

PHASE TRANSFER CATALYZED OXIDATIONS OF ALCOHOLS
AND AMINES BY AQUEOUS HYPOCHLORITE

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Phase transfer catalysis (PTC), using catalytic amounts of lipophilic quaternary ammonium salts for the transfer of anionic species from aqueous to organic media, is being extensively utilized to facilitate a variety of reactions.¹ We now report that PTC with aqueous NaOCl is extremely effective and makes this inexpensive and readily available reagent equal or even superior to more exotic oxidants for the oxidation of many alcohols and amines. Also of interest is an unexpected, specific solvent effect which further extends this method.

Aryl carbinols are smoothly converted to carbonyl compounds by stirring at room temperature an excess of 10% aqueous NaOCl (commercial swimming pool bleach) with a CH₂Cl₂ solution of substrate containing ~5% tetrabutylammonium bisulphate (TBAB) as catalyst. In the absence of phase transfer catalyst, little or no reaction is evident and the alcohol is recovered unchanged. Table 1 lists some representative examples. For benzyl alcohol to benzaldehyde the biphasic PTC method significantly shortens the reaction time over a comparable homogeneous oxidation using aqueous methanolic KOCl.² It is interesting to note that while benzene, carbon tetrachloride, chloroform and dichloromethane function suitably as solvents for these oxidations, ethyl acetate significantly increases the rate and is the solvent of choice. The mechanistic implications of this unusual solvent effect will be presented at a later date.

TABLE 1
OXIDATION OF ARYL CARBINOLS WITH PTC/ OCl_2

<u>Alcohol</u>	<u>Solvent</u>	<u>Reaction Time (Min.)</u>	<u>% Unreacted Alcohol</u>	<u>% Aldehyde or Ketone</u>
Benzyl	CH_2Cl_2	75	23	76
<i>o</i> -Methoxybenzyl	"	90	51	47
<i>p</i> -Methoxybenzyl	"	75	11	79
<i>p</i> -Methylbenzyl	"	83	18	78
<i>p</i> -Chlorobenzyl	"	60	14	82
Benzhydryl	"	150	16	82
9-Fluorenol	"	35	5	92
<i>p</i> -Methylbenzyl	EtOAc	30	—	100
<i>p</i> -Methoxybenzyl	"	28	1	92
<i>o</i> -Methoxybenzyl	"	72	2	94

The efficiency of ethyl acetate as a solvent now also permits certain aliphatic, secondary carbinols to be oxidized at reasonable rates and in good yields using PTC/hypochlorite. Some indicative examples are presented in Table 2. Primary aliphatic alcohols are oxidized more slowly to aldehydes, but these aldehydes (in contrast to aryl aldehydes) are oxidized exceedingly rapidly to carboxylic acids.

TABLE 2
OXIDATION OF SECONDARY ALIPHATIC ALCOHOLS WITH PTC/ OCl_2

<u>Alcohol</u>	<u>Reaction Time (Min.)</u>	<u>% Unreacted Alcohol</u>	<u>% Ketone</u>
Cycloheptanol	58	3	89
2-Norbornanol	78	46 (<i>exo</i>) 16 (<i>endo</i>)	36
		76% <i>exo</i> 24% <i>endo</i>	
4- <i>t</i> -Butylcyclohexanol	75	19 (<i>cis</i>) 17 (<i>trans</i>)	49
		23% <i>cis</i> 77% <i>trans</i>	

Primary amines are also oxidized by PTC/ OCl_2 , but synthetically important reactions are limited to those primary amines having a disubstituted α -carbon. These undergo facile reaction with PTC/ OCl_2 to yield N-chloroimines, reduc-

tion and hydrolysis of which gives excellent overall yields of ketones (see Table 3). This PTC technique appears to be superior to the existing procedures for preparing N-chloroamines⁴ and their derived products.⁵ In particular, the present method obviates the need for a multistep synthesis; under our conditions the initially formed dichloroamine is spontaneously and rapidly dehydrochlorinated to N-chloroimine.

TABLE 3
OXIDATION OF AMINES WITH PTC/ OCI_3

<u>Amine</u> ^a	<u>Reaction Time (Min.)</u>	<u>Product (Yield)</u>
Cyclohexylamine	120	Cyclohexanone (98%) ^b
Norbornylamine	80	Norbornanone (84%) ^b
Benzylhydramine	120	Benzophenone (94%) ^b
<i>o</i> -Methylbenzylamine	140	Acetophenone (98%) ^b
Cyclohexylmethylamine	70	Cyclohexyl nitrile (76%)
1-Octylamine	35	1-Cyanoheptane (60%)

a) In ethyl acetate.

b) N-chloroimine is the primary product which was taken up in methanol and successively treated with 1 equiv. of 1N sodium bisulfate solution and then hydrolyzed with dilute mineral acid.

Similar reaction of primary amines containing a monosubstituted α -carbon gives predominantly nitriles with minor amounts of aldehydes. Amides react with PTC/hypochlorite through successive Hofmann rearrangement and oxidation of the resultant amine to give generally lower overall yields of nitriles and aldehydes, or ketones. A more detailed account of the synthetic utility and mechanism of these transformations will be reported soon.

Typical Oxidation Procedure:

p-Methylbenzyl alcohol (1.25 g, 0.01 mole), 2-chloronaphthalene (.87 g, used as internal gc standard), and tetrabutylammonium bisulfate (0.18 g, 5.4×10^{-4} mole) were dissolved in 25.0 ml methylene chloride and to this solution was added 25.0 ml 10% aqueous sodium hypochlorite (2.95 g NaOCl, 0.04 mole). The biphasic mixture was stirred under ambient conditions ($T \sim 24$, atmospheric pressure) and monitored periodically by gas chromatography.

After 113 min reaction, the mixture was analyzed to contain 85% p-tolualdehyde and 10% p-methylbenzyl alcohol. The structure of the aldehyde product was determined by its gc characteristics (comparison to authentic material), its ir spectrum and by preparing a semi-carbazone derivative, mp 222-223° (lit. 221°).

References:

1. For general reviews see: J. Dockx, Synthesis, 441 (1973); E. V. Dehmlow, Angew. Chem. Int. Ed. Eng., 13, 170 (1974).
2. Meyers reports a 77% yield of benzaldehyde after 12-14 hrs. C. Y. Meyers, J. Org. Chem., 26, 1046 (1961).
3. All oxidations shown in tables were conducted with a 4-fold excess of 10% aqueous NaOCl, 0.4 M organic solution of the substrate and 5 mole % TBAB. Oxidations were successfully accomplished using 0.01 to 0.25 mole alcohol and with 1.85-10 mole excess (based on substrate) of hypochlorite. Other quaternary ammonium salts (such as benzyl triethylammonium chloride) also function as acceptable PTC catalysts, but give slower rates of oxidation. After control of the initial exotherm, stirring was continued at room temperature while the course of reaction was monitored by gc and yields determined using calibrated internal standards. Reaction times shown in the table indicate the time required to give the designated reaction composition.
4. a) S. L. Reid and D. B. Sharp, J. Org. Chem., 26, 2567 (1961); S. L. Reid, U.S. Patent No. 3,137,728, June 16, 1964; b) G. H. Alt and W. S. Knowles, J. Org. Chem., 25, 2047 (1960); G. H. Alt and W. S. Knowles, Org. Syn., 46, 16 (1965).
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