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Oxidation of Aliphatic and Aromatic Amines with Hydrogen Peroxide Catalyzed by Peroxoheteropoly Oxometalates

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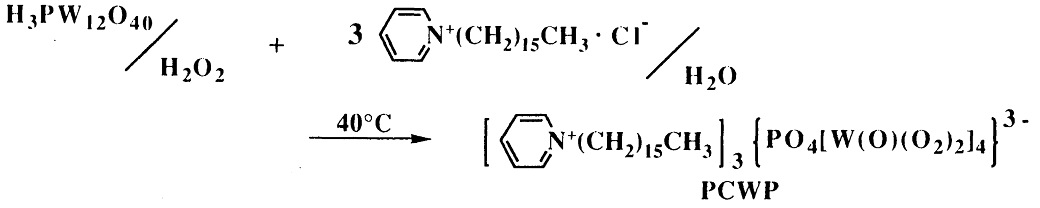
Peroxotungstophosphate (PCWP) was found to be an efficient catalyst for the oxidation of amines with 35% H_2O_2 under the biphasic or homogeneous condition. Thus, primary and secondary amines were oxidized to oximes and nitrones, respectively, in good yields. Aromatic amines afforded to the corresponding nitroso compounds and/or nitrobenzenes.

Oxidation of amines is a useful method for preparing a variety of nitrogen containing compounds such as hydroxyamines, amine N-oxides, oximes, and nitrones etc.1) In general, primary amines possesing α-C-H bond are oxidized to oximes with hydrogen peroxide in the presence of sodium salts of tungstic, molybdic, or vanadic acid,2) and secondary amines gave the corresponding hydroxyamines.2a,3) Recently, Murahashi *et al.* have shown that sodium tungstate4) and selenium dioxide-catalyzed oxidations5) of secondary amines with hydrogen peroxide provide general methods for the preparation of nitrones which are difficult to synthesize by conventional methods.

In a previous paper, we reported that peroxotungstophosphate (PCWP) can be readily prepared by treating 12-tungstophosphoric acid (WPA) in excess 35% H_2O_2 with cetylpyridinium chloride (CPC),6) and the PCWP thus prepared is the same complex class6b) as the peroxocomplex prepared by Venturello et al.7, 8) The PCWP was found to be a unique catalyst which undergoes the oxidation of alkynes to α,β-epoxy ketones6b) and *vic*-diols9) or olefins10) to α-hydroxy ketones.



We now find that the oxidation of a wide variety of amines by the PCWP-H_2O_2 system provides a prominent method for the preparation of oximes, nitrones, and nitrobenzenes etc.

A typical reaction is as follows. To a suspended solution of 35% H_2O_2 (9 mmol) and PCWP (21 mg, 5 wt%) in chloroform (7.5 ml) was added dropwise dibutylamine (**1**) (0.43 g, 3 mmol) at 0°C, and the mixture was stirred at that temperature for 1 h. After stirring for additional 2 h at room temperature, the reaction mixture was extracted with CH_2Cl_2. The extract was dried over anhydrous $MgSO_4$ and evaporated under the reduced pressure to give almost pure N-butylidenebutylamine N-oxide (**2**) in 97% yield by GC based on the internal standard technique. The product was purified by column chromatography on silica gel with ethyl acetate eluent.

In order to examine the potential of polyoxometalates as catalysts, the oxidation of **1** to **2** was chosen as a model reaction and carried out under several reaction conditions (Table 1).

Table 1. Oxidation of Dibutylamine (**1**) to N-butylidenebutylamine N-oxide (**2**) by Several Heteropoly Oxometalates [a)]

Run	Catalyst	Solvent	Product Yield / % [b)]			
1	PCWP	*t*-BuOH	**2**	20	**3**	13
2	PCWP	$CHCl_3$	**2**	97		
3	PCMP	$CHCl_3$	**2**	75		
4	CWP	$CHCl_3$	**2**	20		
5 [c)]	$NaWO_4$	MeOH	**2**	89 [d)]		

a) **1** (3 mmol) was allowed to react with 35% H_2O_2 (9 mmol) in the presence of catalyst (5 wt%) in solvent (7.5 ml) at room temperature for 3 h.
b) GC yield based on internal standard technique.
c) Data were cited from Ref. 4a. d) Isolated yield.

