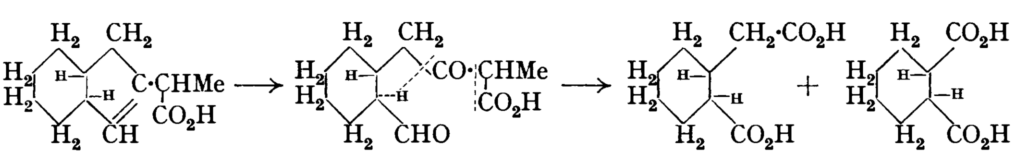
352. *α-Methyl*-trans-*hexahydroindene-2-acetic Acid and the Reduction of Δ^{α}- and Δ^{β}-Unsaturated* trans-*Hexahydrohydrindene* (2) *Compounds.*

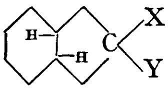
By R. S. Thakur.

Whereas the dehydration of ethyl 2-hydroxy-α-methyl-*trans*-hexahydrohydrindene-2-acetate with phosphoric oxide invariably produces an inseparable mixture of α-methyl-*trans*-hexahydroindene-2-acetic acid (the Δ^{β}-acid) and a $\Delta^{3 \text{ (or } 8)}$-isomeride (J., 1932, 2159), it has now been found that the dehydration with thionyl chloride (Darzens, *Compt. rend.*, 1911, **152**, 1601) yields the Δ^{β}-acid unaccompanied by the $\Delta^{3 \text{ (or } 8)}$-isomeride—the Δ^{α}-acid is produced in considerable quantities in both cases. When the Δ^{β}-*ester* prepared by Darzens' method and subsequent partial esterification is treated with phosphoric oxide, the product obtained does not contain any $\Delta^{3 \text{ (or } 8)}$-isomeride. Therefore the formation of the double bond in a position other than the αβ or βγ which takes place during the dehydration with phosphoric oxide is not due to the action of this agent on the Δ^{β}-ester. The dehydration of ethyl 1-hydroxy*cyclo*pentane- and 1-hydroxy-α-methyl*cyclo*pentane-1-acetates with phosphoric oxide and with thionyl chloride proceeds normally, the expected Δ^{α}- and Δ^{β}-esters being produced and no indication of the formation of a $\Delta^{2 \text{ (or } 3)}$-isomeride being obtained.

The pure α-methyl-*trans*-hexahydroindene-2-acetic acid now obtained gives pure derivatives and forms the same equilibrium mixture (96% of Δ^{α}-acid) as that already obtained from the Δ^{α}-acid (*loc. cit.*, p. 2163). Similarly, the Δ^{β}-ester gives the pure Δ^{α}-ester on treatment with alcoholic sodium ethoxide. The structure of the acid has been confirmed by oxidation to *trans*-hexahydrohomophthalic and *trans*-hexahydrophthalic acids:



Hückel and Friedrich have shown that compounds of the type (I) can exist in one form (racemic) only (*Annalen*, 1926, **451**, 132). The reduction of some Δ^{α}- and Δ^{β}-unsaturated hexahydrohydrindene compounds now carried out supports this view, since only one compound of the type (I) was obtained in every case.



(I.)

trans-Hexahydrohomophthalic acid can be readily prepared pure and in large quantity by the oxidation of *trans*-hexahydro-2-hydrindone with concentrated nitric acid (compare Windaus, Hückel, and Revery, *Ber.*, 1923, **56**, 91; Hückel and Friedrich, *loc. cit.*; Helfer, *Helv. Chim. Acta*, 1926, **9**, 814). A lower-melting substance also formed has not been investigated.

EXPERIMENTAL.

*Dehydration of Methyl and Ethyl 2-Hydroxy-α-methyl-*trans-*hexahydrohydrindene-2-acetate.*—(i) *With phosphoric oxide.* The methyl ester, prepared from the silver salt, had b. p. 155—156°/14 mm., $d_{4^\circ}^{20\cdot8^\circ}$ 1·0391, $n_D^{20\cdot8^\circ}$ 1·4765, $[R_L]_D$ 61·45 (calc., 61·13). On dehydration it gave an ester (yield, 76%), b. p. 144—154°/16 mm., *J* 49·6% (10 mins.), which on equilibration with alcoholic sodium ethoxide gave a product, b. p. 161°/15 mm., $n_D^{21\cdot8^\circ}$ 1·4026, and *J* 16·2%.

