

Model Systems for Cytochrome P450 Dependent Mono-oxygenases. Part 4.¹ The Epoxidation of Alkenes by Peroxyacids in the Presence of Cobalt Complexes

M. Andrew Brook and John R. Lindsay Smith *

Department of Chemistry, University of York, York YO1 5DD

Raymond Higgins and David Lester

Imperial Chemical Industries plc, Petrochemicals and Plastics Division, Research and Technology, P.O. Box 90, Cleveland TS6 8JE

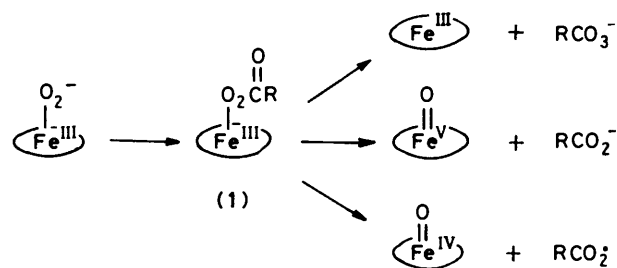
The possible involvement of peroxyacids in oxidations by cytochrome P450 dependent mono-oxygenases has led us to screen the effect of a wide selection of transition metal complexes on the peroxyacid epoxidation of alkenes. This has been achieved by examining the effect that these metal complexes exhibit on the relative reactivities of styrene and 3-chlorostyrene towards epoxidation by 3-chloroperoxybenzoic and peroxybenzoic acids. Cobalt, and to a lesser extent rhodium compounds, produce the largest change in the relative rates. A stepwise radical mechanism for the cobalt(II)-peroxyacid epoxidations has been established using Hammett correlations of data obtained from the epoxidation of 3- and 4-substituted styrenes, stereochemical studies with *cis*- and *trans*-alkenes, and ¹⁸O labelling experiments. An oxy-radical, from the one-electron reduction of the peroxyacid by cobalt(II), reacts with the alkene to give a β-hydroxyalkyl radical, which on further oxidation is cyclised to the epoxide. Alternative concerted two-electron processes and a mechanism involving an alkene radical cation from the one-electron oxidation of the alkene by cobalt(III) have been eliminated.

Cytochrome P450 mono-oxygenases catalyse the transfer of one oxygen atom from dioxygen into a wide range of organic compounds.² Research with hepatic microsomal preparations and with reconstituted systems using purified cytochrome P450 mono-oxygenases has shown that dioxygen can be replaced by oxidants such as hydroperoxides, peroxyacids, and iodosylarenes as the oxygen donor in these reactions.³

The similarity of the oxidations brought about by peroxyacids to those by cytochrome P450 mono-oxygenases, coupled with the ability of peroxyacids to support the enzymic oxidations in the absence of dioxygen,^{3c} has led to suggestions that peroxyacids or peroxyacid derivatives may be involved in the *in vivo* oxidations.^{2a,4,5} Thus acylation of a cytochrome P450 peroxy-intermediate by a protein carboxylate group would lead to an iron peracyl species (I). This could in turn cleave to give a protein bound peroxyacid,^{2a,4} an oxoiron species⁶ or a carboxyl radical as the active oxidant (Scheme 1).⁷ The identification of the biological oxidant and determination as to whether it is the same as that produced in the peroxyacid mediated systems are currently active areas of research.^{4,7,8}

The present interest in oxidations by cytochrome P450 dependent mono-oxygenases and the long-term goal of chemists of devising processes based on the chemistry of these enzymes has led to numerous studies with model systems.^{1,9,10} Those most closely related to the biological systems utilise the same oxidants that promote cytochrome P450 mono-oxygenations with metalloporphyrins as the catalysts.^{10a,c-f,11} This work has recently been extended to include non-porphyrin metal complexes as catalysts.¹²

The aim of the present work has been to determine how catalytic amounts of metal complexes modify peroxyacid oxidations and to examine whether any metal complexes can accentuate the oxidising ability of peroxyacids. We selected the epoxidation of some 3- and 4-substituted styrenes as the standard process for study since this is a reaction brought about by both peroxyacids¹³ and cytochrome P450 mono-oxygenases.¹⁴ By studying the relative reactivities of the styrenes towards the modified peroxyacid systems we have been able to screen a range of metal complexes.



