Hydroxylation of Linear Alkanes Catalysed by Iron Porphyrins: Particular Efficacy and Regioselectivity of Perhalogenated Porphyrins

J. F. Bartoli, O. Brigaud, P. Battioni and D. Mansuy*

Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques, URA 400, Université René Descartes, 45 rue des Saints-Pères, 75270 Paris Cedex 06, France

Iron porphyrins containing perhalogenated pyrroles are found to be much better catalysts for the hydroxylation of poorly reactive alkanes like pentane or heptane by PhIO (yields as high as 80%) than the corresponding iron porphyrins without halogens on the pyrrole rings; the chemoselectivity and regioselectivity of the oxidations are found to vary very much with the presence of pyrrole halogens suggesting a dramatic change in the structure of the oxygenating iron-oxo species.

Many systems using iron or manganese porphyrins as catalysts have been found to mimic cytochrome P-450-dependent monooxygenases.[1] Remarkable progress towards more efficient catalysts has been obtained by introducing halogen substituents on the meso-aryl groups of tetraphenylporphyrin,[2] Fe(tdcpp)Cl and Mn(tdcpp)Cl [tdcpp = tetra-(2,6-dichlorophenyl)porphyrin] being very good and stable catalysts for alkene epoxidation by various oxygen atom donors.[1,2] The stability and activity of these catalysts are much lower in the oxidation of less reactive substrates such as linear alkanes. Very recently, iron tetraarylporphyrins bearing eight halogen substituents (Br,[3] Cl,[4] F[5]) on the pyrrole rings have been prepared. Preliminary results appeared in favour of a better efficacy of these catalysts,[3–5] but very few data on their intrinsic reactivity relative to Fe(tdcpp)Cl, for instance, have been reported to date.

This communication compares the abilities of various iron porphyrins with or without halogen substituents on the pyrrole rings to catalyse the hydroxylation of heptane or pentane by PhIO. It shows that the presence of halogen substituents on the porphyrin ring not only increases dramatically the yields of hydroxylation of these poorly reactive substrates, but also leads to active species exhibiting very different chemo- and regio-selectivities.

All the prepared iron porphyrins (Fig. 1)† belonging either to the tdcpp or tF$_5$pp (tetrapentafluorophenylporphyrin) series and containing different numbers of electron-withdrawing substituents on the meso-aryl or pyrrole rings, catalysed the hydroxylation of heptane by PhIO. However, the total yields based on PhIO were very much dependent on the number of halogen substituents on the porphyrin ring (Table 1). Among the catalysts bearing no halogen substituent on their pyrrole rings, only Fe(tF$_5$pp)Cl gave a good oxidation yield (70%), Fe(tpp)Cl and Fe(tmp)Cl leading only to very low yields (<5%) under the conditions employed. Interestingly, in the tdcpp series, the introduction of eight Cl or Br substituents on the pyrrole rings led to a spectacular increase of the yields (36 to 80%). The same tendency was observed for

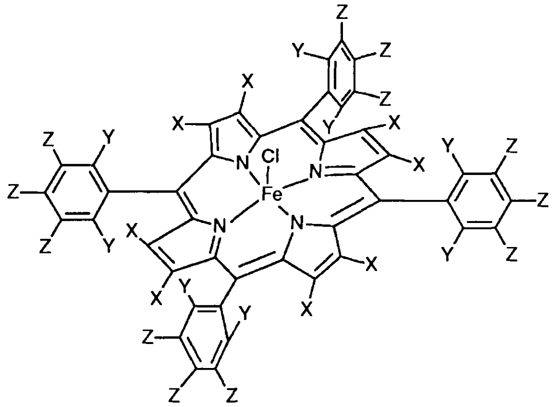
---

† All the Fe(tetra-mesoaryl porphyrin)Cl complexes,[6] Fe(tdcpBr$_8$p)Cl,[3] Fe(tdcpCl$_8$p)Cl[4] and Fe(tF$_5$pCl$_8$p)Cl[4] were prepared by previously described techniques. Their purity was checked by ^{1}H and ^{19}F NMR, mass spectrometry and thin-layer chromatography. Fe(tdcpBr$_6$p)Cl was prepared by iron insertion into tdcpBr$_6$p obtained as a minor product of bromination of tdcpp, the reaction used to prepare tdcpBr$_8$p.[3] The presence of 6 Br substituents on the pyrrole rings was shown by ^{1}H NMR and mass spectrometry, but their relative positions on the pyrrole rings were not determined.

