

Robinson Annulation of 2-Hydroxymethylene-ketones. A New Route to Spiro-diketones

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The adducts formed from methyl vinyl ketone and the 2-hydroxymethylene derivatives of cyclic ketones of ring sizes 5, 6, 7, and 12 have been cyclised to spiro-ketones containing the same number of carbon atoms. Cyclisation under mild conditions gives ketols, the constitution and stereochemistry of which have been investigated. Methanol containing anhydrous calcium chloride converts the adducts of ring sizes 7 and 12 into spiro-ethers: the C₆ adduct gives differently constituted products. The spiro-ketones all have a u.v. absorption band at ca. 224 nm (ϵ ca. 6500) but a second band of approximately the same intensity appears at 246 nm for ring sizes 5 and 12.

It has been reported¹ that the initial adduct (1; R = CHO) from 2-hydroxymethylenecyclohexanone and methyl vinyl ketone, when treated with a catalytic amount of toluene-*p*-sulphonic acid in hot benzene, gave a mixture of products from which was obtained a bright yellow bis-2,4-dinitrophenylhydrazone, which, on the basis of elemental analysis and u.v. absorption [λ_{\max} . (CHCl₃) 360 nm (ϵ 29,880)] was formulated as the bis-2,4-dinitrophenylhydrazone of the aldehyde (2); Prelog² obtained similarly constituted products from cyclisation in acid of compounds similar to (1). The only unexplained feature for the compound was a distinct shoulder on the long-wavelength side of the maximum (λ ca. 393 nm; ϵ ca. 20,000).

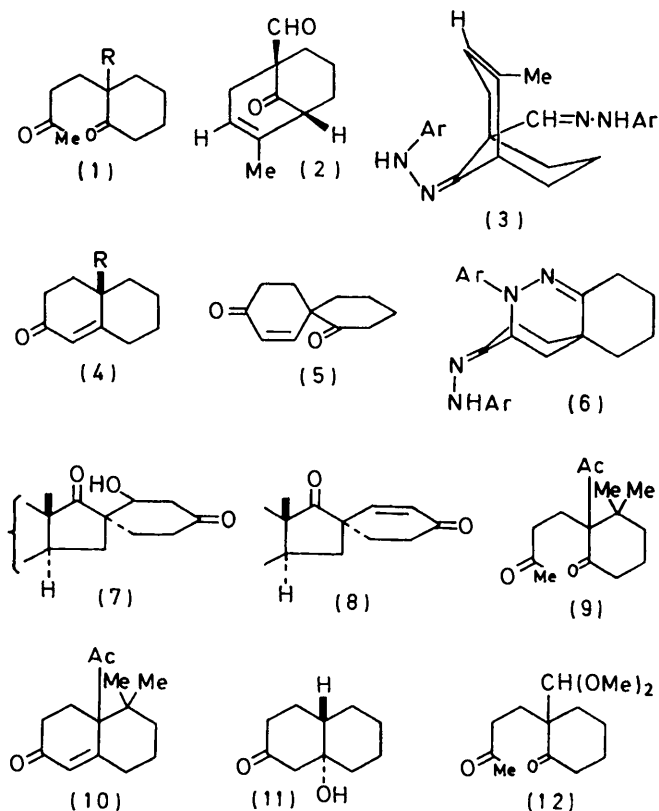
It was felt that the geometry of the system (2) might be responsible for this, as the 2,4-dinitrophenyl system attached at the ketone carbon atom could approach the double bond quite closely in conformation (3) and give rise to what are normally forbidden electron transitions.^{3,4} We have reinvestigated the structure of this compound as, since the original investigation, n.m.r. spectroscopy had become available to us.

Compound (1; R = CHO) was best prepared by stirring 2-hydroxymethylenecyclohexanone with methyl vinyl ketone at room temperature in the presence of catalytic quantities of hydroquinone and potassium hydroxide. Heating the compound with toluene-*p*-sulphonic acid in benzene or, better, slow distillation from a little potassium hydroxide gave a mixture readily separated by preparative g.l.c. into starting material (1; R = CHO), compounds (1; R = H) and (4; R = H), and the spiro-ketone (5) (the major component). The evidence for structure (5) was the presence in its n.m.r. spectrum of a doublet (1H) at τ 2.92 and a second doublet (1H) at τ 3.96 with the same coupling constant (9.6 Hz). The i.r. spectrum showed the presence of two carbonyl groups (ν_{\max} . 1704 and 1680 cm⁻¹). On cautious treatment the compound gave an orange-red mono-2,4-dinitrophenylhydrazone (λ_{\max} . 372 nm; ϵ 27,200) by reaction at the $\alpha\beta$ -unsaturated carbonyl function (the derivative possessed a band at 1712 cm⁻¹); the two olefinic protons gave coincident signals in the n.m.r. spectrum at τ 3.53. Further

¹ D. J. Baisted and J. S. Whitehurst, *J. Chem. Soc.*, 1961, 4089.

² (a) V. Prelog, M. M. Wirth, and L. Ruzicka, *Helv. Chim. Acta*, 1946, **29**, 1425; (b) V. Prelog, L. Ruzicka, P. Barman, and L. Frenkiel, *ibid.*, 1948, **31**, 92; (c) V. Prelog, P. Barman, and M. Zimmermann, *ibid.*, 1949, **32**, 1284.

treatment of this compound with 2,4-dinitrophenylhydrazine gave the same bis-derivative as that obtained previously. The earlier formulation must therefore give



way to one based on the isomeric structure (5). However, the compound was not a simple bis-2,4-dinitrophenylhydrazone. The n.m.r. spectrum had a triplet at τ 5.63 (*J* 4.5 Hz) but lacked olefinic proton signals, and at low field (τ -0.95) there was only one NH signal. The evidence is accommodated if the compound is formulated as the pyridazine (6). The alternative pyrazole structure formed by cyclisation at the β -carbon atom of the $\alpha\beta$ -unsaturated carbonyl system is not in accord with the n.m.r. evidence: the aforementioned triplet would be expected at τ ca. 7; also such a molecule is much less likely on steric grounds.

The use of 2-hydroxymethylene ketones in the

³ H. Labhart and G. Wagniere, *Helv. Chim. Acta*, 1959, **42**, 2219.

⁴ R. C. Cookson and N. Lewin, *Chem. and Ind.*, 1956, 984; R. C. Cookson and N. S. Wariyar, *J. Chem. Soc.*, 1956, 2302.

Robinson annulation is due to Wilds.⁵ Essentially, the formyl group is introduced to activate a methylene group α to a carbonyl group in the cyclic ketone, and is lost during the subsequent cyclisation. Similar loss of CHO is encountered in the alkylation of 2-hydroxymethylene ketones.⁶ However, Petrow and his associates, in work published during the course of the present work,⁷ obtained compounds of types (7) and (8) as minor products in the Robinson annulation of some 16-hydroxymethylene-17-oxo-steroids. Also Büchi, Jeger, and Ruzicka⁸ have reported the retention of an acetyl group in the cyclisation of compound (9) which yielded the octalone (10).

