646. *A Synthesis of Indane-1-carboxylic Acids.*

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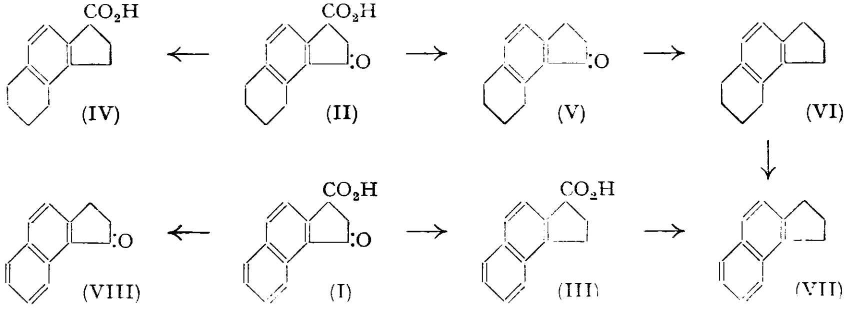
Ring closure of β-naphthyl- and 1 : 2 : 3 : 4-tetrahydro-6-naphthylsuccinic acid, followed by Clemmensen reduction of the intermediate γ-keto-acids, has been shown to lead to 4 : 5-benzindane-1-carboxylic acid and its 1′ : 2′ : 3′ : 4′-tetrahydro-derivative respectively.

As part of a scheme for the synthesis of derivatives of hexahydroindane considered as fragments of the complete steroid nucleus, a general method of preparation of the aromatic derivatives, indane-1-carboxylic acids, was sought. The route described below involves the synthesis and ring closure of various arylsuccinic acids which may be readily prepared from the corresponding aromatic aldehydes. Its utility was first checked by using phenylsuccinic acid itself: ring closure with fluorosulphonic acid (Baker, Coates, and Glockling, *J.*, 1951, 1376) yielded the known 3-oxoindane-1-carboxylic acid. Clemmensen reduction furnished a good yield of indane-1-carboxylic acid (Knowles, Kuck, and Elderfield, *J. Org. Chem.*, 1942, **7**, 377).

The method was next applied to 2-naphthylsuccinic acid and 1 : 2 : 3 : 4-tetrahydronaphthyl-6-succinic acid which were synthesised by standard methods (*Org. Synth.*, 1941, **1**, 451; 1950, **30**, 83). 2-Naphthaldehyde was condensed with ethyl cyanoacetate or diethyl malonate; the products added hydrogen cyanide smoothly, and subsequent hydrolysis yielded β-naphthylsuccinic acid. 1 : 2 : 3 : 4-Tetrahydro-6-naphthaldehyde (obtained by a Gattermann reaction on tetralin) similarly gave the tetrahydro-analogue.

In contrast to experience with phenylsuccinic acid, intramolecular acylation could not be satisfactorily accomplished under Friedel–Crafts conditions and the reagent of choice was anhydrous hydrogen fluoride: this gave an excellent yield of (I) and (II) after 24 hours' condensation at room temperature. Fluorosulphonic acid gave equally satisfactory yields but presented more difficulties in isolation of the product. Clemmensen reduction gave the corresponding 4 : 5-benz- and 1′ : 2′ : 3′ : 4′-tetrahydro-4 : 5-benz-indane-1-carboxylic acids (III) and (IV).



