

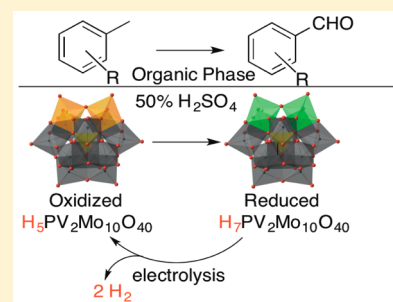
Oxygenation of Methylarenes to Benzaldehyde Derivatives by a Polyoxometalate Mediated Electron Transfer–Oxygen Transfer Reaction in Aqueous Sulfuric Acid

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S Supporting Information

ABSTRACT: The synthesis of benzaldehyde derivatives by oxygenation of methylarenes is of significant conceptual and practical interest because these compounds are important chemical intermediates whose synthesis is still carried out by nonsustainable methods with very low atom economy and formation of copious amounts of waste. Now an oxygenation reaction with a 100% theoretical atom economy using a polyoxometalate oxygen donor has been found. The product yield is typically above 95% with no “overoxidation” to benzoic acids; H₂ is released by electrolysis, enabling additional reaction cycles. An electrocatalytic cycle is also feasible. This reaction is possible through the use of an aqueous sulfuric acid solvent, in an aqueous biphasic reaction mode that also allows simple catalyst recycling and recovery. The solvent plays a key role in the reaction mechanism by protonating the polyoxometalate thereby enabling the activation of the methylarenes by an electron transfer process. After additional proton transfer and oxygen transfer steps, benzylic alcohols are formed that further react by an electron transfer–proton transfer sequence forming benzaldehyde derivatives.



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INTRODUCTION

Carbon–hydrogen bond activation of alkanes and related oxygen insertion leading to hydroxylated products remains a highly desirable and important chemical transformation with broad implications in many areas ranging from the energy sector, for example methane to methanol, to transformations in the fine chemical industry. Much of the more recent research in homogeneous phase catalytic hydroxylation has been devoted to enzymatic reactions and the use of related biomimetic analogues as catalysts.^{1,2} Iron based heme and non-heme catalysts have been the most studied compounds.^{3,4} An important subclass of alkane hydroxylation reactions is the oxygenation of alkylarenes, where the weaker benzylic carbon–hydrogen bond makes such a selective transformation more probable. Surprisingly, despite the perceived easier oxygenation of alkylarenes, a selective, high yield reaction of methylarenes, ArCH₃, to benzaldehyde derivatives, ArCHO, remains a considerable challenge, especially in the context of green, waste free transformations with a high atom economy, because aerobic and peroxide oxidation strongly tends to yield benzoic acid derivatives as the major product.⁵ A perusal of the literature describing the synthesis of benzaldehyde derivatives shows that there are five major reaction pathways. The first pathway is formylation reactions of arenes by various methods such as the Gatterman–Koch reaction,⁶ the Gatterman reaction,⁷ the Vilsmeier–Haack reaction,⁸ the Reimer–Tiemann reaction,⁹ the use of dichloromethyl methyl ether and aluminum chloride,¹⁰ or formyl fluoride/boron trifluoride.¹¹ All these reactions form copious amounts of waste and often use or produce toxic compounds. They are not general for all

substrates and not regioselective, thus requiring product separation. The second pathway is the use of molecular halogens X₂, X = Cl, Br, either through free radical halogenation of methylarenes followed by hydrolysis to yield the required aldehyde¹² or by halogenation of arenes to the corresponding haloarenes followed by carbonylation with carbon monoxide typically using palladium catalysts.¹³ Obviously these reactions produce large quantities of halide waste. Methylarenes can be oxidized to the corresponding carboxylic acids, by a large variety of methods but also catalytically with O₂ using the classic autoxidation Co/Mn/Br catalysts.⁵ The carboxylic acid can then be reduced, typically via formation of an acyl chloride followed by reduction.¹⁴ Single step highly selective catalytic formation of ArCHO from ArCH₃ in high yields with benign oxidants has not been demonstrated, although using stoichiometric reagents such as chromyl chloride,¹⁵ permanganate,¹⁶ manganese dioxide,¹⁷ hypervalent iodine compounds,¹⁸ and cerium oxidants¹⁹ can be effective. Recently, there have been some reports on new catalysts for the oxidation of ArCH₃ compounds such as Pd–Au nanoparticles supported on carbon or TiO₂,²⁰ Cu-based heterogeneous catalysts,²¹ and thermally treated melamine.²² Conversion and/or selectivity to benzaldehyde is low.

