

## Steroid Analogues. Part 3.<sup>1</sup> Preparation of 4-Cyclohexylidenecyclohex-2-enones and 6,7-Dinor-5,8-secoestra-4,9-dien-3-ones by Birch Reduction of 1-*p*-Methoxyphenylcycloalkanols

By David J. Humphreys,\* (Mrs.) Pamela M. Lawrence, Christopher E. Newall, Gordon H. Phillipps, and Peter A. Wall, Organic Chemistry Department, Glaxo Research Ltd., Greenford, Middlesex UB6 0HE

Reduction of 4-substituted 1-(*p*-methoxyphenyl)cyclohexanols (8)—(13) with lithium and ethanol in liquid ammonia, followed by hydrolysis, gave 4-(4-substituted cyclohexylidene)cyclohex-2-enones (14)—(22) as the major products; in some cases the corresponding 4-(4-substituted cyclohexyl)cyclohex-3-enones (36) were isolated.

Similar treatment of 3 $\xi$ -(*p*-methoxyphenyl)-6 $\beta$ -methyl-*trans*-bicyclo[4.3.0]nonane-3 $\xi$ ,7 $\beta$ -diol (47) afforded 17 $\beta$ -hydroxy-6,7-dinor-5,8-secoestra-4,9-dien-3-one (42) in moderate yield as a mixture of  $\Delta^{1,9}$  and  $\Delta^{4,9}$ -isomers.

4-Cyclohexylidenecyclohex-2-enol (57) was reduced with di-imide to give 4-cyclohexylidenecyclohexanol (58) as the major product.

IN continuation of our study of the synthesis of 6,7-dinor-5,8-seco-steroids in which rings A and C are joined by a double bond,<sup>1</sup> we now describe the preparation of some analogues of steroidal 4-en-3-ones. These were of interest both in their own right and as potential precursors of compounds in which ring A is saturated, apart from the exocyclic double bond.

We had two objectives: first, the synthesis of a number of 4-cyclohexylidenecyclohex-2-enones (which might be held to represent rings A and C of the steroid nucleus) bearing suitable substituents in the 4'-position, and of some closer analogues in which ring D was also present; secondly, the selective saturation of the disubstituted double bond in these dienones or derivatives thereof, in order to provide analogues of steroids with a saturated ring A.

Alkylidenecyclohexenones can be prepared conveniently by reduction of  $\alpha$ -substituted *p*-methoxybenzyl alcohols with lithium and ammonia, as described by Inhoffen.<sup>2</sup> Accordingly, the *p*-methoxybenzyl alcohols (8)—(13) were prepared.

**Preparation of *p*-Methoxybenzyl Alcohols.**—The reaction of 4-hydroxycyclohexanone (2)<sup>3</sup> with *p*-methoxyphenylmagnesium bromide yielded a mixture of the diols (9a and b) and their dehydration product (23). The yields were poor, possibly owing to the insolubility of the initially formed bromomagnesium salt of (2). Satisfactory yields were obtained (81% of mixed isomers and little or no dehydrated material) when 4-benzoyloxycyclohexanone (3)<sup>3</sup> was used as the starting material, the benzoyl group being removed during the reaction. In each case the *cis*-diol (9a) was the major product. The diols (9a and b) have been prepared previously<sup>4</sup> as intermediates in the synthesis of the hydroxy-ketone (26) but the isomers were not separated or characterised. The *cis*-diol (9a) was smoothly dehydrated by glacial acetic acid to give the unsaturated alcohol (23) along with some of the acetate (24).

We hoped to prepare the diols (10a and b) by treat-



<sup>1</sup> Part 2, D. J. Humphreys, P. M. Lawrence, and C. E. Newall, preceding paper.

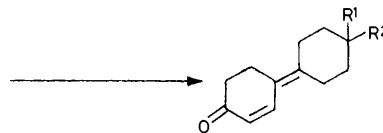
<sup>2</sup> H. H. Inhoffen, D. Kampe, and W. Milkowski, *Annalen*, 1964, **674**, 28.

<sup>3</sup> E. R. H. Jones and F. Sondheimer, *J. Chem. Soc.*, 1949, 615. For a more convenient preparation of 4-hydroxycyclohexanone, see P. Radlick and H. T. Crawford, *J. Org. Chem.*, 1972, **37**, 1669.

ment of the hydroxy-ketone (26)<sup>4</sup> with methyl-lithium. Oxidation of the diols (9a and b) with Jones reagent gave in one instance a 77% yield of the required ketone (26);<sup>4</sup> however, the reaction was not reproducible as dehydration to the unsaturated ketone (25) occurred to



- |   |   |
|---|---|
| (1) R <sup>1</sup> = R <sup>2</sup> = H   | (8) R <sup>1</sup> = R <sup>2</sup> = H   |
| (2) R <sup>1</sup> = H, R <sup>2</sup> = OH   | (9a) R <sup>1</sup> = H, R <sup>2</sup> = OH  |
| (3) R <sup>1</sup> = H, R <sup>2</sup> = OBz  | (9b) R <sup>1</sup> = OH, R <sup>2</sup> = H  |
| (4) R <sup>1</sup> = Me, R <sup>2</sup> = OH  | (10a) R <sup>1</sup> = Me, R <sup>2</sup> = OH  |
| (5) R <sup>1</sup> = H, R <sup>2</sup> = CH <sub>2</sub> CH(OH)Me   | (10b) R <sup>1</sup> = OH, R <sup>2</sup> = Me  |
| (6) R <sup>1</sup> = H, R <sup>2</sup> = CH <sub>2</sub> -  | (11) R <sup>1</sup> , R <sup>2</sup> = H, CH <sub>2</sub> CH(OH)Me  |
| (7) R <sup>1</sup> = H, R <sup>2</sup> = CH <sub>2</sub> CO <sub>2</sub> H  | (12) R <sup>1</sup> , R <sup>2</sup> = H, CH <sub>2</sub> -  |
|   | (13) R <sup>1</sup> , R <sup>2</sup> = H, CH <sub>2</sub> CO <sub>2</sub> H   |



- |  |
|--|
| (14) R <sup>1</sup> = R <sup>2</sup> = H                                     |
| (15) R <sup>1</sup> = H, R <sup>2</sup> = OH                                 |
| (16) R <sup>1</sup> = H, R <sup>2</sup> = OAc                                |
| (17) R <sup>1</sup> R <sup>2</sup> = O                                       |
| (18) R <sup>1</sup> = Me, R <sup>2</sup> = OH                                |
| (19) R <sup>1</sup> = H, R <sup>2</sup> = CH <sub>2</sub> COMe               |
| (20) R <sup>1</sup> = H, R <sup>2</sup> = CH <sub>2</sub> CH(OH)Me           |
| (21) R <sup>1</sup> = H, R <sup>2</sup> = CH <sub>2</sub> CO <sub>2</sub> H  |
| (22) R <sup>1</sup> = H, R <sup>2</sup> = CH <sub>2</sub> CO <sub>2</sub> Me |

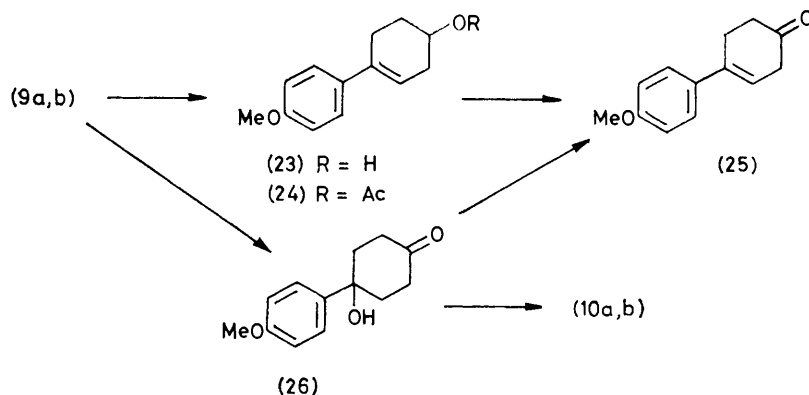
various extents (*cf.* ref. 4). Moffatt oxidation<sup>5</sup> of (9a) gave a mixture of the unsaturated ketone (25) and the corresponding alcohol (23). Reaction of (26) with methyl-lithium on a small scale resulted in a mixture of the diols (10a and b) in which the *cis*-isomer (10a) predominated.

<sup>4</sup> D. Lednicer, D. E. Emmert, R. Lahti, and A. D. Rudzik, *J. Medicin. Chem.*, 1972, **15**, 1239.

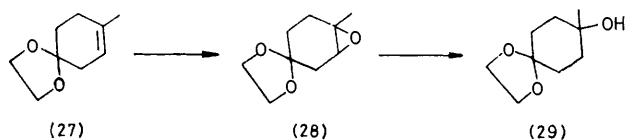
<sup>5</sup> K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, 1965, **87**, 5661, 5670.

4-Hydroxy-4-methylcyclohexanone (4)<sup>6</sup> has not been readily available hitherto and we sought a convenient procedure for its preparation on a larger scale, with mixed success. Birch reduction of *p*-methoxytoluene and treatment of the product with ethylene glycol and toluene-*p*-sulphonic acid afforded the acetal (27) in 86% yield. Payne<sup>7</sup> and others<sup>8</sup> have described an efficient

The ketones (5) and (6) were prepared by Birch reduction of *p*-methoxyphenylacetone and of its ethylene acetal, respectively, followed by acidic hydrolysis and hydrogenation of the resulting cyclohex-3-enones. Their reaction with *p*-methoxyphenylmagnesium bromide led to the *p*-methoxybenzyl alcohols (11) and (12), respectively, the former being obtained as a mixture of



method for epoxidation of olefins using a mixture of a nitrile and hydrogen peroxide, the oxidising species being a peroxyimide acid. Application of this procedure to the acetal (27) resulted in a 92% yield of the epoxide (28), which was reduced in 78% yield by lithium aluminium hydride to the acetal (29);<sup>9</sup> however, prolonged treatment of the reduction mixture with mineral acid produced equal quantities of the desired hydroxy-ketone (4)<sup>6</sup> and 4-methylcyclohex-2-enone. Reaction



of the former with *p*-methoxyphenylmagnesium bromide gave the mixed diols (10a and b); in this case the *trans*-isomer (10b) was the major product. Stereochemical assignments for the diols (9a and b) and (10a and b) were made on the basis of their chromatographic polarity and n.m.r. spectra.

The n.m.r. spectrum of the more polar isomer of the diol (9) showed a signal due to axial CH(OH); that of the less polar isomer showed a signal due to equatorial CH(OH). Assuming that the *p*-methoxyphenyl group is equatorially oriented, it follows that these compounds are the *cis*- (9a) and *trans*- (9b) isomers, respectively. The methylene envelope of the *trans*-isomer (9b) was much broader than that of the *cis*-isomer (9a), owing to deshielding of the axial hydrogens by the axial hydroxy-groups in (9b). The greater chromatographic polarity of (9a) is consistent with a *cis*-arrangement of polar groups.

