[CONTRIBUTION FROM BATTELLE MEMORIAL INSTITUTE]

Preparation of Some Condensed Ring Carbazole Derivatives

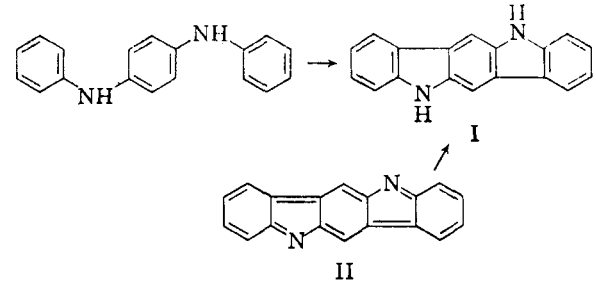
HENRY M. GROTTA, CHARLES J. RIGGLE, AND ARTHUR E. BEARSE

Received September 1, 1960

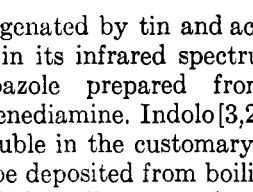
Two new indolocarbazoles have been prepared by vapor phase cyclodehydrogenation of *N,N'*-diphenylphenylenediamines over a platinum-on-magnesia catalyst. This method has also been used for the preparation of benzocarbazoles from phenylnaphthylamines.

Of the five isomeric indolocarbazoles, two have been synthesized and simple derivatives of two others have been reported. Indolo[3,2-*a*]carbazole was first prepared by Tomlinson[1] from biscyclohexanone *m*-phenylenedihydrazone, and its structure was later confirmed by alternate syntheses,[2,3] and indolo[2,3-*a*]carbazole has been made from 1-keto-1,2,3,4-tetrahydrocarbazole and phenylhydrazine.[3,4] 2-Cyanoindolo[2,3-*c*]carbazole[5] and 6-methylindolo[2,3-*b*]carbazole[6] have been prepared but the corresponding unsubstituted compounds have not been described. Indolo[3,2-*b*]carbazole appears to be unknown except possibly as a 5,11-spiro derivative (indoxyl brown) prepared from indoxyl red.[7]

It has been reported[8] that diphenylamine can be cyclodehydrogenated to carbazole when passed in the vapor phase over a platinum-on-carbon catalyst. In attempting to improve on this method and particularly to develop a catalyst capable of regeneration by burning off carbonaceous deposits, we have found that good conversions of diphenylamine to carbazole can be obtained over a catalyst consisting of platinum supported on silica or alumina[9] or on magnesium oxide. It was also found that this method can be used for the preparation of condensed ring carbazole derivatives. When applied to *N,N'*-diphenyl-*p*-phenylenediamine, indolo[3,2-*b*]carbazole (I) is obtained in about 10% yield. None of the isomeric indolo[2,3-*c*]-carbazole, which might be expected from the alternative orientation in the cyclization reaction, was identified in the reaction product. Fearon and Boggust prepared dehydroindolo[3,2-*b*]carbazole ("urorosein") (II) by the acid condensation of two moles of indole-3-aldehyde.[10] This material could



I

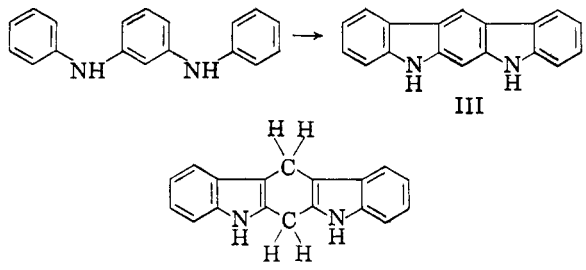


II

be readily hydrogenated by tin and acid to a compound identical in its infrared spectrum with the indolo[3,2-*b*]carbazole prepared from *N,N'*-diphenyl-*p*-phenylenediamine. Indolo[3,2-*b*]carbazole is virtually insoluble in the customary organic solvents, but may be deposited from boiling quinoline solution as fine, light yellow crystals which darken above 470° without apparently melting.

