Nitration of Alkanes with Nitric Acid by Vanadium-Substituted Polyoxometalates

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Abstract: The nitration of alkanes by using nitric acid as a nitrating agent in acetic acid was efficiently promoted by vanadium-substituted Keggin-type phosphomolybdates such as $[H_4PVMo_{11}O_{40}]$, $[H_5PV_2Mo_{10}O_{40}]$, and $[H_6PV_3Mo_9O_{40}]$ as catalyst precursors. A variety of alkanes including alkylbenzenes were nitrated to the corresponding nitroalkanes as major products in moderate yields with formation of oxygenated products under mild reaction conditions. The carbon–carbon bond cleavage reactions hardly proceeded. ESR, NMR, and IR spectroscopic data show that the vanadium-substituted polyoxometalate, for example, $[H_4PVMo_{11}O_{40}]$, decomposes to form free vanadium species and $[PMo_{12}O_{40}]^{3-}$ Keggin anion. The reaction mechanism involving a radical-chain path is proposed. The polyoxometalates initially abstract the hydrogen of the alkane to form the alkyl radical and the reduced polyoxometalates. The reduced polyoxometalates subsequently react with nitric acid to produce the oxidized form and nitrogen dioxide. This step would be promoted mainly by the phosphomolybdates, $[PMo_{12}O_{40}]^{n-}$, and the vanadium cations efficiently enhance the activity. The nitrogen dioxide promotes the further formation of nitrogen dioxide and an alkyl radical. The alkyl radical is trapped by nitrogen dioxide to form the corresponding nitroalkane.

Keywords: alkanes · molybdophosphate · nitration · nitric acid · vanadium

Introduction

Polyoxometalates catalyze transformation of various kinds of functional groups because the acid and redox properties can be controlled at the atomic and molecular levels by changing the constituent elements.[1] Various kinds of polyoxometalate-catalyzed reactions have been reported,[2] and Keggin-type phosphovanadomolybdates such as $[H_4PVMo_{11}O_{40}]$, $[H_5PV_2Mo_{10}O_{40}]$, and $[H_6PV_3Mo_9O_{40}]$ are reported to be catalytically active for liquid-phase oxidation reactions.[3]

Nitration of alkanes is an important reaction in academic and industrial fields because nitroalkanes are important precursors for pharmaceuticals and agrochemicals,[4] and are used as various synthetic intermediates because the nitro group can be removed selectively while maintaing other functional groups; furthermore the reduction of nitro compounds affords various nitrogen derivatives such as amines, oximes, nitroso compounds, and hydroxyl amines.[5] Despite their significant importance, there are only a few useful methods for the nitration of alkanes[6] in contrast to the nitration of aromatics.[7] 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, which results in the formation of the undesirable lower alkanes/nitroalkanes.[8]

Even in the case of rather reactive adamantane, it is known that the nitration with concentrated nitric acid or nitrogen dioxide does not proceed even under the forced conditions.[9] In the presence of ozone, nitrogen dioxide reacts with adamantane at tertiary position to give 1-nitroadamantane as a main product.[6a] Nitration of adamantane under free-radical conditions was carried out by irradiating a solution of adamantane and dinitrogen pentoxide to give a mixture of 1-nitroadamantane, adamantyl nitrate, 2-nitroadamantane, and 2-adamantanone as products.[6d] The nitration of adamantane with nitronium tetrafluoroborate (NO_2^+ BF_4^-) in a carefully purified (nitrile free) nitroalkane solvent gives 1-nitroadamantane in 60–70% yield.[6b] However, these systems have disadvantages; they require special han-
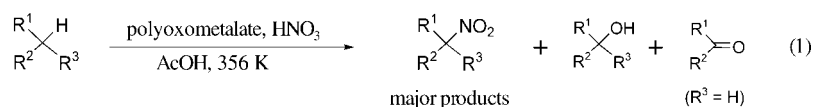
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dling, for example, the use of ozone, and careful purification of solvents; also, they are of limited use for some alkanes, such as adamantane derivatives. In these contexts, efficient, widely usable *catalytic* systems are previously unknown, while the key is activation of unreactive alkanes as well as nitrating agents with catalysts under mild reaction conditions. Recently, Ishii and co-workers have developed an efficient nitration system with nitric acid or nitrogen dioxide by using *N*-hydroxyphthalimide (NHPI) as a catalyst precursor.[10] However, in the nitration of adamantane using nitric acid as a nitrating reagent (employed by our group), the NHPI almost completely decomposed to phthalic acid and other products. Therefore, a large amount of NHPI (at least 10 mol%) was required to achieve the high conversion even in the nitration of adamantane and the catalyst could not be recycled.

We have previously reported that $[VO(H_2O)_5]H[PMo_{12}O_{40}]$ could act as a catalyst for the nitration of alkanes.[11] During the course of our investigation, we found that Keggin-type vanadium-substituted phosphomolybdates such as $[H_4PVMo_{11}O_{40}]$, $[H_5PV_2Mo_{10}O_{40}]$, and $[H_6PV_3Mo_9O_{40}]$ also showed high catalytic activity for the nitration of alkanes by using nitric acid as a nitration agent. Various alkanes including alkylbenzenes were nitrated to the corresponding nitroalkanes in high or moderate yields under mild reaction conditions [Eq. (1)]. In this paper, we report the scope of nitration by using the vanadium-substituted phosphomolybdates as catalyst precursors. Further, we investigate the possible reaction path.

Figure 1. Reaction profiles of the nitration of adamantane with nitric acid catalyzed by $H_4PVMo_{11}O_{40}$; conversion of adamantane (*), yields of 1-nitroadamantane (●), 1,3-dinitroadamantane (◆), 1-adamantanol (▲), 2-adamantanone (■). Reaction conditions: Adamanatane (1 mmol, 0.33 M), $[H_4PVMo_{11}O_{40}]$ (0.5 mol%, 1.67 mM), nitric acid (2 mmol, 0.67 M), acetic acid (3 mL), 356 K, under 1 atm of argon.

