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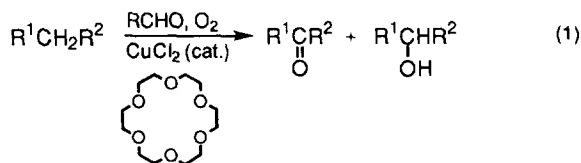
## Aerobic Oxidation of Alkanes in the Presence of Acetaldehyde Catalysed by Copper–Crown Ether

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**Abstract:** Copper–crown ether catalysed oxidation of alkanes with molecular oxygen in the presence of acetaldehyde gives the corresponding ketones and alcohols highly efficiently. High turnover numbers have been obtained for the oxidations of cyclohexane using copper(II) chloride and 18-crown-6 as a catalyst.

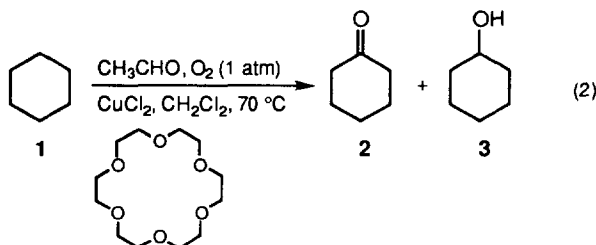
The aerobic oxidation of alkanes is of importance from enzymatic and synthetic points of view.<sup>1</sup> Although many catalytic systems for aerobic oxidations of alkanes have been reported,<sup>1</sup> high catalytic efficiency was achieved only in a limited number of these systems such as Fe(TPPF<sub>20</sub>Br<sub>8</sub>)–O<sub>2</sub><sup>2</sup> and Co naphthenate–O<sub>2</sub>–cyclohexanone<sup>3</sup> systems, which require high reaction temperature and high pressure of O<sub>2</sub>. During the course of our systematic study on the cytochrome P-450 type oxidation of alkanes with peroxides,<sup>4</sup> we have found aerobic oxidation of alkanes with ruthenium,<sup>5a</sup> iron,<sup>5a</sup> and copper<sup>5b</sup> catalysts can be performed efficiently in the presence of an aldehyde. The catalytically active species of these reactions seems to be an oxometal species. In order to improve the turnover numbers of these oxidations, we have been searching for a simple method to generate more reactive and stable oxometal species by using macrocyclic ligands. As a result, we found that the combination of copper chloride and crown ethers gives high catalytic efficiency for the aerobic oxidation of alkanes with acetaldehyde (eq 1).



The catalytic activity of various combinations of copper chloride and crown ethers (0.025 mol%) (1:1) has been examined for the oxidation of cyclohexane with molecular oxygen (1 atm) in the presence of acetaldehyde (10 mol% based on cyclohexane) in CH<sub>2</sub>Cl<sub>2</sub> at room temperature for 24 h. The yields of cyclohexanol and cyclohexanone and the turnover numbers were determined by GLC analyses. A combination of CuCl<sub>2</sub> and crown ethers such as 18-crown-6, dicyclohexyl-18-crown-6, dibenzo-24-crown-8, 15-crown-5, and 12-crown-4 gave high turnover numbers for the formation of cyclohexanol and cyclohexanone. The catalytic activities of these complexes are higher than those of the reported catalysts; Fe-

AcOH,<sup>5a</sup> RuCl<sub>3</sub>·nH<sub>2</sub>O·AcOH,<sup>5a</sup> Cu(OH)<sub>2</sub>,<sup>5b</sup> under the similar conditions. Other host ligands such as calix[n]arenes, cryptands, and azacrown ethers retard the oxidation reactions. Concerning the aldehydes used, excellent results were obtained with aliphatic aldehydes such as acetaldehyde, 2-methylpropanal, and 2,2-dimethylpropanal. As a solvent, dichloromethane gave the best result. Ethyl acetate, benzene, and acetonitrile can be also used.

