to yield 20.7 g. (81%) of the amine, distilling at 150° at 2 mm. The amine rapidly picks up carbon dioxide from the air to form a white solid carbonate, but this can be prevented by distilling and storing under nitrogen.

Anal. Calcd. for $C_{15}H_{17}N$: N, 6.63. Found: N, 6.63.

The hydrochloride of the amine was recrystallized from anhydrous ethanol and melted at 217.5–218.5°.

Anal. Calcd. for $C_{15}H_{18}NCl$: N, 5.66; Cl, 14.34. Found: N, 5.59; Cl, 14.33.

bis-(γ,γ-Diphenylpropyl)-amine.—Upon reducing β,β-diphenylpropionitrile under ammonia, 10% of the secondary amine was obtained which distilled at 270° at 2 mm. Hydrogenating in the absence of ammonia increased the yield to 24%.

Anal. Calcd. for $C_{30}H_{31}N$: N, 3.46. Found: N, 3.42.

The hydrochloride of the amine melted at 193–194° after one recrystallization from ethanol.

Anal. Calcd. for $C_{30}H_{32}NCl$: N, 3.17; Cl, 8.06. Found: N, 3.10; Cl, 8.04.

4-Pyrone.—Chelidonic acid[17] was decarboxylated to 4-pyrone.[2]

N-(9-Aminofluorenyl)-4-pyridone.—To 50 ml. of anhydrous ethanol in a 100-ml. beaker were added 1 g. of 4-pyrone and 1.91 g. of 9-aminofluorene. The solution was evaporated down to about 10 ml., cooled and filtered. The pale yellow crystals were recrystallized twice from benzene yielding 1.1 g. (41%) of a white product melting at 177° dec.

Anal. Calcd. for $C_{18}H_{13}NO$: N, 5.36. Found: N, 5.30.

The following N-substituted 4-pyridones were prepared in the same manner.

N-(α,α-Diphenylmethyl)-4-pyridone.—α,α-Diphenylmethylamine was condensed with 4-pyrone to yield 42.3% of a product which melted at 169.5–170.5° after two recrystallizations from benzene.

Anal. Calcd. for $C_{18}H_{15}NO$: N, 5.33. Found: N, 5.48.

N-(β,β-Diphenylethyl)-4-pyridone.—β,β-Diphenylethylamine and 4-pyrone yielded 31% of a nearly white material melting at 159–160° following two recrystallizations from benzene.

Anal. Calcd. for $C_{19}H_{17}NO$: N, 5.10. Found: N, 5.00.

N-(γ,γ-Diphenylpropyl)-4-pyridone.—Condensing, γ,γ-diphenylpropylamine and 4-pyrone yielded a light brown viscous liquid that resisted attempts to purify it.

N-(β,γ-Diphenylpropyl)-4-pyridone.—Condensation experiments with β,γ-diphenylpropylamine and 4-pyrone yielded viscous liquids similar to that described above.

Attempts to prepare salts of the last two compounds resulted in the formation of brownish-red oils that could not be characterized.

N-(α,α-Diphenylmethyl)-chelidamic Acid.—Condensation was effected by treating 1.8 g. of chelidonic acid with 1.8 g. of α,α-diphenylmethylamine in 50 ml. of anhydrous ethanol. The pale yellow solid that formed after evaporating down the solution was washed with ethanol and yielded 2.8 g. (84%) of a white solid melting at 210° dec.

Anal. Calcd. for $C_{20}H_{15}NO_5$: N, 4.01. Found: N, 3.75.

N-(β,γ-Diphenylpropyl)-chelidamic Acid.—Equimolar amounts of β,γ-diphenylpropylamine and chelidonic acid were condensed as above to yield 76.6% of a pale yellow solid melting at 210° dec.

Anal. Calcd. for $C_{22}H_{19}NO_5$: N, 3.63. Found: N, 3.67.

N-(γ,γ-Diphenylpropyl)-chelidamic Acid.—γ,γ-Diphenylpropylamine and chelidonic acid were condensed to yield 79% of a nearly colorless product melting at 220° dec.

Anal. Calcd. for $C_{22}H_{19}NO_5$: N, 3.63. Found: N, 3.40.

Summary

1. Five new N-aralkyl-4-pyridones have been synthesized: α,α-diphenylmethyl-, β,β-diphenylethyl-, 9-aminofluorenyl-, β,γ-diphenylpropyl- and γ,γ-diphenylpropyl-. The latter two are viscous liquids that resisted attempts to purify them.
2. Three new N-aralkyl chelidamic acids were also prepared: α,α-diphenylmethyl-, β,γ-diphenylpropyl- and γ,γ-diphenylpropyl-.
3. The yields of β,β-diphenylethylamine and β,γ-diphenylpropylamine prepared from their nitriles has been increased over those reported in the literature.
4. The methods of preparation and constants of γ,γ-diphenylpropylamine and bis-(γ,γ-diphenylpropyl)-amine and their hydrochlorides are described for the first time.

