The Iodo-lactones derived from Norborn-5-en-2-*endo*-yl-acetic Acid and -propionic Acid

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The iodolactonisation of norborn-5-en-2-*endo*-ylacetic acid is analogous to that of norborn-5-ene-2-*endo*-carboxylic acid and affords 6-*endo*-hydroxy-5-*exo*-iodonorbornan-2-*endo*-ylacetic acid δ-lactone. The lactone ring is probably in a boat conformation. The iodolactonisation of 3-(norborn-5-en-2-*endo*-yl)propionic acid does not follow a similar pattern; the rearrangement product obtained is 3-(2-*endo*-hydroxy-7-*anti*-iodonorbornan-2-*exo*-yl)propionic acid γ-lactone.

THE iodolactonisation of norborn-5-ene-2-*endo*-carboxylic acid (I) affords the iodo-γ-lactone (VII) in good yield. The reaction is well documented and the structure (VII) rigorously established.[1-3] It is usual to carry out the reaction by dissolving a 9 : 1 mixture of the acid (I) and its 2-*exo*-isomer (II) in aqueous sodium hydrogen carbonate, then treating this solution with iodine and potassium iodide. The neutral iodo-lactone (VII) is readily separated, since unchanged (I) and its relatively unreactive 2-*exo*-isomer (II) remain in solution. We now report that the corresponding reaction of a 10 : 1 mixture of norborn-5-en-2-*endo*-ylacetic acid (III) and its 2-*exo*-isomer (IV) affords the corresponding δ-lactone (VIII), $\nu_{max.}$ ($CHCl_3$) 1 736 cm^{-1} (characteristic [4] of a δ-lactone); the n.m.r. spectral parameters (Table 1) showed a satisfactory correlation with those [3] due to (VII). The values for J(2,8a) and J(2,8b) (6 and 2 Hz, respectively) strongly indicate a boat conformation (VIIIA) for the lactone ring. Values derived from the Karplus equation [5] (7 and 1 Hz) are to be compared with 3 and 3 Hz for the chair alternative (VIIIB). The boat conformation (VIIIA) is also supported by the absence of anisotropic deshielding of H-1 by the lactone carbonyl function. Models suggest that if (VIII) had the chair conformation H-1 would be directly under the deshielding cone of the carbonyl group.

TABLE 1

N.m.r. data for the lactone (VIII)

Proton	1	2	3-*endo*	3-*exo*	4	5	6	7a	7b	8a	8b
δ	2.40br	2.40	1.13	2.15br	2.56br	3.81	5.25	2.25br	1.77	2.61	2.60
Mult.	m	m	oct	sext	d	q	m	d	decet	q	q

J	1,2	1,6	1,7a	1,7b	2,3-*endo*	2,3-*exo*	2,6	2,8a	2,8b	3-*endo*, 3-*exo*, 3-*exo*	3-*endo*, 7a	3-*endo*, 4	4,7a	4,7b	5,6	5,7b	7a,7b	8a,8b
Hz	*ca.* 4	5	1.8	1.6	4.0	12	1.8	6	2	12.8	2.5	5	1.8	1.6	1.9	3.2	10.9	*ca.* 12

