[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY AND THE UNIVERSITY OF GEORGIA]

SUCCINO- AND PHTHALO-HYDROXAMIC ACIDS

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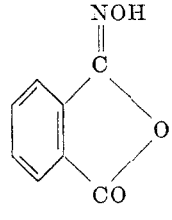
The object of this investigation was to study the rearrangement of succino- and phthalo-hydroxamic acids. The first of these compounds is known (1, 9) but not the second, although its isomers isophthalo- and terephthalo-hydroxamic acids have both been reported (2). Rearrangement of appropriate derivatives of the last two compounds resulted in formation of polyphenyleneureas: n $C_6H_4(CONNa—OCOPh)_2$ → $(—C_6H_4—NHCONH—)_n$. Rearrangement of hydroxamic acids of other dicarboxylic acids (adipic, sebacic) also has been shown to yield polyureas (1).

Although phthalohydroxamic acid has not been reported, its monohydroxylamine analog is known, namely, *o*-carboxybenzohydroxamic acid (3, 10). It was the product of reaction of phthalic anhydride and hydroxylamine.

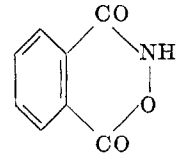
In the present work it was found that although sodium phthalohydroxamate was obtainable by interaction of phthalic ester, hydroxylamine, and sodium ethoxide, precautions were necessary to prevent formation of "phthaloxime".[1] Thus, temperature control (5°) is important and temperature must not be allowed to rise spontaneously, the solvent must be nearly anhydrous, and the salt must not be allowed to stand in moist air. The salt gave the ferric chloride color reaction typical of hydroxamic acids but it contained less sodium than that calculated for the disodium salt. Attempts to purify it by crystallization were unsuccessful, as were attempts to obtain the free phthalohydroxamic acid; instead, phthaloxime was obtained when the salt was acidified. Treatment of a concentrated aqueous solution of the salt with carbon dioxide yielded red plates, and further acidification with hydrochloric acid yielded phthaloxime. The colored substance was probably a salt of phthaloxime, which is known to form several colored salts (5).

It was found that the high temperature employed by Lossen (2) in the prep-

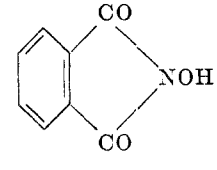
[1] The structure of "phthaloxime", also obtainable from phthalic anhydride or phthaloyl chloride and hydroxylamine, has not been settled. Structures A, B, and C fit the analytical data, but Brady, *et al.* (4) have eliminated B by the isolation of O-methylhydroxylamine by methylation of phthaloxime, then hydrolysis. Other references relating to the structure are listed in reference 5.



A

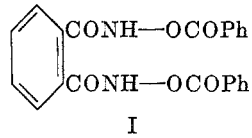


B

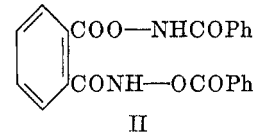


C

aration of the benzoyl derivatives of iso- and tere-phthalohydroxamic acids was not suitable for the preparation of the corresponding derivatives of either phthalo- or succino-hydroxamic acids since these substances tended to form heterocyclic compounds easily (6). Benzoylation was accomplished by the Schotten-Baumann method at approximately 0°, but the benzoyl derivative prepared from crude sodium phthalohydroxamate could not be purified by conventional crystallization techniques due to facile cyclization to form "benzoylphthaloxime" (5). The product was separable, however, into two fractions by washing with cold alcohol. The insoluble fraction proved to be phthalo(benzoylhydroxamic) acid (I). The alcoholic filtrate contained an isomeric substance,



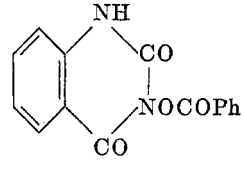
I



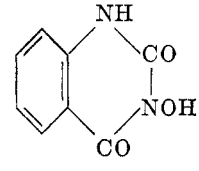
II

benzo[(N-benzoxyphthalamoyl)hydroxamic] acid (II), which separated on dilution with water. Both I and II, when freshly prepared, were soluble in alkali and neither gave a coloration with aqueous ferric chloride.

