

Additions to Alkenes *via* Metal Ion-promoted Oxidation of 2,2'-Dipyridyl Disulphide and Bis-(2-aminophenyl) Disulphide

Alan Bewick, John M. Mellor,* Dorys Milano, and W. Martin Owton
 Department of Chemistry, The University, Southampton SO9 5NH

Vicinal trifluoroacetoxysulphides, which readily afford vicinal hydroxysulphides, are obtained by oxidative addition of 2,2'-dipyridyl disulphide and of bis-(2-aminophenyl) disulphide to alkenes in dichloromethane-trifluoroacetic acid promoted by copper(II) acetate.

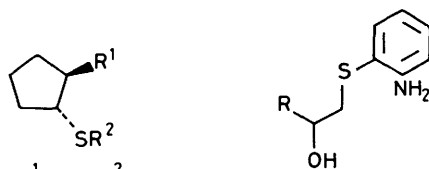
In the previous paper¹ we have described the extension of the Trost methodology² of lead(IV)-promoted addition of organic disulphides to alkenes in dichloromethane-trifluoroacetic acid to give, after hydrolysis, products of hydroxysulphenylation. Such addition products could be obtained using lead(IV) salts as described by Trost² or by using manganese(III) salts, or by a much slower reaction in the absence of added metal salts. However, we found that with lead(IV) salts, or in the absence of added metal salts [although diphenyl disulphide (1) added efficiently], the basic disulphides, 2,2'-dipyridyl disulphide (2) and bis-(2-aminophenyl) disulphide (3), failed to add to cyclohexene, or to other simple alkenes. In contrast to the behaviour of diphenyl disulphide (1) the two disulphides (2) and (3) were recovered unchanged even after long exposure to cyclohexene in dichloromethane-trifluoroacetic acid under air. In view of the good precedents in biological systems and in model studies for catalysis by metal ions of the cleavage of the sulphur-sulphur bond of disulphides by nucleophiles³⁻⁷ we have examined the reaction of the disulphides (2) and (3) with alkenes in the presence of added copper(II) salts. Although copper(II) salts do not increase the efficiency of addition of diphenyl disulphide (1) to alkenes we find that their promotion of the addition of the basic disulphides (2) and (3) to alkenes is efficient.

The results of reaction of the disulphides (2) and (3) with a number of alkenes are shown in the Table. In each instance in the absence of a metal salt no products of addition are observed with either 2,2'-dipyridyl disulphide (2) or with bis-(2-aminophenyl) disulphide (3). However, addition of catalytic quantities of copper(II) acetate leads to slow addition of both disulphides (2) and (3) to alkenes. Reaction of 2,2'-dipyridyl disulphide (2) with cyclohexene in the presence of copper(II) acetate affords, after work-up, the alcohol (6) directly. After purification by chromatography over alumina the alcohol (6) was isolated in 70% yield (w.r.t. 2,2'-dipyridyl disulphide). Direct isolation of the alcohol (6) implies that the intermediate trifluoroacetate (7) is hydrolysed on work-up in contrast to the behaviour of the rather more stable products obtained with diphenyl disulphide. The *trans*-stereochemistry in the alcohol (6) was assigned by observation of the coupling constant associated with the two methine protons. Similarly the alcohol (10) was obtained directly by addition of the disulphide (2) to cyclopentene. In the case of the addition of bis-(2-aminophenyl) disulphide (3) to cyclohexene it was possible to isolate the rather unstable trifluoroacetate (9). However, products were typically isolated as the alcohols (8) and (11)–(13). Addition to oct-1-ene proceeded to give a terminal sulphide (12). The regiochemistry of this addition and that to hexa-1,5-diene is the same as that observed with all previous additions either by electrochemical⁸ or non-electrochemical¹ methods.

