

mixture allowed to come to room temperature during the next 6 hr. Bromine was found to be insoluble in sulfuric acid. The mixture was quenched in crushed ice and worked up in the usual manner. The lachrymatory oil was treated with diethylamine in ether by the method of Lutz⁴¹ to remove phenacyl bromide. After this treatment, only a small amount of acetophenone (b.p. less than 62° at 1 mm.) was obtained.

A mixture of sulfuric acid (184 g.) and anhydrous aluminum chloride (45.7 g.) was also used as a catalyst. The mixture evolved hydrogen chloride and became solid. An additional 100 ml. of sulfuric acid was added to make the system fluid. Acetophenone (40.4 g.) was added dropwise forming a yellow orange complex. Bromine (53.7 g.) was added with stirring over a one hour period and this mixture was allowed to stir overnight. Phenacyl bromide, b.p. 71–73° at 1.5 mm., 30.5 g., 45%, was obtained as a solid. No higher boiling fraction was present in more than a gram quantity.

Chlorosulfonic acid was found to give a completely water-soluble product within the space of 20 min. followed by the addition of bromine within a space of 25 min.

Attempted use of boron trihalides. Boron trichloride (Matheson, 142 g., 1.2 mole) was condensed in a three-necked flask cooled by a slurry of Dry Ice and acetone. Acetophenone (90 g., 0.75 mole) was added dropwise forming a yellow orange colored soluble complex. Bromine (120 g., 0.75 mole) was added dropwise over a period of 20 min. No hydrogen bromide was evolved. The reaction mixture was then allowed to warm up to room temperature over a period of 6 hr. Most of the boron trichloride and some of the bromine evaporated during this period. No product except acetophenone and solid phenacyl bromide (b.p. 71–73° at

1.5 mm.) was obtained. As little as 5 g. of 3-bromoacetophenone would have been detected by the method of isolation.

Boron trifluoride was passed rapidly into 90 g., 0.75 mole of acetophenone. Sufficient heat was liberated to necessitate cooling. After 45 minutes of saturating the mixture with boron trifluoride, bromine (120 g., 0.75 mole) was added dropwise. Some hydrogen bromide seemed to be evolved together with bromine vapor. After six hours of stirring, the mixture became semi-solid and greenish black in color. The usual procedure of isolation gave a dark polymerized mass from which only a few grams of lachrymatory oil could be distilled.

Attempted use of stannic chloride in chlorination of benzaldehyde. Benzaldehyde (51.9 g., 0.49 mole) was added dropwise to 454 g., 1.74 moles of stannic chloride to form a creamy, white slurry that was easily stirred. The heat of reaction seemed comparable to that of benzaldehyde and aluminum chloride. Chlorine (43.8 g., 0.49 mole) was bubbled through the mixture over a period of 3 hr. and the mixture was stirred an additional 5 hr. After the usual isolation, benzaldehyde (b.p. 69° at 15 mm., 37 g., 71%) was first removed leaving a semisolid residue (3 g.) in still pot. The residue was oxidized in quantitative yield to benzoic acid, m.p. and mixed m.p. 122°.

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[CONTRIBUTION FROM UNIVERSITY COLLEGE FOR GIRLS, EIN SHAMS UNIVERSITY,
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Synthesis of Decahydro-5,6-benzindan-1-yl Acetoxymethyl Ketone and 1-Acetoxydecahydro-4,5-benzindan-1-yl Methyl Ketone

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Decahydro-5,6-benzindan-1-yl acetoxymethyl ketone and 1-acetoxydecahydro-4,5-benzindan-1-yl methyl ketone were synthesized from 1-carbethoxy-4,5,6,7,1',2',3',4'-octahydro-5,6-benzindan-3-one and decahydro-4,5-benzindan-1-one, respectively. These compounds are of interest as analogs of adrenal cortical hormones.

