

Communications

Regioselective Ring Cleavage of Phenyl- or/and Alkyl-Substituted Epoxides with *Al*-Trifluoromethanesulfonyldiisobutylalane. Comparison of Its Reactivity with *Al*-Methanesulfonyldiisobutylalane

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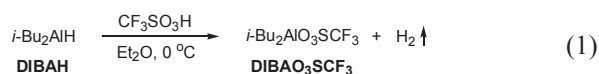
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Received June 23, 2010, Accepted July 16, 2010

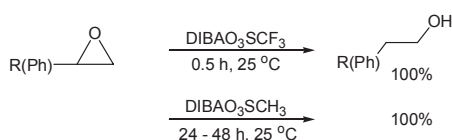
Key Words: Epoxides, Regioselective ring-cleavage, Reduction, *Al*-Trifluoromethanesulfonyldiisobutylalane, MPV type reaction

In the previous note,¹ we reported that *Al*-methanesulfonyldiisobutylalane (DIBAO₃SCH₃), a new Meerwein-Ponndorf-Verley (MPV) type reagent, attacks alkyl- or/and phenyl-substituted epoxides at a moderate rate to afford the regioselective ring-opened product in 100% purity. In addition, we found that the reactivity of *Al*-trifluoroacetoxydiisobutylalane (DIBAO₂CCF₃) is much stronger than that of *Al*-acetoxydiisobutylalane (DIBAOAc) toward carbonyl compounds;² these results indicate that the strong electron-withdrawing fluorine substituent in acetoxy group increases the acidity of the reagent and makes it stronger. From these experimental backgrounds, we designed the fluorinated methanesulfonyl derivative, *Al*-trifluoromethanesulfonyldiisobutylalane (DIBAO₃SCF₃), and applied to the reduction of epoxides. This communication described the reactivity and regioselectivity of DIBAO₃SCF₃ in the reaction of epoxides, and compares with those of DIBAO₃SCH₃.

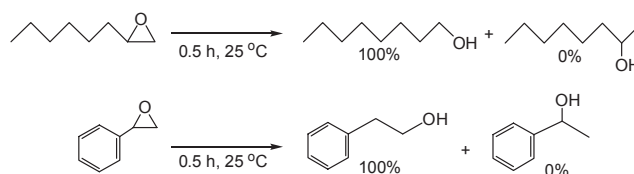
DIBAO₃SCF₃ can be readily prepared by a simple reaction of diisobutylaluminum hydride (DIBAH) with an equivalent of trifluoromethanesulfonic acid in Et₂O at 0 °C (Eq. 1).³



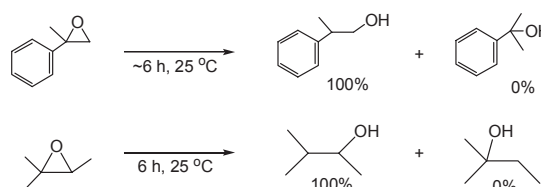
The reactivity and regioselectivity of DIBAO₃SCF₃ toward epoxides in Et₂O at 25 °C, and comparison of its reactivity with DIBAO₃SCH₃ are summarized in Table 1. As shown in the Table, DIBAO₃SCF₃ readily reduced a variety of alkyl- or/and phenyl-substituted epoxides examined to the ring-opened products in 0.5 ~ 6 h at 25 °C. The reactivity of the reagent appeared much higher than that of DIBAO₃SCH₃.¹ These results clearly indicate that the strong electron-withdrawing fluorine substituent in methanesulfonyl group increases the acidity of the reagent, that leads to a stronger coordination of the reagent to epoxy oxygen and in turn an easier attack on epoxy carbon to produce a ring-opened product.



More interestingly, in spite of such high reactivity the regioselectivity achieved by reagent in the reduction of epoxides was rather surprising. For example, the reaction of one alkyl- or phenyl-substituted epoxides such as 1,2-epoxyoctane and styrene oxide provided only the corresponding primary alcohol as a sole product. These results clearly indicate that the reaction proceeds through trapping of β -hydrogen from isobutyl group of the reagent at the site best able to accommodate a carbocation.



Such phenomenon was further verified by the results obtained from the reaction of alkyl-substituted or alkyl- and phenyl-substituted epoxides such as 2,3-epoxy-2-methylbutane and α -methylstyrene oxide: the products were 3-methyl-2-butanol and 2-phenyl-1-propanol, respectively, and the selectivity was also 100%.



