Steroid Analogues. Part 1. Preparation of Intermediates containing Rings C and D

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(±)-7β-Hydroxy-6β-methyl-*trans*-bicyclo[4.3.0]nonan-3-one (6) and (±)-*rel*-(1*R*,6*R*,7*R*)-7-[(1*R*)-1-hydroxyethyl]-6-methylbicyclo[4.3.0]nonan-3-one (10), key intermediates for the synthesis of 6,7-dinor-5,8-secoestr-9-enes, were prepared from (±)-6-methyl-*trans*-bicyclo[4.3.0]nonane-3,7-dione (4). Reduction of (4) with a modified Henbest reagent (hexachloroiridic acid–trimethyl phosphite–triethylamine–aqueous propan-2-ol) gave (±)-3α-hydroxy-6β-methyl-*trans*-bicyclo[4.3.0]nonan-7-one (13) as the major product; with Lalancette's reagent (sulphurated sodium borohydride) the (±)-3β-hydroxy-epimer (15) was formed. Surprisingly, reduction of (±)-6-methyl-*cis*-bicyclo[4.3.0]nonane-3,7-dione (19) with either the Henbest or the Lalancette reagent gave (±)-3α-hydroxy-6β-methyl-*cis*-bicyclo[4.3.0]nonan-7-one (20).

OVER many years series of steroids which possess a wide range of pharmacological action have been developed. Simultaneously there has been a search for non-steroidal analogues possessing the attributes of the therapeutically useful steroids but not their undesirable side-effects. Among these analogues have been compounds based on a structure formed from rings A, C, and D of the steroid nucleus. Derivatives of 3-phenyl-6-methylbicyclo-[4.3.0]nonane [1] [*e.g.* (1)] have not yet found a commercial use, while compounds related to the cyclohexylindanecarboxylic acid (2) are reported [2] to possess systemic anti-inflammatory activity.

In all compounds of this type so far reported, however, rings A and C are joined by a single bond. We wished to prepare compounds with the basic skeleton (3), in which rings A and C are joined by an olefinic linkage, since the lack of rotation about the double bond, combined with the predicted all-chair conformation for rings A and C, would afford new compounds with an overall shape very similar to that of a steroid.

We considered that the most convenient synthetic approach to these compounds lay in the condensation of preformed intermediates corresponding to ring A and rings C and D. This paper describes the preparation of the latter components; the various methods used to couple them with ring A intermediates will be described in later papers.[3-6]

Our principal targets were the hydroxy-ketones (6) and (10); these were prepared by selective modification of the 7-carbonyl group of (±)-6-methyl-*trans*-bicyclo-[4.3.0]nonane-3,7-dione (4), whose synthesis has been reported recently by several groups.[7-10] Selective acetalisation of the six-membered ring carbonyl group of the dione (4) was achieved by treatment with toluene-*p*-sulphonic acid in anhydrous methanol; the dimethyl acetal (5) was not isolated but was reduced *in situ* with sodium borohydride. Deacetalisation of the product gave the desired hydroxy-ketone (6),[10] which was conveniently separated *via* its water-soluble hydrogen sulphite complex from small amounts of the diol (16). The latter probably arose by reduction of the dione (4) which contaminated the acetal (5). The hydroxy-ketone (6), or a suitable derivative thereof, was used as the key intermediate in the synthesis of analogues of 17-oxo-steroids, to be described in later papers.[4-6]

As the dimethyl acetal (5) was very labile, we sought a more stable protecting group for the 3-carbonyl group of (4) before embarking on the preparation of a more complex synthon for use in the preparation of pregnane analogues. Attempted selective formation of an ethylene acetal was unsuccessful, as both carbonyl groups were

[1] See, for example, C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 1960, **4547**; H. Schick and G. Hilgetag, *J. prakt. Chem.*, 1971, **312**, 837.

