Model Systems for Cytochrome P450 Dependent Mono-oxygenases. Part 3.[1] The Stereochemistry of Hydroxylation of *cis*- and *trans*-Decahydronaphthalene by Chemical Models for Cytochrome P450 Dependent Mono-oxygenases

John R. Lindsay Smith * and Paul R. Sleath
Department of Chemistry, University of York, York YO1 5DD

The stereochemistry of hydroxylation of the tertiary C–H bonds of *cis*- and *trans*-decahydronaphthalene by seven chemical models for cytochrome P450 dependent mono-oxygenases has been studied. Oxidations by three of the model systems (H_2O_2–Fe^{2+}–CH_3CN, O_2–Fe^{2+}–2-mercaptobenzoic acid, and diazofluorene–*hν*–O_2) are non-stereospecific giving the same ratio of *cis*- to *trans*-decahydronaphthalen-9-ol from each substrate. However, hydroxylations with pyridine *N*-oxide–*hν* show a partial retention of configuration and with trifluoroperacetic acid or with iron(III) porphyrins and iodosylbenzene the oxidations are >97% stereospecific. The mechanisms of these hydroxylations and their usefulness as models for the cytochrome P450 dependent mono-oxygenases are discussed.

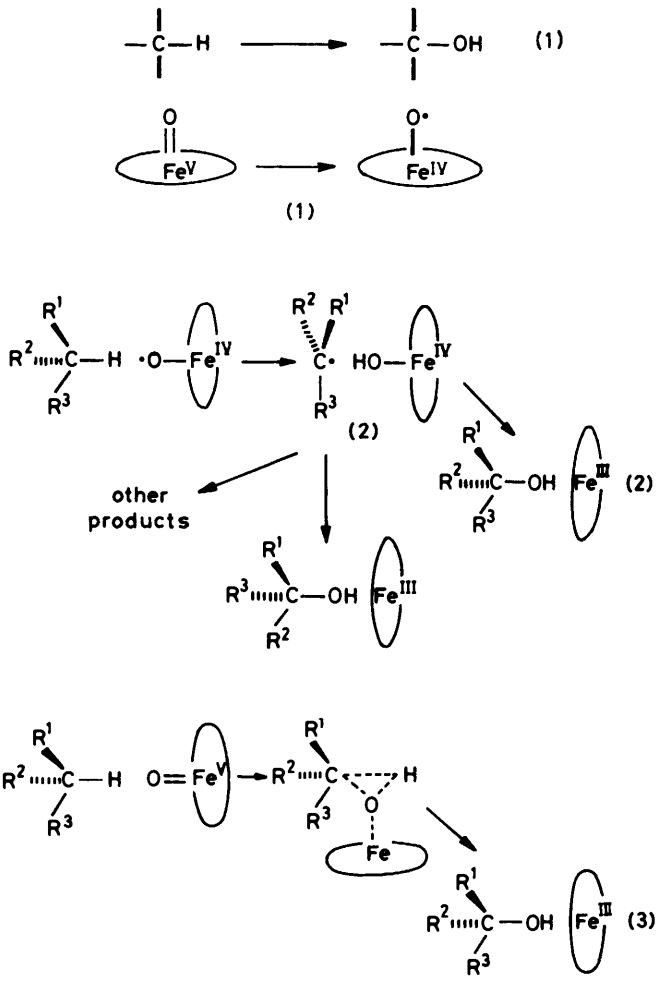
One aspect of the chemistry brought about by the mono-oxygenases that has recently attracted much attention is the hydroxylation of unactivated saturated C–H bonds [reaction (1)].[2] This process has been studied with mono-oxygenases from a variety of sources including bacteria,[2i-k] yeasts,[2e] and mammalian liver.[2c,d,f,l] The interest of chemists in these oxygenations is centred on their mechanism and on the nature of the active oxidant, since a thorough understanding of the biological processes may lead to new, commercially viable, selective oxidations of hydrocarbons.

