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

# POTENTIAL NITROGEN-HETEROCYCLE CARCINOGENS. VIII. POLYCYCLIC CARBAZOLES WITH PHENOLIC GROUPS<sup>1</sup>

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Hydroxylation has been found to be a biochemical process involved in the metabolism of many carcinogenic compounds by the animal body. For instance, 4'-hydroxy-1,2-benzanthracene (1) and 4'-hydroxy-9,10-dimethyl-1,2-benzanthracene (2) are formed from the corresponding hydrocarbons, and 1,2,5,6-dibenzanthracene is oxidized to the 4',8'-dihydroxy derivative (3). Even carcinogenic nitrogen-compounds seem to be metabolized along a similar path, 2-acetaminofluorene being thus converted into 7-hydroxy-2-acetaminofluorene (4).

In view of the carcinogenic activity dispalyed by some polycyclic carbazoles (5), and in anticipation of metabolism studies upon these, the synthesis of some hydroxy derivatives of 1,2-benzocarbazole (I), 1,2,5,6- (II) and 1,2,7,8-dibenzocarbazole (III) was deemed worthy of consideration.

The literature concerning compounds of this series is scanty: 4'-hydroxy-1,2benzocarbazole (6) and 1'-hydroxy-3,4-benzocarbazole (7) are mentioned in patents in connection with their potential use in the preparation of azo and indigoid dyes. Both were prepared by alkaline fusion of the corresponding sulfonic acids, but their properties were not recorded, nor were those of some hydroxy- and aminohydroxy-benzocarbazole sulfonic acids also mentioned in patents (8). We have found that demethylation of benzo- and dibenzo-carbazoles bearing methoxyl groups is readily brought about by a short heating with pyridine hydrochloride. This offers a convenient route for the preparation of substances bearing hydroxyl groups in known positions. The methoxy compounds we have thus treated were previously known, with the exception of those derived from 6-methoxy-1-tetralone (IV).



<sup>1</sup> Paper VII in this series: Buu-Hoï, and Hoán, and Khôi: J. Org. Chem., preceding article.



The often described routine carbazole synthesis (9), applied to the latter ketone and the appropriate arylhydrazines, gave 3'-methoxy-1,2-benzocarbazole, 3'-methoxy-6-methyl-1,2-benzocarbazole, 3'-methoxy-1,2,5,6-dibenzocarbazole, and 3'-methoxy-1,2,7,8-dibenzocarbazole.

All of the hydroxy compounds prepared are colorless alkali-soluble substances, now under biological investigation by Professor A. Lacassagne; in view of the high bactericidal activity of 3,4,5,6-dibenzocarbazole against staphylococci (10), they are also being tested for potential antibiotic properties.

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#### EXPERIMENTAL<sup>2</sup>

6-Methoxy-1-tetralone. This ketone was synthesized from tetralin according to the literature (11). It melted at 79°, and its semicarbazone formed (from ethanol) silky lustrous needles, m.p. 244°. Papa (12) gave m.p. 75-77° for the ketone, and m.p. 235.5-236.5° for the semicarbazone.

3'-Methoxy-3,4-dihydro-1,2-benzocarbazole. Prepared in the usual way by indolization of the phenylhydrazone of ketone IV; crystallized from benzene in colorless needles, m.p. 169°; light yellow coloration with sulfuric acid, and violet *picrate*.

Anal. Calc'd for C<sub>17</sub>H<sub>15</sub>NO: N, 5.6. Found: N, 5.5.

3'-Methoxy-1,2-benzocarbazole. Formed from benzene in colorless needles m.p. 245°; deep yellow coloration with sulfuric acid.

Anal. Calc'd for C<sub>17</sub>H<sub>13</sub>NO: N, 5.6. Found: N, 5.4.

3'-Hydroxy-1,2-benzocarbazole. A solution of 0.5 g. of the foregoing compound in 3 g. of redistilled pyridine hydrochloride was gently boiled for five minutes; water was added after cooling, and the precipitate thus obtained filtered off and recrystallized from xylene. Yield, 0.35 g. of colorless prisms m.p. 265°, slightly soluble in water; deep yellow coloration with sulfuric acid.

Anal. Calc'd for  $C_{16}H_{11}NO: N$ , 6.0. Found: N, 5.9.

3'-Methoxy-6-methyl-3,4-dihydro-1,2-benzocarbazole. From the p-tolylhydrazone of ketone IV; formed from benzene colorless needles, m.p. 191°; yellow coloration with sulfuric acid.

Anal. Calc'd for C<sub>18</sub>H<sub>17</sub>NO: N, 5.3. Found: N, 5.2.

3'-Methoxy-6-methyl-1,2-benzocarbazole. Crystallized from xylene in shiny colorless prisms, m.p. 285°; orange-yellow coloration with sulfuric acid.

Anal. Calc'd for  $C_{18}H_{15}NO: N$ , 5.3. Found: N, 5.2.

3'-Hydroxy-6-methyl-1,2-benzocarbazole. Shiny colorless leaflets, m.p. 295°; this compound and the eight following ones gave an orange-yellow coloration with sulfuric acid.

<sup>2</sup> All melting points are uncorrected and were taken with a Maquenne block.

Anal. Calc'd for C<sub>17</sub>H<sub>12</sub>NO: N, 5.6. Found: N, 5.3.

