

# Communications

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

Jin Soon Cha\* and Seung Jin Park

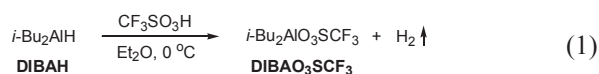
Department of Chemistry, Yeungnam University, Gyongsan 712-749, Korea. \*E-mail: jscha@yu.ac.kr

Received June 23, 2010, Accepted July 16, 2010

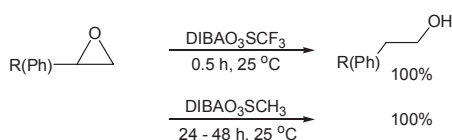
**Key Words:** Epoxides, Regioselective ring-cleavage, Reduction, *Al*-Trifluoromethanesulfonyldiisobutylalane, MPV type reaction

In the previous note,<sup>1</sup> we reported that *Al*-methanesulfonyldiisobutylalane (DIBAO<sub>3</sub>SCH<sub>3</sub>), 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*-trifluoroacetoxidiisobutylalane (DIBAO<sub>2</sub>CCF<sub>3</sub>) is much stronger than that of *Al*-acetoxidiisobutylalane (DIBAOAc) toward carbonyl compounds:<sup>2</sup> 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 (DIBAO<sub>3</sub>SCF<sub>3</sub>), and applied to the reduction of epoxides. This communication described the reactivity and regioselectivity of DIBAO<sub>3</sub>SCF<sub>3</sub> in the reaction of epoxides, and compares with those of DIBAO<sub>3</sub>SCH<sub>3</sub>.

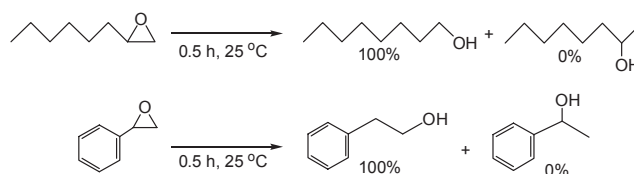
DIBAO<sub>3</sub>SCF<sub>3</sub> can be readily prepared by a simple reaction of diisobutylaluminum hydride (DIBAH) with an equivalent of trifluoromethanesulfonic acid in Et<sub>2</sub>O at 0 °C (Eq. 1).<sup>3</sup>



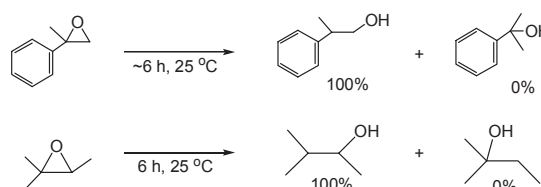
The reactivity and regioselectivity of DIBAO<sub>3</sub>SCF<sub>3</sub> toward epoxides in Et<sub>2</sub>O at 25 °C, and comparison of its reactivity with DIBAO<sub>3</sub>SCH<sub>3</sub> are summarized in Table 1. As shown in the Table, DIBAO<sub>3</sub>SCF<sub>3</sub> readily reduced a variety of alkyl- 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 DIBAO<sub>3</sub>SCH<sub>3</sub>.<sup>1</sup> 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.



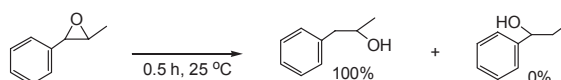
More interestingly, in spite of such high reactivity the regioselectivity achieved by reagent in the reduction of epoxides was rather surprising. For example, the reaction of one alkyl- or phenyl-substituted epoxides such as 1,2-epoxyoctane and styrene oxide provided only the corresponding primary alcohol as a sole product. These results clearly indicate that the reaction proceeds through trapping of  $\beta$ -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  $\alpha$ -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*- $\beta$ -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 DIBAO<sub>3</sub>SCF<sub>3</sub> in Et<sub>2</sub>O<sup>a</sup> at 25 °C

Epoxides	Time (h)	DIBAO <sub>3</sub> SCF <sub>3</sub>	DIBAO <sub>3</sub> SCH <sub>3</sub> <sup>a</sup>	Product	Purity (%) <sup>b</sup>
		Conversion(%) <sup>b</sup>	Conversion(%) <sup>b</sup>		
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 <sup>c</sup>		2-phenylethanol	100
	6		95		100
	24		100		100
$\alpha$ -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> - $\beta$ -methylstyrene oxide	0.5	100		2-phenyl-2-propanol	100
	3		89		100
	6		100		100

<sup>a</sup>10% excess reagent utilized ; 0.5 M concentration. <sup>b</sup>Determined by GC using a suitable internal standard. <sup>c</sup>74% 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 BH<sub>3</sub>-THF in the presence of BF<sub>3</sub>,<sup>4</sup> NaBH<sub>3</sub>CN in the presence of BF<sub>3</sub>,<sup>5</sup> KPh<sub>3</sub>BH in the presence of Ph<sub>3</sub>B,<sup>6</sup> (<sup>t</sup>PrO<sub>3</sub>)B,<sup>7</sup> *Al*-fluorodiisobutylalane (DIBAF),<sup>8</sup> and *Al*-methanesulfonyldiisobutylalane (DIBAO<sub>3</sub>SCH<sub>3</sub>).<sup>1</sup> 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.<sup>9</sup>

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 Et<sub>2</sub>O, tridecane (2 mmol) as an internal standard, and 3.7 mL of a 1.5 M DIBAO<sub>3</sub>SCF<sub>3</sub> (5.5 mmol) in Et<sub>2</sub>O 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 K<sub>2</sub>CO<sub>3</sub> and the organic phase was dried over anhydrous MgSO<sub>4</sub>. 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

1. Cha, J. S.; Park, S. J. *Bull. Korean Chem. Soc.* **2009**, *30*, 2823.
2. Cha, J. S.; Yi, J. E. *J. Incl. Phenom. Macrocycl. Chem.* **2009**, *65*, 15.
3. DIBAO<sub>3</sub>SCF<sub>3</sub> 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 Et<sub>2</sub>O at 0 °C.<sup>10</sup> After the reaction completed, the solution was diluted with Et<sub>2</sub>O to be 1.5 M. The <sup>27</sup>Al NMR spectrum of the solution showed a broad singlet centered at  $\delta$ -18 ppm relative to Al(H<sub>2</sub>O)<sub>6</sub><sup>3+</sup>.
4. Brown, H. C.; Yoon, N. M. *Chem. Commun.* **1968**, 1549.
5. Hutchins, R. O.; Taffer, I. M.; Burgoyne, W. *J. Org. Chem.* **1981**, *46*, 5214.
6. Yoon, N. M.; Kim, K. E. *J. Org. Chem.* **1987**, *52*, 5564.
7. Cha, J. S.; Park, J. H. *Bull. Korean Chem. Soc.* **2002**, *23*, 1377.
8. Cha, J. S.; Park, S. J.; Yu, S. J.; Kim, S. K.; Kwon, O. *Bull. Korean Chem. Soc.* **2008**, *29*, 301.
9. See the review paper, some references cited in: (a) Cha, J. S. *Org. Proc. Res. Devel.* **2006**, *10*, 1032. (b) Cha, J. S. *Bull. Korean Chem. Soc.* **2007**, *28*, 2162.
10. All reactions and manipulations of air- and moisture-sensitive material were carried out using standard techniques for handling air-sensitive materials.<sup>11</sup> THF was dried over sodium-benzophenone ketyl and distilled. All liquid materials were transferred by using hypodermic syringes.
11. Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Synthesis via Boranes*; Wiley-Interscience: New York, N. Y., 1975.