# A Water-Soluble and "Self-Assembled" Polyoxometalate as a Recyclable Catalyst for Oxidation of Alcohols in Water with Hydrogen Peroxide

Dorit Sloboda-Rozner,[†] Paul L. Alsters,[‡] and Ronny Neumann*,[†]

*Department of Organic Chemistry, Weizmann Institute of Science, Rehovot, Israel, 76100, and DSM Life Sciences, Advanced Synthesis and Catalysis, 6160 MD Geleen, The Netherlands*

Received February 4, 2003;  E-mail: Ronny.Neumann@weizmann.ac.il

The selective oxidation of alcohols to carbonyl compounds is a key transformation in organic synthesis. Thus, there have been many recent publications emphasizing environmentally benign methods using molecular oxygen or hydrogen peroxide as oxidants. The research prior to the year 2000 has recently been reviewed.[1] Since then, in the area of aerobic oxidation, many new homogeneous[2] and heterogeneous[3] catalytic systems have been disclosed. Although catalytic aerobic oxidation is certainly of importance, there are also important advantages in the use of aqueous hydrogen peroxide. This is true especially for smaller scale operations such as in fine chemicals manufacture, where the complications involving use of oxygen as a gaseous reagent may be avoided.[4] Research involving catalytic oxidation of alcohols with hydrogen peroxide has been based either on the use of hydrophobic quaternary ammonium salts of molybdenum- and tungsten-containing catalysts[5] or on the use of manganese or iron complexes with polyamine ligands.[6] These types of reactions with the catalyst dissolved in the organic phase inherently require separation of the catalyst from the product, invariably a chromatographic procedure, for recovery of the catalyst. A key advance to the area of alcohol oxidation was the finding that a water-soluble palladium-phenanthroline catalyst may be used in a biphasic reaction medium that allows liquid alcohols to be oxidized with water as solvent; the catalyst is easily recycled from the product by separation of the aqueous phase.[7] Such a system has the disadvantage that it requires the use of both an expensive noble metal and a water-soluble organic ligand.

It would be very advantageous for practical and industrial applications if a water-soluble catalyst were prepared or "self-assembled" by simply mixing salts of the required components even without isolation of the catalyst. Polyoxometalates have recently been nicely shown by Hill and Weinstock et al. to be amenable to this type of synthesis and use for lignin oxidation.[8] We now report on the use of easily prepared water-soluble polyoxometalate, $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$,[9] Figure 1, as an effective catalyst in a biphasic reaction medium with no organic solvent for the selective oxidation of alcohols with aqueous hydrogen peroxide. Furthermore, we show that even the nonisolated polyoxometalate prepared in one step in water from simple salts, and representing a "self-assembled" catalyst, is equally active for alcohol oxidation.

According to the known literature procedure, $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ is prepared by dropwise addition of zinc nitrate to a nitric acid solution of sodium tungstate over 5 h at 90 °C.[9] After isolation, the catalytic activity of $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ for alcohol oxidation was surveyed for a range of substrates, Table 1.

Several trends may be noted. First, liquid secondary alcohols including 2-propanol, 2-pentanol, 2-octanol, 1-phenylethanol, cyclohexanol, and cyclooctanol were all selectively oxidized to the
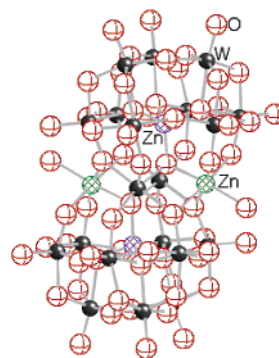


**Figure 1.** The $[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]^{q-}$ polyoxometalate.

**Table 1.** Oxidation of Various Alcohols Catalyzed by $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]^a$

| substrate | conversion mol % | product (selectivity, mol %) |
|---|---|---|
| 1-pentanol | 66 | pentanal (9), pentanoic acid (91) |
| 2-pentanol | 94 | 2-pentanone (100) |
| 2-propanol | 93 | acetone (100) |
| 2-octanol | 91 | 2-octanone |
| 1-pentanol[b] | 62 | pentanal (41), pentanoic acid (59) |
| benzyl alcohol | ~100 | benzoic acid (100) |
| 1-phenylethanol | ~100 | acetophenone (100) |
| cyclohexanol | ~100 | cyclohexanone (100) |
| cyclooctanol | 95 | cyclooctanone (100) |
| 2-ethyl-1,3-hexanediol | ~100 | 2-ethyl-3-oxo-1-hexanol (95), butanoic acid (4) |
| 2-butyl-4-chloro-5-hydroxylmethylimidazole | >95 | 2-butyl-4-chloro-imidazole-5-carboxylic acid (100) |
| 1-cyclohexyl-3,3,3-trifluoro-2-propanol | 0 | 1-cyclohexyl-3,3,3-trifluoro-2-propanone |

