N-*n*-butyl-*p*-anisidine was 56% based on the *p*-anisidine used. Adams platinum catalyst and palladized charcoal were inefficient for this reduction, both with and without added acetic acid.

Acknowledgment.—The authors wish to express their gratitude to Mr. Samuel Blackman for the micro-analyses here recorded.

Summary

1. A series of N,N-disubstituted 4-alkoxy-α-naphthamidines has been prepared.

2. Several of these amidines are local anesthetics of high potency.

TUCKAHOE 7, NEW YORK RECEIVED JUNE 16, 1950

[CONTRIBUTION FROM ABBOTT LABORATORIES]

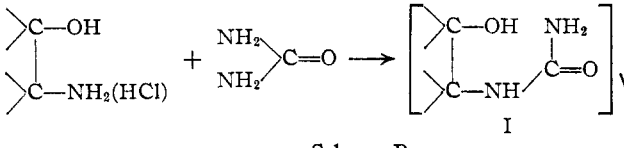
Anticonvulsant Drugs. IV. Some 2-Oxazolidones[1]

BY W. J. CLOSE

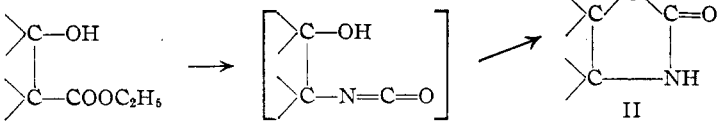
A few years ago it was discovered that certain 2,4-oxazolidinedione derivatives had anticonvulsant properties.[2] It seemed desirable, therefore, to undertake a study of the closely related 2-oxazolidones (II).

Several methods for the synthesis of 2-oxazolidones had been described prior to and during this investigation. The condensation of β-amino alcohols with ethyl carbonate in the presence of a basic catalyst[3] appeared to be the most generally useful procedure. It seemed likely, however, that the oxazolidones could be prepared more simply by heating β-amino alcohols or their hydrochlorides with urea (scheme A).[4] This method proved to be general and convenient, combining ease of manipulation with reasonable yields (generally 50–80%).

Scheme A



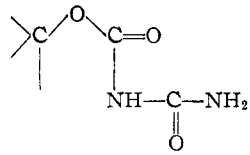
Scheme B



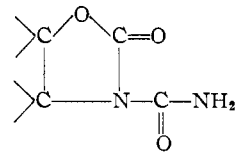
Although the mechanism of this conversion has not been definitely established, it is probable that the urea first breaks down to cyanic acid, which then attacks the basic group with the formation of the intermediate I. Finally, cyclization takes place with the elimination of ammonia. In one case selected for detailed study (5,5-dimethyl-2-oxazolidone) it was possible to isolate the intermediate I in good yield and to convert it to the oxazolidone by continued heating.

Where the requisite amino alcohols were not readily available, the oxazolidones were obtained directly from β-hydroxy esters by means of the Curtius reaction (scheme B), a synthetic method which has found occasional use by others.[5] Over-all yields from the ester were comparable to those obtained by the urea procedure.

During the course of the present work it was discovered that allophanic esters (III) exhibited anticonvulsant activity.[1] It was apparent that



III

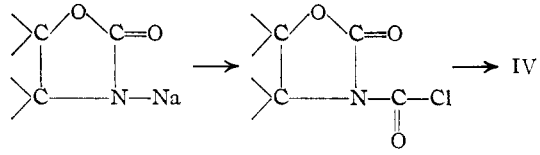


IV

similarly constituted molecules (IV) could be obtained by the introduction of a carbamyl group onto the nitrogen atom of the oxazolidones. A procedure was therefore developed whereby this type of compound could be obtained. The oxazolidone was converted to its sodio derivative, which was then treated with an excess of phosgene, followed by ammonia (scheme C). Over-all yields of 48–78% were obtained.