2'-Hydroxy-6-methyl-1,2-benzocarbazole. Gray-tinged shiny leaflets (from xylene), m.p. 275°.

Anal. Calc'd for C17H13NO: N, 5.6. Found: N, 5.4.

2'-Hydroxy-3'-methyl-1,2-benzocarbazole. Shiny colorless leaflets (from xylene), m.p. 297°.

Anal. Calc'd for C<sub>17</sub>H<sub>13</sub>NO: N, 5.6. Found: N, 5.6.

1'-Methyl-4'-hydroxy-1,2-benzocarbazole. Slightly yellowish needles (from toluene), m.p. 224-225°.

Anal. Calc'd for C<sub>17</sub>H<sub>13</sub>NO: N, 5.6. Found: N, 5.3.

2'-Hydroxy-5,8-dimethyl-1,2-benzocarbazole. Slightly gray-tinged needles (from water), m.p. 227-228°.

Anal. Calc'd for C18H15NO: N, 5.3. Found: N, 5.2.

2'-Hydroxy-3,6-dimethyl-1,2-benzocarbazole. Shiny colorless leaflets (from xylene), m.p. 330°.

Anal. Calc'd for C<sub>18</sub>H<sub>15</sub>NO: N, 5.3. Found: N, 5.0.

2'-Methoxy-3,4-dihydro-1,2-benzocarbazole. Obtained from the phenylhydrazone of 7methoxy-1-tetralone; formed (from benzene) in colorless needles, m.p. 131°.

Anal. Calc'd for C<sub>17</sub>H<sub>15</sub>NO: N, 5.6. Found: N, 5.4.

2'-Methoxy-1,2-benzocarbazole. Crystallized from benzene in colorless microscopic needles, m.p. 190°.

Anal. Calc'd for C<sub>17</sub>H<sub>13</sub>NO: N, 5.6. Found: N, 5.5.

2'-Hydroxy-1, 2-benzocarbazole. Formed (from water) colorless leaflets, m.p. 246°; this compound and the two preceding ones gave a yellow coloration with sulfuric acid.

Anal. Calc'd for C<sub>16</sub>H<sub>11</sub>NO: N, 6.0. Found: N, 5.8.

3'-Methoxy-3,4-dihydro-1,2,5,6-dibenzocarbazole. From the  $\beta$ -naphthylhydrazone of ketone IV; colorless needles from benzene, m.p. 190-191°, giving with sulfuric acid an orange coloration.

Anal. Cale'd for C<sub>21</sub>H<sub>17</sub>NO: N, 4.7. Found: N, 4.5.

3'-Methoxy-1,2,5,6-dibenzocarbazole. Formed from xylene graytinged microcrystals, m.p. 293°; orange-red coloration with sulfuric acid.

Anal. Calc'd for  $C_{21}H_{15}NO: N$ , 4.7. Found: N, 4.6.

3'-Hydroxy-1,2,5,6-dibenzocarbazole. Microscopic colorless needles from xylene, m.p. 303°; same coloration with sulfuric acid as the above.

Anal. Cale'd for C<sub>20</sub>H<sub>13</sub>NO: N, 4.9. Found: N, 4.6.

2'-Hydroxy-3'-methyl-1,2,5,6-dibenzocarbazole. Shiny colorless leaflets from xylene, m.p. 309-310°; brownish-red coloration with sulfuric acid.

Anal. Calc'd for  $C_{21}H_{15}NO: N, 4.7$ . Found: N, 4.5.

1'-Methyl-4'-hydroxy-1,2,5,6-dibenzocarbazole. Colorless microscopic needles from xylene, m.p. 265°; violet-red coloration with sulfuric acid.

Anal. Calc'd for C<sub>21</sub>H<sub>15</sub>NO: N, 4.7. Found: N, 4.4.

3'-Methoxy-3,4-dihydro-1,2,7,8-dibenzocarbazole. From the  $\alpha$ -naphthylhydrazone of ketone IV; colorless needles from benzene, m.p. 169°, giving an orange coloration with sulfuric acid.

Anal. Calc'd for  $C_{21}H_{17}NO: N, 4.7$ . Found: N, 4.6.

3'-Methoxy-1,2,7,8-dibenzocarbazole. Formed from benzene colorless microscopic needles, m.p. 235°; red coloration with sulfuric acid.

Anal. Calc'd for  $C_{21}H_{15}NO: N, 4.7$ . Found: N, 4.5.

3'-Hydroxy-1,2,7,8-dibenzocarbazole. Colorless needles from xylene, m.p. 255°; deep red coloration with sulfuric acid.

Anal. Calc'd for C<sub>20</sub>H<sub>13</sub>NO: N, 4.9. Found: N, 4.8.

1'-Methyl-4'-hydroxy-1,2,7,8-dibenzocarbazole. Colorless needles from xylene, m.p. 311°; brown coloration with sulfuric acid.

Anal. Cale'd for C<sub>21</sub>H<sub>15</sub>NO: N, 4.7. Found: N, 4.8.

#### SUMMARY

1. Several carbazole syntheses from 6-methoxy-1-tetralone have been performed.

2. A series of polycyclic carbazoles bearing phenolic groups has been prepared by demethylation of the corresponding methoxy compounds with pyridine hydrochloride.

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