<sup>6</sup> M. M. Green and C. Djerassi, *J. Amer. Chem. Soc.*, 1967, **89**, 5190; A. Siegel and H. Broll-Keckeis, *Monatsh.*, 1957, **88**, 910.

<sup>7</sup> G. B. Payne, *Tetrahedron*, 1962, **18**, 763.

<sup>8</sup> Y. Ogata and Y. Sawaki, *Tetrahedron*, 1964, **20**, 2065.

racemates which was partially separated by chromatography. The isomers of the acetal (12) could not be distinguished chromatographically.

The hydroxy-acid (13) was similarly prepared in 56% yield from 4-oxocyclohexylacetic acid.<sup>10</sup>

*Preparation of Cyclohexylidenecyclohexanones.*—In common with Inhoffen,<sup>2</sup> we found that Birch reduction of *p*-methoxybenzyl alcohols proceeded with some loss of the benzylic hydroxy-group to give a mixture of the dihydro-compounds (30) and (32), which could be separated easily by rapid column chromatography. The dihydro-compounds (32), on treatment in aqueous methanol with dilute mineral acid, gave rise to the required dienones. This transformation could also be accomplished by heating the dihydro-compound (32) in the same solvent with acetic acid; in the cold, however, hydrolysis of the enol ether function occurred without dehydration, to give the intermediate hydroxy-enone (36). Alternatively, the mixture of dihydro-compounds (30) and (32) could be acidified to give a mixture of the desired dienone and the corresponding  $\beta\gamma$ -unsaturated ketone (34), which was also readily separable by chromatography.

In general, Inhoffen's procedure was followed closely, although in some instances it was marginally advantageous to remove the proton from the benzylic hydroxy-group before reduction, by treating the starting material with methyl-lithium. The yield of dienone from a given *p*-methoxybenzyl alcohol was variable, as has been the experience of others<sup>11</sup> with metal-ammonia reductions.

<sup>9</sup> P. Courtot, *Bull. Soc. chim. France*, 1962, 1493; *Ann. Chim. (France)*, 1963, **8**, 197.

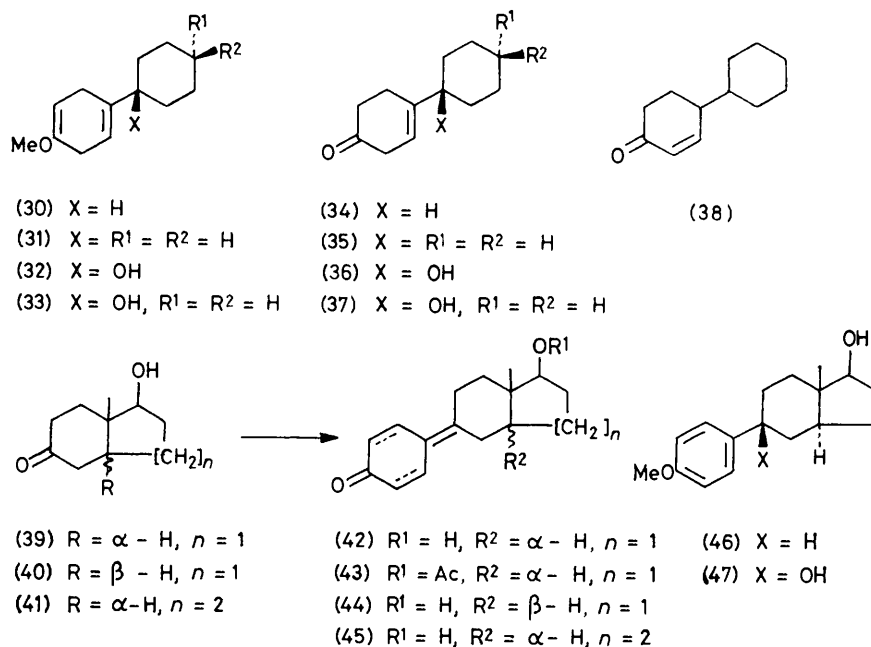
<sup>10</sup> D. D. Phillips and D. N. Chatterjee, *J. Amer. Chem. Soc.*, 1958, **80**, 1360; A. E. Ungnade and F. V. Morriss, *J. Amer. Chem. Soc.*, 1948, **70**, 1898.

<sup>11</sup> H. L. Dryden, G. M. Webber, R. R. Burtner, and J. A. Cella, *J. Org. Chem.*, 1961, **26**, 3237.

Reduction of the alcohol (8)<sup>12</sup> gave, after acidification, a 60–65% yield of the dienone (14) and 20–25% of the corresponding unconjugated ketone (35).<sup>13</sup> Reduction of the diols (9a and b) with lithium and ammonia proceeded in widely varying yields, the highest being 92%, to give the dienone (15), which reacted smoothly with acetic anhydride and pyridine to give the acetate (16). However, attempts to oxidise (15) with Jones reagent were very unsatisfactory, giving a low yield of the dienedione (17) which tended to decompose, even at 0 °C. This is not altogether surprising as all the

$\Delta^{4,9}$ -isomer of (42) is a fairly close analogue of testosterone; its  $\beta$ -phenylpropionate is likewise an analogue of an anabolic drug recently described<sup>14</sup> as an 'interceptive.'

Reaction of the bicyclic hydroxy-ketone (39)<sup>15</sup> with *p*-methoxyphenylmagnesium bromide afforded the corresponding *p*-methoxybenzyl alcohol (47), which was partially purified by chromatography before reduction with lithium and ammonia to give, in 34% overall yield, the dienone (42), presumed to be a 1 : 1 mixture of  $\Delta^1$ - and  $\Delta^4$ -isomers. Treatment of (42) with acetic



hydrogen atoms in (17) are either allylic or adjacent to a carbonyl group, making the compound very susceptible to further oxidation.

The dienones (18)–(21) were similarly obtained by reduction with lithium–ammonia of the *p*-methoxybenzyl alcohols (10)–(13). The dienones (19)–(21) might be considered, in appropriate conformations, to be analogues of progesterone, a pregnan-20-ol, and an estrane-17-carboxylic acid, respectively. The last of these (21) proved rather unstable; treatment with diazomethane and with dimethyl sulphate resulted in complex mixtures from which the desired methyl ester (22) was isolated in very low yield.

*Tricyclic Analogues.*—The compounds described so far bear at best a loose resemblance to steroids and, in an attempt to provide closer analogues, the same procedure was applied to several bicyclic ketones in which the CD portion of the steroid is intact. In particular, the

anhydride in pyridine gave the acetate (43) in poor yield. An attempt to prepare the  $\beta$ -phenylpropionate by treatment of the alcohol (42) with  $\beta$ -phenylpropionic acid and trifluoroacetic anhydride was unsuccessful; among the products isolated were the trifluoroacetate of (42) and the isomeric phenol.

Similarly, the bicyclic ketones (40)<sup>16</sup> and (41)<sup>17</sup> were converted by treatment with *p*-methoxyphenyl-lithium<sup>18</sup> into the corresponding tertiary alcohols and thence into the dienones (44) and (45), respectively, in low overall yields.

*Alternative Approaches to Dienones.*—Unsuccessful attempts were made at benzylic oxidation of the readily available bicyclononane (46)<sup>19</sup> under a wide variety of conditions, in the hope of defining a more convenient route to the intermediate (47). Efforts to convert the unconjugated ketone (35)<sup>13</sup> into the dienone (14) by oxidation or bromination–dehydrobromination were to

<sup>12</sup> S. Goldschmidt and W. L. C. Veer, *Rec. Trav. chim.*, 1948, **67**, 489; I. R. Sherwood, W. F. Short, and R. Stansfield, *J. Chem. Soc.*, 1932, 1832.

<sup>13</sup> A. L. Wilds and N. A. Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5360.

<sup>14</sup> R. H. Naqvi and J. C. Warren, *Steroids*, 1971, **18**, 731.

<sup>15</sup> D. J. Humphreys, C. E. Newall, H. A. Paskins, and G. H. Phillips, *J. C.S. Perkin I*, 1978, 15.

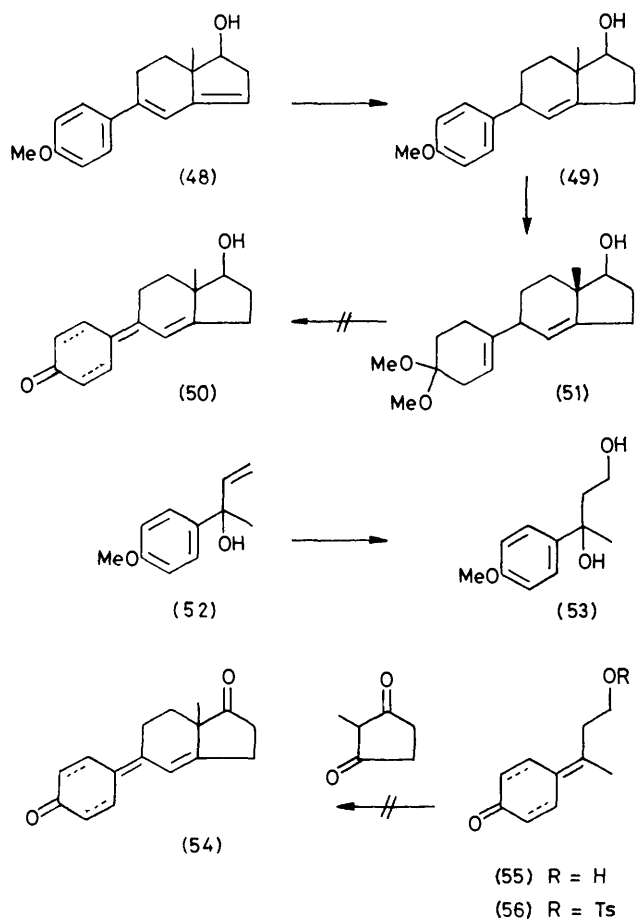
<sup>16</sup> C. B. C. Boyce and J. S. Whitehurst, *J. Chem. Soc.*, 1960, 4547; K. H. Baggaley, S. G. Brooks, J. Green, and B. T. Redman, *J. Chem. Soc. (C)*, 1971, 2671.

<sup>17</sup> A. W. Fort and R. E. Leary, *J. Amer. Chem. Soc.*, 1960, **82**, 2494.

