[VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$]-catalyzed nitration of alkanes with nitric acid†

Kazuya Yamaguchi, Satoshi Shinachi and Noritaka Mizuno*

Department of Applied Chemistry, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan. E-mail: tmizuno@mail.ecc.u-tokyo.ac.jp; Fax: +81-3-5841-7220; Tel: +81-3-5841-7272

[VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$], which contains vanadyl counter cations and PMo$_{12}$O$_{40}$$^{3-}$, can act as a catalyst for the nitration of various alkanes including alkylbenzenes using nitric acid as a nitrating agent in acetic acid at 356 K.

Nitroalkanes are important precursors for a wide variety of chemicals such as pharmaceuticals and agrochemicals,[1] and are used as various synthetic intermediates because the nitro group can be removed selectively with maintenance of the other functional groups and the reduction of nitro compounds affords various nitrogen derivatives.[2] Despite their significant importance, there are only a few useful methods for the nitration of alkanes,[3] in contrast to the nitration of aromatics.[4]

Currently, nitration of lower alkanes such as propane is usually carried out using nitrogen dioxide or nitric acid under forced reaction conditions (523–673 K) because of the difficulty of activation of C–H bonds as well as nitrating agents. Under such conditions, alkanes undergo cleavage of the C–C bonds, resulting in formation of an undesirable mixture of lower alkanes and lower nitroalkanes.[5,6] In the presence of ozone at 195 K, nitrogen dioxide reacts with adamantane at tertiary position to give 1-nitroadamantane in a ~95% yield (Kyodai-nitration).[3a] The nitration of adamantane with nitronium tetrafluoroborate (NO$_2$$^+BF_4$$^-$) in carefully purified (nitrile free) nitroalkane solvent gives 60–70% yields of 1-nitroadamantane.[3b] However, these systems have disadvantages; necessity of special handling, *e.g.*, use of ozone, special purification of solvent, and narrow applicability only to limited alkanes (adamantane derivatives). Very recently, Ishii and coworkers have developed an efficient nitration system with nitric acid or nitrogen dioxide using *N*-hydroxyphthalimide (NHPI) as a catalyst precursor.[7] However, in the nitration of adamantane using nitric acid as a nitrating reagent (in our hands), most of the NHPI was decomposed to phthalic acid and other products. Therefore, a large amount of NHPI (at least 10 mol%) was required to achieve high conversion even in the nitration of rather reactive adamantane, and the catalyst could not be recycled. In these contexts, efficient, widely usable catalytic systems are unknown, while the key is activation of unreactive alkanes as well as nitrating agents with catalysts under mild reaction conditions.

In this paper, we report an efficient nitration of alkanes to the corresponding nitroalkanes using nitric acid by [VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$] which contains vanadyl counter cations and PMo$_{12}$O$_{40}$$^{3-}$. Various alkanes including alkylbenzenes were nitrated to the corresponding nitroalkanes in moderate to high yields under mild reaction conditions. To our knowledge, this is the first example of using polyoxometalates for the nitration of alkanes with nitric acid as a nitration reagent.

The nitration of adamantane (1 mmol) with nitric acid (2 mmol) was first carried out in the presence of [VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$] (1.67 mM, 0.5 mol%) at 356 K in acetic acid (3 mL) under argon. The main product was 1-nitroadamantane and oxygenated products of 1-adamantanol and 2-adamantanone were also produced. After *ca.* 12 h, the successive nitration of 1-nitroadamantane to 1,3-dinitroadamantane proceeded. The yield ratio of (1-nitroadamantane + 1,3-dinitroadamantane):1-adamantanol:2-adamanta-

none changed only slightly with time. The yields of 1-nitroadamantane, 1,3-dinitroadamantane, 1-adamantanol and 2-adamantanone after 24 h were 54, 7, 27 and 5%, respectively. In the absence of [VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$], the nitration did not proceed at all. After the nitration of adamantane was completed, adamantane (1 mmol) and nitric acid (2 mmol) were again added to the reaction solution and the solution was heated to 356 K. The nitration again easily proceeded with a very similar reaction rate and selectivity to those observed for the first run. Thus, the [VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$] catalyst is intrinsically recyclable. After the second run, the total turnover number (TTON) reached 362, approximately 50 times higher than that for the NHPI-catalyzed nitration reported previously.[7]

The nitration of adamantane in various solvents was carried out at 356 K under several reaction conditions. Among the solvents tested, acetic acid gave the highest yields of the corresponding nitro compounds, while the yields of nitro compounds were poor for ethyl acetate and acetonitrile. When the reaction was performed below 343 K, prolonged reaction times were needed to attain high yields of the corresponding nitro compounds. An increase in the reaction temperature to 373 K resulted in decreasing the selectivity to 1-nitroadamantane probably because the acceleration of the nitration of 1-nitroadamanatne to 1,3-dinitroadamantane. Therefore, the nitration was hereafter carried out at 356 K in acetic acid.

