Electrophilic Bromination of Bicyclo[3.2.0]hept-2-en-6-ones

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Bromination of bicyclo[3.2.0]hept-2-en-6-one (3) and 7,7-dimethylbicyclo[3.2.0]hept-2-en-6-one (2) in a variety of solvents gave high yields of the corresponding 2-*exo*-bromo-3-*endo*-substituted bicycloheptanones. The configurations of the products were deduced from n.m.r. spectra. The observed stereospecificity of the reaction is due to the preferential formation of the intermediate bromonium ion on the *exo*-face of the cyclopentene ring. 7-Chlorobicyclo[3.2.0]hept-2-en-6-ones (1) and (4) gave mixtures of the corresponding 2,3-disubstituted bicycloheptenones and 3,8-disubstituted 2-oxatricyclo[3.2.1.$0^{3,6}$]octanones when brominated in solvents capable of addition across the activated carbonyl group. Spectral evidence suggests that the 3-*endo*- and 7-*endo*-substituents determine the preferred conformation of the bicycloheptanones.

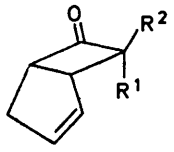
REARRANGEMENTS of 7-halogenobicyclo[3.2.0]heptan-6-ones and -6-ols have been described recently,[1,2] but the chemistry of bicyclo[3.2.0]heptanones halogenated at other sites has not been explored. We describe here the synthesis and configurational assignment of a series of 2-bromobicyclo[3.2.0]heptan-6-ones, which undergo rearrangements of mechanistic and synthetic interest.[3] The bicyclo[3.2.0]hept-2-en-6-ones (1)—(4) used as

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

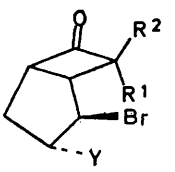
[2] P. R. Brook, A. J. Duke, J. M. Harrison, and K. Hunt, *J.C.S. Perkin I*, 1974, 927; P. R. Brook and A. J. Duke, *J. Chem. Soc.*, 1971, 1764; P. R. Brook, A. J. Duke, and J. M. Harrison, *J.C.S. Chem. Comm.*, 1972, 997; W. T. Brady and J. P. Hieble, *J. Org. Chem.*, 1971, **36**, 2033; H. C. Stevens, J. K. Rinehart, J. M. Lavanish and G. M. Trenta, *ibid.*, p. 2780; D. L. Garin and K. L. Cammack, *J.C.S. Chem. Comm.*, 1972, 333; P. D. Bartlett and T. Ando, *J. Amer. Chem. Soc.*, 1970, **92**, 7518.

[3] S. M. Roberts, *J.C.S. Chem. Comm.*, 1974, 948; M. Rey, S. M. Roberts, E. L. Mitch, Z. Grudzinski, and A. S. Dreiding, unpublished results.

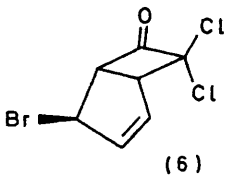
substrates in the bromination reactions were prepared by methods described previously.[4]



(1) $R^1 = R^2 = Cl$
(2) $R^1 = R^2 = CH_3$
(3) $R^1 = R^2 = H$
(4) $R^1 = Cl, R^2 = H$



(5) $R^1 = R^2 = Cl, Y = Br$
(8) $R^1 = R^2 = Me, Y = Br$
(9) $R^1 = R^2 = H, Y = Br$
(10) $R^1 = R^2 = Cl, Y = OAc$
(11) $R^1 = R^2 = Me, Y = OAc$
(12) $R^1 = R^2 = H, Y = OAc$
(13) $R^1 = Cl, R^2 = H, Y = OAc$
(14) $R^1 = R^2 = H, Y = OMe$
(15) $R^1 = R^2 = Me, Y = OMe$
(16) $R^1 = R^2 = Cl, Y = OMe$
(18) $R^1 = Cl, R^2 = H, Y = OMe$
(20) $R^1 = R^2 = Me, Y = OH$
(21) $R^1 = R^2 = H, Y = OH$
(22) $R^1 = R^2 = Cl, Y = OH$
(25) $R^1 = Cl, R^2 = H, Y = OH$



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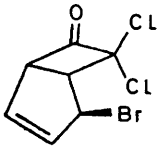

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Bromination Conditions and Products.—Bromination of 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (1) is reported to give a mixture of 2,3-dibromo-7,7-dichlorobicyclo-[3.2.0]heptan-6-one and a bromo-7,7-dichlorobicyclo-[3.2.0]heptenone.[5] We have repeated this reaction and found that the product mixture consisted of 2-*exo*,3-*endo*-dibromo-7,7-dichlorobicyclo[3.2.0]heptan-6-one (5) and 4-*exo*-bromo-7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (6) in the ratio 2 : 3. The products were identified by comparison of an n.m.r. spectrum of the mixture with the spectra of pure samples of the ketones (5) and (6).

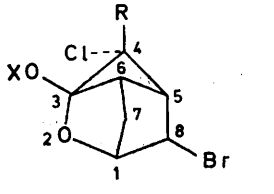
The tetrahalogenobicycloheptanone (5) was obtained pure in 80% yield after recrystallization by conducting the bromination of (1) in cold, buffered solution. The light-catalysed reaction of the dichlorobicycloheptenone (1) with *N*-bromosuccinimide furnished pure ketone (6) after recrystallization to remove the isomeric impurity 2-*exo*-bromo-7,7-dichlorobicyclo[3.2.0]hept-3-en-6-one (7).[6]

Bromination of 7,7-dimethylbicyclo[3.2.0]hept-2-en-6-one (2) under controlled conditions gave 2-*exo*,3-*endo*-dibromo-7,7-dimethylbicyclo[3.2.0]heptan-6-one (8) in 85% yield after recrystallization. Likewise, bicyclo-[3.2.0]hept-2-en-6-one (3) furnished 2-*exo*,3-*endo*-dibromobicyclo[3.2.0]heptan-6-one (9) in high yield.[7] The results of further studies on the dibromoheptanones (8) and (9) will be reported in a separate publication.

