

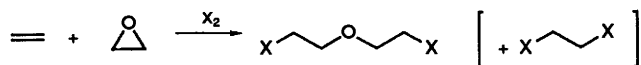
Stereochemistry of Polymethylated β,β' -Dibromoethers Formed by Bromination of Alkene–Epoxide Mixtures

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Examination of β,β' -dibromoethers formed when bromine is added to alkene–epoxide mixtures in pentane at -78°C revealed that opening of the bromonium ion and the epoxide occurs under high stereochemical control, whilst approach of the epoxide and the bromonium ion is subject to lower or no stereochemical control.

Recent reports have described the intramolecular interactions which occur between alkenes and epoxides in the presence of halogens and lead to the generation of cyclic dihalogenated ethers.^{1,2} The intermolecular form of this reaction in which addition of halogen to a mixture of alkene and epoxide produces β,β' -dihaloethers (Scheme) has been known for some time,³ but



Scheme.

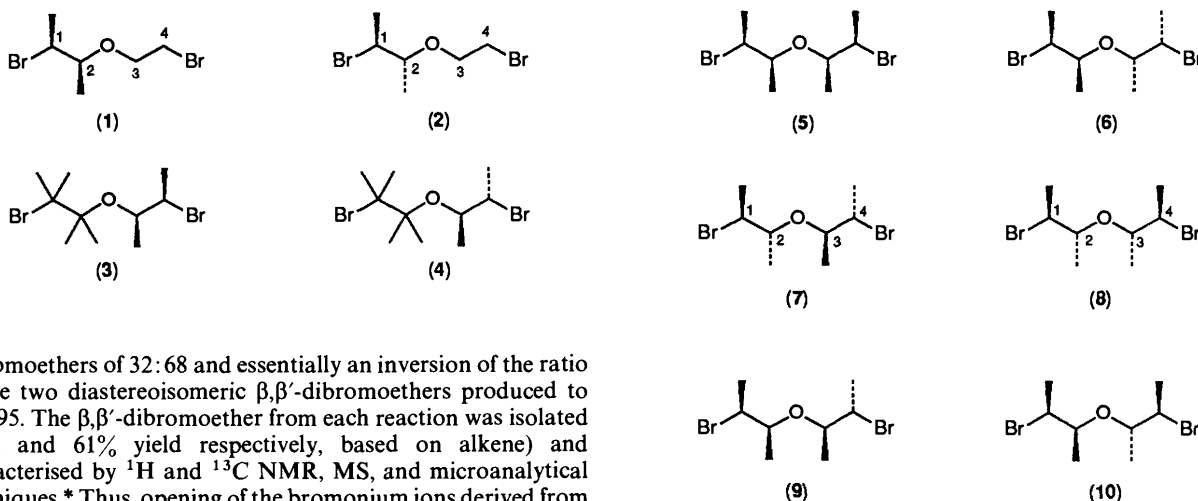
as far as we are aware the stereochemical consequences of this reaction have not been addressed. In view of the potential applications of β,β' -dihaloethers containing an array of chiral centres in, for example, crown ether chemistry or as precursors to novel phosphine ligands, we have examined the stereochemical aspects of this reaction and describe the outcome of our experiments below.

The majority of additions of halogens to alkene–epoxide

mixtures reported previously have been performed without a solvent or in chloroalkane solvents at around room temperature. We carried out investigations designed to increase the ratio of β,β' -dihaloether to dihaloalkane produced, and found that β,β' -dihaloether formation is favoured over dihaloalkane formation by (a) decreasing the polarity of the solvent used, and (b) decreasing the reaction temperature. Accordingly the reactions described below were performed at -78°C in pentane with alkene:epoxide:bromine in the ratio 1:2:1.3.

Initially the degree of stereochemical control over opening of the bromonium ion was investigated by adding bromine to a mixture of *cis*-but-2-ene–ethylene oxide and to a mixture of *trans*-but-2-ene–ethylene oxide. Examination of the 400 MHz ^1H NMR spectrum of the crude products revealed that in the case of *cis*-but-2-ene the ratio of 2,3-dibromobutane to β,β' -dibromoethers was 27:73 and that the ratio of the two diastereoisomeric β,β' -dibromoethers was >95:5. Using *trans*-but-2-ene resulted in a ratio of 2,3-dibromobutane to β,β' -