The dehydration of the ethyl ester was carried out as before (*loc. cit.*, p. 2162). The unsaturated ester was hydrolysed without prior distillation and the resulting acid was separated from α-methyl-*trans*-hexahydrohydrindylidene-2-acetic acid by means of light petroleum, recovered from the extract, and partly esterified. The Δ^β(?)-ester obtained had b. p. 140°/12 mm. and *J* 85% (10 mins.). After equilibration, it had b. p. 157°/14 mm. and *J* 20·1%, the presence of the isomeric ester thus being shown.

(ii) *With thionyl chloride.* The dehydration product from 86 g. of the hydroxy-ester (*loc. cit.*, p. 2162) was fractionally distilled: (i) b. p. 147—163°/21 mm.; (ii) b. p. 168—172°/21 mm. (28 g.). The hydrolysis of the first fraction was incompletely carried out with 8 g. of sodium hydroxide in 300 c.c. of water in a shaking machine, alcohol not being used in order to avoid the conversion of the Δ^β-ester into the Δ^α-isomeride. The acid obtained, which was practically free from the Δ^α-acid, was treated with cold aqueous sodium hydrogen carbonate (compare Wechsler, *Monatsh.*, 1893, **14**, 462; Eccott and Linstead, J., 1929, 2154), and the unreacted acid removed by extraction with ether. The acid (20 g.) recovered from the alkaline layer was partly esterified for 15 hours at room temperature and gave *ethyl α-methyl-*trans-*hexahydroindene-2-acetate*, b. p. 150—151°/22 mm. $d_{4^\circ}^{20\cdot6^\circ}$ 0·9747, $n_D^{20\cdot6^\circ}$ 1·4732, $[R_L]_D$ 63·97 (calc., 63·81), *J* 83·8% (10 mins.) (Found: C, 75·2; H, 9·9. $C_{14}H_{22}O_2$ requires C, 75·6; H, 10·0%).

Treatment of the Δ^β-Ester with Phosphoric Oxide.—The above ester (2·5 g.) was treated with phosphoric oxide (1·5 g.) in dry benzene (25 c.c.) for 16 hours at room temperature and for 1 hour on the steam-bath. The product was worked up as in the dehydration experiments. The ester obtained was, without prior distillation, treated with *N*-sodium ethoxide for a few hours. The recovered ester (1·7 g.) had b. p. 170—171°/21 mm., $d_{4^\circ}^{20\cdot6^\circ}$ 1·0016, $n_D^{20\cdot6^\circ}$ 1·4955, and *J* 3·7% [compare these values with those similarly obtained in (i)].

Hydrolysis of the Δ^β-Ester.—The ester (12 g.) was shaken with sodium hydroxide (7 g.) in 310 c.c. of water and a little methyl alcohol. The acid obtained, m. p. 68—72°, was distilled, b. p. 143—146°/1 mm. The distillate solidified only after seeding and cooling in ice; on crystallisation from dilute alcohol it gave α-methyl-*trans*-hexahydroindene-2-acetic acid in thick plates, *J* 98·4% (10 mins.), m. p. 80—81° after sintering (Found: C, 74·1; H, 9·15; equiv., 193·8. Calc. for $C_{12}H_{18}O_2$: C, 74·2; H, 9·3%; equiv., 194·2), and mixed m. p. 56—66° with the $\Delta^{3\text{ (or }8)}$-acid.

The *amide*, $C_8H_{13}{\gg}C{\cdot}CHMe{\cdot}CO{\cdot}NH_2$, prepared from the undistilled Δ^β-acid chloride and ammonia, melted at 131—132° as prepared and also after crystallisation from benzene, in very small needles (Found: C, 74·2; H, 9·9. $C_{12}H_{19}ON$ requires C, 74·6; H, 9·8%).