*a* Reaction conditions:  1 mmol of substrate, 5 mmol (~17 wt %) of $H_2O_2$, 4 $\mu$mol of $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$, 1 mL of water, 85 °C, 7 h.[10]  *b* 0.012 mmol of TEMPO was added. For more difficult to oxidize substrates, for example, 2-octanol, a 5-fold molar excess of $H_2O_2$ was needed, but for more active substrates, for example, 1-phenylethanol, a 1.5 molar excess was sufficient. Product distributions were not significantly affected by carrying out the reactions under Ar.

corresponding ketone in high yields. There is little discernible effect of the hydrophobicity of the substrate, although not surprisingly the benzylic substrate was more reactive. A secondary alcohol, 1-cyclohexyl-3,3,3-trifluoro-2-propanol, with a strongly electron-withdrawing $CF_3$ moiety adjacent to the carbinol center was not oxidized. Primary alcohols, for example, 1-pentanol and benzyl alcohol, were oxidized to pentanoic acid and benzoic acid, respectively. The formation of the carboxylic acid could be partially inhibited and the oxidation stopped at the aldehyde stage by addition of catalytic amounts of TEMPO. A 1,3 diol, 2-ethyl-1,3-hexanediol, was oxidized almost exclusively at the secondary position to yield

† Weizmann Institute of Science.
‡ DSM Life Sciences.

the appropriate 3-keto alcohol; there was some carbon−carbon bond cleavage. 2-Butyl-4-chloro-5-hydroxylmethylimidazole, an intermediate for angiotensin II inhibitors,[11] also reacted to yield the acid. This experiment indicates that nitrogen-based moieties, at least for cases where the nitrogen atom is not susceptible to oxidation, do not interfere with the catalytic alcohol oxidation.

The synthesis of the $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ polyoxometalate proceeds according to the following stoichiometry, eq 1.[9,12]

$$5Zn(NO_3)_2 + 19Na_2WO_4 + 16HNO_3 \rightarrow$$
$$Na_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2] + 26NaNO_3 + 8H_2O \quad (1)$$
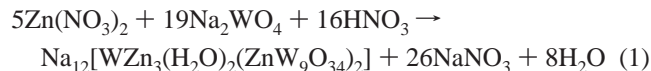
A reaction conducted at 85 °C for 7 h and containing approximately 40 $\mu$mol of $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ (assuming a theoretical 100% yield in the polyoxometalate synthesis) from the solution obtained in the polyoxometalate preparation, 10 mmol of 2-pentanol, and 50 mmol (∼17 wt %) of $H_2O_2$, in 10 mL of water, gave an 88% yield of 2-pentanone. It should be emphasized that control reactions at 95 °C, 18 h with (a) no metal catalyst (1 M 2-pentanol, 5 M $H_2O_2$), (b) only sodium tungstate (1 M 2-pentanol, 0.76 M $Na_2WO_4$, 5 M $H_2O_2$), (c) only zinc nitrate (1 M 2-pentanol, 0.2 M $Zn(NO_3)_2$, 5 M $H_2O_2$), and (d) a combination of zinc nitrate and sodium tungstate without addition of nitric acid (1 M 2-pentanol, 0.76 M $Na_2WO_4$, 0.2 M $Zn(NO_3)_2$, 5 M $H_2O_2$) showed no formation of 2-pentanone in (a) and (c) and only trace formation, ≤1%, of 2-pentanone in (b) and (d). Therefore, it is clear that only a solution of $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ prepared by "self-assembly" of zinc nitrate and sodium tungstate in the presence of nitric acid was catalytically active.