BROOKLYN, N. Y. RECEIVED NOVEMBER 1, 1946

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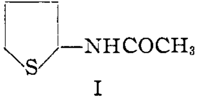
[17] "Organic Syntheses," Coll. Vol. II, p. 126 (1943).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

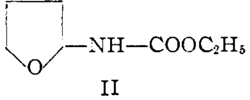
Diazo Reactions in the Thiophene and Furan Series

BY CHARLES D. HURD AND HILL M. PRIESTLEY[1]

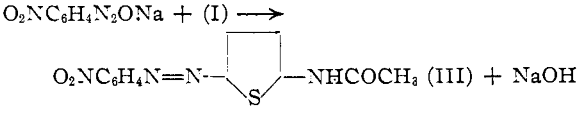
One of the rules in dye chemistry is that when an arylamine is acetylated, its power to couple with diazonium salts is destroyed. Thus, aniline will couple but acetanilide will not.[2] The present investigation has demonstrated that this limitation does not apply to the thiophene or furan series. Aceto-2-thiophenamide[3] (I), the thiophene analog of acetanilide, couples rapidly with sodium *p*-nitrobenzenediazotate



I



II



Still more remarkable is the fact that the coupling may be carried out with *p*-nitrobenzenediazonium

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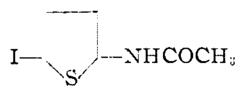
[1] Present address: Pepsodent (Lever Brothers), Chicago, Illinois.

[2] König and Kohler, *Ber.*, **54**, 981 (1921), obtained a 20% yield of an azo dye by allowing to react for five days at 0° a mixture of diazotized *p*-nitroaniline and aceto-1-naphthylamide.

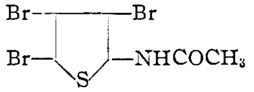
[3] The names aceto-2-thiophenamide and 2-thiophenamine are used in preference to the abridged names aceto-2-thiophenide and 2-thiophenine, respectively.

chloride in acid solution to form the azo dye in high yield. Ethyl 2-furylcarbamate (II) behaves similarly.

The exceptional tendency of the amidothiophenes to couple was also demonstrated in another way. If a halogen atom is present in the 5-position, it is ejected during the coupling reaction. Here, however, the coupling requires a neutral or alkaline solution. Thus, the same azo compound (III) is formed starting either with (I) or with 2-acetamido-5-iodothiophene[4] (IV).



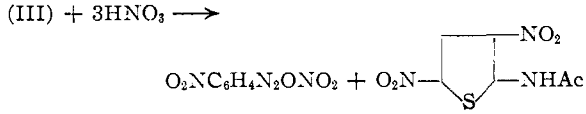
IV



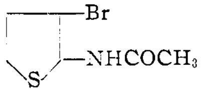
V

In like manner 2-acetamido-3,4,5-tribromothiophene (V) gives rise to 5-*p*-nitrophenylazo-3,4-dibromo-2-acetamidothiophene. The fact that (I) couples in an acid solution, whereas (IV) does not, proves that the dyes formed are aminoazo derivatives and not diazoamino derivatives, since both I and IV possess identical NH groups, and the compounds should possess predictably similar reaction rates if diazoamino compounds were formed.

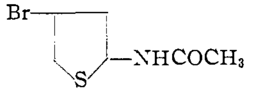
It was shown that the azo compound (III) could be converted into 2-acetamido-3,5-dinitrothiophene by reaction with fuming nitric acid



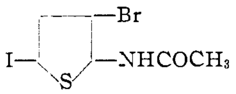
Syntheses of the halogen derivatives employed in this study will be presented briefly. 2-Acetamido-3,5-dibromothiophene (VI) was prepared by the bromination of aceto-2-thiophenamide at room temperature whereas the tribromo derivative (V) was made at higher temperatures, acetic acid serving as solvent in both reactions. 2-Acetamido-3-bromothiophene (VII) and the 4-bromo analog (VIII) were prepared from VI and V, respectively, by reduction with aluminum amalgam. These compounds (VII, VIII) were source materials for the mixed halogen compounds (IX, X), synthesis of which was accomplished by mercuration ($HgCl_2$), followed by iodine cleavage I_2 + aq. KI. The free 5-position in VII and VIII was proved not only by the formation of the chloromercuri compound but also by the coupling reaction in acid solution. Only when an α-position is free does a chloromercuri compound form on treatment with mercuric chloride at a low temperature. Also, only if the α-position is unoccupied does *immediate* coupling with sodium *anti-p*-nitrobenzenediazotate take place in glacial acetic acid solution. Compound (VII) coupled readily in this manner to form 5-*p*-nitrophenylazo-3-bromo-2-acetamidothiophene (XI), and VIII coupled to yield the 4-bromo azo analog. The structure of XI was substantiated by synthesis from III by direct bromination. Fuming nitric acid converted XI into 2-acetamido-3,5-dinitrothiophene, thereby demonstrating replaceability of the bromo group as well as the azo radical by nitro.



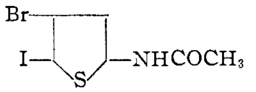
VII



VIII



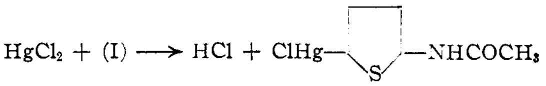
IX



X

Mention has been made of the synthesis of two of the iodo derivatives. In addition, the 5-iodo-, 3,5-diiodo- and the triiodo- derivatives of (I) were prepared and studied. All were prepared by cleavage of the corresponding chloromercuri derivatives with iodine.