Apart from enzymic studies, the following five mechanistic probes have been used by chemists to investigate *in vitro* substrate oxidations: (i) kinetic isotope effect studies with isotopically labelled substrates;[1,2d,j-l,3] (ii) measurement of the relative reactivities of primary, secondary, and tertiary C–H bonds;[2b,c,f] (iii) investigations of the stereochemistry of these oxidations;[2d,f,j-l,4] (iv) studies of the influence of substrate structure on the direction of the oxidation, including the possible involvement of rearrangements;[2d,f,l,5] (v) ^{18}O labelling studies to determine the fate of the dioxygen and the origin of the oxygen in the product.[2g,h,6]

The results can be compared with those from chemical oxidants [2a,b,7] and from modified *in vitro* systems where the dioxygen and NADPH are replaced by oxidants such as iodosylbenzene, hydroperoxides, peracids, and sodium periodate.[1,2h,k,4,8]

These investigations have led to the conclusion that the active oxidant in biological aliphatic hydroxylations with NADPH and dioxygen is an oxoiron porphyrin (1) that reacts by a two-step hydrogen atom abstraction process [reaction (2)] [2d,f] rather than by a concerted oxenoid insertion mechanism [reaction (3)].[9] The main pathway involves the collapse of the radical pair (2) to produce alcohol with retention of configuration. The extent to which alternative products are formed depends on the life-time of the carbon radical and the relative rates of competing processes (*e.g.* rearrangement and loss of stereochemistry).

Our interest in models for cytochrome P450 dependent mono-oxygenases has led us to examine alkane hydroxylation by a selection of model systems. The ability of model systems to hydroxylate saturated C–H bonds is well documented [2b,6,10] and we have directed our attention to the stereochemistry of these processes. The stereospecificity of hydroxylation by some model systems has been reported [7a,d,e,g,11] although uncertainties in some of the published data and experimental details have led us to re-examine several systems. We report here our studies of the oxidation of *cis*- and *trans*-decahydronaphthalene with chemical models for the cytochrome P450 dependent mono-oxygenases.



Results and Discussion

Analysis of Oxidation Products from cis- *and* trans-*Decahydronaphthalene.*—G.c. analysis with a polyethylene glycol

Table 1. Decahydronaphthalen-9-ol isomer distribution from the oxidation of *cis*- and *trans*-decahydronaphthalene by chemical model systems for the cytochrome P450 dependent mono-oxygenases

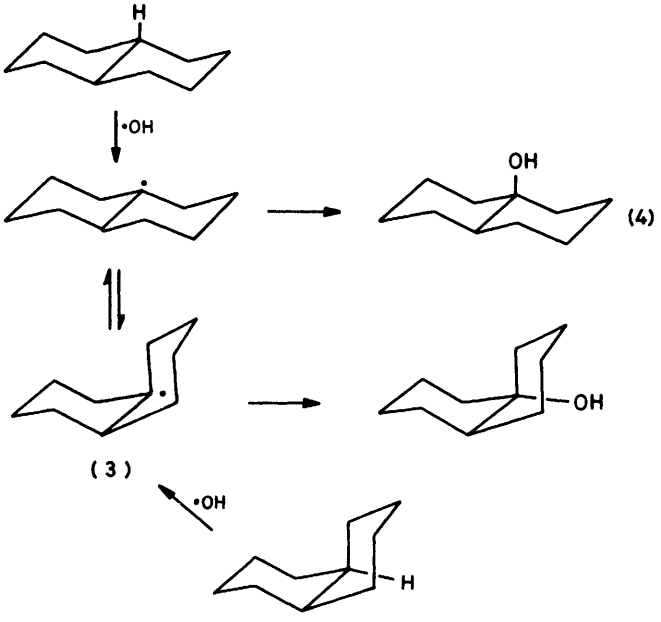
Model systems [a]	Solvent	Decahydronaphthalene isomer	Decahydronaphthalen-9-ol isomer distribution (%) *cis*	*trans*
$Fe^{2+} - H_2O_2$ (Non-aqueous Fenton's reagent) [b]	CH_3CN	*cis*	34	66
		trans	32	68
Fe^{2+}–2-mercaptobenzoic acid–O_2 (Ullrich's system) [c]	H_2O/CH_3COCH_3	*cis*	30	70
		trans	28	72
Diazofluorene–*hν*–O_2 [d]	CH_2Cl_2	*cis*	25	75
		trans	27	73
Pyridine *N*-oxide–*hν* [e]	CH_2Cl_2	*cis*	70	30
		trans	10	90
Trifluoroperacetic acid [f]	CH_2Cl_2	*cis*	98	2
		trans	2	98
Fe^{III}TPPCl–PhIO (Groves' system) [g]	CH_2Cl_2	*cis*	99	1
		trans	3	97
Fe^{III}TFPPCl–PhIO [h]	CH_2Cl_2	*cis*	99	1
		trans	3	97