+ 1,3-dinitroadamantane):1-adamantanol:2-adamantanone changed little with time. This means that the nitration and oxygenation products are formed in parallel. Table 1 shows the results of the nitration of adamantane under several reaction conditions. Among the solvents tested, acetic acid and trifluorotoluene gave the high yields of the corresponding nitro compounds (entries 3 and 5), while the yields were low for ethyl acetate and acetonitrile (entries 6 and 7).

When the nitration was carried out with various solvents, the conversion decreased with decrease in the amount of gaseous nitrogen dioxide evolved. When the reaction was performed below 343 K, prolonged reaction time was needed to attain high yields of the corresponding nitro compounds (entries 1 and 2). The increase in the reaction temperature to 373 K resulted in the decrease in the selectivity to 1-nitroadamantane probably because of the acceleration of the nitration of

major products $(R^3 = H)$ (1)

Results and Discussion

Scope of the present nitration: The nitration of adamantane with nitric acid was first carried out in the presence of $[H_4PVMo_{11}O_{40}]$ (1.67 mM, 0.5 mol%) at 356 K in acetic acid (3 mL) under argon. The time course is shown in Figure 1. The nitration of adamantane proceeded with an induction period (3–4 h). The main product was 1-nitroadamantane and oxygenated products of 1-adamantanol and 2-adamantanone were also produced. After 12 h, the successive nitration of 1-nitroadamantane to 1,3-dinitroadamantane proceeded. The yields of 1-nitroadamantane, 1,3-dinitroadamantane, 1-adamantanol, and 2-adamantanone after 24 h were 51, 7, 17, and 5%, respectively, and the yield ratio of (1-nitroadamantane
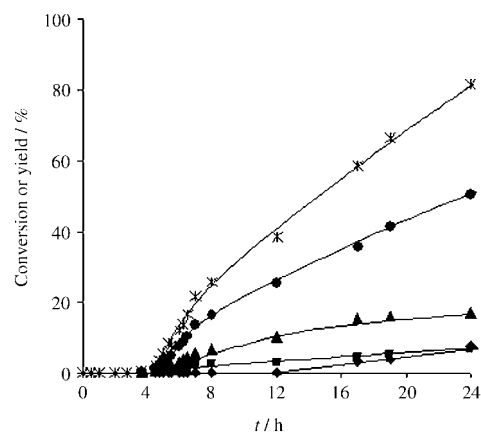
Table 1. Nitration of adamantane with nitric acid under various reaction conditions.[a]

Entry	Solvent	T/K	Yield/%				
			1-nitro	1,3-dinitro	1-ol	2-one	total
1[b]	AcOH	333	trace	n.d.	trace	n.d.	<1
2[b]	AcOH	343	10	1	11	trace	22
3	AcOH	356	51	7	17	5	80
4	AcOH	373	41	20	13	5	81
5	PhCF$_3$	356	59	7	25	4	95
6	AcOEt	356	14	trace	22	3	39
7	CH$_3$CN	356	n.d.	n.d.	n.d.	n.d.	<1

[a] Adamantane (1 mmol), $H_4PVMo_{11}O_{40}$ (1.67 mM, 0.5 mol%), nitric acid (2 mmol), solvent (3 mL), under 1 atm of argon, 24 h. Yields were based on adamantane used and determined by GC using naphthalene as an internal standard. [b] 48 h.

1-nitroadamanatne to 1,3-dini-troadamantane (entry 4). Therefore, the nitration was hereafter carried out at 356 K in acetic acid.

Table 2 summarizes the results of the nitration of various alkanes by [H$_4$PVMo$_{11}$O$_{40}$] in acetic acid at 356 K. The nitration of adamantane proceeded at the tertiary C–H bonds to give mainly 1-nitroadamana-tane and 1,3-dinitroadamantane with oxygenated products (entry 1). 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 proceeded with almost the same induction period, reaction rate and selectivity as those observed for the first run (Figure S1, Supporting Information). Thus, the [H$_4$PVMo$_{11}$O$_{40}$] is intrinsically recyclable. Substituted adamantanes of 1,3-di-methyladamantane and 1-chloroadamantane were also nitrated to the corresponding nitro compounds (entries 2 and 3). Cyclohexane was highly selectively nitrated to nitrocyclo-hexane, while hardly any C–C bond cleavage was observed (entry 4). Cyclooctane was also nitrated to the corresponding mono and dinitro compounds along with cyclooctanone (entry 5). It is noted that alkylbenzenes such as toluene and *p*-xylene 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 and 7), although the nitration of the alkyl side-chain of alkylbenzenes is very difficult with the conventional methods.[1,2] In the case of benzene, nitration as well as hydroxylation of aromatic ring did not occur under the present conditions.

State of catalyst: Next, ESR spectra of [H$_4$PVMo$_{11}$O$_{40}$] in acetic acid were measured to investigate the catalyst state. In the measurements, 1,3-dimethyladamantane was used as a substrate because the solubility of adamantane in acetic acid was low below 298 K (the temperature of ESR measurements) and adamantane added was in part insoluble. The acetic acid solution of [H$_4$PVMo$_{11}$O$_{40}$] (1.67 mM) *without* 1,3-dimethyladamantane was completely ESR silent after the treatment at 356 K under argon. To the solution, 200 equivalents of 1,3-dimethyladamantane with respect to [H$_4$PVMo$_{11}$O$_{40}$] were added and the solution was kept at 356 K under 1 atm of argon. After 4 h, the color of the solution was changed from orange to yellow-green, suggesting the reduction of [H$_4$PVMo$_{11}$O$_{40}$]. Then, the ESR spectrum of the solution was measured at 100 K (solid line in Figure 2a). The hyperfine structure of vanadium was observed and the spectrum was well reproduced by the simulation

Table 2. Nitration of various alkanes catalyzed by H$_4$PVMo$_{11}$O$_{40}$ with nitric acid.[a]

