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H_2O_2-Oxidation of Alcohols Promoted by Polymeric Phosphotungstate Catalysts

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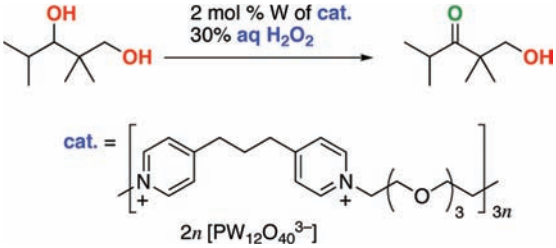
ABSTRACT



A novel polymeric phosphotungstate catalyst bearing a poly(ethylene oxide-pyridinium) matrix was developed that efficiently promoted oxidation of a variety of alcohols, including highly sterically demanding neopentyl alcohols, with hydrogen peroxide, to afford the corresponding carbonyl compounds in up to quantitative yield. The chemoselective oxidation of sterically hindered secondary alcohols in the presence of primary alcohols was achieved. The catalyst could be reused four times without any loss of catalytic activity.

Heterogeneous catalytic systems for the oxidation of alcohols with hydrogen peroxide would realize environmentally benign, secure processes as well as facilitate methods for product purification and catalyst recycling.[1,2] While there has been no lack of pioneering work on alcohol oxidation with aqueous H_2O_2 promoted by a homogeneous catalyst,[3] the heterogeneous-switching of catalytic oxidation to meet green chemical requirements still remains a major challenge.[4] In particular, we were intrigued by the idea of developing a heterogeneous alcohol oxidation catalysis[5] with high activity that would tolerate sterically demanding substrates.

Recently, we have been creating highly active, reusable, heterogeneous polymeric metal catalysts for organic transformations on the basis of our concept, also known as "*molecular convolution*", where a soluble linear polymer having multiple ligand groups is convoluted (noncovalently cross-linked) with transition metals via coordinative or ionic

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(1) For general reviews on green chemistry, see: (a) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, UK, 1998. (b) *Green Chemical Syntheses and Processes: Recent Advances in Chemical Processing*; Anastas, P. T., Heine, L. G., Williamson, T. C., Eds.; American Chemical Society: Washington, DC, 2001. (c) Tundo, P.; Anastas, P.; Black, D. S.; Breen., J.; Collins, T.; Memoli, S.; Miyamoto, J.; Polyakoff, M.; Tumas, W. *Pure Appl. Chem.* **2000**, *72*, 1207.

(2) (a) Wahlen, J.; De Vos, D. Oxidations on immobilized molecular catalysts, In *Handbook of Heterogeneous Catalysis*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2008; Vol. 7, p 3700. (b) Sheldon, R. A.; Arends, I. W. C. E.; Dijksman, A. *Catal. Today* **2000**, *57*, 157. (c) Lu, J.; Toy, P. H. *Chem. Rev.* **2009**, *109*, 815.

(3) For recent examples with tungsten catalysts, see: (a) Hida, T.; Nogusa, H. *Tetrahedron* **2009**, *65*, 270. (b) Zhang, S.; Zhao, G.; Gao, S.; Xi, Z.; Xu, J. *J. Mol. Catal. A: Chem.* **2008**, *289*, 22. (c) Shaikh, T. M. A.; Sudalai, A. *Eur. J. Org. Chem.* **2008**, 4877. (d) Wang, J.; Yan, L.; Qia, G.; Li, S.; Yang, K.; Liu, H.; Wang, X. *Tetrahedron* **2007**, *63*, 1826. (e) Shi, X.-Y.; Wei, J.-F. *J. Mol. Catal. A: Chem.* **2005**, *229*, 13. (f) Sloboda-Rozner, D.; Alsters, P. L.; Neumann, R. *J. Am. Chem. Soc.* **2003**, *125*, 5280, and references cited therein.

(4) For examples with polymer-supported catalysts, see: (a) Lamblin, M.; Nassar-Hardy, L.; Hierso, J.-C.; Fouquet, E.; Felpin, F.-X. *Adv. Synth. Catal.* **2010**, *352*, 33–79. (b) Mitsudome, T.; Noujima, A.; Mizugaki, T.; Jitsukawa, K.; Kaneda, K. *Adv. Synth. Catal.* **2009**, *351*, 1890. (c) Maayan, G.; Neumann, R. *Catal. Lett.* **2008**, *123*, 41. (d) Sarmah, P.; Chakrabarty, R.; Phukan, P.; Das, B. K. *J. Mol. Catal. A: Chem.* **2007**, *268*, 36. (e) Ebitani, K.; Motokura, K.; Mizugaki, T.; Kaneda, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 3423.

