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LETTERS

Highly efficient cleavage of epoxides catalyzed by $B(C_6F_5)_3$[†,‡]

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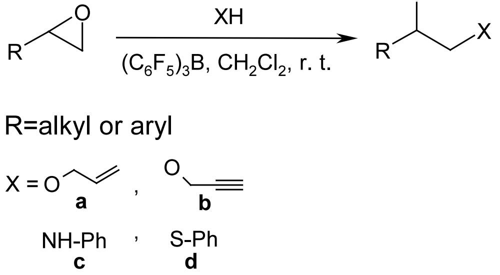
Abstract—A highly effective protocol for ring opening of epoxides with allyl and propargyl alcohols, aniline and thiophenol in the presence of catalytic amounts of $B(C_6F_5)_3$ has been developed. Benzyl, tetrahydropyranyl, *tert*-butyldimethyl silyl protecting groups were stable under the reaction conditions. © 2002 Elsevier Science Ltd. All rights reserved.

Lewis acid mediated cleavage of epoxides with various nucleophiles such as alcohols, amines and thiols is an important transformation in organic synthesis[1] which liberates a free hydroxy group as a handle for further manipulations. The Lewis acids used include metal and lanthanide halides[2–4] and triflates,[5,6] besides others.[7–9] However, the reactions reported are not general and are incompatible with most functional groups, often provide only moderate yields of the products, sometimes require at least stoichiometric amounts of Lewis acid or reflux conditions. Accordingly, the development of a more general, efficient and environmentally benign catalytic methodology for the cleavage of epoxides is desired. Tris(pentafluorophenyl) borane, $[B(C_6F_5)_3]$ has been recently explored as a non-conventional Lewis acid which operates via hypercoordination at the boron center.[10] As part of an ongoing project, we required a general protocol for the ring opening of epoxides with various heteroatoms viz., O, N and S in a combinatorial fashion to generate libraries of β-hydroxy ethers, amines and sulfides. We found that tris(pentafluorophenyl) borane, $[B(C_6F_5)_3]$ was an efficient catalyst for the aforementioned transformation (Scheme 1). $B(C_6F_5)_3$ is a convenient, commercially available non-traditional Lewis acid, which has recently gained prominence.[11] The results pertaining to this transformation are documented herein.

In the first case, styrene oxide was treated with allyl alcohol and $B(C_6F_5)_3$ in anhydrous CH_2Cl_2 at room temperature to give the corresponding allyloxy alcohol **1a** in 92% yield. This result prompted us to explore the possibility of opening epoxides with other nucleophiles viz., propargyl alcohol, aniline and thiophenol. Accordingly styrene oxide was treated with propargyl alcohol, aniline and thiophenol separately in the presence of $B(C_6F_5)_3$ to yield the corresponding propargyloxy alcohol **1b**, amino alcohol **1c** and thio alcohol **1d** in 90, 85 and 84% yields, respectively (entry 1). This success has encouraged us to exploit the generality of the reaction to a few other epoxides with allyl and propargyl alcohols, aniline and thiophenol (Table 1). Cyclopentene oxide gave the corresponding cleavage products **2a**, **2b**, **2c** and **2d** with allyl and propargyl alcohols, aniline and thiophenol 85, 81, 88 and 88% yields, respectively (entry 2). Similarly, benzyloxy propene oxide and benzyloxy butene oxide underwent epoxide cleavage using these reaction conditions (entries 3 and 4). Naphthyloxy propene oxide was also opened with all four nucleophiles under identical reaction conditions to give the corresponding cleavage products **5a**, **5b**, **5c** and **5d** in 95, 90, 90 and 93% yields, respectively. The *tert*-butyldimethylsilyl (TBS) protected epoxide was cleaved to yield the corresponding opening products **6a**, **6b**, **6c** and **6d** in >80% yield, leaving the TBS protecting group



Scheme 1.