Entry	Substrate	Conditions	TTON[b]	Products	Yield/%
1	adamantane	**I**	160	1-nitroadamantane	51
				1,3-dinitroadamantane	7
				1-adamantanol	17
				2-adamantanone	5
2	1,3-dimethyladamantane	**I**	114	1,3-dimethyl-5-nitroadamantane	41
				3,5-dimethyl-1-adamantanol	16
3	1-chloroadamantane	**I**	108	1-chloro-3-nitroadamantane	36
				3-chloro-1-adamantanol	18
4	cyclohexane	**II**	40	nitrocyclohexane	9
				cyclohexanol	1
5	cyclooctane	**I**	100	nitrocyclooctane	25
				dinitrocyclooctanes	14
				cyclooctanone	11
6	toluene	**II**	168	(nitromethyl)benzene	20
				benzyl alcohol	7
				benzaldehyde	15
7	*p*-xylene	**II**	320	1-methyl-4-(nitromethyl)benzene	48
				p-tolualdehyde	32

[a] Reaction conditions **I**: alkane (1 mmol), [H$_4$PVMo$_{11}$O$_{40}$] (1.67 mM, 0.5 mol%), nitric acid (2 mmol), acetic acid (3 mL), 356 K, under 1 atm of argon. Yields were based on alkanes used and determined by GC using naphthalene as an internal standard. Reaction conditions **II**: alkane (18.5 mmol), [H$_4$PVMo$_{11}$O$_{40}$] (1.00 mM, 0.03 mol%), nitric acid (2 mmol), acetic acid (3 mL), 356 K, under 1 atm of argon. Yields were based on nitric acid used and determined by GC using naphthalene as an internal standard. [b] TTON (total turnover number) = products (mol)/[H$_4$PVMo$_{11}$O$_{40}$] used (mol).

with parameters characteristic of V^{4+} as follows; $g_\perp = 1.982$, $g_\| = 1.935$, $A_\perp = 7.0$ mT, and $A_\| = 18.1$ mT (dotted line in Figure 2a).[12,13] The signal intensity corresponds to the extent of reduction of 1.0 electron per polyanion; this shows that all of the V^{5+} was reduced to V^{4+}. Separately, we synthesized [VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$] and measured the ESR spectrum in acetic acid at 100 K. It was found that the parameters of the hyperfine structure were the same as those in Figure 2a. To the yellow-green solution, two equivalents of nitric acid with respect to 1,3-dimethyladamantane were added under argon, resulting in the quick disappearance of ESR signals (Figure 2b) and the evolution of nitrogen dioxide. This fact indicates that the reduced polyoxometalate is easily reoxidized by nitric acid.[13] Then, the nitration reaction proceeded with almost the same rate as that under the catalytic turnover conditions (in Table 2). In the case of [H$_3$PMo$_{12}$O$_{40}$], a very weak broad signal of Mo^{5+} was observed at $g = 1.951$ (100 K).

^{51}V and ^{31}P NMR measurements were carried out at 356 K with the same sample as that used for the ESR measurements. The fresh [H$_4$PVMo$_{11}$O$_{40}$] in acetic acid gave a chemical shift of δ −562.9 in the ^{51}V NMR analysis. The signal intensity became much weaker after the treatment with 1,3-dimethyladamantane at 356 K under argon. The decrease in the intensity can be explained by the reduction of V^{5+} species to V^{4+}.[14] On the other hand, no spectral changes were observed *without* 1,3-dimethyladamantane. These observations are in good agreement with the ESR results. The fresh [H$_4$PVMo$_{11}$O$_{40}$] showed a ^{31}P NMR signal at δ −1.59 in acetic acid. The signal intensity became very weak and an intense signal at δ −2.16 was observed after the treatment with 1,3-dimethyladamantane at 356 K under argon. This signal at δ −2.16 is assigned to [PMo$_{12}$O$_{40}$]$^{3-}$ since the ^{31}P NMR spectra of H$_3$PMo$_{12}$O$_{40}$ and [VO(H$_2$O)$_5$]H[PMo$_{12}$O$_{40}$] in acetic acid (1.67 mM) showed signals at δ −2.20

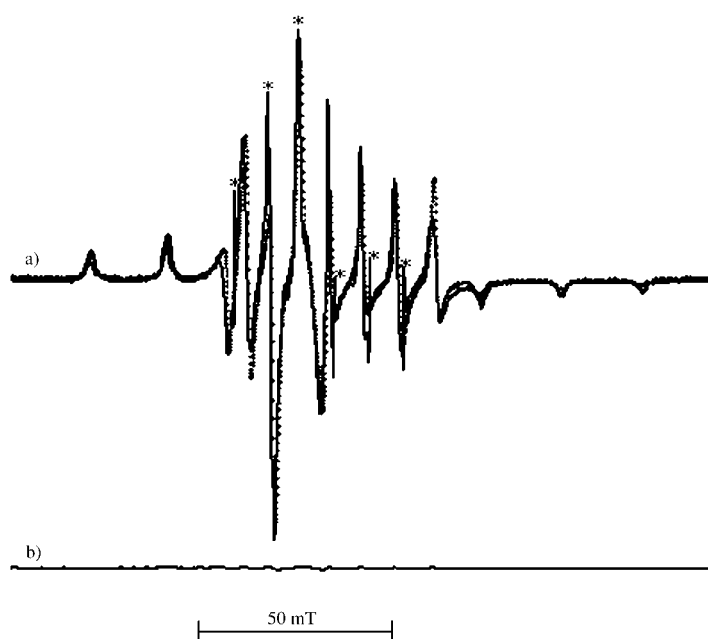Figure 2. ESR spectra of $[H_4PVMo_{11}O_{40}]$ in acetic acid measured at 100 K. a) 1.67 mM $[H_4PVMo_{11}O_{40}]$ in acetic acid was treated by 200 equivalents of 1,3-dimethyladamantane at 356 K for 4 h under 1 atm of argon. b) 2 equivalents of nitric acid with respect to 1,3-dimethyladamantane were added to the above solution. Six asterisks are assigned to the signals of the Mn marker. The dotted line in a) is obtained by the simulation (see text).