The vapor phase catalytic dehydrogenation reaction was also applied at 500° to *N,N'*-diphenyl-*m*-phenylenediamine, prepared from resorcinol and aniline.[11] Two products were isolated from this reaction, separated from each other on the basis of their solubility difference in methanol, and purified by recrystallization from xylene. The methanol insoluble material (m.p. 358–360°) was identified as indolo[2,3-*b*]carbazole (III) on the basis of elemental analysis, infrared spectrum, and nonidentity of melting point with that (299–300°) reported for the alternative product, indolo[3,2-*a*]-carbazole.[1-3] Infrared absorption at 11.3μ is indicative of a 1,2,4,5-substituted benzene ring which would not be present in the alternative indolocarbazole structure. The sharpness of the N—H band suggests a single type of NH group which would not be present in partially dehydrogenated products nor in indolo[3,2-*a*]carbazole. The overall structure of the absorption curve appeared reasonable for an indolocarbazole and no indication of mono-substituted aromatic rings was found. Dobeneck and Maas[12] have reported the preparation of dihydroindolo[2,3-*b*]carbazole (IV) from indole and formaldehyde. It was hoped that this material would provide, by dehydrogenation, a

(1) M. L. Tomlinson, *J. Chem. Soc.*, 809 (1951).
(2) J. A. Hall and S. G. P. Plant, *J. Chem. Soc.*, 116 (1953).
(3) F. G. Mann and T. J. Willcox, *J. Chem. Soc.*, 1525 (1958).
(4) G. V. Bhide, N. L. Tikotkar, and B. D. Tilak, *Chem. & Ind. (London)*, 363 (1957).
(5) P. V. Clifton and S. G. P. Plant, *J. Chem. Soc.*, 461 (1951).
(6) M. L. Swindells and M. L. Tomlinson, *J. Chem. Soc.*, 1135 (1956).
(7) P. Seidel, *Chem. Ber.*, **83**, 20 (1950).
(8) N. D. Zelinsky, I. Titz, and M. Gaverdowskaja, *Ber.*, **59**, 2590 (1926).
(9) H. M. Grotta, U. S. Patent 2,921,942 (Jan. 19, 1960).
(10) W. R. Fearon and W. A. Boggust, *Biochem. J.*, **46**, 62 (1950).
(11) A. Calm, *Ber.*, **16**, 2786 (1883).
(12) H. von Dobeneck and I. Maas, *Chem. Ber.*, **87**, 455 (1954).

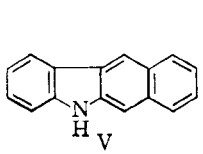


III

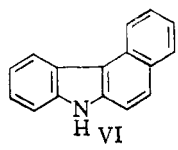
IV

second route to III; however, we, like Swindells and Tomlinson,[6] were unable to duplicate the preparation of IV. The fraction of the product more soluble in boiling methanol was recrystallized from xylene to m.p. 290–291° and may contain the isomeric indolo[2,3-*a*]carbazole or possibly 2-anilinocarbazole from partial dehydrogenation, although such a high melting point would not be expected for the latter compound. Its identity has not been established.

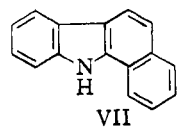
The cyclodehydrogenation reaction has also been applied to the phenyl naphthylamines for the preparation of benzocarbazoles. Graebe has reported the pyrolytic cyclization of phenyl-2-naphthylamine to 2,3-benzocarbazole (V),[13] although no yield was given. The same reaction conducted at 500° over the platinum–magnesium oxide catalyst proceeded to give in 21% yield a product consistent in appearance,[13] and in melting point of its acetyl derivative,[14] with 2,3-benzocarbazole, although its melting point is much higher (347–349°) than that reported by Graebe (330°), and somewhat higher than the value (342°) reported by Clemo and Felton.[15] No 3,4-benzocarbazole (VI)[16] was found in the reaction product.



V



VI



VII

When Graebe pyrolyzed phenyl-1-naphthylamine, he isolated a product melting at 165°.[13] 1,2-Benzocarbazole (VII) first synthesized by Kym[17] is reported to have a melting point of 225° and of 227–228°.[15] Phenyl-1-naphthylamine was found to cyclodehydrogenate at 500° under the influence of the platinum–magnesium oxide catalyst to produce 1,2-benzocarbazole (m.p. 229–230°) in 22% yield. Thus, while pyrolytic and catalytic dehydrogenation give the same product from phenyl-2-naphthylamine, different products arise from phenyl-1-naphthylamine.

(13) C. Graebe and W. Knecht, *Ann.*, **202**, 1 (1880).

(14) F. Kehrmann, A. Oulevay, and F. Regis, *Ber.*, **46**, 3712 (1913).

(15) G. R. Clemo and D. G. I. Felton, *J. Chem. Soc.*, 1658 (1952).

(16) F. Ullmann, *Ber.*, **31**, 1697 (1898).

(17) O. Kym, *Ber.*, **23**, 2458 (1890).

Structures of the two benzocarbazoles prepared in this work are confirmed by the correspondence of the ultraviolet absorption spectra with those already reported. The wave lengths of the absorption maxima and the values of log ϵ_{max} are given in Table I together with the corresponding values of Clemo and Felton[15] (in parentheses).