That I possessed the conventional hydroxamic structure was evident by a study of its rearrangement. When an aqueous solution of its disodium salt was heated a precipitate formed which proved to be 3-benzoxy-1*H*-quinazolinedione (III). This result follows logically by assuming that one of the —CON(Na) OCOPh groups cleaved and became a transient —NCO group, which then added to the other original group to form III. Alkaline hydrolysis of III gave rise to benzoic acid and 3-hydroxy-1*H*-quinazolinedione (IV). III could be



III



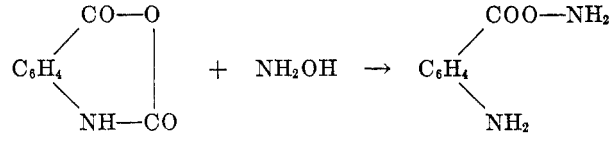
IV

regenerated from IV by benzoylation. IV was soluble in cold alkali. It gave a red color with aqueous ferric chloride, and it reacted with hydrazine to produce the known 3-amino-1*H*-quinazolinedione (7). IV was stable both toward a refluxing 10% sodium hydroxide solution and concentrated hydrochloric acid at 160°. That IV was of the structure shown (or a tautomer) was proved by its synthesis from *o*-carbethoxyphenylurethan, hydroxylamine, and sodium ethoxide.

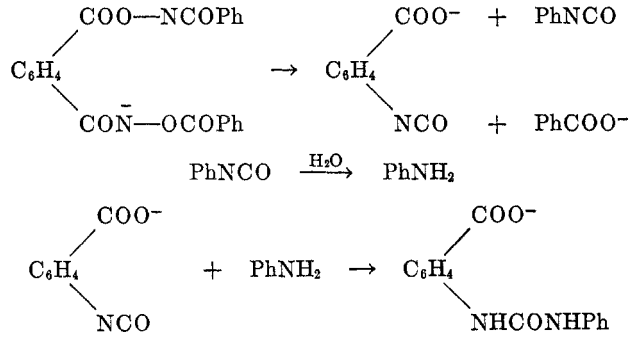
When I was rearranged in the presence of a small excess of alkali IV was formed directly, but a large excess of alkali caused the hydrolysis of I.

The isolation of II as well as I from the mixture resulting from benzoylation of phthalohydroxamic acid suggests that the hydroxamic acid contained not only material of the structure $C_6H_4(CONHOH)_2$ but also HONHCO—C_6H_4-

COO—NH_2. This was quite unexpected. The unusual feature of this is acylation at the oxygen of hydroxylamine, although it is not without precedent since Scott and Wood (8) also found O-acylation in the reaction of hydroxylamine with isatoic anhydride:

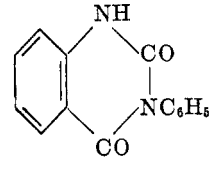


Both hydroxylamine residues in II exist in "dihydroxamic" structures, RCO—NH—OCOR′, the sodium salt of which would rearrange into RNCO and R′COONa. This course of rearrangement was indeed followed by II when the salt was heated briefly:

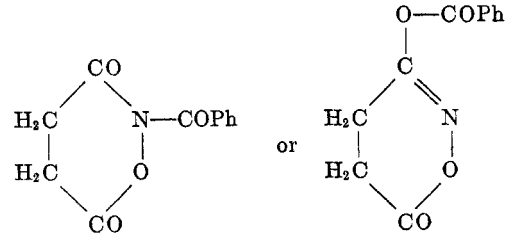


Precipitation of *o*-(3-phenylureido)benzoic acid, PhNHCONH—C_6H_4—COOH, resulted on acidification of the cooled solution.

If the sodium salt of II was heated for a longer time, or if a solution of sodium *o*-(3-phenylureido)benzoate was heated, the product was 3-phenyl-1*H*-quinazolinedione (V) (7).



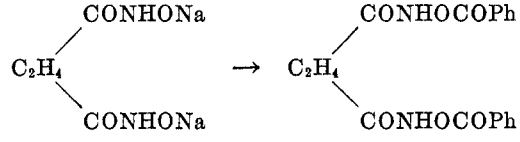
V



VI

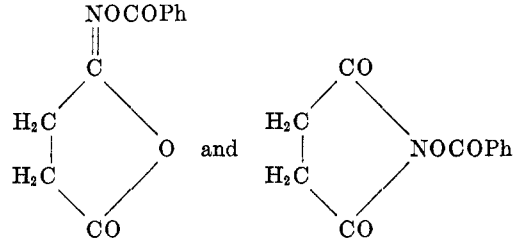
In the succinic series, cyclization to the succinylhydroxylamine derivative (VI) was reported (1) during benzoylation of succinohydroxamic acid with benzoyl chloride in pyridine. Our results confirmed this. Also, the same substance was obtained (10) by treatment of 3-carboxypropiono(benzoylhydroxamic) acid with benzoyl chloride.

