215. 5-*Methyl*-3 : 4-*benzofluorene.*

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The Robinson–Mannich reaction has been used in syntheses of 6 : 7 : 8 : 13-tetrahydro-3 : 4-benzofluoren-6-one and its 5-methyl homologue. These were converted into 3 : 4-benzofluorene and 5-methyl-3 : 4-benzofluorene respectively.

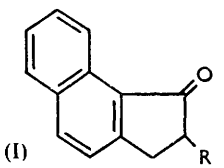
Failing to obtain 5-methyl-3 : 4-benzofluorene by a Bougault-type cyclisation, which provided a satisfactory means of obtaining some of its isomers,[1] we sought another route to this compound.

The Robinson–Mannich reaction, which has been applied to the synthesis of fluorene derivatives,[2] promised to be useful, and initially we examined its use in preparing 3 : 4-benzofluorene itself.

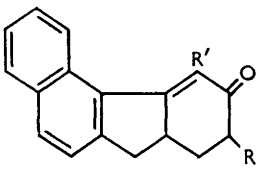
4 : 5-Benzindan-3-one was prepared by Ansell and Hey[3] on a very small scale by cyclising β-2-naphthylpropionic acid with hydrogen fluoride. We found this cyclisation to proceed smoothly and efficiently on the larger scale, and the product (I; R = H) reacted readily with paraformaldehyde and morpholine hydrochloride to give 2-morpholinomethyl-4 : 5-benzindan-3-one hydrochloride (I; R = $-CH_2 \cdot C_4H_8ON,HCl$). The free base, liberated in the cold from this sparingly soluble salt (heat caused decomposition), readily formed a quaternary salt with methyl iodide. The methiodide reacted

[1] Keene and Schofield, *J.*, 1957, 3181.
[2] Harradence and Lions, *J. Chem. Soc. New South Wales*, 1938, 284.
[3] Ansell and Hey, *J.*, 1950, 2874.

quickly with ethyl sodioacetoacetate, to give a moderately good yield of ethyl 6 : 7 : 8 : 13-tetrahydro-6-oxo-3 : 4-benzofluorene-7-carboxylate (II; R = CO_2Et, R′ = H). In the fluorene series Harradence and Lions [2] removed the ethoxycarbonyl group from the compound analogous to (II; R = CO_2Et, R′ = H) by heating it at 190° with glycerol containing 10% of water. With the compound (II; R = CO_2Et, R′ = H) this reagent gave only intractable tars, but hydrolysis and decarboxylation proceeded smoothly when the ester was boiled with 2N-hydrochloric acid in acetic acid.



(I)



(II)

We failed to hydrogenate the resulting 6 : 7 : 8 : 13-tetrahydro-3 : 4-benzofluoren-6-one (II; R = R′ = H), and the amorphous solid formed on reduction with lithium aluminium hydride gave only tars when heated with palladised charcoal. However, the ketone was reduced cleanly by the Meerwein–Ponndorf procedure, with aluminium *iso*propoxide in propan-2-ol, and the resulting oily alcohol underwent dehydration and dehydrogenation when heated with palladised charcoal, giving 3 : 4-benzofluorene in reasonable yield.

To extend this variation of the method to the synthesis of 5-methyl-3 : 4-benzofluorene, we attempted to condense 2-morpholinomethyl-4 : 5-benzindan-3-one methiodide with ethyl sodio-β-oxovalerate. As in the previous case, the reaction solution quickly became red-brown, but no solid separated. Acidification and extraction isolated a brown oil from which no homogeneous product could be obtained directly. When it was heated with hydrochloric–acetic acid only a small quantity of 4 : 5-benzindan-3-one was recovered.

For an application of the alternative type of Robinson–Mannich synthesis, 4 : 5-benzindan-3-one was converted into 2-formyl-4 : 5-benzindan-3-one (I; R = CHO). This reacted with 4-piperidinobutan-2-one methiodide in absolute methanolic sodium methoxide, to give the crystalline diketone (I; R = CH_2·CH_2·COMe) in good yield, the formyl group being eliminated. When heated with a mixture of acetic and hydrochloric acid the diketone was converted into the tetracyclic compound (II; R = R′ = H).

