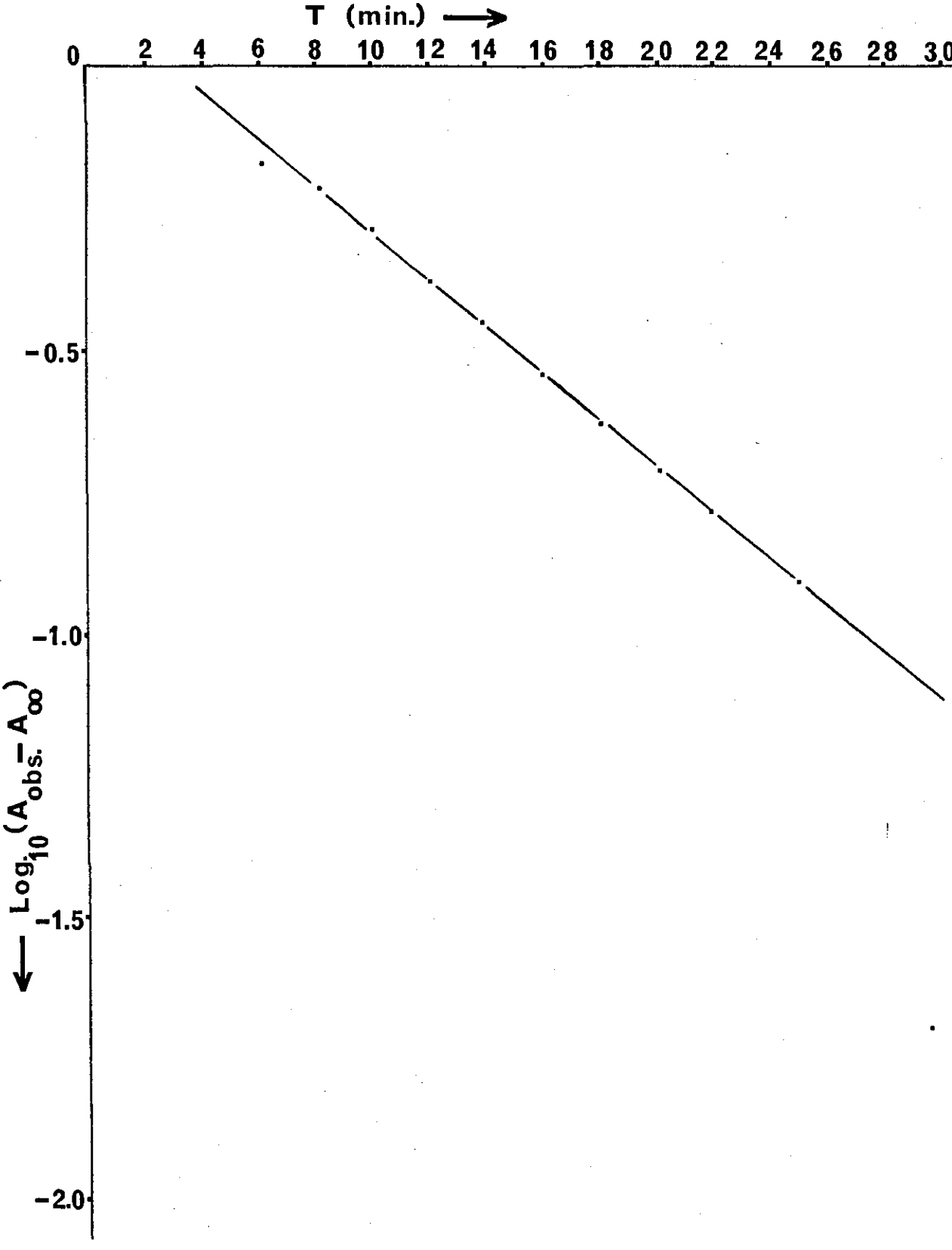


Plate 4

- The calculated rate constants (k) for a series of alcohols are recorded in Table 11. These results show that the relative rates of reaction (discussed earlier) were correct. The hydrolysis constant for argentic picolinate was calculated by a similar method and is included for comparison. It can be seen that the reaction of ethanol with the oxidant is 10 x faster than water with the oxidant.

Possible mechanisms for the oxidation of alcohols.

Present evidence (112, 138) favours a one-electron transfer process for the oxidation reaction by argentic picolinate. If this is so then the oxidation of alcohols (for example) will involve 2 moles of oxidant per mole of alcohol oxidised; and this was found to be true for all cases examined. The kinetics of alcohol oxidation, discussed earlier, showed that the rate of oxidation was proportional to $[Ag^{II}]$ i.e. the reaction was 1st order with respect to concentration of silver II ions. Hence, the initial step in the oxidation, the rate controlling step, will be the attack of 1 mole of alcohol on 1 mole of oxidant to give an intermediate complex. The rate of formation of this intermediate and its subsequent breakdown will depend on factors such as the ability of the alcohol to displace picolinic acid from the silver II complex (115). Following the formation and breakdown of the initial intermediate, the second mole of argentic picolinate will be reduced more quickly otherwise the overall rate of reaction would be proportional to $[Ag^{II}]^2$. As a radical will be involved in the latter reaction, the reduction of silver II would be

MECHANISM OF ALCOHOL OXIDATION

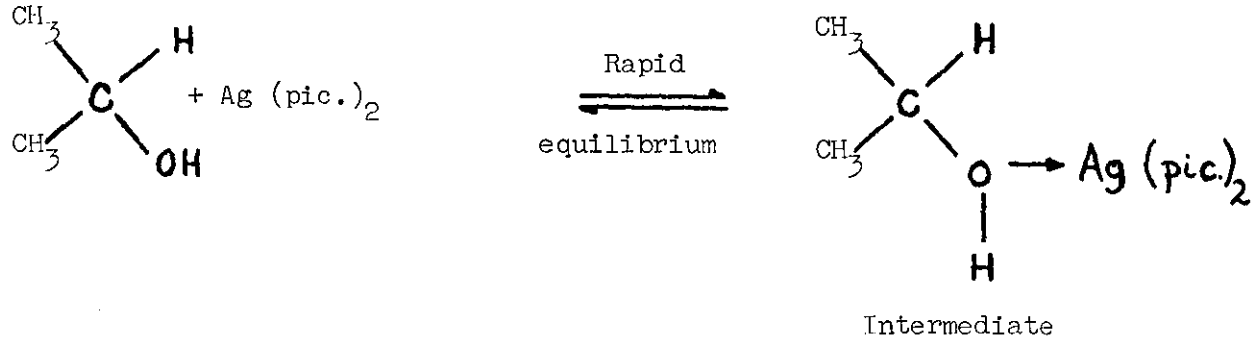


Fig.4

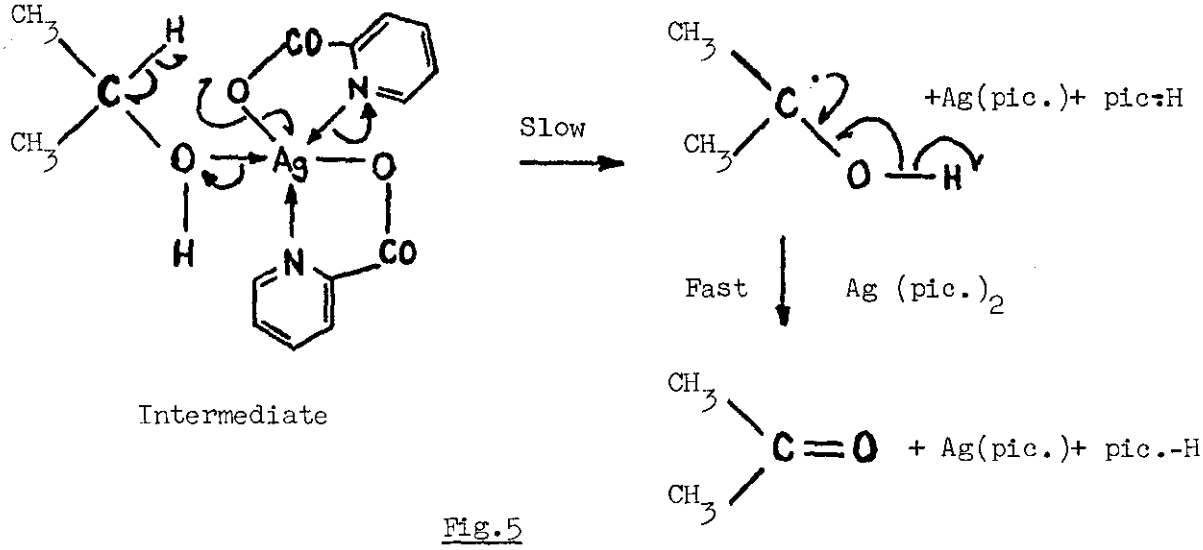


Fig.5

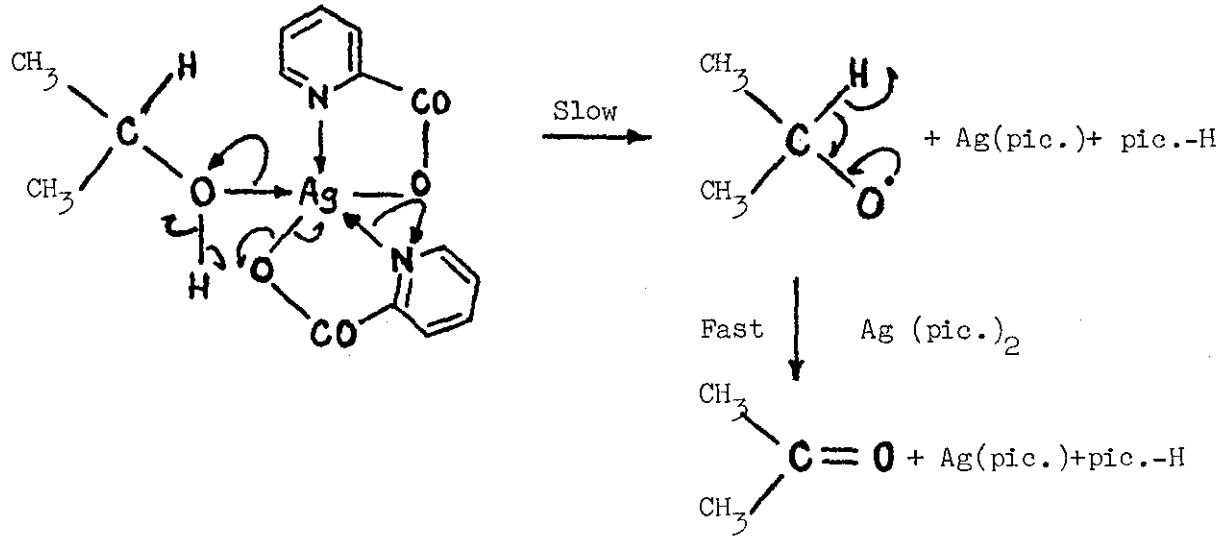


Fig.6

expected to be faster than when attack is by an alcohol molecule.

The exact mechanism of oxidation by argentic picolinate is not known, but oxidations with other transition metal oxidants involving single-electron transfer processes have been partially elucidated. The mechanism of oxidation of alcohols by vanadium V (138) and cobalt III (139) complex ions has been suggested and assuming that silver II picolinate behaves in a similar way, plate 5 shows a possible mechanistic sequence. The initial attack of 1 mole of alcohol on 1 mole of the oxidant will give rise to an intermediate (fig.4) and this can break down in two possible ways (a) to give an alkyl radical (fig.5) and (b) to give an alkyloxy radical (fig.6). In either case the radical formed will be rapidly attacked by the second mole of argentic picolinate to give, in this example, acetone and argentous picolinate.

Proton magnetic resonance spectra of carbonyl 2,4-dinitrophenyl-hydrazone derivatives.

The 2,4-D.N.P. derivatives of the products of oxidation of alcohols were routinely examined by p.m.r. spectrometry to establish whether any skeletal rearrangement had occurred during oxidation. For all products examined, no skeletal rearrangement was recorded. The spectral data for aldehyde derivatives is recorded in table 12 and for ketone derivatives, table 13.

The line spectra recorded can be accounted for by reference to figs. 7 and 8 and plates 6 and 7. The one-proton singlet at -1.1 tau, exchanged by deuterium oxide,

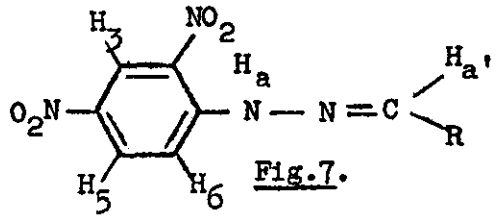


Fig.7.

THE P.M.R.SPECTRAL DATA OF ALDEHYDE 2,4-DINITROPHENYL-HYDRAZONES.

	CHEMICAL SHIFT ($CDCl_3$). Tau							COUPLING CONSTANT (c.p.s.)			
DERIVATIVE.	H_a	H_3	H_5	H_6	$1H_a'$	$2H_a'$	R group	$J_{H_3H_5}$	$J_{H_5H_6}$	$J_{1H_a'R}$	$J_{2H_a',R}$
Formaldehyde	-1.25(s)	0.78(d)	1.55(dd)	1.95(d)	2.75(d)	3.20(d)	R = H	2.75	9.60	11.0	
Acetaldehyde	-1.10(s)	0.86(d)	1.65(dd)	2.05(d)	2.4(q)	-	7.8(d)	2.50	9.65	5.50	
Propionaldenyde	-1.10(s)	0.80(d)	1.60(dd)	2.02(d)	2.3(t)	3.0(t)	7.5(o),8.75(sx)	2.35	10.0	4.87	5.42
Propionaldehyde*	-1.40(s)	1.10(d)	1.60(dd)	2.10(d)	1.9(t)	-	7.85(q),8.85(t)	2.50	9.75	5.0	-
n-Butyraldehyde	-1.02(s)	0.9(d)	1.65(dd)	2.05(d)	2.38(t)	3.0(t)	7.60(m),8.30(m),8.90(t),8.95(t)	2.92	9.65	5.38	5.42
iso-Butyraldehyde	-1.0(s)	0.86(d)	1.60(dd)	2.08(d)	2.50(d)	2.90(d)	7.35(m),8.75(d)	2.50	9.15	5.0	5.33

Table 12

cont. .....

DERIVATIVE	CHEMICAL SHIFT ($CDCl_3$) tau							Coupling constant(c.p.s.)			
	Ha	H_3	H_5	H_6	$1H_a'$	$2H_a'$	R group	$J_{H_3H_5}$	$J_{H_5H_6}$	$J_{1H_a'R}$	$J_{2H_a'R}$
2-Methyl-butyraldehyde	-1.03(s)	0.86(d)	1.66(dd)	2.05(d)	2.53(d)		7.60(m),8.45(q),8.79(d),9.0(t)	2.50	10.0	5.50	
2-Ethyl-butyraldehyde**	-1.15(s)	0.81(d)	1.58(dd)	1.98(d)	2.49(d)	3.18(d)	7.63(m),8.38(m),9.01(t)	2.58	9.67	6.50	8.83
n-Pentan-aldehyde	-1.03(s)	0.85(d)	1.65(dd)	2.05(d)	2.38(t)	3.0(t)	7.55(m),8.40(m),9.0(t)	2.42	9.50	5.32	5.20
iso-Pentan-aldehyde	-1.01(s)	0.90(d)	1.65(dd)	2.06(d)	2.40(t)	2.95(t)	7.65(t),8.20(m),8.95(d)	2.15	9.95	5.92	5.30
Pivalalde-hyde	-1.10(s)	0.80(d)	1.60(dd)	2.00(d)	2.45(s)	-	8.75(s)	2.59	10.0	-	-
n-Hexan-aldehyde	-1.15(s)	0.85(d)	1.60(dd)	2.00(d)	2.30(t)	2.95(t)	7.50(m),8.45(m),9.05(t)	2.59	9.85	5.42	5.42
2-Ethylhex-analdehyde	-1.05(s)	0.84(d)	1.61(dd)	2.00(d)	2.45(d)	-	7.60(m),8.50(m),9.02(t),9.08(t)	2.66	10.0	6.84	-
n-Heptan-aldehyde	-1.0(s)	0.88(d)	1.68(dd)	2.05(d)	2.42(t)	3.01(t)	7.53(m),8.58(m),9.08(t)	2.33	9.64	5.49	5.25

* Spectrum recorded in hexadeutero-dimethyl sulphoxide (DMSO-D_6)

** Prepared by standard procedure (140) for comparison

Table 12 (cont.)

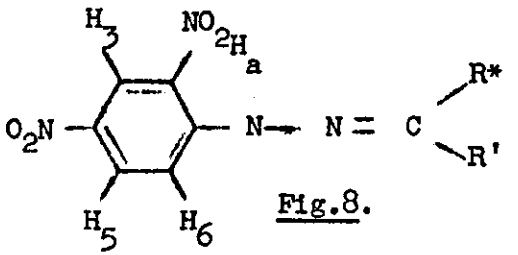


Fig.8.

THE P.M.R.SPECTRAL DATA OF KETONE 2,4-DINITROPHENYLHYDRAZONES.

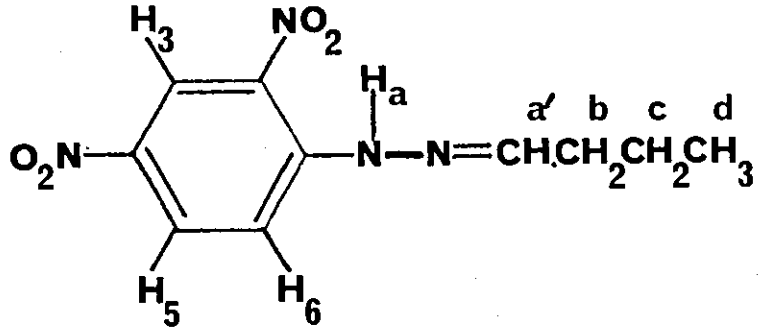
DERIVATIVE	CHEMICAL SHIFT ($CDCl_3$) tau							Coupling constant(c.p.s	
	H_a	H_3	H_5	H_6	IR	2R	R'	$J_{H_3H_5}$	$J_{H_5H_6}$
Acetone	-1.10(s)	0.85(d)	1.65(dd)	2.02(d)	7.82(s)	-	7.89(s)	2.50	9.30
Methyl ethyl ketone	-1.10(s)	0.85(d)	1.65(dd)	2.00(d)	7.85(s)	7.92(s)	7.5(q),7.52(q),8.75(t),8.78(t)	2.25	9.35
Methyl t-butyl ketone**	-1.13(s)	0.80(d)	1.60(dd)	2.00(d)	7.95(s)	-	8.75(s)	2.58	10.0
Ethyl n-butyl ketone**	-1.30(s)	0.78(d)	1.60(dd)	1.95(d)	7.5(m),	8.65(t)	7.5(m),8.4(m),8.92(t)	2.42	9.60
Cyclo-hexanone	-1.32(s)	0.80(d)	1.62(dd)	1.95(d)	7.55(m),8.30(m)		-	2.58	9.67

* R = smaller group where relevant

** Prepared by standard procedure (140) for comparison.

Table 13.

