Clemmensen Reduction. Part III.[1] αβ-Unsaturated Ketones

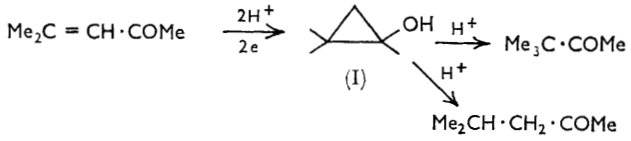
By B. R. Davis and P. D. Woodgate

Further studies on the Clemmensen reduction of αβ-unsaturated ketones support the suggestion that cyclopropanols are intermediates in this reaction. A variety of approaches to, and the successful synthesis of, a hitherto unknown bicyclo[3,1,0]hexan-1-ol are described. Clemmensen reduction of cholest-4-en-3-one gives 5β-cholest-3-ene which has been synthesised by an alternative route. The behaviour of some cyclohex-2-enols under Clemmensen conditions has been investigated.

In Part II [1,2] we showed that cyclohex-2-enone and its methyl derivatives were reduced on comparatively brief treatment under Clemmensen conditions to give a mixture of the corresponding cyclohexanone and the related 2-substituted cyclopentanone. We suggested that this reaction proceeds by way of a cyclopropanol. We have now studied the Clemmensen reduction of some acyclic αβ-unsaturated ketones and isolated both an unrearranged and a rearranged monoketone.

4-Methylpent-3-en-2-one was treated with amalgamated zinc wool and 7M-hydrochloric acid for 30 min. to give a 75% yield of two ketones, identified by their infrared (i.r.) and nuclear magnetic resonance (n.m.r.) spectra, and gas–liquid chromatography (g.l.c.), as 3,3-dimethylbutan-2-one and 4-methylpentan-2-one, in the ratio 72 : 28.

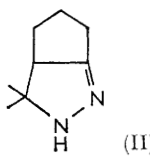
The detailed course of this reaction is not yet clear. However, the most likely path involves the intermediacy



of a cyclopropanol (I). The initial steps may involve the addition of a proton and an electron followed by the transformation of an allyl radical into a cyclopropyl radical;[3,4] the acid-catalysed cleavage of cyclopropanols is well established.[5] Evidence for the correctness of this postulate was provided by the synthesis and acid-catalysed cleavage of 1,2,2-trimethylcyclopropanol [6] to give the same two saturated ketones, in the same relative proportions, as found above.

Clemmensen reduction of an aralkyl αβ-unsaturated ketone, 4-phenylbut-3-en-2-one,[6a] provided further confirmatory evidence. In this case the products were 3-phenylbutan-2-one and 4-phenylbutan-2-one, in the ratio 58 : 42. De Puy and Breitbeil [5] had previously synthesised the expected cyclopropanol intermediate, 1-methyl-2-phenylcyclopropanol, and found that acid-catalysed decomposition gave the same two ketones in the ratio 60 : 40.

In our earlier work on the Clemmensen reduction of cyclohex-2-enones [1] we had postulated the intermediacy of a hitherto unknown bicyclo[3,1,0]hexan-1-ol. The necessity to synthesise such a system and subject it to acid-catalysed cleavage in order to confirm the mechanism was apparent. The two chief synthetic approaches appeared to be (*a*) an extension of Freeman's work [6] involving thermal decomposition of an acetoxypyrazoline, or (*b*) addition of a carbene to a cycloalkenyl acetate. Both routes were examined, the former providing a successful synthesis. 2-Isopropylidenecyclopentanone [7] was treated with 80% hydrazine hydrate to give the bicyclic pyrazoline (II), which had previously been decomposed directly by Kishner and Losik to 6,6-dimethylbicyclo[3,1,0]hexane.[8] Acetoxylation with lead tetra-acetate gave the crude acetoxy-pyrazoline (III) which evolved nitrogen at 170° to give the bicyclic acetate (IV; R = Ac) showing the expected infrared and n.m.r. spectra. Lithium aluminium hydride reduction then gave the desired bicyclic alcohol (IV; R = H). This is unstable but, on treatment with hot 7M-hydrochloric acid for 5 min., gave 2-isopropylcyclopentanone [9] and 2,2-dimethylcyclohexanone [10] in the ratio 1 : 3 (g.l.c.).