When the adduct (1; R = CHO) was treated with diethylamine or adsorbed on alumina in order to obtain the ketol intermediary to (5), the products were compound (1; R = H) and the known^{9,10} *trans*-ketol (11). When compound (1; R = CHO) in methanol was treated with anhydrous calcium chloride in the reasonable hope of obtaining protection at the aldehyde function as in structure (12) it gave two compounds, a solid, m.p. 96–97°, and an oil. The solid, C₁₂H₂₀O₄, showed hydroxy- (ν_{\max} . 3420 cm⁻¹) but no carbonyl absorption. The n.m.r. spectrum showed a singlet at τ 5.19 (O·CH·O), a three-proton singlet at 6.58 (OMe), a singlet at 7.41 (OH, exchangeable with D₂O), and a singlet at τ 8.63 (tertiary Me). These data agree with structure (13). The other compound, C₁₃H₂₂O₄, lacked both hydroxy- and carbonyl functions; the n.m.r. spectrum showed signals at τ 5.34 (1H, s, O·CH·O), 6.69 (3H, s, OMe), 6.85 (3H, s, OMe), and 8.78 (3H, s, tertiary Me). There was no change in the spectrum on addition of D₂O. This compound is formulated as (14). Both compounds (13) and (14) slowly reverted to the starting material (1; R = CHO).

2-Formylcyclopentanone is the least accessible in the series of 2-formyl cyclic ketones; the yield from cyclopentanone and ethyl formate is only about 10%.¹¹ We obtained a slight improvement (*ca.* 20% overall) in a two-step procedure using a Vilsmeier–Haack reaction¹² between 1-ethoxycyclopentene¹³ and phosphoryl chloride–dimethylformamide. The adduct of 2-formylcyclopentanone with methyl vinyl ketone (15; $n = 5$) on slow distillation from potassium hydroxide gave unchanged material (15; $n = 5$) and compounds [(16)–(18); $n = 5$]. The mixture of (15) and (16) was readily separable from that of (17) and (18) by distillation, and the latter two were separated by preparative g.l.c. Compound (15; $n = 7$), when treated similarly gave the corresponding compounds (15), (16), and (18) (all cleanly separated from each other), but none of compound (17; $n = 7$).

Toluene-*p*-sulphonic acid in refluxing benzene con-

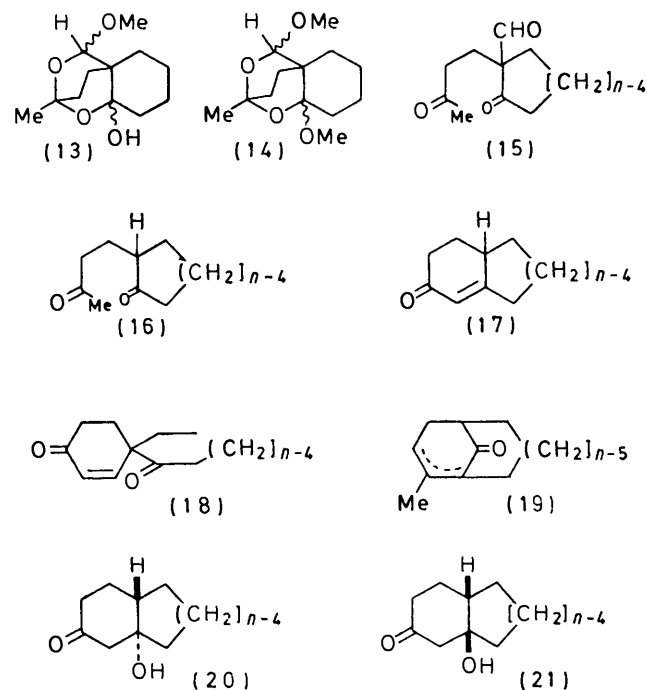
⁵ C. H. Shunk and A. L. Wilds, *J. Amer. Chem. Soc.*, 1949, **71**, 394.

⁶ A. L. Wilds and C. Djerassi, *J. Amer. Chem. Soc.*, 1946, **68**, 1715; R. Robinson and J. Walker, *J. Chem. Soc.*, 1935, 1530; H. K. Sen and K. Mondal, *J. Indian Chem. Soc.*, 1928, **5**, 609.

⁷ J. M. Allison, D. Burn, F. K. Butcher, M. T. Davies, and V. Petrow, *Tetrahedron*, 1967, **23**, 1515.

verted the compounds (15; $n = 5$ or 7) into compounds (17; $n = 5$ or 7) in greater than 90% yield. With this reagent 2-formyl-2-(3-oxobutyl)cyclododecanone (15; $n = 12$) gave directly, without chromatography, the spiro-ketone (18; $n = 12$) in 30% yield. The mother liquors from the crystallisation of (18; $n = 12$) certainly contained the compound (17; $n = 12$) but no attempt was made to secure it in pure form as this compound was the sole isolated product of the action of sodium methoxide in benzene on the formyl ketone (15; $n = 12$). None of these experiments furnished the structurally isomeric compounds (19), which were obtained by Prelog² from the ethoxy-carbonyl analogues of (15), albeit under more drastic conditions.

The spiro-ketone (18; $n = 5$), unlike the six-membered analogue, gave a normal red bis-2,4-dinitrophenylhydrazone. By contrast, the analogous compounds (18; $n = 7$ and 12) gave mono-2,4-dinitrophenylhydrazones by reaction at their $\alpha\beta$ -unsaturated carbonyl functions. The spiro-ketones (18; $n = 5$ or 12) had virtually identical u.v. absorption spectra, λ_{\max} . 222 (ϵ *ca.* 6000) and 246 nm (*ca.* 5200). The spiro-ketones (18; $n = 6$ or 7) possessed only the low wavelength band (λ_{\max} .



226 nm; ϵ *ca.* 7700). This low wavelength band is that of the normal $\pi \rightarrow \pi^*$ transition of the $\alpha\beta$ -unsaturated carbonyl system; the higher wavelength

⁸ G. Büchi, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, 1948, **31**, 241.

⁹ W. S. Johnson, J. J. Korst, R. A. Clement, and J. Dutta, *J. Amer. Chem. Soc.*, 1960, **82**, 614.

¹⁰ J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, 1964, **29**, 2501.

¹¹ W. S. Johnson and W. E. Shelberg, *J. Amer. Chem. Soc.*, 1945, **67**, 1745 and earlier references.

¹² A. Vilsmeier and A. Haack, *Ber.*, 1927, **60**, 119.

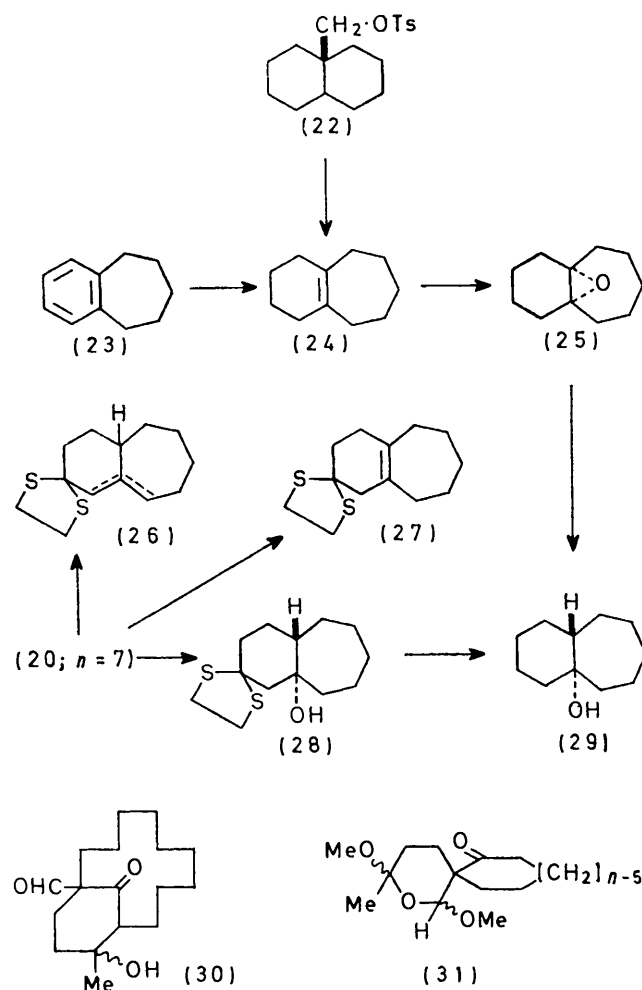
¹³ U. Schmidt and P. Grafen, *Annalen*, 1962, **656**, 97.