N-Alkyloxazolidones were obtained from the parent compounds by treatment of the sodio derivatives with alkyl halides or sulfates in an inert solvent. Alkylation could also be carried out in Cellosolve with the sodium alkoxide as a condensing agent. Alkylation in absolute alcohol with sodium ethoxide gave low yields.

Scheme C



Acetylation was accomplished by prolonged heating of the oxazolidones with acetic anhydride. Pyridine was used as a solvent and catalyst in acylation with higher acid radicals.

The oxazolidones were tested for anticonvulsant activity as described earlier[2] by Drs. R. K. Richards and G. M. Everett, to whom the author is indebted for the pharmacological data reported here

(1) Paper III in this series by Spielman, Barnes and Close, THIS JOURNAL, **72**, 2520 (1950). The present work was presented at the 117th Meeting of the A. C. S. at Philadelphia, April 11, 1950.

(2) Spielman and Everett, THIS JOURNAL, **70**, 1021 (1948); Everett and Richards, *J. Pharmacol.*, **81**, 402 (1944).

(3) Homeyer, U. S. Patents 2,399,188, 2,437,388, 2,437,389, 2,437,390.

(4) (a) Close, Tiffany and Spielman, THIS JOURNAL, **71**, 1265 (1949); (b) Stratton and Wilson, *J. Chem. Soc.*, 1133 (1932).

(5) Newman, THIS JOURNAL, **71**, 378 (1949); Ide and Baltzly, *ibid.*, **70**, 1084 (1948); Baltzly and Buck, *ibid.*, **62**, 164 (1940); Schroeter, German Patent 220,852.

TABLE I

PROPERTIES OF PARENT OXAZOLIDONES

Compd.	Substituents	M. p., °C.[a]	Recrystn. solvent[b]	Formula	Nitrogen, % Calcd.	Found	Prepn. method	Yield,[a] %	Activity[c]
1	5-Chloromethyl[d]	100–103	Alc.	.....	..	..	..[d]	20	0, 0
2	5,5-Dimethyl	79–82	Alc.–Sk.	$C_5H_9NO_2$	12.2	12.2	A	53	0, 0
3	4,4-Dimethyl[e]	56.5–58	Alc.–et.	.....	..	..	A	13	0, 0
4	5,5-Diethyl	55–58	Alc.–Sk.	$C_7H_{13}NO_2$	9.8	9.7	B	57	0, 0
5	5-Isobutyl-5-methyl	69–70	Alc.–Sk.	$C_8H_{15}NO_2$	8.9	8.9	A	60	0, ±
6	4,4-Dimethyl-5-propyl	50–52	Et.–Sk.	$C_8H_{15}NO_2$	8.9	9.1	A	83	0, 0
7	(2,4,4-Trimethylpentyl)[f]	116–117	Alc.–et.	$C_{11}H_{21}NO_2$	7.0	6.9	A	33	±, 0
8	5-Phenyl[g]	88–90	Alc.–Sk.	.....	..	..	B	..	+, 0
9	5-Methyl-5-phenyl	146–147	Alc.	$C_{10}H_{11}NO_2$	7.9	7.9	B	72	0, ++
10	4-Methyl-5-phenyl[h]	.....	.....	.....	..	..	..	..	++, 0
11	5-Ethyl-5-phenyl	119–120	Alc.–Sk.	$C_{11}H_{13}NO_2$	7.3	7.3	A	83	++, ++
12	4,5-Dimethyl-5-phenyl[i]	95–96[j]	Et.–Sk.	$C_{11}H_{13}NO_2$	7.3	7.3	A	83	±, +
13	5,5-Diphenyl	199–200	Alc.	$C_{15}H_{13}NO_2$	5.9	5.9	A	82	0, 0

