Hydrolytically Stable Organic Triester Capped Polyoxometalates with Catalytic Oxygenation Activity of Formula $[RC(CH_2O)_3V_3P_2W_{15}O_{59}]^{6-}$ (R = CH_3, NO_2, CH_2OH)

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Abstract: The apparent instability of fully oxidized (d^0) redox active alkoxypolyoxometalates to hydrolysis inferred from literature studies would appear to obviate complexes involving covalent bonds between polyols (e.g. carbohydrates) and polyoxometalate complexes for applications in aqueous phase catalysis and medicine. The title capped complexes $[RC(CH_2O)_3V^V_3P_2W^{VI}_{15}O_{59}]^{6-}$ ([**1**-R]: R = CH_3, NO_2, and CH_2OH), prepared in very high yield (>90%) by the stoichiometric condensation of 1,1,1-tris(hydroxymethyl)ethane derivatives with $Q_5H_4[V_3P_2W_{15}O_{62}]$, where Q = $(n\text{-}C_4H_9)_4N$, in CH_3CN, however, have *substantial* kinetic stability with respect to hydrolysis (e.g. $\tau_{1/2} \sim 912$ h for 40 mM [**1**-CH_3] in D_2O with pD = 0 at 100 °C). ^1H, ^{31}P, and ^{51}V NMR spectra during and after the condensation synthesis of the triester complexes [**1**-R] indicate the absence of polyoxometalate intermediates in significant concentration during the reactions. These techniques and ^{183}W NMR and IR confirm the only detectable product in each case is the C_{3v} regioisomer involving replacement of the three μ_2-oxo edge-bridging oxygens of the V_3 cap in the parent polyoxometalate, the most basic oxide ions in the complex, with the three μ_2-alkoxy groups of the triols. Two types of experiments, complementary to those addressing hydrolytic removal of the 1,1,1-tris(alkoxymethyl) "caps" of the title complexes, indicate both a kinetic and a thermodynamic preference for reaction of the more electron rich alcohols with the parent heteropolyanion, $Q_5H_4[V_3P_2W_{15}O_{62}]$, to form the title complexes. First, competitive kinetics methods indicate the relative reactivities of CH_3OH, $CH_3C(CH_2OH)_3$, $(HOCH_2)C(CH_2OH)_3$, and $(O_2N)C(CH_2OH)_3$, respectively, with this polyanion were 6:6:5:1. Second, thermodynamic equilibration in cap-cap′ exchange (or triple transesterification) reactions, $RC(CH_2OH)_3 + [R'C(CH_2O)_3HV_3P_2W_{15}O_{59}]^{5-} \rightarrow [RC(CH_2O)_3HV_3P_2W_{15}O_{59}]^{5-} + R'C(CH_2OH)_3$, where R, R′ = NO_2 or CH_2OH (DMF solution, 50 °C, 3 days), indicated a 35-fold preference for binding of the $HOCH_2C(CH_2\text{–})_3$ cap relative to the $O_2NC(CH_2\text{–})_3$ cap. While the title capped complexes showed stability upon reduction on the cyclic voltammetry time scale (nearly reversible voltammograms), preparative electrochemical or chemical reduction in slightly wet CH_3CN resulted in immediate and complete hydrolysis to form the free 1,1,1-tris(alkoxymethyl) caps and $[V_3P_2W_{15}O_{62}]^{9-}$. Potentiometric titration, elemental analysis, and chemical reactivity confirmed that the [**1**-CH_3] complex could be prepared in two different protonation states, Q_5H[**1**-CH_3] and Q_2H_4[**1**-CH_3]. Several experiments with the thioether mustard gas analog tetrahydrothiophene (THT) demonstrated that the [**1**-R] complexes are capable of catalyzing oxygenation. Comparative kinetics methods gave the following order of reactivity for oxidation of THT by *tert*-butyl hydroperoxide (TBHP): Q_2H_4[**1**-CH_3] (fastest catalyst) > $OV(O\text{-}i\text{Pr})_3$ (a monomeric V^V model for breakdown of [**1**-CH_3] during turnover) > $(n\text{-}Bu_4N)_2WO_4$ (a monomeric W^{VI} model) > $Q_5H_4[V_3P_2W_{15}O_{62}]$ (the parent complex) > Q_5H[**1**-CH_3] > $Q_6[P_2W_{18}O_{62}]$ > no catalyst (slowest). These relative rates coupled with other kinetics measurements and the complete lack of degradation of [**1**-CH_3] examined after 30 turnovers (30 equiv of THTO from THT and TBHP) collectively provide strong evidence that kinetically significant fragmentation during catalysis by [**1**-CH_3] is minimal and that [**1**-CH_3] in varying protonation states is probably the active catalyst. One possible activated complex for the rate-determining transition state is given for THT oxidation by TBHP catalyzed by [**1**-CH_3] consistent with the unusual rate law: $v_0 = k[\text{THT}][\text{TBHP}][[\textbf{1}\text{-}CH_3]]^2$. The Arrhenius plot is quite linear ($R = 0.988$) yielding $E_a \sim 10.1$ kcal mol^{-1}.

Introduction

Early transition metal oxygen anion clusters, or polyoxometalates for short, simultaneously exhibit several properties that make them attractive for applications in catalysis, medicine, and many other areas. Among these properties are an ability to be reversibly reduced by several electrons, resistance to thermal and oxidative degradation, and synthetic accessibility and alterability.[1-14] The potential utility of polyoxometalates in both catalysis and chemotherapeutics could be considerably enhanced if a rational and flexible methodology existed for the formation

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of hydrolytically stable linkages between organic and biological groups and the surfaces of the complexes. Such surface groups could facilitate recognition and preassociation of catalytic substrates and biological targets while hydrolytic stability of the linkages would render the organic derivatized polyoxometalates stable in water. Water is not only a solvent of growing value for catalysis in an age of concern about toxic organic solvents and reagents and burgeoning biotechnology industries but also the solvent mandated by medical applications. At present two types of linkages between polyoxometalate oxygen atoms and organic or organometallic groups have demonstrable long term hydrolytic stability in partial or completely aqueous systems, the organosilyl and related main group organometallic derivatives of Knoth and Pope[15–26] and the alkyl-substituted cyclopentadienyltitanium ($RCpTi^{IV}$) polyoxometalate derivatives of Klemperer and Keana.[27–31] A third group of organic derivatized polyoxometalates, the bis(organophosphonyl) polyoxotungstates of formula $[C_6H_5P(O)]_2X^{n+}W_{11}O_{39}^{(8-n)-}$ (where $X^{n+} = P^{5+}, Si^{4+}$) have limited hydrolytic stability with halflives of hours (not too short for chemotherapeutic efficacy but not too long to interfere with bodily clearance).[32] The optimal "handles" for molecular recognition for catalytically or physiologically active water soluble polyoxometalates, however, would be the polyols. Carbohydrates are ubiquitous in biological systems, structurally diverse, and often play key roles in selective molecular binding and consequent physiological activity. By extension carbohydrate–polyoxometalate conjugates with adequate hydrolytic stability might facilitate targeting of polyoxometalates in antiviral chemotherapy.[12,33–36] Unfortunately, definitive work including that of Day, Klemperer, and Schwartz[37] and others has established that alkoxypolyoxometalates (alternative nomenclature: organic esters of polyoxometalates) are notoriously labile to hydrolysis. While the group of Zubieta has used hydrothermal conditions and the chelating triesters to prepare a gallery of polyalkoxyvanadates, these complexes are not likely to be compatible with oxidative catalysis or physiological conditions as nearly all of them contain, in whole or in part, reduced vanadium ions, which dictates, in large part, their stability.[38–40]

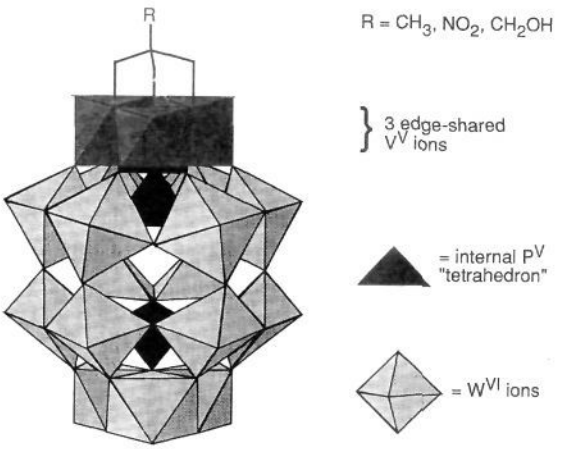

Figure 1. The structures of the title complexes, $[RC(CH_2O)_3V_3P_2W_{15}O_{59}]^{6-}$, R = CH_3, NO_2, CH_2OH ([**1**-CH_3], [**1**-NO_2], and [**1**-CH_2OH], respectively), in polyhedral notation. In this notation the MO_6 and internal PO_4 units are represented as coordination polyhedra: octahedra and tetrahedra, respectively. The vertices of the polyhedra define the oxygen nuclei while the central metal or nonmetal ions are internal to each polyhedron.

