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Studies on Bicyclononanes. Part III.¹ Chair–Boat Equilibria in Bicyclo[3,3,1]nonanes

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The preparation and configurational assignments of the epimeric 3-carboxybicyclo[3,3,1]nonanes are described, and the free energy difference between their methyl esters is measured. The bromination products of bicyclononan-2-one are discussed, and the deamination of a boat cyclohexylamine is reported.

BICYCLO[3,3,1]NONANE and several of its derivatives have been shown to exist as double chair conformers.² It was of interest to equilibrate a pair of epimeric 3-substituted bicyclo[3,3,1]nonanes, and so estimate ΔG for the double-chair to chair-boat isomerisation. The 3-carboxybicyclononanes and their esters seemed most suited to our purpose. Recently a description³ of one of these acids has appeared, though without evidence of configuration.

Diethyl malonate was condensed with the ditosylate of cis-1,3-bishydroxymethylcyclohexane to give a diester which was not purified, but hydrolysed immediately to the diacid (I) (63% overall). The neutral fraction from the reaction consisted of the compounds (II)-(IV) and polymeric material; the structure assignments are based on analyses and spectral properties (see Experimental section).



Decarboxylation of (I) in a melt or in collidine under reflux gave a mixture of two monocarboxylic acids in the ratio 17:3. They could not be separated by partition chromatography; the major product was obtained pure by fractional crystallisation. As proof of structure, the acids were converted into bicyclononan-3-one (an authentic sample of which was obtained by Dieckmann cyclisation of the requisite diester) by way of their dimethylamides, the dimethylaminomethylbicyclononanes, and 3-methylenebicyclononane.

The major decarboxylation product was shown to be the 3α -acid (V) by conversion into both the 3α -ol (by the usual route through the methyl ketone and the acetoxy-

¹ Part II, R. A. Appleton, J. R. Dixon, J. M. Evans, and S. H. Graham, *Tetrahedron*, 1967, 23, 805. ² W. A. C. Brown, K. Eglinton, J. Martin, W. Parker, and G. A. Sim, *Proc. Chem. Soc.*, 1964, 57; W. A. C. Brown, J. Martin, and G. A. Sim, *J. Chem. Soc.*, 1965, 1844; M. Dobler and J. D. Dunitz, Helv. Chim. Acta, 1964, 47, 695.

³ E. Buchta and S. Billenstein, Annalen, 1966, 692, 42.

derivative) and 3α -methylbicyclononane (by reduction to the hydroxymethyl derivative, tosylation, and hydride reduction). Both samples were different from the known 3 β -epimers. The predominant formation of 3α -acid in the decarboxylation is to be expected; ⁴ the presence of 15% of the β -epimer is probably due to partial equilibration. The 3β -acid (VI) was prepared by way of its ester by the action of methoxide on (VII) and the two esters (VII) and (VIII) were equilibrated at 20°; thus equilibrium was approached from both sides. The observed equilibrium [99% (VIII) $\pm 0.5\%$] corresponds to a ΔG value of 2.7 kcal./mole for the double-chair into chair-boat conversion. Attempts to separate this value into enthalpy and entropy terms by repeating the measurements at other temperatures met with no success. Although the g.l.c. separations were of sufficient sharpness to give realistic free energy values, we do not regard our analyses, since the percentage of (VII) is low, as accurate enough to permit the extraction of a meaningful entropy term. However, provided that (VII) exists in substantially a single conformation, no significant entropy change should be anticipated, as both (VII) and (VIII) are rigid and of the same symmetry. Hence the value of 2.7 kcal./mole is probably a fair approximation to the enthalpy of isomerising a chair ring of bicyclononane into a boat.

The assumption has been made that (V) and (VII) represent the only seriously populated conformations for the 3α -acid and its ester. However the view has been expressed ⁵ and challenged ⁶ that a 3a-hydroxygroup at least can be accommodated in a double-chair bicyclononane skeleton. As will be shown later, a 3α -bromine atom undoubtedly necessitates the substituted ring assuming the boat conformation; although the combination of the long C-Br bond with the large atomic radius of bromine results in effectively small steric requirements in ordinary cyclohexane chemistry, it is safer to regard bromine as a large atom in the present connection. In the absence of any experimental confirmation of the conformation of (VII) it seems reasonable to compute the minimum enthalpy change involved in isomerising a 3-ester group from the exo- to the endoposition in a double-chair as twice the ester-methyl 1.3-diaxial repulsion less twice the hydrogen-methyl

⁴ J. A. King, J. Amer. Chem. Soc., 1947, **69**, 2738; H. Musso and V. Biethan, Chem. Ber., 1967, **97**, 2282. ⁵ C.-Y. Chen and R. J. W. Le Fèvre, Tetrahedron Letters,

^{1965,} **12**, 737.