Fig. 1 shows the results of the nitration of adamantane using various catalysts in acetic acid at 356 K. As described above, the nitration did not proceed at all in the absence of catalyst. [VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$] afforded the highest yields of the corresponding nitro compounds. The nitration proceeded in the presence of H$_3$PMo$_{12}$O$_{40}$ to give the corresponding nitroadamantanes in moderate yields with oxygenated products. Vanadium-substituted polyoxomolybdate, H$_4$PVMo$_{11}$O$_{40}$, exhibited higher catalytic activity than that of H$_3$PMo$_{12}$O$_{40}$. VO(acac)$_2$ gave
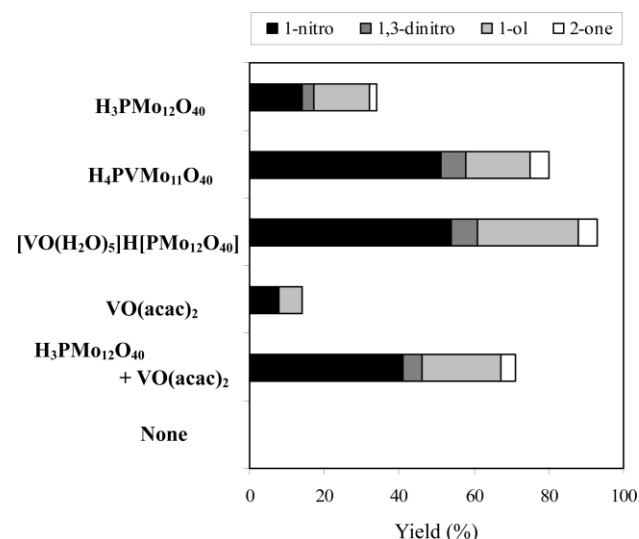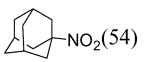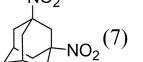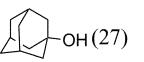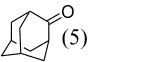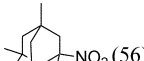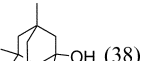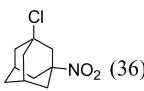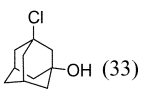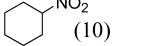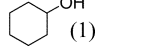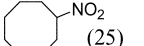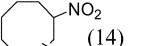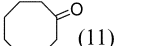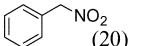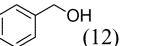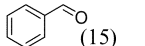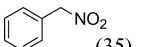
Fig. 1 Nitration of adamantane with nitric acid by various catalysts in acetic acid. Reaction conditions: adamantane (1 mmol), catalyst (0.5 mol%), nitric acid (2 mmol), acetic acid (3 mL), 356 K, argon atmosphere, 24 h.

† Electronic supplementary information (ESI) available: Experimental section. See http://www.rsc.org/suppdata/cc/b3/b314978a/

Table 1 Nitration of various alkanes catalyzed by $[VO(H_2O)_5]H[PMo_{12}O_{40}]$ with nitric acid[a]

Entry	Substrate	Conditions	Products (yield %)				TTON[b]
1	adamantane	A	1-nitroadamantane $-NO_2$ (54)	1,3-dinitroadamantane (7)	1-adamantanol $-OH$ (27)	adamantanone (5)	186
2	1,3-dimethyladamantane	A	$-NO_2$ (56)	$-OH$ (38)			188
3	1-chloroadamantane (Cl)	A	$-NO_2$ (36)	$-OH$ (33)			138
4	cyclohexane	B	NO_2 (10)	OH (1)			44
5	cyclooctane	A	$-NO_2$ (25)	$-NO_2$, NO_2 (14)	cyclooctanone (11)		100
6	toluene	B	$-NO_2$ (20)	$-OH$ (12)	benzaldehyde (15)		188
7	m-xylene	B	$-NO_2$ (35)	(18)			212
8	p-xylene	B	$-NO_2$ (30)	(33)			252

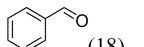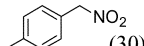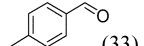[a] Reaction conditions: A: Alkane (1 mmol), $[VO(H_2O)_5]H[PMo_{12}O_{40}]$ (1.67 mM, 0.5 mol%), nitric acid (2 mmol), acetic acid (3 mL), 356 K, argon atmosphere. Yields were based on alkane and were determined by GC using naphthalene as an internal standard. B: Alkane (18.5 mmol), $[VO(H_2O)_5]H[PMo_{12}O_{40}]$ (1.00 mM, 0.03 mol%), nitric acid (2 mmol), acetic acid (3 mL), 356 K, argon atmosphere. Yields were based on nitric acid used and were determined by GC using naphthalene as an internal standard. [b] TTON (total turnover number) = products (mol)/catalyst used (mol).