(5) (a) Uozumi, Y.; Nakao, R. *Angew. Chem., Int. Ed.* **2003**, *42*, 194. (b) Yamada, Y. M. A.; Arakawa, T.; Hocke, H.; Uozumi, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 704. (c) Uozumi, Y.; Nakao, R.; Rhee, H. *J. Organomet. Chem.* **2007**, *692*, 420. (d) Yamada, Y. M. A.; Arakawa, T.; Hocke, H.; Uozumi, Y. *Chem. Asian J.* **2009**, *4*, 1092.

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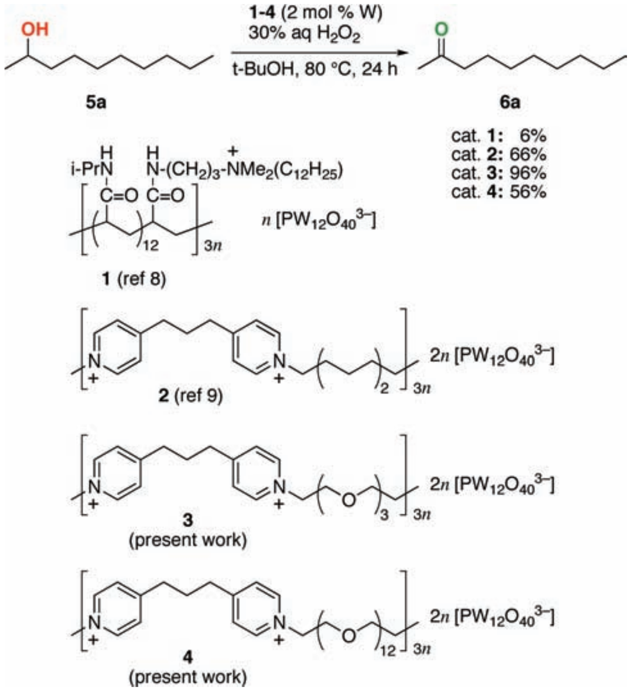
complexation.[6] Previously Yamada and co-workers reported preliminary studies on a convoluted polymeric tungstate catalyst, (isopropylacrylamide)polymer-supported phosphotungstate **1**, for the oxidation of alcohols; however, the catalytic activity was insufficient[7] and the heterogeneous catalyst became emulsive during the reaction, presumably due to its physical fragility, resulting in low recyclability.[8] To overcome these drawbacks, we recently developed a tightly convoluted polymeric catalyst **2** of main-chain polypyridinium and phosphotungstate that exhibited high catalytic activity and recyclability for the oxidative cyclization of alkenols and alkenoic acids and sulfide oxidation.[9] As part of our effort to demonstrate the wide utility of the catalyst system, we decided to examine alcohol oxidation with H_2O_2 with the polypyridinium-phosphotungstate catalyst system.[3,4] Here we report our results, namely that aliphatic alcohols were readily oxidized with aqueous H_2O_2 in the presence of a catalytic amount of a convoluted polypyridinium-phosphotungstate composite bearing an appropriate length of oxyethylene units to exhibit high catalytic performance, recyclability, and chemoselectivity with respect to secondary alcohols.[10]

The catalytic ability of the polypyridinium-phosphotungstates **2**−**4** was examined for H_2O_2-oxidation of 2-decanol (**5**) (Scheme 1). The polymeric composites **3** and **4** having three and twelve units of oxyethylene, respectively, were designed and prepared with a view toward using them in aqueous reaction media.[11,12] The oxidation of 2-decanol was carried out with 6 mol equiv of H_2O_2 (30% aqueous H_2O_2 was used) in *t*-BuOH at 80 °C for 24 h in the presence of 2 mol % W of the polymeric phosphotungstate catalysts. After being cooled to ambient temperature, the reaction mixture was filtered and the filtrate cake was rinsed with EtOAc. The combined filtrate was dried and concentrated in vacuo to give the crude residue, which was chromatographed on silica gel to give 2-decanone.

