Reaction of Epoxides with Boron Triisopropoxide. The Meerwein-Ponndorf-Verley Type Reduction of Boron Alkoxides. 2[1]

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In the preceding communication,[1] we reported that the reaction of some carbonyl compounds with boron triisopropoxide follows exactly the Meerwein-Ponndorf-Verley (MPV) reduction procedure to produce the corresponding alcohols. To our knowledge, this is the first example that boron alkoxides react with carbonyl compounds in a MPV type fashion. This interesting outcome led us to examine other organic functionalities. In the course of systematic study, we found that the reagent reacts with epoxides to produce the ring-opened reduction products. This paper described such a MPV type reduction of epoxides.

First of all, we examined the reaction conditions: the concentration of 0.5 M in reagent appeared to afford the best yield. In addition to that, the solvent effect on the reduction was examined and the results are summarized in Table 1. Among the solvents examined, dimethylformamide appeared the best in conversion yield, whereas tetrahydrofuran (THF) showed the highest selectivity. Accordingly, we chose the reaction conditions of a 0.5 M solution in refluxing THF under a stream of dry nitrogen for further reactions.

As listed in Table 2, boron triisopropoxide showed actually no reactivity toward aliphatic epoxides examined. On the other hand, aromatic epoxides were reactive to reduction in refluxing THF. In general, one mole of boron triisopropoxide can reduce only one mole of epoxy compound even in the presence of exess compound: it usually is capable of involving only one isopropoxy moiety among three in a molecule of reagent in this reduction, except for the case of β-methylstyrene. One mole of the reagent reduced two moles of compound (*i.e.*, the yield of 66% corresponds to the reduction of 2 equiv. among 3 equiv. of compound reacted). In the reactions used equimolar amounts of epoxide and reagent, the yields range from 84 to 98% in refluxing for 7 days.

Table 1. Effect of Solvent on the Reduction of Styrene Oxide with Boron Triisopropoxide[a,b] under Stream of Nitrogen

Solvent	Time (d)	Conversion (%)[c]	Product	Ratio[d]
tetrahydrofuran	3	24	2-phenylethanol	99
			1-phenylethanol	1
toluene	1	11		
	3	24	2-phenylethanol	94
			1-phenylethanol	6
dimethylformamide	1	33		
	3	45	2-phenylethanol	91
			1-phenylethanol	9

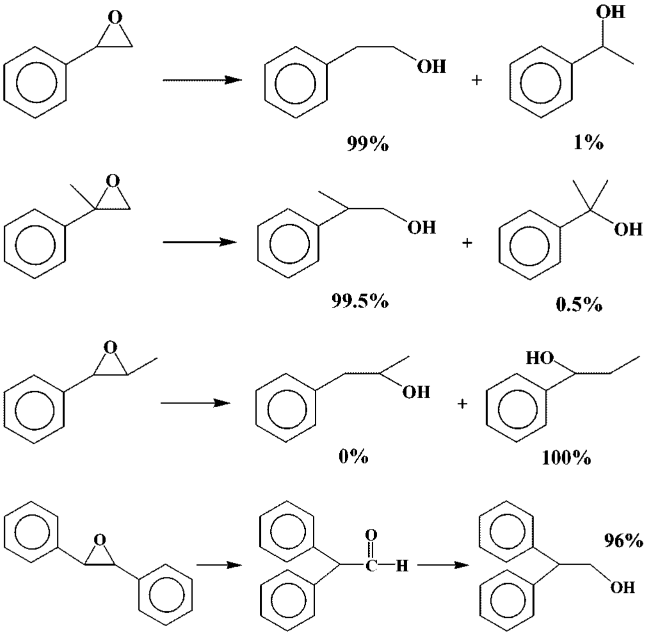
[a]Ratio of compound to reagent is 3 : 1. [b]In refluxing solvent. [c]Analyzed by GC with tridecane as an internal standard. [d]Normalized.

Table 2. Reaction of Epoxides with Boron Triisopropoxide in Refluxing Tetrahydrofuran under Stream of Nitrogen

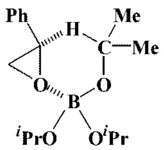
Compound	Comp /rgt	Time (d)	Conversion (%)[a]	Product	Ratio[b]
1,2-epoxybutane	3	7	0		
	1	7	0		
1,2-epoxyoctane	1	7	0		
1,2-epoxycyclohexane	1	7	0		
styrene oxide	3	7	30	2-phenylethanol	99
				1-phenylethanol	1
	1	0.25	18		
		1	60		
		3	89		
		7	98	2-phenylethanol	99
				1-phenylethanol	1
α-methylstyrene oxide	3	7	31	2-phenyl-1-propanol	92
				2-phenyl-2-propanol	8
	1	7	94	2-phenyl-1-propanol	99.5
				2-phenyl-2-propanol	0.5
trans-β-methyl-styrene oxide	3	7	66	1-phenyl-2-propanol	0
				1-phenyl-1-propanol	100
	1	7	89	1-phenyl-2-propanol	0
				1-phenyl-1-propanol	100
α-phenylstyrene oxide	3	7	31	2,2-diphenylethanol	91
				1,1-diphenylethanol	9
	1	7	88	2,2-diphenylethanol	92
				1,1-diphenylethanol	8
trans-stilbene oxide	3	7	28	2,2-diphenylethanol	88
				1,2-diphenylethanol	12
	2	7	54	2,2-diphenylethanol	96
				1,2-diphenylethanol	4
	1	7	84	2,2-diphenylethanol	96
				1,2-diphenylethanol	4

[a]Analyzed by GC with a suitable internal standard and the yields are based on the amount of epoxides applied. [b]Normalized.