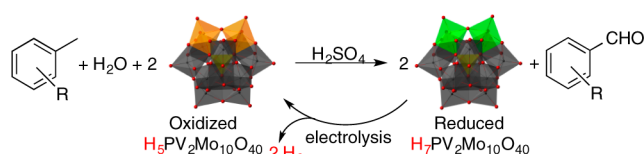
Previous research has shown that phosphovanadomolybdate polyoxometalates, most notably H₅PV₂Mo₁₀O₄₀, are reactive in electron transfer–oxygen transfer (ET–OT) reactions that, for example, can lead to insertion of oxygen from H₅PV₂Mo₁₀O₄₀

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into a C–H bond.²³ For example, an alkylarene with a low oxidation potential, such as xanthene, was shown to react in this manner to yield xanthone as product.^{24,25} However, *no reaction occurred with substrates with higher oxidation potential, notably toluene and alike.* Recently, we have demonstrated that (ET–OT) reactions, active for cleavage of C–C bonds of primary alcohols and vicinal diols,²⁶ can transform carbohydrates to synthesis gas.²⁷ Important in the context of this research, it was observed that such reactions are considerably accelerated using mineral acids as solvents, leading us to the proposition that reactions that were not enabled in typical organic solvents may be possible in mineral acids. Indeed, we now demonstrate for the first time the two stage very high yield and selective oxidation of ArCH₃ to ArCHO with a theoretical atom economy of 100%, Scheme 1. First ArCHO is formed in an

Scheme 1. Scheme for the ET–OT Oxygenation of ArCH₃ to ArCHO Followed by Electrolytic Release of H₂



ET–OT oxygenation reaction, and then H₂ as the additional product is released by electrolysis. The reaction can also be carried out electrocatalytically. Cyclic voltammetry and DFT calculations coupled with mechanistic probe reactions show why mineral acids may be superior solvents for such ET–OT transformations.

RESULTS AND DISCUSSION

Oxygenation of ArCH₃ to ArCHO. As shown in Scheme 1, the oxygenation of ArCH₃ to ArCHO is a four-electron oxidation, and since H₅PV₂Mo₁₀O₄₀ is nominally a two-electron oxidant, stoichiometric reactions between H₅PV₂Mo₁₀O₄₀ and ArCH₃ in a 2:1 ratio were found to be optimal for the formation of ArCHO. In such a process it has been shown that an oxygen atom on the surface of the polyoxometalate framework is the oxygen donor.²⁵ Thus, the ET–OT oxygenation of toluene, PhCH₃, and various substituted derivatives, R₂C₆H₄CH₃, with 2 equiv of H₅PV₂Mo₁₀O₄₀ was carried out in 50% aqueous H₂SO₄ as solvent. Depending on the substrate, the partially optimized conditions of reaction temperature and time to yield an optimal amount of ArCHO products are summarized in Table 1. The results show highly efficient formation of ArCHO in almost all cases with practically no formation (0–0.1 mol %) of the corresponding carboxylic acid, ArCOOH. Also, no sulfonated products were detected. For toluene and halogen substituted derivatives as electron withdrawing moieties nearly quantitative conversions were observed with very high selectivity to ArCHO.

Since the reaction is initiated by electron transfer to yield an electrophilic radical cation, ArCH₃^{•+}, which can then also yield an electrophilic cation ArCH₂⁺ through further proton and electron transfer,²⁵ reaction of these plausible intermediate electrophiles with ArCH₃ yields some small amounts of dimeric compounds, typically as the only byproducts. 4-Nitrotoluene also reacts, however, in this case sublimation of the substrate leads to its removal from the reaction mixture, lowering the yield. For moderately activated toluene derivatives, such as the xylenes, the corresponding tolaldehydes are formed selec-

Table 1. ET–OT Oxidation of ArCH₃ Compounds to ArCHO^a

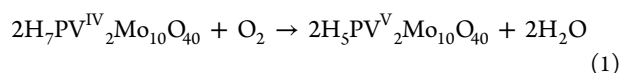
R in R–C ₆ H ₄ CH ₃	time, h	temp, °C	conversion, mol %	selectivity, mol %
H	5	70	99	95
4-Me	5	60	99	94
3-Me	5	70	99	94
2-Me	5	60	99	89
2,4-di-Me ^b	5	50	80	80
1,3,5-tri-Me	5	50	90	85
4-OMe	24	5–22 ^c	85	75
4- <i>i</i> -Pr	24	5–22 ^c	60	30 ^d
4- <i>t</i> -Bu	12	30	93	89 ^e
4-F	5	70	99	98
4-Cl	7	80	99	97
4-Br	10	80	98	96
4-I	10	80	97	96
3-Cl	8	80	98	93
3-Br	7	80	98	94
2,4-di-Cl	12	90	90	96
4-NO ₂ ^f	24	90	45	98