The Diels–Alder reaction of cyclopentadiene with pent-4-enoic acid afforded a *ca.* 5 : 1 mixture of 3-(norborn-5-en-2-*endo*-yl)propionic acid (V) and its 2-*exo*-isomer (VI). This mixture readily reacted under the usual conditions for iodolactonisation but the major product had $\nu_{max.}$ ($CHCl_3$) 1 774 cm^{-1}, consistent [4] with a γ-lactone and not the ε-lactone analogue of (VII) and (VIII). The ^1H n.m.r. spectrum of the product shows no resonance attributable to >CHO–, indicating a spiro structure for the γ-lactone system. The only low-field resonance was at δ 3.90 ($W_{\frac{1}{2}}$ *ca.* 2.5 Hz), consistent [6] with >CHI at C-7, leading to the assignment of structure (XIII) to the spiro γ-lactone. The remaining proton resonances overlap in the region δ 1.8—2.6, apart from a multiplet ($W_{\frac{1}{2}}$ *ca.* 26 Hz) at δ 1.45. This width is consistent [6] with H-5-*endo* or H-6-*endo* in (XIII), and since decoupling experiments show a long-range coupling of 1.7 Hz with the C-7 bridge proton (δ 3.90), the latter is *anti* to to the 5,6-bond, confirming structure (XIII). A likely mechanism for the formation of (XIII) is indicated. Because capture of the iodonium ion in (IX) by the carboxylate anion to form an ε-lactone is slow for steric reasons, either (IX) or the open carbocation (X) derived from (IX) is likely to undergo Wagner–Meerwein rearrangement to afford (XI). This appears to be the sole possible route for rearrangement of (X), since a 5,6-*exo*,-*exo* or a 2,6-*endo*,*endo* hydride shift cannot be envisaged. (The propensity for 5,6-*exo*,*exo* and 2,6-*endo*,*endo* hydride shifts in norbornane systems has been reviewed.)[7] The ion (XI) can then undergo the favourable 2,6-*endo*,*endo* hydride shift to afford the tertiary carbocation ion (XII). Intramolecular cyclisation in (XII) of the carboxylate anion centre on to the carbocation centre then occurs to afford the lactone (XIII). This assumption of *exo*-attack is based on the known high preference for *exo*-attack on tertiary norbornyl cations.[7-9] The structural information derived from the spectral measurements does not rule out the alternative (XIV) derived from *endo*-attack, although its formation would be contradictory to contemporary theory.[7,9]

[1] C. D. Ver Nooy and C. S. Rondestvedt, *J. Amer. Chem. Soc.*, 1955, **77**, 3583.

[2] J. A. Berson and D. A. Ben-Efraim, *J. Amer. Chem. Soc.*, 1959, **81**, 4083; F. R. Jensen and J. J. Miller, *Tetrahedron Letters*, 1966, 4861; G. W. Oxer and D. Wege, *ibid.*, 1969, 3513; R. M. Moriarty, H. Gopal, H. G. Walsh, K. C. Ramey, and D. C. Lini, *ibid.*, 1966, 455; D. N. Ford, W. Kitching, and P. R. Wells, *Austral. J. Chem.*, 1969, **22**, 1157; S. Beckmann and H. Geiger, *Chem. Ber.*, 1961, **94**, 48.

[3] K. C. Ramey, D. C. Lini, R. M. Moriarty, H. Gopal, and H. G. Walsh, *J. Amer. Chem. Soc.*, 1967, **89**, 2401.

[4] L. J. Bellamy, 'The Infra-red Spectra of Complex Molecules,' 2nd edn., Methuen, London, 1958.