Since succinylhydroxylamine is cyclic, it is of interest to report the preparation of acyclic succino(benzoylhydroxamic) acid (VII) by use of benzoyl chloride on aqueous sodium succinohydroxamate at 0°, or on a suspension of the salt in ether:



VII

When VII was heated in acetic anhydride some VI was obtained but there was also obtained an isomer. Two possible structures for the latter (VIII) are presented.

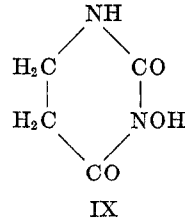


VIII

There was a 20° difference in the melting points of isomers VI and VIII, and one depressed the m. p. of the other. The ultraviolet and infrared spectra of the two substances were nearly identical.

Sodium succinohydroxamate may also be acylated at 5–15° by acetic anhydride to an open-chain diacetyl derivative of structure comparable to VII, and it also undergoes cyclization with hot acetic anhydride.

The sodium salt of VII readily was found to rearrange on heating in water into 3-hydroxy-5,6-dihydrouracil (IX).



IX

As in the rearrangement of I, this result demonstrates that one of the hydroxamic positions rearranges (to isocyanate) whereas the other hydroxamic position is

captured by the transient isocyanate group instead of rearranging. The uracil derivative gave rise to monoacetyl and dibenzoyl derivatives.

No analog of II was isolated as such in the succinic series, but some evidence for its presence in VII was obtained in the isolation of a small amount of *sym*-diphenylurea during rearrangement of VII. It is obvious that a salt of the struc-

$$\begin{array}{l} CH_2COO\text{—}\bar{N}COPh \\ | \\ CH_2CO\bar{N}\text{—}OCOPh \end{array}$$

ture would give rise of PhNCO as an initial product of rearrangement, and in water this usually decomposes into *sym*-diphenylurea.

EXPERIMENTAL

Melting points reported herein are uncorrected.

Disodium phthalohydroxamate. An ethanolic solution of hydroxylamine was prepared by treatment of a refluxing solution of 21.5 g. of hydroxylamine hydrochloride in 500 ml. of hot, absolute ethanol with NaOEt and removal by filtration of the resulting sodium chloride. Ethyl (or butyl) phthalate (33.3 g.) was dissolved in a solution of sodium ethoxide (from 7.2 g. of sodium) in 200 ml. of absolute ethanol. The cooled hydroxylamine solution was added to the solution containing the ester at such a rate as to keep the temperature below 30° (approximately 30 minutes). The flask containing the mixture was then stoppered and allowed to stand in an ice-bath for one hour. Petroleum hexane (250 ml.) was then added. The resulting gelatinous precipitate was separated by suction filtration. In the presence of moist air, the nearly colorless precipitate acquires a red color, probably due to the formation of salts of phthaloxime. The colorless salt was, therefore, transferred as rapidly as possible to a vacuum desiccator charged with concentrated sulfuric acid and paraffin wax. The salt was then dried to constant weight. Light pink or yellow samples were employed successfully in subsequent steps, but orange or red samples yielded large quantities of benzoylphthaloxime with benzoyl chloride. Yield: 33.5 g., 95% based on $C_8H_6N_2Na_2O_4$. The analytical samples were dried *in vacuo* for several days, but the results of analyses on samples dried for 20 hours were not significantly different.

Anal. Calc'd for $C_8H_6N_2Na_2O_4$: Na, 19.2. Found: Na, 16.6, 17.3, 16.9 (different samples).

Attempts were made to fractionate the salt by washing with absolute ethanol. While the salt was found to be slightly soluble in ethanol, no separation was accomplished as evidenced by sodium analyses or a study of the benzoylation products. For example, one analysis of the salt precipitated from the alcohol washings with petroleum hexane showed 17.3% sodium.