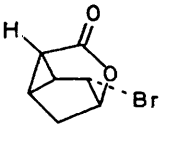
Reactions of equimolar quantities of *N*-bromoacetamide (NBA) and the bicycloheptenones (1)—(4) in glacial acetic acid gave the corresponding 3-*endo*-acetoxy-2-*exo*-bromobicyclo[3.2.0]heptan-6-ones (10)—(13) in 70—80% yields. Similarly, treatment of bicyclo[3.2.0]hept-2-en-6-one (3) and its 7,7-dimethyl derivative (2) with NBA in an excess of methanol gave 2-*exo*-bromo-3-*endo*-methoxy- (14) and 2-*exo*-bromo-3-*endo*-methoxy-7,7-dimethyl-bicyclo[3.2.0]heptan-6-one (15), respectively.

The reaction of 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (1) with NBA in methanol gave a two-component mixture. The minor component (25%) was identified (n.m.r., i.r.) as the expected 2-*exo*-bromo-7,7-dichloro-3-*endo*-methoxybicyclo[3.2.0]heptan-6-one (16). The major component (75%) showed no carbonyl i.r. absorption and the n.m.r. spectrum was consistent with the structure 8-*exo*-bromo-4,4-dichloro-3-*exo*-methoxy-2-oxatricyclo[3.2.1.$0^{3,6}$]octane (17). Similar treatment of a methanolic solution of 7-*endo*-chlorobicyclo[3.2.0]hept-2-en-6-one (4) with NBA gave a mixture of two solid products, separated into 2-*exo*-bromo-7-*endo*-chloro-3-*endo*-methoxybicyclo[3.2.0]heptan-6-one (18) and 8-*exo*-bromo-4-*endo*-chloro-3-*exo*-methoxy-2-oxatricyclo-[3.2.1.$0^{3,6}$]octane (19). The ratio of (18) to (19) was 1 : 3.

On treatment with NBA in aqueous acetone the bicycloheptenones (2) and (3) gave 2-*exo*-bromo-3-*endo*-hydroxy-7,7-dimethyl- (20) and 2-*exo*-bromo-3-*endo*-hydroxy-bicyclo[3.2.0]heptan-6-one (21), respectively. Treatment of the bromohydrins (20) and (21) with acetic anhydride in pyridine gave only the corresponding bromo-acetoxy-compounds (11) and (12). The reaction of 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (1) with NBA in aqueous acetone yielded 2-*exo*-bromo-7,7-dichloro-3-*endo*-hydroxybicyclo[3.2.0]heptan-6-one (22), which exists in solution in equilibrium with 8-*exo*-bromo-4,4-dichloro-2-oxatricyclo[3.2.1.$0^{3,6}$]octan-3-*exo*-ol (23). Thus the n.m.r. spectrum of the reaction product dissolved in carbon tetrachloride exhibited a pattern similar to that obtained when the n.m.r. spectra of



(17) R = Cl, X = Me
(19) R = H, X = Me
(23) R = Cl, X = H
(24) R = Cl, X = Ac
(26) R = X = H



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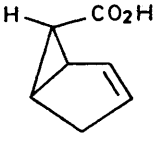

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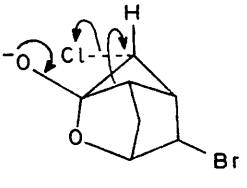

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[4] M. Rey, S. M. Roberts, A. Dieffenbacher, and A. S. Dreiding, *Helv. Chim. Acta*, 1970, **53**, 417; P. A. Grieco, *J. Org. Chem.*, 1972, **37**, 2363; J. C. Martin, P. G. Gott, V. W. Goodlett, and R. H. Hasek, *ibid.*, 1965, **30**, 4175.

[5] W. E. Bissinger, U.S.P. 3,549,769/1970 (*Chem. Abs.*, 1971, **74**, 141,112c); B. Boehner and K. Ruefenacht, S.Afr.P. 6,706,947/1968 (*Chem. Abs.*, 1969, **70**, 106,068p).

[6] C. E. Dahl, R. W. Gray, and A. S. Dreiding, *Helv. Chim. Acta*, 1974, **57**, 1169.

[7] E. Mitch and A. S. Dreiding, *Chimia* (*Switz.*), 1960, **14**, 424.

(16) and (17) were superimposed. The interconversion of the isomers (22) and (23) is therefore slow on the n.m.r. time scale and their ratio (1 : 1.1) could be determined. In deuteriopyridine solution, the n.m.r. spectrum of the product displayed four broad, ill-defined signals δ 4.9—4.5, 3.7—3.1, 2.7—2.3, and 2.2—1.8 suggesting that the ring–chain tautomerism is considerably faster in this basic medium.

Base-catalysed acetylation of the tautomeric mixture takes place at the reactive hemiacetal site to give 3-*exo*-acetoxy-8-*exo*-bromo-4,4-dichloro-2-oxatricyclo-[3.2.1.$0^{3,6}$]octane (24) in 93% yield.

Likewise 7-*endo*-chlorobicyclo[3.2.0]hept-2-en-6-one (4) reacted with NBA in aqueous acetone to give a crystalline product which in solution exhibited properties attributable to the presence of the ring–chain tautomers 2-*exo*-bromo-7-*endo*-chloro-3-*endo*-hydroxybicyclo[3.2.0]heptan-6-one (25) and 8-*exo*-bromo-4-*endo*-chloro-2-oxatricyclo[3.2.1.$0^{3,6}$]octan-3-ol (26). The n.m.r. spectrum suggested that the ratio of bromohydrin (25) to hemiacetal (26) was 4 : 1. The smaller proportion of hemiacetal in the equilibrium mixture (25) ⇌ (26) as compared with that in the mixture (22) ⇌ (23) is probably due to favourable intramolecular hydrogen-bonding between the adjacent 3-*exo*-hydroxy- and 4-*exo*-chloro-substituents in (23).