That the constitutions assigned are correct was shown by the following reactions. (i) Nitric acid oxidation of (II) gave benzene-1 : 2 : 3 : 4-tetracarboxylic acid identified as its tetramethyl ester; (ii) decarboxylation of (II) gave the hitherto unknown 1′ : 2′ : 3′ : 4′-tetrahydro-4 : 5-benzindan-3-one (V) which on Clemmensen reduction yielded the known 1′ : 2′ : 3′ : 4-tetrahydro-4 : 5-benzindane (VI) (Arnold and Barnes, *J. Amer. Chem. Soc.*, 1943, **65**, 2393); (iii) dehydrogenation of (VI) furnished 4 : 5-benzindane (VII) (Kruber, *Ber.*, 1932, **65**, 1382); (iv) decarboxylation of (I) gave 3-oxo-4 : 5-benzindane (VIII) (*idem, loc. cit.*); (v) decarboxylation of (III) gave 4 : 5-benzindane (VII). The direction of ring closure is thus in accord with many analogies. Attempts were made to extend these reactions to 6-hydroxy-2-naphthylsuccinic acid without success. Thus, although 6-methoxy-2-naphthoic acid was smoothly converted into the corresponding aldehyde by McFadyen and Stevens's method (*J.*, 1936, 584) and this was further converted into 6-hydroxy-2-naphthylsuccinic acid, ring closure proved abortive under all conditions tried.

EXPERIMENTAL

Indane-1-*carboxylic Acid*.—3-Oxoindane-1-carboxylic acid (2·5 g.) in acetic acid (75 ml.) was refluxed for 8 hr. with amalgamated zinc (20 g.) and concentrated hydrochloric acid (100 ml.). After working up in the usual way, there resulted an acid (1·4 g.) crystallising from water in colourless needles, m. p. 55—56°. The p-*toluidide* crystallised from light petroleum (b. p. 80—100°) in stout needles, m. p. 162—163° (Found: C, 81·2; H, 6·9; N, 5·5. $C_{17}H_{17}ON$ requires C, 81·3; H, 6·8; N, 5·6%). Neither the acid nor its toluidide depressed the m. p. of samples produced by hydrogenation of indene-1(3)-carboxylic acid (Knowles, Kuck, and Elderfield, *loc. cit.*).

1 : 2 : 3 : 4-*Tetrahydro*-6-*naphthaldehyde*.—Dry tetralin (33 g., 0·25 mole), cuprous chloride (3·7 g., 0·02 mole), and dry benzene (150 ml.) were stirred while finely powdered aluminium chloride (33·6 g., 0·25 mole) was added. Separate streams of dry hydrogen chloride and carbon monoxide were then led into the mixture at 50° for 7 hr. The whole was cooled and poured on ice, and steam-distilled. The distillate was extracted with ether, and the extract dried and evaporated. After an initial fraction consisting of unchanged tetralin there was obtained the required aldehyde, b. p. 117—120°/4 mm. (8·5 g.). The semicarbazone had m. p. 221° in agreement with Newman and Zahn (*J. Amer. Chem. Soc.*, 1943, **65**, 1098). The 2 : 4-*dinitrophenylhydrazone* crystallised from chloroform–ethanol in orange plates, m. p. 222° (Found: C, 59·7; H, 4·9; N, 16·4. $C_{17}H_{16}O_4N_4$ requires C, 60·0; H, 4·7; N, 16·5%).

Ethyl α-*Cyano*-1 : 2 : 3 : 4-*tetrahydro*-6-*naphthylmethyleneacrylate*.—Piperidine (0·5 ml.) was added to a mixture of the above aldehyde (11 g.) and ethyl cyanoacetate (8 g.). Heat was evolved and the mixture was held at 100° for 5 min. On cooling, the whole solidified. A portion crystallised from ethanol in pale buff needles, m. p. 62° (Found : C, 75·6; H, 6·9; N, 5·6. $C_{16}H_{17}O_2N$ requires C, 75·3; H, 6·7; N, 5·5%). The main bulk was carried forward to the next stage.

1 : 2 : 3 : 4-*Tetrahydro-2-naphthylsuccinic Acid*.—The above crude *cyanoacrylate* was dissolved in ethanol (14 ml.) and on addition of sodium cyanide (7 g.) in water (14 ml.) an exothermic reaction ensued. The mixture was kept at 65° for 30 min., cooled, and acidified, a viscous brown oil resulting. The upper aqueous layer was decanted and the bottom layer refluxed with concentrated hydrochloric acid (250 ml.) for 8 hr. The semisolid mass thus formed was triturated with chloroform (3 × 75 ml.), to yield 9·9 g. of the required *acid*, crystallising from 20% aqueous ethanol in colourless plates, m. p. 200° (Found : C, 67·5; H, 6·6%; titration equiv., 125. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5%; equiv., 124).