[a] Abbreviations: Fe^{III}TPPCl, tetraphenylporphinatoiron(III) chloride; Fe^{III}TFPPCl, tetrakis(pentafluorophenyl)porphinatoiron(III) chloride. [b] Ref. 10*a*. [c] Ref. 2*a*. [d] Ref. 12. [e] Ref. 13. [f] Ref. 14. [g] Ref. 7*e*. [h] Ref. 15.

stationary phase (Carbowax 20M) separates the tertiary *cis*- and *trans*-decahydronaphthalen-9-ols from each other and from the products from oxidation at positions 1 or 2 of the decahydronaphthalenes. All the products from oxidation of secondary C–H bonds have longer retention times than the two tertiary alcohols. However, an efficient column is needed to ensure that one secondary alcohol, probably a decahydronaphthalen-1-ol, is well separated from *cis*-decahydronaphthalen-9-ol. Although the problems associated with the g.c. analysis of the decahydronaphthalenols have been reported before [16] it is possible that in some previous work on the oxidation of decahydronaphthalenes adequate product separations for accurate analyses were not obtained.

Oxidation of cis- *and* trans-*Decahydronaphthalene with a Selection of Model Systems.*—Attempts to oxidise *cis*- or *trans*-decahydronaphthalene in aqueous suspension with Udenfriend's system [iron(II)–EDTA–ascorbic acid and dioxygen] [17] or with the tin(II)–pyrophosphate–dioxygen system [18] were unsuccessful. These substrates are not sufficiently water-soluble to be oxidised by these aqueous systems. This observation accounts for the very limited data on the oxidation of alkanes with aqueous model systems and it restricted this investigation to model systems using non-aqueous solvents. The results from the oxidation of *cis*- and *trans*-decahydronaphthalene with seven model systems are given in Table 1.

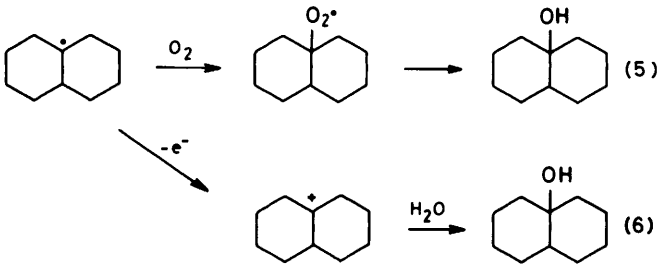
Three of the systems, namely non-aqueous Fenton's, Ullrich's, and the diazofluorene–*hν*–dioxygen system, give the same relative yields of *cis*- to *trans*-decahydronaphthalen-9-ol (*ca.* 30 : 70, respectively) irrespective of whether the substrate is the *cis*- or *trans*-hydrocarbon. The active oxidant in these oxidising systems is most probably an oxy-radical which, when it abstracts a hydrogen atom from the 9-position of decahydronaphthalene, gives a carbon free radical that can interconvert between *cis*- and *trans*-conformers (3) [reaction (4)]. Since the product distributions are independent of substrate stereochemistry the 9-decahydronaphthyl radicals must attain conformational equilibrium faster than they are oxidised to products. The predominance of the more stable *trans*-radical [19] accounts for the higher yield of *trans*-decahydronaphthalen-9-ol. Miyajima and Simamura [20] reached very similar conclusions in their studies of the autoxidation of methylcyclohexanes.

