

644. Perhydroindanes. Part II.* Hexahydroindanonones.

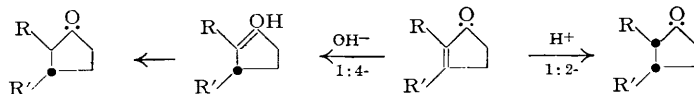
By DAVID W. MATHIESON.

Reduction at a palladium catalyst of a number of 4 : 5 : 6 : 7-tetrahydroindanonones has been shown to lead to the corresponding hexahydroindanonones in good yield.

PREVIOUSLY recorded routes to hexahydroindanone and its derivatives have suffered from the inaccessible nature of the intermediate materials. For instance, synthesis of hexahydroindan-1-one involves Dieckmann ring closure of the diester of β -(2-carboxycyclohexyl)propionic acid (cf., *inter al.*, Hückel, Sachs, Yantschulewitsch, and Nerdel, *Annalen*, 1935, 518, 155; Kon, Linstead, and Simmons, *J.*, 1937, 814). Alternatively, the 8-methyl derivative may be made by a Darzens reaction on β -(2-methylcyclohex-1-enyl)propionic acid followed by reduction of the double bond (Chuang, Tien, and Ma, *Ber.*, 1936, 69, 1494; Nenitzescu and Przemetsky, *Ber.*, 1941, 74, 676, 6841). Obvious difficulties of synthesis arise, however, when hexahydroindanonones more complex than the parent members of the series are required. The elegant work of Johnson and his co-workers on the Stobbe condensation (Johnson and Daub, "Organic Reactions," John Wiley and Sons, 1951, Vol. VI, p. 1) has made available a general route to tetrahydroindan-1-ones of established structure and it seemed likely that, under mild conditions, reduction of the double bond could be achieved to furnish the required hexahydro-derivatives. Several isolated instances of such reductions have been reported. Hückel and Schluter (*Ber.*, 1934, 67, 2107) have claimed the reduction of 4 : 5 : 6 : 7-tetrahydroindan-4-one to the hexahydro-ketone at a palladium catalyst under normal pressure and temperature. More recently Braude and Coles (*J.*, 1952, 1430) have carried out an analogous reduction of 9-oxo- Δ^{12} -decahydrofluorenone with platinic oxide, whilst at 75°/70 atm. the hydrogenation of the $\alpha\beta$ -ethylenic bond in 6 : 7-dihydronaphtho(1' : 2'-4 : 5)indan-1-one has been claimed (Johnson and Posvic, *J. Amer. Chem. Soc.*, 1947, 69, 1362). Insufficient information was available, however, as to the preparative value of such a method for larger quantities of the saturated ketones required in connection with other work, and the investigation of this point is described below.

A number of tetrahydroindanonones were synthesised by Stobbe condensation between the requisite ketone and diethyl succinate, ring closure of the resulting half-ester, and then hydrolysis and decarboxylation. The following were thus smoothly obtained : 4 : 5 : 6 : 7-tetrahydro- (Johnson, Davis, Hunt, and Stork, *ibid.*, 1948, 70, 3022), 4 : 5 : 6 : 7-tetrahydro-6-phenylindan-1-one, 6 : 7-dihydro- (Johnson, Johnson, and Petersen, *ibid.*, 1945, 67, 1360), and 4 : 5 : 6 : 7 : 1' : 2' : 3' : 4'-octahydro-4 : 5-benzindan-1-one.

When $\alpha\beta$ -unsaturated carbonyl compounds are hydrogenated at a palladium catalyst it has been shown (Weidlich and Meyer-Delius, *Ber.*, 1941, 74, 1195, 1213) that in alkaline solution 1 : 4-addition occurs followed by ketonisation of the resulting enol to the *trans*-ketone, whilst in acid solution 1 : 2-addition to the double bond takes place to yield a *cis*-ketone (accompanied by the *cis*-hydrocarbon).