The *dimethyl* ester had b. p. 250°/10 mm. (bath-temp.), m. p. 42° (Found : C, 69·2; H, 7·3. $C_{16}H_{20}O_4$ requires C, 69·6; H, 7·3%).

1′ : 2′ : 3′ : 4′-*Tetrahydro-3-oxo-4 : 5-benzindane-1-carboxylic Acid*.—(a) *By means of hydrogen fluoride.* This reagent was most conveniently handled in "Polythene" ware. To the acid, placed in a narrow-necked screw-capped bottle, liquid anhydrous hydrogen fluoride was added, then the cap was firmly screwed down. Under these conditions the mixture could be safely kept almost indefinitely without evaporation and the use of thin-walled bottles made it possible to observe the contents fairly readily. Such bottles have been in almost constant use for over a year without apparent deterioration. In working up, the reagent is easily evaporated on the steam-bath from a "Polythene" beaker. The above tetrahydronaphthylsuccinic acid (15 g.), dissolved in anhydrous hydrogen fluoride (150 ml.), was kept for 24 hr. Evaporation left a residue (13·2 g.) which crystallised from ethanol–light petroleum (b. p. 100—120°) in stout plates, m. p. 182°. The *semicarbazone* crystallised from aqueous acetic acid in pale yellow plates, m. p. 248° (Found : C, 62·6; H, 6·0; N, 14·2. $C_{15}H_{17}O_3N_3$ requires C, 62·7; H, 5·9; N, 14·6%). The 2 : 4-*dinitrophenylhydrazone* of the *ethyl* ester, crystallised from acetic acid, had m. p. 194° (Found : C, 60·3; H, 5·0; N, 12·8. $C_{22}H_{22}O_6N_4$ requires C, 60·3; H, 5·0; N, 12·8%). The *oxime* crystallised from 50% aqueous alcohol in plates, m. p. 241° (decomp.) (Found : N, 5·7. $C_{14}H_{15}O_3N$ requires N, 5·7%).

(b) *By means of fluorosulphonic acid.* The succinic acid (1 g.) was added to fluorosulphonic acid (8 ml.), and the resulting solution warmed to 100° for 20 min., then poured on ice-water. The product was extracted with ether, to yield the required compound (0·9 g.), crystallising from ethanol–light petroleum in plates, m. p. 182°.

Oxidation of 1′ : 2′ : 3′ : 4′-*Tetrahydro-3-oxo-4 : 5-benzindane-1-carboxylic Acid*.—The keto-acid (1 g.) was refluxed for 180 min. with concentrated nitric acid (15 ml.), a further 15 ml. being added after 90 min. Evaporation left a residue of benzene-1 : 2 : 3 : 4-tetracarboxylic acid which crystallised from ether–light petroleum (b. p. 100—120°) in prisms, m. p. 233—235° (Smith, *J. Amer. Chem. Soc.*, **1933**, **55**, 4305, cites m. p. 238°). The tetramethyl ester crystallised from methanol in plates, m. p. 132—133° (*idem, loc. cit.*, gives m. p. 133—135°).

1′ : 2′ : 3′ : 4′-*Tetrahydro-4 : 5-benzindan-3-one*.—The keto-acid (3 g.) in quinoline (30 ml.) was heated at 240° with copper bronze (3 g.). When evolution of gas had ceased (25 min.) the mixture was cooled, filtered, and diluted with four times its volume of ether. Quinoline was removed by repeated shaking with 50% hydrochloric acid, and any unchanged starting material with 10% aqueous sodium hydroxide. The residue on evaporation of the ether proved to be an oily ketone which gave an oily oxime, but the 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in fine red plates, m. p. 278° (Found : C, 62·3; H, 4·5; N, 15·2. $C_{19}H_{18}O_4N_4$ requires C, 62·3; H, 4·9; N, 15·3%).

