

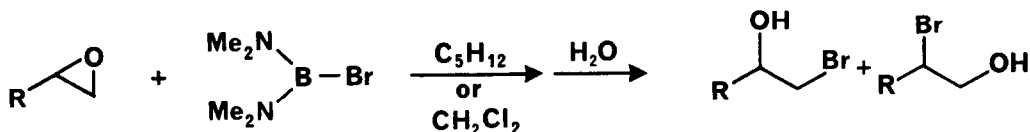
CONVERSION OF EPOXIDES TO BROMOHYDRINS BY
B-BROMOBIS(DIMETHYLAMINO)BORANE

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Abstract: Reaction of the title reagent with 1-alkene oxides regioselectively yields the corresponding 1-bromo-2-alkanols, while the more substituted bromide predominates in the cases of styrene oxide and 1-methylcyclohexene oxide.

Haloboranes, such as boron tribromide,¹ are well known as highly reactive reagents for ether cleavage. Recently, a number of monofunctional haloborane reagents (R_2BX) have been reported in which two of the electronegative halide substituents have been removed, resulting in lower reactivity.² Moderated electrophiles of this type are of particular interest for selective cleavage of dialkyl ethers, including protected alcohols, and for reactions with sensitive substrates, such as epoxides. The resonance stabilization enjoyed by aminoboranes³ suggests that a B-halodiaminoborane might function as a mild and selective reagent for cleaving ethers. We have therefore examined the conversion of epoxides to bromohydrins using B-bromobis(dimethylamino)borane (BDB),⁴ as shown below.



We have found that BDB reacts readily with a large variety of epoxides to afford the corresponding bromohydrins,⁵ as shown in the **Table**. The best yields were obtained when the epoxide was added to a solution of the reagent in pentane at -78°C , then the reaction mixture was stirred at room temperature. Under these conditions, aliphatic terminal epoxides reacted regioselectively, mainly affording the primary bromide (1-bromo-2-alkanol). Reaction of BDB with the TBS, TBDPS or MOM ethers of 5-hexen-1-ol oxide resulted in selective cleavage of the epoxide functionality. In the case of styrene oxide the secondary bromide predominates, while *exo* norbornene oxide yields a mixture of vicinal and rearranged bromohydrins. Cyclohexene oxide and 1-methylcyclohexene oxide opened cleanly to the trans bromohydrins, with the tertiary bromide forming the major product in the latter case. The effect of changing the solvent from pentane to methylene chloride was examined in a few of the cases, leading to lower overall yields and increased proportions of the more substituted bromide, as shown in the **Table** for propylene oxide and 1-methylcyclohexene oxide.

TABLE: REACTIONS OF EPOXIDES WITH B-BROMOBIS(DIMETHYLAMINO)BORANE (BDB).⁵




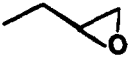


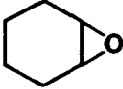

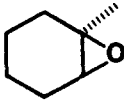


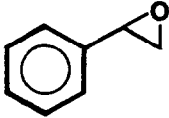
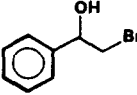
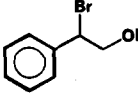
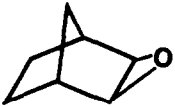
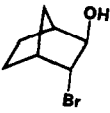
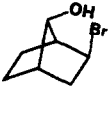
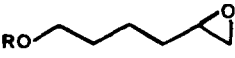
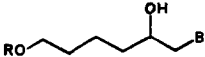
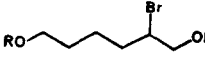
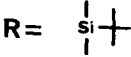
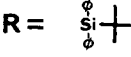
<u>Epoxide</u>	<u>Conditions</u> ^(a)	<u>Product(s)/(Ratios)</u> ^(b)	<u>Yield,%</u> ^(d)	<u>(Ref.)</u>
	Standard 0°C CH ₂ Cl ₂	  (89:11) (77:23) (13:87)	84 69 27	(6,7,10)
	Standard 25°C Std. (<u>in situ</u>) ^(f)	  (92:8) (92:8) (87:13)	90 54 80	
	Standard		91	(7,11)
	Standard CH ₂ Cl ₂	  (40:60) ^(c) (10:90)	70 56	(7,12)
	Standard	  (18:82) ^(c)	75 ^(e)	(7,12,13)
	Standard	  (55:45) ^(c)	68 ^(e)	(14,15)
	Standard	 		
R =  (TBS)		> (92:8)	67	
R =  (TBDPS)		> (92:8)	74	
R = CH ₂ OCH ₃ (MOM)		> (92:8)	66	(16)

Table (continued):

- (a) Standard conditions: epoxide/BDB (1:1.6); addition was at -78°C then the reaction mixture was stirred at room temperature overnight in pentane under N_2 . Exceptions are indicated.
- (b) Determined by glc, except as indicated.
- (c) 300 MHz ^1H NMR.
- (d) Isolated yields for bromohydrins which were free of impurities by glc, ^1H and/or ^{13}C NMR, except as indicated.
- (e) Crude yield.
- (f) See experimental.

The observed products are consistent with the "borderline $\text{S}_{\text{N}}2$ " mechanism typically proposed for electrophile-assisted epoxide cleavage reactions.⁶ Product regio-chemistry is sensitive to solvent polarity, as expected. On the other hand, norbornene oxide yields a mixture of the expected vicinal bromohydrin and an isomeric bromoalcohol, apparently resulting from carbocationic rearrangement.⁶

It is apparent from our results that BDB, though of moderated reactivity relative to BBr_3 , is a potent electrophile. Greater amounts of the more hindered bromide are obtained with BDB than with dilithium tetrabromonickelate,⁷ which was reported to be unreactive with epoxycholestane.⁸ BDB should serve as a useful alternative to trimethylsilyl halides, which yield O-silyl halohydrins,⁹ and also to hydrogen halides, for which the corresponding dibromide is often observed as a reaction by-product.¹⁰ It is important to note that BDB is compatible with common alcohol protecting groups, such as TBS, TBDPS and MOM, whereas trimethylsilyl bromide cleaves MOM ethers at low temperature.¹⁶ In the last case, BDB was found to be superior even to very mildly acidic epoxide cleavage conditions.¹⁷ Finally, the reagent may be prepared in good yield from boron tribromide and tris(dimethylamino)-borane,¹⁸ or BDB may be generated *in situ*, as described in the following procedure.

Experimental: Boron tribromide (2.31 mmole) was added dropwise by syringe to a vigorously stirred solution of tris(dimethylamino)borane (4.75 mmole) in 8 mL of dry pentane at -78° under N_2 . The mixture was warmed to room temperature and filtered to remove by-product amine hydrobromide salts. The BDB solution was cooled to -78°C and a solution of anhydrous 1,2-epoxybutane (3.47 mmole) in 2 ml of dry pentane was added dropwise. The reaction mixture was slowly warmed to room temperature and stirring under N_2 was continued overnight (12 h). Finally, the reaction mixture was treated with several mL of phosphate buffer (pH 7.0) and extracted with diethyl ether. The combined ether extracts were dried over MgSO_4 , filtered and the solvent was removed to afford the product bromohydrins (see Table).

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