Tetrahedron Letters, Vol.27, No.1, pp 51-54, 1986
Printed in Great Britain

0040-4039/86 $3.00 + .00

CATALYTIC HYDROXYLATION ON AROMATIC RINGS BY USE OF AN ARTIFICIAL P-450 SYSTEM ASSISTED BY ACID AND ACID ANHYDRIDE.

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Aromatic compounds are effectively monohydroxylated by the artificial P-450 type catalytic system, consisting of TPP•Mn, N-methylimidazole, colloidal Pt, O_2 and H_2. Addition of benzoic anhydride and/or hydrogen chloride favored o- and p-hydroxylation.

The accumulation of valuable structural and mechanistic information on monooxygenation through dioxygen activation by native cytochrome P-450$^{1)}$ allows one to design a system consisting of totally artificial molecules which mimicks the efficient biological monooxygenation reaction$^{2)}$. In addition, several carefully designed systems which produce P-450 type activity via oxygen atom transfer have been reported recently$^{3)}$. Among the monooxygenation reactions studied by the use of these artificial P-450 type systems, hydroxylation of aromatic rings has gained least achievement. Especially difficult is to gain large turn over$^{4)}$ (mol of product formed/mol of catalyst employed•unit time) and/or number of recycling (i.e., mol of products formed/mol of catalyst consumed). We now wish to report that our effective O_2 activation system, TPP•Mn and H_2/colloidal Pt supported on a synthetic polymer$^{2,5)}$, performs aromatic hydroxylation with good yields and reasonable recycling numbers.

A typical catalytic system consists of 1.4×10^{-5} mol (3.5×10^{-3} M) of TPP•Mn^{III}•Cl^-, 6×10^{-9} particle eqv$^{6)}$ of colloidal Pt supported on PVP (polyvinylpyrrolidone) (1.5×10^{-3} M), a H_2/O_2 mixed gas (1/1 vol/vol) at atmospheric pressure, and an aromatic substrate (1.4×10^{-2} mol) (3.5 M) dissolved in 3 mL of EtOH. After 1-40 h reaction at room temperature, products were conveniently analyzed by GLC. For further structure determination of the products, GLC-Mass and GLC-IR spectroscopy were used. Phenol was obtained from benzene as the sole detectable product at low conversion. Neither quinone nor dihydroxybenzenes were detected up to 1.80 (mol/mol) phenol formation based on the TPP•Mn^{III} employed. Substituted phenols were similarly obtained from substituted benzenes (eqn 1). From toluene, cresols and benzyl alcohol

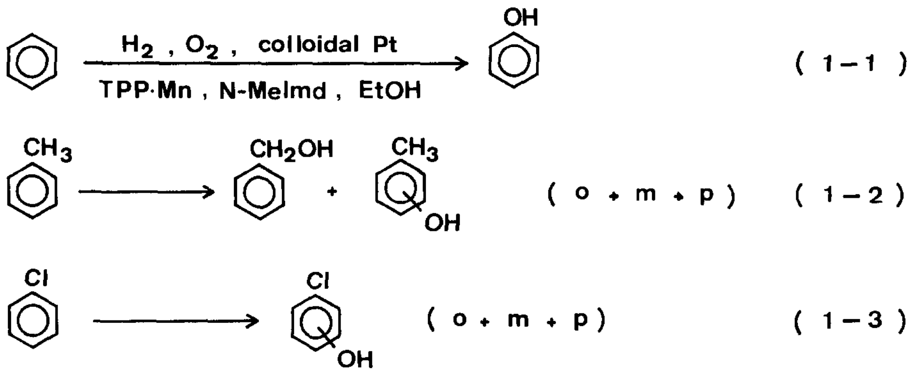


Table 1 Hydroxylation of aromatic compounds by artificial P-450 system

substrate (mol)	HCl (mol)	$(PhCO)_2O$ (mol)	Turnover[a] $\frac{\text{prod mol}}{\text{cat mol}}$		product distribution (%)			
benzene					phenol			
(1.4 x 10^{-2})	0	0	.49	(1.30)[b]				
	2 x 10^{-4}	0	.59	(1.70)				
	2 x 10^{-3}	0	1.03	(7.90)				
	2 x 10^{-3}	2 x 10^{-3}	1.79	(24.80)				
toluene					$PhCH_2OH$	o-	m-	p-cresol
(1.4 x 10^{-2})	0	0	2.40	(5.70)	60	23	6	12
	1 x 10^{-3}	0	3.56	(15.90)	45	30	8	17
	2 x 10^{-3}	0	3.07	(22.90)	34	33	8	25
	0	1 x 10^{-3}	3.02	(10.90)	42	33	7	18
	1 x 10^{-3}	2 x 10^{-3}	4.14	(21.20)	31	40	9	20
	2 x 10^{-3}	2 x 10^{-3}	4.16	(33.30)	12	41	15	32

