Tetrahedron Letters,Vol.26,No.11,pp 1461-1464,1985
Printed in Great Britain

0040-4039/85 $3.00 + .00

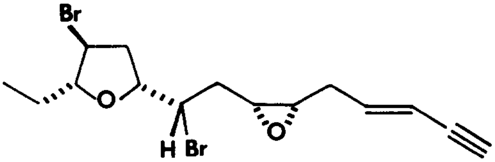
STEREOSELECTIVE SYNTHESIS OF CYCLIC ETHERS VIA BROMINE ASSISTED EPOXIDE RING EXPANSION

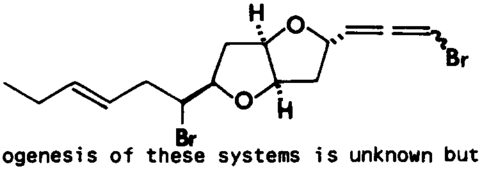
Stephen G. Davies, Mario E.C. Polywka
and Susan E. Thomas*

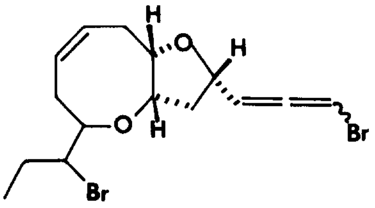
The Dyson Perrins Laboratory, South Parks Road,
OXFORD OX1 3QY

Summary: 9-Oxabicyclo[6.1.0]non-4-ene reacts with bromine to give stereoselectively trans,trans-2,6-dibromo-9-oxabicyclo[3.3.1]nonane and trans,trans-2,5-dibromo-9-oxabicyclo[4.2.1]nonane.

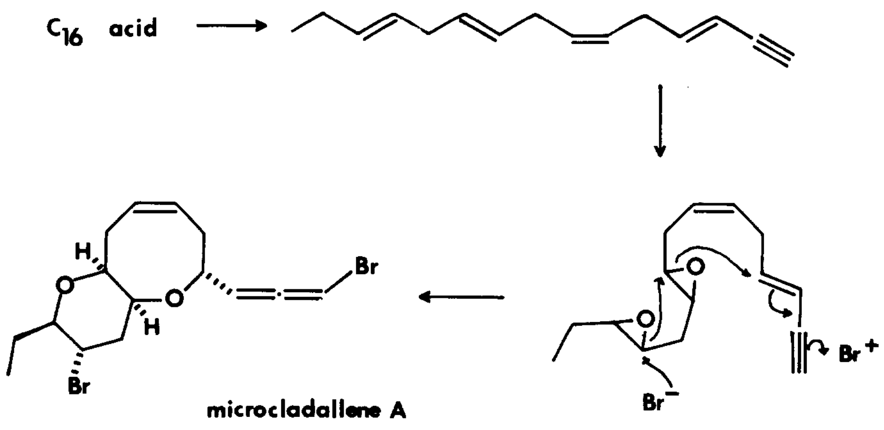
Many dibrominated sesquiterpenes containing ether linkages have been isolated from the red algal genus *Laurencia*;[1-5] three examples are illustrated below.







The biogenesis of these systems is unknown but the bromine-assisted cyclisation of unsaturated epoxides, originally proposed by Bu'Lock,[6] has recently been invoked as a possible biosynthetic route to microcladallene A.[5]



Although the cyclisations of unsaturated epoxides by mercury (II) electrophiles[7] and of unsaturated episulphides by halogens[8] have been established, a bromine-assisted cyclisation of unsaturated epoxides has no chemical precedent as far as we are aware.

