The Rearrangement of a Tetrahydrobiphenylene Derivative to a Bridged Benzocycloheptene

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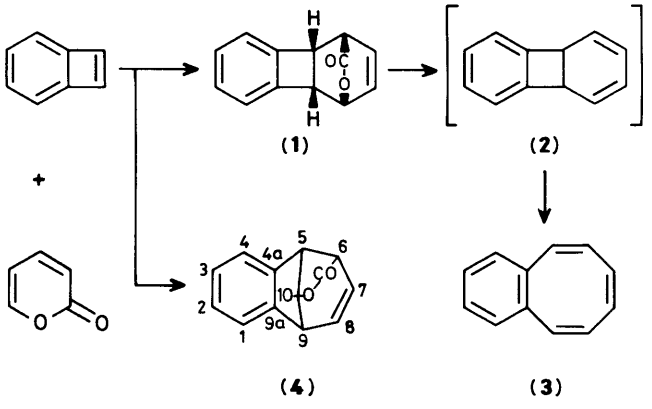
Alkaline hydrolysis of the cycloadduct of benzocyclobutene with 2*H*-pyran-2-one gives 8-hydroxy-4a,5,8,8a-tetrahydrobiphenylene-5-carboxylic acid (**7**) which undergoes an acid-catalysed rearrangement to the lactone of 6,9-dihydro-10-hydroxy-5,9-methano-5*H*-benzocycloheptene-6-carboxylic acid (**4**). A likely mechanism for this rearrangement is discussed.

In a previous paper,[1] we described the reaction of benzocyclobutene with 2*H*-pyran-2-one in DMF at 95—100 °C to give the cycloadduct (**1**), the *endo* stereochemistry being assumed by analogy with previous work. Since this lactone is readily decarboxylated thermally to benzocyclo-octene (**3**), reaction proceeding *via* ring-opening of the 4a,8b-dihydrobiphenylene intermediate (**2**) (Scheme 1), in DMF solution at reflux temperature (**3**) was obtained directly. From a parallel



Scheme 1.

experiment in acetic acid at reflux temperature we isolated, in addition to benzocyclo-octene (**3**), a compound $C_{13}H_{10}O_2$ isomeric with the adduct (**1**). In contrast to (**1**) this isomer shows remarkable thermal stability: thus, it does not decarboxylate below 250 °C and it can be sublimed under reduced pressure. Here we identify this product as the lactone of 6,9-dihydro-10-hydroxy-5,9-methano-5*H*-benzocycloheptene-6-carboxylic acid (**4**), and investigate the mechanism of the rearrangement leading to its formation.

Results and Discussion

Structure. ^{1}H N.m.r. decoupling experiments first indicated the bridged-lactone structure (**4**) for this isomeric product. The ^{1}H n.m.r. spectrum shows distinct multiplets at 3.21 (1 H, t, 6-H), 3.54 (1 H, t, 9-H), 3.98 (1 H, t, 5-H), 5.12 (1 H, t, 10-H), 5.56 (1 H, m, 7-H), 6.17 (1 H, m, 8-H), and 7.22—7.33 (4 H, m, 1-, 2-, 3-, 4-H); $J_{5,6}$ 4.7, $J_{5,10}$ 5.2, $J_{6,7}$ 6.1, $J_{7,8}$ 9.2, $J_{8,9}$ 5.3, and $J_{9,10}$ 5.3 Hz. A small long-range coupling can also be detected between 6-H and 8-H, and between 7-H and 9-H. The bridgehead 10-H does not appear to be significantly affected by the proximity of the benzene ring. The ^{13}C n.m.r. spectrum shows peaks at δ 44.1 and 44.5 (C-6 and C-9, unassigned), 49.5 (C-5), 84.2 (C-10), 121.6 (C-7), 135.1 (C-8), 176.7 (carbonyl C), 121.8, 125.9, 127.5, 127.9 (C-1, -2, -3, -4, unassigned), and 135.6, 149.6 (quaternaries, C-4a and C-9a, unassigned). The olefinic C-7 and C-8 were distinguished by selective decoupling of the associated protons 7-H and 8-H. The mass spectrum of the adduct shows sequential loss of CO_2 and a CH fragment to give the stable benzocycloheptyl radical as the base peak, and this is quite unlike the mass spectrum of (**1**), which shows cycloreversion to benzocyclobutene and 2*H*-pyran-2-one to be the favoured fragmentation. An *X*-ray determination finally established the solid state structure of the adduct as (**4**). The molecular structure with its atomic numbering scheme is shown in the Figure. The final atomic positional parameters are given in Table 1 and selected bond lengths and interbond angles in Table 2. The geometry of the aromatic ring (C-1—C-4a, C-9a) is normal with C–C separations ranging from 1.380(3) to 1.406(3) Å. All other C–C bonds, except C(7)–C(8), indicate single bond lengths with