Monomercuration was accomplished by means of mercuric chloride at 20°



Dimercuration at positions 3 and 5 was performed rapidly at room temperature by reaction of (I) in acetic acid solution with mercuric acetate. For trimercuration, the reaction mixture of (I), acetic acid, and mercuric acetate was heated at 100°. The acetoxymercuri derivatives were changed to the chloromercuri compounds by metathesis with sodium chloride.

2-Acetamido-3,5-diiodothiophene was more reactive toward aluminum amalgam than the corresponding 3,5-dibromo compound because in this reductive cleavage it lost both of its iodine atoms, not merely one of them.

As would be surmised from the above discussion, the 5-halogen in both the dibromo and diiodo derivatives was easily replaced by an azo group during the diazo coupling to form 5-arylazo-3-halo-2-acetamidothiophene. Such couplings proceeded rapidly if the diazotate was produced from the diazonium salt in the presence of an alcoholic solution of the thiophene compound by addition of sodium acetate solution. A slow coupling was realized in these α-halo replacements, however, when the thiophene compound was brought into reaction with sodium *anti-p*-nitrobenzenediazotate in acetic acid solution; but the second of these methods promotes rapid coupling if the 5-position is unsubstituted.

Several of the compounds reported in this paper were tested for possible reactivity toward maleic anhydride but none gave rise to a Diels–Alder reaction.

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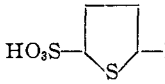
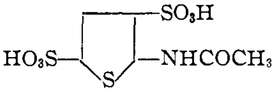
(4) Naming this and similar substituted derivatives of (I) by considering the heterocyclic nucleus as the principal function seems better than by naming them as amides, since it avoids the necessity for parentheses in the name. The amide name for IV would be aceto-(5-iodo-2-thiophen)-amide.

By use of concentrated sulfuric acid it was possible to convert aceto-2-thiophenamide into the sulfonic acid derivative (XII). The disulfonic acid (XIII) was made with fuming sulfuric acid. Conversion of the barium salt of XII into the tribromo compound (V) shows that the sulfonic group may be replaced by bromine.


XII


XIII

Biphenyl-bis-(diazonium chloride) reacts with the sodium salts of XII and XIII to give red and yellow reaction products, respectively. The color is the unusual feature of these compounds, since they appear to be merely the diazonium sulfonates, the substance from XII presumably possessing the structure $(\text{—}C_6H_4N_2^+\ {}^-O_3SC_4H_2SNHCOCH_3)_2$.

2-Thiophenamine is known not to undergo diazotization. It is of interest, therefore, that a sulfonated thiophenamine reacts readily with nitrous acid to form a diazo compound capable of coupling with 2-naphthol.

Experimental

All melting points are uncorrected.

2-Acetamido-3,5-dibromothiophene (VI).—In a 3-necked flask, provided with a thermometer, mechanical stirrer and dropping funnel, and surrounded with cold water, there was placed a solution of 5.0 g. of aceto-2-thiophenamide (m. p. 162°) in 150 g. of glacial acetic acid. With stirring, a solution of 7.5 g. of anhydrous sodium acetate in 25 g. of water was added. None of the (I) separated from the glacial acetic acid solution. Bromination was effected by gradually adding, with stirring, a solution of 4.0 ml. of bromine in 30 ml. of glacial acetic acid. The mixture was poured immediately into 700 g. of cold water. After two hours the product was filtered, washed with water, and air-dried. The yield was 9.0 g. or 85%; m. p., 138–141°. After recrystallization from alcohol, the pure (VI) melted at 142°.

Anal. Calcd. for $C_6H_5Br_2NOS$: N, 4.72. Found: N, 4.65.

2-Acetamido-3,4,5-tribromothiophene (V).—To a suspension of 10.0 g. of (VI), m. p. 142°, in 30 ml. of hot glacial acetic acid, there was added 3.0 ml. of bromine. A complete solution resulted. It was warmed on the water-bath for five minutes. Crystallization was induced by rubbing the side of the flask with a glass rod. The flask was cooled, and its contents were added to 60 ml. of cold glacial acetic acid. The product was filtered, washed with sodium bisulfite solution and water. The yield of (V) was 10.5 g. After two recrystallizations, one from hot glacial acetic acid and another from absolute alcohol, the tribromo derivative melted at 210°.

Anal. Calcd. for $C_6H_4Br_3NOS$: N, 3.70. Found: N, 3.85.

5-Acetamido-2-thiophenemercuric Chloride.—To a solution of 0.50 g. of aceto-2-thiophenamide in 30 ml. of methanol there was added dropwise, with mechanical stirring, in the course of fifteen minutes, a solution of 1.0 g. of mercuric chloride in 20 g. of water. The precipitate was filtered, washed with water, methanol and ether. The yield of 5-acetamido-2-thiophenemercuric chloride was 0.30 g., m. p. 222° (dec.). One gram of the chloromercuri compound is soluble in 2 ml. of pyridine; only one milligram will dissolve in 1 ml. of absolute ethyl alcohol.

Anal. Calcd. for $C_6H_6ClHgNOS$: N, 3.72. Found: N, 3.89.

2-Acetamido-5-iodothiophene (IV).—For conversion into the iodo derivative, 0.20 g. of the above mercuric salt was triturated with 0.10 g. of iodine and 0.30 g. of potassium iodide dissolved in 2 g. of water. After no more free iodine was present, a little water was added, and the substance was extracted with ether. Removal of the ether left 0.10 g. of (IV), m. p. 130° The material was recrystallized from dilute alcohol, and there was obtained 0.060 g. of needles, m. p. 133°.

