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

A NEW SYNTHESIS OF 2-ANTHROL

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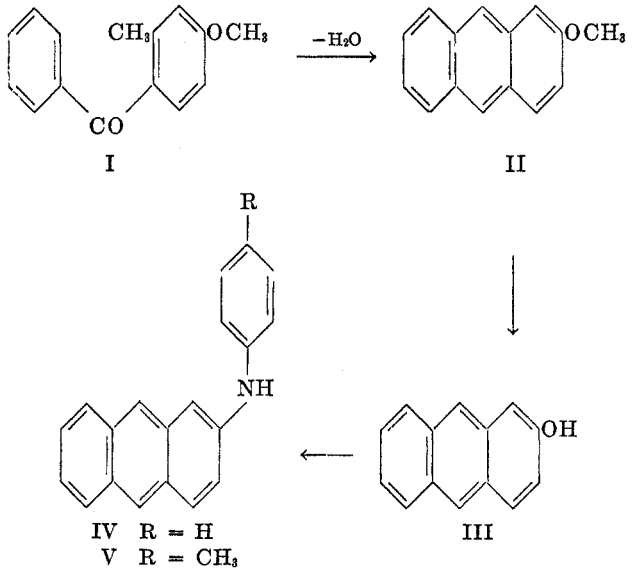
In the course of a research upon the synthesis of condensed nitrogen heterocyclic compounds bearing an anthracene nucleus, and which are of biological interest as potential carcinogens, 2-anthrol was required in quantity. The methods of preparation of this intermediate were therefore investigated.

2-Anthrol had been prepared: (a) by alkaline fusion of anthracene-2-sulfonic acid (1); (b) by reduction of 2-hydroxyanthraquinone with aluminum and ammonia (2) or with phosphorus and hydriodic acid (3); and (c) by the Bucherer reaction on 2-aminoanthracene (4). The first method involves a tedious separation of anthracene-2-sulfonic acid from the isomeric anthracene-1-sulfonic acid, and the other two make use of relatively rare intermediates.

It has now been found that 4-methoxy-2-methylbenzophenone (I) readily undergoes the Elbs reaction (5) to give 2-methoxyanthracene (II) in reasonable yield, demethylation of which with pyridine hydrochloride leads to 2-anthrol (III). This latter compound was further characterized by its acetate, and its ethyl ether which can also be prepared by an Elbs reaction with 4-ethoxy-2-methylbenzophenone.

It is known that Elbs reactions generally lead to poor yields in the synthesis of anthracene derivatives, and cannot be considered as a preparative method in such cases. The present preparation of 2-anthrol, which affords a 13% over-all



I II

IV R = H
V R = CH_3

III

yield of the compound, is a happy exception to this rule; the ready accessibility of 4-methoxy-2-methylbenzophenone from *m*-cresol (6) offers a further advantage.

2-Anthrol easily underwent Knoevenagel reactions with aniline and *p*-toluidine in the presence of iodine (7) to give 2-anilino- (IV) and 2-*p*-toluidino-anthracene (V); the former compound had previously been obtained by Scholl, Semp, and Stix (8) by the dry zinc distillation of 2-anilinoanthraquinone and 3,4-phthalylacridone. These diarylamines are important intermediates for nitrogen-heterocycle syntheses.

EXPERIMENTAL (with P. Mabille)

Preparation of intermediates. 4-Methoxy-2-methylbenzophenone was prepared by the methylation of 4-hydroxy-2-methylbenzophenone, m.p. 129°, with dimethyl sulfate and aqueous sodium hydroxide. It gave on Clemmensen reduction a 70% yield of pure *4-methoxy-2-methyldiphenylmethane* as a colorless oil, b.p. 188–189°/15 mm., n_D^{21} 1.5752.

Anal. Calc'd for $C_{15}H_{16}O$: C, 84.9; H, 7.5.
Found: C, 84.8; H, 7.6.

Demethylation of 4-methoxy-2-methyldiphenylmethane with boiling pyridine hydrochloride gave a quantitative yield of pure *4-hydroxy-2-methyldiphenylmethane*, b.p. 212–215°/14 mm., m.p. 94°.

Elbs reaction with 4-methoxy-2-methylbenzophenone. Ketone I (20 g.) was refluxed at 400–420° on a metal bath for 72 hours, with periodic removal of the water formed. The dark reaction product was vacuum-fractionated, giving 2 g. of recovered 4-methoxy-2-methylbenzophenone, b.p. 220–225°/19 mm., and 4 g. of a viscous oil, b.p. 230–235°/1 mm., which solidified on standing with ethanol. After two recrystallizations from this solvent, *2-methoxyanthracene* was obtained as yellowish needles, m.p. 178.5°; lit. (9) m.p. 175–178°.

Anal. Calc'd for $C_{15}H_{12}O$: C, 86.5; H, 5.8.
Found: C, 86.2; H, 6.0.

When the duration of pyrolysis was shortened to 24 hours, no methoxyanthracene was obtained, and 16 g. of the starting ketone was recovered; 48 hours' pyrolysis yielded 0.8 g. of 2-methoxyanthracene and 13 g. of recovered ketone.

Preparation of 2-anthrol. A mixture of one part of 2-methoxyanthracene and 3 parts of redistilled pyridine hydrochloride was gently refluxed for 30 minutes; on addition of water, a brown solid was obtained, which was purified by dissolution in a dilute aqueous solution of sodium hydroxide followed by precipitation by the addition of acetic acid. After recrystallization from xylene, 2-anthrol was obtained in 65% yield as pale yellow prisms, m.p. 255°. von Braun and Bayer (10) gave the same m.p. for pure 2-anthrol. Treatment with acetic anhydride gave *2-acetoxyanthracene*, which crystallized from xylene in yellowish needles, m.p. 197–198°. Lit. (1), m.p. 198°.

Ethylation with diethyl sulfate and aqueous sodium hydroxide afforded *2-ethoxyanthracene*, crystallizing from ethanol in yellowish prisms, m.p. 147°; lit. (9) m.p. 145–146°. This compound, b.p. 235–240°/1 mm., was also prepared in 15% yield by refluxing 4-ethoxy-2-methylbenzophenone for 72 hours as for the lower homolog. 2-Anthrol yielded with 2,3-dichloro-1,4-naphthoquinone a brown condensation product (11) which gave a greenish coloration with sulfuric acid.

2-Anilinoanthracene. A mixture of 5 g. of 2-anthrol and 10 g. of aniline was gently refluxed for 12 hours with 0.1 g. of iodine, and was poured into dilute aqueous hydrochloric acid; the solid obtained crystallized from ethanol in yellowish needles, m.p. 200°; lit. (8), m.p. 197–198°. Yield: 3 g. This substance could be distilled in a high vacuum without decomposition, and yielded on heating with arsenic trichloride in *o*-dichlorobenzene solution a crystalline precipitate of a yellow *chlorodihydrophenarsazine derivative* (12).

2-p-Toluidinoanthracene. A mixture of 5 g. of 2-anthrol and 10 g. of *p*-toluidine was treated as above; the resulting diarylamine crystallized from ethanol in yellowish prisms, m.p. 208°.

Anal. Calc'd for $C_{21}H_{17}N$: C, 89.0; H, 6.0.
Found: C, 89.3; H, 6.0.

This compound also gave a yellow chlorodihydrophenarsazine with arsenic trichloride.

SUMMARY

A new method of preparation of 2-anthrol, based on an Elbs reaction, is described, and the synthesis of several of its derivatives is reported.

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