⁶ W. D. K. Macrosson, J. Martin, and W. Parker, Tetrahedron Letters, 1965, 30, 2589.

diaxial repulsion. The first of these values is not known but can be interpolated between the known values for the hydroxy- (2.4 kcal./mole) 7 and methyl (3.7 kcal./ mole) ⁷ groups. Provisional assignment of 2.6 kcal/mole for the ester-methyl 1,3-diaxial repulsion would give 3.5 kcal./mole (*i.e.* 5.2 - 1.7 kcal./mole), plus an unknown increment for increased transannular strain, for the enthalpy change involved. Even if the many approximations in the above calculation are allowed for it seems that a double-chair conformation of the 3*a*-ester can be populated to only a small extent. Similar reasoning indicates that chair-boat conformations with the 3α -substituent in the chair ring⁶ can certainly be ignored.

The enthalpy difference between chair and boat cyclohexane rings has been estimated at $6.9 \text{ kcal./mole.}^8$ The presence of two axial substituents should raise the energy of the chair ring relative to the boat since each substituent introduces two skew-methylene interactions into the former and only one into the latter, while the exchange of two hydrogen-hydrogen eclipsing interactions in the boat for two hydrogen-methylene interactions will add only about 0.5 kcal./mole to the energy of the boat.⁹ Hence, transannular strain apart, the enthalpy difference between double-chair and chair-boat conformers should be (6.9 - 1.7 + 0.5) kcal./mole, *i.e.* ca. 5.7 kcal./mole. Subtraction of the observed 2.7 kcal./mole gives 3 kcal./mole as a rough approximation to what may properly be termed transannular strain in the double chair.

This work constitutes the first demonstration that bicyclononanes will exist in the double-chair conformation independently of the constraints of the crystal lattice. It also indicates that bicyclononan-2-ones should have an appreciable population in both conformations, since ΔH_{525} for the cylcohexanone chair \longrightarrow twist-boat conversion is only 3.91 kcal./mole.¹⁰ Bicyclononan-2-one and its 7β -methyl homologue were therefore brominated as a first step to equilibrating two 3-substituted bicyclononan-2-ones, though the dipolar repulsions between bromine and carbonyl make them less suitable for quantitative comparisons.

Bromination of the enol acetates of the two ketones in the presence of a proton scavenger gave two monobromo-ketones, each of which showed in its ¹H n.m.r. spectrum a triplet (1H, J 10 c./sec.) with centre at τ 5.28. After equilibration with hydrobromic acid a second triplet was observed, superimposed on the first, with centre at τ 5.21; the spectra then resembled those of the bromo-ketones obtained by direct acid-catalysed bromination of the 2-ones. No quantitative analysis of the equilibrium mixtures could be made from the spectrum, nor could the epimers be separated by crystallisation or by chromatography. It could in fact only be inferred that the second ketone was a 3-bromo2-one (attack at C-1 could of course be discounted), since the mixtures readily yielded pure 3,3-dibromo-2-ones on further reaction.

Because of steric hindrance to endo-approach, the kinetically controlled reaction products should be the 3β -bromo-2-ones. (If the brominations passed through a chair-boat transition state the rule of axial approach of bromine¹¹ need not be violated.) This was confirmed by reduction to bromohydrins (IXa) and (IXb); the trans-geometry of these was established by their ¹H n.m.r. spectra which included absorptions at τ 5.45 (1H, m, 3-H) and τ 6.17 (1H, q, apparent J 5 and 10 c./sec., 2-H); spin decoupling showed $J_{2,3}$ to be the 10 c./sec. coupling. Since the 3α -bromo- 2β -ols (Xa) and (Xb) could be prepared from the appropriate epoxides and hydrogen bromide, and were different from the bromoketone reduction products, both the latter and the bromo-ketones must have β -oriented bromine. The ¹H n.m.r. spectra of the 3α -bromo- 2β -ols not only confirm their structures but also show that the substituted ring is definitely in the boat form, since the 2-H signal is a doublet $(J_{2,3} \ 10 \ \text{c./sec.})$ and the coupling to 1-H is very small, and leads only to a broadening of the lines of the doublet. The resonance of the 2-protons occurs at almost the same chemical shift value in the spectra of all the bromohydrins, but that of the 3-protons occurs about 0.4 p.p.m. to lower field in the spectra of the double-chair isomers (IX) relative to the chair-boat isomers (X).



Borohydride reduction of the equilibrated mixtures of bromo-ketones gave the same bromohydrins (IXa) and (IXb), but in lower yield (60% as against 85%) than when made from pure 3β -bromo-2-one; this gives a lower limit of about 70% for the β -epimers at equilibrium. The ease with which pure 3β -bromo- 2α -ols could be isolated from the reduction of mixtures of bromo-ketones is probably due to the steric hindrance to reduction of the 3α -bromo-2-ones which makes this process relatively slow.