Adrenal cortical hormones usually have a —CO-CH₂R side chain and an R' group (where R and R' = H or OH) attached to the carbon atom at position 17 in the cyclopentanoperhydrophenanthrene nucleus. Moreover, the presence of cortical activity has been demonstrated in perhydroindan-1-yl hydroxymethyl ketone² I in the life maintenance test. In view of these observations and because the optimum skeleton upon which to attach the side chain has not been determined, it was decided to attempt the preparation of such derivatives of decahydrobenzindans which may be regarded as analogs of the cyclopentanoperhydrophenanthrene nucleus. Thus, decahydro-5,6-benzindan-1-yl ace-

toxymethyl ketone and 1-acetoxy-decahydro-4,5-benzindan-1-yl methyl ketone were synthesized according to the following scheme.

Clemmensen reduction of 1-carbethoxy-4,5,6,7,1',2',3',4'-octahydro-5,6-benzindan-3-one³ II gave mainly an unsaturated ester tentatively assigned the constitution III. A trace of another product was also isolated and shown to be the paraconic acid X. With regard to the absorption properties of the unsaturated ester III, attention was drawn to the investigation of Ungnade and Ortega,⁴ which has established that α,β -unsaturated acids or esters in alcoholic solution show a distinct maximum in the region between 210–225 m μ ($E \approx 9000$).

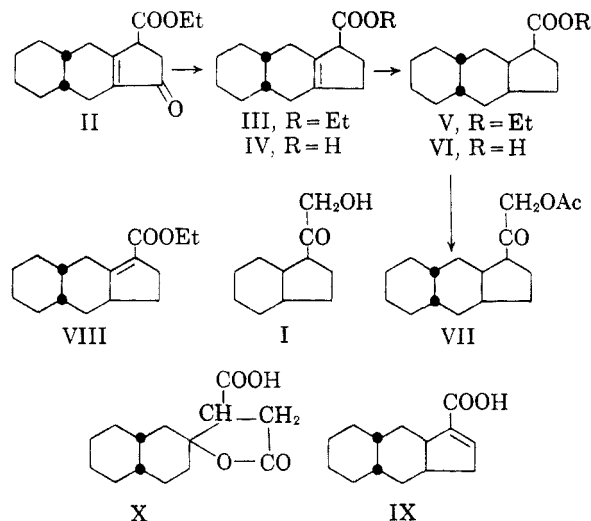
(1) Chemistry Department, University College for Girls, Ein Shams University, Cairo, Egypt.

(2) D. W. Mathieson, Ph.D. thesis, London University, 1951.

(3) A. M. El-Abbady, *J. Am. Chem. Soc.*, **79**, 1757 (1957).

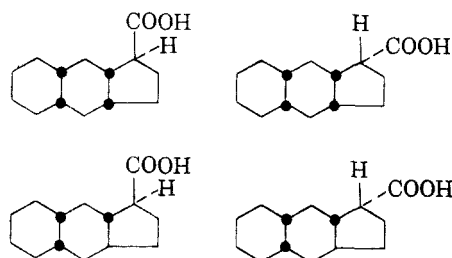
(4) H. E. Ungnade and I. Ortega, *J. Am. Chem. Soc.*, **73**, 1565 (1951).

The observed value for the unsaturated acid IV λ_{\max} 219 $m\mu$ (E 1900) agrees with the above regarding the wave length at which maximum absorption occurs. The low value of E may suggest that during the Clemmensen reduction, the inert double bond in the keto ester II has only partially shifted to be



in conjugation with the carboxy group, as in VIII, giving rise to a mixture of α,β and β,γ -unsaturated esters. Also the observed value of the unsaturated acid IV does not allow any differentiation between it and its isomer IX.