REACTIONS OF THE SALT

Carbon dioxide. Gaseous carbon dioxide was passed into a solution made up of 1.00 g. of the salt in 8 ml. of ice-cold water. Red plates (0.37 g.) precipitated. The color of the salt darkened when a sample was heated to 90° but the salt did not melt up to 300°. The colored salt was dissolved in water and acidified cautiously with dilute hydrochloric acid. "Phthaloxime" precipitated (m.p. and mixture m.p. with an authentic specimen, 232° dec.). With limited amounts of sodium hydroxide, it yielded yellow and then orange solutions; with ammonia, red (5). Cautious acidification of the crude salt in water with dilute hydrochloric acid also yielded "phthaloxime".

Benzoylation. A solution of 17.0 g. of the crude sodium phthalohydroxamate in 90 ml. of ice-cold water was cooled to −5° in an ice-salt bath. A concentrated solution of sodium hydroxide containing 5.7 g. of alkali was added thereto. Then 19.5 g. of benzoyl chloride was added in 1-ml. portions with stirring while the temperature was held below 3°. Stirring was continued for 15 minutes after the addition. Then 30 ml. of benzene was added and the

mixture was filtered. The benzene layer of the filtrate was separated; after some of the benzene was evaporated, the benzoyl derivative of phthaloxime, m.p. 169–170°, was isolated. The aqueous layer was then cooled in an ice-salt bath and acidified with 15 ml. of concentrated hydrochloric acid. The precipitate was separated and washed liberally with water. The residue was then triturated with 50 ml. of 95% ethanol, filtered, and then washed with an additional 20 ml. of ethanol. The residue weighed 18.2 g.; m.p. 125–130° dec. The analytical values obtained on this sample agreed with the theoretical values for a dibenzoyl derivative of phthalohydroxamic acid.

Anal. Calc'd for $C_{22}H_{16}N_2O_6$: C, 65.32; H, 3.99; N, 6.93.
Found: C, 65.69; H, 4.10; N, 6.92.

By further processing, however, it was noticed that the sample was inhomogeneous. The sample was divided into two isomeric fractions as follows.

Benzo[(N-benzoxyphthalamoyl)hydroxamic] acid (II). A 14.00-g. sample of the crude phthalo(benzoylhydroxamic) acid was triturated with three 100-ml. portions of 95% ethanol. Each filtrate was diluted with 200 ml. of water. Thus, from the first filtrate there was precipitated 4.2 g. of needles (m.p. 142–144°); from the second, 1.6 g. of needles, m.p. 152–154°, which was lowered by admixing dibenzohydroxamic acid; from the third, 0.5 g., m.p. 145–146°. The sample from the first filtrate was analyzed and used in the rearrangement experiment described below.

Anal. Found: C, 65.63; H, 4.34.

Phthalo(benzoylhydroxamic) acid (I). The residue from the above washings weighed 6.9 g. and melted at 120–125° with decomposition. Attempts to crystallize this residue from chloroform (dissolved cold) by the addition of ethanol or by conventional crystallization from ethanol or acetic acid resulted in ring closure to the benzoyl derivative of "phthaloxime", m.p. 168–169°. The sample was, therefore, analyzed without further treatment.

Anal. Found: C, 65.24; H, 3.98; N, 6.95.

The melting point of a mixture of the 142–144°- and 120–125°-fractions was 115–120°.

Rearrangement of crude phthalo(benzoylhydroxamic) acid. To a solution of 3.6 g. of sodium hydroxide in 90 ml. of water was added 15.0 g. of phthalo(benzoylhydroxamic) acid, m.p. 125–130°, from which II had not been removed. Insoluble particles were separated by gravity filtration, the filtrate being allowed to drop into 50 ml. of water, which was kept boiling. A solid precipitated. After the mixture cooled the solid was separated: yield, 2.59 g.; m.p. 260–265°. The sample was purified by recrystallization from absolute ethanol, yielding the benzoxyquinazolinedione (III) as colorless prisms, m.p. 264–266°. The latter was sparingly soluble in hot ethanol, essentially insoluble in water and dilute mineral acids, gave no color with aqueous ferric chloride, and dissolved in alkali, as shown below, with hydrolysis.

Anal. Calc'd for $C_{15}H_{10}N_2O_4$: C, 63.82; H, 3.57.
Found: C, 64.18; H, 3.84.

