# Stereospecific Ring Contractions of 7-Chlorobicyclo[3.2.0]hept-2-en-6-ones and Equilibration Studies of 7-Alkylbicyclo[3.2.0]hept-2-en-6-ones [1]

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7-Alkyl-7-*endo*-chlorobicyclo[3.2.0]hept-2-en-6-ones (1b—d) undergo ring contraction readily and stereospecifically with aqueous base. Because of conformational factors, the 7-*exo*-chloro-epimers (2b—d) show an increasing reluctance to undergo ring contraction as the size of the alkyl group increases, and in the case of (2c and d) 2-alkyltropones are also formed. Equilibration studies show that for 7-alkylbicyclo[3.2.0]hept-2-en-6-ones, the large alkyl group prefers the *endo*-configuration, whereas in the 2,3-dihydro-derivatives it prefers the *exo*-configuration: however in both equilibria, energy differences between *endo*- and *exo*-epimers are small.

THE idea of crosswise approach of the two components, proposed by Woodward and Hoffmann for $[_{\pi}2_a + _{\pi}2_s]$ cycloadditions,[2] when applied to keten–cyclopentadiene reactions leads to the prediction that the larger group of an unsymmetrical keten will be found preferentially in the *endo*-position of the product, a 7,7-disubstituted bicyclo[3.2.0]hept-2-en-6-one. Experimentally, this has been confirmed by ourselves [1] and other groups of workers notably those of Brady [3] and Dreiding.[4] Stereoselectivity has also been found in cycloadditions of ketens to other olefins.[5]

Our own investigation consisted of the addition of a series of alkylchloroketens to cyclopentadiene; the size of alkyl group was systematically varied (series a—e). The reactive chloroketens were chosen so that addition occurred under mild conditions, and they were generated by dehydrochlorination of the appropriate α-chloro-acid chlorides. In the route to the ethyl- and isopropyl-chloroketens, chlorination of butyryl chloride and 3-methylbutyryl chloride with sulphuryl chloride led to considerable α-dichlorination in the former case (20%) and some α-dichlorination and β-chlorination (tertiary H) in the second case. Intermediates of satisfactory purity were obtained by chlorination ($SO_2Cl_2$), then

[1] Preliminary communication, P. R. Brook, J. M. Harrison, and A. J. Duke, *Chem. Comm.*, 1970, 589.

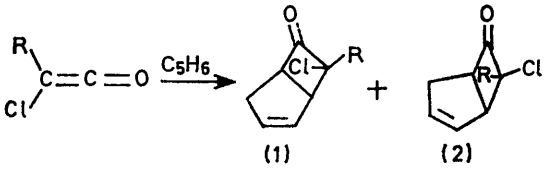
[2] R. B. Woodward and R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 847.

[3] W. T. Brady and R. Roe, *J. Amer. Chem. Soc.*, 1970, **92**, 4618; W. T. Brady and E. F. Hoff, *J. Org. Chem.*, 1970, **35**, 3733, and references cited in these papers.

[4] M. Rey, S. Roberts, A. Dieffenbacher, and A. S. Dreiding, *Helv. Chim. Acta*, 1970, **53**, 417.

[5] T. DoMinh and O. P. Strausz, *J. Amer. Chem. Soc.*, 1970, **92**, 1766.

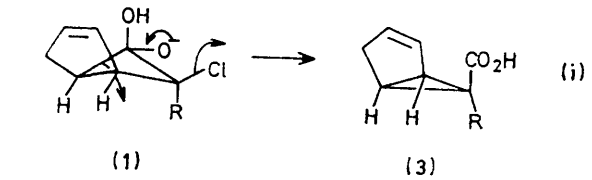
decarboxylation of appropriate monoalkylmalonic acids. The cycloadditions have been fully reported in other papers, and we merely summarise our results and analyses in Table 2. The present paper describes some of the chemistry of the chloroketen adducts.



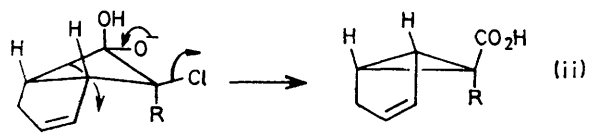
(1) (2)

a; R = H d; R = Pr$^i$
b; R = Me e; R = Ph
c; R = Et f; R = Cl

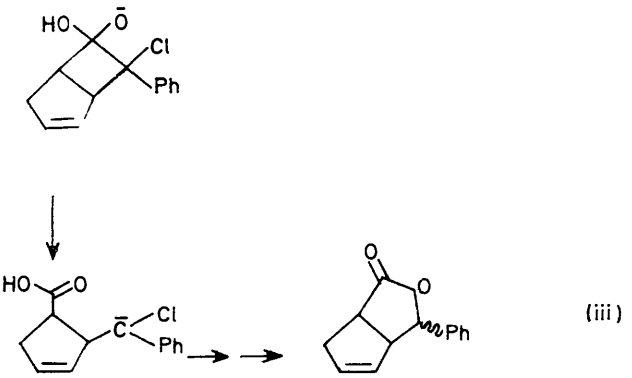
Assignment of stereochemistry in the chloro-adducts (1) and (2) has normally been made by n.m.r. spectroscopy; in particular the H-5 signal occurs at lower field when a 7-*exo*-chloro-group is present.[3] Nuclear Overhauser effects have also been employed.[4] After separation of 7-epimeric adducts by chromatography, we



(1) (3) (i)



(2) (4) (ii)



(iii)

obtained chemical evidence of stereochemistry by making use of the stereospecific base-catalysed ring contractions of α-chlorocyclobutanones first observed in simple cases by Conia and his co-workers.[6] The 7-*endo*-chloro-7-alkyl ketones (1b—d) underwent stereospecific ring contraction in excellent yields with 2N-sodium hydroxide to give 6-*exo*-alkylbicyclo[3.1.0]hex-2-ene-6-*endo*-carboxylic acids (3b—d) [equation (i)]. The stereochemistry at C-6 was readily established by use of an iodolactonisation reaction which demonstrated the *cis*-relationship of acid group and double bond with respect to the cyclopropane.

