Clemmensen Reduction. Part 7.[1] Acid-catalysed Opening of Cyclopropane-1,2-diols

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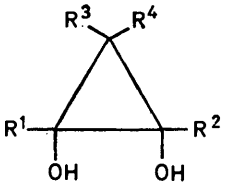
Cyclopropane-1,2-diols are shown to undergo ring opening in acid to give, in most cases, α-ketols, formation of β-ketols occurring only rarely. The α-ketols are often accompanied by αβ-unsaturated ketones of the same carbon skeleton. Unsymmetrical diols open to give usually only one α-ketol, the preference for the terminal group bonded to the carbonyl group being in the order methyl > phenyl > hydrogen. The relationship of these results to the Clemmensen reduction of 1,3-diketones is discussed.

EARLIER work [2a] led us to the conclusion that the key intermediates in the Clemmensen reduction of enolisable 1,3-diketones are rearranged α-ketols and unrearranged αβ-unsaturated ketones, both of which undergo further reduction. It is now well established that non-enolisable 1,3-diketones give rearranged α-ketols through the intermediacy of a cyclopropane-1-2-diol.[2b] In Part 6 [1] we reported the synthesis of a number of these diols using, in most cases, dissolving-metal reduction of a 1,3-diketone and trapping the diols as their diacetates. We now report on the acidolysis of the diols themselves and compare the products with those formed by Clemmensen reduction of the parent diketone.

The acid-catalysed conversion of cyclopropanols to ketones is a well documented reaction; [3] although some groups have studied the acidolysis of cyclopropane-1,2-diols and their derivatives,[4] very few data on unsymmetrical diols have been reported.

RESULTS AND DISCUSSION

In our work, cyclopropane-1,2-diyl diacetates were treated with methyl-lithium to remove the protective ester groups and protolysis was then achieved *in situ* by the action of methanolic hydrochloric acid. In view of the ease with which cyclopropane-1,2-diols are oxidised to diketones,[5] all reactions were performed under an atmosphere of nitrogen. 2,4-Dinitrophenylhydrazine was often added prior to work-up to aid in the isolation of otherwise water-soluble products, while for acid-sensitive products the reaction was performed in the presence of this reagent. In most cases, α-ketols were the major, even the sole, products of acidolysis of the diols and, conversely, β-ketols were conspicuous by their absence. αβ-Unsaturated carbonyl compounds were also obtained from some reactions; their genesis is discussed below. 1,2-Dimethylcyclopropane-1,2-diol (1), 1,2,3,3-tetramethylcyclopropane-1,2-diol (2), and 1,3,3-trimethyl-2-phenylcyclopropane-1,2-diol (3) gave only the α-hydroxy methyl ketones (8), (9), and (10) respectively, while 1,2,3-trimethylcyclopropane-1,2-diol (4) gave mainly 3-methylpent-3-en-2-one (11) which might arise in this case from either the α- or the β-ketol by dehydration, or by a concerted process (see later). Clemmensen reduction of the parent diketones gives, as one of the products, the appropriate α-ketol in each case (ref. 6 and present work). Two cyclopropane-1,2-diols containing one secondary hydroxy group, (5) and (6), also underwent ring opening; in one example (5), the 2,4-dinitrophenylhydrazine used as trapping reagent gave not only the hydrazone of the α-ketol (12) but also its corresponding osazone (13). Clemmensen reduction of the parent β-keto-aldehyde gave the free α-ketol (12). In the other example, (6), the corresponding enone derivative (14) was obtained

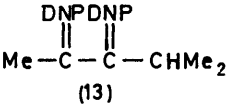


(1) $R^1 = R^2 = Me, R^3 = R^4 = H$
(2) $R^1 = R^2 = R^3 = R^4 = Me$
(3) $R^1 = R^3 = R^4 = Me, R^2 = Ph$
(4) $R^1 = R^2 = R^3 = Me, R^4 = H$
(5) $R^1 = R^3 = R^4 = Me, R^2 = H$
(6) $R^1 = Ph, R^3 = R^4 = Me, R^2 = H$
(7) $R^1 = R^3 = Me, R^2 = Ph, R^4 = H$

$MeCOCMe_2(OH)$ (8)

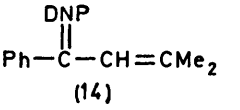
$MeCOCMe(OH)CHMe_2$ (9)

$MeCOCPh(OH)CHMe_2$ (10)



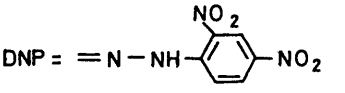
(13)

$MeCOCMe{=}CHMe$ (11)



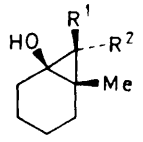
(14)

$MeCOCH(OH)CHMe_2$ (12)

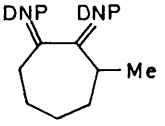


In all the above cases where an unsymmetrical diol was utilised, not only was the direction of ring opening specific in giving an α-ketol, but of the two possible α-ketols only one was obtained. The terminal substituent attached to the carbonyl group showed a well-defined order of preference in the sequence methyl > phenyl > hydrogen. In one unsymmetrical diol two modes of ring opening were observed. Thus, at the temperature of the