The filtrate from the separation of III was acidified to Congo Red with concentrated hydrochloric acid. The resulting precipitate was collected, washed with water, and then dissolved in the minimum amount of cold 95% ethanol. When water was added to this solution and the mixture was allowed to stand, 1.55 g. of a solid separated. This product was recrystallized from a 1:1 water-ethanol mixture and obtained as colorless needles, m.p. 180–182°. The melting point was raised to 189–190° by subsequent recrystallization from this solvent. This was *o*-(3-phenylureido)benzoic acid. An authentic specimen of m.p. 189–190°, prepared by Paal's method (11), did not depress the m.p. of our material. Paal listed 180–181° for the m.p. of his compound, but Riedel (12) showed that this was low. Riedel gave 190–192°.

Rearrangement of pure phthalo(benzoylhydroxamic) acid. A 4.24-g. quantity of freshly prepared and alcohol-washed phthalo(benzoylhydroxamic) acid (I) was stirred vigorously with a solution of 0.82 g. of sodium hydroxide in 25 ml. of water. Insoluble material (0.20 g.; identified as benzoylphthaloxime, m.p. 164–166°) was separated. The filtrate was caused to rearrange and the product was processed as described in the previous experiment. Yield

of III: 1.09 g., 37%, m.p. 260–262°. Recrystallization from ethanol raised the melting point to 265–266°.

Rearrangement of II. *Short heating.* A 3.03-g. sample of II was dissolved in a solution of 0.60 g. of sodium hydroxide in 25 ml. of water. The solution was heated to boiling and then cooled immediately. The solution was acidified and the precipitated *o*-(3-phenylureido)-benzoic acid was crystallized from dilute ethanol: yield, 0.71 g. or 37%; m.p. and mixture m.p. with an authentic specimen, 187–188°.

Longer heating. Identical quantities and procedure were used as in the preceding experiment except that the solution was heated for 15 minutes during the rearrangement. A precipitate separated before the solution was acidified. This was collected, crystallized from dilute ethanol, and identified as 3-phenyl-1*H*-quinazolinedione (V). The yield was 0.52 g. or 29% and its m.p. or mixture m.p. with an authentic sample (7, 8) was 280–281°.

Anal. Calc'd for $C_{14}H_{12}N_2O_2$: C, 70.58; H, 4.23; N, 11.76.

Found: C, 70.79; H, 4.68; N, 11.87.

Synthesis of V *from o-(3-phenylureido)benzoic acid.* A solution of 1.00 g. of the acid in an equivalent quantity of sodium hydroxide solution was refluxed for one hour. The solution was cooled and acidified (V is soluble in sodium hydroxide solutions). The precipitate was collected and crystallized from dilute ethanol: yield, 0.52 g. (60%); m.p. and mixture m.p. with an authentic sample, 280–281°.

Hydrolysis of III. A 0.20-g. sample of III (m.p. 264–266°) was dissolved in 30 ml. of warm, 5% sodium hydroxide solution. The resulting solution was heated on a steam-bath for 20 minutes. After being cooled, the solution was acidified (HCl) carefully to Congo Red. After filtration, the residue was washed with absolute ethanol. On evaporation of the alcoholic solution, 0.55 g. of benzoic acid (m.p. 121–122°) was obtained. The residue remaining from the alcohol wash (0.125 g.; 99%) melted at 320–322° (sealed tube) with decomposition. By recrystallization from hot water, 3-hydroxy-1*H*-quinazolinedione (IV) was obtained as long needles, m.p. 325–326° (dec.).

Anal. Calc'd for $C_8H_6N_2O_3$: C, 53.93; H, 3.40; N, 15.73.

Found: C, 53.81; H, 3.51; N, 15.79.

Samples of IV were not hydrolyzed by concentrated hydrochloric acid in a sealed tube at 160°, although it dissolved at this temperature, or by a refluxing 10% sodium hydroxide solution. Concentrated potassium hydroxide at 180° did cause a reaction, but no pure products were obtainable from the reaction mixture.

Conversion of IV *to 3-amino-1H-quinazolinedione.* A 100-mg. quantity of IV was treated with 1 ml. of 95% hydrazine on a steam-bath for one hour. The excess of hydrazine was removed in a stream of dry air and the residue was crystallized from absolute ethanol: yield, 51 mg. The melting point of the product was 287–288° and this melting point was not lowered by the addition of authentic 3-amino-1*H*-quinazolinedione (7).

Anal. Calc'd for $C_8H_7N_3O_2$: N, 23.72. Found: N, 23.74.

