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Polyfluorinated Quaternary Ammonium Salts of Polyoxometalate Anions: Fluorous Biphasic Oxidation Catalysis with and without Fluorous Solvents

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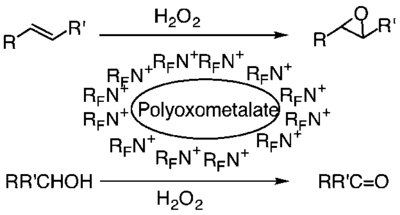
ABSTRACT



Polyfluorinated quaternary ammonium cations, [CF$_3$(CF$_2$)$_7$(CH$_2$)$_3$]$_3$CH$_3$N$^+$ (R$_F$N$^+$), were synthesized and used as countercations for the [WZnM$_2$(H$_2$O)$_2$(ZnW$_9$O$_{34}$)$_2$]$^{12-}$ (M = Mn(II), Zn(II)) polyoxometalate. The (R$_F$N$^+$)$_{12}$[WZnM$_2$(H$_2$O)$_2$(ZnW$_9$O$_{34}$)$_2$] compounds were fluorous biphasic catalysts for alcohol and alkenol oxidation, and alkene epoxidation with aqueous hydrogen peroxide. Reaction protocols with or without a fluorous solvent were tested. The catalytic activity and selectivity was affected by both the hydrophobicity of the solvent and the substrate.

An important area of homogeneous catalysis research remains the quest for practical separation techniques of the intrinsically soluble catalyst from the remaining reaction components. One method that has quite recently attracted significant attention as a separation/recovery method is fluorous biphasic catalysis.[1] The concept espouses modification of known catalytic entities with fluorous "ponytails" yielding catalysts soluble in very hydrophobic perfluorohydrocarbon solvents. Commonly, there are very temperature dependent organic substrate/fluorous solvent liquid/liquid phase miscibilities that allow single phase reactions at elevated reaction temperature and biphasic separation of the organic product from the fluorous solvent containing the catalyst at ambient or subambient temperatures. In the context of catalytic oxidation, fluorous biphasic catalysis has been realized by using various appropriately modified organometallic complexes.[2] Questions concerning the environmental impact and degradability of perfluorinated solvents, along with their relative high cost, have also led to the concept of fluorous phase catalysis without fluorous solvents.[3] In such systems, polyfluorinated thermomorphic catalysts are soluble in normal hydrocarbons at elevated temperatures but are immiscible in the solvent at decreased temperatures, allowing the separation by precipitation of the fluorous catalyst from the product and solvent phase by cooling the reaction mixture.

Polyoxometalate anions have over recent years been investigated as oxidation catalysts with use of a variety of oxidants, including the more sustainable molecular oxygen and hydrogen peroxide.[4] Especially notable in the context of this paper is the use of "sandwich"-type polyoxometalates, [WZnM$_2$(H$_2$O)$_2$(ZnW$_9$O$_{34}$)$_2$]$^{12-}$ (M = Mn(II), Zn(II)), for catalytic oxidation of alkenes, alkenols, and alcohols with

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aqueous hydrogen peroxide.[5] Also in the area of polyoxometalate oxidation catalysis various techniques for separation/recovery of the polyoxometalate from the other reaction components have been considered. These methods include supported catalysts,[6] aqueous biphasic media,[7] solvent anchored catalysts,[8] and others.[9] In this paper we report on our adaptation of the concept of biphasic fluorous phase catalysis into the realm of oxidation catalysis by polyoxometalates. We have found that thermomorphic fluorous polyoxometalates may be prepared and used in fluorous biphasic catalysis despite the *polyanionic* nature of the polyoxometalates by use of perfluorinated quaternary ammonium cations, $[CF_3(CF_2)_7(CH_2)_3]_3CH_3N^+$ or (R_FN^+), as countercations. Consequently, effective catalytic oxidation reactions of alkenes, alkenols, and alcohols can be carried out using "sandwich"-type polyoxometalates, $(R_FN^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$, Figure 1, with aqueous hydrogen peroxide as oxidant with or without fluorous solvents.

