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A Versatile Aerobic Oxidation of Organic Compounds Catalyzed by Cobalt(II) Porphyrins

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Abstract: Co(II)porphyrin (1a-d) acts as a versatile catalyst during the oxidation of a wide range of organic substrates at ambient conditions by using a combination of molecular oxygen and 2-methylpropanal. The versatility of these catalysts is demonstrated by oxidation of alkenes, allylic or benzylic substrates, alcohols, and hydrocarbons to the corresponding oxidized products at ambient conditions. © 1997 Elsevier Science Ltd.

Introduction

Synthetic metalloporphyrin catalyzed oxidation of organic substrates has emerged as a good biological model^{1,2} for oxidations involving enzymatic reactions of mono³ and dioxygenases. These model reactions normally utilize exogenous oxygen donors like iodosyl benzene, periodate, and hydroperoxide as the effective oxygen source in the absence of dioxygen. These efforts have culminated in the development of a new generation of synthetic metalloporphyrin which are able to reproduce and mimic all hemenzyme mediated reactions like oxygenation, oxidation, oxidative chlorination and dismutation.⁴⁻¹³ As a result of these advances, metalloporphyrin derived from Fe, Mn, Cr, Rh and Co, have come to enjoy very prominent position among the class of versatile catalysts for the oxidation of wide range of organic molecules. Metalloporphyrin



catalyzed oxidation using molecular oxygen requires two electrons and two protons to reduce the second oxygen atom of dioxygen to water, and most of the studies reported use borohydride, hydrogen and colloidal particles, Zn or electron from an electrode as reducing agent.¹³ Most of the studies related to metalloporphyrin were undertaken as mimics of CytP450 mediated¹⁴ epoxidation reaction as pioneered¹⁵ by Tabushi in 1979. Subsequent to Tabushi's work^{15,16} some groups have also used ascorbic acid or aldehyde as a reductant during metalloporphyrin catalyzed oxidation with molecular oxygen. In continuation of our studies on Co(II) Schiff's base complex catalyzed dioxygen activation with aldehyde we became interested in the Co(II) porphyrin¹⁷ catalyzed oxidation of organic substrates with dioxygen. We now demonstrate that Co(II) porphyrin complex **1a** functions as a versatile catalyst¹⁸ during the oxidation of these findings are described below.

Results and Discussion

Our earlier studies¹⁹ have indicated that aldehydes and keto-esters promote the oxidation of alkenes and alcohols with dioxygen by cobalt(II)schiff's base complexes. We have demonstrated that carbonyl compounds assist the formation of a Co(III) dioxygen complex and subsequently they act as a reducing agent during oxygen atom transfer to organic substrates. In continuation of these efforts we have also investigated some Co(II) porphyrin catalyzed oxidation of organic substrates with dioxygen in the presence of 2-methyl propanal. Accordingly four Co(II) porphyrin complexes²⁰ (1a-d) were prepared and their role as a catalyst during oxygen activation was studied. We next explored the catalytic activity of complex 1a and according to our previously described protocol,¹⁹ various organic substrates were oxidized in the presence of 2 equivalents of 2-methylpropanal under oxygen balloon at ambient conditions. According to this protocol methyl styrene 2, stilbene 3, farnesyl acetate 4 were transformed to the corresponding epoxides 2a-4a in nearly quantitative yields (Table 1). It is noteworthy that trans stilbene afforded the corresponding trans epoxide 3a whereas highly regioselective monoepoxidation of farnesyl acetate to give 4a was observed under these conditions. Similarly, limonene 6 was readily transformed to a mixture of mono 5b and diepoxide 5a in 1:2.3 ratio in quantitative yields (Table 1). Interestingly, the α , β unsaturated carbonyl compounds i.e. chalcone 6 and ethyl cinnamate 7 were epoxidised in good yields to give stereochemically pure trans epoxides 6a and 7a respectively. Catalyst 1a was also efficient during benzylic oxidation as fluorene 8 was efficiently transformed under these conditions to the corresponding ketone 8a in good yields. Even secondary alcohols like (-)-menthol 9 underwent smooth oxidation to the corresponding ketone 9a in high yields. The versatility of catalyst 1a is also evident during the oxidation of cyclohexane 10 to a mixture of cyclohexanol 10a and cyclohexanone 10b. It is interesting to note that the oxidation of cyclohexane 10 is catalyzed by 1a at ambient conditions. In order to probe the substituent effect in the para position of aromatic ring of porphyrin the catalytic activity of four cobalt porphyrin complex la-d with different para substituents were studied and results indicated that the p-substituent displays some effect during these oxidations. Thus, the oxidation of

substrate	product(s) ^b	yield(%) ^a
Ph H_3C	$\begin{array}{c} Ph & O \\ H_{3}C & 2a \end{array}$	94
PhPh	Ph O $3a$ Ph	100
4 OAc		DAc 80
	5a (2.3 : 1) $5b$	100¢
Ph R=Ph =OEt 7	$\begin{array}{c} Ph \underbrace{\bigcirc}_{O} \\ 6a \\ 7a \\ 0 \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $	83 51
		58
У ОН	9a	76
10	$\bigcup_{10a}^{OH} + \bigcup_{10b}^{O}$	26