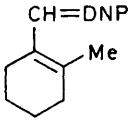
refluxing solution the *cis* bicyclic diol (15) gave the osazone (17) as the major product and the aldehyde 2,4-dinitrophenylhydrazone (18) as the minor product, although only the α-ketol hydrazone (19) was obtained at room temperature. In contrast, the *trans* bicyclic diol (16) was inert at room temperature but at reflux temperature gave the aldehyde derivative (18) as the major and the osazone (17) as the minor product. The αβ-unsaturated aldehyde can arise either in a step-wise manner *via* the α-ketol, or directly from the diol by a concerted ring opening concomitant with loss of water. In this latter case, only one of the two possible disrotatory motions is feasible as a consequence of the steric constraints imposed by the fused cyclohexane ring. Moreover, in the *cis* isomer (15) this inwards disrotation forces the methyl group to move towards the hydroxy-group at the terminus of the cyclopropane bond being broken, whereas in the *trans* isomer (16) this same disrotation causes the methyl group to move towards a hydrogen atom. Such a concerted process, if it occurs at all, would be of greater importance in the ring opening of the *trans* as opposed to the *cis* isomer. Thus the unsaturated aldehyde and not the α-ketol, is the major product in the former case.



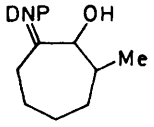
(15) R^1 = OH, R^2 = H
(16) R^2 = OH, R^1 = H



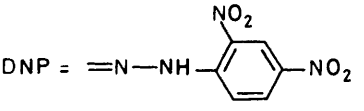
(17)



(18)

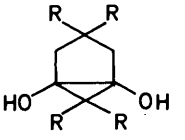


(19)

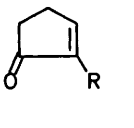


In two examples of bicyclo[3.1.0]hexane-1,5-diols, (20) and (21), ring opening proceeded to give the unsaturated ketones (22), and (23) and (24), respectively, as the only isolable products. The Clemmensen reduction of the corresponding diketones had given the α-ketol (25) and the deoxy-ketone (26) as the main products from 2,2,5,5-tetramethylcyclohexane-1,3-dione,[7] while both 2-methylcyclopentanone and cyclohexanone had been obtained from cyclohexane-1,3-dione.[2]

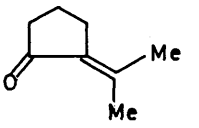
In only one case was evidence obtained for the opening of a cyclopropane-1,2-diol to give a β-ketol. 1,3-Dimethyl-2-phenylcyclopropane-1,2-diol (7) gave, with 4 mol l^{-1} acid, the now expected product (27) and a small amount of the enone (28); this latter compound must arise by dehydration of a β-ketol. When (7) was treated with more dilute acid (0.1 mol l^{-1}) the enone (28) became the major product. The Clemmensen reduction of the corresponding diketone, in 5 mol l^{-1} acid, gave only the α-ketol (27) and its corresponding deoxy-ketone. The



(20) R = H
(21) R = Me



(22) R = Me
(23) R = ^{i}Pr



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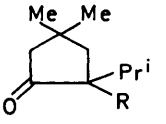
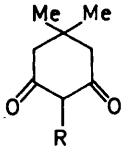


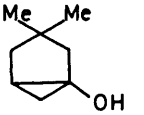
(25) R = OH
(26) R = H

MeCOCPh(OH)CH_2Me
(27)

MeCOCMe=CHPh
(28)



(29) R = H
(30) R = Me



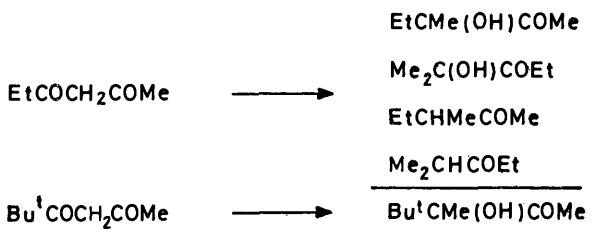
(31)

difference in results depending on the acid concentration suggests that protonation at the non-oxygenated C-3 is of major importance in initiating carbon–carbon bond cleavage in strong acid; in dilute acid, however, the mesomeric effect of the oxygen atom of a non-protonated hydroxy-group assumes the dominant function in 'pushing' the ring open.

Two points are noteworthy in summarising the acid-catalysed ring opening reactions of cyclopropane-1,2-diols. The first is the marked preference for methyl ketone formation where this is possible. Such a preference has been observed previously in the Lewis-acid-catalysed isomerisation of α-ketols and of saturated ketones.[8] Assuming that the observed products are formed by a kinetically controlled process in the present case, it may be that the hyperconjugative effect of the methyl group on the protonated carbonyl group outweighs the conjugative effect of the phenyl group. The second point is the marked preference for α-ketol formation in these ring openings. Inductive effects presumably make the C-1 and C-2 carbon atoms less electron-rich than the C-3 carbon atom, and thus protonation occurs preferentially at this latter position, subsequent electronic shifts then producing the observed α-ketols. We have postulated [2a] the presence of αβ-unsaturated ketones of unrearranged skeleton in the Clemmensen reduction of enolisable diketones. These, in turn, we proposed to arise from β-ketols but the source of these

latter compounds was uncertain. Our present work strongly suggests that acidolysis of cyclopropane-1,2-diols does not produce β-ketols in any appreciable amount, and therefore that these products must arise by direct reduction of the diketone without involving the cyclic diol intermediate. That β-ketols and αβ-unsaturated ketones can be derived from β-diketones under reductive conditions is supported further by our previous observation [1] that treatment of 5,5-dimethylcyclohexane-1,3-dione under modified Clemmensen conditions produced not the cyclopropane-1,2-diol, but the same cyclopropanol that was obtained by reduction of 5,5-dimethylcyclohexenone.