Treatment of the tautomeric mixture (25) ⇌ (26) with aqueous potassium carbonate gave the bromolactone (27), with spectral characteristics identical with those reported.[8] Furthermore, treatment of (27) with zinc in acetic acid gave bicyclo[3.1.0]hex-2-ene-6-*endo*-carboxylic acid (28), identical with an authentic sample.[9]

The rearrangement (25) ⇌ (26) ⟶ (27) presumably proceeds through the anion (29). It is noteworthy that the cyclobutane ring is locked in a non-planar conformation with the chlorine atom pseudo-equatorial. Furthermore, the C(4)–Cl and C(3)–C(6) bonds are antiperiplanar, a favourable disposition leading to the observed ring contraction. The rearrangement is analogous to the stereospecific base-catalysed reactions of 7-*endo*- and 7-*exo*-halogenobicyclo[3.2.0]hept-2-en-6-*endo*-ols which are believed to react through conformations of the cyclobutane ring in which the expelled chlorine atom is pseudoequatorial.[1,10]

Configuration of the 2-Bromobicyclo[3.2.0]heptan-6-ones.—The bromine atom in the fifteen bicyclo[3.2.0]-heptanones (5), (8)—(16), (18), (20)—(22) and (25) has been assigned the 2-*exo*-configuration; the 3-*endo*-configuration was assigned to the appended acetoxy-group [(10)—(13)], methoxy-group [(14)—(16), and (18)], hydroxy-group [(20)—(22) and (25)] or the second bromine atom [(5), (8), and (9)]. These assignments were based on n.m.r. spectral data * and the conclusions are summarised below.

The 4-*exo*- and 4-*endo*-protons are both coupled to H-5 ($J_{4\text{-}exo,5}$ 7.5—9.0, $J_{4\text{-}endo,5}$ 0.5—4.5 Hz) and to a second nucleus presumed to be H-3. The chemical shift of H-3 varies considerably for the brominated products and depends upon whether the substituents at C-2 and C-3 are dibromo- (δ 4.8—4.3), bromo-acetoxy- (5.45—5.28), bromo-methoxy- (4.2—4.1), or bromo-hydroxy- (δ 4.7—4.3). For the same compounds the chemical shift of H-2 is relatively constant (δ 4.85—4.3). It was concluded that a bromine atom always occupies a site at C-2.

Except for the dibromo-compounds [(5) and (8)], the signal due to H-2 appears as a slightly broadened singlet displaying only fine coupling to H-3 and H-1. This can only be rationalized by assuming torsion angles $\omega_{1,2}$ and $\omega_{2,3}$ *ca.* 90° and molecular models demonstrate that H-2 must have therefore an *endo*-configuration, *trans* to H-1 and H-3. The n.m.r. spectra of the dibromo-compounds (5) and (8) show the H-2 signal as a doublet of doublets ($J_{1,2}$ 4.0 ± 1.0 Hz). This is ascribed to a change in conformation (see next section).

Further evidence that H-2 is in an *endo*-configuration is that its chemical shift shows a dependence on the nature of the *endo*-substituent at C-7, *e.g.* (11), (15), and (20) (CH_3-7-*endo*) $\delta_{H\text{-}2}$ 4.30 ± 0.05; (5), (10), (13), (16), and (18) (Cl-7-*endo*) $\delta_{H\text{-}2}$ 4.65 ± 0.05.

Conformation of the 2-Bromobicyclo[3.2.0]heptan-6-ones.—The Karplus relationship of torsion angle $\omega_{x,y}$ between vicinal hydrogen atoms H-*x* and H-*y* and coupling constant $J_{x,y}$ [11] must be used with caution in systems involving electronegative substituents bonded to C-*x* and C-*y*. It is well documented that the orientation of the electronegative units to H-*x* and H-*y* profoundly affects $J_{x,y}$.[12] Nevertheless, a good deal of conformational information can be gleaned from the observed coupling constants (see Supplementary Publication).

The coupling of H-1 to H-5 and H-7 is significantly larger for the 2-bromobicyclo[3.2.0]heptan-6-ones ($J_{1,7}$ 9.5 ± 0.25, $J_{1,5}$ 8.5 ± 0.5 Hz) than for the corresponding bicyclo[3.2.0]hept-2-en-6-ones ($J_{1,7}$ 7.5, $J_{1,5}$ 7.5 ± 0.5 Hz). If the introduction of a double bond into a five-membered ring does not appreciably influence the magnitude of the vicinal coupling constants in the saturated fragment,[12] a change in conformation of the four-membered ring is indicated. We suggest that the four-membered ring is essentially planar in the saturated series whereas the four-membered ring of the bicycloheptenones is buckled such that $\omega_{1,7} \simeq \omega_{1,5} \simeq 20°$.[13] †

* Available as Supplementary Publication No. SUP 21427 (3 pp.). For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1974, Index issue.

† If we assume that the same Karplus curve can be applied to the two series of compounds, then $J^0_{1,5} \simeq 8.75$; $J^0_{1,7} \simeq 10.0$ Hz.

[8] J. Warkentin, E. Singleton, and J. F. Edgar, *Canad. J. Chem.*, 1965, **43**, 3456.

[9] J. Meinwald, S. S. Labana, and M. S. Chadha, *J. Amer. Chem. Soc.*, 1963, **85**, 582.