The unsaturated ester III was then hydrogenated in glacial acetic acid with Adams' catalyst. It absorbed one mole of hydrogen to yield a fully saturated ester V, whence alkaline hydrolysis gave the corresponding saturated acid VI. Theoretically, such a substance is capable of existing in four geometrical isomers: It was found that when the



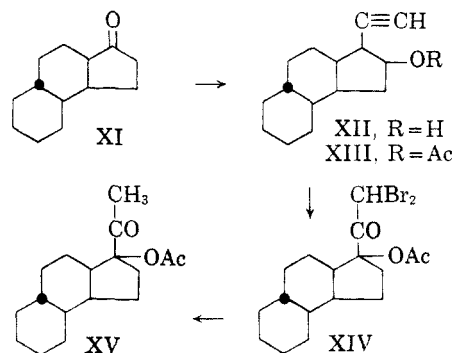
ether-petroleum ether solution of the acid VI was well chilled, a colorless crystalline solid was precipitated. The mother liquor gave the remainder of the substance as colorless oil (the ratio of the solid to the fractions was 1:6). The constitution and configuration of the solid and the liquid fractions are as yet unproved. The liquid fraction of the acid VI on treatment with thionyl chloride,⁵ yielded the corresponding acid chloride which with diazomethane⁶ gave the diazomethyl ketone. This, with

(5) W. S. Knowles, J. A. Kuck, and R. C. Elderfield, *J. Org. Chem.*, **7**, 374 (1942).

(6) M. Steiger and T. Reichstein, *Helv. Chim. Acta*, **20**, 1164 (1937).

glacial acetic acid, yielded decahydro-5,6-benzindan-1-yl acetoxymethyl ketone VII, which failed to give a 2,4-dinitrophenylhydrazone but reduced ammoniacal silver nitrate and Fehling's solution.

Decahydro-4,5-benzindan-1-one⁹ XI was treated with acetylene⁷ in presence of potassium *t*-butoxide, to give 1-ethynyl-1-hydroxydecahydro-4,5-benzindan XII. This was acetylated by prolonged refluxing with acetic anhydride and pyridine,⁸ to give 1-acetoxy-1-ethynyldecahydro-4,5-benzindan XIII. The acetoxy ethynyl derivative XIII when treated



with hypobromous acid⁹ (prepared by adding *N*-bromosuccinimide to a sodium acetate buffer) yielded the dibromoketone XIV. This was reduced easily with zinc dust and acetic acid to 1-acetoxydecahydro-4,5-benzindan-1-yl methyl ketone XV, which gave a 2,4-dinitrophenylhydrazone.

The two final products will be tested for cortical activity and the results may be available at a later date.

EXPERIMENTAL¹⁰

1-Carboethoxy-4,5,6,7,1',2',3',4'-octahydro-5,6-benzindan (III). The solution of 1-carboethoxy-4,5,6,7,1',2',3',4'-octahydro-5,6-benzindan-3-one⁸ (II) (15 g., distilled once) in toluene (100 ml.) was added to amalgamated zinc wool (60 g.) in concentrated hydrochloric acid (120 ml.) and water (50 ml.). The whole was refluxed for 30 hr. (three 30-ml. portions of concentrated hydrochloric acid being added at intervals of 6 hr.). The toluene layer was then separated and the solvent removed; the residue was dissolved in ether. The aqueous layer was extracted with ether and the combined ether extracts were then extracted with sodium carbonate solution. The neutral ethereal solution on evaporation gave a residue which, on distillation, yielded the unsaturated ester (III) at 120° (0.6 mm.) as a colorless oil (6.5 g.), n_D^{25} 1.4545. It was unsaturated to bromine in carbon tetrachloride.

Anal. Calcd. for $C_{16}H_{24}O_2$: C, 77.42; H, 9.67; sapon. equiv., 248. Found: C, 77.61; H, 9.79; sapon. equiv., 247.

Acidification of the alkaline extracts gave an oily substance which partly solidified under benzene-petroleum ether (80-

(7) H. E. Stavely, *J. Am. Chem. Soc.*, **61**, 79 (1939).