^aReaction conditions: 0.461 mmol of ArCH₃, 0.922 mmol of H₅PV₂Mo₁₀O₄₀·32H₂O, 8 mL of 50% H₂SO₄, N₂. The products were quantified by GC-FID and identified by GC-MSD when reference samples were unavailable. Unless otherwise stated the major byproducts were dimers, e.g., a mixture of dimethyl substituted biphenyl isomers from toluene. Traces of other compounds, typically less than 0.5%, were sometimes formed. No arene sulfonation reactions were observed. ^bThree dimethyl benzaldehyde isomers were formed in similar amounts. ^cThe reaction mixture was kept at ~5 °C for 3 h and then left to warm to ambient temperature. ^dThe major product, 65–70%, was 4-methylacetophenone. ^eThe major byproduct, ~8%, was benzaldehyde. ^fThe substrate tended to sublime from the reaction mixture.

tively. Similarly, 4-*tert*-butyltoluene reacts selectively to yield the corresponding 4-*tert*-butylbenzaldehyde with some formation of benzaldehyde likely because of acid catalyzed dealkylation. An interesting substrate is 4-isopropyltoluene, where the tertiary C–H bond is weaker than the primary C–H bond. Activation at the tertiary positions leads to oxygenation coupled with C–C bond cleavage to give the 4-methylacetophenone as the main product. Still there are significant amounts of 4-isopropylbenzaldehyde formed, which is clearly the kinetically preferred product since at higher temperatures only 4-methylacetophenone is formed. Similarly, isopropylbenzene yielded acetophenone (88% yield) and ethylbenzene also yielded the C–C bond cleaved product benzaldehyde (94% yield). With more electron donating substituents, for example, with 1,2,4-trimethylbenzene, dimer formation becomes more pronounced. This dimer formation can be significantly inhibited by reducing the reaction temperature to 5–22 °C and increasing reaction times. This effect is pronounced in the oxidation of 4-methoxytoluene where good yields of 4-methoxybenzaldehyde were achievable. At 50–60 °C there was almost only dimerization and even some formation of oligomers.

After completion of the ET–OT reaction with the formation of ArCHO, the polyoxometalate is reduced. The number of electrons on the polyoxometalate was measured by titration with KMnO₄ on the representative toluene oxidation reaction. About 1.95 electrons per polyoxometalate were found, which is commensurate with the yield of benzaldehyde and the reaction

stoichiometry. The completion of catalytic cycles in typical organic solvents is possible by use of O_2 , eq 1.



However, in 50% H_2SO_4 this reaction is very slow and alternatively the reduced polyoxometalate can be reoxidized by electrolysis with quantitative formation of H_2 .²⁷ A cyclic voltammetric measurement of the reaction mixture after the formation of the reduced polyoxometalate shows a reversible redox wave at ~ 1.1 V versus SCE, Figure S1 in the Supporting Information. Therefore, $H_7PV^{IV}_2Mo_{10}O_{40}$ was reoxidized with a Pt gauze anode and a platinum wire cathode at a potential of 1.3 V or higher between the anode and cathode to quantitatively release H_2 , Figure S2 in the Supporting Information.²⁸ It should be noted that, in a two-cell setup with a Nafion membrane, Figure S3 in the Supporting Information, one visually observes that H_2 is being released at the Pt cathode electrode and that the reduced green polyoxometalate was oxidized to the orange $H_5PV^V_2Mo_{10}O_{40}$ at the anode. In this vein, five oxygenation–electrolysis cycles were carried out without loss of reactivity on three representative substrates, toluene, 4-chlorotoluene, and 4-*tert*-butyltoluene, showing that the catalyst is easily reoxidized and then recovered without its removal from the solvent in a quantitative transformation. The conversions and product selectivity were within $\pm 3\%$ for each cycle.

Alkylarene oxidation can also be carried out electrocatalytically in one step, that is, simultaneous substrate oxygenation and polyoxometalate reoxidation. Thus, 10 mmol of substrate and 0.23 mmol of $H_5PV_2Mo_{10}O_{40}$ in 5 mL of 50% H_2SO_4 were reacted using Pt gauze as working electrode, and Pt wire as counter and reference electrode at a cell potential of 1.5 V between the cathode and anode. The higher cell potential was used to accelerate the reoxidation of the polyoxometalate. When the substrate was toluene at 70 °C, approximately a 65% yield (28 turnovers) of benzaldehyde was obtained after 10 h with >95% selectivity. When *p*-xylene was used as substrate, similar results were obtained. Attempts to use a two half-cell setup as shown in Figure S3 in the Supporting Information suffered from the lack of stability of the Nafion membrane at more elevated temperatures. It should be noted that indirect electrocatalytic oxidation of toluene and derivatives is also possible with Mn^{3+} and Co^{3+} salts in concentrated acid, but these catalysts tend to be less selective to benzaldehyde derivatives under high conversion conditions (see discussion below).²⁹ Ce^{4+} has been more selective, but in order to obtain good results Ag^+ was added as a catalyst or reactions were carried out in CH_3SO_3H .³⁰

