[CONTRIBUTION FROM SCHOOL OF PHARMACY, LONDON UNIVERSITY, AND UNIVERSITY COLLEGE FOR GIRLS, EIN SHAMS UNIVERSITY]

Octahydrobenzindanes. Synthesis of 3-Carbethoxy-Δ^8-octahydro-5,6-benzindan-1-one and 3-Carbethoxy-Δ^8-octahydro-4,5-benzindan-1-one

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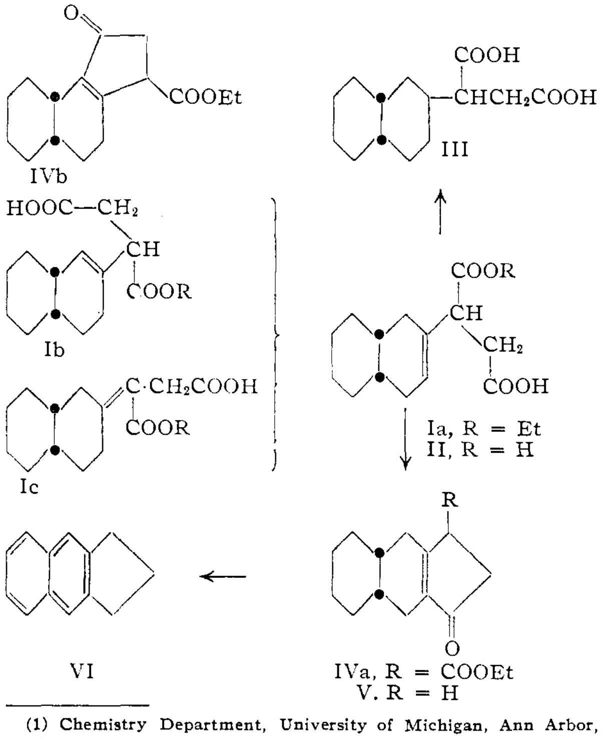
Stobbe condensation was carried on *cis*-2-decalone and *trans*-1-decalone with diethyl succinate. The resulting half-esters when ring closed gave 3-carbethoxy-Δ^8-octahydro-5,6-benzindan-1-one and 3-carbethoxy-Δ^8-octahydro-4,5-benzindan-1-one, respectively. The structures of these compounds were proved.

Octahydrobenzindane compounds are of interest, as they could serve as intermediates in the preparation of analogs of steroid hormones. Their structures represent rings B, C and D of the natural hormones. The procedure applied for their synthesis had been used previously by Johnson, *et al.*,[2] in the preparation of tetrahydroindanones.

cis-2-Decalone was condensed with diethyl or dimethyl succinate in the presence of potassium *t*-butoxide to give the half-ester I (R = Et or Me), as a colorless oil. The constitution of Ia (R = Et) as β-carbethoxy-β-(*cis*-2-Δ^2-octahydronaphthyl)-propionic acid follows from the following observations: The half-ester I failed to give any ketonic material on oxidation with alkaline permanganate. It also failed to reveal an absorption band in the region between 210–225 mμ in ethanol, a characteristic of α,β-unsaturated esters,[3] thus excluding structure Ic. The fact that *cis*- and *trans*-2-decalols when dehydrated give the corresponding *cis*- and *trans*-Δ^2-octalins,[4] shows that the double bond in the octalin is preferentially formed in the 2,3-position and not in the 1,2-position. These findings suggest that structure Ia of the half-ester is more likely to be formed than structure Ib where the double bond is in 1,2-position. Such supposition could explain the formation of the keto ester IVa and not IVb as it is shown later on. Alkaline hydrolysis of the half-ester gave β-carboxy-β-(*cis*-2-Δ^2-octahydronaphthyl)-propionic acid (II). When the half-ester was subjected to catalytic hydrogenation, it absorbed one mole of hydrogen and gave after hydrolysis β-carboxy-β-(*cis*-2-decahydronaphthyl)-propionic acid (III). Treatment of the half-ester Ia (R = Et) with a solution of zinc chloride in acetic acid and acetic anhydride yielded a cyclic keto ester 3-carbethoxy-Δ^8-octahydro-5,6-benzindan-1-one (IVa), that was isolated from the reaction mixture as colorless oil when fractionated on an alumina column. Redistilled samples, however, seemed to be substantially of the stated structure, as acid hydrolysis and decarboxylation gave a homogeneous α,β-unsaturated ketone V in 80% yield. The actual course of the reaction and particularly the structure of the keto ester IV is a matter of interest. Since the reaction is an intramolecular ring closure, the resulting keto ester would then appear to have the proposed structure IVa.