The epimeric 7-*exo*-chloro-7-alkyl ketones (2) showed an increasing reluctance to undergo ring contraction as the size of the alkyl group increased. Whereas (2b) reacted readily to give (4b), the yield was lower for the ethyl ketone (2c) and 2-ethyltropone was also formed.[8] The isopropyl ketone (2d) gave no bicyclohexanecarboxylic acid (4d) although 2-isopropyltropone was formed; the reaction took a different and more complicated course.[9] This systematic change in ease of reaction is attributed to increasing steric interaction between the alkyl group and the 4-*endo*-H, in that conformation in which the chloro-group becomes equatorial [equation (ii)].

Two further anomalies were noted in the ring contractions. The phenylchloro-ketone (2e) did not undergo ring contraction (so giving indirect support to the assignment of the *endo*-configuration to the large phenyl group) but instead appeared to give lactonic products ($\nu_{CO}$ 1763 cm$^{-1}$) by a ring-opening reaction [equation (iii)]. The products were only characterised spectroscopically, but more vigorous treatment with base gave the hydroxy-acids (5), for which satisfactory analytical figures were obtained.

The monochloroketen adduct (1a) did not undergo ring contraction stereospecifically, but instead gave an epimeric mixture of bicyclohexane-6-carboxylic acids (3a) and (4a), separable by the iodolactonisation procedure. As the chloro-ketone (1a) contained an ' enolisable ' proton (H-7), it seemed likely that the lack of stereospecificity was due to epimerisation prior to ring contraction. Evidence that the C-7 enolate was being formed in the reaction was obtained by use of NaOD–$D_2O$: the resulting *endo*- and *exo*-bicyclohexanecarboxylic acids were 86% monodeuteriated and *ca.* 14% dideuteriated. We consider the dideuteriation to arise by replacement of H-5 as well as H-7 in the ketone (1a) before ring contraction. This C-5 enolate anion appears rather strained, but it has been invoked [10] in explanation of *cine*-substitution of the 7-halogeno-group with methoxide ion and other nucleophiles.

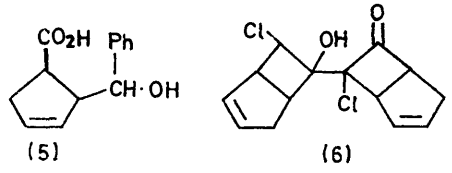
In view of the foregoing results, a route to the 7-*exo*-chloro-ketone (2a) by base-catalysed epimerisation of the corresponding *endo*-chloro-compound appeared feasible. In 0·1N-$Na_2CO_3$–$D_2O$, 87% of H-7 had exchanged after 1 h at 20° (ring contraction was observed at 100°), but without detectable epimerisation. After longer reaction times only *endo*-chloro-derivative was found, but ketol

[6] J. M. Conia and J. Salaun, *Accounts Chem. Res.*, 1972, **5**, 37.
[7] J. Meinwald, S. S. Labone, and M. S. Chadha, *J. Amer. Chem. Soc.*, 1963, **85**, 582.
[8] W. T. Brady and J. P. Hieble, *J. Amer. Chem. Soc.*, 1972, **94**, 4278.
[9] P. R. Brook and J. M. Harrison, *J.C.S. Chem. Comm.*, 1972, 997.
[10] (*a*) D. L. Garin and K. L. Canmalk, *J.C.S. Chem. Comm.*, 1972, 333; (*b*) P. D. Bartlett and T. Ando, *J. Amer. Chem. Soc.*, 1970, **92**, 7518; (*c*) W. T. Brady and J. P. Hieble, *J. Org. Chem.*, 1971, **36**, 2033.

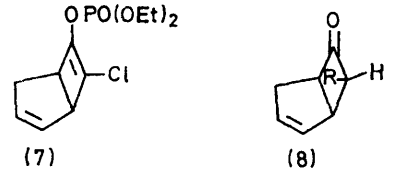
dimer (6) (two stereoisomers by t.l.c.) was also observed. This lack of epimerisation shows that the C-7 enol has a strong preference for protonation from the *exo*-face and with fairly weak base ($Na_2CO_3$) little or no equilibration was being observed. *exo*-Protonation of the 7-enol was confirmed when partial dechlorination of the 7,7-dichloro-ketone (1f) with zinc [11] or triphenylphosphine [12] gave only 7-*endo*-chloro-ketone (1a).

With triethyl phosphite the dichloro-ketone (1f) gave the enol phosphate (7) by a Perkow reaction.[13] Attempted ester interchange of this with methanolic methoxide led to a low yield of ring-contracted methyl esters related to (3a) and (4a), rather than monochloro-ketones (1a and 2a). Milder hydrolysis conditions gave back starting material.