Scheme 1. H_2O_2-Oxidation of 2-Decanol with Polymeric Phosphotungstates



As can be seen from Scheme 1, where the result obtained with (isopropylacrylamide)polymer-supported phosphotungstate **1** is included for comparison, polypyridinium-phosphotungstate **3** bearing three oxyethylene units was identified to be the best catalyst in the alcohol oxidation.[13] Thus, of the polypyridinium-phosphotungstates, composite **3** gave 96% isolated yield of 2-decanone (**6**) while the alkyl-tethered **2** and the deca(oxyethylene)-tethered **4** afforded **6** in 66% and 56% yield, respectively. Poly(acrylamide)-based composite **1** gave only 6% yield of **6** under similar conditions. Though it is difficult to rationalize the appropriate length of the alkyl and oxyethylene tethering units between the pyridinium groups, fine-tuning of the hydrophobicity/hydrophilicity of the main chain cationic polymer should be essential to achieve high performance in the H_2O_2-oxidation catalysis.

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(6) (a) For a review, see: Yamada, Y. M. A. *Chem. Pharm. Bull.* **2005**, *53*, 723. (b) Yamada, Y. M. A.; Watanabe, T.; Torii, K.; Uozumi, Y. *Chem. Commun.* **2009**, 5594. (c) Yamada, Y. M. A.; Guo, H.; Uozumi, Y. *Org. Lett.* **2007**, *9*, 1501. (d) Yamada, Y. M. A.; Uozumi, Y. *Tetrahedron* **2007**, *63*, 8492. (e) Uozumi, Y.; Yamada, Y. M. A.; Beppu, T.; Fukuyama, N.; Ueno, M.; Kitamori, T. *J. Am. Chem. Soc.* **2006**, *128*, 15994. (f) Yamada, Y. M. A.; Maeda, Y.; Uozumi, Y. *Org. Lett.* **2006**, *8*, 4259. (g) Yamada, Y. M. A.; Uozumi, Y. *Org. Lett.* **2006**, *8*, 1375.

(7) Hamamoto, H.; Suzuki, H.; Yamada, Y. M. A.; Tabata, H.; Takahashi, H.; Ikegami, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 4536.

(8) (a) Yamada, Y. M. A.; Ichinohe, M.; Takahashi, H.; Ikegami, S. *Org. Lett.* **2001**, *3*, 1837. (b) Yamada, Y. M. A.; Tabata, H.; Takahashi, H.; Ikegami, S. *Synlett* **2002**, 2031. (c) Yamada, Y. M. A.; Tabata, H.; Ichinohe, M.; Takahashi, H.; Ikegami, S. *Tetrahedron* **2004**, *60*, 4097.

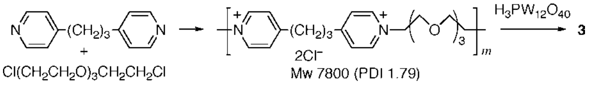
(9) (a) Yamada, Y. M. A.; Guo, H.; Uozumi, Y. *Org. Lett.* **2007**, *9*, 1501. (b) Yamada, Y. M. A.; Guo, H.; Uozumi, Y. *Heterocycles* **2008**, *76*, 645. (c) Jin, C. K.; Yamada, Y. M. A.; Uozumi, Y. *Bull. Korean Chem. Soc.* **2010**, *31*, 547.

(10) For a review, see: (a) Arerburn, J. B. *Tetrahedron* **2001**, *57*, 9765. For selected pioneering works, see: (b) Kaneda, K.; Kawanishi, Y.; Jitaukawa, K.; Teranishi, S. *Tetrahedron Lett.* **1983**, *24*, 5009. (c) Tomioka, H.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 539. (d) Steven, R. V.; Chapman, K. T.; Stubbs, C. A.; Tam, W. W.; Albizani, K. F. *Tetrahedron Lett.* **1982**, *23*, 4647. (e) Jung, M. E.; Spelts, M. L. *J. Am. Chem. Soc.* **1976**, *98*, 7882.

(11) We have been aware of the importance of equipping poly(ethylene oxide) units with polymer-immobilized catalysts to gain high catalytic activity in aqueous reaction media through our research on polystyrene-poly(ethylene oxide) (PS-PEG) resin-supported metal catalysts. For reviews, see: (a) Uozumi, Y. *Top. Curr. Chem.* **2004**, *242*, 77. (b) Uozumi, Y. Heterogeneous Asymmetric Catalysis in Aqueous Media, In *the Handbook of Asymmetric Heterogeneous Catalysis*; Ding, K., Uozumi, Y., Eds.; Wiley-VCH: Weinheim, Germany, 2008; p 209. (c) Uozumi, Y. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1183. (d) Uozumi, Y.; Yamada, Y. M. A. *Chem. Rec.* **2009**, *9*, 51.