band presumably corresponds to electron transfer from the C=C π -bond to the π^* of the saturated carbonyl function (these compounds are not only $\alpha\beta$ - but also $\beta\gamma$ -unsaturated ketones). A check on the u.v. evidence was provided by conversion of the spiro-ketones into their monosemicarbazones and regeneration of the ketones in very pure form from these by hydrolysis with aqueous pyruvic acid under very mild conditions. The low value for the extinction coefficients for the 222—226 nm band was a feature of the presence of the saturated carbonyl group. When the spiro-ketone (18; $n = 12$) was converted into its mono-ethylenethioacetal (reaction at the $\alpha\beta$ -unsaturated carbonyl function), the latter then reduced with lithium aluminium hydride, and the ethylenethioacetal function hydrolysed with mercuric chloride, the alcohol produced (18; $n = 12$, CHO instead of the saturated CO) had an extinction coefficient of 12,000 (λ_{max} , 230 nm).

The compounds (15; $n = 5, 7$, or 12) were separately dissolved in dry ether and the solutions applied to columns of chromatographic alumina. After specified times the products were eluted with more ether. By proper choice of conditions all these compounds could be deformylated cleanly, without any concurrent cyclisations, to compounds (16), always in high and sometimes in quantitative yields. When more active alumina and longer adsorption times were used, further changes occurred. Compound (15; $n = 5$) gave a little of compound (17; $n = 5$); despite a rigorous search no intermediary ketols were detected. The seven-membered analogue (15; $n = 7$) gave a ketol, $\text{C}_{11}\text{H}_{18}\text{O}_2$, the n.m.r. spectrum of which pointed to its being either the *trans*- or the *cis*-compound [(20) or (21)]. The correct structure was found to be (20); proof was provided as follows.

The starting material was bicyclo[5.4.0]undec-1(7)-ene (24). This has been prepared¹⁴ by solvolysis of the *cis*- and *trans*-forms of 9-decalylmethyl toluene-*p*-sulphonate (22) but in view of the fact that some 20% of other isomeric hydrocarbons was present in the product we decided to obtain the compound from tetrahydrobenzocycloheptene^{14,15} (23). Reduction of the latter with lithium in 1,2-diaminoethane¹⁶ gave bicyclo[5.4.0]undec-1(7)-ene (24) in 82% yield (96% purity by g.l.c.), identical with a specimen kindly provided by Professor Dauben. Epoxidation with *m*-chloroperbenzoic acid followed by reduction of the product (25) with lithium aluminium hydride gave the strongly camphor-smelling alcohol (29), m.p. 39°, the stereochemistry of which follows from the known *trans*-ring opening of epoxides with lithium aluminium hydride. The ketol (20; $n = 7$), obtained from (15; $n = 7$), when treated with ethane-1,2-dithiol in dioxan containing zinc chloride and anhydrous sodium sulphate,¹⁷ gave the thioacetal (28). Two previous attempts at this reaction by use of boron

trifluoride-ether complex in acetic acid¹⁸ or neat ethane-1,2-dithiol (solvent and reactant) gave compounds (26) and



(27), respectively. Desulphurisation of compound (28) with Raney nickel gave the alcohol (29), identical with the product prepared by the previous route. Plattner¹⁵ prepared an alcohol, m.p. 30—31°, of constitution (29) but of unknown stereochemistry by oxidation of the dihydro-derivative of (24); since the *cis*-alcohol, m.p. 107° corresponding to (29) is also known¹⁹ it seems likely that Plattner's product was slightly impure *trans*-alcohol (29).

When compound (17; $n = 7$) was subjected sequentially to the reagents sodium borohydride, *m*-chloroperbenzoic acid, lithium aluminium hydride, and finally chromium trioxide-pyridine, two alcohols (ratio 70:30) were produced. The major product, m.p. 118—119° was identical with authentic *trans*-ketol (20; $n = 7$); the minor compound therefore is its *cis*-isomer (21; $n = 7$). The intermediates in the foregoing sequence were not characterised but they did appear to be chromatographically homogeneous. The loss in

¹⁴ W. G. Dauben and J. B. Rogan, *J. Amer. Chem. Soc.*, 1957, **79**, 5002.

¹⁵ Pl. A. Plattner, *Helv. Chim. Acta*, 1944, **27**, 801.

¹⁶ L. Reggel, R. A. Friedel, and I. Wender, *J. Org. Chem.*, 1957, **22**, 891.

¹⁷ J. Romo and A. Romo de Vivar, *J. Amer. Chem. Soc.*, 1959, **81**, 3446.

¹⁸ L. F. Fieser, *J. Amer. Chem. Soc.*, 1954, **76**, 1945.

¹⁹ J.-M. Bessière and H. Christol, *Bull. Soc. chim. France*, 1969, 4063.

stereoselectivity in this sequence presumably occurred in the borohydride reduction, as the epoxidation of an allylic alcohol is normally fairly stereoselective.²⁰ Marshall⁹ obtained even less stereoselectivity in a similar study of the six-membered analogue (17; $n = 6$).

Adsorption on alumina simply deformylated compound (15; $n = 12$). However, when the compound was stirred with diethylamine for 3 h two products were obtained. The minor one was the spiro-ketone (18; $n = 12$); the major product showed i.r. hydroxy-absorption and two carbonyl bands; the n.m.r. spectrum showed the presence of an aldehyde and a tertiary methyl group. The evidence leads to formula (30). This compound was also formed with extreme ease but somewhat unpredictably during the preparation of the adduct (15) from 2-hydroxymethylenecyclododecanone and methyl vinyl ketone. As far as we are aware the formation of this compound represents the first instance of the retention of a formyl group in the cyclisation of a Robinson-type adduct. Dehydration with phosphoryl chloride-pyridine gave an $\alpha\beta$ -unsaturated ketone corresponding to formula (30). However, with sodium methoxide in benzene dehydration took a different course and produced (83%) compound (17; $n = 12$).

2-Formyl-2-(3-oxobutyl)cycloheptanone (15; $n = 7$) reacted readily at room temperature with methanol containing calcium chloride. The product (ca. 70% yield) was a liquid, $C_{14}H_{24}O_4$, whose i.r. spectrum showed the presence of the cycloheptanone carbonyl group (1697 cm^{-1}) and the absence of a hydroxy-group. The n.m.r. spectrum had signals at τ 5.46 (1H, s, O-CH-O), 6.62 and 6.76 (both OMe), and 8.71 (tertiary Me). This evidence leads to formula (31; $n = 7$). 2-Formyl-2-(3-oxobutyl)cyclododecanone (15; $n = 12$) underwent a similar but more sluggish reaction and gave an analogous compound (31; $n = 12$) [ν_{CO} 1692 cm^{-1} (no OH), τ 5.57 (O-CH-O), 6.57 (OMe), 6.84 (OMe), and 8.82 (tertiary Me)]. Clearly, the six-membered compound in the series (15; $n = 6, 7$, or 12) is differentiated from the other members in this reaction, which may prove to be general.