1′ : 2′ : 3′ : 4′-*Tetrahydro-4 : 5-benzindane*.—The above ketone (2·9 g.) in toluene (10 ml.) was refluxed for 16 hr. with amalgamated zinc (10 g.) and concentrated hydrochloric acid (17·5 ml.). On cooling, the whole was extracted with ether and the organic layer evaporated, to give the required hydrocarbon as a colourless oil, b. p. 110°/7 mm. (Found : C, 91·2; H, 8·7. Calc. for $C_{13}H_{16}$: C, 90·8; H, 9·3%).

4 : 5-*Benzindane*.—The above tetrahydro-derivative (1 g.) was heated with a 30% palladium–charcoal for 6 hr. at 265—270°. The residual oil obtained on extraction with ether furnished a picrate, m. p. 108—110° (Kruber, *Ber.*, 1932, **65**, 1382, cites m. p. 109—110°).

1′ : 2′ : 3′ : 4′-*Tetrahydro-4 : 5-benzindane-1-carboxylic Acid*.—1′ : 2′ : 3′ : 4′-Tetrahydro-3-oxo-4 : 5-benzindane-1-carboxylic acid (2 g.) in toluene (5 ml.) was refluxed for 17 hr. with amalgamated zinc (5 g.) and concentrated hydrochloric acid (12 ml.). When worked up by the usual procedure *via* the sodium salt, the required *acid* was obtained, crystallising from 80% aqueous acetic acid in small colourless plates, m. p. 128—129° (1·5 g.) (Found: C, 77·3; H, 7·3. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·4%).

2-*Naphthylsuccinic Acid.*—(*a*) 2-Naphthaldehyde (*Org. Synth.*, 1943, **23**, 63) (1·6 g.) in ethanol (2 ml.) was heated with ethyl cyanoacetate (1·1 g.) and piperidine (0·2 ml.). After 3 min.' warming at 100° the mixture was cooled, yielding *ethyl α-cyano-2-naphthylmethyleneacrylate* (1·4 g.), crystallising from ethanol in clusters of pale yellow needles, m. p. 112° (Found: C, 76·7; H, 5·1; N, 5·5. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2; N, 5·6%).

Sodium cyanide (0·5 g.) in water (2 ml.) was added to a suspension of ethyl α-cyano-2-naphthylmethyleneacrylate (1·25 g.) in ethanol (5 ml.). After 12 hr. at 65—75° the cooled mixture was acidified, yielding a viscous brown oil. The aqueous layer was decanted and the oil refluxed for 6 hr. with concentrated hydrochloric acid (25 ml.). Trituration of the resulting semi-solid mass with chloroform gave the required substance (125 mg.), m. p. 218°. Evaporation of the chloroform and re-treatment of the residue with concentrated hydrochloric acid, as above, yielded a further 105 mg. (total yield, 230 mg.), crystallising from 10% ethanol in water in colourless plates, m. p. 220° (Found: C, 68·1; H, 4·7%; titration equiv., 119. $C_{14}H_{12}O_4$ requires C, 68·8; H, 4·9%; equiv., 122). The *dimethyl* ester crystallised from light petroleum (b. p. 40—60°) in needles (m. p. 65°) (Found: C, 70·5; H, 6·1. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

(*b*) 2-Naphthaldehyde (30 g.) and ethyl malonate (31·5 g.) in dry benzene (90 ml.) were refluxed with piperidine (1 ml.) until no more water was formed (18—24 hr.). The semi-solid ethyl 2-naphthylmethylenemalonate was then isolated by removal of solvent and dissolved in ethanol (600 ml.). Potassium cyanide (13·5 g.) in water (22·5 ml.) was added and the mixture heated to 70—80° for 19 hr. with constant stirring. After cooling, potassium hydrogen carbonate was filtered off and the filtrate acidified. Concentration of the liquors yielded a viscous oil which was refluxed with concentrated hydrochloric acid (650 ml.) for 6 hr. Trituration with chloroform gave the required acid and, from the chloroform layer, a quantity of viscous oil which was reprocessed with concentrated hydrochloric acid as above. The acid (total yield, 11·5 g.) crystallised from water containing 10% of ethanol, in colourless plates, m. p. 220° giving no depression on admixture with a sample synthesised as in (*a*) above.