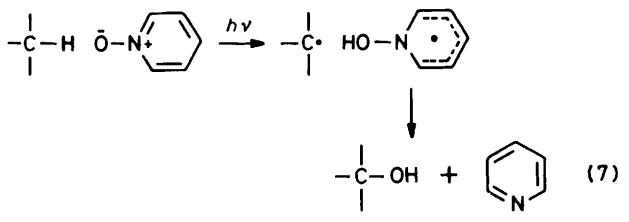


The conversion of the 9-decahydronaphthyl radicals into alcohols can occur by trapping with dioxygen [reaction (5)], a fast reaction of alkyl radicals,[21] or alternatively by electron transfer and reaction with water [reaction (6)].[22]

Results from other studies with the non-aqueous Fenton's reagent are in agreement with the active oxidant being an oxyl-radical (probably the hydroxyl radical).[1,22,23] Likewise the results from Ullrich's system concur with the suggestion that oxidation by this system is also brought about by an oxyl-radical.[24]

In agreement with this study the diazofluorene–*hν*–dioxygen system is reported to oxidise *cis*- and *trans*-1,2-dimethylcyclohexane with loss of stereochemistry, but quantitative data on





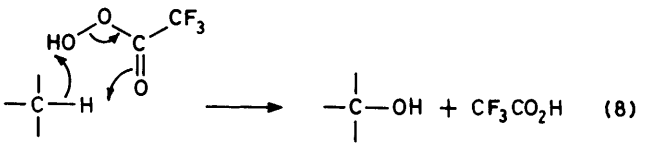


Table 2. The reactivities of aliphatic alkenes, relative to oct-1-ene, towards epoxidation by iron(III) porphyrins and iodosylbenzene in dichloromethane at room temperature

Substrate	Reactivity relative to oct-1-ene	
	$Fe^{III}TPPCl$ [a]	$Fe^{III}TFPPCl$
2,3-Dimethylbut-2-ene	204	32
cis-4-Methylpent-2-ene	28	12
Cyclohexene	20	9
trans-4-Methylpent-2-ene	2	2
Oct-1-ene	1	1

[a] Ref. 28.

product distributions are not given.[7a] These results reinforce the view that this oxidation is a free radical process.[1]

The yield of oxidation products from decahydronaphthalenes with the pyridine *N*-oxide system was low and a variety of unknown compounds, presumably arising from rearrangement of the *N*-oxide,[25] was obtained. However, in contrast with the results of Hamilton and his co-workers [7a,9] who reported this system to be >95% stereospecific we find only a partial retention of configuration. The stereospecificity we have observed resembles that reported for the oxidation of decahydronaphthalenes by $O(^3P)$ atoms generated by the γ-radiolysis of liquid carbon dioxide.[7d] In this latter system *cis*- and *trans*-decahydronaphthalene show 83 and 93% retention of configuration, respectively, and caged radicals are proposed to account for the partial retention of stereochemistry.[7d,26] A similar radical mechanism can be proposed involving hydrogen atom abstraction by a photoexcited pyridine *N*-oxide [reaction (7)] or alternatively, $O(^3P)$ atoms may be the active species as suggested by Ogawa *et al.*[27]

The mechanism of oxidation of alkanes by peracids is not well defined although all the evidence to date,[2b,7g,10b,11] including the results from this study, can be accommodated by the concerted oxidation proposed by Deno and his co-workers [reaction (8)].[9] Consequently, as we noted previously,[1] oxidations mediated by peracids cannot be considered to be good models for those catalysed by cytochrome P450. However, more sophisticated studies are needed, along the lines of those of Groves and his co-workers [2d,f,5,8d] in their investigations of oxidations catalysed by cytochrome P450 and by related metalloporphyrins, to eliminate short-lived radical intermediates in these reactions.

The oxidations brought about by the iron(III) porphyrins with iodosylbenzene show almost 100% retention of configuration and in this respect resemble those of trifluoroperacetic acid. This was unexpected since Goves *et al.* have reported a 17% loss of stereochemistry in the oxidation of *cis*-decahydronaphthalene by the $Fe^{III}TPPCl$–iodosylbenzene system.[7e] The origin of this discrepancy in results remains unclear but may arise from an incomplete separation of oxidative products in the earlier study.