[2] P. F. Juby, T. W. Hudyma, and R. A. Partyka, *J. Medicin. Chem.*, 1972, **15**, 120; P. F. Juby, W. R. Goodwin, T. W. Hudyma, and R. A. Partyka, *ibid.*, p. 1297; S. Noguchi, S. Kishimoto, I. Minamida, and M. Obayashi, *Chem. and Pharm. Bull. (Japan)*, 1974, **22**, 529; S. Noguchi, M. Obayashi, S. Kishimoto, and M. Imanishi, *ibid.* p. 537.

[3] D. J. Humphreys, P. M. Lawrence, and C. E. Newall, following paper.

[4] D. J. Humphreys, P. M. Lawrence, C. E. Newall, G. H. Phillipps, and P. A. Wall, *J.C.S. Perkin I*, 1978, 24.

[5] D. J. Humphreys and C. E. Newall, *J.C.S. Perkin I*, 1978, 33.

[6] D. J. Humphreys, C. E. Newall, G. H. Phillipps, and G. A. Smith, *J.C.S. Perkin I*, 1978, **45**.

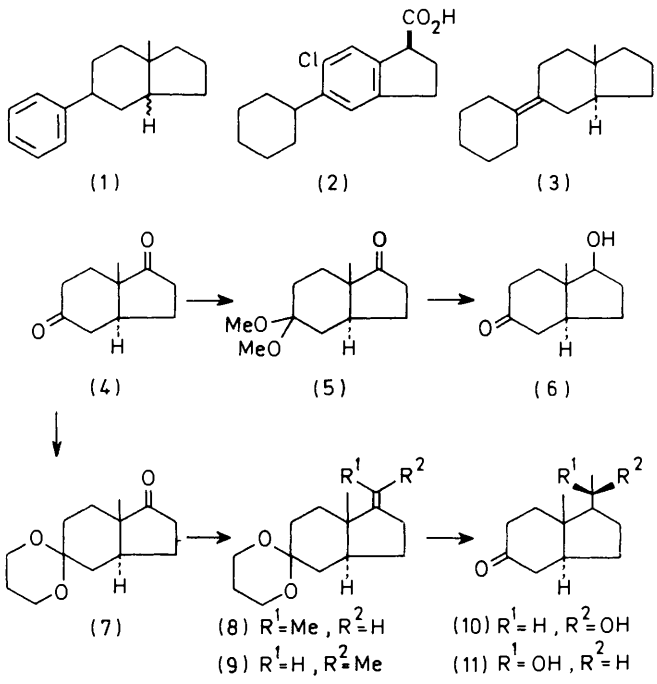
[7] K. H. Baggeley, S. G. Brooks, J. Green, and B. T. Redman, *J. Chem. Soc. (C)*, 1971, 2671.

[8] G. S. Grinenko, E. V. Popova, and V. I. Maksimov, *Zhur. org. Khim.*, 1971, **7**, 935.

[9] U. Eder and H. P. Lorenz (Schering A.G.), Ger. Offen. 2,131,230 (*Chem. Abs.* 1973, **78**, 71,769d).

[10] Z. G. Hajos and D. R. Parrish, *J. Org. Chem.*, 1973, **38**, 3239.

attacked; however, the use of propane-1,3-diol resulted in the mono(trimethylene) acetal (7), the crude product being sufficiently pure for use in subsequent reactions. Reaction of (7) with ethylidenetriphenylphosphorane