We report here the synthesis and characterization of the first alkoxypolyoxometalates with both hydrolytic stability and catalytic oxygenation activity. These complexes of formula $[RC(CH_2O)_3HV_3P_2W_{15}O_{59}]^{5-}$ ([**1**-R]: R = CH_3, NO_2, and CH_2OH), illustrated in Figure 1, are the tris(hydroxymethyl) triesters of $[V_3P_2W_{15}O_{62}]^{9-}$, a complex first reported by Pope, Tézé, and their co-workers[41–43] and subsequently characterized further by Finke and co-workers, who alluded to irreversible changes in the NMR spectra of solutions of the complex containing methanol, a point not further developed.[44] The spectroscopic, hydrolytic, redox, and catalytic oxygenation properties of the new title complexes are described.

Experimental Section

Materials and Methods. *Acetonitrile (Burdick & Jackson)* was dried over 3Å molecular sieves before use. The thioether substrates and oxidants were purchased from Aldrich. The complexes Q_2WO_4[27] (Q = *n*-Bu_4N), $OV(O\text{-}iPr)_3$,[45] and $Q_5H_4[V_3P_2W_{15}O_{62}]$[44] were prepared by literature procedures. The purity and composition of the latter polyoxometalate complex was determined to be very high based on IR, ^{31}P, and ^{51}V NMR and elemental analysis. ^1H NMR spectra were recorded using a General Electric QE-300 instrument. ^{31}P, ^{51}V, and ^{183}W NMR spectra were recorded using an IBM WP-200SY NMR spectrometer at 81.01, 52.58, and 8.34 MHz, respectively. All solvents for use in NMR were dried by storage over activated 3Å molecular sieves for at least a week prior to use. ^1H, ^{31}P, ^{51}V, and ^{183}W NMR chemical shifts were referenced to $(CH_3)_4Si$, 85% H_3PO_4, 100% $VOCl_3$, and 2.0 M Na_2WO_4 in D_2O, respectively. In the case of ^{31}P, ^{51}V, and ^{183}W NMR spectra, referencing was achieved by the substitution method and chemical shifts downfield from the reference are reported as positive ($+\delta$). The probe temperature was 25 °C in all NMR experiments. Infrared spectra were obtained as

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KBr pellets with 2–5 wt % of the sample using a Nicolet 510M FTIR spectrophotometer. Potentiometric titrations of [**1**-CH_3] in acetonitrile solution with 1.0 M methanolic $(n\text{-}C_4H_9)_4NOH$ to assess protonation states were carried out using a Model 240 Corning pH meter equipped with a combination micro glass electrode at room temperature. The numbers of titratable protons in all cases agreed with the formulations of the polyoxometalate complexes based on all other data (*vide infra*). Elemental analyses were conducted by Atlantic Microlab, Inc. (Norcross, GA) for C, H, and N and by E+R Microanalytical Laboratory (Corona, NY) for all other elements.

Preparation of $[(n\text{-}C_4H_9)_4N]_5H[CH_3C(CH_2O)_3V_3P_2W_{15}O_{59}]$, Q_5H[1-CH_3]. To 2.07 g (0.4 mmol) of $Q_5H_4[V_3P_2W_{15}O_{62}]$ in 50 mL of CH_3CN was added 0.06 g (0.5 mmol) of 1,1,1-tris(hydroxymethyl)ethane. The resulting solution was stirred at room temperature for 24 h and a large excess of ether was slowly added to the solution until a precipitate formed. The precipitate was separated by filtration, washed with ether, and dried in vacuo for 2 days, to yield about 2.0 g of [**1**-CH_3] as an orange powder (95% yield based on $Q_5H_4[V_3P_2W_{15}O_{62}]$). The ^1H NMR (CD_3CN) shows one characteristic resonance at $\delta = 5.44$ for the three equivalent methylene groups consistent with attachment to the three vanadium atoms on one cap or end of the C_{3v} starting polyoxometalate complex. The resonance of the ester (triol) methyl group was coincident with the resonance of the terminal methyl of the tetra-*n*-butylammonium groups: δ 1.00 (t, 60H + 3H of cap), 1.43 (sextet, 40H), 1.65 (quintet, 40H), 3.17 (t, 40H), 5.44 (s, 6H, $-CH_2-O$). ^{31}P, ^{51}V, and ^{183}W NMR spectra confirm that effective C_{3v} symmetry is maintained in the capped-catalyst product, [**1**-CH_3]. ^{31}P NMR (0.01 M in CD_3CN at 25 °C): –4.50 ppm ($\Delta\nu_{1/2} = 8.4 \pm 0.4$ Hz) and –9.60 ppm ($\Delta\nu_{1/2} = 8.0 \pm 0.3$ Hz). ^{51}V NMR (0.01 M in CD_3CN at 25 °C): –551.0 ppm ($\Delta\nu_{1/2} = 1243.8 \pm 9.3$ Hz). ^{183}W NMR (0.15 M in CD_3CN at 25 °C, 11 000 acquisitions): –113.4 ppm (1W, $\Delta\nu_{1/2} = 3.1 \pm 0.1$ Hz, $^2J_{W\text{-}O\text{-}W} = 6.3 \pm 0.5$ Hz), –153.6 ppm (2W, $\Delta\nu_{1/2} = 3.5 \pm 0.1$ Hz, $^2J_{P\text{-}O\text{-}W} = 1.4 \pm 0.1$ Hz, $^2J_{W\text{-}O\text{-}W} = 7.9 \pm 0.5$ Hz), and –167.5 ppm (2W, $\Delta\nu_{1/2} = 8.0 \pm 0.3$ Hz, $^2J_{W\text{-}O\text{-}W} = 11.4 \pm 0.5$ Hz). IR (cm^{-1}): 1088 (m), 1067 (w), 1026 (vw), 956 (s), 909 (s), 818 (vs), 798 (s), 733 (m). Potentiometric titration of the isolated complex indicated one proton consistent with the formulation Q_5H[**1**-CH_3].

Anal. Calcd for $C_{85}H_{190}N_5O_{62}P_2V_3W_{15}$: C, 19.45; H, 3.62; N, 1.33; P, 1.18; V, 2.92; W, 52.60. Found: C, 19.20; H, 3.51; N, 1.38; P, 0.97; V, 3.19; W, 52.02.

Preparation of $Q_2H_4[CH_3C(CH_2O)_3V_3P_2W_{15}O_{59}]$. The more acidic form of [**1**-CH_3] was prepared by ion exchange using AG 50W-X2 resin. Ten grams (1.9 mmol) of [**1**-CH_3] were dissolved in 50 mL of CH_3CN and the solution was passed through 20 g of the AG 50W-X2 (BIO-RAD) acidic cation exchange resin charged with H^+ and pre-washed with CH_3CN. Several additional 5-mL portions of 50/50 v/v CH_3CN/H_2O were required to wash all the complex off the column. The eluant was collected and solvent was removed at about 45 °C with a rotary evaporator. The solid was dried in vacuo at room temperature for 2 days yielding 8.3 g (95% based on Q_5H[**1**-CH_3]) of the product as an orange powder. ^1H NMR (CD_3CN at 25 °C): δ 1.00 (t, 28H + 3H of cap), 1.42 (sextet, 18H), 1.64 (quintet, 18H), 3.13 (t, 18H), 5.58 (s, 6H, $-CH_2-O$). ^{31}P NMR (0.01 M in CD_3CN at 25 °C): –4.45 ppm ($\Delta\nu_{1/2} = 9.4 \pm 0.4$ Hz) and –9.40 ppm ($\Delta\nu_{1/2} = 8.8 \pm 0.3$ Hz). ^{51}V NMR (0.01 M in CD_3CN at 25 °C) only one peak at –561.0 ppm ($\Delta\nu_{1/2} = 1143.8 \pm 10.3$ Hz). IR (cm^{-1}): 1089 (m), 1067 (sh), 1025 (vw), 959 (s), 912 (s), 814 (vs), 797 (s), 731 (m). Potentiometric titration of the isolated complex indicated ca. four protons, which is consistent with the formulation Q_2H_4[**1**-CH_3]. The elemental analysis was satisfactory.