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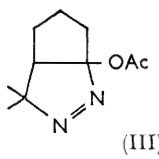

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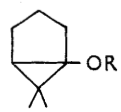


(IV)

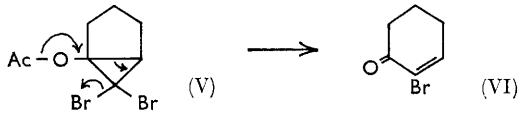
A number of examples of acid-catalysed isomerisation of cyclopropanols have now been studied.[5,11] In a series of deuteration experiments, De Puy and Breitbeil [5] demonstrated that this bimolecular reaction involves electrophilic attack at a saturated carbon atom, subsequent cleavage proceeding with retention of configuration. In the cases studied, bond cleavage takes place

[1] Part II, B. R. Davis and P. D. Woodgate, *J. Chem. Soc.*, 1965, 5943.
[2] For a preliminary account see B. R. Davis and P. D. Woodgate, *Chem. Comm.*, 1966, 65.
[3] R. B. Woodward and R. Hoffmann, *J. Amer. Chem. Soc.*, 1965, **87**, 395.
[4] H. C. Longuet-Higgins and E. W. Abrahamson, *J. Amer. Chem. Soc.*, 1965, **87**, 2045.
[5] C. H. De Puy and F. W. Breitbeil, *J. Amer. Chem. Soc.*, 1963, **85**, 2176.
[6] J. P. Freeman, *J. Org. Chem.*, 1964, **29**, 1379.
[6a] J. F. J. Dippy and R. H. Lewis, *Rec. Trav. chim.*, 1937, **56**, 1000.
[7] J. M. Conia and J.-P. Sandre, *Bull. Soc. chim. France*, 1963, 744.
[8] I. N. M. Kishner and I. B. Losik, *Bull. Acad. Sci. U.S.S.R.*, 1941, 49.
[9] W. Huckel and G. Naher, *Chem. Ber.*, 1958, **91**, 792.
[10] S. V. Kessar and K. P. Mahajan, *J. Indian Chem. Soc.*, 1962, **39**, 147.
[11] C. H. De Puy, L. G. Schnack, J. W. Hausser, and W. Wiedemann, *J. Amer. Chem. Soc.*, 1965, **87**, 4006.

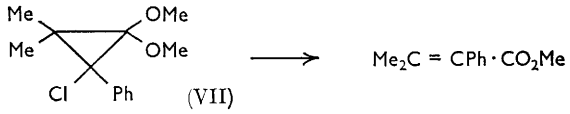
predominantly towards the least alkylated carbon atom. Thus, if the Clemmensen reduction of cyclohex-2-enones involves a cyclopropanol intermediate, the product ratio cyclopentanone : cyclohexanone should increase in the order 2-methylcyclohex-2-enone < cyclohex-2-enone ≃ 5,5-dimethylcyclohex-2-enone < 3-methylcyclohex-2-enone. This order ratio was verified in our earlier work.[1]

All the above results taken together thus confirm the hypothesis that Clemmensen reduction of both cyclic and acyclic αβ-unsaturated ketones proceeds *via* a cyclopropanol intermediate.

In the course of experiments directed towards the synthesis of bicyclo[*n*,1,0]alkan-1-ols ($n = 3$ and 4) we studied the reaction of some carbenes with cycloalkenyl acetates. No reaction was observed when cyclohexenyl acetate was treated with diazomethane. However, reaction of cyclohexenyl acetate with sodium trichloracetate at 125° gave a low yield of 7,7-dichlorobicyclo[4,1,0]heptyl acetate, identified by its analysis, and infrared and n.m.r. spectra. The product from the reaction of dibromocarbene [generated by pyrolysis of phenyl(tribromomethyl) mercury[12]] with cyclopentenyl acetate was not the bicyclic compound, but one presumably derived from it, *viz.*, 2-bromocyclohex-2-enone. The melting point and infrared and n.m.r. spectral properties were fully consistent with the published values[13] for this compound, which may be formed by (V) ⟶ (VI). It is known[14–16] that the