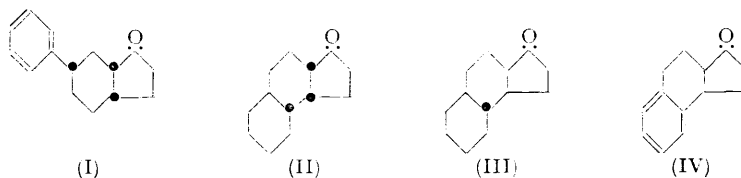


This has been demonstrated where R and R' are not involved in a ring structure, but since the more stable configuration of the hydroindane nucleus is *cis* (Hückel, Sachs, Yantschulewitsch, and Nerdel, *loc. cit.*) it seemed likely that under either acid or alkaline conditions this form would predominate. This proved to be so and when reduced at a 5% palladium-barium sulphate catalyst in alcohol (with or without the addition of sodium hydroxide or hydrogen chloride), tetrahydroindanone rapidly yielded hexahydroindan-1-one in excellent yield. The derived semicarbazone had m. p. 212° and the oxime m. p. 75—90°. These figures are in good agreement with those given by Hückel *et al.* (*loc. cit.*)

* Part I, *J.*, 1951, 177.

for the same derivatives of a hexahydroindan-1-one (*cis* : *trans* ratio 10 : 1). *cis-trans*-Interconversion has, however, been shown to occur on distillation of hexahydroindan-4-one (Hückel and Doll, *Annalen*, 1936, 526, 103) and interconversion seems likely in the present instance also.

Under identical conditions (palladium-barium sulphate in methanol) 4 : 5 : 6 : 7-tetrahydro-6-phenyl- and 4 : 5 : 6 : 7 : 1' : 2' : 3' : 4'-octahydro-4 : 5-benzindan-1-one gave the fully reduced ketones in good yield. Tentative assignments of configuration may be made. In the former case, if a *cis*-hydroindane structure is assumed, conformational analysis indicates that a 6-phenyl substituent may be inserted in either the *cis*- or the *trans*-position with respect to C₍₈₎-hydrogenation, so that the molecule involves one polar and two equatorial bonds: the alternatives are thus of equal stability. During reduction, however, tetrahydro-6-phenylindanone would be preferentially adsorbed on the catalyst in such a way that the phenyl group would be directed away from the body of the catalyst (cf. Linstead and his co-workers, *J. Amer. Chem. Soc.*, 1942, 64, 1985; *J.*, 1950, 1431). *cis*-Addition of hydrogen at C₍₈₎ and C₍₉₎ would then occur, yielding (I). For decahydro-4 : 5-benzindane the *trans-syn-cis*- (II) and the *trans-anti-cis*-conformation (III) are of equal stability, each involving one polar and three equatorial bonds (Johnson, *Experientia*, 1951, p. 315).



The ease of reduction in the above cases is in contrast to the findings by Hamlet, Henbest, and Jones (*J.*, 1951, 2652) that similarly constituted 3-alkyl-4 : 5 : 6 : 7-tetrahydroindan-1-ones are resistant to hydrogenation in acetic acid at a palladium catalyst. This result cannot be confirmed in the present case, as tetrahydroindanone has been found to be easily reduced in acetic acid at a 5% palladium-barium sulphate catalyst.

Such reduction of 6 : 7-dihydro-4 : 5-benzindan-1-one was slow and incomplete, leading to a mixture. However, at 80°/80 atm. the required ketone (IV) was easily obtained, though a mixture with the alcohol was formed: the ketone was assayed by 2 : 4-dinitrophenylhydrazone, and the alcohol present reoxidised to the ketone by using the theoretical amount of chromic anhydride. If tetrahydroindan-1-one was hydrogenated under similar high-pressure conditions, no reduction of the ketonic group occurred and hexahydroindanone was obtained in 90% yield.

