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

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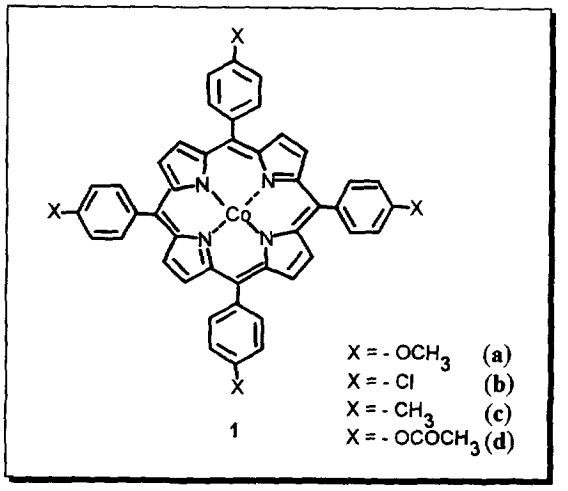
Abstract: Co(II)porphyrin **(1a-d)** acts as a versatile catalyst during the oxidation of a wide range of organic substrates at ambient conditions by using a combination of molecular oxygen and 2-methylpropanal. The versatility of these catalysts is demonstrated by oxidation of alkenes, allylic or benzylic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

Introduction

Synthetic metalloporphyrin catalyzed oxidation of organic substrates has emerged as a good biological model[1,2] for oxidations involving enzymatic reactions of mono[3] 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



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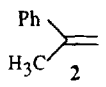
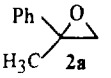
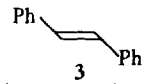
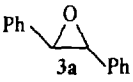
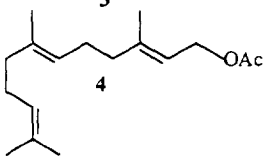
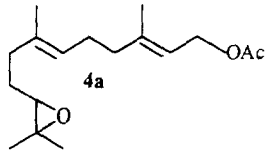
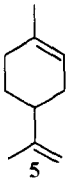
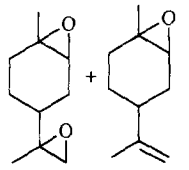
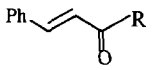
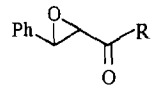
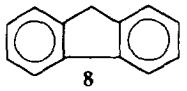
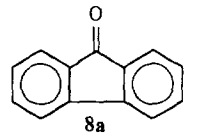
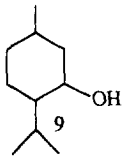
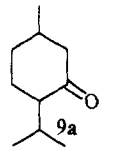
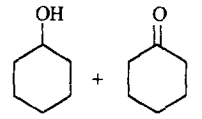
catalyzed oxidation using molecular oxygen requires two electrons and two protons to reduce the second oxygen atom of dioxygen to water, and most of the studies reported use borohydride, hydrogen and colloidal particles, Zn or electron from an electrode as reducing agent.[13] Most of the studies related to metalloporphyrin were undertaken as mimics of CytP450 mediated[14] epoxidation reaction as pioneered[15] 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) porphyrin[17] catalyzed oxidation of organic substrates with dioxygen. We now demonstrate that Co(II) porphyrin complex **1a** functions as a versatile catalyst[18] during the oxidation of wide range of organic substrates with diverse redox potential under aerobic conditions. A detailed account of these findings are described below.

Results and Discussion

Our earlier studies[19] 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 complexes[20] (**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 **1a-d** with different para substituents were studied and results indicated that the p-substituent displays some effect during these oxidations. Thus, the oxidation of

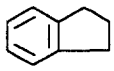
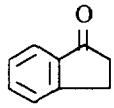
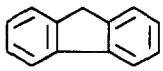
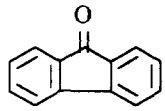
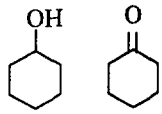
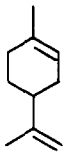
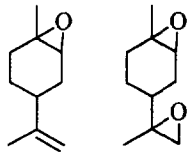
Table 1. Co(II) Porphyrin 1a Catalyzed Oxidation of Organic Substrates using 2-Methylpropanal and Dioxygen

substrate	product(s)[b]	yield(%)[a]
 **2**	 **2a**	94
 **3**	 **3a**	100
 **4**	 **4a**	80
 **5**	 **5a** (2.3 : 1) **5b**	100[c]
 R=Ph **6** =OEt **7**	 **6a** **7a**	83 51
 **8**	 **8a**	58
 **9**	 **9a**	76
 **10**	 **10a** (44:56) **10b**	26

[a] *Isolated yield.* [b] *Yield determined from* ^{1}*H-NMR of the crude reaction mixture.*
[c] *Obtained 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

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

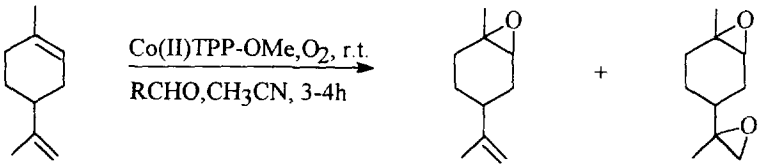
Entry	Substrate	Catalyst	Product(s)	Yield (%)[a]
1		**1a**		86
		1b		82
		1c		54
		1d		26
2		**1a**		58
		1b		39
		1c		36
		1d		29
3		**1a**		26 (44:56)[b,c]
		1b		24 (39:61)
		1c		20 (50:50)
		1d		16 (40:60)
4		**1a**		26 (1:2.3)[c]
		1b		24 (1:3)
		1c		20 (1:--)

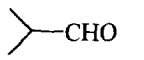
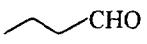
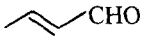
[a]Isolated yield. [b]Ratio determined from GC. [c]Ratio determined from ^{1}H NMR of the crude reaction mixture

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

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

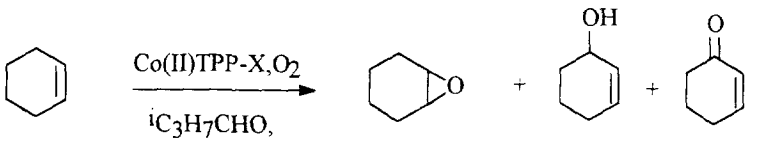


Entry	Carbonyl Compound	Product(s) ratio of products[b,c]	Yield(%)[a]
1.		(2.5:1)	100
2.		(1:3)	80
3.		(1:5)	55
4.	PhCHO	NR	—

[a]Isolated yield based on limonene. [b]Ratio determined from ^{1}H NMR of the crude reaction mixture.
[c]Mono 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 further changes 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(**1a**)	(1:3:1.2)	84
2.	Me(**1b**)	(- :1.2:1)	76
3.	Cl(**1c**)	(1:1.9:1)	82

[a]Isolated yield of the mixture of compounds. [b]Ratio determined from ^{1}H-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 CCl_4 , $CDCl_3$, 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 procedure[20].

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 x 20 mL) and brine solution (3 x 15 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): ^{1}H NMR ($CDCl_3$) 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: ^{1}H-NMR ($CDCl_3$) 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: ^{1}H-NMR ($CDCl_3$) 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}.

Referencees and Notes

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