Oxybromination Catalysed by the Heteropolyanion Compound $H_5PMo_{10}V_2O_{40}$ in an Organic Medium: Selective *para*-Bromination of Phenol

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Selective bromination of phenol and its derivatives and the bromination of ketones and alkenes have been achieved by oxybromination at ambient conditions catalysed by the mixed addenda heteropolyanion compound $H_5PMo_{10}V_2O_{40}$, which is dissolved in a nonpolar chlorohydrocarbon solvent by complexation with tetraglyme.

The vast field of heteropolyanion (HPA) chemistry has been centred around their preparation, structure, properties, and analytical applications,[1] but over the last two decades their potential as catalysts has gained recognition. The major field of research uses HPAs as heterogeneous catalysts in gas phase reactions,[2] where the HPA can act as a strong acid, in transformations such as the dehydration of propan-2-ol[3] or the formation of hydrocarbons from methanol,[4] or as an oxidation catalyst, in reactions such as the dehydrogenation of methacrolein to methacrylic acid.[5] Another field of research is concerned with homogeneous catalysis. Mixed addenda Keggin anions of general formula $XM_{12-n}M'_nO_{40}{}^{q-}$ (X = P, Si; M

= Mo, W; M′ = V, Cr, Mn, Fe, Co) have been used as oxidation catalysts. For example, such compounds have been used to catalyse the epoxidation of alkenes by iodosylbenzene[6] or hydrogen peroxide.[7]

Keggin compounds of the type $H_{3+n}PMo_{12-n}V_nO_{40}$ (PMoV-*n*) have been described by Kozhevnikov and Matveev[8] as effective redox catalysts undergoing the catalytic cycle of equations 1 and 2. The majority of research using this reaction scheme has been on the use of PMoV-*n* instead of $CuCl_2$ in Wacker type chemistry[9] (substrate Pd^0, product Pd^{II}). In addition, the PMoV-*n* catalyst has been reported to oxidize sulphides to sulphones and sulphoxides[10] and aqueous hydrobromic acid to bromine.[11] The latter reaction requires a large excess of concentrated sulphuric acid (itself capable of oxidizing hydrobromic acid[12]) and is not selective. In all cases the successful application of the catalytic cycle requires a water soluble cosolvent to dissolve the substrate and high oxygen pressures (10—15 atm) to obtain reasonable rates of reoxidation of the reduced form of the catalyst. The high pressure severely limits the synthetic utility of the reaction and constitutes a significant safety hazard.

$$H_{3+n}PMo_{12-n}V^{V}{}_{n}O_{40\,(ox)} + \text{Substrate} + 2H^+ \rightarrow H_{5+n}PMo_{12-n}V^{IV}{}_{n}O_{40\,(red)} + \text{Product} \quad (1)$$

$$H_{5+n}PMo_{12-n}V^{IV}{}_{n}O_{40\,(red)} + 1/2O_2 \rightarrow H_{3+n}PMo_{12-n}V^{V}{}_{n}O_{40\,(ox)} + H_2O \quad (2)$$

$$2HBr_{(org)} + \text{PMoV-}2_{(ox)} \rightarrow Br_2 + \text{PMoV-}2_{(red)} \quad (3)$$

$$Br_2 + RH \rightarrow RBr + HBr_{(org)} \quad (4)$$

$$\text{PMoV-}2_{(red)} + 1/2O_2 \rightarrow \text{PMoV-}2_{(ox)} + H_2O \quad (5)$$

$$HBr_{(org)} + 1/2O_2 + RH \rightarrow RBr + H_2O \quad (6)$$

We now report that complexation of PMoV-2 by dimethylethers of ethylene glycol oligomers, *e.g.* tetraglyme, enables dissolution of PMoV-2 in its acidic form in nonpolar organic solvents such as 1,2-dichloroethane. This complexed HPA compound catalyses the oxidation of hydrogen bromide to molecular bromine which reacts with an organic substrate, RH. The reduced catalyst is then reoxidized at *ambient* temperature and oxygen pressure, (p_{oxygen} 0.2 atm), to complete the catalytic cycle, equations 3—5. Summation of the reaction steps shows the oxybromination stoicheiometry (equation 6). The bromine formed converts alkenes to vicinal dibromides, ketones to α-bromoketones, and ring activated aromatic compounds selectively to monobromo aromatic compounds. In phenolic compounds the monobromination is regioselective at the *para* position.