3-*Oxo*-4 : 5-*benzindane*-1-*carboxylic Acid.*—(a) *By means of hydrogen fluoride.* 2-Naphthylsuccinic acid (8 g.) in anhydrous hydrogen fluoride (150 ml.) was kept at room temperature for 24 hr. Evaporation gave a *keto-acid* (6·5 g.), crystallising from 1 : 9 ethanol–water in needles, m. p. 181—182° (Found: Titration equiv., 221. $C_{14}H_{10}O_3$ requires equiv., 226). The *semicarbazone* crystallised from aqueous acetic acid in pale yellow plates, m. p. 235° (Found: C, 63·5; H, 4·8; N, 14·6. $C_{15}H_{13}O_3N_3$ requires C, 63·6; H, 4·6; N, 14·8%). Satisfactory analyses could not be obtained on the keto-acid or its 2 : 4-dinitrophenylhydrazone.

(b) *By means of fluorosulphonic acid.* 2-Naphthylsuccinic acid (0·5 g.) in fluorosulphonic acid (5 ml.) was warmed on the steam-bath for 7 min. After cooling, the mixture was poured on ice-water and extracted with ether. Crystallisation of the residue thus obtained from 1 : 9 ethanol–water gave needles (0·35 g.), m. p. 181—182°, identical with a sample obtained as in (*a*) above.

(c) *By means of aluminium chloride–acid chloride.* To the acid chloride from β-naphthylsuccinic acid (0·5 g.) in dry nitrobenzene (4 ml.) was added aluminium chloride (0·4 g.) in dry nitrobenzene. The mixture was heated at 110° for 30 min., then decomposed with ice-water. Nitrobenzene was removed by steam-distillation and the insoluble non-volatile residue brought into solution by addition of ethanol. After treatment with charcoal and cooling, the keto-acid (0·2 g.) was obtained, having m. p. 182°.

4 : 5-*Benzindan*-3-*one.*—3-Oxo-4 : 5-benzindane-1-carboxylic acid (0·5 g.) in quinoline (10 ml.) was refluxed with copper bronze for 15 min. The products were isolated as described for the tetrahydro-isomer, to give the required ketone, crystallising from acetic acid in almost colourless prisms, m. p. 100—102°. The oxime had m. p. 174°. (Kruber, *loc. cit.*, cites m. p. 102—103° and 175—176° respectively.)

4 : 5-*Benzindane*-1-*carboxylic Acid.*—3-Oxobenzindane-1-carboxylic acid (2 g.) in toluene (5 ml.) was refluxed for 18 hr. with amalgamated zinc (5 g.) and concentrated hydrochloric acid (10 ml.). The resultant *acid* formed colourless plates (m. p. 145°; 1·3 g.) from 50% aqueous acetic acid (Found: C, 78·9; H, 5·8. $C_{14}H_{12}O_2$ requires C, 79·3; H, 5·7%). Decarboxylation with copper bronze gave 4 : 5-benzindane (picrate, m. p. 105—107°) identical with that obtained as described above.

6-*Methoxynaphthalene*-2-*carboxylic Acid.*—To 2-acetyl-6-methoxynaphthalene (Robinson and Rydon, *J.*, 1939, 1394) (60 g.) in dioxan (600 ml.) there was added during 1 hr. a solution of hypobromite [from bromine (60 ml.), sodium hydroxide (168 g.) and water (800 ml.)]. Saturated sodium metabisulphite solution (100 ml.) was added to destroy the excess of hypobromite, and dioxan and bromoform were removed *in vacuo*. Acidification of the remaining liquors gave the required acid (51 g.), m. p. 212°. (Fries and Schimmelschmidt, *Ber.*, 1925, **58**, 2835, cite m. p. 212°.) The *ethyl* ester made in the usual manner had m. p. 96°, crystallising from light petroleum (b. p. 60—80°) in colourless plates (Found: C, 73·3; H, 6·1. $C_{14}H_{14}O_3$ requires C, 73·1; H, 6·1%).