Table 1 Hydroxylation of linear alkanes by PhIO catalysed by various iron-porphyrins[a]

	Heptane						Cyclooctene + heptane	Pentane				
	Product yields (%)						Epoxide: heptanols + heptanones	Product yields (%)				
Catalyst	1-ol	2-ol	3-ol	4-ol	-ones[b]	Total yield	radio[d]	1-ol	2-ol	3-ol	-ones[b]	Total yield
Fe(tdcpp)Cl	1	14	7.5	3.5	6	38	8.2	0.8	16.5	4.5	5	32
		(58)	(30)	(12)[c]					(78)	(22)[c]		
Fe(tdcpBr$_6$p)Cl	1.4	20	12	5.5	2.5	44	3.6					
		(53)	(32)	(14)[c]								
Fe(tdcpBr$_8$p)Cl	1.5	29.5	28	11	5	80	2.8	1	34	15	3	56
		(42)	(41)	(16)[c]					(69)	(31)[c]		
Fe(tdcpCl$_8$p)Cl	1.5	29	27	10.5	5	78	2.9	2	34	16	4	60
		(43)	(40)	(16)[c]					(68)	(32)[c]		
Fe(tF$_5$pp)Cl	1	25.5	24	10.5	4	69	1.7	1	24	11	2	40
		(41)	(39)	(20)[c]					(68)	(32)[c]		
Fe(tF$_5$pCl$_8$p)Cl	1.5	22	21.5	9	5	64	1.5					
		(41)	(40)	(19)[c]								
Fe(tmp)Cl[e]		1.7	0.8	0.3	0.5	4	10					
		(60)	(31)	(9)								
Fe(tpp)Cl[e]		1.2	1.4	0.6	<0.2	3.5	6.2					
		(38)	(42)	(20)								

[a] *Conditions*: Alkane : PhIO : Fe = 800 : 20 : 1 in CH_2Cl_2 (catalyst concentration 2 mmol dm^{-3}), 1 h at 20°C. Yields based on starting PhIO (PhIO was completely consumed in each case). For total yields, it was assumed that 2 moles of PhIO were necessary for ketone formation. [b] Only the total yields of 2-, 3- and 4-heptanones in the case of heptane, and of 2- and 3-pentanones in the case of pentane were given. Their relative proportions were always equal to the indicated relative proportions of the corresponding alcohols. [c] Values in parentheses correspond to the relative proportions of oxidation products (ol + one) on positions 2, 3 and 4 of heptane, or on positions 2 and 3 of pentane. [d] Competition experiments were performed under the conditions: heptane : cyclooctene : PhIO : catalyst = 2000 : 20 : 20 : 1 in CH_2Cl_2 at 20°C for 1 h. The ratios cyclooctene oxide–heptanols + heptanones are indicated. [e] tpp = tetraphenylporphyrin; tmp = tetra-(2,4,6-trimethylphenyl)porphyrin.



Y = Z = X = H Fe(tpp)Cl

Y = Cl, Z = X = H Fe(tdcpp)Cl
Y = Cl, X = Br, Z = H Fe(tdcpBr$_8$p)Cl
Y = Cl, X = Cl, Z = H Fe(tdcpCl$_8$p)Cl

Y = Z = F, X = H Fe(tF$_5$pp)Cl
Y = Z = F, X = Cl Fe(tF$_5$pCl$_8$p)Cl

Fig. 1

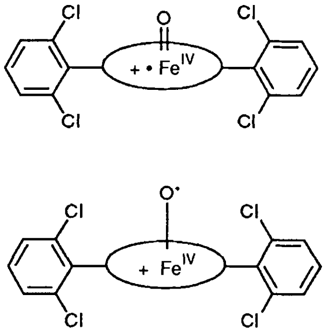


Fig. 2 Possible structures for the porphyrin iron-oxo active species (the possible presence of a Cl ligand or counteranion is not indicated)

pentane hydroxylation, the total yield increasing from 32 to 60% from Fe(tdcpp)Cl to Fe(tdcpCl$_8$p)Cl. This 60% yield obtained under very mild conditions is remarkable for such a poorly reactive linear alkane.[7]

