Metal-ion-promoted Reactions of Organo-sulphur Compounds

By D. P. N. Satchell
DEPARTMENT OF CHEMISTRY, KING'S COLLEGE, STRAND, LONDON WC2R 2LS

1 Introduction

Certain metal ions, especially Hg^{2+} and Ag^{+}, have long been known to react readily with organo-sulphur compounds.[1] Often these reactions facilitate changes in the organo-sulphur compound which can also occur slowly, either spontaneously or under catalysis by hydrogen acids. In a loose sense, the metal ions catalyse such reactions, but since the metal is also frequently consumed as a covalent and often insoluble sulphide the processes are usually better described[2] as 'metal-ion-promoted.'* A typical example is the hydrolysis of thiol esters in aqueous solvents. This reaction occurs spontaneously, is (slightly[4]) catalysed by hydrogen ions [reaction (1)], and is greatly facilitated by Hg^{2+} or Ag^{+} ions[5] [reaction (2)]. In the metal-ion-promoted process the thiol is formed

$$R^1COSR^2 + H_2O \xrightarrow{H_3O^+} R^1CO_2H + R^2SH \tag{1}$$

$$R^1COSR^2 + 2H_2O + Ag^+ \rightarrow R^1CO_2H + R^2SAg + H_3O^+ \tag{2}$$

as a relatively insoluble metal derivative, which must subsequently be decomposed if the free thiol is required. Many such reactions are known, but the information is scattered in the literature and has been only fragmentarily reviewed. The present review will draw examples mainly from reactions of thiols, of disulphides, and of thio-ethers, -acetals, -esters, -acids, -anhydrides, and -amides. In these compounds the S atoms are divalent and can interact directly with the metal. Some of the reactions have been studied kinetically. A difficulty frequently met in kinetic work throughout the field is the low solubility of the metal sulphide products, since the presence of a precipitate can lead to (unwanted) auto-catalytic effects.[6] Homogeneous systems can, however, usually be obtained by careful

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*The notion[3] that if a species accelerates a reaction by its effect on $\Delta S^{\ddagger}$, rather than by its effect on $\Delta H^{\ddagger}$, then that process should be called 'promotion' rather than 'catalysis' runs counter to current usage: catalysis covers both effects. The term promotion is normally used in the sense employed in the present article.

[1] E. E. Reid, 'Organic Chemistry of Bivalent Sulphur' vols. 1—5, Chemical Publishing Co., New York, 1958.

[2] M. L. Bender, *Adv. Chem. Series*, 1963, **37**, 19.

[3] R. W. Hay and P. J. Morris, *J.C.S. Dalton*, 1973, 56.

[4] J. R. Schaefgen, *J. Amer. Chem. Soc.*, 1948, **70**, 1308.

[5] D. P. N. Satchell and I. I. Secemski, *J. Chem. Soc. (B)*, 1970, 1306.

[6] A. J. Hall and D. P. N. Satchell, *J.C.S. Perkin II*, 1975, 1273; A. J. Hall, Thesis, University of London, 1976.

control of reaction conditions. Almost all the reactions reported involve class B (soft[7,8]) metal ions and have heterolytic (*i.e.* Lewis acid–base) mechanisms.

The reactions covered are of interest in a surprising number of contexts. They offer simple examples of catalysis by class B metal ions, and their quantitative study allows some assessment of class B character; they have valuable applications in organic synthesis and in quantitative and qualitative analysis; they are relevant to biochemical processes and they throw light on ligand-substitution reactions in metal ions and upon reactions of co-ordinated ligands. All these points will be illustrated. The reactions of all sulphur compounds are much less susceptible to catalysis by hydrogen acids than are the reactions of their oxygen analogues when protonation of S (or O) underlies the catalysis (H^+ being a hard acid). That is one important reason why the corresponding metal-ion-promoted reactions are of interest for the sulphur-containing compounds.

2 Reactions of Thiols

Thiols readily form compounds (mercaptides) with metals, *e.g.* reactions (3) and (4). Mercaptides of the heavier, and especially class B, metals are poorly soluble.

$$RSH + KOH \rightarrow RSK + H_2O \tag{3}$$

$$2RSH + Hg(NO_3)_2 \rightarrow (RS)_2Hg + 2HNO_3 \tag{4}$$

They have characteristic melting points and are useful for the isolation, identification, and quantitative analysis of thiols.[9] The early isolation and purification of coenzyme-A was based on its precipitation as the mercury or copper derivative, followed by regeneration of the thiol with hydrogen sulphide.[10]

Mercaptides are normally stable, but can decompose to give mainly sulphides, *e.g.* reaction (5). Sometimes, on heating, some disulphide, or olefin, is also formed,

$$(MeS)_2Pb \xrightarrow{\text{heat}} Me_2S + PbS \tag{5}$$

$$(EtS)_2Hg \xrightarrow{\text{heat}} Hg + EtS{-}SEt \tag{6}$$

$$(Me_3CS)_2Hg \xrightarrow{\text{heat}} Me_3CSH + Me_2C{=}CH_2 + HgS \tag{7}$$

e.g. reactions (6) and (7). Mercaptide formation, followed by processes (5) or (7), represents metal-promoted conversion of thiols into thioethers or olefins. Similar reactions occur[11] when the thiol is heated with certain metal sulphides [*e.g.* reactions (8) and (9)], when the changes may also proceed *via* the mercaptide.

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[7] S. Ahrland, J. Chatt, and N. R. Davies, *Quart. Rev.*, 1958, **12**, 265.

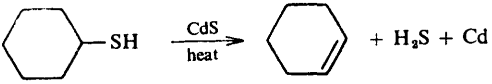
[8] 'Hard and Soft Acids and Bases', ed. R. G. Pearson, Dowden, Hutchinson, and Ross Inc., New York, 1973.

[9] F. Challenger, 'Aspects of the Organic Chemistry of Sulphur', Butterworths, London, 1959.

[10] J. D. Gregory, G. D. Novelli, and F. Lipmann, *J. Amer. Chem. Soc.*, 1952, **74**, 854; H. Beinert, R. W. von Korff, D. E. Green, D. A. Buyske, R. E. Handschumacher, H. Higgins, and F. M. Strong, *ibid.*, 1952, **74**, 854.

[11] D. S. Tarbell and D. P. Harnish, *Chem. Rev.*, 1951, **49**, 1.

However, the detailed mechanisms of all these essentially heterogeneous reactions are unknown.



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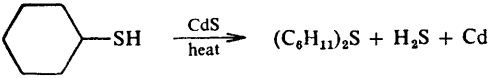

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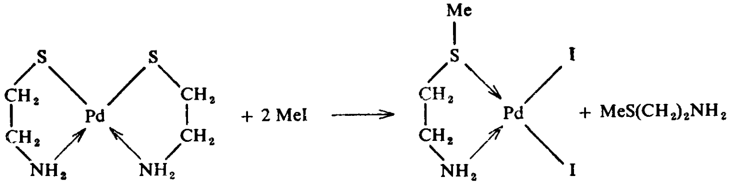
The conversion of thiols into thioethers has been found to occur more readily, and under more controlled conditions, when a mercaptide is treated with an alkyl halide[12] [reaction (10)], and especially[13] when the thiolate group is part of a chelate [reactions (11) and (12)]. Normally the resulting thioether is isolated as the metal complex, from which it can be displaced by more strongly co-ordinating ligands [*e.g.* reaction (12)]. So far, such reactions have always involved class B-like metals. This type of alkylation has been used[13] to synthesize large cyclic ligands [reaction (13)]. The reactions are conducted in solution, or suspension,

$$(EtS)_2Pt + 2\,EtI \longrightarrow Pt(SEt_2)_2I_2 \qquad (10)$$



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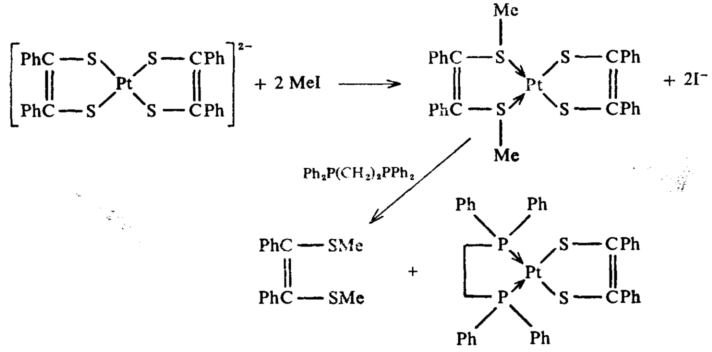

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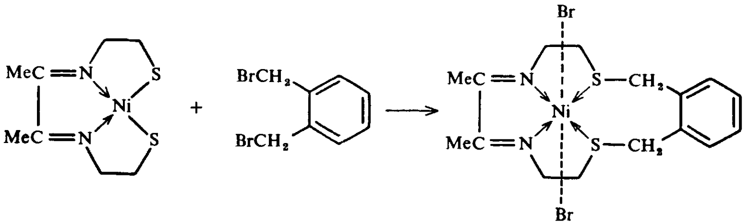
[12] S. Smiles, *J. Chem. Soc.*, 1900, **77**, 160.

[13] D. H. Busch, J. A. Burke, D. C. Jicha, M. C. Thompson, and M. L. Morris, *Adv. Chem. Series*, 1963, **37**, 125.