A comparison of the above results shown in the Table with those reported in the previous paper indicates that, apart from a greater facility for hydrolysis of the trifluoroacetate adducts



- | | |
|--|---|
| (1) R = Ph | (6) R ¹ = OH, R ² = 2-C ₅ H ₄ N |
| (2) R = 2-C ₅ H ₄ N | (7) R ¹ = OCOCF ₃ , R ² = 2-C ₅ H ₄ N |
| (3) R = C ₆ H ₄ NH ₂ - <i>o</i> | (8) R ¹ = OH, R ² = C ₆ H ₄ NH ₂ - <i>o</i> |
| (4) R = 4-C ₅ H ₄ N | (9) R ¹ = OCOCF ₃ , R ² = C ₆ H ₄ NH ₂ - <i>o</i> |
| (5) R = C ₆ H ₄ Me- <i>p</i> | |



- | | |
|---|---|
| (10) R ¹ = OH, R ² = 2-C ₅ H ₄ N | (12) R = C ₆ H ₁₃ ⁿ |
| (11) R ¹ = OH, R ² = C ₆ H ₄ NH ₂ - <i>o</i> | (13) R = CH ₂ CH ₂ CH=CH ₂ |

derived from the disulphides (2) and (3) relative to the adducts from diphenyl disulphide (1) and dialkyl disulphides, reactions proceed to give similar products. The only difference lies in the reactivity of the disulphides and the nature of the activation process used with the different disulphides. The amount of copper(II) acetate which is needed to promote the addition of the two disulphides (2) and (3) is small, and a catalytic role of the metal ion is indicated.

These observations led us to examine three further aspects of this activation of disulphides: (i) the extension to other disulphides having basic sites, (ii) the possibility that copper(II) salts might catalyse the addition of simple dialkyl disulphides and diaryl disulphides to alkenes, and (iii) the possibility that other metal ions might catalyse these additions.

In contrast to the reactivity of 2,2'-dipyridyl disulphide (2) 4,4'-dipyridyl disulphide (4) fails to add to alkenes in the presence of copper(II) acetate. Under a variety of conditions the disulphide (4) is inert. In sharp contrast to the promotion of the addition of the disulphides (2) and (3) to alkenes by copper(II) acetate the addition of diphenyl disulphide (1) to alkenes is not accelerated by addition of copper(II) acetate. The likely explanation of these results is the specific chelation possible in disulphides (2) and (3) which would be absent in complexes formed from either diphenyl disulphide (1) or 4,4'-dipyridyl disulphide (4). By formation of a complex between either disulphide (2) or (3) with copper(II) the metal ion assists the cleavage of the sulphur-sulphur bond by the attacking nucleophilic alkene. In the case of disulphides (1) and (4) no such assistance can be gained because of the absence of strong complexation.

Table. Additions to alkenes by metal ion-promoted oxidation of 2,2'-dipyridyl disulphide (2) and bis-(2-aminophenyl) disulphide (3)

Alkene	Disulphide	Added metal salt	Product	Yield of vicinal hydroxysulphide (%)
Cyclohexene	(2)	Cu(OAc) ₂	(6)	70
Cyclopentene	(2)	Cu(OAc) ₂	(10)	142
Cyclohexene	(3)	Cu(OAc) ₂	(8)	108
Cyclopentene	(3)	Cu(OAc) ₂	(11)	88
Oct-1-ene	(3)	Cu(OAc) ₂	(12)	121
Hexa-1,5-diene	(3)	Cu(OAc) ₂	(13)	29
Cyclohexene	(2)	Fe(OAc) ₃	(6)	0
Cyclohexene	(2)	Hg(OAc) ₂	(6)	55
Cyclohexene	(2)	Mn(OAc) ₃	(6)	65

From the many studies of the interaction of the disulphides (2) and (3), acting as polydentate ligands, with metal ions, strong support for this analysis is found. Although earlier spectroscopic studies⁹ are revealing concerning the nature of the structures of such complexes, X-ray diffraction studies are more powerful in suggesting the origin of the catalysis. The latter studies discriminate between those complexes in which the metal ion is not co-ordinated to sulphur, for example a cobalt(II) complex¹⁰ and a mercury(II) complex¹¹ with the disulphide (2), and a complex¹² such as that formed between copper(II) perchlorate and the disulphide (2) where co-ordination to sulphur occurs. In this copper complex not only is co-ordination of sulphur to copper observed but complexation is accompanied by an increase in the sulphur-sulphur bond length.

