Absolute Configuration of (+)-2-*exo*-Bromonorbornane-1-carboxylic Acid and (-)-1-lodo-2-*exo*-bromonorbornane

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Resolution of (\pm) -2-*exo*-bromonorbornane-1-carboxylic acid was achieved by h.p.l.c. separation of diastereoisomeric amides, obtained from this acid and (+)-(R)-phenylglycinol; the absolute configuration was established by X-ray structure analysis and correlated with c.d. spectra.

Most of the highly strained bridgehead alkenes which have either been prepared or detected as short-lived intermediates possess C_1 symmetry and hence are chiral molecules. Apart from the preparation of (-)-(5S)-bicyclo[3.3.1]non-1-ene for which the absolute configuration has been established,¹ this unique property of Bredt-alkenes has not been investigated. As part of our continuing interest in highly strained bridgehead alkenes² we have prepared 2-exo-bromo-norbornane-1-carboxylic acid (1) and 1-iodo-2-exo-bromonorbornane (2), precursors of $\Delta^{1,2}$ -norbornene, in





Figure 1. X-Ray structure of (-)-(3b).

optically active form and determined their absolute configuration.

racemic 2-exo-bromonorbornane-1-Resolution of carboxylic acid (1) has been achieved by h.p.l.c. separation of the diastereoisomeric amides (3a) and (3b), obtained from reaction of (1) with (+)-(R)-phenylglycinol {(3a): m.p. 129.5 °C, $[\alpha]_{D^{20}}$ -118.2, R_{f} (t-butyl methyl ether) 0.4; (3b): m.p. 171 °C, $[\alpha]_{\rm p}^{20}$ -13.0, $R_{\rm f}$ (t-butyl methyl ether) 0.29}. Since the two diastereoisomeric amides were essentially stable to hydrolysis, they were converted into the oxazolines (4a) and (4b) by treatment with toluene-p-sulphonyl chloride in pyridine. Treatment with aqueous H₂SO₄ gave the esters (5a) and (5b), which subsequently were transformed into the optically active 2-exo-bromonorbornane carboxylic acids (-)-(1) and (+)-(1) by heating with concentrated H_2SO_4 to 35 °C for 1 h $\{(-)-(1): \text{ m.p. 114 °C}, [\alpha]_{D}^{20} - 72.5; (+)-(1): \text{ m.p. 112}-114 °C, [\alpha]_{D}^{20} + 74.9\}.$ From (-)-(1), (-)-1-iodo-2-exo-bromonorbornane (2) $([\alpha]_{D}^{20} - 109.1)$ was prepared by reaction with t-butylhypoiodite followed by photolysis.3

Chiroptical methodology⁴ was used for the tentative assignment of absolute configuration to (-)-(1) and (+)-(1). The C=O group of an acid usually lies *syn*-periplanar to a C_{α}-C_{β} bond, and the dipole interaction between CO₂H and Br will preferably put the C-7–C-1 bond in this position. This conformation resembles that of a β -axial bromoketone, for which 'antioctant' behaviour has been demonstrated.⁵ Since for a ketone and its corresponding acid (or simple derivative) analogous rules are valid⁵ the negative $\Delta \varepsilon$ -value of -1.13 at 215 nm suggests the (1*R*)-configuration for (-)-(1) [$\Delta \varepsilon$ +1.10 for (+)-(1)]. As the Br is in the *exo* position (-)-(1) should thus be the (1*R*,2*R*)-enantiomer.

A chirality rule for secondary iodo alkanes⁵ suggests that the Cotton effect should be positive between 250—270 nm when the ligands on the carbon are arranged clockwise with decreasing size looking along the C–I bond. Compound (-)-(2), which should have the (1S,2R)-configuration since it is derived from (-)-(1), shows two c.d. bands ($\Delta \varepsilon -2.13$ at 246 nm, $\Delta \varepsilon -2.1$ at *ca*. 213 nm). Therefore, for this chirality rule to be applicable to (-)-(2) it has to be assumed that the C-6 methylene group is larger than the C-7 methylene group. However in this case it is probably the (negative) sign of the torsional angle (I–C–C–Br) which determines the signs of the Cotton effects. Proof for the absolute configuration of (+)-(1) and hence of (-)-(2) came from X-ray structure analysis of (3b).[†] Since D-phenylglycinol has (R)-chirality, it is concluded that (+)-(1), prepared from amide (3b), has (1S,2S)-chirality. The 1-iodo-2-*exo*-bromonorbornane (-)-(2), prepared from (-)-(1R,2R)-(1) is consequently assigned (1S,2R)-chirality.

The X-ray structure of (3b), Figure 1, the CONHR moiety of which should have the same conformation as the COOH moiety of (1), is in agreement with the assignment of the absolute configuration of optically active (1) from chiroptical data.

The absolute configuration of (1) and (3b) may also be discussed on the basis of Helmchen's empirical rule, which suggests that the absolute configuration of an acid can be deduced from the relative R_f values of corresponding amides of type (6).⁸ However, because of the ambiguity in assigning the smallest group to the ethylene or the methylene bridge on C-1 of the norbornane skeleton, as well as the difficulty in determining the conformation of the norbornyl moiety relative to the amide functionality, stereochemical assignment of (1) would still have remained speculative. It should be noted that (3b) exhibits, at least in the crystalline state, in a conformation in which one carbon–carbon bond is synplanar to the carbonyl group, whereas in the examples studied by Helmchen, the carbon–hydrogen bond is antiplanar. (+)-

[†] Crystal data: Prismatic crystals, elongated along the *a*-axis, of (**3b**) were obtained by crystallisation from methanol-water: orthorhombic, space group $P2_{12}_{12}_{12}$, a = 6.389(4), b = 11.370(6), c = 21.40(2) Å; $C_{16}H_{20}BrO_2N$, $D_c = 1.45$ g cm⁻³. Diffraction intensities were measured in the range of 1° < 20 < 60° at 20(±2) °C by the ω --20 scan technique (monochromatized Mo-K_{$\bar{\alpha}$} radiation). After averaging multiple measurements 2577 independent reflections remained, of which 1072 with $I < 2.58\sigma(I)$ were unobserved. The structure was solved by Patterson methods, which gave the bromine atom position; the light atoms were found by Fourier calculations using bromine phased structure factors. The structure was refined with least squares techniques with atomic scattering factors taken from ref. 6 (R = 0.075 for observed reflections). All calculations and drawings were done using the KRIPROG program system (ref. 7).

The atomic co-ordinates for this work are available on request from the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

(1S,2S)-2-exo-Bromonorbornane-1-carboxylic acid, (+)-(1), and (-)-(1S,2R)-1-iodo-2-exo-bromonorbornane, (-)-(2), are the first examples of chiral β -bromoacids and stable tertiary iodides for which the c.d. spectra have been correlated with their absolute configuration.

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