Plate 6


H3
NO2
Ha
a′ b c d
O2N
N—N=CH.CH2CH2CH3
H5
H6

H3
H6
1Ha′
H5
Ha
2Ha′
b
c
d
TMS
−1
1
2
3
tau
7
8
9
10

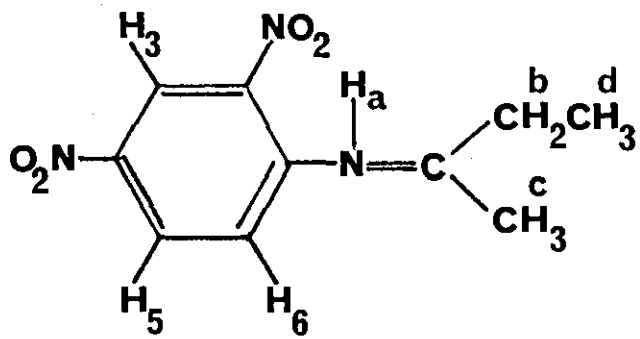
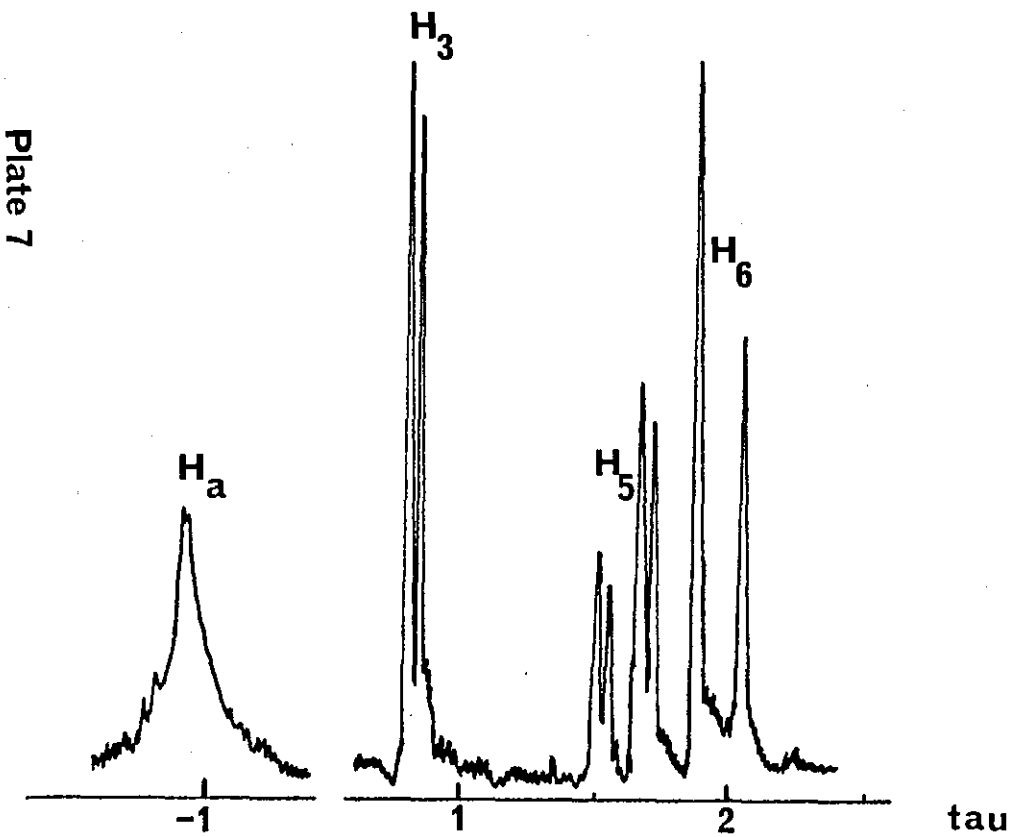
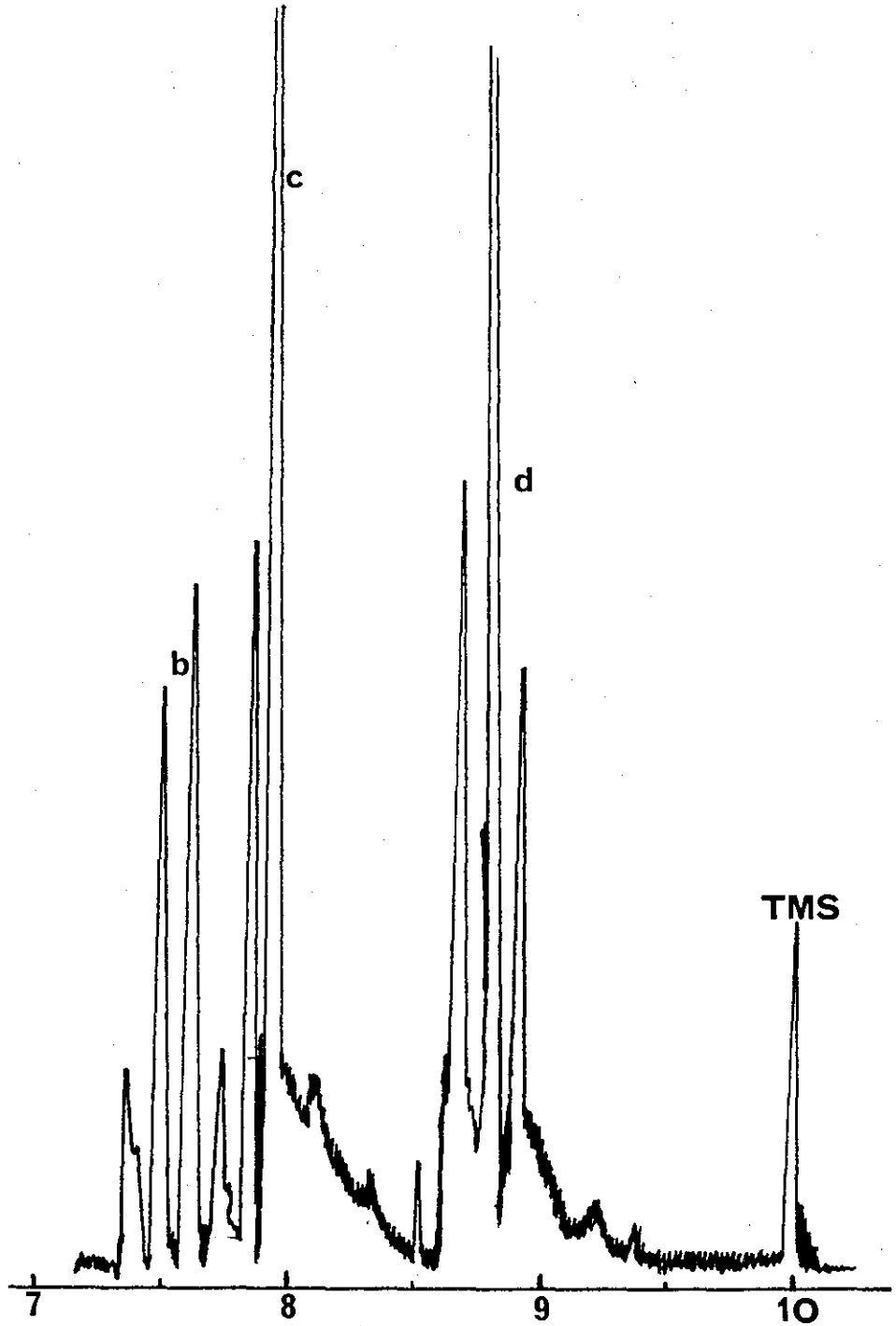

H3
NO2
Ha
b
d
CH2CH3
O2N
N
C
c
CH3
H5
H6

Plate 7


H3
Ha
H5
H6
−1
1
2
tau


c
b
d
TMS
7
8
9
10

can be assigned to proton-H_a. Its presence at a very low field must be due to strong hydrogen-bonding to the nitro-group on ring-carbon$_2$. (When DMSO was the solvent the signal moved down-field to -1.5 tau). The one-proton doublet at approx. 0.8 tau can be assigned to proton -H_3. The doublet arises by meta-coupling to proton -H_5($J_{H_3H_5}$ =ca. 2.5 c.p.s.) and its position approx. 120 c.p.s. down-field from benzene is due to deshielding by the nitro-groups on C_2 and C_4 of the aromatic nucleus. The one-proton double-doublet at approx. 1.6 tau can be assigned to proton-H_5 and the signal multiplicity is due to meta coupling with proton-H_3 and ortho coupling to proton-H_6($J_{H_5H_6}$ = ca. 10 c.p.s.). The doublet at approx. 2 tau is consequently assigned to proton -H_6. Apparently no para coupling between H_3 and H_6 occurred as no further multiplicity (J= ca. 1 c.p.s.) was recorded. The single proton signal pattern at approx. 2.3-3.2 tau can be assigned to proton-$H_{a'}$ (aldehydes only). Its presence at low field is due to the deshielding of the C=N bond in the same plane as proton-$H_{a'}$. The multiplicity of this methine proton is necessarily dependent upon the group R (table 12); eg., $H_{a'}$ appears as a quartet in acetaldehyde. The remaining proton signals can be accounted for by R (and R' for ketones) and appear at 7 to 9.1 tau.

In addition to the spectral data recorded for 2,4-D.N.P. derivatives, the p-nitrophenylhydrazone derivatives of n-hexanaldehyde and methyl ethyl ketone were prepared (142) and their p.m.r. spectral data are recorded in table 14. The assignment of the line spectra can be made with reference to

fig.9. The two-proton double-doublet at 1.9 tau is due to protons-H_3 and $H_{3'}$. Multiplicity is accounted for by ortho coupling ($J_{H_2H_3}$=ca. 9 c.p.s.) and meta coupling ($J_{H_3H_{3'}}$ = ca. 1.4 c.p.s.). Apparently para coupling is zero. The presence of the nitro group on carbon-4 is reflected in the chemical shift of approx. 60 c.p.s. (down field) from the normal benzene singlet (6 protons). Consequently the two-proton double-doublet at approx. 2.9 tau can be assigned to protons-H_2 and $H_{2'}$. Proton -H_a appears at higher yield than in 2,4-D.N.P. derivatives and this is due to lack of hydrogen-bonding as the nitro-group on C_2 is now absent. Groups R and R' protons occur, as expected, between 7 and 9.1 tau and account for the skeletal structure of the respective derivative.

Configurational isomerism about C = N bonds from p.m.r.data.

The possibility of configurational isomerism about the C = N bond of 2,4-D.N.P.derivatives is well accepted as the presence of a mixture of the 2 isomers would account for the variable melting points often recorded for some aldehyde derivatives (140). Recently, Hegarty and Scott (142) published the kinetics of syn-anti conversion of 2,4-D.N.P.derivatives and it was then discovered that Karabatsos (143) had published his findings on the p.m.r. spectral data of some aldehyde 2,4-D.N.P.derivatives.

During the routine analysis by p.m.r. spectra, of the 2,4-D.N.P. derivatives formed by alcohol oxidation products, it was noted that the methine proton (-CH = N -) of some derivatives did not always integrate for one proton. On these occasions, a smaller signal was recorded at ca. 40 c.p.s.

THE P.M.R. SPECTRAL DATA OF CARBONYL p-NITROPHENYLHYDRAZONES.*

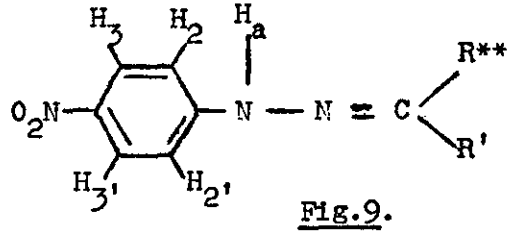


Fig.9.

DERIVATIVE	$H_3(H_{3'})$ $H_2(H_{2'})$ H_a CHEMICAL SHIFT($CDCl_3$)	1R 2R	R'	$J_{H_2H_{2'}}$ $J_{H_2H_3}$ J_R
n-Hexanaldehyde	1.90(dd) 2.98 (dd) 1.13(s)	2.69(t) 3.4(t) (R = H)	7.75(q), 8.62(m), 9.12(t)	1.33 9.0 5.5 (R = H)
Methyl ethyl ketone	1.83(dd) 2.90(dd) 2.33(s)	7.95(s) 8.1(s)	7.7(m), 8.9(t)	1.47 9.35 -

* Prepared by standard procedure (141)

**R = smaller group (or hydrogen).

Table 14.

up-field of the main signal. Close inspection of the spectra of some ketone derivatives showed that the R group proton signals were also duplicated; however the chemical shift was only ca. 4 c.p.s. down-field of the main peak. The results of these observations are recorded under $1H_a$, and $2H_a$, in table 12 and 1R and 2R in table 13. The areas under these signals were computed by use of equation 37 (I_1 and I_2 were the measured values and I_1' and I_2' are the corrected values, recorded in table 15 (a) and 15 (b). From these corrected values the syn-anti ratio was calculated.

$$I_1' = \frac{I_1}{I_1 + I_2} \text{ and } I_2' = \frac{I_2}{I_1 + I_2} \quad \ldots\ldots\ldots\ldots\ldots\ldots 37$$

Syn-anti isomerism (fig.10) occurs because of the lack of rotational freedom around the "rigid" C = N bond and the syn-isomer might be expected to be the dominant isomer because it is thermodynamically more stable than the anti-isomer. The ratios of syn-anti isomers for aldehyde and ketone derivatives are recorded in table 15 (a) and 15 (b) respectively. It can be seen that the syn-isomer is the predominant form but that as much as 20% of the anti-isomer was found to be present for some derivatives. The syn-isomer was assigned

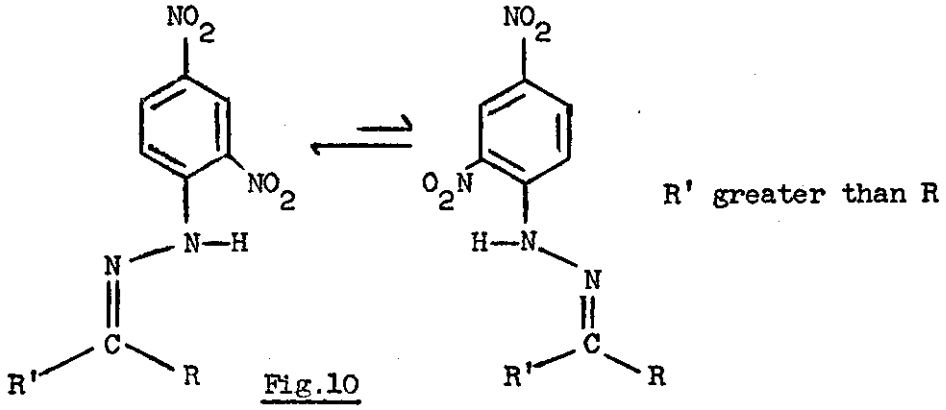


Fig.10

syn-isomer anti-isomer

Syn-anti isomerism of carbonyl 2,4-D.N.P.'s and p-Nitrophenyl-hydrazones by p.m.r. spectral data.

(a) Aldehyde 2,4-D.N.P.derivatives.

Derivative	$1H_a$,*	$2H_a$,	Syn-anti ratio
Formaldehyde	-	-	-
Acetaldehyde	1.0	0	100/0
Propionaldehyde	0.84	0.16	84/16
Propionaldehyde**	1.0	0	100/0
n-Butyraldehyde	0.75	0.25	75/25
iso-Butyraldehyde	0.86	0.14	86/14
2-Methylbutyraldehyde	1.0	0	100/0
2-Ethylbutyraldehyde	1.0	0	100/0
n-Pentanaldehyde	0.81	0.19	81/19
iso-Pentanaldehyde	0.83	0.17	83/17
Pivalaldehyde	1.0	0	100/0
n-Hexanaldehyde	0.81	0.19	81/19
2-Ethylhexanaldehyde	1.0	0	100/0
n-Heptanaldehyde	0.80	0.20	80/20

(b) Ketone 2,4-D.N.P. derivatives.

Derivative	1R*	2R	Syn-anti ratio
Acetone	-	-	-
Methyl ethyl ketone	0.51	2.49	83/17
Methyl t-butyl ketone	0	3.0	100/0
Ethyl n-butyl ketone	Impossible to measure from spectrum		

(c) p-Nitrophenylhydrazones.

Derivative	1R*	2R	Syn-anti ratio
n-Hexanaldehyde	0.82	0.18	82/18
Methylethyl ketone	0.57	2.43	81/19

* Refers to integration of lower field signal in tables 12, 13 and 14.

** Recorded in DMSO - D_6.

Table 15.

to the lower field signal (for aldehydes) on the fact that the syn-isomer should be the major isomer in the mixture and that the proton -H_a, would probably be deshielded (in comparison to when it is in the anti-form) due to the close proximity of the aromatic nucleus. Similarly for ketone derivatives, the R group will be slightly more shielded when it is in the syn form than when it is in the anti-form and the syn-isomer will be thermodynamically more favourable. The p-nitrophenylhydrazone derivatives can be analysed in an identical manner and the results of syn-anti isomerism are recorded in table 15 (c).

All spectral data shown in the preceding tables were recorded on solutions of the precipitated derivative dissolved in deuterochloroform. The solutions were all examined within 20 minutes of being prepared and the results indicate that both the syn-and anti-isomers are present in some cases. However, Karabatsos (143) reported that freshly prepared solutions of aldehyde 2,4-D.N.P.'s showed only the syn-isomer to be present and that the anti-isomer was not formed until the solutions had been standing at room temperature for several hours. Isomerisation of these compounds must involve breakage of one C - N bond; energetically this would be very unfavourable, and it is surprising that Karabatsos observed such rapid isomerisation in the absence of a catalyst.

A.2. THE REACTION OF SILVER II OXIDE WITH ALCOHOLS.

The alcohol was stirred with silver II oxide (molar ratio, 1.1) in water at 70°C. and the reaction was allowed to proceed until only elemental silver appeared to be present.

The results of these reactions are recorded in table 16 and indicate that primary aliphatic alcohols give the carboxylic acid whilst the substituted benzyl alcohols give the corresponding aldehyde. This behaviour is partly in contrast with the reactions of argentic picolinate.

THE REACTION OF SILVER II OXIDE WITH ALCOHOLS AT 70°C. IN WATER.

ALCOHOL	TIME (hours)	PRODUCT	YIELD(%)*
Ethanol	14	Acetic acid	100
n-Propanol	15	n-Propionic acid	100
n-Butanol	13	n-Butyric acid	99.9
		n-Butyraldehyde	0.1
2-Ethyl-n-butanol	13	2-Ethyl-n-butyric acid	33
sec- Butanol	72	Methylethyl ketone	96
n-Pentanol	15	n-Pentanoic acid	100
iso-Pentanol	15	iso-Pentanoic acid	100
n-Hexanol	24	n-Hexanoic acid	35
2-Ethyl-n-hexanol	14	2-Ethyl-n-hexanoic acid	100
n-Octanol	24	n-Octanoic acid	22
Borneol**	15	Camphor	ca.50
iso-Borneol**	72	Camphor	ca.50
Benzhydrol	36	Benzophenone	70
p-Nitrobenzyl alcohol	72	No reaction	-
Benzyl alcohol	12	Benzaldehyde	12
p-Methoxybenzyl alcohol	15	Anisaldehyde	44
3,4-Dimethoxybenzyl alcohol**	60	Veratraldehyde	ca.50
Piperonyl alcohol	13	Piperonaldehyde	48

*Yield calculated from g.l.c. on the basis of 1:1 molar ratio of oxidant:alcohol with the exception of**

Table 16.

The yields of carboxylic acid from the oxidation of primary aliphatic alcohols are high; the yields are calculated on the basis of a molar ratio, 1:1 (alcohol:oxidant) and as the alcohol requires 2 moles of silver II oxide, the conversion is only 50% for an indicated yield of 100%. However, the yield for most acids was quantitative and with the exception

of a trace of butyraldehyde, the aldehyde was not detected as a product. The yield of product decreased with increase in molecular weight of the alcohol even when the reaction time was increased and in general, chain-branching had an adverse affect on the conversion to the acid. Secondary alcohols were converted to the corresponding ketone in high yield. Substituted benzyl alcohols reacted with silver II oxide to give the corresponding benzaldehyde although this reaction did not appear to be as favourable as the reaction of argentic picolinate with benzylic alcohols. p-Nitrobenzyl alcohol was not oxidised by the reagent even after 72 hours; but as the electron-donating power of the substituents on the ring was increased, the yields became higher. Consequently benzaldehyde was formed in 12% yield whilst 48% piperonaldehyde was isolated. The benzaldehydes appeared to be stable towards further oxidation as the corresponding carboxylic acid was not detected.

The reaction of silver II oxide with, for example, alcohols is difficult to follow in comparison to the reactions with argentic picolinate. As the reaction proceeds, elemental silver is deposited and hence it can never be seen with any certainty when the oxidant has been completely reduced. Methods for following the rate of a reaction, such as removal of aliquots at different times, are not practical due to the heterogeneity of the mixture and so the effect of chain-branching, carbon-number etc. on the rate of reaction cannot be discussed. However, the reaction of silver II oxide with alcohols is likely to proceed by a two-electron transfer process and the reaction is most likely aided by electron

availability at the site of oxidation. The reaction of the oxidant with alcohols can be summarised by the following equations:-

$$R.CH_2OH + 2\ AgO \longrightarrow R.COOH + 2\ Ag + H_2O \quad \ldots\ldots\ldots 38$$

$$\begin{matrix} R \\ R \end{matrix}\!\!>\!CHOH + AgO \longrightarrow \begin{matrix} R \\ R \end{matrix}\!\!>\!C = O + Ag + H_2O \quad \ldots\ldots\ldots\ldots 39$$

and $Ar.CH_2OH + AgO \longrightarrow Ar.\ CHO + Ag + H_2O$ 40

It is also evident that the very severe acid conditions employed with $Ag^{II}O$ by Syper (120) are not necessary as the reactions proceed satisfactorily in essentially neutral conditions. Furthermore, $Ag^{II}O$ decomposes in acidic solution with evolution of oxygen, and consequent wastage of oxidising agent.

The reactions of silver II oxide with aliphatic and aromatic alcohols show no consistency in its power as an oxidising agent, i.e. primary aliphatic alcohols are oxidised to the carboxylic acid in a short reaction time whilst attack on benzylic alcohols to give the aldehyde, is difficult to bring about. Scatturin et al.(117) have shown by neutron diffraction that silver II oxide is stoichiometrically AgO but consists of Ag^{I} and Ag^{II} ions bonded in the same lattice structure to atoms of oxygen. Hence, it might be expected that the presence of Ag^{III} and the lack of complexing ligands would render it a more powerful oxidant than argentic picolinate; but the results indicate it to have approximately the same oxidising power but less useful because of the transfer of 2-electrons per mole of oxidant.

B.1 THE REACTION OF ARGENTIC PICOLINATE WITH ALDEHYDES.

The reaction of argentic picolinate with a series of aldehydes was examined by a simple procedure similar to that used with alcohols, i.e. the aldehyde and the oxidant (molar ratio 1:2 respectively) were stirred together at 70°C. in water until the colour change orange-red to white was complete. For the aldehydes examined, the reactions proceeded smoothly to give the expected carboxylic acid, with two exceptions. The results of these reactions are summarised in tables 17 - 19.

The times of reaction of various aldehydes at 50°C. in 50% aqueous dimethyl sulphoxide are recorded in table 17 and the results indicate that aliphatic aldehydes were oxidised rapidly whilst substituted benzaldehydes were generally more stable towards the reagent. (It is well known that aliphatic aldehydes are more susceptible to oxidation than aromatic aldehydes, but even so the rate decreases with increase in chain length). The rapid reaction of p-N,N-dimethylaminobenzaldehyde is almost certainly the result of oxidation at the site of the tertiary amino-group and not at the aldehyde function (see part E.1.). Examination of the results in table 18 shows that the reaction of substituted benzaldehydes is accelerated by the presence of electron-donating groups whilst electron-withdrawing groups hinder the reaction. The overall reaction for the oxidation of aldehydes can be summarised by equation 41.

$$R.CHO + 2\ Ag(pic.)_2 + H_2O \longrightarrow R.COOH + 2\ Ag\ pic. + 2pic.H \quad \ldots 41$$

The results of reaction of argentic picolinate with substituted-benzaldehydes at 70° in aqueous media, are recorded in table 18. It can be seen that p-nitrobenzaldehyde, benzaldehyde and p-methoxybenzaldehyde all gave the corresponding acid in

moderate yields, whilst very anomalous reactions occurred with 3,4-dimethoxybenzaldehyde and piperonaldehyde. These two aldehydes were oxidised very many times faster (see table 19) but no oxidation product was isolated; in fact only starting material was found. This was recovered in good yield. Two possible explanations for these observations, both assuming extensive oxidative breakdown of the aromatic nucleus to the exclusion of the normal reaction at the aldehyde site, are as follows. (a) Due to the enhanced electron availability in the nucleus of these two aldehydes, a π-complex could be formed with Ag^{II} (see part F) which then leads to complete breakdown of the ring with consumption of several moles of the oxidant. (b) $Ag^{+}/S_2O_8^{2-}$ mixtures are known to bring about oxidative decarboxylation of carboxylic acids (100) and argentic picolinate is also reported (114) to convert phenylacetic acid to benzaldehyde (30% yield). If the activated aldehydes were oxidised to the respective acids which then underwent oxidative decarboxylation, the aromatic nucleus would almost certainly be destroyed at the expense of the normal reaction. It is interesting to note that the corresponding alcohols i.e. piperonyl and 3,4-dimethoxybenzyl alcohols were oxidised to the aldehydes at a fast rate with no abnormal reaction; hence, formation of a silver II-alcohol complex must be more favourable than a silver II-aromatic ring complex in these cases.

THE REACTION OF ALDEHYDES SHAKEN WITH ARGENTIC PICOLINATE AT 50°C. IN AQUEOUS DMSO.

ALDEHYDE	TIME (Hours)
p-NN-Dimethylamino-benzaldehyde	Instantaneous
2-Ethyl-n-butyraldehyde	0.33
2-Ethyl-n-hexanaldehyde	0.84
Furfuraldehyde	3
p-Tolualdehyde	4
Benzaldehyde	7
p-Nitrobenzaldehyde	28
p-Chlorobenzaldehyde	Partial reaction at 28.

Table 17.

THE REACTION OF ARGENTIC PICOLINATE WITH SUBSTITUTED-BENZALDEHYDES AT 70°C. IN WATER.

