

Oxidation of Alkylarenes by Nitrate Catalyzed by Polyoxophosphomolybdates: Synthetic Applications and Mechanistic Insights

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Abstract: Alkylarenes were catalytically and selectively oxidized to the corresponding benzylic acetates and carbonyl products by nitrate salts in acetic acid in the presence of Keggin type molybdenum-based heteropolyacids, $H_{3+x}PV_xMo_{12-x}O_{40}$ ($x = 0-2$). $H_5PV_2Mo_{10}O_{40}$ was especially effective. For methylarenes there was no over-oxidation to the carboxylic acid contrary to what was observed for nitric acid as oxidant. The conversion to the aldehyde/ketone could be increased by the addition of water to the reaction mixture. As evidenced by IR and ^{15}N NMR spectroscopy, initially the nitrate salt reacted with $H_5PV_2Mo_{10}O_{40}$ to yield a $N^VO_2^+[H_4PV_2Mo_{10}O_{40}]$ intermediate. In an electron-transfer reaction, the proposed $N^VO_2^+[H_4PV_2Mo_{10}O_{40}]$ complex reacts with the alkylarene substrate to yield a radical-cation-based donor-acceptor intermediate, $N^VO_2[H_4PV_2Mo_{10}O_{40}]-ArCH_2R^{+\bullet}$. Concurrent proton transfer yields an alkylarene radical, $ArCHR^\bullet$, and NO_2 . Alternatively, it is possible that the $N^VO_2^+[H_4PV_2Mo_{10}O_{40}]$ complex abstracts a hydrogen atom from alkylarene substrate to directly yield $ArCHR^\bullet$ and NO_2 . The electron transfer-proton transfer and hydrogen abstraction scenarios are supported by the correlation of the reaction rate with the ionization potential and the bond dissociation energy at the benzylic positions of the alkylarene, respectively, the high kinetic isotope effect determined for substrates deuterated at the benzylic position, and the reaction order in the catalyst. Product selectivity in the oxidation of phenylcyclopropane tends to support the electron transfer-proton transfer pathway. The $ArCHR^\bullet$ and NO_2 radical species undergo heterocoupling to yield a benzylic nitrite, which undergoes hydrolysis or acetolysis and subsequent reactions to yield benzylic acetates and corresponding aldehydes or ketones as final products.

Introduction

Nitrogen oxides, specifically nitrogen dioxide and its dimer, and nitric acid have long been used as reagents in organic chemistry for nitration and oxidation.¹ Also, in the biological realm, nitrate has been shown to be an oxidant for anaerobic enzymatic oxidation of saturated and aromatic hydrocarbons.² The selectivity of reactions with nitrogen oxides or nitric acid is mostly determined by the nature of the substrates. Nitration is usually observed for aromatic substrates, whereas oxidation is more predominant for aliphatic substrates. The most well-known use of nitric acid in oxidation is that of cyclohexanol/cyclohexanone for the production of adipic acid.³ Our interest in the research described herein was in the liquid phase oxidation of alkylarenes. Thus, while aromatic substrates typically undergo nitration,⁴ alkylbenzenes are preferentially nitrated or oxidized

at the benzylic position yielding either α -nitroalkylbenzenes,⁵ coupling products,⁶ or oxygenated products.⁷

Polyoxomolybdates of the Keggin structure, $H_{3+x}PV_xMo_{12-x}O_{40}$ (especially $x = 0-2$), have been attracting considerable interest over recent years as oxidation catalysts for both gas phase and liquid oxidation reactions.⁸ In the area of liquid-phase oxidation, the earliest use was as cocatalysts in Wacker type oxidations of terminal alkenes,⁹ followed later on by various catalytic

- (1) (a) Riebsomer, J. L. *Chem. Rev.* **1945**, *36*, 157–233. (b) Gray, P.; Yoffe, A. D. *Chem. Rev.* **1955**, *55*, 1069–1154. (c) Ogata, Y. In *Oxidation in Organic Chemistry, Part C*; Trahanovsky, W. S., Ed.; Academic Press: New York, 1978; pp 295–342. (d) Bosch, E.; Kochi, J. K. In *N-Centered Radicals*; Alfassi, Z. B., Ed.; John Wiley & Sons: Chichester, 1998; pp 69–128.
- (2) (a) Widdel, F.; Rabus, R. *Curr. Opin. Biotechnol.* **2001**, *12*, 259–275. (b) Spormann, A. M.; Widdel, F. *Biodegradation* **2000**, *11*, 85–105. (c) Knemeyer, O.; Heider, J. *J. Biol. Chem.* **2001**, *276*, 21381–21386.
- (3) (a) Castellan, A.; Bart, J. C. J.; Cavallero, S. *Catal. Today* **1991**, *9*, 285–299. (b) Godt, H. C., Jr; Quinn, J. F. *J. Am. Chem. Soc.* **1956**, *78*, 1461–1464.

- (4) Although these reaction are well-known, the mechanism is still controversial; see for example ref 1d and Esteves, P. M.; Walkimar de M. Carneiro, J.; Cardoso, S. P.; Barbosa, A. G. H.; Laali, K. K.; Rasul, G.; Surya Parkash, G. K.; Olah, G. A. *J. Am. Chem. Soc.* **2003**, *125*, 4836–4849 and references therein.
- (5) (a) Shechter, H.; Brain, D. K. *J. Am. Chem. Soc.* **1963**, *85*, 1806–1812. (b) Nishiwaki, Y.; Sakaguchi, S.; Ishii, Y. *J. Org. Chem.* **2002**, *67*, 5663–5668.
- (6) (a) Puskas, I.; Fields, E. K. *J. Org. Chem.* **1966**, *31*, 4204–4210. (b) Puskas, I.; Fields, E. K. *J. Org. Chem.* **1967**, *32*, 589–592. (c) Puskas, I.; Fields, E. K. *J. Org. Chem.* **1967**, *32*, 3924–3928.
- (7) (a) Ogata, Y.; Tezuka, H.; Kamei, T. *Tetrahedron* **1969**, *25*, 4913–4918. (b) Ogata, Y.; Tezuka, H.; Kamei, T. *Tetrahedron* **1969**, *25*, 4919–4922. (c) Ogata, Y.; Tezuka, H.; Kamei, T. *J. Org. Chem.* **1969**, *34*, 845–847. (d) Ogata, Y.; Tezuka, H.; Kamei, T. *Tetrahedron* **1970**, *26*, 4313–4318. (e) Zaug, E.; Rapala, T. *Org. Synth., Collect. Vol. 3* **1955**, 820–821. (f) Tulry, F. W.; Marvel, C. S. *Org. Synth., Collect. Vol. 3* **1955**, 822–823. (g) Crandall, W.; Beasley, R.; Lambing, L. L.; Moriconi, R. *J. Org. Chem.* **1967**, *32*, 134–136. (h) Ogata, Y.; Tezuka, H. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 3285–3286. (i) Srinivasan, B.; Chandalic, S. B. *Indian J. Technol.* **1971**, *9*, 274–275. (j) Minisci, F.; Recupero, F.; Gambarotti, C.; Punta, C.; Paganelli, R. *Tetrahedron Lett.* **2003**, *44*, 6919–6922. (k) Nyberg, K. *Acta Chem. Scand.* **1970**, *24*, 473–481.