EXPERIMENTAL

All evaporations were carried out under reduced pressure. Silica gel GF 254 (Merck) was used for t.l.c. and p.l.c. G.l.c. was carried out on a Varian Acrograph Autoprep model A-700 [$\frac{3}{8} \times 20$ in aluminium column packed with 30% SE 30 on 45–60 mesh Chromosorb W; helium (occasionally nitrogen) as carrier gas]. U.v. spectra refer to solutions in 95% ethanol. 'Work-up' signifies the successive operations of (a) extraction with ether, (b) washing the extract with water, (c) drying it with anhydrous magnesium sulphate, and (d) evaporation of solvent. All compounds are racemic.

The 2-hydroxymethylene ketones were all known compounds and were made by literature methods.^{10,21-24} 2-Hydroxymethylenecyclopentanone was made from cyclo-

pentanone and ethyl formate¹⁰ as well as by the following method. A solution of freshly distilled phosphoryl chloride (11.25 g) in 1,2-dichloroethane (20 cm^3) was added to a stirred solution of anhydrous dimethylformamide (10 g) in the same solvent (20 cm^3) kept at -40° . After 15 min 1-ethoxycyclopentene (7.5 g) in 1,2-dichloroethane (20 cm^3) was added in one portion; the yellow solution became deep red and after a further 2 h was allowed to reach room temperature. Ice (200 g) was added and after thorough mixing the organic layer was discarded. Concentrated hydrochloric acid (50 cm^3) was added to the aqueous phase, which was then continuously extracted with ether. The extract was dried and evaporated; the crude 2-hydroxymethylenecyclopentanone (2.2 g), m.p. 70–71°, was collected and crystallised from light petroleum (b.p. 40–60°) to give needles, m.p. 78°.

The 2-formyl-2-(3-oxobutyl) derivatives (15; $n = 5, 6, 7$, or 12) were prepared by a general method as follows. The hydroxymethylene ketone (0.1 mol), methyl vinyl ketone (20 cm^3), a trace of hydroquinone, and potassium hydroxide (0.25 g) were stirred at room temperature under nitrogen for 5 h; a few drops of concentrated hydrochloric acid were added and the unchanged methyl vinyl ketone was distilled off at room temperature (ca. 15 \rightarrow 0.1 mmHg).

2-Formyl-2-(3-oxobutyl)cyclopentanone was distilled from the residue, b.p. 108° at 0.05 mmHg (72%), ν_{max} (film) 1715 cm^{-1} , τ (CCl_4) 0.66 (1H, s, CHO), and 7.92 (3H, s, COMe) (Found: C, 66.15; H, 7.2. $C_{10}H_{14}O_3$ requires C, 65.9; H, 7.75%); 2-formyl-2-(3-oxobutyl)cyclohexanone¹ distilled at 112° and 0.05 mmHg (68%), ν_{max} (film) 1715 and 1705 cm^{-1} , τ (CCl_4) 0.37 (1H, s, CHO) and 7.81 (3H, s, COMe) (Found: C, 67.1; H, 8.4. Calc. for $C_{11}H_{16}O_3$: C, 67.3; H, 8.2%); 2-formyl-2-(3-oxobutyl)cycloheptanone distilled at 119–120° and 0.04 mmHg (60%), ν_{max} (film) 1716 and 1696 cm^{-1} , τ ($CDCl_3$) 0.14 (1H, s, CHO) and 7.86 (3H, s, COMe) (Found: C, 68.75; H, 8.55. $C_{12}H_{18}O_3$ requires C, 68.55; H, 8.65%); 2-formyl-2-(3-oxobutyl)cyclododecanone was isolated as for the previous compound and purified by crystallisation from light petroleum [(b.p. 60–80°)], m.p. 88–89° (58%), ν_{max} (Nujol) 1713, 1705, and 1695 cm^{-1} , τ ($CDCl_3$) 0.14 (1H, s, CHO) and 7.89 (3H, s, COMe) (Found: C, 73.4; H, 10.05. $C_{17}H_{26}O_3$ requires C, 72.8; H, 10.05%).

Preparation of the Spiro-ketones (18; $n = 5, 6$, or 7).—A mixture of the 2-formyl-2-(3-oxobutyl) cyclic ketone (0.07 mol) and potassium hydroxide (0.8 g) was slowly distilled (thermometer in the vapour ca. 140–170° at pressures ca. 0.5–1.0 mmHg). The early fractions consisted of mixtures of starting materials and deformylation products (16) which could be separated if desired by p.l.c. The later fractions were preparatively gas chromatographed; the spiro-ketones had the highest retention times in every case.

Cyclohex-2-enespirocyclopentane-2',4-dione was a pale yellow liquid, b.p. 108° at 0.12 mmHg (21%), ν_{max} (film) 1738 and 1678 cm^{-1} , λ_{max} 222 (ϵ 6000) and 247 nm (5550), τ (CCl_4) 3.48 (1H, d, J 10.25 Hz) and 4.09 (1H, d, J 10.25 Hz) (CH=CH) (Found: C, 72.7; H, 7.5. $C_{10}H_{12}O_2$ requires C, 73.15; H, 7.35%). The *bis-2,4-dinitrophenylhydrazones* had m.p. 225° (red needles from ethanol-chloroform), λ_{max} ($CHCl_3$) 370 nm (ϵ 41,900) (Found: C, 50.4; H, 4.2; N, 21.1. $C_{22}H_{20}N_8O_8$ requires C, 50.4; H, 3.85; N, 21.35%).

²² V. Prelog, L. Ruzicka, and O. Metzler, *Helv. Chim. Acta*, 1947, **30**, 1883.

²³ W. Treibs and H. J. Neupert, *Annalen*, 1955, **595**, 219.

²⁴ L. I. Zakharin and V. V. Korneva, *Izvest. Akad. Nauk S.S.S.R., Ser. khim.*, 1964, **12**, 2206 (*Chem. Abs.*, 1965, **62**, 7654).

²⁰ H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1957, 1958; H. B. Henbest and J. McEntee, *ibid.*, 1961, 4478.

²¹ Pl. A. Plattner, P. Treadwell, and C. Shalz, *Helv. Chim. Acta*, 1945, **28**, 771.

Reduction of the spiro-ketone in 95% ethanol with hydrogen and 5% palladium-calcium carbonate gave cyclohexanespirocyclohexane-2',4'-dione, whose 2,4-dinitrophenylhydrazone had m.p. 214° (yellow needles from chloroform-ethyl acetate), λ_{\max} (CHCl₃) 365 nm (ϵ 49,210) (Found: C, 50.05; H, 4.2; N, 21.3. C₂₂H₂₂N₈O₈ requires C, 50.2; H, 4.2; N, 21.3%).