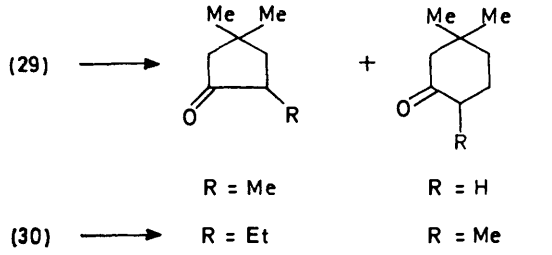
Our results from cleavage of the diols allow us to rationalise the formation of the products of Clemmensen reduction of some other 1,3-diketones with respect to the nature of the group adjacent to the carbonyl group. Two unsymmetrical diketones were treated with amalgamated zinc and aqueous hydrochloric acid (Scheme). Hexane-2,4-dione gave a mixture of both possible α-ketols and the derived deoxy-ketones, with the methyl ketones predominant in each case as expected from consideration of the greater hyperconjugative effect of the methyl group compared with that of the ethyl group. A similar



SCHEME

argument can be invoked to explain the exclusive formation of the methyl ketol from the reduction of 5,5-dimethylhexane-2,4-dione (Scheme 1).

In the cyclic compounds (29) and (30) reduction to a β-ketol becomes important, with dehydration and further reduction of an αβ-unsaturated ketone producing a cyclopropanol, which on acidolysis gives a mixture of rearranged and unrearranged monoketones. No α-ketols were isolated in these reductions. Confirmatory evidence for this pathway was obtained when acid-catalysed opening of the cyclopropanol (31) gave a similar mixture of products to that formed by aqueous reduction of the diketone (29). α-Ketols have been isolated also from reduction of cyclic diketones [2,6]



and thus both the cyclopropanol and cyclopropane-1,2-diol pathways must be operating in these cases.

EXPERIMENTAL

General experimental details can be found in Part 6.[1] All reduction and rearrangement products were purified by p.l.c. and the quoted yields are the isolated yields off p.l.c.

Synthesis of 1,3-Dicarbonyl Compounds.—The synthesis of several of the 1,3-dicarbonyls was described in Part 6.[1]

Hexane-2,4-dione. Condensation of acetone with ethyl propanoate using sodium hydride in ether gave hexane-2,4-dione [9] which was isolated by fractional distillation, b.p. 155—158 °C.

5,5-Dimethylhexane-2,4-dione. Treatment of 3,3-dimethylbutan-2-one with sodium amide in liquid ammonia, followed by the addition of ethyl acetate gave, after purification as its copper(II) salt, 5,5-dimethylhexane-2,4-dione, b.p. 81—82 °C at 30 mmHg (lit.,[10] 70—71 °C at 20 mmHg).

2,5,5-Trimethylcyclohexane-1,3-dione (30). 5,5-Dimethylcyclohexane-1,3-dione (29) was reacted with the equivalent amount of iodomethane and sodium methoxide in methanol to give the trimethyl diketone (30) in 59% yield, m.p. 159—160 °C (aqueous EtOH) (lit.,[11] 158—159 °C).

Rearrangement of Cyclopropane-1,2-diols. General Rearrangement Procedure.—A solution of cyclopropane-1,2-diyl diacetate [1] (0.25 g) in dry ether (5 ml) was treated with a slight excess of methyl-lithium in ether at room temperature and the mixture was stirred under an atmosphere of oxygen-free nitrogen for *ca.* 10 min. Addition of an excess of methanolic hydrochloric acid (4 mol l^{-1}) gave the free diol, which was rearranged *in situ* by stirring either at room temperature or under reflux, for varying times, depending on the nature of the substrate. 2,4-Dinitrophenylhydrazine was often added prior to work-up to aid in the isolation of otherwise water-soluble products, while for acid-sensitive products the rearrangement was performed in the presence of this reagent.

1,2-Dimethylcyclopropane-1,2-diol (1). Rearrangement of 1,2-dimethylcyclopropane-1,2-diol by heating under reflux for 15 min, followed by reaction with 2,4-dinitrophenylhydrazine, gave (*i*) 3-methoxy-3-methylbutan-2-one 2,4-dinitrophenylhydrazone (38%), m.p. 142—143.5 °C (lit.,[12] 139—140 °C); δ_H 1.48 (6 H, s, 3-Me and 4-H_3), 2.06 (3 H, s, 1-H_3), 3.16 (3 H, s, OMe), and 11.06 (1 H, m, NH); and (*ii*) 3-hydroxy-3-methylbutan-2-one 2,4-dinitrophenylhydrazone (20%), m.p. 143—144 °C (lit.,[12] 139—140 °C); δ_H 1.53 (6 H, s, 3-Me and 4-H_3), 2.17 (3 H, s, 1-H_3), 2.67 (1 H, m, exchangeable on deuteriation, OH), and 11.10 (1 H, m, NH).