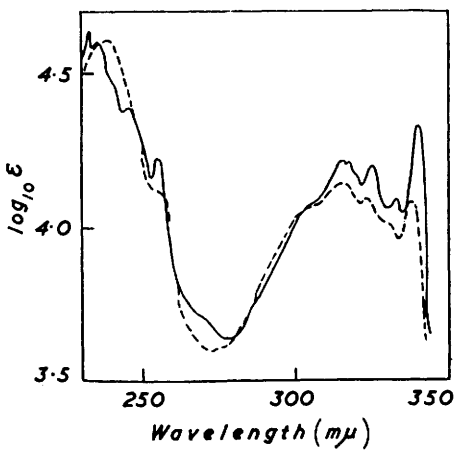
In the same way, 1-diethylaminopentan-3-one methiodide reacted with 2-formyl-4 : 5-benzindan-3-one, to give the diketone (I; R = CH_2·CH_2·COEt), and acid cyclisation then produced the required 6 : 7 : 8 : 13-tetrahydro-5-methyl-3 : 4-benzofluoren-6-one (II; R = H, R′ = Me). The αβ-unsaturated ketones (II; R = H, R′ = H and Me severally) gave ultraviolet extinction curves [4] showing the expected [5] broad band in the 320—350 mμ region. Meerwein–Ponndorf reduction of the ketone (II; R = H, R′ = Me) under the conditions mentioned earlier, and subsequent dehydration and dehydrogenation, afforded 5-methyl-3 : 4-benzofluorene. The overall yield was considerably lower than in the case of the parent compound.

In the 3 : 4-benzophenanthrene series [6] the 5-methyl derivatives show abnormally high m. p.s, and in contrast to their isomers do not form picrates. The m. p. of 5-methyl-3 : 4-benzofluorene was not abnormal, and it did form a picrate. The latter, like others in this series, decomposed rapidly enough to make accurate analysis difficult. Clear evidence of molecular overcrowding in 5-methyl-3 : 4-benzofluorene was provided by its ultraviolet extinction curve. Compared with those of other methyl-3 : 4-benzofluorenes (see Figure) it showed a loss of fine structure and a decrease in the intensity of the three peaks in the 310—340 mμ range. These changes are characteristic of overcrowded

[4] Full curves for a number of compounds described in this paper and in ref. 1 are given by Keene, Ph.D. Thesis, 1957, Exeter University.
[5] Wilds, Beck, Close, Djerassi, Johnson, Johnson, and Shunk, *J. Amer. Chem. Soc.*, 1947, **69**, 1985.
[6] Newman and Wheatley, *ibid.*, 1948, **70**, 1913.

molecules and have been observed in 3 : 4-benzophenanthrenes,[6,7] chrysenes,[8] and 5 : 6-benzophenanthridines.[9]

Unexpected difficulties prevented the extension of these methods to the synthesis of naphtho(2′ : 1′-3 : 4)fluorenes. 3′-Oxo-3 : 4-*cyclo*pentanophenanthrene[10] was conveniently prepared by cyclising β-3-phenanthrylpropionic acid with polyphosphoric acid (hydrogen fluoride produced a mixture of ketones, presumably by causing cyclisation in both possible directions), but we were unable to formylate this ketone. A number of attempts using ethyl formate and sodium methoxide produced only traces of alkali-soluble material, the main product being a purple tar. The ketone was unchanged by treatment



——— 7-*Methyl*-3 : 4-*benzofluorene* (*in* cyclo*hexane*).
The curves for 6- *and* 8-*methyl*-3 : 4-*benzofluorene were very similar.*[4]
– – – – 5-*Methyl*-3 : 4-*benzofluorene* (*in* cyclo*hexane*).

with diethyl carbonate and sodium hydride under a variety of conditions, and with paraformaldehyde and morpholine hydrochloride gave a poor yield of an unidentified substance.

