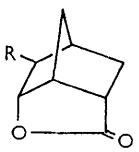
269. *Anomalous Resistance to Oxidation of Hydroxyl Groups in Some Bicyclo[2,2,1]heptane Derivatives.*

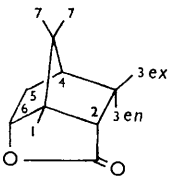
By E. Crundwell and W. Templeton.

The lactones of 5-*exo*-6-*endo*-dihydroxybicyclo[2,2,1]heptane-2-*endo*-carboxylic acid and -2,3-di-*endo*-dicarboxylic acid methyl ester have been found to be unexpectedly resistant to oxidation. Related hydroxy-esters do not show this resistance, and the lactone of 5,6-dihydroxybicyclo[2,2,2]-octane-2-carboxylic acid is readily oxidized.

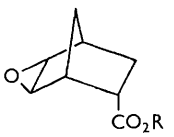
During an investigation of the synthesis of various bicyclo[2,2,1]heptane derivatives it was found that the hydroxy-lactone (I; R = OH) resisted oxidation by a variety of standard procedures. At first it was suspected that formula (I) was incorrect. The hydroxy-lactone



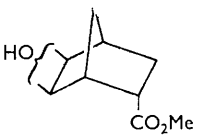
(I)



(II)



(III)



(IV)

was prepared [1] by acid treatment of the product of epoxidation of methyl bicyclo[2,2,1]-heptane-2-*endo* carboxylate with perbenzoic acid. In the related 7-oxa-series it has been reported [2] that perphthalic acid causes epimerization of an *endo*-carboxyl group, and acid conditions of epoxide opening [3] can cause rearrangement leading to a 7-hydroxy-com-compound. Treatment of bicycloheptadiene with t-butyl perbenzoate [4] or benzoyl peroxide [5] gives rise to 7-hydroxy-derivatives, and treatment with peracetic acid [6] causes extensive rearrangement leading to a bicyclo[3,1,0]hexane aldehyde. 7-Hydroxybicyclo-[2,2,1]heptane can be oxidized,[3] though the yield of ketone is poor. The resistance to oxidation would be more readily explicable if the hydroxyl group were tertiary, perhaps on a bridgehead or on a nortricyclene ring. In order to elucidate the structure, proton magnetic resonance (p.m.r.) spectra of the compounds (I; R = H, Br, or OH) were examined. The equations of Karplus [7] were used to calculate coupling constants (J) for the interactions listed in Table 1, in which protons are designated as shown in formula (II). The dihedral angles (ϕ) were estimated from a Dreiding model.

[1] Henbest and Nicholls, *J.*, 1959, 221.
[2] Kunstman, Tarbell, and Autrey, *J. Amer. Chem. Soc.*, 1962, **84**, 4115.
[3] Walborsky and Loncrini, *J. Org. Chem.*, 1957, **22**, 1117.
[4] Story, *J. Org. Chem.*, 1961, **26**, 287.
[5] Tanida and Tsuji, *Chem. and Ind.*, 1963, 211.
[6] Meinwald, Labara, and Chada, *J. Amer. Chem. Soc.*, 1963, **85**, 582.
[7] Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

TABLE 1.

Interactions of protons shown in formula (II).

Protons	ϕ	J (c./sec.)	Anticipated effect of electronegative substituent (see ref. 8)
1, 2*ex*	35°	5·4	
1, 7	60	1·8	
2*ex*, 3*ex*	10	7·9	Decrease J
2*ex*, 3*en*	110	0·8	Increase J

The identifiable peaks observed in the 60 Mc. p.m.r. spectra are listed in Table 2. Except for the peaks around $\tau = 6{\cdot}8$, which is rather low, the τ values are consistent with those found for protons in similar environments in aliphatic compounds. Moreover, the signal at $\tau = 6{\cdot}30$ in (I; R = OH) is close to that reported [8] ($\tau = 6{\cdot}42$) for the equivalent proton in *exo*-norborneol.

None of the spectra showed signals with $\tau > 8{\cdot}4$, so an unsubstituted nortricyclene cyclopropane ring ($\tau = 8{\cdot}99$) [9] is not present. The lactone oxygen cannot be attached

TABLE 2.