(13)

in DMF, chloroform, or methanol. The final complex is normally more soluble than the starting material. In some examples, which can be examined under homogeneous conditions throughout, kinetic studies have been made.[13] The main conclusions are: (i) each alkylation step is first-order in the thio-complex and first-order in the alkyl halide, (ii) complexes of palladium are much less reactive than those of nickel, (iii) the rate constant for alkylation of the second S atom in an overall process such as (12) is *ca.* 30-fold larger than that for alkylation of the first, and in reaction (13) the closure of the ring is more than 300-fold faster than the initial alkylation, (iv) the reactivity of alkyl halides (RHal) is in the sequence RI > RBr > RCl, and (v) the difference in reactivity between benzyl and *p*-nitrobenzyl chloride arises mainly from a change in $\Delta S^{\ddagger}$. These findings, and others subsequently reported[14] for the alkylation of substituted 8-mercapto-quinoline derivatives of nickel [reaction (14)], seem best explained by a mechanism such as reaction (15). A slow intermolecular S_N2 displacement of halide from free RHal by co-ordinated sulphur, or a prior slow dissociation of the metal–sulphur bond in what are essentially square-planar complexes (and therefore unlikely to display dissociation mechanisms[15]) seem less probable. Reaction (15) involves five-co-ordinate intermediates, but the fact that equilibrium constant K_2 is likely to be greater than K_1 readily explains the otherwise surprising rapidity of the second alkylation step. For examples such as reaction (13) the ring-closure stage is entirely intramolecular, and this accounts for its relatively great speed.

Certain Friedel–Crafts (HCl–$AlCl_3$-catalysed) alkylations by thiols have been reported.[16] However, it is not yet known if they involve direct interaction between the S and Al atoms.

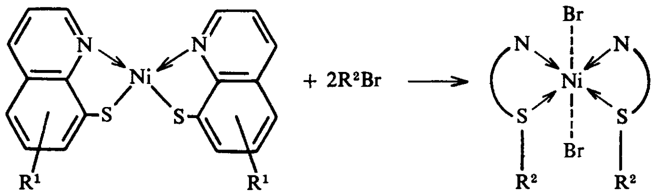
Some sulphur derivatives of ketones that are otherwise difficult to isolate can be obtained by making use of the stability of their chelates with soft metals. For example, *gem*-dithiols, formed in the reaction of hydrogen sulphide with ketones, are very unstable even at low temperatures, but can be isolated as their lead derivatives[17] [reaction (16)]. With β-diketones, hydrogen sulphide leads normally to the monothio-derivative only. However, in the presence of suitable

[14] J. C. Schoup and J. A. Burke, *Inorg. Chem.*, 1973, **12**, 1851.

[15] F. Basolo and R. G. Pearson, 'Mechanisms of Inorganic Reactions', J. Wiley and Sons, New York, 2nd edn., 1967.

[16] J. R. Meadow, *Chem. Abs.*, 1946, **40**, 6502; U.S.P. 2 403 013.

[17] R. Mayer in 'Organosulphur Chemistry', ed. M. J. Jenssen, Wiley, New York, 1967.



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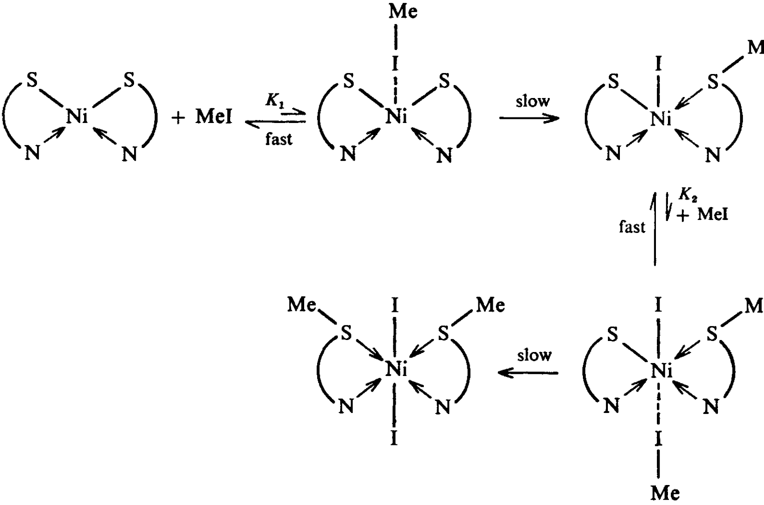
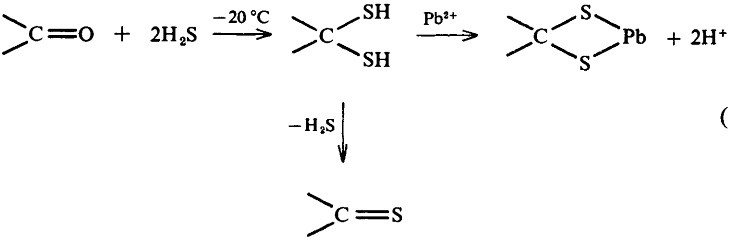


(15)

metal ions the dithiodiketone is formed as its anion. Thus thioacetylacetonate (SAA) can be converted into dithioacetylacetonate (SSAA) *via* its chelated palladium complex [reaction (17)]. Mercury, rhodium, platinum, and cobalt effect similar transformations.[18]



(16)

$$\mathrm{Pd(SAA)_2 + H_2S \rightarrow Pd(SSAA)_2 + H_2O} \qquad (17)$$

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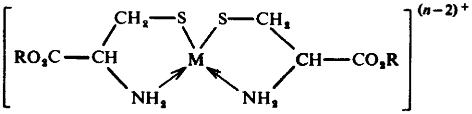
[18] S. Kawanishi, A. Yokoyama, and H. Tanaka, *Chem. and Pharm. Bull. (Japan)*, 1973, **21**, 2653; 1972, **20**, 262.

The great stability of metal chelates involving thiolate ligands has important consequences in many contexts. Two further examples are (i) the preferential co-ordination of cysteine esters as in (1) (rather than *via* their ester groups) and the consequent relatively feeble catalysis by metal ions of their hydrolysis in aqueous solution,[19] and (ii) the displacement of thiazoline–Schiff base equilibria, which normally lie on the thiazoline side in alcohol or DMF, towards the Schiff base in the presence of Ni^{2+}, Cd^{2+}, or similar ions[20] [reaction (18)]. These processes sometimes involve a prior, rate-limiting tautomerism and sometimes a direct attack of the metal on the thiazoline. The latter case constitutes a metal-promoted rearrangement.



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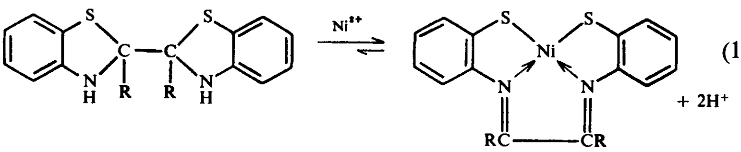


(18)

As a final example of the influence of metal ions on the reactions of thiols, their conversion into disulphides must be mentioned. This reaction has long been known. It can occur simply on heating the mercaptide [equation (6)], when the metal is reduced, or in aqueous solutions of metal–thiol complexes (especially chelate complexes) in the presence of oxygen, when the latter takes up hydrogen. Complexes of Fe^{2+} and Cu^{2+} have been widely studied, but other metals, especially transition metals, can be used.[21,22] Although the picture is by no means clear, kinetic results for the Fe^{2+}–mercaptoacetate system[21] suggest a reaction between a rapidly formed metal chelate and oxygen, probably involving electron transfer and radical formation, as in the outline scheme shown by reactions (19)—(21). Other steps are doubtless involved, and the details seem to depend upon the pH and upon the relative reactant concentrations. Disulphide formation is of widespread interest in protein chemistry, since protein stability can be critically dependent on sulphur-bridging. It is found too that proteins are protected against radiation damage on conversion of their free thiol groups into disulphides with added thiols.[23]

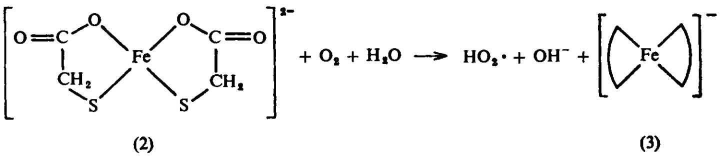
[19] L. J. Porter, D. D. Perrin, and R. W. Hay, *J. Chem. Soc.* (*A*), 1969, 118.

[20] L. F. Lindoy, *Coordination Chem. Rev.*, 1969, **4**, 41.

[21] D. L. Leussing and T. N. Tischer, *Adv. Chem. Series*, 1963, **37**, 216.

[22] S. H. H. Chaston and S. E. Livingstone, *Austral. J. Chem.*, 1967, **20**, 1065.

[23] H. Sakurai, A. Yokoyama, and H. Tanaka, *Chem. and Pharm. Bull.* (*Japan*), 1971, **19**, 1416.