1,2,3,3-Tetramethylcyclopropane-1,2-diol (2). Rearrangement of 1,2,3,3-tetramethylcyclopropane-1,2-diol (2) as above, followed by extraction with ether, gave 3-hydroxy-3,4-dimethylpentan-2-one (79%), one peak by g.l.c.; $\nu_{max.}$ 3 495 (OH), 1 695 (C=O), 1 360 (CMe_2), and 1 160 cm^{-1} (C–O); δ_H 0.72 and 1.02 (6 H, 2 d, *J* 7 Hz, 4-Me and 5-H_3), 1.30 (3 H, s, 3-Me), 2.17 (3 H, s, 1-H_3), and 4.83 (1 H, m, exchangeable on deuteriation, OH); the 2,4-dinitrophenylhydrazone had m.p. 120 °C (lit.,[13] 114—115 °C).

1,3,3-Trimethyl-2-phenylcyclopropane-1,2-diol (3). Rearrangement of the diol (3) gave 3-hydroxy-4-methyl-3-phenylpentan-2-one (34%); $\nu_{max.}$ 3 470 (OH), 1 705 (C=O), and 1 350 cm^{-1} (C–O); δ_H 0.84 and 1.04 (6 H, 2 d, *J* 7 Hz, 4-Me and 5-H_3), 2.12 (3 H, s, 1-H_3), 2.73 (1 H, sextet, *J*

7 Hz, 4-H), 4.22 (1 H, s, exchangeable on deuteriation, OH), and 7.33 (5 H, m, Ar-H); δ_C 16.4 (4-Me and C-5), 23.5 (C-4), 32.5 (C-1), 85.6 (C-3), 126.6 (*ortho*-C), 127.5 (*para*-C), 128.4 (*meta*-C), 140.3 (C-1′), and 209.6 (C-2); the *oxime* had m.p. 92—93 °C (Found: C, 69.65; H, 8.4; N, 6.5. $C_{12}H_{17}NO_2$ requires C, 69.5; H, 8.3; N, 6.75%).

1,2,3-*Trimethylcyclopropane*-1,2-*diol* (4). Rearrangement of 1,2,3-trimethylcyclopropane-1,2-diol (4) gave 3-methylpent-3-en-2-one 2,4-dinitrophenylphydrazone (29%), m.p. 198—199 °C (lit., [14] 198—200 °C); δ_H 1.93 (3 H, d, *J* 7 Hz, 5-H_3), 2.02 (3 H, s, 3-Me), 2.20 (3 H, s, 1-H_3), 6.25 (1 H, q, *J* 7 Hz, 4-H), and 11.22 (1 H, m, NH).

1,3,3-*Trimethylcyclopropane*-1,2-*diol* (5). Rearrangement of the trimethyl diol (5) by heating it under reflux for 1 h in the presence of 2,4-dinitrophenylhydrazine, followed by extraction with dichloromethane, gave: (*i*) 4-methylpentane-2,3-dione bis-(2,4-dinitrophenylhydrazone) (25%), m.p. 220—221 °C (lit.,[15] 226—227 °C); *m/e* 474 ($M^{+\cdot}$, $C_{18}H_{18}N_8O_8$); δ_H 1.56 (6 H, d, *J* 7 Hz, 4-Me and 5-H_3), 2.41 (3 H, s, 1-H_3), 3.90 (1 H, septet, *J* 7 Hz, 4-H), and 11.37 and 11.72 (2 H, NH); and (*ii*) 3-hydroxy-4-methylpentan-2-one 2,4-dinitrophenylhydrazone, m.p. 139.5—142.5 °C (lit.,[16] 139—142 °C); δ_H 0.95 and 1.06 (6 H, 2 d, *J* 6 Hz, 4-Me and 5-H_3), 2.10 (3 H, s, 1-H_3), 2.83 (1 H, m, exchangeable on deuteriation, OH), 4.18 (1 H, d, *J* 6 Hz, 3-H), and 11.12 (NH).