[a] The m. p. data are for analytically pure samples; yields are based on material of reasonable purity. [b] The abbreviations used are: alc. = alcohol, et. = ether, Sk. = Skellysolve B. [c] The symbols have the following significance: 0 = no protection, ± = doubtful protection, + = partial protection at toxic levels, ++ = complete protection at toxic levels or partial protection with no side effects, +++ = complete protection with no side effects. The symbol before the comma refers to activity against electro-shock, the other refers to activity against Metrazol. [d] Thomsen, *Ber.*, **11**, 2136 (1878). [e] Homeyer, U. S. Patent 2,399,188. [f] The intermediate amino alcohol was supplied through the courtesy of Dr. Ralph Conner. [g] Schroeter, German Patent 220,852. [h] Described by Close in a separate publication, in press. [i] The intermediate amino alcohol was kindly supplied by Dr. K. E. Hamlin. [j] A lower melting form (90–91°) was also observed.

(see Tables I and II). Compounds substituted with aliphatic groups in the 4- and 5-positions were either inactive or very weakly active. 5-Phenyl derivatives, on the other hand, had fair to good activity. The activity in both the aliphatic and aromatic series was not improved by N-alkylation or N-acylation with simple acyl groups, but was increased by N-carbamylation. The most effective compound tested was 3-carbamyl-5-ethyl-5-phenyl-2-oxazolidone. It may be of interest to note that 3,5,5-trimethyl-2-oxazolidone, the 4-desoxo analog of the clinically established drug Tridione, was completely inactive.

Experimental[6]

Preparation of Intermediates.—Many of the intermediates used in this work were obtained from commercial sources and were used without further purification. Others were prepared following published procedures. The preparations given below are described in some detail because they involve new compounds or a substantially improved procedure.

1-Amino-2-methyl-2-propanol.—Concentrated ammonium hydroxide (1.5 liters) was cooled in an ice-salt-bath and stirred during the addition of 168 g. of isobutylene oxide over a 40- to 60-minute period. After standing overnight the solution was fractionated, yielding 104 g. (50%) of product, b. p. 147–153°, $n^{25}D$ 1.4439.[7]

α-Hydroxy-α-methylisocaproamide.—The procedure used by Stoughton[8] with related hydroxy amides was followed with 140 g. of 4-methyl-2-pentanone. Since the product was water soluble, it was necessary to isolate it by continuous ether extraction after pouring the reaction mixture onto cracked ice. The product was crystallized in a Skellysolve B–alcohol mixture. A total of 79.8 g. (39%), m. p. 75–78°, was obtained in several crops. The pure leaflets melted at 77–79°.

Anal. Calcd. for $C_7H_{15}NO_2$: N, 9.6. Found: N, 9.9.

1-Amino-2,4-dimethyl-2-pentanol.—Reduction of 29 g. of α-hydroxy-α-methylisocaproamide with 15.2 g. of lithium aluminum hydride in dry ether overnight gave 8.5 g. (32%) of the amino alcohol, b. p. 79–80° (12 mm.), $n^{31}D$ 1.4482.

Anal. Calcd. for $C_7H_{17}NO$: N, 10.7. Found: N, 10.9.

Preparation of Parent Oxazolidones.—All of the N-unsubstituted oxazolidones were prepared using procedures essentially identical to either method A or method B described below. The properties of the specific compounds are given in Table I.

Method A.—A mixture of 1 mole of the amino alcohol or its hydrochloride[9] with 2 moles of urea was prepared and placed in a bath at 170–180° for 20 to 30 minutes. The bath temperature was then increased to 200–210° and maintained for an additional 20 to 60 minutes. The end of the reaction could be determined by the marked decrease in gas evolution (ammonia). The cooled reaction mixture was treated with water and the product was obtained by filtration. Low-melting products were separated by extraction with ether and distillation before crystallization.

Detailed Study of Course of Reaction under Method A.—A mixture of 10 g. of 1-amino-2-methyl-2-propanol and 20 g. of urea was placed in a bath at 170° for 20 minutes. The mixture was cooled and the solid cake was recrystallized from water, yielding 4.0 g., m. p. 165–168°, and 5.7 g., m. p. 162–167° (66%). Further recrystallization brought the melting point to 169–171°.