The 3,3-dibromo-ketones (XIa) and (XIb) were prepared in the hope that dehydrohalogenation followed by reduction would give the pure 3α -bromo-2-ones. The attempt failed because the final hydrogenation removed bromine and regenerated the original ketones. The ¹H n.m.r. spectra of the dibromo-ketones proved of interest since they included a quartet (1H, apparent J 10 and 17 c./sec.) with centre τ 6.30 and a doublet (1H, J 17 c./sec.) with centre τ 6.96 (and superimposed

⁷ E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison,

⁶ Conformational Analysis, ⁷ Interscience, New York, 1965, p. 52. ⁸ J. B. Hendrickson, J. Amer. Chem. Soc., 1961, 83, 4537.

⁹ Ref. 7, p. 9.

N. L. Allinger, H. M. Blatter, L. A. Freiberg, and F. M. Karkowski, J. Amer. Chem. Soc., 1966, 88, 2999.
E. J. Corey, J. Amer. Chem. Soc., 1954, 76, 175.

on more complex absorption). Spin decoupling showed the signals to be mutually coupled; this can only be a geminal coupling, with the lower field signal due to the 4β -H, which is also coupled (10 c./sec.) to 5-H (the two protons eclipse each other). The higher-field signal $(4\alpha-H)$ shows hardly any vicinal coupling (compare the spectra of the 3α -bromo- 2β -ols where, with a dihedral angle also of 120° , the coupling is again very small). Deshielding of vicinal protons by gem-dihalogeno-groups has been reported,¹² but the origin of the effect is obscure. In the present instance the chemical shifts of 4β -H and 4α -H showed marked solvent dependence: they were moved upfield (by 0.33 and 0.37 p.p.m. respectively) on going from deuteriochloroform to deuteriochloroformbenzene (50%). The ¹H n.m.r. spectra of the 3-bromoenones, formed by dehydrobromination of (XIa) and (XIb), were also of interest, as the olefinic proton (4-H) showed a coupling of 1.5 c./sec. to the *anti*-proton on C-9. although the four bonds involved depart seriously from the planar-M geometry.13

OH OH Me Me Me (XII)(X III)

 7α -Methylbicyclononan-2-one (XII), in which the cyclohexane ring is constained into the boat conformation, was synthesised by the route shown. It yielded only a monobromo-ketone, even in the presence of excess of bromine; the configuration of this bromoketone was not investigated, but both kinetic and thermodynamic considerations favour β -substitution. The ¹H n.m.r. spectrum (q, J 6 and 10 c./sec. for 3-H) was consistent with homogeneity of the sample and with the cyclohexanone ring being a fairly normal chair. The other 3β-bromo-2-ones (triplets for 3-H) had marked distortion in the ketonic rings.

Since a 3α -substituted bicyclononane is an example of the comparatively rare true boat ring, we began a study of the chemistry of substituted boat cyclohexanes by preparing 3α -aminobicyclononane (XIII), by the usual stereospecific reactions, and examining its reaction with nitrous acid. The normal course of reaction of equatorial cyclohexylamines is to give an alcohol with retained configuration and comparatively little olefin.¹⁴ The amine (XIII) did not react with nitrous acid at pH 4,¹⁵ and at pH 5 only 10% had reacted after 24 hr., to give approximately equimolar amounts of the 3α -ol and bicyclonon-2-ene. The formation of the alcohol

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with retained configuration was expected; the attack of solvent from the back of the diazonium ion observed by Corey and Dawson¹⁶ could not occur here. Neither can the alcohol be formed by way of a simple carbonium ion, which would certainly exist as a double-chair and lead to the 3β -ol; collapse of a solvated diazonium ion to an asymmetrically solvated (boat-chair) carbonium ion ¹⁷ which reacts with its own solvent envelope would explain the formation of the 3α -ol. If the rule of transdiaxial elimination holds for boat cyclohexane rings, then the olefin cannot be formed by concerted loss of nitrogen and a proton from the diazonium ion,¹⁷ but must involve loss of a proton from the carbonium ion. Although this is not commonly observed in the reactions of equatorial amines, it must be borne in mind that reaction of carbonium ion with solvent in the present instance involves setting up steric strains and it is not surprising that proton loss is able to compete with alcohol formation.