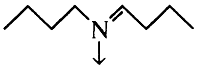
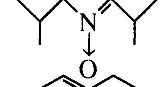
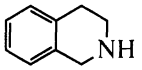
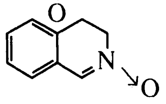
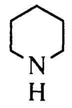
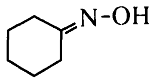
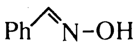
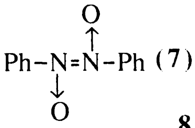
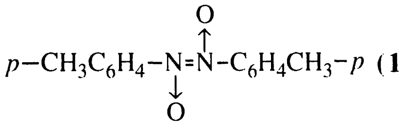
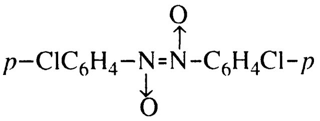
Among the catalysts examined, PCWP was found to be the best catalyst. The oxidation of **1** with 35% H_2O_2 by PCWP under the homogeneous condition using *tert*-butyl alcohol as the solvent gave **2** and butyraldehyde oxime (**3**) in 20% and 13% yields, respectively. The formation of **3** may be due to the over-oxidation of **2**. Under the two-phase condition using chloroform as the solvent, **1** was oxidized to **2** in almost quantitative yield. It is interesting to note that the oxidation of **1** to **2** could be achieved with high yield in non-polar solvent like chloroform, since this type of oxidation has so far been carried out in water or hydrophilic solvents such as acetone and ethanol.[2)] For example, in the sodium tungstate catalyzed oxidation of **1** with H_2O_2, methanol and water were employed as the solvents.[4, 5)]

The corresponding peroxomolybdenum compound, PCMP, was less active than the PCWP under the same reaction conditions. In the oxidation by tris(cetylpyridinium)12-tungstophosphate (CWP), $[\pi\text{-}C_5H_5N^+(CH_2)_{15}CH_3]_3(PW_{12}O_{40})^{3-}$, the yield of **2** was slightly lowered than that by the PCWP.

On the basis of these results, the oxidation of various amines with 35% H_2O_2 under the influence of the PCWP is summarized in Table 2. Secondary aliphatic amines such as **1** and diisobutylamine under the biphasic system were oxidized to the corresponding nitrones in good yields (runs 1 and 2). 1,2,3,4-Tetrahydro-isoquinoline was converted into 3,4-dihydroisoquinoline N-oxide in 90% yield (run 3), but in the oxidation of piperidine, nitrone was difficult to be isolated because of the formation of many side products (run 4).

On the other hand, the oxidation of primary amines occurred smoothly in *tert*-butyl alcohol rather than the biphasic system employing chloroform as the solvent (runs 5-8). For example,

Table 2. Oxidation of Various Amines with 35%H_2O_2 in the Presence of PCWP[a)]

