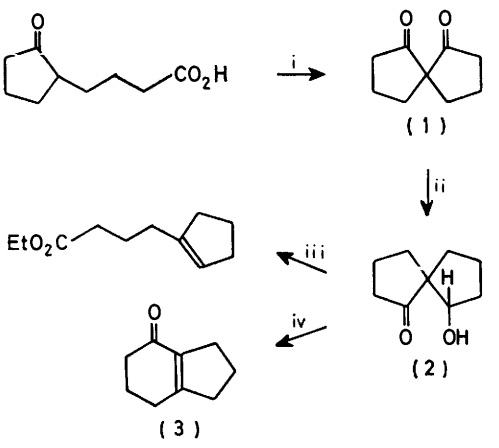
Bicyclo[4.2.1]non-1-en-8-one; a Novel Anti-Bredt Enone. Synthesis of Non-enolisable β-Diketones from Oxo-acids

By **William Carruthers** * and **Andrew Orridge**, Chemistry Department, University of Exeter, Stocker Road, Exeter EX4 4QD

Several cyclic β-diketones were prepared by acid-catalysed intramolecular cyclisation of appropriate oxo-acids. One of them, bicyclo[4.2.1]nonane-2,8-dione, was converted into the bridgehead enone named in the title. Some reactions of this compound are reported. Reaction of (5*R**,6*R**)-6-tosyloxyspiro[4.4]nonan-1-one with boiling collidine gave 1,2,3,5,6,7-hexahydroinden-4-one by elimination and rearrangement.

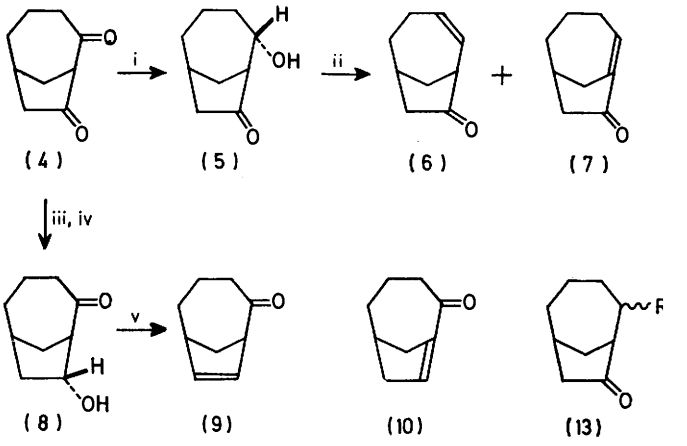
GERLACH and MÜLLER have described [1] the synthesis of a number of non-enolisable cyclic β-diketones from oxo-acids by reaction with polyphosphoric acid in acetic acid, and the method has been employed by others.[2] We have independently obtained similar, and in some cases better, results using naphthalene-2-sulphonic acid in boiling xylene as cyclising agent; thus, 4-(2-oxocyclopentyl)butyric acid was converted into spiro[4.4]nonane-1,6-dione (1) in 80% yield and both 4-(2-oxocyclohexyl)-butyric acid and 5-(2-oxocyclopentyl)valeric acid gave spiro[4.5]decane-1,6-dione (70—75%). With 5-(2-oxocyclohexyl)valeric acid the expected spiro[5.5]undecane-1,7-dione was accompanied by an isomer ($\nu_{max.}$ 1 755 cm^{-1}) which appears to be the enol lactone of the original oxo-acid, since it readily afforded the starting acid on alkaline hydrolysis. Under the same conditions (4-oxocycloheptyl)acetic acid was smoothly converted into bicyclo[4.2.1]nonane-2,8-dione (4) (ν_{CO} 1 742 and 1 695 cm^{-1}). Although two modes of cyclisation are possible here the diketone (4) formed 80—90% of the product (g.l.c.) and was the only compound isolated.



SCHEME 1 Reagents: i, naphthalene-2-sulphonic acid, boiling xylene; ii, $LiAlH(OBu^t)_3$, −30 °C; iii, tosylate with NaOEt–EtOH; iv, tosylate with boiling collidine

Its structure was established by conversion into bicyclo-[4.2.1]nonane by Wolff–Kishner reduction of the bis-semicarbazone or, better, by the stepwise route through the mono-ketone (14) described below.

We have used the diketone (4) in attempts to prepare the two bridgehead enones (7) and (10) (Scheme 2).



SCHEME 2 Reagents: i, $LiAlH(OBu^t)_3$, −78 °C; ii, tosylate with boiling collidine [TsOH in benzene gave (7) only]; iii, $(CH_2OH)_2$, TsOH; iv, $LiAlH_4$, H_3O^+; v, various conditions, *e.g.* tosylate with boiling collidine

Wiseman [3] has related the strain in bridgehead olefins to that in the appropriate *trans*-cycloalkenes; he predicted that since *trans*-cyclo-octene itself is isolable, bridgehead olefins which incorporate a *trans*-cyclo-octene ring should also be isolable. In agreement he obtained [4] the two bridgehead olefins corresponding to (7) and (10) (CH_2 for CO) by pyrolysis of the bridgehead quaternary ammonium hydroxide, but his proposal offers no guidance on the relative stabilities of isomeric bridgehead olefins of this type. Wiseman considers that the isomer with the double bond in the seven-membered ring is here the more stable, but recent work by Becker [5] suggests the reverse. We hoped to obtain further insight into this by synthesis of compounds (7) and (10) and a study of their properties. In the event we were frustrated in this aim by our inability to obtain the isomer (10).