Oxidation of the Δ^β-Acid.—The pure acid was oxidised in cold aqueous sodium hydrogen carbonate with 3% aqueous permanganate. After extraction with ether, the alkaline solution gave a viscous acid which did not solidify. This was oxidised with hot dilute nitric acid, yielding a crystalline product which on recrystallisation from water gave *trans*-hexahydrophthalic acid, m. p. 226—227° (Kon and Khuda, J., 1926, 3073, give m. p. 222°), *trans*-hexahydrohomophthalic acid, m. p. and mixed m. p. 161—162°, and oxalic acid, m. p. and mixed m. p. 102—103°.

Catalytic Hydrogenation of the Δ^β-Acid.—The pure acid was hydrogenated in the manner described for the Δ^α-acid (p. 1487), and the product treated with cold dilute alkaline permanganate to remove any unsaturated acid. α-Methyl-*trans*-hexahydrohydrindeneacetic acid crystallised from dilute methyl alcohol in needles and gave an amide, m. p. and mixed m. p. (with authentic specimens; see below) 99—101° and 195—196° respectively.

Equilibrations.—The Δ^{β}-acid, when heated (two experiments) with an excess of 25% aqueous potash in copper flasks for 3 and for 4 days, gave products having *J* 6·2 and 5·7% respectively—values which agree closely with those obtained for the equilibration product of α-methyl-*trans*-hexahydrohydrindylidene-2-acetic acid (*loc. cit.*, p. 2163, Table II, experiments 10—12). On crystallisation from benzene, the equilibrated Δ^{β}-acid gave the Δ^{α}-acid, m. p. and mixed m. p. 196—197°.

The Isomeric Impurity, $C_8H_{13}{\geqslant}C{\cdot}CHMe{\cdot}CO_2H$.—This acid was obtained by the method already described (*loc. cit.*, p. 2164); after crystallisation from dilute alcohol it melted at 81—83°. The high m. p. 89—90° of the previous specimen is due to the presence of α-methyl-*trans*-hexahydrohydrindylidene-2-acetic acid.

*α-Methyl-*trans*-hexahydrohydrindene-2-acetic Acid.*—α-Methyl-*trans*-hexahydrohydrindylidene-2-acetic acid in rectified spirit was readily and completely reduced by hydrogen in presence of Adams's catalyst (0·2 g.). *α-Methyl-*trans*-hexahydrohydrindene-2-acetic acid* crystallised from petroleum (b. p. 60—80°) or dilute alcohol in needles, m. p. 104—105° (Found: C, 73·3; H, 10·4; equiv., 196·0. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3%; equiv., 196·2). The acid chloride was a colourless liquid, b. p. 150°/23 mm. The *amide*, m. p. 196° (Found: C, 73·6; H, 10·7. $C_{12}H_{21}ON$ requires C, 73·8; H, 10·85%), and the *anilide*, thin needles, m. p. 176—177° (Found: C, 79·35; H, 9·15. $C_{18}H_{25}ON$ requires C, 79·65; H, 9·3%), were crystallised from benzene.

The same acid, m. p. 104—105°, was also obtained by the catalytic reduction of α-methyl-*trans*-hexahydroindeneacetic acid or ethyl α-methyl-*trans*-hexahydrohydrindylidene-2-acetate, by the reduction of the Δ^{α}-acid with sodium and amyl alcohol or with sodium amalgam and aqueous sodium carbonate, and by shaking α-methyl-*trans*-hexahydrohydrindyl-2-acetone (see below) with aqueous sodium hypobromite, but all these methods were unsatisfactory.

