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HYDRAZIDES OF DIPHENIC AND 4-NITRODIPHENIC ACIDS AND SOME OF THEIR REACTIONS

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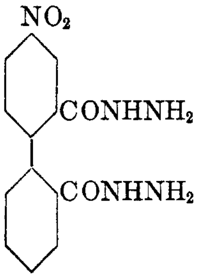
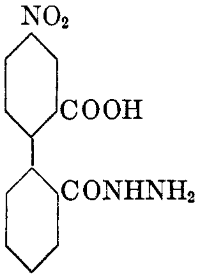
The preparation and study of the diphenic acid hydrazides began comparatively recently. Kalb and Gross (1) obtained the dihydrazide; one of the present authors (2) obtained the monohydrazide and the secondary hydrazide.

Application of the Curtius degradation to the di- and mono-hydrazides was described in a recent work (3). The dihydrazide yielded 2,2′-diphenyleneurea and 2,2′-diaminobiphenyl. The monohydrazide, degraded in alcohol, produces phenanthridone; in alcoholic hydrogen chloride, N-carbethoxyphenanthridone. Similar reactions and preparations have now been carried out on 4-nitrodiphenic acid.

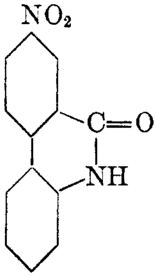
By the action of hydrogen peroxide on 2-nitrophenanthraquinone, an extension of the method of Chapman (4) for phenanthraquinone, 4-nitrodiphenic acid was obtained, which was converted to the dimethyl ester and anhydride. By the action of hydrazine on these derivatives, the dihydrazide (I) and the monohydrazide (II) were obtained. The amount of monohydrazide (II) which is obtained varies between 81–90% of the theoretical; the other isomer could not be isolated from the mother liquors.



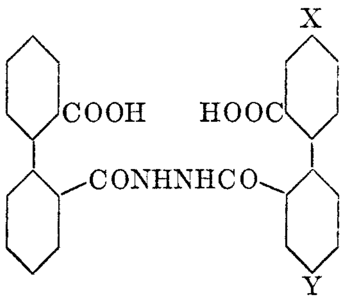
I



II



III



IV:X = H; Y = H
V:X = NO_2; Y = H
VI:X = H; Y = NO_2

By the action of ammonia, Moore and Huntress (5) obtained from 4-dinitrodiphenic anhydride the two amides, that corresponding to the hydrazide (II) in 23% yield, and the isomer in 32% yield.

The structure (I) of the hydrazide obtained by us was determined by degradation with nitrous acid. It produced the same phenanthridone (III) derivative that is formed by the Hofmann degradation of the structurally analogous amide obtained by Moore and Huntress. When heated *in vacuo*, this hydrazide is transformed into a high-melting isomer which may be N-amino-4-nitrodiphenimide.

When the diphenic acid monohydrazide is treated with diphenic anhydride, a symmetrically disubstituted hydrazine is formed which is also a dibasic acid (IV); this substance is also formed in small amount in the preparation of diphenic monohydrazide. The structure of this compound was confirmed by obtaining the dimethyl ester and by determination of the carboxyl and hydrazide groups. A similar substance is formed by the action of 4-nitrodiphenic anhydride, but in this case the two isomers (V) and (VI) are obtained in yields of 18–20%, respectively. The structure of isomer (V) turns out to be the same as that obtained by the action of diphenic anhydride on 4-nitrodiphenic hydrazide (II).

Acetic anhydride reacts readily with these disubstituted hydrazides (IV; V; VI) eliminating from them two molecules of water with the production of crystalline substances of very high melting point, which are insoluble in almost all solvents. If, instead of the free acid (IV), the methyl ester is treated with acetic anhydride, this reaction does not occur, and a monoacetyl derivative is obtained.

Stollé (6) found that treatment of the N,N′ disubstituted hydrazines with dehydrating agents led to formation of cyclic oxadiazoles, and we think that a similar reaction prevails here with the simultaneous formation of the anhydride of the dibasic acid. Most of the oxadiazoles prepared by Stollé were very resistant to the action of alkali. Our preparations hydrolyze relatively easily, yielding the original diphenic acids.

EXPERIMENTAL

4-Nitrodiphenic acid. A sample of 6 g. of 2-nitrophenanthraquinone, 50 cc. of acetic acid, and 50 cc. of hydrogen peroxide (20 volumes strength) was refluxed for 3 hours. The reaction mixture was made alkaline with sodium hydroxide, a small precipitate was filtered off, and the mixture was acidified to Congo red, precipitating 4-nitrodiphenic acid, which melted at 250°; yield 75–80%.