Synthesis of IV *from o-carbethoxyphenylurethan.* This urethan, EtOOC-C_6H_4-NHCOOEt, was prepared from N-bromophthalimide by Bredt's method (13). A 1.32-g. quantity of it was dissolved in a filtered ethanolic solution of hydroxylamine, (equivalent to 0.35 g. of hydroxylamine hydrochloride). To this solution was added sodium ethoxide (from 0.115 g. of sodium in 5 ml. of absolute ethanol). This mixture was heated on a steam-bath for two hours, then cooled, diluted with 25 ml. of water, and acidified with hydrochloric acid. The precipitated 3-hydroxy-1*H*-quinazolinedione (0.39 g.; m.p. 305°) was separated. The melting point was raised to 309–310° (open capillary) by recrystallization from a large volume of absolute ethanol or acetic acid. By recrystallization from water, the product was obtained as long needles (m.p. 311–312°, open capillary; 325–326°, sealed capillary). This material did not depress the m.p. of the IV which was obtained by hydrolysis of III.

Anal. Calc'd for $C_8H_6N_2O_3$: N, 15.73. Found: N, 15.32.

Benzoylation of disodium succinohydroxamate. A. By the Schotten-Baumann technique. A solution of 3.84 g. of sodium succinohydroxamate (prepared as in ref. 1) and 5.4 g. of sodium acetate trihydrate in 40 ml. of water was stirred, in the presence of a little saponin,

with 6.0 ml. of benzoyl chloride. The temperature was held between 5–10°. After 15 minutes, an additional 2.0 ml. of benzoyl chloride was added and the stirring was continued for 30 minutes. The mixture was then acidified with 5.0 ml. of concentrated hydrochloric acid and 50 ml. of a 1:1 mixture of ligroin (60–70°) and benzene was added. The crude benzoyl derivative was separated and recrystallized from 95% ethanol. Succino(benzoylhydroxamic) acid (VII; 2.34 g. or 45%) was thus obtained as soft, colorless needles, m.p. 135° (dec.).

Anal. Calc'd for $C_{18}H_{16}N_2O_6$: C, 60.69; H, 4.53; N, 7.87.

Found: C, 60.83; H, 4.38; N, 8.05.

B. In ether. A suspension of 5.0 g. of disodium succinohydroxamate in 60 ml. of ether was treated with 7.0 ml. of benzoyl chloride. After the vigorous reaction had subsided, the mixture was refluxed for 30 minutes and then, after being cooled, it was filtered. The solid on the filter was washed with ether and then with water. The residue was crystallized from absolute ethanol, yielding 4.1 g. (55%) of VII, m.p. 130° (dec.). Further recrystallizations from this solvent afforded needles, m.p. 135° (dec.), undepressed with a sample prepared by the Schotten-Baumann method. Some impure dibenzohydroxamic acid was isolated from the mother liquors.

Anal. Found: N, 8.07.

Preparation of VI. This benzoyl derivative was prepared essentially by the method of reference 1 by conversion of sodium succinohydroxamate to a copper salt, treatment of the copper salt with hydrogen sulfide, and benzoylation of the resulting organic product with benzoyl chloride in benzene in the presence of pyridine. VI was obtained as colorless rhombs, m.p. 135–136°. A mixture of it with VII obtained by method *B* above melted at 130–131°.

Anal. Calc'd for $C_{11}H_9NO_4$: N, 6.39. Found: N, 6.52.

Cyclization of VII. *Experiment I.* Acetic anhydride (5 g.) and 0.25 g. of succino(benzoylhydroxamic acid) were mixed and heated at 100° for 30 minutes. The excess of anhydride was then removed in a stream of dry air at 100° and the residue was taken up in benzene. Precipitation with petroleum hexane gave an oil. The mixed solvent was decanted and the oil was triturated with ethanol. The product crystallized from the ethanolic solution as the solvent was allowed to evaporate. Several recrystallizations from ethanol afforded 0.08 g. of compound VIII, m.p. 116°.

Anal. Calc'd for $C_{11}H_9NO_4$: C, 60.27; H, 4.14; N, 6.39.

Found: C, 60.36; H, 4.60; N, 6.33.

Experiment II. After a similar heating of 1.0 g. of VII in acetic anhydride the gummy residue obtained after removal of the excess anhydride was taken up in hot ethanol. The first crystals to form on cooling were those of VI, prisms melting at 134°. This m.p. was raised to 136° after several recrystallizations from ethanol and it was undepressed by the sample prepared by the method of reference 1. The second crop of crystals melted at 105° and the third fraction at 114° (rosettes of needles). The third fraction was recrystallized from a mixture of benzene and petroleum hexane, then from ethanol, yielding a sample of VIII melting at 116°. A mixture of the two isomers (136° and 116°) melted at approximately 105°. The ultraviolet and infrared spectra of both were found to be nearly identical.