EXPERIMENTAL

3,3-Dicarboxybicyclo[3,3,1]nonane (I).-To a solution of diethyl malonate (6.4 g.) in dry tetrahydrofuran (200 ml.) was added sodium hydride (50% dispersion in mineral oil; 3.6 g.) in portions during 1 hr. A solution of cis-1,3-bistoluenesulphonyloxymethylcyclohexane (20 g.) in dry tetrahydrofuran (400 ml.) was stirred in and the whole was heated with stirring at 120° in a stainless steel autoclave for 20 hr. The cooled mixture was filtered, the residual salt was washed with solvent, and the filtrates were evaporated. The residue was boiled with 4n-methanolic potassium hydroxide (100 ml.) for 7 hr., the solvent was evaporated off, the residue was taken up in water (300 ml.), and neutral materials were extracted with light petroleum $(3 \times 20 \text{ ml.})$. Acidification of the aqueous phase with 10n-hydrochloric acid and extraction with ether gave the acid (I) as a gum which crystallised after trituration with chloroform as cubes (5.9 g., 63%), m.p. 152-153° (Found: C, 61.8; H, 7.2. C₁₁H₁₆O₄ requires C, 62.2; H, 7.6%). The combined neutral fractions from several runs (76.1 g.) were distilled up a Vigreux column (6 in.) to give fractions b.p. 70-97°/12 mm. (9.0 g.) and 97-98°/12 mm. (24.15 g.) and a polymeric residue (42.1 g.). The lower-boiling fraction (three components; g.l.c. on silicone) was separated by chromatography on alumina into a mobile liquid $(0.52\,\mathrm{g.})$, b.p. 70°/12 mm. (Found: C, 77.5; H, 11.2. C₉H₁₆O requires C, 77.3; H, 11.5%), ν_{max} 889, 1093, 1640, 2819, and 3075 cm.⁻¹, a volatile solid, m.p. 138–141°, ν_{max} 1075 cm.⁻¹ (Found: C, 74.9; H, 11.0. C₇H₁₂O requires C, 74.9; H, 10.8%), and a third component identical with the higher-boiling fraction (total 30.2 g.), b.p. 98°/12 mm., $n_{\rm D}^{23}$ 1.4451, $\nu_{\rm max}$ 1093 and 2819 cm.⁻¹ (Found: C, 70.0; H, 11.7. $C_{10}H_{20}O_2$ requires C, 69.7; H, 11.7%).

Decarboxylation of Acid (I).—(a) The acid (5.6 g.) was heated at 160° in a nitrogen atmosphere until effervescence ceased. Vacuum sublimation at 105°/1 mm. gave a solid (3.88 g.), m.p. 90—113°.

¹² C. W. Shoppee, T. E. Bellas, R. E. Lock, and S. Sternhell, *J. Chem. Soc.*, 1965, 2483.

¹³ C. W. Jefford, B. Waegall, and K. Ramey, J. Amer. Chem. Soc., 1965, 87, 2191.

¹⁴ J. A. Mills, J. Chem. Soc., 1953, 260; W. G. Dauben, R. C. Twist, and C. Mannerskantz, J. Amer. Chem. Soc., 1954, 76, 4420.

¹⁵ N. Kornblum and D. C. Iffland, J. Amer. Chem. Soc., 1949,

^{71, 2137.} ¹⁶ E. J. Corey and R. C. Dawson, J. Amer. Chem. Soc., 1963, 85, 1782.

¹⁷ A. Streitweiser and C. E. Coverdale, J. Amer. Chem. Soc., 1959, 81, 4275.

(b) The acid (I) (1 g.) was heated for 2 hr. in boiling collidine (10 ml.); the cooled mixture was taken up in 2N-hydrochloric acid (50 ml.) and extracted with ether (2 × 20 ml.). Removal of solvent and vacuum sublimation as above gave a solid (0.62 g.), m.p. 90—113°. Esterification (with diazomethane) of the mixed acids gave a mixture of (VII) (85%) and (VIII) (15%) (g.l.c. on tritolyl phosphate at 142°). The crude monocarboxylic acids (15 g.) were recrystallised several times from light petroleum to give plates (10.7 g.), m.p. 126—127° (lit.,³ 122°) (Found: C, 71·3; H, 9·3. Calc. for C₁₀H₁₆O₂: C, 71·4; H, 9·5%). Esterification of the acid (3·0 g.) with diazomethane gave the *methyl ester* (VII) (2·75 g.), b.p. 121°/11 mm., $n_{\rm D}^{23}$ 1·4824, homogeneous on g.l.c. (Found: C, 72·8; H, 10·0. C₁₁H₁₈O₂ requires C, 72·5; N, 10·0%).

The 3-Dimethylcarbamoylbicyclo[3,3,1]nonanes.— To a stirred ice-cold solution of the acid chlorides (4.17 g.) from the epimeric carboxylic acids in dry benzene (10 ml.) 0.6M-dimethylamine in benzene (100 ml.) was added dropwise during 1 hr., and the mixture was heated at 40° for 1 hr. The usual work-up gave the *amides* (4.3 g.) as an oil which crystallised; m.p. 55°, b.p. 110—112°/0.3 mm. (Found: C, 73.6; H, 10.7; N, 7.2. $C_{12}H_{21}NO$ requires C, 73.9; H, 10.8; N, 7.2%).