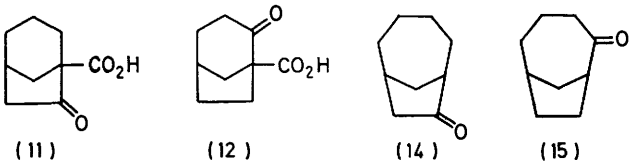
Reduction of the diketone (4) with lithium hydrido-tri-t-butoxyaluminate at −78 °C led, by selective attack on the carbonyl group of the seven-membered ring, to the *endo*-ketol (5). The presence of the carbonyl group in a five-membered ring was suggested by the carbonyl

[1] H. Gerlach and W. Müller, *Angew. Chem. Internat. Edn.*, 1972, **11**, 1030; *Helv. Chim. Acta*, 1972, **55**, 2277.
[2] H. J. Wüthrich, A. Siewinski, H. Schaffner, and O. Jeger, *Helv. Chim. Acta*, 1973, **56**, 239; T. Wheeler, C. A. Jackson, and K. H. Young, *J. Org. Chem.*, 1974, **39**, 1318.
[3] J. R. Wiseman, *J. Amer. Chem. Soc.*, 1967, **89**, 5966; J. R. Wiseman and W. A. Pletcher, *ibid.*, 1970, **92**, 956.
[4] J. R. Wiseman, Hak-Foon Chan, and C. J. Ahola, *J. Amer. Chem. Soc.*, 1969, **91**, 2812.
[5] H. Becker, *Helv. Chim. Acta*, 1977, **60**, 94.

i.r. absorption of the ketol itself (ν_{CO} 1 725 cm^{-1}) and, more decisively, by that of the derived tosylate (ν_{CO} 1 745 cm^{-1}), and the *endo*-configuration was shown by the occurrence of intramolecular hydrogen bonding in the ketol [$\nu_{max.}$ (3.6×10^{-3}M-solution in CCl_4) 3 660 and 3 585 cm^{-1}]. Reaction of the derived tosylate with boiling collidine led, by elimination, to a mixture of the two isomeric olefins (6) and (7) in the ratio 4 : 1. Both compounds on catalytic hydrogenation gave bicyclo-[4.2.1]nonan-8-one (14), which was itself converted into bicyclo[4.2.1]nonane by Wolff–Kishner reduction of the semicarbazone, confirming that no skeletal rearrangement had taken place during the elimination. The major product of the reaction was identified as the unwanted isomer bicyclo[4.2.1]non-2-en-8-one (6) by its weak u.v. absorption and its ^1H n.m.r. spectrum, which includes a signal [τ 3.9—4.4 (m)] corresponding to two olefinic protons. The bridgehead enone (7), the minor product of the elimination, showed strong u.v. absorption [$\lambda_{max.}$ 246 nm (ε 4 700)] clearly indicating the presence of an $\alpha\beta$-unsaturated carbonyl group, and its ^1H n.m.r. spectrum contains a signal [τ 3.1—3.3 (m)] corresponding to only one olefinic proton. The reaction of the tosylate of (5) with collidine gave erratic results and in some experiments none of the enone (7) was obtained. Dehydrochlorination with 1,5-diazabicyclo-[4.3.0]non-5-ene of the chloride derived from (5) with phosphoryl chloride gave only the non-conjugated isomer (6), but a reliable route to (7) was found in the direct dehydration of the ketol (5) with toluene-*p*-sulphonic acid and calcium chloride in boiling benzene.[6] The enone (7) was consistently obtained in 20—25% yield by this method and, remarkably, appeared to be the only product. Although a number of bridgehead enones have been prepared before,[7] compound (7) is apparently the first in which neither the carbonyl group nor the olefinic bond is situated on the bridge.

The alternative ketol (8), which appeared a suitable precursor of the enone (10), was readily obtained from the dione (4) by reduction of the monoacetal (formed at the carbonyl group in the seven-membered ring with ethylene glycol and toluene-*p*-sulphonic acid) with lithium aluminium hydride, followed by hydrolysis. The i.r. spectrum, taken at high dilution, showed that the hydroxy-group again had the *endo*-configuration. However all attempts to convert this compound or derivatives into the desired enone (10) were unsuccessful. Treatment of the tosylate with boiling collidine gave only the alternative elimination product (9), and numerous attempts to dehydrohalogenate the chloride or bromide under a variety of conditions led either to (9) or to no reaction. Direct dehydration of the ketol with toluene-*p*-sulphonic acid and calcium chloride in this case gave only polymeric products.

The greater resistance to the formation of (10) than of (7) may be a consequence of greater strain in the transition state leading to the bridgehead olefin in which the double bond is in the five-membered ring. This would be in line with the observation that the oxo-acid (11) requires a higher temperature for decarboxylation than the isomer (12).[8]



(11) (12) (14) (15)

The u.v. spectrum of the enone (7) suggests that the double bond, although twisted, is still conjugated with the carbonyl group.[7] In agreement, the compound reacted readily with diethyl sodiomalonate and with lithium dimethylcuprate to give the conjugate addition products [13; R = $CH(CO_2Et)_2$ or Me]. In contrast it did not form a Diels–Alder adduct with either furan or 1,3-diphenylisobenzofuran in boiling ether. The two addition reactions presumably take place by way of the bridgehead enolate with the double bond in the five-membered ring, but attempts to trap the enolate from the cuprate reaction[9] with methyl iodide or chlorotrimethylsilane were unsuccessful.

