Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 47 (2006) 4457–4460
Tetrahedron Letters

Highly regioselective ring opening of epoxides and aziridines using (bromodimethyl)sulfonium bromide☆

Biswanath Das,* Maddeboina Krishnaiah and Katta Venkateswarlu

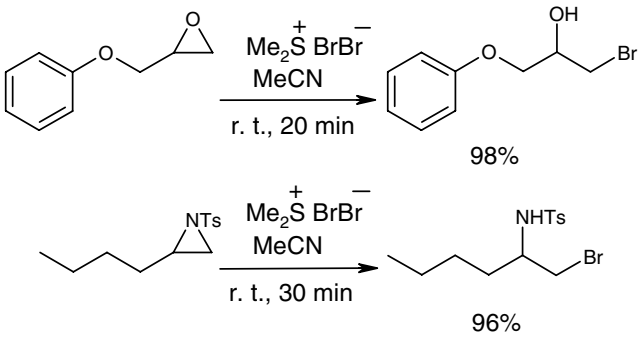
Organic Chemistry Division-I, Indian Institute of Chemical Technology, Uppal Road, Hyderabad 500 007, Andhra Pradesh, India

Received 3 March 2006; revised 3 April 2006; accepted 10 April 2006
Available online 11 May 2006

Abstract—Epoxides and aziridines undergo ring opening efficiently with (bromodimethyl)sulfonium bromide at room temperature to form the corresponding β-bromohydrins and β-bromoamines, respectively. The conversions are highly regioselective and afford the products in excellent yields within a short period of time.

Epoxides[1] and aziridines[2] are versatile intermediates in organic synthesis. They can be easily prepared and cleaved with different nucleophiles, leading to the formation of regio- and stereoselective ring opened products. Vicinal halohydrins and haloamines are useful precursors in the synthesis of halogenated marine natural products and other bioactive molecules.[3] The ring opening of epoxides to form halohydrins can generally be carried out with halogens,[4a,b] hydrogen halides[4c] and metal halides.[4d,e] Aziridine rings can also be opened with metal halides.[3b,4e] However, many of the reported methods suffer from drawbacks, such as unavailability of the reagents, long reaction times, unsatisfactory yields, formation of side products and harsh reaction conditions. Thus, a mild and effective method suitable for opening of both epoxides and aziridines is highly desirable.

In continuation of our work[5] on the development of useful synthetic methodologies, we have observed that (bromodimethyl)sulfonium bromide ($Me_2S^+BrBr^-$)[6] can be utilized efficiently for the cleavage of epoxides and aziridines to produce β-halohydrins and β-haloamines, respectively (Scheme 1).



Scheme 1.

Various epoxides and *N*-tosylaziridines underwent ring cleavage easily with $Me_2S^+BrBr^-$ in MeCN at room temperature (Table 1).[7] The desired products were formed in excellent yields and no side products were observed. The reaction times were short—for opening of epoxides it took only 20 min, while opening of aziridines only 30 min was required. The cleavage of both epoxides and aziridines took place with high regioselectivity. 2-Arylepoxides and *N*-tosyl-2-arylaziridines afforded the products of opening at the benzylic position, while 2-alkylepoxides and *N*-tosyl-2-alkylaziridines gave the products formed by cleavage at the terminal position. These observations demonstrated that in the former case, the products are generated through the formation of a stabilized benzylic cation during the reaction and in the second case, they are formed by predominant attack of the halide ion on the less hindered carbon of the epoxide or aziridine. The structures of

Keywords: Epoxide; Aziridine; (Bromodimethyl)sulfonium bromide; Regioselectivity.

☆ Part 89 in the series, 'Studies on novel synthetic methodologies'; IICT Communication No. 060332.

* Corresponding author. Tel./fax: +91 40 7160512; e-mail: biswanathdas@yahoo.com

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.04.059

Table 1. Ring opening of epoxides and aziridines with $Me_2S^+BrBr^-$ [a]