Table 1. The oxybromination of organic substrates by PMoV-2 with tetraglyme as complexing agent.[a]

Substrate	Product	Yield (%)[b]
Phenol	4-Bromophenol	99
Anisole	2- and 4-Bromoanisole	98
o-Cresol	2-Methyl-4-bromophenol	97
p-Cresol	2-Bromo-4-methylphenol	97
1-Naphthol	4-Bromo-1-naphthol	98
N,*N*-Diethylaniline	2- and 4-Bromo-*N*,*N*-diethylaniline	98
Toluene[c]	2- and 4-Bromotoluene	0
Toluene[d]	α-Bromotoluene	0
Cumene[d]	α-Bromocumene	0
Acetone	α-Bromoacetone	42
	α,α′-Dibromoacetone	37
	α,α-Dibromoacetone	21
Cyclohexanone	α-Bromocyclohexanone	50
	α,α′-Dibromocyclohexanone	28
	α,α-Dibromocyclohexanone	14
1-Octene	1,2-Dibromo-octane	73[e]

[a] *Reaction conditions:* substrate (20 mmol), tetraglyme (5.0 mmol), PMoV-2 (0.1 mmol), 1,2-dichloroethane (25 ml), HBr and air bubbled through the mixture, temperature 20 °C, 5 h. [b] Yields computed from g.l.c. data. [c] About 18 mmol of bromine was formed. [d] Reaction mixture was illuminated with a 300 W tungsten lamp, no bromine was formed. [e] Conversion 100%, byproduct 1-bromo-octane.

In a typical reaction PMoV-2 (0.1 mmol) and tetraglyme (5.0 mmol) were dissolved in 1,2-dichloroethane (25 ml) in the presence of substrate (20 mmol) and hydrogen bromide and air were slowly bubbled through the solution. Turnover numbers were typically about 50 turnovers per mol catalyst per hour and reactions were complete within 4—5 h at 20 °C. The results are summarized in Table 1. With toluene as substrate no bromination takes place, but bromine is formed at rates comparable to cases where bromination proceeds. Attempts at free radical bromination of toluene or at the side chain of cumene under illumination (300 W tungsten lamp) failed and no bromine was formed, indicating that strong illumination deactivates the catalyst. Although the relatively high ratio of *para*-bromination of phenol in certain solvents is well known[13] this system is unique in that complete selectivity is obtained without addition of special *para*-directing reagents such as cyclodextrins[14] or zeolites.[15] We have as yet no satisfactory explanation for this phenomenon although the relatively slow formation of bromine and its immediate reaction (bromine concentration approaches zero) may be a partial answer, implying that for bromination of phenol the *para* position is *always* preferred. Another partial explanation for the *para*-selective bromination may be the formation of a tetraglyme–bromine complex. It is known that a similar dioxane–bromine selectively brominates phenol derivatives.[16] Slow addition of bromine to phenol over 4 h (dichloroethane/tetraglyme) always yielded 7—10% 2-bromophenol and 2,4-dibromophenol even at 0 °C.

Although diethyl ether has been known to form complexes with HPA compounds,[17] the use of polyethers is novel in this respect. The length of the polymer chain in the complexing agent has a pronounced effect on the reaction (Table 2). Ether, tetrahydrofuran, monoglyme, and diglyme can all solubilize the HPA compound by complexation, but the system remains catalytically inactive. Tetraglyme, 18-crown-

Table 2. The effect of the complexing agent on the oxybromination of phenol catalysed by PMoV-2.[a]

Complexing agent	Yield (%)
Diethyl ether	0
Tetrahydrofuran	0
Monoglyme	4.2
Diglyme	3.8
Tetraglyme	100
PEGDME-350[b]	100
18-Crown-6	100
PEGDME-5000[c]	0

[a] *Reaction conditions:* phenol (20 mmol), PMoV-2 (0.1 mmol), complexing agent (1.1 g), (variable molar concentration but approximately constant number of ether functionalities), 1,2-dichloroethane (25 ml), HBr and air bubbled through the solution, temperature 20 °C, 5 h. [b] Dimethyl ether of polyethylene glycol of average molecular weight 350. [c] Dimethyl ether of polyethylene glycol of average molecular weight 5000.

6, or low molecular weight polyethers dissolve the PMoV-2 and promote catalytic oxidation. High molecular weight polyethers do not complex the HPA compound and no reaction takes place. Although the formation of a guest–host cation(proton)–crown ether type complex seems an obvious conclusion, the identity of the complex and its importance in the catalytic cycle is not clear.

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