Scheme 1.

Results and Discussion

Effect of Metal Complexes on the Relative Reactivity of Styrene and 3-Chlorostyrene towards Peroxyacid Epoxidation.— Although benzene and polyhaloalkanes are commonly used as solvents for peroxyacid epoxidations,^{9b,15} chlorobenzene was chosen for these studies with metal complex-peroxyacid systems. It was argued that chlorobenzene, which is more inert than benzene towards electrophiles and electrophilic radicals,¹⁶ would be less likely to react with any active intermediates.

The preliminary screening of the metal complexes was achieved by comparing the relative reactivities of styrene and 3-chlorostyrene towards epoxidation by 3-chloroperoxybenzoic acid (3-CPBA) in the presence of soluble metal complexes. It was hoped that any change in the reactivity of the peroxyacid arising from the presence of the metal complex would show up in a change in this relative reactivity. Each reaction was analysed after 1 h when iodimetric titration showed that all the oxidant had been consumed. The only products (>1% yield) observed by g.l.c. analysis were the styrene epoxides. Control experiments showed that the epoxides are stable for at least 3 h in the presence of 3-CPBA and metal complexes in concentrations comparable to those used in the epoxidation. Table 1 records the yields of epoxides and the relative reactivities of styrene and 3-chlorostyrene using a 3-CPBA to metal complex ratio of 20:1. An analogous, although less

Table 1. Epoxidation of styrene and 3-chlorostyrene in chlorobenzene with 3-chloroperoxybenzoic acid in the presence of transition metal complexes^a: yields and relative reactivities

Metal complex	Yield (%) ^b		Relative reactivity Styrene: 3-chlorostyrene
	Epoxystyrene	3-Chloroepoxystyrene	
Co(octanoate) ₂	46	19	2.4
RhCOCl(PPh ₃) ₂	54	18	3.0
Cr(CO) ₆	63	19	3.3
Ti(stearate) ₃	28	8	3.5
Mn(acetate) ₃	73	20	3.7
Cu(octanoate) ₂	69	18	3.8
W(CO) ₆	73	19	3.8
None	72	19	3.8
Ni(PPh ₃) ₂ (CO) ₃ Br ₃	59	13	4.5
Fe(PPh ₃) ₂ (CO) ₃	61	13	4.7
Mo(CO) ₆	70	15	4.7

^a Ratio of peroxyacid to metal complex, 20:1. ^b Yields based on peroxyacid.**Table 2.** Epoxidation of styrene and 3-chlorostyrene in chlorobenzene with peroxybenzoic acid in the presence of transition metal complexes^a: yields and relative reactivities

Metal complex	Yield (%) ^b		Relative reactivity Styrene: 3-chlorostyrene
	Epoxystyrene	3-Chloroepoxystyrene	
Co(octanoate) ₂	47	18	2.6
W(CO) ₆	71	19	3.7
Mn(acetate) ₃	67	17	3.9
None	68	17	4.0
Mo(CO) ₆	62	15	4.1
Cr(CO) ₆	66	14	4.7

^a Ratio of peroxyacid to metal complex, 20:1. ^b Yields based on peroxyacid.**Table 3.** Epoxidation of styrene and 3-chlorostyrene in chlorobenzene with 3-chloroperoxybenzoic acid in the presence of cobalt compounds^a: yields and relative reactivities

Cobalt complex	Yield (%) ^b		Relative reactivity Styrene: 3-chlorostyrene
	Epoxystyrene	3-Chloroepoxystyrene	
Co(octanoate) ₂	46	19	2.4
Co(salicylaldiminato) ₂	47	19	2.5
Co(pyridine) ₂ Cl ₂	47	19	2.5
Co(pyridine) ₂ (palmitate) ₂	52	19	2.7
Co ₂ (CO) ₈	49	16	3.1
Co(pyridine) ₂ (acetate) ₂	48	15	3.2
Co phthalocyanine	55	16	3.4
No cobalt complex	72	19	3.8
Co(PPh ₃) ₂ Cl ₂	62	16	3.9

^a Ratio of peroxyacid to cobalt complex, 20:1. ^b Yields based on peroxyacid.

comprehensive, study was carried out using peroxybenzoic acid (PBA) as the oxidant (Table 2). The data obtained from both oxidants are in broad agreement [with the exception of those from chromium(O)hexacarbonyl] and show that the metal resulting in the smallest difference in reactivity is cobalt, with rhodium second.