Run	Substrate	Solvent	Time / h	Product	Yield / %[b)]
1	$(C_4H_9)_2NH$ **(1)**	$CHCl_3$	3	 **(2)**	97
2	$(i\text{-}C_4H_9)_2NH$	$CHCl_3$	3		80
3		$CHCl_3$	3		90
4		$CHCl_3$	3	complex mixture	
5	$C_6H_{13}NH_2$ **(4)**	$CHCl_3$	5	 **(5)**	56
6	**4**	*t*-BuOH	5	**5**	72
7	*cyclo*-$C_6H_{11}NH_2$	*t*-BuOH	5		66
8	$PhCH_2NH_2$	*t*-BuOH	5		81
9	$H_2N(CH_2)_6NH_2$	*t*-BuOH	5		60[c)]
10	$PhNH_2$ **(6)**	$CHCl_3$	2	 $Ph{-}\underset{\substack{\downarrow\\ O}}{N}{=}\overset{\substack{O\\ \uparrow}}{N}{-}Ph$ **(7)** 85 , $PhNO_2$ **(8)**	9
11	**6**	$CHCl_3$ (rf.)	4	**8**	71
12	$p\text{-}CH_3C_6H_4NH_2$ **(9)**	$CHCl_3$	2	 $p{-}CH_3C_6H_4{-}\underset{\substack{\downarrow\\ O}}{N}{=}\overset{\substack{O\\ \uparrow}}{N}{-}C_6H_4CH_3{-}p$ **(10)** $p\text{-}CH_3C_6H_4NO_2$ **(11)**	80 14
13	**9**	$CHCl_3$ (rf.)	4	**11**	92
14	$p\text{-}ClC_6H_4NH_2$ **(12)**	$CHCl_3$	2	 $p{-}ClC_6H_4{-}\underset{\substack{\downarrow\\ O}}{N}{=}\overset{\substack{O\\ \uparrow}}{N}{-}C_6H_4Cl{-}p$ **(13)** $p\text{-}ClC_6H_4NO_2$ **(14)**	46 50
15	**12**	$CHCl_3$ (rf.)	4	**14**	87

a) Substrate (3 mmol) was allowed to react with 35% H_2O_2 (3 equiv.) in the presence of PCWP (5 wt% for runs 1 - 4 or 10 wt% for runs 5 - 15) at room temperature.

b) GC yields based on internal standard technique.

c) Isolated yield.

hexylamine (**4**) afforded hexylaldehyde oxime (**5**) in 72% yield in *tert*-butyl alcohol and 56% in chloroform. Benzylamine and cyclohexylamine were converted into the corresponding oximes in good yields. 1,6-Hexadiamine was also oxidized to dioxime in 60% yield.

In a similar manner as aliphatic amines, aromatic amines were successfully oxidized by the PCWP-H_2O_2 system under the two-phase condition to give the corresponding nitrosobenzenes and/or nitrobenzenes, depending on the reaction temperature (runs 10-15). The oxidation of aniline afforded nitrosobenzene (**7**)[11] at room temperature and nitrobenzene under refluxing temperature as a principal product.[12] Similarly, *p*-methyl- and *p*-chloroanilines, **9** and **12**, were oxidized to the corresponding nitroso compounds, **10**[12] and **13**,[12] respectively.

In conclusion, the oxidation of a variety of amines by the PCWP-H_2O_2 system provides a useful method for the preparation of amine derivatives such as nitrones, oximes, nitrosobenzenes and nitrobenzenes.

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8) It has been shown that Venturello complex, $(Q^+)_3\{PO_4[WO(O_2)_2]_4\}^{3-}$, where Q is quarternary ammonium, can be prepared by employing our method upon treatment of WPA in excess 35% H_2O_2 with quarternary ammonium salts such as $Bu_4N^+Cl^-$: J. -M. Brégeault, C. Aubry, G. Chottard, N. Platzer, C. Chauveau, C. Huet, and H. Ledon, "Dioxygen Activation and Homogeneous Catalytic Oxidation," ed by L. I. Simandi, Elsivier Sci. Pub., Amsterdam (1991), p. 521.

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11) H. E. Baumgarten, A. Staklis, and E. M. Miller, *J. Org. Chem.*, **30**, 1203 (1965).

12) Data on **7**: m p 65-67 °C (Lit.[11] 68 °C); ^1H NMR ($CDCl_3$) δ 7.88-7.90 (m, 2H), 7.68-7.72 (m, 1H), 7.59-7.63 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 165.8, 135.6, 129.3, 120.9 **10**: m p 47-49 °C (Lit.[11] 47.5-48 °C); ^1H NMR ($CDCl_3$) δ 7.80 (d, J = 8.1 Hz, 2H), 7.38 (d, J =8.1 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 165.6, 147.2, 129.7, 121.2, 21.9 **13**: m p 85-87 °C (Lit.[2a] 85-87 °C); ^1H NMR ($CDCl_3$) δ 7.86 (d, J = 8.6 Hz, 2H), 7.60(d, J = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 163.7, 142.5, 129.7, 122.2.

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