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Low-Temperature Activation of Dioxygen and Hydrocarbon Oxidation Catalyzed by a Phosphovanadomolybdate: Evidence for a Mars–van Krevelen Type Mechanism in a Homogeneous Liquid Phase**

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Aerobic heterogeneous catalytic oxygenation of hydrocarbons with transition metal oxides often proceeds by a Mars–van Krevelen (M-vK) type mechanism [Eqs. (1) and (2)].[1]

$$\text{cat-O}_{ox} + SH_2 \longrightarrow \text{cat}_{red} + SO + 2\,H_{ads} \quad (1)$$

$$\text{cat}_{red} + 2\,H_{ads} + O_2 \longrightarrow \text{cat-O}_{ox} + H_2O \quad (2)$$

This mechanism involves activation of the C–H bond and transfer of lattice oxygen from the oxide to yield the product and the reduced catalyst. Re-oxidation of the catalyst by dioxygen and formation of water then follows. Heterogenization of homogeneous catalysis seeks to combine the selectivity and mild conditions typical of homogeneous catalysis with the handling advantages inherent in heterogeneous catalysis.[2] Here, we consider the application of the inverse concept, that is, homogenization of heterogeneous catalysis, to M-vK type oxygenations. Since archetypal M-vK oxygenation reactions can both activate C–H bonds in hydrocarbons and utilize dioxygen as a terminal oxidant, such catalysis in homogeneous media could lead to viable, selective low-temperature aerobic oxidation of hydrocarbons.

Polyoxometalates (POMs)[3] are discrete, anionic and soluble (mixed) metal oxides. They have the potential to activate dioxygen[4] and to function as oxidation catalysts.[5] Oxygen transfer in the liquid phase has been demonstrated using chromium(V)-oxo-containing POMs[6] and activation of a C–H bond has been observed using phosphovanadomolybdates.[7] Thus, hydrocarbons such as cyclic dienes are oxydehydrogenated but to our knowledge there are no reports of combined hydrocarbon activation, oxygen transfer, and dioxygen activation through a M-vK type mechanism in homogeneous media.[8]

We now report that the phosphovanadomolybdate $H_5PV_2Mo_{10}O_{40}$ can activate both aromatic and benzylic C–H bonds in hydrocarbons, for example, anthracene and xanthene, in homogeneous liquid phases by electron transfer. Subsequent oxygen transfer from the POM leads to the formation of the quinone/ketone. The reaction occurs by a M-vK type mechanism.

Hydrocarbons (60 mM) and $H_5PV_2Mo_{10}O_{40}\cdot 34\,H_2O$[9] (1 mM) were treated with one atmosphere of O_2 in CH_3CN at 60 °C for 18 h. Analysis of the reaction mixtures showed that selective oxidation (>99 %) of anthracene to anthraquinone, xanthene to xanthone, fluorene to fluorenone, and diphenylmethane to benzophenone occurred with turnover numbers of 24, 30, 13, and 1, respectively. Initial strong support for a M-vK type mechanism, namely, that the source of the oxygen in the product was from the POM lattice and not from atmospheric O_2, was obtained by a classic $^{18}O_2$-labeling experiment. In the oxidation of anthracene or xanthene (20 mM) catalyzed by $H_5PV_2Mo_{10}O_{40}\cdot 34\,H_2O$ (1 mM) in CH_3CN under $^{18}O_2$ (1 atm, 96.1 % purity) at 60 °C, the amount of ^{18}O found in the product by GC-MS increased as the reaction progressed. Incorporation of ^{18}O was 0, 14.8, and 22.5 mol % after 1, 5.4, and 10.2 turnovers for anthraquinone and 0, 12.3, and 19.6 mol % after 1, 4.9, and 11.4 turnovers for xanthone. Full incorporation of ^{18}O is expected from the outset for autooxidation since the initial radical formed will always react with $^{18}O_2$. Second, a reaction (60 °C, 24 h) of equimolar amounts of anthracene or xanthene and $H_5PV_2Mo_{10}O_{40}$ under Ar in an NMR tube also yielded 48 % of anthraquinone and 71 % of xanthone, as evidenced by ^1H NMR spectroscopy. Since each POM molecule can be formally considered as a three-electron oxidant [Eqs. (3) and (4)], the maximum conversions into anthraquinone and xanthone are 50 and 75 %, respectively.