Dimethyl 4-nitrodiphenate. A sample of 2 g. of the acid was dissolved in cold methanol saturated with anhydrous hydrogen chloride. After standing 24 hours, the mixture was concentrated to half its volume, precipitating the diester. Following recrystallization from ethanol, the melting point was 96°; yield 90%.

Anal. Calc'd for $C_{16}H_{13}NO_6$: C, 60.95; H, 4.12.
Found: C, 60.81; H, 4.55.

4-Nitrodiphendihydrazide (I). A sample of 0.85 g. of the diester and 1 cc. of hydrazine monohydrate in 10 cc. of absolute ethanol was heated under reflux for 4 hours. The dihydrazide was precipitated by concentration of the reaction mixture. The melting point following recrystallization from ethanol was 209°; yield 45%. It is soluble in hydrochloric acid, and reduces silver nitrate.

Anal. Calc'd for $C_{14}H_{13}N_5O_4$: C, 53.33; H, 4.12; N, 22.22.
Found: C, 53.60; H, 4.36; N, 21.80.

Monohydrazide of 4-nitrodiphenic acid (II). A sample of 1 g. of 4-nitrodiphenic anhydride was treated with 1 cc. of 50% hydrazine hydrate, with chilling. Following the addition, the mixture was heated on the steam-bath for an hour. The solution was thrown into water and, with vigorous stirring, the monohydrazide was precipitated with diluted (1:2) hydrochloric acid. The precipitate was filtered off and recrystallized from ethanol, melting at 200°; yield 81–90%. It dissolves in alkalies, carbonates and bicarbonates, and likewise in acids when they are in slight excess.

Anal. Calc'd for $C_{14}H_{11}N_3O_5$: C, 55.81; H, 3.65; N, 13.95.
Found: C, 55.98; H, 3.94; N, 14.26.

Curtius degradation of 4-nitrodiphenmonohydrazide (II) to 7-nitrophenanthridone (III). A sample of 0.8 g. of the monohydrazide was dissolved in 10 cc. of 10% hydrochloric acid and the solution was covered with ether. The solution was chilled with ice and 5 cc. of 10% sodium nitrite solution was then introduced. The precipitate of azide readily passed into the ether layer on shaking. The aqueous layer was then separated and the ether thrown into dilute ethanol. The azide decomposed spontaneously and, on concentration, yellow needles of 7-nitrophenanthridone were obtained. After recrystallization from acetic acid or sublimation, it melted at 290° (Moore and Huntress: 284–285°).

Anal. Calc'd for $C_{13}H_8N_2O_3$: C, 65.00; H, 3.53; N, 11.83.
Found: C, 65.01; H, 3.62; N, 11.87.

N-Amino-4-nitrodiphenimide. A sample of 1 g. of the nitrodiphenic acid monohydrazide was placed in a large test tube and heated *in vacuo* to 200°. A $CaCl_2$ tube absorbed the moisture given off. At the outset there was an active decomposition which ended in a short while. The mixture was cooled and the precipitate digested with alcohol. It was filtered and recrystallized from acetic acid, melting at 319°; yield 50%.

Anal. Calc'd for $C_{14}H_9N_3O_4$: C, 59.36; H, 3.18; N, 14.84.
Found: C, 59.47; H, 3.17; N, 14.87.

N,N'-bis-[o(2-carboxyphenyl)benzoyl]hydrazine (IV). A sample of 2 g. of diphenic acid monohydrazide and 1.76 g. of diphenic anhydride in 20 cc. of absolute ethanol was heated under reflux for two hours. On chilling, the di-acid precipitated. It was filtered and, by evaporation of the mother liquor, a new fraction was obtained. On recrystallization from alcohol it formed hexagonal prisms or plates which melted at 253° with decomposition; yield 75–80%. The same product was obtained as an insoluble residue in the preparation of the diphenic hydrazide by the method described by Labriola (2).

Anal. Calc'd for $C_{28}H_{20}N_2O_6$: C, 70.00; H, 4.16; N, 5.83.
Found: C, 70.20; H, 4.35; N, 5.90.

Anal. Calc'd for $C_{26}H_{18}N_2O_2(CO_2H)_2$: two equivalents 448.
Found: 438, 424.

Determination of nitrogen in N,N'-bis-[o(2-carboxyphenyl)benzoyl]hydrazine (IV). A sample of 158.6 mg. of di-acid was dissolved in 10 cc. of 40% KOH in a closed apparatus connected with an azotometer. Air was first eliminated from the apparatus with a strong current of CO_2, and then 6 cc. of saturated aqueous potassium ferricyanide was run in. The nitrogen evolved was collected and the reaction mixture was heated gently and acidified with sulfuric acid. The nitrogen was then displaced in a current of CO_2 until constant volume was reached. A volume of 8 cc. (27°/760 mm.) was obtained.