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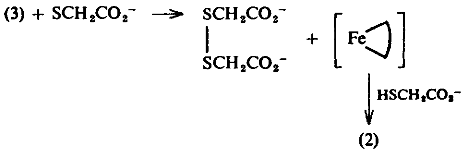
(2) (3)

$$HO_2\cdot + HSCH_2CO_2^- \rightarrow H_2O_2 + \cdot SCH_2CO_2^- \qquad (20)$$

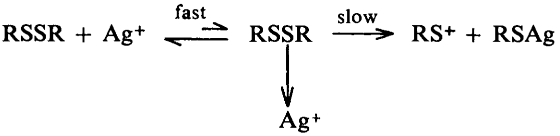


(21)

3 Reactions of Disulphides

Most reactions of these compounds involve S—S bond fission. As noted above, disulphides are of special interest in biochemistry, and an example which nicely illustrates both the dependence of protein structure on disulphide bonds, and their cleavage by soft metal ions, is the disruption of the protein sheath of the T_2 bacteriophage by complexes of Zn^{2+}, Cd^{2+}, and Hg^{2+}. In nature, this phage is able to inject its DNA into the bacterium *E. coli* after an analogous disruption of the sheath by zinc species in the bacterial cell wall.[24]

In view of the importance of cleavage reactions of disulphides, surprisingly little work has been done on their promotion by metal ions. Most studied has been the hydrolysis in aqueous solvents. This occurs *via* a heterolytic path, perhaps as shown in reactions (22) and (23). Despite some kinetic work,[25] this



$$RSSR + Ag^+ \underset{}{\overset{\text{fast}}{\rightleftharpoons}} \underset{\displaystyle Ag^+}{\underset{\downarrow}{RSSR}} \xrightarrow{\text{slow}} RS^+ + RSAg \qquad (22)$$

$$RS^+ + 2H_2O \xrightarrow{\text{fast}} RSOH + H_3O^+ \qquad (23)$$

scheme remains tentative. The sulphenic acid (RSOH) is unstable, and it disproportionates rapidly to sulphinic acid (RSO_2H) and RSH. The hydrolysis is known to be promoted by ions other than Ag^+, notably Hg^{2+} and Cu^{2+}. Disulphides with chelating possibilities tend to react rapidly, and sometimes render one metal ion very much more effective than others.[26]

Cleavage occurs *via* some variety of electron-transfer route when disulphides

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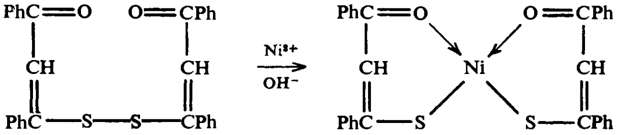
[24] L. M. Kozloff, *Records Chem. Progr.*, 1960, **21**, 49.

[25] R. Cecil and J. R. McPhee, *Biochem. J.*, 1957, **66**, 538.

[26] I. M. Klotz and B. J. Campbell, *Arch. Biochem. Biophys.*, 1962, **96**, 92.

displace carbon monoxide from metal carbonyl complexes,[27] and reaction (24), which occurs in alkaline aqueous alcohol solution,[28] may represent the reverse of a scheme such as that shown in reactions (19)—(21) or may result from initial S—S bond cleavage by hydroxide ion, followed by chelation of the thiolate product.



(24)

4 Reactions of Thioethers

Thioethers have been more extensively studied than disulphides. Most thioethers are very stable towards attack by electrophiles. They are even less readily cleaved than are their oxygen-analogues by hydrogen acids, and they form stable addition compounds with suitable electrophiles, including soft metal ions [reactions (25) and (26)]. Carbon–sulphur bonds are thus difficult to break by

$$Et_2S + EtBr \rightarrow Et_3S^+ Br^- \qquad (25)$$

$$2Et_2S + HgCl_2 \rightarrow (Et_2S)_2HgCl_2 \qquad (26)$$

electrophilic attack on sulphur. It is found, however, that ethers R^1SR^2, in which R^1 is an aryl group and/or R^2 is an aliphatic group having some stability as a carbonium ion, can be cleaved by various metal derivatives, especially under forcing conditions. The ability of R^2 to leave as a cation is probably of particular importance, and various pieces of evidence point to unimolecular C—S bond heterolysis in the metal–ether complex as the usual mechanism of decomposition. Thus, with aqueous mercuric chloride, optically active α-methylbenzylmercapto-acetic acid leads[29] to racemic α-methylbenzyl alcohol [reaction (27)]; with aqueous silver nitrate, alkyl alkenyl sulphides undergo allylic rearrangement [reaction (28)];[30] and the fission of aryl benzyl thioethers by aluminium bromide in a chlorobenzene solvent [reaction (29)] is accelerated by electron-withdrawing substituents in the aryl half of the ether.[11,31] This reaction also leads to some benzylation of the solvent, although this may occur after the formation of the $PhCH_2Br$.

We have seen earlier how chelating thiol compounds can be alkylated at the S atom. [*e.g.* reaction (11)]. The reverse[20,32] also occurs, but normally less

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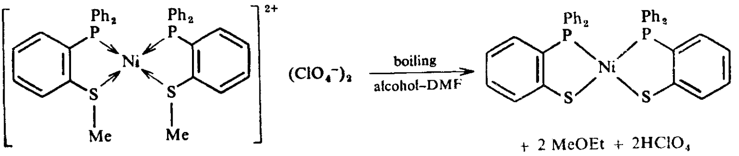
[27] E. W. Abel and B. C. Crosse, *J. Chem. Soc.* (*A*), 1966, 1377.
[28] R. K. Y. Ho, S. E. Livingstone, and T. N. Lockyer, *Austral. J. Chem.*, 1966, **19**, 1179.
[29] B. Holmberg, *Arkiv. Kemi Mineral. Geol.*, 1940, **14A**, No. 2 (*Chem. Abs.*, 1941, **35**, 4364).
[30] B. Saville, *J. Chem. Soc.*, 1962, 4062.
[31] H. F. Wilson and D. S. Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 5200.
[32] S. E. Livingstone and T. N. Lockyer, *Inorg. Nuclear Chem. Letters*, 1967, **3**, 35.

$$\mathrm{PhCH(Me)SCH_2CO_2H + HgCl_2 + H_2O \rightarrow}$$
$$\mathrm{PhCH(Me)OH + ClHgSCH_2CO_2H + HCl} \quad (27)$$

$$\mathrm{Me_2C{=}CHCH(Me)SR + AgNO_3 + H_2O \rightarrow}$$
$$\mathrm{Me_2C{=}CHCH(Me)OH + Me_2C(OH)CH{=}CHMe + AgSR + HNO_3} \quad (28)$$

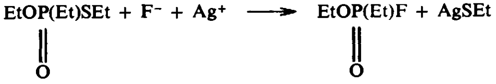
$$\mathrm{ArSCH_2Ph + AlBr_3 \xrightarrow{PhCl} ArSAlBr_2 + PhCH_2Br} \quad (29)$$

readily. Forcing conditions often seem necessary, and also conditions under which it is difficult for the cleaved group to re-alkylate the S atom [reaction (30)]. Aryl alkyl ethers again seem to be those most readily decomposed. These reactions are not yet well understood, but recent work[33] using ligands similar to those used in the alkylation studies[13] suggests that the usual mechanism of dealkylation may well be the microscopic reverse of processes such as reaction (15). As expected, a trityl group is more easily cleaved than is a benzyl group. The dealkylating ability of metal ions is in the sequence $Co^{2+} < Ni^{2+} < Hg^{2+}$. Studies which uncover the factors controlling the equilibrium position in these alkylation–dealkylation systems would be welcome.



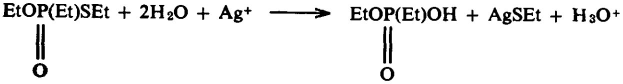
(30)

Compounds somewhat analogous to thioethers are the phosphonothiolates. The replacement of SEt^- in diethyl phosphonothiolate by F^- or OH^- in aqueous solution is promoted by silver ions[34] [reactions (31) and (32)]. A kinetic study shows that the rate equations take the forms (33) and (34), respectively. Equation (33) suggests the scheme outlined in reactions (35)—(37) for the fluoride reaction.



$$\mathrm{EtO\underset{\underset{O}{\|}}{P}(Et)SEt + F^- + Ag^+ \longrightarrow EtO\underset{\underset{O}{\|}}{P}(Et)F + AgSEt} \quad (31)$$

(4) (7)



$$\mathrm{EtO\underset{\underset{O}{\|}}{P}(Et)SEt + 2H_2O + Ag^+ \longrightarrow EtO\underset{\underset{O}{\|}}{P}(Et)OH + AgSEt + H_3O^+} \quad (32)$$

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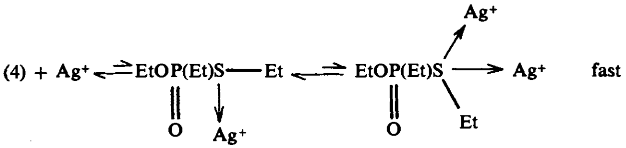
[33] R. W. Hay, A. L. Galyer, and G. A. Lawrence, *J.C.S. Dalton*, 1976, 939.
[34] B. Saville, *J. Chem. Soc.*, 1961, 4624.

$$-\mathrm{d}[(4)]/\mathrm{d}t = \{k_{31}[\mathrm{Ag}^+] + k'_{31}[\mathrm{Ag}^+]^2\}\,[\mathrm{F}^-][(4)] \qquad (33)$$

$$-\mathrm{d}[(4)]/\mathrm{d}t = k_{32}[(4)][\mathrm{Ag}^+]^2 \qquad (34)$$



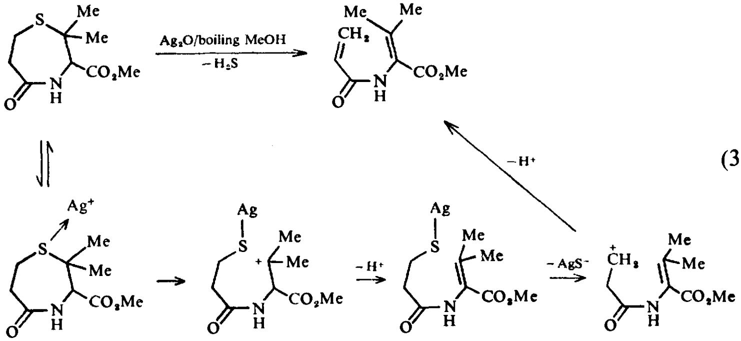
$$(4) + \mathrm{Ag}^+ \rightleftharpoons \underset{\substack{\| \\ \mathrm{O}}}{\mathrm{EtOP(Et)}}\underset{\substack{\downarrow \\ \mathrm{Ag}^+}}{\mathrm{S}}\!-\!\mathrm{Et} \rightleftharpoons \underset{\substack{\| \\ \mathrm{O}}}{\mathrm{EtOP(Et)}}\overset{\mathrm{Ag}^+\nearrow}{\underset{\searrow \mathrm{Et}}{\mathrm{S}}}\!\longrightarrow \mathrm{Ag}^+ \quad \text{fast} \qquad (35)$$