$[H_5PV_2Mo_{10}O_{40}]$, and $[H_6PV_3Mo_9O_{40}]$ exhibited higher activity and selectivity to the nitration products than those of $[H_3PMo_{12}O_{40}]$ (entries 2–4). $[VO(acac)_2]$ gave 1-nitroadamantane and 1-adamantanol in 8 and 6% yields, respectively, and the activity was much lower than those of phosphomolybdates (entry 8). Interestingly, a mixture of $[H_3PMo_{12}O_{40}]$ and $[VO(acac)_2]$ showed higher activity than those of $[H_3PMo_{12}O_{40}]$ and $[VO(acac)_2]$ (entry 9). When $[VO(H_2O)_5]H[PMo_{12}O_{40}]$ was used as a catalyst, the nitration of various alkanes was efficiently promoted and the activity was similar to that of $[H_4PVMo_{11}O_{40}]$ (entry 10 and Table S1 in the Supporting Information).[11] These facts show that there is a synergistic effect between phosphomolybdates and vanadium cations. As mentioned above, $[H_3PMo_{12}O_{40}]$ as intrinsically active for the nitration and the activity was higher than that of vanadium compounds. Therefore, the present nitration would be proceeded mainly by the $[PMo_{12}O_{40}]^{3-}$ anion. Since the metal cations such as Cu^{2+} and Pd^{2+} can promote the reduction of $[PMo_{12}O_{40}]^{3-}$ and the reoxidation of the reduced form,[17] the eliminated vanadium species likely promotes the reduction and reoxidation of the anion, for example, $[PMo_{12}O_{40}]^{4-}+V^{5+} \rightarrow [PMo_{12}O_{40}]^{3-}+V^{4+}$, which results in the acceleration of the nitration by the anion. Similar acceleration of isobutane oxidation by $[H_3PMo_{12}O_{40}]$, in the presence of vanadium species has been reported.[15]

Reaction mechanism: The nitration reactions proceed generally via either ionic or free-radical mechanism. The nitronium ion (NO_2^+) mechanism has been accepted for the nitration of aromatic compounds catalyzed by mixed acids, for example, sulfuric acid and nitric acid. While it is possible that polyoxometalates can act as a strong Brønsted acid to generate nitronium ion, no nitration of aromatic compounds proceeded in the present system. Therefore, the nitronium ion mechanism (ionic mechanism) can be excluded. When nitric acid is used in the vapor-phase nitration, the reaction

and −2.19, respectively. The IR spectrum of fresh $[H_4PVMo_{11}O_{40}]$ showed the bands characteristic of the Keggin structure; $\tilde{v}$(Mo-O-Mo) (787 and 866 cm^{-1}), $\tilde{v}$(Mo= O) (961 cm^{-1}), $\tilde{v}$(P-O-Mo) (1062 cm^{-1}), and $\tilde{v}$(P-O-V) (1078 cm^{-1}). By the treatment with 1,3-dimethyladamantane, the band position and intensities were almost unchanged except that a shoulder $\tilde{v}$(P-O-V) band disappeared (Figure S2).

These ESR, NMR, and IR data show the elimination of the vanadium from the Keggin structure to form free vanadium species and $[PMo_{12}O_{40}]^{3-}$ Keggin anions.[16]

Roles of $[PMo_{12}O_{40}]^{n-}$ and vanadium: Table 3 shows the results of the nitration of adamantane using various catalysts in acetic acid at 356 K. The nitration did not proceed in the absence of catalysts (entry 11), but proceeded in the presence of $[H_3PMo_{12}O_{40}]$ to give the corresponding nitroadamantanes and oxygenated products in moderate yields (entry 1). Vanadium-substituted polyoxomolybdates such as $[H_4PVMo_{11}O_{40}]$,

Table 3. Nitration of adamantane with nitric acid by various catalysts in acetic acid.[a]

Entry	Catalyst	Yield/%				
		1-nitro	1,3-dinitro	1-ol	2-one	total
1	$[H_3PMo_{12}O_{40}]$	14	3	15	2	34
2	$[H_4PVMo_{11}O_{40}]$	51	7	17	5	80
3	$[H_5PV_2Mo_{10}O_{40}]$	45	8	25	5	83
4	$[H_6PV_3Mo_9O_{40}]$	44	11	26	5	86
5	$[H_3PW_{12}O_{40}]$	3	trace	3	trace	6
6	$[H_4PVW_{11}O_{40}]$	33	2	15	trace	50
7	$[H_5PV_2W_{10}O_{40}]$	26	trace	18	trace	44
8	$[VO(acac)_2]$	8	trace	6	trace	14
9[b]	$[H_3PMo_{12}O_{40}]+[VO(acac)_2]$	41	5	21	4	71
10	$[VO(H_2O)_5]H[PMo_{12}O_{40}]$	54	7	27	5	93
11	none	n.d.	n.d.	n.d.	n.d.	<1

[a] Reaction conditions: Adamantane (1 mmol), catalyst (1.67 mM, 0.5 mol%), nitric acid (2 mmol), acetic acid (3 mL), 356 K, under 1 atm of argon, 24 h. Yields were based on adamantane used and determined by GC using naphthalene as an internal standard. [b] Catalyst: A mixture of $[H_3PMo_{12}O_{40}]$ (1.67 mM) and $[VO(acac)_2]$ (1.67 mM).

is initiated by the homolytic decomposition of nitric acid into nitrogen dioxide and a hydroxyl radical. Then, hydroxyl radicals and alkyl radicals are propagated (Scheme S1). If the present nitration by using polyoxometalates proceeds in a similar way, aromatic hydroxylation takes place. However, in the present system, no hydroxylation of aromatic compounds such as benzene, toluene, and *p*-xylene proceeded. Therefore, we exclude the mechanism in the present nitration.

We investigated the reaction mechanism in more detail with [H$_4$PVMo$_{11}$O$_{40}$]. First, the nitration reaction was carried out by using adamantane as a test substrate under the conditions described in Table 2. As above mentioned (Figure 1), the nitration of adamantane proceeded with an induction period (3–4 h). After the period, the nitrogen dioxide gas was evolved, which was confirmed by UV/Vis spectroscopy according to ref. [18]. Without [H$_4$PVMo$_{11}$O$_{40}$], no evolution of nitrogen dioxide was observed and the nitration did not proceed. Further, no evolution of nitrogen dioxide was observed without addition of adamantane. In contrast, nitrogen dioxide was evolved even at room temperature upon the treatment of reduced [H$_4$PVMo$_{11}$O$_{40}$] or [H$_3$PMo$_{12}$O$_{40}$] (one electron per polyanion by using ascorbic acid) with nitric acid, while no nitrogen dioxide was evolved upon the treatment of the oxidized (fresh) polyoxometalates with nitric acid.

