[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY, RADIUM INSTITUTE, UNIVERSITY OF PARIS]

POTENTIAL NITROGEN-HETEROCYCLE CARCINOGENS. IV. SYNTHESIS OF 2,3-BENZOCARBAZOLES AND OF INDENOINDOLES[1]

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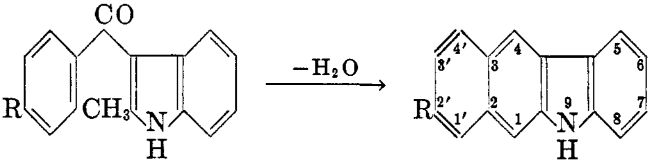
Although the Elbs reaction has been extensively used for syntheses of polycyclic hydrocarbons (1), it has hitherto rarely been applied to heterocyclic ketones with nitrogen-containing rings. To our knowledge, the only work dealing with this subject is that of Fieser and Hershberg (2), who prepared 20-methyl-4-azacholanthrene and 4′-aza-1,2-benzanthracene through pyrolysis of the suitable quinoline ketones.

We have now found that the Elbs reaction can also be performed on certain *o*-methyl ketones belonging to the indole series. Thus, 2-methyl-3-benzoylindole (I) was found to lose water rapidly on refluxing, and yielded small amounts of 2,3-benzocarbazole (II). The latter is an important component of crude anthracene from coal-tar, and had previously been synthesized in various ways: (a) by thermal dehydrogenation of phenyl-β-naphthylamine in a red-hot tube (3); (b) as a by-product in the Graebe-Ullmann synthesis of 1,2-benzocarbazole from "phenylaziminonaphthalene" (4); and (c) by the Bucherer reaction (5), starting from 2-aminonaphthalene-1-sulfonic acid and phenylhydrazine.



I; R = H
III; R = CH_3

II; R = H
IV; R = CH_3

Although the yield of 2,3-benzocarbazole obtained in our synthesis was definitely inferior to those recorded for the above methods (owing to the instability of indole ketones towards heat), it nevertheless provides a very quick procedure for the preparation of small quantities of compound II.

The Elbs reaction was extended to the preparation of certain homologs of 2,3-benzocarbazole which would not be readily accessible through other methods. Thus, 2-methyl-3-*p*-toluoylindole (III) could be cyclized, although in very poor yield, to 2′-methyl-2,3-benzocarbazole (IV), the methyl group being retained in the course of pyrolysis. It may be noted that the m.p. of 2′-methyl-2,3-benzocarbazole is somewhat higher than that of 2,3-benzocarbazole, a fact which is parallel to a similar difference between 2-methylcarbazole and carbazole itself.

Ketones (I) and (III) were prepared from the organomagnesium derivative

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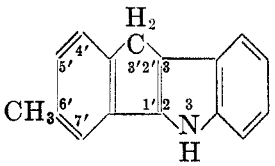
[1] For Part III, see Buu-Hoï and Royer, *J. Org. Chem.*, preceding article.

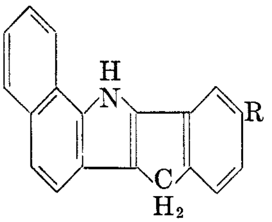
of 2-methylindole and the requisite acid chlorides in ether medium (6). 2-Methyl-3-*p*-ethylbenzoylindole, 2-methyl-3-α-naphthoylindole, 2-methyl-3-β-naphthoylindole, and 2-methyl-3-anisoylindole were also prepared in a similar way, but no pure carbazoles have yet been separated from their pyrolysis products.

A substance whose molecular form closely resembles that of 2′-methyl-2,3-benzocarbazole is 6′-methyl-1′,2′:2,3-indenoindole (V), which we prepared by indolization of 5-methylindan-1-one phenylhydrazone; compound (V) is a homolog of indeno-1′2′:2,3-indole, already synthesized by Hausmann (7). From indan-1-one and 5-methylindan-1-one on the one hand, and α- and β-naphthylhydrazine on the other, the following substances were similarly prepared:

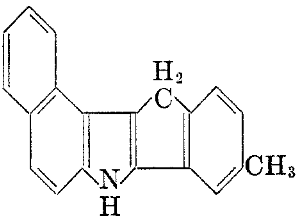


(V)

1′,2′:2,3-indeno(6,7-benzoindole) (VI);
6′-methyl-1′,2′:2,3-indeno(6,7-benzoindole) (VII);
1′,2′:2,3-indeno(4,5-benzoindole) (VIII); and
6′-methyl-1′,2′:2,3-indeno(4,5-benzoindole) (IX).



VI; R = H
VII; R = CH_3



VIII; R = H
IX; R = CH_3

This group of compounds has some biological significance by virtue of its structural connection with the carcinogenic dibenzocarbazoles.

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EXPERIMENTAL

2,3-Benzocarbazole (II). 2-Methyl-3-benzoylindole was prepared as follows: to a solution of ethylmagnesium bromide (made from 2.4 g. of magnesium and 13 g. of ethyl bromide) in anhydrous ether (100 ml.), 13.1 g. of 2-methylindole (dissolved in ether) was added in small portions with frequent shaking. The mixture was then refluxed for thirty minutes, cooled in ice-water, and 14.1 g. of benzoyl chloride (dissolved in ether) was added dropwise. After one hour's refluxing, it was treated with a cold aqueous solution of ammonium chloride and the ether removed by evaporation. The solid precipitate was washed thoroughly with an aqueous solution of sodium carbonate, then with water, dried, and crystallized from methanol; yield, 12 g. of ketone (I), m.p. 181°.