Table 1. Atomic co-ordinates ($\times 10^4$)

	x	*y*	*z*
C(1)	10 608(3)	666(2)	9 607(2)
C(2)	9 493(3)	1 129(3)	10 388(2)
C(3)	8 171(3)	1 611(3)	9 911(2)
C(4)	7 916(3)	1 639(2)	8 620(2)
C(4a)	9 026(2)	1 173(2)	7 847(2)
C(5)	9 053(2)	1 037(2)	6 452(2)
C(6)	9 845(2)	2 107(2)	5 662(2)
C(7)	11 325(3)	2 512(2)	6 242(2)
C(8)	12 090(2)	1 650(2)	6 906(2)
C(9)	11 401(2)	332(2)	7 252(2)
C(9a)	10 364(2)	683(2)	8 332(2)
C(10)	10 221(2)	−66(2)	6 268(2)
O(10)	10 692(2)	39(2)	4 983(1)
C(11)	10 372(3)	1 291(3)	4 565(2)
O(11)	10 588(3)	1 595(2)	3 507(2)

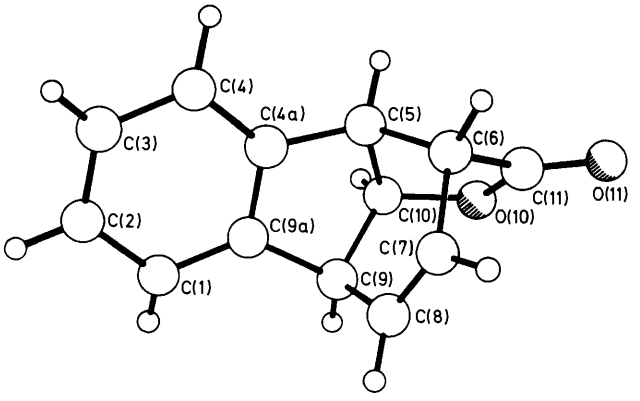


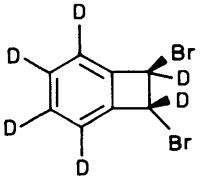
Figure.

Table 2. Selected bond lengths (Å) and interbond angles (°)

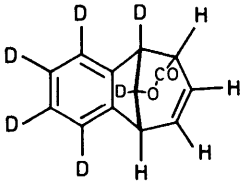
C(1)–C(2)	1.387(4)	C(9a)–C(9)	1.530(3)	C(7)–C(8)	1.318(3)
C(2)–C(3)	1.382(2)	C(9)–C(10)	1.550(3)	C(8)–C(9)	1.512(3)
C(3)–C(4)	1.406(3)	C(10)–C(5)	1.542(3)	C(6)–C(11)	1.513(3)
C(4)–C(4a)	1.380(3)	C(5)–C(4a)	1.504(3)	C(11)–O(10)	1.370(3)
C(4a)–C(9a)	1.400(3)	C(5)–C(6)	1.545(3)	C(10)–O(10)	1.447(3)
C(9a)–C(1)	1.387(3)	C(6)–C(7)	1.524(3)	C(11)–O(11)	1.193(3)
C(9a)–C(1)–C(2)	118.6(2)	C(1)–C(9a)–C(9)	130.5(2)	C(7)–C(8)–C(9)	120.0(2)
C(1)–C(2)–C(3)	121.0(2)	C(1)–C(9a)–C(4a)	120.5(2)	C(6)–C(7)–C(8)	119.9(2)
C(2)–C(3)–C(4)	120.9(2)	C(9)–C(9a)–C(4a)	108.8(2)	C(5)–C(6)–C(7)	111.4(2)
C(3)–C(4)–C(4a)	118.0(2)	C(9a)–C(9)–C(10)	99.2(2)	C(7)–C(6)–C(11)	101.0(2)
C(4)–C(4a)–C(9a)	121.1(2)	C(9a)–C(9)–C(8)	103.5(2)	C(5)–C(6)–C(11)	101.1(2)
C(4)–C(4a)–C(5)	129.9(2)	C(8)–C(9)–C(10)	109.9(2)	C(6)–C(11)–O(11)	130.8(2)
C(9a)–C(4a)–C(5)	109.0(2)	C(9)–C(10)–C(5)	101.0(2)	C(6)–C(11)–O(10)	108.1(2)
		C(9)–C(10)–O(10)	115.2(2)	O(10)–C(11)–C(11)	121.0(2)
		C(5)–C(10)–O(10)	105.6(2)	C(10)–O(10)–C(11)	108.6(2)