Cyclohex-2-enespirocyclohexane-2',4'-dione (a pale yellow liquid) had b.p. 92–94° at 0.015 mmHg (35%), ν_{\max} (film) 1704 and 1680 cm⁻¹, λ_{\max} 226 nm (ϵ 7740), τ (CCl₄) 2.92 (1H, d, *J* 9.5 Hz) and 3.96 (1H, d, *J* 9.5 Hz) (Found: C, 74.25; H, 7.7. C₁₁H₁₄O₂ requires C, 74.15; H, 7.9%). The mono-2,4-dinitrophenylhydrazone formed red needles from ethyl acetate, m.p. 177°, ν_{\max} (KBr) 1712 cm⁻¹, λ_{\max} (EtOH) 372 nm (ϵ 27,200), τ (CDCl₃) 3.53br (2H, s) (Found: C, 57.25; H, 5.15; N, 15.7. C₁₇H₁₈N₄O₅ requires C, 57.0; H, 5.05; N, 15.65%). The monosemicarbazone (needles from benzene-methanol) had m.p. 216° (Found: C, 61.35; H, 7.3. C₁₂H₁₇N₃O₂ requires C, 61.25; H, 7.3%). Treatment of the 2,4-dinitrophenylhydrazone with 1 mol. equiv. of 2,4-dinitrophenylhydrazine in dimethylformamide gave 8-(2,4-dinitrophenyl)-7,8-diazatricyclo[7.3.1.0^{4,6}]-tridec-6-en-10-one 2,4-dinitrophenylhydrazone (6), yellow plates and prisms from ethyl acetate, m.p. ca. 252° (decomp.), λ_{\max} (EtOH) 360 nm (ϵ 29,500), τ (CDCl₃; accumulated spectrum) -0.95br (1H, s, NH), and 5.63 (1H, t, *J* 4.5 Hz, CH) (Found: C, 50.95; H, 4.25. Calc. for C₂₃H₂₂N₈O₈: C, 51.3; H, 4.1%).

Cyclohex-2-enespirocyclohexane-2',4'-dione gave on catalytic reduction cyclohexanespirocyclohexane-2',4'-dione, b.p. 96° at 0.01 mmHg (86%), ν_{\max} (film) 1703br cm⁻¹ (Found: C, 73.1; H, 8.75. C₁₁H₁₆O₂ requires C, 73.3; H, 8.95%). The bis-2,4-dinitrophenylhydrazone crystallised from chloroform-methanol in yellow plates, m.p. 180–183° (Found: C, 51.4; H, 4.65; N, 20.3. C₂₃H₂₄N₈O₈ requires C, 51.05; H, 4.45; N, 20.7%).

Cycloheptanespirocyclohex-2'-ene-2,4'-dione was obtained as a liquid, b.p. 122° at 0.13 mmHg (40%), ν_{\max} (film) 1697 and 1677 cm⁻¹, λ_{\max} 227 nm (ϵ 7620), τ (CCl₄) 3.22 (1H, d, *J* 11 Hz) and 4.04 (1H, d, *J* 11 Hz). The mono-2,4-dinitrophenylhydrazone formed red needles from ethanol-chloroform, m.p. 161°, ν_{\max} (Nujol) 1697 cm⁻¹, λ_{\max} (CHCl₃) 378 nm (ϵ 29,620) (Found: C, 57.75; H, 5.4; N, 14.7. C₁₈H₂₀N₄O₅ requires C, 58.05; H, 5.4; N, 15.05%). The monosemicarbazone, needles from methanol, had m.p. 203°, ν_{\max} 1687 cm⁻¹, λ_{\max} 270 nm (ϵ 20,500) (Found: C, 62.55; H, 7.86; N, 16.35. C₁₃H₁₉N₃O₂ requires C, 62.6; H, 7.7; N, 16.85%).

Catalytic hydrogenation of the foregoing spiroketone gave cycloheptanespirocyclohexane-2,4'-dione, crystals (95%) from ether, m.p. 37–38°, ν_{\max} 1722 and 1704 cm⁻¹ (Found: C, 74.55; H, 9.3. C₁₂H₁₈O₂ requires C, 74.2; H, 9.35%).

Cyclododecanespirocyclohex-2'-ene-2,4'-dione (18; *n* = 12).—2-Formyl-2-(3-oxobutyl)cyclododecanone (5.6 g) in sodium-dried benzene (100 cm³) was refluxed with toluene-*p*-sulphonic acid (1.0 g) under a water separator until the theoretical amount of water (0.36 cm³) had been collected. The solution was washed with water, dried (MgSO₄), and concentrated. The crystalline residue was recrystallised from light petroleum (b.p. 60–80°) to give the spiro-dione (1.6 g, 30%), m.p. 105°, ν_{\max} (Nujol) 1690br cm⁻¹, λ_{\max} 221 (ϵ 6230) and 246 nm (5120), τ (CDCl₃) 2.88 (1H, d, *J* 10 Hz) and 4.03 (1H, d, *J* 10 Hz) (Found: C, 77.55; H, 10.45. C₁₇H₂₆O₂ requires C, 77.8; H, 10.0%). The spiro-dione gave a red mono-2,4-dinitrophenylhydrazone, m.p. 174°

(ethanol), ν_{\max} (Nujol) 1700 cm⁻¹, λ_{\max} (CHCl₃) 380 nm (ϵ 28,600) (Found: C, 63.1; H, 7.1; N, 12.8. C₂₃H₃₀N₄O₅ requires C, 62.4; H, 6.85; N, 12.65%). The monosemicarbazone had m.p. 228° (methanol), ν_{\max} (Nujol) 1688br cm⁻¹, λ_{\max} 272 nm (ϵ 21,850) (Found: C, 67.65; H, 9.35; N, 12.95. C₁₈H₂₉N₃O₂ requires C, 67.65; H, 9.15; N, 13.15%).

Catalytic reduction of the spiro-ketone gave cyclo-dodecanespirocyclohexane-2,4'-dione, needles from light petroleum (b.p. 60–80°), m.p. 100°, ν_{\max} (Nujol) 1710 cm⁻¹ (Found: C, 78.0; H, 10.85. C₁₇H₂₈O₂ requires C, 77.2; H, 10.65%).

General Method of Hydrolysis of the Semicarbazones.—The semicarbazone (0.2 g) in glacial acetic acid (4 cm³), pyruvic acid (2 cm³), and water (2 cm³) was stirred at room temperature for 24 h. Work-up gave, in general, a 90% yield of the spiro-ketone.

2-Hydroxycyclododecanespirocyclohex-2'-en-4'-one (18; *n* = 12, CHOH instead of saturated CO).—To a stirred solution of the spiro-dione (18; *n* = 12) (660 mg) in glacial acetic acid (5 cm³) at room temperature was added a solution of ethanedithiol (290 mg) in glacial acetic acid (1 cm³) followed by freshly distilled boron trifluoride-ether complex (2 cm³). After 4 h the solid was collected and purified by p.l.c. (benzene-ether). The thioacetal (370 mg, 44%) had m.p. 145° (from methanol), ν_{\max} (Nujol) 1700 cm⁻¹, τ (CDCl₃) 4.11br (2H, s, CH=CH) and 6.65 (4H, s, S-CH₂-CH₂-S) (Found: C, 67.6; H, 9.55. C₁₉H₃₀OS₂ requires C, 67.45; H, 8.95%).