Cyclization of 3-carboxypropiono(benzoylhydroxamic) acid. A 1.00-g. sample of this acid (10) was warmed with 2.0. ml. of benzoyl chloride at 100° for 15 minutes. The resulting solution was cooled and the product was crystallized as prisms from absolute ethanol, yielding 0.35 g. of VI, m.p. 135°.

Succino(acetylhydroxamic) acid. A solution of 2.4 g. of disodium succinohydroxamate and 2.8 g. of sodium acetate trihydrate in 12 ml. of water was cooled to approximately 5°. A trace of saponin and then 4 ml. of freshly distilled acetic anhydride was added during one minute while the mixture was vigorously stirred. The temperature rose to 15°. The derivative which crystallized from the reaction mixture was separated immediately, washed with petroleum hexane, and dried *in vacuo* at 25°. The crude product weighed 2.3 g. Part of the sample dissolved in boiling 2-propanol and the solution, upon being cooled, yielded 0.71 g. of succino(acetylhydroxamic) acid, m.p. 140°. Further recrystallizations from

either 2-propanol or a large volume of tetrachloroethane afforded colorless plates, m.p. 147° (dec.). The acid was soluble in water or acetone and was very soluble in ethyl acetate, chloroform, or benzene. It gave no color with aqueous ferric chloride. The compound is unstable on standing and acquires the odor of acetic acid.

Anal. Calc'd for $C_8H_{12}N_2O_6$: C, 41.37; H, 5.21; N, 12.06.

Found: C, 41.34; H, 5.33; N, 12.15.

Cyclization of succino(acetylhydroxamic) acid. A solution of 0.66 g. of this acid in 5 ml. of acetic anhydride was refluxed for ten minutes. The excess anhydride was removed in a dry air stream over a steam-bath. The residue was dissolved in benzene and precipitated with petroleum hexane, yielding 0.37 g. (83%; m.p. 129°) of the heterocyclic acetyl derivative. Recrystallization from benzene afforded colorless prisms, m.p. 131°.

Anal. Calc'd for $C_6H_7NO_4$: C, 45.87; H, 4.49; N, 8.92.

Found: C, 45.56; H, 4.49; N, 9.04.

Disodium succino(benzoylhydroxamate) was prepared by treating a suspension of 8.57 g. of VII in 50 ml. of anhydrous ethanol with an equivalent quantity of sodium ethoxide (1.13 g. of sodium in 24 ml. of ethanol). The acid dissolved and part of the desired salt precipitated. Anhydrous ether (100 ml.) was added and the precipitated salt was collected. The product was dried *in vacuo* over sulfuric acid. Yield: 9.25 g.; 96%.

Anal. Calc'd for $C_{18}H_{14}N_2Na_2O_6$: Na, 11.49. Found: Na, 11.63.

Rearrangement. A. Using the isolated salt. A solution of 7.27 g. of disodium succino(benzoylhydroxamate) in 20 ml. of water was heated at 100° for one hour. A small amount of *sym*-diphenylurea (0.12 g.) separated. The mixture was filtered and the filtrate was cooled and acidified. Benzoic acid, which precipitated, was removed. The aqueous filtrate was treated with Norit and then evaporated to dryness on a steam-bath in a stream of air. Volatile materials were further removed *in vacuo*. The dry residue was then extracted four times with 25-ml. portions of boiling 2-propanol. The combined alcoholic portion was filtered, concentrated to approximately 25 ml. by distillation, and cooled. 3-Hydroxy-5,6-dihydrouracil (IX), 0.70 g., m.p. 205°, deposited. Subsequent recrystallization from 2-propanol raised the melting point to 210°. The uracil is very soluble in water and hot ethanol, very sparingly soluble in acetone and diethyl ketone, and essentially insoluble in ether, benzene, chloroform, ethyl acetate, and camphor. It gives a blood-red color with aqueous ferric chloride, which changes to yellow on acidification. After being refluxed with sodium hydroxide solution, the substance may be recovered in approximately 30% yield by the tedious process described in its isolation from the reaction mixture above.