As far as the regioselectivity of heptane or pentane hydroxylation is concerned, only very low amounts of compounds coming from the hydroxylation of the methyl groups were formed, and the secondary alcohol ratios observed with the non-hindered porphyrins of the tF$_5$pp series corresponded to an almost statistical oxidation only linked to the number of secondary abstractable hydrogen atoms, as previously described for Fe(tpp)Cl[8] (2- : 3- : 4-ol around 40 : 40 : 20). In the case of Fe(tdcpp)Cl, the presence of bulky *ortho* Cl substituents led to a ratio favouring the more accessible position 2 of the alkane.[9] However, surprisingly, the introduction of Cl or Br substituents on the pyrroles of tdcpp led to a progressive change of this regioselectivity towards the statistical one [from a 2- : 3- : 4-ol ratio of 58 : 30 : 12 for Fe(tdcpp)Cl to 43 : 40 : 16 for Fe(tdcpCl$_8$p)]. The same tendency was observed in pentane hydroxylation, the 2- : 3-ol ratio changing from 78 : 22 for Fe(tdcpp)Cl to 67 : 33 for Fe(tdcpCl$_8$p)Cl.

This was presumably due to a dramatic change in the structure and/or intrinsic reactivity of the active oxygen species. In order to know whether this regioselectivity change was accompanied by a change in the chemoselectivity of the active species, we have studied the oxidation of a cyclooctene–heptane (molar ratio 1 : 100) mixture by PhIO in the presence of the various iron porphyrin catalysts. As shown in Table 1, there was a marked variation of the (cyclooctene epoxide–heptanols + heptanones) ratio as a function of the porphyrin structure. This ratio decreased from 10 for the most electron-rich Fe(tmp)Cl catalyst to 1.5 for the most electron-deficient

Fe(tF$_5$pCl$_8$p)Cl catalyst. In the tdcpp series, this ratio varied from 8.2 for Fe(tdcpp)Cl to 3.6 for Fe(tdcpBr$_6$p)Cl and 2.8 for Fe(tdcpBr$_8$p)Cl. The polyfluorinated iron porphyrins of the tF$_5$pp series showed the most pronounced effect with a ratio of 1.7 for Fe(tF$_5$pp)Cl and of 1.5 for Fe(tF$_5$pCl$_8$p)Cl, indicating their better chemoselectivities for C–H bond hydroxylation. Preliminary results indicated the same type of variations of this ratio for identical experiments performed with the corresponding Mn^{III}-porphyrins [from 5.3 for Mn(tdcpp)Cl to 0.9 for Mn(tF$_5$pCl$_8$p)Cl].

For each catalyst, the products obtained appear to be derived from only one active species as the product ratios were found constant as a function of the reaction time. This active species formed upon reaction of all the iron porphyrins studied with PhIO could be a high-valent iron-oxo complex[1,10] acting as an electrophilic radical.[1,11] Accordingly, similar regioselectivity changes were observed in experiments using another oxygen atom donor, magnesium monoperoxyphthalate,[12] instead of PhIO (data not shown). They should be due to a dramatic change either of the porphyrin structure caused by the presence of the bulky Br or Cl pyrrole substituents, or of the electronic structure of the iron-oxo intermediate. More experiments are necessary to conclude between the relative importance of these two factors on the regioselectivity variations.

As far as the observed chemoselectivity changes are concerned, the marked decrease of the epoxide : alcohol ratio obtained by increasing the number of halogen substituents either on the meso-aryl groups [as in Fe(tF$_5$pp)Cl] or on the pyrrole rings [as in Fe(tdcpCl$_8$p)Cl] should be due to a change in the electronic structure and intrinsic reactivity of the iron-oxo species, as it occurs with non-hindered as with hindered porphyrins. This results in its increased tendency to abstract hydrogens even though its addition to double bonds remains predominant [even in the best case of Fe(tF$_5$pCl$_8$p)Cl, each secondary C–H bond of heptane is about 1500-fold less reactive than the cyclooctene double bond]. These data would be in favour of an iron-oxo species with more Fe–O$^{\bullet}$ character in the case of the highly halogenated porphyrins with an easier access of substrates to the active species because of a longer Fe–O bond, and a greater tendency to abstract hydrogen atoms. In fact, when going from the electron-rich Fe(tmp)Cl to the very electron-poor Fe(tdcpCl$_8$p)Cl, the active species could progressively vary from a (porphyrin)$^{+\cdot}$ Fe^{IV}=O[10] [or (porphyrin) Fe^{V+}=O] to a (porphyrin) Fe^{IV+}–O$^{\bullet}$ structure (Fig. 2), because of the decreased ability of electron-deficient porphyrins to exist as radical cations or to stabilize an Fe^{V} species.