(5) (6)

$$(5) + \mathrm{F}^- \rightarrow (7) + \mathrm{AgSEt} \qquad \text{slow} \qquad (36)$$

$$(6) + \mathrm{F}^- \rightarrow (7) + [\mathrm{Ag_2SEt}]^+ \qquad \text{slow} \qquad (37)$$

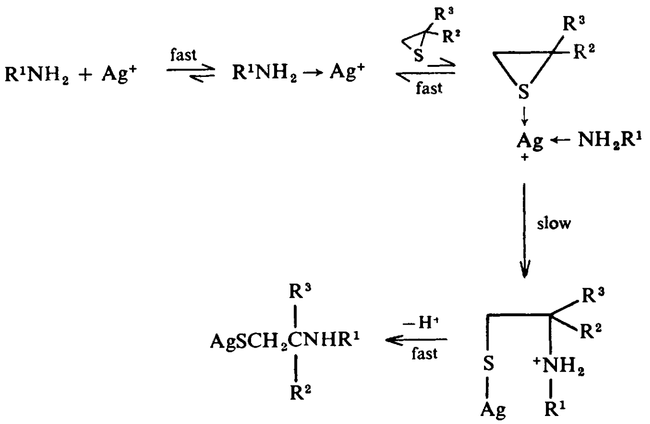
Evidence for species containing two silver ions attached to sulphur is found in other contexts, and it seems that attack by neutral water molecules requires powerful promotion of this sort, since no kinetic term that is first-order in Ag^+ is detected in this case [equation (34)].



(38)

Two interesting examples of silver-ion-promoted reactions of cyclic thioethers may also be mentioned. Processes such as reaction (38) presumably involve cleavage first of thioether and then of thiol.[35] The formation of olefinic rather than of solvolysis products is perhaps aided by the conjugated carbonyl groups, but the detailed mechanisms of these reactions can, at present, only be guessed at. The aminolysis of episulphides in aqueous solution is also promoted by silver ions, and provides a convenient route to aminoethanethiols.[36] Aminolysis is slow in the absence of silver, and it has been suggested that promotion probably proceeds *via* silver–amine complexes [reaction (39)]. This is in line with other work on promoted aminolyses (see p. 360).

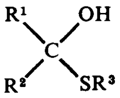
[35] D. Gravel, R. Gauthier, and C. Berse, *J.C.S. Chem. Comm.*, 1972, 1322.
[36] R. Luhowy and F. Meneghini, *J. Org. Chem.*, 1973, **38**, 2405.



(39)

5 Reactions of Thioacetals

Thiols, like alcohols, react with carbonyl compounds, but more readily. The resulting hemi-thioacetals (8), thioacetals (9), and their cyclic analogues (10) and (11) are of great synthetic interest. They are much more stable towards dilute solutions of hydrogen acids than are their oxygen analogues, but can be hydrolysed under mild conditions, using metal-ion promotion [*e.g.* reaction (40)]. They provide, therefore, a convenient means of protecting either —SH or —C=O groups during synthesis. Employed for many years in protein and sugar chemistry, interest has sharpened recently owing to their use by Seebach[37] in indirect acylation, the —C=O group being generated finally by a process such as reaction (40). Species (10) and (11) are also readily reduced to the methylene derivatives by Raney nickel, but this reaction, which has proved particularly useful in the steroid field, is outside the scope of the present review.



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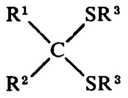

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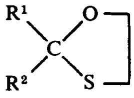

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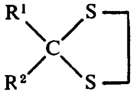

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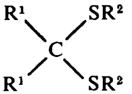

$$+ \ 2Ag^+ + 3H_2O \longrightarrow R^1COR^1 + 2R^2SAg + 2H_3O^+ \qquad (40)$$

The synthetic importance of the metal-ion-promoted hydrolyses has led to the publication of numerous preparative recipes[38] (mostly involving salts or oxides

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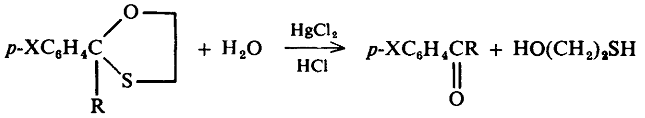
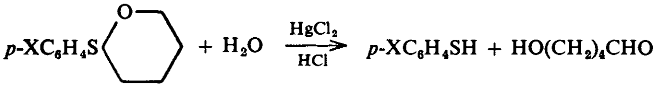
[37] D. Seebach, *Angew. Chem. Internat. Edn.*, 1969, **8**, 639.

[38] *E.g.*, D. Gravel, C. Vaziri, and S. Rahal, *J.C.S. Chem. Comm.*, 1972, 1323; T.-L. Ho and C. M. Wong, *Canad. J. Chem.*, 1972, **50**, 3740.

of soft metals), but to little kinetic work, so that the mechanistic details are in most cases unknown. One unusual (but apparently suitable) catalyst is ceric ammonium sulphate. Some kinetic information is available for catalysis by mercuric chloride. This was one of the earliest salts to be used,[11] often in conjunction with hydrogen chloride, the combination being claimed[11] (although on what evidence is not clear) to be more effective than mercuric chloride alone. The initial kinetic work[39,40] followed this pattern. Reactions (41) and (42) were

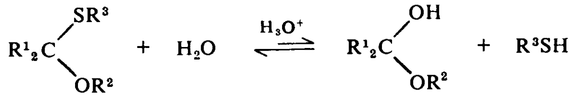


(41)



(42)

studied, using aqueous solvents containing various concentrations of mercury salt and a fixed, relatively large concentration of hydrogen chloride. Under these conditions the hydrolyses are first-order in the thioacetal and in the total mercury concentrations. A recent study[41] of reaction (42) has shown that a reduction in the concentration of chloride ion leads to a marked increase in rate, and the (approximate) relative reactivities of the different mercury species in solution are Hg^{2+} (1) $\simeq$ $HgCl^{+}$ (1) $\simeq$ $HgCl_2$ (1) $>$ $HgCl_3^{-}$ (0.1) $\gg$ $HgCl_4^{2-}$ (< 0.001). The rate constant for reaction *via* Hg^{2+} is *ca.* 10^6-fold larger than that for hydrolysis in the presence of H_3O^+ alone, and the addition of hydrogen chloride leads to a reduction, rather than an increase, in rate. Since the hydrolysis proceeds to completion, if relatively slowly, even in the absence of the metal, it is unlikely that the metal's catalytic role is to remove thiol as it is formed, *via* an equilibrium such as reaction (43), as was once believed.[11] Direct, rapid, pre-equilibrium



$$R^1_2C(SR^3)(OR^2) + H_2O \overset{H_3O^+}{\rightleftharpoons} R^1_2C(OH)(OR^2) + R^3SH \qquad (43)$$

co-ordination of the acetal's S atom to mercury is likely, and substituent effects and values of $\Delta S^{\ddagger}$ suggest[39,40] that reaction (42) involves a slow unimolecular breakdown of the acetal–mercury complex, whereas reaction (41) proceeds *via* the slow attack of water on this complex.

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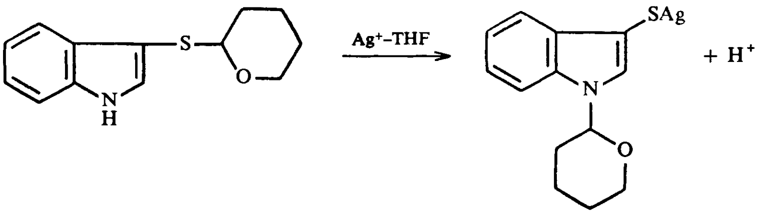
[39] L. R. Fedor, *J. Amer. Chem. Soc.*, 1968, **90**, 7266.

[40] L. R. Fedor and B. S. R. Murty, *J. Amer. Chem. Soc.*, 1973, **95**, 8407.

[41] D. P. N. Satchell and L. Z. Zdunek, unpublished results.

That the metal is interacting directly with the thioacetal and assisting the removal of RS$^-$ is supported by reactions (44) to (46) observed in non-hydroxylic solvents:[42–44] all suggest carbonium ion intermediates. Reaction (46) represents Cu^{2+}-promoted alkylation, and other nucleophiles can replace anisole.

$$R^1R^2CHC(SPh)_2R^3 \xrightarrow{Cu^+SO_3CF_3^- \text{-THF-} C_6H_6} R^1R^2C{=}C(SPh)R^3 + PhSCu + CF_3SO_3H \qquad (44)$$



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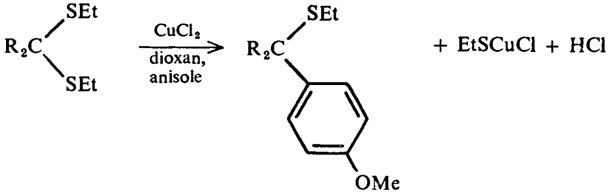

(46)

6 Reactions of Thioesters

Relatively little work exists on the reactions between thioesters and soft metal ions, but a substantial portion of it is of a quantitative and kinetic nature. Virtually all the work refers either to hydrolysis or aminolysis, both these reactions of thioesters being only feebly catalysed by hydrogen ions. The metal-promoted hydrolysis of both thiolesters [reaction (47)] and thionesters [reaction (48)] has been known for some time;[45,46] studies of the aminolysis of thiolesters [reaction (49)] are more recent.[47] Early qualitative reports are somewhat in conflict concerning the relative efficiencies of different metals, but it is clear that

$$R^1COSR^2 + H_2O + HgCl_2 \rightarrow R^1CO_2H + HCl + R^2SHgCl \qquad (47)$$

$$R^1CSOR^2 + H_2O + 2AgNO_3 \rightarrow R^1COOR^2 + Ag_2S + 2HNO_3 \qquad (48)$$

$$R^1COSR^2 + R^3NH_2 + AgNO_3 \rightarrow R^1CONHR^3 + AgSR^2 + HNO_3 \qquad (49)$$