The effect of cobalt complexes was investigated in more detail. The results in Table 3 show that the majority, although not all, of the complexes lead to a significant reduction in the ratio of reactivities of styrene and 3-chlorostyrene. The ligands surrounding the cobalt determine the extent to which the peroxyacid epoxidation is modified. This aspect was not investigated further and subsequent studies used cobalt(II) octanoate and bis(salicylaldiminato)cobalt(II).

The total yields of epoxides from almost all the reactions is lowered by the presence of metal complexes. Since all the

peroxyacid is consumed in each reaction and the epoxides, which are the only products detected, are stable to further reaction, we attribute this to effective competition with the styrenes for the active oxidant by the ligands surrounding the metal ion. Similar observations have been reported in epoxidations by cytochrome P450 mono-oxygenations supported by peroxyacids^{7,8e} and by metalloporphyrin catalysed model systems.^{11a,17}

Experiments with cobalt(II) octanoate, designed to test the validity of the competitive method, showed that the recovered starting materials and products accounted for >99% of the two substrates, whether the reactions were carried out under nitrogen or in air. It is noteworthy that the reaction mixtures had the green colour expected of a cobalt(III) solution. We conclude that the change in relative reactivities towards epoxidation in the presence of cobalt(II) octanoate does not

Table 4. Relative reactivities of substituted styrenes towards epoxidation by peroxybenzoic acids in the presence of cobalt(II) complexes^a

Oxidising system	Relative reactivities of X-styrenes					Hammett ρ value
	X = 4-Me	H	4-Cl	3-Cl	4-NO ₂	
3-CPBA	2.1	1.0	0.7	0.3	0.2	-1.04
3-CPBA ^b	2.2	1.0	0.9	0.5	0.2	-0.93
3-CPBA + Co(II) octanoate	1.3	1.0	0.8	0.4	0.3	-0.66
3-CPBA + bis(salicylaldiminato)cobalt(II)	1.6	1.0	0.9	0.5	0.3	-0.72
PBA + Co(II) octanoate	1.5	1.0	0.8	0.5	0.3	-0.64

^a Ratio of peroxyacid to cobalt(II) complex, 20:1. ^b Solvent benzene

Table 5. Epoxidation of *cis*- and *trans*-alkenes in chlorobenzene with 3-chloroperoxybenzoic acid and cobalt(II) octanoate: ^a yields and stereochemical composition

Substrate	Yield of epoxide (%) ^b			Composition of product (%)	
	<i>trans</i>	<i>cis</i>	Total	<i>trans</i>	<i>cis</i>
<i>trans</i> -Stilbene	63	8	71	89	11
<i>cis</i> -Stilbene	20	48	68	29	71
<i>trans</i> -4-Methylpent-2-ene	64	2	66	97	3
<i>trans</i> -4-Methylpent-2-ene ^c	41	3	44	93	7
<i>cis</i> -4-Methylpent-2-ene	5	60	65	8	92
<i>cis</i> -4-Methylpent-2-ene ^c	18	34	52	35	65

^a Ratio of peroxyacid to cobalt(II) octanoate, 40:1. ^b Yields based on peroxyacid. ^c Solvent MeCN.

arise from the selective removal of styrene in a cobalt-initiated free radical polymerisation. Such a selective removal of one of the two substrates would have invalidated the competitive method used in this study.

Epoxidation of 3- and 4-Substituted Styrenes by Peroxyacid-Cobalt Complex Systems.—Styrene and five substituted styrenes were epoxidised with solutions of 3-CPBA in benzene and in chlorobenzene. The yield of epoxide from each of the reactions, except that of 4-methoxystyrene, was >93%. Presumably the electron-donating methoxy substituent makes the 4-methoxystyrene epoxide very susceptible to acid catalysed ring opening, analogous to the acid lability of vinyl ether epoxides.¹⁸ However, repeating these oxidations in the presence of solid disodium hydrogenphosphate, previously utilized to minimise acid catalysed ring opening of epoxides in solution,¹⁹ had no observable effect on any of these reactions. 4-Methoxystyrene was omitted from subsequent studies.

