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REGIOSELECTIVITY CHANGES IN HEXANE HYDROXYLATION BY IODOZOBENZENE CATALYZED BY TETRAARYLPORPHYRINATOIRON COMPLEXES

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Summary: Regioselectivity of hexane hydroxylation by iodozobenzene was correlated with electronic and steric constants of substituted porphyrins and revealed the increase of the relative rate of an attack at terminal methyl- and methylene-groups of hexane in sterically hindered and electron-deficient porphyrinatoiron complexes.

Some forms of cytochrome P-450 and ω-hydroxylase demonstrate an unusual selectivity in alkane oxidation with preferable hydroxylation of terminal methyl and methylene groups next to methyl.[1] Well-known chemical models of alkane hydroxylation based on tetraphenylporphyrinatoiron do not result in such unusual selectivity,[2,3] Recently the increase of relative hydroxylation rate has been observed at more accessible alkane terminal C-H bonds, catalyzed by sterically hindered iron porphyrins[4] or in the reactionsin microheterogeneous systems.[5]

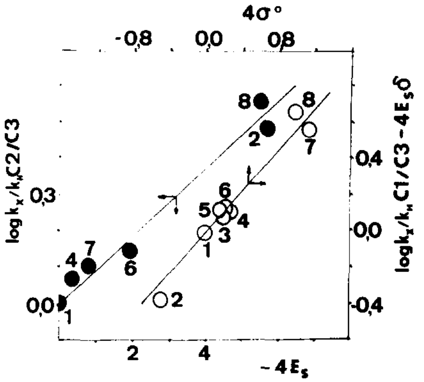
By modifying porphyrin ligands we have now succeeded in regioselectivity changes in hydroxylation at terminal C-H bond in hexane catalytically with iodozobenzene as an oxygen source. As the Table show, substitution of phenyl groups considerably changes the distribution of hexylic alcohols.

Table. Distribution of Isomeric Hexylic Alcohols Calculated per C-H Bond in Ironporphyrin-Catalyzed Hydroxylation of Hexane with PhIO.

Porphyrin	Hexanol -1	Hexanol -2	Hexanol -3	Yield of Alcohol on PhIO(%)
1 Tetraphenylporphyrin	0.010	1.0	1	13
2 Tetrmesytilporphyrin	0.028	2.5	1	23
3 Tetra(p-fluorophenyl)porphyrin	0.012	1.1	1	19
4 Tetra(o-fluorophenyl)porphyrin	0.014	1.2	1	35
5 Tetra(p-chlorophenyl)porphyrin	0.012	1.1	1	19
6 Tetra(o-chlorophenyl)porphyrin	0.025	1.4	1	30
7 Tetra(pentafluorophenyl)porphyrin	0.043	1.3	1	40
8 Tetra(o-nitrophenyl)porphyrin	0.320	4.0	1	32

In a typical experiment, 1.25 μmol of FePCl are dissolved in 0.5 mL C_6H_6; 0.5 mL of hexane and 68 μmole PhIO are added and the reaction mixture is stirred magnetically at room temperature. After 3 h, the mixture is analyzed by GLC.

Evidently, the regioselectivity in hexane oxidation may be attributed to electronic and steric effects of active species. We have found that the ratio of hexanol-2 formed to hexanol-3 correlates with steric constants of substituents in ortho-position (Eq. 1) and the ratio of hexanol-1 to hexanol-3 depends on the steric[6] and electronic[7] constants of the substituents of phenyl groups (Eq. 2) (Figure).



$$\log k_X/k_H(C2/C3) = -0.38\ E_s \qquad (1)$$

$$\log k_X/k_H(C1/C3) = 0.15\sigma^{\circ} - 0.60E_s \qquad (2)$$

Figure. A Taft plot for the hexane hydroxylation reaction (numbers in the Figure correspond to those in the Table).

Thus we can suppose that just these two effects, electronic and steric created from proximal protein surrounding of hydroxylase active species, promote the unusual selectivity in alkane hydroxylation. We hope that the mysterious enzymatic hydroxylation can be understood in simple chemical terms.

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