ALDEHYDE	TIME (Hours)	PRODUCT	YIELD (%)
p-Nitrobenzaldehyde	26	p-Nitrobenzoic acid	31
Benzaldehyde	25	Benzoic acid	58
p-Methoxybenzaldehyde	8	p-Methoxybenzoic acid	57
3,4-Dimethoxybenzaldehyde	2.1	-	85*
Piperonaldehyde	0.5	-	60*

*% starting material recovered unchanged.

Table 18.

THE RELATIVE RATE OF OXIDATION OF ALDEHYDES BY ARGENTIC PICOLINATE

ALDEHYDE	RELATIVE RATE*
p-Nitrobenzaldehyde	93
Benzaldehyde	100
p-Tolualdehyde	180
Furfuraldehyde	240
Anisaldehyde	300
Veratraldehyde	870
2-Ethyl-n-hexanaldehyde	895
2-Ethyl-n-butyraldehyde	2040
Piperonaldehyde.	5000
Benzyl alcohol**	2170
p-Nitrobenzyl alcohol**	915

* Rate Relative to benzaldehyde = 100
**Included for comparison.

Table 19.

The relative rates of oxidation of the aldehydes, compared with benzaldehyde = 100, are recorded in table 19 and from this it can be seen that the effect of electron-releasing groups on the rate of oxidation is marked. (Piperonaldehyde is oxidised at a rate 50 times greater than the parent aldehyde). Included in table 19 are the relative rates of oxidation of benzyl and p-nitrobenzyl alcohols under comparable conditions. The successful oxidation of alcohols to aldehydes depends on the lower reactivity of the latter and it can be seen that benzyl alcohol was oxidised by the reagent approx. 20 times faster than was benzaldehyde.

Possible mechanism of oxidation.

As for the oxidation of alcohols by argentic picolinate, no detailed evidence is available but on the assumption that the behaviour is similar to other one-electron transfer reactions (144) schemes can be suggested. Equations 42 and 43 show that the initial attack could be the abstraction of a hydrogen radical by one mole of argentic picolinate and this step would be rate-determining. Hence in the example shown (equation 42) a benzoyl radical would be formed which then undergoes further attack by the second mole of oxidant in the presence of water to yield the carboxylic acid (equation 43). The removal of the

e.g. $C_6H_5 - C\overset{H}{\underset{O}{=}} + Ag(pic.)_2 \longrightarrow C_6H_5\dot{C} = O + Ag(pic.) + pic\text{-}H$ 42

$C_6H_5\dot{C}=O + Ag(pic.)_2 + H_2O \longrightarrow C_6H_5C\overset{O}{\underset{OH}{=}} + Ag(pic.) + pic\text{-}H$ ...43

hydrogen atom leading to the formation of the radical could be

brought about by (a) the loss to a picolinate ligand with a subsequent one-electron removal (fig.11; plate 8) or (b) the formation of a complex by donation of an electron pair from the oxygen followed by subsequent ligand displacement and the formation of the radical (fig.12).

B.2 THE REACTION OF SILVER II OXIDE WITH ALDEHYDES.

The reaction of silver II oxide with aldehydes at 70°C. in aqueous media was investigated. As might be expected the reaction yields the carboxylic acid in a similar manner to argentic picolinate; however piperonaldehyde and 3,4-dimethoxybenzaldehyde reacted normally to give the carboxylic acids. This is perhaps surprising since the oxidant is potentially a more powerful agent than the picolinate complex. The results are recorded in table 20 and it will be noted that the yields of aliphatic carboxylic acid are high in comparison to the yields of substituted benzoic acids. This is probably accounted for by the comparative ease with which aliphatic aldehydes undergo oxidation. In general α-branched aldehydes gave a lower yield of the acid and this might indicate that steric hindrance at the site of oxidation, slowed the reaction. Since the exact reaction time for the oxidation of the various aldehydes was not easily measured, the effects of substitution and steric hindrance are not readily distinguished.

The main difference between the oxidation of aldehydes with argentic picolinate and silver II oxide is that in the latter case, molar ratios of 1:1 (oxidant:aldehyde) may be used and this results in the formation of elemental silver. Hence, the overall

MECHANISM OF ALDEHYDE OXIDATION

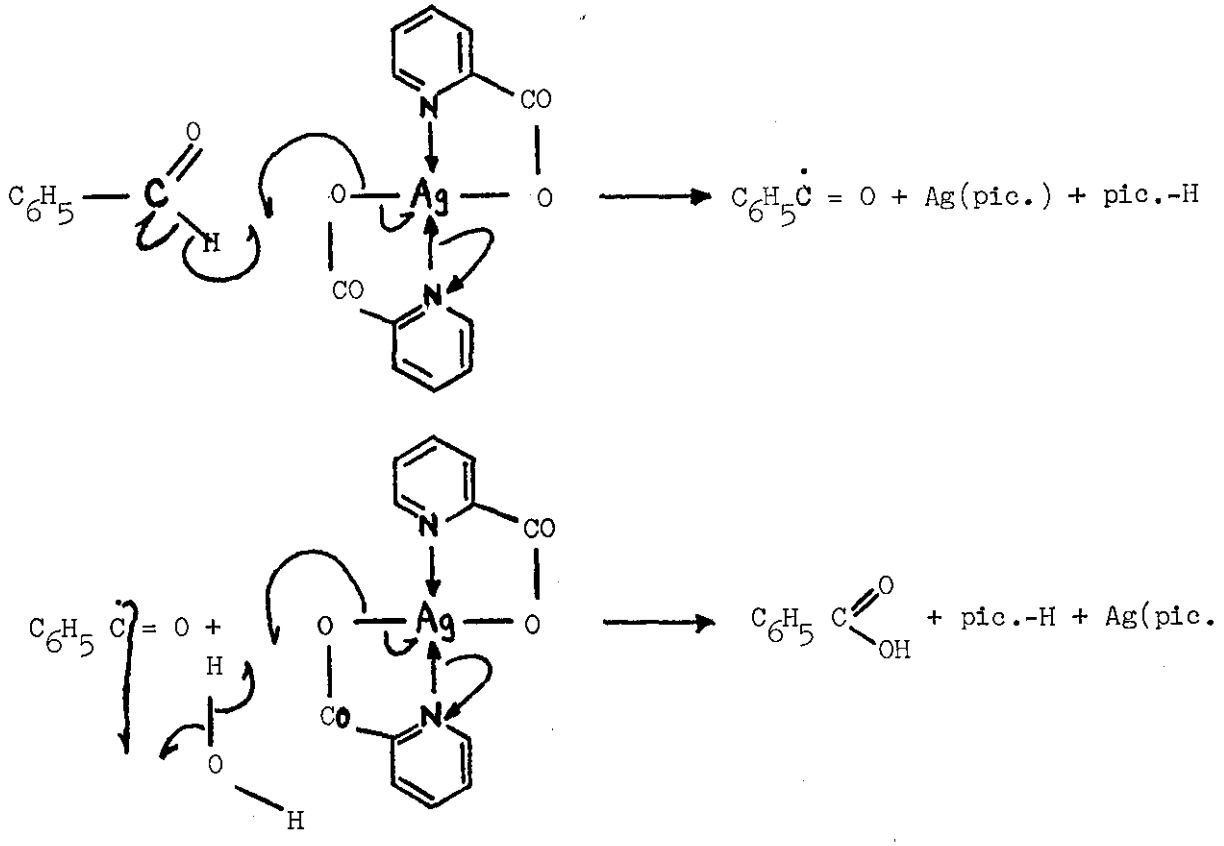
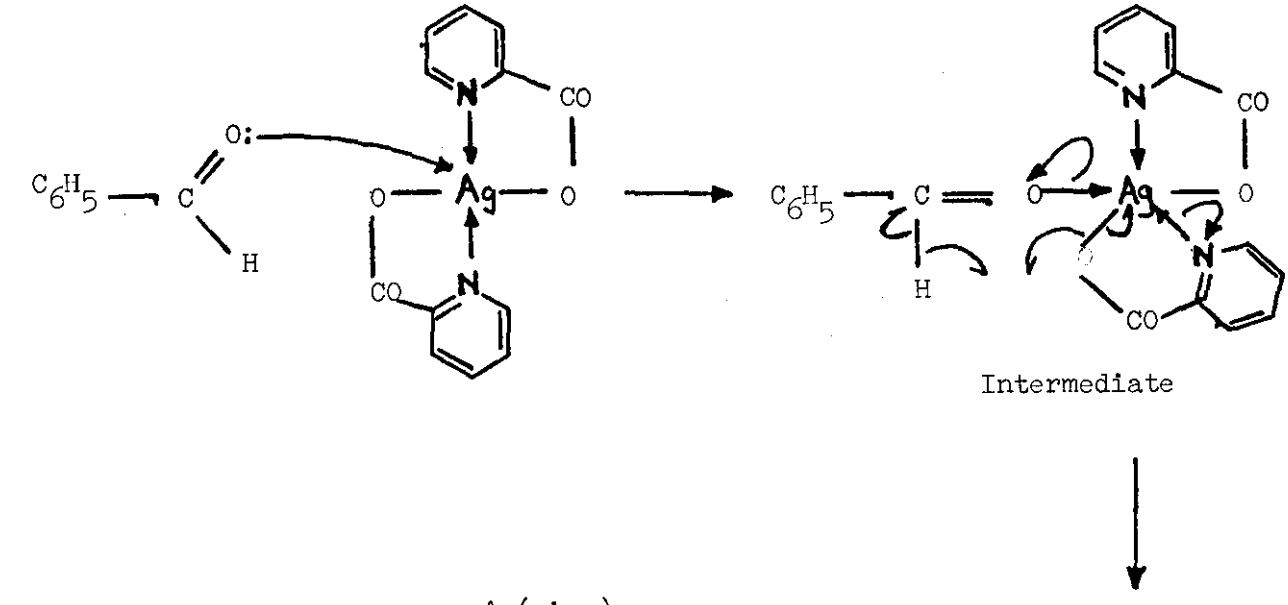


Fig.11



$$Ag(pic.) + C_6H_5COOH + pic.-H \xleftarrow[H_2O]{Ag(pic.)_2} C_6H_5\dot{C} = O + Ag(pic.) + pic. - H$$

(as for fig. 11).

Fig.12

Plate 8

reaction between aldehydes and silver II oxide may be written as equation 44. In this way, silver II oxide again behaves as a two-electron transfer agent.

$$R.CHO + AgO \longrightarrow R.COOH + Ag. \quad \ldots\ldots\ldots\ldots\ldots\ldots 44$$

THE REACTION OF SILVER II OXIDE WITH ALDEHYDES AT 70°C.IN WATER.

ALDEHYDE	TIME (Hours)	PRODUCT	YIELD(%)
2-Ethyl-n-butyraldehyde	18	2-Ethyl-n-butyric acid	93*
n-Hexanaldehyde	22	n-Hexanoic acid	100*
2-Ethyl-n-hexanaldehyde	25	2-Ethyl-n-hexanoic acid	68*
p-Nitrobenzaldehyde	21	p-Nitrobenzoic acid	38
Benzaldehyde	22	Benzoic acid	51
p-Methoxybenzaldehyde	10	p-Methoxybenzoic acid	57
3,4-Dimethoxybenzaldehyde	12	3,4-Dimethoxybenzoic acid	47
Piperonaldehyde	20	Piperonylic acid	30

* Yield calculated from g.l.c.data.

Table 20.

C. THE REACTIONS OF ARGENTIC PICOLINATE AND SILVER II OXIDE WITH ORGANO-PHOSPHORUS COMPOUNDS.

The reactions of phosphite esters and triphenylphosphine with both argentic picolinate and silver II oxide were carried out at 70°C. in water. The procedures used were similar to those outlined in the preceding discussion (i.e. parts A and B). The mixtures of products were examined by thin layer chromatography and the results of the oxidation reactions are summarised in tables 22 and 23. For the chromatographic examination, the respective phosphate esters were prepared by the standard method of Rydon and Tonge (145) (the action of bromine on the phosphite ester and subsequent hydrolysis to give the phosphate ester). Triphenylphosphine oxide was examined by T.L.C. and also separated and its identity confirmed by comparison of the infra-red spectrum with that of the authentic material.

The results of the oxidation reactions with argentic picolinate (table 22) show that in general the phosphite esters were converted to the phosphate esters in moderate yields, whilst triphenylphosphine gave the oxide in 100% yield. All of the chromatograms examined, showed the presence of free alcohol (or phenol) in the mixture but whether it was formed during the oxidation step or by acid-catalysed hydrolysis of the phosphate ester during the separation of inorganic salts, is difficult to establish. However, the oxidation of phosphite esters by argentic picolinate can be best summarised by equation 45.

eg. $(C_6H_5O)_3P + 2Ag(pic.)_2 + H_2O \longrightarrow (C_6H_5O)_3P{=}O + 2Agpic. + 2pic.-H$ ...45

Table 23 records the results of the oxidation of the same five phosphorus compounds with silver II oxide and it can be seen that the yields of phosphate esters are slightly higher than recorded with the other oxidant. However, triphenylphosphine is not converted quantitatively to triphenylphosphine oxide. As in the preceding reactions, the respective alcohol (or phenol) was found to be present in the reaction mixtures. The reaction between silver II oxide and the compounds can be summarised by equation 46. From this reaction it can be seen that

eg. $(C_6H_5O)_3P + AgO \longrightarrow (C_6H_5O)_3 P = O + Ag$ 46

1:1 molar quantities of ester and oxidant were employed and therefore the oxide behaves as a two-electron transfer agent whilst argentic picolinate (equation 45) was seen to behave as a one-electron transfer agent i.e. 2:1 molar ratio (oxidant/ester).

THE REACTION OF ARGENTIC PICOLINATE WITH ORGANO-PHOSPHORUS COMPOUNDS AT 50°C. IN AQUEOUS DMSO.

COMPOUND	TIME (mins.)
Tri-iso-propyl phosphite	Instantaneous
Tributyl phosphite	"
Triamyl phosphite	"
Trihexyl phosphite	"
Tri(2-ethyl hexyl)phosphite	5
Triphenyl phosphite	5
Tridecyl phosphite	10
Triphenyl phosphite	10
Dibenzyl phosphite	10
Triauryl phosphite	35

Table 21.

THE OXIDATION OF ORGANO-PHOSPHORUS COMPOUNDS BY ARGENTIC PICOLINATE

COMPOUND	YIELD (%)*	PRODUCT
Triphenylphosphine	100	Triphenylphosphine oxide
Triphenyl phosphite	30	Triphenyl phosphate
	70	Phenol
Trihexyl phosphite	40	Trihexyl phosphate
	20	n-Hexanol
Tridecyl phosphite	20	Tridecyl phosphate
	25	n-Decanol
Trilauryl phosphite	80	Trilauryl phosphate
	20	n-Dodecanol

* Yields (± 10% accuracy) estimated from T.L.C. examination.

Table 22.

THE OXIDATION OF ORGANO-PHOSPHORUS COMPOUNDS BY SILVER II OXIDE

COMPOUND	YIELD (%)*	PRODUCT
Triphenylphosphine	40	Triphenylphosphine oxide
Triphenyl phosphite	30	Triphenyl phosphate
	70	Phenol
Trihexyl phosphite	75	Trihexyl phosphate
Tridecyl phosphite	40	Tridecyl phosphate
	20	n-Decanol
Trilauryl phosphite	60	Trilauryl phosphate
	25	n-Dodecanol

* Yield (± 10% accuracy) estimated from T.L.C. examination.

Table 23.

From the results presented, it can be seen that the yields of phosphate esters from reactions with both oxidants are only poor to moderate. Yields of greater than 80% are obtained by oxidation of phosphite esters with p-benzoquinone in benzyl alcohol at room temperature (146) or with N,N-diethyltrichloroacetamide (147). These latter reagents however, give poorer yields than the silver II compounds in the oxidation of triphenylphosphine. Moderate to good yields of phosphate esters and phosphine oxides have been obtained by aerial oxidation in refluxing iso-propanol (148).

The relative rates of oxidation of some phosphite esters and triphenylphosphine, by argentic picolinate at 50°C. in 50% aqueous dimethyl sulphoxide, are recorded in table 21. It can be seen that even at moderate temperatures, the reaction of all compounds was extremely fast. Tri-iso-propyl, tributyl, triamyl and trihexylphosphites reacted instantaneously upon contact with the oxidant. Although the reaction rates are fast, it does seem that the rate is dependent upon chain length (see earlier parts). The rate of reaction with silver II oxide is also rapid; triethyl phosphite in the absence of solvent was found to react explosively (149).

Possible mechanism of reaction.

Complexes between silver I compounds and tertiary phosphines are known to exist (150) and it has been suggested (151) that these complexes are bonded by π -bonds formed by phosphorus. Nitrogen is unable to form π -bonds and yet complexes between amines and Ag^{I} are known and it has been further suggested that amines complex with Ag^{II} (112). As phosphorus is less electro-

negative than nitrogen, it is reasonable to assume that some form of complex or intermediate could be formed between silver II and tertiary phosphorus compounds. (The lone pair of electrons is more available on phosphorus than on nitrogen and because the element is less electronegative the tetrahedral structure is distorted such that the bond angle is further reduced from the normal $109^{\circ}28'$ leaving the lone pair of electrons more vulnerable to attack). A mechanism for oxidation of the compounds examined and a possible explanation for the formation of either phenol or the alcohol is schematically represented in plate 9. Figure 13 (plate 9) shows the intermediate which can rearrange by a series of one-electron shifts to give the phosphorus radical which then undergoes rapid oxidation to the phosphate ester (fig.14). However, it is possible that the electron transfer mechanism shown in figure 15 could participate and hence diphenyl phosphate would be formed.

D.1 THE REACTION OF ARGENTIC PICOLINATE WITH AMINO-ACIDS AND α-AMINO-ACID ESTERS.

The reactions of amino-acids and α-amino-acid esters with argentic picolinate were examined. The procedure for these reactions, carried out at $70^{\circ}C.$ in aqueous media, followed that outlined in preceding parts of the discussion. α-Amino-acids were oxidised and the volatile products were swept from the flask by a stream of nitrogen and trapped in 2,4-dinitrophenyl-hydrazine reagent. The derivatives were isolated and routinely examined by p.m.r. spectrometry and the data are incorporated in table 12. Examination of the p.m.r. spectra of the products showed that α-amino-acids were oxidatively-cleaved

MECHANISM OF PHOSPHITE OXIDATION

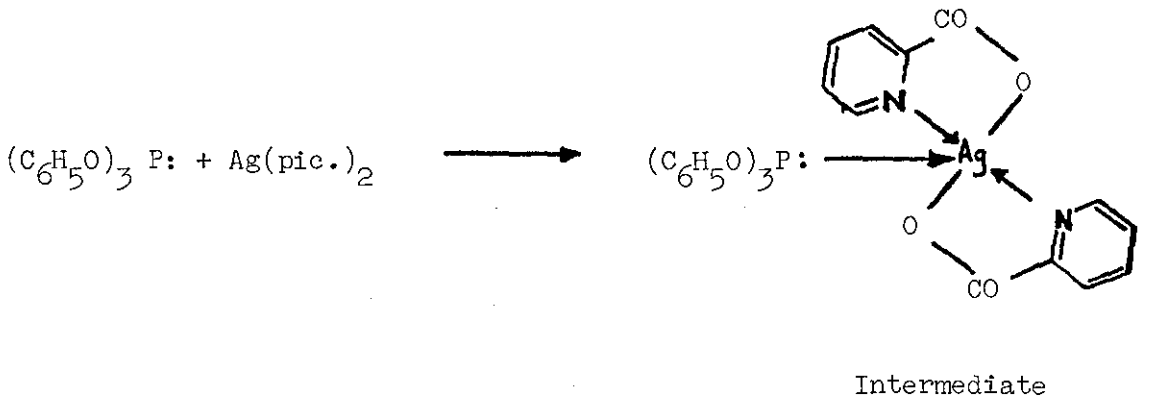


Fig.13

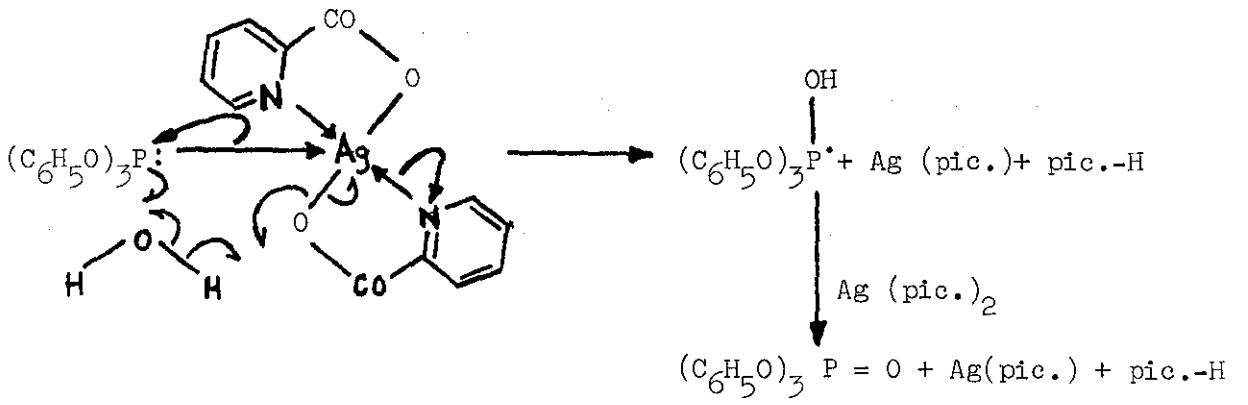


Fig.14

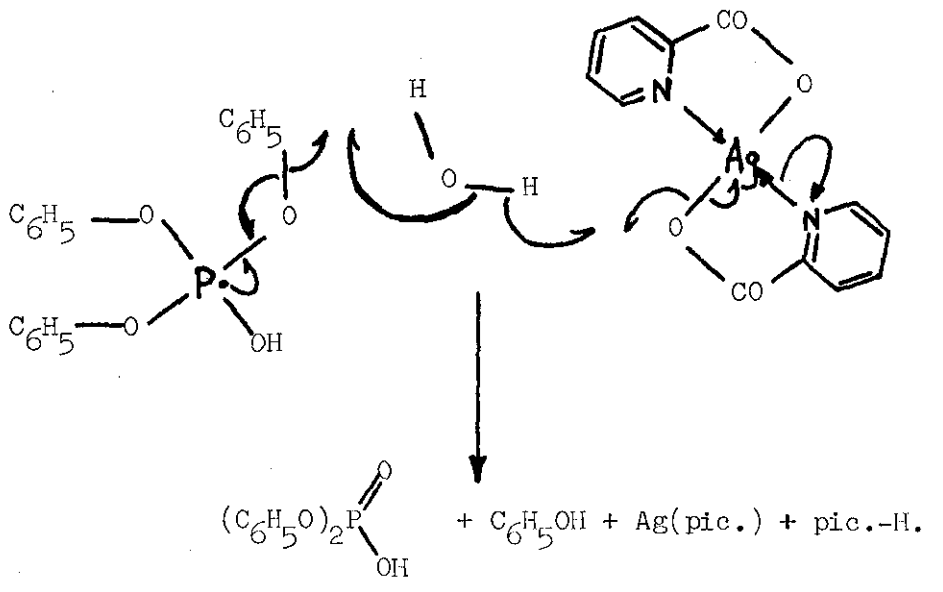


Fig.15.

to give the lower homologous aldehyde. Non-volatile products were isolated by addition of 2,4-D.N.P. reagent to the aqueous reaction mixtures after the silver salts had been removed.