We wish to report a bromine-mediated transformation of unsaturated epoxides into dibrominated cyclic ethers. Treatment of 1,5 cyclo-octadiene 1 with one equivalent of bromine at 0°C gave trans-1,2-dibromocyclo-oct-5-ene which was oxidised with mCPBA to the expected product 4,5-dibromo-9-oxa-bicyclo[6.1.0]nonane 2. Oxidation of 1 with one equivalent of mCPBA to give 3 followed by bromination in carbon tetrachloride at 0°C, however, led to a 1.22:1 mixture of trans,trans isomers of 2,6-dibromo-9-oxabicyclo-[3.3.1]nonane 6 and 2,5-dibromo-9-oxabicyclo [4.2.1]nonane 7. The products 6 and 7 were identified by comparison of their spectroscopic properties with literature data[9-12] and the product ratio was determined from the ^{13}C-{^{1}H} spectrum of the mixture. No other diastereoisomers of 6 or 7 were detected. A mechanism involving neighbouring group participation by the epoxide oxygen in the opening of the bromonium ion 4 to give the oxonium species 5 is consistent with the observed stereoselective formation of only trans,trans-6 and 7.

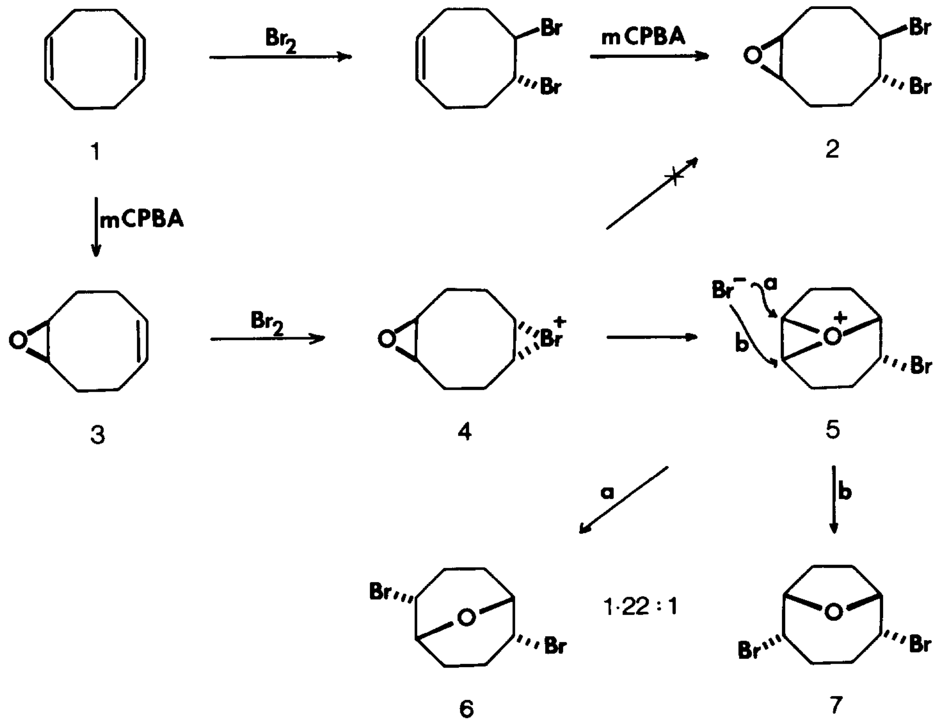
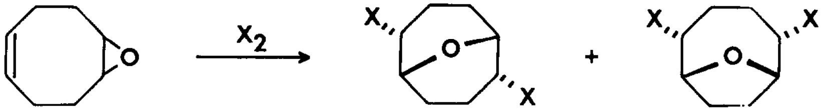


Table 1 records the ratios of dihalogenated bicyclic ethers obtained on treatment of 3 with halogen under various conditions.