The 3-Dimethylaminomethylbicyclo[3,3,1]nonanes.— The epimeric amides (4.2 g.) were boiled with lithium aluminium hydride (1.5 g.) in tetrahydrofuran (70 ml.) for 3 hr. After cautious addition of water, solvent was decanted from precipitated salts, which were washed with ether. Drying and removal of solvent gave the amines (3.86 g.), b.p. 101—102°/11 mm. (Found: C, 79.3; H, 12.9; N, 7.8. $C_{12}H_{23}N$ requires C, 79.6; H, 12.7; N, 7.7%).

3-Methylenebicyclo[**3**,**3**,**1**]nonane.— Hydrogen peroxide (100 vol.; 20 ml.) was added to the amines (**3**-86 g.) in methanol (**35** ml.) during **15** min. The mixture was left for 1 hr. at room temperature, and boiled for 4 hr. After destruction of excess of peroxide and removal of solvent, the residue was heated at $120^{\circ}/0.5$ mm. and the products were collected in a cold trap. The residue was taken up in solvent, washed, dried, and chromatographed on alumina with light petroleum as eluant to give **3**-methylenebicyclononane, m.p. 20°, b.p. $182^{\circ}/760$ mm., τ 5.34 (2H, m, $W_{\rm H}$ **4**·5 c./sec.), 7.57 (4H, m), and 8·0—8·5 (10H) (Found: C, 88·3; H, 11·7. C₁₀H₁₆ requires C, 88·2; H, 11·8%).

Bicyclo[3,3,1]nonan-2-one.—(a) Sodium periodate (3 g.) was added in three portions to a solution of methylenebicyclononane (0.5 g.) and osmic acid (20 mg.) in tetrahydrofuran (20 ml.) and water (10 ml.) during 30 min., and stirring was continued for 3 hr. Then 2N-sodium hydroxide (15 ml.) was added, the solvent was removed, and the ketone was extracted into methylene chloride. The ketone was sublimed at $80^{\circ}/12$ mm. to give prisms (0.32 g.), m.p. 180—182° (lit.,¹⁸ 180—182°), v_{max} . ¹⁸ 1706 and 1717 cm.⁻¹ (Found: C, 77.9; H, 10.1. Calc. for C₉H₁₄O: C, 78.2; H, 10.1%); the 2,4-dinitrophenylhydrazone had m.p. 208—209° (lit.,¹⁸ 208—209°); the semicarbazone gave plates, m.p. 182° (from ethanol-water) (Found: C, 61.4; H, 8.7; N, 21.0. C₁₉H₁₇N₃O requires C, 61.5; H, 8.8; N, 21.5%).

(b) The dimethyl ester of cis-cyclohexane-1,3-diacetic acid (5 g.) and sodium hydride (1.5 g.) in benzene (15 ml.) were boiled for 18 hr.; the usual work-up gave the ketone (0.49 g.), m.p. and mixed m.p. with product of (a) 180–182°.

 3α -Acetylbicyclo[3,3,1]nonane.—An ethereal solution (0.34M) of methyl-lithium (180 ml.) was added in one batch to the acid (V) (3 g.) in ether (100 ml.) under nitrogen. The

mixture was stirred for 15 min. at room temperature and for 30 min. under reflux, then worked up. The resulting oil (3.08 g.) was chromatographed on alumina to give the *ketone* (1.37 g. after distillation), b.p. 122—124°/13 mm., n_p^{23} 1.4913 (Found: C, 79.9; H, 11.0. C₁₁H₁₈O requires C, 79.5; H, 10.9%); the *semicarbazone* gave plates, m.p. 217—218° (Found: C, 64.6; H, 9.6; N, 18.6. C₁₂H₂₁N₃O requires C, 64.6; H, 9.5; N, 18.8%). From the later fractions of the chromatographic separation 3α -(2-hydroxy-2-propyl)bicyclo[3,3,1]nonane (0.92 g.) was isolated as needles, m.p. 82.5—83.5° (Found: C, 79.0; H, 11.9. C₁₂H₂₂O requires C, 79.1; H, 12.2%).

Bicyclo[3,3,1]nonan-3 α -ol.—Monoperphthalic acid (2·1 g.) in dry ether (60 ml.) was added during 20 min. to a solution of the above ketone (1·37 g.) in dry ether (20 ml.), and the mixture was left for some days. Removal of acids and fractionation gave 3α -acetoxybicyclo[3,3,1]nonane (1·18 g.), b.p. 113—115°/12 mm. (Found: C, 72·7; H, 9·9. C₁₁H₁₈O₂ requires C, 72·5; H, 9·9%). Hydrolysis of this ester (0·5 g.) with methanolic alkali for 4 hr. at the boiling point gave the alcohol (0·33 g.) as needles, m.p. 95—95·5°, depressed on admixture with the 3 β -ol (Found: C, 77·3; H, 11·6. C₉H₁₆O requires C, 77·1; H, 11·5%).