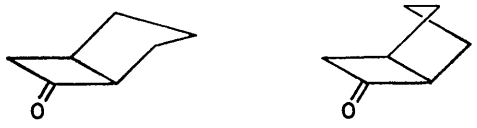
[10] P. R. Brook and A. J. Duke, *Chem. Comm.*, 1970, 652; P. R. Brook, *ibid.*, 1968, 565; P. R. Brook, A. J. Duke, J. G. Griffiths, S. M. Roberts, M. Rey, and A. S. Dreiding, in preparation.

[11] M. Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

[12] L. M. Jackman and S. Sternhell, 'Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 1969.

[13] J. M. Conia and J. R. Salaun, *Accounts Chem. Res.*, 1972, **5**, 33; P. R. Brook, A. J. Duke, and J. R. C. Duke, *Chem. Comm.*, 1970, 574.

Under the constraint of an almost planar four-membered ring, the cyclopentane ring of the 2-bromobicyclo[3.2.0]heptan-6-ones can assume any conformation between the limiting *exo*- and *endo*-envelope forms (see Figure): the five-membered ring might also rapidly flip between two or more conformations within these limits. In the latter case the observed coupling constants will be the arithmetic means of the coupling constants associated with the contributing conformations.



FIGURE

Consider first the bromo-methoxy- [(15), (16), and (18)], bromo-acetoxy- [(10)—(13)], and bromo-hydroxy-compounds [(20), (21), and (22)], and also 2,3-dibromobicyclo[3.2.0]heptan-6-one (9). The values $J_{4\text{-}exo,5}$ 8.2 ± 0.8, $J_{4\text{-}endo,5}$ 2.25 ± 0.75 Hz require that $\omega_{4\text{-}exo,5}$ is small in comparison with $\omega_{4\text{-}endo,5}$. In addition, the small couplings $J_{2,3} = J_{1,2} = J_{3,4\text{-}endo} = 0.75 \pm 0.75$ Hz suggest $\omega_{3,2} \simeq \omega_{2,1} \simeq \omega_{3,4endo} \simeq 90°$. Molecular models suggest that these requirements are only satisfied by the *endo*-envelope conformation (Table), which must therefore be the sole or major contributing conformation. In this conformation the bulky groups at C-2 and C-3 are *trans*-diaxial and eclipsing of Br-2 and H-1 is minimized.

Torsion angles between protons on contiguous carbon atoms as a function of the conformation of the five-membered ring

	Torsion angle (°) [a]						
Conformation	$\omega_{1,2}$	$\omega_{2,3}$	$\omega_{3,4\text{-}exo}$	$\omega_{3,4\text{-}endo}$	$\omega_{4\text{-}exo,5}$	$\omega_{4\text{-}endo,5}$	$\omega_{1,5}$
endo-Envelope	90	75	45	80	45	80	*ca.* 0
exo-Envelope	145	160	135	165	15	130	*ca.* 0

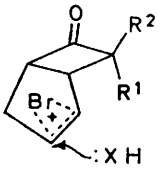
[a] Measured from molecular models.

The dibromobicycloheptanones (5) and (8) display larger values for $J_{1,2}$, $J_{2,3}$, $J_{3,4\text{-}endo}$, $J_{3,4\text{-}exo}$, $J_{4\text{-}exo,5}$, indicating that in comparison with the preceding series of compounds the torsion angles between these pairs of hydrogen atoms move away from 90°. This is exactly what occurs on ring-flipping of the five-membered ring to the *exo*-envelope conformation; the torsion angles are summarized in the Table. The latter conformation thus makes a significant (if not major) contribution to the mobile conformation of the dibromobicycloheptanones (5) and (8). For these compounds it seems that the steric influences mentioned above are outweighed by the unfavourable transannular interaction of Br-3-*endo* and the bulky *endo*-substituent at C-7.

The locked conformation of the oxatricyclo[3.2.1.$0^{3,6}$]-octanes (17), (19), (23), (24), and (26) leads to the observation of distinct long-range coupling in the n.m.r. spectra ($^4J_{8,7\text{-}syn}$, $^4J_{1,6}$ 1.5 Hz) reminiscent of similar interactions in the norbornane system.[12] Note also that while $\omega_{1,7\text{-}anti} = \omega_{1,7\text{-}syn} = 60°$, $J_{1,7\text{-}anti} < 0.2$ and $J_{1,7\text{-}syn}$ 2.0 Hz: this is a similar effect to that observed previously, whereby coupling constants are diminished when an electronegative substituent is antiperiplanar to the coupling path.[14]

Mechanism of Bromination.—The additions to the double bond of bicyclo[3.2.0]hept-2-en-6-ones reported above are stereospecific.* This is rationalized by postulating the preferential formation of the *exo*-bromonium ion intermediate (30) [15] which is attacked from the *endo*-face by the attendant nucleophile at the less hindered C-3 position.

The marked preference for the formation of an *exo*- rather than an *endo*-bromonium ion is further illustrated by silver tetrafluoroborate-promoted conversion of 2-*exo*,3-*endo*-dibromo-7,7-dimethylbicyclo[3.2.0]heptan-6-one (8) into 2-*exo*-bromo-3-*endo*-methoxy-7,7-dimethylbicyclo[3.2.0]heptan-6-one (15) in 70% yield. The unreactivity of the more accessible *exo*-bromine atom in the ketone (8) is due to the inability of the neighbouring



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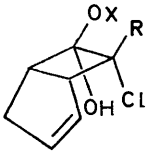

(31) R = Cl, X = Me
(32) R = H, X = Me
(33) R = Cl, X = H
(34) R = X = H

bromine atom (at C-3) to form an *endo*-bromonium ion. On the other hand, silver-catalysed abstraction of the hindered bromine atom at C-3 is promoted by participation of the *exo*-bromine atom to give a bromonium ion (30) which is consequently attacked by methanol from the *endo*-face to give (15).