Experimental

4 : 5-*Benzindan*-3-*one*.—β-2-Naphthylpropionic acid (13·1 g.), set aside with hydrogen fluoride (130 g.) until most of the latter had evaporated, gave in the usual way the ketone (10·1 g.), m. p. 102—104° (un-recrystallised) (lit.,[11] m. p. 102—103°).

2-*Morpholinomethyl*-4 : 5-*benzindan*-3-*one*.—From a boiling solution of 4 : 5-benzindan-3-one (8 g.), morpholine hydrochloride (5·36 g.), and paraformaldehyde (1·45 g.) in absolute ethanol (10 c.c.), solid began to separate after 30 min. After 90 min. more of heating, the hydrochloride (13·0 g.), m. p. 203—205° (decomp.), was collected. A vigorously stirred suspension of this compound in water (750 c.c.) and ether (500 c.c.) was basified with 2N-sodium carbonate. When no solid remained the ether layer was separated, dried (Na_2SO_4), and evaporated. 2-*Morpholinomethyl*-4 : 5-*benzindan*-3-*one* (6·54 g.) formed needles, m. p. 127—128° (Found: C, 77·1; H, 6·9. $C_{18}H_{19}O_2N$ requires C, 76·8; H, 6·8%), from ethanol.

Ethyl 6 : 7 : 8 : 13-*Tetrahydro*-6-*oxo*-3 : 4-*benzofluorene*-7-*carboxylate*.—Crude 2-morpholinomethyl-4 : 5-benzindan-3-one (6·54 g.) and methyl iodide (15 ml.) were heated under reflux for 30 min., then set aside, with occasional shaking, for 30 min. more. Excess of methyl iodide was removed in a vacuum-desiccator, and the methiodide (m. p. 137—140°) was treated with a solution of ethyl sodioacetoacetate [from sodium (0·8 g.), ethyl acetoacetate (4·55 g.), and ethanol (25 c.c.)]. The mixture was heated under reflux for 2 hr., and the product (3·94 g.) was collected and washed with much warm water. The *ester* formed straw-coloured needles, m. p. 171—173° (Found: C, 78·3; H, 6·2. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9%), from ethyl acetate.

6 : 7 : 8 : 13-*Tetrahydro*-3 : 4-*benzofluoren*-6-*one*.—(i) The keto-ester (2·63 g.), 2N-hydrochloric acid (120 c.c.), and acetic acid (180 c.c.) were heated under reflux for 6—7 hr. The

[7] Badger and Walker, *J.*, 1954, 3238.
[8] Jones, *J. Amer. Chem. Soc.*, 1941, **63**, 313.
[9] Mills and Schofield, *J.*, 1956, 4213.
[10] Bachmann and Kloetzel, *J. Amer. Chem. Soc.*, 1937, **59**, 2207.
[11] Cook and Hewett, *J.*, 1933, 1098.

solution was diluted with ice-water, and after 12 hr. the substantially pure product (1·32 g.) was collected. Straw-coloured plates of 6 : 7 : 8 : 13-*tetrahydro*-3 : 4-*benzofluoren*-6-*one*, m. p. 117—118° (Found: C, 87·0; H, 6·0. $C_{17}H_{14}O$ requires C, 87·15; H, 6·0%), $\lambda_{max.}$ 237, 251, 266, 321, 338, 352 mμ ($\log_{10}\varepsilon$ 4·44, 4·36, 4·02, 4·19, 4·18, 4·20), separated from a small volume of ethyl acetate. The 2 : 4-*dinitrophenylhydrazone* formed dark-red needles, m. p. 250—260° (decomp.) (Found: C, 66·6; H, 4·3. $C_{23}H_{18}O_4N_4$ requires C, 66·7; H, 4·4%), from benzene.