The product decomposed slowly in boiling water with the evolution of ammonia. It was appreciably soluble in cold water, and more soluble in dilute hydrochloric acid. The compound was recovered unchanged by evaporation of the acid solution. These data indicated that the material was (2-hydroxy-2-methylpropyl)-urea, which was confirmed by analysis.

Anal. Calcd. for $C_5H_{12}N_2O_2$: C, 45.4; H, 9.2; N, 21.2. Found: C, 45.8; H, 9.1; N, 21.2.

The urea derivative (6.0 g., m. p. 169–171°) was heated at 210° for 30 minutes. Crystallization in benzene–Skellysolve B gave 4.6 g. (88%) of 5,5-dimethyl-2-oxazolidone, m. p. 70–81°. The same oxazolidone could be obtained directly from the amino alcohol by method A in a 53% yield of material melting at 72–81°. It was difficult to get a product which melted sharply; a large number of recrystallizations from ether or alcohol–Skellysolve B brought the melting point to 79–82°.

Anal. Calcd. for $C_5H_9NO_2$: N, 12.2. Found: N, 12.2.

Method B.—A solution of 2 moles of β-hydroxy ester and 3 moles of 85% hydrazine hydrate was prepared by the addition of enough alcohol to form a single phase while hot. The solution was refluxed for 4 to 6 hours. Where possible, the hydrazide was separated by filtration; in other cases, all of the solvents were removed under reduced pressure and the residue was used directly in the next step.

(6) Microanalyses by E. F. Shelberg and staff. All melting points are uncorrected.

(7) Cairns and Fletcher, THIS JOURNAL, **63**, 1034 (1941), prepared the amino alcohol in 29% yield by a somewhat different procedure and recorded the boiling point as 145–155°.

(8) Stoughton, *ibid.*, **63**, 2376 (1941).

(9) It appeared to make no difference in the reaction whether the free base or its salt were used.

TABLE II

PROPERTIES OF N-SUBSTITUTED OXAZOLIDONES

Parent compd.[a]	N-Substituent	M. p., °C.[b]	Recrystn. solvent[c]	Formula	Nitrogen, % Calcd.	Found	Yield,[b] %	Activity[d]
2	Methyl	.....[e]	.....	$C_6H_{11}NO_2$	10.8	10.6	51	0, 0
2	Carbamyl	118–120	Alc.	$C_6H_{10}N_2O_3$	17.7	17.4	48	0, 0
2	Acetyl	42.5–44	Alc.–Sk.	$C_7H_{11}NO_2$	8.9	9.0	75	0, 0
2	Carbethoxy	54–55.5	Et.	$C_8H_{13}NO_4$	7.5	7.6	79	0, 0
2	Isoamyl	.....[f]	.....	$C_{10}H_{19}NO_2$	7.6	7.6	75	0, 0
2	Isovaleryl	49.5–51	Sk.	$C_{10}H_{17}NO_3$	7.0	6.9	70	0, 0
2	Trimethylacetyl	80–81	Sk.	$C_{10}H_{17}NO_3$	7.0	6.9	48	0, 0
4	Methyl	.....[g]	.....	$C_6H_{15}NO_2$	8.9	8.6	68	0, +
4	Carbamyl	82–84	Bz.–Sk.	$C_8H_{14}N_2O_3$	15.1	15.2	78	++, +
6	Carbamyl	102–105	Alc.	$C_9H_{16}N_2O_3$	14.0	14.1	55	+, +
6	Acetyl	29.5–30	Sk.	$C_{10}H_{17}NO_3$	7.0	7.1	80	0, 0
8	Carbamyl	132.5–133.5	Alc.	$C_{10}H_{10}N_2O_3$	13.6	13.7	67	++, +
9	Carbamyl	113–114	Alc.	$C_{11}H_{12}N_2O_3$	12.7	12.9	54	+, ++
10	Methyl[h]	.....	.....	.....	..	..	..	0, 0
11	Methyl	.....[i]	.....	$C_{12}H_{15}NO_2$	6.8	6.7	78	++, ++
11	Carbamyl	112–113	Bz.–Sk.	$C_{12}H_{14}N_2O_3$	12.0	11.7	63	+++, ++
13	Carbamyl	181–185	Alc.	$C_{16}H_{14}N_2O_3$	9.9	9.8	68	0, 0
13	Acetyl	142–143	Alc.	$C_{17}H_{15}NO_3$	5.0	5.1	76	0, 0