Proton magnetic resonance spectra of compounds (I; R = H, Br, or OH).

R in formula (I)	τ	Multiplicity: Main	Multiplicity: Subsidiary	J (c./sec.)	Assigned to proton	Coupled with protons	Remarks
H *	5·22	3	2	6, 1	6*ex*	5*ex* and 1, 5*en*	
H	6·80	3	2	5, 1	2*ex*	3*ex* and 1, 3*en*	
Br †	5·05	2	2	5·5, 1	6*ex*	1, 5*en*	
Br	6·14	2	—	2	5*en*	6*ex*	
Br	6·72	3	2	5, 1	2*ex*	3*ex* and 1, 3*en*	
OH ‡	5·57	2	2	5, 1	6*ex*	1, 5*en*	Deshielding?
OH	6·30	2	—	1—2	5*en*	6*ex*	Poorly resolved
OH	6·61	1	—		Hydroxyl		Solvent-dependent
OH	6·82	3	2	5, 1	2*ex*	3*ex* and 1, 3*en*	

* Beckman and Geiger, *Chem. Ber.*, 1961, **94**, 48. † Roberts, Trumbull, Bennett, and Armstrong, *J. Amer. Chem. Soc.*, 1950, **72**, 3116. ‡ See ref. 1.

to the 7-position in any of the compounds as the coupling constant of the proton attached to the same carbon atom is too large; it is therefore at the 6-position. The change in multiplicity (3 to 2) in the substituted lactones shows the substituent to be at either the 5-*exo*- or the 1-position. The appearance of a signal due to the proton attached to the carbon bearing the substituent shows that substitution cannot be at the tertiary 1-position or in a nortricyclene cyclopropane ring. The spectra therefore support the structures assigned but are not consistent with the alternatives considered above.

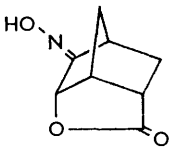
Further support for structure (I; R = OH) was obtained when the epoxy-ester (III; R = Me) [1] was hydrolysed with cold dilute alkali to give not only an acid (III; R = H) but also a large proportion of the hydroxy-lactone (I; R = OH). This easy opening of the epoxide, under conditions in which skeletal rearrangement is unlikely and epimerization probably minimal, is in contrast to the extreme resistance [10,11] of 2,3-epoxybicyclo[2,2,1]heptane to nucleophilic attack.

In order to check the behaviour of hydroxyl groups towards the oxidizing agents used, the mixture of esters (IV) was prepared by hydroboronation. This reaction is not apparently directed by a 2-substituent,[12] so that a 1 : 1 mixture of 5-*exo*- and 6-*exo*-alcohols is formed. The mixture of esters (IV) was readily oxidized in at least 65% yield to a mixture of keto-esters.

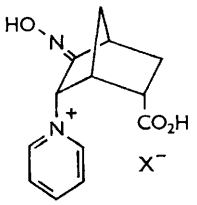
In an alternative approach to the desired keto-lactone, nitrosyl chloride was added to

[8] Williamson, *J. Amer. Chem. Soc.*, 1963, **85**, 516.
[9] Dauben and Cargill, *Tetrahedron*, 1961, **15**, 197.
[10] Meinwald and Wiley, *J. Amer. Chem. Soc.*, 1958, **80**, 3667.
[11] Kwart and Takeshita, *J. Org. Chem.*, 1963, **28**, 670.
[12] McGreer, *Canad. J. Chem.*, 1962, **40**, 1554.

bicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acid, and the product treated with pyridine, which caused slow isomerization of the nitrosyl group. From the minor (neutral) fraction, the oximino-lactone (V) was obtained. This was very difficult to hydrolyse, and the keto-lactone could not be isolated. The major (acidic) fraction was a monobasic acid, very



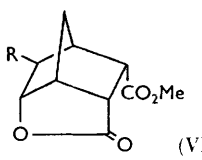
(V)



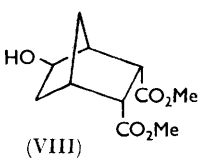
(VI)

soluble in water, with empirical formula about $C_{13}H_{15}ClN_2O_3$. With silver nitrate it gave a quantitative precipitate of silver chloride and another very water-soluble acid of empirical formula about $C_{13}H_{15}N_3O_6$. It seems likely that these compounds should be formulated as (VI; X = Cl and NO_3, respectively), and that pyridinium salts of oximes prepared in this way [13] should be re-formulated as quaternary compounds.