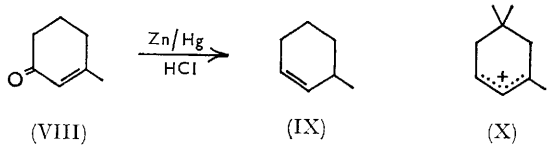


dihalogenocyclopropane adduct formed by the addition of a dihalogenocarbene to a small cyclic system can undergo ring enlargement on heating. An exactly analogous reaction occurred[17] when 2-chloro-2-phenyl-3,3-dimethylcyclopropanone dimethyl acetal (VII) was pyrolysed to give α-phenyl-β-methyl crotonate.



Ethoxycarbonylcarbene, generated by the copper sulphate-catalysed decomposition of ethyl diazoacetate, added to the double bond of both cyclopentenyl acetate and cyclohexenyl acetate to give the corresponding ethoxycarbonyl acetates, identified by their analyses and infrared and n.m.r. spectra. The n.m.r. spectra of both compounds showed the ethyl group of the ethoxycarbonyl moiety as two triplets and two quartets, suggesting that both *endo* and *exo* isomers were present.

During work on cyclohex-2-enones,[1] we found that an alkyl group on C(3) resulted in the appreciable formation of an alkene, with the double bond at C(1), *viz.*, (VIII) ⟶ (IX). Extension of this work to a steroidal



enone has produced a similar result. Clemmensen reduction of cholest-4-en-3-one gave, as the only isolable product, 5β-cholest-3-ene in 48% yield. This compound was unambiguously characterised by comparison of its m. p. and infrared and n.m.r. spectra with those of an authentic sample, synthesised by the general method developed by Shoppee *et al.*[18] In the present work cholest-4-en-3-one was hydrogenated[19] to 5β-cholestan-3-one, which, on bromination with pyridinium bromide perbromide, gave 4β-bromo-5β-cholestan-3-one.[20] Sodium borohydride reduction gave a mixture of epimeric bromohydrins which were treated with zinc in acetic acid[21] to give 5β-cholest-3-ene (27%) together with 5β-cholestan-3α-ol, its acetate, and the corresponding ketone. The isolation of the alcohol, acetate, and ketone is somewhat surprising since Fieser and Ettore[21] utilised the zinc–acetic acid reduction of the appropriate bromohydrin to synthesise methyl-Δ^3-cholenate in 92% yield.

Although the isolation of the Δ^3-steroid from the Clemmensen reduction is consistent with the isolation of similarly constituted alkenes in the cyclohexane series, the stereochemistry at the A/B ring junction is unusual in that it results from attack of hydrogen at C(5) from above the plane of the molecule (*i.e.*, most hindered side). However, an analogous reduction involving a surface–molecule interaction is the palladium-catalysed hydrogenation of cholest-4-en-3-one to 5β-cholestan-3-one.[19]

Norymberski[22] converted a number of steroidal enones into alkenes with double-bond migration using zinc in acetic acid at room temperature. In four cases, involving unsaturation of C(5), the products had *trans* (5α) ring-junctions, but in two cases both the *cis* (5β) and *trans* (5α) isomer were isolated.

We also examined the reaction of allylic alcohols

[12] D. Seyferth and J. M. Burlitch, *J. Organometallic Chem.*, 1965, **4**, 127.
[13] F. G. Bordwell and K. M. Wellman, *J. Org. Chem.*, 1963, **28**, 2544.
[14] S. Winstein and J. Sonnenberg, *J. Org. Chem.*, 1962, **27**, 748.
[15] C. W. Jefford, *Proc. Chem. Soc.*, 1963, 64.
[16] C. W. Jefford, S. Mahajan, J. Waslyn, and B. Waegell, *J. Amer. Chem. Soc.*, 1965, **87**, 2183.
[17] S. M. McElvain and P. L. Weyna, *J. Amer. Chem. Soc.*, 1959, **81**, 2579.
[18] D. R. James, R. W. Rees, and C. W. Shoppee, *J. Chem. Soc.*, 1955, 1370.
[19] H. Grasshof, *Z. physiol. Chem.*, 1934, **223**, 249.
[20] C. Djerassi and C. R. Scholz, *J. Amer. Chem. Soc.*, 1948, **70**, 417.
[21] L. F. Fieser and R. Ettore, *J. Amer. Chem. Soc.*, 1953, **75**, 1700.
[22] J. K. Norymberski, B.P. 887,706 (*Chem. Abs.*, 1962, **57**, 2292).

