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Rapid, highly efficient and stereoselective deoxygenation of epoxides by $ZrCl_4$/NaI

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Abstract—An effective and highly chemoselective method is described for the rapid deoxygenation of different epoxides to the corresponding olefins using $ZrCl_4$/NaI in anhydrous CH_3CN, in excellent yields and with retention of relative stereochemistry.

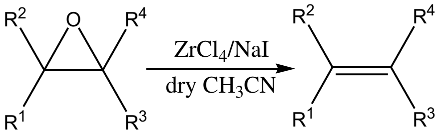
The ability of transition metals to mediate organic reactions either catalytically or stoichiometrically constitutes one of the most powerful strategies to achieve both selectivity and efficiency in synthetic chemistry.[1] However, the choice of mediator is important with respect to environmental and economic considerations. For example, $TiCl_4$ is an efficient mediator in organic reactions, however, its applications are limited considerably by its high toxicity and its requirement for special handling.[2] $ZrCl_4$ is less costly, easily available[3] and relatively safe [LD_{50} [$ZrCl_4$, oral rat] = 1688 mg/kg].[4] Additionally, Zr^{4+} with a high charge-to-size ratio (22.22 $e^2 m^{-10}$)[5] enables reactions with high to excellent yields due to strong coordination of Zr^{4+}. Thus, zirconium(IV) compounds are excellent catalysts or reagents in synthetic chemistry,[6] as evidenced by their increasing commercial use for this purpose.[7]

It is well-known that epoxides are versatile intermediates in organic chemistry.[8] The deoxygenation of epoxides to olefins allows the use of the oxirane ring as a protective group for double bonds.[9] Thus, it is an important protocol to control olefin stereochemistry,[10] for conversion of biomass-derived substrates to useful organic compounds[11] and also for structural analysis of natural products.[12] Relatively few general methods exist for removing oxygen atoms from epoxides.[13] Most of them require expensive reagents and harsh reaction conditions which may affect other sensitive functional groups in the molecule.[14]

In the course of our research on new applications of $ZrCl_4$ in organic synthesis, we have explored its use as an effective catalyst for highly chemoselective transthioacetalization of acetals.[15] Very recently, we have employed $ZrCl_4$/NaI as an efficient reagent for chemoselective iodination of alcohols.[16] Now, we introduce $ZrCl_4$/NaI as an expedient reagent for immediate and stereospecific deoxygenation of epoxides to olefins in excellent yields (Scheme 1).

The results given in Table 1 illustrate the high efficiency of this protocol for the deoxygenation of structurally different epoxides in short reaction times. Complete conversion of diverse epoxides, carrying alkyl, aryl, ether, carbonyl, ester and hydroxyl groups α or β to the oxirane ring, were all converted in excellent yields.

Among the epoxides we have studied, *cis*-stilbene oxide deoxygenation required the longest reaction time (15 min). We suggest that this retardation is caused by the requirement for attack by the large I^- on the epoxide ring, which encounters pronounced steric hindrance from the phenyl groups present in the molecule.



Scheme 1.

Keywords: Zirconium tetrachloride; Sodium iodide; Epoxide; Deoxygenation.

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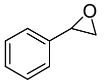
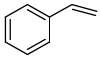
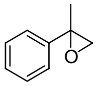
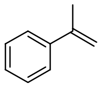
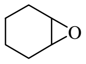
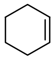
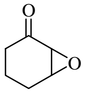
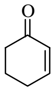
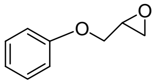
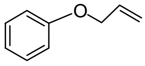
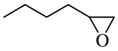
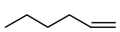
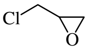
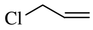
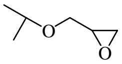
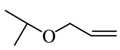
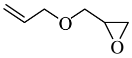
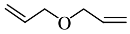
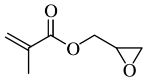
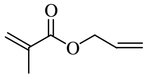
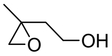
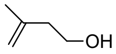
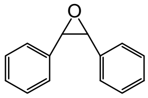
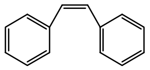
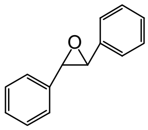
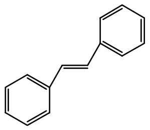
Table 1. Deoxygenation of epoxides using $ZrCl_4$/NaI in anhydrous CH_3CN[a]

Entry	Epoxide	Product	GC yield (%)	Isolated yield (%)	Time (min)
1			100	93	<1
2[b]			96	90	<1
3			97	87	<1
4[b]			100	92	<1
5			95	87	<1
6			100	88	<1
7			100	87	<1
8			100	90	<1
9			100	90	<1
10			95	88	<1
11[b]			98	90	<1
12[b]			90[c]	82	15
13[b]			100[c]	94	3

[a] The molar ratio of epoxide: NaI:$ZrCl_4$ was 1:2:0.5.

