(0.03 mole) of 4-methyl-5-phenyloxazolidine (from *l*-norpseudoephedrine), 3.02 g. (0.0306 mole) of succinimide, 5.0 g. (0.06 mole) of 36% aqueous formaldehyde, and 35 ml. of absolute ethanol. Crystallization from absolute ethanol gave the product as a white crystalline solid, m.p. 74–77.5° and α_D −57.6°.

Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.22. Found: C, 65.99; H, 6.56; N, 10.18.

Acknowledgment. The help of the following persons who contributed materially to this research is acknowledged: Dr. Robert T. Dillon and his associates for analyses and determination of physical properties; Mr. William Selby and his associates for the running of all catalytic reductions and pressure reactions; Drs. C. G. Van Armen and C. Kagawa and their associates for diuretic assays; Dr. R. E. Ranney and his associates for the appetite inhibition assays; Drs. F. Saunders and L. Herschberger and their associates for the anti-inflammatory assays. I would also like to acknowledge the assistance of Varian Associates, Palo Alto, California, for the NMR spectra and analysis of the data.

CHICAGO 80, ILL.

[CONTRIBUTION FROM THE RADIUM INSTITUTE, UNIVERSITY OF PARIS]

Some Reactions of 5H-Benzo[b]carbazole

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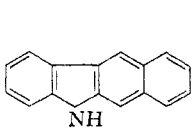
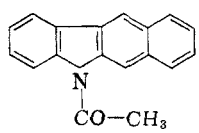
Chrysene obtained from commercial sources, even purified by recrystallization, has been found to contain from 10 to 12% 5H-benzo[b]carbazole. This heterocycle, especially in dilution with chrysene, readily undergoes Friedel-Crafts diacylations with aliphatic and aromatic acid chlorides.

In the course of an investigation on potential antileukemic agents derived from chrysene,[1] large quantities of chrysene were submitted to various chemical reactions, especially Friedel-Crafts acylations. The product used was commercial chrysene purified by recrystallization from toluene and treated with maleic anhydride to remove naphthacene, and was thus obtained as a colorless material having the melting point indicated in the literature. Friedel-Crafts acetylation of this substance yielded, as reported earlier,[1a] 6-acetylchrysene. It is now shown that it is possible to isolate in sizable amounts, from the mother liquors of this ketone, a new compound containing nitrogen, whose composition corresponds to the formula $C_{20}H_{15}NO_2$; it was therefore suspected to arise from a nitrogen-containing impurity that must have been present in appreciable quantities in the starting chrysene. Such an impurity could be one of the benzocarbazoles known to exist in coal tar,[2] for instance, 5H-benzo[b]carbazole (I). Should this be so, the compound $C_{20}H_{15}NO_2$ would be a product of Friedel-Crafts diacetylation of I. Indeed, the same compound was obtained, although in very low yield, along with the known 5-acetyl-5H-benzo[b]carbazole (II), when 5H-benzo[b]carbazole was submitted to acylation under similar conditions. That the compound $C_{20}H_{15}NO_2$ was a diketone, *i.e.*, that the —NH— group was not acetylated, was proven by its ready conversion into a diethyl-5H-benzo[b]-carbazole by means of a Wolff-Kishner reaction. The ultraviolet spectrum of this reduction product closely resembles that of 5H-benzo[b]carbazole itself (see Fig. 1).



I



II

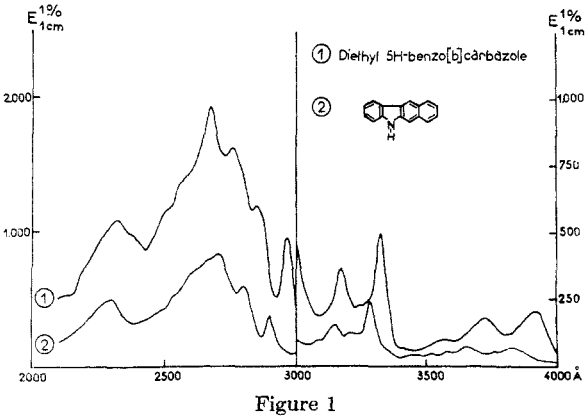


Figure 1

As so little is known of the chemistry of 5H-benzo[b]carbazole, the sites occupied by the substituents in the molecule of its diacetyl compound could not be established, but in view of the rules governing substitution in carbazole itself,[3] one of

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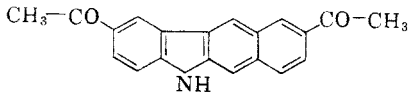
(1) (a) P. Mabille and N. P. Buu-Hoï, *J. Org. Chem.*, **25**, 216 (1960). (b) P. Mabille and N. P. Buu-Hoï, *J. Org. Chem.*, **25**, 1092 (1960). (c) P. Mabille and N. P. Buu-Hoï, *J. Org. Chem.*, **25**, 1094 (1960).