Mechanism of Activation of $ArCH_3$. The key experimental observation that oxygenation of toluene with $H_5PV_2Mo_{10}O_{40}$ is possible in a mineral acid solvent but not in an organic solvent such as acetonitrile requires detailed explanation. It was hypothesized that the strongly acidic medium led to the increase in the redox potential of $H_5PV_2Mo_{10}O_{40}$. In Figure 1, we present the cyclic voltammetry measurements that show the changes in the oxidation potential as a function of H_2SO_4 concentration. See Figure S4 in the Supporting Information for all the cyclic voltammograms. At increasing H_2SO_4 concentrations from 0.1 to 5% there is a relatively small change in the oxidation potential from ~ 0.41 to 0.54 V versus SCE. At concentrations between 10 and 25% it was difficult to observe the redox wave; however at 30% to 50%

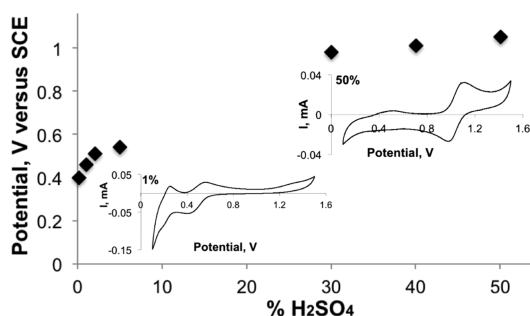
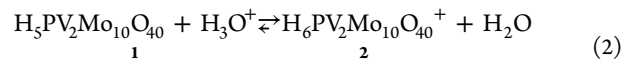


Figure 1. Oxidation potential, $E_{1/2}$, versus SCE of $H_5PV_2Mo_{10}O_{40}$ at various concentrations of aqueous H_2SO_4 . The measurements were carried out at 2 mM $H_5PV_2Mo_{10}O_{40}$ using a glassy carbon working electrode, a platinum wire counter electrode, and a calomel reference electrode; scan rate 50 mV/s. Representative cyclic voltammograms at 1% (left inset) and 50% (right inset) H_2SO_4 are shown.

H_2SO_4 the oxidation potential clearly and very strongly shifted to 1.0–1.1 V versus SCE. This shift in the redox potential is attributed to the formation of a protonated polyoxometalate at higher H_2SO_4 concentrations (see below).

DFT calculations show that the oxidation of $PhCH_3$ to $PhCHO$ according to Scheme 1 is thermodynamically favorable with $\Delta G_{298} = -39.0$ and -36.9 kcal/mol in acetonitrile and sulfuric acid, respectively. It is shown above that protonation dramatically increased the oxidation potential and reactivity of $H_5PV_2Mo_{10}O_{40}$. This has also been observed with other oxidants such as manganese and cobalt acetate,³¹ and has been attributed (i) to the lowering of orbital energies including that of the LUMO, (ii) to an increase of electrophilicity through formation of a positively charged species, and (iii) specifically for $H_5PV_2Mo_{10}O_{40}$ by formation of coordinatively unsaturated sites that become available for coordination of a reactant.³² In a nonprotic regime, polyoxometalates such as $H_5PV_2Mo_{10}O_{40}$ are neutral where the negative charge of the polyanion is fully compensated by the corresponding number of protons chemically bound to the bridging oxygen atoms, preferably around vanadium atoms.^{33,34} In sulfuric acid, calculations show that further protonation of $H_5PV_2Mo_{10}O_{40}$ is favorable with $\Delta G_{298} = -2.4$ kcal/mol, eq 2.



Moreover, the proton affinity of reduced species is even higher, Table S1 in the Supporting Information. Thus, protonation favors the reduction of this polyoxometalate both kinetically and thermodynamically. As predicted by the calculations, the protonation increases the electron affinity or oxidative “power” of $H_5PV_2Mo_{10}O_{40}$ and $H_6PV^V_2Mo_{10}O_{40}$ by 10.6 and 9.3 kcal/mol, respectively.

Activation of the reactants through electron transfer (ET) or proton coupled electron transfer (PCET) usually precedes oxygen transfer from the polyoxometalate to a substrate. Figure 2 displays the calculated energetics for the possible initial outer-sphere reactions for the oxidation of toluene. Although ET presents a plausible initial step for a neutral complex **1** in acetonitrile and, especially, in sulfuric acid, all the outer-sphere reactions of this complex are endergonic at 298 K. The outer-sphere reactions of **2** with toluene are energetically more favorable. Thus, electron transfer becomes exergonic in sulfuric acid. In the gas phase as well as in the less polar acetonitrile solution PCET is energetically preferred, although **2** is not