oxidations of halides,¹⁰ alcohols, ketones and amines,¹¹ phenols,¹² (alkyl)aromatics,¹³ dienes,¹⁴ alkanes,¹⁵ and sulfur containing compounds.¹⁶ From a mechanistic point of view there is now quite abundant information indicating that the polyoxomolybdates act as electron-transfer oxidants toward one of the reaction components, commonly, the organic substrate or oxidant. The specific complete reaction pathway, thus, much depends on the both the targeted oxidative transformation and the oxidant employed. We have, in the past, studied the mechanism of polyoxomolybdate-catalyzed reactions using various oxidants including molecular oxygen,^{13e,14b} nitrous oxide,^{11e} sulfoxides,^{13a} and alkylhydroperoxides.¹⁵ Now we present our studies on a novel system; the oxidation of alkylaromatic substrates to acetates and aldehydes using nitrate as the primary oxidant/oxygen donor.¹⁷ Synthetic aspects and mechanistic insights are presented.

Results and Discussion

Synthetic Aspects. The synthetic objective of this research was to carry out the selective oxidation of alkyl aromatic substrates at the benzylic position with emphasis on preventing over oxidation, i.e., avoiding the formation of the corresponding carboxylic acid, eq 1. Classical aerobic $\text{Co}^{2+/3+}/\text{Mn}^{2+/3+}/\text{Br}^-$ aerobic oxidations typically yield carboxylic acids as major

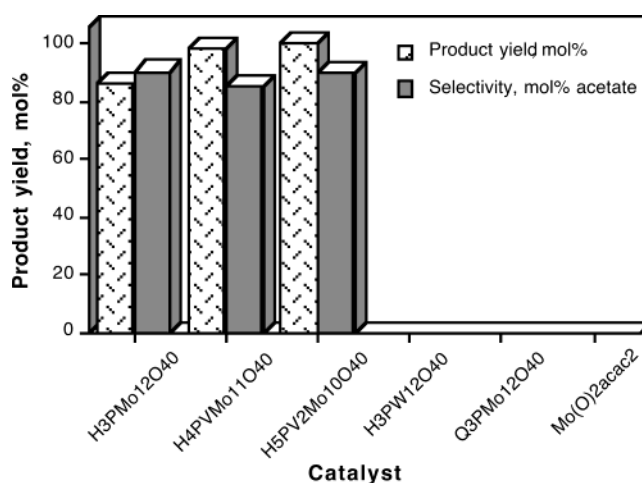
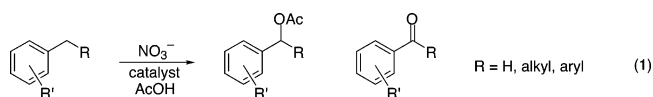


Figure 1. Oxidation of durene by nitrate in acetic acid with different catalysts. 0.5 M durene, 0.1 M lithium nitrate, and 0.01 M polyoxometalate in AcOH, 80 °C, Ar. Product yields defined as % mol alkylarene reacted/mol nitrate vary slightly, $\pm 2\%$. Q = tetrabutylammonium.



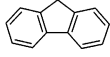
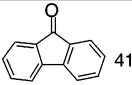
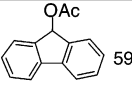
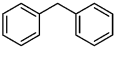
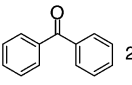
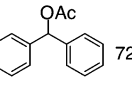
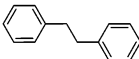
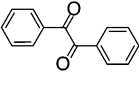
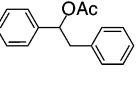
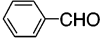


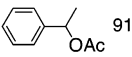


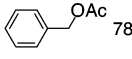


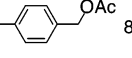
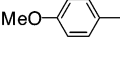
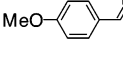
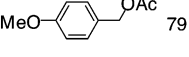


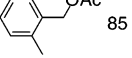


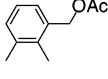
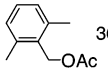

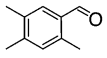
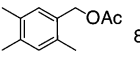