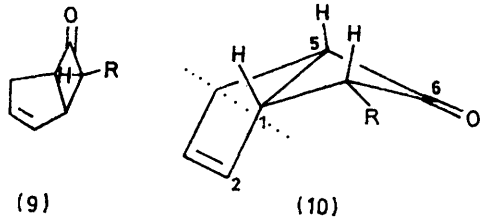
Our failure to epimerise the chloro-ketone led us to suspect initially that it was the *exo*-derivative (2a) and




(5) (6)




(7) (8)




(9) (10)

the more thermodynamically stable epimer. However the *endo*-configuration was firmly established by *X*-ray crystallography and n.m.r. studies.[14] Ghosez and Roussel have successfully epimerised the 7-*endo*-chloro-ketone (1a) by treatment with triethylamine in benzene,[15] but the equilibrium mixture only contained 22% of *exo*-chloro-epimer. This result is surprising; most workers have assumed that the larger group would prefer the *exo*-configuration and that only kinetic control in the cycloadditions leads to a greater proportion of epimer with the larger group *endo*.[16]

We have now extended this observation that a large 7-substituent has a slight preference for the *endo*-configuration to the alkyl-substituted compounds (8) and (9). Dechlorination of the epimeric 7-chloro-7-alkylbicyclo[3.2.0]heptenones (1) and (2) with zinc led to a product consisting mainly of one epimer, as in the case of the dichloro-ketone (1f). In the methyl case, n.m.r. confirmed that the major product was the 7-*endo*-methyl isomer (8b) the methyl doublet appearing at higher field (δ 0·98) than in the case of the minor product (1·25) owing to shielding by the five-membered ring. The major product of dechlorination in the ethyl and isopropyl series was assigned the *endo*-alkyl structure only by analogy with the methyl case, as here the n.m.r. spectra were more complicated. Base-catalysed epimerisation of these 7-alkylbicycloheptenones (8) and (9) proceeded readily to equilibrium as reported in Table 1. Because of the unexpected preference for an *endo*-alkyl group the equilibrium in the methyl series was approached from both sides to confirm that true thermodynamic equilibrium had been established. The results are in line with that reported for the chloro-ketone and so suggest that torsional strain and steric effects are major factors in all cases; any dipole–dipole interaction in the chloro-ketone case appears to operate in the same direction.

The dihydro-ketones were readily obtained by catalytic reduction of the double bonds in the epimeric mixtures of (8) and (9), and again these compounds were readily equilibrated with base. In the dihydro-compounds the *exo*-alkyl configuration was preferred but not to a great extent (Table 1). Clearly, the change of C-2 from an $sp^2$- to an $sp^3$-hybridised centre leads to increased unfavourable interaction of it with a 7-*endo*-alkyl group.

TABLE 1

Base-catalysed equilibria of 7-alkylbicyclo[3.2.0]hept-2-en-6-ones and their 2,3-dihydro-derivatives

| | Bicycloheptenones (8) and (9) | | Bicycloheptanones [dihydro-(8)] and [dihydro-(9)] | |
|---|---|---|---|---|
| R | *exo* | *endo* | *exo* | *endo* |
| Me | 34 | 66 | 58 | 42 |
| Et | 37 | 63 | 73 | 27 |
| Pr$^i$ | 46 | 54 | 86 | 14 |

From Dreiding models of 7-alkylbicycloheptenones, it appears that a planar cyclobutanone ring requires a cyclopentene ring fused to it also to be planar. In this situation unfavourable torsional strains arise, particularly for atoms adjacent to the 1,5- and 5,4-bonds; again, with planar rings the terminal hydrogen atoms of the 7-*endo*-ethyl or -isopropyl group approach within 1 Å of C-2, directly above the double bond. If the cyclobutanone ring is bent by moving C-6 in the *endo*-direction, much of the unfavourable interaction is removed: the cyclopentene ring adjusts to an envelope conformation with C-5 out of the plane of the double

[11] Zinc–acetic acid has also been used: for a brief report see M. Rey, U. A. Hüber and A. S. Dreiding, *Tetrahedron Letters*, 1968, 3583.

[12] For other examples of dehalogenation with this reagent see I. T. Borowitz, K. C. Kirby, and R. Wirkhaus, *J. Org. Chem.*, 1966, **31**, 4031.

[13] This reaction has been reported earlier: S.A. P. 6,706,947/1968 (*Chem. Abs.*, 1968, **70**, 106,068).

[14] P. R. Brook, A. J. Duke, and J. R. C. Duke, *Chem. Comm.*, 1970, 574.

[15] Albert Roussel, D.Sc. Thesis, Université Catholique de Louvain, 1970. We thank Professor Ghosez for a copy of this thesis.

[16] See for example refs. 1, 3, and 4; and also for comments on a 'masochistic steric effect,' B. M. Jacobson and P. D. Bartlett, *J. Org. Chem.*, 1973, **38**, 1036.

bond containing atoms 1, 2, 3, and 4, and the *endo*-alkyl group swings away from the cyclopentene ring, becoming equatorial with respect to the four-membered ring as in conformation (10). Bending of the cyclobutanone ring by movement of C-6 in the *exo*-direction again brings the cyclopentene ring into an envelope conformation but the 7-*endo*-alkyl group, now axial, is brought across the five-membered ring close to the C-4 methylene group, also axial with respect to the cyclobutanone ring. This 1,3-diaxial interaction produces a less favoured situation.