A stirred slurry of lithium aluminium hydride (32 mg) in dry ether (7 cm³) was kept at 4°. To it a solution of the preceding thioacetal (300 mg) in dry tetrahydrofuran (3 cm³) was added. After 4 h dilute hydrochloric acid was added. Work-up gave a crystalline solid (285 mg) which was purified by p.l.c. (benzene-ether). The alcohol (170 mg, 55%) had m.p. 159° (methanol), ν_{\max} (Nujol) 3475 cm⁻¹, τ (CDCl₃) 3.94 (1H, dd, *J* 10.5 and 4.5 Hz) and 4.49 (1H, complex doublet, *J* 10.5 Hz, CH=CH), and 6.64 (4H, s, S-CH₂-CH₂-S) (Found: C, 67.0; H, 9.2. C₁₉H₃₂OS₂ requires C, 67.05; H, 9.45%).

A mixture of the alcohol (170 mg), methanol (80 cm³), water (0.5 cm³), mercuric chloride (1.7 g), and yellow mercuric oxide (1.7 g) was refluxed for 4 h.²⁵ Solvent was evaporated and the residue extracted with hot light petroleum (b.p. 60–80°). 2-Hydroxycyclododecanespirocyclohex-2'-en-4'-one was obtained as needles, m.p. 131–132°, ν_{\max} (Nujol) 3440 and 1672 cm⁻¹, τ (CDCl₃) 3.07 (1H, dd, *J* 10.5 and 1.5 Hz), 3.96 (1H, slightly split doublet, *J* 10.5 Hz, CH=CH), and 7.92 (1H, s, exchangeable with D₂O, OH) (Found: C, 77.75; H, 10.65. C₁₇H₂₈O₂ requires C, 77.2; H, 10.65%).

1-Formyl-12-hydroxy-12-methylbicyclo[9.3.1]pentadecan-15-one (30).—(a) A mixture of 2-formyl-2-(3-oxobutyl)-cyclododecanone (15; *n* = 12) (1 g) and diethylamine (10 cm³) was stirred at room temperature for 3 h. The amine was then pumped off (temp. < 15°). P.l.c. (benzene-ether) gave two bands, *R_F* 0.28 and 0.65. The latter gave cyclododecanespirocyclohex-2'-ene-2,4'-dione (18; *n* = 12) (0.26 g), m.p. 101–103°, identical with that already obtained. The former furnished a crystalline solid (0.58 g) which was recrystallised from light petroleum (b.p. 60–80°) and gave the bicyclopentadecanone (30), m.p. 157°, ν_{\max} (CHCl₃) 3600, 1724, and 1703 cm⁻¹, τ (CDCl₃) 0.0 (1H,

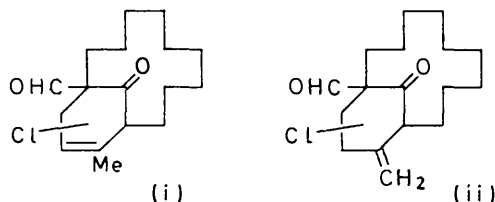
²⁵ E. J. Corey and R. B. Mitra, *J. Amer. Chem. Soc.*, 1962, **84**, 2938.

s, CHO), 7.1 (1H, d, J 10.5 Hz, CH-CO, coupling to only one adjacent alicyclic proton), and 8.61 (3H, s, tertiary Me) (Found: C, 73.35; H, 10.1. $C_{17}H_{28}O_3$ requires C, 72.8; H, 10.5%).

(b) The ketol (30) was formed occasionally as sole product in the reaction between 2-hydroxymethylenecyclo-dodecanone and methyl vinyl ketone. The amount of potassium hydroxide used for this reaction seemed to be critical. The i.r. spectrum of the ketol, m.p. 155–157°, thus produced was *not* identical with that of the ketol prepared by the diethylamine method; the i.r. spectra of the two products in chloroform solution were, however, identical.

11-Formyl-14-methylbicyclo[9.3.1]pentadec-1(14)-en-15-one. —The ketol (30) (0.5 g) in pyridine (10 cm³) was added to a stirred solution of phosphoryl chloride (3 cm³) in pyridine (3 cm³). After 3 h, work-up in the usual way gave two products (85 : 15). The principal product (65%) was the bicyclopentadecanone, m.p. 97° (from isopentane), ν_{\max} (Nujol) 1651 cm⁻¹, λ_{\max} 252 nm (ϵ 10,650), τ (CCl₄) -0.71 (1H, s, CHO) and 8.04br (3H, s, MeC=C) (Found: C, 77.9; H, 10.05. $C_{17}H_{26}O_2$ requires C, 77.8; H, 10.0%).

The minor product was a crystalline solid, m.p. 136–138° [from light petroleum (b.p. 40–60°)], ν_{\max} 1738 and 1726 cm⁻¹, τ (CDCl₃) 0.01 (1H, s, CHO), 4.4br (s), 5.2 (d, J 11 Hz), and 6.4 (d, J 11 Hz) (CH=C and H₂C=C), and 8.28 (MeC=C) (Found: C, 68.7; H, 9.05; Cl, 11.85. Calc. for $C_{17}H_{23}ClO_2$: C, 68.8; H, 8.45; Cl, 12.0%). This product is probably a mixture of the illustrated compounds (i) and (ii). Introduction of chlorine with thionyl chloride-



pyridine is known.²⁶ Hydrogenation of the mixture over 5% palladium-charcoal in ethyl acetate gave a dihydro-product, m.p. 76–80°, τ (CDCl₃) 0.06 (1H, s, CHO) and 9.18 (3H, d, J 8 Hz) (CH·CH₃).

Bicyclo[10.4.0]hexadec-11-en-13-one (17; $n = 12$).—(a) A mixture of 2-formyl-2-(3-oxobutyl)cyclododecanone (15; $n = 12$) (0.5 g), sodium methoxide (0.11 g), and sodium-dried benzene (10 cm³) was refluxed for 3 h. Work-up gave a light yellow oil (0.36 g) which was purified by p.l.c. (benzene-ether). The bicyclohexadecanone (17; $n = 12$) was obtained as needles (0.13 g) from light petroleum (b.p. 40–60°), ν_{\max} (Nujol) 1665 and 1622 cm⁻¹, λ_{\max} 240 nm (ϵ 16,600), τ (CDCl₃) 4.05 (1H, s, CH=C) (Found: C, 82.15; H, 11.5. $C_{18}H_{28}O$ requires C, 82.0; H, 11.2%). The 2,4-dinitrophenylhydrazone formed red plates (from ethanol), m.p. 145°, λ_{\max} (CHCl₃) 390 nm (ϵ 31,800) (Found: C, 63.6; H, 7.65; N, 13.4. $C_{22}H_{30}N_4O_4$ requires C, 63.75; H, 7.3; N, 13.5%).

(b) 1-Formyl-12-hydroxy-12-methylbicyclo[9.3.1]penta-decan-15-one (30) (0.5 g), sodium methoxide (0.33 g), and sodium-dried benzene (10 cm³) were refluxed for 5 h. Work-up as before gave crystals, m.p. 77° (0.34 g, 73%) of compound (17; $n = 12$).

²⁶ H. Kugita and M. Takeda, *Chem. and Pharm. Bull. (Japan)*, 1963, **11**, 986; R. T. Parfitt, M. Takeda, and H. Kugita, *J. Org. Chem.*, 1967, **32**, 419.