The products from the oxidation of α-amino-acids are recorded in table 24 and it can be seen that the aldehydes are formed in high yield after a short reaction time. The rates of reaction at 70°C.were too fast to permit the differentation of those factors which affect the oxidation but by analogy with other systems examined, it is probable that increase in chain length and chain-branching will adversely affect the rate of reaction. The very high yield of product is especially noteworthy as it is in contrast with many other reported procedures (152). Hence, oxidative-decarboxylation (the Strecker degradation) of α-amino-acids gives rise to poor to moderate yields of the aldehyde when, for example, silver I oxide (96), sodium hypochlorite (153) or $S_2O_8^{2-}/Ag^+$ mixtures (106) are employed as the oxidising agents.

The reaction of argentic picolinate with α-amino-acid esters gave two products (table 25). DL-Ethyl-α-alaninate reacted to give a 50/50 mixture of ethyl pyruvate and ethyl acrylate whilst DL-methyl-α-valinate and L-methyl-α-leucinate gave 87 and 62% of the α-keto-ester, respectively and one other product in each case. The ethyl acrylate and ethyl pyruvate were separated by preparative g.l.c. and their identity was established by examination of their p.m.r.spectra and

comparison with the authentic material. The products of oxidation of methyl valinate and methyl leucinate could not be separated by g.l.c. because of pyrolysis on the column but their mixtures were examined by p.m.r. and I.R. spectra and g.l.c. The p.m.r. spectra could be analysed to show the presence of the α-keto-ester and the possible presence of a β-hydroxy-ester. The I.R. spectra showed a broad band at 3400 $cm.^{-1}$ (valinate product) and 3380 $cm.^{-1}$ (leucinate product). This data could be attributed to the presence of a β-hydroxy-function in each product. β-Hydroxy-ester formation could be accounted for by hydration of the αβ-unsaturated ester. In acid solution, the unsaturated ester can undergo acid-catalysed hydration at the β-position to give the hydroxy-ester (see fig.16). The difference in ratio of the α-keto- to β-hydroxy esters formed from reaction of

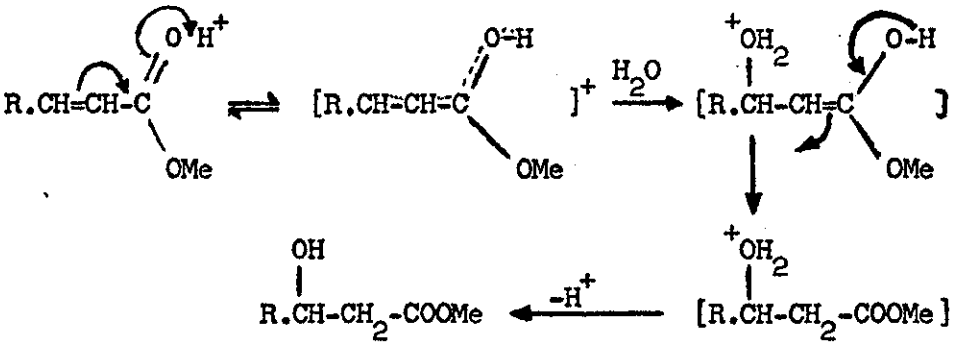


Fig.16.

the two amino-acid esters might be accounted for statistically i.e. a molecule of ammonia will be eliminated more readily from methyl leucinate because there are two β-hydrogen atoms present whereas there is only one in methyl valinate. Hence, more of the unsaturated ester might be expected from methyl leucinate and consequently more of the β-hydroxy ester.

THE OXIDATION OF AMINO-ACIDS BY ARGENTIC PICOLINATE IN WATER AT 70°C.

AMINO-ACID	TIME (mins.)	PRODUCT	YIELD(%)
DL-α-Alanine	26	Acetaldehyde	88
DL-α-Amino-n-butyric acid	25	Propionaldehyde	72
DL-Valine	28	iso-Butyraldehyde	90
DL-nor-Valine	18	n-Butyraldehyde	93
DL-Leucine	46	iso-Pentanaldehyde	88
DL-nor-Leucine	38	n-Pentanaldehyde	95
DL-iso-Leucine	33	2-Methyl-n-butyraldehyde	91
DL-2-Amino-n-octanoic acid	39	n-Heptanaldehyde	75
DL-Phenylglycine	25	Benzaldehyde	75
DL-Phenylalanine	25	Phenylacetaldehyde	73
4-Amino-n-butyric acid	32	Succinaldehydic acid	79
L-Glutamic acid	22	Succinaldehydic acid	80

Table 24.

THE OXIDATION OF α-AMINO-ACID ESTERS BY ARGENTIC PICOLINATE IN WATER AT 70°C.

α-AMINO-ACID ESTER	TIME (mins.)	PRODUCT	YIELD (%)
DL-Ethyl-α-alaninate	30	Ethyl pyruvate	49
		Ethyl acrylate	51
DL-Methyl-α-valinate	20	Methyl 2-oxo-3-methyl-n-butyrate	87
		Methyl 3-hydroxy-3-methyl-n-butyrate*	13
L-Methyl-α-leucinate	20	Methyl 2-oxo-4-methyl-n-pentanoate	62
		Methyl 3-hydroxy-4-methyl-n-pentanoate*	38

* Possible product but not confirmed.

Table 25.

Possible mechanisms for the oxidation of α-amino acids and esters.

It has been shown that the oxidative decarboxylation of α-amino-acids in the Strecker degradation, is not dependent upon the presence of an α-hydrogen atom (153), and hence the oxidation of the amino-group to the imine followed by hydrolysis

and decarboxylation is discounted. The mechanism suggested here for the oxidation by argentic picolinate (plate 10) does not require the presence of an α-hydrogen atom either. The reaction, summarised in equation 47, is initiated by attack of the nitrogen lone-pair of electrons at the Ag^{II} site to give an initial intermediate (fig.17). This is followed by a rearrangement of bonds to displace a picolinate ligand and thus involves the amino-acid in direct bonding with the silver II atom (fig. 18). This complex, in the presence of the second mole of

$$\underset{\underset{NH_2}{|}}{R\text{-}CH\text{-}COOH} + 2\ Ag(pic.)_2 + H_2O \longrightarrow R\ CHO + 2\ Ag(pic.) + 2\ pic\text{-}H + CO_2 + NH_3 \qquad \ldots\ldots 47$$

argentic picolinate can undergo a concerted elimination of carbon dioxide resulting in the oxidation of the amino-acid to the imine (fig.19). This is then hydrolysed to the aldehyde and ammonia. To support this mechanism, pyruvic acid was reacted with (a) argentic picolinate, (b) argentous picolinate and (c) picolinic acid. Acetaldehyde was not found in any of these three reaction mixtures and hence decarboxylation of pyruvic acid in this system is unlikely to occur.

The mechanism of oxidation of α-amino-acid esters is complicated by the competing elimination. However, a mechanism involving the initial intermediate formed by donor bond between the oxidant and the amine can be postulated (fig.20, plate 11). This intermediate can then undergo the electronic rearrangements shown (fig.21) with further oxidation to give the imine or the mechanism (fig.22) could occur in which case the αβ-unsaturated ester would be formed. Presumably the amino-group will remain bonded to the silver I picolinate formed.

MECHANISM OF α-AMINO-ACID OXIDATION

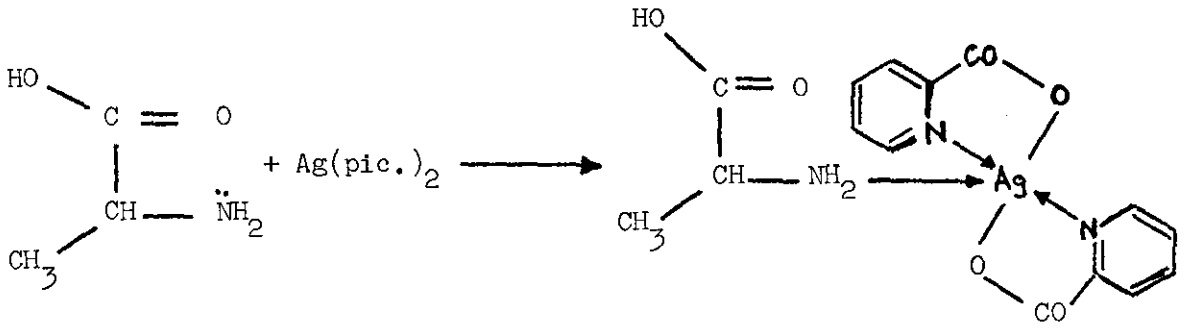


Fig.17

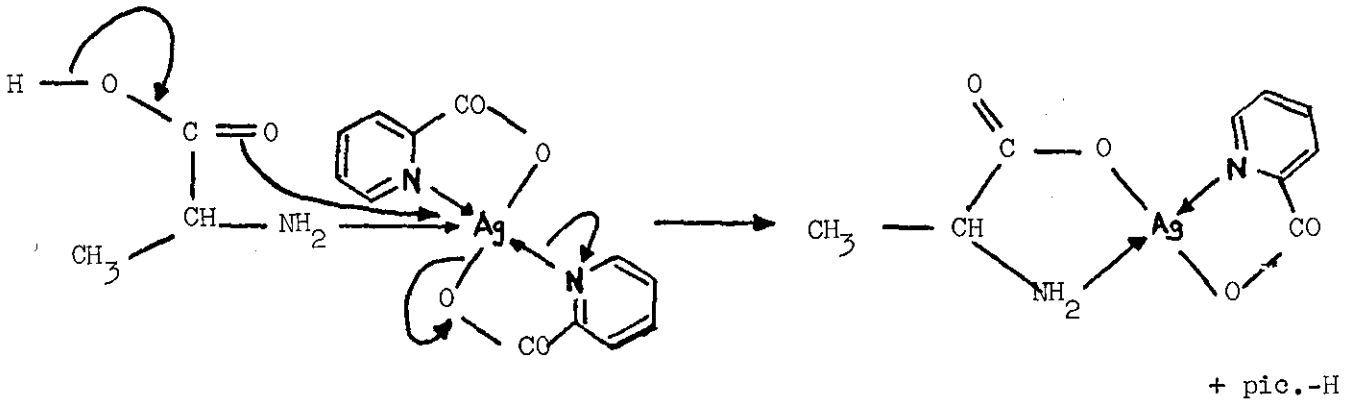


Fig.18

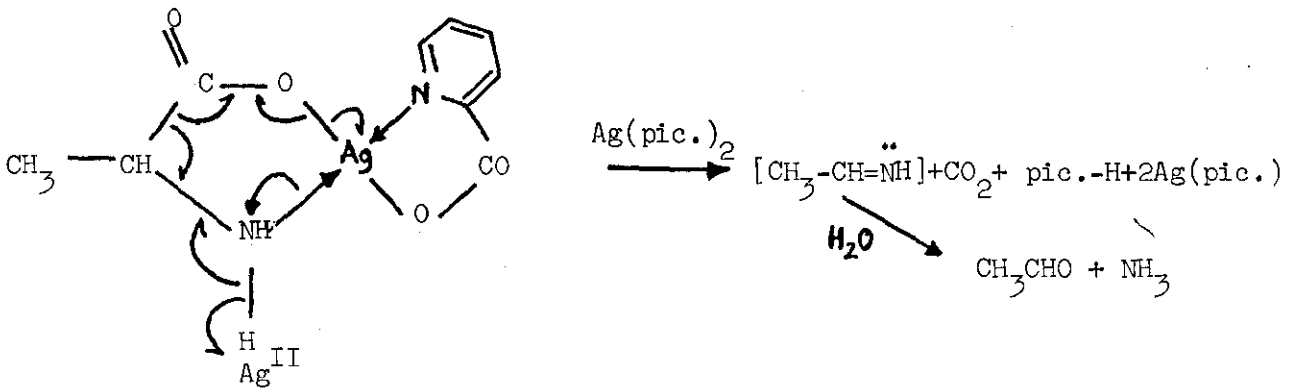


Fig.19

MECHANISM OF α-AMINO-ACID ESTER OXIDATION.

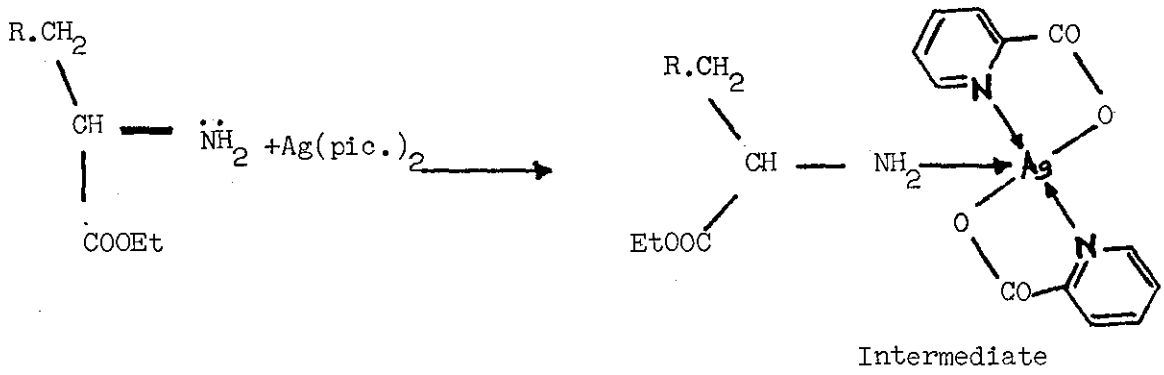


Fig. 20

Route to α-keto-ester

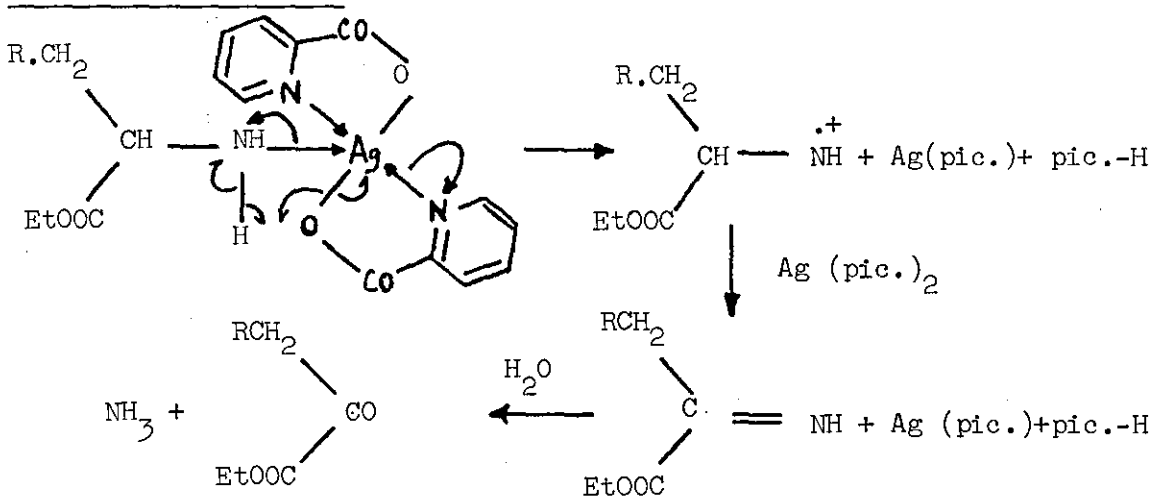


Fig.21

Route to αβ-unsaturated ester

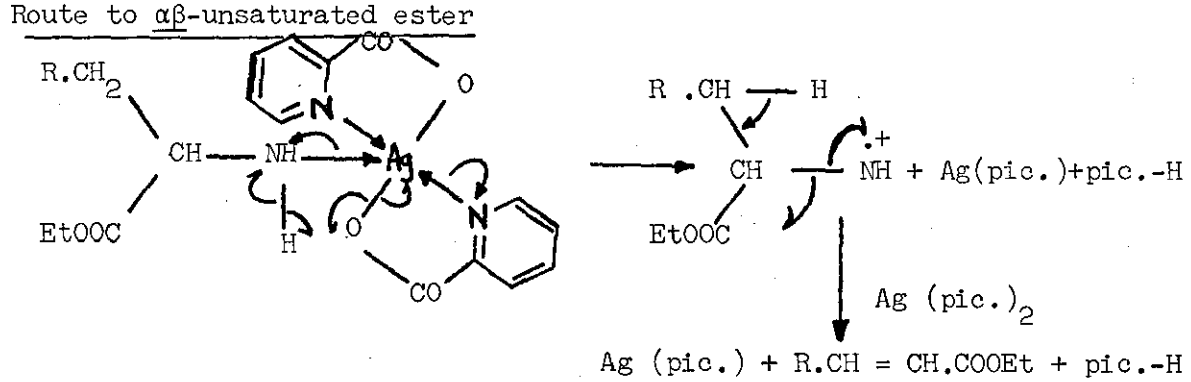


Fig.22

D.2 THE REACTION OF SILVER II OXIDE WITH α-AMINO-ACIDS.

The reaction of silver II oxide with α-amino acids at 70°C. in water was investigated. A procedure, similar to that used for the oxidation of alcohols was employed and the products were examined by g.l.c., p.m.r. and I.R. spectroscopy. The reaction of DL-2-amino-n-butyric acid was also carried out under a stream of nitrogen. The volatile product was swept into 2,4-D.N.P.reagent and the derivative was shown to be that of n-butyraldehyde. With the exception of the latter and phenylglycine which gave benzaldehyde, the product of oxidation was the lower homologous carboxylic acid. However for the amino-acids with a carbon number greater than 5, a second product was also isolated. The acid-products of these latter reactions were isolated and their identity established by examination of their p.m.r. spectra. The lower acids were examined by g.l.c. against authentic compounds as standard, and showed the appropriate bands in their I.R.spectra. The second product of the reactions with the leucines and α-amino-n-octanoic acid were all shown to be neutral compounds, pure by g.l.c. but remain unidentified because p.m.r. and I.R. spectra are inconclusive. However, the p.m.r. spectrum of each indicated the presence of the N - H grouping.

THE OXIDATION OF α-AMINO-ACIDS BY SILVER II OXIDE IN H_2O AT 70°C.

α-AMINO ACID	TIME(hours)	PRODUCT	YIELD(%)
DL-α-Alanine	12	Acetic acid	100*
DL-2-Amino-n-butyric acid	14 (a)	Propionic acid	100*
DL-nor-Valine	12	n-Butyric acid	100*
DL-Valine	20	iso-Butyric acid	100*
DL-nor-Leucine	12	n-Pentanoic acid	49
DL-Leucine	12	iso-Pentanoic acid	61
DL-iso-Leucine	12	2-Methyl-n-butyric acid	53
DL-2-Amino-n-octanoic acid	24	n-Heptanoic acid	58
DL-Phenylglycine	10	Benzaldehyde	79
DL-2-Amino-n-butyric acid	14 (b)	Propionaldehyde	37

* Yield calculated from g.l.c.data.

Table 26

The results of these reactions are recorded in table 26 and show that oxidation proceeds to the carboxylic acid unless the first product of oxidation (the aldehyde) is removed from the sphere of oxidation. Benzaldehyde was not removed from the reaction mixture and therefore the relative stability of aromatic aldehydes towards further oxidation is again shown. Equation 48, summarises the reaction of silver II oxide with α-amino-acids and shows that the oxidant behaves as a two-electron transfer agent.

$$R\text{-}\underset{\underset{NH_2}{|}}{CH}.COOH + 2\ AgO \longrightarrow R.COOH + 2\ Ag + NH_3 + CO_2 \quad \ldots\ldots\ldots 48$$

E.1 THE REACTION OF ARGENTIC PICOLINATE WITH SOME ORGANO-NITROGEN COMPOUNDS.

In an initial survey carried out to establish the scope of the reactions of argentic picolinate with various functional groups (154), a series of nitrogen compounds was examined with the reagent. The results shown in table 27 indicate the products obtained when some of these nitrogen compounds were reacted with argentic picolinate in either dimethyl sulphoxide or water as solvent. The effect of the solvent on the condition of reaction is immediately obvious: benzylamine was oxidised to benzaldehyde in approx. 10 min. in DMSO whilst in water at 70°C, the reaction took 1 hour. It can be seen that DMSO only affected the reaction rate and not the product of the reaction. DMSO was used in an attempt to make the reaction mixture more homogeneous and this may be the factor leading to faster reaction. The electron-transfer process may take place across the solvent/solid interface (112), therefore the greater the

homogeneity of the mixture the faster the reaction will occur.

The results in table 27 indicate that two main types of reaction were occurring for the compounds examined. Compounds such as benzylamine, t-butylamine and N-acetylbenzylamine underwent oxidation whilst cinnamide, benzylidene p-nitroaniline, benzoin-oxime and cyclohexanone-oxime were hydrolysed. Bacon and Hanna (112) have reported the reaction of argentic picolinate with primary and secondary amines and find that, in general, the carbonyl compound was isolated although $Me_3C.CH_2$ $CH(Me)CH_2CH_2NH_2$ gave the corresponding nitrile. On the basis of their results they proposed the mechanism outlined in equations 49 and 50; to support this they reported that the imine, when stable to hydrolysis under the conditions used, was isolated. From these two equations it can be seen that oxidation occurs by the successive removal of two electrons from one mole of amine by two moles of argentic picolinate to give the imine which then undergoes hydrolysis.

$$R.CH_2\text{-}\overset{\overset{Ag(II)}{|}}{N}H.R' \longrightarrow Ag(I) + R.CH_2\text{-}\overset{\cdot+}{N}H.R' \longrightarrow R.\dot{C}H\text{-}NH.R' + H^+ \quad \ldots\ldots 49$$

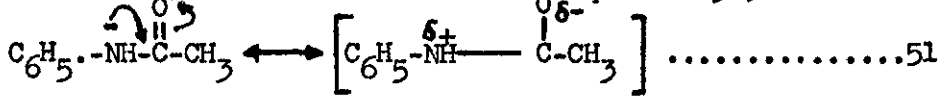
$$Ag(II) + R.\dot{C}H\text{-}NH.R' \begin{cases} \xrightarrow{(+H_2O)} H^+ + Ag(I) + R.CH{=}NR \\ \xrightarrow{(+H_2O)} H^+ + Ag(I) + R.\underset{\underset{OH}{|}}{CH}\text{-}NH.R' \end{cases} \quad \ldots\ldots\ldots 50$$

$$\Rightarrow R.CHO + R\,NH_2$$

The formation of benzaldehyde from benzylamine, reported by Bacon and Hanna was confirmed in this work and the reaction was shown to be aided by use of DMSO, as solvent.