The fluorous quaternary ammonium salt $\{[CF_3(CF_2)_7(CH_2)_3]_3CH_3N^+\}CH_3OSO_3^-$ was prepared by quaternization of the known fluorous tertiary aliphatic amine,[10] by dimethyl sulfate (see Supporting Information for details). The fluorous polyoxometalates, $(R_FN^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$, were then prepared by mixing 12 equiv of $\{[CF_3(CF_2)_7(CH_2)_3]_3CH_3N^+\}CH_3OSO_3^-$ with 1 equiv of $Na_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$ polyoxometalate.[11] The fluorine content by weight of $(R_FN^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$ is 51.5%.

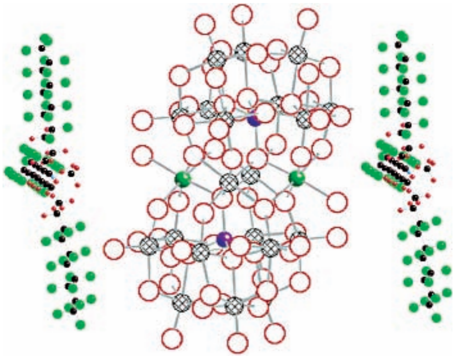

Figure 1. Representation of the $[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]^{12-}$ polyoxometalate with two (out of twelve) (R_FN^+) countercations.

Thus, despite the polyanionic character of the polyoxometalate, $(R_FN^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$ is freely soluble in perfluorohydrocarbons at room temperature. In other common solvents such as ethyl acetate and toluene $(R_FN^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$ is insoluble at room temperature, but dissolves upon heating to 60−80 °C. This property leads to two different reaction protocols for the fluorous biphasic catalysis, Figure 2: (a) with a perfluorohydrocarbon (perfluorodecalin) solvent and (b) without a fluorous solvent, e.g. EtOAc. Results with the two catalytic reaction protocols for the oxidation of alcohols, alkenols, and alkenes are presented in Tables 1−3, respectively.

Table 1. Oxidation of Aliphatic Alcohols with 30% Aqueous H_2O_2 Catalyzed by $(R_FN^+)_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2]$[a]

substrate	conversion, mol % fluorous solvent	conversion, mol % nonfluorous solvent
2-butanol	3	8
2-pentanol	32	36
2-hexanol	44	55
2-heptanol	46	48
2-octanol	67	28
cyclohexanol	43	82
1-octanol	50[b]	19[c]

[a] Reaction conditions: 1 mmol of alcohol, 2 mmol of 30% aq.H_2O_2, 1 mL of perfluorodecalin or EtOAc, 5 μmol of $(R_FN^+)_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2]$, 80 °C, 8 h. Analysis by GC; ketones were the only observed product. [b] 4% octanal, 76% octanoic acid, 20% octyloctanoate. [c] 15% octanal, 36% octanoic acid, 39% octyloctanoate.

One may observe that secondary aliphatic alcohols were rather effectively oxidized to the expected ketones without