Anal. Calcd. for C_6H_6INOS: N, 5.24. Found: N, 5.16.

A good source for this monoiodo derivative is the filtrate obtained from the recrystallization of (I) from methanol. The chloromercuri compound is obtained quite pure on the addition of a cold solution of mercuric chloride. The conversion to the iodo compound is then carried out as described above.

5-Acetamido-2,4-thiophene-bis-(mercuric Chloride).—To a solution of 0.50 g. of (I) in 10 g. of glacial acetic acid there was added a solution of 7.0 g. of mercuric acetate in 25 g. of water. The golden-green solution was allowed to stand for five minutes at room temperature. There was then added, with stirring, a solution of 4 g. of sodium chloride in 165 g. of water. The mixture was warmed on the steam-bath until the precipitate had settled out and a clear supernatant solution resulted. This procedure usually required about thirty minutes. The precipitate was filtered off, washed successively with water and then with 10 ml. of alcohol and 10 ml. of ether. The yield of colorless 5-acetamido-2,4-thiophenebis-(mercuric chloride) was 2.05 g. (calcd., 2.06 g.). The compound has no definite melting or decomposition point, as in the case with the analogous compounds containing one or three chloromercuri groups. In a capillary tube, the compound turns brown at about 110°, and decomposes at about 250°, without melting; at that temperature it has the appearance of burnt rubber. Raising the temperature to 280° does not cause any further change in the decomposition of the substance. One gram of the mercury compound is soluble in 30 ml. of pyridine.

Anal. Calcd. for $C_6H_5Cl_2Hg_2NOS$: N, 2.29. Found: N, 2.32.

2-Acetamido-3,5-diiodothiophene.—The 2.05 g. of the mercuric salt was treated for thirty minutes with 1.8 g. of iodine, 4.5 g. of potassium iodide and 30 g. of water. Excess iodine was removed with 3 ml. of 10% sodium bisulfite solution. The substance was washed with water and dried. The yield was 1.25 g. (calcd. 1.39 g.). It was recrystallized from 20 ml. of 95% alcohol, giving 0.90 g. of a gray-colored solid, m. p. 168°. Further crystallization brought the m. p. to 172°.

Anal. Calcd. for $C_6H_5I_2NOS$: N, 3.56. Found: N, 3.73.

5-Acetamido-2,3,4-thiophene-tris-(mercuric Chloride).—To a hot solution of 0.50 g. of (I) in 10 g. of glacial acetic acid, there was added all at once a hot solution of 7.0 g. of mercuric acetate in 20 ml. of 50% glacial acetic acid. The solution was warmed on the steam-bath for ninety minutes. There was then rapidly added a solution of 2.0 g. of sodium chloride in 140 g. of water. The precipitate was digested on the water-bath for one hour, then collected on a filter, washed with much water and then with a little alcohol and ether. The alcoholic washings on coming in contact with water should yield no precipitate. The presence of a precipitate indicates the presence of the mono- or bis-chloromercuri derivatives. The yield of the tris-chloromercuri compound was 2.9 g.; it softened at 240° and decomposed at 250°, with the formation, apparently, of black mercuric sulfide. The substance is colorless and completely insoluble in pyridine.

Anal. Calcd. for $C_6H_4Cl_3Hg_3NOS$: N, 1.66. Found: N, 1.66.

2-Acetamido-3,4,5-triiodothiophene.—With the tris-mercuric salt was placed 2.8 g. of iodine, 6.8 g. of potassium iodide and 30 ml. of water. Directions were the same as above listed for the diiodo analog. The yield of greenishgray colored triiodo product was 1.55 g. It melted at 225°, but iodine vapors were visible in the capillary tube at temperatures above 200°.

Anal. Calcd. for $C_6H_4I_3NOS$: N, 2.70. Found: N, 2.83.

5-Acetamido-4-bromo-2-thiophenemercuric Chloride.—A solution of 0.50 g. of the dibromo compound (VI) in 30 ml. of water-saturated ether was treated with 0.5 g. of amalgamated aluminum. After thirty minutes, two drops of water and 0.5 g. more of the amalgam were added. The next day, 15 ml. more of the wet ether was added, and the mixture was refluxed for three hours. From this mixture there was obtained 0.4 g. of crude 2-acetamido-3-bromothiophene (VII), m. p. 70–115.°

This was mercurated directly by dissolving it in 30 ml. of methanol and adding an equal volume of saturated aqueous mercuric chloride solution. The resulting gray organic mercury compound which separated weighed 0.050 g. It melted sharply at 222° (dec.).

Anal. Calcd. for $C_6H_5ClBrHgNOS$: N, 3.08. Found: N, 3.33.

2-Acetamido-3-bromo-5-iodothiophene (IX).—The above mercury derivative was placed in reaction with a mixture of 40 mg. of iodine, 100 mg. of potassium iodide and 1.0 g. of water. A gray solid was obtained. After recrystallization from alcohol, the (IX) melted at 159°.

Anal. Calcd. for $C_6H_5BrINOS$: N, 4.05. Found: N, 4.35.