B. Using the acid. Into a solution of 1.2 g. of sodium hydroxide in 20 ml. of water was dissolved 5.34 g. of VII. The resulting solution was heated on a steam-bath for one hour. The details of processing were the same as in method *A*. Both diphenylurea and benzoic acid were obtained as before. From the 2-propanol extractions (eight 25-ml. portions were taken) there was obtained 1.06 g. of the crude 3-hydroxy-5,6-dihydrouracil by concentration, cooling, and dilution with chloroform. After recrystallization, the m.p. was 206°.

Anal. Calc'd for $C_4H_6N_2O_3$: C, 36.92; H, 4.65; N, 21.53.

Found: C, 36.64; H, 4.81; N, 21.86.

Acetylation of IX. To 0.26 g. of the uracil was added 15 ml. of acetic anhydride and the solution was heated at 100° for 30 minutes. Volatile solvents were then removed with a dry air stream. The residue was desiccated *in vacuo* and the resulting dry residue weighed 0.19 g. A test with aqueous ferric chloride was negative. The product was sparingly soluble in cold water but soluble in hot. It was not precipitated when hot aqueous solutions were cooled. The sample was crystallized first from a mixture of chloroform and petroleum hexane and then from ethyl acetate, yielding colorless rhombs, m.p. 162°. It was a monoacetyl derivative.

Anal. Calc'd for $C_6H_8N_2O_4$: C, 41.88; H, 4.69; N, 16.28.

Found: C, 41.77; H, 4.63; N, 16.30.

Benzoylation of IX. A 160-mg. quantity of the uracil was dissolved in 2.5 ml. of pyridine containing 0.5 g. of benzoyl chloride and the resulting solution was heated at 100° for one

hour. The solution was then diluted with 5 ml. of water and the precipitate (320 mg.) was separated, washed with water, and dried. This compound was found to be essentially insoluble in methanol and ethanol. The derivative was crystallized from acetic acid, yielding a sample with a melting point of 245° (dec.). It was a dibenzoyl derivative.

Anal. Calc'd for $C_{18}H_{15}N_2O_5$: C, 63.71; H, 4.46; N, 8.26.
Found: C, 63.70; H, 4.16; N, 8.17.

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SUMMARY

As examples of compounds with two hydroxamic acid groups attached to adjacent carbon atoms suitable for rearrangement studies, phthalo(benzoylhydroxamic) acid and succino(benzoylhydroxamic) acid have been prepared. These acyclic compounds underwent cyclization very readily.

Rearrangement of phthalo(benzoylhydroxamic) salt gives rise to 3-benzoxy-1*H*-quinazolinedione; of succino(benzoylhydroxamic) salt, 3-hydroxy-5,6-dihydrouracil.

Evidence is presented that benzo[(N-benzoxyphthalamoyl)hydroxamic] acid is obtained along with phthalo(benzoylhydroxamic) acid in its preparation from ethyl phthalate.

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REFERENCES

(1) HURD AND BOTTERON, *J. Org. Chem.*, **11**, 207 (1946).
(2) LOSSEN, *Ann.*, **281**, 227 (1894).
(3) ERRERA, *Gazz. chim. ital.*, **24**, 469 (1894).
(4) BRADY, *et al.*, *J. Chem. Soc.*, 529 (1928).
(5) *Cf.* LASSAR-COHN, *Ann.*, **205**, 295 (1880); LACH, *Ber.*, **16**, 1781 (1883); ERRERA, *Gazz. chim. ital.*, **25**, II, 25 (1895); ORNDORFF AND PRATT, *Am. Chem. J.*, **47**, 99 (1912); PUTOKHIN, *J. Russ. Phys.-Chem.*, **62**, 2203 (1930) [*Chem. Abstr.*, **25**, 3993 (1931)].
(6) *Cf.* ERRERA, *Gazz. chim. ital.*, **25**, II, 21 (1895).
(7) KUNCKEL, *Ber.*, **38**, 1212 (1905).
(8) SCOTT AND WOOD, *J. Org. Chem.*, **7**, 508 (1942).
(9) HANTZSCH AND URBAHN, *Ber.*, **28**, 753 (1895).
(10) HURD, BUESS, AND BAUER, *J. Org. Chem.*, **17**, 865 (1952).
(11) PAAL, *Ber.*, **27**, 978 (1894).
(12) RIEDEL, *Chem. Zentr.*, I, 1774 (1912).
(13) BREDT, *Ber.*, **33**, 27 (1900).