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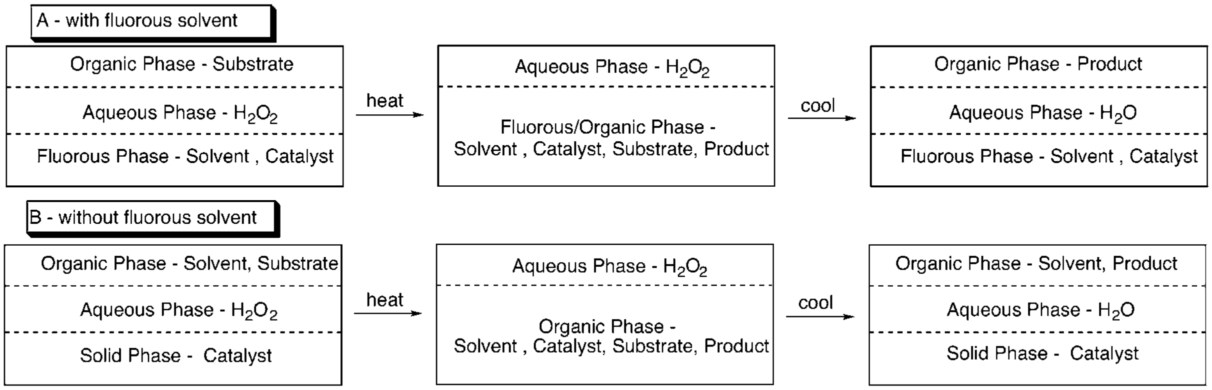

Figure 2. Reaction protocols for oxidation with aqueous hydrogen peroxide catalyzed by $(R_FN^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$.

formation of byproducts. For a representative primary alcohol, 1-octanol, one observes low selectivity, with formation first of octanal. Octanal may be further oxidized to octanoic acid or a reaction between octanal and 1-octanol leads to formation of a hemiacetal that is oxidized to the octyloctanoate ester. It is also interesting to note that there appear to be interesting trends of reactivity as a function of the length of the aliphatic chain. Fairly water soluble 2-butanol hardly reacts due to its limited solubility in EtOAc and perfluorodecalin in the presence of aqueous H_2O_2. For the shorter chain alcohols, e.g. 2-pentanol, 2-hexanol, and also cyclohexanol, probably better solubility in EtOAc versus perfluorodecalin leads to higher conversion in the nonfluorous solvent. As the aliphatic chain is lengthened, the relative activity EtOAc/perfluorodecalin is inverted. 2-Octanol is more reactive in the fluorous phase.

Analysis of the results of the oxidation of alkenols needs to take into account at least five factors: (i) allylic versus nonallylic alcohols, (ii) secondary versus primary alcohols, (iii) secondary versus primary alkenes, (iv) fluorous versus nonfluorous solvents, and (v) the hydrophilicity or hydrophobicity of the substrate. One general observation was that allylic alkenols were more reactive (reactions at ambient temperature) than nonallylic alkenols (reactions at 60 °C). Furthermore, a general selectivity trend was observed: for alkenols with primary alcohol moieties, epoxidation is the predominant reaction, whereas for alkenols with secondary alcohol moieties, alcohol oxidation is the predominant reaction. Selectivity to epoxidation was highest in 3-methyl-2-buten-1-ol due to the higher nucleophilicity of the alkene.

Table 2. Oxidation of Alkenols with 30% Aqueous H_2O_2 Catalyzed by $(R_FN^+)_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2]^a$

	conversion (selectivity),[b] mol %	
substrate	fluorous solvent	nonfluorous solvent
E-2-hexen-1-ol	95 (94, 6)	53 (72, 28)
Z-2-hexen-1-ol	95 (98, 2)	66 (65, 35)
3-Me-2-buten-1-ol	43 (100, 0)	100 (100, 0)
Z-3-hexen-1-ol	71 (82, 18)	94 (90, 10)
5-hexen-1-ol	58 (97, 3)	56 (96. 4)
1-octen-3-ol	66 (0, 100)	35 (0, 100)
1-cyclohexen-3-ol	82 (0, 100)	89 (0, 100)
(−)-isopulegol[c]	87 (0, 100)	40 (0, 100)

[a] Reaction conditions: 1 mmol of alcohol, 2 mmol of 30% aq H_2O_2, 1 mL of perfluorodecalin or EtOAc, 5 μmol of $(R_FN^+)_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2]$, 22 °C (allylic alcohols), 60 °C (other alkenols), 8 h. Analysis by GC, GC-MS. [b] Selectivity is given as mol % product/all products (% epoxide, % ketone or aldehdye). [c] (1*R*,2*S*,5*R*)-2-Isopropenyl-5-methylcyclohexanol.