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dibromoethers of 32:68 and essentially an inversion of the ratio of the two diastereoisomeric β,β' -dibromoethers produced to <5:95. The β,β' -dibromoether from each reaction was isolated (58% and 61% yield respectively, based on alkene) and characterised by ^1H and ^{13}C NMR, MS, and microanalytical techniques.* Thus, opening of the bromonium ions derived from *cis*- and *trans*-but-2-ene by the oxygen atom of ethylene oxide occurs under good stereochemical control. Assuming that the opening occurs with inversion of configuration, then the product isolated from the *cis*-but-2-ene-ethylene oxide reaction is the β,β' -dibromoether (1), and the product isolated from the *trans*-but-2-ene-ethylene oxide reactions is its diastereoisomer (2) (one enantiomer depicted for clarity).†

The degree of stereochemical control over epoxide opening was then examined by adding bromine to a mixture of 2,3-dimethylbut-2-ene-*cis*-but-2-ene oxide and to a mixture of 2,3-dimethylbut-2-ene-*trans*-but-2-ene oxide. The 400 MHz ^1H NMR spectra of the crude products from these reactions revealed that epoxide opening occurs under good stereochemical control. The *cis*-but-2-ene oxide experiment gave a crude product which contained β,β' -dibromoethers and 2,3-dibromo-2,3-dimethylbutane in a 90:10 ratio. The ratio of the two diastereoisomeric β,β' -dibromoethers present was >95:5. Addition of bromine to the 2,3-dimethylbut-2-ene-*trans*-but-2-ene oxide mixture yielded a crude product in which the ratio of β,β' -dibromoethers to 2,3-dibromo-2,3-dimethylbutane was 43:57 and the ratio of the diastereoisomeric β,β' -dibromoethers was inverted to <5:95. The major diastereoisomer from each reaction was isolated (56% and 23% yield respectively, based on

alkene) and fully characterised. Assuming that the stereochemical control over opening of the epoxides by bromide is achieved by an $\text{S}_{\text{N}}2$ -type process, then the ether isolated from the 2,3-dimethylbut-2-ene-*trans*-but-2-ene oxide reaction is the β,β' -dibromoether (3) and the ether isolated from the 2,3-dimethylbut-2-ene-*cis*-but-2-ene oxide reaction is its diastereoisomer (4).

Finally, experiments were performed to determine the relative stereochemistry of products containing chiral centres at the α -, α' -, β -, and β' -carbon atoms in order to determine whether the reaction exerts control over the relative stereochemistry of the α and α' chiral centres. Bromine was added to four pairs of reagents, (a) *cis*-but-2-ene-*cis*-but-2-ene oxide, (b) *trans*-but-2-ene-*trans*-but-2-ene oxide, (c) *cis*-but-2-ene-*trans*-but-2-ene oxide, and (d) *trans*-but-2-ene-*cis*-but-2-ene oxide. The reactions each produced essentially two diastereoisomeric β,β' -dibromoethers and 2,3-dibromobutane in ratios of 59:41, 57:43, 55:45, and 71:29 respectively. The ratios of the two diastereoisomers were 1:1, 1:1, 2:1, and 1:3 respectively,‡ and in each case the ratio of the two major diastereoisomers to other diastereoisomers was >95:5. The diastereoisomeric pairs were isolated and their ^1H and ^{13}C NMR spectra examined. These were entirely consistent with the spectra expected for β,β' -dibromoethers (5) and (6) [from case (a)], (7) and (8) [from case (b)], (9) and (10) [from case (c)], and (9) and (10) [from case (d)], i.e. from reactions in which opening of the bromonium ion and the epoxide occurs stereospecifically, as observed in the examples described above, but little [cases (c) and (d)] or no [cases (a) and (b)] control is exerted over the relative stereochemistry of the α and α' chiral centres.

Synthetically, it is of note that addition of bromine to but-2-ene-but-2-ene oxide mixtures led in each case to the generation of only two of the six possible diastereoisomeric β,β' -dibromoethers. The properties and applications of the chiral C_2 -symmetrical β,β' -dibromoethers (6) and (7) are under investigation.

References

- (a) S. G. Davies, M. E. C. Polywka, and S. E. Thomas, *Tetrahedron Lett.*, 1985, **26**, 1461; (b) S. G. Davies, M. E. C. Polywka, and S. E. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1277.
- (a) E. Alvarez, E. Manta, J. D. Martin, M. L. Rodriguez, and C. Ruiz-Perez, *Tetrahedron Lett.*, 1988, **29**, 2093; (b) E. Alvarez, E. Manta, J. D. Martin, M. L. Rodriguez, C. Ruiz-Perez, and D. Zurita, *ibid.*

* β,β' -Dibromoethers (1)–(10) are novel compounds.