The efficiency of the present catalysts is highlighted by extremely high turnover numbers in the aerobic oxidation of cyclohexane (1), which is an important aspect in view of industrial applications. Actually, the oxidation of cyclohexane in the presence of CuCl<sub>2</sub> (2.50 × 10<sup>-4</sup> mol%) and 18-crown-6 (2.50 × 10<sup>-4</sup> mol%) and acetaldehyde (10 mol%) at 70 °C under O<sub>2</sub> atmosphere (1 atm) gave cyclohexanone (2) (61 % yield based on acetaldehyde) and cyclohexanol (3) (10 %) with turnover number of 1.62 × 10<sup>4</sup> (eq 2).



The representative results of the CuCl<sub>2</sub>-18-crown-6-catalysed oxidation of alkanes with molecular oxygen (1 atm) and acetaldehyde in CH<sub>2</sub>Cl<sub>2</sub> are shown in Table 1. Various alkanes and alkylated arenes can

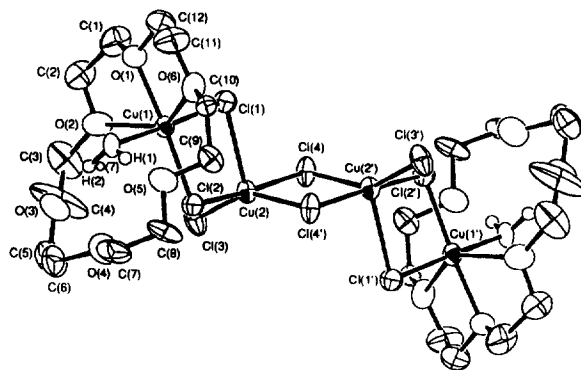
**Table 1.** CuCl<sub>2</sub>-18-crown-6-Catalysed Oxidation of Alkanes with Molecular Oxygen in the Presence of Acetaldehyde.<sup>a</sup>

Entry	Alkane	Temp., °C	Yields, <sup>b</sup> %		Turnover number <sup>c</sup>
			Alcohol(s)	Ketone(s)	
1	cyclohexane	70	10 <sup>f</sup>	61 <sup>g</sup>	1.62 × 10 <sup>4</sup>
2 <sup>d</sup>	cyclohexane	70	9.7 <sup>f</sup>	61 <sup>g</sup>	1.60 × 10 <sup>4</sup>
3	cyclooctane	70	9.1 <sup>h</sup>	74 <sup>i</sup>	1.86 × 10 <sup>4</sup>
4	<i>n</i> -hexane	70	2.3 <sup>j</sup>	44 <sup>k</sup>	9.77 × 10 <sup>3</sup>
5 <sup>e</sup>	ethylbenzene	rt	2.0 <sup>l</sup>	13 <sup>m</sup>	3.48 × 10 <sup>3</sup>
6 <sup>e</sup>	indane	rt	11 <sup>n</sup>	50 <sup>o</sup>	1.41 × 10 <sup>4</sup>
7 <sup>e</sup>	tetraline	rt	9.2 <sup>p</sup>	56 <sup>q</sup>	1.48 × 10 <sup>4</sup>

<sup>a</sup> A mixture of CuCl<sub>2</sub> (1.00 × 10<sup>-4</sup> mmol) and 18-crown-6 (1.00 × 10<sup>-4</sup> mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was stirred for 20 min. A mixture of yellow homogeneous solution obtained, alkane (40.0 mmol), and acetaldehyde (4.00 mmol) was placed in an autoclave (300 mL) and flushed with molecular oxygen (1 atm). The mixture was reacted with stirring for 24 h. <sup>b</sup> Determined by GLC analyses based on the starting acetaldehyde using an internal standard. It was assumed that 2 moles of acetaldehyde were necessary for ketone formation. <sup>c</sup> Results are given in mole of products formed per mole of catalyst. <sup>d</sup> CuCl<sub>2</sub>-18-crown-6 complex (4) was used as a catalyst. <sup>e</sup> Alkane (4.00 mmol) was used. <sup>f</sup> Cyclohexanol. <sup>g</sup> Cyclohexanone. <sup>h</sup> Cyclooctanol. <sup>i</sup> Cyclooctanone. <sup>j</sup> 2-Hexanol and 3-hexanol (53:47). <sup>k</sup> 2-Hexanone and 3-hexanone (49:51). <sup>l</sup> 1-Phenylethanol. <sup>m</sup> Acetophenone. <sup>n</sup> 1-Indanol. <sup>o</sup> 1-Indanone. <sup>p</sup> α-Tetralol. <sup>q</sup> α-Tetralone.

be converted into the corresponding alcohols and ketones with high turnover numbers. It is noteworthy that the extremely high yields of alcohols and ketones based on acetaldehyde can be achieved, when the reactions are carried out at 70 °C. The crown ether coordinated to copper is not oxidized under the reaction conditions.