On the basis of all these results, it is probable that nitrogen dioxide is produced according to the following mechanism (Scheme 1): An alkane reacts with a polyoxometalate (POM$_{ox}$) to form the polyoxometalate (POM$_{red}$) and an alkyl radical (step 1). The reduced species then reacts with nitric acid to regenerate the oxidized form along with nitrogen dioxide (step 2). Addition of 2,2′-azobis(isobutyronitrile) (AIBN, 2 mol % with respect to adamantane) as an alkyl radical initiator to the reaction mixture did not affect the induction period, reaction rate, and product selectivity. Further, AIBN alone yielded no nitration products in the absence of polyoxometalates (<1 % conversion after 36 h). When copper metal (50 μmol)[19] was added to the system without polyoxometalates, nitrogen dioxide was quickly evolved and the induction period disappeared (▲ in Figure 3). The initial rate was almost the same as the postinduction rate without copper metal (■ in Figure 3). When nitrogen dioxide was introduced to the reaction system, the induction period disappeared. The initial rate was almost the same as the postinduction rate and product selectivity was unchanged. These observations suggest that [H$_4$PVMo$_{11}$O$_{40}$] is not directly involved in the nitration of an alkane, but initiates formation of nitrogen dioxide and an alkyl radical species with nitric acid and an alkane and that the formation of nitrogen dioxide is a key reaction for the present nitration. An induction period would be needed to build up the sufficient chain carrier of nitrogen dioxide by the reaction among [H$_4$PVMo$_{11}$O$_{40}$], alkanes, and nitric acid according to the Scheme 1.

Next, the kinetic studies on the nitration of adamantine by using [H$_4$PVMo$_{11}$O$_{40}$] were carried out. The dependence of the rate on the concentration of [H$_4$PVMo$_{11}$O$_{40}$] (0.03–1.67 mM) was investigated. The rate (R_0) was estimated by
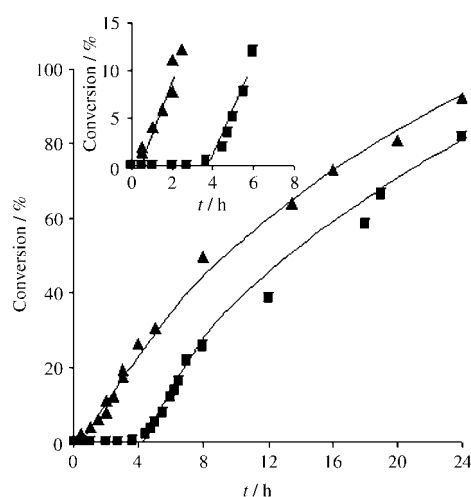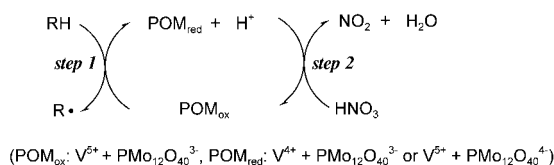

Figure 3. Reaction profiles of the nitration of adamantane with nitric acid. Adamantane (1 mmol, 0.33 M), [H$_4$PVMo$_{11}$O$_{40}$] (0.5 mol %, 1.67 mM), nitric acid (2 mmol, 0.67 M), acetic acid (3 mL), 356 K, under 1 atm of argon (■). The other reaction was carried out under the same conditions as those above described except that copper metal (50 μmol) was used instead of H$_4$PVMo$_{11}$O$_{40}$ (▲).

(POM$_{ox}$: V^{5+} + PMo$_{12}$O$_{40}^{3-}$, POM$_{red}$: V^{4+} + PMo$_{12}$O$_{40}^{3-}$ or V^{5+} + PMo$_{12}$O$_{40}^{4-}$)

Scheme 1.

the slope of the linear line after the induction period. Figure 4 shows the dependence of R_0 on the concentration of [H$_4$PVMo$_{11}$O$_{40}$]. The slope of $\log(R_0)$ versus $\log([$H$_4$PVMo$_{11}$O$_{40}])$ was 0.53 (inset in Figure 4), and the dependence of R_0 on the concentration of [H$_4$PVMo$_{11}$O$_{40}$] was positive. Approximately first-order dependences on the concentration of adamantane (Figure 5) and nitric acid (Figure 6) were observed for the nitration. The same dependences of the rates on the concentrations of [H$_4$PVMo$_{11}$O$_{40}$], nitric acid, and adamantane were observed for the formation rates of the nitration and oxidation products.