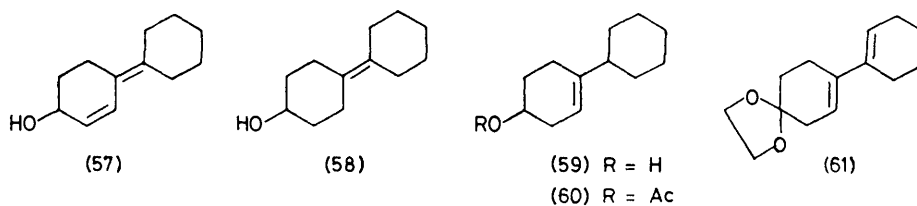
<sup>18</sup> A. J. Birch, E. Pride, and H. Smith, *J. Chem. Soc.*, 1958, 4688.

<sup>19</sup> H. Schick and G. Hilgetag, *Ger. Offen.* 1 930 955.

no avail. Oxidation by benzoquinone of the unconjugated diene (51), prepared from (48)<sup>19</sup> by low-temperature reduction with sodium-ammonia to give (49)



and subsequent reduction with lithium-ammonia, was equally unsuccessful.



Finally, it occurred to us that a convenient approach to the ACD tricyclic system might lie in condensation of the tosylate (56), which bears a preformed cyclohexenone moiety, with 2-methylcyclopentane-1,3-dione<sup>20</sup> to give the trienone (54). The alcohol (55) was accordingly prepared in 30–40% yield by hydroboration of the

<sup>20</sup> V. J. Grenda, G. W. Lindberg, N. L. Wendler, and S. H. Pines, *J. Org. Chem.*, 1967, **32**, 1236.

<sup>21</sup> E. Wenkert, S. K. Bhattacharya, and E. M. Wilson, *J. Chem. Soc.*, 1964, 5617.

<sup>22</sup> D. Burn, D. N. Kirk, and V. Petrow, *Tetrahedron*, 1965, **21**, 1619.

<sup>23</sup> E. Farkas and N. J. Bach, *J. Org. Chem.*, 1971, **36**, 2715.

<sup>24</sup> C. H. Shunk and A. L. Wilds, *J. Amer. Chem. Soc.*, 1949, **71**, 3946.

vinyl alcohol (52)<sup>19</sup> to the diol (53) and subsequent reduction with lithium-ammonia. Its n.m.r. spectrum showed that it was a 1:1 mixture of *E*- and *Z*-forms. However, attempts to condense the tosylate (56) with 2-methylcyclopentane-1,3-dione under a variety of conditions were unsuccessful.

*Reduction of the Dienone (14).*—The dienone (14) was readily reduced by sodium borohydride to the dienol (57), but most of our attempts at selective reduction of (14) or (57) to cyclohexylidenecyclohexanone or -ol were unsuccessful, and the results illustrate the inherent instability of these systems. The exocyclic double bond shows a marked tendency to migrate into the ring when conjugated to a second double bond or a carbonyl group, as exemplified by the thermal isomerisation of 2-cyclohexylidenecyclohexanone to 2-(cyclohex-1-enyl)-cyclohexanone.<sup>21</sup> An attempted exchange hydrogenation of the dienone (14) with cyclohexene and palladised charcoal<sup>22</sup> led to the exclusive formation of the isomeric 4-cyclohexylphenol, illustrating the strong tendency of such systems to aromatise.<sup>23</sup>

Hydrogenation of (14) over palladium proceeded in accordance with Inhoffen's findings<sup>2</sup> to give a mixture of 4-cyclohexylcyclohexanone<sup>24</sup> and the corresponding  $\alpha\beta$ -unsaturated ketone (38), together with some cyclohexylphenol. When an iridium catalyst was used, a mixture of the isomeric 4-cyclohexylcyclohexanols<sup>25</sup> was obtained.

Reduction of (14) by lithium and ammonia gave a mixture of the unsaturated alcohol (59) (70%) and the desired 4-cyclohexylidenecyclohexanol<sup>1</sup> (58) (30%). Similar reduction of the acetal (61) also gave a mixture.

Attempts to reduce the dienol (57) were more successful. Hydrogenation of (57) over palladium, platinum, or nickel boride<sup>26</sup> proceeded mainly by 1,4-addition to give the  $\gamma\delta$ -unsaturated alcohol (59) as the major product. In contrast, the reaction of (57) with diimide<sup>27</sup> proceeded *via cis*-addition of hydrogen to the

less hindered  $\beta\gamma$ -double bond to give the required alcohol<sup>1</sup> (58) as the major product (64%), accompanied by some of the starting material and some fully saturated products. However, since by this time other more efficient ways of preparing the desired seco-steroids had become available,<sup>28,29</sup> this approach was not investigated further.

<sup>25</sup> H. E. Ungnade, *J. Org. Chem.*, 1948, **13**, 361.

<sup>26</sup> C. A. Brown and H. C. Brown, *J. Amer. Chem. Soc.*, 1963, **85**, 1003, 1005; C. A. Brown, *J. Org. Chem.*, 1970, **35**, 1900.

<sup>27</sup> Y. J. Abul-Hajj, *J. Org. Chem.*, 1971, **36**, 2730.

<sup>28</sup> D. J. Humphreys and C. E. Newall, following paper.

<sup>29</sup> D. J. Humphreys, C. E. Newall, G. H. Phillipps, and G. A. Smith, *J.C.S. Perkin I*, 1978, 45.

## EXPERIMENTAL

For preamble see Part 1.<sup>15</sup>

**8-Methyl-1,4-dioxaspiro[4.5]dec-7-ene (27).**—4-Methyl-anisole (122 g, 1 mol) in tetrahydrofuran (500 ml) and *t*-butyl alcohol (500 ml) was added over 30 min to a solution of lithium (45 g, 6.4 mol) in liquid ammonia (2.5 l). After a further 30 min sufficient methanol (300 ml) was added to discharge the colour. The ammonia was evaporated off and the residue was partitioned between water and dichloromethane. Drying and evaporation of the organic phase left a homogeneous (t.l.c.) oil (110 g).

Ethylene glycol (250 ml) and toluene-*p*-sulphonic acid (250 mg) were added and the mixture was heated at 90–95 °C and 12–15 mmHg for 1.5 h, then poured into aqueous sodium hydrogencarbonate. The product was extracted into dichloromethane, and the extract was washed with water, dried, and evaporated to give the *acetal* (27) as an oil (133 g, 86%),  $\nu_{\max}$  1 059 cm<sup>-1</sup> (C–O),  $\tau$  8.31 (3 H, s, CH<sub>3</sub>), 6.04 (4 H, s, OCH<sub>2</sub>CH<sub>2</sub>O), and 4.68 (1 H, m, =CH–) (Found: C, 69.9; H, 9.2. C<sub>9</sub>H<sub>14</sub>O<sub>2</sub> requires C, 70.1; H, 9.15%).

**6-Methyl-7-oxabicyclo[4.1.0]heptane-3-spiro-2'-1',3'-dioxolan (28).**—The olefin (27) (133 g, 0.86 mol), acetonitrile (44.3 g, 1.08 mol), methanol (720 ml), 30% hydrogen peroxide (123 g, 1.08 mol), and 0.1M-disodium hydrogen-phosphate (21.5 ml) were heated together at 50 °C. 0.5M-Sodium hydroxide (21.5 ml) was added and the solution was stirred at 50–60 °C. More 0.5M-sodium hydroxide (5 × 21.5 ml) was added as necessary to maintain the pH at *ca.* 8. T.l.c. (CHCl<sub>3</sub>) indicated that the reaction was incomplete.

Further quantities of acetonitrile (37.3 g) and 30% hydrogen peroxide (103 g) were added, followed by 0.5M-sodium hydroxide (5 × 21.5 ml), the mixture being stirred at 50–60 °C. As the reaction was still incomplete, the process was repeated once more and the mixture was then partitioned between water and dichloromethane. The organic phase was washed with water, dried, and evaporated to give the *epoxide* (28) as an oil (135 g, 92%),  $\nu_{\max}$  1 060 (C–O) and 837 cm<sup>-1</sup> (epoxide),  $\tau$  8.68 (3 H, s, CH<sub>3</sub>), 7.01 (1 H, t, *J* 2.5 Hz, 1-H), and 6.08 (4 H, s, OCH<sub>2</sub>CH<sub>2</sub>O) (Found: C, 63.3; H, 8.2. C<sub>9</sub>H<sub>14</sub>O<sub>3</sub> requires C, 63.5; H, 8.3%).

**8-Methyl-1,4-dioxaspiro[4.5]decan-8-ol (29).**—The epoxide (28) (1.70 g, 10 mmol) in dry tetrahydrofuran (25 ml) was added to a stirred suspension of lithium aluminium hydride (500 mg, 13 mmol) in dry tetrahydrofuran (25 ml) and the mixture was heated under reflux for 2 h. Water was added cautiously, followed by 2N-hydrochloric acid, and the mixture was extracted with dichloromethane. The extract was washed with water, dried, and evaporated to give the alcohol (29) as an oil (1.35 g, 78%),  $\nu_{\max}$  3 600 and 3 415 (OH) and 1 081 and 1 036 cm<sup>-1</sup> (C–O),  $\tau$  8.79 (3 H, s, CH<sub>3</sub>) and 6.07 (4 H, s, OCH<sub>2</sub>CH<sub>2</sub>O), which crystallised (lit.,<sup>9</sup> m.p. 70–71°).

**4-Hydroxy-4-methylcyclohexanone (4).**—The epoxide (28) (66 g, 0.39 mmol) in dry tetrahydrofuran (1 l) was added to a stirred slurry of lithium aluminium hydride (15 g, 0.4 mol) in dry tetrahydrofuran (1 l) under nitrogen and the mixture was heated under reflux for 21 h. Water was added, followed by 2N-hydrochloric acid, and the mixture was stirred for 1 h, then extracted with dichloromethane. The extract was washed with water, dried, and evaporated to a yellow oil (37 g). G.l.c. indicated that this was a mixture containing two major components (51 and 40%). Chro-

matography on alumina gave (i) 4-methylcyclohex-2-enone<sup>30</sup> (16.6 g, 33%) as a pale yellow oil; (ii) impure hydroxy-ketone (4) (4.55 g, 9%) as a pale yellow oil; (iii) 4-hydroxy-4-methylcyclohexanone (4) (12.05 g, 24%) as an oil which solidified (lit.,<sup>6</sup> m.p. 36–38°).