Preparation of $Q_5H[O_2NC(CH_2O)_3V_3P_2W_{15}O_{59}]$, [1-$NO_2$]. The same procedure was used as for [**1**-CH_3] but the triol $(O_2N)C(CH_2OH)_3$ was used in place of $CH_3C(CH_2OH)_3$. The single ^1H NMR resonance of the capped polyanion moiety of $Q_5H[O_2NC(CH_2O)_3V_3P_2W_{15}O_{59}]$ was observed at $\delta = 5.82$. IR (cm^{-1}): 1086 (m), 1066 (w), 1024 (vw), 954 (s), 909 (s), 820 (vs), 806 (s), 733 (m). The elemental analysis was satisfactory.

Preparation of $Q_5H[HOCH_2C(CH_2O)_3V_3P_2W_{15}O_{59}]$, [1-$CH_2OH$]. Pentaerythritol (0.08 g; 0.6 mmol; 1.5 equiv) and 2.07 g (0.4 mmol) of $Q_5H_4[V_3P_2W_{15}O_{62}]$ were stirred in 30 mL of DMF contained in a 100-mL round-bottom flask covered with aluminum foil for 30 h at 40 °C. The stirred solution was cooled to ambient temperature and added dropwise to 300 mL of diethyl ether to precipitate the product which was separated by filtration. Acetonitrile (20 mL) was added to the separated product and the mixture filtered to remove insoluble impurities if any. The supernatant was treated with 150 mL of diethyl ether to reprecipitate the product which was separated by filtration, washed with diethyl ether, and dried in vacuo at ambient temperature for 2 days to yield 1.8 g (85% yield based on $Q_5H_4[V_3P_2W_{15}O_{62}]$) of the title complex. All spectra and elemental analyses were consistent with the formulation of the complex. ^1H NMR (CD_3CN at 25 °C): δ 0.99 (t, 60H + 3H of cap), 1.40 (sextet, 40H), 1.67 (quintet, 40H), 2.90 (s, 1H, OH), 3.16 (t, 40H), 5.54 (s, 6H, $-CH_2-O$). IR (cm^{-1}): 1088 (m), 1065 (w), 1023 (vw), 958 (s), 912 (s), 811 (vs), 794 (s), 732 (m). The elemental analysis was satisfactory.

Esterification of $[V_3P_2W_{15}O_{62}]^{9-}$ by Alcohols. The kinetic and thermodynamic affinities of alcohols toward $[V_3P_2W_{15}O_{62}]^{9-}$ were assessed. In a competitive kinetics experiment, 0.2 mmol of $O_2NC(CH_2OH)_3$ and 0.2 mmol of one of the alcohols, methanol, $CH_3C(CH_2OH)_3$, or $(HOCH_2)C(CH_2OH)_3$, were dissolved in 10 mL of DMF. To this solution was added 0.1 mmol of $Q_5H_4[V_3P_2W_{15}O_{62}]$, and the solution was stirred at 40 °C for 24 h. Aliquots were removed for analysis and added dropwise to ca. 200 mL of diethyl ether to precipitate the product. The precipitate was collected by filtration, washed three times with diethyl ether, and dried in vacuo prior to analysis by ^1H NMR. Products were quantified by ^1H NMR. By this method, the relative reactivities of the alcohols for $[V_3P_2W_{15}O_{62}]^{9-}$ were determined to be 6:6:5:1 for CH_3OH: $CH_3C(CH_2OH)_3$:$(HOCH_2)C(CH_2OH)_3$:$(O_2N)C(CH_2OH)_3$.

Hydrolytic Stability of Q_5H[1-CH_3]. One hundred equivalents of D_2O were added to a 0.1 M CD_3CN solution of the title compound and the resulting solution was kept at 60 °C for 72 h. The spectral properties confirmed that there was no apparent hydrolysis of the tris(hydroxymethyl) "cap" from the complex: ^1H NMR: δ 5.47 ($-CH_2-O$). ^{31}P NMR: –4.50 ($\Delta\nu_{1/2} = 8.4 \pm 0.4$ Hz) and –9.80 ppm ($\Delta\nu_{1/2} = 8.9 \pm 0.5$ Hz).

Determination of Rate Constant for Hydrolysis of Li_5H[1-CH_3]. Solubility limitations compelled us to prepare the analogous lithium salt of [**1**-CH_3], $Li_5H[CH_3C(CH_2O)_3V_3P_2W_{15}O_{59}]$ (Li_5H[**1**-CH_3] for convenience), for this study. The lithium salt was prepared in the following manner. Fifteen milliliters of an acetonitrile solution of 2.5 g (0.5 mmol) of Q_5H[**1**-CH_3] was added dropwise to 20 mL 50/50 v/v CH_3CN/H_2O saturated solution of $(CH_3)_4NBr$ with stirring. The resulting $(CH_3)_4N^+$ salt was filtered, washed with three 15-mL portions of H_2O, and then dissolved in 100 mL of 50/50 v/v CH_3CN/H_2O and passed through a 50-mL bed of AG 50W-X2 resin (BIO RAD) charged with Li^+ at the rate of 2 mL/min. The eluant was concentrated with a rotary evaporator and the product was dried in vacuo at 50 °C for 2 days, yielding 2.5 g (70%) of the hydroscopic product. ^1H NMR (D_2O) shows two characteristic resonances at $\delta = 1.07$ and 5.51. ^{31}P NMR (0.01 M in D_2O at 25 °C): –6.56 ($\Delta\nu_{1/2} = 19.8 \pm 0.9$ Hz) and –12.66 ppm ($\Delta\nu_{1/2} = 19.0 \pm 0.8$ Hz). ^{51}V NMR (0.01 M in D_2O at 25 °C): –540.8 ppm ($\Delta\nu_{1/2} = 891.8 \pm 9.3$ Hz). Anal. Calcd for $Li_5H[CH_3C(CH_2O)_3V_3P_2W_{15}O_{59}]$: Li, 0.86. Found: Li, 0.85.

The hydrolysis was conducted as follows: To 0.5 mL of acidified D_2O (1 N HCl, pD = 0), 0.0815 g (0.02 mmol) of Li_5H[**1**-CH_3] and about 0.5 μL of DMSO, as an internal standard, were added. The solution was transferred to a NMR tube, which was placed in a 100 °C oil bath. The hydrolysis process was monitored by ^1H NMR. The rate constant for hydrolysis was determined by either the rate of disappearance of the reactant ^1H NMR signal or the appearance of the organic triol ^1H NMR signal to be $k_{obs} = 7.6 \times 10^{-4}$ h^{-1} at this temperature and pH.

Exchange of Tris(hydroxymethyl) "Caps" on $[V_3P_2W_{15}O_{62}]^{9-}$. In one case, the relative thermodynamic stabilities of two different tris(hydroxymethyl) derivatives as triesters for $[V_3P_2W_{15}O_{62}]^{9-}$ could be assessed. This was done by using the triple transesterification cap-cap' exchange reaction involving the nitrocapped complex and the free hydroxymethylcap, pentaerythritol, and the reverse reaction involving the hydroxymethyl-capped complex and the free nitrocap, tris(hydroxymethyl)nitromethane. To 5.0 mL of DMF in a 10-mL round-bottom flask was added 0.05 mmol of $Q_5H[O_2NC(CH_2O)_3V_3P_2W_{15}O_{59}]$ and 0.05 mmol of $HOCH_2C(CH_2OH)_3$. The flask was capped with a rubber stopper and wrapped with aluminum foil to exclude light, and the solution was stirred at 25 °C for 3 days. The solution was added to 100 mL of ether with stirring. The resulting precipitate was filtered, washed with ether, and dried in vacuo for 24 h. ^1H NMR showed that 35 ± 5% of the original cap ($O_2NC(CH_2-)_3$) had been replaced by the new one ($HOH_2CC(CH_2-)_3$). The same procedure and conditions were used starting with $Q_5H[HOH_2CC(CH_2O)_3V_3P_2W_{15}O_{59}]$ and $O_2NC(CH_2OH)_3$. ^1H NMR showed that $Q_5H[HOH_2CC(CH_2O)_3V_3P_2W_{15}O_{59}]$ did not react with $O_2NC(CH_2OH)_3$ (detectability limit in analysis <2%).