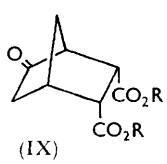
The bicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acid used in these experiments was freed from *exo*-isomer by iodolactonization [14] and reduction,[15] which generates pure endo-acid. It was esterified with diazomethane, and prolonged heating of any derivative was avoided to reduce thermal isomerization.[16] Similar procedures gave the iodo-lactone-ester (VII; R = I), which was reduced, esterified, and hydroboronated to give the hydroxy-diester (VIII). This was readily oxidized to the keto-diester (IX; R = Me), which was



(VII)



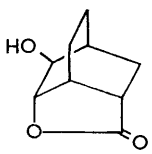
(VIII)



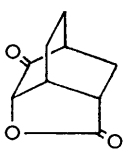
(IX)

hydrolysed to the keto-diacid (IX; R = H). The infrared absorption spectrum showed a clear peak at 1750 cm.$^{-1}$ typical of a ketone in a five-membered ring. In contrast, the hydroxy-lactone-ester [17] (VII; R = OH) was unaffected under the same conditions of oxidation.

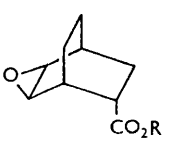
To see if this resistance to oxidation was shown by hydroxy-lactones in other bicyclic systems, bicyclo[2,2,2]oct-5-ene-2-carboxylic acid [18] was treated with peracid. The resultant hydroxy-lactone (X) was easily oxidized to the keto-lactone (XI). The epoxy-ester (XII; R = Me) was hydrolysed with cold alkali to an epoxy-acid (XII; R = H), but no lactone (X) was obtained.



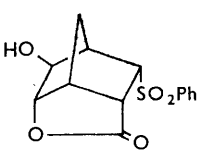
(X)



(XI)



(XII)



(XIII)

The resistance to oxidation of compounds (I; R = OH) and (VII; R = OH) is surprising. The mechanism of oxidation by chromic acid has not been fully elucidated.

[13] Gaddis and Butz, *J. Amer. Chem. Soc.*, 1947, **69**, 1203.
[14] Ver Nooy and Rondestvedt, *J. Amer. Chem. Soc.*, 1955, **77**, 3583.
[15] Berson and Ben Ephraim, *J. Amer. Chem. Soc.*, 1959, **81**, 4083.
[16] Baldwin and Roberts, *J. Amer. Chem. Soc.*, 1963, **85**, 115.
[17] Alder, Mölls, and Reeber, *Annalen*, 1958, **611**, 7.
[18] Jenkins, U.S.P. 2,797,227.

Westheimer and his co-workers [19] proposed preliminary formation of a chromate ester, and Kwart and Francis [20] have suggested that the rates of oxidation of bicycloheptanols depend on relief of strain in ester decomposition. Rocek and Krupicka [21] have proposed the direct removal of hydrogen from the secondary carbon without ester formation. Richer *et al.*[22] have observed that relief of conformational strain in the product facilitates oxidation; the easy formation of an acetate [1] (I; R = OAc) indicates that the hydroxyl group is not very hindered, so it seems likely that resistance to oxidation is related to greatly increased strain in the product. Bonincontro *et al.*[23] reported the oxidation of the hydroxy-lactone (XIII) by chromium trioxide in refluxing acetic acid. The product is clearly highly strained since lactone absorption is found at 1798 cm.$^{-1}$ and ketonic absorption at 1758 cm.$^{-1}$. These forcing conditions caused some oxidative break-down of the hydroxy-lactone (I; R = OH) but did not give a keto-lactone. Perhaps the rate of fragmentation of (XIII) is reduced by the presence of the powerfully electron-withdrawing substituent, so that isolation of the ketone is possible. It seems unlikely, however, that an electronic effect of the lactone ring accounts for the resistance to oxidation of the adjacent hydroxyl group, since the monoacetate of *p*-menthane-*trans*-2,3-diol can be oxidized with chromic acid.[24]

Experimental

P.m.r. spectra were determined, for deuterochloroform solutions, on a Varian A60 spectrometer. Infrared (i.r.) spectra were measured, for thin films unless otherwise stated, on a Perkin-Elmer 137 spectrophotometer.