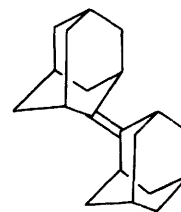
The typical reaction of the disulphides (2) and (3) with alkenes in the presence of copper(II) acetate is accompanied by striking colour changes indicating that a number of different complexes are probably present in the course of reaction. However, we attribute the role of the copper in promotion of the alkene addition to formation of a complex in which weakening of the sulphur-sulphur bond facilitates alkene attack. Copper(II)-promoted cleavage of the disulphide bond in compound (2) has previously been observed,¹³ and similarly the disulphide bond of another pyridine-containing disulphide¹⁴ has recently been cleaved by copper(II). Our observation that only catalytic quantities of copper(II) are required to promote addition of alkenes to the disulphides (2) and (3) compares with the observation that in analogous systems¹⁴ after cleavage of the sulphur-sulphur bond copper(I) is reoxidised by dioxygen to give copper(II). Hence in the presence of dioxygen a catalytic role for copper(II) is not unexpected.

It is the catalytic role of copper(II) which distinguishes the copper(II)-promoted cleavage of the disulphides (2) and (3) from reactions with other metal salts. In the absence of added metal salts neither disulphide reacts with alkenes but reaction can be promoted either by catalytic quantities of copper(II) or non-catalytically by manganese(III) and mercury(II) salts. No reaction is observed in the presence of iron(III) acetate. Lead(IV) acetate reacts with the disulphide (3) but neither of the disulphides (2) and (3) undergoes efficient addition to alkenes in the presence of lead(IV) acetate.

Previous studies¹⁵ have used exchange experiments to show the lability of the sulphur-sulphur bond in disulphides. When diphenyl disulphide (1) and di-p-tolyl disulphide (5) are dissolved in trifluoroacetic acid-dichloromethane, h.p.l.c. analysis shows the rapid equilibration of the disulphides. In contrast, under the same reaction conditions, disulphides (2) and (4) do not equilibrate. This failure to equilibrate is attributed to protonation on nitrogen which inhibits the acid-catalysed cleavage of the disulphide bond with concomitant

attack by a disulphide acting as nucleophile. Even in the presence of added copper(II) acetate the disulphides (2) and (4) do not equilibrate but this can be attributed to the reduced nucleophilicity of the protonated disulphides. The ability of copper salts to promote the solvolysis of allylic sulphides¹⁶ has recently been noted.

In summary the results in this and the two previous papers^{1,8} show that a variety of organic disulphides can be added to alkenes using different conditions. Anodic cleavage in acetonitrile proceeds *via* cation-radical intermediates. Cleavage by lead(IV) salts and manganese(III) salts proceeds *via* oxidation of the disulphide with an irreversible reduction of the metal salt, whereas copper(II) salts in the presence of oxygen can be used catalytically. Copper(II) salts are particularly efficient in the cleavage of the disulphides (2) and (3). Finally, slow addition of diphenyl disulphide to alkenes is possible in the absence of metal salts. These three papers clearly establish the preparative utility of these additions but leave a number of mechanistic questions unanswered. For example a number of intermediates might explain the oxidative addition in the absence of added metal salts. As the addition of thiol sulphinates to alkenes in trifluoroacetic anhydride has previously been reported¹⁷ one route might involve a catalytic role for such intermediates or thiol sulphinates. Alternatively the recent suggestion¹⁸ that the alkene (14) is oxidised in trifluoroacetic acid in air *via* a cation-radical intermediate indicates that a route involving formation of the cation radical from diphenyl disulphide (1) and related disulphides cannot be excluded. Trifluoroacetic acid is known to favour cation-radical formation and the relative ionisation potentials [8.3 eV for (1) and 7.84 eV for (14)] suggests that a single-electron transfer process with the disulphide (1) might be possible.



(14)

Further work to distinguish between the different possible mechanisms is in progress.

Experimental

General methods are described earlier.¹

2-(2-Aminophenylthio)cyclohexanol (8).—Copper(II) acetate (200 mg) was dissolved in a mixture of dichloromethane (50 ml) and trifluoroacetic acid (4 ml) at room temperature. Bis-(2-aminophenyl) disulphide (3) (1.6 g) and then cyclohexene (3.2 g) were added in rapid succession. The solution was stirred at room temperature under air for 5 days and then poured into water (150 ml). Excess of acid was neutralised by careful addition of solid sodium carbonate, and the solution was extracted with chloroform (3 × 50 ml). The combined organic extracts were washed with water, dried over magnesium sulphate, and filtered. Evaporation of solvents afforded an oil which was purified by column chromatography [eluant light petroleum-chloroform (1:1)] to afford, as a yellow oil, 1-(2-aminophenylthio)-2-trifluoroacetoxycyclohexane (9) [2.23 g, 108% w.r.t. disulphide (3)] (Found: M^+ , 319.0691. $C_{14}H_{16}F_3NO_2S$ requires M , 319.0707); m/z 319 (M^+ , 41%) and 125 (100); v_{max} (film) 3 480, 3 380, 2 950, 2 860, 1 790, 1 610, 1 480, 1 450,