The relative reactivities of the five remaining styrenes towards epoxidation by 3-CPBA in benzene and in chlorobenzene were measured by competition experiments (Table 4) and were used to construct Hammett correlations. Good linear relationships were obtained against σ^+ with ρ values of -0.93 ± 0.04 and -1.04 ± 0.04 for reactions in benzene and in chlorobenzene, respectively (Table 4). Similar treatment of epoxidations with 3-CPBA acid and with PBA in the presence of cobalt(II) octanoate or bis(salicylaldiminato)cobalt(II) also gave good linear Hammett correlations but with ρ values between -0.64 ± 0.04 and -0.72 ± 0.04 (Table 4). The ρ values for reactions in the absence of cobalt complexes agree very well with those reported for the epoxidation of substituted stilbenes (-1.08)²⁰ and styrenes (-1.30)²¹ with PBA. The better correlation with σ^+ than with σ and the size and sign of these ρ values are consistent with significant positive charge development on the α -carbon of the styrene in the epoxidation transition state.¹³

The smaller ρ values for the reactions in the presence of cobalt(II) complexes indicate that for these systems there is less

Table 6. Change of product distribution with time in epoxidation of *trans*-4-methylpent-2-ene with 3-chloroperoxybenzoic acid (0.2 mmol) and cobalt(II) octanoate (4.2×10^{-3} mmol) in acetonitrile

Time (min)	Yield of epoxide (%)			Product composition (%)	
	<i>trans</i>	<i>cis</i>	Total	<i>trans</i>	<i>cis</i>
1	14	2	16	88	12
5	24	2	16	92	8
10	35	2	37	95	5
30	49	2	51	96	4
60	62	2	64	97	3

build-up of positive charge, suggesting that the attacking species may be either a more reactive electrophile or a free radical (see discussion below).

Oxidation of *cis*- and *trans*-Alkenes by Peroxyacid-Cobalt(II) Complex Systems.—The epoxidation of *cis*- and *trans*-stilbene using 3-CPBA-cobalt(II) octanoate (molar ratio 40:1) is not completely stereospecific. Thus each stilbene gives a mixture of *cis*- and *trans*-epoxides with retention of configuration in the major product (Table 5). Very similar results were obtained with *cis*- and *trans*-4-methylpent-2-ene using dichloromethane or acetonitrile as the solvent, although the loss of stereochemistry is less for these substrates (Table 5). Control experiments demonstrated that the epoxides are stable to the reaction conditions, that the product distributions are unaffected by whether the reactions are carried out in air or under nitrogen, and that the reactions are stereospecific in the absence of cobalt(II) octanoate.

The product distributions in Table 5 were obtained by h.p.l.c. or g.l.c. analyses of the reaction mixtures when iodometric titration showed that all the oxidant had been consumed. In some oxidations the product distribution and yields were also monitored during the course of the reaction (Table 6) and these data reveal that the epoxidation occurs *via* two mechanisms.

This duality of mechanism is interpreted as a fast, non-stereospecific, cobalt(II) initiated epoxidation followed by a slower *syn* epoxidation. The latter is probably a peroxyacid epoxidation that continues after the metal complex has been rendered inactive to further participation in the reaction. Increasing the concentration of the cobalt complex in the reaction, as would be expected, increases the proportion of the epoxidation proceeding *via* the cobalt(II) initiated process but it also lowers the overall yield of epoxide (Table 7). Very comparable results are observed from reactions in dichloromethane and in acetonitrile. Clearly the active species in the cobalt initiated reaction leads to other oxidation products besides epoxides. As described above, we suspect that these arise from the oxidation of the ligands of the metal complex.