$$\text{anthracene} + 2\,H_5PV^{V}_{2}Mo^{VI}_{10}O_{40} \longrightarrow \text{anthraquinone} + 2\,H_5PV^{IV}_{2}Mo^{VI}_{9}O_{39} \quad (3)$$

$$2\,H_5PV^{IV}_{2}Mo^{VI}_{9}O_{39} + 1.5\,O_2 \longrightarrow 2\,H_5PV^{V}_{2}Mo^{VI}_{10}O_{40} + H_2O \quad (4)$$

Third, similar anaerobic reactions of equimolar amounts of anthracene and $H_5PV_2Mo_{10}O_{40}$ enriched with ^{17}O or ^{18}O yielded labeled anthraquinone as measured by ^{17}O NMR spectroscopy ($\delta = 515$) and GC-MS (^{18}O), respectively. An approximately 75 % ^{18}O-enriched $H_5PV_2Mo_{10}O_{40}$ yielded

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anthraquinone labeled with 70% ^{18}O. Fourth, the reaction stoichiometry that conforms with a M-vK mechanism [Eqs. (3) and (4)] indicates that 1.5 equivalents of O_2 are consumed per catalytic cycle for the oxidation of anthracene, while a 3:1 O_2:anthracene stoichiometry is expected for autooxidation with a significant number of propagation chains. Indeed, oxygen consumption was 1.45 ± 0.2 equivalents per reaction cycle.

Since $H_5PV_2Mo_{10}O_{40}$ is a hydrate one needs to exclude the possibility of water as the source of oxygen leading to the formation of products by its nucleophilic attack on the radical cation intermediate (see also below).[10] Thus, an excess of AcOH was added to the reaction mixture (anthracene or xanthene (20 mM), $H_5PV_2Mo_{10}O_{40} \cdot 34\,H_2O$ (1 mM), AcOH (160 mM), 60 °C, 1 atm O_2, 16 h). Only anthraquinone and xanthone at 90 and 95% conversion were obtained; there was no acetylation by the nucleophilic AcOH. In a reaction carried out in an anhydrous medium (anthracene (20 mM), $Q_5PV_2Mo_{10}O_{40}$ (1 mM, $Q = (C_4H_9)_4N$), hexafluoro-2-propanol (1 mL), 55 °C, 1 atm O_2, 16 h) anthraquinone was the only product. The addition of water had no significant effect.

The experiments described above indicated that oxygenation occurred by oxygen transfer from a lattice oxygen atom of the POM to the hydrocarbon substrate. Further aspects of the oxidation mechanism and catalytic cycle were studied. Of initial interest was the mode of activation of the C–H bond, which can occur by the formation of a donor–acceptor complex, electron transfer,[11] or hydrogen abstraction.[12] The interaction of hydrocarbons with $H_5PV_2Mo_{10}O_{40}$ was studied by measuring the appearance of the absorbance corresponding to the reduced POM at 750 nm. Kinetic profiles obtained from the reaction of $H_5PV_2Mo_{10}O_{40} \cdot 34\,H_2O$ (1 µmol) and the hydrocarbon (10 µmol) in CH_3CN (3 mL) under Ar at 60 °C showed that the reactions were pseudo-first-order in $H_5PV_2Mo_{10}O_{40}$. The rate constants correlated very well ($r^2 = 0.89$) with the gas-phase ionization potential[13] of the hydrocarbon (Figure 1). Hydrocarbons with both weaker benzylic C–H bonds (80–85 kcal mol) found in xanthene and stronger aromatic C–H (ca. 105 kcal mol) bonds found in anthracene were purposely used in the comparison. Clearly, the initial interaction is by formation of a donor–acceptor complex between the hydrocarbon and the POM, or electron transfer to form a radical cation and the mono-reduced $PV^{IV}V^{V}Mo_{10}O_{40}^{6-}$ species. ESR experiments (see Supporting Information) clearly showed significant formation the radical cation intermediate.