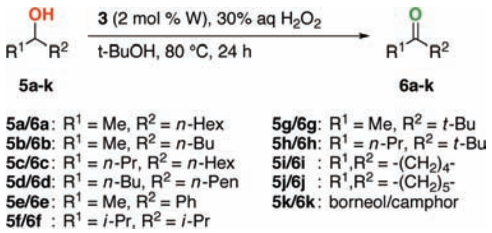
(12) For recent typical examples, see: (a) Hirai, Y.; Uozumi, Y. *Chem. Commun.* **2010**, *46*, 1103. (b) Suzuka, T.; Okada, Y.; Ooshiro, K.; Uozumi, Y. *Tetrahedron* **2010**, *66*, 1064. (c) Uozumi, Y.; Matsu-ura, A. T.; Yamada, Y. M. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 2708. (d) Oe, Y.; Uozumi, Y. *Adv. Synth. Catal.* **2008**, *350*, 18771. (e) Uozumi, Y.; Suzuka, T. *Synthesis* **2008**, 1960. (f) Uozumi, Y.; Takenaka, H.; Suzuka, T. *Synlett* **2008**, 1557. (g) Uozumi, Y.; Suzuka, T. *J. Org. Chem.* **2006**, *71*, 8644. (h) Nakai, Y.; Kimura, T.; Uozumi, Y. *Synlett* **2006**, 3065. (i) Uozumi, Y.; Suzuka, T. *J. Org. Chem.* **2006**, *71*, 8644, and references cited therein. Also see ref 5.

(13) Catalyst **3** (W 60.5 wt %; ICP-AES analysis) was readily prepared starting with 1,3-di(4-pyridyl)propane and tetraethylene glycol dichloride (below). Details are provided in the Supporting Information.

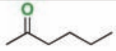
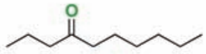
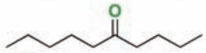
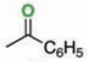
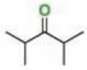
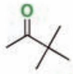
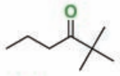
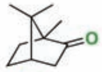
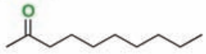


The heterogeneous catalytic oxidation was examined with a variety of secondary alcohols under similar conditions and exhibited wide substrate tolerance. Representative results are summarized in Table 1. Thus, 2-hexanol (**5b**), 4-decanol (**5c**), and 5-decanol (**5d**) were oxidized with H_2O_2 under similar conditions to give the corresponding ketones **6b**, **6c**, and **6d** in 99% isolated yield in all three cases (entries 1−3). The oxidation of a benzylic secondary alcohol **5e** was completed in 12 h to give acetophenone (**6e**) in 98% yield (entry 4). While the reactivity of sterically hindered alcohols is generally lower than less hindered ones,[3] surprisingly the oxidation of diisopropyl carbinol **5f** proceeded more smoothly than the sterically less hindered *n*-alkyl carbinols, such as **5a**−**d**, to afford diisopropyl ketone (**10c**) in 97% yield over 12 h (entry 5). It should also be noted that the reactivity of the much more sterically hindered neopentyl-type *tert*-butyl methyl carbinol **5g** was similar to that of the less hindered *n*-butyl methyl carbinol (= 2-hexanol (**5b**)), providing *tert*-butyl methyl ketone (**10e**) in 97% yield in 24 h (entry 6 vs entry 1). This tendency of the reactivity was observed in the reaction of *tert*-butyl *n*-propyl carbinol **5h** and *n*-butyl *n*-pentyl carbinol (= 5-decanol (**5d**)) to provide *tert*-butyl *n*-propyl ketone (**6h**) in 96% yield (entry 7 vs entry 3). Cyclopentanol (**5i**) and cyclohexanol (**5j**) also underwent catalytic H_2O_2-oxidation to give the corresponding cyclic ketones **6i** and **6j**, both in 97% yield (entries 8 and 9). The oxidation of the neopentyl alicyclic alcohol borneol (**5k**) proceeded more smoothly (7 h) than that of cyclopentanol (**5i**) and cyclohexanol (**5j**) to afford camphor (**6k**) in 87% isolated yield (entry 10). It is also noteworthy that the neopentyl alcohols, in particular borneol (**5k**), do not undergo any carbocation-based 1,2-rearrangement reactions, such as the Wagner−Meerwein rearrangement, that are generally promoted under acidic conditions.[14]