In a separate experiment, nitrogen monoxide was generated in situ by the reaction of nitric acid with FeSO$_4$·7H$_2$O[19,20] in acetic acid and then adamantane was added. Adamantane was easily nitrated to give 1-nitroadamantane (64 %), 1,3-dinitroadamantane (9 %), 1-adamantanol (16 %), and 2-adamantanone (4 %) after 24 h with a very similar reaction profile to that observed for a [H$_4$PVMo$_{11}$O$_{40}$]/nitric acid system. When nitrous acid was generated in situ by the reaction of nitric acid with NaNO$_2$ or Ba(NO$_2$)$_2$[21,22] in acetic acid followed by the addition of adamantane, a similar profile to that with nitrogen monoxide was obtained. These results suggest that nitrogen monoxide and nitrous acid can take part in the further formation of an alkyl radical and nitrogen dioxide from an alkane and nitric acid; for example, NO$_2$+RH→HNO$_2$+R·, 3HNO$_2$→2NO+HNO$_3$+H$_2$O, and NO+2HNO$_3$→3NO$_2$+H$_2$O.[20,21] Fi-
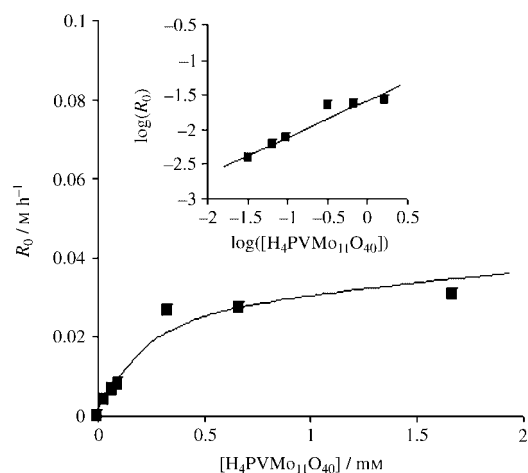
Figure 4. Dependence of initial rate R_0 on the concentration of [$H_4PVMo_{11}O_{40}$]. Adamanatane (0.33 M), [$H_4PVMo_{11}O_{40}$] (0.03–1.67 mM), nitric acid (0.67 M), acetic acid (3 mL), 356 K, under 1 atm of argon. R_0 values were determined from the reaction profiles (conversion vs time curves) at low conversion (<10%) of adamantane. Slope from the inset = 0.53.
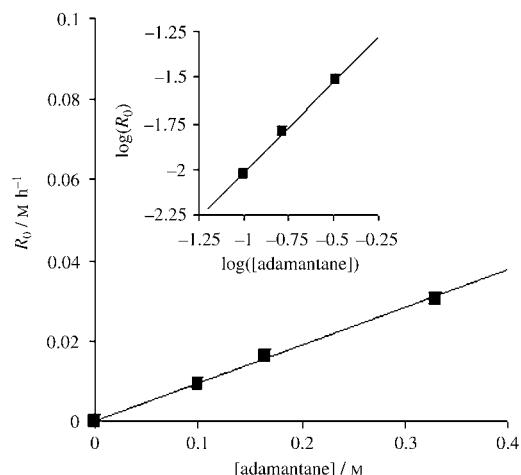

Figure 6. Dependence of initial rate R_0 on the concentration of nitric acid. Reaction conditions: Adamanatane (0.33 M), [$H_4PVMo_{11}O_{40}$] (1.67 mM), nitric acid (0.33–1.67 M), H_2O (2.62 M), acetic acid (3 mL), 356 K, under 1 atm of argon. R_0 values were determined from the reaction profiles (conversion vs time curves) at low conversion (<10%) of adamantane. Slope from the inset = 1.05.

Figure 5. Dependence of initial rate R_0 on the concentration of adamantane. Reaction conditions: Adamanatane (0.10–0.33 M), $H_4PVMo_{11}O_{40}$ (1.67 mM), nitric acid (0.67 M), acetic acid (3 mL), 356 K, under 1 atm of argon. R_0 values were determined from the reaction profiles (conversion vs time curves) at low conversion (<10%) of adamantane. Slope from the inset = 0.97.

nally, the alkyl radical formed is trapped by nitrogen dioxide to afford the corresponding nitroalkane.

In the present system, oxygenated products such as alcohols and ketones (aldehydes) were formed as side products in all cases. Oxygenated products would be produced from the corresponding alkyl nitrates formed through the reaction of alkyl radicals with nitrogen dioxide. Nitrogen dioxide radical molecule is a resonance hybrid; the chief contributing forms are as follows [Eq. (2)]:[8a]
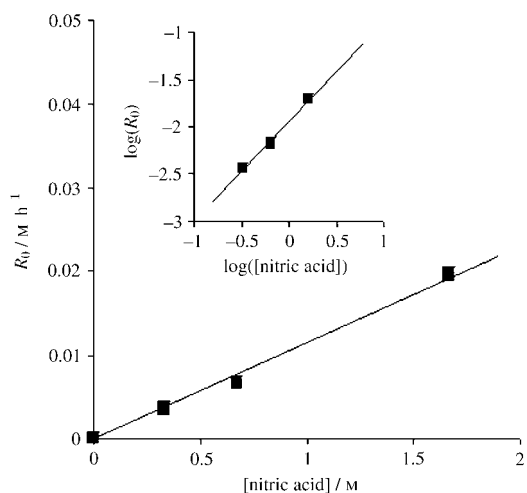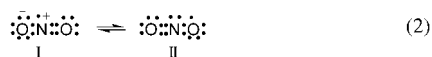
$$ \underset{\textbf{I}}{:\!\overset{\cdot}{\underset{}{O}}\!:\!\overset{+}{\underset{}{N}}\!:\!:\!\overset{\cdot}{\underset{}{O}}\!:} \quad \rightleftharpoons \quad \underset{\textbf{II}}{:\!\overset{\cdot}{\underset{}{O}}\!:\!:\!\overset{\cdot}{\underset{}{N}}\!:\!\overset{\cdot}{\underset{}{O}}\!:} \qquad (2) $$

When an alkyl radical reacts with nitrogen dioxide in form **I**, the product is a nitroalkane. On the other hand, when in form **II**, the product is an alkyl nitrate. It is well known that alkyl nitrates are unstable and the hydrolytic decomposition of alkyl nitrates to the corresponding alcohols proceeds smoothly in acidic media.[23] Alcohols formed are further oxidized to the corresponding ketones (aldehydes) under the present reaction conditions. The reaction mechanism for the formation of oxygenated products is summarized in Scheme 2.

R• + NO₂ ⟶ RONO

RONO + H₃O⁺ ⟶ ROH + HNO₂ + H⁺
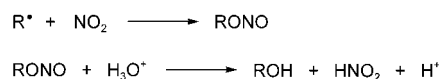
Scheme 2.

Conclusions

In conclusion, we have developed a system using polyoxometalates as catalyst precursors for the nitration of various alkanes to nitroalkanes with nitric acid. Not only normal alkanes, but also alkylbenzenes can be nitrated under mild conditions. Especially, vanadium-substituted Keggin-type phosphomolybdates such as [$H_4PVMo_{11}O_{40}$], [$H_5PV_2Mo_{10}O_{40}$], and [$H_6PV_3Mo_9O_{40}$] can act as efficient catalyst precursors for the present nitration. Under the present conditions, carbon–carbon bond cleavage reactions hardly proceed. The kinetic and mechanistic studies show a catalytic reaction mechanism involving a radical-chain path. Initially, the phosphomolybdates abstract the hydrogen of an alkane to form an alkyl radical and the reduced form of phosphomolybdates. Then, the reduced phosphomolybdates subsequently react with nitric acid, generating the original oxidized form and nitrogen dioxide. This initial formation of

nitrogen dioxide is a key step. The initial formation of nitrogen dioxide can take place mainly on polyoxomolybdates, that is, $[PMo_{12}O_{40}]^{n-}$, and vanadium species enhance the reaction. Then, the nitration is proceeded via a chain formation of nitrogen dioxide and an alkyl radical.