When 10 g. of this compound was gently boiled at normal pressure for ten minutes in a Claisen flask with a Vigreux column evolution of water and extensive carbonization was soon observed. The volatile fractions were then distilled, and the distillate treated with a large volume of methanol, which dissolved the recovered ketone and left a residue which was recrystallized from benzene. 2,3-Benzocarbazole was thus obtained in the form of grey-tinged prisms m.p. 330–331°, giving a yellow coloration with sulfuric acid (the literature indicates m.p. 330°, for this compound). The yield was 0.5 g. (*circa* 5%), barely increased by addition of zinc powder.

2-Methyl-3-p-toluoylindole (III). Obtained as above from *p*-toluoyl chloride (15.5 g.), 2-methylindole (13 g.), and ethylmagnesium bromide; from methanol it formed rose-tinged needles m.p. 210° (sublimation above 180°), giving a violet picrate; yield: 15 g.

Anal. Calc'd for $C_{17}H_{16}NO$: N, 5.6. Found: N, 5.4.

2'-Methyl-2,3-benzocarbazole (IV). Pyrolysis of the foregoing ketone (10 g.), performed as above, gave 2'-methyl-2,3-benzocarbazole in the form of almost colorless needles m.p. 343°, giving a yellow coloration with sulfuric acid (yield, 0.6 g.).

Anal. Calc'd for $C_{17}H_{14}N$: N, 6.0. Found: N, 5.8.

2-Methyl-3-p-ethylbenzoylindole. Obtained from *p*-ethylbenzoyl chloride (11.6 g.), 2-methylindole (10 g.), and ethylmagnesium bromide in the usual way. Yield, 8 g. of a ketone crystallizing from methanol in rose-tinged needles, m.p. 204°.

Anal. Calc'd for $C_{18}H_{18}NO$: N, 5.3. Found: N, 5.2.

2-Methyl-3-α-naphthoylindole. Obtained from α-naphthoyl chloride (19.3 g.), 2-methylindole (13.1 g.), and ethylmagnesium bromide in the form of colorless prisms (from methanol), m.p. 209°, giving with sulfuric acid an orange coloration (yield, 20 g.).

Anal. Calc'd for $C_{20}H_{15}NO$: N, 4.9. Found: N, 4.6.

2-Methyl-3-β-naphthoylindole. From 19.3 g. of β-naphthoyl chloride and 13.1 g. of 2-methylindole, there was obtained 14 g. of a ketone crystallizing from methanol in colorless needles, sparingly soluble in ether, m.p. 225°, giving an orange coloration with sulfuric acid.

Anal. Calc'd for $C_{20}H_{15}NO$: N, 4.9. Found: N, 4.9.

2-Methyl-3-anisoylindole. From 1.7 g. of anisoyl chloride and 1.3 g. of 2-methylindole, there was obtained 0.8 g. of a ketone crystallizing from benzene in colorless needles, soluble in ether, m.p. 206°.

Anal. Calc'd for $C_{17}H_{16}NO_2$: N, 5.2. Found: N, 5.0.

The above four ketones underwent extensive carbonization and loss of water on boiling.

6'-Methyl-1',2':2,3-indenoindole (V). 5-Methylindan-1-one (2 g.) and 2 g. of phenylhydrazine were heated at 120–130° until steam ceased to evolve; 20 ml. of acetic acid saturated with hydrogen chloride was added, the mixture was brought to the boil, and then poured into water. The solid precipitate was collected, washed, and recrystallized from ethanol, giving colorless needles, m.p. 206–207° (yield, 2 g.).

Anal. Calc'd for $C_{16}H_{13}N$: N, 6.4. Found: N, 6.3.

1',2':2,3-Indeno(6,7-benzoindole) (VI). A mixture of 1.5 g. of indan-1-one 3 g. of α-naphthylhydrazine hydrochloride, 2.5 g. of sodium acetate, and 50 ml. of ethanol was refluxed two hours, then poured into water; the precipitate was filtered off and treated with acetic acid saturated with hydrogen chloride as above. The indole (1.5 g.) crystallized from benzene in colorless prisms, m.p. 234°.

Anal. Calc'd for $C_{19}H_{13}N$: N, 6.1. Found: N, 6.0.

6'-Methyl-1',2':2,3-indeno(6,7-benzoindole) (VII). Similarly obtained from 5-methylindan-1-one (1.5 g.) and α-naphthylhydrazine hydrochloride (2.9 g.); crystallized from benzene in almost colorless needles, m.p. 223–224° (yield, 1.2 g.).

Anal. Calc'd for $C_{20}H_{15}N$: N, 5.2. Found: N, 5.3.

1',2':2,3-Indeno(4,5-benzoindole) (VIII). This compound (1.2 g.), obtained from 1.5 g. of indan-1-one and 3 g. of β-naphthylhydrazine hydrochloride, formed colorless needles, m.p. 157–158° from benzene.

Anal. Calc'd for $C_{19}H_{13}N$: N, 6.1. Found: N, 5.8.

6'-Methyl-1',2':2,3-indeno(4,5-benzoindole) (IX). From 1.5 g. of 5-methylindan-1-one and 2.9 g. of β-naphthylhydrazine hydrochloride there was obtained 1.2 g. of a substance forming yellowish needles, m.p. 230° from benzene.

Anal. Calc'd for $C_{20}H_{15}N$: N, 5.2. Found: N, 5.1.

SUMMARY

1. Certain ketones belonging to the indole series are shown to be susceptible to the Elbs reaction. 2,3-Benzocarbazole and one of its methyl homologs have been obtained, although in poor yields, by that means.

2. Some new indenoindoles structurally related to 2,3-benzocarbazole have been prepared.

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