[b] The epoxides in entries 2, 4 and 11–13 were prepared according to the literature.[17,18]

[c] ^1H NMR yield.

In all the reactions, the immediate development of a deep brown colour was observed which is consistent with the generation of molecular iodine in the reaction mixture. By considering this observation, we suggest a mechanism for the reaction (Scheme 2).

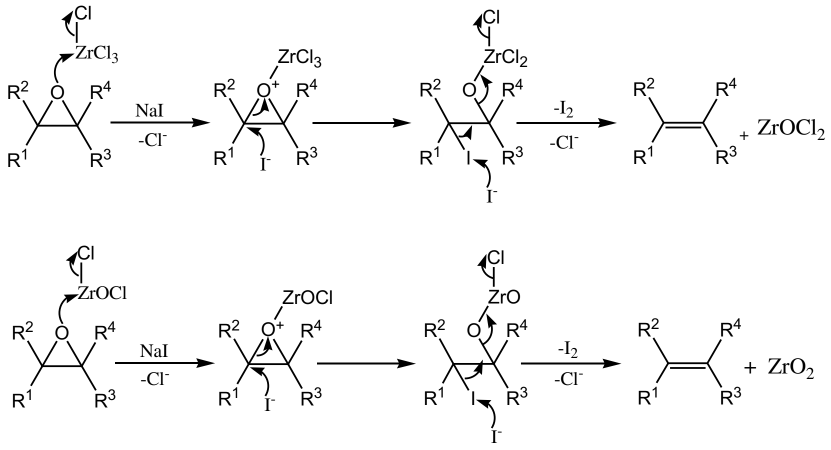
The important feature of this method is its high stereospecificity as demonstrated by the deoxygenation of *cis*-stilbene oxide to *cis*-stilbene and *trans*-stilbene oxide to *trans*-stilbene (entries 12 and 13).

The chemoselectivity of the method is also noteworthy, as exemplified by a molecule which carries both an epoxide ring and a hydroxyl group (entry 11). Deoxygenation of the epoxide ring proceeded well in high yield, the hydroxyl group remaining intact.

In order to show the advantages of the presented method, in Table 2, we have compared some of the results obtained by other methods with those using the $ZrCl_4$/NaI system.

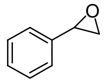
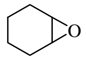
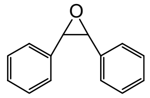
In conclusion, we have reported that $ZrCl_4$/NaI is a safe, inexpensive and highly efficient reagent for rapid chemoselective deoxygenation of various epoxides in excellent yields. We have also found that the reaction proceeded with absolute stereospecificity.

Typical procedure: To a solution of styrene oxide (0.120 g, 1 mmol) and NaI (0.3 g, 2 mmol) in dry CH_3CN (2 ml) solid $ZrCl_4$ (0.116 g, 0.5 mmol) was added in several portions. The mixture was stirred at reflux and the progress of the reaction was monitored



Scheme 2.

Table 2. Comparison of the $ZrCl_4$/NaI system with previously reported methods for deoxygenation of epoxides

Substrate	$ZrCl_4$/ NaI min [yield (%)]	$[Co(salen)_2]$/ Na(Hg)[13f] h [yield (%)]	$MoO(Et_2dtc)_2$[14j] h [yield (%)]	$LReO_3$/ PPh_3[13b] h [yield (%)]	LiI/ Amberlyst 15[13g] h [yield (%)]	$(EtO)_2P(O)TeNa$[14o] h [yield (%)]	$[n\text{-}Bu_3SnAlMe_3]^-Li^+$[10o] h [yield (%)]
	<1 [100]	1 [100][a]	—	2 [32]	3 [85][b]	—	—
	<1 [100]	6 [100]	36 [92]	—	—	42 [88]	—
	15 [90][c]	24 [100][d]	—	2 [33]	8 [93][e]	—	6 [88][f]

[a] The product was a mixture of 2-phenylethanol and styrene.

[b] The product was the halohydrin.

[c] *cis*-Stilbene.

[d] The product was a mixture of *cis*-stilbene, *trans*-stilbene and 1,2-diphenylethanol.

[e] *trans*-Stilbene.

[f] 34% *trans*-stilbene, 66% *cis*-stilbene.

by GC. After less than 1 min, the reaction mixture was diluted with cold water (10 ml) and ether (10 ml). The organic layer was separated and washed with a solution of $Na_2S_2O_3$ (aq 10%, 10 ml), and then H_2O (10 ml). The organic layer was separated and dried over anhydrous Na_2SO_4. Evaporation of the solvent under reduced pressure at room temperature gave the pure olefin (0.097 g, 93%) (Table 1, entry 1). In the case of low boiling products (Table 1, entries 3, 6, 7, 8 and 9) liquid air cooled, bulb-to-bulb distillation was used for purification.

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