TABLE I

ULTRAVIOLET SPECTRA OF THE BENZOCARBAZOLES[a]

1,2-Benzocarbazole		2,3-Benzocarbazole	
mμ	log ϵ_{max}	mμ	log ϵ_{max}
243 (246)[b]	4.55 (4.47)	268 (268)	4.74 (4.81)
251 (252)	4.60 (4.56)	282 (282)	4.62 (4.69)
256 (258)	4.55 (4.52)	292 (292)	4.48 (4.56)
279 (280)	4.62 (4.63)	317 (317)	3.90 (4.03)
301 (302)	4.28 (4.29)	331 (332)	4.04 (4.13)
305 (306)	4.30 (4.30)	373 (374)	3.56 (3.70)
322 (323)	3.76 (3.76)	391 (394)	3.60 (3.72)
337 (338.5)	3.76 (3.75)		
354 (355)	3.81 (3.79)		

[a] Taken in ethanol solution with a Cary Model 14 spectrophotometer. [b] Values in parentheses taken in ethanol by Clemo and Felton (Ref. 15).

It may be added that this cyclodehydrogenation method failed to produce 3-fluorocarbazole from 4-fluorodiphenylamine, 9-ethylcarbazole from *N*-ethyldiphenylamine, 3,6-dimethylcarbazole from di-*p*-tolylamine, or 3-hydroxycarbazole from 4-hydroxydiphenylamine. In each case the only materials identified in the products of these reactions were starting compound and unsubstituted carbazole. Details of the development of this synthetic procedure for carbazole will be reported elsewhere.

EXPERIMENTAL[18]

Catalyst preparation. Magnesium oxide (light powder, U.S.P., J. T. Baker Co.) was made denser by pelleting in a press, the pellets ground, and material of 70–140 mesh collected. Fifty-seven grams of the magnesia so treated was stirred overnight with two ounces of 5% chloroplatinic acid solution which had been neutralized with ammonia and diluted with sufficient water to bring all the platinum salt into solution. The resulting slurry was centrifuged, the supernatant liquid decanted, and the solid residue dried for 20 hr. at 60° under vacuum. This solid was ground to −70 mesh and pelleted in a 1/8-inch die to give about 70 cc. (bulk volume) of catalyst which was heated during 5 hr. to 340° under a slow stream of nitrogen and finally during 20 hr. to 475° under a stream of hydrogen.

Indolo[3,2-b]carbazole (I). (a) *From N,N'-diphenyl-p phenylenediamine.* To 38 g. (60 ml. bulk volume) of 2% platinum–magnesium oxide pelleted catalyst in an electrically heated stainless steel tube containing a preheat section of about 50 ml. packed with glass beads, *N,N'*-diphenyl-*p*-phenylenediamine (10 g.) dissolved in xylene (45 ml.) was introduced through a motor-driven screw-impelled hypodermic syringe during 255 min. The temperature of the

(18) Melting points are uncorrected. All elemental analyses were by Clark Microanalytical Laboratory, Urbana, Ill. Infrared spectra were taken as dispersions in potassium bromide with the Perkin-Elmer Model 21 spectrophotometer (sodium chloride optics).

catalyst bed was maintained at 500 ± 5°, and hydrogen at about 170 ml./min. and water at 6.5 g./hr. were fed continuously during the run. The contents of the receiver were extracted with 100 ml. of boiling xylene and the xylene-insoluble residue was recrystallized from boiling quinoline, to give 0.95 g. of fine light yellow crystals which darken without melting at about 470°.

Anal. Calcd. for $C_{18}H_{12}N_2$. C, 84.38; H, 4.69; N, 10.94. Found. C, 84.44; H, 4.72; N, 11.13.

(b) *From indole-3-aldehyde.* One gram of urorosein (II) prepared from indole-3-aldehyde according to Fearon and Boggust[10] was dissolved with warming in 150 ml. of ethanol; 25 ml. of water, 30 ml. of hydrochloric acid, and 5 g. of tin were added, and the mixture was kept for 2 days with occasional warming and addition of three 10-ml. increments of acid. The solvent containing suspended solids was decanted from undissolved tin, filtered, and the solid residue extracted on the filter with ethanol. The ethanol-insoluble residue was recrystallized from boiling quinoline to give 60 mg. of I identical in infrared spectrum with the material prepared in (a) above.

Anal. Found. C, 84.37; H, 4.93; N, 10.96.

Infrared spectrum (μ). 2.93 (N—H); 3.28 (C—H); 6.19 (N—H bend and aromatic C=C stretch); 6.56; 6.86; 6.91; 7.57; 7.89; 8.10; 8.48; 8.76; 9.05; and, 11.67, 11.78, 13.12, 13.27, 13.47, and 14.48 (C—H out of plane deformation).