The tricyclic acetals (17) and (19) are probably formed from the hemiacetals (31) and (32); intramolecular attack by OH-6-*endo* at C-3 in the intermediate bromonium ion would lead directly to the acetals (17) and (19), respectively. It is possible that the hemiacetals (22) and (26) are formed in a similar manner through the ketone hydrates (33) and (34), respectively. However, it is also possible that water attacks the bromonium ion (30; R^1 = Cl, R^2 = H or Cl, X = OH) to give bromohydrins (22) and (25) with secondary ring–chain tautomerism giving (23) and (26). Previously attempted intramolecular reactions between an *endo*-hydroxy-group at C-6 and a transient carbocation at C-3 in the bicyclo[3.2.0]heptane system were unsuccessful.[1]

EXPERIMENTAL

N.m.r. spectra were obtained with a Varian A60 or HA100 spectrometer for solutions in carbon tetrachloride unless otherwise stated. I.r. spectra were run with a Perkin-Elmer 257 spectrophotometer. Silica gel (B.D.H.)

* N.m.r. spectra of crude reaction products showed no evidence of other stereoisomers.

[14] H. Booth, *Tetrahedron Letters*, 1965, 411.
[15] B. E. Smart, *J. Org. Chem.*, 1973, **38**, 2366.

was used for preparative chromatography and silica gel G (Merck) for analytical chromatography. Distillations were accomplished by using the Büchi Kugelröhr (bulb-to-bulb) system and the temperatures reported are oven temperatures at distillation. *N*-Bromoacetamide (Koch–Light) was used without further purification.

Dibromobicyclo[3.2.0]*heptan*-6-*ones*.—Bromine in carbon tetrachloride was added dropwise to a stirred solution of the ketone in carbon tetrachloride containing sodium hydrogen carbonate (2.0 g) at 0 °C. Stirring was continued for 3 h at this temperature before the solution was cooled to −20° C over 16 h. The colourless solution was filtered and the filtrate evaporated. The residue was taken up in the minimum quantity of solvent and crystallised at −20 °C.

(a) 2-exo,3-endo-*Dibromo*-7,7-*dichlorobicyclo*[3.2.0]*heptan*-6-*one* (5). Treatment of 7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (1) (1.72 g) in carbon tetrachloride (10 ml) with bromine (1.60 g) in carbon tetrachloride (5 ml) gave the dibromodichlorobicycloheptanone (5) (2.6 g, 79%), m.p. 78—79° (from petroleum) (lit.,[5] 77—78°), $\nu_{max.}$ 1 815 cm^{-1} (Found: C, 25.2; H, 1.9. Calc. for $C_7H_6Br_2Cl_2O$: C, 25.0; H, 1.8%).

Reaction of the bicycloheptenone (1) with bromine in carbon tetrachloride at room temperature in the absence of sodium hydrogen carbonate gave a viscous oil which displayed an n.m.r. spectrum indicating a mixture of dibromodichloroheptanone (5) (40%) and 4-*exo*-bromo-7,7-dichlorobicyclo[3.2.0]hept-2-en-6-one (6) (60%). An authentic sample of (6) was obtained by dissolving the bicycloheptenone (1) (1.4 g) and *N*-bromosuccinimide (1.8 g) in carbon tetrachloride (10 ml). Irradiation with a tungsten lamp (500 W) induced a rapid reaction. After 1 h the mixture was cooled to −20 °C, the succinimide filtered off and the solution evaporated. Crystallization of the residue from carbon tetrachloride at −20 °C gave the bromodichlorobicycloheptenone (6) (0.75 g, 37%), m.p. 81—82° (lit.,[6] 80—81), $\nu_{max.}$ 1 810 cm^{-1}, δ 6.33 (1 H, ddd, *J* 6.0, 2.0, and 2.0 Hz, H-2 or H-3), 6.03 (1 H, ddd, *J* 6.0, 2.0, and 1.0 Hz, H-3 or H-2), 5.12 (1 H, ddd, *J* 2.0, 2.0 and 1.0 Hz, H-4), 4.54 (1 H, d, *J* 6.5 Hz, H-5), and 4.28 (1 H, dddd, *J* 6.5, 2.0, 2.0, and 2.0 Hz, H-1) (Found: C, 33.0; H, 2.1. Calc. for $C_7H_5BrCl_2O$: C, 32.8; H, 1.95%). The mother liquors were rich in 2-*exo*-bromo-7,7-dichlorobicyclo[3.2.0]hept-3-en-6-one (7) as evidenced by the n.m.r. spectrum: δ 6.45—6.20 (2 H, m, H-3 and H-4), 5.35 (1 H, ddd, *J* 3.0, 3.0, and 3.0 Hz, H-2), 4.85 (1 H, dddd, *J* 7.0, 3.0, 3.0, and 1.5 Hz, H-5), and 3.85 (1 H, dd, *J* 9.0 and 3.0 Hz, H-1).

(b) 2-exo,3-endo-*Dibromo*-7,7-*dimethylbicyclo*[3.2.0]*heptan*-6-*one* (8). Treatment of 7,7-dimethylbicyclo[3.2.0]-hept-2-en-6-one (2) (5.0 g) in carbon tetrachloride (30 ml) with bromine (5.9 g) in carbon tetrachloride (5 ml) gave the *dibromodimethylbicycloheptanone* (8) (10.3 g, 95%), m.p. 73.5—74° (from diethyl ether), $\nu_{max.}$ 1 780 cm^{-1} (Found: C, 36.8; H, 3.85. $C_9H_{12}Br_2O$ requires C, 36.5; H, 4.1%).

(c) 2-exo,3-endo-*Dibromobicyclo*[3.2.0]*heptan*-6-*one* (9). The reaction of bicyclo[3.2.0]hept-2-en-6-one (3) (1.0 g) in carbon tetrachloride (13 ml) with bromine (1.54 g) in carbon tetrachloride (4 ml) gave the *dibromobicycloheptanone* (9) (2.14 g, 86%), m.p. 59—60° (from diethyl ether), $\nu_{max.}$ 1 780 cm^{-1} (Found: C, 31.05; H, 3.1. $C_7H_8Br_2O$ requires C, 31.4; H, 3.0%).