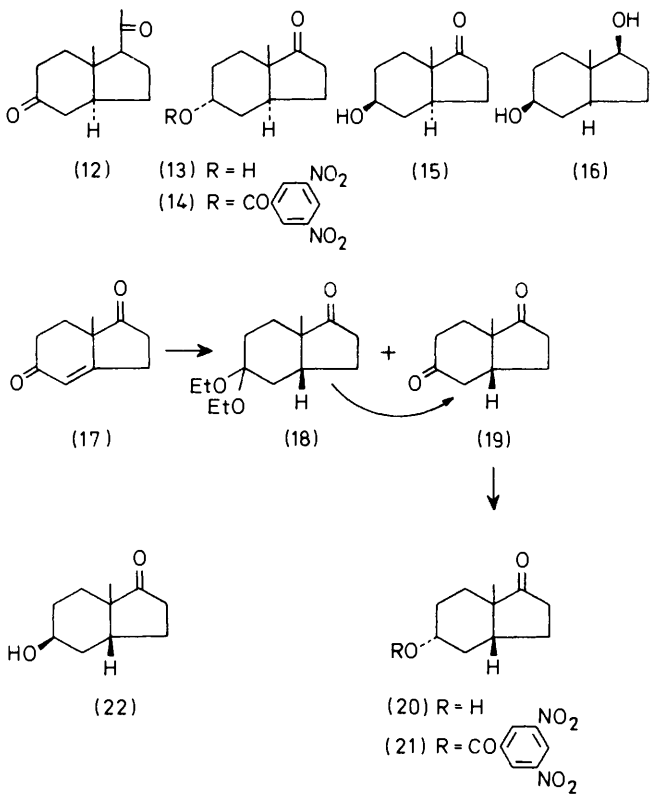


gave a mixture of the *Z*- and *E*-ethylidene acetals (8) and (9), respectively, in the ratio 20 : 1 (by g.l.c.). This mixture was subjected to hydroboration–oxidation to give, after deacetalisation, a mixture of the hydroxy-ketones (10) and (11) in the ratio 8 : 1. Their structures were assigned by analogy with similar reaction sequences in the steroid series.[11] Oxidation of the mixture of hydroxy-ketones gave a single product, the dione (12); their reactions with ring A synthons to give pregnane analogues will be described in a later paper.[5]

We also examined methods for selective reduction of the carbonyl group in the six-membered ring of the dione (4). The hexachloroiridic acid–propan-2-ol–trimethyl phosphite reagent reported by Henbest [12] and further studied by Browne and Kirk [13] is both regiospecific and highly stereoselective; 5α- and 5β-3-oxosteroids are thereby reduced to the corresponding axial alcohols in high yield. Reduction of (4) with a modification [14] of the Henbest reagent gave, in high yield, a mixture of the axial and equatorial hydroxy-ketones (13) and (15), respectively, in the ratio 85 : 15; there was no evidence for attack on the 7-carbonyl group. The pure axial alcohol (13) was obtained by crystallisation of the mixture of 3,5-dinitrobenzoates,[15] followed by hydrolysis.

Lalancette *et al.*[16] have reported the selective reduction of steroidal 3-ketones by sulphurated sodium borohydride to give equatorial (3β-) alcohols in good yield. Reduction of the dione (4) with Lalancette's reagent gave a mixture comprising the axial alcohol (13) (3%), the equatorial alcohol (15) (36%), the diol (16) (21%), and starting material. The relative lack of stereospecificity with the modified Henbest reagent and of regiospecificity with Lalancette's reagent, as compared with the performance of these reagents in the steroid series, probably reflects the greater conformational mobility of the dione (4) relative to a steroid such as 5α-androstane-3,17-dione.

The *cis*-dione (19),[7] obtained by hydrogenation of the unsaturated dione (17), was also treated with the Henbest and Lalancette reagents; in each reaction the same hydroxy-ketone was obtained as the major product. This compound exhibited a carbonyl stretching band at 1 720 cm^{-1} ($CHBr_3$), indicating that reduction had taken place in the six-membered ring. The presence of a



broad multiplet ($W_{\frac{1}{2}}$ *ca.* 20 Hz) at τ 6.40 in the ^1H n.m.r. spectrum revealed that the hydroxy-group was in an equatorial configuration. Dreiding models of the epimeric alcohols (20) and (22) showed that either could exist in a conformation in which the hydroxy-group is equatorial to the chair form of the six-membered ring. In these conformations, the angular methyl group would