Base-catalysed hydrogen–deuterium exchange, taking place through intermediate enolate ions with a bridgehead double bond, has been observed on a number of occasions.[10] Both the ketones (14) and (15) formed trideuterio-derivatives in which the third deuterium atom occupies the bridgehead position (from ^1H n.m.r. spectroscopy; see Experimental section) when heated at 95 °C with sodium deuterioxide in dioxan containing deuterium oxide. The five-membered-ring ketone (14) did so considerably faster than (15), presumably because of the greater reactivity of the intermediate enolate in which the double bond is in the five-membered ring. The reactivity of these ketones contrasts with that of bicyclo[3.2.1]octan-2-one [as (15) with a six- instead of a seven-membered ring], which formed only a dideuterio-derivative even at 170 °C,[11] possibly because in this case replacement of the bridgehead hydrogen atom requires an intermediate enolate with a *trans*-cycloheptene ring.

The 4-oxocycloheptylacetic acid required for preparation of the diketone (4) was obtained by ring expansion of 4-oxocyclohexylacetic acid with diazomethane. The acetic acid was best made by catalytic hydrogenation of *p*-hydroxyphenylacetic acid followed by Jones oxidation of the resulting cyclohexanol, as described by Ungnade

[6] E. Wenkert and T. E. Stevens, *J. Amer. Chem. Soc.*, 1956, **78**, 2318.

[7] *Cf.* G. L. Buchanan, *Chem. Soc. Rev.*, 1974, **3**, 41.

[8] J. P. Ferris and N. C. Miller, *J. Amer. Chem. Soc.*, 1966, **88**, 3522.

[9] *Cf.* H. O. House and M. J. Umen, *J. Amer. Chem. Soc.*, 1972, **94**, 5495; G. H. Posner, J. J. Sterling, C. E. Whitten, C. M. Lenz, and D. J. Brunelle, *ibid.*, 1975, **97**, 107.

[10] See, for example, K. W. Turnbull, S. J. Gould, and D. Arigoni, *J.C.S. Chem. Comm.*, 1972, 597; D. H. Bowen, C. Cloke, and J. MacMillan, *J.C.S. Perkin I*, 1975, 378.

[11] A. Nickon, D. F. Covey, Fu-Chih Huang, and Yu-Neng Kuo, *J. Amer. Chem. Soc.*, 1975, **97**, 904.

and Morriss.[12] This procedure gave better results than an alternative involving initial Birch reduction of *p*-methoxyphenylacetic acid,[13] the results of which were unreliable in our hands.

In separate experiments (Scheme 1) spiro[4.4]nonane-1,6-dione (1), obtained as described above, was reduced with lithium hydridotri-t-butoxyaluminate at −30 °C to give, selectively, (5*R**,6*R**)-6-hydroxyspiro[4.4]nonan-1-one (2), previously obtained, along with its epimer, by catalytic hydrogenation of the diketone.[14] Reaction of the corresponding tosylate with boiling collidine was not straightforward; elimination was accompanied by rearrangement and 1,2,3,5,6,7-hexahydroinden-4-one (3) was formed in high yield. A similar reaction took place with the tosylate of (5*R**,6*R**)-6-hydroxyspiro[4.5]decan-1-one to give 3,4,5,6,7,8-hexahydronaphthalene-1(2*H*)-one. Rearrangement of derivatives of spiro[4.4]nonan-1-one and spiro[4.5]decan-1-one to the same fused bicyclic ketones during attempted Schmidt and Beckmann reactions under acidic conditions has been observed previously.[15] Formation of intermediate ring-opened carbocations was established for these reactions and it seems likely that carbocations formed by solvolysis of the tosyloxy-group are concerned in the present reactions. Reaction of the tosylate of (2) with sodium ethoxide led to a different product; fragmentation took place to give ethyl 4-(cyclopent-1-enyl)butyrate formed, apparently, by a *cis*-' elimination.'

EXPERIMENTAL

U.v. spectra were obtained for ethanolic solutions, and i.r. spectra (with a Perkin-Elmer Infracord instrument) for liquid films or for solutions in chloroform; i.r. spectra at high dilution were measured with a Hilger–Watts H900 double-beam instrument. ^{1}H N.m.r. spectra were recorded with a Perkin-Elmer R10 spectrometer (at 60 MHz) or a JEOL MH-100 instrument (at 100 MHz) for solutions in deuteriochloroform or carbon tetrachloride, with tetramethylsilane as internal standard. Preparative t.l.c. was carried out on Merck Kieselgel GF 254 1 mm thick activated at 100 °C. Petroleum refers to the fraction of b.p. 60—80 °C.