5-Acetamido-3-bromo-2-thiophenemercuric Chloride.—Five grams of the pure tribromo compound (V) was powdered and dissolved at room temperature in 300 ml. of water-saturated ether. Nine grams of amalgamated aluminum was added in gram portions, every three hours for three days. A test portion of the ether solution when evaporated yielded a solid melting at 160°. The bulk of the solution was filtered, and the residue on the filter washed with ether. The ether was then distilled off. Of the reduction product (VIII), 1.5 g. was dissolved in 20 ml. of absolute alcohol and treated with a solution containing 5.0 g. of mercuric chloride in 100 g. of water. After half an hour, the white precipitate was filtered off and washed successively with 50% alcohol, absolute alcohol, and ether. The yield was 0.99 g., m. p. 245° (dec.).

Anal. Calcd. for $C_6H_5ClBrHgNOS$: N, 3.08. Found: N, 3.28.

2-Acetamido-4-bromo-5-iodothiophene (X).—Details of this synthesis were the same as for IX, using 0.40 g. of iodine, 1.20 g. of potassium iodide, and 6 g. of water; yield, 0.37 g.; m. p., 165°. The product (X) was dissolved in 0.50 ml. of absolute alcohol, the warm solution centrifuged, and decanted; yield, 30 mg.; m. p. 170°. The solid possessed a light brown color.

Anal. Calcd. for $C_6H_5BrINOS$: N, 4.05. Found: N, 4.13.

Coupling Experiments

5-*p*-Nitrophenylazo-2-acetamidothiophene (III). **First Method, from** (I).—To a suspension of 0.28 g. of *p*-nitroaniline in 3 g. of water and 0.6 ml. of concentrated hydrochloric acid, there was added, with cooling, 0.15 g. of sodium nitrite in 1 g. of water. The filtered diazonium chloride solution was added dropwise to a solution of 0.28 g. of aceto-2-thiophenamide in 5 ml. of absolute alcohol. A red precipitate resulted which was collected on a filter, washed with 50% alcohol, then with water, and desiccated over sulfuric acid. The substance melted at 250°, with decomposition. Its alcoholic solution was purple. A drop of this solution added to water rendered the color orange when acid, and purple when alkaline.

Anal. Calcd. for $C_{12}H_{10}N_4O_3S$: S, 11.03. Found: S, 11.22.

Second Method, from (I).—A purer product was obtained when the coupling was carried out in glacial acetic acid solution. A suspension of 0.80 g. of sodium *anti-p*-nitrobenzenediazotate[5] in 4 g. of water was treated with 6 g. of glacial acetic acid, and this was added to a solution of 0.50 g. of (I) in 10 g. of glacial acetic acid. The material was rubbed with a glass rod until all the white particles of the salt had disappeared. It was then allowed to stand for half an hour, with occasional shaking. There was then added 20 ml. of water. The azo compound was collected on a filter, washed with 10 ml. of 50% alcohol, and with 3 ml. of 95% alcohol. The yield of dried product was 1.02 g. (theory, 1.03 g.), melting at 262° (dec.). The product (III) may be recrystallized from 100 parts of hot dioxane, or 100 parts of nitrobenzene, or from 10 parts of hot pyridine. The crystals were dark red.

Anal. Calcd. for $C_{12}H_{10}N_4O_3S$: N, 19.31. Found: N, 19.27.

Third Method, from IV.—To a solution of 0.18 g. of 2-acetamido-5-iodothiophene (IV) in 4 g. of glacial acetic acid there was added 0.12 g. of sodium *anti-p*-nitrobenzenediazotate in 4 g. of glacial acetic acid. The clear red solution was set aside in a cool place for half an hour. The dye which separated was washed (with glacial acetic acid, water and alcohol) and digested with hot absolute alcohol. The yield of (III) was 20 mg.; m. p. 260° (dec.). A sodium fusion showed the absence of iodine in the sample. Mixed with a sample made from (I) by the second method, the substance still melted at 260°.

Hydrolytic Cleavage of the Azo Dye.—The cleavage of (III) with fuming nitric acid was carried out according to the general method of O. Schmidt.[6] To 8 ml. of fuming nitric acid at 0–5° there was added, in small portions, 0.90 g. of the azo compound. After twenty minutes, the solution was poured onto ice. A gelatinous precipitate formed which was removed by filtration and rinsed with water. The yield of crude nitro product was 0.55 g., and the melting point 176° (dec.). After recrystallization from a mixture of nitrobenzene and alcohol, the light yellow substance melted at 180°. No depression in the melting point was obtained on adding some 2-acetamido-3,5-dinitrothiophene of m. p. 180°, prepared according to the method of Steinkopf.[7]

The cold nitric acid filtrate was poured into 130 ml. of 10% sodium hydroxide solution containing 0.60 g. of 2-naphthol. The amount of 1-*p*-nitrophenylazo-2-naphthol obtained was 0.70 g. (77% yield), m. p. 250°.

Ethyl 5-(*p*-Nitrophenylazo)-2-furylcarbamate, $O_2NC_6H_4N_2C_4H_2ONHCOC_2H_5$.—Two separate batches of ethyl 2-furylcarbamate (II) were prepared, one by the method of Curtius and Leimbach[8] and the other by the procedure of Marquis.[9] The azide, before rearrangement, did not react with the *p*-nitrobenzenediazoic acid. One gram of the azide was converted into the urethan by warming for two hours under reflux with 5 ml. of absolute alcohol.