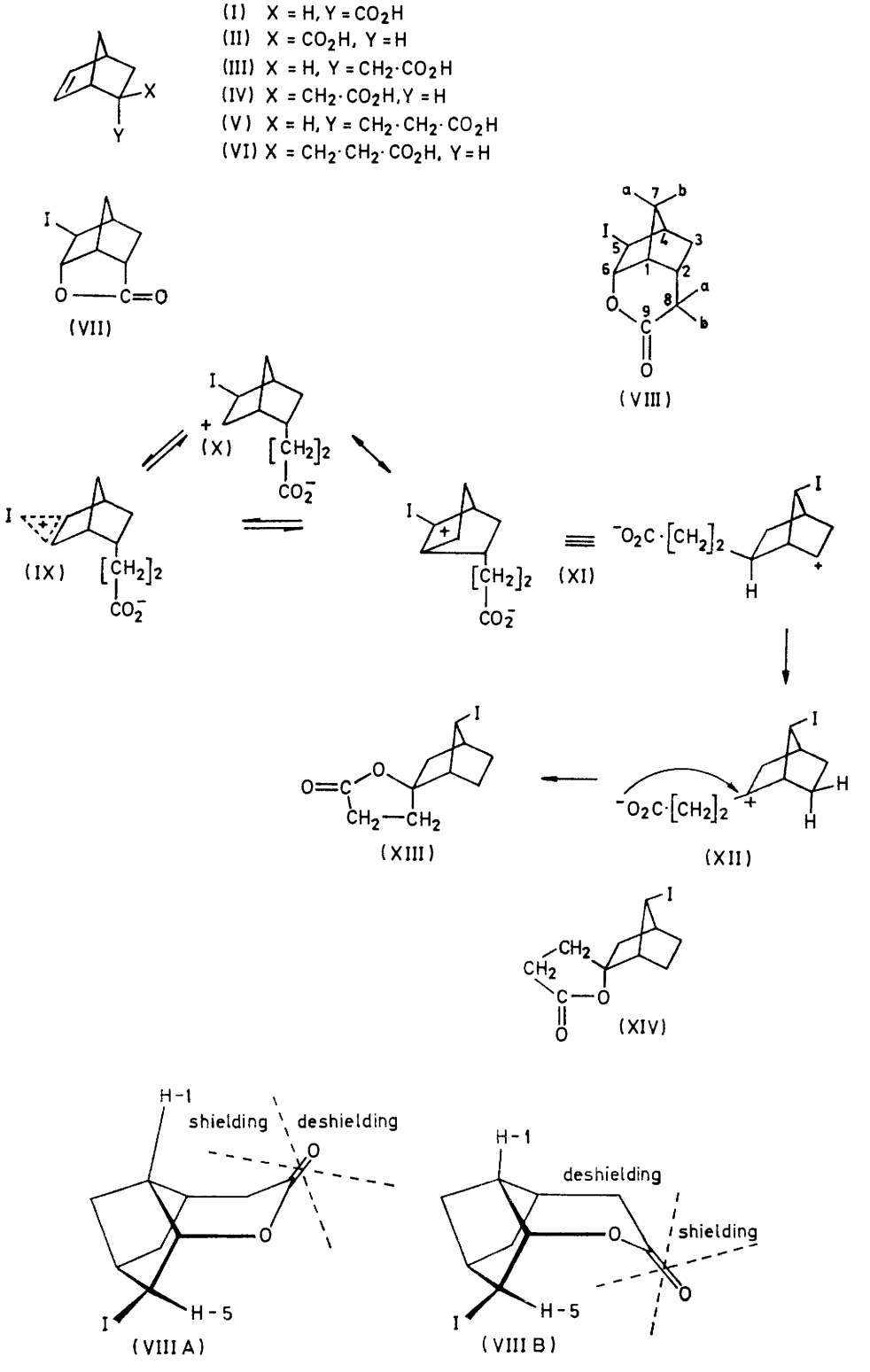
[5] M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11; H. Conroy, *Adv. Org. Chem.*, 1960, **2**, 265.

[6] See Tables in L. M. Jackman, S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford, 1969.

[7] G. D. Sargent in 'Carbonium Ions,' vol. 3, eds. G. A. Olah and P. von R. Schleyer, Wiley, New York, 1972, p. 1114.

[8] See for example H. C. Brown and S. Ikegami, *J. Amer. Chem. Soc.*, 1968, **90**, 7122; S. Ikegami, D. L. Vander Jagt, and H. C. Brown, *ibid.*, p. 7124.

[9] H. C. Brown, *Tetrahedron*, 1976, **32**, 179.



Further support for structure (XIII) is provided by the ^{13}C n.m.r. spectral data which are compared in Table 2 with those for the lactones (VII) and (VIII). Assignments were made by comparison with the work of Roberts [10] on the ^{13}C n.m.r. of norbornane derivatives. In (VII) and (VIII) C-5 and -6, respectively, carry the iodo and oxygen substituents, and their signals appear at positions comparable with those of the corresponding

[10] J. B. Grutzner, M. Jautelat, J. B. Dence, J. A. Smith, and J. D. Roberts, *J. Amer. Chem. Soc.*, 1970, **92**, 7107.

C-7 and -2 respectively in (XIII). However in (XIII) the C-2 signal is a singlet on account of the spiro nature of this carbon atom. The positions of the >C=O signals for the three lactones appear to be related to the size of the lactone ring. It is therefore possible, as previously proposed,[11] that ^{13}C n.m.r. measurements on cyclic ketones and lactones can be developed into a method to determine ring size.