It is also notable that $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ appears to be stable under reaction conditions. Thus, the $^{183}W$ NMR of $Na_{12}$-$[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ shows 10 peaks at $\delta$ (ppm) 22.6(1), −16.5(2), −41.6(2), −84.2(2), −89.4(2), −93.8(2), −153.9(2), −187.3(2), −226.6(2), and −304.7(2) as expected.[9] Upon addition of $H_2O_2$ and for at least 12 h, a 10-line slightly shifted $^{183}W$ NMR spectrum is retained, $\delta$ (ppm) 22.7(1), −28.2(2), −45.6(2), −93.4-(2), −94.3(2), −96.8(2), −158.4(2), −192.6(2), −231.3(2), and −299.4(2), together with formation of peroxo related peaks at −655.4 and −697.3 ppm. There is no $^{183}W$ NMR evidence for mononuclear tungsten species or peroxotungstate species.[13] Reisolation of the $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$ after completion of the reaction by evaporation of the water phase showed by IR that the integrity of the catalyst was retained (peaks at 925, 880, and 772 cm$^{-1}$). Furthermore, a catalyst recycle experiment (10 mmol of 2-pentanol, 50 mmol of $H_2O_2$, 40 $\mu$mol of $Na_{12}[WZnZn_2(H_2O)_2$-$(ZnW_9O_{34})_2]$, 10 mL of water, 85 °C, 7 h) carried out simply by separation of the organic phase and re-addition of 2-pentanol (10 mmol) and hydrogen peroxide (50 mmol) showed 95%, 90%, and 96% conversions over three reaction cycles with 2-pentanone as the only product. There was no discernible loss in activity or selectivity. Eventually, to avoid excess accumulation of water, the aqueous phase should be concentrated.

We have shown that a water-soluble polyoxometalate is an effective, stable, and recyclable catalyst for alcohol oxidation with $H_2O_2$ in biphasic reaction media. The in situ prepared catalyst was as active as the isolated catalyst, while an independent "assembly" of reaction components was inactive.