To the filtrate was added one gram of sodium *anti-p*-nitrobenzenediazoate in 10 ml. of glacial acetic acid. The yellow dye was filtered off and washed with 20 ml. of 50% alcohol and then with 5 ml. of 95% alcohol. The yield was 0.70 g., m. p. 195° (dec.).

Anal. Calcd. for $C_{13}H_{12}N_4O_5$: N, 18.42. Found: N, 17.74.

5-*p*-Nitrophenylazo-3-bromo-2-acetamidothiophene, $O_2NC_6H_4N_2C_4HSBrNHCOCH_3$.—**A.** The coupling in glacial acetic acid, without the addition of sodium acetate, was effected as follows: To a solution of 0.50 g. of 2-acetamido-3,5-dibromothiophene (VI), m. p. 142°, in 15 g. of glacial acetic acid, there was added 2 g. of water, then 0.50 g. of sodium *anti-p*-nitrobenzenediazotate. A red color was produced almost instantly. The solution was placed in a refrigerator at 0°. The following day, some of the dye had already separated. The reaction was allowed to continue for another five days. Then the dye

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[5] Prepared as described by Schraube and Schmidt, *Ber.*, **27**, 518 (1894).

[6] O. Schmidt, *Ber.*, **38**, 320 (1905).

[7] Steinkopf, *Ann.*, **403**, 44 (1914).

[8] Curtius and Leimbach, *J. prakt. Chem.*, [2] **65**, 21 (1902).

[9] Marquis, *Ann. chim. phys.*, [8] **4**, 284 (1905).

was filtered off, washed with 5 ml. of 50% alcohol, and then with 2 ml. of 95% alcohol. The yield was 0.25 g., m. p. 210° (dec.). It was recrystallized from a mixture of 2.5 ml. of pyridine with 2.5 ml. of absolute alcohol. There was obtained 0.15 g. of substance, m. p. 235° (dec.). The yield of crude material was 40% of the theory; that of the purified dye, 24%.

B. Coupling in the presence of sodium acetate solution was carried out thus: A solution of 1.30 g. of (VI) in 60 ml. of absolute alcohol was treated with a suspension of 0.95 g. of sodium *anti-p*-nitrobenzenediazotate in 12 ml. of water containing 1.0 ml. of concentrated hydrochloric acid. There was then added a solution of 13 g. of sodium acetate in 40 ml. of water. After standing for fifteen minutes on ice, 30 ml. of water was added, and the precipitated dye filtered. The precipitate was washed with 50% alcohol, water, absolute alcohol and ether. The yield was 0.60 g., m. p. about 190°. The red substance was recrystallized from a mixture of 2 ml. of pyridine with 4 ml. of absolute alcohol. The yield was 0.14 g., m. p. 231° (dec.). This was recrystallized from a mixture of 1.5 ml. of pyridine with 2 ml. of absolute alcohol. There was obtained 0.10 g. of pure dye, m. p. 235° (dec.).

Anal. Calcd. for $C_{12}H_9BrN_4O_3S$: N, 15.18. Found: N, 14.79.

C. From (VII).—About 0.30 g. of crude 2-acetamido-3-bromothiophene (VII) was prepared from 0.40 g. of (VI) by reduction with aluminum amalgam. It was dissolved in 7 g. of glacial acetic acid and treated with 0.5 g. of sodium *anti-p*-nitrobenzenediazotate. After fifteen minutes, a precipitate appeared. It was collected, washed on the filter with glacial acetic acid, water, alcohol and ether. Two such runs yielded 0.22 g. This was recrystallized from a mixture of 3 ml. of pyridine and 3 ml. of absolute alcohol. The yield was 0.10 g., m. p. 235° (dec.).

Anal. Calcd. for $C_{12}H_9BrN_4O_3S$: N, 15.18. Found: N, 14.19.

D. From III.—The bromination of 5-*p*-nitrophenylazo-2-acetamidothiophene (III) was carried out in three different solvents (glacial acetic acid, pyridine and nitrobenzene). The same product was formed from all three. The bromination in pyridine is here described.

One gram of (III) was dissolved in 17 ml. of hot pyridine, and treated with 0.55 g. of bromine in 10 ml. of pyridine. The mixture was allowed to stand at room temperature for an hour and then warmed on the water-bath for fifteen minutes. There was then added 30 ml. of absolute alcohol. The precipitate was filtered and washed with a pyridine–alcohol mixture, then with absolute alcohol, water, again absolute alcohol, and finally with ether. The yield was 0.75 g., m. p. 233° (dec.). After recrystallization from dioxane, the melting point was 235° (dec.).

Anal. Calcd. for $C_{12}H_9BrN_4O_3S$: N, 15.18. Found: N, 14.58.

Reaction with Nitric Acid.—Reaction ensued when 0.5 ml. of fuming nitric acid was placed with 0.1 g. of 5-*p*-nitrophenylazo-3-bromo-2-acetamidothiophene. After twenty minutes ice was added. The crystals were filtered off and recrystallized from alcohol. The light yellow colored substance formed was 2-acetamido-3,5-dinitrothiophene; melting point and mixed m. p. 180°.