The ultraviolet absorption spectra of the unsaturated keto ester, the unsaturated ketone, their 2,4-dinitrophenylhydrazones and their semicarbazones confirm the presence of an α,β-unsaturated ketone grouping when compared with some general examples from the literature,[5,6] and, more specifically, with similar derivatives of tetrahydroindanones[7] and octahydrobenzindanone.[8] To establish the structure of the keto ester IVa, the α,β-unsaturated ketone V was dehydrogenated using 30% palladized charcoal, to give the known 5,6-benzindane (VI), as shown from its melting point (94°) and the melting point of its picrate (120–121°).[9] Its ultraviolet spectrum showed three maxima at 226 mμ (log E 4.89), 279 mμ (log E 3.78) and 320 mμ (log E 3.17), characteristic of naphthalene and 4,5-benzindane.[10]

trans-α-Decalone was similarly condensed in the presence of potassium *t*-butoxide with diethyl suc-

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[1] Chemistry Department, University of Michigan, Ann Arbor, Mich.

[2] W. S. Johnson, H. C. E. Johnson and J. W. Petersen, THIS JOURNAL, **67**, 1360 (1945).

[3] H. E. Ungnade and I. Ortega, *ibid.*, **73**, 1565 (1951).

[4] W. Borsch and E. Large, *Ann.*, **434**, 219 (1923).

[5] (a) H. S. French, THIS JOURNAL, **74**, 514 (1952); (b) E. A. Braude and E. R. H. Jones, *J. Chem. Soc.*, 498 (1945).

[6] L. K. Evans and A. E. Gillam, *ibid.*, 565 (1943).

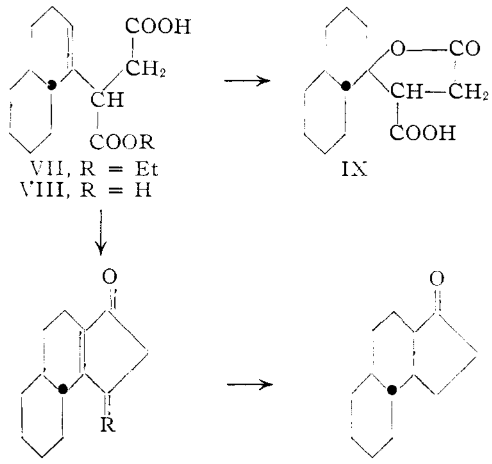
[7] D. W. Mathieson, *ibid.*, 177 (1951); J. C. Hamlet, H. B. Henbest and E. R. H. Jones, *ibid.*, 2652 (1951).

[8] D. W. Mathieson, *ibid.*, 3248 (1953).

[9] S. C. Sen-Gupta, *J. Indian Chem. Soc.*, **16**, 89 (1939). He reported exactly the same melting points.