For the tetrahydroindanones the position of the ethylenic link $\alpha\beta$ to the carbonyl group is confirmed by the position of the main band at 2370 Å in the ketone (3950 Å in the dinitrophenylhydrazones and 2650 Å in the semicarbazones; Hamlet, Henbest and Jones, *loc. cit.*; Braude and Coles, *J.*, 1952, 1430). On hydrogenation, a hypsochromic shift is observed of 300 Å in the position of the main bands of the dinitrophenylhydrazones and semicarbazones. The position of these at 3660 Å and 2300 Å respectively is normal for saturated aliphatic ketones (Braude and Jones, *J.*, 1945, 498). With the ketones themselves reduction of the conjugated double bond is marked by the expected disappearance of the high-intensity band at 2370 Å and the appearance of the usual low-intensity carbonyl peak at 2880 Å. The bathochromic shift of 500 Å observed on passage from 4 : 5 : 6 : 7-tetrahydroindanone to 6 : 7-dihydro-4 : 5-benzindanone where extra conjugation with an aromatic nucleus obtains is in line with similar cases recorded by Wilds *et al.* (*J. Amer. Chem. Soc.*, 1947, 69, 1985). This conjugation is destroyed on hydrogenation and the position of the main band of the 2 : 4-dinitrophenylhydrazone of (IV) is normal for saturated ketones. The presence of the benzene ring in (IV) is confirmed by low-intensity vibrational structure between 2500 and 2750 Å typical of tetrahydronaphthalene (Friedel and Orchin, "Ultra-violet Spectra of Organic Compounds," John Wiley and Sons, New York, 1951). That no reduction of the benzene ring in the ketone (I) had occurred is likewise confirmed by the appearance of absorption due to the phenylcyclohexane chromophore.

EXPERIMENTAL

Microanalyses in this and the following paper are by Mr. G. S. Crouch. Light absorptions were measured in EtOH for the ketones and semicarbazones, and in CHCl_3 for the 2 : 4-dinitrophenylhydrazones (main band only given).

4 : 5 : 6 : 7-Tetrahydroindanone.—Ethyl β -carboxy- α -cyclohexenylpropionate (40 g.) in acetic anhydride (580 ml.) was refluxed with zinc chloride (8 g.) in acetic acid (400 ml.) for 5 hr. under nitrogen. Acetic acid and anhydride were removed *in vacuo* and the residue refluxed for 3 hr. with concentrated hydrochloric acid (100 ml.) in acetic acid (100 ml.). To the residue left after removal of solvent, sufficient sodium hydroxide was added to make the suspension faintly alkaline to litmus, and the whole was extracted with ether. There resulted on distillation a colourless oil, b. p. 83.5–85°/2 mm. (10.9 g.), n_D^{20} 1.5260 (cf. Johnson, Davis, Hunt, and Stork, *loc. cit.*). Absorption max.: ketone 2370 (E 12,700), 2 : 4-dinitrophenylhydrazone 3950 (E 27,500), semicarbazone 2650 Å (E 26,500).

4 : 5 : 6 : 7-Tetrahydro-6-phenylindanone [with Dr. E. I. HAIBA].—Under the above conditions methyl 4 : 5 : 6 : 7-tetrahydro-3-oxo-5-phenylindane-1-carboxylate (unpublished work) (5 g.) was converted into the tetrahydro-6-phenylindanone (2 g.), colourless needles [from light petroleum (b. p. 60–80°)], m. p. 79–80° (Found: C, 84.6; H, 7.5. $\text{C}_{15}\text{H}_{16}\text{O}$ requires C, 84.9; H, 7.5%). Absorption max.: 2370 (E 12,750). The 2 : 4-dinitrophenylhydrazone crystallised from acetic acid in orange-red needles, m. p. 235–236° (Found: C, 64.4; H, 5.3; N, 14.4. $\text{C}_{21}\text{H}_{20}\text{O}_4\text{N}_4$ requires C, 64.3; H, 5.1; N, 14.3%). Absorption max.: 3940 Å (E 33,000).