[11] J. Fried and J. A. Edwards, 'Organic Reactions in Steroid Chemistry,' vol. II, Van Nostrand–Reinhold, New York, 1972, p. 132.
[12] H. B. Henbest and T. R. B. Mitchell, *J. Chem. Soc.* (*C*), 1970, 785.
[13] P. A. Browne and D. N. Kirk, *J. Chem. Soc.* (*C*), 1969, 1653.
[14] J. C. Clayton, P. J. Faulkner, W. R. Jones, and G. H. Phillipps, U.S. 3,822,298.
[15] T. M. Dawson, P. S. Littlewood, B. Lythgoe, T. Medcalfe, M. W. Moon, and P. M. Tomkins, *J. Chem. Soc.* (*C*), 1971, 1292.
[16] J. M. Lalancette, A. Freche, J. R. Brindle, and M. Laliberté, *Synthesis*, 1972, 526.

be pseudo-axial to the five-membered ring in (20) and pseudo-equatorial in (22). On changing the ^1H n.m.r. solvent from deuteriochloroform to hexadeuteriobenzene an upfield shift of 0.28 p.p.m. was observed in the signal due to the angular methyl group. This shift is consistent [17] with an axial orientation of the methyl group relative to the five-membered ring, and the compound was therefore assigned structure (20).

In hexadeuteriobenzene the *cis*-dione (19) exhibits a large upfield shift (0.42 p.p.m.) in the resonance of the methyl group, suggesting that in this compound also the methyl group is axial to the five-membered ring. In this conformation there appears to be little difference in the degree of steric hindrance on either side of the six-membered ring, and we are unable to account for the reversal of the normal stereoselectivity of the Henbest reagent experienced in the reduction of the *cis*-dione (19).

EXPERIMENTAL

Unless otherwise stated, m.p.s were determined for samples in unsealed capillaries and are corrected; i.r. spectra were measured on solutions in bromoform; u.v. spectra were determined on solutions in ethanol; and n.m.r. spectra were obtained for solutions in deuteriochloroform. Preparative thin-layer chromatography (p.l.c.) was carried out using plates coated with a 2 mm layer of Merck Kieselgel $PF_{254+366}$. 'Petrol' refers to light petroleum (b.p. 40—60 °C). Solutions in organic solvents were dried over sodium sulphate or magnesium sulphate.

(±)-7β-*Hydroxy*-6β-*methyl*-trans-*bicyclo*[4.3.0]*nonan*-3-*one* (6).—(±)-6-Methyl-*trans*-bicyclo[4.3.0]nonane-3,7-dione (4) (1.88 g, 11.3 mmol) in dry methanol (20 ml) was treated with toluene-*p*-sulphonic acid hemihydrate (3 mg) and Type 4A molecular sieve (1 g), and the mixture was set aside at room temperature overnight. The solution was rapidly adjusted to pH 8 with sodium ethoxide in ethanol and filtered, and the sieves were washed with propan-2-ol (40 ml). The combined filtrates were stirred with sodium borohydride (440 mg, 11.6 mmol) in water (5 ml) for 30 min. Acetic acid (1 ml) was added and the solution was evaporated to small bulk and stirred for 30 min with acetone (50 ml) and 2N-sulphuric acid (10 ml). The acetone was removed, water (30 ml) was added,* and the mixture was extracted with dichloromethane. The extracts were washed with water, dried, and evaporated to give the ketol (6) [10] (1.55 g, 81%) as a light brown oil, $\nu_{max.}$ 3 595 and 3 425 (OH) and 1 700 cm^{-1} (C=O), τ 9.01 (3 H, s, CH_3) and 6.21 (1 H, m, C*H*OH), g.l.c. purity 94% (Found: C, 69.8; H, 9.5. Calc. for $C_{10}H_{16}O_2,0.25H_2O$: C, 69.55; H, 9.65%).