characteristic shortening adjacent to sp^2 atoms *viz*: C(8)–C(9), C(7)–C(6), C(4a)–C(5), and C(9)–C(9a). Similarly, the two C–O bonds show C(11–O(10) to be shorter than C(10)–O(10), but both fall into the normal C–O ranges. The bond angles in the various five- and six-membered rings distort from tetrahedral values most markedly at the ring junctions, *i.e.* at points of maximum ring strain, *e.g.* C-9, C-10, C-5, and C-6.

Mechanism. Preliminary experiments indicated that the adduct (**1**) did not rearrange to the lactone (**4**) in acetic acid containing zinc and zinc bromide, benzocyclo-octene (**3**) being the only detectable product. In order to identify the carbon atoms involved in the skeletal rearrangement a partially deuteriated derivative of (**4**) was prepared in the following way. Reaction of perdeuterio-*o*-xylene with *N*-bromosuccinimide (4 equiv.), followed by cyclisation with sodium iodide in DMF, gave the dibromohexadeuteriobenzocyclobutene (**5**). Generation of perdeuteriobenzocyclobutene, by debromination of (**5**) with zinc, in the presence of 2*H*-pyran-2-one in acetic acid gave the deuteriated lactone (**6**). The ^1H n.m.r. spectrum of (**6**) shows

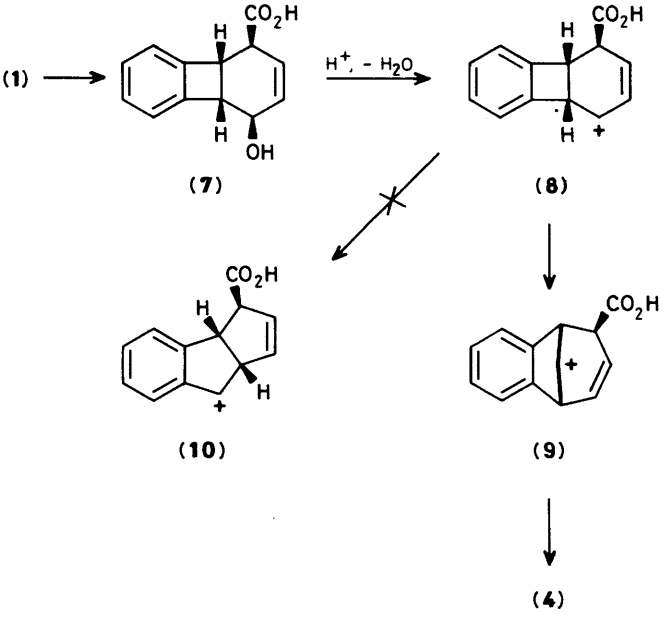


(**5**)



(**6**)

signals for 6-, 7-, 8-, and 9-H only, the multiplets at 3.98 and 5.12 in the spectrum of (**4**) being absent. This, despite our earlier observations, suggested initial formation of adduct (**1**), and a further reaction proceeding *via* rearrangement of the cationic intermediate (**8**) (Scheme 2). This is supported by our subsequent findings. Hydrolysis of the adduct (**1**) with potassium hydroxide in aqueous digol gave 8-hydroxy-4a,5,8,8a-tetrahydrobiphenylene-5-carboxylic acid (**7**). A solution of the acid (**7**) in acetic anhydride containing a trace of sulphuric acid rearranged rapidly at 25 °C to the lactone (**4**). The adduct (**1**) also rearranges under these conditions, but the reaction is considerably slower, taking several days at room temperature. Molecular models indicate that the mechanistic sequence (Scheme 2) leading to (**4**) is also in keeping with the assumed *endo* configuration of (**1**), the stereoisomeric carbon corresponding to (**9**), derived from the *exo* isomer, not being capable



Scheme 2.

of cyclising to (**4**). No products derived from the thermodynamically favoured benzylic cation (**10**) could be found. Here again, this cation would be sterically incapable of cyclisation to a lactone.