Ethyl 4-*Oxocycloheptylacetate*.—A solution of diazomethane (0.19 g) in ether [distilled from *N*-methyl-*N*-nitrosotoluene-4-sulphonamide (1.07 g), potassium hydroxide (0.2 g), 95% ethanol (10 ml), and ether (60 ml)] was added to a solution of ethyl 4-oxocyclohexylacetate (0.56 g) (prepared by the method of Ungnade and Morriss [12]) at 0 °C, and the solution was allowed to come to room temperature. Next morning solvents were removed *in vacuo* and the resulting yellow oil was purified by preparative g.l.c. (15% SE 30; 150 °C). *Ethyl* 4-*oxocycloheptylacetate* (0.25 g) was obtained as an oil, b.p. 135 °C at 0.15 mmHg (air-bath temperature) (Found: C, 66.8; H, 9.3%; M^+, 198. $C_{11}H_{18}O_3$ requires C, 66.6; H, 9.15%; *M*, 198); $\nu_{max.}$ (film) 1 690 and 1 730 cm^{-1}. The *semicarbazone* had m.p. 98—100 °C (from water) (Found: C, 56.4; H, 8.3; N, 16.3%. $C_{12}H_{21}N_3O_3$ requires C, 56.45; H, 8.3; N, 16.5%).

In large-scale runs (10 g) the ethyl 4-oxocycloheptylacetate was purified by fractional distillation instead of by preparative g.l.c.

Bicyclo[4.2.1]*nonane*-2,8-*dione* (4).—4-Oxocycloheptylacetic acid (0.3 g), obtained from the foregoing ester by hydrolysis as a viscous oil, b.p. 158—162 °C at 0.1 mmHg (air-bath temperature) (Found: C, 63.65; H, 8.45%. Calc. for $C_9H_{14}O_3$: C, 63.5; H, 8.3%), was heated in xylene solution (40 ml) with naphthalene-2-sulphonic acid (0.1 g) for 48 h, with azeotropic removal of the water formed. The recovered product showed only one major spot on t.l.c. Purification by preparative t.l.c. (2 : 1 ethyl acetate–petroleum as eluant) gave a gum (0.16 g) from which *bicyclo*[4.2.1]*nonane*-2,8-*dione* was readily obtained by sublimation *in vacuo* as crystals, m.p. 130—132 °C (Found: C, 70.9; H, 8.0%; M^+, 152. $C_9H_{12}O_2$ requires C, 71.0; H, 7.95%; *M*, 152); $\nu_{max.}$ ($CHCl_3$) 1 690 and 1 740 cm^{-1}; τ ($CDCl_3$) 6.7 (1 H, t, COC*H*CO) and 7.0—8.8 (11 H, envelope); τ [$CDCl_3$ with Eu(fod)$_3$] 4.3 (1 H, d), 6.05 (2 H, t), 6.6br (3 H, s), 6.9br (2 H, s), and 7.55br (4 H, s). The *mono*-2,4-*dinitrophenylhydrazone* formed orange needles in ethanol–ethyl acetate, m.p. 183—185 °C (Found: C, 54.2; H, 4.95; N, 16.8. $C_{15}H_{16}N_4O_5$ requires C, 54.2; H, 4.85; N, 16.9%); $\nu_{max.}$ (KBr disc) 1 735 cm^{-1}.

The derived bis-semicarbazone (m.p. 212—213 °C; 0.15 g) was heated at 210 °C with a solution of sodium (0.3 g) in diethylene glycol (6 ml). Bicyclo[4.2.1]nonane, m.p. 88—91 °C, collected in the condenser, and was identified by mixed m.p. (86—92 °C) with an authentic specimen [16] (m.p. 88—94 °C). Dilution of the mixture with water and extraction with petroleum gave a gum (24 mg) which appeared to contain bicyclo[4.2.1]nonane (g.l.c.), but it could not be induced to crystallise.

2-endo-*Hydroxybicyclo*[4.2.1]*nonan*-8-*one* (5).—Bicyclo-[4.2.1]nonane-2,8-dione (0.5 g) in tetrahydrofuran (50 ml) was added to a stirred solution of lithium hydridotri-t-butoxyaluminate (3.4 g) in tetrahydrofuran (50 ml) at −78 °C. After 24 h at this temperature the mixture was carefully acidified with 2M-hydrochloric acid and the product was extracted with ether and purified by preparative t.l.c. [ethyl acetate–petroleum (2 : 1) as eluant]. 2-endo-*Hydroxybicyclo*[4.2.1]*nonan*-8-*one* (0.42 g) was obtained as a crystalline solid, m.p. 127—129 °C, after vacuum sublimation (100 °C at 0.1 mmHg) (Found: C, 70.4; H, 9.0%; M^+, 154. $C_9H_{14}O_2$ requires C, 70.1; H, 9.15%; *M*, 154); $\nu_{max.}$ (film) 3 600—3 100 and 1 730 cm^{-1}; $\nu_{max.}$ (3.6×10^{-3}M in CCl_4) 3 600 and 3 585br cm^{-1}; τ ($CDCl_3$) 5.8—6.05br (1 H, q, C*H*OH), 6.3—6.6br (1 H, s, removed by D_2O, CHO*H*), and 7.2—8.8 (12 H, envelope). The *toluene*-p-*sulphonate* formed needles in petroleum–toluene, m.p. 99—101 °C (Found: C, 62.3; H, 6.5. $C_{15}H_{20}O_4S$ requires C, 62.4; H, 6.6%); $\nu_{max.}$ (CCl_4) 1 745 cm^{-1}; τ ($CDCl_3$) 5.0—5.3 (1 H, m, C*H*OTs).