Acetoxybromobicyclo[3.2.0]*heptan*-6-*ones*.—Bicycloheptenone was dissolved in glacial acetic acid (10—20 ml). *N*-Bromoacetamide (1.25 equiv.) was added and the mixture was stirred until dissolution was complete. After 16 h at room temperature the solution was diluted with ether (30—50 ml) and extracted with saturated sodium hydrogen carbonate solution until neutral. The aqueous washings were back-extracted with ether (2 × 30 ml). The combined extracts were dried and evaporated and the residue was distilled and/or recrystallized.

(a) 3-endo-*Acetoxy*-2-exo-*bromo*-7,7-*dichlorobicyclo*[3.2.0]-*heptan*-6-*one* (10). 7,7-Dichlorobicyclo[3.2.0]hept-2-en-6-one (1) (0.65 g) gave a solid product which was recrystallized from carbon tetrachloride to give the *acetoxybromobicycloheptanone* (10) (1.0 g, 86%), m.p. 70—72°, $\nu_{max.}$ 1 815 and 1 750 cm^{-1} (Found: C, 34.4; H, 2.7. $C_9H_9BrCl_2O_3$ requires C, 34.2; H, 2.9%).

(b) 3-endo-*Acetoxy*-2-exo-*bromo*-7,7-*dimethylbicyclo*-[3.2.0]*heptan*-6-*one* (11). 7,7-Dimethylbicyclo[3.2.0]hept-2-en-6-one (2) (1.5 g) gave a residue which was recrystallized from petroleum to give the *acetoxybromobicycloheptanone* (11) (2.5 g, 82%), m.p. 68—70°, $\nu_{max.}$ 1 780 and 1 750 cm^{-1} (Found: C, 47.8; H, 5.5. $C_{11}H_{15}BrO$ requires C, 48.0; H, 5.5%).

(c) 3-endo-*Acetoxy*-2-exo-*bromobicyclo*[3.2.0]*heptan*-6-*one* (12). Bicyclo[3.2.0]hept-2-en-6-one (3) (0.85 g) gave a residue which was distilled (110 °C at 0.01 mmHg) and recrystallized from petroleum at −20 °C to give the *acetoxybromobicycloheptanone* (12) (1.75 g, 90%), m.p. 38°, $\nu_{max.}$ 1 785 and 1 745 cm^{-1} (Found: C, 43.9; H, 4.7. $C_9H_{11}BrO_3$ requires C, 43.75; H, 4.5%).

(d) 3-endo-*Acetoxy*-2-exo-*bromo*-7-endo-*chlorobicyclo*-[3.2.0]*heptan*-6-*one* (13). 7-*endo*-Chlorobicyclo[3.2.0]hept-2-en-6-one (4) (1.3 g) gave a residue which was distilled (105 °C at 0.005 mmHg) and crystallized from petroleum to give the *acetoxybromobicycloheptanone* (13) (1.5 g, 58%), m.p. 80—82°, $\nu_{max.}$ 1 800 and 1 745 cm^{-1} (Found: C, 38.1; H, 3.8. $C_9H_{10}BrClO_3$ requires C, 38.4; H, 3.6%).

Treatment of Bicyclo[3.2.0]*hept*-2-*en*-6-*ones* (1)—(4) *with NBA in Methanol*.—The bicycloheptenone was dissolved in methanol and NBA (1.25 equiv.) was added with stirring. After 18 h at room temperature the solution was diluted with ether (50 ml) and extracted with water (6 × 30 ml). The aqueous extracts were separately washed with ether (2 × 30 ml). The combined organic fractions were dried ($MgSO_4$) and evaporated.

(a) 2-exo-*Bromo*-7,7-*dichloro*-3-endo-*methoxybicyclo*-[3.2.0]*heptan*-6-*one* (16) *and* 8-exo-*bromo*-4,4-*dichloro*-3-exo-*methoxy*-2-*oxatricyclo*[3.2.1.0^{3,6}]*octane* (17). 7,7-Dichlorobicyclo[3.2.0]hept-2-en-6-one (1) (2.0 g) in methanol (25 ml) gave a crude product (2.6 g) which partially solidified on cooling to −20 °C. The solid was filtered off and recrystallized from petroleum to give the *oxatricyclo-octane* (17) (1.2 g, 37%), m.p. 58—60°, δ ($CDCl_3$) 4.64 (1 H, ddd, $^3J_{1.8}$ 1.5, $^3J_{1.7\text{-}syn}$ 1.5, $^4J_{1.6}$ 1.5 Hz, H-1), 4.36 (1 H, dd, $^4J_{8.7\text{-}syn}$ 1.5 Hz, H-8), 3.47 (3 H, s, OMe), 3.27 (1 H, dddd, $^3J_{5.6}$ 4.5, $^3J_{6.7\text{-}syn}$ 1.5, $^3J_{6,7\text{-}anti}$ 1.5 Hz, H-6), 3.06 (1 H, d, H-5), 2.47 (1 H, dd, $^2J_{7\text{-}syn,7\text{-}anti}$ 12 Hz, H-7-*anti*), and 1.90 (1 H, dddd, H-7-*syn*) (Found: C, 32.7; H, 2.7. $C_8H_9BrCl_2O_2$ requires C, 33.3; H, 3.1%).

Column chromatography of the residual oil over silica with benzene–petroleum as eluant gave in the first fraction the acetal (17) (0.3 g, 9%), followed by the *bromomethoxybicycloheptanone* (16) (0.5 g, 15%), b.p. 110° at 0.005 mmHg, $\nu_{max.}$ 1 815 cm^{-1} (Found: C, 33.6; H, 2.8. $C_8H_9BrCl_2O_2$ requires C, 33.3; H, 3.1%).