Experimental

Preparative t.l.c. was performed using Kieselgel HF (Merck) and column chromatography using aluminium oxide MFC (BDH). ^1H N.m.r. spectra were recorded on a JEOL JNM FX200 spectrometer, and ^{13}C spectra on a JEOL JNM FX90Q spectrometer. Samples were run at ambient temperature and chemical shifts are recorded as p.p.m. downfield from internal tetramethylsilane. I.r. spectra were run as Nujol mulls. Mass spectra were obtained on an AEI MS902 instrument operated at 70 eV and a source temperature of 200 °C. The following starting materials were prepared by literature routes: the lactone (**1**),[1] *trans*-1,2-dibromo-1,2-dihydrobenzocyclobutene,[2] and 2*H*-pyran-2-one.[3]

Lactone of 6,9-*Dihydro*-10-*hydroxy*-5,9-*methano*-5H-*benzocycloheptene*-6-*carboxylic Acid* (**4**).—A solution of *trans*-1,2-dibromo-1,2-dihydrobenzocyclobutene (2.7 *g*) and 2*H*-pyran-2-one (0.5 g) in acetic acid (10 ml) was added over a period of 20 min to a stirred suspension of zinc dust (5 g) in boiling acetic acid (35 ml) containing 2*H*-pyran-2-one (0.7 g). The mixture was heated under reflux for a further 20 min, cooled, extracted with ether, and the extract washed with water followed by aqueous sodium hydrogen carbonate. The organic phase was dried (Na_2SO_4), evaporated to *ca.* 10 ml, and diluted with light petroleum (b.p. 40—60 °C; 40 ml), to precipitate the crystalline lactone (**4**) (0.4 g, 20%), m.p. 137—139 °C (from light petroleum) (Found: C, 78.7; H, 5.1. $C_{13}H_{10}O_2$ requires C, 78.8; H, 5.05%); n.m.r. spectra, see text; $\nu_{max.}$ 1 760, 1 121, 1 046, 1 019, 965, and 705 cm^{-1}; *m*/*z* (%) 198 (M^+, 17), 154 (81), 153 (8), 141 (100), and 115 (26). Evaporation of the filtrate and chromatography of the residue on alumina using light petroleum (b.p. 40—60 °C) as the eluant gave benzocyclo-octene (**3**) (0.47 g, 30%), m.p. 49—50 °C (from aqueous EtOH).

[4-^{2}H]-1,2-*Dibromo*-1,2-*dideuteriobenzocyclobutene* (**5**).—The photobromination of [10-^{2}H]-*o*-xylene (2.0 g) with *N*-bromosuccinimide (12.5 g) in dry carbon tetrachloride (60 ml) by heating to reflux over a 250 W bulb for 3.5 h gave, after removal of succinimide by filtration and evaporation of the filtrate, [4-^{2}H]-1,2-bis(dibromodeuteriomethyl)benzene (7.1 g, 90%), m.p. 116—117 °C (from $CHCl_2$–EtOH) (Found: C, 22.6; H, 3.0; Br, 74.6. $C_8D_6Br_4$ requires C, 22.4; H, 2.8; Br, 74.8%). A solution of this tetrabromide (7.0 g) and sodium iodide (13 g) in DMF (50 ml) was stirred at 65 °C for 5.5 h. The reaction mixture was cooled, diluted with water, and extracted with ether. The extract was washed with aqueous sodium hydrogen sulphite and then water, dried (Na_2SO_4), and evaporated to give a mixture of bromo- and iodo-cyclised products. This crude product was dissolved in carbon tetrachloride (50 ml) containing bromine (2.0 g) and the solution kept at room temperature for 36 h; it was then again washed, dried, and evaporated as above to give the benzocyclobutene (**5**) containing a small proportion of the *cis*-isomer (2.50 g, 57%), m.p. 35—50 °C [from light petroleum (b.p. 40—60 °C)] (Found: C, 35.7; H, 4.3; Br, 60.1. $C_8H_6Br_2$ requires C, 35.8; H, 4.5; Br, 59.7%).