For the 7-*exo*-alkyl series the planar cyclobutanone arrangement is still disfavoured, but, for the two bent cyclobutanones (C-6 moved *endo* or *exo*, respectively) the best conformation is not so obvious. The former reduces torsional strains between H-1 and H-2, H-4 (*exo*) and H-5, and H-4 (*endo*) and C-6, but at the expense of increasing the 1,3-diaxial interaction of the 7-*exo*-alkyl group with H-5. The latter conformation (C-6 *exo*) increases the torsional strains while reducing the 1,3-diaxial interaction. On balance we suggest that conformation (10) for the bicyclic system is again preferred, with the *exo*-alkyl group axial.

## EXPERIMENTAL

Details of general experimental techniques and the instruments used have been given in earlier papers.[17]

*Chloro(ethyl)malonic Acid.*[18]—Sulphuryl chloride (28·35 g, 0·21 mol) was added dropwise to a solution of ethylmalonic acid (26·4 g, 0·2 mol) in anhydrous ether (120 ml). After the initial vigorous reaction the mixture was heated under reflux for 3 h and the ether was removed. The chloro-acid, crystallised from AnalaR benzene, had m.p. 109—110° (yield 21 g, 63%). When this acid (10 g) had been heated to 120—125° for 0·5 h, distillation then gave 2-chlorobutyric acid (5·9 g, 81%), b.p. 85—86° at 15 mmHg.

*Chloro(isopropyl)malonic Acid.*[18]—Similarly, isopropylmalonic acid (21·9 g, 0·15 mol) gave the chloro-acid (17·0 g, 64%), m.p. 104—106° [from benzene–petroleum (b.p. 60—80°)]. On decarboxylation at 120—130° 2-chloro-3-methylbutyric acid was obtained (7·1 g, 93%), b.p. 98—100° at 15 mmHg, m.p. 25—28°.

*Chloroketen–Cyclopentadiene Cycloadditions.—General procedure.* Triethylamine (5—10% excess over acid chloride) was added to a refluxing rapidly stirred mixture of the α-chloroacyl chloride with a four-fold excess of freshly distilled cyclopentadiene in sufficient pentane to maintain a mobile suspension of base hydrochloride during the reaction (about twice the volume of cyclopentadiene). The mixture was poured into water, the organic phase was washed with 2N-sodium carbonate, 2N-hydrochloric acid, and water; removal of the solvent left the crude adducts which were analysed by n.m.r. and g.l.c. Chromatography on Kieselgel G (Merck) with benzene–petroleum (b.p. 40—60°) as eluant gave good separation of the stereoisomers in proportions agreeing with the results of n.m.r. analysis. The yields and ratios of adducts are reported in Table 2. All adducts had spectroscopic properties in agreement with those reported. Chromatography was not used where the product was homogeneous: the monochloroketen adduct (1a) was merely purified by distillation, and the phenylchloroketen adduct (2c) after removal of solvent appeared pure; attempts to distil or chromatograph the adduct resulted in loss of product.

*Base-catalysed Ring Contractions of 7-Alkyl-7-chlorobicyclo[3.2.0]hept-2-en-6-ones.—General method.* The pure stereoisomer in 2N-sodium hydroxide (about 10-fold excess) was shaken until the solution was homogeneous, or until no further reaction was occurring (t.l.c.). After extraction with dichloromethane to remove any neutral product, acidification gave the pure acid.

(*a*) The 7-*endo*-methylchloro-ketone (2b) (1·0 g) after 10 min gave 6-endo-*methylbicyclo*[3.1.0]*hex-2-ene-6-carboxylic acid* (4b) (0·92 g, 97%), m.p. (from aqueous acetone) 75·5—76° (Found: C, 68·9; H, 7·1%. $C_8H_{10}O_2$ requires C, 69·6; H, 7·25%), $\nu_{CO}$ 1695 cm$^{-1}$, δ 11·2 (1H, s, OH), 5·85—5·55 (2H, m, olefinic), 2·97—1·87 (4H, m, bridgehead and allylic protons), and 1·01 (3H, s, Me).

TABLE 2

Yields, ratios, and analyses of chloroketen–cyclopentadiene adducts

| Compound | Yield (%) | Ratio | Found (%) C | Found (%) H | Found (%) Cl | Required (%) C | Required (%) H | Required (%) Cl |
|---|---|---|---|---|---|---|---|---|
| (1a) | 33 | 100 | 58·85 | 4·9 | 24·95 | 58·9 | 4·95 | 24·9 |
| (1b) | 88 | 27 | 61·2 | 5·8 | 22·7 | 61·4 | 5·75 | 22·7 |
| (2b) | | 73 | 61·9 | 5·85 | 22·9 | | | |
| (1c) | 70 | 11·5 | 63·5 | 6·45 | 20·5 | 63·4 | 6·45 | 20·8 |
| (2c) | | 88·5 | 63·5 | 6·45 | 20·85 | | | |
| (1d) | 58 | 5·5 | 65·15 | 7·3 | 19·2 | 65·00 | 7·05 | 19·3 |
| (2d) | | 94·5 | 65·25 | 6·95 | 19·0 | | | |
| (2e) | 95 | 100 | 71·7 | 6·35 | | 71·6 | 6·4 | |

(*b*) The 7-*exo*-methylchloro-ketone (1b) (0·5 g) after 10 min gave 6-exo-*methylbicyclo*[3.1.0]*hex-2-ene-6-carboxylic acid* (3b), m.p. 95—96·5° (0·46 g, 96%) (Found: C, 69·4; H, 7·15%), *m/e* 138 ($M^+$) and 93 (100%; $M^+ - CO_2H$), $\nu_{CO}$ 1700 cm$^{-1}$, δ 11·1 (1H, s, OH), 5·80—5·45 (2H, m, olefin), 2·75—1·53 (4H, extended m, bridgehead and allylic protons), and 1·33 (3H, s, Me).