 Table 1. Co(II) Porphyrin 1a Catalyzed Oxidation of Organic Substrates using 2-Methylpropanal and Dioxygen

^aIsolated yield. ^bYield determined from ¹H-NMR of the crude reaction mixture. ^cObtained as a mixture of syn-anti diastereomers

indane and fluorene in the presence of **1a** or **1b** provided better yields as compared with the oxidation using ' **1c** or **1d** (Table 2, entries 1 and 2). Similarly, oxidation of cyclohexane to a mixture of cyclohexanol and cyclohexanone was achieved in moderate yields using **1a** or **1b** whereas catalysis using **1c** or **1d** provided comparatively low yields of these products (Table 2, entry 3). Interestingly, limonene underwent oxidation using of **1a** or **1b** to afford a diastereomeric (1:1 anti-syn) mixture of corresponding di and monoepoxide in quantitative yields (Table 2, entry 4) and it is noteworthy that the diepoxide was found to be the major product in both these reactions. On the other hand the oxidation of limonene in the presence of **1c** afforded a low yield of monoepoxide only. The results described in table 2 clearly show that Co(II)porphyrin having electron donating groups in the para position of the aromatic ring of the porphyrin (**1a-b**) act efficiently during the oxidation of benzylic, allylic and double bond oxidations whereas the presence of a para chloro or acetoxy substituent (**1c-d**) provides moderate to low yields of the oxidized products. It is also clear that

Entry	Substrate	Catalyst	Product(s)	Yield (%) ^a
1		1a 1b 1c 1d		86 82 54 26
2		1a 1b 1c 1d		58 39 36 29
3	\bigcirc	1a 1b 1c 1d	OH O	26 (44:56) ^b ,c 24 (39:61) 20 (50:50) 16 (40:60)
4		1a 1b 1c		26 (1:2.3)¢ 24 (1:3) 20 (1:)

Table 2. Cobalt(II) Porphyrin 1a-d Catalysed Oxidation of Organic substrates with Dioxygen

alsolated yield. ^bRatio determined from GC. ^cRatio determined from ¹H NMR of the crude reaction mixture

the oxidation of cyclohexane is not affected to any significant extent by the para substituent of the catalyst 1a-d.

We have also observed the effect of structure of aldehyde during the oxidation of limonene in the presence of catalyst 1a (Table 3). Thus the oxidation using 2-methylpropanal afforded a diastereomeric(1:1 syn and anti) mixture of di and mono epoxide in 2.5:1 ratio whereas this ratio is reversed to 1:3 in the

	Co(II)TPP-OMe,O ₂ , r.t. RCHO,CH ₃ CN, 3-4h	+	↓° ↓°
Entry	Carbonyl Compound	Product(s) ratio of products ^b ,c	Yield(%) ^a
1.	>сно	(2.5:1)	100
2.	<u> </u>	(13)	80
3.	СНО	(1:5)	55
4.	PhCHO	NR	

Table 3. Cobalt(II) porphyrin 1a Catalyzed Epoxidation of Limonene with Dioxygen

^aIsolated yield based on limonene. ^bRatio determined from ¹H NMR of the crude reaction mixture. ^cMono and diepoxide are obtained as a 1:1 mixture of syn and anti diastereomers. NR: No Reaction

reaction using n-butanal (Table 3, entry 2). Interestingly this ratio turther enanges to 1:5 when crotonaldehyde is used for this oxidation (Table 3, entry 3). It is also noteworthy that no significant oxidation of limonene is observed in the presence of benzaldehyde (Table 3, entry 4). This dramatic change in the ratio of di and monoepoxide in going from 2-methylpropanal to crotonaldehyde is quite intriguing and we don't have a plausible explanation for this observation. In order to elucidate the mechanism of this reaction we have

Table 4. Cobalt(II) porphyrin 1a-c Catalyzed Oxidation of Cyclohexene with Dioxygen



Entry	X	Products ratio(epoxide:alcohol:ketone) ^b		Yield(%) ^a	
1.	OMe(la)	*	(1:3:1.2)	84	
2.	Me(1 b)		(-:1.2:1)	76	
3.	Cl(1 c)		(1:1.9:1)	82	

^alsolated yield of the mixture of compounds. ^bRatio determined from ¹H-NMR of the crude reaction mixture.

carried out the oxidation of cyclohexene with catalyst **1a-c**. Thus oxidation of cyclohexene using **1a** as catalyst afforded a mixture of corresponding epoxide, cyclohexenol, cyclohexenone in 1:3:1.2 ratio (Table 4, entry 1). On the other hand oxidation of cyclohexene in the presence of **1b** yielded only a mixture of cyclohexenol and cyclohexenone whereas catalysis under **1c** gave rise to a mixture of epoxide, cyclohexenol, and cyclohexanone respectively (Table 4, entries 2-3). These results are similar to oxidation of cyclohexene in the presence of Fe-porphyrin^{2a-e} and it is conceivable that the oxidation described herein are also proceeding via an analogous cobalt oxo species.

