Efficient Nucleophilic Cleavage of Oxiranes to Chlorohydrins†

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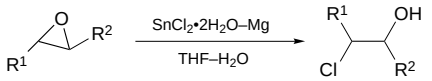
$SnCl_2 \cdot 2H_2O$–Mg and THF–H_2O is an efficient system for the conversion of oxiranes into chlorohydrins.

Epoxides are valuable intermediates in organic synthesis partly because of their nucleophilic cleavage leading to 1,2-difunctionalized systems and partly because such cleavages usually occur specifically with *trans* stereochemistry. The formation of halohydrins from epoxides has been extensively studied with a variety of reagents.[1–8] Although there is precedent for the Lewis acid assisted cleavage of oxiranes to halohydrins, these reactions often afford only modest yields. The present work was undertaken in order to determine the general applicability of the reaction with epoxides. In continuation of our earlier studies on the uses of metal reagents,[9,10] we found that $SnCl_2 \cdot 2H_2O$–Mg and THF–H_2O is a promising system for the regioselective ring opening of oxiranes to the corresponding chlorohydrins in good yields.



In acidic medium[1] there is usually a greater tendency for nucleophilic attack at the more substituted carbon atom. Phenyl substituents at the epoxide ring can stabilize an intermediate positive charge by conjugation, and hence attack occurs at the more substituted carbon atom. However, in the case of epoxides with electron withdrawing substituents, nucleophilic attack at the unsubstituted carbon is usually favoured. Under these conditions, substituted epoxides (Table 1, entries 4, 7 and 8) reacted regioselectively affording the primary chloride. The cyclohexene oxide and the epoxide (entries 2 and 3 respectively) opened cleanly to afford the *trans* chlorohydrins, with the tertiary chloride being the major product in the latter case. However in the case of styrene oxide the secondary chloride predominates. The yield of the products corresponds to the total yield of the regioisomers.

Cleavage of the oxirane ring has also been unsuccessfully attempted using $SnCl_2 \cdot 2H_2O$–THF alone. However, the use of a stoichiometric amount of magnesium facilitated the reaction. In addition, the possibility of active zero-valent tin (generated *in situ* by the reduction of Sn^{II} to Sn^0 in the presence of magnesium) could effectively induce regioselective nucleophilic attack.

Owing to the general interest in the smooth and selective cleavage of these compounds, mild reaction conditions, good yields and some possible synthetic applications, the $SnCl_2 \cdot 2H_2O$–Mg–THF system will be a useful addition to the existing findings.

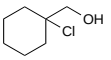
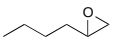
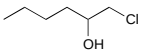
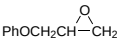
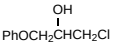
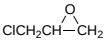
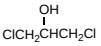
Experimental

^{1}H NMR spectra were recorded on deuteriochloroform on a JEOL FX-90 instrument. IR spectra were recorded on a JASCO FT/IR-5300 instrument in chloroform. Mass spectra were recorded on an MS-30 instrument. TLC and preparative TLC were performed on silica gel (E. Merck).

General Procedure.—In a typical procedure, a mixture of $SnCl_2 \cdot 2H_2O$ (442 mg, 2 mmol), Mg powder (36.5 mg, 1.5 mmol) and oxirane (1 mmol) in THF (10 ml) was stirred at room temperature. An exothermic reaction occurred with the liberation of hydrogen. The reaction mixture was stirred for 30 min. After completion of the reaction (TLC), usual work-up and purification by preparative chromatography yielded the corresponding chlorohydrins.

Selected ^{1}H *NMR spectral data*. For *trans*-2-chlorocyclohexanol: δ_H ($CDCl_3$) 1.1–1.95 (8 H, m), 2.65 (1 H, br s), 3.05–3.5 (2 H, m). For 1-chloromethylcyclohexanol: δ_H ($CDCl_3$) 1.2–1.75 (10 H, m), 2.15 (1 H, br s), 3.15 (2 H, s). For 1-chlorohexan-2-ol: δ_H ($CDCl_3$) 1.15 (3 H, s), 1.35–1.95 (6 H, m), 2.6 (1 H, br s), 3.8 (2 H, d), 4.85 (1 H, t). For 2-chloro-2-phenylethanol: δ_H ($CDCl_3$) 2.36 (1 H, s), 3.95–1.95 (2 H, d), 5.05 (1 H, t), 7.48 (5 H, m).

Table 1 Oxirane ring opening with $SnCl_2 \cdot 2H_2O$–Mg–THF–H_2O

Entry	Oxirane	Product[a]	Yield (%)[b]
1			64
2			72
3			75
4			77
5			90
6			78
7			86
8			74

[a]All the products gave satisfactory spectral data. [b]Total yield of the regioisomers.

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