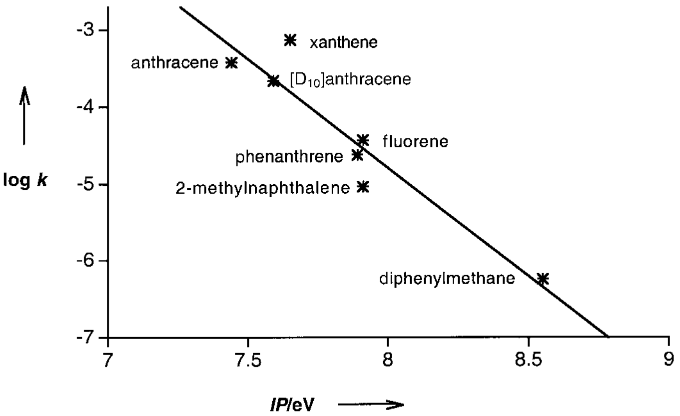


Figure 1. The reaction of $H_5PV_2Mo_{10}O_{40}$ with hydrocarbons as a function of the gas-phase ionization potential of the hydrocarbon. The reduction of $H_5PV_2Mo_{10}O_{40}$ was followed by a diode-array UV/Vis spectrometer at 750 nm. Conditions: $H_5PV_2Mo_{10}O_{40}$ (1 µmol) and hydrocarbon (10 µmol) in CH_3CN (3 mL) under Ar at 60 °C. Pseudo-first-order rate constants (s^{-1}) were obtained from the initial rates for up to 20% conversion.

Although the reduction of the POM with [D10]anthracene as the substrate was about twice as slow as when anthracene was used, an inverse kinetic isotope effect, $k_H/k_D = 0.85 \pm 0.05$ for the formation of anthraquinone, was measured in a competitive reaction (anthracene (10 mM), [D10]anthracene (10 mM), $H_5PV_2Mo_{10}O_{40} \cdot 34\,H_2O$ (1 mM), 60 °C, 1 atm O_2). This result is consistent with a change of hybridization from sp^2 to sp^3 at the 9(10) aromatic carbon atom of anthracene in the rate-determining step.[14] Therefore, formation of a C–O bond must occur in the rate-determining step. More insight into the oxygen-transfer step was obtained by measurement of the IR spectra of ^{18}O-enriched $H_5PV_2Mo_{10}O_{40}$ after catalytic reaction with anthracene under $^{16}O_2$ (Figure 2). In ^{18}O-labeled $H_5PV_2Mo_{10}O_{40}$ (middle) there is a shift relative to unlabeled $H_5PV_2Mo_{10}O_{40}$ of the $M{=}O_t$ (terminal) absorption (two distinct peaks) from 960 to 919 cm^{-1}. Additionally, there are absorption shifts from 865 to 831 cm^{-1} and 774 to 758 cm^{-1} for corner and edge-shared oxygen atoms, respectively. A 69% incorporation of ^{18}O into anthraquinone was observed along with an increase in the peak ratio of 960 (^{16}O) to 919 cm^{-1} (^{18}O) after ten turnovers (bottom; anthracene (60 mM), $H_5PV_2Mo_{10}O_{40}$ (1 mM), CH_3CN, 60 °C, $^{16}O_2$). Shifts from 831 to 843 cm^{-1} and 761 to 758 cm^{-1} were also observed in the spectra. Clearly, there is re-incorporation of ^{16}O into the POM from $^{16}O_2$. The results show that hydrocarbon oxygenation

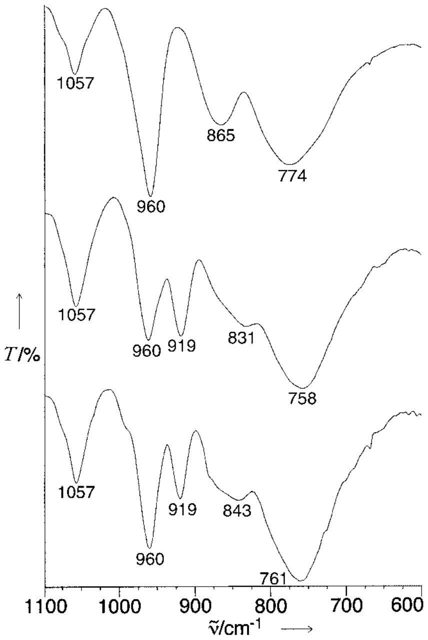
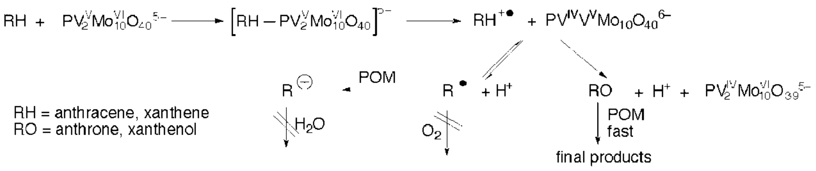


Figure 2. The IR spectrum of ^{18}O-labeled $H_5PV_2Mo_{10}O_{40}$ before and after reaction with anthracene and $^{16}O_2$. Top: unlabeled $H_5PV_2Mo_{10}O_{40}$; middle: ^{18}O-labeled $H_5PV_2Mo_{10}O_{40}$; bottom: ^{18}O-labeled $H_5PV_2Mo_{10}O_{40}$ after reaction with anthracene and $^{16}O_2$ after ten turnovers.