(±)-6-*Methyl*-3,3-*trimethylenedioxy*-trans-*bicyclo*[4.3.0]-*nonan*-7-*one* (7).—The dione (4) (607 mg, 3.66 mmol) in propane-1,3-diol (5 ml) was treated with toluene-*p*-sulphonic acid (18 mg) and set aside at 20 °C in the dark for 5 days. 5% Sodium hydrogen carbonate (20 ml) was added and the mixture was extracted with dichloromethane. The extracts were filtered, treated with a drop of pyridine, and evaporated to give a yellow viscous oil (851 mg), which was purified by passage through alumina. It gave (from petrol) crystals of the *acetal* (7), m.p. 85—89°, $\nu_{max.}(CS_2)$ 1 730 cm^{-1} (C=O), τ 9.09 (3 H, s, CH_3) (Found: C, 69.3; H, 8.9. $C_{13}H_{20}O_3$ requires C, 69.6; H, 9.0%).

* It is important that after removal of the acetone sufficient water be added to give a fairly dilute solution, otherwise the 3β,7β-diol (16) [18] may be salted out into the organic phase.

(±)-(Z)-7-*Ethylidene*-6-*methyl*-trans-*bicyclo*[4.3.0]*nonan*-3-*one Trimethylene Acetal* (8).—80% Sodium hydride in oil (1.5 g, 50 mmol) was washed with dry hexane (3 ×), dried in a stream of dry nitrogen, and stirred at 60—70 °C under nitrogen with dry dimethyl sulphoxide (40 ml) until a green solution was obtained, which was then allowed to cool to room temperature. A solution of ethyltriphenylphosphonium iodide (20.9 g, 50 mmol) in dry dimethyl sulphoxide (80 ml) was added to give a red solution. The acetal (7) (2.55 g, 11.4 mmol) in dry benzene (50 ml) was added and the mixture was stirred at 50—70 °C under nitrogen for 2 h, then poured into ice–water (600 ml). The mixture was extracted with petrol (4 × 100 ml) and the extracts were washed with water (2 × 50 ml), filtered, treated with a few drops of pyridine, and kept at 5 °C overnight. After removal of crystalline triphenylphosphine oxide, the solution was evaporated and the residue was chromatographed on alumina. Petrol eluted triphenylphosphine and ether eluted the *ethylidene derivative* (8) as a golden oil (1.545 g, 57%), τ 9.09 (3 H, s, CH_3), 8.40 (3 H, d, *J* 7 Hz, =CHC*H*$_3$), and 4.86 (1 H, q, *J* 7 Hz, =C*H*CH_3) (some coupling with 8-H) (Found: C, 76.3; H, 10.2. $C_{15}H_{24}O_2$ requires C, 76.2; H, 10.2%).

(±)-rel-(1R,6R,7R)-7-[(1R)-1-*Hydroxyethyl*]-6-*methylbicyclo*[4.3.0]*nonan*-3-*one* (10).—Boron trifluoride–diethyl ether complex (10 ml) in dry ether (10 ml) and dry bis-(2-methoxyethyl) ether (10 ml) was added slowly under nitrogen to a stirred suspension of sodium borohydride (4.0 g) in dry bis-(2-methoxyethyl) ether (40 ml). The resulting stream of diborane was passed into a solution of the acetal (8) (1.24 g, 5.25 mmol) in dry tetrahydrofuran (50 ml) at room temperature. After 1 h, the diborane generator was disconnected and the mixture was cooled to 0—5 °C, stirred, and treated cautiously with 2N-sodium hydroxide (20 ml) followed by 30% hydrogen peroxide (5 ml). Vigorous stirring was continued for a further 15 min, after which water (50 ml) was added and the mixture was extracted with dichloromethane. The extracts were washed with freshly prepared 4% iron(II) sulphate and water, dried, and evaporated to a gum (1.388 g).

The product was dissolved in acetone (25 ml) and treated with 2N-sulphuric acid. After 1 h, most of the acetone was removed *in vacuo* and the residue was treated with water and extracted with dichloromethane. The extracts were washed with water, filtered, and evaporated to a gum (955 mg) which was stirred for 10 min with aqueous 20% sodium hydrogen sulphite (25 ml). Ether (25 ml) was added and the mixture was stirred vigorously for a further 15 min. The aqueous phase was treated with potassium carbonate (10 g) and 2N-sodium hydroxide (to pH 10) and extracted with dichloromethane. The extracts were washed with water, filtered, and evaporated to give the *hydroxy-ketone* (10) as a gum (825 mg, 80%), $\nu_{max.}$ 3 600 (OH) and 1 700 cm^{-1} (C=O), τ 9.08 (3 H, s, CH_3), 8.75 [3 H, d, *J* 7 Hz, CH(OH)C*H*$_3$], and 6.18 [1 H, q, *J* 7 Hz, C*H*(OH)CH_3] (Found: C, 73.3; H, 10.4. $C_{12}H_{20}O_2$ requires C, 73.4; H, 10.3%).