5-*p*-Nitrophenylazo-3,4-dibromo-2-acetamidothiophene, $O_2NC_6H_4N_2C_4Br_2SNHCOCH_3$.—To a solution of 7.0 g. of acetamidotribromothiophene (V) in 40 ml. of absolute alcohol, there was added a suspension of 4.0 g. of sodium *anti-p*-nitrobenzenediazotate in 35 g. of water which contained 5.0 ml. of concd. hydrochloric acid. A clear solution resulted. There was then added 40 g. of dry sodium acetate dissolved in 150 g. of water. An additional 10 g. of water was added ten minutes later, and the mixture was stirred for half an hour while surrounded in an ice-bath. The precipitate was filtered off, and washed successively with 30-ml. portions of 50% alcohol, 30% alcohol, water and 95% alcohol. The product was then suspended in 50 ml. of warm pyridine and filtered off. The dry solid weighed 2.7 g., and melted with decomposition at 240°. Another crop of 0.9 g. of the red dye was obtained by adding 15 g. of water to the pyridine filtrate. This fraction melted at 230°. After washing with 5 ml. of warm pyridine and 10 ml. of absolute alcohol, the second fraction weighed 0.7 g.; m. p. 240° (dec.). In contrast to the azo compound formed from (I) or (VI), that from (V) was insoluble in pyridine.

Anal. Calcd. for $C_{12}H_8Br_2N_4O_3S$: N, 12.50. Found: N, 12.61.

5-*p*-Nitrophenylazo-4-bromo-2-acetamidothiophene, $O_2NC_6H_4N_2C_4HSBrNHCOCH_3$.—Reduction of 0.42 g. of V by amalgamated aluminum (see above) yielded 0.23 g. of crude 2-acetamido-4-bromothiophene (VIII), melting about 160°. This was dissolved in 3 g. of glacial acetic acid and treated with a solution of 0.20 g. of sodium *anti-p*-nitrobenzenediazotate in 4 g. of glacial acetic acid. An immediate red color was obtained on mixing, and a red precipitate separated after several minutes. Altogether, the reaction proceeded for thirty minutes. The precipitate was collected on a filter, washed with 5 g. of glacial acetic acid and then with a little alcohol. The yield was 0.14 g., m. p. about 220° (dec.). After recrystallization from a pyridine–alcohol solution, 0.020 g. of the pure azo dye was obtained, m. p. 234° (dec.).

Anal. Calcd. for $C_{12}H_9BrN_4O_3S$: N, 15.18. Found: N, 15.09.

5-*p*-Nitrophenylazo-3-iodo-2-acetamidothiophene, $O_2NC_6H_4N_2C_4HSINHCOCH_3$.—To a solution of 3.0 g. of 2-acetamido-3,5-diiodothiophene in 135 ml. of absolute alcohol, there was added a suspension of 1.5 g. of sodium *anti-p*-nitrobenzenediazotate in 15 g. of water which contained 1.5 ml. of concd. hydrochloric acid. The clear solution was treated with 10 g. of sodium acetate dissolved in 60 g. of water. After ten minutes another 60 g. of water was added. The mixture was stirred for half an hour while cooled with ice. The dye was collected and washed successively with 50, 30, 10 and 95% alcohol. The yield was 1.0 g., m. p. 210–222° (dec.). The dark red product was dissolved in 5 ml. of warm pyridine and then treated with 8 ml. of absolute alcohol. The dye was filtered and washed with absolute alcohol. It amounted to 0.40 g., m. p. 222° (dec.).

Anal. Calcd. for $C_{12}H_9IN_4O_3S$: N, 13.46. Found: N, 13.23.

Barium 5-Acetamido-2-thiophenesulfonate.—One part of 25% fuming sulfuric acid was added to three parts of 95% acid. Then, 10 ml. of this mixture was added with stirring to 5 g. of (I). The mixture was left for ninety minutes at 25°, diluted, ether extracted to remove 0.7 g. of (I) and neutralized with barium carbonate. The barium salt was crystallized. Even after drying at 120°, it retained water of crystallization.

Sulfonation occurred also with concentrated sulfuric acid, but the reaction was slower.

Anal. Calcd. for $C_{12}H_{12}N_2O_8S_4Ba\cdot H_2O$: Ba, 22.40. Found: Ba, 22.43.

Bromination.—A suspension of 0.1 g. of the barium salt in 2 g. of acetic acid warmed when 0.20 ml. of bromine was added. After five minutes on the steam-bath, it was poured into 20 ml. of water. The precipitate of acetamidotribromothiophene was collected and rinsed with alcohol; yield 0.03 g.; m. p. 207°; mixed m. p. with pure V (210°), 207–210°.

Reaction with Diazotized Benzidine.—The diazo solution was prepared from 0.35 g. of benzidine hydrochloride, 0.25 g. of sodium nitrite, and 3 ml. of dilute hydrochloric acid. To it was added a solution of 0.65 g. of the sodium salt of XII (prepared from the barium salt with sodium carbonate) in 2 ml. of water. The precipitate which formed at once weighed 0.5 g. It was intensely red colored, insoluble in acids, soluble in alkali.

Anal. Calcd. for $C_{24}H_{20}N_6O_3S_4$: S, 19.75. Found: S, 19.48.

Barium 5-Acetamido-2,4-thiophenedisulfonate.—A solution of 0.7 g. of (I) in 2 ml. of 60% fuming sulfuric acid was left at 25° for an hour, poured into ice water, and neutralized with barium carbonate. There was no unchanged (I). The barium salt, precipitated from 7 ml. of aqueous solution by addition of alcohol, weighed 1.5 g. For analysis, a sample was dried at 140° for three hours.