(2) S. Kikkawa, *J. Chem. Soc. Japan (Ind. Chem. Section)*, **54**, 631 (1951).

(3) For a review of this subject, see N. P. Buu-Hoï and R. Royer, *Rec. trav. chim.*, **66**, 533 (1947).

the acetyl groups could perhaps be assumed to occupy position 2; the other substituent might be placed either in position 6 or in position 9 (as, for instance, in Formula III). It is interesting to note



III

that the yield of the diacetyl compound was considerably higher when the reaction was performed with 5H-benzo[b]carbazole diluted in chrysene (shown by nitrogen determinations to contain 10 to 12% of I) than when the heterocycle was used in the pure state.

In the benzoylation of chrysene which, as is shown, was heavily polluted with I, an x,y-dibenzoyl-5H-benzo[b]carbazole could be isolated from the mother liquors of crystallization of 6-benzoylchrysene.[1b] This diketone underwent Wolff-Kishner reduction to x,y-dibenzyl-5H-benzo[b]carbazole. Similarly, an x,y-di-(*o*-toluoyl)-5H-benzo[b]-carbazole and an x,y-di(2,4-dimethylbenzoyl)-5H-benzo[b]carbazole could be isolated from the mother liquors of crystallization of 6-(*o*-toluoyl)- and 6-(2,4-dimethylbenzoyl)-chrysene, respectively. The first of these two could be reduced to x,y-di(*o*-methylbenzyl)-5H-benzo[b]carbazole.

Chrysene could be freed of 5H-benzo[b]carbazole by treatment with acetic anhydride in the presence of zinc chloride, which converted the impurity into its *N*-acetyl derivative (II), a compound more soluble in acetic acid than chrysene.

EXPERIMENTAL

The chrysene used in this work was prepared by purification of commercial chrysene, m.p. 252°, by refluxing its toluene solution with maleic anhydride, removal of the adduct of maleic anhydride and naphthacene by alkaline treatment, and crystallization from toluene. The chrysene thus purified melted at 256–258° and was practically colorless, but its solutions in sulfuric acid showed a slight yellow halochromism. Its nitrogen content was 0.77%, which corresponds to *circa* 12% of 5H-benzo[b]carbazole.

x,y-Diacetyl-5H-benzo[b]carbazole. The acetylation of 100 g. of the above chrysene with acetyl chloride, performed in methylene chloride as already reported,[1a] afforded 92 g. of 6-acetylchrysene after recrystallization from acetone. Concentration of the mother liquors of this operation furnished 9 g. of a yellow, crystalline precipitate, m.p. 185–188°, which on recrystallization from 300 ml. of acetone afforded 6 g. of short, golden yellow needles, m.p. 189°. This compound gave an orange-yellow halochromism in sulfuric acid; its solutions in sulfuric acid with traces of nitric acid gave a green coloration characteristic of carbazole derivatives.

Anal. Calcd. for $C_{20}H_{15}NO_2$: C, 79.7; H, 5.0; N, 4.7; O, 10.6. Found: C, 79.9; H, 5.1; N, 4.8; O, 10.8.

