dure described for 5,5-diethyl-3-methyl-2-oxazolidone gave 78% of product, b. p. 141–142°, $n^{25}D$ 1.5282.

3-Acetyl-5,5-diphenyl-2-oxazolidone.—The procedure described for the acetylation of 4,4-dimethyl-5-propyl-2-oxazolidone was followed except that sufficient acetic acid was added to bring the diphenyloxazolidone into solution at the boiling point. The product precipitated upon the addition of water; recrystallization from alcohol gave 76%, m. p. 140–143°.

Summary

A number of 2-oxazolidone derivatives have been prepared, principally by the reaction of urea with β-amino alcohols. Procedures have been developed for N-acylation and N-alkylation of the compounds.

Approximately one-third of the compounds was found to have anticonvulsant action. The 3-carbamyl and 5-phenyl groups were particularly effective in this connection.

NORTH CHICAGO, ILL. RECEIVED JUNE 20, 1950

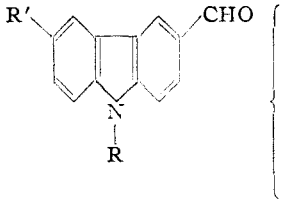
[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, RADIUM INSTITUTE, UNIVERSITY OF PARIS]

Carbazole Aldehydes

BY NG. PH. BUU-HOÏ AND NG. HOÁN

Notwithstanding the great amount of work already done in the field of carbazole chemistry, no aldehyde from that series has yet been prepared, presumably for want of a suitable method. The synthesis of aldehydes by means of N-methylformanilide and phosphorus oxychloride had proved of great value in many series,[1] including N-dialkylanilines, and has recently been extended to the preparation of thiophene aldehydes. We have now found it to be readily applicable to 9-alkylcarbazoles, which are today produced on a large scale[2] but which still have limited synthetical uses.

From 9-methyl-, 9-*n*-butyl- and 9-isoamylcarbazole[3] were thus obtained, with excellent yields in all instances, 9-methyl- (I), 9-*n*-butyl- (II), and

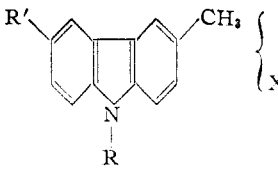


I, R = CH_3 R′ = H
II, R = *n*-C_4H_9 R′ = H
III, R = *i*-C_5H_{11} R′ = H
IV, R = *n*-C_4H_9 R′ = CH_3
V, R = CH_3 R′ = Br
VI, R = *n*-C_4H_9 R′ = Br
VII, R = CH_3 R′ = NO_2
VIII, R = *n*-C_4H_9 R′ = NO_2
IX, R = *i*-C_5H_{11} R′ = NO_2

9-isoamylcarbazole-3-aldehyde (III). The position entered by the formyl group was assumed from analogy with other cases of substitution reactions with 9-alkylcarbazoles,[4] and verified by reduction of aldehyde (I) into 3,9-dimethylcarbazole identical with a sample prepared by N-methylation of 3-methylcarbazole. In the present case, there is thus analogy between 9-alkylcarbazoles and N-dialkylanilines. It should be mentioned that the action of free formaldehyde in acid medium[5] upon carbazole and (9-ethylcarbazole) has been found to yield 3,3′-methylene-bis-carbazole (and its 9-ethyl derivative); in alkaline medium, 9-hydroxymethylcarbazole was obtained.[6]

Reductions of carbazole aldehydes into methyl compounds were found to be best achieved by means of the Wolff–Kishner method as modified by Huang-Minlon[7]: in addition to 3,9-dimethylcarbazole, 3-methyl-9-*n*-butyl- and 3-methyl-9-isoamylcarbazole were thus obtained in high yield. These 3,9-dialkylcarbazoles were also susceptible to the N-methylformanilide method, and 3-methyl-9-*n*-butylcarbazole, for instance, gave 6-methyl-9-*n*-butylcarbazole-3-aldehyde (IV), which, in its turn, was easily and almost quantitatively converted as above into 3,6-dimethyl-9-*n*-butylcarbazole.