Deuteriated Lactone (**6**).—A reaction between [6-^{2}H]benzocyclobutene and 2*H*-pyran-2-one, as described above, gave, after recrystallisation from chloroform–hexane, the lactone (**6**) (16%), m.p. 140—141 °C (sublimes above 125 °C) (Found: C, 76.8; H, 8.0%; M^+, 204.1061. $C_{13}D_6H_4O_2$ requires C, 76.5; H, 7.8%; *M*, 204.1057); $\delta_H(CDCl_3)$ 3.21 (d, $J_{6,7}$ 6.1 Hz), and 3.54 (d, $J_{8,9}$ 0.6 Hz, 8-H); $\delta_C(CDCl_3)$ 44.1 and 44.5 (unassigned), 121.6 (C-7), and 135.1 (C-8); *m*/*z* (%) 204 (M^+, 13), 160 (93), and 146 (100).

8-*Hydroxy*-4a,5,8,8a-*tetrahydrobiphenylene*-5-*carboxylic Acid* (**7**).—A solution of the lactone (**1**) (0.5 g) and potassium hydroxide (0.2 g) in dioxane (3 ml) and water (3 ml) was stirred at room temperature for 2 h after which it was diluted with water (25 ml). The solution was washed with ether, acidified with hydrochloric acid, and the product collected by extraction with chloroform. The dried (Na_2SO_4) organic phase was evaporated to give the acid (**7**) (0.50 g, 92%), m.p. 170—171 °C (from $CHCl_3$) (Found: C, 72.2; H, 5.6. $C_{13}H_{12}O_3$ requires C, 72.2; H, 5.6%); $\delta_H(CD_3COCD_3)$ 3.40 (1 H, m, 4a-H), 3.68 (1 H, m, 5-H), 3.86 (1 H, m, 8a-H), 4.30 (1 H, m, 8-H), 5.90 (1 H, m, 6-H), 6.08 (1 H, m, 7-H), and 7.21 (4 H, m, 1—4-H); $\nu_{max.}$ 1 687, 1 213, 1 001, and 740 cm^{-1}; *m*/*z* (%) 216 (M^+, 0.9), 198 (2), 153 (100), and 102 (69).

Rearrangements of (**7**) *and* (**1**) *to the Lactone* (**4**).—(*a*) A solution of the acid (**7**) (100 mg) in acetic anhydride (3 ml) containing sulphuric acid (1 drop) was stirred at room temperature for 1 h after which it was worked up as described for (**4**) above to give the lactone (70%), identical with an authentic sample.

(*b*) The reaction was carried out as in (*a*) using a solution of the lactone (**1**). After 48 h the reaction mixture was worked up and the product purified by preparative t.l.c. on silica using chloroform as eluant, to give the lactone (**4**) (28%). The residue consisted of a complex mixture of esterified products.

Crystallography.—Crystal data for (**4**): $C_{13}H_{10}O_2$, M = 198.2, space group orthorhombic $P2_12_12_1$ (No. 19), a = 8.982(2), b = 10.080(2), c = 10.739(2) Å, V = 972.3(4) Å^3, (293 K) Z = 4, D_c = 1.35 g cm^{-3}, $F(000)$ = 416; graphite monochromated Mo-K_α radiation, λ = 0.710 69 Å, μ = 0.85 cm^{-1}.

Intensity data were recorded from a clear transparent crystalline fragment (0.3 × 0.5 × 0.9 mm) in the range $2.9 \leqq 2\theta \leqq 65°$. From the 1 464 unique data, 1 351 were observed with $I \geqq \sigma(I)$ and these were used to refine the structure after solution by direct methods. All hydrogen atoms were located from difference density syntheses and were refined with isotropic displacement parameters, while all non-hydrogen atoms were refined with anisotropic displacement parameters. The programme used throughout was SHELXTL on a Data General S230 Eclipse; scattering factors were taken from ref. 4, including corrections for anomalous dispersion. Refinement converged at R (R_w) 0.047 (0.050) using a weighting scheme of the form $\{w = (\sigma^2(F) = gF^2)^{-1}\}$, where g = 0.001. The latter scheme gave a satisfactory analysis of variance and the final difference synthesis showed maximum residuals of ±0.02 e Å^{-3}. The atomic co-ordinates given are those of the enantiomorph which satisfies the normal enantiomorph tests. The atomic co-ordinates are given in Table 1 and selected bond lengths and angles in Table 2; full listings of the latter together with the hydrogen co-ordinates and thermal parameters are available on request from the Cambridge Crystallographic Data Centre.*

Acknowledgements

We thank the S.E.R.C. for studentships to M. K. S. and A. M. S.

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Received 13*th November* 1986; *Paper* 6/2172