1 390, and 1 170 cm^{-1} ; δ_{H} 1.1—1.9 (6 H, complex), 2.25 (2 H, m), 3.04 (1 H, m), 4.30 (2 H, s), 4.94 (1 H, m), and 6.5—7.3 (4 H, complex).

The trifluoroacetate (9) was hydrolysed (2M KOH in ethyl alcohol) to afford, quantitatively after work-up, 2-(2-aminophenylthio)cyclohexanol (8), m.p. 79—80 °C (from dichloromethane-pentane) (Found: M^+ , 223.1067. $\text{C}_{12}\text{H}_{17}\text{NOS}$ requires M , 223.1063; m/z 223 (M^+ , 20%) and 125 (100); ν_{max} (CHCl_3) 3 420, 3 330, 2 930, 2 850, 1 620, 1 480, 1 445, 1 300, 1 210, and 1 070 cm^{-1} ; δ_{H} 1.0—1.8 (6 H, complex), 2.08 (2 H, m), 2.62 (1 H, m), 3.25 (1 H, dt, J 9, 9, and 4 Hz), 4.25 (3 H, br), 6.67 (2 H, m), 7.10 (1 H, m), and 7.38 (1 H, m); δ_{C} 24.35 (CH_2), 26.1 (CH_2), 32.9 (CH_2), 34.4 (CH_2), 56.6 (CH), 72.5 (CH), and 115.5, 115.7, 118.8, 130.5, 138.2, and 149.4 p.p.m. (aromatic carbons).

2-(2'-Aminophenylthio)cyclopentanol (11).—Copper(II) acetate (200 mg) was dissolved in a mixture of dichloromethane (50 ml) and trifluoroacetic acid (4 ml) at room temperature. Bis-(2-aminophenyl) disulphide (3) (1.23 g) and then cyclopentene were added, and after reaction as described above for 4 days and work-up, the crude trifluoroacetate was hydrolysed. Purification by column chromatography (eluant chloroform) afforded 2-(2-aminophenylthio)cyclopentanol (11) [915 mg, 88% w.r.t. disulphide (3)] m.p. 74—75 °C (from dichloromethane-pentane) (Found: M^+ , 209.1095. $\text{C}_{11}\text{H}_{15}\text{NOS}$ requires M , 209.1073; m/z 209 (M^+ , 14%) and 125 (100); ν_{max} (CHCl_3) 3 600, 3 440, 3 360, 3 000, 2 960, 1 610, 1 480, 1 450, 1 220, and 1 030 cm^{-1} ; δ_{H} 1.4—2.2 (6 H, complex), 3.07 (1 H, m), 3.93 (1 H, m), 4.15 (2 H, br), 6.72 (2 H, m), 7.14 (1 H, m), and 7.40 (1 H, m).

1-(2-Aminophenylthio)octan-2-ol (12).—Copper(II) acetate (310 mg) was dissolved in a mixture of dichloromethane (50 ml) and trifluoroacetic acid (5 ml) at room temperature. Bis-(2-aminophenyl) disulphide (3) (1.04 g) and then oct-1-ene (3.1 g) were added and after reaction as described above for 5 days, and work-up, the crude trifluoroacetate was hydrolysed. Purification by column chromatography [eluant light petroleum-chloroform (1:4)] afforded 1-(2-aminophenylthio)octan-2-ol (12) [1.30 g, 121% w.r.t. bis-(2-aminophenyl) disulphide (3)] as a yellow oil (Found: M^+ , 253.1479. $\text{C}_{14}\text{H}_{23}\text{NOS}$ requires M , 253.1477; m/z 253 (M^+ , 23%) and 125 (100); ν_{max} (film) 3 450, 3 360, 2 960, 2 860, 1 610, 1 490, 1 450, and 1 310 cm^{-1} ; δ_{H} 0.90 (3 H, t), 1.1—1.7 (10 H, complex), 2.65—2.9 (2 H, m), 3.50 (1 H, m), 4.4 (2 H, br), 6.70 (2 H, m), 7.06 (1 H, m), and 7.40 (1 H, m); δ_{C} 14.1 (CH_3), 25.6 (CH_2), 29.3 (CH_2), 31.7 (CH_2), 36.1 (CH_2), 42.9 (CH_2), 64.0 (CH_2), 69.9 (CH), and 115.7, 118.0, 119.2, 129.9, 137.6, and 148.6 p.p.m. (aromatic carbons).