[10] W. V. Mayneord and E. M. F. Roe, *Proc. Roy. Soc.* (*London*), **A152**, 299 (1935).

cinate to yield β-carbethoxy-β-(1-Δ^1-octahydronaphthyl)-propionic acid (VII).[8] This on alkaline hydrolysis gave the corresponding diacid VIII, and when refluxed with a mixture of glacial acetic acid and hydrochloric acid yielded the paraconic acid (IX). The half-ester VII was then cyclized with zinc chloride–acetic anhydride in acetic acid to give exclusively 3-carbethoxy-Δ^8-octahydro-4,5-benzindan-1-one (X) as a colorless oil. Hydrolysis and decarboxylation of the keto ester X yielded the known Δ^8-octahydro-4,5-benzindan-1-one (XI).[8] This was hydrogenated at a palladium catalyst and gave the decahydro-4,5-benzindan-1-one (XII).[8]



VII, R = Et
VIII, R = H
IX
X, R = COOEt
XI, R = H
XII

Experimental[11]

β-Carbethoxy-β-(*cis*-2-Δ^2-octahydronaphthyl)-propionic Acid (I).—To a solution of potassium *t*-butoxide (from potassium, 5.6 g., and dry *t*-butyl alcohol, 100 ml.) were added *cis*-2-decalone (18 g.) (b.p. 105–106° (7 mm.), n^{20}D 1.4927)[12] and diethyl succinate (30 g.). The mixture was refluxed under nitrogen for 45 min. and then cooled in ice. Concentrated hydrochloric acid (20 ml.) in ice-water (20 ml.) was slowly added so that the temperature did not exceed 20°. Excess of *t*-butyl alcohol was removed on the steam-bath *in vacuo* and the residue extracted with ether. The acid fraction was isolated in the usual way with 10% aqueous sodium carbonate. There resulted a viscous oil, b.p. 179–180° (0.2 mm.), n^{21}D 1.5013 (yield 23 g., 68%).

Anal. Calcd. for $C_{16}H_{24}O_4$: C, 68.6; H, 8.57. Found: C, 68.98; H, 8.44.

Repeating the above experiment using dimethyl succinate, yielded the half-ester Ia (R = Me) as a colorless oil, b.p. 172–173° (0.5 mm.), n^{20}D 1.5043 (65%).

Anal. Calcd. for $C_{15}H_{22}O_4$: C, 67.67; H, 8.27. Found: C, 67.81; H, 8.05.

β-Carboxy-β-(*cis*-2-Δ^2-octahydronaphthyl)-propionic Acid (II).—The ethyl half-ester Ia (2 g.) was refluxed in 10% sodium hydroxide solution (20 ml.) for 3 hr. Working up the reaction mixture as usual, gave an oil which solidified under light petroleum (b.p. 60–80°). This was crystallized from benzene; m.p. 121–123° (1.6 g.).

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.66; H, 7.94; neut. equiv., 126. Found: C, 66.91; H, 7.99; neut. equiv., 126.

β-Carboxy-β-(*cis*-2-decahydronaphthyl)-propionic Acid (III).—The ethyl half-ester Ia (1 g.), dissolved in a mixture of ethanol (5 ml.) and glacial acetic acid (15 ml.), was hydrogenated with Adams platinum oxide (0.1 g.). Uptake was almost complete in one hour. The product was refluxed for 2 hr. with 10% sodium hydroxide solution, after which acidification yielded a colorless solid (0.8 g.) crystallizing from ethanol–light petroleum (b.p. 60–80°); m.p. 174–176°.

Anal. Calcd. for $C_{14}H_{22}O_4$: C, 66.1; H, 8.66. Found: C, 65.7; H, 8.2.

3-Carbethoxy-Δ^8-octahydro-5,6-benzindan-1-one (IVa).—The half-ester Ia (R = Et) (40 g.) in freshly distilled acetic anhydride (700 ml.) was refluxed (under nitrogen) with 2% solution of fused zinc chloride in glacial acetic acid (350 ml.) for 6 hr. Excess anhydride and acid were removed *in vacuo* and the residue poured into water which was made alkaline with sodium carbonate. A dried ethereal extract on evaporation gave a dark brown resinified oil, which on distillation gave a pale yellow heavy oil, b.p. 160–162° (0.2 mm.), n^{21}D 1.5160 (20 g., 54%). It gave a semicarbazone, m.p. 210–211°, from ethanol, λ_{max} 268 mμ (*E* 26,000).