3,3-*Dimethyl*-1-*phenylcyclopropane*-1,2-*diol* (6). Rearrangement of the diol (6) by heating it under reflux for 4 h in the presence of 2,4-dinitrophenylhydrazine gave: (*i*) 3-methyl-1-phenylbut-2-en-1-one 2,4-dinitrophenylhydrazone (19%), m.p. 184—185 °C (lit.,[17] 185—186 °C); δ_H 1.67 (3 H, s, *trans*-3-Me), 2.17 (3 H, d, *J* 2 Hz, *cis*-4-H_3), 5.95 (1 H, m, $W_{\frac{1}{2}}$ 4 Hz, 2-H), and 11.55 (1 H, apparent br s, NH); (*ii*) 2,2-*dimethyl*-3-*oxo*-3-*phenylpropanal bis*-(2,4-*dinitrophenylhydrazone*) (11%), m.p. 229—230 °C (dichloromethane–methanol) (Found: C, 51.1; H, 3.7; N, 20.4. $C_{23}H_{20}N_8O_8$ requires C, 51.5; H, 3.8; N, 20.9%); *m/e* 536 ($M^{+\cdot}$, $C_{23}H_{20}N_8O_8$); $\nu_{max.}$ 3 280 (N-H) and 1 610 and 1 595 cm^{-1} (C=N and C=C); δ_H 1.63 (6 H, s, 2-Me_2), 7.87 (1 H, s, 1-H), and 10.7 and 11.18 (2 H, 2 s, NH). This compound had identical m.p. and spectroscopic properties to material obtained by treatment of the keto-aldehyde with an excess of 2,4-dinitrophenylhydrazine in refluxing acidic methanol; and (*iii*) a number of minor unidentified products.

6-*Methylbicyclo*[4.1.0]*heptane*-1,2-*diol* (15, 16). Rearrangement of the *cis*-isomer of the bicyclic diol (15), by heating it under reflux for 2 h in the presence of 2,4-dinitrophenylhydrazine. gave: (*i*) 2-methylcyclohex-1-enecarbaldehyde 2,4-dinitrophenylhydrazone (18) (9%), m.p. 190—191 °C (lit.,[18] 190—191 °C); δ_H 1.70 (4 H, m, 4- and 6-H_2), 1.95 (3 H, s, 2-Me), 2.30 (4 H, m, 3- and 6-H_2), 8.22 (1 H, s, 1-H), and 11.17 (1-H, m, NH); (*ii*) 3-*methylcycloheptane*-1,2-*dione bis*-(2,4-*dinitrophenylhydrazone*) (17) (51%), as orange needles from dichloromethane–methanol, m.p. 215—216 °C (Found: C, 47.9; H, 4.0; N, 22.4. $C_{20}H_{20}N_8O_8$ requires C, 48.0; H, 4.0; N, 22.4%); *m/e* 500 ($M^{+\cdot}$, $C_{20}H_{20}N_8O_8$); $\nu_{max.}$ 3 300 (N–H) and 1 605 and 1 595 cm^{-1} (C=C and C=N); δ_H 1.41 (3 H, d, *J* 7 Hz, 3-Me), 1.92 (6 H, m, 4-, 5-, and 6-H_2), 2.87 (3 H, m, 3-H and 7-H_2), and 11.43 and 12.73 (2 H, 2 s, NH); and (*iii*) a complex mixture of other minor products. Repeating the same reaction at room temperature for 3 h gave: trans-2-*hydroxy*-3-*methylcycloheptanone* 2,4-*dinitrophenylhydrazone* (19) (26%) as yellow needles, m.p. 154.5—155.5 °C (CH_2Cl_2–MeOH) (Found: C, 52.0; H, 5.6; N, 17.0. $C_{14}H_{18}N_4O_5$ requires C, 52.2; H, 5.6; N, 17.4%); *m/e* 322 ($M^{+\cdot}$, $C_{14}H_{18}N_4O_5$); $\nu_{max.}$ 3 500 (O–H), 3 310 (N–H), and 1 610 and 1 595 cm^{-1} (C=C and C=N); δ_H 1.20 (3 H, d, *J* 6 Hz, 3-Me), 2.63 (2 H, m, 7-H_2), 3.23 (1 H, m, exchangeable on deuteriation, OH), 4.16 (1 H, d, *J* 7 Hz, 2-H), and 11.18 (NH); δ_H 19.8 (3-Me), 22.9, 27.1, and 27.6 (C-5, -6, and -7), 33.5 (C-4), 41.4 (C-3), 78.8 (C-2), and 162.2 (C-1); and a number of minor unidentified products. Although treatment of the *trans*-isomer at room temperature failed to induce any rearrangement, heating it under reflux gave the same two products as above, in 16 and 2.3% yield respectively.

Bicyclo[3.1.0]*hexane*-1,5-*diol* (20). 1,5-Bis(trimethylsilyoxy)(bicyclo[3.1.0]hexane (0.26 g, 1 mmol) was dissolved in a mixture of methanol (30 ml) and conc. hydrochloric acid (10 ml), and 2,4-dinitrophenylhydrazine (0.5 g) in acidic methanol (20 ml) was added. The mixture was stirred and heated under reflux beneath at atmosphere of nitrogen for 30 min, then cooled and extracted with dichloromethane. P.l.c. [hexane–dichloromethane (1 : 1)] gave 2-methylcyclopent-2-enone 2,4-dinitrophenylhydrazone (0.11 g, 40%), m.p. 223—224 °C (lit.,[19] 221—222 °C); $\nu_{max.}$ 3 310 (N–H) and 1 615 and 1 590 cm^{-1} (C=C and C=N); *m/e* 276 ($M^{+\cdot}$, $C_{12}H_{12}N_4O_4$); δ_H 1.96 (3 H, m, $W_{\frac{1}{2}}$ 4 Hz, 2-Me), 2.70 (4 H, m, $W_{\frac{1}{2}}$ 3 Hz, 4- and 5-H_2), 6.50 (1 H, m, $W_{\frac{1}{2}}$ 4 Hz, 3-H), 7.96 (1 H, d, *J* 9.5 Hz, 6′-H), 8.30 (1 H, dd, *J* 2.5 and 9.5 Hz, 5′-H), 9.10 (1 H, d, *J* 2.5 Hz, 3′-H), and 10.82 (1 H, m, NH). The same product was obtained when the trimethylsilyl groups were removed by treatment with methyl-lithium prior to the addition of acid. Performing the reaction in the absence of 2,4-dinitrophenylhydrazine gave a complex mixture from which no pure compounds could be isolated.