2-(2-Pyridylthio)cyclohexanol (6).—Copper(II) acetate (200 mg) was dissolved in a mixture of dichloromethane (50 ml) and trifluoroacetic acid (5 ml) at room temperature. 2,2'-Dipyridyl disulphide (Aldrithiol-2) (2) (1.19 g) and then cyclohexene (2.84 g) were added and after reaction as described above for 4 days, work-up and column chromatography [alumina, eluant benzene-chloroform (3:1)] afforded directly, as a yellow oil, 2-(2-pyridylthio)cyclohexanol (6) [1.13 g, 70% w.r.t. Aldrithiol-2 (2)] (Found: M^+ , 209.0763. $\text{C}_{11}\text{H}_{15}\text{NOS}$ requires M , 209.0774; m/z 209 (M^+ , 13%), 191 (14), and 112 (100); ν_{max} (film) 3 400, 2 950, 2 870, 1 580, 1 560, 1 450, 1 415, and 1 130 cm^{-1} ; δ_{H} 1.1—1.9 (6 H, complex), 2.20 (2 H, m), 3.4—3.6 (2 H, m), 5.5 (1 H, br), 7.06 (1 H, m), 7.38 (1 H, m), 7.50 (1 H, m), and 8.37 (1 H, m); δ_{C} 24.0 (CH_2), 26.0 (CH_2), 32.2 (CH_2), 35.7 (CH_2), 51.8 (CH), 75.0 (CH), and 120.0, 123.3, 136.5, 148.7, and 159.4 p.p.m. (aromatic carbons).

2-(2'-Pyridylthio)cyclopentanol (10).—Copper(II) acetate (200 mg) was dissolved in a mixture of dichloromethane (50 ml) and

trifluoroacetic acid (4 ml) at room temperature. 2,2'-Dipyridyl disulphide (Aldrithiol-2) (2) (1.00 g) and then cyclopentene (2.02 g) were added and after reaction as described above for 5 days, work-up and column chromatography [alumina, eluant light petroleum-chloroform (4:1)] afforded directly, as a yellow oil, 2-(2-pyridylthio)cyclopentanol (10) [1.26 g, 142% w.r.t. Aldrithiol-2 (2)] (Found: M^+ , 195.0954. $\text{C}_{10}\text{H}_{13}\text{NOS}$ requires M , 195.0930; m/z 195 (M^+ , 13%), 178 (23), and 111 (100); ν_{max} (film) 3 400, 2 960, 2 860, 1 580, 1 555, 1 450, 1 420, 1 125, and 1 020 cm^{-1} ; δ_{H} 1.4—2.4 (6 H, complex), 3.72 (1 H, m), 4.25 (1 H, m), 6.4 (1 H, br), 7.04 (1 H, m), 7.30 (1 H, m), 7.50 (1 H, m), and 8.35 (1 H, m).

1-(2-Aminophenylthio)hex-5-en-2-ol (13).—Copper(II) acetate (200 mg) was dissolved in a mixture of dichloromethane (50 ml) and trifluoroacetic acid (5 ml) at room temperature. Bis-(2-aminophenyl) disulphide (3) (1.27 g) and then hexa-1,5-diene (3.8 g) were added and after reaction as described above for 3 days, and work-up, the crude trifluoroacetate was hydrolysed. Purification by column chromatography (eluant chloroform) afforded 1-(2-aminophenylthio)hex-5-en-2-ol (13) [340 mg, 29% w.r.t. disulphide (3)] as a yellow oil (Found: M^+ , 223.1152. $\text{C}_{12}\text{H}_{17}\text{NOS}$ requires M , 223.1140; m/z 223 (M^+ , 27%) and 125 (100); ν_{max} (film) 3 460, 3 350, 3 060, 2 930, 1 610, 1 480, 1 450, and 1 310 cm^{-1} ; δ_{H} 1.5—1.7 (2 H, m), 2.20 (2 H, m), 2.6—2.9 (2 H, m), 3.58 (1 H, m), 3.8 (2 H, br), 4.8—5.1 (2 H, m), 5.6—5.9 (1 H, m), 6.72 (2 H, m), 7.10 (1 H, m), and 7.40 (1 H, m).