Keywords: amino alcohols; catalysts; cleavage reactions; epoxides; hydroxy ethers; hydroxy sulfides.

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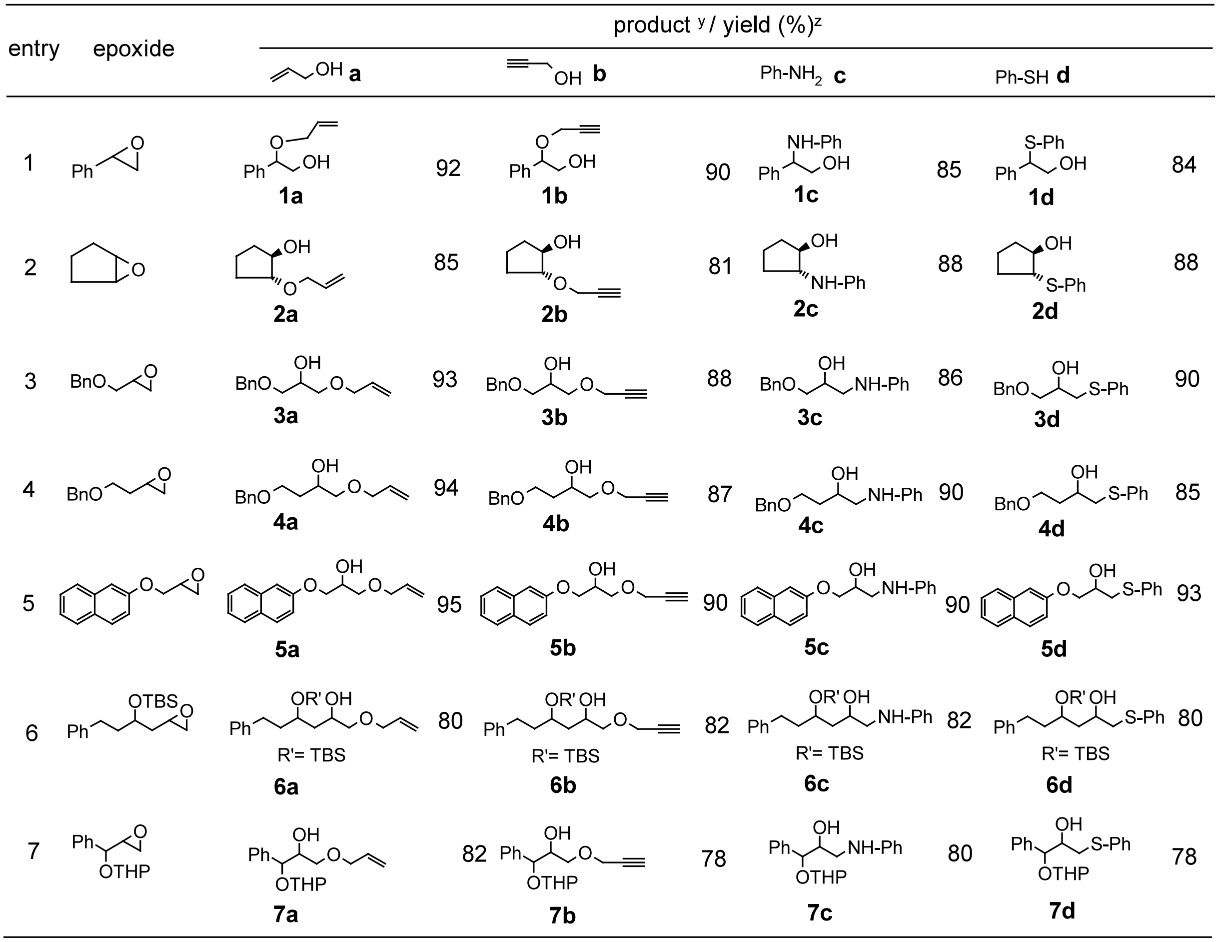
Table 1. $B(C_6F_5)_3$-catalyzed cleavage of epoxides with nuceophiles **a**–**d**