Like all the derivatives of carbazole having a free position *para* to the nitrogen atom, the 9-alkylcarbazole-3-aldehydes cited above readily lent themselves to substitution reactions. With



X, R = CH_3 R′ = Br
XI, R = CH_3 R′ = NO_2
XII, R = *n*-C_4H_9 R′ = NO_2
XIII, R = *n*-C_4H_9 R′ = Br

bromine, in acetic acid solution in the cold,[8] were thus obtained 6-bromo-9-methyl- (V) and 6-bromo-9-*n*-butylcarbazole-3-aldehyde (VI). Fuming nitric acid also reacted in the cold and in acetic acid medium[9] to give the high-melting 6-nitro-9-methyl- (VII), 6-nitro-9-*n*-butyl (VIII) and 6-nitro-9-isoamylcarbazole-3-aldehyde (IX). The 3,9-dialkylcarbazoles mentioned above were also easily monobrominated and mononitrated in the same conditions. 6-Bromo-3,9-dimethyl- (X), 6-nitro-3,9-dimethyl- (XI), 6-nitro-3-methyl-9-*n*-butyl (XII) and 6-bromo-3-methyl-9-*n*-butylcarbazole (XIII) were thus obtained.

A highly sensitive reaction characteristic of 9-alkylcarbazole-3-aldehydes was the intensely blue coloration they gave with β-naphthol in acid medium, due probably to the formation of xanthene derivatives.[10]

Experiments upon the successful extension of the N-methylformanilide aldehyde synthesis both to the indole series and to the carcinogenic benzocarbazoles and dibenzocarbazoles will be described in forthcoming papers.

(1) See, for instance, Vilsmeier and Haak, *Ber.*, **60**, 119 (1927); Fieser, *et al.*, THIS JOURNAL, **60**, 2547, 2556 (1938); King and Nord, *J. Org. Chem.*, **13**, 635 (1948).

(2) 9-Ethylcarbazole, 9-*n*-butylcarbazole and other homologs are now produced on a large scale by the Reilly Corp., Indianapolis.

(3) Levy, *Monatsh.*, **33**, 180 (1912).

(4) See, for instance, Buu-Hoï and Royer, *Rec. trav. chim.*, **66**, 533 (1947).

(5) Pulvermacher and Loeb, *Ber.*, **25**, 2766 (1892).

(6) German Patent 256,757 Kl. 12 pp. (10.5.1912).

(7) Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).

(8) In the case of 9-alkylcarbazoles (ref. 4), bromination gave almost exclusively 3,6-dibromo derivatives, except with N-bromosuccinimide.

(9) This nitration method is far more convenient than those described in the literature, using, for instance, nitrobenzene as a solvent.

(10) Wolff, *Ber.*, **26**, 84 (1893); Claisen, *Ann.*, **237**, 265 (1887).

TABLE I

CARBAZOLE ALDEHYDES

Number	Appearance	B. p., °C.	Mm.	M. p., °C.	%	Empirical formula	Analyses: Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
II	Colorless prisms[a]	267–269	13	57	81	$C_{17}H_{17}NO$	81.27	81.0	6.77	6.89
III	Crystalline mass[b]	268–269	12	>25	85	$C_{18}H_{19}NO$	81.5	81.3	7.16	7.2
IV	Colorless prisms[c]	284–285	13	73	85	$C_{18}H_{19}NO$	81.5	81.3	7.16	7.2
V	Yellowish prisms[d]			164	90	$C_{14}H_{10}BrNO$				
VI	Yellowish prisms			100	90	$C_{17}H_{16}BrNO$	61.81	61.6	4.84	4.9
VII	Yellow leaflets			279	80	$C_{14}H_{10}N_2O_3$	66.14	66.0	3.93	3.8
VIII	Yellowish needles			222	85	$C_{17}H_{16}N_2O_3$	68.9	68.6	5.4	5.5
IX	Yellow leaflets			219	85	$C_{18}H_{18}N_2O_3$	69.67	69.5	5.8	6.0

[a] Crystallized from ligroin. Aldazine, fine pale yellow needles from ethanol, m. p. 203°, giving a deep red color with sulfuric acid (Calcd. for $C_{34}H_{34}N_4$: N, 11.2. Found: N, 11.1). [b] n^{20} 1.6516; semicarbazone, colorless microneedles from ethanol, m. p. 212–213°. Aldazine, pale yellow needles from ethanol, m. p. 176° (Calcd. for $C_{36}H_{33}N_4$: N, 10.6. Found: N, 10.4. [c] Semicarbazone, fine colorless needles from ethanol, m. p. 203°. [d] Orange color with sulfuric acid. *Anal.* Calcd.: N, 4.86. Found: N, 4.60.