Attempted Oxidation of 5-exo-6-endo-*Dihydroxybicyclo*[2,2,1]*heptane*-2-endo-*carboxylic Acid γ-Lactone.*—The hydroxy-lactone [1] was unaffected by treatment with 0·24N-chromium trioxide in acetone at room temperature for 1 hr., 0·6N-chromium trioxide in dimethylformamide at room temperature for 17 hr., 1·4N-chromium trioxide in pyridine at 0° for 17 hr., 0·27N-potassium permanganate in acetic acid at 100° for 3 hr., and 0·44N-*N*-bromosuccinimide in t-butyl alcohol at room temperature for 2 days. On treatment with 0·75N-chromium trioxide in acetic acid at room temperature for 6 days, the compound was partially converted into unidentified acidic products, but no keto-lactone was formed. From the products of treatment with 5·4N-chromium trioxide in acetic acid at 100° for 24 hr., no neutral material could be isolated.

Treatment of Methyl 5,6-exo-*Epoxybicyclo*[2,2,1]*heptane*-2-endo-*carboxylate* (III; R = Me) *with Base.*—The epoxy-ester [1] (0·9 g.) was stirred with 2N-sodium hydroxide (10 ml.) at room temperature overnight. Continuous extraction of the solution with ether gave a hydroxy-lactone (0·35 g., 43%), m. p. 155—157° (from ether), which was identified by mixed m. p. and i.r. spectrum as (I; R = OH).

The alkaline solution was acidified with 2N-sulphuric acid and subjected to continuous extraction with ether. The ether extract afforded 5,6-exo-*epoxybicyclo*[2,2,1]*heptane*-2-endo-*carboxylic acid* (III; R = H) (0·3 g., 37%), m. p. 83—84°, $\nu_{max.}$ (chloroform) 1700 and 850 cm.$^{-1}$ (Found: C, 62·35; H, 6·45. $C_8H_{10}O_3$ requires C, 62·3; H, 6·55%).

Methyl 5(6)-exo-*Hydroxybicyclo*[2,2,1]*heptane*-2-endo-*carboxylate* (IV).—Bicyclo[2,2,1]hept-5-ene-2-*endo*-carboxylic acid [14] was converted with diazomethane into its methyl ester, b. p. 80—83°/13 mm. This ester (10·8 g.) in dry tetrahydrofuran (50 ml.) was cooled in an ice-bath, stirred, and treated for 1 hr. with the diborane from sodium borohydride (1·05 g.) in dry di-2-methoxyethyl ether (200 ml.) dripped into a stirred solution of redistilled boron trifluoride etherate (7 ml.) and dry di-2-methoxyethyl ether (10 ml.). The diborane generator was then heated to ~80° for 1 hr. A slow stream of nitrogen was passed through the apparatus throughout. The tetrahydrofuran solution was allowed to stand for 1 hr., stirred, and treated with 2N-sodium hydroxide (12 ml.) (which caused evolution of gas) followed by 30% hydrogen peroxide (8 ml.). The temperature of the solution was kept between 20—40°. It was kept in

[19] Holloway, Cohen, and Westheimer, *J. Amer. Chem. Soc.*, 1951, **73**, 65.
[20] Kwart and Francis, *J. Amer. Chem. Soc.*, 1959, **81**, 2116.
[21] Rocek and Krupicka, *Coll. Czech. Chem. Comm.*, 1958, **23**, 2068.
[22] Richer, Pilato, and Eliel, *Chem. and Ind.*, 1961, 2007.
[23] Bonincontro, Maccagnani, and Montanari, *Gazzetta*, 1963, **92**, 1182.
[24] Sasaki, Ito, and Fujise, *Chem. and Ind.*, 1963, 1119.

ice for 1 hr., and then diluted with water and extracted with ether. The ether extract was washed with N-sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated *in vacuo* on a steam-bath, to give an oil (10·2 g.) which was distilled under nitrogen, the fraction of b. p. 87—89°/0·3 mm. being collected (7·8 g., 65%). A sample of the *ester* had b. p. 69—72°/0·1 mm. (Found: C, 63·5; H, 8·3. $C_9H_{14}O_3$ requires C, 63·5; H, 8·3%), $\nu_{max.}$ ~3400 and 1730 cm.$^{-1}$.