Experimental Section

Materials: Phosphometalates except for $[H_3PMo_{12}O_{40}]$, $[H_4PVMo_{11}O_{40}]$, and $[VO(H_2O)_5]H[PMo_{12}O_{40}]$ were supplied by Nippon Inorganic Colour and Chemical Co., Ltd. and used after recrystallization from water. $[H_3PMo_{12}O_{40}]$ (Kanto) was used as received. $[H_4PVMo_{11}O_{40}]$[24] and $[VO(H_2O)_5]H[PMo_{12}O_{40}]$[25] were synthesized according to the literature procedures. Solvents and concentrated aqueous nitric acid (69 wt%) were of analytical grade (Tokyo Kasei) and used without the further purification. Alkanes used in the nitration reactions were commercially obtained from Tokyo Kasei or Aldrich (reagent grade) and purified prior to use.[26]

Instrumentation: GC analyses were performed on Shimadzu GC-14B with a flame ionization detector equipped with a TC-WAX capillary or SE-30 packed column. Mass spectra were determined on Perkin–Elmer TurboMass at an ionization voltage of 70 eV. NMR spectra were recorded on JEOL JNM-EX-270. ^1H and ^{13}C NMR spectra were measured at 270 and 67.5 MHz, respectively, in CDCl$_3$ with TMS as an internal standard. ^{31}P NMR spectra of polyoxometalates were measured at 109.25 MHz in acetic acid. 85% H$_3$PO$_4$ was used as an external standard. ^{51}V NMR spectra of polyoxometalates were measured at 70.90 MHz in acetic acid. VOCl$_3$ was used as an external standard. Infrared spectra were measured on Jasco FT/IR-460 Plus using KBr disks. ESR measurements at 100 K (X-band) were performed with a JEOL JES-RE-1X spectrometer. The microwave power, resonance frequency, modulation, and time constant were 1.0 mW, 9.21 GHz, 0.5 mT, and 0.1 s, respectively. A reactor directly connected to an ESR tube was used to avoid the exposure of the sample to the air. After a certain catalytic reaction period, the reaction solution was transferred into the ESR tube and the ESR tube was sealed by firing. The simulation was carried out according to the literature,[27] assuming the axial symmetry for vanadium.

Procedure for catalytic nitration: Nitration of alkanes was carried out in a glass vial containing a magnetic stir bar. A typical procedure was as follows. Into a glass vial were successively placed adamantane (0.33 M), $[H_4PVMo_{11}O_{40}]$ (1.67 mM, 0.5 mol%), acetic acid (3 mL), and nitric acid (0.67 M). The glass reactor was then attached to a vacuum line, cooled to 77 K, and degassed by three freeze-pump-thaw cycles. The vial was allowed to warm to 298 K and 1 atm of argon was introduced to the system. Then, reaction mixture was heated at 356 K for 24 h. All of the products were confirmed by GC analysis in combination with mass and ^1H and ^{13}C NMR spectroscopy as reported previously.[10,28] The yields were determined by GC analyses using naphthalene or diphenyl as an internal standard.

Kinetic study: Nitration of alkanes was performed via the same procedure as those described above. The reaction conditions are given in the Figure captions (Figures 4–6). The reaction was monitored every 30 min by GC analyses showing no reaction during the induction period in every case. Reaction rates (R_0) for the kinetic analyses were determined from the slope of reaction profiles (conversion vs time plots, see Figure 3, inset) at low conversion ($<10\%$) of the substrate after the induction period.

Acknowledgement

[1] a) R. Neumann, *Prog. Inorg. Chem.* **1998**, *47*, 317; b) N. Mizuno, M. Misono, *Chem. Rev.* **1998**, *98*, 199; c) T. Okuhara, N. Mizuno, M. Misono, *Adv. Catal.* **1996**, *41*, 113; d) C. L. Hill, C. M. Prosser-McCartha, *Coord. Chem. Rev.* **1995**, *143*, 407; e) M. T. Pope, A. Müller, *Angew. Chem.* **1991**, *103*, 56; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 34.

[2] Examples of recent works, see: a) K. Kamata, K. Yonehara, Y. Sumida, K. Yamaguchi, S. Hikichi, N. Mizuno, *Science* **2003**, *300*, 964; b) W. Adam, P. L. Alsters, R. Neumann, C. R. Saha-Möller, D. Sloboda-Rozner, R. Zhang, *J. Org. Chem.* **2003**, *68*, 1721; c) D. Sloboda-Rozner, P. L. Alsters, R. Neumann, *J. Am. Chem. Soc.* **2003**, *125*, 5280; d) N. M. Okun, T. M. Anderson, C. L. Hill, *J. Am. Chem. Soc.* **2003**, *125*, 3194; e) H. Weiner, A. Trovarelli, R. G. Finke, *J. Mol. Catal. A* **2003**, *191*, 253; f) A. M. Khenkin, R. Neumann, *Adv. Synth. Catal.* **2002**, *344*, 1017; g) S. Ellis, I. V. Kozhevnikov, *J. Mol. Catal. A* **2002**, *187*, 227; h) R. Ben-Daniel, L. Weiner, R. Neumann, *J. Am. Chem. Soc.* **2002**, *124*, 8788; i) H. Tsuji, Y. Koyasu, *J. Am. Chem. Soc.* **2002**, *124*, 5608; j) J. T. Rhule, W. A. Neiwert, K. I. Hardcastle, B. T. Do, C. L. Hill, *J. Am. Chem. Soc.* **2001**, *123*, 12101; k) I. A. Weinstock, E. M. G. Barbuzzl, M. W. Wemple, J. J. Cowan, R. S. Reiner, D. M. Sonnen, R. A. Heintz, J. S. Bond, C. L. Hill, *Nature* **2001**, *414*, 191; l) Y. Nishiyama, Y. Nakagawa, N. Mizuno, *Angew. Chem.* **2001**, *113*, 3751; *Angew. Chem. Int. Ed.* **2001**, *40*, 3639; m) T. Hayashi, A. Kishida, N. Mizuno, *Chem. Commun.* **2001**, 381.