TABLE II

SUBSTITUTED CARBAZOLES

Compound	Appearance	B. p. °C.	Mm.	M. p., °C.	Yield, %	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
3-Methyl-9-*n*-butyl-	Pale yellow oil[a]	222–223	13		85	$C_{17}H_{19}N$	86.07	86.0	8.01	8.2
3,6-Dimethyl-9-*n*-butyl-	Long colorless needles	236–238	13	61	98	$C_{18}H_{21}N$	86.05	86.0	8.36	8.4
3-Methyl-9-isoamyl-	Pale yellow oil[b]	227–228	15		95	$C_{18}H_{21}N$	86.05	86.0	8.36	8.4
6-Nitro-3,9-dimethyl-	Yellow needles[c]			217		$C_{14}H_{12}N_2O_2$	70.0	69.8	5.0	5.0
6-Nitro-3-methyl-9-*n*-butyl-	Pale yellow prisms			130		$C_{17}H_{18}N_2O_2$	72.34	72.05	6.38	6.5
6-Bromo-3,9-dimethyl-	Colorless needles[d]			115	90	$C_{14}H_{12}BrN$	61.31	61.2	4.37	4.5
6-Bromo-3-methyl-9-*n*-butyl-	Silky colorless needles[e]	260–265	13	64–65	90	$C_{17}H_{18}BrN$				

[a] $n^{21.5}$ 1.6256. [b] n^{20} 1.5840. [c] Deep violet color with sulfuric acid. [d] Transient pale green color with sulfuric acid. [e] *Anal.* Calcd.: N, 4.43. Found: N, 4.28.

Experimental

Intermediates.—The 9-methylcarbazole was prepared by adding dimethyl sulfate to an acetone solution of carbazole and concentrated aqueous sodium hydroxide; 9-*n*-butylcarbazole and 9-isoamylcarbazole were prepared according to Levy's procedure, and purified by vacuum redistillation. The latter substance, described by Levy as an oil, was now obtained as a solid, m. p. 43°.

9-Methylcarbazole-3-aldehyde (I).—A solution of 65 g. of redistilled 9-methylcarbazole and 64 g. of N-methylformanilide in 64 g. of phosphorus oxychloride and 50 cc. of *o*-dichlorobenzene was heated on a boiling water-bath for six hours. After cooling, the reaction product was treated with a 30% aqueous solution of sodium acetate, and steam distillation was used to remove the *o*-dichlorobenzene and the N-methylaniline formed. The dark green sticky mass obtained was heated with acetic acid, the resulting solution filtered and diluted with water, and the aldehyde extracted with benzene. The benzene solution was washed with dilute hydrochloric acid, and then with an aqueous solution of sodium carbonate. After drying over sodium sulfate, the solvent was distilled, and the residue vacuum fractionated. There were obtained 46 g. (61% yield) of the aldehyde, b. p. 262–264° at 13 mm., crystallizing from ether in almost colorless needles m. p. 74°, giving with sulfuric acid a deep orange coloration. *Anal.* Calcd. for $C_{14}H_{11}NO$: C, 80.38; H, 5.26. Found: C, 80.25; H, 5.28.

The semicarbazone formed from ethanol fine shiny colorless prisms which turned orange-yellow on heating, and melted at 305°. *Anal.* Calcd. for $C_{15}H_{14}N_4O$: N, 21.0. Found: N, 20.8.

The aldazine, prepared by refluxing a mixture of the aldehyde (2 moles) with hydrazine hydrate (1 mole) in ethanol for two hours, formed from that solvent long pale yellow needles m. p. 309°, giving with sulfuric acid a deep red coloration. *Anal.* Calcd. for $C_{28}H_{22}N_4$: N, 13.5. Found: N, 13.3.