Treatment of this *endo*-acid (3b) (0·25 g) with sodium hydrogen carbonate–potassium tri-iodide yielded a 6-exo-*methyliodo-lactone* * (0·41 g), m.p. 84—84·5° (from methylcyclohexane) (Found: C, 68·65; H, 8·3; I, 48·4. $C_8H_9IO_2$ requires C, 68·6; H, 8·6; I, 48·2%). The epimeric *exo*-acid on similar treatment only gave back starting acid.

Catalytic hydrogenation (Pt in MeOAc) of the 6-*endo*-methylbicyclohexene-6-carboxylic acid (4b) gave the corresponding 6-endo-*methylbicyclohexane acid* [dihydro-(4b)], m.p. 74—76° (from water–5% acetone) (Found: C, 68·35; H, 8·4. $C_8H_{12}O_2$ requires C, 68·6; H, 8·6%), $M^+$ 140 (100%); δ 1·15 (3H, s, Me). In a similar way the 6-*exo*-

* The i.r. spectrum of the crude product indicated a mixture of δ- and γ-lactones, the latter predominating. The structure of the purified product was not established.

[17] P. R. Brook and A. J. Duke, *J.C.S. Perkin I*, 1973, 1013.

[18] The method of R. H. Horn, R. B. Miller, and S. N. Slater, *J.* 1950, 2900.

methyl epimer gave the 6-exo-*methylbicyclohexane-6-carboxylic acid* [dihydro-(3b)], m.p. 75—76·5° (Found: C, 68·65; H, 8·3%), $M^+$ 140 (100%), δ 1·25 (3H, s, Me).

The 2,3-double bond in the methylchloroketen adducts played no part in the stereochemical course of the ring contraction. Hydrogenation of the 7-*endo*-methylchloroketone (2b) afforded the 2,3-dihydro-compound, not fully characterised, but having the expected spectral properties, and this when treated with base gave the ring-contracted 6-*endo*-methylbicyclohexane acid [dihydro-(4b)]. In the same way, the 2,3-dihydro-7-*exo*-methyl adduct [dihydro-(1b)] gave the 6-*exo*-methylbicyclohexane acid [dihydro-(3b)]. Stereochemical purity of the acids was >98% (g.l.c. analysis of the methyl esters).

(*c*) The 7-*endo*-ethyl-7-chloro-ketone (2c) (1·0 g) with 2N-sodium hydroxide after 45 min gave 6-endo-*ethylbicyclo*[3.1.0]*hex-2-ene-6-carboxylic acid* (4c) (0·59 g, 65%), m.p. 68—69° (from methylcyclohexane, after sublimation) (Found: C, 70·8; H, 7·85. $C_9H_{12}O_2$ requires C, 71·0; H, 7·85%), δ 11·1 (1H, s, OH), 5·75 (2H, m, olefinic), 3·0—2·5 (2H, m, allylic $CH_2$), 2·45—1·9 (2H, m, H-1 and H-5), and 1·9—0·7 p.p.m. (5H, m, Et). A small neutral fraction gave 2-ethyltropone, $\nu_{max.}$ 1630 $cm^{-1}$ (C=O), δ 6·95 (5H, m, aromatic H), 2·55 (2H, distorted q, $CH_2{\cdot}CH_3$), and 1·13 (3H, distorted t, $CH_2{\cdot}CH_3$), $\lambda_{max.}$ (MeOH) 232 (ε 21,000) and 311 nm (7000).

(*d*) The 7-*exo*-ethyl-7-chloro-ketone (1c) (0·52 g) after 30 min gave in the same way 6-exo-*ethylbicyclo*[3.1.0]*hex-2-ene-6-carboxylic acid* (3c), purified as before, m.p. 53·5—54° (0·44 g, 94%) (Found: C, 70·9; H, 7·9), δ 11·07 (1H, s, OH), 5·83—5·44 (2H, m olefin), 3·0—2·4 (2H, m, allylic $CH_2$), and 2·30—0·80 (7H, remaining H). No neutral tropone was formed in this case. This *endo*-acid afforded a 6-exo-*ethyliodo-lactone*,* m.p. 53—54° (from aqueous methanol) (Found: C, 38·95; H, 3·95; I, 45·25. $C_9H_{11}IO_2$ requires C, 38·85; H, 4·0; I, 45·7%).

(*e*) The 7-*exo*-isopropyl-7-chloro-ketone (1d) (0·2 g) after 24 h gave 6-exo-*isopropylbicyclo*[3.1.0]*hex-2-ene-6-carboxylic acid* (3d) (0·165 g, 93%), m.p. 68—71·5° (Found: C, 71·9; H, 8·3. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·5%), δ 10·47 (1H, s, OH), 5·76 and 5·51 (2H, 2 × m, olefin), 2·92—2·4 (2H, m, allylic $CH_2$), 2·10 (1H, m, H-1), 1·67 (1H, m, H-5), and 1·08 (7H, m, including apparent t, non-equivalent methyls and CH of $Pr^i$).

The *endo*-acid gave a 6-exo-*isopropyliodo-lactone*,* m.p. 56—57° (from methylcyclohexane) (Found: C, 41·5; H, 4·6; I, 43·2. $C_{10}H_{13}IO_2$ requires C, 41·2; H, 4·45; I, 43·4%).