Anal. Calc'd for $C_{14}H_{10}O_3$-NH-NH-$C_{14}H_{10}O_3$: N, 5.83.
Found: N, 5.75, 6.24.

N,N'-bis-[o-(2-carbomethoxyphenyl)benzoyl]hydrazine. A sample of 5 g. of (IV) was dissolved in methanol and saturated with hydrogen chloride. After 24 hours a precipitate was obtained; purified from ethanol, m.p. 182°; yield 83%.

Anal. Calc'd for $C_{30}H_{24}N_2O_6$: C, 70.86; H, 4.72; N, 5.51.
Found: C, 70.99; H, 4.90; N, 5.50.

The saponification of the diester produces the original acid.

N-[o-(2-carboxyphenyl)benzoyl]-N'-[o-(2-carboxy-4-nitrophenyl)benzoyl]hydrazine (V) and

N-[o-*(2-carboxyphenyl)benzoyl*]*-N′-*[*2-(2′-carboxyphenyl)-5-nitrobenzoyl*]*hydrazine (VI).* A sample of 2 g. of 4-nitrodiphenic anhydride and 1.9 g. of the appropriate monohydrazide in 25 cc. of absolute ethanol was refluxed for 2 hours. On chilling, the isomer of m.p. 261° came out, and the m.p. was unchanged by subsequent recrystallizations; yield 0.7 g. (18%). On concentration of the alcoholic solution, the other isomer precipitated, and after successive recrystallizations reached the m.p. 252°; yield, 0.8 g. (20%).

A sample of 0.5 g. of 4-nitrodiphenic acid monohydrazide and 0.38 g. of the diphenic anhydride was heated with reflux for two hours. On concentrating and chilling, the crystals of the hydrazide came out, m.p. 261° after recrystallization from ethanol. On mixture with the isomer of the same m.p. previously obtained, no depression of the m.p. was observed.

Anal. Calc'd for $C_{28}H_{19}N_3O_8$: C, 64.00; H, 3.61; N, 8.00.
Found, isomer of m.p. 261°: C, 64.12; H, 3.81; N, 8.18.
Found, isomer of m.p. 252°: C, 64.40; H, 4.04; N, 8.01.

"Oxadiazole" derivatives of the N,N′ disubstituted hydrazines. Oxadiazole(A). A sample of 10 g. of (IV) was boiled for 15–20 minutes with acetic anhydride. It dissolved, but soon formed a rather heavy precipitate. It was filtered off, washed repeatedly with hot alcohol and a portion was recrystallized from nitrobenzene, yielding prisms melting at 400°; yield 95%.

Anal. Calc'd for $C_{28}H_{16}N_2O_4$: C, 75.67; H, 3.60; N, 6.30.
Found: C, 75.67; H, 3.84; N, 6.16.

Oxadiazole (B). This compound was prepared similarly from V. Rectangular plates were formed which melted at 351°.

Anal. Calc'd for $C_{28}H_{15}N_3O_6$: C, 68.71; H, 3.06; N, 8.58.
Found: C, 68.67; H, 3.40; N, 8.75.

Oxadiazole (C). This compound was prepared from VI in the form of small plates which melted at 360°.

Anal. Calc'd for $C_{28}H_{15}N_3O_6$: C, 68.71; H, 3.06; N, 8.58.
Found: C, 68.77; H, 3.29; N, 8.71.

These oxadiazoles do not possess acetyl groups. All of the above described oxadiazoles heated with an excess of 10% alcoholic KOH for 30 minutes are converted into the original acids (mixed m.p.).

Acetylation of N,N′-bis-[o-*(2-carbomethoxyphenyl)benzoyl*]*hydrazine.* A sample of 2 g. of the di-ester was boiled for 4 hours with an excess of acetic anhydride. The excess was evaporated off and the residue crystallized from alcohol, m.p. 141–142°; yield 1.3 g.

Anal. Calc'd for $C_{32}H_{26}N_2O_7$: C, 69.81; H, 4.72; N, 5.09; CH_3CO, 7.81.
Found: C, 69.98; H, 4.74; N, 5.07; CH_3CO, 7.78.

SUMMARY

The hydrazides of 4-nitrodiphenic acid were prepared and the structure of the single monohydrazide obtained was determined.

N,N′-bis-[*o*-(2-carboxyphenyl)benzoyl]hydrazines were prepared from the substituted diphenic acids and it was shown that treatment with acetic anhydride removes water, forming products that may be oxadiazoles.

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