TABLE 2

^{13}C N.m.r. chemical shifts [a]

	(VII) [b]		(VIII)		(XIII) [c]	
Carbon	δ	Mult.	δ	Mult.	δ	Mult.
1	46.2	d	39.1	d	53.8	d
2	36.7	d	30.2	d	87.7	s
3	34.0	t	35.8	t	43.2	t
4	46.4	d	46.9	d	44.6	d
5	30.8	d	33.2	d	29.1	t
6	88.1	d	91.4	d	21.3	t
7	37.0	t	38.3	t	30.3	d
8	178.3	s	33.1	t	26.8	t
9			168.0	s	36.4	t
10					176.0	s

[a] Fourier transform mode spectra recorded at room temperature with a Bruker HFX 90 spectrometer operating at 22.628 2 MHz; shifts in p.p.m. from Me_4Si. [b] Assignments of C-1 and -4 may perhaps be reversed. [c] Off-resonance multiplicities.

In the non-classical ion theory, σ-bridging in the norbornyl cation has been considered the controlling factor stabilising the ion and leading to products derived from *exo*-attack.[7] The ready formation of the lactones (VII) and (VIII) from the acids (I) and (II), respectively, in iodolactonisation reactions involving *endo*-attack may seriously call into question the importance of σ-bridging in controlling the direction of attack on secondary norbornyl cations.

EXPERIMENTAL

The 220 MHz n.m.r. spectral measurements were carried out by the P.C.M.U., Harwell; the ^{13}C measurements were made with a Bruker HFX 90 spectrometer operating at 22.628 2 MHz. 5-*exo*-Iodonorbornane-2-*endo*,6-*endo*-carbolactone (VII) was prepared by the procedure of Ver Nooy and Rondestvedt;[1] a 10 : 1 mixture of norborn-5-en-2-*endo*-ylacetic acid (III) and its 2-*exo*-isomer (IV) was prepared by the method of Alder and Windemuth.[12]

Pent-4-enoic Acid.—Magnesium turnings (1.0 g, 0.04 mol) were washed with acetone and dried at 80 °C for *ca.* 0.5 h; after cooling they were covered with ether (10 ml). A solution of 4-bromobut-1-ene (5.4 g, 0.04 mol) in ether (10 ml) was added dropwise over 1 h with continuous stirring. The resulting solution of but-4-enylmagnesium bromide was saturated with carbon dioxide gas, which was then bubbled through the solution for a further 0.5 h. Water (20 ml) was then added and the mixture acidified with concentrated hydrochloric acid. The ether layer was separated and the aqueous layer extracted with ether (3 × 25 ml). The combined ether layer and extracts were dried ($MgSO_4$) and evaporated and the product was distilled to afford pent-4-enoic acid (3.2 g), b.p. 46—48° at 0.45 mmHg (lit.,[13] 186—187° at 745 mmHg), n_D^{20} 1.430 1 (lit.,[14] $n_D^{7.5}$ 1.434 1); $\nu_{max.}$ 3 650—2 300br, m (OH) and 1 711s cm^{-1} (C=O); δ($CDCl_3$) 11.74 (s, CO_2H), 5.83 (m, CH_2=C*H*–CH_2), 5.30—4.83 (m, CH_2=CH), and 2.70—2.29 (m, CH_2·CH_2).

3-(*Norborn-5-en-2-yl*)*propionic Acids* (V) *and* (VI).—A mixture of cyclopentadiene (13.52 g, 0.20 mol) and pent-4-enoic acid (19.29 g, 0.20 mol) was heated (Carius furnace) in a sealed tube at 180—185 °C for 30 h. Distillation of the crude product afforded unchanged pent-4-enoic acid (3.82 g), b.p. 25—81° at 0.04 mmHg, followed by a liquid (6.33 g), b.p. 81—89° at 0.04 mmHg. This liquid was dissolved in aqueous sodium hydrogen carbonate (10%; 100 ml) and the solution was washed with ether (3 × 50 ml) and then acidified with aqueous sulphuric acid (10%; 100 ml). The mixture was extracted with ether (3 × 75 ml) and the combined extracts were dried ($MgSO_4$), filtered, and evaporated at room temperature and 15 mmHg to afford a mixture (2.12 g) of 3-(norborn-5-en-2-*endo*-yl)propionic acid (V) and its 2-*exo*-isomer (VI) as a liquid, b.p. 102—106° at 0.05 mmHg, n_D^{20} 1.485 2; $\nu_{max.}$ 3 650—2 200m,br (OH) and 1 708s cm^{-1} (C=O); δ($CDCl_3$) 11.38 (s, CO_2H), 6.15 (q, C*H*=CH, *J* 6 and 3 Hz), 5.92 (q, CH=C*H*, *J* 6 and 2.5 Hz), 2.78br (H-1 and H-4), 2.64—1.00 (8 H, complex), and 0.52 [q, H-3-*endo* in (V), *J* 7 and 3 Hz] in the ratio 5 : 1 (by n.m.r.) (Found: C, 71.95; H, 8.45. Calc. for $C_{10}H_{14}O_2$: C, 72.25; H, 8.5%).