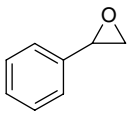
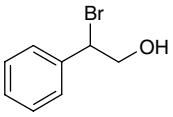
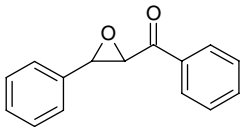
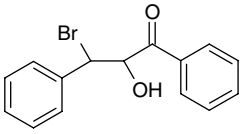
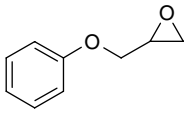
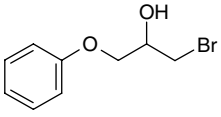
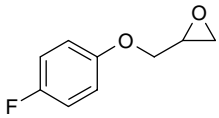
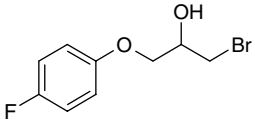
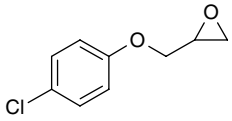
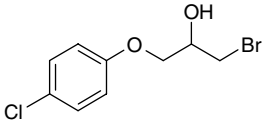
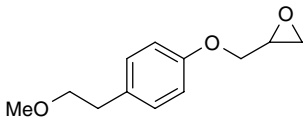
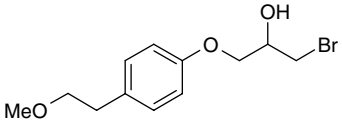
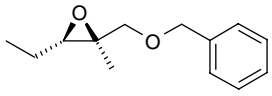
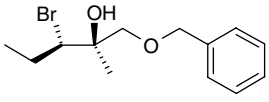
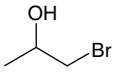
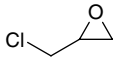
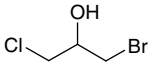
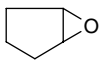
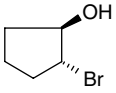
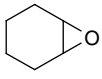
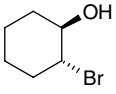
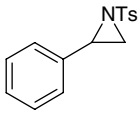
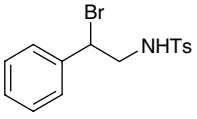
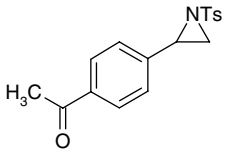
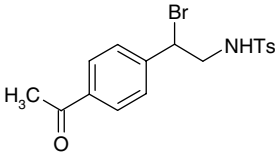
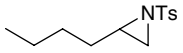
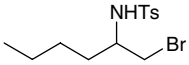
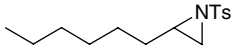
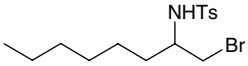
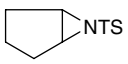
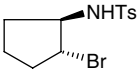
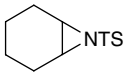
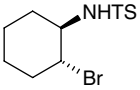
Entry	Epoxide/aziridine **1**	Product **2**	Isolated yield (%)
a			98
b			84
c			98
d			98
e			98
f			98
g			78
h			95
i			98
j			98
k			98
l			84
m			84

Table 1 (*continued*)

Entry	Epoxide/aziridine **1**	Product **2**	Isolated yield (%)
n			96
o			95
p			98
q			98

[a] The structures of the products were established from their spectral (^{1}H and ^{13}C NMR and MS) data.

the products were established from their spectral (^{1}H and ^{13}C NMR and MS) data.[7]

The data for known products were compared with those reported in the literature.[4] In the EIMS, **2b** showed significant peaks at m/z 171 and 169 (each 7%) (resulting from benzylic cleavage), while **2g** demonstrated a peak at m/z 165 (5%) (resulting from β-cleavage with respect to the hydroxyl group) which suggested the regiochemistry of these two compounds. The regiostructures of other products were also similarly determined from their mass fragmentation patterns along with ^{1}H NMR spectral values. The regiochemistries of **2b** and **2g** were further confirmed from 2D-NMR and chemical evidence. Thus, the HMBC spectrum of **2b** showed that the proton of the hydroxyl group (δ 3.56, 1H, d, $J = 6.0$ Hz) was correlated with the carbonyl group (δ 196.8) and also with the benzylic carbon (δ 53.2). Similarly, the HMBC spectrum of **2g** revealed that the hydroxyl group proton (δ 2.56, 1H, br s) correlated with the carbons of a methyl group (δ 18.5), $C(OH)CH_3$, a $–CH_2O–$ group (non-benzylic) (δ 74.9) and a –CHBr– group (δ 56.3). The ^{1}H–^{1}H COSY spectrum of **2g** indicated the absence of a proton at the adjacent carbon atom with respect to this hydroxyl group. Compound **2g** did not afford an acetylation product on overnight treatment with Ac_2O and pyridine at room temperature, suggesting it to be a *tertiary* alcohol.

Ring-opening of bicyclic epoxides and aziridines with (bromodimethyl)sulfonium bromide afforded products whose stereochemistry was found to be trans (^{1}H NMR spectra).[7]

(Bromodimethyl)sulfonium bromide[6] is an inexpensive reagent. It works under mild reaction conditions and was employed earlier to carry out some synthetic transformations, mainly as a catalyst. In the present case, it has been applied efficiently for cleavage of both epoxides and aziridines with equal ease. No additional catalyst was required.

In conclusion, we have described a simple and efficient procedure for ring-opening of epoxides and aziridines using (bromodimethyl)sulfonium bromide at room temperature for the preparation of β-bromohydrins and β-bromoamines, respectively. The present method is associated with several advantages, such as application of an inexpensive reagent, operational simplicity, short reaction times, high yields and excellent regioselectivity. A novel useful utilization of the reagent is also disclosed.