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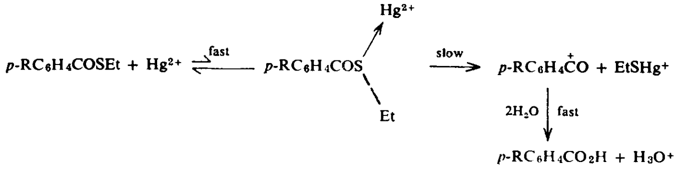
[42] T. Cohen, G. Herman, J. R. Falck, and A. J. Mura, *J. Org. Chem.*, 1975, **40**, 812.
[43] T. D. Lee, M. V. Pickering, and G. D. Daves, *J. Org. Chem.*, 1974, 39, 1106.
[44] T. Mukaiyama, K. Narasaka, and H. Hokonok, *J. Amer. Chem. Soc.*, 1969, **91**, 4315.
[45] G. Sachs, *Chem. Ber.*, 1921, **54**, 1849.
[46] T. Matsui, *Mem. Coll. Sci. Eng. Kyoto Imp. Univ.*, 1912, **3**, 247.
[47] R. Schwyzer and C. Hurlimann, *Helv. Chim. Acta*, 1954, **37**, 155.

Hg^{2+} and Ag^{+} can promote hydrolysis, Hg^{2+} being particularly effective. For aminolysis, preparative experiments by Schwyzer[47] suggest the sequence $Pb^{2+} < Cu^{2+} < Hg^{2+} < Ag^{+}$.

A recent kinetic study[5,48] of the hydrolysis of esters *p*-RC_6H_4COSEt, under homogeneous conditions in aqueous solutions of various metal perchlorates, leads to the following conclusions.

(i) with Hg^{2+} the rate equation is $-d[S\text{-ester}]/dt = k[Hg^{2+}][S\text{-ester}]$, but with Ag^{+} it is $-d[S\text{-ester}]/dt = \{k_1[Ag^{+}] + k_2[Ag^{+}]^2\}[S\text{-ester}]$.

(ii) substituent effects, solvent isotope effects, and the activation parameters indicate that the mechanism of the Hg^{2+}-promoted hydrolysis changes from one [reaction (50)] that is analogous to an *A*1 mechanism, when R = OMe, to a mechanism (51) analogous to an *A*2 scheme, when R = NO_2. With Ag^{+} the mechanism remains *A*2-like for all substituents for both the routes involving one [reaction (52)] and two [reaction (53)] silver ions. Route (53) is important for electron-repelling substituents (*e.g.* R = OMe). This kinetic behaviour in the presence of silver resembles that found for the phosphonothiolate reactions (33) and (34).



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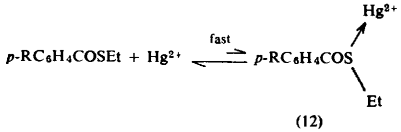
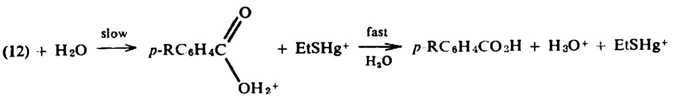
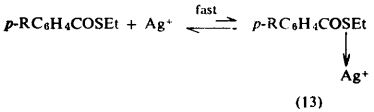


(51a)



(51b)



(52a)

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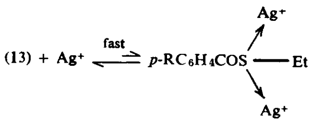
[48] D. P. N. Satchell and I. I. Secemski, *Tetrahedron Letters*, 1969, **24**, 1991.

$$(13) + H_2O \xrightarrow{\text{slow}} p\text{-}RC_6H_4COOH_2^+ + EtSAg \xrightarrow[H_2O]{\text{fast}} p\text{-}RC_6H_4CO_2H + H_3O^+ + EtSAg \qquad (52b)$$



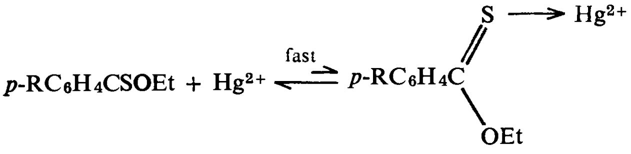
$$(13) + Ag^+ \overset{\text{fast}}{\rightleftharpoons} p\text{-}RC_6H_4CO\overset{Ag^+}{\underset{Ag^+}{S}}\text{—}Et \qquad (53a)$$

(14)

$$(14) + H_2O \xrightarrow{\text{slow}} p\text{-}RC_6H_4CO_2H_2^+ + EtSAg_2^+ \xrightarrow[H_2O]{\text{fast}} p\text{-}RC_6H_4CO_2H + H_3O^+ + EtSAg_2^+ \qquad (53b)$$

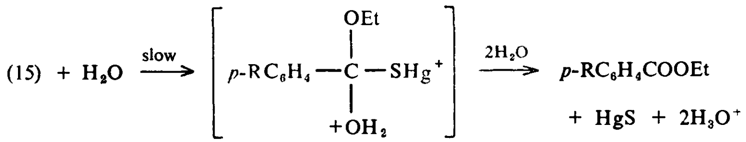
(iii) Hg^{2+} and Ag^+ are *ca.* 10^6 and *ca.* 10^3 times more effective, respectively, in accelerating the hydrolyses of these esters than the same concentration of hydrogen ions. Other soft ions tested (Pb^{2+}, Cu^{2+}, Cd^{2+}, and Ni^{2+}) are less effective than the hydrogen ion.

A similar pattern of metal ion efficiencies was also found in a recent kinetic study[49] of the related thionesters p-RC_6H_4CSOEt. These esters are hydrolysed *ca.* 10^6 times more rapidly in the presence of metal ions than are their thiol analogues. This is probably because the pre-equilibrium (54a) lies further to the right than in reaction (51a), and because the positive charge on the metal can more readily be transmitted to the carbonyl carbon atom. This great difference in reactivity has been used to estimate the compositions of thiol–thionester mixtures.[50]



(54a)

(15)



$$(15) + H_2O \xrightarrow{\text{slow}} \left[p\text{-}RC_6H_4\text{—}\overset{OEt}{\underset{+OH_2}{C}}\text{—}SHg^+ \right] \xrightarrow{2H_2O} p\text{-}RC_6H_4COOEt + HgS + 2H_3O^+ \qquad (54b)$$

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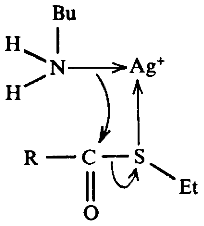
[49] D. P. N. Satchell, M. N. White, and T. J. Weil, *Chem. and Ind.*, 1975, 791.
[50] S. A. Karjala and S. M. McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 2966.

The kinetics of the homogeneous n-butylaminolysis of ethyl thiolbenzoate in aqueous solution over a range of pH values have recently been examined.[51] It is found that aminolysis proceeds *via* a slow reaction of the ester with the rapidly formed complexes $[Ag(BuNH_2)]^+$ and $[Ag(BuNH_2)_2]^+$. Transition states such as (16) and (17) are likely, similar to that suggested by Schwyzer.[47] The kinetic



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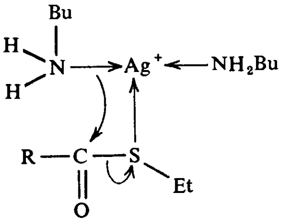
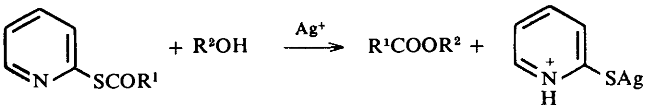


(17)

benefits arising from the intramolecular nature of the aminolysis step apparently more than compensate for the inevitable loss of nucleophilicity of the N atom when co-ordinated to Ag^+. How it is that Ag^+ is more effective than is Hg^{2+} in thiolester aminolyses,[47] whereas the reverse is true in hydrolysis,[5] and how Cu^{2+} and Pb^{2+} are effective in aminolysis,[47] but almost entirely without effect in hydrolysis,[5] is not yet clear. It is to be remembered, however, that preparative experiments[47] often involve heterogeneous systems in which powerful surface catalysis may also be present. More work is needed on the kinetics of aminolysis.

The fact that the silver-ion-promoted reactions of thiolesters proceed readily at neutral pH has been exploited in a recent[52] *O*-ester synthesis [reaction (55)], using such conditions.



(55)

Another class of *S*-esters to have had their metal-ion-promoted hydrolyses studied kinetically are thiolbenzimidate esters (18). These esters are relatively basic and exist in dilute aqueous solutions of H-acids predominantly as (19). Hydrolysis proceeds slowly under these conditions, and leads[53] initially to $R^1C_6H_4COSR^2$ [see reaction (56)], which undergoes further slow hydrolysis to $R^1C_6H_4CO_2H$. The sulphur atoms of these thiolbenzimidate esters are apparently

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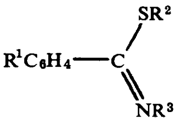
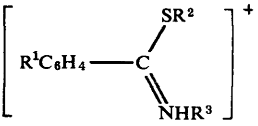
[51] B. Boopsingh and D. P. N. Satchell, *J.C.S. Perkin II*, 1972, 1702.