3,3,6,6-*Tetramethylbicyclo*[3.1.0]*hexane*-1,5-*diol* (21). Rearrangement of the bicyclic diol (21) gave: (*i*) 2-isopropylidene-4,4-dimethylcyclopentanone (24) (0.1 g, 23%); $M^{+\cdot}$ 152; $\nu_{max.}$ 1 705 (C=O) and 1 635 cm^{-1} (C=C); δ_H 0.92 (6 H, s, 4 Me_2), 1.83 (3H, s, Me), 2.17 (3 H, s, Me), 2.20 (2 H, s, 5-H_2), and 2.37 (2 H, br s, 3-H_2); the 2,4-dinitrophenylhydrazone had m.p. 210—212 °C (lit.,[20] 212—213 °C); and (*ii*) 2-isopropyl-4,4-dimethylcyclopent-2-enone (23) (0.03 g, 7%); $\nu_{max.}$ 1 705 (C=O) and 1 630 cm^{-1} (C=C); δ_H 1.08 (6 H, d, *J* 7 Hz, 2-CMe_2), 1.19 (6 H, s, 3-Me_2), 2.27 (2 H, s, 5-H_2), 2.52 (1 H, sextet, *J* 7 Hz, 1′-H), and 6.97 (1 H, br s, 3-H); the 2,4-*dinitrophenylhydrazone* had m.p. 181—183 °C (methanol–chloroform) (Found: C, 57.9; H, 6.1; N, 17.0. $C_{16}H_{20}N_4O_4$ requires C, 57.8; H, 6.1; N, 16.9%). When a sample of 2-hydroxy-2-isopropyl-4,4-dimethylcyclopentanone, dissolved in acidic methanol, was heated under reflux for 30 min the two enones (23) and (24) were shown by g.l.c. to be the products of elimination.

1,3-*Dimethyl*-2-*phenylcyclopropane*-1,2-*diol* (7). Rearrangement of the diol (7) by heating it under reflux for 2 h gave: (*i*) 3-methyl-4-phenylbut-3-en-2-one (28) (9%) $\nu_{max.}$ 1 670 (C=O) and 1 615 cm^{-1} (C=C); δ_H 2.00 (3 H, d, *J* *ca.* 1 Hz, 3-Me), 2.38 (3 H, s, 1-H_3), and 7.33 (6 H, apparent br s, 4-H and Ar-H); the 2,4-dinitrophenylhydrazone had m.p. 199—200 °C (lit.,[21] 190—191 °C); and (*ii*) 3-hydroxy-3-phenylpentan-2-one (27) (23%); $\nu_{max.}$ 3 480 (OH), 1 705 (C=O), 1 665 (C=C), and 1 135 cm^{-1} (C–O); δ_H 0.87 (3 H, t, *J* 7 Hz, 5-H_3), 2.03 (3 H, s, 1-H_3), 2.13 (2 H, q, *J* 7 Hz, 4-H_2), 4.18 (1 H, s, exchangeable on deuteriation, OH), and 7.33 (5 H, m, Ar-H); the oxime had m.p. 90—91 °C (lit.,[22] 80 °C). Performing the above rearrangement with dilute acid (0.1 mol l^{-1}) resulted in the exclusive formation of the αβ-unsaturated enone.

Clemmensen Reduction of 1,3-*Dicarbonyl Compounds; General Reduction Procedure.*—A mixture of diketone (1 g), amalgamated zinc wool (2.5 g), ethanol (15 ml), conc. hydrochloric acid (10 ml), and water (5 ml) was heated under reflux for 15 min, and a few crystals of ferric chloride were then added to the cooled solution to oxidise any unrearranged cyclopropanediol. The reduction products were normally isolated by direct extraction with ether, although water-soluble compounds were converted to their 2,4-dinitrophenylhydrazones and extracted with dichloromethane.

2,2-*Dimethyl*-1-*phenylbutane*-1,3-*dione*. Clemmensen reduction of the phenyldiketone, and work-up as before, gave: (*i*) 4-methyl-3-phenylpentan-2-one (22%); $\nu_{max.}$ 1 710 cm^{-1} (C=O); δ_H 0.65 and 0.96 (6 H, 2 d, *J* 6 Hz, 4-Me and 5-H_3), 2.00 (3 H, s, 1-H_3), 3.73 (1 H, m, 4-H), 3.21 (1 H, d, *J* 9 Hz, 3-H), and 7.22 (5 H, s, Ar-H); the 2,4-*dinitrophenylhydrazone* had m.p. 113—115 °C (dichloromethane–methanol) (Found: C, 60.6; H, 5.7; N, 15.5. $C_{18}H_{20}N_4O_4$ requires C, 60.7; H, 5.7; N, 15.7%); (*ii*) 3-hydroxy-4-methyl-3-phenylpentan-2-one (10) (25%), identical by ^1H n.m.r. and i.r. spectroscopy with an authentic sample; and (*iii*) starting material (12%).