Electrochemistry of [1-CH_3]. An acetonitrile solution 1.0 mM in Q_5H[**1**-CH_3] and 0.1 M in tetrabutylammonium hexafluorophosphate ($TBAPF_6$) electrolyte was reduced and reoxidized electrochemically using carbon cloth as the working electrode and platinum wire as the counter electrode. Two reduction peaks, at –0.31 and –0.72 V relative to ferrocene (F_c^+/F_c), indicate that two distinct reduced complexes should, in principle, be obtainable by control potential electrolysis. Ce(IV) titration confirmed the implication from the cyclic voltammetry that the first (–0.31 V) and

second (–0.72 V) reduced species both represented 2-e⁻ reductions. ^{31}P NMR of the first reduced and then reoxidized complex (0.01 M in CD_3CN, with 1 M $TBAPF_6$, 25 °C) shows two peaks at –3.91 ($\Delta\nu_{1/2}$ = 6.9 ± 0.4 Hz) and –9.99 ppm ($\Delta\nu_{1/2}$ = 8.7 ± 0.3 Hz). ^{51}V NMR of the same sample gives one peak at –534.5 ppm ($\Delta\nu_{1/2}$ = 1943.8 ± 10.3 Hz). These NMR data demonstrate that the organic cap of [**1**-CH_3] comes off upon reduction and the inorganic product is $[V_3P_2W_{15}O_{62}]^{9-}$.

Catalytic Oxidation of Tetrahydrothiophene (THT) and Stability of Catalyst. The following concentrations were required for NMR studies. To 3 mL of CH_3CN, 6 μmol of $Q_2H_4[CH_3C(CH_2O)_3V_3P_2W_{15}O_{59}]$ (2 mM), 0.24 mmol of THT (0.08 M), 0.24 mmol of TBHP (0.08M), and 3 μL of bromobenzene as internal standard were added. NMR spectra were taken immediately. The ^{31}P NMR spectrum exhibited two peaks: –4.42 ($\Delta\nu_{1/2}$ = 8.8 ± 0.5 Hz) and –9.48 ppm ($\Delta\nu_{1/2}$ = 8.8 ± 0.5 Hz). ^{51}V NMR gave one peak at –554.4 ppm ($\Delta\nu_{1/2}$ = 1071.9 ± 10.5 Hz). After reaction for 12 h at 40 °C, gas chromatographic analysis indicated 75% of the THT (30 turnovers) had been converted to tetrahydrothiophene oxide (THTO). At this time, ^{31}P NMR showed two peaks at –4.58 ($\Delta\nu_{1/2}$ = 13.8 ± 0.4 Hz) and –9.89 ppm ($\Delta\nu_{1/2}$ = 13.5 ± 0.5 Hz). ^{51}V NMR gave one peak at –552.3 ppm ($\Delta\nu_{1/2}$ = 1278.7 ± 8.6 Hz). The presence of the THTO, THT, and TBHP was shown to provide the small perturbation to the observed resonances.

Determination of Rate Law for Catalytic Oxidation of Tetrahydrothiophene (THT) by *tert*-Butyl Hydroperoxide (TBHP). The reaction rates were determined by measuring the amount of oxidation product (tetrahydrothiophene oxide = THTO) as a function of time using gas chromatography (HP 5890 instrument with a 5% methyl phenyl silicone column, nitrogen carrier gas, flame ionization detection and product quantitation using authentic products and internal standard techniques). In a typical reaction, 5 μmol of polyoxometalate catalyst, if not specified elsewhere, 0.284 mmol of substrate tetrahydrothiophene (THT), and 5 μL of internal standard bromobenzene were added to 5 mL of CH_3CN containing 50 mmol of $[(n\text{-}C_4H_9)_4N]HSO_4$ to prevent precipitation. The solution was degassed and placed under argon, and 0.284 mmol of degassed TBHP (90% aqueous solution) was added with a gas tight syringe. Aliquots of ca. 0.2 mL were taken out each time with the gas tight syringe. An excess amount of triphenylphosphine was added to destroy the remaining TBHP before injecting on the gas chromatograph. For initial rate measurements, the conversions of THT substrate were kept below 2% to minimize complications from side reactions. For determination of reaction orders, all reaction conditions were kept constant. The slopes of conventional log–log plots (logarithm of the initial rate as a function of logarithm of reactant concentration) indicated the oxidation of THT by TBHP catalyzed by [**1**-CH_3] was first order in THT and TBHP and second order in [**1**-CH_3]. The temperature dependence of this reaction was determined under the same reaction conditions.

Results and Discussion

Synthesis and Spectroscopic Properties of Triester Capped Polyoxometalates, $[RC(CH_2O)_3V_3P_2W_{15}O_{59}]^{6-}$, [1-R], R = CH_3, NO_2, and CH_2OH. The condensation of tris(hydroxymethyl) derivatives with the Q_5H_4 salt of $[V_3P_2W_{15}O_{62}]^{9-}$ in neutral polar aprotic media proceeds readily and in high yield at ambient temperature to form the corresponding triesters, [**1**-CH_3], [**1**-NO_2], and [**1**-CH_2OH], eq 1. The reaction and purification

$$RC(CH_2OH)_3 + H_4[V_3P_2W_{15}O_{62}]^{5-} \xrightarrow[25\text{–}40\ ^\circ C,\ no\ h\nu]{CH_3CN\ or\ DMF} [RC(CH_2O)_3HV_3P_2W_{15}O_{59}]^{5-} + 3H_2O \quad (1)$$

[**1**-R] (80–95% yield)

where R = CH_3, NO_2, and CH_2OH

conditions are described in the Experimental Section. The ^{31}P, ^{51}V, and ^{183}W NMR spectra of both the crude product mixture and the isolated purified products indicate for all three reactions that a single isomer is present after the condensation and through all workup and spectral acquisition procedures. This virtually quantitative regioselectivity with respect to the position of attachment of three alkoxy groups was unexpected as carefully characterized reactions involving the binding of organic[37] and

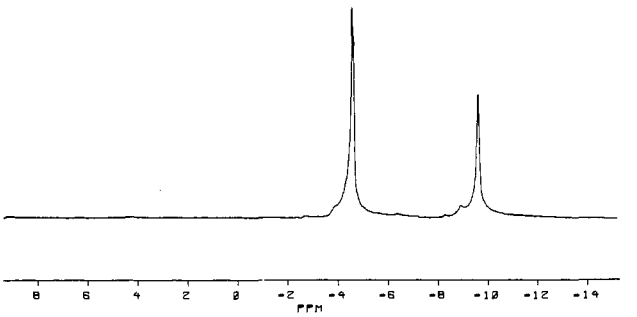


Figure 2. ^{31}P NMR spectrum of Q_5H[**1**-CH_3] (Q = n-Bu_4N^+) (10 mM in CD_3CN at 25 °C; line broadening = 5; chemical shifts are relative to 85% H_3PO_4).

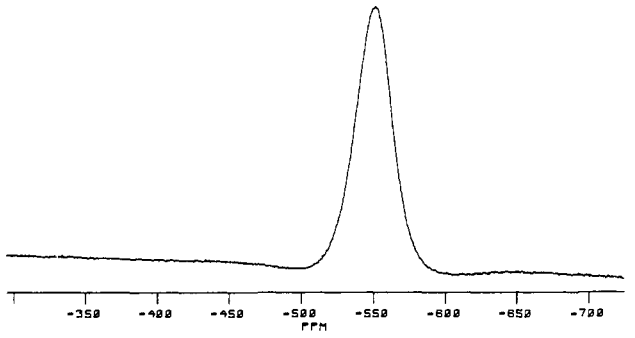


Figure 3. ^{51}V NMR spectrum of Q_5H[**1**-CH_3] (10 mM in CD_3CN at 25 °C; line broadening = 5; chemical shift is relative to neat $VOCl_3$).