**References**

(1) Sheldon, R. A.; Arends, I. W. C. E.; Dijksman, A. *Catal. Today* **2000**, *57*, 157−160.
(2) (a) Steinhoff, B. A.; Fix, S. R.; Stahl, S. S. *J. Am. Chem. Sox.* **2002**, *124*, 766−767. (b) Steinhoff, B. A.; Stahl, S. S. *Org. Lett.* **2002**, *4*, 4179−4181. (c) Nishimura, T.; Maeda, Y.; Kaikiuchi, N.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 4301−4305. (d) Hasan, M.; Musawir, M.; Davey, P. N.; Kozhevnikov, I. V. *J. Mol. Catal.* **2002**, *180*, 77−84. (e) Wolfson, A.; Stijn, S.; de Vos, D. E.; Vankelecom, I. F. J.; Jacobs, P. A. *Tetrahedron Lett.* **2002**, *43*, 8107−8110. (f) Ben-Daniel, R.; Alsters, P.; Neumann, R. *J. Org. Chem.* **2001**, *66*, 8650−8653. (g) Fabbrini, M.; Galli, C.; Gentilli, P.; Macchitella, D. *Tetrahedron Lett.* **2001**, *42*, 4551−4553. (h) Ragagnin, G.; Betzemeier, B.; Quici, S.; Knochel, P. *Tetrahedron* **2002**, *58*, 3985−3991. (i) Cecchetto, A.; Fontana, F.; Minisci, F.; Rucupero, F. *Tetrahedron Lett.* **2001**, *42*, 6651−6653. (j) Dijksman, A.; Marino-Gonzalez, A.; Mairata, I.; Payeras, A.; Arends, I. W. C. E.; Sheldon, R. A. *J. Am. Chem. Soc.* **2001**, *123*, 6826−6833. (k) Iwahama, T.; Yoshino, Y.; Ketitoku, T.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2000**, *65*, 6502−6507. (l) Ishii, Y.; Sakaguchi, S.; Iwahama, T. *Adv. Synth. Catal.* **2001**, *343*, 393−427. (m) Minisci, F.; Punta, C.; Recupero, F.; Fontana, F.; Pedulli, G. F. *Chem. Commun.* **2002**, 688−689. (n) d'Alessandro, N.; Liberatore, L.; Tonucci, L.; Morvillo, A.; Bressan, M. *J. Mol. Catal.* **2001**, *175*, 83−90. (o) Shapley, P. A.; Zhang, N.; Allen, J. L.; Pol, D. H.; Liang, H.-C. *J. Am. Chem. Soc.* **2000**, *122*, 1079−1091. (p) Csjernyik, G.; Ell, A. H.; Fadini, L.; Pugin, B.; Bäckvall, J. E. *J. Org. Chem.* **2002**, *67*, 1657−1662.
(3) (a) Son, Y.-C.; Makwana, V. D.; Howell, A. R.; Suib, S. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 4280−4283. (b) Makwana, V. D.; Son, Y.-C.; Howell, A. R.; Suib, S. L. *J. Catal.* **2002**, *210*, 46−52. (c) Choudary, B. M.; Kantam, M. L.; Rahman, A.; Reddy, C. V.; Rao, K. K. *Angew. Chem., Int. Ed.* **2001**, *40*, 763−766. (d) Mori, K.; Yamaguchi, K.; Hara, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2002**, *124*, 11572−11573. (e) Keresszegi, C.; Buergi, T.; Mallat, T.; Baiker, A. *J. Catal.* **2002**, *211*, 244−251. (f) Nishimura, T.; Kakiuchi, N.; Inoue, M.; Uemura, S. *Chem. Commun.* **2000**, 1245−1246. (g) Kakiuchi, N.; Nishimura, T.; Inoue, M.; Uemura, S. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 165−172. (h) Besson, M.; Gallezot, P. *Catal. Today* **2000**, *57*, 127−141. (i) Ji, H.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Tetrahedron Lett.* **2002**, *43*, 7179−7183. (j) Yamaguchi, K.; Mizuno, N. *New J. Chem.* **2002**, *26*, 972−974. (k) Yamaguchi, K.; Mizuno, N. *Angew. Chem., Int. Ed.* **2002**, 4538−4540.
(4) Sheldon, R. A. *J. Chem. Technol. Biotechnol.* **1997**, *68*, 381−388.
(5) (a) Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 12386−12387. (b) Bortolini, O.; Conte, V.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1986**, *51*, 2661−2663. (c) Venturello, C.; Gambaro, M. *J. Org. Chem.* **1991**, *56*, 5924−5931. (d) Ishii, Y.; Yamawaki, K.; Ura, T.; Yamada, H.; Yoshida, T.; Ogawa, M. *J. Org. Chem.* **1988**, *53*, 3587−3593. (e) Neumann, R.; Gara, M. *J. Am. Chem. Soc.* **1995**, *117*, 5066−5074.
(6) (a) Berkessel, A.; Sklorz, C. A. *Tetrahedron Lett.* **1999**, *40*, 7965−7968. (b) Brinksma, J.; Rispens, M. T.; Hage, R.; Feringa, B. L. *Inorg. Chim. Acta* **2002**, *337*, 75−82. (c) Ligtenbarg, A. G. J.; Oosting, P.; Roelfes, G.; La Crois, R. M.; Hage, R.; Feringa, B. L.; Lutz, M.; Spek, A. L. *Chem. Commun.* **2001**, 385−386.
(7) (a) ten Brink, G. J.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636−1639. (b) ten Brink, G. J.; Arends, I. W. C. E.; Sheldon, R. A. *Adv. Synth. Catal.* **2002**, *344*, 355−369.
(8) Weinstock, I. A.; Barbuzzi, E. M. G.; Wemple, M. W.; Cowan, J. J.; Reiner, R. S.; Sonnen, D. M.; Heintz, R. A.; Bond, J. S.; Hill, C. L. *Nature* **2001**, *414*, 191−195.
(9) Tourné, C. M.; Tourné, G. F.; Zonnevijlle, F. *J. Chem. Soc., Dalton Trans.* **1991**, 143−151.
(10) Reactions were carried out in 10−25 mL flasks using the conditions described above. Reactions were quantified by GLC in the presence of an external standard using a 30 m 5% phenylmethyl silicone capillary column with an ID of 0.32 mm and 0.25 $\mu$m coating, and products were identified by GC-MS with the same column and conditions.
(11) Binder, D.; Weinberger, J. Eur. Pat. Appl. EP 535420 A1, 1993.
(12) The preparation of the polyoxometalate is not affected by the presence of a substrate (2-pentanol), but addition of $H_2O_2$ prevents the formation of $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$.
(13) $Na_2WO_4$ ($\delta$ = 0 ppm) upon addition of $H_2O_2$ (0.76 M $Na_2WO_4$, 5 M $H_2O_2$) gave a peak at $\delta$ = −1242 ppm only as expected for tungsten in the presence of excess hydrogen peroxide.

JA0344821