[3] a) T. Yokota, M. Tani, S. Sakaguchi, Y. Ishii, *J. Am. Chem. Soc.* **2003**, *125*, 1476; b) M. Vennat, P. Herson, J.-M. Bregeault, G. B. Shul'pin, *Eur. J. Inorg. Chem.* **2003**, *5* 908; c) R. Ben-Daniel, R. Neumann, *Angew. Chem.* **2003**, *115*, 96; *Angew. Chem. Int. Ed.* **2003**, *42*, 92; d) T. Yokota, S. Sakaguchi, Y. Ishii, *Adv. Synth. Catal.* **2002**, *344*, 849; e) A. M. Khenkin, L. Weiner, Y. Wang, R. Neumann, *J. Am. Chem. Soc.* **2001**, *123*, 8531; f) A. M. Khenkin, A. Rosenberger, R. Neumann, *J. Catal.* **1999**, *182*, 82.

[4] a) H. Feuer, T. Nielsen, *Nitrocompounds: Recent Advances in Synthesis and Chemistry*, VCH, New York, **1990**; b) A. F. Bollmeier Jr., in *Encyclopedia of Chemical Technology*, Vol. 17 (Ed.: J. I. Kroschwitz), Wiley, New York, **1996**, pp. 205–225.

[5] N. Ono, *The Nitro Group in Organic Synthesis*, Wiley-VCH, Weinheim, **2001**.

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

[7] a) G. A. Olah, R. Malhotra, S. C. Narahg, *Nitration: Methods and Mechanism*, VCH, New York, **1989**; b) T. Mori, H. Suzuki, *Synlett* **1995**, 383; c) N. L. Lancaster, V. Llopis-Mestre, *Chem. Commun.* **2003**, 2812, and references therein.

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

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

[10] a) Y. Nishiwaki, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **2002**, *67*, 5663; b) S. Sakaguchi, Y. Nishiwaki, T. Kitamura, Y. Ishii, *Angew. Chem.* **2001**, *113*, 228; *Angew. Chem. Int. Ed.* **2001**, *40*, 222; c) S. Isozaki, Y. Nishiwaki, S. Sakaguchi, Y. Ishii, *Chem. Commun.* **2001**, 1352.

[11] K. Yamaguchi, S. Shinachi, N. Mizuno, *Chem. Commun.* **2004**, 424.

[12] When the ESR spectrum was measured at 4 K, a signal at $g=2.005$ was observed in addition to the hyperfine structure of vanadium. The signal may be assignable to an alkyl radical species.

[13] The formation of V^{4+} by the treatment of $[H_4PVMo_{11}O_{40}]$ with cyclohexane and toluene, and the reoxidation with nitric acid to form nitrogen dioxide were observed.

[14] A ^{51}V NMR signal appeared at δ −559.0 after addition of nitric acid to the solution. The signal at δ −559.0 is assigned to monomeric VO$_2^+$ species since the chemical shift is almost the same as that of VO$_2^+$ species prepared from V$_2$O$_5$ in acetic acid (δ −559.4).[15]

[15] K. Inumaru, A. Ono, H. Kubo, M. Misono, *J. Chem. Soc. Faraday Trans.* **1998**, *94*, 1765.

[16] S. E. O'Donnell, M. T. Pope, *J. Chem. Soc. Dalton Trans.* **1976**, 2290.

[17] M. Akimoto, K. Shima, H. Ikeda, E. Echigoya, *J. Catal.* **1984**, *86*, 173.

[18] M. S. Norris, S. A. Fleck, D. H. Lichtenfels, *Anal. Chem.* **1955**, *27*, 1565.

[19] It is known that nitric acid quickly reacts with copper metal to generate nitrogen dioxide according to the following equation: $Cu+4HNO_3 \rightarrow Cu(NO_3)_2+2NO_2+2H_2O$. See: R. Lee, F. L. Albright, *Ind. Eng. Chem. Process Des. Dev.* **1965**, *4*, 441.

[20] a) J. J. Carberry, *Chem. Eng. Sci.* **1959**, *9*, 189; b) L. F. Albright in *Encyclopedia of Chemical Technology*, *Vol. 17* (Ed.: J. I. Kroschwitz), Wiley, New York, **1996**, pp. 68–80.

[21] K. Jones in *Comprehensive Inorganic Chemistry* (Ed.: A. F. Trotman-Dickenson), Pergamon Press, New York, **1973**, pp. 147–388.

[22] O. Pestovsky, A. Bakac, *J. Mol. Catal. A* **2003**, *200*, 21.

[23] a) E. Iglesias, L. G. arcía-Río, J. R. Leis, M. E. Peòa, D. L. H. Williams, *J. Chem. Soc. Perkin Trans. 2* **1992**, 1673; b) S. E. Aldred, D. L. H. Williams, *J. Chem. Soc. Perkin Trans. 2* **1982**, 777; c) A. D. Allen, *J. Chem. Soc.* **1954**, 1968.

[24] G. T. Tsigdinos, C. J. Hallada, *Inorg. Chem.* **1968**, *7*, 437.

[25] R. Bayer, C. Marchal, F. X. Liu, A. Tézé, G. Hervé, *J. Mol. Catal. A* **1996**, *110*, 65.

[26] *Purification of Laboratory Chemicals*, 3rd ed. (Eds.: D. D. Perrin, W. L. F. Armarego), Pergamon Press, Oxford (UK), **1988**.

[27] C. P. Stewart, A. L. Porte, *J. Chem. Soc. Dalton Trans.* **1972**, 1661.

[28] a) R. W. Murray, R. Jeyaraman, L. Mohan, *Tetrahedron Lett.* **1986**, *27*, 2335; b) K. A. Turner, *Synthesis* **1998**, 139; c) J. K. Gallos, T. V. Koftis, *J. Chem. Soc. Perkin Trans. 1* **2001**, 415.