under Clemmensen conditions. Risinger, Mach, and Barnett [23] found that cyclohexanol gave a quantitative yield of cyclohexene; the unsaturated alcohols behave similarly and give the products of dehydration rather than of reduction. Thus, 3,5,5-trimethylcyclohex-2-enol afforded, after 30 min., a mixture of dienes separated by preparative g.l.c. and identified by their infrared [24] and n.m.r. spectra as 5,5-dimethyl-3-methylenecyclohexene and a mixture of 1,5,5-trimethyl- and 3,5,5-trimethylcyclohexadiene. These dehydrations clearly proceed *via* a mesomeric carbonium ion (X), which may lose a proton from any one of the three available sites. Dehydration [24] of this cyclohexenol with alumina yielded the same homoannular dienes and the methylenecyclohexene in the ratio 7 : 3. Reaction of cholest-4-en-3-ol with amalgamated zinc and hydrochloric acid gave only cholesta-3,5-diene.

The failure of acidolysis of the monocyclic 2-en-1-ols to yield the products isolated from the Clemmensen reduction of the corresponding cycloalkenones rules out the possibility of their being an intermediate in the reaction, as opposed to the bicyclic cyclopropanol derivative.

EXPERIMENTAL

For general experimental details, see Part II.[1]

Clemmensen Reduction of 4-*Methylpent*-3-*en*-2-*one*.—4-Methylpent-3-en-2-one (5 g., 0·051 mole) was heated under reflux for 30 min. with amalgamated zinc wool (14·3 g., 0·218 mole) and 7M-hydrochloric acid (25 ml.). Ether extraction yielded a yellow liquid (3·81 g.) separated by preparative g.l.c. into two fractions, identified with authentic samples, by i.r. and n.m.r. spectra and g.l.c. retention volumes, as 3,3-dimethylbutan-2-one, n_D^{20} 1·3960 (lit.,[25] n_D^{25} 1·3950), 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 125° (lit.,[26] m. p. 125°) and 4-methylpentan-2-one. Analytical g.l.c. showed the two ketones to be present in the ratio 72 : 28. The use of unamalgamated zinc and hydrochloric acid gave no rearranged or reduced products under these conditions.

1,2,2-*Trimethylcyclopropanol*.— 4-Methylpent-3-en-2-one was converted into the corresponding acetoxypyrazoline by successive reaction with hydrazine hydrate and lead tetra-acetate. Thermal decomposition gave 1,2,2-trimethylcyclopropyl acetate [6] which on reduction with lithium aluminium hydride gave 1,2,2-*trimethylcyclopropanol*, b. p. 42—44°/15 mm., n_D^{20} 1·4256, $\nu_{max.}$ 3320 (OH) and 3065 cm.$^{-1}$ (cyclopropane), δ 0·15 and 0·44 [2d, J = 5 c/sec., 2, C(3) methylene protons], 1·03 and 1·17 (2s, 6, CMe_2) 1·38 [s, 3, *C*(1)Me], 4·45 (s, 1, OH, reduced on deuteration). The cyclopropanol's instability prevented an accurate analysis being obtained.

Acid-catalysed Isomerisation of 1,2,2-*Trimethylcyclopropanol*.—1,2,2-Trimethylcyclopropanol (2·6 g., 0·026 mole, freshly distilled) was heated under reflux with 7M-hydrochloric acid (11 ml.) for 5 min. Ether extraction and distillation yielded a liquid (2·11 g.) which was shown by analytical g.l.c. to contain 3,3-dimethylbutan-2-one and 4-methylpentan-2-one in the ratio 73 : 27. The n.m.r. spectrum of the total product confirmed this analysis.