Bicyclo[4.2.1]*non*-2-*en*-8-*one* (6) *and Bicyclo*[4.2.1]*non*-1-*en*-8-*one* (7).—A solution of the foregoing toluene-*p*-sulphonate (1.4 g) in 2,4,6-collidine (30 ml) was boiled for 20 h; the cooled mixture was acidified with 2M-hydrochloric acid and extracted with ether. The recovered oil (0.7 g) was purified by preparative t.l.c. (eluant ethyl

[12] H. E. Ungnade and F. V. Morriss, *J. Amer. Chem. Soc.*, 1948, **70**, 1898.
[13] J. A. Marshall and R. H. Ellison, *J. Org. Chem.*, 1975, **40**, 2070.
[14] E. Hardegger, E. Maeder, H. M. Semarne, and D. J. Cram, *J. Amer. Chem. Soc.*, 1959, **81**, 2729.
[15] R. K. Hill and R. T. Conley, *J. Amer. Chem. Soc.*, 1960, **82**, 645; R. T. Conley and B. E. Nowak, *J. Org. Chem.*, 1961, **26**, 692.
[16] C. W. Jefford, U. Burger, and F. Delay, *Helv. Chim. Acta*, 1973, **56**, 1083.

acetate–petroleum, 2 : 1) and preparative-scale g.l.c. (10% SE30; 150 °C) and gave two products. *Bicyclo*[4.2.1]*non-2-en-8-one* (0.25 g), the major product, formed crystals, m.p. 38—40 °C, by sublimation at 70 °C and 0.1 mmHg (Found: C, 79.1; H, 9.2%; M^+, 136. $C_9H_{12}O$ requires C, 79.4; H, 8.9%; *M*, 136); $\nu_{max.}$ (film) 1 740 and 1 630 cm^{-1}; u.v. (95% EtOH) end absorption only; τ ($CDCl_3$) 3.9—4.4 (2 H, m, CH=CH), and 7.1—8.6 (10 H, envelope).

The minor product, *bicyclo*[4.2.1]*non-1-en-8-one* (0.15 g), was isolated as a liquid, unstable in air, b.p. 70—75 °C at 0.05 mmHg (air-bath temperature) (Found: C, 79.6; H, 9.2%; M^+, 136. $C_9H_{12}O$ requires C, 79.4; H, 8.9%; *M*, 136); $\nu_{max.}$ (CCl_4) 1 720 and 1 655 cm^{-1}; $\lambda_{max.}$ (95% ethanol) 246 nm (ε 4 700); τ ($CDCl_3$) 3.1—3.3 (1 H, m, CO–C=CH), and 7.2—9.2 (11 H, envelope). This compound was more easily obtained from the alcohol by heating it (0.2 g) in dry benzene (20 ml) with toluene-*p*-sulphonic acid (0.1 g) and anhydrous calcium chloride (0.2 g) for 3 h. The recovered oil gave bicyclo[4.2.1]non-1-en-8-one (50 mg), b.p. 70 °C at 0.1 mmHg, after preparative t.l.c.; the i.r., u.v., and ^1H n.m.r. spectra were identical with those of the product obtained as described above.

Both the above unsaturated ketones were rapidly converted by hydrogenation over 5% palladium–charcoal into *bicyclo*[4.2.1]*nonan-8-one*, m.p. 97—99 °C after sublimation at 40 °C and 0.2 mmHg (Found: C, 78.2; H, 10.4%; M^+, 138. $C_9H_{14}O$ requires C, 78.2; H, 10.2%; *M*, 138); $\nu_{max.}$ ($CHCl_3$) 1 740 cm^{-1}. The *semicarbazone* formed needles in aqueous methanol, m.p. 194—195 °C (decomp.) (Found: C, 61.3; H, 8.9; N, 21.2. $C_{10}H_{17}N_3O$ requires C, 61.5; H, 8.8; N, 21.5%). When this semicarbazone (50 mg) was heated at 220 °C with the solution obtained from sodium (100 mg) in diethylene glycol (3 ml), bicyclo[4.2.1]-nonane (15 mg) collected in the condenser as flaky crystals, m.p. 85—87 °C, identical (mixed m.p.) with an authentic specimen. G.l.c. analysis of material recovered from the diethylene glycol solution showed that it was a complex mixture.

8-endo-*Hydroxybicyclo*[4.2.1]*nonan-2-one* (8).—Bicyclo-[4.2.1]nonane-2,8-dione (3 g) was converted into the 2-ethylene acetal by reaction with ethylene glycol (15 g) in boiling toluene (500 ml) containing toluene-*p*-sulphonic acid (0.2 g) for 60 h, with azeotropic removal of water. The crude product was purified by chromatography on silica gel, but could not be separated completely from some dione. This product [$\nu_{max.}$ (film) 1 740 cm^{-1} (five-membered ring ketone)] (1 g) was reduced directly with lithium aluminium hydride (1 g) in ether and the acetal group in the crude product was hydrolysed with hydrochloric acid (10N; 1 ml) in acetone (60 ml) at room temperature for 1 h. Preparative t.l.c. (ethyl acetate–petroleum, 2 : 1) gave 8-endo-*hydroxybicyclo*[4.2.1]*nonan-2-one* (0.8 g) as plates, m.p. 131—135 °C after sublimation (100 °C at 0.1 mmHg) (Found: C, 70.0; H, 9.2%; M^+, 154. $C_9H_{14}O_2$ requires C, 70.1; H, 9.15%; *M*, 154); $\nu_{max.}$ (film) 3 600—3 200 and 1 685 cm^{-1}; $\nu_{max.}$ (3.4×10^{-3}M in CCl_4) 3 600, 3 585—3 500, and 1 695 cm^{-1}; τ ($CDCl_3$) 5.2—5.6 (1 H, m, C*H*OH), 6.0 (1 H, s, removed by D_2O, CHO*H*), and 7.0—9.0 (12 H, envelope). The toluene-*p*-sulphonate was a gum; $\nu_{max.}$ (film) 1 690 cm^{-1}; τ ($CDCl_3$) 6.0—6.2 (1 H, q, C*H*OTs). Treatment of the tosylate with ethanolic sodium ethoxide or with potassium t-butoxide in dimethyl sulphoxide at room temperature gave no reaction; with the t-butoxide at 75 °C only highly polar products which did not migrate in t.l.c. were formed.