The present results show the remarkable activity of iron perhalogenated porphyrins in the catalysis of linear alkane hydroxylation, and indicate that it is possible to induce large variations in the intrinsic reactivity and regioselectivity of the active species derived from reaction of PhIO with iron porphyrins by introducing halogen substituents on their pyrrole rings.

We thank Profs P. S. and T. G. Traylor for fruitful discussions on the interpretation of the data.

Received, 17th October 1990; Com. 0/04672H

References

1 For recent reviews: T. J. McMurry and J. T. Groves, in *Cytochrome P-450, Structure, Mechanism and Biochemistry*, ed. P. R. Ortiz de Montellano, Plenum Press, New York and London, 1986, pp. 1–28; B. Meunier, *Bull. Soc. Chim. Fr.*, 1986, II, **4**, 578–594; D. Mansuy, *Pure Appl. Chem.*, 1987, **59**, 759–770; D. Mansuy, P. Battioni and J. P. Battioni, *Eur. J. Biochem.*, 1989, **184**, 267–285.

2 C. K. Chang and F. Ebina, *J. Chem. Soc., Chem. Commun.*, 1981, 778; P. S. Traylor, D. Dolphin and T. G. Traylor, *J. Chem. Soc., Chem. Commun.*, 1984, 279; M. J. Nappa and C. A. Tolman, *Inorg. Chem.*, 1985, **24**, 4711.

3 T. G. Traylor and S. Tsuchiya, *Inorg. Chem.*, 1987, **26**, 1338.

4 D. H. Dolphin, T. Nakano, T. K. Kirk, T. E. Marone, R. L. Farrell and T. P. Wijesekera, Patent PCT Int. Appl. WO 88/07 988, 1988.

5 S. Tsuchiya and M. Seno, *Chem. Lett.*, 1989, 263.

6 J. S. Lindsey and R. W. Wagner, *J. Org. Chem.*, 1989, **54**, 828.

7 P. Battioni, J. P. Lallier, L. Barloy and D. Mansuy, *J. Chem. Soc., Chem. Commun.*, 1989, 1149.

8 D. Mansuy, J. F. Bartoli and M. Momenteau, *Tetrahedron Lett.*, 1982, **23**, 2781.

9 P. Battioni, J. P. Renaud, J. F. Bartoli, M. Reina-Artiles, M. Fort and D. Mansuy, *J. Am. Chem. Soc.*, 1988, **110**, 8462.

10 J. T. Groves, R. C. Haushalter, M. Nakamura, T. E. Nemo and B. J. Evans, *J. Am. Chem. Soc.*, 1981, **103**, 2884; B. Boso, G. Lang, T. J. McMurry and J. T. Groves, *J. Chem. Phys.*, 1983, **79**, 1122; A. L. Balch, L. Latos-Grazynski and M. W. Renner, *J. Am. Chem. Soc.*, 1985, **107**, 2983; T. S. Calderwood and T. C. Bruice, *Inorg. Chem.*, 1986, **25**, 3722; H. Sugimoto, H-C. Tung and D. T. Sawyer, *J. Am. Chem. Soc.*, 1988, **110**, 2465; A. Gold, K. Tayaraj, P. Doppelt, R. Weiss, G. Chottard, E. Bill, X. Ding and A. X. Trautwein, *J. Am. Chem. Soc.*, 1988, **110**, 5756.

11 P. Inchley, J. R. Lindsay Smith and R. J. Lower, *New J. Chem.*, 1989, **13**, 669.

12 C. Querci and M. Ricci, *Tetrahedron Lett.*, 1990, **31**, 1779.