Anal. Calcd. for $C_6H_5NO_7S_3Ba$: Ba, 31.49. Found: Ba, 31.20.

Reaction with Diazotized Benzidine.—To the filtered diazo solution made (as above) from 0.35 g. of benzidine hydrochloride was added a solution of 0.6 g. of the barium salt in 5 ml. of water. An orange precipitate appeared after a couple of minutes; yield, 0.3 g. The color of this salt is intensified by mineral acids but becomes nearly colorless in alkaline solution.

Anal. Calcd. for $C_{18}H_{13}N_5O_7S_3$: S, 18.93. Found: S, 18.60.

Diazotization.—In view of the inability of 2-thiophenamine to undergo diazotization, the following experiment strikingly demonstrates the fact that a sulfonated 2-thiophenamine does diazotize. A few drops of 60% fuming sulfuric acid were added to 50 mg. of 2-thiophenammonium chlorostannate, $(C_4H_3SNH_3)_2SnCl_6$. Fumes were evolved. After dilution with ice and water the mixture was treated with a few drops of sodium nitrite solution, then with alkaline 2-naphthol. An intense red dye formed. As a matter of fact, a red color appeared before addition of the naphthol, caused, no doubt, by coupling of the diazotized portion on some of the unreacted thiophene nuclei.

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Summary

Syntheses of several halogen, azo and organic mercury derivatives of aceto-2-thiophenamide are described.

Aceto-2-thiophenamide couples readily in the 5-position with diazo compounds, even in acid solution. The halogen derivatives of this amide also couple not only when the 5-position is unsubstituted but also when a 5-halogen substituent is present, the latter requiring neutral or alkaline conditions. In reactions of the latter type the halogen is ejected, but halogen atoms on positions 3,4 are not disturbed.

Fuming nitric acid causes replacement of a 5-azo group or a 3-halogen substituent by nitro.

Sulfonic derivatives of aceto-2-thiophenamide are described. The diazotizability of a sulfonated 2-thiophenamine is demonstrated.

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[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF INDIANA UNIVERSITY]

Diquinolylmethanes

BY C. E. KASLOW AND R. A. RECK[1,2]

Very few diquinolylmethanes have been recorded in the literature. Schuller[3] prepared 5,5′-methylenebis-8-hydroxyquinoline by treatment of 8-hydroxyquinoline with formaldehyde in concentrated sulfuric acid 6,6′-methylenebisquinoline[4] was obtained by a Skraup reaction on 4,4′-diaminodiphenylmethane. Borsche and Meyer[5] synthesized 6,6′-methylenebis-2-methylquinoline by the action of alcoholic alkali and acetone on 5,5′-diisatylmethane and decarboxylation of the 6,6′-methylenebis-2-methylcinchoninic acid which was obtained from the reaction. The corresponding 2-phenyl derivative was prepared in a similar manner. Monti and Verona[6] have reported a methylenebis-6-hydroxyquinoline.

The present paper reports on the synthesis of several 6,6′-methylenebislepidine derivatives from corresponding 6,6′-methylenebisacetoacetanilides through the carbostyrils and chlorolepidine derivatives. The latter have also been converted to 2-alkyl ethers and two cyclic tertiary amino derivatives.

Experimental[7]

4,4′-Methylenebisacetoacetanilide.—A stirred solution of 59.4 g. (0.3 mole) of 4,4′-diaminodiphenylmethane in 400 ml. of warm acetone contained in a three-necked flask was treated dropwise with 54.6 g. (0.65 mole) of diketene. The rate of addition was regulated so as to cause the acetone to reflux rapidly. The 4,4′-methylenebisacetoacetanilide did not start to precipitate until most of the diketene has been added. The stirred reaction mixture was heated on a steam-bath for an additional hour. The solid was removed by filtration, washed with three 100-ml. portions of acetone and dried at 80–85°. The yield was 86.2 g. (78.5%); m. p. 167.5–168.5°. Recrystallization of 4 g. of the substance from 135 ml. of a boiling solution of absolute ethyl alcohol–acetone (3:1) gave 3.7 g. of white granular solid, m. p. 168.5–169°. The melting point could not be raised further.

Anal. Calcd. for $C_{21}H_{22}N_2O_4$: N, 7.65. Found: N, 7.60.

An additional 16.5 g. was obtained by concentration of the combined mother liquor and filtrate; m. p. 161–164°. One recrystallization of the low melting material raised the m. p. to 166–168°; yield 11.3 g.

6,6′-Methylenebis-4-methylcarbostyril.—To 90 ml. of concentrated sulfuric acid at 70–75° was added 54.9 g. (0.15 mole) of 4,4′-methylenebisacetoacetanilide in 2–3 g. portions. The temperature was not allowed to go above 95°. After all of the substance had been added, the reaction mixture was heated in a boiling water-bath for fifteen minutes, then cooled until much solid had separated and water was added cautiously, and cooled from time to time, until 300–350 ml. had been added. The solid was

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(3) Schuller, *J. prakt. Chem.*, [2] **88**, 180 (1913).

(4) Borsche and Kienitz, *Ber.*, **43**, 2334 (1910).

(5) Borsche and Meyer, *ibid.*, **54**, 2841 (1921).

(6) Monti and Verona, *Gazz. chim. ital.*, **62**, 878 (1932).

(7) All melting points are corrected.