**4-(2-Hydroxypropyl)cyclohexanone (5).**—Lithium (14.3 g, 2 g atom) was added over 20 min to *p*-methoxyphenylacetone (16.4 g, 0.1 mol) in dry tetrahydrofuran (500 ml), *t*-butyl alcohol (500 ml), and liquid ammonia (1 l), and the mixture was stirred for 2 h. Methanol was then added to discharge the colour and the ammonia was evaporated off. The residue was partitioned between aqueous ammonium chloride and chloroform, and the organic phase was washed with water, dried, and evaporated. The residual oil was heated under reflux in methanol (300 ml) containing 2N-sulphuric acid (70 ml) for 1 h, then poured into aqueous sodium hydrogen carbonate. The product was extracted into dichloromethane and the extracts were washed with water, dried, and evaporated to give crude 4-(2-hydroxypropyl)cyclohex-3-enone as a pale yellow oil (11.53 g). The product was hydrogenated in ethyl acetate (1 l) over 10% palladium-charcoal (600 mg) to give a pale yellow oil (10.8 g, 70%). Chromatography on alumina (500 g) (chloroform as eluant) yielded (i) impure saturated ketone (5) (5.66 g, 36%) (62% pure); (ii) 4-(2-hydroxypropyl)cyclohexanone (5) (4.76 g, 30%),  $\nu_{\max}$  3 615 (OH) and 1 700 cm<sup>-1</sup> (C=O),  $\tau$  8.77 (3 H, d, *J* 6 Hz, CHCH<sub>3</sub>), 6.03 (1 H, m, CHCH<sub>3</sub>) (Found: C, 67.3; H, 10.3. C<sub>9</sub>H<sub>16</sub>O<sub>2</sub>·0.25H<sub>2</sub>O requires C, 67.25; H, 10.3%).

**2-(p-Methoxybenzyl)-2-methyl-1,3-dioxolan.**—*p*-Methoxyphenylacetone (20 g, 122 mmol) and toluene-*p*-sulphonic acid (200 mg), dissolved in ethylene glycol (200 ml), were heated on a rotary evaporator at 95 °C and 1 mmHg for 2 h, then poured into aqueous sodium hydrogen carbonate. The product was extracted into dichloromethane and the extract was dried and evaporated to give the *acetal* (26.25 g) as a yellow oil,  $\lambda_{\max}$  225.5 ( $\epsilon$  9 800), 276.5 (1 540), and 283 nm (1 330),  $\nu_{\max}$  1 030 cm<sup>-1</sup> (C–O),  $\tau$  8.70 (3 H, s, CH<sub>3</sub>), 7.13 (2 H, s, CH<sub>2</sub>), and 6.20 (3 H, s, OCH<sub>3</sub>) (Found: C, 69.4; H, 7.7. C<sub>12</sub>H<sub>16</sub>O<sub>3</sub> requires C, 69.2; H, 7.7%).

**4-(2,2-Ethylenedioxypropyl)cyclohexanone (6).**—The above acetal (24 g, 115 mmol) in tetrahydrofuran (300 ml) and *t*-butyl alcohol (300 ml) was added to liquid ammonia (600 ml), and lithium (5 g, 730 mmol) was added to the stirred solution over 15 min. After a further 1 h, sufficient methanol was added to discharge the colour and most of the ammonia was evaporated off. The residue was partitioned between aqueous ammonium chloride and dichloromethane and the organic phase was washed with water, dried, and evaporated to give the dihydro-compound as a yellow oil (23.8 g).

The product in methanol-water (9:1; 300 ml) was treated with acetic acid (75 ml) at 50 °C for 2 h, then poured into water (375 ml) and extracted with dichloromethane. The extracts were washed with water, dried, and evaporated to give 4-(2,2-ethylenedioxypropyl)cyclohex-3-enone as a yellow oil (20.5 g).

The crude unsaturated ketone was hydrogenated in ethanol (500 ml) over 5% palladium-charcoal (2 g). The product was chromatographed on alumina to give an oil (18.89 g, 83%), which was distilled to give compound (6) (16.07 g) as an oil, b.p. 107–110 °C at 0.5 mmHg,  $\nu_{\max}$  (CS<sub>2</sub>) 1 704 cm<sup>-1</sup> (C=O),  $\tau$  8.64 (3 H, s, CH<sub>3</sub>) and 6.03 (4 H, s,

<sup>30</sup> M. F. Ansell, J. E. Emmett, and B. E. Grimwood, *J. Chem. Soc. (C)*, 1969, 141.

OCH<sub>2</sub>CH<sub>2</sub>O), for which a correct elemental analysis was not obtained.

*General Method for Preparation of 1-(p-Methoxyphenyl)cyclohexanols.*—A Grignard solution was prepared under nitrogen from 4-bromoanisole and magnesium in dry tetrahydrofuran and was heated under reflux for 1 h. The ketone in dry tetrahydrofuran was added slowly to the cooled solution and the mixture was heated under reflux until the reaction was complete (1–8 h), then poured into aqueous ammonium chloride and extracted with dichloromethane. The extracts were washed with water, dried, and evaporated and the residue was purified by chromatography or crystallisation.

*1-(p-Methoxyphenyl)cyclohexane-1,4-diol (9).*—4-Benzoyloxycyclohexanone (3) (43.6 g, 0.2 mol) was treated as above with *p*-methoxyphenylmagnesium bromide (0.64 mol). The crude product was triturated with petrol–dichloromethane to give a white crystalline solid (19.5 g, 44%), which gave (from aqueous methanol) crystals of 1-(*p*-methoxyphenyl)cyclohexane-*cis*-1,4-diol (9a), m.p. 154–156°,  $\lambda_{\text{max}}$  223.5 ( $\epsilon$  11 000), 274 (1 700), and 281 nm (1 500),  $\lambda_{\text{infl}}$  267.5 nm ( $\epsilon$  1 300),  $\nu_{\text{max}}$  3 590 cm<sup>-1</sup> (OH),  $\tau[(\text{CD}_3)_2\text{SO}]$  6.22 (3 H, s, OCH<sub>3</sub>) and 6.50br (1 H, m, CHOH) (Found: C, 70.3; H, 8.2. C<sub>13</sub>H<sub>18</sub>O<sub>3</sub> requires C, 70.2; H, 8.2%). The mother liquors were chromatographed on alumina; dichloromethane eluted non-polar material and subsequent elution with chloroform, then ether, gave (i) a gum (5.34 g) from which the *trans*-diol (9b) (1.42 g, 3%) was isolated; (ii) a white solid (12.7 g, 29%) which gave (from methanol) crystals of 1-(*p*-methoxyphenyl)cyclohexane-*trans*-1,4-diol (9b), m.p. 101–102°,  $\lambda_{\text{max}}$  223.5 ( $\epsilon$  9 100), 274 (1 350), and 280.5 nm (1 200),  $\lambda_{\text{infl}}$  267.5 nm ( $\epsilon$  1 000),  $\nu_{\text{max}}$  3 610 and 3 460 cm<sup>-1</sup> (OH),  $\tau[(\text{CD}_3)_2\text{SO}]$  6.25 (3 H, s, OCH<sub>3</sub>) and 6.13 (1 H, m, CHOH) (Found: C, 69.0; H, 8.2. C<sub>13</sub>H<sub>18</sub>O<sub>3</sub>·0.25H<sub>2</sub>O requires C, 68.85; H, 8.2%); (iii) a gum (5.84 g) from which the *cis*-diol (9a) (2.26 g, 5%) was isolated.

*Oxidation of 1-(p-Methoxyphenyl)cyclohexane-cis-1,4-diol (9a).*—(a) *With Jones reagent.* The *cis*-diol (9a) (222 mg, 1 mmol) in acetone (30 ml) was treated dropwise with stirring with Jones reagent (0.3 ml) and the mixture was partitioned between water and chloroform. The organic phase was washed with water, dried, and evaporated to give an off-white solid (217 mg). P.l.c. (CHCl<sub>3</sub>) gave as the major product a solid (170 mg, 77%) which, from benzene–petrol, gave needles of 4-hydroxy-4-(*p*-methoxyphenyl)cyclohexanone (26), m.p. 105–106° (lit.<sup>4</sup> 103–104.5°),  $\lambda_{\text{max}}$  223.5 ( $\epsilon$  11 500) and 274 nm (1 800),  $\nu_{\text{max}}$  3 600 (OH) and 1 705 cm<sup>-1</sup> (C=O),  $\tau$  6.19 (3 H, s, OCH<sub>3</sub>) (Found: C, 71.0; H, 7.3. Calc. for C<sub>13</sub>H<sub>16</sub>O<sub>3</sub>: C, 70.9; H, 7.3%).

(b) *With dimethyl sulphoxide–dicyclohexylcarbodi-imide.* The *cis*-diol (9a) (1.1 g, 5 mmol) in dry dimethyl sulphoxide (7.5 ml) and dry benzene (7.5 ml) containing pyridine (0.4 ml, 5 mmol) and trifluoroacetic acid (0.2 ml, 2.5 mmol) was treated with dicyclohexylcarbodi-imide (3.09 g, 15 mmol) and the mixture was stirred until all the starting material had been consumed. Standard work-up<sup>5</sup> gave a gum (1.43 g) which was chromatographed over silica gel in dichloromethane to give (i) 4-(*p*-methoxyphenyl)cyclohex-3-enone (25) (600 mg, 59%); (ii) 4-(*p*-methoxyphenyl)cyclohex-3-enol (23) (160 mg, 16%).

*4-(p-Methoxyphenyl)cyclohex-3-enol (23) and the Acetate (24).*—The *cis*-diol (9a) (222 mg, 1 mmol) was heated under reflux for 30 min in acetic acid (50 ml), then poured into water. The product was extracted into dichloromethane and the extracts were washed with aqueous sodium hydrogen

carbonate and water, dried, and evaporated to a white solid (208 mg). P.l.c. (CHCl<sub>3</sub>) yielded (i) a gum (46 mg, 19%) which solidified. It gave (from petrol) crystals of 4-(*p*-methoxyphenyl)cyclohex-3-enyl acetate (24), m.p. 83–84°,  $\lambda_{\text{max}}$  253 ( $\epsilon$  15 400) and 288 nm (1 800),  $\nu_{\text{max}}$  1 720 cm<sup>-1</sup> (ester),  $\tau$  7.93 (3 H, s, OCOCH<sub>3</sub>), 6.19 (3 H, s, OCH<sub>3</sub>), 4.90 (1 H, m, CHOAc), and 4.08 (1 H, m, =CH-) (Found: C, 73.2; H, 7.6. C<sub>15</sub>H<sub>18</sub>O<sub>3</sub> requires C, 73.15; H, 7.4%); (ii) a white solid (142 mg, 70%) which gave (from petrol) crystals of 4-(*p*-methoxyphenyl)cyclohex-3-enol (23), m.p. 118–119°,  $\lambda_{\text{max}}$  253 ( $\epsilon$  15 300) and 288 nm (1 800),  $\nu_{\text{max}}$  3 610 cm<sup>-1</sup> (OH),  $\tau$  6.27 (3 H, s, OCH<sub>3</sub>), 6.20 (1 H, m, CHOH), and 4.08 (1 H, m, =CH-) (Found: C, 76.35; H, 8.0. C<sub>13</sub>H<sub>16</sub>O<sub>2</sub> requires C, 76.4; H, 7.9%).