Clemmensen Reduction of 4-*Phenylbut*-3-*en*-2-*one*.—4-Phenylbut-3-en-2-one (7·45 g., 0·051 mole) was heated under reflux for 30 min. with amalgamated zinc wool (14·3 g., 0·218 mole) and 7M-hydrochloric acid (25 ml.). Ether extraction yielded a yellow oil (6·3 g.) which deposited a little colourless solid (possibly a dimer). Analytical g.l.c. of the oil showed the presence of 3-phenylbutan-2-one and 4-phenylbutan-2-one in the ratio 58 : 42. The n.m.r. spectrum of the total reduction product showed all the signals found in the spectra of the two authentic ketones.

6,6-*Dimethylbicyclo*[3,1,0]*hexan*-1-*ol*.— 6,6-*Dimethylcyclopentano*[c]-2-*pyrazoline* (I). 2-Isopropylidenecyclopentanone, prepared from cyclopentanone, acetone, and aqueous sodium hydroxide,[7] was made to react with hydrazine hydrate solution to give 6,6-dimethylcyclopentano[*c*]-2-pyrazoline,[8] $\nu_{max.}$ 3238 (NH), 1646 (C=N), 1373 and 1360 cm.$^{-1}$ (CMe_2).

7-*Acetoxy*-6,6-*dimethylcyclopentano*[c]-1-*pyrazoline* (III). The crude pyrazoline (23·2 g., 0·168 mole) in dry dichloromethane (40 ml.) was added during 15 min. to a stirred solution of lead tetra-acetate (81·8 g., 0·185 mole) in dry dichloromethane (300 ml.) held at 2—5°. The mixture was stirred at 20° for a further 40 min. Working up gave the acetoxypyrazoline (26·5 g., 81%) as a brown oil, $\nu_{max.}$ 1748 and 1235 (acetate) and 1652 cm.$^{-1}$ (N=N).

6,6-*Dimethylbicyclo*[3,1,0]*hex*-1-*yl acetate* (IV; R = Ac). The crude acetoxypyrazoline (26·5 g., 0·135 mole) was heated at 170° until nitrogen evolution ceased (1½ hr.). Distillation yielded a liquid, b. p. 76—78°/20 mm. (10·2 g., 45%) which was purified by preparative g.l.c. to give the *bicyclic acetate*, n_D^{21} 1·4509 (Found: C, 71·6; H, 9·5; O, 19·4. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6; O, 19·0%); $\nu_{max.}$ 1745 and 1233 cm.$^{-1}$ (acetate), δ 1·01 and 1·04 (2s, 6, CMe_2), 1·13—1·85 [m, 4, CH_2 on C(3) and C(4)], 1·93 (s, 3, acetate), 1·93—2·48 [m, 3, CH_2 at C(3), CH at C(5)].

6,6-*Dimethylbicyclo*[3,1,0]*hexan*-1-*ol* (IV; R = H). A solution of 6,6-dimethylbicyclo[3,1,0]hex-1-yl acetate (IV; R = Ac) in ether (60 ml.) was added to lithium aluminium hydride (9·3 g., 0·244 mole) in ether during 60 min. The mixture was heated under reflux for 90 min. and saturated ammonium chloride solution added. The mixture was then stirred for 24 hr. and yielded a pale yellow liquid (6·3 g.) to ether. Distillation yielded the unstable 6,6-dimethylbicyclo[3,1,0]hexan-1-ol (4·3 g., 57%), b. p. 84—86°/19 mm., $\nu_{max.}$ 3375 and 1156 cm.$^{-1}$ (OH).

Acid-catalysed Isomerisation of 6,6-*Dimethylbicyclo*[3,1,0]-*hexan*-1-*ol*.—6,6-Dimethylbicyclo[3,1,0]hexan-1-ol (3·84 g., 0·0305 mole) was heated under reflux for 5 min. with 7M-hydrochloric acid (12 ml.). Ether extraction yielded a liquid (3·6 g.), b. p. 63—68°/19 mm., $\nu_{max.}$ 1738 (cyclopentanone) and 1710 cm.$^{-1}$ (cyclohexanone). The n.m.r. spectrum indicated the presence of 2-isopropylcyclopentanone [9] and 2,2-dimethylcyclohexanone [10] in the ratio 1 : 3, by comparison with the spectra of authentic samples. The two ketones were not completely resolved on g.l.c. but 2-isopropylcyclopentanone was identified in the mixture by its retention volume, alone and mixed with an authentic sample.