(*f*) The 7-*endo*-isopropyl-7-chloro-ketone (2d) (2·0 g) after 36 h yielded 2-isopropyltropone (0·3 g, 18%), but the acidic fraction contained no 6-*endo*-isopropylbicyclohexane-6-carboxylic acid.[9] The 2-isopropyltropone was characterised as 2-amino-7-isopropyltropone, obtained by treatment with hydrazine hydrate in ethanol; m.p. 88—89° (lit., 88°).

(*g*) The 7-*endo*-chloro-ketone (1a) was treated with base under various conditions. Thus the ketone (1a) (5·83 g) was added dropwise to a stirred solution of potassium hydroxide (16·0 g) in 70% aqueous dioxan (250 ml). Acidification after 30 min at room temperature, followed by extraction with dichloromethane yielded the bicyclohexene-6-*endo*- and 6-*exo*-carboxylic acids (3a) and (4a) (ratio *ca.* 40 : 60 by g.l.c. analysis of their methyl esters) (4·35 g, 86%). Iodolactonisation of this mixture in the normal way gave the known δ- and γ-iodolactones[7] (4·92 g) and the 6-*exo*-bicyclohexenecarboxylic acid (4a) (1·60 g), m.p. 77—79° [from methylcyclohexane after sublimation (97° and 0·1 mmHg)].

Treatment of the iodo-lactones with zinc–methanolic ammonium chloride and normal work-up gave the 6-*endo*-carboxylic acid (3a), m.p. 92°.[7]

Formation of a similar mixture of ring-contracted acids (3a) and (4a) was observed when the monochloro-ketone was boiled in 2N-sodium carbonate.

*Ring Contraction with Sodium Deuteroxide–Deuterium Oxide.*—When the monochloro-ketone (1a) was added to a rapidly stirred solution of sodium deuteroxide [sodium (0·9 g) in deuterium oxide (20 ml)] an 88% yield of *endo*- and *exo*-acids (3a) and (4a), ratio 81 : 19 by g.l.c. analysis of their methyl esters, was obtained. After separation of the two epimers by the iodolactonisation procedure, the pure deuteriated *endo*- and *exo*-acids were analysed by mass spectrometry and compared with undeuteriated material. Although the comparison was hindered by the presence of an $M - 1$ peak it was estimated that 88% of *endo*-acid contained one (non-exchangeable) deuterium atom and 13% had two such atoms. For the *exo*-acid the figures were 87 and 16%. The error in these values is difficult to judge but appears to be at least ±4%.

(*h*) The 7-*endo*-phenyl-7-chloro-ketone (2e) on treatment with 2N-sodium hydroxide gave non-crystalline lactonic material, $\nu_{max.}$ 1763 $cm^{-1}$ (C=O), not fully characterised.

Vigorous treatment of the phenyl ketone (2e) (3·00 g) with potassium hydroxide (20 g) in water (30 ml) at the boil gave a dark oil which after bulb-to-bulb distillation [180—200° (air-bath) and 0·1 mmHg] gave 2-(α-*hydroxybenzyl*)-*cyclopent-3-ene-1-carboxylic acid* (5) as a gum (diastereoisomers) (1·85 g, 65%) (Found: C, 71·7; H, 6·35. $C_{13}H_{14}O_3$ requires C, 71·6; H, 6·4%), $\nu_{max.}$ 3700—2400 (OH and $CO_2H$), 1730 (CO), and 1618 and 1610 $cm^{-1}$ (double bond and phenyl group).

*Dechlorination of the Chloroketen Adducts.*—(a) 7,7-*Dichlorobicyclo*[3.2.0]*hept-2-en-6-one* (1f). The dichloro-ketone (3·0 g), stirred and heated in methanol (15 ml) with zinc dust (4 g) and ammonium chloride (1 g), gave after 30 h bicyclo[3.2.0]hept-2-en-6-one (92%), b.p. 70—75° at 18 mmHg. The semicarbazone had m.p. 226° (from ethanol) (lit.,[19] 221—222°).

Slow passage of the dichloro-ketone (1f) (2 g) in methanol (30 ml) and ammonium chloride (1 g) down a column of zinc wool (1 × 10 in) previously activated with methanolic ammonium chloride and set up over refluxing methanol gave 7-*endo*-chlorobicyclo[3.2.0]hept-2-en-6-one (1a) (0·85 g, 53%), characterised spectroscopically (>99% pure by g.l.c.).

The dichloro-ketone (1f) (0·8 g) in 80% aqueous dioxan (10 ml) was heated with triphenylphosphine (1·2 g) on a water-bath for 48 h. After aqueous work-up g.l.c. analysis indicated that the major product was the 7-*endo*-monochloro-ketone (1a), produced together with a little starting ketone and some fully dechlorinated ketone.

The dichloro-ketone (10 g) was heated under reflux in benzene (250 ml) with triethyl phosphite (25 g) for 10 days under nitrogen. Distillation yielded 7-*chlorobicyclo*[3.2.0]-*hepta-2,6-dien-6-yl diethyl phosphate* (7), b.p. 120—125° at 0·3 mmHg (15·7 g, 99%) (Found: C, 47·3; H, 5·95; Cl, 12·8. $C_{11}H_{16}ClO_4P$ requires C, 47·4; H, 5·75; Cl, 12·75%), $M^+$ 278 and 280 (4 : 1), $\nu_{max.}$ 1680 (enol ester double bond), 1612 (olefin), 1295 (P=O), and 1040 $cm^{-1}$ (P–O), δ 6·01—5·61 (2H, m, olefinic H), 4·46—3·90 (4H, dq, *J* 8·6 and 7·4 Hz re-

* Same footnote as on page 930.