*4-(p-Methoxyphenyl)cyclohex-3-enone (25).*—The hydroxy-ketone (26) (200 mg, 0.9 mmol) in benzene (15 ml) was treated overnight with toluene-*p*-sulphonic acid (20 mg). Aqueous sodium hydrogen carbonate was added and the mixture was stirred for 30 min. The organic layer was separated, dried, and evaporated to a yellow oil (183 mg) which solidified. Recrystallisation from petrol yielded the *unsaturated ketone* (25) as pale yellow needles, m.p. 65–66°,  $\lambda_{\text{max}}$  255 nm ( $\epsilon$  14 500),  $\nu_{\text{max}}$  1 705 (C=O) and 1 605 cm<sup>-1</sup> (C=C),  $\tau$  6.19 (3 H, s, CH<sub>3</sub>) and 3.98 (1 H, t, *J* 4 Hz, =CH-) (Found: C, 75.4; H, 6.8. C<sub>13</sub>H<sub>14</sub>O<sub>2</sub>·0.25H<sub>2</sub>O requires C, 75.5; H, 7.1%).

*1-(p-Methoxyphenyl)-4-methylcyclohexane-1,4-diol (10).*—(a) *From 4-hydroxy-4-(p-methoxyphenyl)cyclohexanone (26).* The ketone (26) (220 mg, 1 mmol) in tetrahydrofuran (40 ml) was treated under nitrogen with ethereal methyl-lithium (2 ml of a 2M-solution) and the mixture was heated under reflux for 30 min, then left overnight at room temperature. The product was partitioned between aqueous ammonium chloride and dichloromethane. The organic phase was washed with water, dried, and evaporated to give a gum (230 mg). P.l.c. (CHCl<sub>3</sub>–MeOH, 19 : 1) afforded (i) the starting material (26) (55 mg); (ii) 1-(*p*-methoxyphenyl)-4-methylcyclohexane-*trans*-1,4-diol (10b) (58 mg, 24%) as a white solid, m.p. 123–125°,  $\lambda_{\text{max}}$  223.5 ( $\epsilon$  10 300), 267.5 nm (1 300), 274 (1 700), and 280.5 nm (1 500),  $\nu_{\text{max}}$  3 620 cm<sup>-1</sup> (OH),  $\tau$  8.70 (3 H, s, CH<sub>3</sub>) and 6.20 (3 H, s, OCH<sub>3</sub>) (Found: C, 69.85; H, 8.6. C<sub>14</sub>H<sub>20</sub>O<sub>3</sub>·0.25H<sub>2</sub>O requires C, 69.8; H, 8.6%); (iii) 1-(*p*-methoxyphenyl)-4-methylcyclohexane-*cis*-1,4-diol (10a) (95 mg, 40%) as a white solid, m.p. 150–151°,  $\lambda_{\text{max}}$  223.5 ( $\epsilon$  10 700), 268.5 nm (1 300), 274 (1 600), and 280.5 nm (1 400),  $\nu_{\text{max}}$  3 615 and 3 475 cm<sup>-1</sup> (OH),  $\tau$  8.73 (3 H, s, CH<sub>3</sub>) and 6.20 (3 H, s, OCH<sub>3</sub>) (Found: C, 68.3; H, 8.3. C<sub>14</sub>H<sub>20</sub>O<sub>3</sub>·0.5H<sub>2</sub>O requires C, 68.5; H, 8.6%).

(b) *From 4-hydroxy-4-methylcyclohexanone (4).* The hydroxy-ketone (4) (13.25 g, 103 mmol) was treated with *p*-methoxyphenylmagnesium bromide (217 mmol) and the crude product was triturated with dichloromethane to give the *cis*-diol (10a) (3.77 g, 15.5%). Chromatography of the mother liquor on alumina (dichloromethane as eluant) removed non-polar material, and further elution with chloroform, then ether, yielded the *trans*-diol (10b) (9.18 g, 37%). Finally, elution with methanol afforded more *cis*-diol (10a) (4.14 g, 17%).

*4-(2-Hydroxypropyl)-1-(p-methoxyphenyl)cyclohexanol (11).*—4-(2-Hydroxypropyl)cyclohexanone (5) (22.0 g, 140 mmol) was treated as above with *p*-methoxyphenylmagnesium bromide (280 mmol). The product was a mixture of two racemates. Trituration with petrol yielded a gum which was further triturated with dichloromethane to give the

less polar isomer of the diol (11) as a white solid (650 mg), m.p. 134–136°,  $\lambda_{\text{max}}$  224.5 ( $\epsilon$  10 500), 275.5 (1 600), and 282 nm (1 400),  $\nu_{\text{max}}$  3 570 and 3 430  $\text{cm}^{-1}$  (OH),  $\tau$  8.79 (3 H, d,  $J$  6 Hz,  $\text{CH}_3$ ), 6.19 (3 H, s,  $\text{OCH}_3$ ), and 6.06 (1 H, m,  $\text{CHOH}$ ) (Found: C, 71.35; H, 9.0.  $\text{C}_{19}\text{H}_{24}\text{O}_3 \cdot 0.25\text{H}_2\text{O}$  requires C, 71.4; H, 9.2%). The petrol solution was evaporated and the residue was triturated with ether-petrol to give the more polar isomer as a white solid (760 mg), m.p. 89–91°,  $\lambda_{\text{max}}$  225.5 ( $\epsilon$  10 000), 275 (1 500), and 282 nm (1 300),  $\nu_{\text{max}}$  3 590 and 3 430  $\text{cm}^{-1}$  (OH),  $\tau$  8.83 (3 H, d,  $J$  6 Hz,  $\text{CH}_3$ ), 6.19 (3 H, s,  $\text{OCH}_3$ ), and 6.10 (1 H, m,  $\text{CHOH}$ ) (Found: C, 72.3; H, 9.0.  $\text{C}_{19}\text{H}_{24}\text{O}_3$  requires C, 72.7; H, 9.15%). The combined liquors were chromatographed on alumina to give the mixed isomers of the diol (11) (24.37 g, 67%).

4-(2,2-Ethylenedioxypropyl)-1-(*p*-methoxyphenyl)cyclohexanol (12).—4-(2,2-Ethylenedioxypropyl)cyclohexanone (6) (16.0 g, 80 mmol) was treated as above with *p*-methoxyphenylmagnesium bromide (110 mmol). Chromatography of the crude product over alumina in dichloromethane yielded the tertiary alcohol (12) (15.5 g, 63%) as a 1:1 mixture of *cis*- and *trans*-isomers which gave (from ether-petrol) crystals, m.p. 92–93°,  $\lambda_{\text{max}}$  225 ( $\epsilon$  10 900), 272.5 (1 700), and 282 nm (1 500),  $\nu_{\text{max}}$  ( $\text{CS}_2$ ) 3 585  $\text{cm}^{-1}$  (OH),  $\tau$  8.62 and 8.68 (3 H, both s,  $\text{CH}_3$ ), 6.19 (3 H, s,  $\text{OCH}_3$ ), 6.03 and 6.07 (4 H, both s,  $\text{OCH}_2\text{CH}_2\text{O}$ ) (Found: C, 70.25; H, 8.6.  $\text{C}_{18}\text{H}_{26}\text{O}_4$  requires C, 70.55; H, 8.55%).

4-Hydroxy-4-(*p*-methoxyphenyl)cyclohexylacetic Acid (13).—4-Oxocyclohexylacetic acid<sup>10</sup> (7) (1.56 g, 10 mmol) was treated in the usual way with *p*-methoxyphenylmagnesium bromide. When the reaction was complete, the mixture was poured into aqueous ammonium chloride and the whole was partitioned between ether and aqueous 10% sodium carbonate. The aqueous phase was acidified to pH 5 with acetic acid and extracted with chloroform. Evaporation of the dried extract gave an off-white solid (2.5 g, 94%), which was recrystallised from benzene to give the hydroxy-acid (13) (1.48 g, 56%), m.p. 93–94.5°,  $\lambda_{\text{max}}$  224 ( $\epsilon$  11 200), 269 nm (1 300), 274 (1 600), and 281 nm (1 400),  $\nu_{\text{max}}$  3 580, 3 490, and 3 400–2 300 (OH), and 1 730 and 1 705  $\text{cm}^{-1}$  ( $\text{CO}_2\text{H}$ ),  $\tau$  6.20 (3 H, s,  $\text{OCH}_3$ ) (Found: C, 67.9; H, 7.5.  $\text{C}_{15}\text{H}_{20}\text{O}_4$  requires C, 68.2; H, 7.6%).

General Method for Reduction of 1-(*p*-Methoxyphenyl)cyclohexanols with Lithium-Ammonia.—Method A. The alcohol (10 mmol) in ethanol (4 ml) and tetrahydrofuran (30 ml) was added over 15 min to a solution of lithium (0.2 g atom) in liquid ammonia (150 ml) and tetrahydrofuran (15 ml). The mixture was stirred rapidly for 10 min, after which ethanol was added to discharge the blue colour. The ammonia was evaporated off and the residue was partitioned between aqueous ammonium sulphate and dichloromethane. The organic phase was washed with water, dried, and evaporated. The mixture of dihydro-compounds obtained was hydrolysed by heating under reflux in methanol with acetic acid or 2*N*-sulphuric acid. Dilution with water and extraction with dichloromethane afforded a mixture of dienone and  $\beta\gamma$ -unsaturated ketone which was separated by chromatography.

Method B. The alcohol (10 mmol) in tetrahydrofuran (45 ml) was treated with ethereal methyl-lithium (10 mmol for each hydroxy-group). Liquid ammonia (170 ml), ethanol (4 ml), and lithium (0.2 g atom) were added successively and the mixture was stirred rapidly for 10 min, then worked up as in method A.

4-Cyclohexylidenecyclohex-2-enone (14).—(a) The alcohol<sup>12</sup>

(8) (2.06 g, 10 mmol) was reduced with lithium and ammonia (Method A) and the mixture of dihydro-compounds produced was chromatographed rapidly on alumina. Elution with petrol yielded 1-cyclohexyl-4-methoxycyclohexa-1,4-diene (31) (747 mg, 39%) which gave (from petrol) plates, m.p. 62–63° (lit.<sup>13</sup> 65–66°). Further elution with ether gave 1-(4-methoxycyclohexa-1,4-dienyl)cyclohexanol (33) (548 mg, 26%) which gave (from petrol) crystals, m.p. 71–72°,  $\nu_{\text{max}}$  ( $\text{CS}_2$ ) 3 580 (OH) and 1 678 and 1 640  $\text{cm}^{-1}$  ( $\text{C}=\text{C}$ ),  $\tau$  6.44 (3 H, s,  $\text{OCH}_3$ ), 5.31 (1 H, m,  $\text{C}=\text{CH}-$ ), and 4.21 (1 H, m,  $\text{MeO}\cdot\text{C}=\text{CH}-$ ). Compound (33) (104 mg, 0.5 mmol) was heated under reflux for 30 min in methanol (5 ml) and 2*N*-sulphuric acid (2 ml). After neutralisation with sodium hydrogen carbonate, the product was extracted into ether and the extract was dried and evaporated to give a pale yellow oil (88 mg). P.l.c. ( $\text{C}_6\text{H}_6$ ) furnished the dienone (14) as a viscous oil (55 mg, 66%).