Competitive Oxidations with Iron(III) Porphyrin Model Systems.—Since the two iron(III) porphyrin–iodosylbenzene systems oxidise the 9-position of the decahydronaphthalenes with high stereospecificity it is possible to measure the relative reactivity of the *cis*- and *trans*-isomers in the two systems. Preliminary separate oxidations of the two substrates showed that the *cis*-decahydronaphthalene gives the higher yield of decahydronaphthalen-9-ol. The greater reactivity of the *cis*-isomer was confirmed by measuring the yields of tertiary alcohols from competition experiments. The relative reactivity of *cis*- to *trans*-decahydronaphthalene is 9.4 : 1 for the $Fe^{III}TPPCl$–iodosylbenzene system and 17.3 : 1 for Fe^{III}-TFPPCl and iodosylbenzene. It is likely that the greater reactivity of the *cis*-isomer arises from this substrate being able to approach the active oxidant, at the centre of the porphyrin ring, more easily than the *trans*-isomer. Similar steric arguments have been used to explain the greater ease of epoxidation of *cis*- over isomeric *trans*-alkenes by these model systems.[1,7e]

The greater selectivity of the $Fe^{III}TFPPCl$–iodosylbenzene system was unexpected since with alkene epoxidation the fluoroporphyrin system is less selective than $Fe^{III}TPPCl$–iodosylbenzene (Table 2). With the latter system we have shown that the electron-donating properties of the alkyl groups on the alkene tend to dominate their steric effects [28] and thus we interpret the lower substrate selectivity in epoxidations by the fluoroporphyrin system to an increased reactivity of the active oxidant arising from electron-withdrawal by the fluorine substituents. A similar trend has been observed for the effect of substituents on the rate of epoxidation by perbenzoic acids.[29] However, with the decahydronaphthalenes the electronic effects of the substrates are equivalent and less important than for alkenes and the difference in reactivity must arise from the slightly larger steric hindrance from the fluorines (van der Waal's radius 0.135 nm) in $Fe^{III}TFPPCl$ over the hydrogens (van der Waal's radius 0.12 nm) in $Fe^{III}TPPCl$.

The mechanism of oxidation of saturated C–H bonds by the $Fe^{III}TPPCl$–iodosylbenzene system has been described in terms of the oxidant being an oxoiron intermediate (I)[5,7e,i] that reacts by two one-electron steps [reaction (2)].[7e] The minor extent to which there is loss of stereochemistry can be rationalised by assuming that the initially formed carbon radical (9-decahydronaphthyl) is generated next to the oxidant in a solvent cage and is rapidly trapped to give product (decahydronaphthalen-9-ol). A similar explanation has been used to account for the retention of configuration in the oxidation of alkanes by chromic(VI) acid in aqueous acetic acid.[30] The alternative concerted oxidation mechanism although consistent with almost all the data cannot explain the partial rearrangement in the allylic hydroxylation of 1,2-

dideuteriocyclohexene,[5] the formation of cyclohexane derivatives, other than cyclohexanol and cyclohexanone, in the oxidation of cyclohexane,[31] and the large kinetic isotope effect in the oxidative *O*-demethylation of anisole and [*Me*-$^2H_3$]-anisole.[1]

Conclusion.—The initial step in the hydroxylation of saturated C–H bonds by all the model systems used in this study, with the probable exception of that with trifluoroperacetic acid, can be rationalised as a hydrogen atom abstraction to generate a carbon radical. The stereochemical outcome of the oxidation depends on the life-time of this radical. It is almost stereospecific where the radical is trapped rapidly by the oxidant within a solvent cage [iron(III) porphyrin–iodosylbenzene systems]; however, with longer lived radical intermediates the product distribution reflects the equilibrium distribution of the radical conformers (Ullrich's, non-aqueous Fenton's, and the diazofluorene–*hv*–dioxygen systems). Of the chemical oxidants examined in this and our previous study[1] the iron(III) porphyrin–iodosylbenzene systems most closely resemble the cytochrome P450 dependent monooxygenases.