† Diastereoisomeric ethers (1)/(2) and (3)/(4) were readily distinguishable by ^1H and ^{13}C NMR spectroscopy e.g. δ_{H} (1) (400 MHz; CDCl_3) 1.22 (3 H, d, J 6.3 Hz, C^2CH_3), 1.62 (3 H, s, J 6.8 Hz, C^1CH_3), 3.41 (2 H, t, J 6.2 Hz, C^4H_2), 3.56 (1 H, dq, J 4.4, 6.3 Hz, C^2H), 3.73 (1 H, dt, J 10.8, 6.2 Hz, 1 H of C^3H_2), 3.82 (1 H, dt, J 10.8, 6.2 Hz, 1 H of C^3H_2), and 4.11 (1 H, dq, J 4.4, 6.8 Hz, C^1H); δ_{H} (2) (400 MHz; CDCl_3) 1.25 (3 H, d, J 6.2 Hz, C^2CH_3), 1.66 (3 H, s, J 6.8 Hz, C^1CH_3), 3.44 (2 H, t, J 6.4 Hz, C^4H_2), 3.49 (1 H, dq, J 4.8, 6.2 Hz, C^2H), 3.80 (1 H, dt, J 10.7, 6.4 Hz, 1 H, of C^3H_2), 3.81 (1 H, dt, J 10.7, 6.4 Hz, 1 H of C^3H_2), and 4.11 (1 H, dq, J 4.8, 6.8 Hz, C^1H); δ_{C} (1) (100.6 MHz; CDCl_3) 15.8 (C^2CH_3), 20.3 (C^1CH_3), 30.4 (C^4), 51.4 (C^1), 69.4 (C^3), and 79.1 (C^2); δ_{C} (2) (100.6 MHz; CDCl_3) 17.1 (C^2CH_3), 21.4 (C^1CH_3), 30.4 (C^4), 52.8 (C^1), 69.5 (C^3), and 79.7 (C^2).

‡ Diastereoisomers (5)–(10) each gave unique ^1H and ^{13}C NMR data, e.g. δ_{H} [more polar diastereoisomer of (7)/(8)] (400 MHz; CDCl_3) 1.22 (6 H, d, J 6.2 Hz, C^2Me , C^3Me), 1.67 (6 H, d, J 6.9 Hz, C^1Me , C^4Me), 3.57 (2 H, dq, J 4.7, 6.2 Hz, C^2H , C^3H), and 4.11 (2 H, dq, J 4.7, 6.9 Hz, C^1H , C^4H); δ_{H} [less polar diastereoisomer of (7)/(8)] (400 MHz; CDCl_3) 1.25 (6 H, d, J 6.2 Hz, C^2Me , C^3Me), 1.64 (6 H, d, J 6.8 Hz, C^1Me , C^4Me), 3.59 (2 H, dq, J 4.7, 6.2 Hz, C^2H , C^3H), and 4.06 (2 H, dq, J 4.7, 6.8 Hz, C^1H , C^4H); δ_{C} [more polar diastereoisomer of (7)/(8)] 18.1 (C^2CH_3 , C^3CH_3), 21.8 (C^1CH_3 , C^4CH_3), 53.6 (C^1 , C^4), and 78.1 (C^2 , C^3); δ_{C} [less polar diastereoisomer of (7)/(8)] 17.5 (C^2CH_3 , C^3CH_3), 21.3 (C^1CH_3 , C^4CH_3), 53.5 (C^1 , C^4), and 77.5 (C^2 , C^3).

- 1988, **29**, 2097; (c) E. Alvarez, D. Zurita, C. Ruiz-Perez, M. L. Rodriguez, and J. D. Martin, *ibid.*, 1989, **30**, 3729.
- 3 (a) C. K. Egeonu, P. A. Gurbanov, M. M. Movsumzade, and A. E. Agaeva, *Dokl. Akad. Nauk Az. SSR*, 1983, **39**, 56 (*Chem. Abstr.*, 1984, **101**, 55012q); (b) G. K. Khodzhaev, F. K. Agaev, and Z. M. Tsalikova, *Azerb. Khim. Zh.*, 1985, 55 (*Chem. Abstr.*, 1986, **105**, 6249w); (c) J. Rodriguez, J. P. Dulcere, and M. Bertrand, *Tetrahedron Lett.*, 1983, **24**, 4423; (d) I. G. Dinulescu, M. Avram, C. T. Jijovici, M. Farcasiu, and C. D. Nenitzescu, *Chem. Ind. (London)*, 1964, 840.

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