We succeeded in the isolation of  $\text{CuCl}_2$ -18-crown-6 complex (**4**) from the reaction of  $\text{CuCl}_2$  and 18-crown-6 in  $\text{CH}_2\text{Cl}_2$ -ether at room temperature, although stable transition metal complexes of crown ethers are rarely isolated.<sup>6</sup> The aerobic oxidation of cyclohexane with the complex **4** under the same reaction conditions (Table 1, entry 2) proceeds as efficiently as the combined use of  $\text{CuCl}_2$  with 18-crown-6. The structure of **4** was determined by X-ray analysis<sup>7</sup> as shown in Figure 1. The complex consists of tetrameric  $(\text{CuCl}_2)_4$ , two



**Fig.1** The X-ray crystal structure of  $[(\text{CuCl}_2)_4(18\text{-crown-6})_2(\text{H}_2\text{O})_2]$  (**4**). Hydrogen atoms on carbons are omitted for clarity. Atoms related by inversion center are primed.

crown ethers, and two  $\text{H}_2\text{O}$  molecules. The centrosymmetric molecule contains copper atoms in two distinct coordination geometries: the central pair of copper ions have 4+1 coordination, while the outer pair have a distorted-octahedral geometry. Each outer copper ion is hexacoordinate with three oxygen atoms of the crown ether, two bridged chlorine atoms, and one oxygen atom of  $\text{H}_2\text{O}$ .

In order to gain insight into the mechanism of the present oxidation of alkanes, the relative reaction rates of the  $\text{CuCl}_2$ -18-crown-6-catalysed oxidation of three substituted toluenes ( $\text{X-C}_6\text{H}_4\text{Me}$ ,  $\text{X} = p\text{-Me}$ ,  $\text{H}$ ,  $p\text{-Cl}$ ) with molecular oxygen in the presence of acetaldehyde, in  $\text{CH}_2\text{Cl}_2$  at room temperature, were determined by GLC analyses of the products. The rate data correlate well ( $\gamma = 0.999$ ) with Hammett linear free-energy relationship with use of  $\sigma^+$  values. The  $\rho$  value is  $-1.59$ , which is close to the values obtained for the competitive oxidation of substituted toluenes by  $\text{Cu}(\text{OH})_2$  and acetaldehyde ( $-1.21$ ),<sup>5b</sup>  $\text{Mn}(\text{TPP})\text{Cl}$  and  $\text{Fe}(\text{TPP})\text{Cl}$  and  $\text{PhIO}$  ( $-1.36$  and  $-1.69$ , respectively).<sup>8</sup> The intramolecular deuterium isotope effect of the  $\text{CuCl}_2$ -18-crown-6-catalysed oxygenation of 1,1-dideuterio-1,3-diphenylpropane was determined to be 4.1 (3.6,  $\text{Cu}(\text{OH})_2$ ) by GC-MS analysis of the product ketones. The observed  $k_{\text{H}}/k_{\text{D}}$  values suggest that the C-H bond breaking is a crucial step. Although it is premature to discuss the precise mechanism at the present stage, this system can be rationalized by assuming the following pathway. The reaction of acetaldehyde with molecular oxygen in the presence of copper-crown ether complex would give peracetic acid. The presence of peracetic acid under the reaction conditions has been detected by the NMR study. A peracid subsequently reacts with the metal complex to afford an oxocopper species.<sup>9</sup> Hydrogen abstraction of alkanes by the oxocopper species, followed by hydroxy ligand transfer to the resulting radical, would give alcohol and metal

to complete the catalytic cycle. The alcohols can be converted into the corresponding ketones under the reaction conditions. The reason why the copper-crown ether complex gives higher turnover number and high yields of oxidation products based on the aldehyde in comparison with  $\text{Cu}(\text{OH})_2$  is due to the stabilization of oxocopper species by coordination of crown ethers to prevent self-decomposition before hydrogen abstraction of hydrocarbons.