(b) 2-exo-*Bromo*-3-endo-*methoxy*-7,7-*dimethylbicyclo*-[3.2.0]*heptan*-6-*one* (15). 7,7-Dimethylbicyclo[3.2.0]hept-2-en-6-one (2) (1.5 g) in methanol (10 ml) gave by the above

procedure the *bromomethoxybicycloheptanone* (15) (2.05 g, 75%), b.p. 70° at 0.01 mmHg, $\nu_{max.}$ 1 780 cm^{-1} (Found: C, 47.95; H, 5.9. $C_{10}H_{15}BrO_2$ requires C, 48.6; H, 6.1%).

(c) 2-exo-*Bromo*-3-endo-*methoxybicyclo*[3.2.0]*heptan*-6-*one* (14). Bicyclo[3.2.0]hept-2-en-6-one (3) (8.5 g) in methanol (100 ml) treated in the above manner gave the *bromomethoxybicycloheptanone* (14) (17.0 g, 99%), b.p. 70° at 0.005 mmHg, $\nu_{max.}$ 1 785 cm^{-1} (Found: C, 43.6; H, 4.9. $C_8H_{11}BrO_2$ requires C, 43.9; H, 5.1%).

(d) 2-exo-*Bromo*-7-endo-*chloro*-3-endo-*methoxybicyclo*[3.2.0]*heptan*-6-*one* (18) *and* 8-exo-*bromo*-4-endo-*chloro*-3-exo-*methoxy*-2-*oxatricyclo*[3.2.1.$0^{3,6}$]*octane* (19). 7-*endo*-Chlorobicyclo[3.2.0]hept-2-en-6-one (4) (2.5 g) in methanol (30 ml) gave a crude product which was dissolved in carbon tetrachloride and cooled to −20 °C. The crystals formed were filtered off to give the *dihalogenomethoxybicycloheptanone* (18) (0.85 g, 19%), m.p. 114—116°, $\nu_{max.}$ 1 785 cm^{-1} (Found: C, 38.4; H, 3.9. $C_8H_{10}BrClO_2$ requires C, 37.9; H, 4.0%). The mother liquors were evaporated and the residue crystallized from petroleum–chloroform to give the *oxatricyclo-octane* (19) (2.55 g, 57%), m.p. 70—72°, δ 4.65—4.35 (3 H, m, H-1, H-4, and H-8), 3.26 (3 H, s, OMe), 2.95—2.75 (2 H, m, H-5 and 6), 2.46 (1 H, dm, *J* 12.0 Hz, H-7-*anti*), and 1.92 (1 H, dm, H-7-*syn*) (Found: C, 37.5; H, 3.7. $C_8H_{10}BrClO_2$ requires C, 37.9; H, 4.0%).

Treatment of Bicyclo[3.2.0]*hept*-2-*en*-6-*ones* (1)—(4) *with NBA in Aqueous Acetone*.—The bicycloheptenone was dissolved in acetone (40 ml) and water (10 ml). NBA (1.25 equiv.) was added with stirring. After 18 h at room temperature, water (10 ml) was added and the acetone was removed *in vacuo*. Ether (40 ml) was added and the organic phase was separated and washed with water (6 × 30 ml). The aqueous washes were back-extracted with ether (2 × 30 ml). The combined organic fractions were dried and evaporated.

(a) 2-exo-*Bromo*-7,7-*dichloro*-3-endo-*hydroxybicyclo*[3.2.0]*heptan*-6-*one* (22) *and* 8-exo-*bromo*-4,4-*dichloro*-2-*oxatricyclo*[3.2.1.$0^{3,6}$]*octan*-3-exo-*ol* (23). 7,7-Dichlorobicyclo[3.2.0]hept-2-en-6-one (1) (3.0 g) gave after crystallization from carbon tetrachloride the *bromohydrin* (22) (2.6 g, 56%), m.p. 76.5—78°, $\nu_{max.}$ 3 480, 3 380br, and 1 810 cm^{-1} (Found: C, 30.4; H, 2.5. $C_7H_7BrCl_2O_2$ requires C, 30.7; H, 2.55%). The n.m.r. spectrum of the crystalline product dissolved in carbon tetrachloride displayed signals attributable to bromohydrin (22). Other peaks in the spectrum were assigned to the ring–chain tautomer (23): δ 3.30 (1 H, dm, $J_{5,6}$ 4.2 Hz, H-6) and 3.06 (1 H, dm, H-5). Integration of the latter peaks and those assigned to H-5 and H-1 in the *bromohydrin* (22) indicated that the ratio (22) : (23) was 1 : 1.1.

(b) 2-exo-*Bromo*-3-endo-*hydroxy*-7,7-*dimethylbicyclo*[3.2.0]*heptan*-6-*one* (20). 7,7-Dimethylbicyclo[3.2.0]hept-2-en-6-one (2) (1.9 g) gave after distillation (100° at 0.01 mmHg) and crystallization from petroleum the *bromohydrin* (20) (2.5 g, 77%), m.p. 66—69°, $\nu_{max.}$ 3 420 and 1 768 cm^{-1} (Found: C, 46.55; H, 5.5. $C_9H_{13}BrO_2$ requires C, 46.4; H, 5.6%).

(c) 2-exo-*Bromo*-3-endo-*hydroxybicyclo*[3.2.0]*heptan*-6-*one* (21). Bicyclo[3.2.0]hept-2-en-6-one (3) (1.5 g) gave after crystallization from carbon tetrachloride the *bromohydrin* (21) (1.7 g, 60%), m.p. 87—89°, $\nu_{max.}$ 3 400br and 1 770 cm^{-1} (Found: C, 40.5; H, 4.1. $C_7H_9BrO_2$ requires C, 41.0; H, 4.4%).

