Determination of the Configuration and Conformation of Some Epoxybicycloalkanones using the Epoxide Ring Current Effect

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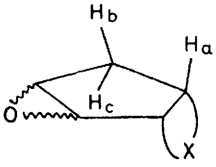
A ring current effect due to the oxiran ring has been used as an aid to structure elucidation of various novel epoxides derived from the 6-azabicyclo[3.2.0]hept-2-en-7-ones (1) and (4), the 2-oxabicyclo[3.3.0]oct-6-en-3-ones (7), (8), and (11), and the bicyclo[3.2.0]hept-2-en-6-one (14).

WE have been engaged in studies involving the utilisation of the reactive oxiran ring system in stereocontrolled syntheses of naturally occurring materials and selected analogues.[1] The oxiran moiety is generally part of a tricyclic ring system incorporating a central cyclopentane unit (Figure) and a knowledge of the mutual orientation of the two outer rings was crucial to the design and implementation of the synthetic route. Since the position of the three-membered ring was not always predictable from the mode of preparation, we were obliged to use two magnetic effects due to the epoxide ring to clarify the stereochemistry of the molecules.

The first aid to structure determination was the shielding effect of the epoxy-ring current on the proton (H_a) transannular to and coaxial with the epoxy-ring. While this shelding effect has been noted in n.m.r. spectra of tailored, model epoxy-compounds,[2] its application to the identification of isomers as described herein is unprecedented, to our knowledge. Secondly, a more standard anisotropic downfield shift of the proton (H_b or H_c) directly adjacent to the oxygen atom in the three-membered ring can be discerned in the n.m.r. spectra.



FIGURE

The relevant chemical shift data are summarised in the Table.

For example, two epoxides can be obtained from the unsaturated β-lactam (1).[3] One shows a pronounced upfield shift of the signal from H_a [relative to the reference compound (1)] while the other does not. For the former compound, the signal due to H_b (identified by the large *cis*-coupling to H_a) is at low field, while in the latter compound the signal due to H_c (weakly coupled to H_a) is at low field; on this evidence, the former compound was assigned to be the *exo*-epoxide (2) and the latter to be the *endo*-epoxide (3).

Chemical shifts of protons in some bicycloheptanones, 6-azabicycloheptanones, and 2-oxabicyclo-octanones

	Chemical shift (δ) [a]		
Compound	H_a	H_b	H_c
(1)	3.75	2.50	2.50
(2)	3.34	2.10	2.10
(3)	3.66	1.68	2.27
(4)	3.78	2.54	2.54
(5)	3.35	2.14	2.14
(6)	3.70	1.80	2.40
(7)	5.10	2.75	2.75
(8)	5.10	2.70	2.70
(9)	4.65	2.75	2.10
(10)	4.65	2.70	2.10
(11)	5.10	2.70	2.70
(12)	4.95	2.15	2.50
(13)	4.95	2.25	2.25
(14)	3.80	2.43	2.63
(15)	3.62	1.85	2.30
(16)	3.01	1.78	2.22
(17)	← 2.80—1.85 [b] →		

[a] Measured in carbon tetrachloride or deuteriochloroform using tetramethylsilane as internal standard. [b] Signals appear as a complex multiplet.

The isomeric epoxides, m.p.s 103 and 114°, derived from the β-lactam (4)[3] could be differentiated on the same basis and assigned to be the *exo*-epoxy-β-lactam (5) and the *endo*-epoxy-β-lactam (6), respectively.

The *endo*-halogeno-lactones (7) and (8) each give a single epoxide on oxidation using *m*-chloroperbenzoic acid in chloroform.[4] Both compounds display a high field shift of the signal for H_a relative to the starting material (Δδ 0.45). Two conclusions may be drawn: first the epoxy-ring is present on the *exo*-face of the molecule (this is substantiated by the low-field position of the signal from H_b) Secondly, the proton attached to the bridgehead carbon atom (H_a) is present as an axial substituent on the cyclopentane ring and is affected by

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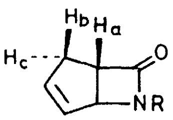
[1] S. M. Ali and S. M. Roberts, *J.C.S. Chem. Comm.*, 1976, 584.

[2] K. Tori, K. Kitahonoki, Y. Takano, H. Tanida, and T. Tsuji, *Tetrahedron Letters*, 1965, 869; K. Tori, K. Aono, K. Kitahonoki, R. Muneguki, Y. Takano, H. Tanida, and T. Tsuji, *ibid.*, 1966, 2921; P. J. Jefferies, R. S. Rosich, and D. E. White, *ibid.*, 1963, 1853.