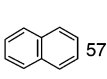
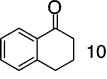
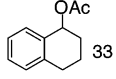
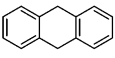
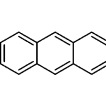
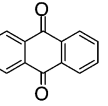
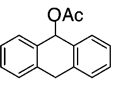
- (8) (a) Pope, M. T. *Isopoly and Heteropoly Anions*; Springer: Berlin, Germany, 1983. (b) Müller, A. *Polyoxometalate Chemistry*; Kluwer Academic: Dordrecht, The Netherlands, 2001. (c) Kozhevnikov, I. V. *Catalysis by Polyoxometalates*; Wiley: Chichester, U.K., 2002. (d) Hill, C. L.; Prosser-McCartha, C. M. *Coord. Chem. Rev.* **1995**, *143*, 407–455. (e) Mizuno, N.; Misono, M. *Chem. Rev.* **1998**, *98*, 171–192. (f) Neumann, R. *Prog. Inorg. Chem.* **1998**, *47*, 317–370.
- (9) (a) Matveev, K. I. *Kinet. Catal.* **1977**, *18*, 716–729. (b) Matveev, K. I.; Kozhevnikov, I. V. *Kinet. Catal.* **1980**, *21*, 855–861. (c) Grate, J. R.; Mamm, D. R.; Mohajan, S. *Mol. Eng.* **1993**, *3*, 205. (d) Grennberg, H.; Bergstad, K.; Bäckvall, J.-E. *J. Mol. Catal.* **1996**, *113*, 355–358. (e) Yokota, T.; Fujibayashi, S.; Nishiyama, Y.; S. Sakaguchi, Y. Ishii, *J. Mol. Catal.* **1996**, *114*, 113–119. (f) Bergstad, K.; Grennberg, H.; Bäckvall, J.-E. *Organometallics* **1998**, *17*, 45–50.
- (10) (a) Neumann, R.; Assael, I.; *J. Chem. Soc., Chem. Commun.* **1998**, 1285–1287. (b) Branytskaya, O.; Neumann, R. *J. Org. Chem.* **2003**, *68*, 9510–9512.
- (11) (a) Brégault, J.-M.; El Ali, B.; Mercier, J.; Martin, J.; Martin, C. C. R. *Acad. Sci. II* **1989**, *309*, 459–462. (b) El Ali, B.; Brégault, J.-M.; Mercier, J.; Martin, J.; Martin, C.; Convert, O. *J. Chem. Soc., Chem. Commun.* **1989**, 825–826. (c) Atlamsani, A.; Ziyad, M.; Brégault, J.-M. *J. Chim. Phys., Phys.-Chim. Biol.* **1995**, *92*, 1344–1364. (d) A. M. Khenkin, A. M.; Neumann, R. *J. Org. Chem.* **2002**, *67*, 7075–7079. (e) Ben-Daniel, R.; Neumann, R. *Angew. Chem., Int. Ed.* **2003**, *42*, 92–95. (f) Neumann, R.; Levin, M. *J. Org. Chem.* **1991**, *56*, 5707–5710. (g) Ben-Daniel, R.; Alsters, P. L.; Neumann, R. *J. Org. Chem.* **2001**, *66*, 8650–8653. (h) El Aakel, L.; Launay, F.; Atlamsani, A.; Bregeault, J.-M. *Chem. Commun.* **2001**, 2218–2219. (i) Khenkin, A. M.; Vigdergauz, I.; Neumann, R. *Chem.-Eur. J.* **2000**, *6*, 875–882.
- (12) (a) Kholdeeva, O. A.; Golovin, A. V.; Maksimovskaya, R. I.; Kozhevnikov, I. V. *J. Mol. Catal.* **1992**, *75*, 235–244. (b) Lissel, M.; Jansen van de Wal, H.; Neumann, R. *Tetrahedron Lett.* **1992**, *33*, 1795–1798. (c) Kolesnik, I. G.; Zhizhina, E. G.; Matveev, K. I. *J. Mol. Catal. A: Chem.* **2000**, *153*, 147–154.
- (13) (a) Khenkin, A. M.; Neumann, R. *J. Am. Chem. Soc.* **2002**, *124*, 4198–4199. (b) Neumann, R.; de la Vega, M. *J. Mol. Catal.* **1993**, *84*, 93–108. (c) Nomiyama, K.; Yanagibayashi, H.; Nozaki, C.; Kondoh, K.; Hiramatsu, E.; Shimizu, Y. *J. Mol. Catal. A* **1996**, *114*, 181–190. (d) Khenkin, A. M.; Neumann, R. *Angew. Chem., Int. Ed.* **2000**, *39*, 4088–4090. (e) Khenkin, A. M.; Weiner, L.; Wang, Y.; Neumann, R. *J. Am. Chem. Soc.* **2001**, *123*, 8531–8542.
- (14) (a) Neumann, R.; Lissel, M. *J. Org. Chem.* **1989**, *54*, 4607–4610. (b) Neumann, R.; Levin, M. *J. Am. Chem. Soc.* **1992**, *114*, 7278–7286.
- (15) Khenkin, A. M.; Neumann, R. *J. Am. Chem. Soc.* **2001**, *123*, 6437–6438.
- (16) (a) Gall, R. D.; Faraj, M.; Hill, C. L. *Inorg. Chem.* **1994**, *33*, 5015–5021. (b) Kozhevnikov, I. V.; Simagina, V. I.; Varnakova, G. V.; Matveev, K. I. *Kinet. Catal.* **1979**, *20*, 506–511. (c) Dzhumakaeva, B. S.; Golodov, V. A. *J. Mol. Catal.* **1986**, *35*, 303–307. (d) Harrup, M. K.; Hill, C. L. *Inorg. Chem.* **1994**, *33*, 5448–5455. (e) Harrup, M. K.; Hill, C. L. *J. Mol. Catal. A* **1996**, *106*, 57–66. (c) Gall, R. D.; Hill, C. L.; Walker, J. E. *J. Catal.* **1996**, *159*, 473–478.
- (17) Recently, there has been a report on the oxidation of sulfides to sulfoxides catalyzed by polyoxometalate/nitrate catalysts: Okun, N. M.; Anderson, T. M.; Hardcastle, K. I.; Hill, C. L. *Inorg. Chem.* **2003**, *42*, 6610–6612.

products.¹⁸ Toward this goal, the activity of different Keggin type heteropolyacids, namely $\text{H}_{3+x}\text{PV}_x\text{Mo}_{12-x}\text{O}_{40}$ and $\text{H}_3\text{-PW}_{12}\text{O}_{40}$, as catalysts was initially tested for the oxidation of 1,2,4,5-tetramethylbenzene (durene) as a model substrate with nitrate salts to yield 2,4,5-trimethylbenzyl acetate and 2,4,5-trimethylbenzaldehyde under the following reaction conditions: 0.5 M durene, 0.1 M lithium nitrate, and 0.01 M polyoxometalate in acetic acid at 80 °C under argon, Figure 1. As may be observed, the vanadium-containing polyoxomolybdates were slightly more active compared to the simple $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ compound, while $\text{H}_3\text{PW}_{12}\text{O}_{40}$ was not effective nor was $\text{Mo}(\text{O})_2\text{acac}_2$ or the neutral $\text{Q}_3\text{PMo}_{12}\text{O}_{40}$ (Q = tetrabutylammonium). One may preliminarily conclude that both a sufficiently high oxidation potential and acidic conditions are needed for catalytic activity. No reaction takes place in the absence of nitrate. In addition, it should also be noted that the use of nitric acid in place of a nitrate salt (NaNO_3 and LiNO_3 gave virtually the same results) yielded 2,4,5-trimethylbenzoic acid instead of the acetate or aldehyde.

After the initial experiments on durene, the oxidation reaction was tested on a series of substrates as presented in Table 1. As a rule the acetate ester of the benzylic alcohol was observed to be the major product, in most cases $>80\%$, while the aldehyde was the minor product. For substrates susceptible to aromatization, such as tetralin and dihydroanthracene, the formation of the aromatic product, naphthalene and anthracene, respectively, was significant. There was virtually no nitration at either the aromatic ring or benzylic position for the substrates noted, except for highly ring-activated substrates such as 4-methylanisole where 10 mol % ring nitration was observed. The use of $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ as catalyst yielded by and large similar acetate/aldehyde ratios; however, there was sometimes considerable nitration, $\sim 20\text{--}30\%$ at the aromatic ring, presumably because $\text{H}_3\text{PMo}_{12}\text{O}_{40}$ is a weaker oxidant compared to $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.