[19] B. T. Brooks and G. Wilbert, *J. Amer. Chem. Soc.*, 1941, **63**, 870.

spectively, $CH_2$·O), 3·84—3·39 (2H, m, H-1 and H-5), 2·91—1·92 (2H, m, allylic $CH_2$), and 1·56—1·23 (6H, dt, *J* 0·7 and 7·4 Hz, $CH_3$·$CH_2$).

(b) 7-endo- *and* exo-*Methylbicyclo*[3.2.0]*hept-2-en-6-ones* (8b) *and* (9b). The 7-chloro-7-methyl ketones (1b) and (2b) in the ratio 27 : 73 (10 g) were dechlorinated by zinc in methanolic ammonium chloride as in (a) for 3 h, to yield a mixture of dechlorinated ketones (7·1 g, 91%), b.p. 95—100° at 15 mmHg. G.l.c. analysis indicated two components, ratio 7 : 93, the minor product being the first eluted. The mixture showed $\nu_{max.}$ 1778 $cm^{-1}$ (C=O), δ 1·25 (d, with some inner lines due to virtual coupling, *J* 7·5 Hz, *exo*-Me) and 0·98 (d, *J* 6·9 Hz, with virtual coupling, *endo*-Me) in the ratio 7 : 93. Samples of the dechlorinated ketones (8b) and (9b) were obtained pure by preparative g.l.c. The *endo*-methyl ketone (8b) yielded a *semicarbazone*, m.p. 202—204° (Found: C, 60·15; H, 7·35; N, 23·55. $C_9H_{13}N_3O$ requires C, 60·3; H, 7·3; N, 23·6%). An attempt to form the corresponding derivative for the *exo*-methyl epimer (9b) failed.

(c) 7-endo- *and* 7-exo-*Ethylbicyclo*[3.2.0]*hept-2-en-6-ones* (8c) *and* (9c). 7-*exo*-Chloro-7-*endo*-ethylbicyclo[3.2.0]*heptenone* (2c) (172·5 mg) was dechlorinated as with zinc in methanolic ammonia chloride for 1 h to yield 7-*exo*- and 7-*endo*-ethyl ketones [(9c) and (8c)] (114 mg, 84%), b.p. 120° at 30 mmHg in the ratio 11 : 89 (g.l.c.) (Found: C, 79·25; H, 8·85. Calc. for $C_9H_{12}O$: C, 79·4; H, 8·9%), $\nu_{max.}$ 1770 $cm^{-1}$ (C=O), δ 5·81 (2H, m, H-2 and H-3), 3·60 (3H, m, H-1, H-5, and H-7), 2·52 (2H, m, allylic $CH_2$), 1·48 (2H, m, $CH_2$·$CH_3$), and 0·95 (3H, m, $CH_2$·$CH_3$).

(d) 7-endo- *and* 7-exo-*Isopropylbicyclo*[3.2.0]*hept-2-en-6-ones* (8d) *and* (9d). 7-*exo*-Chloro-7-isopropylbicycloheptenone (2d) (2 g) in the same way during 1 h gave a mixture of 7-*endo*- and 7-*exo*-isopropyl ketones (8d) and (9d); ratio 88 : 12, b.p. 115—120° at 3 mmHg (Found: $M^+$, 150·104093. Calc. for $C_{10}H_{14}O$: *M*, 150·104459), $\nu_{max.}$ 1770 $cm^{-1}$ (C=O), δ 5·87 (2H, narrow m, olefinic H), 3·70 (3H, m, H-1, H-5, and H-7), 2·25 (2H, m, allylic $CH_2$), 2·13 (1H, m, C*H*$Me_2$), and 8·95 and 9·10 (6H, 2 × d, CH*Me*$_2$).

*Hydrogenation of Dechlorinated Adducts.*—The epimeric 7-alkylbicycloheptenones were hydrogenated in ethyl acetate over Adams catalyst ($PtO_2$). Uptake was 1 mol. equiv. in all cases, and g.l.c. analysis indicated no change in the ratio of epimers during the hydrogenation.

(a) *Epimeric 7-methylbicyclo*[3.2.0]*heptan-6-ones* [dihydro-(8b)] *and* [dihydro-(9b)]. The epimeric 7-methylbicycloheptenones yielded 95% of dihydro-compounds, b.p. 70° at 20 mmHg; ratio 93 ± 1 : 7 ± 1 (g.l.c.), $M^+$ 124 ($C_8H_{12}O$), $\nu_{max.}$ 1777 $cm^{-1}$ (C=O), δ 3·77—2·70 (3H, m, cyclobutane CH), 2·15—1·2 (6H, m, $CH_2$), and 1·18 and 0·97 (3H, 2 × d, ratio 8 : 92, *exo*- and *endo*-Me).

(b) 7-endo- *and* 7-exo-*Ethylbicyclo*[3.2.0]*heptan-6-ones* [dihydro-(8c)] *and* [dihydro-(9c)]. The epimeric 7-ethylbicycloheptenones (8c) and (9c), ratio 89 : 11, gave 94% of dihydro-epimers (ratio 91 : 9 by g.l.c.), b.p. 120° at 30 mmHg (Found: C, 77·9; H, 10·2. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·15%), $\nu_{max.}$ 1770 $cm^{-1}$ (C=O), δ 3·53 (1H, m, H-5?), 3·08 (2H, m, H-1 and H-7?), and 2·00—0·90 (11H, m, including distorted t at 0·94, remainder).