Bicyclo[4.2.1]*non-7-en-2-one* (9).—A solution of the foregoing toluene-*p*-sulphonate (0.5 g) in 2,4,6-collidine (15 ml) was boiled for 18 h, cooled, and acidified with 2M-hydrochloric acid. The recovered product was purified by preparative t.l.c. and gave *bicyclo*[4.2.1]*non-7-en-2-one* (0.11 g) as flakes on sublimation (40 °C at 0.1 mmHg), m.p. 39—41 °C (Found: C, 79.5; H, 9.0%; M^+, 136. $C_9H_{12}O$ requires C, 79.4; H, 8.9%; *M*, 136); $\nu_{max.}$ (film) 1 695 and 760 cm^{-1}; $\lambda_{max.}$ (95% EtOH) 292 nm (ε 204); τ ($CDCl_3$) 4.0—4.4 (2 H, m, CH=CH) and 6.8—8.6 (10 H, envelope). Hydrogenation over palladium–charcoal gave bicyclo[4.2.1]nonan-2-one, m.p. 91—92 °C (lit.,[17] 91—92 °C); the semicarbazone formed needles, m.p. and mixed m.p. 193—194 °C.

Bicyclo[4.2.1]non-7-en-2-one was also produced in varying amounts by treatment of 8-*exo*-chlorobicyclo[4.2.1]-nonan-2-one (prepared from the *endo*-alcohol with phosphoryl chloride in pyridine) with potassium t-butoxide in tetrahydrofuran at −78 °C, or with sodium amide in boiling toluene. Other experiments with the chloride using 2,4,6-collidine, 1,5-diazabicyclo[4.3.0]non-5-ene, potassium t-butoxide in dimethyl sulphoxide, or lithium chloride in dimethylformamide, at room temperature or higher, led either to no reaction or to the formation of material which did not migrate in t.l.c.

Reactions of Bicyclo[4.2.1]*non-1-en-8-one*.—(a) *With diethyl malonate*. A solution of the ketone (50 mg) in ethanol (2 ml) was added to a cooled (−10 °C) solution of diethyl sodiomalonate [from diethyl malonate (60 mg) and sodium (90 mg) in ethanol (20 ml)]. After 3 h at room temperature the product (110 mg) was isolated and purified by preparative t.l.c. [ethyl acetate–petroleum (2 : 1)], giving *diethyl* 2-(8-*oxobicyclo*[4.2.1]*nonan-1-yl*)*malonate* as an oil, b.p. 150 °C at 0.1 mmHg (air-bath temperature) (Found: C, 64.7; H, 8.5%; M^+, 296. $C_{16}H_{24}O_5$ requires C, 64.8; H, 8.2%; *M*, 296); $\nu_{max.}$ (film) 1 750 and 1 730 cm^{-1}; τ ($CDCl_3$) 5.7—6.0 (4 H, qd, $CO_2{\cdot}CH_2{\cdot}CH_3$), 7.3—7.45 [1 H, d, $CH(CO_2Et)_2$], 7.1—7.4 (1 H, m, CHCO), and 7.5—9.0 (12 H, envelope). The compound showed only one spot on t.l.c. (eluant ethyl acetate–petroleum, 1 : 1) and gave only one peak on g.l.c. (3% SE 30; 165 °C).

(b) *With lithium dimethylcuprate*. A solution of bicyclo-[4.2.1]non-1-en-8-one (50 ml) in ether (3 ml) was added to a cold (−10 °C) solution of lithium dimethylcuprate [from methyl-lithium (50 mg) and copper(I) iodide (200 mg) in ether (15 ml)]. The mixture was stirred at −10 °C for 1 h, then decomposed with aqueous ammonium chloride. The recovered product (60 mg) was purified by preparative t.l.c. (ethyl acetate–petroleum, 1 : 4) and gave 2-*methylbicyclo*[4.2.1]*nonan-8-one* as an oil, b.p. 80 °C at 0.05 mmHg (Found: C, 79.1; H, 11.1%; M^+, 152. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%; *M*, 152); $\nu_{max.}$ (film) 1 740 cm^{-1}; τ ($CDCl_3$) 7.5—9.0 (13 H, envelope, ring CH_2 and CH) and 9.0—9.3 (3 H, two d in ratio 6 : 1, CH_3). An attempt to trap the intermediate enolate by reaction with methyl iodide or trimethylsilyl chloride at −10 °C gave only the above 2-methyl compound.