(±)-7β-*Acetyl*-6β-*methyl*-trans-*bicyclo*[4.3.0]*nonan*-3-*one* (12).—A solution of the hydroxy-ketone (10) (2.00 g, 10.2 mmol) in acetone (50 ml) was cooled to 0—5 °C and treated

[17] N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964.

[18] V. Prelog and D. Zäch, *Helv. Chim. Acta*, 1959, **42**, 1862.

dropwise with Jones reagent. Water (200 ml) was then added and the product was extracted into dichloromethane. The extracts were washed with water and evaporated to an oil (1.96 g, 99%) which solidified. It gave (from ether) crystals of the *dione* (12), m.p. 68.5—71.5°, $\nu_{max.}$ 1 700 cm^{-1} (C=O), τ 9.10 (3 H, s, CH_3) and 7.84 (3 H, s, $COCH_3$) (Found: C, 73.9; H, 9.3. $C_{12}H_{18}O_2$ requires C, 74.2; H, 9.3%).

(±)-3α-(3,5-*Dinitrobenzoyloxy*)-6β-*methyl*-trans-*bicyclo*-[4.3.0]*nonan*-7-*one* (14).—The dione (4) (2.0 g, 12 mmol) was heated under reflux in a stock solution of hexachloroiridic acid [14] (15 ml) adjusted to pH 5 with triethylamine immediately before use. After 24 h the solution was evaporated to low volume, diluted with water, and extracted with dichloromethane, followed by chloroform. The combined extracts were washed with water, dried, and evaporated to give the crude 3α-hydroxy-ketone (13) as an oil (2.02 g, 99%).

This material (420 mg, 2.5 mmol) was treated with pyridine (5 ml) and 3,5-dinitrobenzoyl chloride (690 mg, 3 mmol) for 16 h at 20 °C, then 1 h at 100 °C. Water was added, followed by 2N-sulphuric acid, and the product was collected and dried under suction to give a fawn powder (508 mg). Extraction of the aqueous liquors yielded a further 532 mg of this fawn solid. The combined products were stirred with 5% sodium hydrogen carbonate and extracted with dichloromethane. The extract was filtered and evaporated to give a light brown gum (577 mg, 62%). Chromatography of the product on silica gel (ether as eluant) yielded the less polar component, which crystallised from ether to give the *dinitrobenzoate* (14) as rods (176 mg), m.p. 147.5—150° (Kofler), $\nu_{max.}$ 1 722 (C=O and ester), and 1 550 and 1 345 cm^{-1} (NO_2), $\lambda_{max.}$ 230 nm (ε 20 450), τ 9.03 (3 H, s, CH_3) and 4.50 (1 H, m, C*H*OCOAr) (Found: C, 56.5; H, 5.1; N, 7.7. $C_{17}H_{18}N_2O_7$ requires C, 56.35; H, 5.1; N, 7.7%).

(±)-3α-*Hydroxy*-6β-*methyl*-trans-*bicyclo*[4.3.0]*nonan*-7-*one* (13).—The dinitrobenzoate (14) (1.9 g, 5.25 mmol) in ethanol (150 ml) was stirred under nitrogen for 3 days with 2N-sodium hydroxide (10 ml). The mixture was filtered and the filtrate was evaporated to small volume and partitioned between water and dichloromethane. The organic phase was washed with water, dried, and evaporated to give the *axial alcohol* (13) [15] as a yellow oil (788 mg, 89%), $\nu_{max.}$ 3 625 (OH) and 1 730 cm^{-1} (C=O), τ 9.13 (3 H, s, CH_3) and 5.85 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz, *eq*-3-*H*) (Found: C, 71.4; H, 9.7. $C_{10}H_{16}O_2$ requires C, 71.5; H, 9.5%).