3,9-Dimethylcarbazole.—A mixture of 15 g. of the foregoing aldehyde and 25 g. of 80% hydrazine hydrate was heated with 30 g. of potassium hydroxide in 150 cc. of diethylene glycol, allowing the water formed to distil. Refluxing was then effected until complete disappearance of the yellow coloration of the supernatant layer, due to the presence of the hydrazone (about three hours). After cooling, water was added, and the reduction product extracted with benzene. The benzene solution was washed with dilute hydrochloric acid, then with water, and dried over sodium sulfate; after evaporation of the solvent and vacuum distillation of the residue, 12.6 g. of 3,9-dimethylcarbazole, b. p. 205–207° at 13 mm. were obtained. It crystallized from methanol in colorless leaflets m. p. 81°, giving a yellow coloration with sulfuric acid; the benzene solutions showed an intense violet fluorescence. *Anal.* Calcd. for $C_{14}H_{13}N$: C, 86.15; H, 6.66. Found: C, 86.0; H, 6.80.

The same compound was obtained by treatment of 3-methylcarbazole[11] in alkaline acetone solution with dimethyl sulfate as in the case of carbazole.

Bromination and Nitration of Carbazole Derivatives.—The bromination was performed by adding dropwise a solution of the calculated amount of bromine in acetic acid to a cooled, stirred solution of the carbazole compound in acetic acid; the reaction product was poured into water, extracted with benzene, and recrystallized from ethanol or vacuum fractionated. The nitration was effected by dropping a small excess of fuming nitric acid (d. 1.48) dissolved in acetic acid into a cooled, stirred solution of the carbazole derivative. After ten minutes of further stirring, water was added, the solid precipitate collected, washed thoroughly with water, and recrystallized twice from acetic acid.

Reaction of Carbazole Aldehydes with β-Naphthol.—A solution of 2 g. of 9-*n*-butylcarbazole-3-aldehyde and of 3 g. of β-naphthol in 25 cc. of acetic acid containing 2 cc. of concentrated hydrochloric acid was refluxed for some minutes. An intense blue color appeared rapidly, and after cooling, a solid indigo-blue precipitate (soluble in organic solvents) was obtained. The constitution of this dye was not investigated, but the presence of a xanthene structure was assumed from analogy with the behavior of aromatic aldehydes. The other carbazole aldehydes gave similar reactions.

Summary

1. The N-methylformanilide method for the synthesis of aldehydes has been found readily

(11) Prepared according to Borsche, *Ann.*, **359**, 77 (1908).

applicable to 9-alkyl- and 3,9-dialkylcarbazoles, and many carbazole aldehydes can thus be prepared.

2. Some reactions of these aldehydes (reduction, bromination, nitration) have been investigated, and several new compounds have been prepared in connection herewith.

PARIS (V), FRANCE RECEIVED MAY 31, 1950

[CONTRIBUTION FROM THE BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, AGRICULTURAL RESEARCH ADMINISTRATION, U. S. DEPARTMENT OF AGRICULTURE]

Constituents of *Heliopsis* Species. I. Scabrin, an Insecticidal Amide from the Roots of *H. scabra* Dunal[1]

BY MARTIN JACOBSON

The isolation of an insecticidal amide from the roots of a Mexican plant submitted to this Bureau as *Erigeron affinis* D. C., and its identification as N-isobutyl-2,6,8-decatrienamide (I), were reported in 1945 by Acree, *et al.*[2] In 1947 the plant was shown to be actually *Heliopsis longipes* (A. Gray.) Blake[3] (family *Compositae*), and a detailed report of its insecticidal activity was published by McGovran, *et al.*[4]

$$CH_3CH{=}CHCH{=}CH(CH_2)_2CH{=}CHC(=O)NHCH_2CH(CH_3)_2 \quad (I)$$

An investigation was undertaken to determine the insecticidal activity of three species of *Heliopsis* native to the United States, and it was found[5] that all of these species—namely, *H. scabra* Dunal., *H. gracilis* Nutt., and *H. parvifolia* A. Gray—particularly the roots, were toxic to house flies (*Musca domestica* L.). The roots of *H. scabra* were especially toxic to this insect.