Methyl 5(6)-*Oxobicyclo*[2,2,1]*heptane*-2-endo-*carboxylate*.—The foregoing ester (7·8 g.) was dissolved in purified acetone (150 ml.) cooled in ice, stirred, and 8N-chromic acid solution [25] (35 ml.) added during 20 min. Much green solid separated. Stirring was continued for 2½ hr. The mixture was then diluted with water, extracted with ether, and the extract was washed with N-sodium hydrogen carbonate, dried (Na_2SO_4), and concentrated *in vacuo* on a steam-bath, to give an oil (5·8 g.) which was distilled under nitrogen, b. p. 64—68°/0·2 mm. (4·7 g., 61%). A sample of this *ester* had b. p. 65—66°/0·2 mm. (Found: C, 64·1; H, 7·1. $C_9H_{12}O_3$ requires C, 64·3; H, 7·2%), $\nu_{max.}$ ~1740 cm.$^{-1}$.

Addition of Nitrosyl Chloride to Bicyclo[2,2,1]*hept*-5-*ene*-2-endo-*carboxylic Acid*.—Nitrosyl chloride (25 g.) was bubbled through a solution of the acid (44 g.) in cyclohexane (500 ml.) at room temperature. The precipitated adduct, a pale green solid (65 g., 100%), subliming at 90—100°, m. p. 140—155°, $\nu_{max.}$ (Nujol) 1705, 1555, and 1230 cm.$^{-1}$, which gave a positive Beilstein test, was filtered off and dried *in vacuo*.

Treatment of the Nitrosyl Chloride Adduct with Pyridine.—The adduct (65 g.) was dissolved in absolute ethanol (500 ml.) and heated with dry pyridine (50 ml.) on a steam-bath for 5 hr. Upon being concentrated, the solution deposited a pyridinium salt (44 g., 68%), m. p. 255—260° (decomp.), very soluble in water and difficult to purify. It was shown to be an acid by its i.r. spectrum, and to contain ionic chlorine by its reaction with silver nitrate.

The ethanolic filtrate was freed from solvent, and the residue was dissolved in saturated sodium hydrogen carbonate solution and extracted continuously with ether. Evaporation of the ether extract afforded a brown oil, which was dissolved in ethyl acetate–light petroleum (b. p. 40—60°) and cooled in ice. The solution slowly deposited 6-endo-*hydroxy*-5-*hydroxy*-*iminobicyclo*[2,2,1]*heptane*-2-endo-*carboxylic acid lactone* (V) (4·6 g., 8·5%), m. p. 150—154°, $\nu_{max.}$ (chloroform) 3280, 1780, and 1170 cm.$^{-1}$ (Found: C, 57·65; H, 5·6; N, 8·2. $C_8H_9NO_3$ requires C, 57·5; H, 5·45; N, 8·4%).

Methyl 6-endo-*Hydroxy*-5-exo-*iodobicyclo*[2,2,1]*heptane*-2,3-*di*-endo-*carboxylate Lactone* (VII; R = I).—Methyl bicyclo[2,2,1]hept-5-ene-2,3-dicarboxylate [26] (75 g.) dissolved in N-sodium hydrogen carbonate (1125 ml.) was added to a solution of iodine (188 g.) and potassium iodide (375 g.) in water (1500 ml.). The mixture was set aside overnight, extracted with chloroform, and the extract was washed with 10% aqueous sodium pyrosulphite, dried (Na_2SO_4) and concentrated *in vacuo* on a steam-bath, to give an oil which solidified, m. p. 95—96° (26 g., 21%). The *lactone* crystallized from benzene–light petroleum (b. p. 60—80°) as plates, m. p. 97—98 (Found: C, 37·6; H, 3·8; I, 41·0. $C_9H_{11}IO_5$ requires C, 37·3; H, 3·4; I, 41·0%), $\nu_{max.}$ (Nujol) 1775 and 1730 cm.$^{-1}$.