Deuterium Incorporation Experiments on Bicyclo[4.2.1]-*nonan-2-one and -8-one*.—These were carried out by the method of Schaefer and Lark.[18]

[17] K. H. Baggaley, J. R. Dixon, J. M. Evans, and S. H. Graham, *Tetrahedron*, 1967, **23**, 299; M. Hartmann, *Annalen*, 1969, **724**, 102.

[18] J. P. Schaefer and J. C. Lark, *J. Org. Chem.*, 1965, **30**, 1337.

The ketone (130 mg) in dioxan (5 ml) was heated at 95 °C for 7 days in a sealed tube with a solution prepared from sodium (15 mg) and deuterium oxide (5 ml). The incorporation of deuterium was estimated from the intensities of the peaks in the mass spectrum at *m/e* 139, 140, and 141 (Table). In the ^1H n.m.r. spectrum of bicyclo-[4.2.1]nonan-2-one determined in the presence of the shift reagent $Eu(fod)_3$, the signals due to the three hydrogen atoms adjacent to the carbonyl group were clearly discernible as a quartet (bridgehead CH) and a triplet (CH_2) at τ 6.4 and 6.8; after deuteriation the triplet was not observed and the quartet was reduced to *ca.* 60% of its original relative intensity. Similarly in the ^1H n.m.r. spectrum of bicyclo[4.2.1]nonan-8-one in the presence of $Eu(fod)_3$, the signals due to the α-protons gave a complex group of peaks at τ 4.8—5.6; these signals had almost completely disappeared after deuteriation.

Mass spectral data from deuteriated bicyclo[4.2.1]nonan-2-one and -8-one

	Rel. intensities (total 100%)	
m/e	Bicyclo[4.2.1]nonan-2-one	Bicyclo[4.2.1]nonan-8-one
139	3.2	1.9
140	59.9	11.1
141	36.9	86.9

Cyclisation of Oxo-acids with Naphthalene-2-sulphonic Acid.—In a typical experiment (first carried out by Dr. M. I. Qureshi), 4-(2-oxocyclopentyl)butyric acid (1.08 g) and naphthalene-2-sulphonic acid (0.2 g) were heated under reflux in xylene (40 ml) for 24 h, with azeotropic removal of water. The recovered neutral oil (0.8 g) gave spiro[4.4]-nonane-1,6-dione (0.6 g) as plates, m.p. 38—39 °C (from petroleum) (lit.,[19] 37—38 °C) after distillation at 109—111 °C and 12 mmHg; $\nu_{max.}$ (CCl_4) 1 750 and 1 725 cm^{-1}. The bis-semicarbazone had m.p. 264—265 °C (lit.,[19] 262 °C) and the bis-oxime had m.p. 231—233 °C, undepressed when mixed with an authentic specimen (lit.,[19] 234—235 °C).

In a similar way 5-(2-oxocyclopentyl)valeric acid and 4-(2-oxocyclohexyl)butyric acid were converted into spiro-[4.5]decane-1,6-dione [70—75% yield after distillation at 66—68 °C and 0.05 mmHg (air-bath temperature)]; $\nu_{max.}$ (film) 1 740 and 1 730 cm^{-1} (doublet). The *monosemicarbazone* formed needles in water, m.p. 204—206 °C (Found: C, 59.4; H, 7.8; N, 18.6. $C_{11}H_{17}N_3O_2$ requires C, 59.2; H, 7.7; N, 18.8%).

With 5-(2-oxocyclohexyl)valeric acid (2.0 g) and naphthalene-2-sulphonic acid (0.4 g) in boiling xylene (160 ml) for 48 h a mixture of two products (1.6 g) was obtained in the ratio 3 : 2 (g.l.c.). These were separated by preparative g.l.c. (15% SE 30; 150 °C). The minor product, with the shorter retention time, was *spiro[5.5]undecan-1,7-dione*, which formed crystals, m.p. 38—40 °C, after distillation at 100—102 °C at 0.05 mmHg (air-bath temperature) (Found: C, 73.5; H, 9.0%; M^+, 180. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%; *M*, 180); $\nu_{max.}$ (KBr) 1 710 and 1 700 cm^{-1}; $\lambda_{max.}$ (95% EtOH) 288 nm (ε 72). The other product was distilled (b.p. 100—102 °C at 0.05 mmHg) and crystallised from petroleum, giving *2-oxabicyclo[6.4.0]dodec-1(8)-en-3-one* as blades, m.p. 77—79 °C (Found: C, 73.0; H, 9.1%; M^+, 180. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%; *M*, 180); $\nu_{max.}$ (KBr) 1 760 cm^{-1}; the u.v. spectrum showed only end absorption; τ ($CDCl_3$) 7.5—9.0 (envelope). The compound was resistant to hydrogenation over 10% palladium–charcoal at room temperature; it dissolved readily on warming with alcoholic 10% potassium hydroxide to give, on acidification of the solution, 5-(2-oxocyclohexyl)valeric acid, identified by mixed m.p. of the crystalline 2,4-dinitrophenylhydrazone.