Experimental

Materials.—All the materials were commercial reagent grade unless otherwise stated and were obtained from Aldrich Chemical Co. Ltd., Fisons Scientific Apparatus Ltd., or Koch-Light Ltd.

Commercial *cis*- and *trans*-decahydronaphthalene were shown, by g.c. analysis, to be 99.9 and 99.8% pure, respectively, and were used without further purification. *trans*-Decahydronaphthalen-9-ol was prepared by oxidation of *trans*-decahydronaphthalene with chromic(VI) acid following Wiberg and Foster.[32] The alcohol was obtained by preparative g.c. and had m.p. 53—55 °C (lit.,[32] 54 °C); δ_C ($CDCl_3$) 70.1 (C-9), 44.2 (C-10), and 39.8, 28.6, 26.3, and 23.6 p.p.m. (-CH_2-) (all resonances gave the expected couplings in the off-resonance spectrum); *m/z* 154 (M^+, 34%), 111 (100), 98 (37), 97 (21), 79 (18), 67 (18), and 55 (28). *cis*-Decahydronaphthalen-9-ol was identified by g.c.–m.s. as the major product in oxidations of *cis*-decahydronaphthalene but was not purified by preparative g.c. (the mass spectra of the two tertiary alcohols are identical and significantly different from those of the secondary alcohols).

The iron(III) porphyrins, iron(II) perchlorate, iodosylbenzene, and diazofluorene were prepared as described previously.[1,28]

Methods.—Mass, g.c.–mass, and n.m.r. spectroscopic methods have been described previously.[28] Preparative and analytical g.c. used Pye 105 and Pye-Unicam 204 gas chromatographs, respectively, with flame ionisation detectors. The packing material was Carbowax 20M (20% w/w) on Celite AW (80—120 mesh).

Oxidation of Decahydronaphthalene with Model Systems.—(i) *Pyridine N-oxide–hv system.* A solution of the decahydronaphthalene (1 cm^3) and pyridine *N*-oxide (0.1 g) in dichloromethane (1 cm^3) was irradiated under nitrogen in a quartz cell (1 cm path length) with a 15-W Hanovia low-pressure mercury lamp. After 30 min the reaction was analysed directly by g.c.

(ii) *Non-aqueous Fenton's reagent, Udenfriend's system Ullrich's system, tin(II) chloride–pyrophosphate–dioxygen, diazofluorene–hv–dioxygen, Fe^{III}TPPCl–iodosylbenzene, Fe^{III}TFPPCl–iodosylbenzene, and trifluoroperacetic acid.* Oxidations with these model systems were as described in the previous paper[1] with anisole replaced by an equivalent amount of decahydronaphthalene.

Competitive Oxidations of cis- *and* trans-*Decahydronaphthalene and of Aliphatic Alkenes.*—The competition experiments with the iron(III) porphyrin–iodosylbenzene model systems were carried out as described previously[28] with 5 mmol of each substrate.

Acknowledgements

One of us (P. R. S.) thanks the S.E.R.C. for the award of a research studentship.