In the selectivity sense, the reagent shows a very high regioselectivity of 96-100% in opening the epoxy ring. The reagent usually attacks the carbon site where phenyl group is attached, except for the case of *β*-methylstyrene. The reaction of *trans*-*β*-methylstyrene yielded 1-phenyl-1-propanol in a 100% selectivity. The reaction of *trans*-stilbene oxide exhibited an interesting result to produce 2,2-diphenylethanol and 1,2-diphenylethanol in a ratio of 96 : 4. This result indicates that the oxide readily undergoes rearrangement with the migration of a phenyl group under the reaction conditions. Thus, boron triisopropoxide seems to involve the reaction as a Lewis acid to lead the epoxide to be rearranged, and followed by the MPV type reduction of the resultant aldehyde.



In a similar to the reaction of carbonyl compounds with aluminum triisopropoxide,[2] the reaction of epoxides with boron triisopropoxide seems to involve the formation of a coordination complex and followed by the hydride transfer *via* a cyclic transition state. The *β*-hydrogen to the boron atom attacks preferentially the phenyl group-attached carbon atom of the epoxy ring, which possesses more positive charge.



Such an anti-Markovnikov reductive opening of epoxides has previously been achieved with borane-THF in the presence of boron trifluoride.[3] However, attention should be called to an additional major advantage of the present procedure. Boron triisopropoxide is a much milder reducing agent than BH_3-THF[4] and almost all functional groups except aldehydes and ketones will tolerate exposure to the reagent under the recommended reaction conditions. This makes possible the anti-Markovnikov reductive opening of aryl epoxides containing a large variety of substituents in the molecule.

The following procedure is representative. Into a 50-mL flask with a side-arm equipped with a 50-cm Vigreux column, the upper end of which is connected to a downward-directed, water-cooled condenser leading to a mercury bubbler,[5] 5 mL of a 0.8 M solution of boron triisopropoxide (4 mmol) in THF,[6] 2 mL of a 2.0 M solution of styrene oxide (4 mmol) in THF, tridecane (2 mmol) as an internal standard and 1 mL of THF were injected.[7] A slow stream of dry nitrogen just over the surface of reaction mixture in order to remove the acetone formed using a 6-inch needle was allowed while the reaction mixture was stirring. Then the flask was immersed into an oil bath and the mixture was maintained under a gentle reflux. After the 72-hour reaction, the reaction mixture was hydrolyzed with water. The aqueous phase was saturated with K_2CO_3 and the organic phase was dried over anhydrous $MgSO_4$. GC analysis of the organic layer revealed the presence of 2-phenylethanol and 1-phenylethanol in a ratio of 99 : 1 in a total chemical yield of 98%. The products were further confirmed by GC-Mass spectrometer. The other results in appropriate time intervals were listed in Table 2.

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References and Notes

1. The preceding article: Cha, J. S.; Park, J. H. *Bull. Korean Chem. Soc.* **2002**, *23*, 1051.
2. (a) Meerwein, H.; Bock, B.; Kirschnick, B.; Lenz, W.; Migge, A. *J. Prakt. Chem.* **1936**, *147*, 211. (b) Woodward, R. B.; Wendler, N. L.; Brutschy, F. J. *J. Am. Chem. Soc.* **1945**, *67*, 1425.
3. Brown, H. C.; Yoon, N. M. *Chem. Commun.* **1968**, 1549.
4. Brown, H. C.; Heim, P.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 1637.
5. All glassware used was dried thoroughly in an oven, assembled hot, and cooled under a stream of dry nitrogen prior to use.
6. Boron triiopropoxide was prepared by reaction of 10 mL of a 1.0 M solution in THF (10 mmol) and 2.0 g of isopropyl alcohol (33 mmol, 10% excess) at room temperature. See ref 1.
7. All reactions and manipulations of air- and moisture-sensitive materials were carried out using standard techniques for handling air-sensitive materials.[9] THF was dried over sodium-benzophenone ketyl and distilled. All liquid materials were transferred by using hypodermic syringes.
8. In cases where a slow stream of dry nitrogen was not employed, the ring-opening reactions of epoxides examined were very sluggish and the conversion yields were much lower.
9. Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. *Organic Synthesis via Boranes*; Wiley-Interscience: New York, N. Y., 1975.