1-nitroadamantane and 1-adamantanol in only 8 and 6% yield, respectively, and the activity was much lower than those of polyoxomolybdates. Interestingly, a mixture of $H_3PMo_{12}O_{40}$ and $VO(acac)_2$ showed much higher catalytic activity than those of $H_3PMo_{12}O_{40}$ and $VO(acac)_2$. These facts show that there is a synergistic effect between polyoxomolybdates and vanadium cations. Since the existence of reducible metal cations such as Cu^{2+} and Pd^{2+} can promote the reduction and reoxidation of $H_3PMo_{12}O_{40}$,[8] vanadium species, which are more easily reduced and reoxidized,[9] likely accelerate the reduction and reoxidation of $H_3PMo_{12}O_{40}$, resulting in the promotion of the nitration by the anion.

Table 1 summarizes the results of $[VO(H_2O)_5]H[PMo_{12}O_{40}]$-catalyzed nitration of various alkanes in acetic acid at 356 K. The nitration of adamantane proceeded at the tertiary C–H bonds to give mainly 1-nitroadamantane and 1,3-dinitroadamantane with oxygenated products (entry 1). Substituted adamantanes, 1,3-dimethyladamantane and 1-chloroadamantane were also nitrated to form the corresponding nitro compounds (entries 2 and 3). The nitration of cyclohexane yields nitrocyclohexane with high selectivity (entry 4). In this case, C–C bond cleavage products could hardly be detected. Cyclooctane was also nitrated to form the corresponding mono and dinitro compounds along with cyclooctanone (entry 5). It is noted that alkylbenzenes such as toluene and m- and p-xylenes were also nitrated only at the alkyl side-chain C–H bonds and that no nitration of the aromatic ring was observed under these reaction conditions (entries 6–8) although the nitration of the alkyl side-chains of alkylbenzenes is very difficult with conventional methods.[1,2] In the case of benzene and naphthalene, nitration as well as hydroxylation of aromatic ring did not proceed under the present conditions.

In conclusion, we have developed a system using polyoxometalate catalysts for the nitration of not only normal alkanes but also alkylbenzenes, to the corresponding nitroalkanes using nitric acid under mild conditions.

Notes and references

1 (a) H. Feuer and T. Nielsen, *Nitrocompounds: Recent Advances in Synthesis and Chemistry*, VCH, New York, 1990; (b) A. F. Bollmeier, Jr., in *Encyclopedia of Chemical Technology*, ed. J. I. Kroschwitz, John Wiley & Sons, Inc., New York, 1996, vol. 17, pp. 205–225; (c) J. J. Carberry, *Chem. Eng. Sci.*, 1959, **9**, 189; (d) L. F. Albright, in *Encyclopedia of Chemical Technology*, ed. J. I. Kroschwitz, John Wiley & Sons, Inc., New York, 1996, **vol. 17**, pp. 68–80.

2 N. Ono, *The Nitro Group in Organic Synthesis*, John Wiley-VCH, New York, 2001.

3 (a) H. Suzuki and N. Nonomiya, *Chem. Commun.*, 1996, 1783; (b) G. A. Olah, P. Ramaiah, B. C. Rao, G. Sandford, R. Golam, N. J. Trivedi and J. A. Olah, *J. Am. Chem. Soc.*, 1993, **115**, 7246; (c) G. A. Olah and C. H. Lin, *J. Am. Chem. Soc.*, 1971, **93**, 1259; (d) I. Tabushi, S. Kojo and Z. Yoshida, *Chem. Lett.*, 1971, 1431.

4 (a) G. A. Olah, R. Malhotra and S. C. Narahg, *Nitration: Methods and Mechanism*, VCH, New York, 1989; (b) T. Mori and H. Suzuki, *Synlett*, 1995, 383, and references cited therein.

5 (a) G. B. Bachman, L. M. Addison, J. V. Hewett, L. Kohn and A. G. Millikan, *J. Org. Chem.*, 1952, **17**, 906; (b) G. B. Bachman, H. B. Hass and L. M. Addison, *J. Org. Chem.*, 1952, **17**, 914; (c) G. B. Bachman, H. B. Hass and J. V. Hewett, *J. Org. Chem.*, 1952, **17**, 928; (d) G. B. Bachman, J. V. Hewett and A. G. Millikan, *J. Org. Chem.*, 1952, **17**, 935; (e) G. B. Bachman and L. Kohn, *J. Org. Chem.*, 1952, **17**, 942.

6 (a) G. W. Smith and H. D. Williams, *J. Org. Chem.*, 1961, **26**, 2207; (b) H. Stetter, *Angew. Chem.*, 1954, **66**, 217.

7 (a) Y. Nishiwaki, S. Sakaguchi and Y. Ishii, *J. Org. Chem.*, 2002, **67**, 5663; (b) S. Sakaguchi, Y. Nishiwaki, T. Kitamura and Y. Ishii, *Angew. Chem., Int. Ed.*, 2001, **40**, 222; (c) S. Isozaki, Y. Nishiwaki, S. Sakaguchi and Y. Ishii, *Chem. Commun.*, 2001, 1352.

8 M. Akimoto, K. Shima, H. Ikeda and E. Echigoya, *J. Catal.*, 1984, **86**, 173.

9 K. Inumaru, A. Ono, H. Kubo and M. Misono, *J. Chem. Soc., Faraday Trans.*, 1998, **94**, 1765.