- (18) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981.

Table 1. Oxidation of Alkylarenes by Nitrate Catalyzed by $H_5PV_2Mo_{10}O_{40}$ (Reaction Conditions: 0.5 mmol of Substrate, 0.3 mmol of $NaNO_3$, 0.01 mmol of $H_5PV_2Mo_{10}O_{40}$, Ar, 1 mL of AcOH, 14 h, 80 °C)

Substrate	Products and Selectivity, mol% ^a		Product yield, mol% ^a
	 41	 59	91
	 28	 72	72
	 6	 79	 15
	 9	 91	52
	 22	 78	33 ^b
	 13	 87	57
	 11	 79	92 ^c
	 15	 85	66
	 8	 57	 36
	 13	 87	99
	 57	 10	 33
	 38	 15	 42

^a Product yield = % mol alkylarene reacted/mol of nitrate; selectivity = % mol product/all products. ^b 120 °C, 28 h. ^c 10% nitration. ^d 5% nitration.

³¹P NMR of the reaction mixtures indicated about a 10% loss after 14 h of $H_5PV_2Mo_{10}O_{40}$ to $H_4PVMo_{11}O_{40}$ and $H_3PMo_{12}O_{40}$ coupled with formation of insoluble $NaVO_3$. The latter was identified by elemental analysis. $H_3PMo_{12}O_{40}$ was stable under reaction conditions. To maximize conversions to the organic product, stepwise addition of $NaNO_3$ seems to be the most effective method compared to use of one large portion. For example, addition of three portions of 2.5 mmol of $NaNO_3$ at 8 h intervals to 5 mmol of *p*-xylene in 1 mL of AcOH in the presence of 0.01 mmol of $H_5PV_2Mo_{10}O_{40}$ gave a 98% conversion of *p*-xylene to 9:1 4-tolyl acetate/4-tolylaldehyde. It is also possible to partially control the ratio of the acetate versus aldehyde product by adding water to the solvent, Figure 2, although total product yields are reduced approximately 2-fold going from 100% AcOH to 50% AcOH%/50% H_2O . Water decreased both the rate of consumption of alkylarene and the rate of formation of the acetate.

Thus, a rather convenient method has been developed for the oxidation of alkyl aromatic substrates to the corresponding

benzylic acetates or benzaldehyde derivatives using nitrate as the primary oxidizing agent and acidic polyoxomolybdate catalysts.

Mechanistic Insights. In the context of this research, we were also interested in gaining insight into the mechanism of these reactions. In general, surprisingly little has been reported on the mechanism of nitrate oxidations. The first obvious important factor is the fate of the nitrate salt in these reactions. Thus, various alkylarenes (0.5 M) were reacted with $Na^{15}NO_3$ (0.1 M)¹⁹ in AcOH at 80 °C under 1 atm of Ar in the presence of $H_5PV_2Mo_{10}O_{40}$ (0.01 M). After 8 h the gas phase was sampled with a gastight syringe and analyzed by MS. Typically, ratios of $^{15}NO/^{15}N_2O/^{15}N_2$ of 20–25:1:1 were measured for substrates such as dihydroanthracene, diphenylmethane, and 1,2,4-trimethylbenzene; NO is clearly the major product from the nitrate salt. Thus, the nitrate is a three-electron oxidant in this system. In principle, a general mechanistic scenario for such a catalytic

(19) ^{15}N labeled $NaNO_3$ was used to allow differentiation from background N_2 and O_2 .

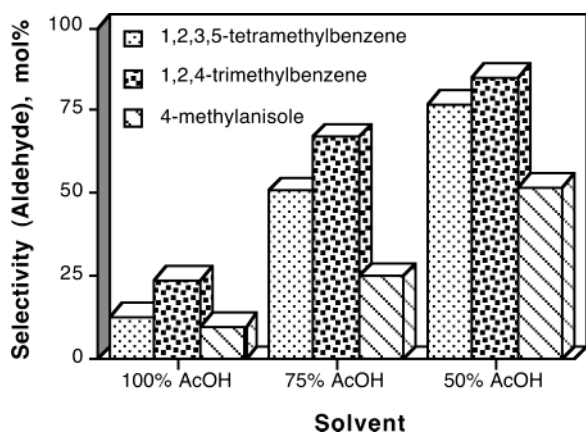


Figure 2. Oxidation of various alkylarenes by nitrate in different concentrations of acetic acid. Reaction conditions: 0.5 mmol of substrate, 0.3 mmol of NaNO_3 , 0.01 mmol of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, 1 atm of Ar, 1 mL of AcOH/ H_2O , 14 h, 80 °C. Selectivity = mol % aldehyde/all products.

oxidation could first involve either the activation of the alkylarene or the nitrate anion by the $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ catalyst. Since, under the reaction conditions studied, but in the absence of nitrate, the oxidation of alkylarenes to benzylic acetates did not take place, we surmised that the initial activation mechanism was by an interaction between the nitrate salt and the $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ polyoxometalate. This interaction was studied in three ways. First, ^{15}N NMR experiments showed that by mixing 0.1 M $\text{Na}^{15}\text{NO}_3$ with 0.1 M $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in CD_3COOD one peak at 339 ppm, $\Delta\nu_{1/2} = 1.82$ was observed (NH_3 external standard) versus a peak at 370 ppm, $\Delta\nu_{1/2} = 1.64$ Hz for $\text{Na}^{15}\text{NO}_3$ alone in CD_3COOD . Importantly, use of noncatalytically active acids such as $\text{H}_3\text{PW}_{12}\text{O}_{40}$ (339 ppm) and H_2SO_4 (341 ppm) instead of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ yielded almost identical ^{15}N NMR spectra. This shift in the ^{15}N NMR indicated the formation of a NO_2^+ species.²⁰ The formation of the NO_2^+ cation in such a system would indicate probable ion pairing between NO_2^+ and the polyoxometalate anion. In fact, addition of 20 μL of a saturated solution of NaNO_3 in AcOH to 2 mL of 25 μM $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in AcOH lead to an ~7% increase in the optical density at $\lambda_{\text{max}} = 310$ nm (from 1.028 to 1.098 au) despite slight dilution of the solution. Attempts to structurally describe this proposed ion pair were not successful. Thus, the cocrystallization of 0.1 M NaNO_3 and 0.1 M $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ from acetic acid yielded typical orange cubic single crystals. X-ray diffraction analysis clearly showed the presence of the polyanion, but neither solvent atoms nor counterions including the proposed NO_2^+ cation could be resolved due to disorder.²¹ Acetate/acetic acid was also not observed. Crystallization of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ with authentic NO_2^+ from nitronium tetrafluoroborate gave similar results. However, the IR spectrum of the crystal clearly showed a peak at 1384 cm^{-1} attributable to a N–O stretch, in addition to the fingerprint peaks of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ between 1100 and 700