Acknowledgements

We thank the S.E.R.C. and Smith Klyne for financial support and Dr. T. Laird for helpful discussions.

References

- 1 A. Bewick, J. M. Mellor, and W. M. Owton, preceding paper.
- 2 B. M. Trost, M. Ochiai, and P. G. McDougal, *J. Am. Chem. Soc.*, 1978, **100**, 7103.
- 3 J. D. Lydon, R. C. Elder, and E. Deutsch, *Inorg. Chem.*, 1982, **21**, 3186.
- 4 R. D. Bach, S. J. Rajan, H. B. Vardhan, T. J. Lang, and N. G. Albrecht, *J. Am. Chem. Soc.*, 1981, **103**, 7727.
- 5 J. M. Downes, J. Whelan, and B. Bosnich, *Inorg. Chem.*, 1981, **20**, 1081.
- 6 A. Ichimura, D. L. Nosco, and E. Deutsch, *J. Am. Chem. Soc.*, 1983, **105**, 844.
- 7 F. A. Davis, A. J. Friedman, E. W. Kluger, E. B. Skibo, E. R. Fretz, A. P. Milicia, W. C. Le Masters, M. D. Bentley, J. A. Lacadie, and I. B. Douglass, *J. Org. Chem.*, 1971, **42**, 967.
- 8 A. Bewick, D. Coe, J. M. Mellor, and W. M. Owton, *J. Chem. Soc., Perkin Trans 1*, 1985, 1033.
- 9 S. E. Livingstone and J. D. Nolan, *Austr. J. Chem.*, 1973, **26**, 961; C. A. McAuliffe, F. P. McCullough, and A. Werfalli, *Inorg. Chim. Acta*, 1978, **29**, 57; S. P. Bag, A. Busu, and A. B. Chatterjee, *J. Indian Chem. Soc.*, 1982, **59**, 787; M. Keeton, A. B. P. Lever, and B. S. Ramaswamy, *Can. J. Chem.*, 1970, **48**, 3185; M. Keeton and A. B. P. Lever, *Inorg. Chem.*, 1971, **10**, 47; J. R. Ferraro, B. B. Murray, and N. J. Wieckowicz, *J. Inorg. Nucl. Chem.*, 1972, **34**, 231; M. Bridson and W. R. Walker, *Austr. J. Chem.*, 1974, **27**, 87; M. Cano, L. Ballester, and A. Santos, *J. Inorg. Nucl. Chem.*, 1981, **43**, 200.
- 10 M. M. Kadooka, L. G. Warner, and K. Seff, *Inorg. Chem.*, 1976, **15**, 812.
- 11 M. M. Kadooka, E. Hilti, L. G. Warner, and K. Seff, *Inorg. Chem.*, 1976, **15**, 1186.
- 12 M. M. Kadooka, L. G. Warner, and K. Seff, *J. Am. Chem. Soc.*, 1976, **98**, 7569.
- 13 L. S. Higashi, M. Lundeen, E. Hilti, and K. Seff, *Inorg. Chem.*, 1977, **16**, 310.

- 14 A. Odani, T. Maruyama, O. Yamauchi, T. Fujiwara, and K. Tomita, *J. Chem. Soc., Chem. Commun.*, 1982, 646.
- 15 R. E. Benesch and R. Benesch, *J. Am. Chem. Soc.*, 1958, **80**, 1666; J. L. Kice, *Acc. Chem. Rev.*, 1981, **1**, 58.
- 16 D. Uguen, *Tetrahedron Lett.*, 1984, **25**, 541.
- 17 T. Morishita, N. Furukawa, and S. Oae, *Tetrahedron*, 1981, **37**, 2539.
- 18 R. Akaba, H. Sakuragi, and K. Tokumaru, *Tetrahedron Lett.*, 1984, **25**, 665.

Received 26th July 1984; Paper 4/1312