7,8-Dihydroindan-5(6H)-one (17; $n = 5$).—A mixture of 2-formyl-2-(3-oxobutyl)cyclopentanone (1 g), sodium-dried benzene (20 cm³), and toluene-*p*-sulphonic acid (0.5 g) was refluxed for 3 h. Work-up gave an oil (0.64 g, 90%) which by g.l.c. and t.l.c. was shown to be a single compound (17; $n = 5$), λ_{\max} 242 nm (ϵ 11,070), τ 4.12 (1H, d, J 2.4 Hz, -CH=). The 2,4-dinitrophenylhydrazone had m.p. 200° (methanol-chloroform) (lit.,²⁷ 199.5°), τ (CDCl₃) 3.75 (1H, d, J 1.2 Hz, -CH=C, allylic coupling to one alicyclic proton at C-3).

Cyclisation of 2-formyl-2-(3-oxobutyl)cyclopentanone in sodium-dried benzene containing sodium methoxide gave identical material in 88% yield.

Bicyclo[5.4.0]undec-7-en-9-one (17; $n = 7$).—2-Formyl-2-(3-oxobutyl)cycloheptanone (5 g), toluene-*p*-sulphonic acid (2 g), and sodium-dried benzene (100 cm³) were refluxed under a water separator for 2 h, at the end of which the theoretical amount of water had been collected. Work-up gave the bicycloundecanone (17; $n = 7$), b.p. 90–91° at 0.1 mmHg (3.60 g, 92%), ν_{\max} (film) 1667 and 1612 cm⁻¹, λ_{\max} 242 nm (ϵ 13,700), τ (CDCl₃) 4.28 (1H, d, J 0.7 Hz, CH=C) (Found: C, 80.1; H, 9.6. Calc. for $C_{11}H_{16}O$: C, 80.45; H, 9.85%). The semicarbazone had m.p. 209° (lit.,^{2a} 218°) (Found: C, 65.15; H, 8.65; N, 19.1. Calc. for $C_{12}H_{18}N_3O$: C, 65.1; H, 8.65; N, 19.0%).

2-(3-Oxobutyl)cycloheptanone, obtained from 2-formyl-2-(3-oxobutyl)cycloheptanone by treatment with alkaline alumina (see later), could be used in the foregoing reaction (yield 91%).

trans-7-Hydroxybicyclo[5.4.0]undecan-9-one (20; $n = 7$).—(a) Alkaline alumina (Hopkin and Williams; Brockmann Activity I) was treated with 5% by weight of water and the mixture was agitated for 3 h. A column of this alumina (240 g) was prepared in sodium-dried ether, and 2-formyl-2-(3-oxobutyl)cycloheptanone (4 g) in ether (20 cm³) was applied to it. The solution was run into the alumina followed by more ether (20 cm³). After 40 h the column was eluted with ether. The early fractions gave 2-(3-oxobutyl)cycloheptanone (3.1 g) (see preceding experiment). Later fractions crystallised. These were combined and recrystallised from light petroleum (b.p. 60–80°) containing some chloroform. The hydroxybicycloundecanone (20) (0.34 g, 10%) had m.p. 120°, ν_{\max} (Nujol) 3345 and 1710 cm⁻¹, τ (CDCl₃) 7.82br (1H, s, exchangeable with D₂O, OH) (Found: C, 72.25; H, 10.0. $C_{11}H_{18}O_2$ requires C, 72.5; H, 9.95%).

trans-9-Ethylenedithiobicyclo[5.4.0]undecan-7-ol (28). To a stirred mixture of the foregoing ketol (0.16 g) in dioxan (5 cm³) containing zinc chloride (0.16 g) (B.D.H. granular) at room temperature, a solution of ethanedithiol (0.16 g) in dioxan (3 cm³) was added, followed by anhydrous sodium sulphate (0.16 g). After 2 days work-up gave a crystalline solid (0.164 g). Crystallisation from light petroleum (b.p. 40–60°) gave the thioacetal (28) as needles (0.122 g, 55%), m.p. 93–94°, τ (CDCl₃) 6.76 (4H, s, S·CH₂·CH₂·S) and 7.38 (1H, s, exchangeable with D₂O, OH) (Found: C, 60.25; H, 8.95. $C_{13}H_{22}OS_2$ requires C, 60.45; H, 8.6%).

(b) To a stirred solution of bicyclo[5.4.0]undec-7-en-9-one (17; $n = 7$) (3.3 g) in methanol (60 cm³) was added, at room temperature, powdered sodium borohydride (3.3 g) during 30 min. After a further 2 h the solution was made acid with acetic acid. Addition of chloroform and normal

²⁷ V. Prelog and M. Zimmermann, *Helv. Chim. Acta*, 1949, **32**, 2360.

work-up gave bicyclo[5.4.0]undec-7-en-9-ol as a viscous liquid (3.0 g, 84%) (ν_{\max} 3323 cm^{-1} ; no CO), t.l.c. of which showed only one spot; no starting material was present.

To a stirred solution of the alcohol (2.1 g) in chloroform (15 cm^3) at room temperature was added *m*-chloroperbenzoic acid (3.0 g) in chloroform (30 cm^3) during 30 min. After 2 h the solution was washed with aqueous sodium sulphite, potassium hydrogen carbonate, and then water before being dried and concentrated. The epoxy-alcohol was a viscous oil (2.2 g) (n.m.r. showed $\text{CH}=\text{C}$).

Lithium aluminium hydride (0.6 g) was stirred with dry tetrahydrofuran (15 cm^3) at room temperature and a solution of the foregoing epoxy-alcohol (1.9 g crude) in tetrahydrofuran (15 cm^3) was added during 15 min. After 12 h dilute hydrochloric acid was added. Work-up gave the diol as a viscous oil (1.6 g, 85%), t.l.c. of which showed the absence of starting material (ν_{\max} 3400 vs cm^{-1}).

To a stirred slurry of chromium trioxide (1.5 g) in dry pure pyridine (15 cm^3) kept at 10° was added a solution of the foregoing diol (1.5 g) in dry pyridine (15 cm^3) during 30 min. After a further 12 h chloroform (50 cm^3) was added and the solution was filtered through Celite. The organic layer was washed with water, then dried and concentrated. T.l.c. (benzene-ether) of the product showed the presence of some starting material, in addition to two other compounds (70:30). P.l.c. gave, from the larger band, *trans*-7-hydroxybicyclo[5.4.0]undecan-9-one (20), m.p. 119–120°, identical with that obtained by method (a).

The smaller band gave *cis*-7-hydroxybicyclo[5.4.0]undecan-9-one (21), m.p. 76–77° [needles from light petroleum (b.p. 40–60°)], ν_{\max} (Nujol) 3387 (Found: C, 72.45; H, 10.0. $\text{C}_{11}\text{H}_{18}\text{O}_2$ requires C, 72.5; H, 9.95%). The compound underwent spontaneous dehydration more readily than the *trans*-ketol.

cis-9-Ethylenedithiobicyclo[5.4.0]undecan-7-ol (28; *cis*-ring junction). To a stirred mixture of the ketol (21) (75 mg), dioxan (1 cm^3), and zinc chloride (75 mg; B.D.H. granular) at 15° was added a solution of ethanedithiol (75 mg) in dioxan (1 cm^3), followed by anhydrous sodium sulphate (75 mg). After 2 days, work-up gave a crystalline solid (73 mg) which was purified by p.l.c. (benzene-ether). The *thioacetal* was obtained (52 mg, 50%) as needles, m.p. 98–99°, ν_{\max} (Nujol) 3447 cm^{-1} (Found: C, 60.4; H, 8.4. $\text{C}_{13}\text{H}_{22}\text{OS}_2$ requires C, 60.45; H, 8.6%).