6-*Methoxy*-2-*naphthaldehyde*.—The above ethyl ester (50 g.) was refluxed with 90% hydrazine hydrate in alcohol (130 ml.) for 7 hr. After cooling, the resulting *hydrazide* (45 g.) was collected and crystallised from ethanol in colourless plates, m. p. 183° (Found: C, 66·2; H, 5·6; N, 13·1. $C_{12}H_{12}O_2N_2$ requires C, 66·7; H, 5·6; N, 13·0%). It was then dissolved in pyridine (675 ml.), and benzenesulphonyl chloride (48 ml.) added slowly at 0°. Stirring was continued thereafter for 2 hr. After pouring on ice and hydrochloric acid there resulted 67 g. of the *benzenesulphonyl* derivative. Crystallisation from 80% ethanol in water gave plates, m. p. 202° (Found: C, 60·3; H, 4·7; N, 7·9; S, 8·9. $C_{18}H_{16}O_4N_2S$ requires C, 60·6; H, 4·5; N, 7·9; S, 9·0%). This derivative (24 g.) was suspended in ethylene glycol (540 ml.) and heated to 160°, partial dissolution resulting. Anhydrous sodium carbonate (5 equivs.) was then added and after 60 seconds the vigorous reaction was terminated by cautious addition of boiling water. On cooling, the whole was extracted with benzene–ether (1 : 3) and the dried extract evaporated. Recrystallisation of the residue from methanol (charcoal) gave the required aldehyde in yellow prisms (8 g.), m p. 80° (Hudson, *J.*, 1946, 76, gives m. p. 80—81°). The semicarbazone crystallised from acetic acid in colourless plates, m. p. 275° (*idem, ibid.*, gives m. p. 277—278°).

Ethyl α-*Cyano*-6-*methoxy*-2-*naphthylmethyleneacrylate*.—To the above aldehyde (5·6 g.) in ethanol (6·5 ml.) was added ethyl cyanoacetate (3·4 g.) and piperidine (0·3 ml.), the mixture being warmed on the steam-bath for 2—3 min. The resulting *cyanoacrylate* (5·6 g.) crystallised from light petroleum (b. p. 100—120°) in pale yellow plates, m. p. 122° (Found: C, 72·5; H, 5·3; N, 4·9. $C_{17}H_{15}O_3N$ requires C, 72·6; H, 5·3; N, 5·0%).

6-*Hydroxy*-2-*naphthylsuccinic Acid*.—Sodium cyanide (1·2 g.) in water (5 ml.) was added to a suspension of ethyl α-cyano-6-methoxy-2-naphthylmethyleneacrylate (4·6 g.) in ethanol (5 ml.). After several min. at 100° complete solution resulted. Dilute hydrochloric acid was then added, to precipitate a heavy brown oil. This was refluxed with concentrated hydrochloric acid (75 ml.) for 4 hr. On cooling, the resulting *succinic acid* was filtered off (3·7 g.). Crystallisation from water containing a few drops of dilute hydrochloric acid gave the substance in pale buff-coloured plates, m. p. 210° (Found: C, 64·8; H, 4·7%; titration equiv., 136. $C_{14}H_{12}O_5$ requires C, 64·6; H, 4·6%; equiv., 130). Zeisel estimation indicated absence of methoxyl and demethylation must have occurred during the acid hydrolysis of the intermediate dicyano-acid. The *diethyl* ester, prepared by the Fischer–Speier method, was a yellow oil, b. p. 200°/0·5 mm. (bath-temp.) (Found: C, 68·2; H, 6·6. $C_{18}H_{20}O_5$ requires C, 68·4; H, 6·3%).

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