[a] The numbers correspond to the compound numbers in Table I. [b] The m. p. and b. p. data are for analytically pure samples; yields are based on material of reasonable purity. [c] The abbreviations used are: alc. = alcohol, bz. = benzene, et. = ether, Sk. = Skellysolve B. [d] The symbols have the same significance as in Table I. [e] B. p. 128–132° (24 mm.); $n^{26}D$ 1.4420. [f] B. p. 102–104° (0.3 mm.); $n^{27}D$ 1.4450. [g] B. p. 92–94° (0.3 mm.); $n^{25}D$ 1.4535. [h] Described by Close in a separate publication, in press. [i] B. p. 141–142° (0.25 mm.); $n^{25}D$ 1.5282.

The hydrazide was dissolved in a slight excess of 1 *N* hydrochloric acid, covered with ether, and cooled below 10° during the addition of a slight excess of sodium nitrite. The ether layer was then separated, dried, diluted with benzene and warmed cautiously on the steam-bath until nitrogen evolution had ceased. The solvents were then removed completely and the product was recrystallized from a suitable solvent.

Acylation and Alkylation of Parent Oxazolidones.—All N-carbamyl derivatives were prepared in essentially the same manner by using method C below. The preparation of other N-substituted compounds is described in detail. The properties of all the compounds are given in Table II, and to avoid duplication data included in the table are, in general, not given below.

Method C.—One mole of the oxazolidone dissolved in benzene was refluxed overnight with 1 equivalent of sodium powder. The suspension of the sodio derivative was added slowly to 5 moles of phosgene dissolved in benzene and cooled in ice.[10] The mixture was refluxed for one hour with provision to trap the evolved phosgene; residual phosgene was removed by passing a stream of air through the mixture. The material was finally poured into a large excess of concentrated ammonium hydroxide. The product was isolated from the benzene layer and recrystallized from a suitable solvent.

3,5,5-Trimethyl-2-oxazolidone.—The procedure described earlier[11] for the alkylation of benzoxazolone derivatives was followed except that to avoid loss of the water soluble product no water was added after removal of the Cellosolve. An excess of methyl bromide gas was used as the alkylating agent; the sodium bromide formed was removed by filtration. Processing gave 51% of product boiling at 130–150° (25 mm.), $n^{27}D$ 1.4390, together with 29% of starting material, b. p. 90–110° (0.2 mm.).

5,5-Dimethyl-3-isoamyl-2-oxazolidone.—The procedure described[11] was used to give 75% of the product boiling at 102–104° (0.35 mm.), $n^{27}D$ 1.4433.

3-Acetyl-5,5-dimethyl-2-oxazolidone.—A solution of 15 g. of dimethyloxazolidone in 25 cc. of acetic anhydride was heated on a steam-bath overnight. The material was then fractionated. The product (15.3 g.) boiled at 127–135° (15 mm.) and solidified in the receiver. A second fraction (2.1 g.) boiling at 135–160° (15 mm.) was shown to contain starting material.

(10) This inconvenient manipulation was avoided in later runs by adding the phosgene solution all at once to a cold suspension of the sodio oxazolidone with efficient stirring.

(11) Ref. 4a, method C.