Acetylation of pure 5H-benzo[b]carbazole. To a stirred solution of 4 g. of aluminum chloride in 100 ml. of anhydrous methylene chloride containing 5 ml. of acetyl chloride, a suspension of 5 g. of 5H-benzo[b]carbazole in 70 ml. of methylene chloride was added portionwise. The brown mixture was left to stand at room temperature for 3 hr., then refluxed for 3 hr., and finally left again to stand for 12 hr. at room temperature. After decomposition with ice and hydrochloric acid, methylene chloride was added and the organic layer washed with 5% aqueous sodium hydroxide, then with water, and dried over sodium sulfate. The resinous brown mass remaining after evaporation of the solvent was taken up in ethanol (charcoal), and after standing for several days in the refrigerator, it formed a pale yellow, crystalline precipitate, m.p. 100–110°. Fractional crystallization of this from acetone furnished 0.5 g. of x,y-diacetyl-5H-benzo[b]carbazole, m.p. 189–190°, showing no depression of melting point when mixed with a sample prepared as above. Evaporation of the mother liquors left a residue which was extracted with hexane; concentration of the hexane solution afforded 0.5 g. of *5-acetyl-5H-benzo[b]carbazole* (II), which crystallized from ethanol in two forms, either colorless leaflets, m.p. 117–118°, or colorless needles, m.p. 120°. The literature,[4] gives m.p. 117° and 121°, respectively.

x,y-Diethyl-5H-benzo[b]carbazole. A mixture of 1.4 g. of the diketone, 2 g. of 98% hydrazine hydrate, and 30 ml. of diethylene glycol was refluxed for 9 hr. with 1.5 g. of potassium hydroxide. After cooling, dilute hydrochloric acid was added, and the precipitate was collected. Crystallization first from hexane, then from ethanol, yielded 0.7 g. of almost colorless needles, m.p. 129°. Sulfuric acid produced a brownish halochromism.

Anal. Calcd. for $C_{20}H_{19}N$: C, 87.9; H, 7.0. Found: C, 87.9; H, 7.3.

x,y-Dibenzoyl-5H-benzo[b]carbazole. Benzoylation of chrysene was effected in the usual way,[1b] and the mother liquors from the preparation of 6-benzoylchrysene were evaporated, leaving 5 g. of a solid residue. This was treated with hot carbon tetrachloride, leaving 1 g. of undissolved material, which on recrystallization from acetic acid afforded silky yellow needles, m.p. 232°, giving a blood-red halochromism in sulfuric acid.

Anal. Calcd. for $C_{30}H_{19}NO_2$: C, 84.7; H, 4.5; N, 3.3; O, 7.5. Found: C, 84.7; H, 4.8; N, 3.5; O, 7.2.

x,y-Dibenzyl-5H-benzo[b]carbazole. One gram of the foregoing diketone was reduced with 1.5 g. of hydrazine hydrate and 1 g. of potassium hydroxide in 25 ml. of diethylene glycol as above. The reaction product crystallized from a mixture of benzene and ethanol in fine colorless prisms (0.5 g.), m.p. 191–192°. Its solutions in sulfuric acid were brownish.

Anal. Calcd. for $C_{30}H_{23}N$: C, 90.7; H, 5.8; N, 3.5. Found: C, 90.4; H, 5.7; N, 3.8.

x,y-Di-(o-toluoyl)-5H-benzo[b]carbazole. This compound was obtained as a by-product in the preparation of 6-(*o*-toluoyl)chrysene,[1c] from which it could easily be separated because of its greater solubility in carbon tetrachloride. Recrystallization from acetic acid afforded golden-yellow needles, m.p. 249°, giving an orange-red halochromism in sulfuric acid; yield, 1.5 g. (from 22.8 g. of chrysene).

Anal. Calcd. for $C_{32}H_{23}NO_2$: C, 84.7; H, 5.1; O, 7.1. Found: C, 85.0; H, 5.3; O, 7.3.

x,y-Di-(o-methylbenzyl)-5H-benzo[b]carbazole was obtained by reduction of 1 g. of the foregoing ketone with 1.5 g. of hydrazine hydrate and 1 g. of potassium hydroxide in 35 ml. of diethylene glycol; the reaction was considerably slower than in the previous cases, and the mixture had to be refluxed for 12 hr. The product crystallized from acetic acid in almost colorless needles (0.7 g.), m.p. 236°.

Anal. Calcd. for $C_{32}H_{29}N$: C, 89.9; H, 6.8; N, 3.3. Found: C, 90.0; H, 6.4; N, 3.3.

x,y-Di-(2,4-dimethylbenzoyl)-5H-benzo[b]carbazole. Obtained from the mother liquors of crystallization of 6-(2,4-dimethylbenzoyl)chrysene,[1c] this diketone crystallized from acetic acid or acetone in shiny yellow needles, m.p. 222°, giving an orange halochromism in sulfuric acid; yield, 0.2 g. (from 22.8 g. of chrysene).