Work is in progress to provide definitive mechanistic information and to apply the present methods to other systems.

### Acknowledgment

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### References and Notes

- (a) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press: New York, 1981. (b) Hill, C. L. *Activation and Functionalization of Alkanes*, Wiley: New York, 1989. (c) *Selective Hydrocarbon Oxidation and Functionalization*, Davis, J. A.; Watson, P. L.; Greenberg, A.; Liebman, J. F., Eds.; VCH: New York, 1990. (d) Shilov, A. E.; Karasevich, E. I. *Metalloporphyrins Catalyzed Oxidations*, Montanari, F.; Casella, L., Eds.; Kluwer Academic Publishers: Dordrecht, 1994; pp. 87-120. (e) Meunier, B. *Chem. Rev.* **1992**, *92*, 1411.
- Ellis, P. E., Jr.; Lyons, J. E. *Coord. Chem. Rev.* **1990**, *105*, 181.
- Murray, E. J.; Winstrom, L. O. *U. S. Patent*, 3671588.
- (a) Murahashi, S.-I.; Oda, Y.; Naota, T.; Kuwabara, T. *Tetrahedron Lett.* **1993**, *34*, 1299. (b) Murahashi, S.-I.; Oda, Y.; Komiya, N.; Naota, T. *Tetrahedron Lett.* **1994**, *35*, 7953.
- (a) Murahashi, S.-I.; Oda, Y.; Naota, T. *J. Am. Chem. Soc.* **1992**, *114*, 7913. (b) Murahashi, S.-I.; Oda, Y.; Naota, T.; Komiya, N. *J. Chem. Soc., Chem. Commun.* **1993**, 139.
- (a) *Crown Ethers and Analogs*, Patai, S.; Rappoport, Z., Eds.; Wiley: New York, 1989. (b)  $\text{CuCl}_2$ -12-crown-4 (1:1) complex: van Remoortere, F. P.; Boer, F. P.; Steiner, E. C. *Acta Cryst.* **1975**, *B31*, 1420. (c)  $\text{CuCl}_2$ -benzo-15-crown-5 (1:1) complex: Sakurai, T.; Kobayashi, K.; Tsuboyama, S.; Kohno, Y.; Azuma, N.; Ishizu, K. *Acta Cryst.* **1983**, *C39*, 206.
- Crystal structure data for **4**,  $\text{C}_{24}\text{H}_{52}\text{Cl}_8\text{Cu}_4\text{O}_{14}$ ,  $M = 1102.47$ , monoclinic, space group  $P2_1/n$ ,  $a = 10.460(7)$ ,  $b = 13.727(5)$ ,  $c = 14.738(7)$  Å,  $\beta = 95.88(5)^\circ$ ,  $V = 2104(1)$  Å<sup>3</sup>,  $Z = 2$ ,  $D_c = 1.739$  g/cm<sup>3</sup>, Mo-K $\alpha$  radiation,  $\omega$  scans,  $2\theta = 25.2$ – $29.6$ , 3374 measured reflections, 3149 independent, 1661 observed [ $I > 3.0\sigma(I)$ ], empirical absorption correction based on azimuthal scans. Full-matrix refinement with 221 parameters led to  $R = 0.082$  and  $R_w = 0.083$ , GOF = 2.48. Detailed X-ray crystallographic data are available from the Cambridge Crystallographic Data Centre.
- Khanna, R. K.; Pauling, T. M.; Vajpayee, D. *Tetrahedron Lett.* **1991**, *32*, 3759.
- $\text{Cu}=\text{O}$  and  $\text{Cu}-\text{O}^\bullet$  have been reported: (a) oxidation of alkanes with Cu cat.  $-\text{H}_2\text{O}_2$ : Barton, D. H. R.; Doller, D. *Acc. Chem. Res.* **1992**, *25*, 504; (b) oxidation of amines with  $\text{Cu}-\text{O}_2$ -AcOH: Rousselet, G.; Capdevielle, P.; Maumy, M. *Tetrahedron Lett.* **1995**, *36*, 4999.

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