Cycloalkenyl Acetate–Carbene Addition Reactions.—(*a*)

[23] G. E. Risinger, E. E. Mach, and K. W. Barnett, *Chem. and Ind.*, 1965, 679.

[24] H. Pines and R. H. Kozlowski, *J. Amer. Chem. Soc.*, 1956, **78**, 3776.

[25] H. Adkins and S. H. Watkins, *J. Amer. Chem. Soc.*, 1951, **73**, 2184.

[26] A. I. Vogel, "Practical Organic Chemistry," Longmans, 3rd ed., 1964, p. 346.

Addition of a solution of diazomethane in ether to an ether solution of cyclohexenyl acetate [27] containing anhydrous copper sulphate gave starting material identified by its i.r. spectrum.

(*b*) *Dichlorocarbene–cyclohexenyl acetate.* A mixture of cyclohexenyl acetate [27] (5·0 g., 0·026 mole), dry sodium trichloroacetate (13·30 g., 0·072 mole), and diethylene glycol diethyl ether (10 ml.) were heated at 125° for 1½ hr. Removal of sodium chloride, solvent, and some cyclohexanone, followed by distillation yielded 7,7-*dichlorobicyclo*[4,1,0]*hept*-1-*yl acetate* (0·64 g., 13%), b. p. 78°/0·3 mm., n_D^{19} 1·4840 (Found: C, 48·0; H, 5·45; O, 16·5. $C_9H_{12}Cl_2O_2$ requires C, 48·4; H, 5·4; O, 14·35%); $\nu_{max.}$ 1760 (α-chloro-acetate) 1221 cm.$^{-1}$ (acetate), δ 1·25—1·60 [m, 4, CH_2 on C(3), C(4)], 1·64—1·93 [m, 2, CH_2 on C(5)] 2·03 (s, 3, acetate), 2·09—2·67 [m, 2, CH_2 on C(2)], 3·31—3·67 [m, 1, CH on C(6)].

(*c*) *Dibromocarbene–cyclopentenyl acetate.* Phenyl(tribromomethyl)mercury [12] (7·0 g., 0·132 mole), cyclopentenyl acetate (5·0 g., 0·0396 mole), and benzene (17 ml.) were heated in nitrogen under reflux for 1½ hr., benzene (8 ml.) being added after ½ hr. Removal of precipitated phenylmercuric bromide (4·5 g., 97%), solvent, and excess of cyclopentenyl acetate left a brown solid (3·0 g.). Chromatography on silica gel in benzene gave 2-bromocyclohex-2-enone (0·32 g., 14%) as flakes (from chloroform–light petroleum), m. p. 74·5° (lit.,[13] m. p. 74°), $\nu_{max.}$ 1713 (α-halogeno- αβ-unsaturated carbonyl), 1612 (conj. C=C), δ 7·34 [t, J = 4·3 c./sec., 1, vinyl H on C(3)] (lit.,[13] δ 7·36 t, J = 4·2 c./sec.).

(*d*) *Ethoxycarbonylcarbene–cyclopentenyl acetate.* Ethyl diazoacetate (13·06 g., 0·115 mole) in cyclopentenyl acetate (15·1 g., 0·120 mole) was added to cyclopentenyl acetate (48 g., 0·42 mole) containing anhydrous copper sulphate (0·20 g.) at 100°. After addition (2½ hr.), stirring and heating were continued for 30 min. Excess of cyclopentenyl acetate was distilled off *in vacuo* and the residue, in ether, washed with 2% aqueous potassium permanganate solution, to remove maleic and fumaric esters. Working up and distillation gave cis- *and* trans-6-*ethoxycarbonylbicyclo*-[3,1,0]*hex*-1-*yl acetate* (4·60 g., 18%), b. p. 76—78°/0·3 mm., n_D^{17} 1·4595 (Found: C, 62·2; H, 7·8; O, 30·4. $C_{11}H_{16}O_4$ requires C, 62·25; H, 7·6; O, 30·15%); $\nu_{max.}$ 3020 (cyclopropane), 1753, 1733 (ester C=O) 1229 (acetate) and 1197 cm.$^{-1}$ (ethoxycarbonyl), δ 1·25 and 1·29 (2t, J = 7 c./sec., 3, $CO_2{\cdot}CH_2{\cdot}C\mathbf{H}_3$), 1·96 (s, 3, acetate), 4·08 and 4·15 (2q, J = 7 c./sec., 2, $CO_2{\cdot}C\mathbf{H}_2{\cdot}CH_3$).