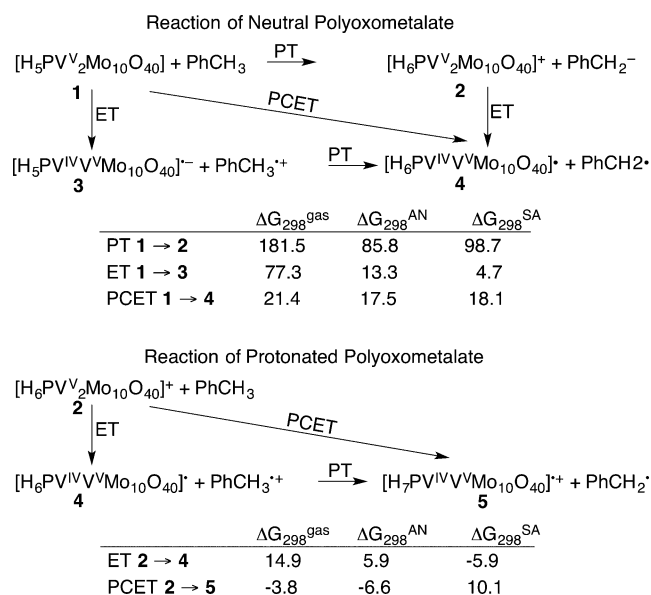
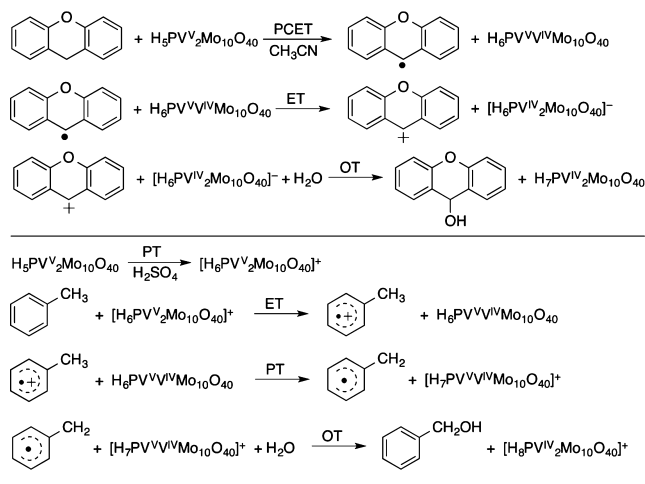


Figure 2. Possible initial outer-sphere reactions for the oxidation of toluene and the calculated energetics. AN and SA refer to acetonitrile and sulfuric acid, respectively.

experimentally accessible under these conditions; ET is still endergonic. Thus, in contrast to PCET in neutral complexes as observed previously for more reactive alkylarenes such as xanthene,²⁵ toluene activation in sulfuric acid presents a sequential protonation of the polyoxometalate by the solvent followed by electron transfer and then proton transfer from the substrate to the polyoxometalate, Scheme 2.

Scheme 2. Reaction Pathways for Hydroxylation of Xanthene in Acetonitrile (Top) and Toluene (Bottom) in Aqueous H₂SO₄



Substitution Effects. The results from Table 1 clearly show that toluene derivatives with electron donating groups are more reactive than those with electron withdrawing groups. This observation is commensurate with the calculations presented above showing that activation of PhCH₃ by 2 is initiated by ET. Thus, one might expect that the rate of oxidation of a series of substrates RC₆H₄CH₃ for various substituents R would be 4-Me > H > 4-Br > 4-Cl > 4-F. Indeed, the vertical ionization energy of these compounds, which represents the driving force for ET, approximated by the

HOMO level in sulfuric acid, is appropriate for this order, Table S2 in the Supporting Information. It was, therefore, initially surprising to observe that in the oxidation of 4-RC₆H₄CH₃ to 4-RC₆H₄CHO the relative first order rate constants, Figure S5 in the Supporting Information, were 4-Me (1.24) > H (1.0) > 4-F (0.88) > 4-Cl (0.43) > 4-Br (0.24); the relative rates of the 4-halogen substituted compounds are very noticeably inverted. Further analysis of calculated data shows that the adiabatic ionization energy, Table S2 in the Supporting Information, which represents the thermodynamic effect of ET, shows a trend for the halogen substituted compounds that is proportional to the observed rates. One may rationalize these results by noting that spin delocalization is the main factor that determines the stability of a benzylic radical.³⁵ Thus, spin localization on the electron withdrawing halogen substituents may lead to destabilization of the benzylic radical. Indeed, for the isodesmic reaction, eq 3, we have found that there is a correlation between the experimentally observed substituent induced change in the reaction rate and the computed stabilization or destabilization energies, Figure 3. Thus, the

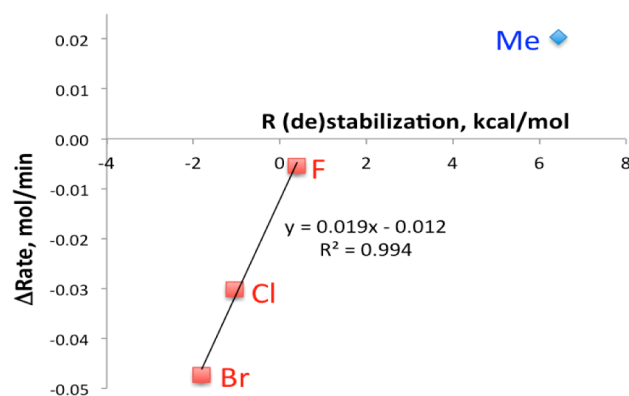
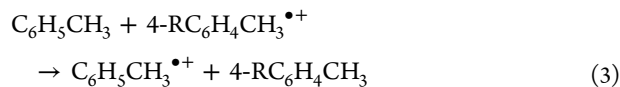