Scheme 1. Activation and oxygenation of aromatic hydrocarbons by $H_5PV_2Mo_{10}O_{40}$.

through a M-vK type mechanism is possible in a homogeneous liquid phase using POMs as catalysts (Scheme 1).

The reaction is initiated by the relatively fast formation of a donor–acceptor complex and then a radical cation. Subsequent formation of a free radical and oxygenation is discounted from the isotope incorporation experiments and anaerobic reactions. Homolytic cleavage of the C–H bond (not shown) does not occur because compounds that easily react in this way (for example, cyclohexene) did not react in this system. Nucleophilic attack of water was also discounted. The rate-determining step appears to be the oxygen transfer from the POM[15] to the activated hydrocarbon as indicated by the inverse deuterium isotope effect. Consequent reaction steps are fast, since no intermediates such as anthrone are observed, and benzylic alcohols react much faster.

Experimental Section

Reactions were carried out in 15-mL glass pressure tubes. Typically, appropriate amounts of hydrocarbon substrate (all highest purity commercial products) and $H_5PV_2Mo_{10}O_{40}\cdot 34\,H_2O$[9] were dissolved in CH_3CN. The gases $^{18}O_2$ (96.1 %) or $^{16}O_2$ were added by four consecutive pump/thaw cycles on a Schlenk line. Conversions were measured by gas-liquid chromatography (HP 6890) on a 5 % phenylmethylsilicone (30 m, 0.32 mm ID, 0.25 μm coating) column. Isotope incorporation was quantified by GC-MS (HP 5973 (same column)). Reactions under anaerobic conditions in CD_3CN, similarly carried out in high-pressure NMR tubes, were quantified by ^1H NMR spectroscopy. Labeled $H_5PV_2Mo_{10}O_{40}$ was prepared by drying the POM at 120 °C for 24 h and then adding 50 equivalents of $H_2{}^{17}O$ (10.2 %) or $H_2{}^{18}O$ (94.3 %) in dry CH_3CN and mixing for 18 h. The drying/exchange cycle was repeated three times. ^{18}O enrichment (see Figure 2, middle) is estimated as about 50 % at the terminal oxygen atoms and to be greater than 90 % (by deconvolution by assuming a 40 cm^{-1} shift, and from the equal intensities of the peaks) at the edge and corner-shared oxygen atoms. Total enrichment for potentially transferable oxygen atoms is therefore about 75 %. Anhydrous reactions were carried out using $((C_4H_9)_4N)_5PV_2Mo_{10}O_{40}$ in dried solvents. The isotope effect in the oxidation of [H_{10}]- and [D_{10}]anthracene in a competitive reaction was measured by mixing anthracene (10 mM), [D_{10}]anthracene (10 mM), $H_5PV_2Mo_{10}O_{40}\cdot 34\,H_2O$ (1 mM) at 60 °C, in O_2 (1 atm). The isotope ratio was computed by comparing the ratio of [H_{10}]- and [D_{10}]anthracene remaining under pseudo-first-order conditions at up to 35 % conversion. Samples for IR spectra (Nicolet Protégé 460) were prepared by placing a few drops of the POM-containing solution on a NaCl plate and evaporating off the solvent. ESR spectra were measured in 1-mm tubes at ambient temperature. UV/Vis kinetic measurements were performed on a diode-array instrument (HP 5842) equipped with a magnetic stirrer and a temperature bath (60 ± 0.1 °C). ^{17}O NMR spectra (Bruker DMX 400) were measured at 54.244 MHz and referenced to $H_2{}^{17}O$.

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Oxidosqualene Cyclase Residues that Promote Formation of Cycloartenol, Lanosterol, and Parkeol[**]

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Eukaryotes make sterols from three different cyclic intermediates.[1] Lanosterol (**7**) is the initial carbocyclic sterol precursor in animals[2] and fungi.[3] Cycloartenol (**5**) and parkeol (**8**) are isomeric sterol biosynthetic intermediates in plants[4, 5] and sea cucumbers,[6] respectively. Lanosterol, cycloartenol, and parkeol synthases cyclize (*S*)-2,3-oxidosqualene ((*S*)-**1**) [7] to the intermediate protosteryl cation **2**[8] and form different products by promoting cationic cyclization

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