Anal. Calcd. for $C_{17}H_{25}O_3N_3$: C, 63.95; H, 7.84; N, 13.17. Found: C, 63.57; H, 7.62; N, 13.77.

Its 2,4-dinitrophenylhydrazone crystallized from ethanol in red crystals, m.p. 133–134°, λ_{max} 388 mμ (*E* 33,000).

Anal. Calcd. for $C_{22}H_{26}O_6N_4$: C, 59.72; H, 5.88; N, 12.67. Found: C, 59.58; H, 5.65; N, 12.88.

When the crude keto ester (2 g.) in dry thiophene-free benzene (100 ml.) was passed over alumina (Savory and Moore, Brockmann Standardized, 50 g., column size 13 × 2.4 cm.), a colorless oily fraction (0.6 g.) was obtained, b.p. 125–130° (0.05 mm.), λ_{max} 239 mμ (*E* 10,000).

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.28; H, 8.39. Found: C, 73.05; H, 8.26.

Δ^8-Octahydro-5,6-benzindan-1-one (V).—A mixture of the ethyl keto ester (5.2 g.) and concentrated hydrochloric acid (80 ml.) was refluxed for one hour. After dilution with water, it was ether-extracted. The ether extract was washed with sodium carbonate solution, water and dried over anhydrous sodium sulfate. Removal of the solvent gave a residue which was distilled at 120° (0.8 mm.) as a colorless oil, n^{20}D 1.5415, λ_{max} 238 mμ (*E* 12,000), yield 3 g. (80%).

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.11; H, 9.47. Found: C, 81.81; H, 9.55.

Its semicarbazone crystallized from *n*-butyl alcohol; m.p. 227.5–228.5° dec., λ_{max} 265 mμ (*E* 23,000).

Anal. Calcd. for $C_{14}H_{21}ON_3$: C, 68.02; H, 8.5; N, 17.0. Found: C, 67.97; H, 8.69; N, 16.8.

Its 2,4-dinitrophenylhydrazone crystallized from ethanol-xylene as dark red crystals, m.p. 216–218° dec., λ_{max} 395 and 265 mμ (*E* 27,600 and 10,250, resp.).

Anal. Calcd. for $C_{19}H_{22}O_4N_4$: C, 61.62; H, 5.94; N, 15.13. Found: C, 61.59; H, 5.80; N, 15.24.

Dehydrogenation of Δ^8-Octahydro-5,6-benzindan-1-one (V) to 5,6-Benzidane (VI).—The unsaturated ketone (1 g.) was heated with (0.5 g.) of 30% palladized charcoal[13] for 4 hr. at 280–300° in a stream of carbon dioxide. About 90% of the calculated amount of hydrogen was evolved. The contents of the flask was then ether-extracted. The ethereal solution was filtered and the solvent removed. The brown crystalline residue (0.6 g.) was then distilled under vacuum giving a colorless solid crystallizable from methanol as plates, m.p. 94° (lit.[9] m.p. 94°); λ_{max} 226, 279 and 320 mμ (log *E* 4.89, 3.78 and 3.17, resp.).

Anal. Calcd. for $C_{13}H_{12}$: C, 92.8; H, 7.2. Found: C, 92.32; H, 7.24.

It gave a picrate crystallizable from ethanol in long golden needles, m.p. 120–121° (lit.[9] m.p. 120–121°).

β-Carboxy-β-(*trans*-1-Δ^1-octahydronaphthyl)-propionic Acid (VIII).—β-Carbethoxy-β-(*trans*-1-Δ^1-octahydronaphthyl)-propionic acid (VII)[8] was prepared by the Stobbe condensation of *trans*-1-decalone (m.p. 32–33°, n^{20}D 1.4856, and diethyl succinate. This half-ester (2 g.) was heated with 5% sodium hydroxide solution (20 ml.) on a steam-bath for 3 hr. The mixture was cooled, ether extracted, then carefully acidified with dilute hydrochloric acid. The colorless solid obtained was crystallized from benzene–light petroleum (b.p. 60–80°); m.p. 173° (1.2 g.).