 3α -Methylbicyclo[3,3,1]nonane.— Aluminohydride reduction of the acid (V) in the usual way gave the hydroxymethyl derivative (90%), b.p. 91—92°/1 mm., $n_{\rm p}^{25}$ 1.5055 (Found: C, 77.6; H, 11.6. C₁₆H₁₈O requires C, 77.9; H, 11.8%); the tosylate gave needles, m.p. 111-112.5° (from methanol) (Found: C, 66.1; H, 7.8; S, 10.2. $C_{17}H_{24}O_3S$ requires C, 66.2; H, 7.8; S, 10.4%). The tosylate (2 g.) and lithium aluminohydride (1.25 g.) in ether (50 ml.) were heated under reflux for 20 hr., and, after the usual work-up, the products were chromatographed on alumina with light petroleum as eluant. This gave the hydrocarbon (0.52 g.), b.p. 179—180°/760 mm., $n_{\rm D}^{25}$ 1.4749 (Found: C, 86.7; H, 13.2. C₁₀H₁₈ requires C, 86.9; H, 13.1%), $\nu_{max.}$ 1445 and 2971 cm.⁻¹, in addition to normal scissoring and stretching frequencies; these peaks did not appear in the spectrum of the 3β-epimer.¹⁹ The ¹H n.m.r. absorptions at τ 9.12 (3H, d, J 5.5 c./sec.) and the pattern of methylene absorption were different from those shown by the 3β -epimer, which had also a different retention time on g.l.c. (tritolyl phosphate).

3 β -Carboxybicyclo[3,3,1]nonane (VI).—The methyl esters (6 g.) from the mixture of monocarboxylic acids were left for several weeks in 0.4M-sodium methoxide. Hydrolysis of the ester gave the acid (VI) (3.52 g.), m.p. 132—133.5° (Found: C, 71.6; H, 9.5. C₁₀H₁₆O₂ requires C, 71.4; H, 9.6%. The methyl ester (VIII) had b.p. 120°/13 mm., $n_{\rm D}^{25}$ 1.4805 (Found: C, 73.0; H, 9.7. C₁₁H₁₈O₂ requires C, 72.5; H, 9.9%).

Equilibration of Esters (VII) and (VIII).—Small glass ampoules were charged in an atmosphere of oxygen-free nitrogen with 0.5 ml. each of a 2% solution of one of the epimeric esters in 0.4M-sodium methoxide, and sealed. After 8 weeks at 20° the ampoules were crushed and the contents were immediately neutralised with glacial acetic acid and analysed [g.l.c. on a column (12 ft.) of 3% tritolyl phosphate on deactivated Celite at 125°]. The equilibrium composition (from a number of runs) was 99% (VIII) and 1% (VII) $\pm 0.5\%$.

7β-Methylbicyclononane-2-one.—A mixture of the epimeric

¹⁸ H. K. Hall, J. Org. Chem., 1963, 28, 3213.

¹⁹ R. A. Appleton, C. Egan, and S. H. Graham, to be published. 7β-methyl-2-(pyrrolidin-1-yl)bicyclononanes 19 (4.5 g.) and mercuric acetate (32.4 g.) in 5% acetic acid (100 ml.) was stirred and heated at 100° for 3 hr. The precipitated salts were filtered off and washed with acetone, and mercuric ion was removed from the combined filtrates with hydrogen sulphide. The aqueous phase was basified (K_2CO_3) and the *ketone* was obtained by ether extraction as an oil (1.92 g.), b.p. 103—105°/10 mm., $n_{\rm p}^{23}$ 1·4876 (Found: C, 78·9; H, 10.8. C₁₀H₁₆O requires C, 78.9; H, 10.6%); the 2,4-dinitrophenylhydrazone gave orange prisms, m.p. 139-140° (from benzene-light petroleum) (Found: C, 57.6; H, 6.1. $C_{16}H_{20}N_4O_4$ requires C, 57.8; H, 6.1%); the semicarbazone had m.p. 165° (Found: C, 63·2; H, 9·1; N, 19·7. C₁₁H₁₉N₃O requires C, 63.2; H, 9.1; N, 20.1%); the enol acetate, b.p. 100°/10 mm., $n_{\rm p}^{22}$ 1.4812 (not analysed), was prepared by exchange with isopropenyl acetate.

2-Acetoxy[3,3,1]bicyclonon-2-ene, similarly prepared, had b.p. 105—108°/10 mm., $n_{\rm D}^{25}$ 1·4835 (Found: C, 73·2; H, 8·8. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%).