5,5-Dimethyl-3-isovaleryl-2-oxazolidone.—Dimethyloxazolidone (9.2 g.) was dissolved in 14.5 g. of isovaleryl chloride and 20 cc. of pyridine. The solution was warmed overnight on a steam-bath. The reaction mixture was poured into water and the product was extracted with ether. After washing the ether solution with water and sodium bicarbonate solution, it was concentrated and the residue was distilled. The product (11.0 g.) was collected at 137–141° (13 mm.) and solidified in the receiver.

5,5-Dimethyl-3-trimethylacetyl-2-oxazolidone.—The procedure described for the isovaleryl derivative above was followed. Two liquid phases were present throughout the reaction. Distillation gave 48% of product boiling at 123–126° (12 mm.) which solidified in the receiver.

3-Carbethoxy-5,5-dimethyl-2-oxazolidone.—The sodio derivative was prepared from 9.2 g. of dimethyloxazolidone by refluxing overnight with 1.84 g. of sodium powder suspended in 100 cc. of dry benzene. Ethyl chlorocarbonate (11.5 cc.) was added dropwise to the cooled suspension, after which the reaction mixture was refluxed briefly, cooled and treated with sufficient water to dissolve the inorganic salt. The organic layer yielded 10.2 g., m. p. 52–55°, and 1.7 g., m. p. 50–54°.

5,5-Diethyl-3-methyl-2-oxazolidone.—The sodio derivative of diethyloxazolidone was prepared by dissolving 5.72 g. in 200 cc. of dry benzene containing 0.92 g. of sodium powder. The mixture was refluxed for 6 hours, after which it was treated with 3.6 cc. of dimethyl sulfate and refluxed with stirring for 90 minutes. Water was added; the organic layer was separated and washed with dilute sodium hydroxide solution, water, dilute hydrochloric acid, and again with water. Concentration and fractionation in a modified Claisen flask gave 4.3 g. of product boiling at 94–98° (0.3 mm.), $n^{25}D$ 1.4535. There was no higher boiling residue in the distilling flask corresponding to unreacted starting material.

An attempt to carry out the reaction in absolute alcohol with sodium ethoxide as the condensing agent gave only 21% of the desired material.

3-Acetyl-4,4-dimethyl-5-propyl-2-oxazolidone.—4,4-Dimethyl-5-propyl-2-oxazolidone (7.9 g.) was refluxed for 65 hours with 10 cc. of acetic anhydride. The reaction mixture was poured into water and allowed to stand with occasional shaking to destroy excess anhydride. The product was taken up in ether, washed with sodium bicarbonate, and distilled; 8.0 g., b. p. 135–138° (12 mm.), $n^{25}D$ 1.4600, was obtained and crystallized upon standing. When the reflux time was decreased to 20 hours, the yield fell to 37% with 47% of the starting material recovered.

5-Ethyl-3-methyl-5-phenyl-2-oxazolidone.—The proce-

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

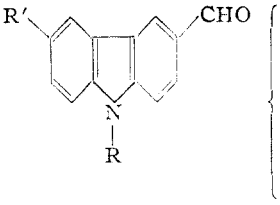
[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, RADIUM INSTITUTE, UNIVERSITY OF PARIS]

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

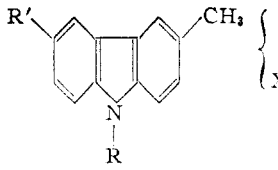


I, R = CH_3 R′ = H
II, R = *n*-C_4H_9 R′ = H
III, R = *i*-C_5H_{11} R′ = H
IV, R = *n*-C_4H_9 R′ = CH_3
V, R = CH_3 R′ = Br
VI, R = *n*-C_4H_9 R′ = Br
VII, R = CH_3 R′ = NO_2
VIII, R = *n*-C_4H_9 R′ = NO_2
IX, R = *i*-C_5H_{11} R′ = NO_2

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).