More interestingly, the reaction of *trans*- β -methylstyrene oxide yielded only 1-phenyl-2-propanol as a sole product within 0.5 h at 25 °C, showing 100% selectivity. This reagent can discriminate between the phenyl-group and the alkyl-group substituted carbon sites.

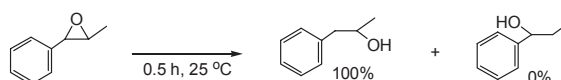


Table 1. Reaction of epoxides with DIBAO₃SCF₃ in Et₂O^a at 25 °C

Epoxides	Time (h)	DIBAO ₃ SCF ₃	DIBAO ₃ SCH ₃ ^a	Product	Purity (%) ^b
		Conversion(%) ^b	Conversion(%) ^b		
1,2-epoxybutane	0.5	100		1-butanol	100
	6		79		100
	24		92		100
	48		99		100
1,2-epoxyoctane	0.5	100		1-octanol	100
	6		75		100
	24		90		100
	48		100		100
2,3-epoxy-2-methylbutane	0.5	94		3-methyl-2-butanol	100
	3	97			100
	6	100	72		100
	24		88		100
	72		95		100
styrene oxide	0.5	100 ^c		2-phenylethanol	100
	6		95		100
	24		100		100
α -methylstyrene oxide	0.5	90		2-phenyl-1-propanol	100
	3	95	93		100
	6	99	98		100
	12	100			100
	24		100		100
<i>trans</i> - β -methylstyrene oxide	0.5	100		2-phenyl-2-propanol	100
	3		89		100
	6		100		100

^a10% excess reagent utilized ; 0.5 M concentration. ^bDetermined by GC using a suitable internal standard. ^c74% of 2-phenylethanol was isolated from the 40 mmol scale reaction.

Such an anti-Markovnikov reductive ring-opening of epoxides has previously been achieved with BH₃-THF in the presence of BF₃,⁴ NaBH₃CN in the presence of BF₃,⁵ KPh₃BH in the presence of Ph₃B,⁶ (tPrO₃)B,⁷ *Al*-fluorodiisobutylalane (DIBAF),⁸ and *Al*-methanesulfonyldiisobutylalane (DIBAO₃SCH₃).¹ However, each reagent possesses its own limitations of the reduction, such as a relatively low regioselectivity requirement for drastic reaction conditions, as undesirable rearrangement product, a relatively low chemoselectivity, etc.⁹

The following procedure is illustrative. Into a 50 mL flask with a sidearm equipped with a condenser leading to a mercury bubbler, 0.60 g of styrene oxide (5 mmol), 6.0 mL of Et₂O, tri-decane (2 mmol) as an internal standard, and 3.7 mL of a 1.5 M DIBAO₃SCF₃ (5.5 mmol) in Et₂O were injected. Then the flask was immersed into a water bath and the mixture was maintained at 25 °C. At the appropriate reaction periods (0.5 and 1 h) an aliquot of the reaction mixture was withdrawn and quenched with water. The aqueous phase was saturated with K₂CO₃ and the organic phase was dried over anhydrous MgSO₄. GC analysis of the organic layer revealed the presence of 2-phenylethanol as a sole product in a yield of 100% at 0.5 h-period. The product was further confirmed by GC-Mass spectrometer.

Despite of such a high reactivity toward epoxides, the reagent appears to be extremely mild toward other organic functional groups. Therefore, this reagent should find a unique application in the selective reduction of organic functionalities. The full

scope of reducing characteristics of the reagent is now underway.

References and Notes

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2. Cha, J. S.; Yi, J. E. *J. Incl. Phenom. Macrocycl. Chem.* **2009**, *65*, 15.
3. DIBAO₃SCF₃ was prepared by reaction of diisobutylaluminum hydride (DIBAH, 75 mmol) with an equivalent of trifluoromethanesulfonic acid (15 mL of 5.0 M, 75 mmol) in Et₂O at 0 °C.¹⁰ After the reaction completed, the solution was diluted with Et₂O to be 1.5 M. The ²⁷Al NMR spectrum of the solution showed a broad singlet centered at δ -18 ppm relative to Al(H₂O)₆³⁺.
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10. All reactions and manipulations of air- and moisture-sensitive material were carried out using standard techniques for handling air-sensitive materials.¹¹ THF was dried over sodium-benzophenone ketyl and distilled. All liquid materials were transferred by using hypodermic syringes.
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