

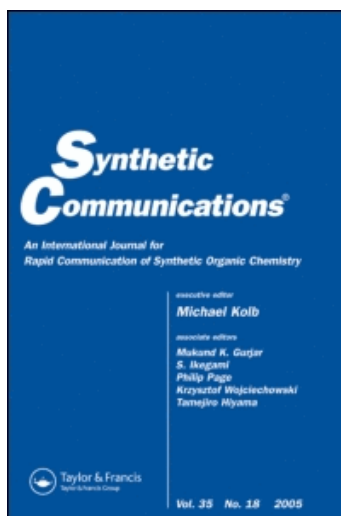
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NOVEL IODINE REAGENT SYSTEM FOR REGIOSELECTIVE CLEAVAGE OF EPOXIDES TO ALCOHOLS

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Epoxides are converted regioselectively to corresponding higher substituted alcohols with greater yields using diphosphorus tetraiodide (P_2I_4) as a reducing agent and a catalytic amount of tetraethylammonium bromide at room temperature.

Keywords: Alcohols; diphosphorus tetraiodide; epoxides; reduction; tetraethylammonium bromide

INTRODUCTION

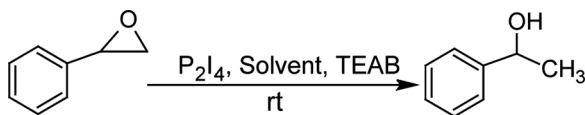
The reductive cleavage of epoxides to alcohols is one of the most important reactions in organic synthesis. In principle, an unsymmetrical alkyl-substituted epoxide can produce the more substituted carbinol by reduction of epoxides with nucleophilic hydride transferring reagents or less substituted alcohol with electrophilic hydride reagents,^[1–5] depending on the cleavage of the C–O bond to the less-substituted or more-substituted carbon atom. Drawbacks of most of these available methods are formation of mixtures of more- and less-substituted alcohols, which means that there is still scope for alternative reagent systems for regioselective preparation of alcohols from epoxides.

Our group is developing new methodologies using an iodine reagent system.^[6] Diphosphorus tetraiodide (P_2I_4) is an orange crystalline solid and is commercially available. It exhibits a high affinity for oxygen and acts as a unique reagent to promote reduction reactions. It is known that P_2I_4 reduces, under mild conditions, aminoxides, sulfoxides, and selenoxides to amines, sulfides, and selenides, respectively,^[7] as well as reducing diols at room temperature in the presence of a base to corresponding alkenes.^[8]

During our study, we proposed that diphosphorus tetraiodide in combination with tetraethylammonium bromide (TEAB) might be advantageous for regioselective opening of epoxides in which the more substituted alcohol would be preferentially produced by trapping the hydride at the site best able to accommodate a

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Scheme 1. Transformation of epoxide to alcohol.

carbonium ion. After considerable exploration, a combination of diphosphorus tetraiodide and a catalytical amount of tetraethyl ammonium bromide was demonstrated to offer the most reliable and convenient reductive system. To the best of our knowledge, there are no reports on P_2I_4 -mediated regioselective reductive transformation of epoxides to alcohols (Scheme 1).

In this communication, we report on our preliminary result on regioselective cleavage of epoxides using P_2I_4 and TEAB to form higher substituted alcohols.