Figure 3. Correlation between observed substituent induced changes in the total reaction rate with computed stabilization (+) and destabilization (-) energies (ΔG_{298} in sulfuric acid, kcal/mol) relative to toluene cation found using isodesmic reaction 3.

radical cation of *p*-xylene is more stable (less reverse ET) relative to that of toluene, leading to a faster rate for *p*-xylene. On the other hand, the radical cations of 4-XC₆H₄CH₃ (X = F, Cl, Br) are less stable (more reverse ET) than that of toluene, Br < Cl < F. Thus, in the range of reversible ET, the less stable the intermediate radical cation, the slower the rate.



Therefore, one may suggest that although the ET from all the tested para substituted compounds, 4-RC₆H₄CH₃, is exergonic, radical cation intermediates of low stability as observed for 4-halogen substituted compounds may reverse the ET step and reduce the rate of reaction measured as formation of product. In contrast, for substrates with electron donating groups, the benzylic radical is stable enough to slow or inhibit reverse ET reactions and the total rate of oxidation is mainly determined by the energy of the HOMO, the driving force for ET (see also below).

Mechanism of the ET–OT Reaction. The proposed calculated mechanism for the ET–OT oxygenation of toluene is presented in Figure 4. As can be seen from the results and as

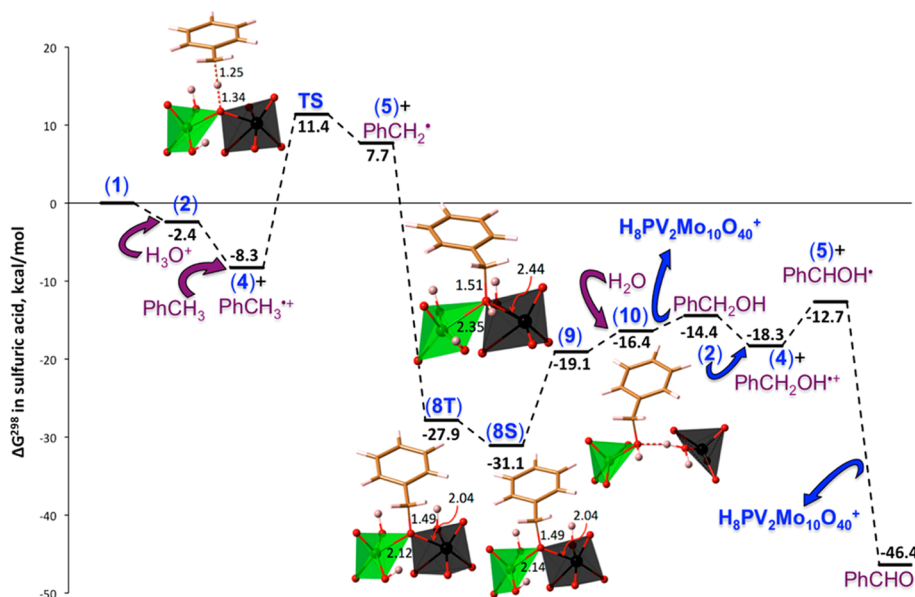


Figure 4. A DFT calculation derived mechanism for oxidation of toluene $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in 50% sulfuric acid. Green, V; black, Mo; red, O; brown, C; whitish, H.

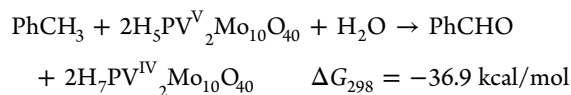
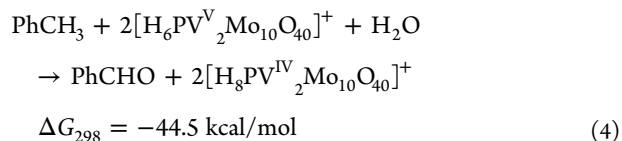
discussed above, after the initial ET reaction to yield $\text{PhCH}_3^{\bullet+}$, the rate-determining step is the sequential PT reaction leading to formation of the highest energy intermediates, the benzylic radical PhCH_2^\bullet and $[\text{H}_7\text{PV}^{\text{IV}}\text{V}^{\text{V}}\text{Mo}_{10}\text{O}_{40}]^{\bullet+}$ (5); $\Delta G_{298}^\ddagger = 19.7$ kcal/mol. This is quite comparable to the experimental value of $\Delta G_{298}^\ddagger = 22.8$ kcal/mol ($\Delta H_{298}^\ddagger = 15.8$ kcal/mol; $\Delta S_{298}^\ddagger = -23.3$ cal/(mol K)) obtained from the Eyring equation, Figure S6 in the Supporting Information. In the transition state (TS) the proton being transferred has short bonds with both the benzylic carbon atom (1.25 Å) and a bridging oxygen atom of the polyoxometalate (1.34 Å). It should be expected that a PT limiting step would be associated with a kinetic isotope effect (KIE). Indeed, such a measurement, Figure S7 in the Supporting Information, showed a KIE = 4.95 in a comparative experiment between the oxidation of C_7H_8 in $\text{H}_2\text{SO}_4/\text{H}_2\text{O}$ and C_7D_8 in $\text{D}_2\text{SO}_4/\text{D}_2\text{O}$. A competitive experiment using a 1:1 mixture of C_7H_8 and C_7D_8 also indicated a similar KIE, but the GC–MS analysis was complicated by competing H–D exchange reactions at both the benzylic and ring positions.