cm^{-1} . A crystal grown using $\text{Na}^{15}\text{NO}_3$ as reagent absorbed at 1352 cm^{-1} , which is in excellent agreement with the expected isotope shift to 1359 cm^{-1} calculated from the reduced mass ratio for N–O. Finally the electrochemical behavior of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in the presence of LiNO_3 was measured by cyclic voltammetry. Thus, a solution containing 3.3 mM $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, 66 mM LiNO_3 , and 100 mM LiClO_4 in acetic acid showed an approximately 3-fold increase in the cathodic current from 60 μA to 186 μA upon electrochemical reduction of the $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ polyoxometalate. There was no shift in the cathodic potential and only a slight decrease in the anodic current. At higher nitrate concentrations there is a further significant increase in the cathodic current. Thus, one may conclude that nitrate would oxidize any reduced polyoxometalate species at relatively very fast rates. Indeed during the oxidation of the alkylarene substrates described above, there is no evidence of formation of reduced (green or blue-green) polyoxometalate species, and chemical oxidation of reduced polyoxometalate species with nitrate is immediate.

The source of the oxygen atom(s) in the reaction product was investigated by using isotopically labeled $\text{NaN}^{18}\text{O}_3$ and $\text{H}_5\text{PV}_2\text{Mo}_{10}^{18}\text{O}_{40}$ and by addition of $^{18}\text{O}_2$. When using 70% ^{18}O in $\text{H}_5\text{PV}_2\text{Mo}_{10}^{18}\text{O}_{40}$ or 96% ^{18}O in $^{18}\text{O}_2$ for the oxidation of durene, no ^{18}O containing product was observed. However, when using 75.2% ^{18}O in $\text{NaN}^{18}\text{O}_3$, approximately 10% ^{18}O incorporation in both 2,4,5-trimethylbenzyl acetate and 2,4,5-trimethylbenzaldehyde was observed. The isotope labeling effect was much diluted due to a secondary competitive reaction whereby acetate and nitrate exchange oxygen atoms under acid conditions.²² Apparently, oxygen is transferred to the product from the nitrate anion. To understand how a NO_2^+ –polyoxometalate complex could activate an alkylarene substrate, kinetic measurements were carried out to see if the reaction rate could be correlated with a property of the organic substrate. The rate of oxidation of various alkylarenes, measured as disappearance of the organic substrate, showed a reasonable correlation ($r^2 = 0.81$) between the rate constants and the ionization potential of the alkylarenes,²³ Figure 3 (left). Since relative gas-phase ionization potentials are proportional to liquid-phase oxidation potentials, the rate-potential correlation notable in Figure 3 (left) would indicate activation of the alkylarenes by electron transfer to a NO_2^+ –polyoxometalate complex. On the other hand, Figure 3 (right), there was also a similar correlation of the rate as a function of the C–H bond strength ($r^2 = 0.82$, after normalization to take into account the number of reactive C–H bonds). This would indicate the possibility of a hydrogen abstraction mechanism for the activation of the alkylarene substrate.

The isotope effect in the electron-transfer step was measured by comparing the rate of oxidation of several nondeuterated and deuterated alkylarenes. For xanthene/xanthene-9- d_2 , diphenylmethane/diphenylmethane- d_2 , and ethylbenzene/ethylbenzene- d_{10} , ratios $k_{\text{H}}/k_{\text{D}} = 9.3, 5.9,$ and 5.4 , respectively, were measured for formation of xanthone and the benzylic acetates of diphenylmethane and ethylbenzene. Such significant kinetic isotope effects are consistent with reactions proceeding either by a hydrogen abstraction mechanism or with electron-transfer oxidations where there is oxidative C–H activation of hydro-

(20) Prakash, G. K. S.; Heiliger, L.; Olah, G. A. *Inorg. Chem.* **1990**, *29*, 4965–4968.

(21) Crystal data and structure refinement. Empirical formula $\text{PMo}_{10}\text{V}_2\text{O}_{40}$; formula weight 1732.23; space group monoclinic, $P2(1)/m$; temperature 120 K; λ 0.710 73 Å; a 13.062(3) Å; b 20.422(4) Å; c 20.213(4) Å; β 107.59(3)°; V 5139.8(19) Å³; Z 4; d_{calc} 2.355 mg/cm³; μ 2.935 mm⁻¹; Theta range for data collection $2.58^\circ \leq \theta \leq 17.22^\circ$; Limiting indices $-10 \leq h \leq 10, 0 \leq k \leq 16, -16 \leq l \leq 0$; reflections collected/unique 3196/3196 [$R(\text{int}) = 0.0000$]; completeness to $\theta = 17.22^\circ$ 98.6%; refinement method full-matrix least-squares on F^2 ; data/restraints/parameters 3196/0/513; goodness-of-fit on F^2 1.151; final R indices [$I > 2\sigma(I)$] $R1 = 0.1107, wR2 = 0.3306$; R indices (all data) $R1 = 0.1270, wR2 = 0.3422$; largest difference peak and hole -2.686 and -1.224 e/Å^3 .

(22) Heating 100 μmol of $\text{NaN}^{18}\text{O}_3$ (75, 2% ^{18}O) and 5 μmol of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ with 300 μmol of AcOH at 80 °C for 8 h gave acetic acid that was 23 mol % enriched with ^{18}O as measured by GC–MS.

(23) Taken from the NIST database at <http://webbook.nist.gov/chemistry>.