RESULTS AND DISCUSSION

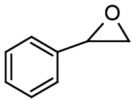
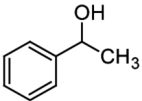
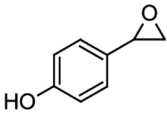
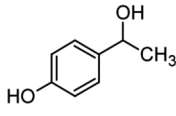
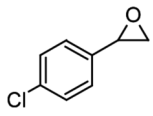
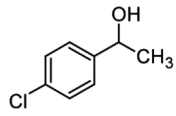
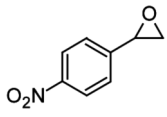
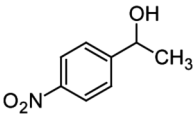
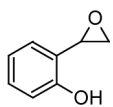
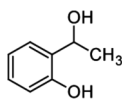
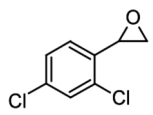
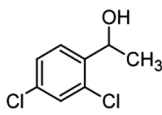
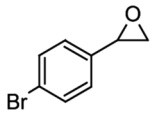
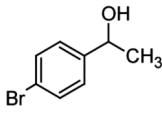
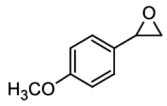
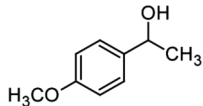
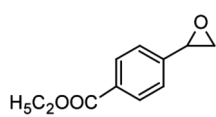
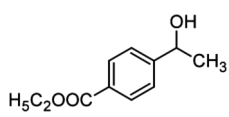
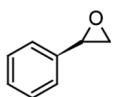
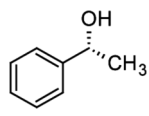
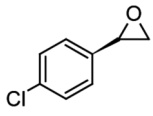
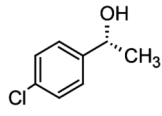
For initial studies, we selected styrene epoxide as a model substrate. We observed that without TEAB, the reaction does not take place. Instead of TEAB, we tried other quaternary ammonium salts such as tetraethylammonium chloride and tetraethylammonium iodide as catalyst, but no reaction was observed. Screening with alternative solvents led us to conclude that dichloromethane was the most suitable solvent for the conversion. Although complete conversion was also observed in carbon disulfide, it was not selected because of its toxicity and flammability.

It has been well studied for reduction of cyclic and acyclic dithioacetals using P_2I_4 and found that the proton required for the reduction comes from the moisture present in the solvent.^[9,10] In this case, the transformation required traces of moisture, which comes from solvent used in the reaction mixture. We confirmed this by conducting the reaction in absolute dry conditions, where reduction to corresponding alcohol was not observed in either dry carbon disulfide or dry dichloromethane.

To explore the reaction scope, a variety of aromatic, aliphatic epoxides were converted into alcohols, and results are presented in Table 1. Table 1 clearly shows that reactions completed within 5–6 h with good yield. It was found that either electron-rich or electron-deficient aromatic epoxides were suitable for this reaction, giving desired alcohols in good yield (Table 1, entries 2–7). It was noted that a variety of functional group tolerated these reaction conditions (Table 1, entries 8 and 9). Reductive cleavage of epoxide occurs with retention of configuration, producing (1R)-1-phenylethanol exclusively from (2R)-2-phenyloxirane and (1R)-1-(4-chlorophenyl) ethanol from (2R)-2-(4-chlorophenyl)oxirane (Table 1, entries 10 and 11).


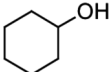

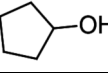
The major advantages of this methodology are availability of this reagent, safer reaction conditions, and complete regioselectivity in the reductive cleavage of epoxide compared with existing reagents. Moreover, with the combination of the excellent methods available for the synthesis of optically active epoxides, the present method can provide easy access to optically active alcohols with retention of configuration.

Table 1. Synthesis of alcohols from epoxides using P_2I_4 and catalytical TEAB^a

Entry	Substrate ^b	Product	Time (h)	Yield ^c (%)
1			5	90
2			5	87
3			6	84
4			5	83
5			5	80
6			6	84
7			6	85
8			6	88
9			7	86
10			6	87 ^d
11			6	85 ^d

(Continued)

Table 1. Continued

Entry	Substrate ^b	Product	Time (h)	Yield ^c (%)
12			6	80
13			6	82

^aTypically, P₂I₄ (0.01 mol) reacted with epoxide (0.01 mol) in dichloromethane (50 ml, 1–3% moisture) in the presence of a catalytic amount of TEAB at room temperature.

^bStarting compounds were prepared by standard literature procedures.

^cIsolated yields after column chromatography and structure confirmed by comparison of IR and ¹H NMR with those of authentic materials.

^dOptical purity was confirmed by chiral HPLC and optical rotation matches with literature values.^[11,12]

GENERAL PROCEDURE

Preparation of Alcohols

Epoxide (0.01 mol) was added to a stirred solution of diphosphorus tetraiodide (0.01 mole) and a catalytical amount of TEAB in dichloromethane (50 mL contains 1–3% moisture). The resultant mixture was stirred at rt until the starting material had been completely consumed (thin-layer chromatography, TLC). The reaction mixture was filtered, and the filtrate was washed successively with saturated aq. NaHCO₃ (2 × 20 mL) and H₂O (1 × 20 mL). The organic layer was separated, dried over Na₂SO₄, and concentrated in vacuo. The residue obtained was purified by silica-gel column chromatography (15% EtOAc–hexane) to afford pure alcohols.

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