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Stereospecific Ring-Opening Reaction of Epoxy Sulfides with Phenylboronic Acid via Episulfonium Ions

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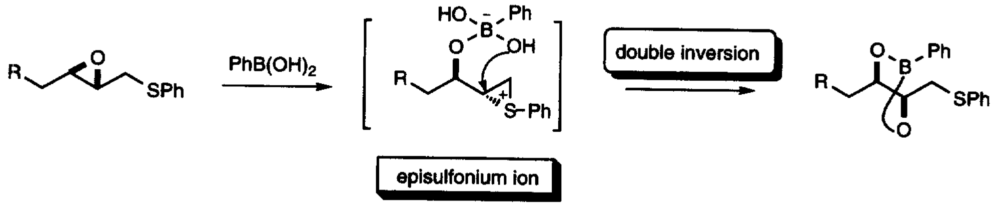
Abstract: The ring-opening reaction of epoxy sulfides with phenylboronic acid in benzene has been demonstrated to occur stereospecifically via episulfonium ions, i.e., with double inversion of configuration, giving rise to phenylboronic esters of 2,3-diols in quantitative yields.

Stereoselective epoxide-opening reactions have been known as one of the most important reactions in organic synthesis and are widely used as key reactions in natural product synthesis.[1] Although a variety of regio- and/or stereo-selective ring-opening reactions of epoxides have been reported so far,[1] no synthetic method for vicinal diols via stereoselective epoxide-opening with double inversion of configuration has been known. We have developed such methodology which involves stereospecific ring-opening reaction of epoxy sulfides with phenylboronic acid via episulfonium ions.[2]

Although phenylboronic acid itself has been little used as a Lewis acid in organic synthesis due to its extremely weak Lewis acidity,[3] we assumed that the ring-opening reaction of epoxy sulfides with phenylboronic acid presumably occurs stereoselectively via episulfonium ions as shown in Scheme 1, i.e., with double inversion of configuration, to give phenylboronic esters of 2,3-diols. Indeed, this type of reaction occurred cleanly and stereospecifically by the use of 1.3 equiv. of phenylboronic acid in hot benzene, giving rise to boronate esters of 2,3-diols



Scheme 1

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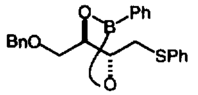
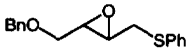
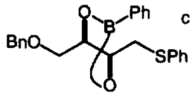
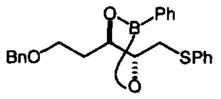
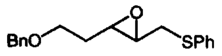
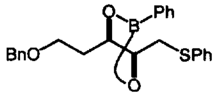
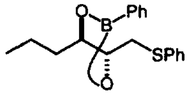
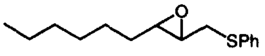
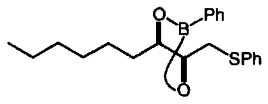
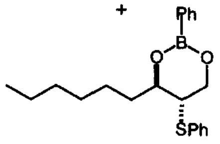
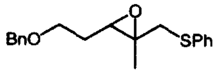
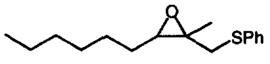
Table 1. Reaction of Epoxy Sulfides with Phenylboronic Acid in Benzene[a]

Entry	Substrate	Conditions		Product	Isolated Yield (%)	Diastereo-selectivity[b]
		Temp. (°C)	Time (h)			
1		70	3		99	>99
2		70	20	 [c]	100	>99
3		70	13.5		97	>99
4		70	17.5		98	>99
5		70	21		98	>99
6		BF$_3$•Et$_2$O (1 eq) 60	48	 + 	30 [d] 70 [d]	
7		70	72	— [e]		
8		70	72	— [e]		

[a] The reaction was carried out using 1.3 equiv. of PhB(OH)$_2$.

[b] The diastereoselectivity was determined by ^{1}H NMR (270 MHz).

[c] Susceptible to silica gel.

[d] The yield was determined by ^{1}H NMR (270 MHz).