The factors influencing the oxidation of amines by argentic picolinate were outlined in the introduction to this

section. From these factors it becomes evident that the "availability" of the lone pair of electrons on the nitrogen atom will affect the displacement of a ligand from the square-planar Ag(II) complex i.e. the more basic the amine, the greater the "availability" of the electrons and presumably the stronger the complex formed by donor bond to the Ag^{II} ion. Thus a molecule having a less basic nitrogen atom than a primary amine should react more slowly. In amido-compounds the electrons on the nitrogen atom are delocalised due to participation in resonance structures summarised in equation 51; and reaction



.....51

of N-acetylbenzylamine was shown to be extremely slow in comparison to benzylamine. However, N-acetylbenzylamine will similarly not complex as easily with Ag^{I} (formed in the oxidation) and therefore it is less likely to be removed from the sphere of oxidation.

The oxidation of t-butylamine was shown to give iso-butylene by elimination of ammonia and a mechanism which will account for this is proposed in figs.20 and 21, (plate 11). In contrast, benzylidene p-nitroaniline gave benzaldehyde and p-nitroaniline by a hydrolysis reaction which involved the reduction of the silver II picolinate. Similarly cinnamide gave cinnamic acid and ammonia. There are two possible mechanisms for these reactions:- (a) the nitrogen portion of the molecule is oxidised in situ and the product is hydrolysed or (b) the molecule is hydrolysed in the presence of argentic picolinate and then the liberated nitrogen-compound is oxidised. The latter might seem more probable as p-nitro-aniline and ammonia (respectively) were

found to be products of the reactions; approx. 14% of the liberated ammonia will be oxidised by the argentic picolinate (see equation 52).

$$6\ Ag^{II} + 14\ NH_3 \longrightarrow 6\ Ag\ (NH_3)_2^+ + 6H^+ + N_2 \quad \ldots\ldots\ldots\ldots 52$$

Cyclohexanone-oxime gave an emerald green complex when it was reacted with argentic picolinate; the complex was soluble in chloroform but unstable and breakdown led to a deposit of a silver salt and cyclohexanone. The fact that 2-methylcyclohexanone semicarbazone did not react with the reagent under similar conditions must be accounted for in terms of steric hindrance at the site of the tertiary nitrogen atom.

THE REACTION OF ARGENTIC PICOLINATE WITH ORGANO-NITROGEN COMPOUNDS.

COMPOUND	SOLVENT	TEMP.(°C)	TIME (hours)	PRODUCT	YIELD(%)
Benzylamine	DMSO	40	0.15	Benzaldehyde	-
	H_2O	70	1	"	46
t-Butylamine	DMSO	70	4	iso-Butylene	ca.40
	H_2O	70	64	"	-
N-Acetylbenzylamine					
	DMSO	50	0.3	Benzaldehyde	-
	H_2O	70	20	"	49
Cinnamide	DMSO	40	0.2	Cinnamic acid	53
	H_2O	60	0.7	" "	-
Benzylidene p-nitro-aniline	DMSO	40	0.1	(Benzaldehyde)	-
	H_2O	65	3.5	(p-nitroaniline)	-
Benzoin-oxime	DMSO	40	0.2	Benzoin + trace of benzil.	-
Cyclohexanone-oxime	DMSO	40		Green complex	-
2-Methylcyclohexanone semicarbazone	DMSO	40	1 week	No reaction	-

Table 27.

E.2 THE REACTION OF SILVER II OXIDE WITH AMINES.

The reaction of silver II oxide with amines at 70°C. in aqueous media has been examined (149). The procedure employed was similar to that outlined for the reaction of the oxide with

alcohols and the molar ratio of reactants was again 1 mole of oxidant per mole of amine. The products of these reactions were isolated and examined by g.l.c. (see table 28). The results of these reactions indicate that primary amines were oxidised to the aldehydo-compound and the nitrile; the Schiff's base was also isolated in most cases. Only two α-chain-branched primary amines were reacted with the reagent; one gave the corresponding ketone in poor yield and one other compound which was not identified; whilst t-butylamine gave 2-nitro-2-methylpropane. Diphenylamine was reacted with the reagent and gave a mixture of 10 products by T.L.C.; the mixture was not separated. In addition to the products identified from the reaction of primary amines; the iso-cyanide was suspected to be present in most reaction mixtures but its presence was only established, by g.l.c., in the product from the reaction of benzyl-amine. In this case it was only present in a trace amount.

The results of the oxidation of primary amines by the reagent show little consistency in the ratio of products, but it can be seen that the aldehyde was usually formed in small yield. The other oxidation product, the nitrile, was usually formed in moderate yield. The formation of the aldehyde can be accounted for by a two-electron transfer process in which two atoms of hydrogen are removed to give the imine which undergoes hydrolysis to the aldehyde (equation 53). However, for the formation of the nitrile a further 2 atoms of hydrogen have to be removed and this would involve another two-electron transfer process and a second mole of silver II oxide (equation 54). Oxidation of amines to nitriles

$R.CH_2.NH_2 + AgO \longrightarrow Ag + R.CH{=}NH + H_2O \longrightarrow R\,CHO + NH_3$.....53

$R.CH{=}NH + AgO \longrightarrow R.C = N + H_2O + Ag$ 54

is known to occur with bromine (155), iodine pentafluoride (156) and lead tetra-acetate (157). If this is the case for the reaction as carried out (molar ratio 1:1, oxidant:amine) then there will be less oxidant present than will be required to oxidise all of the amine. Schiff's base formation could account for the removal of the excess amine and the aldehyde from the sphere of oxidation; hence the products of oxidation, before the isolation of the products from silver by acid-treatment, might be the nitrile and the Schiff's base. During the separation procedure, the Schiff's base will be partially hydrolysed to the aldehyde and the amine. This could account for the varying yields of the aldehydes isolated since the rate of hydrolysis will vary from one Schiff's base to another. The formation of the iso-cyanide can only be accounted for by a 1:2 migration of, for example, a phenyl group and its bond electrons. Equations 55 and 56 show how this might occur.

$C_6H_5.CH{=}NH: \longrightarrow AgO \longrightarrow [C_6H_5.CH{=}\overset{+}{N}] + Ag + OH^-$ 55

$[N^+{=}CH(\text{-}\phi)] \longrightarrow [C_6H_5N{=}\overset{+}{C}H] \longrightarrow C_6H_5NC + H^+$.....56

THE OXIDATION OF AMINES BY SILVER II OXIDE AT 70°C. IN WATER.

AMINE	TIME (hours)	PRODUCT	YIELD(%)
n-Butylamine	5	n-Butyronitrile	87
		Schiff's base	13
2-Ethyl-n-butylamine	12	2-Ethyl-n-butyraldehyde	17
		2-Ethyl-n-butyronitrile	40
		Schiff's base	43
Sec-Butylamine	2.5	Methyl ethyl ketone	10
		Unknown compound	90
n-Pentylamine	12	n-Pentanaldehyde	13

(continued)

THE OXIDATION OF AMINES BY SILVER II OXIDE AT 70°C. IN WATER (cont'd)

AMINE	TIME (hours)	PRODUCT,	YIELD(%)
		n-Pentonitrile	87
n-Hexylamine	12	n-Hexanaldehyde	1
		n-Hexonitrile	26
		Schiff's base	73
2-Ethyl-n-hexylamine	13	2-Ethyl-n-hexanaldehyde	25
		2-Ethyl-n-hexonitrile	75
Cyclohexylamine	4	Cyclohexanone	100
Benzylamine	4	Benzaldehyde	23
		Benzonitrile	77
		Phenyl isocyanide	-
t-Butylamine	48	2-Nitro-2-methylpropane	100
Diphenylamine	18	Mixture of ten products	-

* Yield calculated from g.l.c. data

Table 28.

F.1 THE REACTION OF ARGENTIC PICOLINATE WITH OLEFINE AND AROMATIC HYDROCARBONS.

Olefins. In an initial investigation, the reaction of olefins with argentic picolinate at 50°C. in aqueous DMSO was examined and the specific oxidation of styrene and trans-stilbene at 70°C. in water was investigated. The procedures employed for all these reactions were similar to those outlined for the oxidation of alcohols by the reagent. The results of the rate of reaction of silver II with olefins are shown in tables 29-31 whilst the products of oxidation of styrene and trans-stilbene are recorded in table 32.

It can be seen from the results in tables 29 and 30 that the rate of reaction of cyclic mono-olefins decreases with increase in ring size and that 4-methylcyclohexene reacted more slowly than cyclohexene. For straight chain olefins (tables 29 and 31), the rate of reaction decreases with (a) the increase in chain length and (b) the increase in chain-branching. Also, cis-olefins appear to be oxidised at a

faster rate than the trans-isomer (compare maleic and fumaric acids) whilst terminal olefins react more slowly than the symmetrical isomer (compare cis-pent-2-ene and pent-1-ene). In general the substitution of an electron-withdrawing group, such as a carboxyl group, in conjugation with the carbon-carbon double bond will hinder the reaction by limiting the formation of a donor bond to the silver atom.

The oxidation of styrene and trans-stilbene is recorded in table 32. Examination of the products by g.l.c. showed that benzaldehyde was formed in each case but surprisingly, acetaldehyde was not found as an oxidation product of styrene. The reactions were carried out with 2 moles of oxidant per mole of olefin and on this basis, the yields of benzaldehyde are low especially from trans-stilbene because 2 moles of benzaldehyde might have been expected per mole of stilbene.

THE RATE OF REACTION OF ARGENTIC PICOLINATE WITH OLEFINS IN AQUEOUS DMSO AT 50°C.

OLEFIN	TIME (Hours)
cis-Pent-2-ene	0.25
Cyclopentene	1.25
Cyclohexene	1.5
4-Methylcyclohexene	2
Indene	2.5
Hex-2-ene	3
Cycloheptene	3
Methylene cyclohexane	3.25
Cyclododecene	3.5
Hept-3-ene	4
α-Methyl styrene	4
2-Ethyl-n-hex-1-ene	5
Styrene	11
trans-Stilbene	17
Cyclo-octene	19.5
Oct-1-ene	20.5
Di-iso-butylene	23
2,4,4-Trimethylpent-2-ene	24
2-Methylbut-1-ene	27
Pent-1-ene	46
Maleic acid	99
2-Methylbut-2-ene	100
Fumaric acid	no reaction after 102.

Table 29.

THE RELATIVE RATE OF REACTION OF CYCLO-OLEFINS WITH ARGENTIC PICOLINATE

CYCLO-OLEFIN	RELATIVE RATE *
Cyclopentene	108
Cyclohexene	100
4-Methylcyclohexene	75
Indene	60
Cycloheptene	50
Cyclododecene	43
Cyclo-octene	8

*Rate, relative to cyclohexene = 100 at 50°C.in aqueous DMSO.

Table 30.

THE RELATIVE RATE OF REACTION OF OLEFINS WITH ARGENTIC PICOLINATE

OLEFIN	RELATIVE RATE*
cis-Pent-2-ene	1600
Hex-2-ene	133
Methylene-cyclohexane	123
Hept-3-ene	100
α-Methylstyrene	100
2-Ethyl-n-hex-1-ene	80
Styrene	36
trans-Stilbene	24
Oct-1-ene	20
Di-iso-butylene	17
2,4,4-Trimethylpent-2-ene	17
2-Methylbut-1-ene	15
Pent-1-ene	9
Maleic acid	4
2-Methylbut-2-ene	4
Fumaric acid	-

*Rate relative to Hept-3-ene = 100; at 50°C. in aqueous DMSO.

Table 31.

THE OXIDATION OF AROMATIC HYDROCARBONS AND OLEFINS BY ARGENTIC PICOLINATE AT 70°C. IN WATER.

COMPOUND	TIME (Hours)	PRODUCT	YIELD(%)
Toluene*	1	Benzyl alcohol	-
Ethylbenzene	75	Acetophenone	27
p-Cymene	17	p-Cuminaldehyde	32
Styrene	175	Benzaldehyde	46
trans-Stilbene	3.75	Benzaldehyde	23

*Reaction carried out at 65°C. in aqueous DMSO.

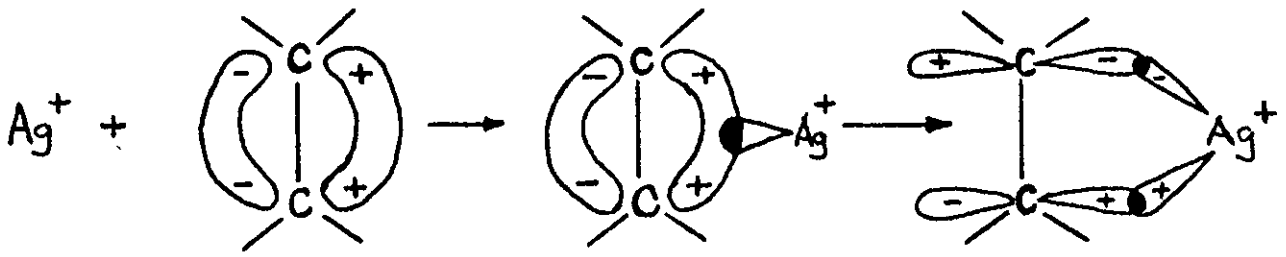
Table 32.

Due to the low yield of benzaldehyde from trans-stilbene and the absence of acetaldehyde and acetic acid as products of the oxidation of styrene, it is difficult to postulate a reasonable mechanism to account for the oxidation reaction by argentic picolinate. However, the oxidation almost certainly proceeds via an olefin-silver II intermediate. Silver I-olefin complexes are well known, sometimes as crystalline compounds (158) and therefore, even if unstable, some form of complex with silver II should exist. The bonding of silver I compounds to olefins can be explained in terms of a simplified molecular orbital theory as the overlap of π -orbitals from the olefin with empty d-orbitals on the silver I atom followed by back-bonding to acceptor π-orbitals on the carbon atoms (see fig.23). Silver I compounds complex more easily to cis-olefins than the trans-isomer and only with cyclic olefins when strain in the ring system can be reduced by so doing (158). Complexes between palladium IV and olefins are known and it is via such intermediates that olefins are oxidised to carbonyl compounds (159). Hence, an intermediate such as shown in fig.24 might be the initial complex in the oxidation of olefins by silver II picolinate.

Aromatic hydrocarbons.

The reaction of argentic picolinate with aromatic hydrocarbons at 70°C. in either water or aqueous DMSO, was examined. The procedure employed was similar to that already outlined in previous parts of the discussion. The results of these reactions are recorded in table 32 from which it can be seen that toluene (molar ratio 1:2, compound to oxidant) gave the alcohol whilst a molar ratio of 1:4 used with ethylbenzene and p-cymene gave the respective carbonyl compounds. The reaction

SILVER-OLEFIN COMPLEXES



π - bond overlap with empty Ag^+ orbitals.

Backbonding from filled Ag^+ orbitals to acceptor π^*-orbitals on carbon atoms.

Fig.23

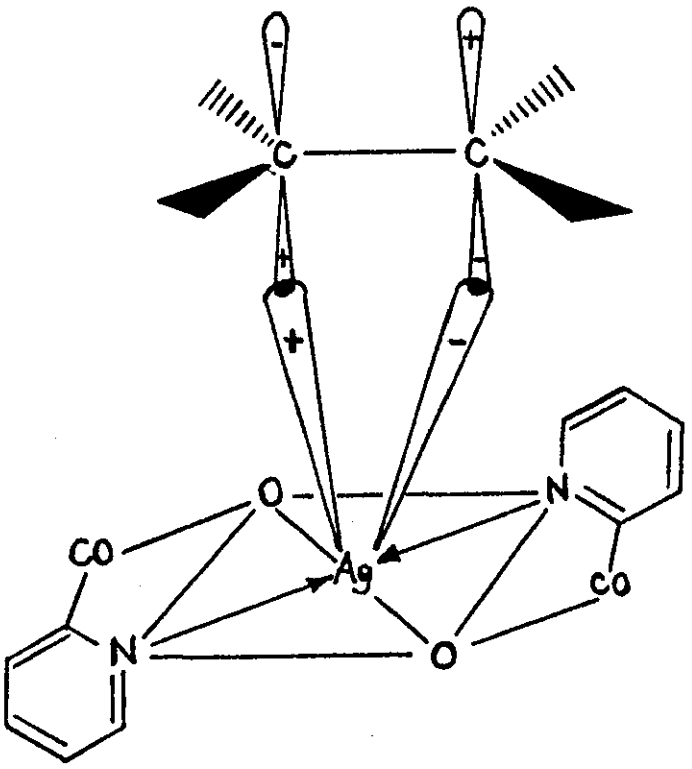


Fig.24

times indicate that the use of DMSO increased the rate of reaction.

In section I of this thesis (p.20), the results of reactions of toluene and o-toluenesulphonamide with argentic picolinate were recorded. It was seen that 1 mole of toluene was oxidised to benzyl alcohol by 2 moles of argentic picolinate and that by the successive addition of 2 moles of oxidant to each product, benzaldehyde and ultimately benzoic acid. The stepwise oxidation was controlled by reactant ratios i.e. the addition of 2 moles of oxidant per mole of compound at each stage. The reaction of o-toluenesulphonamide with argentic picolinate (table 2) showed that no oxidation product was isolated although the oxidant was reduced. The oxidation of ethylbenzene gave acetophenone and p-cymene gave cuminaldehyde and in the latter case there are two types of α-carbon atom at which attach could take place. Apparently, attack takes place at the site of the primary hydrogen and not at the tertiary atom.

The oxidation of toluene by homolytic bond fission at the α-carbon atom was discussed in section I and there it was suggested that a one-electron transfer process would yield the benzyl radical which would be stabilised by delocalisation of the electron around the nucleus. The mechanism of oxidation by a one-electron transfer process is not well established (e.g. oxidation by cobaltic salts (160)). However, it can be assumed that a possible mechanism of reaction will involve the removal of a hydrogen radical from the α-carbon atom by a complex either between the alkyl group and the silver II atom or the π -electron system of the nucleus and the transition element. The latter might be discounted because (a) the π-electron

system is more"tightly" held than in the case of an isolated carbon-carbon double bond system and (b) such a complex would possibly lead to oxidation of the aromatic nucleus and the consumption of many moles of the oxidant. Homolytic bond fission at the α-carbon atom then leads to the attack of water and the second mole of oxidant (equations 57 and 58).

$$C_6H_5.CH_3 + Ag(pic.)_2 \longrightarrow C_6H_5.CH_2^{\bullet} + Ag(pic.) + pic\text{-}H \quad .....57$$

$$C_6H_5.CH_2^{\bullet} + Ag(pic.)_2 + H_2O \longrightarrow C_6H_5CH_2OH + Ag(pic.) + pic\text{-}H \quad ...58$$

In the case of o-toluenesulphonamide, where a strongly electron-withdrawing group such as the sulphonamido-group is present, the homolytic bond fission to give a hydrogen radical will be less favourable than for toluene and the group being ortho-substituted will sterically hinder the formation of the initial complex with the silver II atom. It is possible that the oxidation of aromatic hydrocarbons by argentic picolinate proceeds via hydrogen atom transfer by an outer sphere mechanism (equation 59).

$$C_6H_5.CH_2\text{-}H + pic. \text{ - } Ag(pic.) \longrightarrow C_6H_5CH_2^{\bullet} + H\text{-}pic. + Ag(pic.) \quad ..59$$

F.2 THE REACTION OF ARGENTIC PICOLINATE WITH OTHER ORGANIC COMPOUNDS.

The reaction of 1 mole of 1:4-hydroquinone with 2 moles of argentic picolinate at 70°C. in water gave 1:4-benzoquinone in high yield. The product (table 33) was identified by g.l.c. and infra-red spectroscopy by comparison with authentic material. The reaction proceeded smoothly and all of the oxidant was reduced in 30 minutes. The reaction of other hydroquinones was complicated by the instability of the products e.g. 2,6-dihydroxynaphthalene gave a mixture of products.

An examination of the reaction by argentic picolinate with α-hydroxyacids at 70°C. in water was carried out; the results

are shown in table 33. Lactic acid and mandelic acid underwent oxidative-decarboxylation to the lower homologous aldehyde. The reactions gave a moderate yield of acetaldehyde and an excellent yield of benzaldehyde. For a possible mechanism see plate 10 (oxidation of α-amino-acids).

The reaction of argentic picolinate and α-hydroxy-esters at 70°C. in aqueous media was examined and the results are recorded in table 33. Ethyl lactate was oxidised to ethyl pyruvate which was isolated and identified as the 2,4-D.N.P. derivative and ethyl mandelate gave ethyl benzoylformate. This α-keto ester was established by g.l.c. and p.m.r. spectrum of the resulting mixture and the yield indicated from both g.l.c. and p.m.r. data agreed within 10%.

THE OXIDATION OF OTHER COMPOUNDS BY ARGENTIC PICOLINATE AT 70°C. IN WATER.

COMPOUND	TIME (Hours)	PRODUCT	YIELD(%)
1,4-Hydroquinone	0.5	1,4-Benzoquinone	89
Mandelic acid	0.17	Benzaldehyde	90
Lactic acid	1.33	Acetaldehyde	43
Ethyl mandelate	4.25	Ethyl mandelate	35
Ethyl lactate	3.75	Ethyl pyruvate	30

Table 33.

EXPERIMENTAL.

Infra-red spectra (I.R.) were recorded on Perkin-Elmer spectrophotometers 237 and 257. The abbreviations used in the data quoted are as follows :- s = strong, m = medium, w = weak, sh = shoulder and b = broad. The values quoted have the wave-number ($cm.^{-1}$) as units and have been corrected. Ultra-violet (u.v.) spectroscopic data were recorded on a Unicam-S.P.800 instrument.

Proton magnetic resonance (p.m.r.) spectra were recorded on a Perkin-Elmer R.10, 60 Mc.p.s. spectrometer. The chemical shifts are quoted with reference to tetramethylsilane as standard and the tau-values recorded for any multiplet are at the midpoint of that multiplet and may not be at its centre of gravity. The abbreviations s = singlet, d =doublet, t = triplet, q = quartet, q_t=quintet, s_x = sextet, h = heptet, o = octet, m = multiplet and b = broad are used throughout.

Thin layer chromatography (T.L.C.), unless stated, was carried out with plates (7.5 x 7.5 cm.) prepared by dipping in a Kieselgel-GF/chloroform slurry and spots were identified by adsorption of iodine vapour. Other T.L.C. examinations were carried out on plates (20 x 5 cm.) spread with Kieselgel-GF_{254} which had been activated at 150°C. for 3 hours. Spots were identified by use of a Mineralight UVS-11, ultraviolet lamp.