[52] H. Gerlach and A. Thalmann, *Helv. Chim. Acta*, 1974, **57**, 2661.

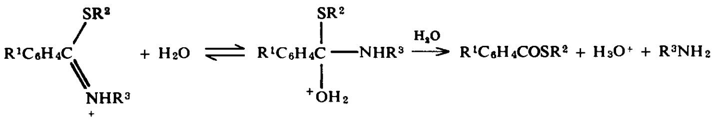
[53] R. K. Chaturvedi, A. F. MacMahon, and G. L. Schmir, *J. Amer. Chem. Soc.*, 1967, **89**, 6984.



(18)



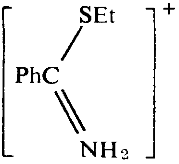
(19)



(56)

very feebly basic, since the usually powerful silver ion has a negligible effect[54] on their rate of decomposition at low pH. The addition of Ag^+ does, however, affect the products that can be isolated, since in its presence[5] the species $R^1C_6H_4COSR^2$ are very rapidly desulphurized [reaction (52)].

Addition of Hg^{2+} ions to a solution of a suitable thiolbenzimidate ester in the presence of hydrogen ions does lead to a considerable increase in the rate of disappearance of the ester.[54] With (20) the product is benzonitrile; with (21) it is the corresponding *O*-amide. The rate equations for these two reactions have the forms (57) and (58), respectively. A mechanism for (20), compatible with the reaction orders, is outlined in the reactions (59)—(64). For (21) the same mechan-



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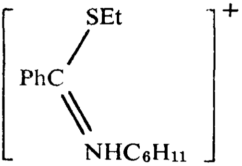

(21)

$$-\mathrm{d}[(20)]/\mathrm{d}t = \left(k_1 \frac{[Hg^{2+}]}{[H_3O^+]} + k_2 \frac{[Hg^{2+}]^2}{[H_3O^+]^2}\right)[(20)] \qquad (57)$$

$$-\mathrm{d}[(21)]/\mathrm{d}t = k[Hg^{2+}][(21)]/[H_3O^+] \qquad (58)$$

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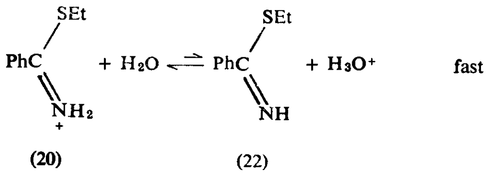
[54] A. J. Hall and D. P. N. Satchell, *J.C.S. Perkin II*, 1976, 1274.



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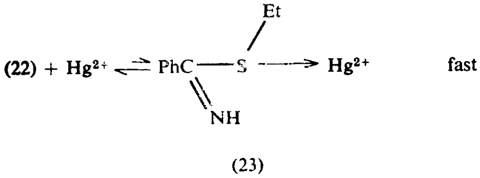

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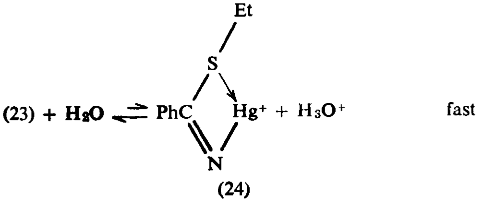
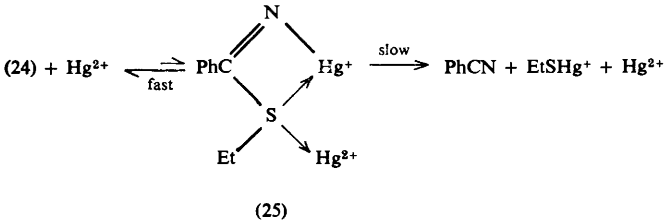


(61)

$$(23) \xrightarrow{\text{slow}} PhC\equiv\overset{+}{N}H + EtSHg^+ \xrightarrow{H_2O} PhCN + H_3O^+ + EtSHg^+ \qquad (62)$$

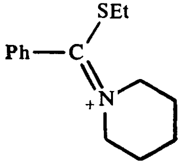
$$(24) \xrightarrow{\text{slow}} PhCN + EtSHg^+ \qquad (63)$$



(64)

ism is satisfactory, except that, since now only one proton is available on nitrogen, it necessarily reduces to three steps, the analogues of reactions (59), (60), and (62).

These steps again account for the observed rate equation, now equation (58). For (21), the analogue of step (62) will necessarily produce the *O*-amide, *via* attack of water on the carbon atom, rather than the nitrile *via* attack on the proton; again as found. The essential role of the protons bound to nitrogen in these reactions is confirmed by the total unreactivity of compound (26), which cannot lose its charge by the dissociation of a proton. The mechanisms of these imidate ester hydrolyses are analogous to those of thioamides to be discussed below. Reaction (64), which emphasizes the value in thiolester reactions of a leaving group with more than one positive charge, is reminiscent of reaction (53). The difference in reactivity between mercury and silver in the benzimidate ester reactions is rather surprising. Gold(III) and thallium(III) ions also promote *S*-imidate ester hydrolyses.[55]



(26)

7 Reactions of Thiocarboxylic Acids and Anhydrides

There has been little relevant work of any kind in this area. One kinetic study examined the hydrolyses of thiolbenzoic acid and of thiobenzoic anhydride, $(PhCO)_2S$, in dilute solution in aqueous perchloric acid in the presence of Hg^{2+} and other soft ions.[5] Hydrogen ions alone catalyse these hydrolyses relatively little.[56] When Ag^+ or Cu^{2+} ions are added to solutions of thiolbenzoic acid it is rapidly precipitated as the corresponding salt. With Ni^{2+}, Cd^{2+}, or Pb^{2+} there is little precipitation, but no detectable increase in hydrolysis rate. Only for Hg^{2+} ions is an increase in rate observed. With this metal the initial precipitation of the salt is negligible when $[PhCOSH] \lesssim 10^{-4}$ mol l^{-1} and $[Hg^{2+}] \gtrsim 10^{-3}$ mol l^{-1}. The ensuing stoicheiometric reaction (65) is firstorder in $[Hg^{2+}]$ and in $[PhCOSH]$, and is independent of the ratio $[PhCOS^-]/[PhCOSH]$ (which can be controlled by choosing different initial values of $[H_3O^+]$). The value of $\Delta S^{\ddagger} \simeq 0$. These results suggest the scheme outlined in reactions (66)—(69). The benefit

$$PhCOSH + Hg^{2+} + 3H_2O \rightarrow PhCO_2H + HgS + 2H_3O^+ \qquad (65)$$

$$PhCOSH + H_2O \rightleftharpoons PhCOS^- + H_3O^+ \quad \text{fast} \qquad (66)$$

$$PhCOS^- + Hg^{2+} \rightleftharpoons PhCOSHg^+ \quad \text{fast} \qquad (67)$$

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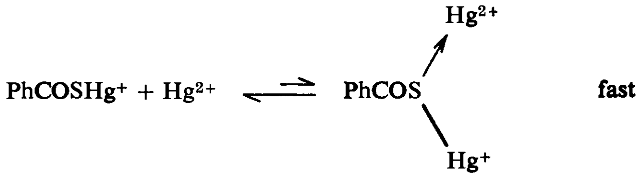
[55] A. J. Hall and D. P. N. Satchell, *J.C.S. Perkin II*, 1976, 1278.

[56] J. Hipkin and D. P. N. Satchell, *Tetrahedron*, 1965, **21**, 835; *J. Chem. Soc.* (*B*), 1966, 345.



$$PhCOSHg^{+} + Hg^{2+} \rightleftharpoons PhCOS\overset{\nearrow Hg^{2+}}{\underset{\searrow Hg^{+}}{}} \qquad \textbf{fast} \qquad (68)$$

(27)

$$(27) \xrightarrow{\text{slow}} \overset{+}{PhCO} + HgS + Hg^{2+} \xrightarrow[\text{fast}]{3H_2O}$$

$$PhCO_2H + 2H_3O^{+} + HgS + Hg^{2+} \qquad (69)$$

from the involvement of a second metal ion when the first-formed substrate–metal complex carries only one positive charge is again indicated.

The hydrolysis of the anhydride[5] occurs in two stages [reactions (70) and (71)], the second being much the slower and, as expected, having kinetics identical

$$(PhCO)_2S + 2H_2O + Hg^{2+} \rightarrow PhCOSHg^{+} + PhCO_2H + H_3O^{+} \qquad (70)$$

$$PhCOSHg^{+} + 2H_2O \rightarrow PhCO_2H + HgS + H_3O^{+} \qquad (71)$$

with those found for the hydrolysis of thiolbenzoic acid. Reaction (70) is kinetically first-order in $[Hg^{2+}]$ and in $[(PhCO)_2S]$, and may proceed *via* reaction (72) and then reaction (73). For Hg^{2+}-promoted hydrolysis, under

$$(PhCO)_2S + Hg^{2+} \rightleftharpoons (PhCO)_2S \rightarrow Hg^{2+} \qquad \text{fast} \qquad (72)$$

$$(PhCO)_2S \rightarrow Hg^{2+} + H_2O \longrightarrow PhCOSHg^{+} + PhCO_2H_2^{+} \qquad \text{slow} \qquad (73)$$

comparable conditions, the relative reactivities of PhCOSEt, PhCOSH, and $(PhCO)_2S$ (first stage) are *ca.* $1:2.3 \times 10^2:1.4 \times 10^4$.