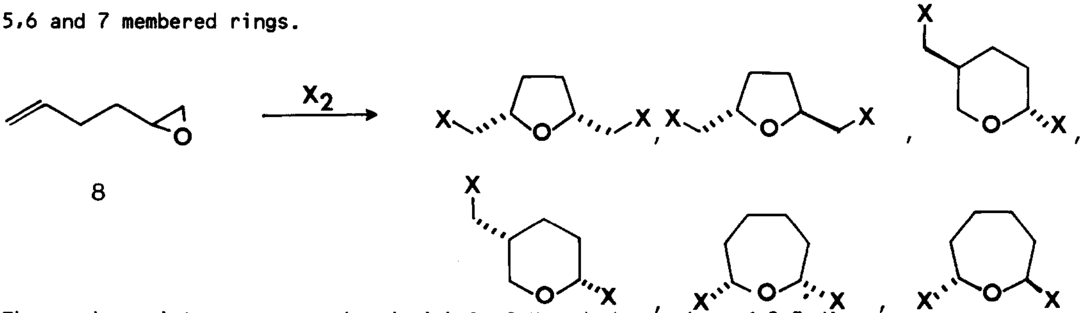
Table 1: Halogenation of 9-oxabicyclo[6.1.0]non-4-ene 3.



3

X_2	Temp	Solvent	Ratio 6:7
Br_2	0°C	CCl_4	1.2:1
Br_2	20°C	CH_3CN	1:1.3
Br_2	-78°C	CH_2Cl_2	1.7:1
I_2	20°C	CH_3CN	1.7:1

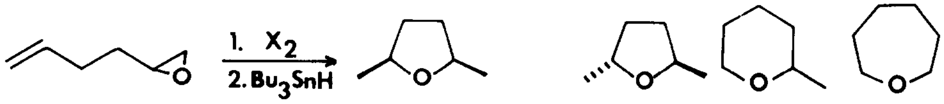
Investigations into the reactivity of 1,2-epoxyhex-5-ene 8 indicate that this bromine-assisted cyclisation is a general phenomenon, independent of the conformation of the cyclo-octane ring. Halogenation of 1,2-epoxyhex-5-ene 8 leads to products containing 5,6 and 7 membered rings.



8

The product mixtures were reduced with Bu_3SnH and the ratios of 2,5-dimethyltetrahydrofuran (cis and trans) : 2-methyltetrahydropyran : oxepane determined by g.c. analysis (See Table 2). These ratios are assumed to reflect the ratios of dihalogenated products obtained.

Table 2: Cyclisation of 1,2-epoxyhex-5-ene 8



X_2	Temp.	Solvent				
Br_2	20°C	CCl_4	75		20	5
Br_2	-78°C	CH_2Cl_2	25	35	40	0
I_2	20°C	CH_3CN	60	20	20	0

Acknowledgement: We thank Interox Chemicals Ltd., for a studentship (to S.E.T.).

References

1. A. Fukuzawa, E. Kurosawa and I. Tobetsu, Tetrahedron Lett., 1980, 1471.
2. T. Suzuki, K. Koizumi, M. Suzuki and E. Kurosawa, Chem. Letts., 1983, 1639.
3. M. Suzuki, K. Koizumi, H. Kikuchi, T. Suzuki and E. Kurosawa, Bull. Chem. Soc. Jpn., 1983, 56, 715.
4. A. Fukuzawa and E. Kurosawa, Tetrahedron Lett., 1979, 2797.
5. D.J. Kennedy, I.A. Selby, H.J. Cowe, P.J. Cox and R.H. Thomson, J. Chem. Soc., Chem. Commun., 1984, 153.
6. J.D. Bu'Lock in 'Comparative Phytochemistry', ed. T. Swain, Academic Press, London, 1966, p.79.
7. J.L. Jernow, D. Gray and W.D. Closson, J. Org. Chem., 1971, 36, 3511.
8. P.H. McCabe and A. Stewart, J. Chem. Soc., Chem. Commun., 1980, 100.
9. G. Haufe, Tetrahedron Lett., 1984, 4365.
10. A.J. Bloodsworth, J.A. Khan and M.E. Loveitt, J. Chem. Soc., Perkin Trans. I, 1981, 621.
11. G. Haufe, E. Kleinpeter and M. Muhlstadt, Monatsh. Chem., 1978, 109, 575.
12. N.V. Averina, N.S. Zefirov, P.P. Kadzyauskas, S.V. Rogozina, N.K. Sadovaya and N.M. Soldatov, Zhur. Org. Khim., 1974, 10, 1442.

(Received in UK 20 December 1984)