Epoxidation of Cyclohexene with Peroxyacid-Cobalt(II) Complex Systems.—The reaction of cyclohexene with 3-CPBA in the presence of cobalt(II) octanoate leads to epoxycyclohexane, cyclohexen-3-ol, and cyclohexen-3-one (Table 8). The allylic oxidation, which only occurs in the presence of a cobalt complex, suggests that the metal initiates a one-electron process with the formation of the cyclohexen-3-yl radical. The oxidation is not the well documented metal-catalysed autoxidation of cyclohexene²² nor the epoxidation of alkenes by dioxygen and cobalt(II) complexes²³ since the product distribution is unaffected by carrying out the reactions under nitrogen. However, it may be analogous to the allylic oxidations that occur with peroxyacid promoted oxidations by cytochrome P450 mono-oxygenases^{3f,8d} and with metalloporphyrin catalysed model systems.^{3f,11a,b,17c,24}

Table 7. Change of product distribution and yield with cobalt(II) octanoate concentration in epoxidation of *cis*-4-methylpent-2-ene with 3-chloroperoxybenzoic acid

$10^3[\text{Co}^{II}]/$ mmol cm ⁻¹	Yield of epoxide (%) ^a			Product composition (%)	
	<i>trans</i>	<i>cis</i>	Total	<i>trans</i>	<i>cis</i>
Solvent CH ₂ Cl ₂					
0	0	92	92	0	100
0.17	1	80	81	1	99
1.7	3	67	70	4	96
8.3	5	46	51	10	90
Solvent MeCN					
0	0	86	86	0	100
0.17	12	54	66	18	92
1.7	18	35	53	34	66
8.3	15	30	45	33	67

^a Yields based on peroxyacid.

Table 8. Oxidation of cyclohexene with 3-chloroperoxybenzoic acid in the presence of cobalt(II) octanoate^a

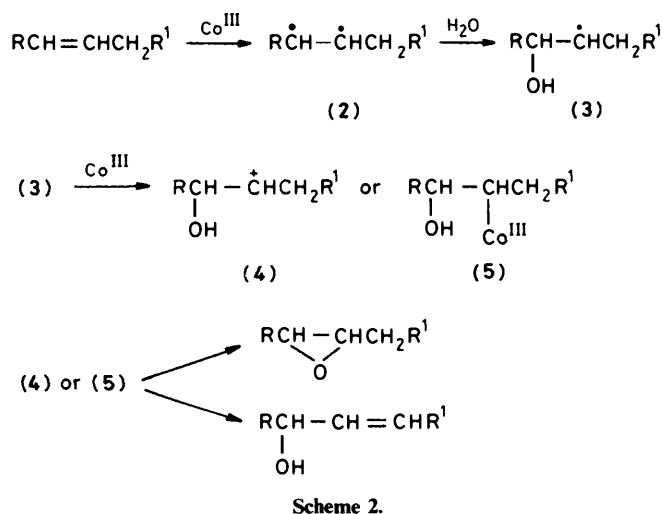
Reaction conditions	Product yield %		
	Epoxycyclohexane	Cyclohexen-3-ol	Cyclohexen-3-one
No Co ^{II} , CH ₂ Cl ₂ , air	94	0	0
No Co ^{II} , MeCN, air	89	0	0
Co ^{II} , CH ₂ Cl ₂ , air	76	5	4
Co ^{II} , CH ₂ Cl ₂ , N ₂	75	5	4
Co ^{II} , MeCN, air	69	5	4
Co ^{II} , MeCN, N ₂	68	5	5

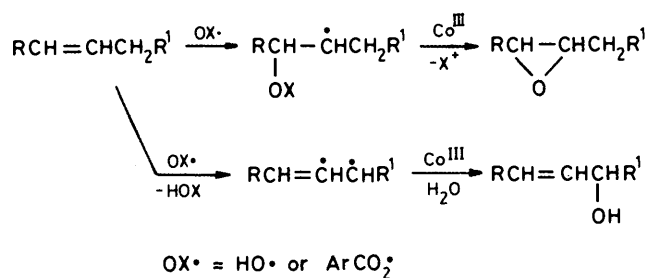
^a Ratio of peroxyacid to cobalt(II) octanoate, 20:1.