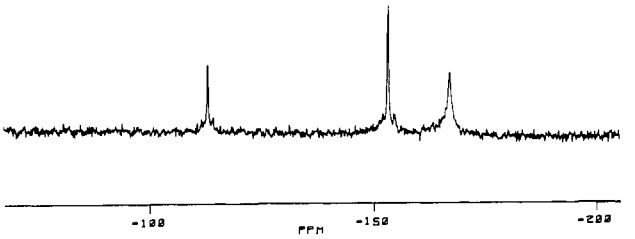


Figure 4. ^{183}W NMR of Q_5H[**1**-CH_3] (0.15 M in CD_3CN at 25 °C, 11 000 acquisitions). The chemical shifts of the three peaks relative to 2.0 M Na_2WO_4 in D_2O and $^2J_{W\text{–}O\text{–}W}$ and $^2J_{P\text{–}O\text{–}W}$ values are given in the Experimental Section.

organometallic[46,47] units to similar mixed addenda polyoxometalates and tris(hydroxymethyl) derivatives with other polyoxometalate precursors[38–40] often lead to more than one detectable type of product or more than one detectable ester regioisomer.

The ^{31}P, ^{51}V and ^{183}W NMR spectra of one representative complex, [**1**-CH_3], are given in Figures 2, 3, and 4, respectively. The observed NMR parameters are given in the Experimental Section. In the ^{31}P NMR spectra the upfield line (–9.60 ppm) is attributed to the phosphorus atom in the PW_9 half of the complex and the downfield line (–4.50 ppm) is attributed to the phosphorus in the PV_3W_6 half based on the increased P–O π bonding in the P–O–V unit relative to the P–O–W unit. These assignments are consistent with those made for the parent complex $[V_3P_2W_{15}O_{62}]^{9-}$.[43] The relative intensities of the two lines depend on the delay between pulses. The relaxation rate for the downfield P resonance is more rapid as this P atom is proximal to the quadrupolar V^V ions. The three resonances in the ^{183}W NMR of [**1**-CH_3] are analogous (relative chemical shifts, line widths, and intensities) to those in the parent complex that were unequivocally assigned by Finke, Domaille, and co-workers using $^{183}W\{^{51}V\}$ 2D INADEQUATE NMR:[44] the resonances at –113.4, –153.6, and –167.5 ppm are assigned to the 3 W atoms in the cap,

(46) For example, see Besecker, C. J.; Day, V. W.; Klemperer, W. G.; Thompson, M. R. *J. Am. Chem. Soc.* **1984**, *106*, 4125–4136.
(47) For example, see: Besecker, C. J.; Klemperer, W. G.; Day, V. W. *J. Am. Chem. Soc.* **1982**, *104*, 6158–6159.

the 6 W atoms in the belt adjacent to the W_3 cap, and the 6 W atoms in the belt adjacent to the V_3 cap, respectively.

The ^{31}P, ^{51}V, and ^{183}W NMR spectra also collectively yield two other types of useful information. First, they establish that the isomer in all three reactions forming [**1**-CH_3], [**1**-NO_2], and [**1**-CH_2OH] is that shown in Figure 1. This C_{3v} structure involves alkoxide formation (esterification) at the three symmetry equivalent μ_2-oxo oxygens in the edge-bridging triad of three V^V ions that comprise the cap of the parent complex. The NMR parameters of the [**1**-R] complexes are similar but distinct from those of the parent complex in the same medium. Second, the numbers of peaks and the line widths are all consistent with proton exchange between water oxygen atoms and polyoxometalate oxygens that is slow on the NMR time scale. Slow proton exchange can lead to line broadening, as in the case of the [**1**-R] complexes, or even multiple peaks, as well as slight changes in chemical shifts in the NMR spectra of protonated polyoxometalate complexes in highly dried dipolar aprotic media.[44] This is confirmed by addition of 100 equiv of D_2O which sharpens the NMR peaks as proton exchange between water oxygen atoms and polyoxometalate oxygens approaches the fast exchange limit. For example, the ^{51}V resonance in dry CD_3CN (δ = –551.0 ppm with $\Delta\nu_{1/2}$ = 1243.8 ± 9.3 Hz) transforms upon addition of 100 equiv of D_2O to a sharper single resonance (δ = –549.5 ppm with $\Delta\nu_{1/2}$ = 1057.2 ± 9.5 Hz).

The IR spectra also strongly suggest retention of the effective C_{3v} structure of the parent polyoxometalate, $[V_3P_2W_{15}O_{62}]^{9-}$, and the tris(hydroxymethyl) group in the product [**1**-R] complexes. Two distinguishing features exhibited by the [**1**-R] complexes that are not present in $[V_3P_2W_{15}O_{62}]^{9-}$ are the ν_{C-O} from the tris(hydroxymethyl) cap (~1027 cm^{-1}) and a slight splitting in one of the ν_{M-O-M} stretching fundamentals (800–820 cm^{-1}).

The more highly protonated complex Q_2H_4[**1**-CH_3], readily prepared by ion exchange, is much more electrophilic and active as an oxygenation catalyst than Q_5H[**1**-CH_3] (*vide infra*) yet appears to be indefinitely stable in CH_3CN solution at ambient temperature. Potentiometric titration in CH_3CN, the solvent chosen for catalytic studies reported below, elemental analysis, and chemical reactivity indicate the more highly protonated formulation.

All the physical and spectroscopic data (Experimental Section) collectively indicate that the formation of covalently or strongly bonded dimers or oligomers of the capped complexes, [**1**-R], in solution is negligible. Furthermore, this data coupled with kinetics and other data discussed below do not indicate that weak intermolecular interactions between these complexes in solution are of sufficient magnitude to have an experimentally significant effect on the redox behavior of these complexes.

Esterification Chemistry of $[V_3P_2W_{15}O_{62}]^{9-}$ with Alcohols. Despite a number of definitive papers published recently that address the formation and chemistry of alkoxypolyoxometalates (organic esters of polyoxometalates), there is paucity of actual kinetic or thermodynamic information on these processes and the complexes. Three types of experiments were conducted to assess the kinetic and thermodynamic aspects of polyoxometalate esterification, depicted by eq 1, and the reverse reaction, hydrolysis of the capped complexes, depicted principally by the reverse of eq 1. Full details (conditions of reaction, analytical methods, etc.) for each of the subsequently described experiments are given in the Experimental Section.

In the first experiment, equimolar quantities of a representative monodentate primary alcohol, methanol, and one of the three triols $CH_3C(CH_2OH)_3$, $(HOCH_2)C(CH_2OH)_3$, or $(O_2N)C(CH_2OH)_3$ were allowed to compete with each other for reaction with $[V_3P_2W_{15}O_{62}]^{9-}$. The products were determined to be stable under the reaction conditions and the relative quantities of the capped products, [**1**-R], were proportional to the relative reactivities of the different alcohols. The relative reactivities for $[V_3P_2W_{15}O_{62}]^{9-}$ were determined to be 6:6:5:1 for CH_3OH, $CH_3C(CH_2OH)_3$, $(HOCH_2)C(CH_2OH)_3$, and $(O_2N)C(CH_2OH)_3$, respectively. The more electron rich alcohols clearly have a kinetic preference for esterification relative to the more electron poor alcohols. This is consistent with the d^0 metal centers being electrophilic and alcohols nucleophilic and the fact that polyoxometalate esterifications take place under neutral or acidic conditions.

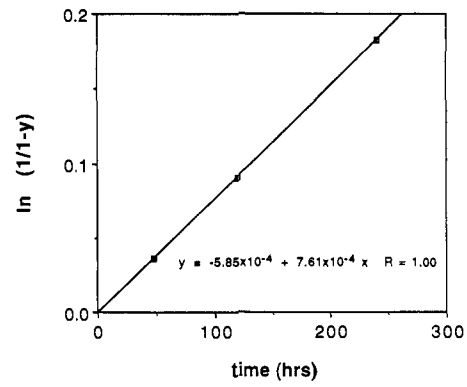


Figure 5. Hydrolysis of Li_5H[**1**-CH_3] to 1,1,1-tris(hydroxymethyl)ethane and $[V_3P_2W_{15}O_{62}]^{9-}$, the reverse of eq 1. Conditions: 40 mM Li_5H[**1**-CH_3], pD = 0; 100 °C. Conversion = $y = (C_0 - C)/C_{0o}$, where C_0 and C = initial concentration and concentration at time t, respectively, of Li_5H[**1**-CH_3].