trans-Bicyclo[5.4.0]undecan-1-ol (29).—(a) A mixture of *trans*-9-ethylenedithiobicyclo[5.4.0]undecan-7-ol (28) (100 mg, m.p. 93°), 95% ethanol (10 cm^3) (distilled from Raney nickel) and freshly made Raney nickel (4 g; W-2) was refluxed for 3 h and then filtered hot. Evaporation gave an oil (89 mg), which on trituration with isopentane at –10° for 2 days solidified, m.p. 34–36°. Recrystallisation from its solution in isopentane at –30° gave *trans*-bicyclo[5.4.0]undecan-1-ol (29) as needles, m.p. 37.5–39°, with a strong camphor-like odour (pure by t.l.c.), ν_{\max} (Nujol) 3602 and 3482 cm^{-1} , τ (CDCl_3) 8.00 (1H, s, exchangeable with D_2O , OH) (Found: C, 78.55; H, 12.25. $\text{C}_{11}\text{H}_{20}\text{O}$ requires C, 78.5; H, 12.0%).

(b) From 6,7,8,9-Tetrahydro-5H-benzocycloheptene (23). δ -Phenylvaleric acid²⁸ (10 g) was added to polyphosphoric acid (200 g; B.D.H., P_2O_5 content 82–85%) maintained at 90°. After 2 h the solution was cooled and poured on ice and the benzocycloheptenone (7.7 g, 92%) was isolated with benzene. The compound was reduced to the hydrocarbon (23) by the method of Dauben and Rogan.¹⁴

To a solution of compound (23) (1.1 g) in 1,2-diamino-

ethane (30 cm^3 ; distilled from sodium) at 80°, lithium pieces (3.5 g) were added during 30 min. After a further 2 h, the mixture was cooled and then treated with water and a little dilute hydrochloric acid. Extraction with ether and work-up gave a pale yellow oil which was dissolved in petroleum (b.p. 40–60°) and chromatographed on Hopkin and Williams neutral alumina (Brockmann Activity III). Bicyclo[5.4.0]undec-1(7)-ene (24) was obtained as a liquid (0.9 g, 82%). G.l.c. on SE-30 showed >96% of this material under one peak; the retention time was identical with that of the major component in a specimen (a total of three peaks) provided by Professor Dauben; τ (CDCl_3) 7.9–8.2 (8H, m, $[\text{CH}_2]_2$ and $\text{C}=\text{C}[\text{CH}_2]_2$).

A solution of bicyclo[5.4.0]undec-1(7)-ene (24) (0.45 g) in chloroform (5 cm^3) was treated, at room temperature, with a solution of *m*-chloroperbenzoic acid (0.85 g) in chloroform (10 cm^3) added during 30 min. The flask was loosely stoppered and kept in the dark for 7 days. The mixture was then washed successively with aqueous sodium sulphite, potassium hydrogen carbonate, and water, after which it was dried and concentrated. The epoxide (25) was an oil (0.4 g, 80%).

The epoxide (0.3 g) in dry tetrahydrofuran (3 cm^3) was added, during 15 min, to a stirred slurry of lithium aluminium hydride (0.3 g) in dry tetrahydrofuran, and the mixture was then refluxed gently for 6 h. Addition of dilute hydrochloric acid and work-up, followed by p.l.c. (benzene-ether) of the product gave needles (0.165 g), m.p. 27–30°, which were recrystallised from isopentane (at ca. –30°). The product, *trans*-bicyclo[5.4.0]undecan-1-ol (29) (0.11 g, 36%), m.p. 37.5–39°, had a pronounced camphor-like odour and was identical (mixed m.p., i.r. and n.m.r. spectra) with that previously obtained.

10-Methoxy-8-methyl-7,9-dioxatricyclo[6.2.2.0^{4,6}]dodecan-6-ol (13) and 6,10-Dimethoxy-8-methyl-7,9-dioxatricyclo[6.2.2.0^{4,6}]dodecane (14).—A mixture of 2-formyl-2-(3-oxobutyl)cyclohexanone (4.3 g), methanol (43 cm^3), and anhydrous calcium chloride (2.0 g, B.D.H. granular, finely powdered) was kept at room temperature for 12 h. Extraction with ether and work-up gave an oil (3.9 g), which, kept at –10° for 12 h deposited a crystalline solid (0.50 g). This was recrystallised from petroleum (b.p. 60–80°) to give the *alcohol* (13), m.p. 96–97° (t.l.c.-homogeneous in benzene-ether), ν_{\max} 3420, τ (CDCl_3) 5.19 (O·CH·O), 6.58 (3H, s, OMe), 7.41 (1H, s, exchangeable with D_2O , OH), and 8.63 (3H, s, tertiary Me) (Found: C, 63.2; H, 9.1. $\text{C}_{12}\text{H}_{20}\text{O}_4$ requires C, 63.15; H, 8.85%). P.l.c. of the filtrate (benzene-ether) gave the *dimethyl ether* (14) as an oil (0.75 g), ν_{\max} 1387 cm^{-1} , τ (CDCl_3) 5.34 (1H, s, O·CH·O), 6.69 (3H, s, OMe), 6.85 (3H, s, OMe), and 8.78 (3H, s, tertiary Me) (Found: C, 64.55; H, 9.05. $\text{C}_{13}\text{H}_{22}\text{O}_4$ requires C, 64.45; H, 9.15%).

1,3-Dimethoxy-3-methyl-2-oxaspiro[5.6]dodecan-7-one (31; $n = 7$) and 1,3-Dimethoxy-3-methyl-2-oxaspiro[5.11]heptadecan-7-one (31; $n = 12$).—2-Formyl-2-(3-oxobutyl)cycloheptanone (1.3 g) was treated with methanol-calcium chloride exactly as for the cyclohexanone analogue. P.l.c. of the crude product (1.09 g) [petroleum (b.p. 60–80°)-ether] gave the *spiro-ketone* (31; $n = 7$) as a liquid, ν_{\max} (film) 1697 cm^{-1} , τ (CCl_4) 5.46 (1H, s, O·CH·O), 6.62 (3H, s, OMe), 6.76 (3H, s, OMe), and 8.71 (3H, s, CMe) (Found: C, 65.9; H, 9.3. $\text{C}_{14}\text{H}_{24}\text{O}_4$ requires C, 65.6; H, 9.4%).

2-Formyl-2-(3-oxobutyl)cyclododecanone (2.0 g) was

²⁸ A. T. Blomquist, R. E. Stahl, Y. C. Meinwald, and B. H. Smith, *J. Org. Chem.*, 1961, **26**, 1687.

refluxed with methanol (30 cm³) and calcium chloride (1 g; finely powdered) for 3 h and set aside overnight. Work-up gave an oil (1.95 g) which was purified by p.l.c. (benzene-ether) to yield the *spiro-ketone* (31; $n = 12$) (0.5 g) as needles, m.p. 116–117.5° (from isopentane), ν_{\max} . (Nujol) 1692 cm⁻¹, τ (CDCl₃) 5.57 (1H, s, O·CH·O), 6.57 and 6.84 (OMe), and 8.82 (tertiary Me) (Found: C, 69.7; N, 10.3.

C₁₉H₃₄O₄ requires C, 69.9; H, 10.5%). The mother liquors from these preparations failed to reveal the presence of any other compounds.

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