TPP·Mn^{III} Cl: 1.4 x 10^{-5} mol, N-methylimidazole: 2.8 x 10^{-3} mol
Pt/PVP: 6 x 10^{-9} particle equiv. 40 h

a) Yields based on the aromatic hydrocarbons consumed were practically quantitative throughout the experiments.

b) Turnover in parenthese were based on TPP·Mn^{III}·Cl consumed.

were formed; the ratio of these products was markedly affected by the addition of HCl (present in a form of N-MeImd·H^+Cl^-) and/or benzoic anhydride to favor ring hydroxylation as shown in Table 1. The combined yield of the products also increased by the addition of HCl and/or benzoic anhydride, up to 4.16

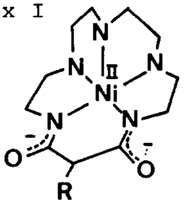
mol/mol of TPP•Mn emplyed, while the recycling number increased from 5.7 to 33.3 (mol/mol). These recycling numbers or turn over are much better than similar O_2 activation system reported in literature[4)] as shown in Table 2,

Table 2 Aromatic Monooxygenation by Native and Artificial P-450 Type Catalyst Systems

substrate	catalysts	combined product mol/mol catalyst			ref.
		(A)	(B)	(C)	
PhH	TPP•Mn^{III}/Pt	1.79	—	0.002	this work
	PhIO/Fe^{III}•TPP	0			4a
	complex I[b)]	ca 0.40	—	—	4b
$Ph\text{-}CH_3$	TPP•Mn^{III}/Pt	4.16	—	0.004	this work
	PhIO/Fe^{III}•TPP		0.009		4a
	rabbit microsome	—	—	0.06	8

a) A: based on catalyst used, B: on O source, C: on substate

b) complex I



but are much worse than epoxidation of olefins. In the epoxidation of nerol 143.9 mol of epoxide (per mol of T_{SO_3Na}PP•Mn employed) was obtained or recycling number of T_{SO_3Na}PP•Mn is 533^{3}mol/mol). The observed poor reactivity of aromatic compounds compared with olefins are partly due to inherent reactivity difference between aromatics and alkenes but also partly due to the remarkable retardation of P-450 type activity by phenol formed in the course of the reaction. The retardation capacity of phenols were clearly shown for epoxidation of nerol when phenol was initially added to the reaction system (see Fig 1), where formation of epoxide were decreased by more than factor of 2. Remarkable adsorption of phenol on colloidal Pt was ascertained by separated experiments but coordination of phenol to Mn was not detected under the condition, suggesting the inhibition effect is important for automatic retardation of further oxidation due to adsorption of the phenols on the colloidal Pt surface, activity of which is important in the rate-determining conversion $Mn^{III} \rightarrow Mn^{II}$

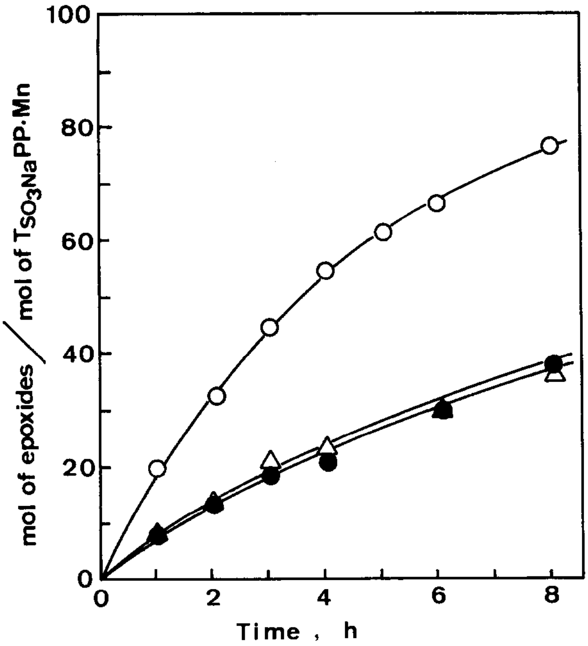


Fig. 1
Inhibition of nerol epoxidation by the addition of phenols

○ : Nerol: 2.8×10^{-3} mol,
$T_{SO_3Na}PP\cdot Mn^{III}$: 2.8×10^{-5} mol
Pt/PVA: 3.0×10^{-6} g equiv.,
Imidazole: 2.8×10^{-3} mol
● : Addition of phenol
(2.8×10^{-4} mol)
△ : Addition of p-chlorophenol
(2.8×10^{-4} mol)

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(Received in Japan 15 October 1985)