(8) L. Ruzicka and K. Hofmann, *Helv. Chim. Acta*, **20**, 1280 (1937).

(9) I. Salamon and T. Reichstein, *Helv. Chim. Acta*, **30**, 1616 (1947).

(10) All melting points and boiling points are uncorrected; microanalyses are by G. S. Crouch, School of Pharmacy, and by A. Bernhardt, Max Plank Institute, Mulheim (Ruhr).

100°). From this mixture two products were obtained. One was a colorless crystalline material (0.72 g.) crystallizable from benzene m.p. 170–172°. Its analysis and equivalent weight fitted for spiro-*cis*-decahydronaphthalene-2-2'[3'-carboxy-5'-ketotetrahydrofuran] (X).

Anal. Calcd. for $C_{14}H_{20}O_4$: C, 66.7; H, 7.94; neut. equiv., 252. Found: C, 67.6; H, 7.71; neut. equiv., 253.

The other was a colorless viscous oil (3.4 g.), which was found to be the unsaturated acid (IV), b.p. 138–140° (0.3 mm.), n_D^{25} 1.5139. It decolorized bromine in carbon tetrachloride and absorbed one mole of hydrogen in microhydrogenation.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.09. Found: C, 75.2; H, 9.46.

1-Carboxydecahydro-5,6-benzindan (V). A solution of the unsaturated ester (III) (4.5 g.) in glacial acetic acid (50 ml.) was shaken with hydrogen in the presence of Adams' catalyst (0.5 g.). Uptake of the required hydrogen was complete in 3 hr. After removal of the solvent under reduced pressure, the residual oil was distilled at 107–110° (0.4 mm.) was a colorless liquid, n_D^{25} 1.4970 (yield, 4 g., 90%).

Anal. Calcd. for $C_{16}H_{22}O_2$: C, 76.80; H, 10.40. Found: C, 76.72; H, 10.17.

Decahydro-5,6-benzindan-1-carboxylic acid (VI). The saturated ester (V) (4 g.) was hydrolyzed, using 5% sodium hydroxide solution (40 ml.). The mixture was refluxed for 3 hr.; after cooling it was ether extracted. The alkaline solution was acidified with hydrochloric acid then ether extracted. The ethereal solution was dried over sodium sulfate and the solvent was removed. The crude saturated acid (VI) was obtained as an oil. By chilling its ether-petroleum ether solution to –70°, two fractions were obtained. One was a colorless crystalline material (0.4 g.), crystallizable from ethanol-petroleum ether (b.p. 40–60°), m.p. 173–174°.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.67; H, 9.91. Found: C, 75.58; H, 9.86.

It gave a *p*-toluidide as colorless crystals from benzene-petroleum ether (b.p. 40–60°), m.p. 147–149°.

Anal. Calcd. for $C_{23}H_{29}ON$: C, 81.03; H, 9.32; N, 4.50. Found: C, 80.6; H, 9.49; N, 4.76.

The other was a colorless viscous oil distilled at 112–115° (0.1 mm.), n_D^{25} 1.5100 (yield 2.4 g.).

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.67; H, 9.91. Found: C, 74.91; H, 10.04.

Decahydro-5,6-benzindan-1-yl acetoxyethyl ketone (VII). Decahydro-5,6-benzindan-1-carboxylic acid (VI) (2.4 g., liquid fraction) in dry benzene (8 ml.) was allowed to stand 48 hr. with redistilled thionyl chloride (10 ml.). Excess thionyl chloride and solvent were removed *in vacuo* and the final traces of acidic material removed by the addition and subsequent removal of two 10-ml. portions of dry benzene. The residue was distilled, b.p. 110–112° (0.4 mm.), to yield the corresponding acid chloride as colorless liquid (2.4 g.). This was then dissolved in dry ether (15 ml.) and added to an ethereal solution of diazomethane (200 ml. from 8 g. nitrosomethylurea). After standing overnight at room temperature, removal of the ether *in vacuo* left a light yellow oil which was dissolved in glacial acetic acid (30 ml.), placed in a water bath and the temperature slowly raised. After 45 min. at 100° no further nitrogen was observed. The contents of the flask were diluted with water and ether extracted. The ether extract was washed with 5% sodium

carbonate and water and dried over anhydrous sodium sulfate. Evaporation of the solvent gave an oil, b.p. 111–112° (0.1 mm.), yield, 1.96 g. (71%), n_D^{25} 1.5051.

Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.4; H, 9.4; COCH₃, 15.4. Found: C, 74.4; H, 9.6; COCH₃, 13.4.

It failed to give a 2,4-dinitrophenylhydrazone, but it reduced ammoniacal silver nitrate and Fehling's solution.

1-Ethynyl-1-hydroxydecahydro-4,5-benzindan (XII). A solution of potassium *t*-butoxide (from potassium metal, 2 g., and dry *t*-butyl alcohol, 30 ml.) kept under nitrogen, was mixed with a solution of decahydro-4,5-benzindan-1-one⁸ (XI) (2.7 g.) in dry ether (20 ml.). The resulting mixture was added over a period of 2 hr. to a saturated solution of acetylene in dry ether (40 ml.) at minus 15°. Acetylene was passed into the mixture for another 2 hr. Decomposition of the reaction mixture was carried out with a saturated solution of ammonium chloride (20 ml.) and concentrated hydrochloric acid till acidic to congo red. The ether layer was separated, washed with water and dried over sodium sulfate. Removal of the solvent gave a residue which was distilled at 104–106° (1.0 mm.) as colorless oil (1.9 g.).

Anal. Calcd. for $C_{16}H_{22}O$: C, 82.57; H, 10.09. Found: C, 82.08; H, 10.13.

1-Ethynyl-1-acetoxydecahydro-4,5-benzindan (XIII). *1-Ethynyl-1-hydroxydecahydro-4,5-benzindan* (XII) (1.5 g.), acetic anhydride (10 ml.) and dry pyridine (10 ml.) were refluxed for 15 hr. The reaction was allowed to cool, poured into water (50 ml.), and then extracted with ether. The ether extract was successively washed with dilute hydrochloric acid, sodium bicarbonate solution, and water and was finally dried over sodium sulfate. After removal of the solvent, the residue was distilled at 135° (5.0 mm.), yield (1.1 g.). This product was not analyzed because of the small quantity obtained.

1-Acetoxydecahydro-4,5-benzindan-1-yl methyl ketone (XV). The above ethynyl ethoxy compound (XIII) (1.1 g.) in *t*-butyl alcohol (20 ml.) was added to a solution of *N*-bromosuccinimide (5 g.) and sodium acetate (5 g.) in water (25 ml.). To this mixture, acetic acid (25 ml.) was added dropwise with stirring. The dibromo compound (XIV) was separated after a while as a solid (0.9 g.) which was dissolved in acetic acid (50 ml.). To this solution a mixture of sodium acetate (4 g.) and zinc dust (4 g.) was added and then shaken for 10 min. at 80°. The mixture was allowed to cool down, then diluted with ether. The zinc dust was filtered off and washed with ether. The ethereal solution was washed free from acetic acid and dried. Evaporation of the solvent left a viscous oil which solidified on standing. The solid was crystallized from petroleum ether (b.p. 60–80°) as colorless crystals (0.5 g.), m.p. 116°.

Anal. Calcd. for $C_{17}H_{26}O_3$: C, 73.33; H, 9.35. Found: C, 73.0; H, 9.30.

Its 2,4-dinitrophenylhydrazone crystallized from ethanol in orange crystals, m.p. 221–222°.

Anal. Calcd. for $C_{23}H_{30}O_6N_4$: N, 12.23. Found: N, 12.14

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CAIRO, EGYPT