(±)-3β-*Hydroxy*-6β-*methyl*-trans-*bicyclo*[4.3.0]*nonan*-7-*one* (15).—Dry tetrahydrofuran (20 ml) was added with stirring to sulphurated sodium borohydride premix [Lalancette's reagent [16] (Alfa Inorganics), 800 mg, 6.03 mmol] at 0 °C under nitrogen, and the mixture was stirred for 1 h. The dione (4) (2.0 g, 12.06 mmol) in dry tetrahydrofuran (50 ml) was added dropwise with stirring, and the mixture was stirred under nitrogen for 2.5 h. 2N-Sodium hydroxide (15 ml) was added, then water (100 ml), and the product was extracted into dichloromethane. The extracts were washed with water, dried, and evaporated to a yellow oil (1.79 g). Traces of the dione (4) were removed by partition of the product between ether and 10% sodium hydrogen sulphite. The aqueous phase was thoroughly extracted with dichloromethane and the combined organic phases were evaporated to a gum (1.485 g). P.l.c. ($CHCl_3$–MeOH, 19 : 1) yielded as the less polar component the *equatorial alcohol* (15) [15] (796 mg, 39%), $\nu_{max.}$ 3 640 (OH) and 1 730 cm^{-1} (C=O), τ 9.09 (3 H, s, CH_3) and 6.32 (1 H, m, $W_{\frac{1}{2}}$ *ca.* 20 Hz, *ax*-3-*H*) (Found: C, 70.3; H, 9.7. $C_{10}H_{16}O_2$,-$0.125H_2O$ requires C, 70.5; H, 9.55%). G.l.c. showed that this material contained 8.6% of the axial alcohol (13). Further p.l.c. (acetone–petrol, 1 : 4) yielded material which contained only 2% of the axial isomer. The more polar component was identified as (±)-6β-methyl-*trans*-bicyclo[4.3.0]nonane-3β,7β-diol (16).[18]

(±)-6-*Methyl*-cis-*bicyclo*[4.3.0]*nonane*-3,7-*dione* (19).[17]—(a) *From* (±)-6-*methylbicyclo*[4.3.0]*non*-1-*ene*-3,7-*dione* (17). The enedione (17) [19] (416 mg, 2.54 mmol) was hydrogenated in ethanol (30 ml) over 5% palladium–charcoal (120 mg). P.l.c. (ether–benzene, 1 : 4) of the resulting oil gave as the more polar component the *cis*-dione (19) [7] (114 mg, 27%) as an oil which solidified, $\nu_{max.}$(CS_2) 1 730 [C(3)=O)] and 1 711 cm^{-1} [C(7)=O], τ($CDCl_3$) 8.75 (3 H, s, CH_3), τ(C_6D_6) 9.17 (3 H, s, CH_3), g.l.c. purity 97.8%. The less polar component, an oil (354 mg, 58%), was identified as (±)-3,3-*diethoxy*-6-*methyl*-cis-*bicyclo*[4.3.0]*nonan*-7-*one* (18), $\nu_{max.}$(CS_2) 1 719 cm^{-1} (C=O), τ 9.00 (3 H, s, CH_3), 8.88 and 8.83 (2 × 3 H, t, *J* 7 Hz, 2 × OCH_2CH_3), and 6.53 (2 × 2 H, q, *J* 7 Hz, 2 × OCH_2CH_3) (Found: C, 70.15; H, 10.1. $C_{14}H_{24}O_3$ requires C, 69.95; H, 10.05%).

(b) *From the diethyl acetal* (18). The diethyl acetal (18) (187 mg) in acetone (10 ml) was treated with 2N-sulphuric acid (1 ml) for 30 min, after which the solution was diluted with ether, washed with water, and evaporated. P.l.c. (ether–benzene, 1 : 4) of the residue afforded the *cis*-dione (19) (81 mg, 63%).