entry	product ^{y} / yield (%)^z: a	yield	b	yield	Ph-NH$_2$ c	yield	Ph-SH d	yield
1	**1a**	92	**1b**	90	**1c**	85	**1d**	84
2	**2a**	85	**2b**	81	**2c**	88	**2d**	88
3	**3a**	93	**3b**	88	**3c**	86	**3d**	90
4	**4a**	94	**4b**	87	**4c**	90	**4d**	85
5	**5a**	95	**5b**	90	**5c**	90	**5d**	93
6	R'= TBS **6a**	80	R'= TBS **6b**	82	R'= TBS **6c**	82	R'= TBS **6d**	80
7	**7a**	82	**7b**	78	**7c**	80	**7d**	78

^{y} reaction times are generally 2-4 hours

^{z} all yields calculated after purification by column chromatography

intact (entry 6). In addition we observed that the tetrahydropyranyl (THP) ether was also stable to the present protocol (entry 7).

In summary, we have developed an effective protocol for epoxide cleavage with allyl and propargyl alcohols, aniline and thiophenol in the presence of catalytic amounts of the unusual Lewis acid, $B(C_6F_5)_3$. Various epoxides underwent the epoxide opening reaction smoothly, under mild conditions to give the corresponding cleavage products[12] in high yields. The acid labile protecting groups TBS and THP were stable under these reaction conditions.

Typical experimental procedure: To a stirred solution of styrene epoxide **1** (8.3 mmol) in dry CH_2Cl_2 was added $B(C_6F_5)_3$ (25 mg, 5 mol%), allyl alcohol **a** (8.3 mmol) and the reaction mixture was stirred at room temperature for 2 h. After completion of the reaction (monitored by TLC) the solvent was evaporated and the crude product was purified by column chromatography to afford the pure product **1a** (1.36 g, 92%).

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12. (a) In the case of entry 1 and 5, the cleavage products were confirmed by acetylation and oxidation; (b) **Spectral data for selected products**: (**3d**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.4–7.12 (m, 10H), 4.5 (s, 2H), 3.94–3.8 (m, 1H), 3.58–3.46 (m, 2H), 3.1–3 (m, 2H); IR (neat): 3623, 2876, 2832, 866 cm^{-1}; EIMS (m/z): 274 (M$^+$), 123, 91, 43. (**5b**): ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.74–7.6 (m, 3H), 7.45–7.2 (m, 2H), 7.18–7.02 (m, 2H), 4.42–4.36 (m, 1H), 4.22 (d, J = 1.2 Hz, 2H), 4.18–4.1 (m, 2H), 3.8–3.66 (m, 2H), 2.42–2.38 (m, 1H); IR (KBr): 3622, 3312, 2132, 766 cm^{-1}; EIMS (m/z): 256 (M$^+$), 144, 115, 69. (**6b**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.36–7.1 (m, 5H), 4.26–4.18 (m, 1H), 3.98–3.4 (m, 5H), 2.65 (t, J = 8.5 Hz, 2H), 2.42–2.34 (m, 1H), 1.96–1.6 (m, 4H), 0.92 (s, 9H), 0.1 (s, 6H); IR (neat): 3624, 3318, 2140, 1276, 853 cm^{-1}; EIMS (m/z): 362 (M$^+$), 249, 117, 91. (**7a**): ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.4–7.2 (m, 5H), 5.98–5.74 (m, 1H), 5.3–5.06 (m, 3H), 4.78 (d, J = 4.3 Hz, 1H), 4.04–3.92 (m, 3H), 3.7–3.58 (m, 2H), 3.5–3.36 (m, 2H), 1.78–1.52 (m, 6H); IR (neat): 3626, 2890, 1436, 935 cm^{-1}; EIMS (m/z): 191 (M$^+$–101), 101, 85, 41.