In a second experiment, the kinetics of hydrolysis of [**1**-CH_3] was conducted using the highly water soluble Li_5H salt of [**1**-CH_3] which was prepared by two successive cation exchange procedures from analytically pure Q_5H[**1**-CH_3]. The observed hydrolytic process was the effective reverse of eq 1 and the free 1,1,1-tris(hydroxymethyl)ethane "cap" and the parent heteropolytungstate, $[V_3P_2W_{15}O_{62}]^{9-}$, were formed cleanly. The rate, monitored by ^1H NMR under pseudo-first-order conditions at pD = 0 and 100 °C is given as a conversion plot in Figure 5. The k_{obs} = 7.6 × 10^{-4} h^{-1} (or 2.1 × 10^{-7} s^{-1}), which translates to a half-life of 912 h under these fairly brutal hydrolytic conditions! Although the rate of forward reaction (i.e. eq 1) could not be assessed under the same conditions in order to experimentally evaluate a thermodynamic binding constant for eq 1, $K = k_1/k_{-1}$, it is clear that K is orders of magnitude greater than 1. The rate data indicate that some types of alkoxypolyoxometalates clearly have the requisite stability in water to be compatible with medical applications and environmentally attractive catalytic processes in water. With the myriad of polysaccharides currently of interest in biotechnology and other research areas, the possibilities for functional covalent polysaccharide–polyoxometalate conjugates would seem considerable.

A third experiment permitted an evaluation of the thermodynamic affinities of triol caps for the parent heteropolytungstate, $[V_3P_2W_{15}O_{62}]^{9-}$. Cap-cap′ exchange (or triple transesterification) reactions, eq 2, were conducted in DMF. Reaction with 1.0 equiv

$$RC(CH_2OH)_3 + [R'C(CH_2O)_3HV_3P_2W_{15}O_{59}]^{5-} \xrightarrow{DMF} [RC(CH_2O)_3HV_3P_2W_{15}O_{59}]^{5-} + R'C(CH_2OH)_3 \quad (2)$$

$$R = CH_2OH,\ R' = NO_2 \text{ and } R = NO_2,\ R' = CH_2OH$$

(0.05 mmol) of $Q_5H[O_2NC(CH_2O)_3V_3P_2W_{15}O_{59}]$ and 1.0 equiv of $(HOCH_2)C(CH_2OH)_3$ in DMF at 25 °C for 3 days produced the free $O_2NC(CH_2OH)_3$ cap and $Q_5H[HOCH_2C(CH_2O)_3V_3P_2W_{15}O_{59}]$ in 35 ± 5% yield based on the starting complex. In contrast, the reverse cap-cap′ exchange reaction involving $Q_5H[HOCH_2C(CH_2O)_3V_3P_2W_{15}O_{59}]$ and $O_2NC(CH_2OH)_3$ under identical conditions produced no detectable triple transesterification products. This indicates that the more electron rich tris(hydroxymethyl) compounds form thermodynamically more stable caps on the $[V_3P_2W_{15}O_{62}]^{9-}$ than the electron poor tris(hydroxymethyl) compounds. Not surprisingly then, the reaction

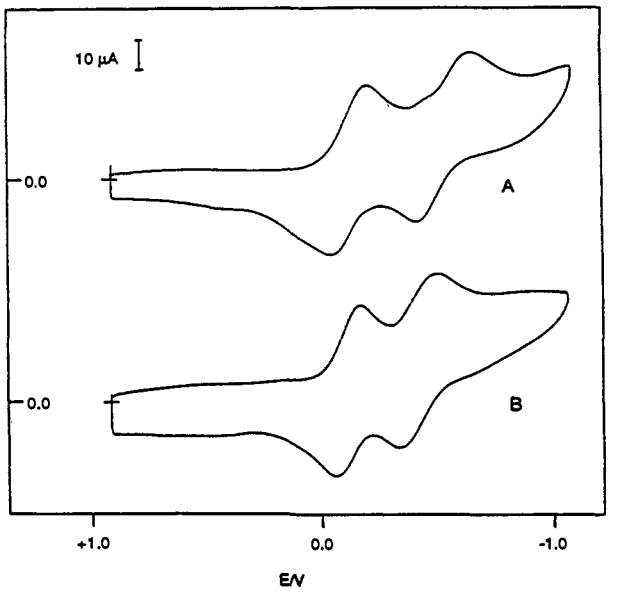


Figure 6. Cyclic voltammograms of $Q_5H[1\text{-}CH_3]$ and the precursor polyoxometalate. (A) $[1\text{-}CH_3]$; (B) the precursor complex, $Q_5H_4[V_3P_2W_{15}O_{62}]$ ($Q = n\text{-}Bu_4N^+$). Conditions in both voltammograms: ~ 1 mM complex; 0.1 M $(n\text{-}Bu_4N)PF_6$ supporting electrolyte in CH_3CN; 25 °C at glassy carbon working electrode; potentials relative to Fc^+/Fc; scan rate 200 mV s^{-1}.

of a more electron rich alcohol with $[V_3P_2W_{15}O_{62}]^{9-}$ is both kinetically and thermodynamically favored. This result should be substantially extrapolatable to d^0 polyoxometalates in general as these compounds, as a class, are all electron poor and electrophilic. It is appropriate to note that steric and not just electronic contributions are important to esterification of polyoxometalates.[37] The research of Day, Klemperer, and Schwartz on the alkylation and esterification of $C_{2v}\text{-}Nb_2W_4O_{19}^{4-}$ with a variety of electrophiles, RX (X = chlorides, sulfonates, and triflates), or alcohols, respectively, to yield the $Nb_2W_4O_{19}R^{3-}$ complexes provides one elegant experimental example of the importance of steric effects in binding aliphatic organic groups to polyoxometalates. For both alkylation and esterification reactions, the less sterically hindered groups (R = CH_3, CH_3CH_2) end up on the more sterically hindered but more nucleophilic doubly bridging oxygens while the more sterically hindered groups (R = $(CH_3)_2CH$, $(CH_3)_3Si$, or $[(CH_3)_3C](CH_3)_3Si$) end up on the less sterically hindered but less nucleophilic terminal oxygens.[37]

Redox Stability of $[1\text{-}CH_3]$. The cyclic voltammograms of $Q_5H[1\text{-}CH_3]$ and the precursor polyoxometalate $Q_5H_4[V_3P_2W_{15}O_{62}]$ at 1.0 mM in CH_3CN are given Figure 6. The following experimentally reproducible points regarding the voltammograms are noted (formal potentials (E^f), = $(E_{pc} + E_{pa})/2$ versus Fc^+/Fc): (1) There are two quasi-reversible redox processes for $Q_5H[1\text{-}CH_3]$, a 2-electron process at –0.31 V and a 2-electron process at –0.72 V. The number of electrons in each redox process was confirmed independently by Ce^{IV} titration. (2) Two analogous redox processes are seen in $Q_5H_4[V_3P_2W_{15}O_{62}]$ (–0.31 and –0.60 V). That the processes are analogous is a point consistent with a minimal change in the electronic structures of the most anodic portion of the molecules, the V_3O_{13} caps, upon replacing the formal $\mu_2\text{-}O^{2-}$ ions with the formal $\mu_2\text{-}RO^-$ ions during the esterification, eq 1.

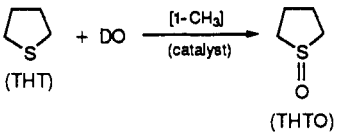
In contrast to the apparent implied stability of the reduced forms of $[1\text{-}CH_3]$ on the cyclic voltammetry time scale (tens of seconds), these forms are neither thermodynamically nor kinetically stable on slightly longer time scales in this medium (CH_3CN with a few equivalents of H_2O). Controlled potential reduction after the first reduction wave at –0.31 V leads to decomposition in minutes. In both cases the dominant products are those of hydrolysis, 1,1,1-tris(hydroxymethyl)ethane and reduced $[V_3P_2W_{15}O_{62}]^{9-}$ as confirmed by ^1H, ^{31}P, and ^{51}V NMR after reoxidation. The conditions and details of these reactions are given in the Experimental Section.

Table I. Oxidation of Tetrahydrothiophene (THT) by Three Oxidants Catalyzed by $Q_2H_4[1\text{-}CH_3]$[a]

oxidant	THT conversion (turnovers)[b]	product (selectivity)[c]
TBHP	32 (18)	THTO (>99%)
H_2O_2	75 (43)	THTO (>99%)
PhIO	23 (13)	THTO (>99%)

[a] $Q = n\text{-}Bu_4N^+$. Conditions: 5×10^{-6} mol of $Q_2H_4[1\text{-}CH_3]$, 0.28 mmol of THT, and 0.28 mmol of oxidant in 5.0 mL of CH_3CN under Ar for 2 h at 25 °C. [b] Conversion = [1 – (moles of substrate at the end of the reaction/moles of substrate initially)] × 100. Turnover = moles of THTO product/moles of catalyst. [c] Selectivity = (moles of THTO product/moles of all detectable THT-derived products) × 100.