(b) The alcohol (8) (2.06 g, 10 mmol) was reduced with lithium and ammonia as above and the mixture of dihydro-compounds obtained was dissolved in methanol-water (9:1; 50 ml) and treated with acetic acid (15 ml). After 16 h at room temperature there was no trace of either dihydro-compound; water and sodium hydrogen carbonate were added and the product was extracted into dichloromethane. Drying and evaporation left a pale yellow oil (1.81 g) which was chromatographed on silica gel in dichloromethane to give (i) the unconjugated ketone<sup>13</sup> (35) (376 mg, 21%); (ii) a pale yellow oil (402 mg, 23%) which was further purified by p.l.c. ( $\text{CHCl}_3$ ) to give the dienone (14) as a pale yellow waxy solid, m.p. 33°,  $\lambda_{\text{max}}$  305 nm ( $\epsilon$  17 500),  $\nu_{\text{max}}$  1 662 ( $\text{C}=\text{O}$ ), 1 615, and 1 572  $\text{cm}^{-1}$  ( $\text{C}=\text{C}$ ),  $\tau$  4.13 (1 H, d,  $J$  10 Hz, 2-H) and 2.62 (1 H, d,  $J$  10 Hz, 3-H) (Found: C, 79.9; H, 8.9.  $\text{C}_{12}\text{H}_{16}\text{O}$ , 0.25 $\text{H}_2\text{O}$  requires C, 79.7; H, 9.2%); (iii) 4-(1-hydroxycyclohexyl)cyclohex-3-enone (37) as a yellow oil (822 mg, 42%),  $\nu_{\text{max}}$  3 585 and 3 500 (OH), and 1 708  $\text{cm}^{-1}$  ( $\text{C}=\text{O}$ ),  $\tau$  7.38–7.57 (4 H, m, 2- and 6-H), 7.00–7.16 (2 H, m, 5-H), and 4.15 (1 H, t,  $J$  4 Hz,  $=\text{CH}-$ ) for which a correct elemental analysis was not obtained; on treatment with 2*N*-sulphuric acid in methanol the dienone (14) was produced.

(c) The alcohol (8) (5.15 g, 25 mmol) was reduced with lithium and ammonia and the product was kept overnight with acetic acid, as described above. T.l.c. showed the presence of the ketone (35), the dienone (14), and the hydroxy-ketone (37). The solution was heated under reflux for 1 h, after which all the hydroxy-ketone had disappeared. Chromatography of the product on silica gel yielded 4-cyclohexylcyclohex-3-enone (35) (1.1 g, 25%) and 4-cyclohexylidenecyclohex-2-enone (14) (2.7 g, 60%).

4-Cyclohexylcyclohex-2-enone (38).—The unconjugated ketone (35) (440 mg, crude) in ethanol (15 ml) and 2*N*-sulphuric acid (25 ml) was heated under reflux for 8 h, after which some starting material remained. The mixture was partitioned between water and dichloromethane and the organic phase was washed with water, dried, and evaporated to a pale yellow oil (390 mg). P.l.c. (petrol-acetone, 4:1) yielded the conjugated ketone (38) (125 mg) as a pale yellow oil,  $\lambda_{\text{max}}$  226 nm ( $\epsilon$  10 200),  $\nu_{\text{max}}$  1 670  $\text{cm}^{-1}$  ( $\text{C}=\text{O}$ ),  $\tau$  4.00 (1 H, dd,  $J$  10 and 2 Hz, 2-H) and 3.04 (1 H, d,  $J$  10 Hz, 3-H) (Found: C, 80.0; H, 10.2.  $\text{C}_{12}\text{H}_{18}\text{O}$ , 0.125 $\text{H}_2\text{O}$  requires C, 79.8; H, 10.2%).

4,4-Ethylenedioxybi(cyclohex-1-enyl) (61).—The dienone (14) (1.056 g, 6 mmol) and toluene-*p*-sulphonic acid (50 mg) were heated in ethylene glycol (110 ml) at 90 °C and 0.1 mmHg for 2 h. The mixture was poured into aqueous

sodium hydrogen carbonate and the product was extracted into dichloromethane. The extract was washed with water, dried, and evaporated to a yellow oil (1.10 g, 83%), g.l.c. purity 88%. P.l.c. ( $\text{CH}_2\text{Cl}_2$ ) yielded the *acetal* (61),  $\lambda_{\text{max}}$  235.5 ( $\epsilon$  15 800), 229nm (14 700), and 243 nm (11 000),  $\tau$  6.01 (4 H, s,  $\text{OCH}_2\text{CH}_2\text{O}$ ) and 4.16 and 4.33 (2 H, each m, =CH-) (Found: C, 74.65; H, 8.9.  $\text{C}_{14}\text{H}_{20}\text{O}_2 \cdot 0.25\text{H}_2\text{O}$  requires C, 74.8; H, 9.2%).

**4-Cyclohexylidenecyclohex-2-enol (57).**—A stirred solution of the dienone (14) (176 mg, 1 mmol) in methanol (25 ml) containing a few drops of water was treated with sodium borohydride (38 mg, 1 mmol). After 30 min, more sodium borohydride (10 mg) was added, and after a further 30 min the mixture was acidified to pH 4 with 2*N*-hydrochloric acid. The product was extracted into dichloromethane and the extracts were washed with water, dried, and evaporated to give a gum (255 mg). Crystallisation from petrol (2 ml) afforded the *dienol* (57) as crystals, m.p. 83–85°,  $\lambda_{\text{max}}$  248 ( $\epsilon$  23 000), 242nm (20 600), and 255nm (17 000),  $\nu_{\text{max}}$  ( $\text{CS}_2$ ) 3 600 and 3 480 (OH) and 1 661  $\text{cm}^{-1}$  (C=C),  $\tau$  5.7 (1 H, m, *CHOH*), 4.30 (1 H, dd, *J* 10 and 3 Hz, 2-H), and 3.41 (1 H, dd, *J* 10 and 1 Hz, 3-H) (Found: C, 80.8; H, 10.2.  $\text{C}_{12}\text{H}_{18}\text{O}$  requires C, 80.85; H, 10.2%).

**Reduction of the Dienol (57).**—(a) *With hydrogen.* The dienol (57) (89 mg, 0.5 mmol) was hydrogenated in ethyl acetate (30 ml) over pre-reduced 2% palladium-charcoal (20 mg). The product was a gum (89 mg), identified as 4-cyclohexylcyclohex-3-enol (59) by comparison with an authentic sample.

(b) *With di-imide.*<sup>27</sup> To a stirred solution of the dienol (57) (375 mg, 2.1 mmol) in methanol (15 ml) were added hydrazine hydrate (7 g) and copper(II) acetate (1.9 mg). After 24 h the mixture was filtered through kieselguhr and evaporated to a light brown gum (381 mg). G.l.c. indicated that it was a mixture of the starting material (57) (41%), 4-cyclohexylidenecyclohexanol (58) (41%), and 4-cyclohexylcyclohexanol (5%). P.l.c. ( $\text{CH}_2\text{Cl}_2$ ) yielded starting material (57) (80 mg) and a solid (138 mg, 36%) which gave (from petrol) needles of 4-cyclohexylidenecyclohexanol (58), m.p. 109–110° (lit.,<sup>1</sup> 115°), identical with an authentic sample. In subsequent experiments, up to 64% of (58) was obtained.

**4-Cyclohexylcyclohex-3-enol (59).**—1-Cyclohexyl-4-methoxycyclohexa-1,4-diene<sup>13</sup> (31) (1.2 g, 6.25 mmol) [prepared by reduction with lithium-ammonia of 1-(*p*-methoxyphenyl)cyclohexene] in methanol-water (9 : 1; 50 ml), was treated with acetic acid (2 ml) and the solution was heated under reflux for 20 min. Most of the methanol was evaporated off and the residue was partitioned between ether and 5% sodium hydrogen carbonate. The organic phase was washed with water and evaporated to low volume. The resulting solution of 4-cyclohexylcyclohex-3-enone (35) was treated with methanol (50 ml) and stirred with sodium borohydride (250 mg) in water (5 ml). After 1.5 h, acetic acid (1 ml) was added and the solution was partitioned between ether and 5% sodium hydrogen carbonate. The organic layer was washed with water, dried, and evaporated to give an oil (1.01 g) which solidified. Chromatography on silica gel (chloroform as eluant) yielded the *alcohol* (59) (740 mg, 66%) as a very low-melting crystalline solid,  $\nu_{\text{max}}$  3 600  $\text{cm}^{-1}$  (OH),  $\tau$  6.10br (1 H, m, *CHOH*) and 4.72 (1 H, m, =CH-) (Found: C, 78.8; H, 10.9.  $\text{C}_{12}\text{H}_{20}\text{O} \cdot 0.125\text{H}_2\text{O}$  requires C, 78.9; H, 11.2%).

**4-Cyclohexylcyclohex-3-enyl Acetate (60).**—The alcohol (59) (600 mg, 3.3 mmol) was kept with acetic anhydride (5 ml)

and pyridine (5 ml) for 20 h at room temperature. The solvents were evaporated off and the residue was evaporated with benzene to give the *acetate* (60) as an oil (621 mg, 84%),  $\nu_{\text{max}}$  1 720  $\text{cm}^{-1}$  (ester),  $\tau$  7.98 (3 H, s,  $\text{OCOCH}_3$ ), 5.03 (1 H, m, *CHOAc*), and 4.72 (1 H, m, =CH-) (Found: C, 74.1; H, 10.0.  $\text{C}_{14}\text{H}_{22}\text{O}_2 \cdot 0.25\text{H}_2\text{O}$  requires C, 74.1; H, 10.0%).