8 Reactions of Thioamides

Thioacetamide held a particular interest in the 1950's when it was found that it could be used as an alternative to hydrogen sulphide for precipitating certain soft metal ions as their sulphides. The reactions leading to precipitation depend[57] upon the pH and upon the metal. Normally, thioacetamide undergoes prior hydrolysis to hydrogen sulphide and/or thioacetic acid[57,58] [reaction (74)]. Either

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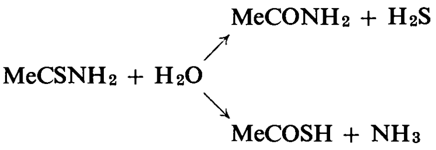
[57] E. H. Swift and E. A. Butler, *Analyt. Chem.*, 1956, **28**, 146; E. H. Swift in 'Advances in Analytical Chemistry and Instrumentation', ed. C. N. Reilly, Interscience, New York, 1960; S. Washizuka, *Bunseki Kagaku*, 1961, **10**, 580.

[58] O. M. Peeters and C. J. De Ranter, *J.C.S. Perkin II*, 1974, 1832; A. J. Hall and D. P. N. Satchell, *ibid.*, p. 1077.



$$MeCSNH_2 + H_2O \rightarrow MeCONH_2 + H_2S \quad \text{or} \quad MeCSNH_2 + H_2O \rightarrow MeCOSH + NH_3 \qquad (74)$$

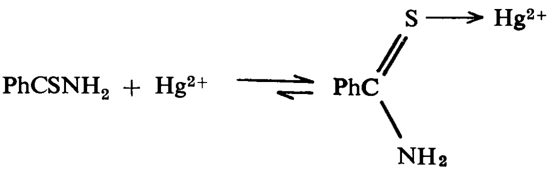
compound can then lead rapidly to the metal sulphide. However, under some conditions a direct reaction between metal ion and thioacetamide is detected, whose rate falls as the pH falls. The early work[57] on these reactions involved heterogeneous conditions, and was primarily concerned with rates of precipitation. The organic product was never identified. Recently, the mechanisms of some similar reactions have been studied, using homogeneous conditions. It is found[6,59–61] that, at 25 °C in dilute aqueous perchloric acid, under which conditions the rate of the hydrogen-ion-catalysed hydrolysis is negligible, thiobenzamide undergoes direct reactions with Hg^{2+}, Ag^+, Cu^{2+}, and Tl^{3+} ions [*e.g.* reaction (75)], always producing the metal sulphide and benzonitrile (not the *O*-amide). The kinetic details differ with each metal. The mercury reaction

$$PhCSNH_2 + 2H_2O + Hg^{2+} \rightarrow PhCN + HgS + 2H_3O^+ \qquad (75)$$

will serve as an example.[59] Here a 2:1 *S*-amide–Hg^{2+} complex is formed rapidly and stoicheiometrically under all concentration conditions. With a ten-fold excess of Hg^{2+} over thioamide, the rate equation, at any fixed value of $[H_3O^+]$, takes the form (76). As $[H_3O^+]$ is raised, k_{obs} falls, reaching a constant, minimum

$$-d[2{:}1\ \text{complex}]/dt = k_{obs}[Hg^{2+}][2{:}1\ \text{complex}] \qquad (76)$$

value when $[H_3O^+] > 1.0$ mol l^{-1}. These facts, the details of the dependencies of k_{obs} and of the spectrum of the 2:1 complex on $[H_3O^+]$, and the behaviour of *N*-substituted *S*-amides[59] (see below) all point to the mechanism of reaction (77)—(85). The fall in k_{obs} with increase in $[H_3O^+]$ cannot be attributed to



$$PhCSNH_2 + Hg^{2+} \rightleftharpoons PhC(=S \rightarrow Hg^{2+})NH_2 \qquad \text{fast} \qquad (77)$$

(28)

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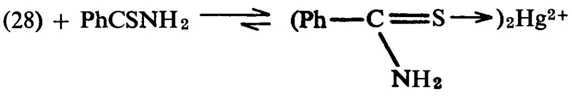
[59] A. J. Hall and D. P. N. Satchell, *J.C.S. Perkin II*, 1975, 778.

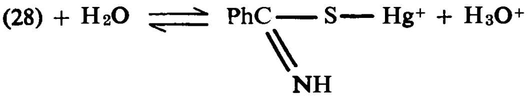
[60] A. J. Hall and D. P. N. Satchell, *J.C.S. Perkin II*, 1975, 953; *J.C.S. Chem. Comm.*, 1975, 50.

[61] A. J. Hall and D. P. N. Satchell, *J.C.S. Perkin II*, 1975, 1351; *ibid.* 1977, 1366.



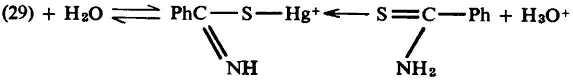
(29)

fast (78)



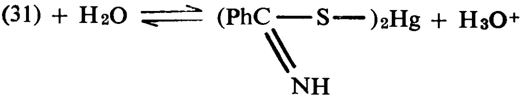
(30)

fast (79)



(31)

fast (80)



(32)

fast (81)

$(29) + \mathrm{Hg^{2+}} \rightarrow 2\,(28)$ slow (82)

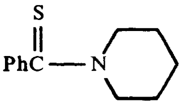
$(31) + \mathrm{Hg^{2+}} \rightarrow (28) + (30)$ slow (83)

$(32) + \mathrm{Hg^{2+}} \rightarrow 2\,(30)$ slow (84)

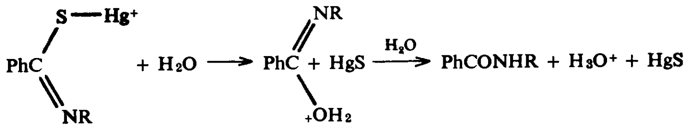
$(30) \rightarrow \mathrm{PhC{\equiv}\overset{+}{N}H} + \mathrm{HgS} \xrightarrow{\mathrm{H_2O}} \mathrm{PhCN} + \mathrm{H_3O^+} + \mathrm{HgS}$ fast (85)

reduction of attack by $\mathrm{OH^-}$ on the thiocarbonyl group since in such a mechanism the product would have to be the *O*-amide. For $\mathrm{Hg^{2+}}$-promotion only the (low concentration) deprotonated 1:1 adduct (30) leads to decomposition. Confirmation of the requirement of *N*-bound protons for rapid reaction comes from the study of (33), whose decomposition is, by comparison, negligibly promoted by $\mathrm{Hg^{2+}}$ ions.

The reaction of the mono-*N*-substituted compound *N*-cyclohexylthiobenzamide displays a kinetic form compatible[59] with a scheme like that of reactions (77)—(85), modified to include only one N—H ionization, and a product-forming step (86); *N*-substituted *S*-amides lead, of necessity, to the *O*-amide as product (*cf.* thiobenzimidate esters, p. 363).

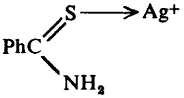


(33)

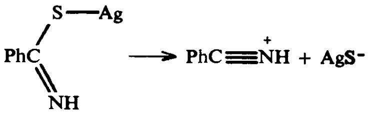


(86)

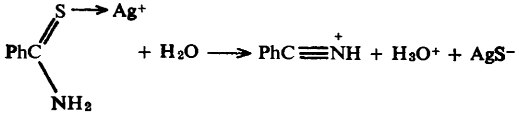
The reactions of Ag^+ and Cu^{2+} with these thiobenzamides are broadly analogous to those of Hg^{2+}. With Ag^+ only 1:1 complexes are formed. For thiobenzamide the stoicheiometrically formed complex (34) loses just one *N*-bound proton in an equilibrium like reaction (79), and the slow steps are (87) and (88). The reaction with copper[60] is similar to that of silver, except that only



(34)



(87)

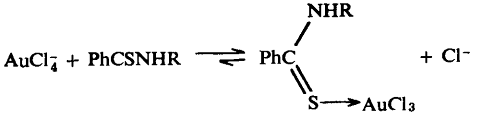


(88)

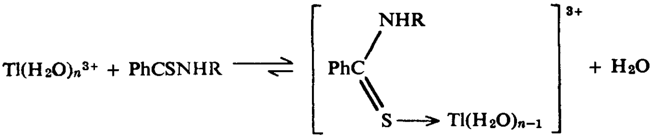
a small concentration of (probably *N*,*S*-chelated) 1 : 1 complex is formed. Because of the differences in the details of the mechanisms, exact comparisons are impossible, but for equal initial concentrations at 25 °C the reactivities of the metals are $Hg^{2+} > Ag^{+} \gg Cu^{2+}$. The ions Pb^{2+}, Ni^{2+}, Cd^{2+}, and Tl^{+} have no detectable effect at 25 °C, and are less effective in decomposing thiobenzamides at moderate ambient hydrogen ion concentrations than is the hydrogen ion itself. This is probably because these ions form little 1 : 1 complex and because the equilibria analogous to (79) lie far to the left. Some small degree of catalysis by Pb^{2+} and Cd^{2+} can be detected at very low H_3O^+ concentrations.[6]

The long-known[11] desulphurization of thioureas [$(R_2N)_2C{=}S$, where R = H or alkyl] by mercury and lead species, under mildly alkaline conditions, displays a qualitative behaviour pattern with interesting parallels to the thiobenzamide reactions discussed above. Again the ability to lose *N*-bound protons is apparently a crucial feature.