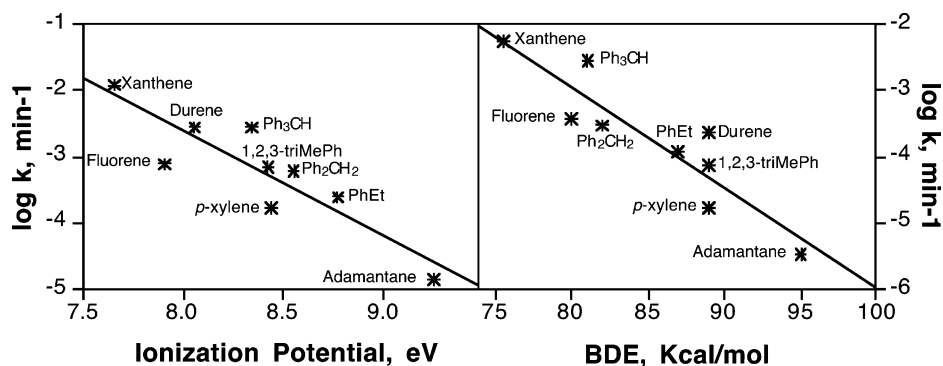
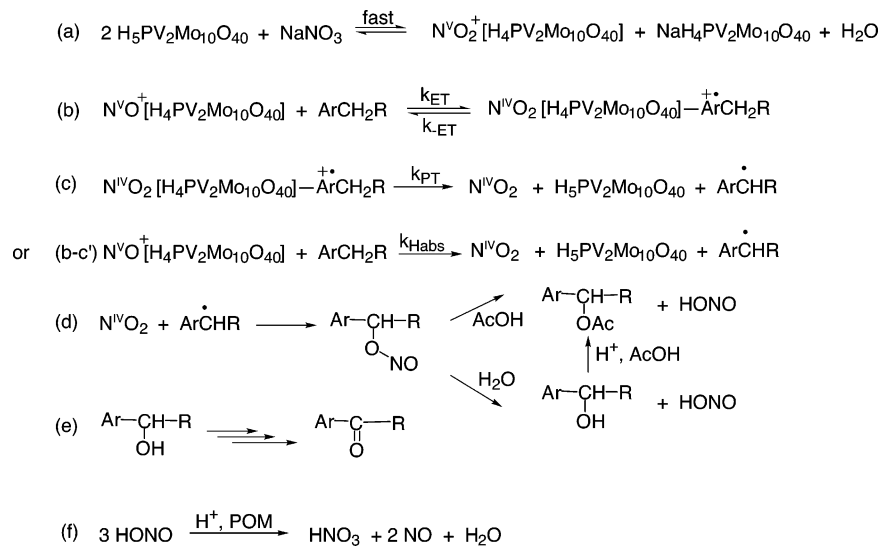


Figure 3. Initial rate of oxidation of alkylarenes as a function of the ionization potential. Reaction conditions: 0.5 mmol of substrate, 0.1 mmol of LiNO_3 , 0.01 mmol of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, 1 atm of Ar, 1 mL of AcOH, 80 °C. Observed rate constants were obtained from initial reaction rates (pseudo first conditions, measured from disappearance of the organic substrate). For the correlation with bond dissociation energies, the rate constants were normalized taking into account the number of reactive C–H bonds.

Scheme 1. Reaction Pathway for the Oxidation of Alkylarenes by Nitrate Catalyzed by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$



carbons involving endergonic electron-transfer steps and where the reverse electron-transfer step is competitive with the proton transfer.²⁴ The proton transfer is concurrent with the electron transfer.

By combining the data presented above, reaction schemes consistent with the experimental findings may be formulated as follows, Scheme 1. Initially there is a reaction (a) that is dehydration of the nitrate anion by the polyoxometalate to yield the $\text{N}^{\text{V}}\text{O}_2^+[\text{H}_4\text{PV}_2\text{Mo}_{10}\text{O}_{40}]$ complex as borne out mainly by the IR and ^{15}N NMR evidence upon interaction of $\text{Na}^{15}\text{NO}_3$ and $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$. Note also the addition of water inhibited the reaction. In one scenario, the rate-determining step is the activation of the alkylarene substrate by $\text{N}^{\text{V}}\text{O}_2^+[\text{H}_4\text{PV}_2\text{Mo}_{10}\text{O}_{40}]$ via electron transfer (b) followed by concurrent proton transfer to yield the reduced $\text{N}^{\text{V}}\text{O}_2$ radical and the benzylic radical possibly within a “radical cage” (c).²⁵ Alternatively, the rate-determining step is the activation of the alkylarene to directly yield the $\text{N}^{\text{V}}\text{O}_2$ and the benzylic radicals (b–c’).²⁶ In both cases, fast heterocoupling²⁷ of the benzylic radical and NO_2 followed by hydrolysis yields the benzylic alcohol and nitrous acid as initial products (d).^{28,29} The benzylic alcohols either undergo esterification to yield the benzylic acetates or are oxidized to

the corresponding carbonyl compounds. Alternatively, the benzylic nitrite intermediate may directly undergo acetolysis to yield the benzylic acetate. Nitrous acid is quickly decomposed under acidic conditions to NO, nitrate, and water. NaNO_2 when added to 0.01 M $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in AcOH is violently decom-

(24) (a) Bockmam, T. M.; Hubig, S. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1998**, *120*, 2826–2830. (b) Ebersson, L.; Jonsson, L. *Acta Chem. Scand. B* **1986**, *40*, 79–91.

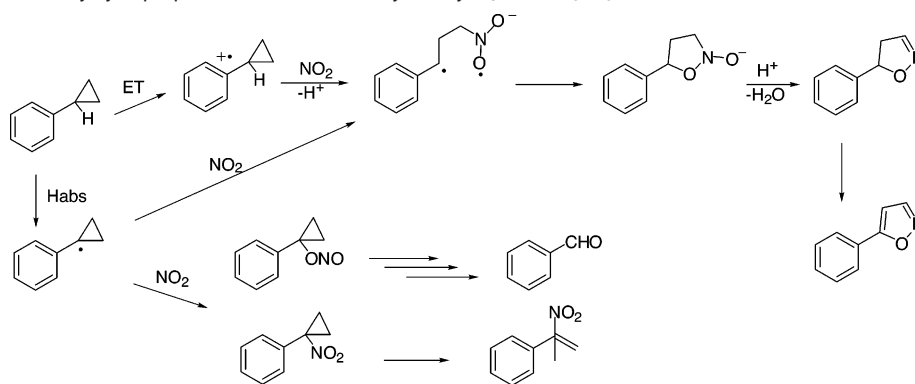
(25) A rate equation developed on the basis of a steady-state concentration of the intermediate $\text{N}^{\text{V}}\text{O}_2^+[\text{H}_4\text{PV}_2\text{Mo}_{10}\text{O}_{40}] - \text{ArCH}_2\text{R}^{\bullet+}$ and concurrent proton transfer step can be written as follows, where $[I] \equiv \text{N}^{\text{V}}\text{O}_2^+[\text{H}_4\text{PV}_2\text{Mo}_{10}\text{O}_{40}] - \text{ArCH}_2\text{R}^{\bullet+}$, $S_A \equiv \text{N}^{\text{V}}\text{O}_2^+[\text{H}_4\text{PV}_2\text{Mo}_{10}\text{O}_{40}]$, $S_B \equiv \text{ArCH}_2\text{R}$, and $P \equiv \text{ArCHR}^{\bullet} \rightarrow \text{products}$. $dI/dt = k_{\text{ET}}S_A S_B - k_{\text{ET}}I - k_{\text{PT}}I = 0$. $I = [k_{\text{ET}}/(k_{\text{ET}} + k_{\text{PT}})]S_A S_B$. $dP/dt = k_{\text{PT}}I - [(k_{\text{PT}}k_{\text{ET}})/(k_{\text{ET}} + k_{\text{PT}})]S_A S_B$. Since the polyoxometalate is the limiting reagent with the nitrate and alkylarene in excess, the observed reaction rate should be first order in S_A . Since in order to obtain S_A 2 equiv of the $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ polyoxometalate are required (see Scheme 1), the reaction should be in fact second-order in $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$. A log dP/dt versus $\log[\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}]$ plot for the oxidation of durene (0.5 M durene, 0.1 M LiNO_3 , and 0.003–0.02 M $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in AcOH at 80 °C) yielded a linear curve of slope 2.03, $r^2 = 0.98$ indicating the reaction is indeed second-order in $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.