4 : 5 : 6 : 7 : 1' : 2' : 3' : 4'-Octahydro-4 : 5-benzindan-1-one.—*trans*- α -Decalone (15.2 g.) and diethyl succinate (19 g.) were condensed in presence of potassium *tert.*-butoxide [from potassium (4 g.) and excess of *tert.*-butanol] in the usual way, to yield ethyl β -carboxy- α -(1- Δ^1 -octahydro-naphthyl)propionate as a viscous colourless oil, b. p. 165–169°/0.5 mm. (19.5 g.) (Found: C, 68.4; H, 8.6. $\text{C}_{16}\text{H}_{24}\text{O}_4$ requires C, 68.6; H, 8.6%). This (38 g.) was cyclised with zinc chloride-acetic anhydride in acetic acid as above. The resulting ketone was obtained as a colourless oil, b. p. 130–132°/0.5 mm. (12.2 g.) (Found: C, 81.9; H, 9.2. $\text{C}_{13}\text{H}_{18}\text{O}$ requires C, 82.1; H, 9.5%). Absorption max.: 2390 Å (E 13,000).

The 2 : 4-dinitrophenylhydrazone crystallised in dark red plates, m. p. 203–204°, from glacial acetic acid (Found: C, 61.7; H, 5.8; N, 14.8. $\text{C}_{19}\text{H}_{22}\text{O}_4\text{N}_4$ requires C, 61.6; H, 5.9; N, 15.1%). Absorption max.: 3960 Å (E 29,300). The semicarbazone crystallised from glacial acetic acid in colourless needles, m. p. 265° (decomp.) (Found: C, 68.1; H, 8.5; N, 17.0. $\text{C}_{14}\text{H}_{21}\text{ON}_3$ requires C, 68.0; H, 8.5; N, 17.0%). Absorption max.: 2660 Å (E 26,000).

Hydrogenation of the Tetrahydroindanones to Hexahydroindanones. General Method.—The tetrahydroindanone (5 g.) was dissolved in methanol or isopropanol (40 ml.) and hydrogenated at a 10% palladium-barium sulphate catalyst (1 g.) at atmospheric temperature and pressure. The time of hydrogen uptake varied from 1 to 5 hr. with different compounds and in every case uptake ceased when one mol. had been absorbed. The crude ketone was assayed by precipitation of the 2 : 4-dinitrophenylhydrazone and weighing of the crude precipitate. In every case 95–98% was present and no significant amount of alcohol appeared therefore to have been produced. Under the above conditions the following were thus obtained.

Hexahydroindanone, a colourless oil, b. p. 72–73/6 mm., n_D^{25} 1.4813. Absorption max.: 2880 Å (E 23). The 2 : 4-dinitrophenylhydrazone crystallised from glacial acetic acid in orange yellow plates, m. p. (various batches) variable, 163–165° to 130–140°. All samples, however, contained 17.4–17.6% of nitrogen and showed an absorption peak at 3670 Å (E 28,000). The semicarbazone, crystallised from aqueous acetic acid, had m. p. 211–212° (Found: N, 21.6. Calc. for $\text{C}_{10}\text{H}_{11}\text{ON}_3$: N, 21.5%). Absorption max.: 2300 Å (E 14,200) (Hamlet, Henbest, and Jones, *loc. cit.*; Part I, *loc. cit.*).

6-Phenylhexahydroindanone, crystallising from light petroleum (b. p. 40–60°) in colourless prisms, m. p. 57–60 (Found: C, 83.7; H, 8.0. $\text{C}_{15}\text{H}_{18}\text{O}$ requires C, 84.0; H, 8.4%). Absorption max.: 2090, 2480, 2530, 2585, 2640, 2675 Å (E 8250, 132, 181, 218, 166, 155 respectively). The 2 : 4-dinitrophenylhydrazone crystallised in orange needles (from glacial acetic acid), m. p. 169–179° (Found: C, 63.8; H, 5.7; N, 14.4. $\text{C}_{21}\text{H}_{22}\text{O}_4\text{N}_4$ requires C, 63.9; H, 5.6; N, 14.2%) [absorption max.: 3670 Å (E 25,000)], and the semicarbazone from aqueous acetic acid in colourless plates, m. p. 254–255° (Found: C, 70.7; H, 7.9; N, 15.4. $\text{C}_{16}\text{H}_{21}\text{ON}_3$ requires C, 70.8; H, 7.8; N, 15.5%).