Acknowledgements

The authors thank CSIR, New Delhi, for financial assistance.

References and notes

1. Parker, R. E.; Isaacs, N. S. *Chem. Rev.* **1959**, *59*, 737–799.
2. Kemp, J. E. G. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergomon: Oxford, 1991; Vol. 7, pp 469–513.
3. (a) Moore, R. E. In *Marine Natural Products*; Scheuer, P. J., Ed.; Academic Press: New York, 1978; Vol. 1, Chapter 2; (b) Righi, G.; Franchini, T.; Bonini, C. *Tetrahedron Lett.* **1998**, *39*, 2385–2388; (c) Babudri, F.; Fiandanese, V.; Marchese, G.; Punzi, A. *Tetrahedron* **2001**, *57*, 549–554; (d) Boukhris, S.; Souizi, A. *Tetrahedron Lett.* **2003**, *44*, 3259–3261.
4. (a) Konnaklieva, M. L.; Dahi, M. L.; Turos, E. *Tetrahedron Lett.* **1992**, *33*, 7093–7096; (b) Sharghi, H.; Eskandari, M. M. *Tetrahedron* **2003**, *59*, 8509–8514; (c) Stewart, C. A.; Vander Werf, C. A. *J. Am. Chem. Soc.* **1954**, *76*, 1259–1264; (d) Kotsuki, H.; Shimanouchi, T. *Tetrahedron Lett.* **1996**, *37*, 1845–1848; (e) Sabitha, G.; Babu, R. S.; Rajkumar, M.; Reddy, C. S.; Yadav, J. S. *Tetrahedron Lett.* **2001**, *42*, 3955–3958.
5. (a) Das, B.; Ramu, R.; Reddy, M. R.; Mahendar, G. *Synthesis* **2005**, 250–254; (b) Das, B.; Venkateswarlu, K.; Mahendar, G.; Mahendar, I. *Tetrahedron Lett.* **2005**, *46*, 3041–3044; (c) Das, B.; Majhi, A.; Banerjee, J.; Chowdhury, N.; Venkateswarlu, K. *Tetrahedron Lett.* **2005**, *46*,

7913–7915; (d) Das, B.; Majhi, A.; Banerjee, J.; Chowdhury, N.; Venkateswarlu, K. *Chem. Lett.* **2005**, *34*, 1492–1493.
6. (a) Furukawa, N.; Inoue, T.; Aida, T.; Oae, S. *J. Chem. Soc., Chem. Commun.* **1973**, 212; (b) Olah, G. A.; Vankar, Y. D.; Arvanaghi, M.; Prakash, G. K. S. *Synthesis* **1979**, 720–721; (c) Khan, A. T.; Mondal, E.; Ghosh, S.; Islam, S. *Eur. J. Org. Chem.* **2004**, 2002–2009, and references therein; (d) Kudrimoti, S.; Bommena, V. R. *Tetrahedron Lett.* **2005**, *46*, 1209–1210.
7. General procedure for ring opening of epoxides and aziridines: To a solution of an epoxide or *N*-tosylaziridine (1 mmol) in MeCN (5 mL), $Me_2S^+BrBr^-$ (1 mmol) (prepared by the reported method[6b]) was added. The mixture was stirred at room temperature for 20 or 30 min. The reaction was quenched with water (10 mL) and the mixture was extracted with EtOAc (3×5 mL). The combined organic portion was dried and concentrated. The residue was purified by column chromatography over silica gel (hexane–EtOAc, 9:1) to afford pure β-bromohydrin (or *N*-tosyl-β-bromoamine).

   The spectral and analytical data of some representative compounds are given below.

   Product **2b**: ^{1}H NMR (200 MHz): δ 7.85 (2H, d, $J = 8.0$ Hz), 7.62 (1H, t, $J = 8.0$ Hz) 7.50 (2H, t, $J = 8.0$ Hz), 7.29–7.10 (5H, m), 5.52 (1H, dd, $J = 6.0$, 2.0 Hz), 5.28 (1H, d, $J = 2.0$ Hz), 3.56 (1H, d, $J = 6.0$ Hz); ^{13}C NMR (50 MHz): δ 196.8, 135.5, 134.0, 132.2, 128.9, 128.6, 128.2, 128.0, 127.4, 77.0, 53.2; EIMS: *m*/*z* (%) 306 (2) 304 (2) ($M^{+\cdot}$), 225 (5), 171 (7), 169 (7), 135 (4), 105 (100); Anal. Calcd for $C_{15}H_{13}BrO_2$: C, 59.02; H, 4.26%. Found: C, 59.18; H, 4.34%.