Table 1. The Oxidation of a Variety of Secondary Alcohols with Hydrogen Peroxide Promoted by **3**[a]



5a/6a: R^1 = Me, R^2 = *n*-Hex
5b/6b: R^1 = Me, R^2 = *n*-Bu
5c/6c: R^1 = *n*-Pr, R^2 = *n*-Hex
5d/6d: R^1 = *n*-Bu, R^2 = *n*-Pen
5e/6e: R^1 = Me, R^2 = Ph
5f/6f : R^1 = *i*-Pr, R^2 = *i*-Pr
5g/6g: R^1 = Me, R^2 = *t*-Bu
5h/6h: R^1 = *n*-Pr, R^2 = *t*-Bu
5i/6i : R^1,R^2 = -$(CH_2)_4$-
5j/6j : R^1,R^2 = -$(CH_2)_5$-
5k/6k: borneol/camphor

entry	substrate/product		time (h)	yield (%)
1	**5b/6b**		24	99
2	**5c/6c**		24	99
3	**5d/6d**		24	99
4	**5e/6e**		12	98
5	**5f/6f**		12	97
6	**5g/6g**		24	97
7	**5h/6h**		24	96
8	**5i/6i**		24	97
9	**5j/6j**		12	97
10	**5k/6k**		7	87
11	**5a/6a**		24	96
12[b]		(2nd use)		97
13[b]		(3rd use)		95
14[b]		(4th use)		99
15[b]		(5th use)		98

[a] Conditions: **5** (1 mmol), **3** (0.02 mmol W), 30% aq H_2O_2 (6 mmol), *t*-BuOH (3 mL), 80 °C. [b] Recovered catalyst **3** was used.

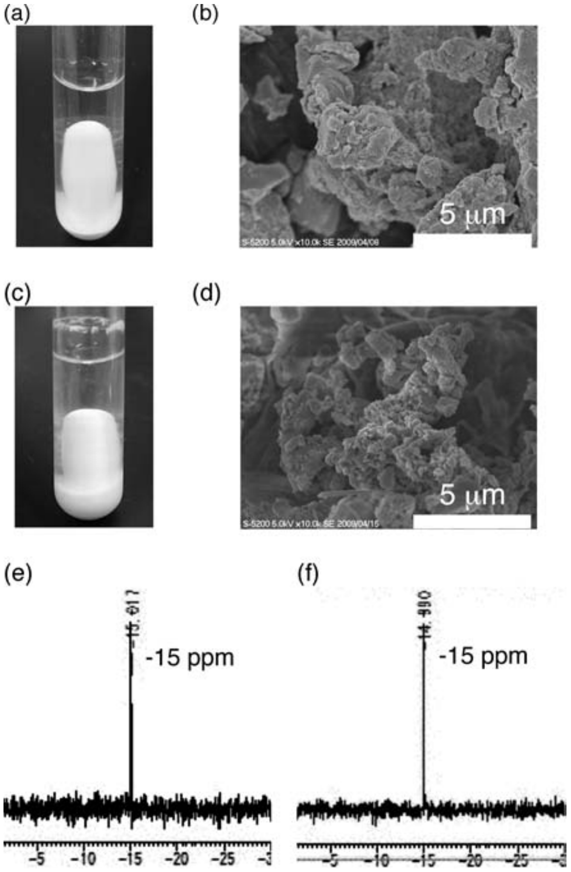
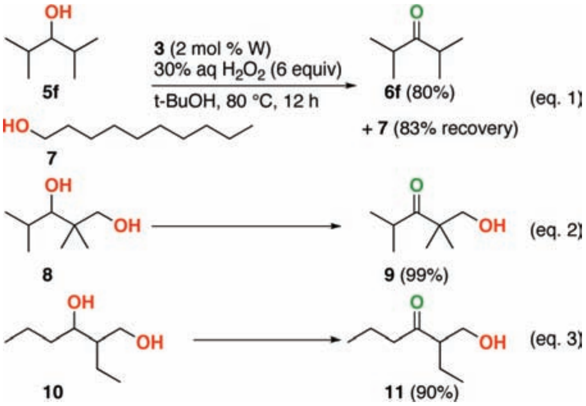


Figure 1. Photo, SEM images, and $^{31}P\{^1H\}$ NMR charts of the catalyst **3** (before and after catalytic use): (a) a photo image before use; (b) a SEM image before use; (c) a photo image after use; (d) a SEM image after use; (e) $^{31}P\{^1H\}$ NMR before use; and (f) $^{31}P\{^1H\}$ NMR after use.

