Catalysis by μ-Oxo Diiron(III) Complexes of the Methanolysis of Epoxides and the Addition of Alcohols and Thiols to Phenyl Isocyanate

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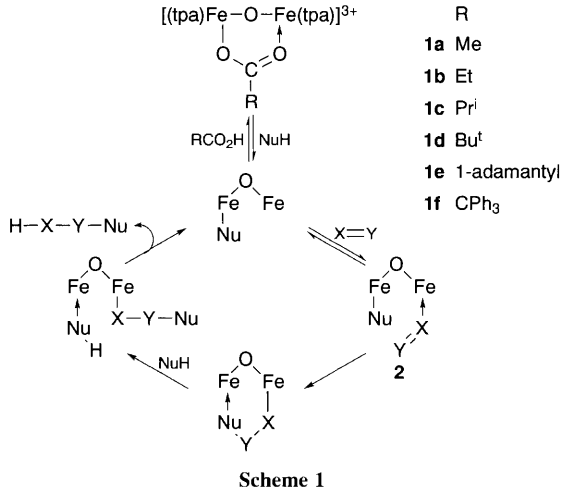
Carboxylate-bridged μ-oxo diiron(III) complexes of the type **1** very efficiently catalyse (*a*) the addition of alcohols and thiols to phenyl isocyanate and (*b*) the ring-opening of epoxides by methanol, with their efficiency being dependent upon the size of the group R.

Because of the presence of an Fe–O–Fe centre in an number of enzymes, *e.g.* the purple acid phosphatases and methane monooxygenase,[1] the roles of these centres is a matter of considerable debate (see, for example, ref. 2) and, in this connection, numerous model compounds which contain an Fe–O–Fe unit have been synthesised and studied.[3,4] However, apart from those investigations into the oxidation of alkanes by reagents such as dioxygen[5] and *tert*-butyl hydroperoxide,[6] no attempts appear to have been made to use these diiron complexes to catalyse organic reactions, even those reactions which are of the same mechanistic types as those catalysed by the enzymes. We have examined the ability of several of these complexes to catalyse specific types of nucleophilic additions and substitutions, and we report some of our findings in this Communication.

By analogy with the reversible hydrolysis of the corresponding dipyridyl and phenanthroline complexes,[6] it was anticipated that the acetate-bridged bis(tpa) cation **1a** [tpa = tris(2-pyridylmethyl)amine] would undergo reversible alcoholysis, and that in the presence of a suitable multiply bonded σ-donor ligand (X=Y) this alcoholysis would give rise to a σ-alkoxy species of the type **2**, Nu = OR′ (charge, tpa ligands, and other related species which would participate in the equilibria have been omitted from Scheme 1 for clarity). This would allow intramolecular nucleophilic attack by the alkoxy group on the σ-donor ligand. A number of reactions with hydroxy binuclear complexes (in most cases involving metals other than iron) in which the hydroxy group is added to a σ donor such as acetonitrile[7] and carbon dioxide[8] to form a new bridging ligand have already been reported. While these reactions almost certainly involve σ-hydroxy species that are analogous to **2** (Nu = OH), they are stoichiometric. It was reasoned, however, that with a σ-alkoxy complex and an excess of the alcohol the catalytic cycle shown in Scheme 1 would be established.

In the presence of the tetraphenylborate salt† of the cation **1a** (10^{-3} mol dm^{-3}), phenyl isocyanate and butanol (both 0.15 mol dm^{-3}) reacted in dichloromethane at room temperature to form the expected urethane. The allophanate and isocyanurate formed as minor products in the base-catalysed addition of



Scheme 1

alcohols to isocyanates[9] were not detected. The half-life of the reaction was about 10 h; in the absence of the salt the half-life was about 17 h.

Molecular models indicate that an increase in the size of the group R in cations of the type **1** results in steric interactions between that group and the tpa ligands. These interactions have already been proposed for the dichromium(III) analogues of **1d–f**,[10] and have now been confirmed for **1e** and **1f** by their X-ray structures.[11] These steric interactions should increase the rate at which the cations **1** undergo alcoholysis, and therefore increase their ability to catalyse the formation of the urethane. Under the reaction conditions specified above, the catalytic activity of the following cations increased in the order **1a** < **1b** < **1c** < **1d** < **1e**. With the cation **1e** the reaction was essentially complete within 24 h with a half-life of *ca.* 3 h (poor solubility prevented the use of **1f**). Tris(2-pyridylmethyl)amine was considerably less effective as a catalyst than the cation **1a**. This is consistent with the steric interactions in the cations causing the displacement of the carboxylate group rather than of all, or part of, one of the tpa ligands which then functions as a basic catalyst for urethane formation.