   Product **2f**: ^{1}H NMR (200 MHz): δ 7.08 (2H, d, $J = 8.0$ Hz), 6.75 (2H, d, $J = 8.0$ Hz), 4.07 (1H, m), 4.02–3.92 (2H, m), 3.57–3.42 (4H, m), 3.31 (3H, s), 2.76 (2H, t, $J = 7.0$ Hz); EIMS: *m*/*z* (%) 290 (7), 288 (7) ($M^{+\cdot}$), 245 (22), 243 (22), 195 (14) 108 (100); Anal. Calcd for $C_{12}H_{17}BrO_3$: C, 49.83; H, 5.88%. Found: C, 49.79; H, 5.92%.

   Product **2g**: ^{1}H NMR (200 MHz): δ 7.41–7.23 (5H, m), 4.59 (1H, d, $J = 12.8$ Hz), 4.52 (1H, d, $J = 12.8$ Hz), 3.96 (1H, dd, $J = 12.0$, 2.0 Hz), 3.77 (1H, d, $J = 9.0$ Hz), 3.35 (1H, d, $J = 9.0$ Hz), 2.56 (1H, br s), 2.19 (1H, m), 1.62 (1H, m), 1.21 (3H, s), 1.04 (3H, t, $J = 7.0$ Hz); ^{13}C NMR (50 MHz): δ 137.8, 128.4, 128.0, 127.8, 127.4, 75.2, 74.9, 73.6, 56.3, 25.1, 18.5, 12.2; FABMS: *m*/*z* 289, 287 $[M+H]^+$; EIMS: *m*/*z* (%) 165 (5), 121 (9), 107 (6); Anal. Calcd for $C_{13}H_{19}BrO_2$: C, 54.36; H, 6.62%. Found: C, 54.44; H, 6.68%.

   Product **2j**: ^{1}H NMR (200 MHz): δ 4.31 (1H, ddd, $J = 10.0$, 9.0, 4.0 Hz), 3.99 (1H, ddd, $J = 10.5$, 9.0,4.0 Hz), 3.27 (1H, br s), 2.32 (1H, m), 2.23 (1H, m), 1.98 (1H, m), 1.92–1.74 (2H, m), 1.55 (1H, m); EIMS: *m*/*z* (%) 166 (46), 164 (46), ($M^{+\cdot}$) 137 (12), 135 (12), 86 (71); Anal. Calcd for C_5H_9BrO: C, 36.36; H, 5.45%. Found: C, 36.42; H, 5.49%.

   Product **2l**: ^{1}H NMR (200 MHz): δ 7.72 (2H, d, $J = 8.0$ Hz), 7.36–7.19 (7H, m), 4.90 (1H, dd, $J = 8.0$, 6.0 Hz), 4.69 (1H, br s), 3.59–3.47 (2H, m), 2.42 (3H, s); EIMS: *m*/*z* (%) 355 (6), 353 (6) ($M^{+\cdot}$), 234 (22), 171 (88), 169 (88); Anal. Calcd for $C_{15}H_{16}BrNO_2S$: C, 50.85; H, 4.50; N, 3.96%. Found: C, 50.81; H, 4.58; N, 3.92%.

   Product **2n**: ^{1}H NMR (200 MHz): δ 7.62 (2H, d, $J = 8.0$ Hz), 7.30 (2H, d, $J = 8.0$ Hz), 5.09 (1H, d, $J = 6.0$ Hz), 3.42–3.29 (3H, m), 2.45 (3H, s), 1.57–1.40 (2H, m), 1.32–1.05 (4H, m), 0.82 (3H, t, $J = 7.0$ Hz); EIMS: *m*/*z* (%) 335 (5) 333 (5) ($M^{+\cdot}$), 278 (11), 276 (11), 240 (16), 214 (9), 163 (27); Anal. Calcd for $C_{13}H_{20}BrNO_2S$: C, 40.71; H, 5.99; N, 4.19%. Found: C, 40.76; H, 5.92; N, 4.23%.

   Product **2q**: ^{1}H NMR (200 MHz): δ 7.80 (2H, d, $J = 8.0$ Hz), 7.32 (2H, d, $J = 8.0$ Hz), 5.71 (1H, d, $J = 6.0$ Hz), 4.10 (1H, ddd, $J = 10.0$, 9.0, 4.0 Hz), 3.67 (1H, m) 2.45 (3H, s), 2.22 (1H, m), 2.13 (1H, m), 1.95 (1H, m), 1.84–1.62 (2H, m), 1.42 (1H, m); EIMS: *m*/*z* (%) 333 (42), 331 (42) ($M^{+\cdot}$), 252 (18), 186 (78), 167 (16); Anal. Calcd for $C_{13}H_{18}BrNO_2S$: C, 46.99; H, 5.42; N, 4.22%. Found: C, 47.02; H, 5.46; N, 4.28%.