2. A series of diethylaminoethoxyethanols have been prepared and some of their physical properties determined. Two members of this series have not been reported previously.

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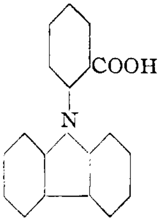
Stereochemistry of N-Phenylpyrroles. XXIX.[1] Preparation and Properties of *o*-N-Carbazyl- and *o*-N-(3-Nitrocarbazyl)-benzoic acid

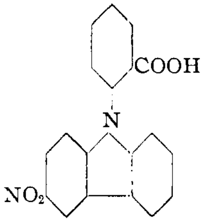
BY W. I. PATTERSON[2] AND ROGER ADAMS

A discussion of the optical isomerism of substituted phenylpyrroles and dipyrryls[3] has been given in previous papers and representative compounds of both classes have been prepared and resolved (III and IV). The experimental evidence all pointed to the conclusion that the isomerism is essentially of the same type and due to essentially the same causes as are found in substituted diphenyls.

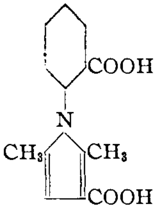
The present investigation has involved the extension of this work to certain substituted N-phenylcarbazoles. In *o*-N-carbazylbenzoic acid (I) there is a symmetrical substitution of the pyrrole ring and, therefore, the compound should be resolvable only if the nitrogen atom retains a more or less fixed tetrahedral structure. No resolution was accomplished. On the other hand, if a substituting group is introduced into the carbazole nucleus, unsymmetrical substitution of the pyrrole is present and substitution conditions resembling those necessary for resolution in the diphenyl series obtain. The *o*-(3-nitrocarbazyl)-benzoic acid (II) was resolved into enantiomorphic forms. The fact that the introduction of a substituting group so far removed from the carbazole nitrogen atom is all that is necessary to render the molecule capable of being resolved, is a potent argument against the probability that optical activity is due to the nitrogen atom.



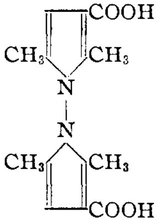
I



II



III



IV

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[1] For the last paper, XXVIII, see Kleiderer and Adams, THIS JOURNAL, **55**, 716 (1933).

[2] The experimental work was done by W. I. Patterson and is part of his thesis for the Degree of Doctor of Philosophy at the University of Illinois.

[3] Bock and Adams, THIS JOURNAL, **53**, 374, 3519 (1931); Chang and Adams, *ibid.*, **53**, 2353 (1931).

The active forms of *o*-(3-nitrocarbazyl)-benzoic acid are racemized very slowly at room temperature in chloroform, but readily by warming in chloroform, alcohol, or sodium hydroxide solution (see Table I). Racemization takes place much more easily than in the active forms of N-2-carboxyphenyl)-2,5-dimethyl-3-carboxypyrrole (III), indicating that the methyls have a greater interfering effect than the CH of the benzene nucleus in compounds of this type.

Experimental

The carbazylbenzoic acids were prepared by condensation of *o*-iodobenzoic acid with carbazole or 3-nitrocarbazole in boiling nitrobenzene with solid potassium hydroxide.

***o*-Carbazylbenzoic Acid and its Salts.**—This compound was prepared in 66% yields by the method of Eckert, Seidel and Endler;[4] m. p. when pure 184°. The brucine salt was formed in ethyl acetate. On long standing, large colorless rhombohedra separated, m. p. 214–215°. No resolution was observed after many trials. In one experiment an ethyl acetate solution of the brucine salt was evaporated slowly at room temperature and six separate fractions of salt taken. The rotation of the mother liquor was determined after each removal and an allowance was made for each change in concentration. The rotation of the solution remained practically constant. An alcoholic solution at 0° with concentrated hydrochloric acid gave, on addition of water, colorless white needles of the inactive acid.

The strychnine, morphine, quinine and dicinchonine salts were also prepared, but in no instance could two different salts be obtained. The method of preparation of the salts and the constants for them are given in Table II.

***o*-(3-Nitrocarbazyl)-benzoic Acid and its Resolution.**—The compound was prepared by the condensation of *o*-iodobenzoic acid with 3-nitrocarbazole[5] by the method of Hayashi.[6] The yields were poor, 10–35%. The product was purified by repeated recrystallization from hot glacial acetic acid followed by one crystallization from alcohol after treatment with norite. Lemon yellow needles were obtained, m. p. 226–227° (corr.) (Hayashi 230°).

A hot solution of 2.2 g. of *o*-(3-nitrocarbazyl)-benzoic acid in 20 cc. of anhydrous ethyl acetate was added to a hot solution of 2.6 g. of anhydrous brucine in 60 cc. of anhydrous ethyl acetate. After standing for twenty-four hours at room temperature, a crystalline precipitate weighing 2.5 g. resulted. This fraction was purified by dissolving in chloroform and adding an excess of absolute alcohol. After twenty-four hours at room temperature the product had separated as large lemon colored crystals, m. p. 246–247°.

Rotation. 1.2574 g. made up to 25 cc. with chloroform at 20° gave α_D $-1.05°$; $l = 2$; $[\alpha]^{20}_D$ $-10.44°$.

Anal. Calcd. for $C_{42}H_{38}O_8N_4$: N, 7.71; C, 69.39; H, 5.27. Found: N, 7.78; C, 69.29; H, 5.33.