Decahydro-4 : 5-benzindanone, crystallising from light petroleum (b. p. 40–60°) in colourless prisms, m. p. 58–59° (Found: C, 81.1; H, 10.0. $\text{C}_{13}\text{H}_{20}\text{O}$ requires C, 81.3; H, 10.4%). Absorption max.: 2880 Å (E 24). The 2 : 4-dinitrophenylhydrazone crystallised from glacial acetic

acid in orange-yellow plates, m. p. 204—206° (Found : C, 61.4; H, 6.6; N, 15.2. $C_{19}H_{24}O_4N_4$ requires C, 61.3; H, 6.5; N, 15.1%). Absorption max. : 3680 Å (*E* 24,000). The *semicarbazone* crystallised from aqueous acetic acid in colourless crystals, m. p. 247—248° (Found : C, 67.7; H, 9.2; N, 17.1. $C_{14}H_{23}ON_3$ requires C, 67.5; H, 9.2; N, 16.9%). Absorption max. : 2300 Å (*E* 14,000).

When the above conditions were applied to 4 : 5 : 6 : 7-tetrahydro-4 : 5-benzindanone uptake of gas was very uneven and incomplete. The resulting material proved to be a mixture. The following conditions were found to be successful (cf. Johnson and Posvic, *J. Amer. Chem. Soc.*, 1947, **69**, 1362).

4 : 5 : 6 : 7-Tetrahydro-4 : 5-benzindanone.—6 : 7-Dihydro-4 : 5-benzindan-1-one (Johnson, Johnson, and Petersen, *ibid.*, 1945, **67**, 1360) (9 g.) in *isopropanol* (400 ml.) was hydrogenated in presence of a 5% palladium-barium sulphate catalyst at 80°/80 atm. After remaining 2 hr. under these conditions the autoclave was allowed to cool during some 3 hr., whereafter the contents were worked up in the usual fashion. A mixture (8.9 g.) of alcohol and ketone resulted. The ketonic content was estimated and the mixture then oxidised by the theoretical quantity of chromic anhydride in glacial acetic acid. On working up in the usual way, the *ketone* was obtained as a colourless oil, b. p. 135—140°/6 mm., n_D^{20} 1.5680 (Found : C, 83.2; H, 7.7. $C_{13}H_{14}O$ requires C, 83.9; H, 7.5%). The 2 : 4-dinitrophenylhydrazone crystallised in orange plates, m. p. 214—215°, from glacial acetic acid (Found : C, 62.3; H, 4.6; N, 15.3. $C_{19}H_{19}O_4N_4$ requires C, 62.3; H, 4.9; N, 15.3%). The *semicarbazone* crystallised from dioxan in colourless needles, m. p. 231—232° (Found : C, 68.9; H, 7.0; N, 17.4. $C_{14}H_{17}ON_3$ requires C, 69.1; H, 7.0; N, 17.3%).

The following absorption max. were recorded. 6 : 7-Dihydro-4 : 5-benzindanone, 2340 (*E* 11,600) and 2970 Å (*E* 16,650) [2 : 4-dinitrophenylhydrazone, 4100 Å (*E* 35,500); semicarbazone, 3260 Å (*E* 32,000)]. 6 : 7 : 8 : 9-Tetrahydro-4 : 5-benzindanone, 2520, 2660, and 2740 Å (*E* 570, 714, 700 respectively) [2 : 4-dinitrophenylhydrazone, 3660 Å (*E* 24,000)]. Phenylcyclohexane, 2090, 2480, 2530, 2585, 2610, 2640, and 2675 (*E* 7750, 123, 176, 212, 208, 158, and 161 respectively).

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