(26) A rate equation based on a hydrogen abstraction rate-determining step can be written as follows where $S_A \equiv \text{N}^{\text{V}}\text{O}_2^+[\text{H}_4\text{PV}_2\text{Mo}_{10}\text{O}_{40}]$, $S_B \equiv \text{ArCH}_2\text{R}$, and $P \equiv \text{ArCHR}^{\bullet} \rightarrow \text{products}$. $P/dt = k_{\text{Habs}}S_A S_B$.

(27) There was no significant homocoupling of benzylic radicals to yield dimeric dibenzylic products. See also: Weiner, B.; Barhard, K. I. *N-Centered Radicals*; Alfassi, Z. B., Ed.; John Wiley & Sons: Chichester, 1998; pp 39–67.

(28) In a separate reaction it was shown that 1-pentyl nitrite reacts immediately in acetic acid to yield mostly >95% 1-pentanol.

(29) A referee suggested the possibility of fast further oxidation of the benzylic radical to a benzylic cation followed by reaction of the benzylic cation with nitrate to yield benzyl nitrate. We found no evidence for formation of nitrate esters that have some stability under reaction conditions. Also this pathway is not compatible with the results observed for the oxidation of phenylcyclopropane (see below).

Scheme 2. Reaction of Phenylcyclopropane with Nitrate Catalyzed by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ **Table 2.** Comparative Oxidation of Alkylarenes and Corresponding Alcohols by Nitrate Catalyzed by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ ^a

substrate	products, selectivity mol %		initial rate, mM/min
	acetate	carbonylate	
diphenylmethane	72	28	0.3
diphenylcarbinol	75	25	72
ethylbenzene	76	24	0.12
1-phenylethanol	82	18	40
1,4-dimethylbenzene	87	13	0.05
4-methylbenzyl alcohol	71	29	6.6

^a Reaction conditions: 0.5 mmol of substrate, 0.1 mmol of LiNO_3 , 0.01 mmol of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in 1 mL of AcOH, 1 atm of Ar, 80 °C. Selectivity = mol % product/all products.

posed. The NO formed does not appear to react with the alkylarene substrate. Control experiments with NO and NO^+ yielded a very different product not observed in the reactions with nitrate. Thus a solution of 0.5 M durene and 0.01 M $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in AcOH under 1 atm of NO at 80 °C for 14 h showed an 18 mol % conversion of durene, but mostly (95% selectivity) to the homo-radical coupling product (dimer), 1,2-bis-(2,4,5-trimethylphenyl)ethane. Similarly a reaction of durene (0.5 M) and NO^+BF_4^- (0.5 M) in AcOH at 80 °C under 1 atm Ar gave 23 mol % conversion after 14 h to the same dimer (93% selectivity).

The question of the fate of the initial benzylic nitrite intermediate was also investigated. One possibility is a nitrite \rightarrow alcohol \rightarrow acetate or carbonylate pathway; another possibility is a nitrite \rightarrow acetate or alcohol pathway, where the alcohol is then oxidized to the carbonylate.³⁰ Comparative oxidations of diphenylmethane and diphenylcarbinol, ethylbenzene and 1-phenylethanol, and 1,4-dimethylbenzene and 4-methylbenzyl alcohol showed the rates of the benzylic alcohol oxidation were significantly higher than that of the corresponding alkylarene but the product selectivity was similar, Table 2.³⁰ This would at least indicate that the benzylic alcohol could be a common intermediate in the obviously faster transformation of benzylic alcohols to the benzylic acetate and carbonyl products. Finally, as noted above the known fast decomposition of nitrite under acidic conditions was verified under the present reaction conditions.

Using phenylcyclopropane as a probe substrate, we attempted to gain additional information regarding an electron transfer versus hydrogen abstraction mechanism,³¹ Scheme 2. Reaction of phenylcyclopropane with nitrate (0.5 M phenylcyclopropane,

0.3 M NaNO_3 , 0.01 M $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in AcOH, 1 atm of Ar, 80 °C, 8 h) yielded 5-phenylisoxazoline (59% selectivity) and 5-phenylisoxazole (29% selectivity) as major products at a conversion of 41%. Benzaldehyde (10% selectivity and α -nitro- α -methylstyrene (2% selectivity) were formed as minor products. It appears from the results that the major products were obtained via a ring-opened intermediate to yield first 5-phenylisoxazoline, and then further by oxydehydrogenation 5-phenylisoxazole. Hydrogen abstraction to yield the neutral benzylic radical could reasonably lead to the formation of the minor products observed according to Scheme 2. It has been often concluded that ring opening products in the oxidation of phenylcyclopropane are good probes for an electron-transfer mechanism,³¹ lending support to such a pathway in the present case; however, it has also been suggested that the ring opening from the neutral radical may also be fast^{31c,d} and therefore competitive with radical coupling. Therefore, the product distribution observed could conceivably be a result of hydrogen abstraction. In the context of the present inconclusive mechanistic research, it should be noted that the long standing discussion of the mechanism of aromatic nitration⁴ has yet to yield a consensus mechanism. In this case as for aromatic nitration, the mechanism may be a function of the properties of the substrate with lower oxidation potentials and higher bond dissociation energies favoring an electron transfer pathway and higher oxidation potentials and lower bond dissociation energies favoring a hydrogen abstraction mechanism.