Origin of Epoxide Oxygen in Peroxyacid-Cobalt(II) Complex Epoxidations.—The oxidations of *cis*- and of *trans*-4-methylpent-2-ene were studied using 3-CPBA and cobalt(II) octanoate in dried acetonitrile to which was added [¹⁸O]water. For each reaction the epoxide with inverted configuration was analysed by g.c.-m.s. and found to contain no observable ¹⁸O. Control reactions showed that the addition of water, in amounts equivalent to the ¹⁸O labelling experiments, had no detectable effect on the yields and product distributions. These experiments show that the epoxide oxygen arises from the peroxyacid and not from trace amounts of water in the reaction medium.

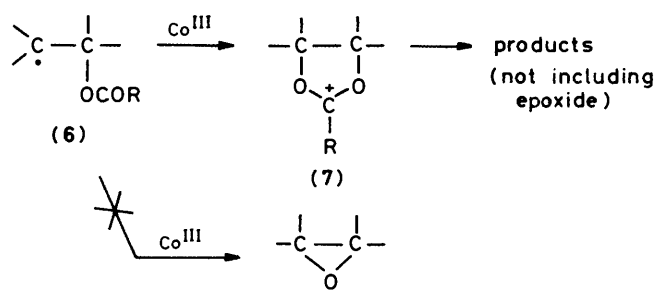
Mechanism of Epoxidation of Alkenes by the Peroxyacid-Cobalt(II) Complex Systems.—Two alternative one-electron mechanisms need to be considered for the cobalt initiated epoxidation of alkenes with peroxyacids. A two-electron reduction of the peroxyacid by cobalt(II) is an unlikely process.

(i) **Electron-transfer epoxidation initiated by cobalt(III).** Cobalt(III) compounds are known to be powerful electron-transfer oxidants and they have been used in this capacity to bring about reactions with alkenes²⁵ and aromatic compounds.²⁶ Furthermore it is clear, from the green colour of the reaction mixtures in this study, that the peroxyacids oxidise cobalt(II) complexes to cobalt(III). Electron transfer from the alkene to cobalt(III) would generate the alkene radical cation [(2), Scheme 2] which on reaction with water and further oxidation of the resultant hydroxyalkyl radical (3) would give the epoxide either *via* a β-hydroxyalkyl cation (4), or a cobalt-alkyl intermediate (5). Allylic oxidation would then occur by the alternative loss of a proton from (4) or *via* a concerted loss of a proton and cobalt(II) from (5). In a footnote in a recent paper,²⁷





Scheme 3.

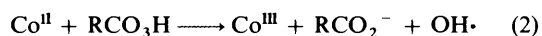
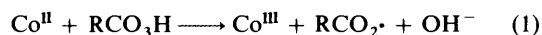


Scheme 4.

Groves and Subramanian suggest that styrenes may be epoxidised by cytochrome P450 mono-oxygenases and by their metalloporphyrin models by an electron-transfer mechanism. This mechanism bears a strong resemblance to the copper(II)-persulphate oxidation of alkenes²⁸ where the persulphate radical anion generates the alkene radical cation. The oxidation of the β -hydroxyalkyl radical to the epoxide by copper(II) probably involves an alkyl copper intermediate rather than the β -hydroxyalkyl cation.²⁹ It is noteworthy that in this system allylic oxidation is not observed.

Although the electron-transfer mechanism can account for the loss of stereospecificity in the peroxyacid-cobalt(II) epoxidations as arising from rotation about the central carbon-carbon bond in the intermediate, it cannot explain the results from the ¹⁸O labelling experiments. Thus the mechanism predicts that labelled ¹⁸O from [¹⁸O]water should be incorporated into the epoxide product. Furthermore, the electron-transfer mechanism might be expected to show a more negative ρ value than is found with the 3-CPBA epoxidation and the reverse is observed. Finally, reactions carried out with small concentrations of cobalt(II) demonstrate that the epoxide is formed *via* two independent mechanisms; the rapid cobalt initiated process is followed by the slower peroxyacid epoxidation. This is not the result expected from the electron-transfer mechanism since the cobalt initiated epoxidation is maximal when the cobalt(III) concentration is smallest. Additionally the lack of reaction of *cis*- and of *trans*-4-methylpent-2-enes with cobalt(III) acetate under the more forcing conditions of acetic acid at 85 °C for 17 h, confirms that the initial oxidation, under our experimental conditions, does not involve electron-transfer from the alkene to cobalt(III).