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[11] All melting points and boiling points are uncorrected; microanalyses are by G. S. Crouch, School of Pharmacy, and by A. Bernhardt, Max-Plank-Institute, Mülhein (Ruhr). Light absorptions were measured in ethanol for the ketones, in 2% chloroform in ethanol for the semicarbazones and in chloroform for the 2,4-dinitrophenylhydrazones.

[12] A. M. El Abbady, *J. Org. Chem.*, **21**, 828 (1956).

[13] Prepared according to R. P. Linstead and S. L. S. Thomas, *J. Chem. Soc.*, 1127 (1940).

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.7; H, 7.94. Found: C, 66.8; H, 7.95.

β-Carboxy-γ-(*trans*-1-decalyl)-spirobutyrolactone (IX).—β-Carbethoxy-β-(*trans*-1-Δ^1-octahydronaphthyl)-propionic acid (2 g.) was refluxed with a mixture of glacial acetic acid (15 ml.) and concentrated hydrochloric acid (15 ml.) for 30 min. After cooling, the mixture was diluted, and the resulting semi-solid was isolated and crystallized from benzene–petroleum ether (b.p. 60–80°) as colorless prisms, m.p. 181–182° (0.7 g.).

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.7; H, 7.94. Found: C, 66.6; H, 7.96.

3-Carbethoxy-Δ^8-octahydro-4,5-benzindan-1-one (X).—The half-ester VII (14 g.) in acetic anhydride (200 ml.) was refluxed with anhydrous zinc chloride (2 g.) in glacial acetic acid (100 ml.) for 5 hr. under nitrogen. Acetic acid and anhydride were removed *in vacuo* and the residue poured into water which was made alkaline with sodium carbonate. A dried ethereal extract on evaporation gave an almost colorless viscous oil, b.p. 163–165° (0.5 mm.) (8.9 g.), $n^{20}\text{D}$ 1.5190.

Anal. Calcd. for $C_{16}H_{22}O_3$: C, 73.28; H, 8.39. Found: C, 72.9; H, 8.32.

The semicarbazone crystallized from ethanol; m.p. 222–223°. *Anal.* Calcd. for $C_{17}H_{25}O_3N_3$: C, 63.95; H, 7.84; N, 13.17. Found: C, 64.1; H, 7.96; N, 13.13.

The 2,4-dinitrophenylhydrazone, m.p. 199–200°, crystallized from ethanol–ethyl acetate as red prisms. *Anal.* Calcd. for $C_{22}H_{26}O_6N_4$: N, 12.67. Found: N, 12.99.

Δ^8-Octahydro-4,5-benzindan-1-one (XI).[8]—A mixture of the keto ester X (5.2 g.) and concentrated hydrochloric acid (80 ml.) was refluxed for one hour. The reaction mixture, after dilution with equal volume of water, was ether-extracted. The ethereal solution was washed with sodium carbonate solution, water then dried. There resulted on distillation Δ^8-octahydro-4,5-benzindan-1-one (XI), as colorless oil, b.p. 104–105° (0.2 mm.), $n^{20}\text{D}$ 1.5370 (yield 3 g.). The 2,4-dinitrophenylhydrazone, m.p. 203–204°, crystallized from ethanol–xylene as dark red plates.

Anal. Calcd. for $C_{19}H_{22}O_4N_4$: C, 61.62; H, 5.94; N, 15.13. Found: C, 61.49; H, 6.09; N, 14.73.