Reduction of 6β-*Methyl*-cis-*bicyclo*[4.3.0]*nonane*-3,7-*dione* (19).—(a) *With sulphurated sodium borohydride.* Lalancette's reagent [16] (1.2 g, 9.2 mmol) was stirred under nitrogen at 0 °C for 1 h in dry tetrahydrofuran (30 ml). A solution of the *cis*-dione (19) (3.0 g, 18.4 mmol) in dry tetrahydrofuran (50 ml) was added dropwise and the mixture was stirred for a further 3.5 h at 20 °C. 2N-Sodium hydroxide (20 ml) and water (100 ml) were added and the mixture was extracted with dichloromethane. The extracts were washed with water, dried, and evaporated and the residual yellow oil (2.69 g) was chromatographed over silica gel. Dichloromethane eluted sulphur, and the crude product (2.5 g) was eluted with ether. P.l.c. ($CHCl_3$–MeOH, 19 : 1) yielded as the main component (±)-3α-hydroxy-6β-methyl-*cis*-bicyclo[4.3.0]nonan-7-one (20) as a pale yellow oil, g.l.c. purity 92%, identical with that described below.

(b) *With hexachloroiridic acid.* The *cis*-dione (19) (5.0 g, 30.1 mmol) was heated under reflux in a stock solution of hexachloroiridic acid [14] (125 ml) adjusted to pH 5 with triethylamine immediately before use. After 22 h the mixture was partitioned between chloroform and brine and the organic phases were dried and evaporated. The residual yellow gum was treated with dry pyridine (50 ml) and 3,5-dinitrobenzoyl chloride (13.4 g, 58.1 mmol) for 65 h at 20 °C and 2 h at 100 °C. The mixture was then treated with water (100 ml) and ice-cold 2N-hydrochloric acid (500 ml), and extracted with dichloromethane. The extracts were washed with 5% sodium hydrogen carbonate and water, dried, and evaporated. Chromatography of the residue in ether over silica gel yielded a brown gum (11.0 g) which gave, from ether–dichloromethane, off-white rods, m.p. 114°. Two recrystallisations from acetone–petrol

[19] C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 1959, 2022; Z. G. Hajos, D. R. Parrish, and E. P. Oliveto, *Tetrahedron*, 1968, **24**, 2039.

yielded rods of the *dinitrobenzoate* (21), m.p. 130—132°, $\nu_{max.}$ 1 722 (C=O and ester) and 1 548 and 1 342 cm^{-1} (NO_2), $\lambda_{max.}$ 226 nm (ε 21 200), τ 8.95 (3 H, s, CH_3) and 4.92 (1 H, m, 3-H) (Found: C, 56.7; H, 5.1; N, 7.5. $C_{17}H_{18}N_2O_7$ requires C, 56.4; H, 5.0; N, 7.7%).

The dinitrobenzoate (21) (1.85 g, 5.1 mmol) was stirred for 2 h with ethanol (150 ml) and 2N-sodium hydroxide (10 ml). The mixture was filtered, evaporated to small volume, diluted with water, and extracted with dichloromethane. The extracts were washed with water, dried, and evaporated to give (±)-3α-*hydroxy*-6β-*methyl*-cis-*bicyclo*[4.3.0]*nonan*-7-*one* (20) as a dark yellow oil (771 mg, 90%), $\nu_{max.}$ 3 600 and 3 440 (OH) and 1 720 cm^{-1} (C=O), τ($CDCl_3$) 9.03 (3 H, s, CH_3) and 6.40 (1 H, m, $W_{\frac{1}{2}}$ *ca.* 20 Hz, *ax*-3-H), τ(C_6D_6) 9.31 (3 H, s, CH_3) and 6.68 (1 H, m, 3-H) (Found: C, 71.3; H, 9.7. $C_{10}H_{16}O_2$ requires C, 71.5; H, 9.5%).

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