Bromination of Enol Acetates.—The enol acetates (1 g.) and potassium carbonate (2 g.) in carbon tetrachloride (25 ml.) were treated with bromine (0.82 g.) at 0°. Filtration and evaporation gave 3β -bromobicyclo[3,3,1]nonan-2-one (1.16 g.), m.p. 75° (Found: C, 49.7; H, 5.8; Br, 36.8. C₉H₁₃BrO requires C, 49.8; H, 6.0; Br, 36.9%), ν_{max} 1709 and 697 cm.⁻¹, τ 5.28 (1H, t, J 10 c./sec., 3-H).

3β-Bromo-7β-methylbicyclo[3,3,1]nonan-2-one (0.88 g.) had m.p. 96° (Found: C, 51.9; H, 6.7. $C_{10}H_{15}BrO$ requires C, 52.0; H, 6.5%), ν_{max} . 1715 cm.⁻¹, τ 5.28 (1H, t, J 10 c./sec., 3-H).

Equilibration of 3-Bromo-2-ones.—Samples of the above bromo-ketones (0.1 g.) were dissolved in acetic acid (5 ml.) and a few drops of hydrobromic acid were added; after some days the solutes were recovered and were then identical with the products of bromination of the 2-ones in acetic acid. The mixture of 3-bromo-2-ones melted over the range 78—89°; the melting range was not altered by recrystallisation. The mixture of 3-bromo-7 β -methyl-2-ones melted at 111—111.5°. The ¹H n.m.r. spectra of both samples included a multiplet (1H) which could be seen to consist of two triplets with centres τ 5.28 and 5.21.

Reduction of 3-Bromo-2-ones.—The bromo-ketone (0.66 g.) and sodium borohydride (0.33 g.) in absolute ethanol were stirred at room temperature for 3 hr., then worked up to give 3 β -bromobicyclo[3,3,1]nonan-2 α -ol (85% from 3 β -bromoketone and 60% from the equilibrium mixture), m.p. 80° (Found: C, 49.7; H, 6.7; Br, 36.1. C₉H₁₅BrO requires C, 49.3; H, 6.8; Br, 36.5%), v_{max} 3584 and 656 cm.⁻¹, τ 5.45 (1H, m) and 6.17 (1H, q, apparent J 5 and 10 c./sec.); the latter was displaced to τ 4.9 on acetylation and collapsed to a doublet (J 5 c./sec.) on irradiation at τ 5.45. On irradiation at τ 8.2—8.3 the τ 5.45 multiplet collapsed to a triplet (apparent J values 10 c./sec.).

3β-Bromo-7β-methylbicyclo[3,3,1]nonan-2α-ol (75% from pure 3β-bromo-ketone, 56% from the equilibrium mixture) had m.p. 90—91° (Found: C, 51·9; H, 7·3; Br, 34·3. C₁₀H₁₇BrO requires C, 51·9; H, 7·3; Br, 34·3%). The ¹H n.m.r. spectrum included absorptions at τ 5·45 (1H, m) and 6·16 (1H, q) which behaved as did the previous sample on spin decoupling.

 3α -Bromobicyclo[3,3,1]nonan-2 β -ols.—Hydrogen bromide was bubbled through stirred ice-cold solutions of 2β , 3β epoxybicyclononane (0.9 g.) and of 7 β -methyl- 2β , 3β -epoxybicyclononane ¹ (0.71 g.) in carbon tetrachloride (50 ml.). The usual work-up gave the bromohydrin (Xa) (1 g.), m.p.

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70—71°, depressed on admixture with (IXa) prepared as above (Found: C, 49·1; H, 6·9; Br, 34·2. C₉H₁₆BrO requires C, 49·3; H, 6·8; Br, 34·5%), v_{max} 3577 and 664 cm.⁻¹, τ 5·96 (1H, m) and 6·35 (1H, d, J 9 c./sec.). The bromohydrin (Xb) (0·91 g.) had m.p. 70°, depressed on admixture with (IXb) (Found: C, 52·0; H, 7·3. C₁₀H₁₇BrO requires C, 51·9; H, 7·3%), τ 5·98 (1H, m) and 6·30 (1H, d, J 10 c./sec.); the latter collapsed to a broad singlet on irradiation at τ 5·98.