Analytical gas-liquid chromatography (g.l.c.) was carried out on Pye, series-104 chromatographs with flame-ionisation detectors. Nitrogen, as carrier-gas, at 60 ml. per min. was used with the following columns :- 10% silicon

oil (S.E.- 30) on firebrick; 5% silicon oil (S.E.- 52) on firebrick; 5% polyethylene glycol adipate (PEG.A) on celite; 5% dinonyl phthalate (DNP) on chromosorb-W and 10% apiezon-L on chromosorb-W. (All columns were 1.5 m.x 4 mm.). Preparative g.l.c. was carried out on an Aerograph autoprep, 705 chromatograph with flame ionisation detection using a 30% PEG.A on chromosorb-W column (30'x3/8")with nitrogen as carrier-gas at 200 ml. per min.

Preparation of α-Picolinic acid.(161)

α-Picoline (50g.; 0.54 M), potassium permanganate (90g.; 0.57 M) and water (2.5 l.) were heated under reflux until the purple colour had dispersed. Potassium permanganate (90g.; 0.57M) in water (500 ml.) was added and the heating was continued until the purple colour was again dispersed. The mixture was allowed to cool partially and the solid manganese dioxide was removed by filtration under reduced pressure. The residue was washed thoroughly with hot water (1 l.) and the filtrate and washings were concentrated to a volume of approx. 200 ml. by rotary evaporation. This solution was acidified to pH5 (congo red paper) with concentrated hydrochloric acid and then evaporated to dryness. The solid residue was heated under reflux with ethanol (95%; 250 ml.) for 1 hr. and the mixture was filtered. This procedure was repeated with a further portion of ethanol (95%; 150 ml.) and the alcohol was removed from the filtrates to give a white solid (40 g.); m.p. = 128 - 130°C. (lit. (162) m.p.=136°C.); yield, 60%. I.R.spectrum showed absorption at the following $\nu_{max.}$ (cm^{-1}):- 3660-2600(s,b), 3100 (w),

1862 (w), 1720 (w), 1655 (m), 1600 (s), 1580 (sh), 1562 (m), 1516 (w), 1446 (w), 1378 (s), 1338 (w), 1286 (m), 1242 (w), 1212 (w), 1148 (w), 1079 (w), 1037 (w), 990 (w), 827 (w), 790 (w), 743 (s), 695 (m) and 672 (s). P.m.r. spectrum was recorded in deuterium oxide showed signals at the following tau values :- 1.1 (d, J=5 c.p.s.), 1 proton; 1.6 (m), 3 protons.

Preparation of Argentic picolinate.

Picolinic acid (61.5 g.; 0.5 M) was dissolved in water (approx. 2 l.) and a solution of silver nitrate (42.5 g.; 0.25 M) in water (500 ml.) was added slowly whilst the bulk solution was stirred. The argentous picolinate separated as a white solid. A solution of potassium persulphate (33.8.; 0.125M) in water (500 ml.) was added to the aqueous suspension of the argentous material and the mixture was stirred and left to stand in the dark for 3 days. (The mixture was stirred occasionally during this time). The argentic picolinate, which separated as a red-orange solid, was removed from the solution by filtration under reduced pressure and washed several times with cold water (6 x 250 ml.). The material was partially dried on the filter and finally in a darkened vacuum oven at 30°C to constant weight (76 g.); yield, 87%. The solid material was ground to a fine powder and stored in the dark. I.R.spectrum showed absorption at the following $\nu_{max.}$ (cm^{-1}):-
1655 (w), 1650 (w), 1638 (w), 1605 (s), 1582 (s), 1565 (s), 1440 (m), 1415 (s), 1405 (s,b), 1295 (w), 1240 (w), 1090 (w), 1045 (w), 1005 (w), 995 (w), 850 (w), 840 (w), 750 (m), 710 (m) and 705 (m). U.V. spectrum, recorded in water, showed

absorption at the following $\lambda_{max.}$:- 217 mμ ($\epsilon_{max.}$= 5,985), 263 mμ ($\epsilon_{max.}$=6,110) and 325 mμ ($\epsilon_{max.}$=1,660).

Preparation of silver II oxide. (116)

Pelleted sodium hydroxide (72 g.; 1.7M.) was dissolved in water (1 l.) and brought to approx. 80°C. on a water-bath. Potassium persulphate (75 g.; 0.28M.) was added to the solution followed by the slow addition of silver nitrate (51g.; 0.33M.) in water (250 ml.). The mixture was stirred for 5 min. and then left to stand at 80°C. for 1 hr. The silver II oxide, which separated as a grey-black solid, was removed by filtration under reduced pressure after the solution had been cooled. Potassium persulphate was removed from the solid by washing with water (500 ml.) containing sodium hydroxide (5g.; 0.125 M.) and then water (500 ml.). The material was partially dried on the filter and then dried to constant weight (36.5 g.) in a darkened oven at 30°C. The material was ground to a fine powder and stored in the dark. Yield, 98.5%.

A.1. The reaction of argentic picolinate with alcohols.

Initial investigation of rate of reaction.

(a) A series of alcohols was treated with argentic picolinate at 40°C. The alcohol (0.5 mM.) was mixed with the oxidant (0.35g.; 1mM.) and 50% aqueous dimethyl sulphoxide (10ml.) and kept at a constant 40°C. until the colour change red-orange to white had been completed. The time for the reaction was recorded (see Table 3).

(b) A series of alcohols was treated with argentic picolinate at 40°C. The procedure was identical with (a) except that the mixtures were shaken throughout the duration of the reaction. (see Table 4).

Detailed investigation of reactions.

In general, two procedures were undertaken for the isolation of the products of oxidation of alcohols. One procedure involved the formation of the 2,4-dinitrophenylhydrazone derivative; the second involved the separation of the product(s) and their subsequent identification.

Procedure 1. The alcohol (3mM.) was reacted with argentic picolinate (2.1g.; 6mM.) in water (50ml.). The mixture was heated under reflux at 70°C. and stirred for the duration of the reaction. Nitrogen gas was bubbled slowly through the mixture and any volatile product was swept into a trap containing 2,4-dinitrophenylhydrazine reagent (50ml.). The reaction was continued until the colour change orange-red to white had been completed; the mixture was then acidified with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and the filtrate was treated with 2,4-dinitrophenylhydrazine reagent until precipitation (if any) was complete. The solid derivatives were combined and carefully washed free from the reagent on a filter. The derivative was dried to a constant weight at 80°C. and the conversion of alcohol to carbonyl compound was calculated on the basis of the weight recorded.

Procedure 2. Procedure 2 was identical to procedure 1 with the exception that (a) nitrogen was not passed through the mixture and (b) the aqueous solution (after the solid material had been removed by filtration) was extracted with chloroform or the product was isolated by rotary evaporation and subsequent extraction of the resulting solid. (The physical properties of the product(s) determined the method of isolation). The following data were recorded for the alcohols named:-

Methanol. The alcohol (0.096g.) was treated by procedure 1 (0.8 hr.) and the formaldehyde was isolated as the 2,4-dinitrophenylhydrazone (2,4-D.N.P.) derivative (0.48g.); m.p.=160°C; yield, 80%. The proton magnetic spectrum (p.m.r.), recorded in deuterochloroform ($CDCl_3$), see Table 12.

Ethanol. The alcohol (0.14g.) was treated by procedure 1 (0.83 hr.) and the acetaldehyde was isolated as the 2,4-D.N.P.derivative (0.49g.); m.p.=141°C; yield 77%. The p.m.r.spectrum, recorded in $CDCl_3$, see Table 12.

n-Propanol. The alcohol (0.18g.) was treated by procedure 1 (1 hr.) and the propionaldehyde was isolated as the 2,4-D.N.P.derivative (0.48g.); m.p.=151°C.; yield, 71%. The p.m.r. spectrum, recorded separately in $CDCl_3$ and deuterodimethyl sulphoxide, see Table 12.

iso-Propanol. The alcohol (0.18g.) was treated by procedure 1 (1.4 hr.). The acetone was isolated as the 2,4-D.N.P.derivative (0.56g.); m.p.=120-122°C.; yield, 79%. The p.m.r.spectrum, recorded in $CDCl_3$, see Table 13.

n-Butanol. The alcohol (0.22g.) was treated by procedure 1 (1.4 hr.) and the n-butyraldehyde was isolated as the 2,4-D.N.P.derivative (0.55g.); m.p.= 119-121°C.; yield, 76%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

iso-Butanol. The alcohol (0.22g.) was treated by procedure 1 (1.1 hr.) and the iso-butyraldehyde was isolated as the 2,4-D.N.P.derivative (0.41g.); m.p.=183°C.; yield, 57%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

sec-Butanol. The alcohol (0.22g.) was treated by procedure 1 (2.5 hr.) and the methyl ethyl ketone was isolated as the 2,4-D.N.P.derivative (0.49g.); m.p.=111-113°C.; yield, 68%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 13.

n-Pentanol. The alcohol (0.26g.) was treated by procedure 1 (1.5 hr.). The n-valeraldehyde was isolated as the 2,4-D.N.P.derivative (0.57g.); m.p.= 106°C.; yield, 74%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

iso-Pentanol. The alcohol (0.26g.) was treated by procedure 1 (1.25 hr.). The iso-valeraldehyde was isolated as the 2,4-D.N.P.derivative (0.47g.); m.p.=119-121°C.; yield, 61%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

neo-Pentanol. The alcohol (0.26g.) was treated by procedure 1 (1.3 hr.) and the pivalaldehyde was isolated as the 2,4-D.N.P.derivative (0.54 g.); m.p.=199-201°C (Lit.(162), 210°C.); yield, 70%. The p.m.r.spectrum, recorded in $CDCl_3$; see Table 12.

n-Hexanol. The alcohol (0.31g.) was treated by procedure 1 (1.5 hr.) and the n-hexanaldehyde was isolated as the

2,4-D.N.P.derivative (0.56g.); m.p.=102°C.; yield, 69%. The p.m.r.spectrum, recorded in $CDCl_3$; see Table 12.

Cyclohexanol. The alcohol (0.30g.) was treated by procedure 1 (1.3 hr.) and the cyclohexanone was isolated as the 2,4-D.N.P.derivative (0.48g.); m.p. =158°C.; yield, 66%. The p.m.r.spectrum, recorded in $CDCl_3$; see Table 13.

2-Ethylhexanol. The alcohol (0.39g.) was treated by procedure 1 (1.5 hr.) and the 2-ethylhexanaldehyde was isolated as the 2,4-D.N.P.derivative (0.48g.); m.p.= 119°C.; yield, 52%. The p.m.r. spectrum, recorded in $CDCl_3$; see Table 12.

n-Heptanol. The alcohol (0.35g.) was treated by procedure 1 (1.5 hr.) and the n-heptanaldehyde was isolated as the 2,4-D.N.P.derivative (0.46g.); m.p.=105°C; yield, 54%. The p.m.r. spectrum, recorded in $CDCl_3$; see Table 12.

n-Decanol. The alcohol (0.47g.) was treated by procedure 1 (2.3 hr.). The n-decanaldehyde was isolated as the 2,4-D.N.P. derivative (0.66g.); m.p.=98°C.; yield, 68%.

DL-1-Phenylethanol. The alcohol (0.37g.) was treated by procedure 1 (2.6 hr.) and the acetophenone was isolated as the 2,4-D.N.P.derivative (0.66g.); m.p.=247-249°C.; yield, 73%.

DL-2-Phenylethanol. The alcohol (0.37g.) was treated by procedure 1 (1.1 hr.) and the phenylacetaldehyde was isolated as the 2,4-D.N.P.derivative (0.55g.); m.p.=114-116°C.; yield, 61%.

Benzhydrol. The alcohol (0.53g.) was treated by procedure 2 (5.75 hr.). The product in chloroform was examined by g.l.c. on a silicon oil (S.E.-30) column at 250°C. A single peak was recorded at R_t=4.2 min. whilst benzophenone was shown to have an identical retention time under identical conditions. Removal of the solvent yielded benzophenone (0.42g.); yield, 80%.

Borneol. The alcohol (0.46g.) was treated by procedure 1 (1.75 hr.) and the camphor was isolated as the 2,4-D.N.P. derivative (0.79g.); m.p.=172°C.; yield, 79%.

iso-Borneol. The alcohol (0.46g.) was treated by procedure 2 (7 hr.). The product in chloroform was examined by T.L.C. on Kieselgel-GF_{254}(0.5mm.) in 10% $CH_3OH/CHCl_3$ solvent. A single spot at R_f=0.62 was recorded, which ran concurrently with an authentic sample of camphor. Removal of the solvent gave a white solid (0.24g.); yield, 53%. The p.m.r. spectrum, recorded in carbon tetrachloride (CCl_4), showed signals at the following tau values:- 8.15 (multiplets), 7 protons; 9.05(s), 3 protons; 9.15 (s), 6 protons. The p.m.r. spectrum of authentic DL-camphor, recorded in CCl_4), was identical with the above unresolved spectrum.

2-Ethoxyethanol. The alcohol (0.27g.) was treated by procedure 1 (1.75 hr.) and the 2-ethoxyacetaldehyde was isolated as the 2,4-D.N.P.derivative (0.41g.); m.p.=118°C. (Lit.(163),115-116°C.); yield, 53%.

Tetrahydrofurfuryl alcohol. The alcohol (0.35g.) was treated by procedure 1 (1.6 hr.) and the tetrahydrofurfuraldehyde was isolated as the 2,4-D.N.P.derivative (0.57g.); m.p.=120°C.; yield, 62%.

Benzyl alcohol. The alcohol (0.32g.) was treated by procedure 1 (1.1 hr.) and the benzaldehyde was isolated as the 2,4-D.N.P. derivative (0.65g.); m.p.=232°C.; yield, 79%.

p-Nitrobenzyl alcohol. The alcohol (0.46g.) was treated by procedure 2 (2.5 hr.) and the product, in chloroform, was examined by g.l.c. on a silicon oil (S.E.-30) column at 250°C. A single peak was recorded at R_t= 2.75 min. whilst p-nitrobenzaldehyde was found to have a R_t=2.70 min. under identical conditions. Removal of the solvent gave p-nitrobenzaldehyde (0.38g.); yield, 84%.

Anisyl alcohol. The alcohol (0.41g.) was treated by procedure 2 (0.42 hr.) and chloroform extract was examined by g.l.c. on a silicon oil (S.E.-30) column at 210°C. A peak was recorded at R_t=3.56 min. whilst anisaldehyde was recorded at R_t=3.60 min. under identical conditions. Removal of the solvent gave anisaldehyde (0.36g.); yield, 87%.

3,4-Dimethoxybenzyl alcohol. The alcohol (0.5g.) was treated by procedure 2 (0.08 hr.) and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 230°C. A peak was recorded at R_t=2.80 min. whilst veratraldehyde was recorded at R_t=2.79 min. under identical conditions. The solvent was removed to give veratraldehyde (0.42 g.); yield, 83%. The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values :- 0.20 (s), 1 proton, 2.65 (double d, $J_{H_2H_6}$=2 c.p.s., $J_{H_5H_6}$=10.c.p.s.), 1 proton; 2.7 (d, $J_{H_2H_6}$ = 2 c.p.s.), 1 proton; 3.15 (d, $J_{H_5H_6}$=10 c.p.s.), 1 proton; 6.15 (s), 6 protons.

Piperonyl alcohol. The alcohol (0.46g.) was treated by procedure 2 (0.12 hr.) and the product was examined by g.l.c.

on a silicon oil (S.E.=30) column at 230°C. A peak was recorded at R_t=2.2 min. whilst piperonaldehyde was recorded at R_t=2.2 min. under identical conditions. Removal of the solvent gave piperonaldehyde (0.36 g.); yield, 77%. The p.m.r.spectrum, recorded in CCl_4, showed signals at the following tau values:- 0.2(s), 1 proton; 2.65 (double d, $J_{H_2H_6}$=2 c.p.s., $J_{H_5H_6}$=10 c.p.s.), 1 proton; 2.72 (d, $J_{H_2H_6}$= 2 c.p.s.), 1 proton, 3.10 (d, $J_{H_5H_6}$=10 c.p.s.), 1 proton; 3.92 (s), 2 protons.

A KINETIC STUDY OF ALCOHOL OXIDATION BY U.V. SPECTROPHOTOMETRY.

Two graduated flasks (50.0ml.) were each charged with the alcohol (approx.0.007 mM.) and the volume was made up to 50.00ml. with distilled water. The flasks were placed in the cell compartment of the u.v.spectrophotometer and allowed to reach ambient temperature (30°C; 1 hr.). Argentic picolinate (approx.0.014 mM.) was added to one of the flasks and the clock was started as the oxidant was virogously shaken with the aqueous alcohol solution. The quartz cells (10 mm. path length) were filled (a) with the aqueous alcohol solution and placed in the reference beam whilst (b) the oxidant/aqueous alcohol mixture was placed in the sample beam. A measure of the decreasing absorbance at 325 mμ was recorded against time. The recorded data for the alcohols examined were as follows :-

1. Ethanol. The reaction of argentic picolinate (5.18 mg.) and ethanol (0.34 mg.; 0.043 ml.).

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$
1.5	0.700	0.095	-1.02
2.0	0.675	0.070	-1.155
2.5	0.655	0.050	-1.30
3.0	0.640	0.035	-1.46
3.5	0.635	0.030	-1.52
6.0	0.615	0.010	-2.00
∞	0.605	-	-

2. n-Butanol. The reaction of argentic picolinate (5.08mg.) with n-butanol (0.528 mg.; 0.066 ml.).

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$
1.5	0.84	0.25	-0.60
2.5	0.70	0.11	-0.96
3.5	0.64	0.05	-1.30
4.5	0.63	0.04	-1.40
5.5	0.62	0.03	-1.52
∞	0.59	-	-

3. Cyclohexanol. The reaction of argentic picolinate (5.095 mg.) and cyclohexanol (0.714 mg.; 0.075 ml.)

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$.
0.75	0.84	0.22	-0.66
1.0	0.81	0.19	-0.72
1.5	0.74	0.12	-0.92
2.0	0.70	0.08	-1.10

3. Cyclohexanol (continued)

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$
2.5	0.68	0.06	-1.22
3.0	0.66	0.04	-1.40
4.0	0.64	0.02	-1.70
6.0	0.63	0.01	-2.00
∞	0.62	-	-

4. iso-Pentanol. The reaction of argentic picolinate (5.098 mg.) and iso-pentanol (0.641 mg.; 0.079 ml.).

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$
1.5	0.67	0.09	-1.05
2.5	0.63	0.05	-1.30
3.5	0.61	0.03	-1.52
5.0	0.60	0.02	-1.70
∞	0.58	-	-

5. sec.-Butanol. The reaction of argentic picolinate (4.824 mg.) and sec-butanol (0.526 mg.; 0.065 ml.).

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$
2.5	0.84	0.24	-0.62
3.5	0.76	0.16	-0.80
4.5	0.71	0.11	-0.96
5.5	0.67	0.07	-1.15
7.0	0.63	0.03	-1.52
∞	0.60	-	-

6. 2-Pentanol. The reaction of argentic picolinate (4.901 mg.) and 2-pentanol (0.615 mg.; 0.076 ml.).

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$
2.5	0.92	0.32	-0.495
3.5	0.82	0.22	-0.66
4.5	0.73	0.13	-0.89
5.5	0.68	0.08	-1.10
7.0	0.64	0.04	-1.40
9.0	0.62	0.02	-1.70
12.0	0.61	0.01	-2.00
∞	0.60	-	-

7. Benzyl alcohol. The reaction of argentic picolinate (4.824 mg.) and benzyl alcohol (0.771 mg.; 0.072 ml.).

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$
1.0	0.70	0.10	-1.0
1.25	0.68	0.08	-1.09
1.50	0.67	0.07	-1.155
1.75	0.66	0.06	-1.22
2.25	0.64	0.04	-1.40
3.0	0.625	0.025	-1.60
4.0	0.62	0.02	-1.70
8.0	0.615	0.015	-1.82
∞	0.60	-	-

8. Hydrolysis of argentic picolinate. The reaction of argentic picolinate (5.195 mg.) with water (50.0 ml.).

t (min.)	$A_{obs.}$	$A_{obs.}-A_{\infty}$	$\log_{10}(A_{obs.}-A_{\infty})$.
1.5	1.32	0.74	-0.13
6.0	1.26	0.68	-0.17
8.0	1.19	0.61	-0.215
10.0	1.10	0.52	-0.28
12.0	1.00	0.42	-0.38
14.0	0.92	0.34	-0.47
16.0	0.86	0.28	-0.55
18.0	0.81	0.23	-0.64
20.0	0.77	0.19	-0.72
22.0	0.74	0.16	-0.80
25.0	0.70	0.12	-0.92
30.0	0.60	0.02	-1.70
∞	0.58	-	-

A.2. THE REACTION OF SILVER II OXIDE WITH ALCOHOLS.

The alcohol (4mM.) was reacted with silver II oxide (0.5g.; 4mM.) in water (5 ml.). The mixture was heated under reflux at 70°C.; and the mixture was stirred for the duration of the reaction. The reaction was allowed to proceed until only elemental silver appeared to be present. The mixture was treated with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and the filtrate was extracted with chloroform. The residue was extracted with chloroform (approx. 5ml.) and the extracts were combined, dried and examined.

Ethanol. The alcohol (0.19 g.) was reacted for 14 hr. and the product was examined by g.l.c. on a PEG.A column at 170°C. A single peak was recorded at R_t=2.8 min. An authentic sample of acetic acid was recorded at R_t=2.76 min. under identical conditions. The I.R. spectrum, recorded in chloroform solution, showed absorbance at $\nu_{max.}$(cm^{-1}):- 3480 - 2560 (m,b) and 1720 (s). Yield, 100%.

n-Propanol. The alcohol (0.25g.) was reacted for 15 hr. and the product was examined by g.l.c. on a PEG.A column at 170°C. A single peak was recorded at R_t=3.6 min., propionic acid showed R_t=3.6 min. under identical conditions. The I.R.spectrum, recorded in chloroform solution, showed absorbance at ν_{max}(cm^{-1}):- 3580-2600 (m,b) and 1720 (s). Yield, 100%.

n-Butanol. The alcohol (0.28 g.) was reacted for 13 hr. and the product was examined by g.l.c. on a PEG.A column at 175°C. Peaks were found to be present at R_t=1.8 min. and R_t=5.7 min. n-Butyraldehyde was recorded at R_t=1.8 and n-butyric acid at R_t=5.7 min. under identical conditions. Yield, n-butyraldehyde, 0.1%; n-butyric acid, 99.9%.

sec-Butanol. The alcohol (0.28 g.) was reacted for 72 hr. and the product was examined by g.l.c. on a PEG.A column at 60°C. Peaks were recorded at R_t=6 min. (sec-butanol concurrent) and R_t=6.9 min. (methyl ethyl ketone concurrent). Yield, 96%.

n-Pentanol. The alcohol (0.35g.) was reacted for 15 hr. and the product was examined by g.l.c. on a PEG.A column at 170°C. A peak at R_t=9.35 min. was recorded which was concurrent with authentic n-pemtanoic acid. The I.R. spectrum, recorded in

chloroform solution, showed absorbance at $\nu_{max.}$ (cm^{-1}):- 3380 - 2300 (m,b) and 1720 (s). Yield, 100%.

iso-Pentanol. The alcohol (0.35g.) was reacted for 15 hr. and the product was examined by g.l.c. on a PEG.A column at 170°C. A peak was recorded at R_t=5.25 min. Calculation of the boiling point from a plot of b.p. vs. $\log_{10}R_t$. for the homologous acid series indicated a value of 176.7°C. (iso-pentanoic acid, b.p.=177°C.) The I.R. spectrum, recorded in chloroform, showed absorbance at $\nu_{max.}$ ($cm.^{-1}$):- 3400 - 2300 (m,b) and 1720(s).