Heliopsis scabra Dunal. is indigenous to most of the United States, growing as a weed from 2.5 to 4.5 feet tall. The only reference in the literature to the chemistry of the plant is that by Kuhn and Winterstein,[6] who reported the isolation of lutein, m. p. 193°, and its palmitic acid ester, m. p. 92°, from the flower heads of *H. scabra* var. *major* and *H. scabra* var. *cinniaeflorae*.

A quantity of air-dried *H. scabra*[7] was obtained from Ruidoso Canyon in the White Mountains of New Mexico and the roots were separated from the rest of the plant. Successive extraction of the roots with petroleum ether, ethyl ether, chloroform, and ethanol showed that only the petroleum ether extractive was toxic to house flies.[8]

The insecticidal material was extracted from the hydrocarbon solution with nitromethane, which was then removed and the residue taken up in ethyl ether. The neutral fraction, obtained following extraction with dilute acid and alkali, was chromatographed on successive columns of alumina, and the main toxic fraction was obtained in pure form in 0.12% yield (based on dry root) as a pale yellow, viscous oil which could not be distilled without decomposition, even under high vacuum.

A trace of this material, when placed on the tongue, produced, after about ten minutes, an intense burning, paralytic effect on the tongue and lips lasting for about two hours. It proved to be appreciably more toxic than the pyrethrins to house flies.

In addition to this toxic oil, there was obtained, in 0.08% yield, a very viscous, yellow oil showing strong blue fluorescence, which also possessed considerable toxicity to house flies, but which was not pungent. It appears to contain a small amount of impurity which is very difficult to separate. There were also isolated from the neutral fraction a colorless crystalline compound, $C_{20}H_{22}O_6$, m. p. 133.5–135.0°, and a yellow crystalline compound, $C_{10}H_6O_3$, m. p. 235°, showing strong blue fluorescence in solution, neither of which is insecticidal. The latter compound contains a lactone structure. The detailed investigation of these compounds will be reported separately.

The non-fluorescent, active substance, for which the name "scabrin" is proposed, is not stable at room temperature for more than a week, changing to a dark orange resin which is neither pungent nor insecticidal. However, it is stable in the cold for several weeks under nitrogen or in sealed ampoules. It is also stable in solution at room temperature, a property which is also shown by herculin from *Zanthoxylum clava-herculis* bark.[9]

Scabrin contained nitrogen and rapidly decolorized a dilute carbon tetrachloride solution of bromine. Acid hydrolysis yielded an acid which was too unstable to be characterized, and a nitrogenous base which was identified as isobutylamine by means of melting point and chlorine determination of its hydrochloride, by melting point of the chloroplatinate, and by comparison with authentic materials. The compound was thus established as the isobutylamide of an unsaturated acid.

Analysis and molecular weight determination indicated the formula $C_{22}H_{35}NO$ for scabrin. Hydrogenation with platinum oxide catalyst yielded decahydroscabrin, $C_{22}H_{45}NO$, m. p. 77–

(1) Report of a study made under the Research and Marketing Act of 1946. Article not copyrighted. This paper was presented before the Division of Organic Chemistry, at the Chicago meeting of the American Chemical Society, September 5, 1950.

(2) F. Acree, Jr., M. Jacobson and H. L. Haller, *J. Org. Chem.*, **10**, 236 (1945); **10**, 449 (1945).

(3) (a) M. Jacobson, F. Acree, Jr., and H. L. Haller, *J. Org. Chem.*, **12**, 731 (1947); (b) E. L. Little, *J. Wash. Acad. Sci.*, **38**, 269 (1948).

(4) E. R. McGovran, *et al.*, Bur. Ent. and Plant Quar. E-736, 5 pp. (1947).

(5) W. A. Gersdorff and N. Mitlin, *J. Econ. Entom.*, **43**, 554 (1950).

(6) R. Kuhn and A. Winterstein, *Naturwiss.*, **18**, 754 (1930).

(7) This material was very kindly collected by Prof. A. H. Berkman, Texas Western College, and its identity was verified by S. F. Blake, Bureau of Plant Industry, Soils, and Agricultural Engineering, U. S. Department of Agriculture, Beltsville, Md.

(8) The tests against house flies were made by W. A. Gersdorff and N. Mitlin of this Bureau.

(9) M. Jacobson, THIS JOURNAL, **70**, 4234 (1948).