In conclusion, the present studies indicate that cobalt(II)porphyrin (1a-d) are efficient catalysts during the aerobic oxidation of wide range of organic substrates. These studies have also shown that the para substituent in the aromatic ring of the cobalt(II)porphyrin (1a-d) play a significant role during aerobic oxidation of organic substrates.

Experimental Section

Materials and Methods. Acetonitrile was purified by the standard procedure. Pyrrole was purchased from Aldrich. Column Chromatography was performed by using ACME silica gel(60-120). Aldehydes and alkenes were purchased commercially and purified prior to use. H^1 -NMR spectra were recorded at 60 and 80 MHz in CCl₄, CDCl₃, IR spectra were recorded on a Perkin-Elmer 1320 spectrometer. HPLC was carried out on Shimadzu LC-6A liquid chromatography using zorbax sil column. GC was carried out on 5765 Nucon Gas Chromatograph using silica gel (80-100 mesh) column. All the known compounds were characterized by comparison with the data from the literature. Cobalt(II)porphyrin 1a-d were prepared accordingly to literature procedure²⁰.

General Procedure for Epoxidation and Allylic oxidation. Aldehyde (10 mmol), alkene (5 mmol) and cobalt(II) porphyrin complex (2.5 mol%) were stirred in anhydrous acetonitrile (25 mL) at ambient temperature under oxygen balloon for 3 hours. The solvent was removed in vacuo and the residue was dissolved in ethyl acetate (30 mL). The ethyl acetate layer was washed with saturated sodium carbonate solution (3 x 15 mL), the brine solution (3 x 10 mL). Drying over anhydrous sodium sulphate and evaporation yielded a residue which was subjected to silica gel column chromatography. Compounds 2a, 3a, 5b, 6a (Table 1) and cyclohexenol, cyclohexenone, and cyclohexene epoxide (Table 4) were prepared according to this procedure and characterized by comparing their NMR, IR and GC analysis with literature^{19b} and standard samples.

General Procedure for the Oxidation of Alcohols and Benzylic Compounds. Aldehyde (10 mmol), alcohol or benzylic compound (5 mmol) and cobalt(II) porphyrin complex (2.5 mol%) were stirred in anhydrous acetonitrile (25 mL) at ambient temperature for 3 hours under oxygen balloon. Usual workup as described above gave the residue which was purified by silica gel column chromatography or analyzed by HPLC Compounds 8a, 9a (Table 1) and inadanone (Table 2, Entry 1) were prepared according to this general

procedure and characterized by comparing their NMR, IR and HPLC data with authentic samples.

General Procedure for Aliphatic Hydrocarbon Oxidation. Hydrocarbon (30 mmol), aldehyde (60 mmol) and cobalt(II) porphyrin complex (~2.5 mol%) were stirred at ambient pressure or 1 atm of oxygen in acetonitrile (30 mL) for 3 hours. Removal of solvent yielded the residue which was dissolved in diethyl ether (30 mL) and successively washed with sodium bicarbonate solution ($3 \times 20 \text{ mL}$) and brine solution ($3 \times 15 \text{ mL}$). Drying over anhydrous sodium sulphate and removal of the solvent in vacuo, gave the crude compound which was subjected to GC or distilled by kugelrohr. Compounds 10a-b were prepared according to this procedure and characterized by comparing their NMR, IR and GC data with standard samples.

1-Acetoxy-3,7,11-trimethyl-10,11-epoxydodeca-2,6-diene. Alkene 4 (0.53g, 2 mmol), aldehyde (0.30g, 4 mmol) and cobalt(II) complex 1a (~2.5 mol%) were reacted according to the reaction conditions as described in the above procedure to give a liquid (0.45g, 80%) after purification on silica gel column chromatography (5% ethyl acetate in hexane): ¹H NMR (CDCl₃) δ 5.5-4.9 (m, 2H), 4.4 (d, 2H, J=6.0 Hz), 2.5 (t, 1H, J=6.0 Hz), 2.2-19 (m, 11H), 1.6 (s, 3H), 1.1 (s, 3H), 0.9 (s, 3H); IR (neat) 1720, 1365, 1230 cm⁻¹.

1,2-Epoxy-methyl-4-(1-methylethyl) cyclohexane. Alkene 5 (0.96g, 5 mmol), aldehyde (0.72g, 10 mmol) and cobalt(II) porphyrin complex 1a (~2.5 mol%) were subjected to the above reaction conditions to afford as a liquid (1.52g, 100%) after purification on silica gel column chromatography (2% ethyl acetate in hexane): Monoepoxide: ¹H-NMR (CDCl₃) δ 4.6 (s, 2H), 3.0(m, 1H), 2.5(q, 1H), 2.0-1.5(m, 7H), 1.3-1.1(m, 5H); IR(neat) 3080, 1640, 1370 cm⁻¹. Diepoxide: ¹H-NMR (CDCl₃) δ 3.0(m, 1H), 2.5(q, 1H), 2.1(s, 2H), 2.0-1.5(m, 7H), 1.3-1.1(m, 5H); IR(neat) 3080, 1370 cm⁻¹.

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