After the formation of PhCH_2^\bullet there is a “rebound” where the PhCH_2^\bullet is bonded to the bridging atom of the polyoxometalate to form stable triplet and singlet intermediates of similar energy (8T and 8S). Subsequently, proton transfer to the bridging oxygen atom leads to formation of PhCH_2OH still strongly bonded to the polyoxometalate, intermediate 9, although the V–O/Mo–O bonds are considerably elongated to 2.35/2.44 Å from 2.12 to 2.14/2.04 Å in 8. Benzyl alcohol is released through the formation of defect species with coordinatively unsaturated sites and coordination of water (10), Figure S8 in the Supporting Information, by the scission of a V–O/Mo–O bond. It should be noted that after short reaction times (20–30 min) small amounts of benzyl alcohol are indeed observed in the GC analyses. Furthermore, separate experiments also showed that benzyl alcohol is readily oxidized to benzaldehyde; relative first order rate constants $\text{PhCH}_2\text{OH}:\text{PhCH}_3 = 4.9$.

Further in the course of the reaction pathway, calculations show the feasibility of subsequent oxidative dehydrogenation of PhCH_2OH by another protonated complex 2 initiated by an

outer-sphere ET, where the propensity for ET is similar to that of PhCH_3 , Table S2 in the Supporting Information. However, since the formation of PhCHO does not require the breaking of M–O bonds in the polyoxometalate, it proceeds with energies that are overall more favorable.

As stated above, contrary to organic solvents where ET–OT oxygenation of toluene does not occur, H_2SO_4 can react with $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ to yield a protonated, cationic $[\text{H}_6\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^+$ species. Thus, an ET reaction of $[\text{H}_6\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^+$ with toluene in H_2SO_4 is favored compared to a reaction between $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ and toluene in acetonitrile by 19 kcal/mol, in good agreement with the experimentally observed increase of the oxidation potential of $\text{H}_2\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ by ~ 0.7 eV when moving from diluted to concentrated sulfuric acid, Figure 1. It should be also noted that the protonation of the polyoxometalate and therefore inter alia the use of mineral acid solvents leads to more favorable thermodynamics and kinetics throughout the reaction profile. Moreover, the total energy of the reaction is also favored by the protonation of the polyoxometalate, eq 4.



The hallmark of the transformation reported here is the very high selectivity obtained for ArCHO without formation of benzoic acid derivatives, ArCOOH. This is easily explained by the much less favored ionization energies and ΔG_{298} for ET for PhCHO compared to PhCH_3 and PhCH_2OH , Table S2 in the Supporting Information. In this context, it is also worthwhile to discuss the intrinsic differences and advantages of ET–OT oxidation of PhCH_3 with $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ compared to (a) ET oxidation catalyzed by $\text{Co}^{\text{III}}(\text{OAc})_3$ using O_2 as oxygen donor

and on the other hand (b) the use of stoichiometric oxidants such as Étard's reagent, CrO_2Cl_2 ,¹⁵ and permanganate.^{16,36} The ET oxidation of ArCH_3 with $\text{Co}^{\text{III}}(\text{OAc})_3$ is long known,³⁷ but the required use of O_2 as an oxygen donor leads to formation of peroxy radicals, $\text{ArCH}_2\text{OO}^\bullet$, and then alkoxy radicals, $\text{ArCH}_2\text{O}^\bullet$. Especially the latter easily abstracts a hydrogen atom from benzaldehyde to promote a competing autoxidation reaction pathway by a hydrogen atom transfer (HAT) mechanism and formation of ArCOOH . The slow kinetic formation of $\text{Co}^{\text{III}}(\text{OAc})_3$ in aerobic reactions has also led to use of promoters, notably bromide typically together with $\text{Mn}(\text{OAc})_2$ which further attenuates ArCOOH formation by autoxidation.³⁸ Thus, it is difficult to obtain high yields of ArCHO using $\text{Co}^{\text{III}}(\text{OAc})_3/\text{O}_2$. Although the stoichiometric oxidation of ArCH_3 by CrO_2Cl_2 or permanganate^{16,36} is long known, the selectivity to ArCHO is low.^{18,16} Interestingly, however, Mayer and co-workers have convincingly argued that these reactions proceed by a HAT or hydride transfer mechanism, concluding that the key feature in these reactions is affinity of the oxidant to $\text{H}^\bullet/\text{H}^-$ that represents the thermodynamic driving force for oxygen transfer. The mechanism of oxidation of alkylarenes with CrO_2Cl_2 or KMnO_4 is very different from that observed here with $\text{H}_3\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.