(*e*) *Ethoxycarbonylcarbene–cyclohexenyl acetate.* Ethyl diazoacetate (27·8 g., 0·244 in mole) in cyclohexenyl acetate (35·9 g., 0·257 mole) was added to cyclohexenyl acetate (125 g., 0·893 mole) containing anhydrous copper sulphate (0·41 g.), as described for cyclopentenyl acetate. Distillation gave cis- *and* trans-7-*ethoxycarbonylbicyclo*[4,1,0]*hept*-1-*yl acetate* (19·0 g., 35%), b. p. 110°/2·0 mm., 87—88°/0·1 mm., n_D^{18} 1·4677 (Found: C, 64·1; H, 7·7; O, 28·6. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0; O, 28·3%); $\nu_{max.}$ 3021 (cyclopropane), 1751, 1733 (ester C=O), 1234 (acetate) and 1179 cm.$^{-1}$ (ethoxycarbonyl), δ 1·20 and 1·25 (2t, J = 7 c./sec., 3, $CO_2{\cdot}CH_2{\cdot}C\mathbf{H}_3$), 1·86 (s, 3, acetate), 3·98 and 4·05 (2q, J = 7 c./sec., 2, $CO_2{\cdot}C\mathbf{H}_2{\cdot}CH_3$).

Clemmensen Reduction of Cholest-4-en-3-one.—Cholest-4-en-3-one (6·70 g., 0·0173 mole) in toluene (21 ml.) was heated under reflux for 2½ hr. with amalgamated zinc wool (13·4 g., 0·205 mole) and 7M-hydrochloric acid (24 ml.). Chromatography of the oil (5·80 g.) on alumina gave 5β-cholest-3-ene (3·10 g., 48%) as an oil which crystallised on long standing. Recrystallisation from ethanol or acetone gave needles, m. p. 46·5—47·5°, $[\alpha]_D^{23}$ +22° (*c* 1·25) [lit.,[28] m. p. 48°, $[\alpha]_D$ +21° (*c* 1·1)], i.r. and n.m.r. spectra identical with those of an authentic sample (Found: C, 87·3; H, 12·5. Calc. for $C_{27}H_{46}$: C, 87·5; H, 12·5%).

5β-*Cholest*-3-*ene*.—5β-*Cholestan*-3-*one*. Cholest-4-en-3-one (5·0 g.) in ether (50 ml.) was hydrogenated over 10% palladium–charcoal (0·5 g.) until absorption ceased. Removal of catalyst and solvent gave a yellow oil (4·8 g.) which was chromatographed on alumina to yield 5β-cholestan-3-one, (4·5 g., 90%), m. p. 57·5—58·5° (lit.,[19] m. p. 58—60°), $[\alpha]_D^{23}$ +46° (*c* 1·04); $\nu_{max.}$ 1713 cm.$^{-1}$, δ 0·69 [*C*(18)Me], 1·03 [*C*(19)Me].

4β-*Bromo*-5β-*cholestan*-3-*one*.[20] 5β-Cholestan-3-one (1·0 g., 2·59 mmole) and pyridinium bromide perbromide (0·83 g., 2·59 mmole) in absolute ethanol (40 ml.) were heated at 50° for 10 min. with stirring. The mixture was kept at 20° for 30 min., then water was added to precipitate the product. Crystallisation from ethanol gave 4β-bromo-5β-cholestan-3-one (0·93 g., 79%) as needles, m. p. 108·5—109·5° (lit.,[20] m. p. 111—113°), $\nu_{max.}$ 1734 cm.$^{-1}$ δ 0·69 [*C*(18)Me], 1·09 [*C*(19)Me].