6-endo-*Hydroxy*-5-exo-*iodonorbornan*-2-endo-*ylacetic Acid* δ-*Lactone* (VIII).—(*Cf.* iodolactonisation procedures of Ver Nooy and Rondestvedt [1] and van Tamelen and Shamma [15]). A solution of iodine (127.2 g, 0.50 mol) and potassium iodide (498.4 g, 3.0 mol) in water (1.15) was added, with protection from light, to a solution of norborn-5-en-2-*endo*-ylacetic acid (III) and its 2-*exo*-isomer (IV) (76.27 g, 0.50 mol of a 10 : 1 mixture) in aqueous sodium hydrogen carbonate (0.5N; 3 l) at 10 °C (ice–water bath). The mixture was shaken vigorously and stored in the dark for *ca.* 3 h while the temperature rose to 25 °C. After a further 12 h the mixture was extracted with chloroform (6 × 500 ml) and the combined extracts were washed successively with aqueous sodium hydrogen carbonate (5%; 2 × 500 ml) and water (2 × 500 ml), dried ($MgSO_4$), filtered, and evaporated at room temperature and 0.1 mmHg for 3 h. Recrystallisation of the residue from carbon tetrachloride afforded the *lactone* (VIII) (74.3 g) as white needles, m.p. 101—103.5° (Found: C, 38.8; H, 3.9; I, 45.3. $C_9H_{11}IO_2$ requires C, 38.85; H, 4.0; I, 45.65%); for spectral data see Tables 1 and 2 and text. Concentration and evaporation of the mother liquor from the recrystallisation afforded crude lactone (VIII) (22 g).

3-(2-endo-*Hydroxy*-7-anti-*iodonorbornan*-2-exo-*yl*)*propionic Acid* γ-*Lactone* (XIII).—A solution of iodine (9.972 g, 0.060 mol) in water (30 ml) was added at room temperature, with protection from light, to a solution, in aqueous sodium hydrogen carbonate (0.5M, 60 ml), of a 5 : 1 mixture (1.638 g, 0.010 mol) of 3-(norborn-5-en-2-*endo*-yl)propionic acid (V) and its 2-*exo*-isomer (VI). The mixture was shaken vigorously, stored in the dark for 12 h, then extracted with chloroform (3 × 100 ml). The combined extracts were washed with aqueous sodium hydrogen carbonate (2 × 50

[11] A. M. Bui, A. Cavé, M.-M. Janol, J. Parello, and P. Potier, *Tetrahedron*, 1974, **30**, 1327.
[12] K. Alder and E. Windemuth, *Ber.*, 1939, **71B**, 1938.
[13] R. Marburg, *Annalen*, 1897, **294**, 89.
[14] J. H. Gladstone, *J. Chem. Soc.*, 1891, **59**, 293.
[15] E. E. van Tamelen and M. Shamma, *J. Amer. Chem. Soc.*, 1954, **76**, 2315.

ml) and water (2 × 50 ml), dried ($MgSO_4$), filtered, and evaporated at room temperature and 0.1 mmHg. Purification of the resulting oil (1.56 g) by preparative layer chromatography (60 × 20 × 0.1 cm silica plates; ether as eluant) gave a pale yellow crystalline solid which was recrystallised from carbon tetrachloride to afford the *lactone* (XIII) (1.32 g), m.p. 92.5—96.5° (Found: C, 41.15; H, 4.4; I, 43.8. $C_{10}H_{13}IO_2$ requires C, 41.1; H, 4.5; I, 43.45%), for spectral data see text and Table 2.

We thank Professor G. A. Olah for discussions, Professor H. C. Brown for his comments, and the S.R.C. for a Research Studentship (to M. D. D.).

[6/682 *Received*, 7*th April*, 1976]