(d) 2-exo-*Bromo*-7-endo-*chloro*-3-endo-*hydroxybicyclo*[3.2.0]*heptan*-6-*one* (25) *and* 8-exo-*bromo*-4-endo-*chloro*-2-*oxabicyclo*[3.2.1.$0^{3,6}$]*octan*-3-exo-*ol* (26). 7-*endo*-Chlorobicyclo[3.2.0]hept-2-en-6-one (4) (1.1 g) gave on crystallization from chloroform the *bromohydrin* (25) (1.2 g, 65%), m.p. 111—114° (decomp.), $\nu_{max.}$ 3 350 and 1 790 cm^{-1} (Found: C, 34.65; H, 3.3. $C_7H_8BrClO_2$ requires C, 35.1; H, 3.4%). The n.m.r. spectrum of the crystalline product displayed a multiplet attributed to the tautomer (26), δ 3.0—2.7 (2 H, m, H-5 and -6). Other signals due to the hemiacetal (26) were hidden under the stronger signals of the bromohydrin (25). Integration of observable signals of the isomers indicated the ratio of (25) to (26) to be 4 : 1.

Treatment of the Bromohydrins (20)—(22) *with Acetic Anhydride in Pyridine*.—The bromohydrin was dissolved in pyridine (3.0 ml) containing acetic anhydride (1.0 g). After 32 h at room temperature, ether (20 ml) was added. The solution was poured into ice-cold 4N-sulphuric acid (10 ml); the ethereal phase was separated, washed with 4N-sulphuric acid and with saturated aqueous sodium hydrogen carbonate (3 × 10 ml). The aqueous washes were separately back-extracted with ether (2 × 20 ml) and the combined organic fractions were dried ($MgSO_4$) and evaporated.

(a) 3-endo-*Acetoxy*-2-exo-*bromo*-7,7-*dimethylbicyclo*[3.2.0]*heptan*-6-*one* (11). The bromohydrin (20) (0.45 g) gave the bromo-acetate (11) (0.43 g, 81%), identical (t.l.c., i.r., n.m.r., mixed m.p.) with the sample obtained above.

(b) 3-endo-*Acetoxy*-2-exo-*bromobicyclo*[3.2.0]*heptan*-6-*one* (12). The bromohydrin (21) (0.23 g) gave the bromo-acetate (12) (0.15 g, 54%), identical (t.l.c., i.r., mixed m.p.) with the sample prepared above.

(c) 3-exo-*Acetoxy*-8-exo-*bromo*-4,4-*dichloro*-2-*oxatricyclo*[3.2.1.$0^{3,6}$]*octane* (24). The bromohydrin (22) (0.28 g) gave, after crystallization from petroleum, the 2-*oxatricyclo-octane* (24) (0.3 g, 93%), m.p. 106—108°, $\nu_{max.}$ 1 765 cm^{-1}, δ 4.77 (1 H, ddd, *J* 1.5, 1.5, and 1.5 Hz, H-1), 4.43 (1 H, d, *J* 1.5 Hz, H-8), 3.74 (1 H, dddd, *J* 4.5, 1.5, 1.5, and 1.5 Hz, H-6), 3.25 (1 H, d, *J* 4.5 Hz, H-5), 2.6—2.5 (2 H, m, 2 × H-7), and 2.12 (3 H, s, Ac) (Found: C, 33.7; H, 2.7. $C_9H_9BrCl_2O_3$ requires C, 34.2; H, 2.85%).

7-exo-*Bromo*-2-*oxatricyclo*[3.2.1.$0^{4,6}$]*octan*-3-*one* (27).—The tautomeric mixture (25) ⇌ (26) (0.5 g) was dissolved in ether (10 ml) and shaken vigorously for 2 min with saturated aqueous potassium carbonate (20 ml). The ethereal layer was separated and the carbonate solution was washed with ether (2 × 15 ml). The combined ethereal fractions were dried ($MgSO_4$) and evaporated to give the 2-oxatricyclo-octanone (27) (0.35 g, 83%), m.p. 93—95° (lit.,[8] 89—90.5°), i.r. and n.m.r. spectra as reported.

The lactone (27) (1.2 g) was treated with zinc (1.4 g) in glacial acetic acid (4.0 ml) at 70 °C for 3 h. After cooling, ether (20 ml) was added; zinc and the precipitated zinc salts were filtered off and the filtrate was extracted with 4N-sodium hydroxide (2 × 10 ml). The alkaline extracts were combined and washed with ether (2 × 10 ml). Neutralization of the aqueous phase with 4N-sulphuric acid and extraction with ether furnished, after removal of the ether and crystallization of the residue from petroleum, bicyclo[3.1.0]hex-2-ene-6-*endo*-carboxylic acid (28) (0.4 g, 55%), m.p. 86—88°, identical (mixed m.p.) with an authentic sample.[9]

Reaction of 2,3-*Dibromo*-7,7-*dimethylbicyclo*[3.2.0]*heptan*-6-*one* (8) *with Silver Tetrafluoroborate in Methanol*.—The dibromobicycloheptanone (8) (0.6 g) and silver tetrafluoroborate (0.6 g) were stirred in boiling methanol (30 ml) for

1 h. The precipitate was filtered off and the filtrate evaporated *in vacuo*. The residue was dissolved in ether (30 ml) and washed with water (2 × 30 ml). The aqueous washes were back-extracted with ether. The combined ethereal fractions were dried ($MgSO_4$) and evaporated to give 2-*exo*-bromo-3-*endo*-methoxy-7,7-dimethylbicyclo-[3.2.0]heptan-6-one (15) (0.34 g, 68%), b.p. 70° at 0.01 mmHg, identical (t.l.c., i.r., n.m.r.) with the sample prepared above.

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