

Carbonate Ion on a Polymeric Support: Hydrolysis of Alkyl Halides and Cyclic Iodocarbonates

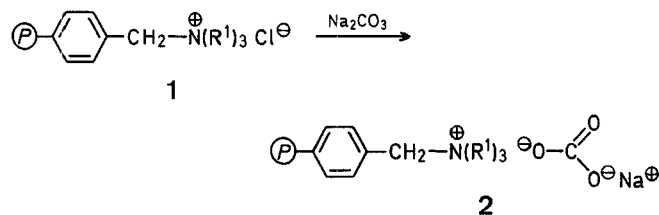
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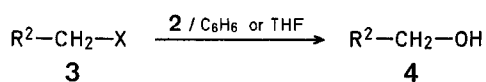
A frequent reaction in organic synthesis is the conversion of alkyl halides to alcohols. A commonly used method consists in the nucleophilic displacement of halogen by hydroxide ion in aqueous solution, although milder reagents (sodium carbonate or water) can be usefully employed with more reactive halides. Nevertheless, in some cases, these reactions are better performed using an inert co-solvent or a phase-transfer catalyst or in the presence of electrophilic cations [silver(I), mercury(II) ions]^{1,2}. These procedures frequently involve some difficulties, the chief being the reaction mixture work-up and purification, particularly when the reaction product is a water soluble alcohol.

In connection with our synthetic problems, an efficient and very mild process to convert alkyl halides to the corresponding alcohols is frequently required. Concerning the investigations in progress in our laboratory on the applicability of polymer supported reagents in organic synthesis³⁻⁸, we now report a new, convenient preparation of alcohols starting from alkyl halides. This reaction can be easily performed by means of carbonate ion supported on anion exchange resin. It is well-known that supported reagents are particularly convenient, since the reaction conditions are very mild and the reaction products can be isolated by simply filtering off the resin.

We supported the carbonate ion by washing with aqueous sodium carbonate a macroreticular resin containing quaternary ammonium groups, in the chloride form (Amberlyst A 26). The reagent **2**, so obtained contains ~3.7 mmol carbonate ion per g of resin.

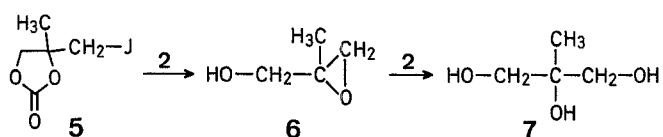


The hydrolysis reaction is performed by a batch technique on stirring an excess of reagent **2** with alkyl halides **3** in tetrahydrofuran or benzene solution at reflux temperature. The solvent does not appear to be critical, except for the reaction time which decreases when a solvent with a higher boiling point is employed.



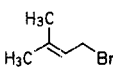
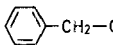
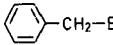
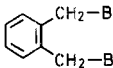
As reported in the Table, good yields of alcohols **4** are obtained with primary alkyl, allyl, and benzyl halides. The easiness of halogen displacement follows the usual sequence: J > Br > Cl. In the case of secondary alkyl halides, elimination predominates with respect to the substitution reaction. In fact, after 5 h in refluxing benzene, 2-bromooctane gives a mixture of starting material, 2-octanol, and olefins (1- and 2-octene). Under the same conditions, bromocyclohexane affords cyclohexene in about 90% yield, the rest being starting material. These findings agree with the Ingold prediction that elimination products should predominate in typical organic media while substitution should match or exceed elimination in a highly aqueous environment⁹.

In the course of further investigations aimed to find new practical methods in organic synthesis, we devised a new, noteworthy application of the polymeric reagent **2**. We observed that it is able to promote the hydrolysis of cyclic iodocarbonates (e.g. **5**), new intermediates recently synthesized in our laboratory¹⁰. The reaction can be accomplished in mild conditions (5 h in refluxing benzene) and affords the corresponding triol **7** in good yield. We have ascertained that the reaction proceeds through the formation of an α -epoxy-alcohol (e.g. **6**), which has been isolated on performing the reaction in boiling tetrahydrofuran for 1 h. This intermediate **6** can be converted to triol **7** in the presence of the polymeric supported reagent in boiling benzene. However, under the same conditions, undecene-1,2-epoxide, refluxed for 5 h with **2** in benzene solution, remains unchanged. Therefore this synthetic method allows the opening of an epoxy ring having a hydroxy group at the α -carbon atom.



As the reaction proceeds, the triol **7** is adsorbed on the resin and can be obtained pure in good yield by washing the resin with methanol. After the reaction, the resin can be easily regenerated by washing with hydrochloric acid, water, and then aqueous sodium carbonate solution.

Table. Hydrolysis of Alkyl Halides **3** using Polymer Supported Carbonate Ion (**2**) to Alcohols **4**

Alkyl halide 3	Reaction conditions	Yield [%] ^{a,b}	m.p. [°C] or b.p. [°C]/torr	
	(time/solvent)		found	reported
<i>n</i> -C ₈ H ₁₇ -Cl	5 h/THF	40	194°/760	194.45°/760 ¹¹
	7 h/C ₆ H ₆	90		
<i>n</i> -C ₈ H ₁₇ -Br	2 h/THF	55		
	5 h/THF	80		
	4 h/C ₆ H ₆	90		
<i>n</i> -C ₈ H ₁₇ -I	2 h/THF	65		
	5 h/THF	90		
	4 h/C ₆ H ₆	95		
	1 h/THF	95	140°/760	140°/760 ¹²
	2 h/C ₆ H ₆	90	204°/760	205.35°/760 ¹¹
	2 h/THF	85		
	2 h/C ₆ H ₆	95		
	2 h/C ₆ H ₆	85°	64-65°	65-66.5° ¹¹

^a Yield of pure, isolated product **4**.