(ii) 2-3′-Oxobutyl-4 : 5-benzindan-3-one (1·0 g.) (see below), acetic acid (25 c.c.), concentrated hydrochloric acid (15 c.c.), and water (7 c.c.) were heated under reflux, under nitrogen, for 3 hr. A benzene extract of the cooled, diluted solution was washed with sodium carbonate solution and evaporated. The residue was triturated with ethyl acetate–light petroleum (b. p. 60—80°), giving a solid (0·4 g.; m. p. 110—112°). The ketone formed yellow prisms, m. p. 117—118°, from aqueous dioxan, identical with the compound described above.

2-*Formyl*-4 : 5-*benzindan*-3-*one*.—4 : 5-Benzindan-3-one (9·1 g.) in dry benzene (80 c.c.) was added to an ice-cold mixture of ethyl formate (7·4 g.), dry benzene (80 c.c.), and sodium methoxide (prepared from 2·4 g. of sodium and baked at 180—200°/0·5 mm. for 1½ hr.). The mixture was set aside, with occasional shaking, for 1 hr. at room temperature, and then heated under reflux for 1 hr. The benzene extract of the diluted and acidified mixture was washed with water and with dilute aqueous potassium hydroxide. Acidification of the alkaline extract with 10% hydrochloric acid gave the substantially pure product (7·58 g.). 2-*Formyl*-4 : 5-*benzindan*-3-*one* formed clusters of biscuit-coloured needles, m. p. 170—172° (decomp.) (Found: C, 81·3; H, 4·7. $C_{14}H_{10}O_2$ requires C, 80·0; H, 4·8%), from ethyl acetate.

2-3′-*Oxobutyl*-4 : 5-*benzindan*-3-*one*.—4-Piperidinobutan-2-one (7·6 g.) [12] was treated gradually at 0°, with swirling and shaking, with methyl iodide (7·6 g.). After being kept at 0° for 2 hr. the mixture was allowed to reach room temperature and the product was washed by decantation with ether and then freed at reduced pressure from traces of this solvent. The methiodide in methanol (30 c.c.) was added to 2-formyl-4 : 5-benzindan-3-one (3·93 g.) in methanolic sodium methoxide [from sodium (0·43 g.) and methanol (30 c.c.)]. After 36 hr. the yellow solution was diluted with water and extracted with benzene. The brown oil (3·34 g.) from the dried (Na_2SO_4) extract crystallised when scratched. 2-3′-*Oxobutyl*-4 : 5-*benzindan*-3-*one* formed platelets, m. p. 64—65° (Found: C, 81·0; H, 6·3. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%), from aqueous methanol.

3 : 4-*Benzofluorene*.—6 : 7 : 8 : 13-Tetrahydro-3 : 4-benzofluoren-6-one (0·5 g.), aluminium *iso*propoxide (1 g.), and absolute propan-2-ol (15 c.c.) were heated under reflux in such a way that the acetone produced distilled from the mixture. When acetone was no longer formed the propanol was removed and the residue was decomposed with ice-cold dilute hydrochloric acid. The yellow-brown gum (0·46 g.) obtained by benzene extraction did not crystallise. It was heated with 30% palladised charcoal (0·1 g.) at 240° in nitrogen for 1½ hr. Sublimation (120°/0·05 mm.) of the gum extracted by ether from the cooled reaction mixture gave 3 : 4-benzofluorene (0·13 g.), which formed flakes, m. p. 125—126°, from ethanol (lit.,[13] m. p. 124—125°).

2-3′-*Oxopentyl*-4 : 5-*benzindan*-3-*one*.—1-Diethylaminopentan-3-one methiodide [prepared from 1-diethylaminopentan-3-one (1·45 g.) [14] in the way described for the lower homologue] in methanol (10 c.c.) was added to 2-formyl-4 : 5-benzindan-3-one (1·05 g.) in methanolic sodium methoxide [from sodium (0·12 g.) and methanol (10 c.c.)]. After 24 hr. the solution was processed as before, giving 2-3′-*oxopentyl*-4 : 5-*benzindan*-3-*one* (0·99 g.) which formed needles, m. p. 54—55° (Found: C, 81·6; H, 7·4. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·8%), from aqueous methanol.