3,3-Dibromo-7β-methylbicyclononan-2-one (XIb).— 78-Methylbicyclononan-2-one (0.5 g.) in acetic acid (10 ml.) was treated with bromine (1 g.); addition of water precipitated the *dibromo-ketone*, m.p. 64–65°, λ_{max} 309 mµ (ϵ 101), ν_{max} 1724 cm.⁻¹ (Found: C, 38.9; H, 4.5. $C_{10}H_{14}Br_2O$ requires C, 38.7; H, 4.5%). The ¹H n.m.r. spectrum (CDCl₃) included absorptions at τ 6.30 (1H, q, I 10 and 17 c./sec.) and 6.96 (1H, d, I 17 c./sec., superimposed on other absorption). In 50% chloroformbenzene these absorptions occurred at τ 6.67 and 7.28. The quartet collapsed to a doublet $(J \ 10 \ c./sec.)$ on irradiation at τ 6.96, and to a doublet (J 17 c./sec.) on irradiation at τ 7.64. On irradiation at τ 6.30 the τ 6.96 doublet collapsed to a singlet. Bromination of the various samples of 3-bromo-7\beta-methyl-2-ones gave the same dibromoketone. Bromination of bicyclononan-2-one gave only an oily, unstable dibromo-ketone (not analysed) which had a ¹H n.m.r. spectrum identical with the above (except for the methyl doublet).

3-Bromo-7β-methylbicyclo[3,3,1]non-2-en-4-one.— A solution of (XIb) (0.5 g.), sodium carbonate (1 g.), and sodium bromide (1 g.) in dimethylformamide (50 ml.) was stirred at 95° for 2 hr. and poured into 0.5N-sulphuric acid (400 ml.). Solvent extraction and vacuum sublimation gave the enone (0.32 g.), m.p. 94—94.5° (Found: C, 52.4; H, 5.8. $C_{10}H_{13}$ BrO requires C, 52.4; H, 5.7%) ν_{max} . 1686 and 1600 cm.⁻¹, τ 2.55 (1H, q, J 7 and 1.5 c./sec., 2-H). Partial dehydrobromination of the dibromo-ketone occurred during chromatography on alumina. Hydrogenation of the enone (0.3 g.) in ethanol (10 ml.) over 5% palladium– carbon gave 7β-methylbicyclononan-2-one; the semicarbazone had m.p. and mixed m.p. 165°.

7a-Methylbicyclononan-2-one (XII).-3-Methylbicyclonon-2-en-6 β -ol¹ (0.9 g.) in ethanol (20 ml.) was hydrogenated over 5% palladium-carbon at room temperature and 760 mm. pressure. Removal of solvent left a solid mixture of alcohols containing 95% 7α -methyl-2 β -ol and 5% 7β methyl-2 β -ol (g.l.c. on tricyanoethoxypropane at 100°). Recrystallisation from methanol-water (1:1) gave the major product pure (0.66 g.), m.p. 61° (Found: C, 77.9; H, 11.6. C₁₀H₁₈O requires C, 77.9; H, 11.7%). Oxidation of this alcohol (0.3 g.) in ether (25 ml.) with aqueous chromic acid gave the *ketone* (XII) (0.26 g.), b.p. $90^{\circ}/0.5$ mm., $n_{\rm p}^{25}$ 1.5261, ν_{max} 1709 cm.⁻¹ (Found: C, 78.4; H, 10.5. C₁₀H₁₆O requires C, 78.9; H, 10.5%). Bromination of this ketone (0.06 g.) in acetic acid with varying quantities of bromine gave a monobromo-ketone (0.06 g.), m.p. 65°, τ 4.83 (1H, q, J 6 and 12 c./sec., 3-H) (not analysed).

 3α -Bicyclo[3,3,1]nonylamine (XIII) Hydrochloride.— A mixture of the acid chloride from the acid (V) (2 g.) and thionyl chloride (2·12 g.) was fractionated (b.p. 118°/10 mm.) and dissolved in acetone (25 ml.). To the solution was added, with shaking, sodium azide (1·5 g.) in water (4 ml.) and after 15 min. the azide was precipitated as an oil with more water. The dried azide in ethanol (40 ml.) was boiled for 4 hr. The ethanol was removed and the residue sub-

limed to give ethyl 3α -bicyclo[3,3,1]nonylcarbamate (2.04 g.), m.p. $73\cdot5-75^{\circ}$ (Found: C, $67\cdot8$; H, $10\cdot0$; N, $6\cdot7$. C₁₂H₂₁NO₂ requires C, $68\cdot3$; H, $10\cdot0$; N, $6\cdot6$ %). The urethane (1 g.) was boiled with 10N-hydrochloric acid (50 ml.) for 9 hr., water (20 ml.) was added, and neutral materials were extracted into ether. Evaporation of the aqueous phase left the amine hydrochloride as a solid (0.79 g.), m.p. 300° . The free base sublimed rapidly at room temperature and so was not isolated. The pH of an ice-cold solution of the hydrochloride (0.1 g.) in water (20 ml.) was brought to 4 and sodium nitrite (0.1 g.) was added. The solution was allowed to warm to room temperature and aqueous acetic acid was added periodically to maintain pH 5. Ether extraction after 12 hr. yielded an oil (8 mg.) which consisted of bicyclonon-2-ene (50%) and bicyclononan- 3α -ol (50%) (g.l.c. on tritolyl phosphate at 80°).

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