(5R*,6R*)-6-*Hydroxyspiro*[4.4]*nonan*-1-*one* (2) *and* (5R*,6R*)-6-*Hydroxyspiro*[4.5]*decan*-1-*one*.—A solution of spiro[4.4]nonane-1,6-dione (1 g) in tetrahydrofuran (10 ml) was added to a stirred solution of lithium hydridotri-t-butoxyaluminate (3 g) in tetrahydrofuran (140 ml) under nitrogen at −30 °C. After 24 h the mixture was acidified and extracted with ether. The recovered oil (0.95 g) was largely (95%) one product (g.l.c.), and on distillation gave (5*R**,6*R**)-6-hydroxyspiro[4.4]nonan-1-one, b.p. 112 °C at 0.05 mmHg (air-bath temperature) (Found: C, 70.3; H, 9.25. Calc. for $C_9H_{14}O_2$: C, 70.1; H, 9.15%); $\nu_{max.}$ (2.7 × 10^{-3}M in CCl_4) 3 650 and 3 520 cm^{-1}. The *p*-nitrobenzoate had m.p. 83.5 °C (lit.,[14] 86.5—87 °C), and the *toluene-p-sulphonate* formed needles, m.p. 99.5—100.5 °C (from toluene–petroleum) (Found: C, 62.5; H, 6.8; S, 10.1. $C_{16}H_{20}O_4S$ requires C, 62.3; H, 6.5; S, 10.3%).

Reduction of spiro[4.5]decane-1,6-dione (0.75 g) under the same conditions gave (5*R**,6*R**)-6-hydroxyspiro[4,5]-decan-1-one [2] (90%), b.p. 80—82 °C at 0.05 mmHg (air-bath temperature) (Found: C, 71.45; H, 9.6%. Calc. for $C_{10}H_{16}O_2$: C, 71.4; H, 9.6%); $\nu_{max.}$ (film) 3 500—3 300 and 1 730 cm^{-1}; $\nu_{max.}$ (1.25 × 10^{-3}M in CCl_4) 3 650 and 3 530 cm^{-1}. The *toluene-p-sulphonate* formed needles in toluene–petroleum, m.p. 89—90 °C (Found: C, 63.1; H, 6.7. $C_{17}H_{22}O_4S$ requires C, 63.3; H, 6.9%); $\nu_{max.}$ ($CHCl_3$) 1 735 cm^{-1}.

1,2,3,5,6,7-*Hexahydroinden*-4-*one and* 3,4,5,6,7,8-*Hexahydronaphthalen*-1(2H)-*one*.—A solution of (5*R**,6*R**)-6-tosyloxyspiro[4.4]nonan-1-one (0.3 g) in collidine (10 ml) was boiled for 20 h. The cooled solution was acidified with dilute hydrochloric acid and extracted with ether. The recovered oil (0.11 g) showed one major spot on t.l.c. Purification by preparative t.l.c. and distillation gave 1,2,3,5,6,7-hexahydroinden-4-one, b.p. 90 °C at 0.05 mmHg (Found: C, 79.2; H, 9.15%; M^+, 136. Calc. for $C_9H_{12}O$: C, 79.4; H, 8.9%; *M*, 136); $\nu_{max.}$ (film) 1 650 cm^{-1}; $\lambda_{max.}$ (95% ethanol) 250 (ε 13 400) and 305 nm (65.4). The oxime had m.p. 132—133 °C (lit., 135.5—136.5 °C), and the dark red 2,4-dinitrophenylhydrazone, m.p. 245—247 °C (decomp.) [lit.,[15] 252.5 (decomp.)]. Hydrogenation over 5% palladium–charcoal gave *cis*-perhydroindan-4-one; oxime, m.p. 132—133 °C (lit.,[20] 136 °C).

(5*R**,6*R**)-6-Tosyloxyspiro[4.5]decan-1-one similarly gave 3,4,5,6,7,8-hexahydronaphthalen-1(2*H*)-one, b.p. 140—145° at 0.25 mmHg (air-bath temperature); $\nu_{max.}$ (film) 1 660 cm^{-1}; semicarbazone, m.p. 233—235 °C (lit.,[21] 243 °C); 2,4-dinitrophenylhydrazone, m.p. 264—165 °C (lit.,[15] 264—265 °C).

Reaction of (5*R**,6*R**)-6-tosyloxyspiro[4.4]nonan-1-one (480 mg) with the solution from sodium (36 mg) in ethanol (20 ml) under reflux for 20 h gave ethyl 4-(1-cyclopentenyl)-butyrate (280 mg), b.p. 70 °C at 0.05 mmHg (air-bath temperature); $\nu_{max.}$ (film) 1 725 cm^{-1}; τ ($CDCl_3$) 4.75 (1 H, s, C=CH), 5.8—6.1 (2 H, q), 7.6—8.4 (12 H, envelope), and 8.7—8.9 (3 H, t); M^+ 182. Hydrogenation over 5% palladium–charcoal gave ethyl 4-cyclopentylbutyrate, identified by mixed m.p. of the *anilide* with an authentic

[19] D. J. Cram and H. Steinberg, *J. Amer. Chem. Soc.*, 1954, **76**, 2753.

[20] W. Hückel and R. Schlüter, *Ber.*, 1934, **67B**, 2107.

[21] W. Hückel and M. Blohm, *Annalen*, 1933, **502**, 114.

specimen, m.p. 79—81° (feathers from toluene–petroleum) (Found: C, 78.1; H, 9.05; N, 6.0%. $C_{15}H_{21}NO$ requires C, 77.9; H, 9.15; N, 6.05%).

We are indebted to Allen and Hanburys Limited for financial support to A. O.

[7/689 *Received*, 25*th April*, 1977]