The direct reactions of Tl^{3+} and of $AuCl_4^-$ ions with thiobenzamides in dilute aqueous perchloric acid are also of considerable interest.[61] These metal species have reactivities comparable with that of Hg^{2+}. Under conditions involving an excess of metal ion over thiobenzamide, they both lead to effectively stoicheiometric 1 : 1 complex formation [reactions (89) and (90)]. In contrast to the cases of Hg^{2+}, Ag^{+}, and Cu^{2+}, the water molecules co-ordinated to Tl^{3+} undergo significant dissociation [*e.g.* reaction (91)] at the hydrogen ion concentrations



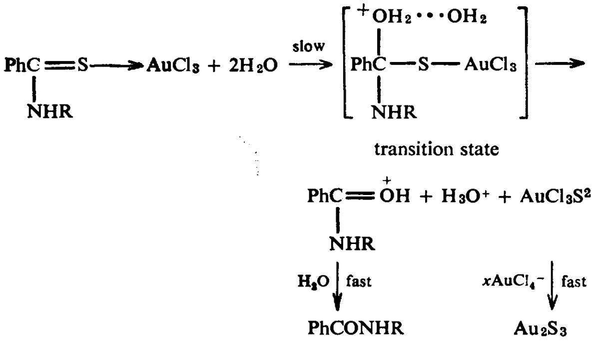
(89)



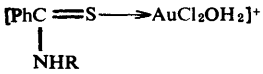
(90)

$$Tl(H_2O)_n^{3+} + H_2O \rightleftharpoons [Tl(H_2O)_{n-1}OH]^{2+} + H_3O^+ \qquad (91)$$

used, and the same is true of the water molecule in the species $AuCl_3(H_2O)$ formed from $AuCl_4^-$ at low ambient chloride concentrations. In spite of such dissociations, and in spite of the behaviour found with Hg^{2+}, Cu^{2+}, and Ag^{+}, the rate of decomposition of thiobenzamides by Tl^{3+} and $AuCl_4^-$ is always independent of $[H_3O^+]$. Clearly, the prior ionization of an *N*-bound proton either does not occur or does not facilitate the decomposition of the complexes in these instances.

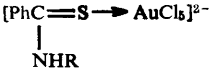


(92)



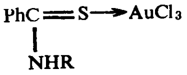
$[\underset{\mathrm{NHR}}{\mathrm{PhC}}{=}\mathrm{S}\rightarrow \mathrm{AuCl_2OH_2}]^+$

(35)



$[\underset{\mathrm{NHR}}{\mathrm{PhC}}{=}\mathrm{S}\rightarrow \mathrm{AuCl_5}]^{2-}$

(36)



$\underset{\mathrm{NHR}}{\mathrm{PhC}}{=}\mathrm{S}\rightarrow \mathrm{AuCl_3}$

(37)

For the gold reaction the steps following (89) are thought to be given by reaction (92). Variation of the ambient chloride ion concentration shows[61] that reaction also occurs *via* (35) at low and *via* (36) at high chloride ion concentrations, both these complexes being more reactive than (37).

For the thallium reaction,[61] not only is k_{obs} independent of $[H_3O^+]$, but it is inversely related to the excess thallium ion concentration. This effect, not found in other systems studied so far, suggests that the reactive complex is the 2:1 *S*-amide–Tl^{3+} species, whose low equilibrium concentration at high thallium ion concentrations falls proportionately as $[Tl^{3+}]$ is increased. For thiobenzamide, both the 1:1 and the 2:1 complexes contribute to the decomposition, but for *N*-substituted thiobenzamides the contribution of the 2:1 complex is dominant. The reason is not obvious; the involvement of a second substrate molecule does not appear beneficial to the decomposition step in any other *S*-substrate system studied. The fact that N—H ionization is kinetically unimportant in the Tl^{3+}- and $AuCl_4^{2-}$-promoted reactions permits the tertiary amide *N*-thiobenzoylpiperidine to react with these ions at a rate comparable to those found for thiobenzamide and *N*-cyclohexylthiobenzamide. The gold and thallium ions are therefore especially useful for the promoted hydrolyses of tertiary *S*-amides.

A final point of interest concerns the $AuCl_4^{2-}$ reaction. For all the other metal ions studied the rate of formation of the initial complex between the *S*-amide and metal species is too fast to be studied, even by the stopped-flow method.

However, for $AuCl_4^{2-}$ (where Cl^- rather than H_2O is being displaced when the complex is formed), the establishment of the pre-equilibrium (89) can be studied.[62] It proceeds *via* a five-co-ordinate gold intermediate, and the kinetic and mechanistic details are similar to those established[63] for the replacement of Cl^- by SCN^- [reaction (93)]. Both the initial uptake of SCN^- (i) and the rate at which

$$\begin{tikzcd}
SCN^- + AuCl_4^- \arrow[r, shift left, "(i)"] \arrow[d, shift left] & {[AuCl_4SCN]^{2-}} \arrow[l, shift left] \arrow[r, "(ii)"] \arrow[d, shift left] & AuCl_3SCN^- + Cl^- \\
SCN^- + AuCl_5^{2-} \arrow[r, shift left] \arrow[u, shift left, "Cl^-"'] & {[AuCl_5SCN]^{3-}} \arrow[l, shift left] \arrow[r] \arrow[u, shift left, "Cl^-"'] & AuCl_3SCN^- + 2Cl^-
\end{tikzcd} \qquad (93)$$

it enters the square plane (ii) are catalysed by added chloride ions. These processes are, therefore, easier when octahedral complexes are involved.

9 General Summary, and Consideration of the Effectiveness of Different Metals

In nearly all metal-ion-catalysed reactions, some special feature is present which renders the concentration of the metal–substrate intermediate kinetically significant. Thus most of the metal-ion-promoted reactions discussed in this review have as an important part of their driving force the exceptional covalent affinity of the soft metal for sulphur; the size of the metal ion and the magnitude of its charge are of secondary importance. Neither soft nor hard metal species will normally promote reactions of the oxygen analogues of the sulphur-containing substrates considered, unless the oxygen-analogue can behave as a chelating ligand.

All the reactions considered probably involve a rapid pre-equilibrium between the metal centre and the sulphur atom of the substrate. In those reactions (the majority) which involve subsequent cleavage of the substrate, the sulphur atom is, or is part of, the leaving group. The products therefore normally include either the metal sulphide or a mercaptide. When the sulphur atom is removed by the metal, the remainder of the substrate either loses protons (as in nitrile formation from primary thioamides and in olefin formation from thiols) or is attacked by an ambient nucleophile. This nucleophile has usually been water, it being convenient to use metal ions in aqueous solution. Most of the known reactions are therefore promoted hydrolyses. Few aminolyses have been reported. There is evidence nevertheless that attack by a variety of nucleophiles occurs readily in non-aqueous solvents, but this type of reaction has been little exploited. Virtually any thio-compound in which the sulphur atom is available to co-ordinate to a metal can be cleaved.

The metal species that have been used most are those derived from silver and from mercury(II). It is clear that, of these two metals, mercury is by far (usually

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[62] A. J. Hall and D. P. N. Satchell, *Chem. and Ind.*, 1976, 373.
[63] A. J. Hall and D. P. N. Satchell, *J.C.S. Dalton*, 1977, 1403.

ca. 10^3-fold) the more reactive under comparable conditions. Two other metals, so far rarely used, with reactivities similar to mercury(II), are thallium(III) and gold(III). In quantitative studies using non-chelating thio-compounds and homogeneous solutions, all other metal ions tested have been found to lead to negligible reaction rates under conditions where silver, mercury, thallium, and gold ions react very rapidly. For example, in hydrolyses where, under similar conditions, the Hg^{2+}-promoted reaction is usually *ca.* 10^6-fold faster than the hydrogen-ion-catalysed process, the ions Cu^{2+}, Ni^{2+}, Cd^{2+}, Pb^{2+}, and Zn^{2+} all lead to rates either comparable with, or sometimes less than, that produced by the (hard) hydrogen ion. There is evidently another large step after silver in the reactivity scale of the soft metals. This conclusion is not compatible with various theoretical estimates[8,64] of softness, and Cd^{2+}, in particular, seems surprisingly unreactive. Although preparative (and some kinetic) work suggests that Cu^{2+}, Pb^{2+}, Cd^{2+}, and other ions can be very effective with sulphur-containing substrates, it seems at present probable that they are so only under heterogeneous conditions or at high temperatures, or when the substrate is a chelating species (so that a significant amount of metal–substrate complex can form), or when the metal acts as a template (thus providing an intramolecular route for the process). The successful applications of catalysts based on copper, nickel, and lead can be explained this way, but then even hard metals can be effective in such circumstances.

It appears that although soft metal ions (by definition) prefer a substrate that contains sulphur to an analogous one containing oxygen, nevertheless the separate hard and soft reactivity scales for acids towards a particular class of base can show considerable overlap, for, as we have seen, only four of the soft metals tested display significantly greater reactivities towards sulphur-containing substrates than does hydrogen in promoted hydrolyses. This is not the sort of result that the hard–soft principle leads us to expect, at least superficially. Although it could be urged that the comparison of the hydrogen ion reactions with the others, if close, is not exact mechanistically, it may be countered that hard–soft comparisons rarely will be exact. Many more systematic quantitative measurements with simple, non-chelating systems are needed before a reliable picture of metal ion acidity can be drawn towards either hard or soft bases. It is unfortunate that the term 'Super-acid catalysis', which arose from the very large catalytic effects occasionally displayed by metal ions, is sometimes used[65] to describe acidic catalysis by metal ions as a whole. This usage gives the misleading impression that metal ions always provide 'super' catalysis; in reality, their catalysis with both hard and soft substrates is usually feeble compared to that provided by the hydrogen ion, for the special effects which give rise to powerful catalysis are by no means always available.

[64] M. Misono and Y. Saito, *Bull. Chem. Soc. Japan*, 1970, **43**, 3680; G. Klopman, *J. Amer. Chem. Soc.*, 1968, **90**, 223; S. Ahrland, *Chem. Phys. Letters*, 1968, **2**, 303; A. Yingst and D. H. McDaniel, *Inorg. Chem.*, 1967, **6**, 1067.

[65] M. L. Bender, 'Mechanisms of Homogeneous Catalysis from Protons to Proteins', Wiley, New York, 1971.