Anal. Calcd. for $C_{34}H_{27}NO_2$: C, 84.8; H, 5.7; O, 6.6. Found: C, 84.8; H, 5.7; O, 6.7.

(4) F. Kehrmann, A. Oulévay, and F. Régis, *Ber.*, **46**, 3713 (1913).

Separation of 5H-benzo[b]carbazole from chrysene. A mixture of 50 g. of commercial chrysene purified as described above, 500 ml. of acetic anhydride, 2 g. of finely powdered anhydrous zinc chloride, and 2500 ml. of acetic acid was gently refluxed for 1 hr. After cooling, the precipitate of pure chrysene (42 g.) was filtered, washed with acetic acid, and recrystallized from toluene. A sample of this hydrocarbon gave no coloration in sulfuric acid. Dilution of the filtrate with water to a volume of 6000 ml. produced a precipitation of 4 g. of less pure chrysene. Dilution of the second filtrate to a volume of 10 l. yielded 4 g. of 5-acetyl-5H-benzo[b]carbazole, from which the nonacetylated heterocycle could be recovered by treatment with potassium hydroxide in ethanol. 5H-benzo[b]carbazole gave a brown-yellow halochromism in sulfuric acid.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF IRWIN, NEISLER & CO.]

Pyridylethylation of Skatole, Benzotriazole, and Benzimidazole

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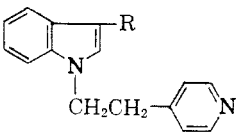
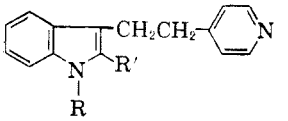
Skatole, 2-methylindole, benzimidazole, and benzotriazole have been pyridylethylated. Under alkaline conditions skatole yielded the 1-substituted derivative, 4-(3-methyl-1-indolylethyl)pyridine. The same product was obtained, in poor yield, when the reaction was carried out in boiling glacial acetic acid. Base catalyzed pyridylethylations of benzotriazole afforded mixtures of two, separable products. Ultraviolet spectral evidence indicates these to be the corresponding 1- and 2-substituted benzotriazole derivatives.

An earlier report[1] from these laboratories was concerned with the pyridylethylation of indole, *N* substitued indoles, and indene. The finding that certain of the derived indolylethylpyridines displayed an interestingly selective spectrum of central depressant effects[2] has stimulated further work in this area. The present paper deals with some aspects of this work, and in particular examines the course of the pyridylethylation reaction with related ring systems.

It is well known that indoles undergo substitution by electrophilic reagents preferentially at the 3-position—no doubt owing to the necessary participation of quinoid forms in the α-substitution process—but the orientation of further substituents is not so clear. Thus, apparently rate control in the Mannich reaction under either acidic or basic conditions results in the order of substitution, 3, *N*, 2[3]—except when stability of the product (as in the intramolecular Mannich-type cyclizations of tryptamines to tetrahydro-β-carbolines) overridingly directs reaction to the 2-position. On the other hand, presumably equilibrium control in Erlich-like reactions with aldehydes under more strongly acid conditions causes substitution to occur at the 3- and then the 2-position, the nitrogen being apparently unaffected.[4] Perhaps more pertinent is the report that skatole reacted with methyl vinyl ketone in a mixture of acetic acid and acetic anhydride to give (in poor yield) the more stable 2-substituted adduct.[5] It was, therefore, of interest to examine the pyridylethylation of skatole. Under alkaline conditions (sodium ethoxide in ethanol) skatole reacted with 4-vinylpyridine to yield 4-(3-methyl-1-indolylethyl)pyridine (I). The structural assignment is unequivocal in view of the reaction of indole under the same conditions to give I(R=H)[1] and of analogous experience with base catalyzed cyanoethylation (see references cited[1]). It would appear that the indole anion is involved in the rate determining step of these base catalyzed reactions. More interesting was the finding that the acid, boiling glacial acetic acid, catalyzed reaction of skatole with 4-vinylpyridine also afforded I, although in poor yield and accompanied by large



I. R = CH_3



II. R = H, R′ = CH_3
III. R = C_2H_5, R′ = H

(1) A. P. Gray and W. L. Archer, *J. Am. Chem. Soc.*, **79**, 3554 (1957).

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