Conclusion

In this new catalytic application of the phosphovanadomolybdate acid, $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, it has been shown that the reaction of the polyoxometalate with the nitrate anion leads to formation of a nitronium complex of the polyanion, $\text{N}^+\text{VO}_2^-[\text{H}_4\text{PV}_2\text{Mo}_{10}\text{O}_{40}]$, which does not lead to nitration of alkylarenes but rather to oxidation at the benzylic position. It would appear that the nitronium complex reacts with the alkylarene substrate by either electron and concurrent proton transfer or hydrogen abstraction leading to formation of an alkylarene radical and NO_2 that undergo radical heterocoupling to yield benzylic nitrites. The latter are not observed, but rather they undergo

(30) The oxidation of benzylic alcohols with nitric acid is known; cf. Strazzolini, P.; Runcio, A. *Eur. J. Org. Chem.* **2003**, 526–536 and references therein.

(31) (a) Riley, P.; Hanzlik, R. P. *Tetrahedron Lett.* **1989**, *30*, 3015–3018. (b) Kim, E. K.; Kochi, J. K. *J. Am. Chem. Soc.* **1991**, *113*, 4962–4974. (c) Wang, Y.; Tanko, J. M. *J. Am. Chem. Soc.* **1997**, *119*, 8201–8208. (d) Wang, Y.; Tanko, J. M. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2705–2711. (e) Dinnocenzo, J. P.; Simpson, T. R.; Zuilhof, H.; Todd, W. P.; Heinrich, T. *J. Am. Chem. Soc.* **1997**, *119*, 987–993. (f) Dinnocenzo, J. P.; Zuilhof, H.; Lieberman, D. R.; Simpson, T. R.; McKechney, M. W. *J. Am. Chem. Soc.* **1997**, *119*, 994–1001.

hydrolysis or acetylation and subsequent reactions leading to the formation of benzylic acetates and carbonyl derivatives as final products. The possible synthetic outcome of such a procedure has been noted for a series of alkylarene substrates.

Experimental Part

Instruments and Measurements. ^{31}P NMR spectra (101.27 MHz, 85% H_3PO_4 external standard) were taken on a Bruker Avance 250 DPX instrument and ^{15}N NMR spectra (40.55 MHz, NH_3 external standard) were taken on a Bruker Avance 400 instrument. GC and GC-MS measurements were recorded on HP 6890 (FID detector) and HP 5973 instruments equipped with a 5% phenyl methylsilicone 0.32 mm ID, 0.25 μm coating, 30 m column (Restek 5MS) using helium as eluant. IR spectra for (2% samples in KBr) were measured on a Nicolet Protege 460 FTIR instrument. Samples were prepared by mixing 1 mmol of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ and 0.3 mmol of NaNO_3 or $\text{Na}^{15}\text{NO}_3$ which were stirred in 0.4 mL of acetic acid at 80 °C for 30 min. The acetic acid was evaporated under vacuum, and the solid obtained was redissolved in 0.5 mL of acetonitrile. To this solution 1 mL of decane was added, and the reaction mixture was slowly evaporated. After a week, nice yellow crystals appeared, which were analyzed by X-ray diffraction (typical Keggin structure was observed) and IR. Cyclic voltammetry was carried on a BAS-1 instrument. The electrochemical data were collected using a glass carbon cathode, a platinum anode, and a calomel reference electrode. The measurements were of solutions of 3.3 mM POM and 66 mM lithium nitrate in 100 mM lithium perchlorate in acetic acid at 100 mV/s; $I/V = 500 \mu\text{A/V}$.

Materials. The $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40} \times 34\text{H}_2\text{O}$ polyoxometalate was prepared using a known literature method.³² Thermogravimetric analysis (Mettler 50) indicated 34 water molecules per polyoxometalate and the elemental analysis was the following: found (calculated) % P, 1.31 (1.34); V, 4.38 (4.41); Mo, 41.32 (41.56). IR 1057, 960, 865, and 774 cm^{-1} . ^{31}P NMR (CD_3COCD_3 , 85% H_3PO_4 external standard) -3.96 (6), -3.42 (1), -3.37 (4), -3.31 (2), and -3.22 (2) ppm (area of peak). $\text{Q}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ ($\text{Q} = (\text{C}_4\text{H}_9)_4\text{N}$) was prepared mixing 10 equiv of QBr

dissolved in water to $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ also dissolved in water. The precipitate formed was filtered and dried overnight in a vacuum oven at 80 °C. The thermogravimetric analysis showed no water was present. Elemental analysis: found (calculated) % C, 32.09 (32.64); H, 5.99 (6.16); N, 2.13 (2.38). Solvents and substrates available from commercial sources were of the highest purity available and used without further purification. $^{18}\text{O}_2$ (Enritech) was 96.1% ^{18}O labeled. Sodium nitrate- ^{15}N , 98% enrichment was from Cambridge Isotope Laboratories and sodium nitrate, ^{18}O 75.2% enrichment was from D-Chem Ltd.. Diphenylmethane- d_2 and xanthene-9- d_2 were prepared by reduction of benzophenone and xanthone, respectively, by reduction with $\text{AlCl}_3\text{-LiAlD}_4$. ^1H NMR and GC-MS were used to verify the absence of benzylic hydrogen atoms and the presence of deuterium. ^{18}O labeled $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ was prepared by drying the polyoxometalate at 120 °C for 24 h and then by adding 50 equiv of H_2^{18}O (96.2%) in dry CH_3CN and mixing for 6 days in order to obtain a fully equilibrated compound.

Oxidation Reactions. Reactions were carried out under anaerobic conditions in 20 mL Schlenk tubes equipped with a vacuum/pressure valve. Typically, the tubes were loaded with the catalyst, nitrate, solvent, and the substrate and degassed by three successive "freeze-pump-thaw" cycles and loaded with Ar. The solution was brought to the appropriate temperature in a thermostated oil bath. The progress of the reactions was then followed periodically by sampling via a gastight syringe; analysis was by GC and GC-MS. Kinetic isotope effects were measured in competitive reactions by reacting equimolar concentrations of deuterated and protonated substrates. Peaks were quantified by comparing molecular peak intensities of the benzylic acetate products.

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Supporting Information Available: ^{15}N NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

(32) Tsigidinos, G. A.; Hallada, C. J. *Inorg. Chem.* **1968**, *7*, 437-441.