[e] Starting material was recovered unchanged.

in quantitative yields.

The results are summarized in Table 1. As shown, the reaction of the disubstituted epoxy sulfides with phenylboronic acid proceeded stereospecifically via episulfonium ions giving rise to the corresponding phenylboronic esters of vicinal diols in quantitative yields regardless of the stereochemistry of epoxides (entries 1 ~ 5). The stereochemistry of the products was unambigously confirmed by comparison with that of authentic samples.[4] Consequently, all the reactions of entries 1 ~ 5 have been demonstrated to have occurred via episulfonium ions, i.e., with complete double inversion of configuration, as shown in Scheme 1. It should be noted that the stereochemistry of the products derived from the present method is contrary to that of the products formed by the Payne rearrangement-opening reactions of 2,3-epoxy alcohols with thiolates which has been discovered by Sharpless.[5] On the other hand, 1-phenylthiononene-2,3-oxide did not react under the same conditions, while the reaction gradually proceeded in the presence of 1 equiv. of $BF_3{\cdot}Et_2O$ at 60 °C giving rise to an inseparable mixture of 2,3- and 1,3-boronates in a 3 : 7 ratio (entry 6). The data of Table 1 shows the following trends: 1) The reaction of *cis*-epoxy sulfides generally proceeds faster than that of the corresponding *trans*-analogs, presumably due to ease of accessibility of phenylboronic acid to the *cis*-epoxides; 2) Substrates having an ether oxygen function in the side chain react faster than those bearing no oxygen atom by the chelation effect (entries 3 and 5, and 4 and 6).

In contrast with the disubstituted epoxy sulfides, trisubstituted ones did not react under the same conditions and the starting materials were recovered unchanged (entries 7 and 8), which may be ascribed to the weak Lewis acidity of phenylboronic acid.

Noteworthy is that the 2,3-*anti*- and the 2,3-*syn*-phenylboronates thus obtained exhibited characteristic ^1H NMR spectra, respectively; namely, C_1 methylene protons adjacent to the thiophenyl group in the 2,3-*anti*-phenylboronates appear as a close pair of double of doublets (J=13.5~14.0, 6.0~7.5 Hz) at ca. 3.15 and 3.25 ppm, respectively, while those in the 2,3-*syn*-series appear as a separate pair of double of doublets at 3.05-3.10 ppm (J=13.5~14.0, 7.0~7.6 Hz) and 3.30-3.35 ppm (J=13.5~14.0, 5 Hz), respectively. Moreover, the C_2 proton in the 2,3-*anti*-phenylboronates appears always in the lower field (ca. 4.70-4.75 ppm) than the corresponding C_2 proton (4.30-4.40 ppm) in the 2,3-*syn*-phenylboronates. Therefore, the stereochemistry of the products is easily determined by their ^1H NMR spectra.

Since the optically active epoxy sulfides are readily available from the corresponding epoxy alcohols by sulfenylation with diphenyl disulfide[6] and the ring-opening reaction of epoxy sulfides with phenylboronic acid proceeds regio- and stereo-specifically to give phenylboronic esters in quantitative yields, the present method should provide an excellent access to chiral diols, triols and polyols.

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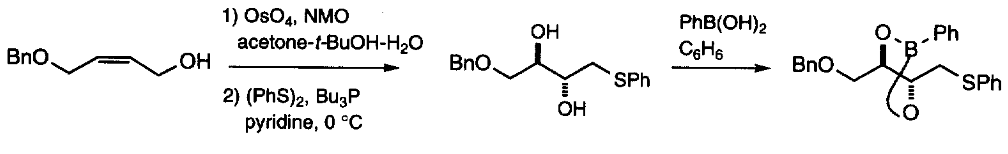
4 Authentic samples can be readily prepared from the starting allylic alcohols by the three-step reaction sequence:1) osmylation; 2) sulfenylation of the resulting triols with diphenyl disulfide; 3) boronation of 2,3-diols with phenylboronic acid in benzene, in good overall yields.



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