(ii) *Oxy-radical epoxidation initiated by the peroxyacid-cobalt complex system.* The one-electron reductive cleavage of peroxyacids by cobalt(II) is a rapid process that can occur by two competing pathways to give a benzenecarboxyl or hydroxyl radical,³⁰ the relative rates of which are solvent dependent [Reactions (1) and (2)]. The alternative oxidative cleavage^{31,32}



of the peroxyacid occurs much more slowly, if at all.³³ The oxy-radicals (OX \cdot) or metal complexed oxy-radicals, from reductive cleavage can either add to the alkene to give a β -hydroxyalkyl radical or abstract a hydrogen atom to give an allylic radical. These intermediates lead to epoxide and allylic oxidation, respectively (Scheme 3).

It is unlikely that the oxy-radical is the 3-chlorobenzene-carboxyl radical for the following reasons. (a) The oxidation of β -acyloxyalkyl radicals (6) by cobalt(III) has been found to give products from a cyclic acyloxonium ion (7) rather than an epoxide (Scheme 4).³⁴ (b) Products from the free-radical polymerisation of styrene by the iron(II) catalysed

reductive cleavage of 4-bromoperoxybenzoic acid contain no bromine, indicating that polymerisation is not initiated by the 4-bromobenzenecarboxyl or 4-bromophenyl radical.³²

However, attempts to confirm the involvement of hydroxyl radicals or of cobalt complexed hydroxyl radicals by epoxidising *cis*-4-methylpent-2-ene with hydrogen peroxide-cobalt(II) (analogous to Fentons reagent) were unsuccessful. The cobalt(III) that is generated in this system brings about the rapid oxidative degradation of hydrogen peroxide with the evolution of dioxygen. The equivalent reaction is unimportant with oxidations by Fentons reagent, since iron(III) is a much weaker oxidant than cobalt(III).³⁵

The non-stereospecific nature of alkene epoxidation by oxy-radicals is well documented.³⁶ Most closely related to this study are the epoxidations by hydrogen peroxide in the presence of tris(acetylacetonato)iron(III)^{36d} or of iron(II) perchlorate³⁷ which are probably brought about by the hydroxyl radical or its iron bound equivalent. Recently Fontecave and Mansuy have suggested an iron-oxy radical as the active oxidant in epoxidations with iron(III) compounds and iodosylbenzene.^{12b}

The lack of incorporation of ¹⁸O with epoxidations in the presence of [¹⁸O]water, which is incompatible with the electron-transfer mechanism, is to be expected from an oxy-radical process, since the oxygen of the epoxide is derived from the peroxyacid.

In the presence of cobalt(II) compounds alkene epoxidation by peroxyacids proceeds *via* two distinct processes, one initiated by the peroxyacid with cobalt(II) and the other by the peroxyacid alone. Consequently, the measured Hammett values are a combination of the ρ values from both processes. The reduction in the magnitude of ρ from reactions in the presence of cobalt(II) complexes is consistent with the rate-determining step for the cobalt initiated reaction being the addition of the oxy-radical to the styrene. Although these radicals are electrophilic, the transition state for such a step is unlikely to involve the development of significant positive charge, hence the observed value in the presence of cobalt(II) is diminished.

Experimental

Materials.—All the materials were commercial reagent grade unless otherwise stated and were obtained from Aldrich Chemical Co. Ltd., Koch-Light Ltd., or Fisons Scientific Apparatus Ltd. The nitrogen gas was British Oxygen white-spot grade. The ¹⁸O enriched water (20.3 atom %) was from Prochem B.O.C. Ltd. The organic soluble metal complexes that were not commercially available were kindly supplied by ICI.