References

1 Part 2, J. R. Lindsay Smith and P. R. Sleath, *J. Chem. Soc., Perkin Trans. 2*, 1983, 621.
2 (*a*) V. Ullrich, *Z. Naturforsch., Teil B*, 1969, **24**, 699; (*b*) U. Frommer and V. Ullrich, *Z. Naturforsch.*, 1971, **26**, 322; (*c*) U. Frommer, V. Ullrich, and S. Orrenius, *FEBS Lett.*, 1974, **41**, 14; (*d*) J. T. Groves, G. A. McClusky, R. E. White, and M. J. Coon, *Biochem. Biophys. Res. Commun.*, 1978, **81**, 154; (*e*) H. G. Müller, W. H. Schunck, P. Riege, and H. Honeck, *Acta Biol. Med. Ger.*, 1979, **38**, 345; (*f*) R. E. White, J. T. Groves, and G. A. McClusky, *ibid.*, p. 475; (*g*) S. G. Sligar, K. A. Kennedy, and D. C. Pearson, *Proc. Nat. Acad. Sci. U.S.A.*, 1980, **77**, 1240; (*h*) D. C. Heimbrook and S. G. Sligar, *Biochem. Biophys. Res. Commun.*, 1981, **99**, 530; (*i*) H. Dalton, B. T. Golding, B. W. Waters, R. Higgins, and J. A. Taylor, *J. Chem. Soc., Chem. Commun.*, 1981, 482; (*j*) E. Caspi, S. Shapiro, and J. U. Piper, *Tetrahedron*, 1981, **37**, 3535; (*k*) M. Gelb, D. C. Heimbrook, P. Malkönen, and S. G. Sligar, *Biochemistry*, 1982, **21**, 370; (*l*) S. Shapiro, J. U. Piper, and E. Caspi, *J. Am. Chem. Soc.*, 1982, **104**, 2301.
3 L. M. Hjelmeland, L. Aronow, and J. R. Trudell, *Biochem. Biophys. Res. Commun.*, 1977, **76**, 541.
4 R. E. McMahon, H. R. Sullivan, J. C. Craig, and W. E. Pereira, *Arch. Biochem. Biophys.*, 1969, **132**, 575.
5 J. T. Groves, O. F. Akinbote, and G. E. Avaria, in 'Microsomes, Drug Oxidations, and Chemical Carcinogenesis,' eds. M. J. Coon, A. H. Conney, R. W. Estabrook, H. V. Gelboin, J. R. Gillette, and P. J. O'Brien, Academic Press, New York, 1980, p. 253.
6 (*a*) H. S. Mason, *Adv. Enzymol.*, 1957, **19**, 79; (*b*) D. Samuel, in 'Oxygenases,' ed. O. Hayaishi, Academic Press, New York, 1973, p. 31.
7 (*a*) G. A. Hamilton, J. R. Giacin, T. M. Hellman, M. E. Snook, and J. W. Weller, *Ann. N.Y. Acad. Sci.*, 1973, **212**, 4; (*b*) T. M. Hellman and G. A. Hamilton, *J. Am. Chem. Soc.*, 1974, **96**, 1530; (*c*) L. M. Hjelmeland and G. H. Loew, *ibid.*, 1977, **99**, 3514; (*d*) A. Hori, S. Takamuku, and H. Sakurai, *J. Org. Chem.*, 1977, **42**, 2318; (*e*) J. T. Groves, T. E. Nemo, and R. S. Myers, *J. Am. Chem. Soc.*, 1979, **101**, 1032; (*f*) J. T. Groves, W. J. Kruper, and R. C. Haushalter, *ibid.*, 1980, **102**, 6377; (*g*) H. J. Schneider and W. Müller, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 146; (*h*) E. Zadok and Y. Mazur, *ibid.*, p. 303; (*i*) D. Mansuy, J. F. Bartoli, and M. Momenteau, *Tetrahedron Lett.*, 1982, **23**, 2781.
8 (*a*) E. G. Hrycay, J. A. Gustafsson, M. Ingelman-Sundberg, and L. Enster, *Biochem. Biophys. Res. Commun.*, 1975, **66**, 209; (*b*) F. Lichtenberger, W. Nastainczyk, and V. Ullrich, *ibid.*, 1976, **70**, 939; (*c*) J. A. Gustafsson, L. Rondahl, and J. Bergman, *Biochemistry*, 1979, **18**, 865; (*d*) J. T. Groves, S. Krishnan, G. E. Avaria, and T. E. Nemo, *Adv. Chem. Ser.*, 1980, **191**, 277; (*e*) R. C. Blake and M. J. Coon, *J. Biol. Chem.*, 1981, **256**, 12127.
9 G. A. Hamilton, in 'Molecular Mechanisms of Oxygen Activation,' ed. O. Hayaishi, Academic Press, New York, 1974, p. 405.
10 (*a*) J. T. Groves and M. Van de Puy, *J. Am. Chem. Soc.*, 1976, **98**, 5290; (*b*) N. C. Deno, E. J. Jedziniak, L. A. Messner, M. D. Meyer, S. G. Stroud, and E. S. Tomezsko, *Tetrahedron*, 1977, **33**, 2503; (*c*) D. Mansuy, J. F. Bartoli, J. C. Chottard, and M. Lange, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 909; (*d*) I. Tabushi, T. Nakajima, and K. Seto, *Tetrahedron Lett.*, 1980, **21**, 2565; (*e*) C. L. Hill and B. C. Schardt, *J. Am. Chem. Soc.*, 1980, **102**, 6374.