2-Ethylbutanol. The alcohol (0.41g.) was reacted for 13 hr. and the product was examined by g.l.c. on a PEG.A column at 160°C. Peaks were recorded at R_t=1.95 and R_t=8.25 min. Authentic 2-ethylbutanol (R_t=1.95 min.) and 2-ethylbutyric acid (R_t=8.25 min.) were recorded under identical conditions. Yield, 33%.

n-Hexanol. The alcohol (0.41g.) was reacted for 24 hr. and the product was examined by g.l.c. on a PEG.A column at 170°C. Peaks were recorded at R_t=2.25 min. and R_t=10.35 min. whilst authentic samples of the alcohol and acid were recorded at R_t=2.25 and 10.35 min. respectively. Yield, 35%.

2-Ethylhexanol. The alcohol (0.52g.) was reacted for 14 hr. and the product was examined by g.l.c. on a PEG.A column at 170°C. A single peak was recorded at R_t=12.15 min. This peak was shown to be equivalent to 2-ethyl-n-hexanoic acid recorded under identical conditions. The I.R. spectrum, recorded in chloroform, showed absorbance at $\nu_{max.}$ (cm^{-1}):- 3360 - 2620 (m,b) and 1720 (s). Yield, 100%.

n-Octanol. The alcohol (0.52g.) was reacted for 24 hr. and

the product was examined by g.l.c. on a PEG.A column at 170°C. Peaks were recorded at R_t=3.9 min. and R_t=21.3 min. and found to be equivalent to authentic samples of the alcohol (R_t=3.9 min.) and n-octanoic acid (R_t=21.3 min.) Yield, 22%.

Borneol. The alcohol (0.62g.) was reacted for 15 hr. and the product was examined by T.L.C. on Kieselgel-GF_{254} (0.5mm.) by development in 20% $CH_3OH/CHCl_3$. Two spots were recorded at R_f=0.91 (minor intensity) and R_f=0.84. Borneol and camphor run concurrently showed camphor to be the major material present. Yield, ca. 50%.

iso-Borneol. The alcohol (0.62g.) was reacted for 72 hr. and the product was compared with the product from the borneol reaction. Camphor was shown to be the major material present.

Benzhydrol. The alcohol (0.75g.) was reacted for approx. 36 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 250°C. A peak was recorded at R_t=3.75 min. whilst under identical conditions; benzhydrol, R_t=4.2 min. and benzophenone, R_t=3.75 min. were recorded.

p-Nitrobenzyl alcohol. The alcohol (0.62g.) was reacted for 72 hr. and the product was examined by T.L.C. in 50/50 ether/petroleum ether. A single spot at R_f=0.25 was recorded. p-Nitrobenzyl alcohol and p-nitrobenzaldehyde, examined as internal standards, showed R_f=0.25 and R_f=0.6 respectively. Starting material recovered unchanged.

Benzyl alcohol. The alcohol (0.43g.) was reacted for 12 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 150°C. Peaks were recorded at R_t=3.3 min. and R_t=6.75 min. Benzaldehyde (R_t=3.3 min.) and benzyl alcohol (6.75 min.) were recorded under identical conditions. The extract was shaken with sodium hydrogen carbonate and subsequent acid treatment and examination showed benzoic acid to be absent. Yield, 12% (benzaldehyde).

Anisyl alcohol. The alcohol (0.56g.) was reacted for 15 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 200°C. Peaks were recorded at R_t=3.15 min. and R_t=3.6 min. Anisaldehyde and anisyl alcohol were recorded at R_t=3.15 min. and R_t=3.6 min., respectively, under identical conditions. Yield, 44%. The extract was shaken with aqueous sodium hydrogen carbonate solution and subsequent acid treatment and examination showed anisic acid to be absent.

Piperonyl alcohol. The alcohol (0.62 g.) was reacted for 13 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 230°C. Peaks were recorded at R_t=2.7 min. and R_t=3.3 min. and were shown to be equivalent to piperonaldehyde and piperonyl alcohol, respectively. The product was shaken with aqueous sodium hydrogen carbonate and subsequent acid treatment and examination showed piperonylic acid to be absent. Yield, 48% (piperonaldehyde).

3,4-Dimethoxybenzyl alcohol. The alcohol (0.68g.) was reacted for 60 hr. and the product was examined by T.L.C.

Spots were recorded at R_f=0.61 (veratraldehyde) and R_f=0.41 (veratryl alcohol) when developed with 10% $CH_3OH/CHCl_3$ on Kieselgel-GF_{254} (0.5 mm.). Relative intensities of the two spots indicated that the yield of the aldehyde was approx. 50%.

B.1. THE REACTION OF ARGENTIC PICOLINATE WITH ALDEHYDES.

(a) Initial investigation of rate of reaction.

A series of aldehydes was treated with argentic picolinate at 50°C. The aldehyde (0.5 mM.) was shaken with the oxidant (1mM.) and 50% aqueous dimethyl sulphoxide (10ml.) and kept at a constant 50°C. until the colour change red-orange to white had been completed. The time for the reaction was recorded. (see Table 17).

(b) The aldehyde (3mM.) was reacted with argentic picolinate (2.0g.; 6mM.) in water (50 ml.). The mixture was heated under reflux at 70°C. and stirred for the duration of the reaction. The reaction was allowed to proceed until the colour change red-orange to white had been completed and the mixture was then treated with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and the residue was washed with a small portion of chloroform (approx.10ml.). The filtrate was extracted with chloroform and the organic extracts were combined, dried and examined.

p-Nitrobenzaldehyde. The aldehyde (0.43g.) was reacted for 26 hr. and the product was examined by T.L.C. The extract was shown to contain a spot at R_f=0.75 (concurrent with

p-nitrobenzoic acid) when run in 100% ether. The extract was shaken with aqueous sodium hydrogen carbonate solution and subsequent isolation gave p-nitrobenzoic acid (0.15g.). Yield, 31%.

Benzaldehyde. The aldehyde (0.3g.) was reacted for 25 hr. and the product was isolated by formation of the sodium salt and acid precipitation. A white solid (0.2g.) separated, m.p.=119°C. Yield, 58%.

Anisaldehyde. The aldehyde (0.39g.) was reacted for 8 hr. and the product was examined by T.L.C. The chromatogram (run in 50% ether/petroleum ether) showed spots at R_f=0.9 (anisaldehyde), R_f=0.6 (anisic acid) and R_f=0.05 (picolinic acid). The product was isolated from the mixture by treatment with aqueous sodium hydrogen carbonate solution, acid treatment and extraction with chloroform. Removal of the solvent gave a white solid (0.25g.); yield, 57%.

Piperonaldehyde. The aldehyde (0.43g.) was reacted for 0.5 hr. and the product was examined by T.L.C.; a single spot at R_f=0.8 was observed in 50% ether/petroleum ether. Piperonaldehyde ran concurrently. Removal of the solvent gave a solid (0.25g.). Recovery of starting material, approx. 60%.

3,4-Dimethoxybenzaldehyde. The aldehyde (0.47g.) was reacted for 2.1 hr. and the product was examined by T.L.C.; a single spot at R_f=0.75 (veratraldehyde) was recorded in 50% ether/petroleum ether. Removal of the solvent gave a solid (0.4g.); recovery of starting material, 85%.

B.2. THE REACTION OF SILVER II OXIDE WITH ALDEHYDES.

The aldehyde (4mM.) was reacted with silver II oxide (0.5g.; 4mM.) in water (5ml.). The mixture was heated under reflux at 70°C. and was stirred for the duration of the reaction. The reaction was allowed to proceed until only elemental silver appeared to be present. The mixture was treated with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and the residue was extracted with chloroform (approx. 5ml.). The filtrate was extracted with chloroform and the extracts were combined, dried and examined.

2-Ethylbutyraldehyde. The aldehyde (0.4g.) was reacted for 18 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-52) column at 95°C. Peaks were recorded at R_t=1.32 min. and R_t=3.9 min. 2-Ethylbutyraldehyde and 2-ethylbutyric acid had R_t=1.30 and 3.90 min., respectively. Yield, 93%.

n-Hexanaldehyde. The aldehyde (0.4g.) was reacted for 22 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 170°C. A single peak at R_t=2.40 min. (n-hexanoic acid) was recorded. Yield, 100%.

2-Ethylhexanaldehyde. The aldehyde (0.52 g.) was reacted for 25 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-52) column at 130°C. Peaks were recorded at R_t=1.35 min. (aldehyde) and R_t=2.85 min. (2-ethyl-n-hexanoic acid). Yield, 68%.

p-Nitrobenzaldehyde. The aldehyde (0.60g.) was reacted for 21 hr. and the product was examined by T.L.C. Spots were recorded at R_f=0.6 and R_f=0.14 when run in 10% petroleum ether/chloroform. p-Nitrobenzoic acid ran at R_f=0.14. Isolation of the acid by treatment with aqueous sodium hydrogen carbonate and subsequent re-extraction (after acid treatment) gave a solid (0.25g.); m.p.= 176 - 178°C. Yield, 38%.

Benzaldehyde. The aldehyde (0.43 g.) was reacted for 22 hr. and the product was isolated by treatment with aqueous sodium hydrogen carbonate solution and subsequent re-extraction. Removal of the solvent gave a white solid (0.25g.) which was shown to be benzoic acid by T.L.C. (R_f=0.9 in ether solution). Yield, 51%.

Anisaldehyde. The aldehyde (0.55g.) was reacted for 10hr. and the product was isolated by treatment with aqueous sodium hydrogen carbonate solution and subsequent re-extraction. A solid (0.35g.) was formed and shown to be anisic acid by T.L.C. (R_f=0.35 in 50% chloroform/petroleum ether). Yield, 57%.

3,4-Dimethoxybenzaldehyde. The aldehyde (0.66 g.) was reacted for 12 hr. and the product was examined by T.L.C. on a Kieselgel-GF_{254}(0.5mm.) plate. Spots were recorded at R_f=0.78 (veratraldehyde) and R_f=0.43 in 10% $CH_3OH/CHCl_3$. The acid was isolated as a pale yellow solid (0.34g.); m.p.=170 - 172°C (subl.). Yield, 47%.

Piperonaldehyde. The aldehyde (0.6g.) was reacted for 20 hr. and the product was examined by T.L.C. on Kieselgel-GF_{254}

(0.5mm.). Spots were recorded at R_f=0.77 (aldehyde) and R_f=0.18 in 10% $CH_3OH/CHCl_3$ solution. The acid was isolated by treatment with aqueous sodium hydrogen carbonate solution and subsequent re-extraction gave a solid (0.2g.); m.p.= 215 - 217°C. (subl.); yield, 30%. I.R. spectrum absorptions at the following $\nu_{max.}$ (cm^{-1}):- 3220 - 2400 (b), 2620 (w), 2560 (w), 1680 (s,b), 1610 (s), 1580 (w), 1300 (s,b), 1260 (s) and 1115 (s).

C. THE REACTION OF ARGENTIC PICOLINATE AND SILVER II OXIDE WITH ORGANIC-PHOSPHORUS COMPOUNDS.

(a) A series of organic phosphorus compounds was treated with argentic picolinate at 50°C. The compound (0.5mM.) was mixed with the oxidant (0.35g.; 1mM.) and 50% aqueous dimethyl sulphoxide (10ml.) and kept at a constant 50°C. until the colour change red-orange to white was noted. This time of the reaction was noted; see Table 21.

(b) The phosphorus compound (0.8 mM.) was reacted with argentic picolinate (0.57g.; 1.6mM.) and aqueous dimethyl sulphoxide (10ml.; 25% DMSO) at 60°C. The mixture was shaken intermittently until the colour change red-orange to white had occurred and the mixture was acidified with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and extracted with chloroform. The filtrate was extracted with chloroform, washed with water to remove DMSO and filtered. The extracts were combined, dried and examined by T.L.C.

(c) The phosphorus compound (0.8 mM.) was reacted with silver II oxide (0.1g.; mM.) and water (10ml.) at 60°C. The mixture was shaken intermittently until elemental silver was present. The product was isolated as described above and examined by T.L.C. Comparison was made with the product from reaction with argentic picolinate.

Triphenyl phosphine. The phosphine (0.21g.) was reacted separately with the two oxidants and the products were examined by T.L.C. in chloroform. The argentic picolinate product showed a single spot at R_f=0.26 (triphenylphosphine oxide) whilst the other product showed spots at R_f=0.7, 0.3 and 0.26. The product of the former reaction (a white solid) was isolated and the I.R. spectrum was recorded. Absorptions were recorded at the following $\nu_{max.}$ (cm^{-1}):- 3060 (w), 2930 (w), 1980 (w), 1910 (w), 1820 (w), 1740 (w), 1590 (w), 1480 (m), 1435 (s), 1310 (w), 1190 (s), 1160 (w), 1120 (s), 1090 (m), 1070 (w), 1025 (w), 970 (m), 850 (w), 755 (s), 745 (s), 720 (s) and 695 (s).

Triphenyl phosphite. The phosphite (0.25g.) was reacted separately with the two oxidants and the products were examined by T.L.C. in 50% chloroform/petroleum ether. Both products showed spots at R_f=0.83 and 0.52. Phenol ran concurrently at R_f=0.83 and triphenylphosphate (145) at R_f=0.52.

Trihexyl phosphite. The phosphite (0.27 g.) was reacted separately with the two oxidants and the products were examined by T.L.C. in 50% chloroform/petroleum ether. Both products

showed spots at R_f=0.9 and 0.52 whilst the product of argentic picolinate reaction also showed spots at R_f=0.74, 0.65 and 0.30. Trihexyl phosphite, trihexylphosphate (145) and n-hexanol were shown to have R_f=0.90, 0.52 and 0.74 respectively, when run concurrently.

Tridecyl phosphite. The phosphite (0.41g.) was reacted separately with the two oxidants and the products were examined by T.L.C. in 20% chloroform/petroleum ether. Spots were recorded at R_f=0.95, 0.73 and 0.36 for both reaction products. Tridecyl phosphite, tridecyl phosphate (145) and n-decanol were shown to have R_f=0.95, 0.73 and 0.36 respectively, when run concurrently.

Trilauryl phosphite. The phosphite (0.48g.) was reacted separately with the two oxidants and the products were examined by T.L.C. in 5% chloroform/petroleum ether. Spots were recorded at R_f=0.85, 0.64 and 0.30 for both products. Trilauryl phosphite, trilauryl phosphate (145) and n-dodecanol were shown to have R_f=0.96, 0.64 and 0.85 respectively, when run concurrently.

D.1. THE REACTION OF ARGENTIC PICOLINATE WITH AMINO-ACIDS AND α-AMINO-ACID ESTERS.

(a) Amino-acids. The amino-acid (3mM.) was reacted with argentic picolinate (2.0g.; 6mM.) in water (50 ml.). The mixture was heated at 70°C. under reflux and stirred for the duration of the reaction. Nitrogen gas was bubbled through the mixture and any volatile product(s) was swept into a trap

containing 2,4-dinitrophenylhydrazine reagent (50 ml.). The reaction was continued until the colour change orange-red to white had been completed; the mixture was then treated with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and the filtrate was treated with 2,4-dinitrophenylhydrazine reagent until precipitation (if any) was complete. The solid derivatives were combined and carefully washed free from the reagent. The derivative was dried to constant weight and the conversion to the carbonyl compound was calculated on the basis of the weight recorded.

DL-α-Alanine. The amino-acid (0.26g.) was reacted for 26 min. and acetaldehyde was isolated as the 2,4-D.N.P. derivative (0.54g.); m.p.= 141°C.; yield, 88%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

DL-α-Amino-n-butyric acid. The amino-acid (0.3g.) was reacted for 25 min. and propionaldehyde was isolated as the 2,4-D.N.P.derivative (0.5g.); m.p.=148 - 150°C.; yield, 72%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

DL-Valine. The amino-acid (0.34g.) was reacted for 28 min. and iso-butyraldehyde was isolated as the 2,4-D.N.P. derivative (0.65g.); m.p.=187°C.; yield, 90%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

DL-nor-Valine. The amino-acid (0.34g.) was reacted for 18 min. and n-butyraldehyde was isolated as the 2,4-D.N.P. derivative (0.67g.); m.p.=119°C.; yield, 93%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

DL-Leucine. The amino-acid (0.38g.) was reacted for 18 min. and iso-valeraldehyde was isolated as the 2,4-D.N.P.derivative (0.65g.); m.p.=119°C.; yield, 88%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

DL-nor-Leucine. The amino-acid (0.38g.) was reacted for 38 min. and n-valeraldehyde was isolated as the 2,4-D.N.P. derivative (0.70g.); m.p.=122°C.; yield, 95%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

DL-iso-Leucine. The amino-acid (0.38g.) was reacted for 33 min. and 2-methylbutyraldehyde was isolated as the 2,4-D.N.P. derivative (0.67g.); m.p.=120-121°C. (Lit.(162), 120.5°C.); yield, 91%. The p.m.r.spectrum, recorded in $CDCl_3$, see Table 12.

DL-2-amino-n-octanoic acid. The amino-acid (0.46g.) was reacted for 39 min. and n-heptanaldehyde was isolated as the 2,4-D.N.P.derivative (0.8g.); m.p.=104°C.; yield, 75%. The p.m.r.spectrum, recorded in $CDCl_3$, see Table 12.

DL-Phenylglycine. The amino-acid (0.43g.) was reacted for 25 min. and the product was isolated by extraction with chloroform (exception to general procedure; N_2 was not passed into the reaction mixture) and examined by g.l.c. on a silicon oil (S.E.-30) column at 130°C. A single peak was recorded at R_t=4.65 min. Benzaldehyde, R_t=4.65 min., was recorded under identical conditions. Removal of the solvent gave benzaldehyde (0.2g.); yield, 75%.

DL-Phenylalanine. The amino-acid (0.47g.) was reacted for 25 min. The product was extracted with chloroform and examined by g.l.c. on a silicon oil (S.E.-30) column at 170°C. when a peak was recorded at R_t=2.7 min. (Phenylacetaldehyde was recorded at R_t=2.7 min. under identical conditions). T.L.C. examination on Kieselgel-GF_{254}(0.5mm.) in chloroform showed spots at R_f=0.83 (phenylacetaldehyde) and R_f=0.17 (phenylacetic acid, very minor spot). Treatment with aqueous sodium hydrogen carbonate solution and subsequent extraction gave phenylacetaldehyde (0.25g.). Yield, 73%.

4-Amino-n-butyric acid. The amino-acid (0.3g.) was reacted for 32 min. Succinaldehydic acid was isolated as the 2,4-D.N.P. derivative (0.65g.); m.p.=196°C. (Lit.(162), 200.5°C.); yield, 79%.

L-Glutamic acid. The amino-acid (0.42g.) was reacted for 22 min. and succinaldehydic acid was isolated as the 2,4-D.N.P. derivative (0.65g.); m.p.=194°C.(Lit.(162), 200.5°C.); yield 80%.

Reaction of pyruvic acid with argentic picolinate.

Pyruvic acid (164) (0.5 g.; approx. 0.6mM) and argentic picolinate (4.0g.; 1.2mM.) were heated together under reflux at 70°C. in water (50ml.). Nitrogen was slowly passed through the mixture into a trap containing 2,4-dinitrophenylhydrazine reagent (approx. 50ml.). After 40 min. the oxidant had been reduced but no precipitate was found in the trap. The mixture was treated with hydrochloric acid (2N), cooled and the solid material was removed by filtration under reduced pressure. The filtrate was distilled at atmospheric pressure and the fraction

distilling at 100°C. was collected (approx.10ml.). Examination by g.l.c. on an apiezon-L column at 100°C. showed no peak to be recorded. Under identical conditions, acetic acid had an R_t=40 sec.

Reaction of pyruvic acid with picolinic acid.

Pyruvic acid (0.5g.; 0.57mM.), picolinic acid (0.7g.; 0.57mM.) and water (50ml.) were heated together under reflux at 70°C. for 19 hr. Nitrogen was passed through the reaction mixture and into a trap containing 2,4-dinitrophenylhydrazine reagent (approx. 25ml.). No derivative was found in the trap at the end of the reaction.

Reaction of pyruvic acid with argentous picolinate.

The mixture from the above reaction was treated with freshly precipitated silver hydroxide (1g.; 8mM.) and the reaction was allowed to proceed for a further 26 hr. At the end of this time, no precipitate was found in the trap.

(b). α-AMINO-ACID ESTER HYDROCHLORIDES.

The amino-acid ester hydrochloride (3mM.) was added to sodium hydrogen carbonate (0.24g.; 3mM.) in water (50ml.) After the evolution of carbon dioxide had ceased, argentic picolinate (2.0g.; 6mM.) was added and the mixture was stirred under reflux at 70°C. The reaction was allowed to proceed until the oxidant had been completely reduced (i.e. colour change red-orange to white). The mixture was treated with hydrochloric acid (2N), cooled and the precipitated silver salt was removed by filtration. The residue was extracted with chloroform. The filtrate was extracted with chloroform and the extracts were combined, dried and examined.

DL-α-Ethyl alaninate hydrochloride. The ester hydrochloride (0.44g.) was reacted for approx. 30 min. The product was examined by g.l.c. on an apiezon-L column at 100°C. Peaks were recorded at R_t=0.8 min. and R_t=1.3 min. whilst under the same conditions, ethyl acetate and ethyl pyruvate (165) had identical retention times with the product peaks. The mixture was separated by preparative g.l.c. on a PEG.A column at 120°C. to give ethyl pyruvate; yield, 49%. The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- 5.75 (q,J=8 c.p.s.), 2 protons; 7.65 (s), 3 protons; 8.65 (t,J=8 c.p.s.), 3 protons. Ethyl acrylate; yield, 51%; p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- 4.0 (m), 3 protons; 6.88 (q, J=7 c.p.s.), 2 protons; 8.7 (t, J=7 c.p.s.), 3 protons.