Dimethyl 5-exo-*Hydroxybicyclo*[2,2,1]*heptane*-2,3-*di*-endo-*carboxylate* (VIII).—The foregoing lactone was reduced with zinc in glacial acetic acid and methylated with diazomethane, to give dimethyl bicyclo[2,2,1]hept-5-ene-2,3-di-*endo*-carboxylate, b. p. 73—75°/0·15 mm. This ester (11 g.) was treated with diborane, as described above for the hydroboration of (IV), to give a solid which was oxidized with hydrogen peroxide to give, on extraction with ethyl acetate, a viscous oil (10 g.). This was distilled under nitrogen, the fraction of b. p. 130—135°/0·2 mm. being collected (7·5 g., 63%). A sample of this *ester*, had b. p. 130°/0·15 mm. (Found: C, 57·6; H, 5·9. $C_{11}H_{16}O_5$ requires C, 57·9; H, 7·1%), $\nu_{max.}$ ~3500 and 1730 cm.$^{-1}$.

Dimethyl 5-*Oxobicyclo*[2,2,1]*heptane*-2,3-*di*-endo-*carboxylate* (IX; R = Me).—The foregoing ester (7·5 g.) was oxidized with chromic acid as described above, for the oxidation of (IV), to give, on extraction with ethyl acetate, a viscous oil (5 g.) which was distilled under nitrogen, the fraction of b. p. 115—120°/0·15 mm. being collected (3·9 g., 52%). A sample of this *ester* had b. p. 118—120°/0·15 mm. (Found: C, 58·8; H, 6·4. $C_{11}H_{14}O_5$ requires C, 54·4; H, 6·2%), $\nu_{max.}$ ~1740 cm.$^{-1}$.

5-*Oxobicyclo*[2,2,1]*heptane*-2,3-*dicarboxylic Acid* (IX; R = H).—The foregoing ester (2·9 g.) dissolved in methanol (30 ml.) was added to potassium hydroxide (3 g.) in water (20 ml.). The

[25] Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39.
[26] Walton, *J. Org. Chem.*, 1957, **22**, 308.

solution was kept at reflux for 90 min., cooled, diluted with water, washed with ethyl acetate, acidified with 2N-hydrochloric acid (50 ml.), and extracted with ethyl acetate. The extract was dried (Na_2SO_4), and concentrated *in vacuo* on a steam-bath, to give a solid (2 g.). The *acid* crystallized from a small quantity of ethyl acetate as rosettes of very small needles, m. p. 182—184° (Found: C, 54·5; H, 5·0. $C_9H_{11}O_5$ requires C, 54·5; H, 5·1%), $\nu_{max.}$ (Nujol) 1755 and 1710 cm.$^{-1}$.

5-exo-6-endo-*Dihydroxybicyclo*[2,2,2]*octane*-2-endo-*carboxylic Acid γ-Lactone* (X).—Bicyclo-[2,2,2]oct-5-ene-2-carboxylic acid [18] (2 g.) was dissolved in 90% formic acid (4 ml.). To the stirred solution, heated to 45—50°, was added dropwise 30% hydrogen peroxide (2 ml.). The mixture was stirred at 45—50° for 1 hr., cooled, made alkaline with saturated sodium hydrogen carbonate, and extracted continuously overnight with ether. Removal of the ether and crystallization of the crude solid product from ethyl acetate–light petroleum (b. p. 40—60°) gave the *hydroxy-lactone* (1·3 g., 60%), m. p. 235—237°, $\nu_{max.}$ 3400 and 1775 cm.$^{-1}$ (Found: C, 64·20; H, 7·05. $C_9H_{12}O_3$ requires C, 64·25; H, 7·2%).

Acetylation with acetic anhydride–pyridine gave the *acetoxy-lactone*, m. p. 106—108°, $\nu_{max.}$ 1775, 1700, 1240, and 1045 cm.$^{-1}$ (Found: C, 62·75; H, 6·95. $C_{11}H_{14}O_4$ requires C, 62·85; H, 6·7%).