For the acyclic allylic primary alcohols tested, *E*-2-hexen-1-ol, *Z*-2-hexen-1-ol, and 3-methyl-2-buten-1-ol, the mentioned chemoselectivity for epoxidation versus alcohol oxidation was retained. However, activity and selectivity was strongly dependent on the carbon chain length (hydrophobicity) and the nature of the solvent. 3-Methyl-2-buten-1-ol was more reactive in EtOAc compared to perfluorodecalin because it is relatively more hydrophilic. For 2-hexen-1-ol the opposite was observed, presumably because of improved solubility in perfluorodecalin. Importantly, the alcohol moiety was less reactive for 2-hexen-1-ol in perfluorodecalin than in EtOAc leading to improved chemoselectivity due to the limited miscibility of the OH group in the fluorous phase. Comparison of the reactivity of remaining substrates also reveals that the more hydrophobic substrates were more

Table 3. Epoxidation of Alkenes with 30% Aqueous H_2O_2 Catalyzed by $(R_FN^+)_{12}[WZnMn_2(H_2O)_2(ZnW_9O_{34})_2$

substrate	conversion, mol %
1-octene	0
E-2-octene	3
cyclooctene	52
2-methyl-2-heptene	64
cyclohexene	100
4-methylcyclohexene	97
1-methylcyclohexene	100

[a] Reaction conditions: 1 mmol of alkene, 2 mmol of 30% aq H_2O_2, 1 mL of toluene, 20 μmol of $(R_FN^+)_{12}[WZnMn_2(H_2O)_2(ZnW_9O_{34})_2]$, 60 °C, 13 h. Analysis by GC, GC-MS. Only epoxides were formed.

reactive in perfluorodecalin compared to EtOAc and vice versa.

The reactivity of weakly nucleophilic alkenes (1-octene, 2-octene) was very low with use of the fluorous polyoxometalate catalyst; however, the more reactive cyclohexene derivatives reacted very nicely with this catalyst with no evidence of acid-catalyzed epoxide ring opening and diol formation, which is unusual for such acid-sensitive epoxides in the absence of a buffer. Alkenes of moderate nucleophilicity such as 2-methyl-2-heptene showed intermediate reactivity.

Importantly, one can demonstrate the catalyst recovery protocols described in Figure 2. Thus, in a fluorous solvent 1-cyclohexen-3-ol was used as a model substrate (1 mmol of 1-cyclohexen-3-ol, 2 mmol of H_2O_2, 5 μmol of $(R_FN^+)_{12}$-$[WZn_3(H_2O)_2(ZnW_9O_{34})_2]$, in 1 mL of perfluorodecalin at 22 °C). After 8 h of reaction the fluorous phase was separated and used as is for another reaction cycle. This process was repeated; no loss of reactivity was noted as conversions to 1-cyclohexen-3-one for each cycle were 80, 83, and 79 mol %, respectively. Similarly, with EtOAc as solvent, cyclohexanol was reacted (1 mmol of cyclohexanol, 2 mmol of H_2O_2, 5 μmol of $(R_FN^+)_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2]$ in 1 mL of EtOAc at 80 °C). After 8 h of reaction and cooling the precipitated catalyst was collected by filtration and reused. Three repetitions showed no significant loss of reactivity; 81, 80, and 78 mol % of cyclohexanone were formed in each cycle. ^{19}F NMR of the organic product phases showed no measurable (by NMR) presence of the catalyst in the product phase.

Polyfluorinated quaternary ammonium salts of polyoxometalate anions can be used in fluorous biphasic oxidation catalysis with and without fluorous solvents for oxidation of alkenes, alkenols, and alcohols with hydrogen peroxide. The solvent (fluorous or “normal”) has an effect on reactivity and selectivity.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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