Decahydro-4,5-benzindan-1-one (XII).[8]—The unsaturated ketone XI (4 g.) was dissolved in ethanol (40 ml.) and hydrogenated at a 10% palladium–barium sulfate catalyst (1 g.) at atmospheric temperature and pressure. The uptake ceased when one mole had been absorbed. There resulted, after removal of the catalyst and solvent, a viscous oil which solidified under light petroleum (b.p. 40–60°) to give decahydro-4,5-benzindan-1-one (XII) as colorless prisms, m.p. 57.5–59° (yield 3.2 g.).

The 2,4-dinitrophenylhydrazone crystallized from ethanol–xylene in orange plates, m.p. 213–214° (lit.[8] gave a lower m.p. 204–205° from acetic acid).

Anal. Calcd. for $C_{19}H_{24}O_4N_4$: C, 61.3; H, 6.5; N, 15.1. Found: C, 61.2; H, 6.4; N, 15.0.

Acknowledgment.—The author wishes to thank Professor W. H. Linnell of the School of Pharmacy for his interest and advice in the execution of part of this research.

LONDON, ENGLAND
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[COMMUNICATION NO. 1855 FROM THE KODAK RESEARCH LABORATORIES]

The Preparation of Some Vinylpiperidines

BY H. L. COHEN AND L. M. MINSK

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The preparation of 2- and 4-vinylpiperidines and their N-methyl derivatives is reported. None of the compounds could be homopolymerized by the usual methods.

Introduction

It has been reported by Heidrich[1] that 1-methyl-2-vinylpiperidine polymerizes on distillation or on standing for several months at room temperature. Since it is known that allylic amines, to which the 2-vinylpiperidines are formally similar, do not homopolymerize readily, it appeared of interest to prepare some of the vinylpiperidines and study their polymerization tendencies.

The preparation of 2-vinylpiperidine by the dehydration of 2-(2-hydroxyethyl)-piperidine, using a concentrated sulfuric acid–glacial acetic acid mixture at 165°, was reported by Ladenburg.[2] This compound was said to form a readily crystallizable picrate, although no details on the preparation or properties of this derivative were given. Dehydration, using concentrated hydrochloric acid at 165°, of 1-methyl-2-(2-hydroxyethyl)-piperidine was reported by Heidrich[1] to give 1-methyl-2-vinylpiperidine. No reports on the preparation of 4-vinylpiperidine or its N-methyl derivative could be found.

Attempts to dehydrate 2-(2-hydroxyethyl)-piperidine in these Laboratories, with Ladenburg's procedure, gave inconsistent results. At best, only a small yield (1 to 3%) of 2-vinylpiperidine was obtained. The major portion of the product consisted of material of unknown structure with a much higher boiling point than the starting material. It was only slightly soluble in ether and miscible with water. The fact that treatment with picric acid gave an oil from which only a small amount of crystalline material could be isolated would seem to indicate that this high-boiling material was not homogeneous. Dehydration of (2-hydroxyethyl)-piperidine in an alumina-packed column at various temperatures in the 375–425° range gave only small yields of basic material from which no pure vinylpiperidine could be isolated.

Since the yields in the dehydration studies were not encouraging, a synthetic sequence based on the pyrolysis of 2-(2-piperidinoethyl)-trimethylammonium hydroxide was tried (structures I–XII in the diagram). Addition of dimethylamine to 2-vinylpyridine in a steel bomb at 150° gave 2-(2-dimethylaminoethyl)-pyridine (I) in good yield.[3] Hydrogenation of this compound over Raney nickel at high pressure was not successful since

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[1] M. Heidrich, *Ber.*, **34**, 1889 (1901).

[2] A. Ladenburg, *ibid.*, **22**, 2583 (1889).

[3] (a) Preparation of 2-(2-dimethylaminoethyl)-pyridine has been reported by H. E. Reich and R. Levine, THIS JOURNAL, **77**, 4913 (1955); (b) preparation of 4-(2-dimethylaminoethyl)-pyridine has been reported by A. J. Matuszko and A. Taurins, *Can. J. Chem.*, **32**, 538 (1954).