6-endo-*Hydroxy*-5-*oxobicyclo*[2,2,2]*octane*-2-endo-*carboxylic Acid Lactone* (XI).—To a stirred solution of the hydroxy-lactone (X) (8 g.) in acetone (100 ml.) at 0° was added dropwise 8N-chromium trioxide [22] (12·5 ml.). The solution was stirred for 45 min. at 0°, made alkaline with sodium hydrogen carbonate, and continuously extracted with ether overnight. On evaporation, the extract afforded a yellow gum (5 g.), which was dissolved in benzene and chromatographed on silica gel (100 g.). Elution with 1 : 1 ether–benzene gave an oily material in 9 fractions (3·75 g.), of which fractions 4—9 (2·75 g.) had virtually identical i.r. spectra. Elution with ethyl acetate–ether gave a further 3 fractions (0·9 g.) of unidentified material.

Fractions 4—9 were combined and re-chromatographed, in benzene, on neutral alumina, activity 3 (80 g.). Elution with 9 : 1 benzene–ether gave the *keto-lactone* (0·75 g., 10%), m. p. 213—215° (from ether), $\nu_{max.}$ 1780 and 1770 cm.$^{-1}$ (Found: C, 64·8; H, 6·3. $C_9H_{10}O_3$ requires C, 65·05; H, 6·05%). Further elution with benzene–ether gave unchanged starting material (0·4 g.), m. p. 227—228° (from ether).

Methyl 5,6-exo-*epoxybicyclo*[2,2,2]*octane*-2-endo-*carboxylate* (XII; R = Me).—A solution of bicyclo[2,2,2]oct-5-ene-2-carboxylic acid [18] (6 g.) in dry methanol (75 ml.) was refluxed with concentrated sulphuric acid (5 ml.) for 1 hr. The solution was diluted with water and extracted with ether. The ether extract afforded, on evaporation, a methyl ester, which was used without purification.

The methyl ester was treated with 0·715M-monoperphthalic acid in ether (65 ml.) for 5 days at room temperature. The ether solution was washed with sodium hydrogen carbonate solution and water, dried (Na_2SO_4) and evaporated. The residue (4·7 g.) was distilled *in vacuo*. Five fractions were taken: (i) b. p. 135—137°/19 mm., n_D^{18} 1·4857 (0·9 g.); (ii) b. p. 137—139°/19 mm., n_D^{18} 1·4901 (1 g.); (iii) b. p. 139—140°/19 mm., n_D^{18} 1·4907 (1·1 g.); (iv) b. p. 140—141°/19 mm., n_D^{18} 1·4908 (1·1 g.); (v) b. p. 141—145°/19 mm., n_D^{18} 1·4916 (0·3 g.). A portion of fraction (iv) was dried and redistilled, giving the *epoxy-ester*, b. p. 140—141°/19 mm., n_D^{18} 1·4908 (Found: C, 65·3; H, 7·8. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·75%), $\nu_{max.}$ 1725, 1200, and 860 cm.$^{-1}$.

5,6-exo-*Epoxybicyclo*[2,2,2]*octane*-2-endo-*carboxylic Acid* (XII; R = H).—The epoxy-ester (XII; R = Me) (2·5 g.) was stirred with 2N-sodium hydroxide at room temperature overnight. Extraction with ether gave no neutral product. The alkaline solution was acidified with ice-cold 2N-sulphuric acid and continuously extracted with ether for 17 hr. Evaporation of the ether and crystallization of the residue from acetone–cyclohexane gave the *epoxy-acid* (2 g., 87%) as white needles, m. p. 129—131°, $\nu_{max.}$ 1700, 1250, and 845 cm.$^{-1}$ (Found: C, 64·2; H, 7·05. $C_9H_{12}O_3$ requires C, 64·25; H, 7·2%).

We are grateful to Professor R. C. Cookson for helpful comment, and to Cynthia E. Coleman for much technical assistance.

Miles-Ames Research Laboratories, Stoke Court,
Stoke Poges, Buckinghamshire.

[*Received, August 13th,* 1963.]