**4-(4-Hydroxycyclohexylidene)cyclohex-2-enone (15).**—1-(*p*-Methoxyphenyl)cyclohexane-*cis*-1,4-diol (9a) (6.66 g, 30 mmol) was reduced with lithium and ammonia (Method A) and the crude ketonic product was chromatographed on alumina. Chloroform eluted the *dienone* (15) (5.26 g, 92%) which gave (from petrol-dichloromethane) off-white crystals, m.p. 114–115°,  $\lambda_{\text{max}}$  302 ( $\epsilon$  17 500) and 229.5nm (6 500),  $\nu_{\text{max}}$  3 610 and 3 460 (OH), and 1 660, 1 610, and 1 570  $\text{cm}^{-1}$  (C=C–C=C=O),  $\tau$  6.01 (1 H, m, *CHOH*), 4.11 (1 H, d, *J* 10 Hz, 2-H), and 2.44 (1 H, d, *J* 10 Hz, 3-H) (Found: C, 73.1; H, 8.2.  $\text{C}_{12}\text{H}_{16}\text{O}_2 \cdot 0.25\text{H}_2\text{O}$  requires C, 73.25; H, 8.45%).

**4-(4-Acetoxy-cyclohexylidene)cyclohex-2-enone (16).**—The dienone (15) (400 mg, 2.08 mmol) was treated overnight with pyridine (15 ml) and acetic anhydride (5 ml). The solvents were removed under reduced pressure and the residue was evaporated with toluene to leave a yellow oil (505 mg). P.l.c. ( $\text{CH}_2\text{Cl}_2$ ) yielded an oil (430 mg, 88%) which solidified. It gave (from petrol) crystals of the *acetate* (16), m.p. 98–100°,  $\lambda_{\text{max}}$  300 ( $\epsilon$  15 500) and 222 nm (6 700),  $\nu_{\text{max}}$  1 721 (ester) and 1 662, 1 618, and 1 575  $\text{cm}^{-1}$  (C=C–C=C=O),  $\tau$  7.85 (3 H, s,  $\text{OCOCH}_3$ ), 5.00 (1 H, m, *CHOAc*), 4.08 (1 H, d, *J* 10 Hz, 2-H), and 2.47 (1 H, d, *J* 10 Hz, 3-H) (Found: C, 71.5; H, 7.7.  $\text{C}_{14}\text{H}_{18}\text{O}_3$  requires C, 71.8; H, 7.7%).

**4-(4-Oxocyclohexylidene)cyclohex-2-enone (17).**—The dienone (15) (500 mg, 2.6 mmol) in acetone (50 ml) was treated dropwise with Jones reagent (0.65 ml). Water was added and the mixture was extracted with dichloromethane. The extract was washed with water, dried, and evaporated to give a pale yellow gum (382 mg). P.l.c. ( $\text{CHCl}_3$ ) yielded a white solid (168 mg, 34%) which gave (from ether) pale yellow crystals of the *dienedione* (17), m.p. 142–144°,  $\lambda_{\text{max}}$  299.5 nm ( $\epsilon$  14 100),  $\nu_{\text{max}}$  1 709 (C=O) and 1 662, 1 620, and 1 576  $\text{cm}^{-1}$  (C=C–C=C=O),  $\tau$  4.06 (1 H, d, *J* 10 Hz, 2-H) and 2.50 (1 H, d, *J* 10 Hz, 3-H) (Found: C, 73.9; H, 7.5.  $\text{C}_{12}\text{H}_{14}\text{O}_2 \cdot 0.25\text{H}_2\text{O}$  requires C, 74.0; H, 7.5%).

**4-(4-Hydroxy-4-methylcyclohexylidene)cyclohex-2-enone (18).**—1-(*p*-Methoxyphenyl)-4-methylcyclohexane-*cis*-1,4-diol (10a) (3.54 g, 15 mmol) was reduced with lithium and ammonia (Method B) to give, as the crude ketonic product, a pale yellow gum (1.84 g, 60%). It gave (from ether-petrol) crystals of the *dienone* (18), m.p. 88–89°,  $\lambda_{\text{max}}$  305 nm ( $\epsilon$  19 600),  $\nu_{\text{max}}$  3 600 (OH) and 1 662 and 1 619  $\text{cm}^{-1}$  (C=C–C=C=O),  $\tau$  8.76 (3 H, s,  $\text{CH}_3$ ), 4.11 (1 H, d, *J* 10 Hz, 2-H), and 2.41 (1 H, d, *J* 10 Hz, 3-H) (Found: C, 75.5; H, 8.8.  $\text{C}_{13}\text{H}_{18}\text{O}_2$  requires C, 75.7; H, 8.8%).

**4-(4-Acetoxy-cyclohexylidene)cyclohex-2-enone (19).**—4-(2,2-Ethylenedioxypropyl)-1-(*p*-methoxyphenyl)cyclohexanol (12) (3.06 g, 10 mmol) was reduced with lithium and ammonia (Method B) and the mixture of dihydro-compounds produced was hydrolysed by heating with acetic acid in aqueous methanol. The mixture was poured into rapidly stirred water (400 ml); needles (1.55 g, 67%) separated and were collected. Recrystallisation from ether-petrol yielded the *dienone* (19), m.p. 113–113.5°,  $\lambda_{\text{max}}$  303 nm ( $\epsilon$  18 450),  $\nu_{\text{max}}$  1 704 (C=O) and 1 659, 1 613, and 1 571  $\text{cm}^{-1}$  (C=C–C=C=O),  $\tau$  7.88 (3 H, s,  $\text{CH}_3$ ), 4.14



(1 H, d,  $J$  10 Hz, 2-H), and 2.48 (1 H, d,  $J$  10 Hz, 3-H) (Found: C, 77.2; H, 8.7.  $C_{15}H_{20}O_2$  requires C, 77.5; H, 8.7%). Extraction of the aqueous liquors with dichloromethane yielded a gum (820 mg) which on p.l.c. afforded the dienone (19) (360 mg, 15%).

4-[4-(2-Hydroxypropyl)cyclohexylidene]cyclohex-2-enone (20).—4-(2-Hydroxypropyl)-1-(*p*-methoxyphenyl)cyclohexanol (11) (3.9 g of mixed isomers, 14.8 mmol) was reduced with lithium and ammonia (Method B) to give as the crude ketonic product a brown gum (2.3 g). P.l.c. ( $CHCl_3$ ) yielded the dienone (20) (1.6 g, 46%) which gave (from ether-petrol) crystals, m.p. 68–70°,  $\lambda_{max}$  305 ( $\epsilon$  17 900) and 234 nm (5 000),  $\nu_{max}$  3 600 (OH) and 1 660 and 1 616  $cm^{-1}$  (C=C–C=C=O),  $\tau$  8.80 (3 H, d,  $J$  6 Hz,  $CH_3$ ), 6.10 (1 H, m,  $CHOH$ ), 4.12 (1 H, d,  $J$  10 Hz, 2-H), and 2.43 (1 H, d,  $J$  10 Hz, 3-H) (Found: C, 76.7; H, 9.6.  $C_{15}H_{22}O_2$  requires C, 76.9; H, 9.5%).

4-(4-Carboxymethylcyclohexylidene)cyclohex-2-enone (21).—4-Carboxymethyl-1-(*p*-methoxyphenyl)cyclohexanol (13) (21.3 g, 81 mmol) was reduced with lithium and ammonia by Method A. The residue left after evaporation of the ammonia was diluted with water and acidified to pH 1 with concentrated hydrochloric acid. The product was extracted into ether and the extracts were washed with water, dried, and evaporated to a white solid (13.6 g, 70%). A portion was purified by p.l.c. ( $CHCl_3$ ) with large loss, followed by crystallisation from aqueous ethanol, to give the dienone (21) as crystals, m.p. 135° (decomp.),  $\lambda_{max}$  304 ( $\epsilon$  18 700) and 230 nm (5 900),  $\nu_{max}$  3 600, 3 500, and 3 500–3 200 (OH), 1 720 and 1 700 ( $CO_2H$ ), and 1 660 and 1 611  $cm^{-1}$  (C=C–C=C=O),  $\tau$  4.09 (1 H, d,  $J$  10 Hz, 2-H) and 2.42 (1 H, d,  $J$  10 Hz, 3-H) (Found: C, 70.3; H, 7.6.  $C_{14}H_{18}O_3 \cdot 0.25H_2O$  requires C, 70.4; H, 7.8%).

4-(4-Methoxycarbonylmethylcyclohexylidene)cyclohex-2-enone (22).—The dienone (21) (2.8 g, 12 mmol) in ether (100 ml) was treated with an excess of ethereal diazomethane. The usual work-up gave a brown gum (2.59 g). Repeated p.l.c. ( $CHCl_3$ ) yielded the ester (22) as a yellow gum (250 mg, 8%) which gave (from ether-petrol) crystals, m.p. 61–62°,  $\lambda_{max}$  225 ( $\epsilon$  2 800) and 304.5 nm (6 000),  $\nu_{max}$  1 722 (ester) and 1 661 and 1 617  $cm^{-1}$  (C=C–C=C=O),  $\tau$  6.32 (3 H, s,  $CO_2CH_3$ ), 4.12 (1 H, d,  $J$  10 Hz, 2-H), and 2.48 (1 H, d,  $J$  10 Hz, 3-H) (Found: C, 71.5; H, 8.0.  $C_{15}H_{20}O_3 \cdot 0.25H_2O$  requires C, 71.3; H, 8.2%).

(±)-17 $\beta$ -Hydroxy-6,7-dinor-5,8-secoestra-4,9-dien-3-one and the  $\Delta^{1,9}$ -Isomer (42).—(±)-7 $\beta$ -Hydroxy-6 $\beta$ -methyl-trans-bicyclo[4.3.0]nonan-3-one (39) (5.05 g, 30 mmol; 86% pure) was treated in the usual way with *p*-methoxyphenylmagnesium bromide (66 mmol). The product was partially purified by chromatography on alumina; dichloromethane removed non-polar material, and chloroform, then ether, eluted the crude tertiary alcohol (6.35 g, 89%), which was reduced with lithium and ammonia (Method A) without further purification. The crude ketonic product was a golden gum (4.59 g) which was subjected to p.l.c. (petrol-acetone, 4 : 1) to give the dienone (42) (2.16 g, 30%) as a golden gum,  $\lambda_{max}$  305.5 nm ( $\epsilon$  14 000),  $\nu_{max}$  3 605 (OH), 1 663, 1 611, and 1 573  $cm^{-1}$  (C=C–C=C=O),  $\tau$  9.11 (3 H, s,  $CH_3$ ), 6.35 (1 H, m,  $CHOH$ ), 4.13 [1 H, d,  $J$  10 Hz, 4-(or 2-)H], and 2.32 [1 H, d,  $J$  10 Hz, 5-(or 1-)H] (Found: C, 75.6; H, 8.7.  $C_{16}H_{22}O_2 \cdot 0.5H_2O$  requires C, 75.3; H, 9.0%).