11 W. Müller and H. J. Schneider, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 407.
12 G. A. Hamilton and J. R. Giacin, *J. Am. Chem. Soc.*, 1966, **88**, 1584.
13 D. M. Jerina, D. R. Boyd, and J. W. Daly, *Tetrahedron Lett.*, 1970, 457.
14 A. J. Davison and R. O. C. Norman, *J. Chem. Soc.*, 1964, 5404.
15 C. K. Chang and F. Ebina, *J. Chem. Soc., Chem. Commun.*, 1981, 778.
16 N. C. G. Cambell, J. R. P. Clarke, R. R. Hill, P. Oberhänsli, J. H. Parrish, R. M. Southam, and M. C. Whiting, *J. Chem. Soc. B*, 1968, 349.
17 S. Udenfriend, C. T. Clark, J. Axelrod, and B. B. Brodie, *J. Biol. Chem.*, 1954, **208**, 731.
18 V. Ullrich and H. J. Staudinger, *Z. Naturforsch., Teil B*, 1969, **24**, 583.
19 L. Kaplan, in ' Free Radicals,' ed. J. K. Kochi, Wiley, New York, 1973, vol. 2, p. 407.
20 S. Miyajima and O. Simamura, *Bull. Chem. Soc. Jpn.*, 1975, **48**, 526.
21 (*a*) F. R. Mayo, *Acc. Chem. Res.*, 1968, **1**, 193; (*b*) R. A. Sheldon and J. K. Kochi, *Oxid. Combust. Rev.*, 1973, **5**, 135.
22 (*a*) J. K. Kochi, *Rec. Chem. Prog.*, 1966, **37**, 207; (*b*) L. Castle, J. R. Lindsay Smith, and G. V. Buxton, *J. Mol. Catal.*, 1980, **7**, 235.
23 (*a*) T. Yamamoto and M. Kimura, *J. Chem. Soc., Chem. Commun.*, 1977, 948; (*b*) M. A. Brook, L. Castle, J. R. Lindsay Smith, R. Higgins, and K. P. Morris, *J. Chem. Soc., Perkin Trans. 2*, 1982, 687.
24 J. R. Lindsay Smith, B. A. J. Shaw, D. M. Foulkes, A. M. Jeffrey, and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 2*, 1977, 1583.
25 (*a*) J. Streith, B. Danner, and C. Sigwalt, *Chem. Commun.*, 1967, 979; (*b*) A. Alkaitis and M. Calvin, *ibid.*, 1968, 292.
26 E. Zadok and Y. Mazur, *J. Org. Chem.*, 1982, **47**, 2223.
27 Y. Ogawa, S. Iwasaki, and S. Okuda, *Tetrahedron Lett.*, 1981, **22**, 2277 and 3637.
28 J. R. Lindsay Smith and P. R. Sleath, *J. Chem. Soc., Perkin Trans. 2*, 1982, 1009.
29 S. A. Khan, M. Ashraf, and N. A. Chugtai, *Pak. J. Sci. Ind. Res.*, 1970, **13**, 30.
30 K. B. Wiberg, in ' Oxidation in Organic Chemistry,' ed. K. B. Wiberg, Academic Press, New York, 1965, p. 69.
31 (*a*) C. R. Hill and J. A. Smegal, *Nouv. J. Chim.*, 1982, 287; (*b*) J. R. Lindsay Smith, unpublished observations.
32 K. B. Wiberg and G. Foster, *J. Am. Chem. Soc.*, 1961, **83**, 423.

Received 3*rd December* 1982; *Paper* 2/2019