6 : 7 : 8 : 13-*Tetrahydro*-5-*methyl*-3 : 4-*benzofluoren*-6-*one*.—The above diketone (0·9 g.), acetic acid (37·5 c.c.), concentrated hydrochloric acid (22·5 c.c.), and water (12 c.c.) were heated under reflux, under nitrogen, for 3 hr. Dilution and extraction with benzene recovered a brown oil which when triturated with methanol gave the product (0·41 g.). The *ketone* formed pale yellow tablets, m. p. 147—148° (Found: C, 86·2; H, 6·1. $C_{18}H_{16}O$ requires C, 87·1; H, 6·5%), $\lambda_{max.}$ 240, 269, 321, 337, 350 mμ ($\log_{10}\varepsilon$ 4·43, 3·97, 4·13, 4·12, 4·14), from methanol.

5-*Methyl*-3 : 4-*benzofluorene*.—The ketone (0·2 g.) was reduced with aluminium *iso*propoxide (1 g.) in propan-2-ol as described above. Similar processing gave a viscous yellow oil which

[12] Wilds and Werth, *J. Org. Chem.*, 1952, **17**, 1149.
[13] Cook, Dansi, Hewett, Iball, Mayneord, and Roe, *J.*, 1935, 1319.
[14] Adamson, McQuillin, Robinson, and Simonsen, *J.*, 1937, 1576.

was heated under nitrogen with 30% palladised charcoal, initially at 190°, rising to 240° in 30 min., and being maintained there for 15 min. Sublimation of the ether-soluble product (0·05 g.), and crystallisation from aqueous ethanol gave fibrous needles of 5-*methyl*-3 : 4-*benzofluorene*, m. p. 85—86° (Found: C, 93·3; H, 6·3. $C_{18}H_{14}$ requires C, 93·9; H, 6·1%).

The picrate formed red needles, m. p. 130—131° (Found: C, 64·3; H, 4·1. Calc. for $C_{18}H_{14},C_6H_3O_7N_3$: C, 62·7; H, 3·7%), from ethanol. Satisfactory analyses could not be obtained because of the fairly rapid decomposition of the compound.

β-3-*Phenanthrylpropionic Acid*.—β-3-Phenanthrylacrylic acid [10] (5 g.), 10% palladised strontium carbonate (0·5 g.), and dioxan (500 c.c.) were shaken with hydrogen until uptake ceased. Filtration, removal of the solvent, and trituration of the residue with benzene gave the acid (3·3 g.), m. p. 155—156° (lit.,[10] m. p. 158·5—159·5°).

3′-*Oxo*-3 : 4-cyclo*pentenophenanthrene*.—The above acid (0·5 g.) and polyphosphoric acid (20 g.) were stirred vigorously at 95—100° until a deep red solution was formed (*ca.* 1¾ hr.). This was poured on ice, and the product was extracted with benzene. The ketone (0·37 g.) formed pale yellow needles, m. p. 139—141°, from aqueous acetic acid (lit.,[10] m. p. 142°).

The *oxime* gave yellow prisms, m. p. 222—223° (decomp.) (Found: C, 81·9; H, 4·9. $C_{17}H_{13}ON$ requires C, 82·6; H, 5·3%), from acetone–ethanol.

When the ketone (0·23 g.), morpholine hydrochloride (0·12 g.) and paraformaldehyde (0·03 g.) were boiled together in absolute ethanol (15 c.c.) for 3 hr. no solid separated. Removal of the solvent and trituration of the residue with ethanol gave a solid (0·19 g.), m. p. 164—165° (Found: C, 68·7; H, 6·15; N, 3·5%) after crystallisation from chloroform. It appeared to contain ionic chlorine.

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