^b Products were identified by G.L.C. (column 2 m long, 6 mm diameter, packed with 15% Carbowax 20 M on Chromosorb W 80-100 mesh) and by comparison of ¹H-N.M.R. spectra (recorded with a Perkin-Elmer R 12 B spectrometer) with data reported in Ref. ¹⁴.

^c The reaction product, 2-hydroxymethylbenzyl alcohol, is recovered by washing the resin with methanol.

The high yields and the easy work-up make this procedure remarkably useful, introducing a significant improvement with respect to the usual methods.

Amberlyst A 26, Carbonate Form (**2**):

A 1 molar solution of sodium carbonate (900 ml) is slowly percolated through a column filled with Amberlyst A 26 (15 g; Rohm and Haas) in the chloride form (average capacity ~3.7 meq/g), until a negative test for chloride ion in the eluate is obtained. The resin is then washed with methanol, acetone, and ether, and dried in vacuo for 2 h at room temperature.

1-Octanol (**4**; R = *n*-C₇H₁₅); Typical Procedure:

Amberlyst A 26 in the carbonate form (**2**; 11 g, ~40 meq) and 1-bromooctane (2.12 g, 11 mmol) are vigorously stirred in refluxing benzene (20 ml) for 4 h. The resin is then filtered off, washed with dichloromethane and methanol; the solvent is removed in vacuo and the residue is purified by silica gel chromatography eluting with hexane/ether (7:3) to give 1-octanol; yield: 1.25 g (90%), see Table.

2-Hydroxymethyl-2-methyloxirane (**6**):

Amberlyst A 26 in the carbonate form (**2**; 4 g, ~15 meq) and the cyclic iodocarbonate¹⁰ **5** (1.2 g, 5 mmol) are stirred in refluxing tetrahydrofuran (15 ml) for 1 h. The resin is then filtered off and washed with methanol (40 ml). The organic solution is evaporated in vacuo and the α -epoxyalcohol **6** is obtained pure after silica gel column chromatography, eluting with 7:3 hexane/ethyl acetate; yield: 0.3 g (70%).

C₄H₈O₂ calc. C 54.53 H 9.15
(88.1) found 54.47 9.11

¹H-N.M.R. (CDCl₃): δ = 1.35 (s, 3 H); 2.75 (AB-q, 2 H, *J* = 5 Hz); 3.75 (d, 2 H, *J* = 2 Hz); 6.0 ppm (br s, 1 H).

2-Methyl-1,2,3-trihydroxypropane (**7**):

Amberlyst A 26 in the carbonate form (**2**; 4 g, ~15 meq) and the cyclic iodocarbonate¹⁰ **5** (1.2 g, 5 mmol) are refluxed in benzene (15 ml)

for 5 h. The resin is then filtered off and washed with methanol. The methanolic solution is evaporated in vacuo and the pure triol **7** is obtained; yield: 0.42 g (80%); b.p. 165-170°C/20 torr (Ref. ¹³, b.p. 115-120°C/1.6 torr).

¹H-N.M.R. (D₂O): δ = 1.15 (s, 3 H); 3.45 ppm (s, 4 H).

Dehydrobromination of Bromocyclohexane:

Amberlyst A 26 in the carbonate form (**2**; 3 g, ~11 meq) and bromocyclohexane (0.5 g, 3 mmol) are vigorously stirred in refluxing benzene (10 ml) for 5 h. The resin is filtered off, washed with methanol and the resulting solution is submitted to G.L.C. analysis using a Perkin-Elmer Sigma 3 instrument, equipped with a Perkin-Elmer Sigma 10 Data Station (column: 15% Carbowax 20 M on Chromosorb G 80-100 mesh). The G.L.C. analysis, performed by comparison with authentic samples, reveals the formation of cyclohexene in 88% yield, the rest being starting material.

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- S. G. Wilkinson in *Comprehensive Organic Chemistry*, D. H. R. Barton, W. D. Ollis, Eds., Vol. 1 (J. F. Stoddart, Ed.), Pergamon Press, Oxford, 1979, p. 595 and references therein.
- S. L. Regen, *Angew. Chem.* **91**, 464 (1979); *Angew. Chem. Int. Ed. Engl.* **18**, 421 (1979).
- K. Shimo, S. Wakamatsu, *J. Org. Chem.* **28**, 504 (1963).
- C. G. Overberger, K. N. Sannes, *Angew. Chem.* **86**, 139 (1974); *Angew. Chem. Int. Ed. Engl.* **13**, 99 (1974).
- C. C. Leznoff, *Q. Rev. Chem. Soc.* **3**, 65 (1974).
- G. Cainelli, F. Manescalchi, *Synthesis* **1975**, 723.
- G. Cainelli, F. Manescalchi, M. Panunzio, *Synthesis* **1976**, 472.
- G. Cainelli, G. Cardillo, M. Orena, S. Sandri, *J. Am. Chem. Soc.* **98**, 6737 (1976).
- F. Manescalchi, M. Orena, D. Savoia, *Synthesis* **1979**, 735.
- K. A. Cooper et al., *J. Chem. Soc.* **1948**, 2043.
- G. Cardillo, M. Orena, G. Porzi, S. Sandri, *J. Chem. Soc. Chem. Commun.* **1981**, 465.
- Handbook of Chemistry and Physics*, 52nd Edn., The Chemical Rubber Co., Cleveland, Ohio, 1971-1972.
- A. Courtot, *Bull. Soc. Chim. Fr.* **35**, 660 (1906).
- G. Hearne, A. W. De Jong, *Ind. Eng. Chem.* **33**, 940 (1941).
- The Aldrich Library of NMR Spectra*, Aldrich Chemical Co., Milwaukee, Wisconsin, 1974.