Catalyzed Oxygenation of an Organic Substrate, Tetrahydrothiophene (THT), by $[1\text{-}CH_3]$. The oxidation of thioethers by oxygen donors was chosen to evaluate potential catalytic oxygenation activity by an exemplary tris(hydroxymethyl) capped complex, $[1\text{-}CH_3]$, for three reasons: (i) it is of practical interest in decontamination (selective oxidation of the prominent thioether chemical warfare agent mustard or HD is a major goal)[48] and other areas, (ii) it is generally simple, facile, and amenable to ready quantitation, and (iii) it has been investigated for regular nonderivatized polyoxometalate catalysts.[49] The particular reaction examined is illustrated in eq 3. The addition of a catalytic



(3)

DO = oxygen donor oxidant (TBHP, H_2O_2, and PhIO used)

amount (1 equiv) of $[1\text{-}CH_3]$ to 57 mM (57 equiv) of both THT substrate and one of three oxidants, *tert*-butyl hydroperoxide (TBHP), hydrogen peroxide, or iodosylbenzene, in CH_3CN leads to the rapid and selective oxidation of THT to the corresponding sulfoxide, tetrahydrothiophene oxide (THTO), in effectively quantitative yields with all three oxidants (Table I). More significantly, the catalyst, $[1\text{-}CH_3]$, recovered after 20 to 30 turnovers is still intact in all reactions.

The recovery of a catalyst after reaction does not, however, say anything definitive regarding its actual role in catalysis. Catalyst-derived species isolated during or after reaction often represent kinetic cul-de-sacs,[50] that is, they do not lie along the principal catalysis reaction coordinate. The actual catalyst is often an altered form or a fragment of the initial species added at the outset of the reaction. To address the issue of the active form of $[1\text{-}CH_3]$ in catalysis of the THT oxidation by TBHP we examined the time course of product generation by several complexes and determined the rate law for oxidation by the most active catalyst of those complexes evaluated. The complexes examined as potential catalysts were $Q_5H[1\text{-}CH_3]$, the more highly protonated form, $Q_2H_4[1\text{-}CH_3]$, $(n\text{-}Bu_4N)_2WO_4$ and $OV(O\text{-}iPr)_3$, models for possible W^{VI} and V^V monomeric fragments of $[1\text{-}CH_3]$, respectively, the parent complex, $Q_5H_4[V_3P_2W_{15}O_{62}]$, and the isostructural all-W^{VI} Wells–Dawson complex, $Q_6[P_2W_{18}O_{62}]$. Figure 7 shows the rates of THTO production from oxidation of THT by TBHP in the presence of the above complexes and in the absence of any catalyst. The rates are in the following order: $Q_2H_4[1\text{-}CH_3]$ (fastest) > $OV(O\text{-}iPr)_3$ > $(n\text{-}Bu_4N)_2WO_4$ > Q_5H_4-

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(49) Hill, C. L.; Faraj, M. In *Proceedings of the 1989 U.S. Army Chemical Research, Development and Engineering Center Scientific Conference on Chemical Defense Research*; US Army Armament, Munitions & Chemical Command, 1989; pp 131–134.

(50) For example, see: Chan, A. S. C.; Pluth, J. J.; Halpern, J. *J. Am. Chem. Soc.* **1980**, *102*, 5952–5954.

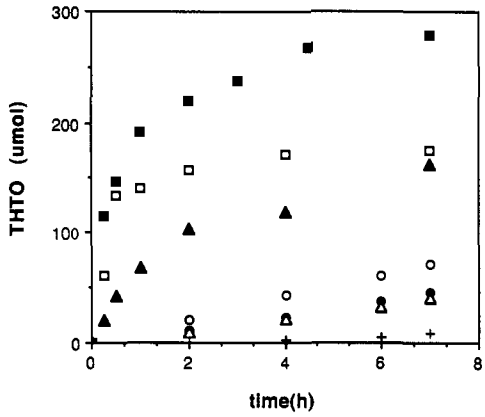


Figure 7. Relative rates of formation of tetrahydrothiophene oxide (THTO) in the oxidation of tetrahydrothiophene (THT) by *tert*-butyl hydroperoxide (TBHP) catalyzed by [1-CH_3] in two different protonation states, Q_2H_4[1-CH_3] (■) and Q_5H[1-CH_3] (●), by the uncapped precursor complex, $Q_5H_4[V_3P_2W_{15}O_{62}]$ (○), by monomeric V^V (□) and W^{VI} (▲) degradation model compounds (WO_4^{2-} and $OV(O\text{-}iPr)_3$, respectively), and by the Wells–Dawson heteropolytungstate, $Q_6[P_2W_{18}O_{62}]$ (△). The control oxidation reaction with no catalyst is also shown (+).

$[V_3P_2W_{15}O_{62}]$ > Q_5H[1-CH_3] > $Q_6[P_2W_{18}O_{62}]$ > no catalyst (slowest). These data provide four mechanistically useful inferences or observations: (1) All the species exhibit a catalytic effect; the ratio of catalyzed to uncatalyzed processes, k_{cat}/k_{uncat}, ranges from ca. 8.7 (for the least active complex, $Q_6[P_2W_{18}O_{62}]$) to ca. 833 (for the most active complex, Q_2H_4[1-CH_3]). (2) Catalysis by [1-CH_3] is acid dependent with the tetraprotonated form (from elemental analysis and potentiometric titration), being ca. 87 times more active than the monoprotonated form. (3) The most active of the catalysts is Q_2H_4[1-CH_3]. It is significantly more active than all the likely fragments that might form in small quantities in situ from it. (4) At parity of protonation state (4 titratable protons), [1-CH_3] is more active than the parent uncapped heteropolyanion, $[V_3P_2W_{15}O_{62}]^{9-}$. These data and the spectroscopic data delimiting the extent of decomposition of [1-CH_3] under turnover conditions (negligible) collectively imply that kinetically significant fragmentation during catalysis by [1-CH_3] is minimal and that [1-CH_3] in varying protonation states is most likely the principal catalyst.

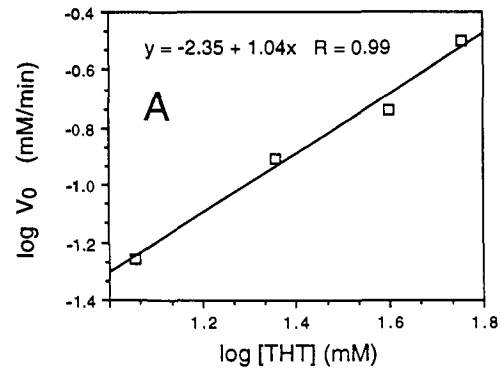
A plausible mechanism for the process depicted in eq 3 involves the direct oxidation of THT by the oxidized form of the polyoxometalate catalyst, eq 4, followed by reoxidation of the

$$\text{THT} + \text{oxidized polyoxometalate} + H_2O \rightarrow \text{THTO} + 2H^+ + \text{reduced polyoxometalate} \quad (4)$$

$$\text{reduced polyoxometalate} + 2H^+ + \text{OX} \rightarrow \text{RED} + \text{oxidized polyoxometalate} + H_2O \quad (5)$$

OX = oxidant (TBHP in this study) and RED = corresponding reduced form (*t*-BuOH = TBA in this study)

reduced form of the catalyst, eq 5, given the considerable number of organic substrate oxidations catalyzed by strongly oxidizing vanadium-containing polyoxometalates that probably proceed by this general mechanism.[8,9,49,51-55] Furthermore, the oxidation of thioethers by TBHP catalyzed by vanadium-substituted heteropolytungstic acids, and in particular, $H_5PV_2Mo_{10}O_{40}$, had been



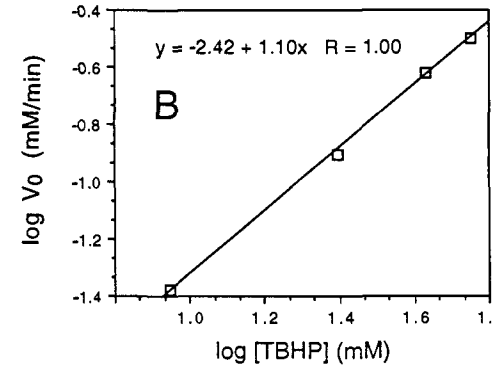


Figure 8. log–log plots for the initial rates of reaction of THT with TBHP catalyzed by Q_2H_4[1-CH_3]: (A) dependence on THT; (B) dependence on TBHP. For conditions see the Experimental Section.