(±)-17 $\beta$ -Acetoxy-6,7-dinor-5,8-secoestra-4,9-dien-3-one and the  $\Delta^{1,9}$ -Isomer (43).—The hydroxy-dienone (42) (850 mg, 3.45 mmol) was kept for 70 h in pyridine (15 ml) and acetic anhydride (5 ml). The solvents were removed *in vacuo*

and the residue was azeotroped with toluene to give a brown oil (1.03 g). P.l.c. ( $CH_2Cl_2$ ) gave the acetate (43) (210 mg, 21%) as a low-melting yellow solid,  $\lambda_{max}$  303.5 nm ( $\epsilon$  13 450),  $\nu_{max}$  1 720 (ester) and 1 660 and 1 606  $cm^{-1}$  (C=C–C=C=O),  $\tau$  9.05 (3 H, s,  $CH_3$ ), 7.98 (3 H, s,  $OCOCH_3$ ), 5.33 (1 H, m,  $CHOAc$ ), 4.11 [1 H, d,  $J$  10 Hz, 4-(or 2-)H], and 2.42 [1 H, d,  $J$  10 Hz, 5-(or 1-)H] (Found: C, 73.4; H, 8.3.  $C_{18}H_{24}O_3 \cdot 0.25H_2O$  requires C, 73.8; H, 8.4%).

(±)-17 $\beta$ -Hydroxy-6,7-dinor-5,8-seco-14 $\beta$ -estra-4,9-dien-3-one and the  $\Delta^{1,9}$ -Isomer (44).—*p*-Bromoanisole (7.15 g, 38.25 mmol) in dry ether (50 ml) was added dropwise over 10 min to a stirred mixture of *n*-butyl-lithium in hexane (9.5 ml of a 2.4M-solution) and ether (45 ml) at 0 °C under nitrogen, and the mixture was stirred for 30 min at 0 °C. A solution of (±)-7 $\beta$ -hydroxy-6 $\beta$ -methyl-*cis*-bicyclo[4.3.0]nonan-3-one<sup>16</sup> (40) (1.5 g, 8.9 mmol) in dry ether (50 ml) was added at –30 °C. Dry tetrahydrofuran (75 ml) was added in an attempt to solubilise the resulting precipitate. The mixture was stirred at –15 °C for 30 min, then allowed to warm to room temperature, evaporated to small volume, and partitioned between water and ether. The aqueous phase was extracted with ether and the combined ethereal solutions were washed with water, dried, and evaporated to a yellow oil (5.5 g). Chromatography on alumina, eluting successively with dichloromethane and ether, yielded the crude tertiary alcohol (930 mg, 38%), which was reduced with lithium and ammonia (Method A). The crude ketonic product was a foam (380 mg) which, on p.l.c. (ether-petrol, 1 : 4), yielded the dienone (44), a 1 : 1 isomeric mixture, as a pale yellow gum (101 mg, 4.6%),  $\lambda_{max}$  305.5 nm ( $\epsilon$  15 800),  $\nu_{max}$  3 610 (OH) and 1 655 and 1 610  $cm^{-1}$  (C=C–C=C=O),  $\tau$  8.92 and 8.96 (3 H, both s,  $CH_3$ ), 6.19 (1 H, m,  $CHOH$ ), 4.13 [1 H, d,  $J$  10 Hz, 4-(or 2-)H], and 2.48 and 2.50 [1 H, both d,  $J$  10 Hz, 5-(and 1-) H] (Found: C, 75.3; H, 8.8.  $C_{16}H_{22}O_2 \cdot 0.5H_2O$  requires C, 75.3; H, 9.1%).

(±)-17 $\alpha\beta$ -Hydroxy-6,7-dinor-5,8-seco-D-homoestra-4,9-dien-3-one and the  $\Delta^{1,9}$ -Isomer (45).—(±)-7 $\beta$ -Hydroxy-6 $\beta$ -methyl-trans-bicyclo[4.4.0]decan-3-one<sup>18</sup> (41) (1.0 g, 5.5 mmol) was treated as above with *p*-methoxyphenyl-lithium (23.6 mmol) and the product was purified by chromatography on alumina. The resulting tertiary alcohol (850 mg, 53%) was reduced with lithium and ammonia (Method A). P.l.c. [EtOAc-petrol (1 : 2) then  $CHCl_3$ ] of the ketonic product (720 mg) yielded the dienone (45) (210 mg, 15%) as a gum,  $\lambda_{max}$  306.5 ( $\epsilon$  19 100) and 221 nm (6 000),  $\nu_{max}$  3 600 (OH) and 1 660, 1 612, and 1 570  $cm^{-1}$  (C=C–C=C=O),  $\tau$  9.03 (3 H, s,  $CH_3$ ), 6.80 (1 H, m,  $CHOH$ ), 4.12 [1 H, d,  $J$  10 Hz, 4-(or 2-)H] and 2.41 [1 H, d,  $J$  10 Hz, 5-(or 1-)H] (Found: C, 75.8; H, 9.15.  $C_{17}H_{24}O_2 \cdot 0.5H_2O$  requires C, 75.5; H, 9.35%).

(±)-7 $\beta$ -Hydroxy-6 $\beta$ -methyl-3 $\xi$ -(*p*-methoxyphenyl)bicyclo[4.3.0]non-1-ene (49).—Sodium (1.21 g) was added in small pieces to a solution of (±)-7 $\beta$ -hydroxy-6 $\beta$ -methyl-3-(*p*-methoxyphenyl)bicyclo[4.3.0]nona-2,9-diene<sup>19</sup> (48) (2.5 g, 9.75 mmol) in dry tetrahydrofuran (25 ml) and liquid ammonia (75 ml) at –60 °C and the mixture was stirred at –40 to –70 °C for 1.5 h. The blue colour was discharged with ammonium chloride, the ammonia was evaporated off, and the residue was partitioned between water and ether. The organic phase was washed with water, dried, and evaporated to a gum (2.45 g). P.l.c. (EtOAc-petrol, 1 : 2) afforded the olefin (49) (1.75 g, 69.5%) which gave (from ether-petrol) prisms, m.p. 87–88°,  $\nu_{max}$  3 610  $cm^{-1}$  (OH),  $\tau$  8.98 (3 H, s,  $CH_3$ ), 6.69 (1 H, m,  $ArCH$ ), 6.30 (1 H, m,  $CHOH$ ), 6.21

(3 H, s, OCH<sub>3</sub>), and 4.62br (1 H, s, =CH-) (Found: C, 78.9; H, 8.6. C<sub>17</sub>H<sub>22</sub>O<sub>2</sub> requires C, 79.0; H, 8.6%).

(±)-3-(4,4-Dimethoxycyclohex-1-enyl)-7β-hydroxy-6β-methylbicyclo[4.3.0]non-1-ene (51).—A solution of the olefin (49) (1.6 g, 6.2 mmol) in tetrahydrofuran (20 ml) and *t*-butyl alcohol (20 ml) was added over 5 min to a stirred mixture of lithium (1.2 g) and liquid ammonia (320 ml) and the mixture was stirred for 1 h. The colour was discharged with ethanol and the ammonia was evaporated off. The residue was partitioned between water and ether, and the organic phase was washed with water, dried, and evaporated. A solution of the residue in methanol (60 ml) was acidified to pH 4 with 2N-sulphuric acid. After 30 min it was neutralised with saturated aqueous sodium hydrogen carbonate and evaporated to small volume, then diluted with water and extracted with ether. The extract was washed with water, dried, and evaporated. P.l.c. (EtOAc-petrol, 1 : 4) of the residue gave the *acetal* (51) (970 mg, 54%) as a gum,  $\nu_{\max}$  (CS<sub>2</sub>) 3 630 cm<sup>-1</sup> (OH),  $\tau$  9.04 (3 H, s, CH<sub>3</sub>), 6.76 (6 H, s, 2 × OCH<sub>3</sub>), 6.20 (1 H, m, CHOH), and 4.70 (2 H, m, 2 × =CH-) (Found: C, 73.2; H, 9.5. C<sub>18</sub>H<sub>28</sub>O<sub>3</sub>·0.25H<sub>2</sub>O requires C, 72.8; H, 9.7%).

3-(*p*-Methoxyphenyl)butane-1,3-diol (53).—A mixture of boron trifluoride-ether complex (10 ml), ether (10 ml), and bis-(2-methoxyethyl) ether (10 ml) was added slowly under nitrogen to a stirred mixture of sodium borohydride (4 g) and bis-(2-methoxyethyl) ether (40 ml), and the resulting stream of diborane was passed through a solution of 2-(*p*-methoxyphenyl)but-3-en-2-ol<sup>19</sup> (52) (3.56 g, 20 mmol) in

dry tetrahydrofuran (20 ml). After 40 min, aqueous 2N-sodium hydroxide (20 ml) was added very cautiously, followed by 30% hydrogen peroxide (5 ml), and the mixture was stirred vigorously for 20 min, then diluted with water and extracted with ether. The extracts were washed successively with water, freshly prepared aqueous 5% iron(II) sulphate, and water, dried, and evaporated to a gum (2.63 g). A portion (375 mg) was subjected to p.l.c. (EtOAc-petrol, 1 : 1) to give as the major, more polar component the *diol* (53) as a gum (210 mg, 37.5%) which crystallised,  $\nu_{\max}$  3 600 and 3 490 cm<sup>-1</sup> (OH),  $\tau$  8.47 (3 H, s, CH<sub>3</sub>), 6.33 (2 H, m, CH<sub>2</sub>OH), 7.98 (2 H, m, CH<sub>2</sub>CH<sub>2</sub>OH), and 6.22 (3 H, s, OCH<sub>3</sub>) (Found: C, 67.0; H, 8.1. C<sub>11</sub>H<sub>16</sub>O<sub>3</sub> requires C, 67.3; H, 8.2%). The minor component (100 mg, 19%) was identified as 3-(*p*-methoxyphenyl)butan-2-ol.<sup>16</sup>

(E)- and (Z)-4-(3-Hydroxy-1-methylpropylidene)cyclohex-2-enone (55).—The diol (53) (1 g, 5.1 mmol) was reduced with lithium and ammonia (Method A) and the crude ketonic product (570 mg) was subjected to p.l.c. (EtOAc-petrol, 3 : 2) to give the *dienones* (55) as a gum (240 mg, 28%),  $\lambda_{\max}$  222 ( $\epsilon$  4 790) and 302.5 nm (14 200),  $\nu_{\max}$  3 620 (OH) and 1 655 and 1 612 cm<sup>-1</sup> (C=C-C=C=O),  $\tau$  8.04 and 8.06 (3 H, both s, CH<sub>3</sub>), 6.21 (2 H, t, *J* 7 Hz, CH<sub>2</sub>OH), 4.11 (1 H, d, *J* 10 Hz, 3-H), and 2.47 and 2.50 (1 H, both d, *J* 10 Hz, 2-H) (Found: C, 68.35; H, 8.6. C<sub>10</sub>H<sub>14</sub>O<sub>2</sub>·0.5H<sub>2</sub>O requires C, 68.55; H, 8.65%).

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