3-*Methylpentane*-2,4-*dione*. Clemmensen reduction of 3-methylpentane-2,4-dione, followed by reaction of the products with 2,4-dinitrophenylhydrazine gave: 3-methylpentan-2-one 2,4-dinitrophenylhydrazone (12%), m.p. 65—68 °C (lit.,[23] 68—70 °C); δ_H 0.77 (3 H, t, *J* 7 Hz, 5-H_3), 1.20 (3 H, d, *J* 7 Hz, 3-Me), 1.67 (2 H, m, 4-H_2), 2.05 (3 H, s, 1-H_3), 2.53 (1 H, sextet, *J* 7 Hz, 3-H), and 14.37 (1 H, m, NH); and (*ii*) 3-hydroxy-3-methylpentan-2-one 2,4-dinitrophenylhydrazone (23%), m.p. 95—100 °C (lit.,[24] 107—109 °C); δ_H 0.90 (3 H, t, *J* 7 Hz, 5-H_3), 1.50 (3 H, s, 3-Me), 1.82 (2 H, q, *J* 7 Hz, 4-H_2), 2.00 (3 H, s, 1-H_3), 3.70 (1 H, m, exchangeable on deuteriation, OH), and 14.42 (1 H, m, N-H).

2,2-*Dimethyl*-3-*oxobutanal*. Clemmensen reduction of the β-keto-aldehyde gave 3-hydroxy-4-methylpentan-2-one (12) (28%) as the only identifiable product; $\nu_{max.}$ 3 460 (OH) and 1 700 cm^{-1} (C=O); δ_H 0.72 and 1.08 (6 H, 2 d, *J* 6 Hz, 4-Me and 5-H_3), 2.17 (3 H, s, 1-H_3), 3.20 (1 H, br s, exchangeable on deuteriation, OH), and 3.93 (1 H, d, *J* 3 Hz, 3-H); the 2,4-dinitrophenylhydrazone was identical with a previously isolated sample.

2,2,5,5-*Tetramethylcyclohexane*-1,3-*dione*. Clemmensen reduction of the tetramethyldione by the method of Kariv *et al.*,[7] followed by work-up involving treatment with ferric chloride, gave: (*i*) 2-isopropyl-4,4-dimethylcyclopentanone (26) (31%); (*ii*) 2-hydroxy-2-isopropyl-4,4-dimethylcyclopentanone (25) (16%); and (*iii*) starting material (13%). No trace of 3-hydroxy-2,2,5,5-tetramethylcyclohexanone was observed.

2-*Methyl*-1-*phenylbutane*-1,3-*dione*. Clemmensen reduction of the phenyldiketone, followed by treatment with ferric chloride and extraction with ether, gave: (*i*) 3-phenylpentan-2-one (29%); $\nu_{max.}$ 1 705 cm^{-1} (C=O); δ_H 0.82 (3 H, t, *J* 7 Hz, 5-H_3), 1.37—2.30 (2 H, m, 4-H_2), 2.00 (3 H, s, 1-H_3), 3.43 (1 H, t, *J* 7 Hz, 3-H), and 7.20 (5 H, br s, Ar-H); the 2,4-*dinitrophenylhydrazone* had m.p. 129—130 °C (dichloromethane–methanol) (Found: C, 59.4; H, 5.4; N, 16.1. $C_{17}H_{18}N_4O_4$ requires C, 59.6; H, 5.3; N, 16.4%); (*ii*) 3-hydroxy-3-phenylpentan-2-one (27) (9%), identical by ^1H n.m.r. and i.r. spectroscopy with authentic material previously isolated; and (*iii*) starting material (8%).

Hexane-2,4-*dione*. Clemmensen reduction of hexane-2,4-dione for 5 min, followed by treatment with ferric chloride and 2,4-dinitrophenylhydrazine, gave: (*i*) a mixture (26%) of 3-methylpentan-2-one (70%) and 2-methylpentan-3-one (30%) 2,4-dinitrophenylhydrazones; and (*ii*) a mixture (30%) of 3-hydroxy-3-methylpentan-2-one (70%) and 2-hydroxy-2-methylpentan-3-one (30%) 2,4-dinitrophenylhydrazones. The major component in each mixture was identical by ^1H n.m.r. spectroscopy with authentic material (see above), while the minor components were identified from non-ambiguous signals: (*i*) δ_H 1.23 (d, *J* 7 Hz, 1-H_3 and 2-Me) and 14.53 (NH); and (*ii*) δ_H 1.55 (s, 1-H_3 and 2-Me), 2.65 (q, *J* 7 Hz, 4-H_2), and 14.60 (NH).