Indolo[2,3-b]carbazole (III). Twenty-two grams of *N,N'*-diphenyl-*m*-phenylenediamine was passed over the 2% platinum-magnesium oxide catalyst during 283 min. Water and hydrogen were added continuously as above while the temperature of the catalyst was maintained at 500°. The reaction product was extracted with methanol leaving a residue which was recrystallized five times from boiling xylene (about 600 ml. for each recrystallization) to give 0.7 g. of III, m.p. 358–360°.

Anal. Calcd. for $C_{18}H_{12}N_2$. C, 84.38; H, 4.69; N, 10.94. Found. C, 84.46; H, 4.99; N, 11.01.

Infrared spectrum (μ). 2.93 (N—H); 3.28 (C—H); 6.08 and 6.19 (N—H bend and aromatic C=C stretch); 6.85; 6.89; 7.56; 7.93; 8.20; 8.65; 9.00; and 11.30, 12.11, 13.01, 13.32, 13.75, and 14.56 (C—H out of plane deformation).

2,3-Benzocarbazole (V). Twenty grams of molten phenyl-2-naphthylamine was vaporized and passed over the platinum-magnesium oxide catalyst during 107 min. at 500–505° while hydrogen at about 170 ml./min. and water at 2.1 g./hr. were fed concurrently. The contents of the receiver were slurried with 300 ml. of hot benzene and filtered to give 3.49 g. of insoluble material, m.p. 344–348°. Concentration of the filtrate provided an additional 0.62 g. of product, m.p. 335–344°. Recrystallization of the combined products from boiling toluene produced glistening white plates, m.p. 347–349°. Warming a 1-g. portion of the product with 5 ml. of acetic anhydride containing a small lump of fused zinc chloride, provided the acetyl derivative, light tan needles from ethanol m.p. 117–118° (lit. m.p. 117° or 123°[14]).

1,2-Benzocarbazole (VII). Twenty grams of phenyl-1-naphthylamine was catalytically dehydrogenated under conditions identical with those used for V above. The benzene solution of the reaction product was treated with anhydrous hydrogen chloride to precipitate 13.56 g. of phenyl-1-naphthylamine hydrochloride and from the filtrate 4.38 g. of VII (m.p. 229–230°) was obtained on evaporation of most of the solvent. Recrystallization from aqueous ethanol provided glistening white plates of the same melting point. The reported value is 227–228°.[15]

Acknowledgment. The authors are indebted to Mr. R. E. Heffelfinger, Mr. R. J. Jakobsen, and Dr. P. W. Davis for the spectral data, and to the Southern Dyestuff Company Division of American-Marietta Company for permission to publish this work conducted under their sponsorship.

COLUMBUS 1, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

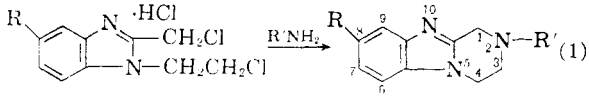
Syntheses of 1,2,3,4-Tetrahydropyrazino[1,2-a]benzimidazoles and 3-Carbethoxy-3-phenyl-1,2,3,4-tetrahydropyrido[1,2-a]benzimidazole

HOWARD MATRICK[1] AND ALLAN R. DAY

Received June 27, 1960

Several 2- and 2,3-substituted 1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazoles have been synthesized. 3-Carbethoxy-3-phenyl-1,2,3,4-tetrahydropyrido-[1,2-a]benzimidazole, a Demerol-like compound, has also been synthesized.

The syntheses of the compounds mentioned in the title were of interest for several reasons. In 1957, Gross and Turian reported the synthesis of a series of benzimidazole derivatives which were active analgesics.[2] The most active compound in the series was 1-(diethylaminoethyl)-2-(4-ethoxybenzyl)-5-nitrobenzimidazole. It occurred to us that the 1,2,3,4-tetrahydropyrazino[1,2-a]benzimidazoles (A), being 1,2-disubstituted benzimidazoles, might have similar properties. Two methods were used for the synthesis of this ring system. The first involved the reaction of a primary amine with 1-(2-chloroethyl)-2-chloromethylbenzimidazole. The other involved the cyclization of 2-bis-(2-chloroethyl)aminomethylbenzimidazole with a base.



(1)

A

R = H, Cl, NO_2, NH_2, $COOC_2H_5$

R' = $C_6H_5CH_2$, $C_6H_5CH_2CH_2$, *n*-C_4H_9

(1) Smith Kline and French Fellow, 1958–59; Eastman Kodak Fellow, 1959–60.

(2) G. Gross and H. Turian, *Experientia*, **13**, 401 (1957).