

Regioselective Cleavage of Phenyl- or Alkyl-Substituted Epoxides with *Al*-Fluorodiisobutylalane

Jin Soon Cha,* Seung Jin Park, Se Jin Yu, Seung Kook Kim, and Oh Oun Kwon

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

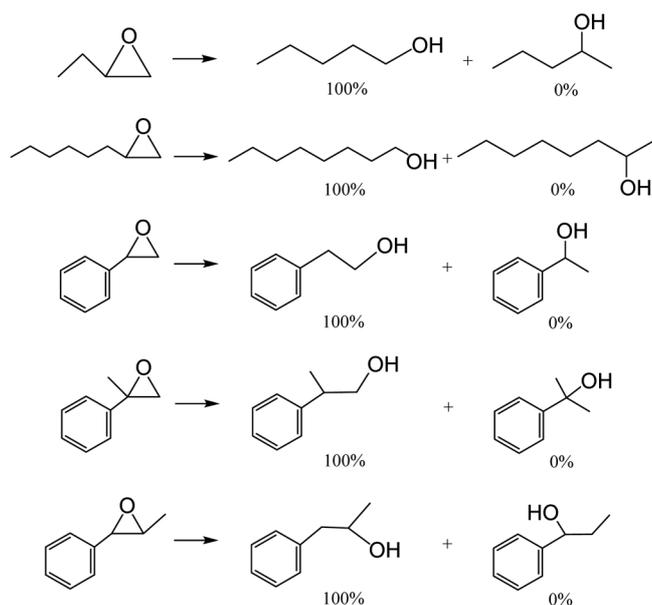
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In the previous communication,¹ we reported that boron triisopropoxide attacked aryl epoxides slowly but regioselectively to produce the anti-Markovnikov ring-opened reduction products in the Meerwein-Ponndorf-Verley (MPV) type reduction procedure. In the course of our successive efforts to devise new unique MPV type reagents, we found *Al*-fluorodiisobutylalane (DIBAF), a new MPV type reagent, reacts readily with both aromatic and aliphatic epoxides to produce the corresponding alcohols in an essentially perfect regioselectivity. This paper described such a regioselective MPV type reduction of epoxides.

As listed in Table 1, DIBAF reduced both aliphatic and aromatic epoxides examined in hexane²-THF in 24 h at 25 °C. However, it is noteworthy that the reagent attacks aromatic epoxides more readily than aliphatic ones. DIBAF shows substituted alcohol is produced as a sole product by trapping of β -hydrogen from isobutyl group of the reagent at the site best able to accommodate a carbonium ion.

Furthermore, the most interesting example should be found in the reaction of *trans*- β -methylstyrene oxide. Thus, the reaction yield 1-phenyl-2-propanol in a 100% selectivity. It is rather surprising that the reagent discriminates between the phenyl group- and the alkyl group- attacked carbon site.



In the mechanistic point of view, the reaction of epoxides

with DIBAF seems to involve the formation of a coordination complex, in which the aluminum atom bound to the epoxy oxygen, and followed by the hydride transfer *via* a cyclic transition state as in a usual reaction of carbonyl compounds with a MPV reagent.^{1,3}

Such an anti-Markovnikov reductive 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 and (*i*PrO)₃B.¹ However, each reagent possesses its own limitations of the reduction, such as a relatively low selectivity, requirement for drastic reaction conditions, an undesirable rearrangement product, etc. The following procedure is illustrative. Into a 50 mL flask with a side-arm equipped with a downward-directed, water-cooled condenser leading to a mercury bubbler,⁷ 0.60 g of styrene oxide (5 mmol), 5.5 mL of THF, tridecane (2 mmol) as an internal standard, and 5.5 mL of a 1.0 M solution of DIBAF

Table 1. Reaction of Epoxides with *Al*-Fluorodiisobutylalane (DIBAF) in Hexane-THF^a at 25 °C^b

Epoxides	Time (h)	Conversion (%) ^c	Product	Purity (%)
1,2-epoxybutane	6	87	1-butanol	100
	12	93	1-butanol	100
	24	100	1-butanol	100
1,2-epoxyoctane	6	78	1-octanol	100
	12	86	1-octanol	100
	24	96	1-octanol	100
	48	100	1-octanol	100
Styrene oxide	6	94	2-phenylethanol	100
	12	99	2-phenylethanol	100
	24	100 ^d	2-phenylethanol	100
α -methylstyrene oxide	6	98	2-phenyl-1-propanol	100
	12	100	2-phenyl-1-propanol	100
	24	100	2-phenyl-1-propanol	100
<i>trans</i> - β -methylstyrene oxide	1	96	1-phenyl-2-propanol	100
	3	100	1-phenyl-2-propanol	100

^aA mixture of hexane-THF (1:1). ^bTen % excess reagent utilized: 0.5 M concentration. ^cDetermined by GC using a suitable internal standard. ^dSeventy six % of 2-phenylethanol was isolated from the 40 mmol scale of reaction mixture.

(5.5 mmol) in hexane⁸ were injected.⁹

Then the flask was immersed into a water bath and the mixture was maintained at 25 °C. At the appropriate reaction periods (6 h and 24 h) an aliquot of 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 94% at 6 h-period and 100% at 24 h-period. The product was further confirmed by GC-Mass spectrometer.

In conclusion, *Al*-fluorodiisobutylalane (**DIBAF**) provides the regioselective cleavage of phenyl- or alkyl-substituted epoxides to the less substituted alcohols resulting from anti ring opening. Especially, the reagent attacks only at the phenyl-substituted site where both phenyl and alkyl groups are attached separately at each carbon site of epoxy ring. Further, the inertness of **DIBAF** toward most other functional groups except aldehyde and ketone functions recommends the reagent when chemoselectivity is important.¹¹

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References and Notes

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2. The reaction is very slow in hexane alone as a solvent, but the addition of equivalent of THF accelerates the reduction rate tremendously.
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7. All glassware used was dried thoroughly in an oven, assembled hot, and cooled under a stream of dry Nitrogen prior to use.
8. **DIBAF** in hexane was used as purchased from Aldrich, or prepared from the reaction of diisobutylaluminum hydride and dry HF.
9. All reactions and manipulations of air- and moisture-sensitive material were carried out using standard techniques for handling air-sensitive materials.¹⁰ THF was dried over sodium-benzophenone ketyl and distilled. All liquid materials were transferred by using hypodermic syringes.
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11. See the review paper, some references cited in: Cha, J. S. *Bull. Korean Chem. Soc.* **2007**, *28*, 2162.