The cations also catalysed the addition of thiols to phenyl isocyanate, with an increase in the size of the group R having the same accelerating effect as in urethane formation. Use of **1e** (10^{-3} mol dm^{-3}) in a reaction in which the butanol in the urethane-forming reaction was replaced by dodecane-1-thiol resulted in half the isocyanate having reacted after 90 min (*cf.* below). In the absence of the cation virtually no reaction had occurred after 24 h; this is consistent with the observation that, under neutral conditions, thiols react extremely slowly with isocyanates.[12] With 2-hydroxyethanethiol and 3-hydroxypropanethiol the additions to the isocyanate involved only the thiol group. As the sulfur atom in 2-hydroxyethanethiol is less nucleophilic towards isocyanates than the oxygen atom,[13] this regioselectivity indicates that the additions did not involve attack on the activated isocyanate by uncoordinated hydroxythiol, *i.e.* the regioselectivity involves (at least, in part) the activation of the thiol group.

The additions with the thiols were faster than those with butanol but, unlike those with butanol, did not proceed to completion. When 2-hydroxyethanethiol was used with the cation **1e**, for example, about 50% of the isocyanate had reacted after 3 min, but the reaction stopped completely after 20 min by which time about 90% of the isocyanate had reacted. Possibly, this was due to the reduction and attendant deactivation of the iron(III) cation by the thiol. Significantly, the additions involving the two hydroxythiols proceeded considerably faster than those involving simple thiols, with those involving 2-hydroxyethanethiol being the fastest. One possible explanation for this is that hydroxy group facilitates the formation of the catalytically active species **2** (Nu = thiolate anion) by bonding to some extent with the second iron atom.

On the basis of reasoning similar to that given earlier, it was predicted that cations of type **1** should also catalyse certain nucleophilic substitutions at saturated carbon. In refluxing methanol and in the presence of the cations **1** (10^{-3} mol dm^{-3}), epoxycyclohexane (0.33 mol dm^{-3}) was converted into *trans*-2-methoxycyclohexanol, with excellent yields being obtained after relatively short reaction times. Here also the rate of

reaction was determined by the size of the group R; after 30 min of reflux the extent of methanolysis observed with the cations **1a** and **1f** was *ca.* 60 and > 95%, respectively. In the absence of the cations about 15% of the epoxide had reacted after 24 h of reflux.

The cations do not effect exchange reactions of carboxylic esters, and so their use to catalyse the methanolyses of the acetate and the 4-*tert*-butylbenzoate esters of glycidol resulted in the formation of the expected monoesters of 1-methoxypropane-1,2-diol. Use of the cations in the methanolysis of *threo*-(1-bromoethyl)oxirane[14] afforded only *threo*-3-bromo-1-methoxybutan-2-ol. This is informative from the viewpoint of the reaction mechanism, for reactions of negatively charged nucleophiles with (1-bromoalkyl)oxiranes usually result in ring-opening followed by displacement of bromide and the formation of a new oxirane ring.[15]

While the coordination chemistry of the reactions described in this Communication is almost certainly more complex than that shown in Scheme 1, the results reported here could lead to a better understanding not only of the role of the diiron centres in certain non-haem enzymes, but also of the mode of action of other enzymes which utilise two oxygen-bridged metal atoms (not necessarily iron) at their active site, *e.g.* some of the phosphoesterases.[3] It should be noted also that some μ-oxo dimetal complexes have been used as catalysts for specific organic reactions, *e.g.* the polymerization of alkenes[16] and oxiranes,[17] and their catalytic role in these reactions can be rationalised in terms of mechanisms similar to that shown in Scheme 1. μ-Oxo dimetal and related μ-hydroxy systems are, of course, also present on the surface of many metal oxides which act as heterogeneous catalysts for a wide range of organic reactions.[18,19]

Finally, in connection with the urethane-forming reactions described here, we note that urethane formation can be catalysed by the addition of a wide range of mononuclear inorganic compounds.[20] In a number of cases, for example with the tris(acetylacetonate) of iron(III),[21] evidence has been presented that the catalysed reactions are initiated by the inorganic compound undergoing alcoholysis to give a metal alkoxide, and it is this which is the active catalyst for the reaction. We believe that many of these metal alkoxides exist, at least in part, as μ-alkoxy binuclear complexes, which are able to catalyse urethane formation by a mechanism similar to that suggested in Scheme 1 for the μ-oxo diiron system.

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Footnote

† The tetraphenylborate salts described in this Communication were prepared by metathesis of the corresponding perchlorate salts.[22] **CAUTION**: the latter are potentially explosive and should be handled with care.

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