DL-Methyl valinate hydrochloride.The ester hydrochloride (0.48g) was reacted for 20 min. The product was examined by g.l.c. on a PEG.A.column at 120°C. when peaks were recorded at R_t=3.6 min. and 4.95 min.; ratio of peak areas was 13% and 87% respectively. The I.R. spectrum of the mixture showed absorptions at the following $\nu_{max.}$ ($cm.^{-1}$):- 3400 \(b,w), 2980 (m), 2940 (w), 2880 (w), 1755 (sh), 1740 (s), 1735 (s), 1680 (w), 1515 (m), 1465 (m), 1435 (m), 1385 (w), 1370 (w), 1270 (s), 1255 (sh), 1170 (w), 1110 (w), 1045 (s), 930 (w), 865 (w), 790 (s), 770 (s) and 685 (w). The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- 6.2 (s), 3 protons; 6.8 (h,J=7.5 c.p.s.), 1 proton; 7.9 (s), 2 protons; 8.7 (d), 6 protons; 8.85 (d, J=7.5 c.p.s.), 6 protons.

L-Methyl leucinate hydrochloride. The ester hydrochloride (0.52g.) was reacted for 20 min. and the product was examined by g.l.c. on a PEG.A column at 120°C. Peaks were recorded at R_t=2.55 min. and R_t=9.3 min.; ratio of peak areas was 38% and 62% respectively. The I.R. spectrum showed absorptions at the following $\nu_{max.}$ ($cm.^{-1}$):- 3380 (b,w), 2960 (s), 2930 (s), 2860 (m), 1745 (s), 1680 (m), 1590 (w), 1570 (w), 1515 (m), 1465 (m), 1435 (m), 1370 (w), 1265 (m), 1205 (w), 1165 (w), 1120 (b,w), 1020 (w), 800 (m) and 750 (m). The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- 6.2 (s), 3 protons; 6.25 (m), 1 proton; 7.3 (d,J=7.5 c.p.s.), 7.8 (m), 2 protons;8.2 (m), 1 proton; 8.9 (d, J=6 c.p.s.), 6 protons; 9.0 (d, J=6 c.p.s.), 6 protons.

D.2. THE REACTION OF SILVER II OXIDE WITH α-AMINO-ACIDS.

The α-amino-acid (4mM.) was reacted with silver II oxide (0.5g.; 4mM.) in water (5ml.). The mixture was heated under reflux at 70°C. and the mixture was stirred for the duration of the reaction. The reaction was allowed to proceed until only elemental silver appeared to be present. The mixture was treated with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and extracted with chloroform (approx. 5ml.). The filtrate was extracted with chloroform and the extracts were combined, dried and examined.

DL-α-Alanine. The amino-acid (0.36g.) was reacted for 12 hr. and the product was examined by g.l.c. on a PEG.A.column at 170°C.

A single peak was recorded at R_t=2.55 min.; acetic acid, R_t=2.55 min. was recorded under identical conditions. The I.R.spectrum, recorded in chloroform, showed absorptions at the following $\nu_{max.}$ ($cm.^{-1}$):- 3520 - 2460 (b), 1720 (s). Yield, 100%.

DL-2-Amino-n-butyric acid. The amino-acid (0.41g.) was reacted for 14 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 130°C. A peak was recorded at R_t=1.35 min. Propionic acid was recorded at 1.35 min. under identical conditions. Yield, 100%.

The above reaction was repeated under identical conditions with the exception that nitrogen was passed slowly through the mixture. Any volatile material was swept into a trap containing 2,4-dinitrophenylhydrazine reagent (approx. 50ml.). Propionaldehyde was isolated as the 2,4-D.N.P. derivative (0.35g.); m.p.=146-149°C.; yield, 37%. The p.m.r. spectrum, recorded in $CDCl_3$, see Table 12.

DL-nor-Valine. The amino-acid (0.47g.) was reacted for 12 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-52) column. A peak at R_t=3.75 min. (n-butyric acid) was recorded. Examination on a PEG.A column at 175°C. showed a single peak at R_t=5.7 min. (n-butyric, 5.7 min. under identical conditions). The I.R. spectrum, recorded in $CHCl_3$, showed absorptions at the following $\nu_{max.}$ (cm^{-1}):- approx.3500 - 2400 (b), 1720 (s). Yield, 100%.

DL-Valine. The amino-acid (0.47g.) was reacted for approx. 20 hr. and the product was examined by g.l.c. on a PEG.A

column at 170°C. A peak was recorded at R_t=4.2 min. from which a b.p.= 159°C. was calculated (iso-butyric acid, b.p. = 155°C.). The I.R. spectrum, recorded in chloroform, showed absorptions at the following $\nu_{max.}$ ($cm.^{-1}$):- 3500 - 2450 (b), 1720 (s). Yield, 100%.

DL-nor-Leucine. The amino-acid (0.52 g.) was reacted for approx. 12 hr. and the product was treated with aqueous sodium hydrogen carbonate solution. Subsequent acid treatment and isolation gave n-pentanoic acid (0.2g.); yield, 49%. The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- -1.85 (s), 1 proton; 7.75 (t, J=6 c.p.s.), 2 protons; 8.48 (m), 4 protons; 9.05 (t, J=6 c.p.s.), 3 protons. Examination by g.l.c. on a PEG.A column at 170°C., showed the product to have an identical retention time to authentic material.

The chloroform extract, containing a single, neutral compound (by g.l.c.), showed a p.m.r. spectrum which was inconclusive.

DL-Leucine. The amino-acid (0.52g.) was reacted for approx. 12 hr. and the extract was treated with aqueous sodium hydrogen carbonate solution. Subsequent acid treatment and isolation gave iso-pentanoic acid (0.25g.); yield, 61%. The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- -2.05 (s), 1 proton; 7.8 (d, J=2.5 c.p.s.), 2 protons; 7.9 (m), 1 proton; 9.0 (d, J=6 c.p.s.), 6 protons.

The chloroform extract, containing a single, neutral compound (by g.l.c.), showed a p.m.r. spectrum which was inconclusive.

DL-iso-Leucine. The amino-acid (0.52g.) was reacted for approx. 12 hr. and the product was treated with aqueous sodium hydrogen carbonate solution. Subsequent acid treatment and isolation gave 2-methylbutyric acid (0.22g.); yield, 53%. The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- -1.95 (s), 1 proton; 7.6 (m), 1 proton; 8.35 (m), 2 protons; 8.8 (d, J=7 c.p.s.), 3 protons; 9.05 (t, J=7 c.p.s.), 3 protons.

The chloroform extract, containing a single, neutral compound (by g.l.c.), showed a p.m.r. spectrum which was inconclusive.

DL-2-Amino-n-octanoic acid. The amino-acid (0.64g.) was reacted for 24 hr. and the extract was treated with aqueous sodium hydrogen carbonate solution. Subsequent acid treatment and isolation gave n-heptanoic acid (0.3g.); yield, 58%. The p.m.r. spectrum, recorded in CCl_4, showed signals at the following tau values:- -1.7 (s), 1 proton; 7.7 (t, J=6 c.p.s.), 2 protons; 8.5 (m), 8 protons; 9.1 (coll.t), 3 protons.

The chloroform extract, containing a single neutral compound (by g.l.c.), showed a p.m.r. spectrum which was inconclusive. The I.R. spectrum showed absorptions at the following $\nu_{max.}$ ($cm.^{-1}$):- 3580 (b,s), 3210 (b,s), 2970 (m), 2950 (s), 2870 (m), 1710 (w), 1670 (s,b), 1635 (s,b), 1470 (m), 1420 (s), 1410 (s), 1355 (w), 1320 (m), 1270 (m), 1220 (m), 1140 (m), 875 (w), 810 (w), 725 (w) and 700 (b,s).

DL-Phenylglycine. The amino-acid (0.61g.) was reacted for 10 hr. and the product was examined by g.l.c. on a silicon

oil (S.E.-30) column at 130°C. A peak was recorded at R_t=4.65 min.; benzaldehyde, examined under identical conditions was recorded at R_t=4.65 min. Removal of the solvent, after the product had been shaken with aqueous sodium hydrogen carbonate solution, gave benzaldehyde (0.3g.); yield, 79%.

E.1. THE REACTION OF ARGENTIC PICOLINATE WITH SOME ORGANO-NITROGEN COMPOUNDS.

Procedure (a) The nitrogen-compound (0.01M.), argentic picolinate (0.02M.), dimethyl sulphoxide (10ml.) and water (10ml.) were heated together under reflux. The time for the colour change orange-red to white was recorded and the mixture was poured into water (250ml.). After treatment with hydrochloric acid (2N), the precipitated silver salt was removed by filtration under reduced pressure and the filtrate was extracted with chloroform.

Procedure (b) Procedure (a) was followed with the exception that dimethyl sulphoxide was omitted from the reaction mixture. Hence the necessity to pour the reacted mixture into excess water was removed.

Benzylamine. (a) The amine (1.07g.) was reacted for 10 min. at 40°C. and the product, after isolation, was shown to be benzaldehyde; the I.R. spectrum was identical with authentic material.

(b) The reaction was carried out at 70°C. for 1 hr. and the product was isolated as the 2,4-D.N.P.derivative (1.3g.) from the aqueous filtrate. Yield, 46%.

t-Butylamine. (b) The amine (0.73g.) was reacted for 64 hr. at 70°C. and nitrogen was passed slowly through the mixture. Any volatile material was swept into a trap containing bromine/carbon tetrachloride solution. The contents of the trap were treated with aqueous sodium metabisulphite solution and the organic phase was dried and examined by g.l.c. on a silicon oil (S.E.-30) column at 130°C. A peak was recorded at R_t=4.0 min. whilst on an apeizon-L column at 100°C. a peak was recorded at R_t=3.3 min. On both columns, under identical conditions, 1,2-dibromo-2-methylpropane recorded similar retention times. Removal of the solvent gave a liquid (1g.); N^D_{22}= 1.4830 (Lit.(166), 1.5160). Further examination by g.l.c., showed solvent to be present to a small extent. Yield, approx. 40%.

N-Acetylbenzylamine. (a) The compound (1.5g.) was reacted for 20. min. at 50°C. The product was isolated and examined by I.R. spectroscopy. Benzaldehyde gave an identical spectrum. (b) The compound was reacted at 70°C. for 20 hr. and the product was isolated from the aqueous filtrate by formation of the 2,4-D.N.P.derivative (1.4g.); yield, 49%.

Cinnamide. (a) The compound (1.47g.) was reacted at 40°C. for 10 min. During this time ammonia was evolved. The product was isolated and examined by its p.m.r.spectrum. The spectrum, recorded in $CDCl_3$, showed signals at the following tau values:- -0.1 (s), 1 proton; 2.23 (d,J=16 c.p.s.), 1 proton; 2.55 (m), 5 protons; 3.6 (d,J=16 c.p.s.) 1 proton. The low field proton was exchanged

when shaken with deuterium oxide. Cinnamic acid (0.4g.) was isolated; yield, 53%.

(b) The reaction was repeated at 60°C. for 40 min. Cinnamic acid was again isolated.

Benzylidene-p-nitroaniline. (a) The compound (2.7g.) was reacted at 40°C. for 5 min. A brown complex was formed which disappeared upon addition of dilute acid. The chloroform extract was shown to contain benzaldehyde (I.R.spectroscopy) whilst the aqueous layer upon treatment with aqueous sodium hydrogen carbonate and subsequent extraction gave p-nitroaniline; m.p.= 142-145°C.

(b) The reaction was repeated at 65°C. for 3.5 hr. Benzaldehyde and p-nitroaniline were isolated.

Benzoin-oxime. (a) The compound(2.3g.) was reacted at 40°C. for 10 min. and T.L.C. examination showed three components to be present. By comparison with authentic materials run concurrently, benzoin, benzil and benzoin-oxime were identified.

E.2. THE REACTION OF SILVER II OXIDE WITH AMINES.

The amine (4mM.) was reacted with silver II oxide (0.5g.; 4mM.) in water (5ml.). The mixture was heated under reflux at 70°C. and the mixture was stirred for the duration of the reaction. The reaction was allowed to proceed until only elemental silver appeared to be present. The mixture was treated with hydrochloric acid (2N) and cooled. The precipitated silver salt was removed by filtration under reduced pressure and the residue was extracted with chloroform (approx. 5ml.). The filtrate was extracted with chloroform and the two extracts were combined, dried and examined.

n-Butylamine. The amine (0.3g.) was reacted for 5 hr. and the product was examined by g.l.c. on a D.N.P.column at 80°C. Peaks were recorded at R_t=3.3 min., R_t=4.2 min. and R_t=44.7 min.; whilst under the same conditions n-butyraldehyde, n-butyronitrile and the Schiff's base (167) were recorded at the following retention times respectively: R_t=1.5 min., R_t=3.3 min. and R_t=43.4 min. Yields: nitrile, 87%; Schiff's base approx. 0.1%; unknown, 13%.

2-Ethylbutylamine. The amine (0.41g.) was reacted for 12 hr. and the product was examined by g.l.c. on a D.N.P.column at 100°C. Peaks were recorded at R_t=6.45 min., R_t=8.25 min. and R_t=22.8 min. whilst 2-ethylbutyraldehyde, 2-ethylbutyronitrile and the Schiff's base (167) were shown to have the same retention times, respectively, under the same conditions. Yields: 43% Schiff's base; 40% nitrile and 17% aldehyde.

sec.-Butylamine. The amine (0.3g.) was reacted for 2.5 hr. and the product was examined by g.l.c. on a PEG.A column at 60°C. Peaks were recorded at R_t=5.7 min. and R_t=8.85 min. whilst under identical conditions, R_t=5.7 min. was recorded for methyl ethyl ketone. The unknown compound (R_t=8.85 min.) co-distilled with chloroform. Yield of ketone, 10%.

n-Pentylamine. The amine (0.35g.) was reacted for 12 hr. and the product was examined by g.l.c. on a D.N.P. column at 90°C. Peaks were recorded at R_t=3.45 min. and R_t=7.05 min. under identical conditions; n-valeraldehyde, R_t=3.45 min. and n-valeronitrile, R_t=7.05 min. were recorded. Yields: 13% aldehyde; 87% nitrile.

n-Hexylamine. The amine (0.41g.) was reacted for 12 hr. and the product was examined by g.l.c. on a PEG.A column at 100°C. Peaks were recorded at R_t=3.9 min., R_t=10.2 min. and R_t=29.55 min. Under identical conditions; n-hexanaldehyde, capronitrile (168) and Schiff's base (167) were found to have comparable retention times, respectively. Yields: 1% n-hexanaldehyde; 26% capronitrile and 73% Schiff's base.

2-Ethylhexylamine. The amine (0.52g.) was reacted for 13 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 130°C. Peaks were recorded at the following R_t values:- 2.1min., and 3.3 min. and were shown to be 2-ethylhexanaldehyde and 2-ethylcapronitrile, respectively, by comparison with authentic materials. Yields: 25% aldehyde and 75% nitrile.

Cyclohexylamine. The amine (0.40g.) was reacted for 4 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 150°C. A peak was recorded at R_t=2.85 min. and was shown to be cyclohexanone (authentic material, R_t=2.85 min.) Examination on a D.N.P. column at 100°C. showed a peak at R_t=9.15 min. corresponding to cyclohexanone. Yield, 100%.

Benzylamine. The amine (0.43g.) was reacted for 4 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 160°C. A peak was recorded at R_t=2.85 min. whilst both benzaldehyde and benzonitrile were recorded at 2.85 min. under the same conditions. Examination on a D.N.P.column at 100°C. showed the following peaks; R_t=13.2 min., R_t=16.65 min. and R_t=22.05 min. Under identical conditions phenylisocyanide (169),benzaldehyde and benzonitrile were recorded at R_t=13.2

min., R_t=16.65 min. and R_t=22.05 min.; respectively. Yields: 23% benzaldehyde and 77% benzonitrile.

t-Butylamine. The amine (0.3g.) was reacted for 48 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 90°C. A single peak was recorded at 3.3 min. and shown to be 2-nitro-2-methylpropane by comparison with authentic material. The I.R. spectrum, recorded as a thin-film, showed absorptions at the following $\nu_{max.}$ ($cm.^{-1}$):- 3000 (m), 2950 (w), 2880 (w), 1565 (sh), 1545 (s,b), 1480 (m), 1465 (w), 1405 (m), 1375 (s), 1350 (s), 1255 (w), 1220 (w), 1180 (w), 935 (w), 860 (m), 800 (w), 760 (s) and 670 (w). (Identical with authentic material). Yield, 100%.

Diphenylamine. The amine was reacted for 18 hr. and the product was examined by T.L.C. on Kieselgel-GF_{254} (0.40mm.) in 10% ether/petroleum ether. Nine spots were recorded at R_f=0.72; 0.55; 0.48; 0.19; 0.15; 0.07; 0.04; 0.01 and a baseline spot. The I.R. spectrum of the mixture showed absorptions at the following $\nu_{max.}$ ($cm.^{-1}$):- 3030 (w), 1590 (m), 1510 (sh), 1490 (s), 1305 (m), 1265 (m), 1170 (w), 1150 (w), 1070 (w), 1025 (w), 990 (w), 820 (w), 745 (m) and 690 (m).

F.1. THE REACTION OF ARGENTIC PICOLINATE WITH OLEFINS AND AROMATIC HYDROCARBONS.

Initial investigation of the rate of reaction of Ag^{II} with olefins.

A series of olefins was treated with argentic picolinate at 50°C. The olefin (0.5 mM.) was shaken with the oxidant (0.35g.; 1mM.) and 50% aqueous dimethyl sulphoxide (10ml.) and kept at a constant 50°C. until the colour change red-orange to white was

completed. The time of this reaction was recorded (see Table 29).

Styrene. Styrene (0.59g.; 6mM.), argentic picolinate (4.0g.; 12mM.) and water (75 ml.) were stirred under reflux at 70°C. for 1.75 hr. The mixture was treated with hydrochloric acid (2N), cooled and the precipitated silver salt was removed by filtration under reduced pressure. The residue and the filtrate were extracted with chloroform and the combined extracts were dried and examined by g.l.c. on a PEG.A column at 130°C. Peaks were recorded at R_t=4.5 min. and R_t=14.5 min. Under identical conditions, benzaldehyde and styrene were recorded at R_t=4.5 min. and 14.5 min., respectively. Yield, 46%.

The reaction was repeated with a stream of nitrogen passing through the mixture. A trap containing 2,4-dinitrophenylhydrazine reagent (50ml.) was employed to isolate any volatile material; but no derivative was formed.

trans-Stilbene. Stilbene (0.51g.; 3mM.) and argentic picolinate (2.0g.; 6mM.) in water (50ml.) were stirred together under reflux at 70°C. for 3.75 hr. The product was isolated as for the styrene product and examined by g.l.c. on a silicon oil (S.E.-30) column programmed from 100-250°C. (24°C. per min. temp. rise). Peaks were recorded at R_t=3.3 min. and 9.45 min. Benzaldehyde and trans-stilbene were shown to have R_t=3.3 min. and 9.3 min., respectively, under identical conditions. Yield, 23%.

Aromatic hydrocarbons.

Toluene. See experimental to section I, p.35

Ethylbenzene. Ethylbenzene (0.30g.; 3mM.) and argentic picolinate (4.0g.; 12mM.) and water (100ml.) were stirred together under reflux at 70°C. for 75 hr. The mixture was treated with hydrochloric acid (2N), cooled and the precipitated silver salt was removed by filtration under reduced pressure. The filtrate was extracted with chloroform, dried and examined by g.l.c. on a PEG.A column at 180°C. A single peak was recorded at R_t=9.4 min. and acetophenone was shown to have a comparable retention time under identical conditions. The solvent was removed and 2,4-D.N.P. reagent (20ml.) was added. The acetophenone was isolated as the 2,4-D.N.P.derivative (0.49g.); recryst. m.p.=236°C.; yield, 27%.

p-Cymene. The hydrocarbon (0.38g.; 3mM.), argentic picolinate (4.0 g.; 12mM.) and dimethyl sulphoxide (20ml.) in water (50ml.) were stirred together at 70°C. under reflux for approx. 17 hr. The product was extracted as for toluene reaction and after the removal of the solvent, 2,4-D.N.P.reagent (20ml.) was added; the cuminaldehyde was isolated as the 2,4-D.N.P. derivative (0.3g.); m.p.= 210°C.; yield, 32%.

F.2. THE REACTION OF ARGENTIC PICOLINATE WITH OTHER ORGANIC COMPOUNDS.

1:4-Hydroquinone. Hydroquinone (0.31g.; 3mM.), argentic picolinate (2.0g.; 6mM.) and water (50ml.) were stirred together at 70°C. for 30 min. The product was extracted as for the ethylbenzene reaction and removal of the solvent gave 1:4-benzoquinone (0.27g.); yield, 89%. The product was established by g.l.c. Comparison with authentic material on

a silicon oil (S.E.-30) column at 200°C. and the I.R. spectrum, recorded in KBr disc, was identical with the quinone.

Mandelic acid. Mandelic acid (0.87g.; 6mM.), argentic picolinate (4.0g.; 12mM.) and water (50ml.) were stirred together at 70°C. under reflux. The reaction was allowed to proceed for 10 min. and the product was isolated as for the styrene reaction. The product was examined by g.l.c. on a silicon oil (S.E.-30) column at 150°C. A peak was recorded which was shown to be benzaldehyde by comparison with authentic material. The solvent was removed to give benzaldehyde (0.55g.); yield, 90%.

Lactic acid. The acid (0.52g.; 6mM.), argentic picolinate (4.0g.; 12mM.) and water (50ml.) were stirred together under reflux at 70°C. The reaction was allowed to proceed for 80 min. whilst nitrogen was passed through the mixture. Volatile material was swept into a trap containing 2,4-dinitrophenylhydrazine reagent (25ml.) and acetaldehyde was isolated as the 2,4-D.N.P.derivative (0.55g.); m.p.=139-140°C.; yield, 43%.

Ethyl mandelate. The ester (0.52g.; 3mM.), argentic picolinate (2.0g.; 6mM.) and water (50ml.) were stirred together under reflux at 70°C. The reaction was allowed to proceed for 4.25 hr. and the product was examined by g.l.c. on a silicon oil (S.E.-30) column at 210°C. Peaks were recorded at R_t=4.95 min. and R_t=5.40 min. whilst ethyl mandelate was shown to be the latter under identical conditions. Yield 31%. (g.l.c.). The p.m.r. spectrum, recorded in CCl_4,

showed signals at the following tau values:- 1.9 (m), 2 protons; 2.45 (m), 3 protons; 2.65 (m), 5 protons; 3.85 (s), 1 proton; 5.62 (q, J=7.0 c.p.s.), 2 protons; 5.85 (q, J=7.0 c.p.s.), 2 protons; 8.65 (t, J=7.0 c.p.s.), 3 protons; 8.85 (t, J=7.0 c.p.s.), 3 protons. Yield (p.m.r.), 38%. Mean yield, 35%.

Ethyl lactate. The ester (0.67g.; 6mM.), argentic picolinate (4.0g.; 12mM.) and water (50ml.) were stirred together at 70°C. under reflux. The reaction was allowed to proceed for 3.75 hr. and the product was extracted as for the styrene reaction. The ethyl pyruvate (0.2g.); yield, 30% was isolated and identified by p.m.r. spectrum (see DL-ethyl alaninate product).

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