[3] J. M. Berge, S. M. Roberts, H. Suschitzky, and J. E. G. Kemp, *J. Chem. Research*, (*S*), 1978, 255.

[4] S. M. Ali, N. M. Crossland, S. M. Roberts, and R. F. Newton, *J.C.S. Perkin I*, in the press.



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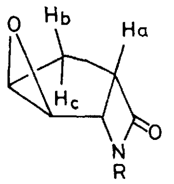

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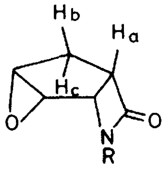

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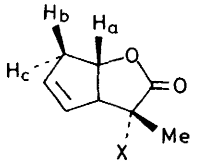
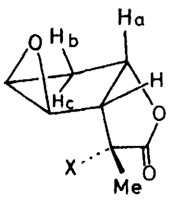


(7) X = Br
(8) X = Cl



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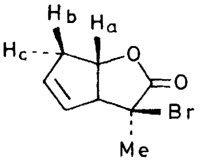

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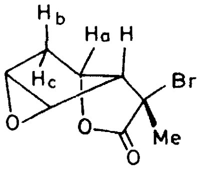

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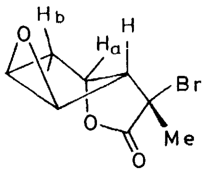

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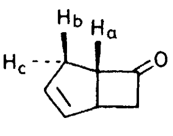

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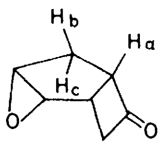

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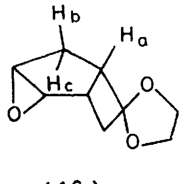

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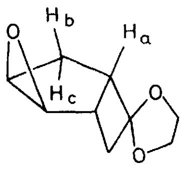

(17)

the current induced in the oxiran unit. It follows that the conformation of the lactone ring is that which allows the halogen atom to adopt the preferred axial position and the epoxides may thus be represented by the formulae (9) and (10) [5]

Two epoxides are formed on peracid oxidation of the *exo*-bromo-oxabicyclo-octenone (11) [4] Neither show a significant high field shift of the signal due to H_a. The major product was assigned to be the *endo*-epoxide (12) on the basis of the low-field signal due to H_c. The minor component, the *exo*-epoxy-lactone (13) must therefore adopt the conformation shown with H_a in an equatorial configuration on the carbocyclic ring and unaffected by the epoxy-ring current. This conformation is adopted to allow the halogen atom to occupy an axial position on the lactone ring.[5]

The influence of an epoxide ring on the chemical shifts of neighbouring protons has been used to define the configuration of some new, useful prostaglandin intermediates. Thus the epoxide (15) derived from the bicycloheptenone (14) [6] is assigned to have the two small rings *cis*-fused to the cyclopentane ring through the observation of the low field position of the signal from H_c in the epoxy-ketone (15) and the insignificant shift in the signal due to H_a on introduction of the oxiran function.

The isomeric epoxy-acetals (16) and (17) have been synthesised from the ketone (14) by independent routes.[7] The important prostaglandin synthon, the *endo*-epoxide (16), is characterised by the low field position of the signal from H_a (δ 3.0) relative to the position of the corresponding signal from H_a in the *exo*-epoxide (17) ($\delta < 2.8$). As expected, the signal due to H_c in the *endo*-epoxide (16) is at low field.

EXPERIMENTAL

Preparation of the epoxy-β-lactams (2), (3), (5), and (6),[3] the halogeno-lactones (9), (10), (12), and (13),[4] the epoxy-ketone (15),[6] and the epoxy-acetals (16) and (17) [7] will be described elsewhere.

N.m.r. spectra were recorded on a Perkin-Elmer EM360 instrument employing tetramethylsilane as the internal standard on 1M solutions of the compounds in carbon tetrachloride or deuteriochloroform. We found that change of solvent or small changes in concentration did not affect the chemical shifts markedly.

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[8/138 *Received, 27th January,* 1978]

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[7] R. F. Newton, C. C. Howard, D. P. Reynolds, A. H. Wadsworth, N. M. Crosshand, and S. M. Roberts, *J.C.S. Chem. Comm.*, 1978, 662.