The commercially available alkenes were purified by distillation or recrystallisation before use. The preparation and purification of other alkenes and of the epoxides have been described.^{17b} Peroxybenzoic acid was prepared from dibenzoyl peroxide following Furniss *et al.*³⁸ and its purity was assessed iodimetrically. Cobalt(III) acetate was prepared from cobalt(II) acetate in acetic acid and acetic anhydride with ozone.³⁹

Methods.—The chromatographic and spectroscopic methods used in this study have been described.^{17b}

Oxidation Procedures.—(a) *Competitive epoxidation of styrene and 3-chlorostyrene in the presence of a selection of metal complexes.* The substrates (1 mmol of each styrene) were oxidised with peroxyacid (0.2 mmol) and metal complex (5×10^{-3} mmol) in chlorobenzene (2.5 cm³) in air at 23 °C. The extent of reaction was monitored by removing aliquots from the reaction mixtures for iodimetric titration. When the reaction was complete (1 h) the products were analysed directly by g.l.c. For reactions in the absence of air, the solution was first thoroughly saturated with nitrogen and the reaction was then carried out under a positive pressure of nitrogen.

(b) *Competitive epoxidations of substituted styrenes by peroxyacids and cobalt complexes.* The following pairs of substrates were used in the competition experiments: (i) styrene and 4-methylstyrene; (ii) styrene and 4-chlorostyrene; (iii) styrene and 3-chlorostyrene; (iv) 4-chloro- and 4-nitro-styrene; and (v) 3-chloro- and 4-nitro-styrene. The oxidations with 3-CPBA and with PBA were carried out as described above for solutions in chlorobenzene and in benzene.

(c) *Epoxidation of cis- and trans-alkenes.* *cis*- and *trans*-isomers of stilbene and of 4-methylpent-2-ene (0.5 mmol) were epoxidised with 3-CPBA (0.2 mmol) and cobalt(II) octanoate (5×10^{-3} mmol for stilbenes and 4.2×10^{-3} mmol for methylpent-2-enes) in acetonitrile or dichloromethane (2.5 cm³). At the end of the reaction the stilbene product mixtures were analysed by h.p.l.c. and those of the 4-methylpent-2-enes by g.l.c.^{17b} In reactions of *trans*-4-methylpent-2-ene where the product distribution was monitored during the course of the oxidation, aliquots of the reaction mixture were removed at measured time intervals and analysed directly by g.l.c.

The dependence of the yield and stereochemistry of the products from the oxidation of *cis*- and *trans*-4-methylpent-2-ene on cobalt(II) concentration was studied as described above using cobalt(II) octanoate (0–10.5 mmol).

Epoxidation of cyclohexene. Cyclohexene (0.5 mmol) in dichloromethane or acetonitrile (2.5 cm³) was epoxidised in air or under nitrogen at 23 °C with 3-CPBA (0.2 mmol) and cobalt(II) octanoate (5×10^{-3} mmol). The products were analysed by g.l.c.^{17b}

Epoxidation of cis- and of trans-4-methylpent-2-enes in the presence of [¹⁸O]water. *cis*- or *trans*-4-methylpent-2-ene (0.5 mmol) in dried acetonitrile (2.5 cm³), containing water or [¹⁸O]water (20 μl), was epoxidised with 3-CPBA (0.2 mmol) and cobalt(II) octanoate (2.5×10^{-3} mmol). The [¹⁸O] content of the products was analysed by g.c.–m.s.

Attempted epoxidation of 4-methylpent-2-enes by cobalt(III) compounds. (a) Cobalt(III) acetate or trifluoroacetate (0.2 mmol) was added to a solution of *cis*- or *trans*-4-methylpent-2-ene (2 mmol) in acetonitrile (2.5 cm³) in air at 23 °C. These reactions were repeated in the presence of water (20 μl). G.l.c. was used to analyse the reactions for products.

(b) Cobalt(III) acetate (6.0 mmol) and *cis*- or *trans*-4-methylpent-2-ene (6.0 mmol) were reacted in acetic acid (15 cm³) under nitrogen at 85 °C. After 17 h the reaction was cooled, and the excess of acetic acid was removed on a rotary evaporator. The residue was basified with 20% sodium carbonate, extracted into ether and analysed by g.l.c.

Attempted epoxidation of 4-methylpent-2-enes by cobalt(II) octanoate and hydrogen peroxide. *cis* or *trans*-4-methylpent-2-ene (0.5 mmol) was mixed with a suspension of hydrogen peroxide (8 μl of 86% aqueous solution) in dichloromethane (2.5 cm³). The cobalt(II) octanoate (5×10^{-3} mmol) in dichloromethane was added slowly over 15 min. This experiment was repeated with acetonitrile in place of dichloromethane.

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