4β-*Bromo*-5β-*cholestan*-3-*ol*. The bromo-ketone (6·6 g., 0·0146 mole) in absolute ethanol (150 ml.) was treated with a solution of sodium borohydride (0·27 g., 0·0071 mole) in absolute ethanol (40 ml.) and the mixture kept at 20° for 3 days. Working up as usual gave the oily mixture of epimeric 4β-bromo-5β-cholestan-3-ols (6·3 g., 96%), $\nu_{max.}$ (film) 3445, 1275, and 1051 cm.$^{-1}$ (OH).

5β-*Cholest*-3-*ene* (*Coprost*-3-*ene*). The crude bromohydrin mixture (6·3 g.) and zinc dust (19·2 g.) were heated under reflux with glacial acetic acid (250 ml.) for 30 min. Removal of zinc and acetic acid gave an oil (4·7 g.) which was chromatographed on alumina and the compounds eluted as described.

(i) With light petroleum: 5β-Cholest-3-ene (1·40 g., 27%), m. p. 44° (acetone), $[\alpha]_D^{22}$ +23° (*c* 0·92), δ 0·66 [*C*(18)Me], 0·94 [*C*(19)Me], 5·43 [q, J = 11 c./sec., C(3) and C(4) vinyl protons].

(ii) With light petroleum–benzene (1 : 1): Probably 5β-cholestan-3α-yl acetate (0·54 g.) as an oil, $\nu_{max.}$ 1740 and 1240 cm.$^{-1}$.

(iii) With benzene: 5β-Cholestan-3-one (0·38 g.) as an oil, identical i.r. spectrum.

(iv) With ether: 5β-Cholestan-3α-ol (0·51 g.) needles m. p. 101—103° (from methanol) identified by its i.r. spectrum.[29]

Clemmensen Reduction of 3,5,5-*Trimethylcyclohex*-2-*enol*.—Lithium aluminium hydride reduction of 3,5,5-trimethylcyclohex-2-enone gave 3,5,5-trimethylcyclohex-2-enol, b. p. 92·5°/14 mm., n_D^{20} 1·4700 (lit.,[30] b. p. 79·5—81·5°/8 mm., n_D^{20} 1·4727). 3,5,5-Trimethylcyclohex-2-enol (5·0 g. 0·036 mole), amalgamated zinc wool (10 g., 0·153 mole) and 7M-hydrochloric acid (17·5 ml.) were heated under reflux for 30 min. Ether yielded an oil (3·0 g.) which showed the presence of three compounds on g.l.c., two of similar retention volume. Preparative g.l.c. gave two fractions: (*a*) 1,5,5-Trimethyl and 3,5,5-trimethyl-cyclohexa-1,3-diene (85%), the i.r. spectrum showing all the peaks present in the

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spectra of the two isomers.[24] (*b*) 5,5-Dimethyl-3-methylenecyclohex-1-ene (15%), i.r. spectrum identical with published spectrum,[24] δ 0·91 [s, 6, CMe_2 at C(5)], 4·73 (m, 2, $C{:}CH_2$), 5·61 (2t) and 6·05 (2t) [1 proton each, $J_{1,2} = 9{\cdot}5$ c./sec., $J_{1,6} = 4{\cdot}5$ c./sec., $J_{2,6} = 1{\cdot}5$ c./sec., vinyl protons at C(1) and C(2)].

Clemmensen Reduction of Cholest-4-en-3-ol.—A mixture of the epimeric cholest-4-en-3-ols (1·0 g.) (from lithium aluminium hydride reduction of cholest-4-en-3-one) in ethanol (30 ml.) was heated under reflux with amalgamated zinc wool (2·0 g.) in 7M-hydrochloric acid (1·3 ml.) for 30 min. Working up gave cholesta-3,5-diene, m. p. 78° (lit.,[31] m. p. 79°), also identified by its i.r., u.v., and n.m.r. spectra.

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