CONCLUSIONS

The transformation of toluene and its derivatives to the corresponding benzaldehyde compounds as presented in Scheme 1 shows both the ET–OT oxidation of the substrate and the formation of H_2 in a second step to form a cyclic repeatable process, for the high yield formation of products with a 100% theoretical atom economy, considering that H_2 has value. The oxidation potential of $\text{H}_3\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in this medium, 1.1 V SCE (1.34 V NHE), is higher than the potential for aerobic formation of water (1.23 V NHE), eq 1. This prevents the thermal reoxidation of the reduced polyoxometalate and precludes an aerobic reaction requiring an electrochemical oxidation of the reduced polyoxometalate. The generally very high reaction yield lends an important practical aspect to such a reaction with potential to replace common nonbenign procedures. Notably, the use of aqueous H_2SO_4 as solvent leads to an aqueous biphasic reaction medium,³⁹ and therefore a simple cascade of operations, (i) thermal substrate oxygenation, (ii) phase separation of the organic and catalyst phase, and (iii) catalyst recycle and recovery by electrolysis, can be implemented. However, one-stage electrocatalytic reactions are also viable. The stability of the Nafion membrane in a two half-cell configuration at elevated temperatures sometimes needed is a remaining technical issue to be solved.

In summary, the use of strong mineral acids as solvents allows significantly improved reactivity due to the higher redox potential of $\text{H}_3\text{PV}_2\text{Mo}_{10}\text{O}_{40}$. There are also advantages in catalyst recovery that are intrinsic to biphasic media. Together with the unique ET–OT oxygenation reactions that $\text{H}_3\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ catalyzes, this research opens up new prospects for selective oxidative transformations, demonstrated here by the selective oxygenation of methylarenes.

EXPERIMENTAL SECTION

Materials. Alkylarenes were of analytical grade. Deuterated compounds were purchased from Cambridge Isotope Laboratories. $\text{H}_3\text{PV}_2\text{Mo}_{10}\text{O}_{40}\cdot 32\text{H}_2\text{O}$ was prepared by a known procedure.⁴⁰

Reactions. Typically the oxidation reactions of ArCH_3 were carried out in 50 mL pressure tubes under N_2 under the conditions given in the tables and figures. The products were decanted and diluted by dichloromethane for analysis by gas chromatography. GC-FID (HP 6890) and GC-MSD (HP 5973) instruments were used equipped with a 5% phenyl methylsilicone 0.32 mm i.d., 0.25 mm coating, 30 m column (Restek SMS) using helium as carrier gas. H_2 was volumetrically quantified by calibration by GC-TCD using a 20 ft \times 1/8 in. stainless steel column packed with molecular Sieve 5 Å in series with a 4 ft \times 1/8 in. stainless steel column packed with HayeSep T. The carrier gas was Ar, column $T = 90^\circ\text{C}$.

Electrolysis and Cyclic Voltammetry Experiments. Cyclic voltammetry experiments were performed using a potentiostat (CHI660A) connected to a personal computer. The measurements were performed in a three-electrode cell configuration consisting of (i) a glassy carbon working electrode, (ii) a Pt wire counter electrode, and (iii) a calomel reference electrode. Experiments were performed at room temperature. The scan rate was 50 mV s^{-1} . Electrolysis in a one cell configuration was carried out using (i) Pt gauze (working electrode), (ii) a Pt wire (counter electrode), and (iii) Pt (a reference electrode). The experiments were performed at 25–80 $^\circ\text{C}$. Electrolysis in a two half-cell configuration was carried out in the presence of Pt gauze as working electrode, and Pt wire as counter and reference electrode at different potentials from 1.3 to 1.5 V between the anode and cathode. The higher the potential, the faster the reoxidation reaction. The two half cells were separated by a Nafion 212 membrane washed before use with 5 wt % H_2O_2 and 8% H_2SO_4 consecutively.

Computational Method. All computations were done using the same methodology previously described by us for calculations involving $\text{H}_3\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.³² Bulk solvent effects of the sulfuric acid medium have been calculated at the M06/PC1 level using the continuum solvation model COSMO with a static dielectric constant, $\epsilon = 100$.⁴¹

ASSOCIATED CONTENT

Supporting Information

Additional experimental information and data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b01745.

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Notes

The authors declare no competing financial interest.

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