The filtrate from the 2.5 g. fraction was allowed to evaporate to half its volume and a small amount of crystalline material which separated was filtered and consisted primarily of the less soluble salt. The more soluble salt remained as a resin after all the solvent had been evaporated from the filtrate. All attempts to crystallize the salt failed. The ro-

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(4) Eckert, Seidel and Endler, *J. prakt. Chem.*, **104**, 85 (1922).

(5) Ruff and Stein, *Ber.*, **34**, 1677 (1901).

(6) Hayashi, *Bull. Inst. Phys.-Chem. Res.* (*Tokyo*), **9**, 970 (1930).

TABLE I

Acid	Solvent	Concn.[c]	α^{20}_D	$[\alpha]^{20}_D$	Temp., rac., °C.	k	Av. deviation	Half-life, min.
d	Chloroform	1.78	+0.15	+ 7.0	60	0.01	0.0006	72
l	Abs. alcohol	1.80	−1.51	−45.0	78.5	.254	.034	29
l	0.1 *N* NaOH	0.88	−0.91	−51.7	27[a]	.00032	.0001	2190
d	Na in alcohol[b]	0.80	+1.08	+67.3	27[a]	.00065	.00002	1080

[a] Completely racemized in 140 and 97 hrs., respectively. [b] 0.5 g. of sodium in 50 cc. of absolute alcohol. [c] Grams per 100 cc.

TABLE II

ALKALOIDAL SALTS[a] OF *o*-CARBAZYLBENZOIC ACID

Alkaloid	Wt., g.	Solv. (dry)	Solv. cc.	Acid, wt.	Solv. (dry)	Vol., cc.	Formula	Concn.[b]	α^{25}_D[c]	$[\alpha]^{25}_D$	Calcd. N, %	Found N, %
Brucine	2.7	Eth. ac.	70	2.0	Eth. ac.	10	$C_{42}H_{39}O_6N_3$	0.63	+0.23	+ 18.2	6.16	6.35
Strychnine	2.5	$CHCl_3$	25	2.1	Eth. ac.	25	$C_{40}H_{35}O_4N_3$	1.61	−0.53	− 16.4	6.76	6.52
Morphine	2.1	CH_3OH	30	2.0	Eth. ac.	20	$C_{36}H_{34}O_6N_2$	0.81	−0.43	− 54.0[c]	4.75	4.94
Quinine	0.8	Eth. ac.	25	0.7	.....	..	$C_{39}H_{37}O_4N_3$	0.43	−0.46	− 26.5	6.87	6.84
Cinchonine	0.9	$CHCl_3$	200	1.7	.....	..	$C_{57}H_{48}O_5N_4$	0.35	+1.15	+166.2	6.45	6.39

[a] The salts crystallized from the solutions after standing at room temperature for a few hours, with the exception of the dicinchonine salt which required a week.

[b] Grams per 100 cc.

[c] Rotations were measured at 25° and in chloroform solution with sodium light in tubes 2 dm. long; for the morphine salt dioxane was the solvent used.

tation of the crude material varied from $[\alpha]_D^{20}$ +21.7 to +46.7°. It decomposed at 160–180°.

Rotation. 0.3104 g. made up to 25 cc. with chloroform at 20° gave α_D +0.90°; $l = 2$; $[\alpha]_D^{20}$ +21.7°.

d- and l-o-(3-nitrocarbazyl)-benzoic Acid.—The active acids were liberated from the individual salts by shaking with ether and 6 *N* hydrochloric acid in a separatory funnel until complete solution of the solid matter occurred. Regardless of the rate of evaporation of the ether solution, either moist or dry, an oil, sometimes containing a small amount of crystalline material, was always obtained when the evaporation was carried out at room temperature.[7] Alcohol and chloroform gave similar results. After long standing in a desiccator the oil gradually changed to a glassy solid which, on powdering, melted at 225–226°, and gave a negative test for brucine with concentrated nitric acid. The rotation of the acid thus obtained from different samples of the less soluble salt varied from $[\alpha]_D^{20}$ −56° to $[\alpha]_D^{20}$ −62°.

Rotation. *l*-Acid, 0.2924 g. made up to 25 cc. with chloroform at 20° gave α_D −1.45°; $l = 2$; $[\alpha]_D^{20}$ −62°.

Anal. Calcd. for $C_{19}H_{12}O_4N_2$: N, 8.44. Found: N, 8.36.

The *d*-acid obtained similarly from the crude more soluble salt was also an oil which gradually solidified. A rotation was taken on the crude acid melting at 224–225°. Different samples of the salt produced acids with widely variable rotations, but the rotation was always positive.

Rotation. *d*-Acid, 0.2497 g. made up to 16.1 cc. with chloroform at 20° gave α_D +1.26°; $l = 2$; $[\alpha]_D^{20}$ +40.57°.

Racemization Experiments.—Data on racemization tests on the active acid are given in Table II.

Summary

1. *o*-N-Carbazylbenzoic acid and *o*-N-(3-nitrocarbazyl)-benzoic acid were prepared by condensing carbazole or 3-nitrocarbazole with *o*-iodobenzoic acid.

2. *o*-N-(3-Nitrocarbazyl)-benzoic acid was resolved into enantiomorphs but *o*-N-carbazylbenzoic acid could not be resolved.

3. With a fixed asymmetric structure for nitrogen both compounds should be resolvable. It appears that the fundamental conditions found necessary for resolution of diphenyl compounds hold in this series.

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(7) After the alcoholic solution of the oil had been boiled for a few minutes, dilution with water until a permanent clouding occurred, followed by cooling, gave a crystalline acid which melted at 226–227°. This crystalline acid always possessed optical activity, provided that the heating was not continued too long.