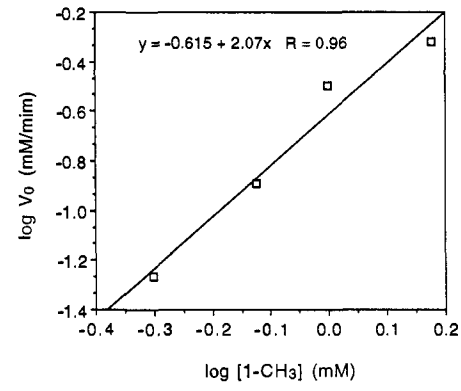


Figure 9. Concentration dependence on Q_2H_4[1-CH_3] for the initial rates of reaction of THT with TBHP catalyzed by Q_2H_4[1-CH_3]. Conditions given in the Experimental Section.

investigated recently and established to proceed by the above mechanism (eqs 4 and 5).[49] It was of some surprise and considerable interest that the control reaction involving the direct oxidation of THT by Q_2H_4[1-CH_3] was several orders of magnitude slower ($\tau_{1/2}$ of months) than the rate of oxidation in the complete reaction system (THT/TBHP/Q_2H_4[1-CH_3]). Clearly, eqs 4 and 5 are not an important mechanism for THT oxidation by TBHP catalyzed by Q_2H_4[1-CH_3]. A number of rate measurements on this reaction were made and the log–log plots for THT and TBHP are given in Figure 8. Not surprisingly, the rate is first order with respect to both THT and TBHP. More interesting and unusual is the second order dependence on the catalyst, Q_2H_4[1-CH_3] (Figure 9), resulting in the rate law in eq 6. The *y*-intercepts in log–log plots from kinetics studies are

$$v_0 = k[\text{THT}][\text{TBHP}][[\text{1-CH}_3]]^2 \quad (6)$$

often marginally meaningful and usually not mentioned. In the

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case here, the strikingly close values on the y intercepts of the two first order terms, THT and TBHP in eq 6 (Figure 8), indirectly confirm the rate law (see Appendix). Independent calculation of the rate constant from Figures 8A, 8B, and 9 respectively yields 7.8, 6.7, and 7.5 × 10^{-5} mM^{-3} min^{-1}.

Both component d^0 ions in the catalyst, W^{VI} and V^V, were previously known[11,56-61] and demonstrated in this study (Figure 7) to catalyze heterolytic electrophilic oxidations using TBHP. These reactions as a class are very well studied[62,63] and all proceed via d^0 peroxometal intermediates without a change in the oxidation state of the d^0 transition metal center. It is more likely that V^V than W^{VI} is directly involved in the THT oxidation by TBHP catalyzed by Q_2H_4[**1**-CH_3] for three reasons. First, the V^V sites are more labile than the W^{VI} sites. Second, V^V species are usually more active as catalysts in the electrophilic oxygenation of organic substrates than analogous W^{VI} which was found to be the case for monomeric V^V and W^{VI} model compounds examined in this study (Figure 7). Third and most importantly, the V^V sites are the most basic and thus the μ_2-oxygens between two V^V sites are most likely to be protonated first. Although considerable literature on d^0 transition metal catalyzed oxygenation by peroxides and the data here would implicate formation of a peroxovanadium(V) intermediate that attacks substrate (THT),[64] the exact structure of this intermediate cannot be inferred from the data.

A final experimental datum of mechanistic value is the temperature dependence of the reaction, THT by TBHP catalyzed by Q_2H_4[**1**-CH_3]. The Arrhenius plot was quite linear (correlation coefficient = 0.988) and gave an activation energy of 10.1 kcal/mol.

The rate law necessarily requires the involvement of one molecule each of THT and TBHP and two molecules of [**1**-CH_3] prior to or including the rate limiting activated complex. Whereas more than one well precedented activated complex could be drawn for a rate law first order in substrate, oxidant, and catalyst, and other rate law, the one operable here, eq 6, does not lend itself to any well-delineated activated complex. One of many possible activated complexes we favor is shown in Figure 10. As drawn, this model of the activated complex does not specify exact bond connectivity around the V^V centers. For example, the substrate-attacking peroxyvanadium and protonated V^V centers cannot be specifically identified and neither μ_2-O^{2-} nor μ_2-RO^- is specifically implicated. We visualize this as effectively a bimolecular nucleophilic attack of THT on a complex of one molecule of TBHP and two molecules of [**1**-CH_3] and not a mechanistically unreasonably quadramolecular process. In the TBHP·([**1**-CH_3])$_2$ complex, the principal role of the first [**1**-CH_3] is to activate TBHP by binding to a V^V center, while the principal role of the second [**1**-CH_3] is to further electrophilically activate the bound TBHP group via H-bonding as shown. The μ_2-η^1-OOR binding mode of alkylperoxides is precedented[65] and the electrophilic

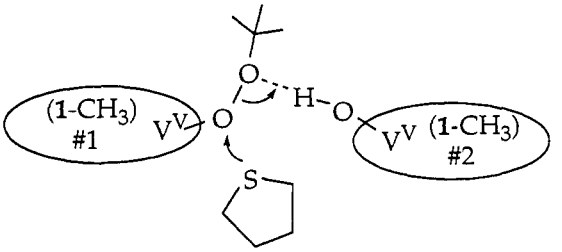

Figure 10. One model for the activated complex in the rate determining transition state for THTO production via TBHP oxidation of THT catalyzed by [**1**-CH_3] that is consistent with the rate law (eq 6), other kinetic and spectroscopic data, and literature investigations. This is effectively a bimolecular nucleophilic attack of THT on a complex of TBHP and two molecules of [**1**-CH_3], where one [**1**-CH_3] activates TBHP via bonding to V^V and the other [**1**-CH_3] activates by H bonding to the bound TBHP. As drawn, this model of the activated complex does not specify exact bond connectivity around the V^V centers. For example, the V^V centers (μ_2-O^{2-} or μ_2-RO^-) associated with protonation or with formation of the peroxyvanadium intermediate cannot be unequivocally identified.

activation roles of both the V^V center and the protonated oxygen of the second [**1**-CH_3], to facilitate attack by the reasonably nucleophilic THT sulfur atom, are reasonable. This activated complex is consistent with all the rate, spectroscopic, acid–base, and other data in this manuscript. Although one can argue that protons associated with one of the [**1**-CH_3] complexes can bind THT via a salt bridge (formation of the protonated $THTH^+$ would function as a countercation to the two negatively charged [**1**-CH_3] complexes) or via hydrogen bonding, both scenarios are unlikely. Either protonation of sulfur or hydrogen bonding to sulfur would deactivate this atom with respect to receiving an electrophilic oxygen atom. Furthermore, the pK_a values of $THTH^+$ (~ -5.4)[66] versus $TBHPH^+$ (~ -1.7)[67] argue against proton activation of the former and for proton activation of the latter.

Acknowledgment. C.L.H. thanks the U.S. Army Research Office (DAAL03-87-K-0131) for support.

Appendix

From the rate law, eq 6, one can write eqs 7–9, which isolate

$$\log v_1 = \log (k[\text{TBHP}][[\textbf{1}\text{-}CH_3]]^2) + \log [\text{THT}] \quad (7)$$

$$\log v_2 = \log (k[\text{THT}][[\textbf{1}\text{-}CH_3]]^2) + \log [\text{TBHP}] \quad (8)$$

$$\log v_3 = \log (k[\text{THT}][\text{TBHP}]) + 2 \log [[\textbf{1}\text{-}CH_3]] \quad (9)$$

[THT], [TBHP], and [**1**-CH_3], respectively. From these equations it is not only apparent that the slopes of these plots, yield the orders, are 1, 1, and 2 respectively for THT, TBHP, and [**1**-CH_3], but as the concentrations of [TBHP] and [THT] were the same in the experiments, the y intercepts should also be similar in the first two plots and distinct in the third plot. This is the case (Figures 8 and 9). This simple treatment illustrates one reason it can be more informative to evaluate orders of reactions in kinetics investigations by not using pseudo-first-order conditions (flooding all concentrations but the limiting one) but instead keeping the concentrations of all reactants in a comparable regime.

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(63) Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 113–126.
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