(c) 7-endo- *and* 7-exo-*Isopropylbicyclo*[3.2.0]*heptan-6-ones* [dihydro-(8d)] *and* [dihydro-(9b)]. The epimeric 7-*endo*- and 7-*exo*-isopropylbicycloheptenones (8d) and (9d) gave 93% of dihydro-epimers (ratio 87 : 13 by g.l.c.), b.p. 120° at 30 mmHg (Found: $M^+$, 152·120424. Calc. for $C_{10}H_{16}O$: 152·120109), $\nu_{max.}$ 1768 $cm^{-1}$ (C=O).

*Equilibration Studies of 7-Alkylbicycloheptenones and their Dihydro-derivatives.* (a) *7-Methyl series.* Pure 7-*exo*-methylbicyclohepten-6-one (9b) (40 mg) in N-sodium methoxide in dry methanol (0·4 ml) during 1 h at 25° gave a mixture with an *exo*-methyl : *endo*-methyl ratio of 35 : 65, as judged by n.m.r. analysis. In the same way pure 7-*endo*-methyl epimer (8b) gave an *exo* : *endo* ratio of 33 : 67 in 1 h. The equilibrium mixture is regarded as comprising 34 ± 1% *exo*-epimer and 66 ± 1% *endo*-epimer.

An epimeric mixture of 7-*exo*-methylbicycloheptan-6-one [dihydro-(9b)] and the 7-*endo*-methyl isomer [dihydro-(8b)] (ratio 7 : 93, *exo* : *endo*) was isomerised as above: the *exo* : *endo* ratios observed by n.m.r. analysis [time (min) in parentheses] were: 56 : 44 (30); 58 : 42 (60); and 58 : 42 (150). The final figures were taken as the equilibrium ratio.

(b) *Ethyl series.* As n.m.r. spectra were complicated, epimerisation was followed by g.l.c. analysis. The original epimeric mixture of 7-ethylbicyclo[3.2.0]hept-2-en-6-ones (8c) and (9c) from dechlorination (11% *exo*-epimer) gave the following *exo* : *endo* ratios [time (min) in parentheses]: 11 : 89 (0); 34 : 66 (5); 35 : 65 (10); 35 : 65 (15); 36 : 64 (30); and 37 : 63 (60), after treatment with N-sodium methoxide in methanol at 20°. The dihydro-epimers [dihydro-(8c)] and [dihydro-(9c)] similarly gave the following figures: 9 : 91 (0); 69 : 31 (5); 71 : 29 (15); 73 : 27 (30); and 73 : 27 (60).

(c) *Isopropyl series.* In the same way N-sodium methoxide with epimeric 7-isopropylbicyclohept-2-en-6-ones (8d) and (9d) gave the following *exo* : *endo* ratios: 12 : 87 (0); 29 : 71 (5); 42 : 58 (15); 44 : 56 (30); and 46 : 54 (1320).

The dihydro-epimers [dihydro-(8d)] and [dihydro-(9d)], equilibrated in the same way, gave the following figures: 13 : 87 (0); 81 : 19(5); 86 : 14 (30); and 86 : 14 (1020).

(d) 7-endo-*Chlorobicyclo*[3.2.0]*hept-2-en-6-one.* The monochloro-ketone (1a) (0·5 g) was vigorously shaken with a solution of sodium carbonate (0·1 g) in deuterium oxide (99%; 2·0 ml). A parallel run with water was also carried out. After 1 h a sample was withdrawn and the chloroketone was analysed by n.m.r. The integrated intensity of the CHCl signal at δ 5·14 had been reduced by (87 ± 2%) as compared with the olefinic proton signals in the deuteriation experiment. The n.m.r. spectrum of the chloroketone in water–sodium carbonate had not changed perceptibly after 1 h and it was concluded that no epimerisation was occurring.

After 18 h 4% of C*H*Cl remained in the deuterium exchange experiment. The n.m.r. spectrum of the chloroketone recovered from aqueous base indicated the formation of ketols, confirmed by t.l.c.

The chloro-ketone (1a) (2 g), after 72 h shaking with water (12 ml)–sodium carbonate (0·6 g) yielded 21% of unchanged ketone and 75% of the 7-chloro-7-(7-chloro-6-hydroxybicyclo[3.2.0]hex-2-en-6-yl)bicyclo[3.2.0]hex-2-en-6-ones (6), b.p. 125—130° at 0·15 mmHg, as a thick oil (Found: C, 58·95; H, 4·9; Cl, 24·9. Calc. for $C_{14}H_{14}Cl_2O_2$: C, 59·3; H, 5·15; Cl, 24·8%), $\nu_{max.}$ 3590 (OH), 1785 (C=O), and 1610 $cm^{-1}$ (olefin), δ 6·18—5·6 (4H, m, olefinic), 5·16—4·90 (1H, m, CHCl), 4·12—3·13 (4H, m, bridgehead protons), 3·05—2·11 (4H, m, methylenes), and 2·9—2·78 (1H, 2 × s, 2 × OH of isomers). T.l.c. (benzene) showed two almost coincident spots of approximately equal intensity ($R_F$ 0·35), suggesting two isomers.

[3/2240 *Received*, 30*th October*, 1973]