*α-Methyl-*trans*-hexahydrohydrindyl-2-acetone.*—α-Methyl-*trans*-hexahydrohydrindylidene-2-acetone (*loc. cit.*, p. 2165) in rectified spirit was readily hydrogenated in presence of Adams's catalyst (0·2 g.). The product (b. p. 140—142°/14 mm.) gave a semicarbazone, which crystallised from methyl alcohol in flat needles or elongated plates, m. p. 179—180° (Found: C, 66·8; H, 10·1. Calc. for $C_{14}H_{25}ON_3$: C, 66·9; H, 10·0%), identical with the semicarbazone described before (*loc. cit.*, p. 2166). α-Methyl-*trans*-hexahydrohydrindyl-2-acetone, regenerated from the semicarbazone by dilute sulphuric acid, had b. p. 149°/23 mm., $d_{4^\circ}^{20\cdot3^\circ}$ 0·9406, $n_D^{20\cdot3^\circ}$ 1·4761, $[R_L]_D$ 58·24 (calc., 57·92), and formed an *oxime* which crystallised from dilute methyl alcohol in colourless needles, m. p. 85—86° after shrinking (Found: C, 74·3; H, 10·9. $C_{13}H_{23}ON$ requires C, 74·65; H, 11·0%).

trans-Hexahydrohydrindene-2-acetic Acid.—*trans*-Hexahydrohydrindylidene-2-acetic acid (*loc. cit.*, p. 2153) was catalytically reduced. The product, which did not decolorise alkaline permanganate, crystallised from light petroleum (b. p. 60—80°) in rhombic plates, m. p. 102—103° after sintering (Found: C, 72·3; H, 9·8; equiv., 181·8. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·9%; equiv., 182·1). Kandiah (J., 1931, 938) gives m. p. 120°. The *amide* crystallised from benzene in needles, m. p. 180° after shrinking (Found: C, 72·6; H, 10·3. $C_{11}H_{19}ON$ requires C, 72·9; H, 10·5%). The anilide crystallised from benzene or benzene–petroleum in needles, m. p. 132° (Kandiah, *loc. cit.*, gives m. p. 135°).

The same acid, m. p. 102—103°, was obtained: (i) by the catalytic reduction of *trans*-hexahydroindene-2-acetic acid, m. p. 65—66° (*loc. cit.*, p. 2154); (ii) by the oxidation of *trans*-hexahydrohydrindene-2-acetone (see below) with aqueous sodium hypobromite, which proceeded readily, giving a good yield.

trans-Hexahydrohydrindyl-2-acetone.—The addition of hydrogen to *trans*-hexahydrohydrindylidene-2-acetone (*loc. cit.*, p. 2156) was carried out as in previous cases. The product (b. p. 130—134°/16 mm.) gave a *semicarbazone*, m. p. 202°, which crystallised from methyl alcohol in clusters of prismatic rods, m. p. 202—203° (decomp.), mixed m. p. with the semicarbazone of the Δ^{α}-ketone 195° after shrinking (Found: C, 65·8; H, 9·6. $C_{13}H_{23}ON$ requires C, 65·8; H, 9·7%). The ketone regenerated from it had b. p. 141°/25 mm., $d_{4^\circ}^{20\cdot1^\circ}$ 0·9396, $n_D^{20\cdot1^\circ}$ 1·4719, $[R_L]_D$ 53·68 (calc., 52·72). The *oxime* crystallised from dilute alcohol in flat needles, m. p. 68—70° (slow heating) after sintering (Found: C, 73·8; H, 10·8. $C_{12}H_{21}ON$ requires C, 73·9; H, 10·8%).

Oxidation of trans-Hexahydro-2-hydrindone.—The ketone (semicarbazone, m. p. 245°) was added in portions to boiling nitric acid (*d* 1·42), and the mixture heated for a short time on the steam-bath and then kept at room temperature. *trans*-Hexahydrohomophthalic acid, which crystallised, was washed with a little ice-cold water and light petroleum; m. p 156—157°, and 160—162° after recrystallisation from water. The nitric acid mother-liquor deposited more of the acid. The filtrate (nitric acid) was concentrated on the steam-bath, kept for a few days, and then transferred to a porous plate. The solid residue was crystallised from water: first crop, m. p. 132—134°, clearing at 144°; second crop, m. p. 134°, clearing at 147° (*cis*-hexahydrohomophthalic acid melts at 147°; Windaus, Hückel, and Reverey, *loc. cit.*).

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