5,5-*Dimethylhexane*-2,4-*dione*. Clemmensen reduction of 5,5-dimethylhexane-2,4-dione gave 3-hydroxy-3,4,4-trimethylpentan-2-one (23%) as the sole isolated product; $\nu_{max.}$ 3 470 (OH), 1 695 (C=O), 1 365 and 1 350 (CMe_3), and 1 125 cm^{-1} (C–O); δ_H 0.95 (9 H, s, CMe_3), 1.28 (3 H, s, 3-Me), 2.22 (3 H, s, 1-H_3), and 3.45 (1 H, m, exchangeable on deuteriation, OH).

5,5-*Dimethylcyclohexane*-1,3-*dione* (29). Clemmensen reduction of 5,5-dimethylcyclohexane-1,3-dione (29) gave: (*i*) 2,4,4-trimethylcyclopentanone; $\nu_{max.}$ 1 740 cm^{-1} (C=O); δ_H 1.07 (3 H, d, *J* 7 Hz, 2-Me), 1.10 and 1.18 (6 H, 2 s, 4-Me_2), and 2.00 (2 H, s, 5-H_2); (*ii*) 3,3-dimethylcyclohexanone; $\nu_{max.}$ 1 705 cm^{-1} (C=O); δ_H 1.00 (6 H, s, 3-Me_2) and 2.08 (2 H, s, 2-H_2); and (*iii*) 3-ethoxy-5,5-dimethylcyclohex-2-enone; $\nu_{max.}$ 1 710 (C=O) and 1 605 cm^{-1} (C=C); δ_H 1.07 (6 H, s, 5-Me_2), 1.37 (3 H, t, *J* 7 Hz, ethyl Me), 2.09 (2 H, s, 6-H_2), 2.22 (2 H, s, 4-H_2), 3.90 (2 H, q, *J* 7 Hz, ethyl CH_2), and 5.20 (1 H, s, 2-H).

2,5,5-*Trimethylcyclohexane*-1,3-*dione* (30). Clemmensen reduction of the trimethyldione (30) gave, in addition to a small amount of hydrocarbons, a mixture of two monoketones which showed carbonyl absorptions at 1 750 (five-membered ring ketone) and 1 710 cm^{-1} (six-membered ring ketone) in the i.r. spectrum. Formation of the 2,4-dinitrophenylhydrazones and recrystallization to constant melting point gave 2-*ethyl*-4,4-*dimethylcyclopentanone* 2,4-*dinitrophenylhydrazone*, m.p. 160—161 °C (methanol–chloroform) (Found: C, 56.0; H, 6.4; N, 17.3. $C_{15}H_{20}N_4O_4$ requires C, 56.2; H, 6.3; N, 17.5%); *m/e* 320 ($M^{+\cdot}$, $C_{15}H_{20}N_4O_4$); $\nu_{max.}$ 1 615 and 1 585 (C=C and C=N), and 1 330 cm^{-1} (NO_2); δ_H 1.02 (3 H, t, *J* 6 Hz, ethyl Me), 1.10 and 1.26 (6 H, 2 s, 4-Me_2), 1.56 (2 H, m, $W_{\frac{1}{2}}$ 4 Hz, 3-H_2), 1.95 (2 H, apparent q, *J* 6 Hz, ethyl CH_2), 2.33 (2 H, m, $W_{\frac{1}{2}}$ 6 Hz, 5-H_2), 2.77 (1 H, m, 2-H), and 14.13 (1 H, br s, NH). Concentration of the mother liquors gave a mixture of the above compound and 2,5,5-trimethylcyclohexanone 2,4-dinitrophenylhydrazone; δ_H 0.92 and 1.10 (6 H, 2s, 5-Me_2), 1.25 (3 H, d, *J* 6 Hz, 2-Me), and 11.25 (1 H, br s, NH). The ratio of five- to six-membered ring ketones was 3 : 1 by ^1H n.m.r. spectroscopic analysis of the initial hydrazone mixture.

Rearrangement of 3,3-*Dimethylbicyclo*[3.1.0]*hexan*-1-*ol* (31). —3,3-Dimethylbicyclo[3.1.0]hexan-1-yl acetate (0.5 g, 3 × 10^{-3} mol) in dry ether was treated with an excess of methyllithium in ether, and the solution was stirred at room temperature for 15 min. Neutralisation (litmus) with dilute acid and ether work-up gave 3,3-dimethylbicyclo[3.1.0]-hexan-1-ol (31) (0.38 g, 100%), δ_H 0.48 (1 H, t, *J* 5 Hz), 0.92 and 1.13 (6 H, 2 s, 3-Me_2), 1.86 (2 H, br s, 2-H_2), and 4.28 (1 H, exchangeable on deuteriation, br s, OH). The alcohol (31) was heated under reflux for 1 h in methanolic acid (20 ml, 4 mol l^{-1}) and worked up to give a mixture (0.25 g) of two compounds (g.l.c. >5 : 1) which were separated by

p.l.c. [hexane–ether (9 : 1)] to give 2,4,4-trimethylcyclopentanone and 3,3-dimethylcyclohexanone, identical by ^{1}H n.m.r. and i.r. spectroscopy with the monoketones obtained from the Clemmensen reduction of 5,5-dimethylcyclohexane-1,3-dione (29).

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