The recyclability of the polymeric phosphotungstate catalyst **3** was examined for the oxidation of 2-decanol (**5a**). Thus, after the first reaction (Scheme 1), which gave a quantitative yield of the carbonyl product **6a** (Table 1, entry 11), the polymeric catalyst was recovered by simple filtration. The recovered catalyst was washed with water, dried in vacuo, and successively subjected to 5 more runs of the oxidation under the same conditions to afford **6a** in 97%, 95%, 99%, and 98% yield, respectively, (entries 12−15), during which hardly any tungsten residue could be detected by ICP-AES analysis from the aqueous or organic filtrates (lower than the detection limit of this analysis; <0.035 ppm). Furthermore, hot filtration examined for the oxidation of **5a** (after 60 min, 80 °C) terminated the formation of **6a** within 3 h to demonstrate no leaching of the catalytic species under the reaction conditions.[15] SEM observations as well as $^{31}P\{^1H\}$ NMR measurements of the recovered catalyst indicated that the catalyst **3** was undamaged under the oxidation conditions (Figure 1).

During the screening of the substrates, we encountered significantly lower reactivity of primary alcohols under similar catalytic conditions, which prompted us to examine the chemoselective oxidation of secondary alcohols in the presence of primary alcohols. Thus, a mixture of diisopropyl carbinol **5f** and 1-decaanol (**7**) in a molar ratio of 1:1 was subjected to the H_2O_2-oxidation in the presence of 2 mol % W of **3** at 80 °C. Whereas the oxidation of **5f** was almost complete within 12 h to give an 80% isolated yield of diisopropyl ketone (**6f**), the unreacted 1-decanol (**7**) was recovered in 83% yield (Scheme 2, eq 1). Next, the reaction of 2,2,4-trimethylpentane-1,3-diol (**8**) was carried out under similar conditions (2 mol % W of **3**, 6 mol equiv of 30% aqueous H_2O_2, in *t*-BuOH, 80 °C), and the selective oxidation took place efficiently to afford 1-hydroxy-2,2,4-trimethylpentan-3-one (**9**) in 99% yield, where the primary alcohol group remained completely intact (Scheme 2, eq 2). The chemoselective oxidation of 2-ethylhexane-1,3-diol (**10**) was also examined under otherwise similar conditions to give a 90% yield of 3-hydroxymethylheptan-4-one (**11**) where again a secondary alcohol group was the predominant group oxidized (Scheme 2, eq 3).

Scheme 2. The Chemoselective Oxidation of Secondary Alcohols in the Presence of Primary Alcohols[a]



[a] Conditions: **5f**, **7**, **8**, or **10** (1 mmol), **3** (0.02 mmol W), 30% aq H_2O_2 (6 mmol), *t*-BuOH (3 mL), 80 °C.

In conclusion, a novel convoluted poly(ethylene oxide-pyridinium) phosphotungstate catalyst **3** was developed, which catalyzed H_2O_2-oxidation of alcohols with high recyclability. The chemoselective and steric bulkiness-unretarded oxidation of secondary alcohols was achieved via oxidation catalysis with polymeric phosphotungstate. Installation of polymeric catalysts into flow-reaction devices is currently in progress in our laboratory and will be reported in due course.

Acknowledgment. We thank the Chemical Analysis Team in RIKEN for ICP-AES analyses. We also acknowledge the JSPS (Grant-in-Aid for Scientific Research no. 20655035; Grant-in-Aid for Scientific Research on Innovative Area no. 2105) for partial financial support of this work.

Supporting Information Available: Detailed experimental procedure as well as NMR, GC, and GCMS data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) For a review, see: Kaupp, G. *Top. Curr. Chem.* **1988**, *146*, 57.

(15) The time-lag observed for the termination of the ketone formation should be attributed to the thermal decomposition of decane-2-hydroperoxide, the possible reaction intermediate. Experimental details are provided in the Supproting Information, S-18.