Summary

1. By fusion of benzalamino-benzoselenazoles with sulfur, and with selenium, selenazolo-benzothiazoles and benzo-bis-selenazoles, new heterocyclic types, have been prepared and studied, together with some of their derivatives. The bis-selenazole was also obtained from the dibenzal-*p*-phenylenediamine, by heating it with selenium.

2. The formation of another new base, $C_{27}H_{18}N_2S_2Se$, was observed in one of these experiments, but it could not be obtained a second time and was not identified.

3. Fusion of furalamino-benzoselenazoles with either selenium or sulfur gave only decomposition products.

4. The following new compounds were prepared: 2,6-diphenyl-*p*-β-benzo-bis-selenazole, its acetyl chloride addition product, mononitro, dinitro, mono-amino and benzalamino derivatives; 6-furalamino-2-phenylbenzoselenazole; 2,6-diphenyl-*p*-β-selenazolo-benzothiazole, its tetra-bromide, acetyl chloride addition product and dinitro derivative; a base, $C_{27}H_{18}N_2S_2Se$, its dinitro derivative and a reduction product of the latter.

New York, N. Y.

[Contribution from the Laboratory of Organic Chemistry of the University of Wisconsin]

DIPHENEINS FROM RESORCINOL AND SUBSTITUTED DIPHENIC ANHYDRIDES. STRUCTURE OF CERTAIN DIPHENYL DERIVATIVES

By Homer Adkins, Edw. F. Steinbring and Elizabeth Pickering[1]

Received May 9, 1924 Published August 5, 1924

Experimental work based upon the idea that diphenic anhydride should behave similarly to phthalic anhydride has been described in two papers dealing with the condensation of the former with resorcinol. These papers appeared in successive months, the first by Dutt,[2] and the second by Bischoff and Adkins.[3] The two reports are in essential agreement, to the effect that the resorcinol condenses with diphenic anhydride to form a strongly fluorescent compound, analogous to fluorescein, which may be brominated to form a compound analogous to eosin. Later Underwood and Kochmann[4] questioned these results and claimed first, that the condensation product of diphenic anhydride and resorcinol is not fluorescent and second, that the previous investigators had not touched upon the

---

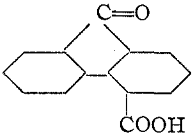
[1] Mr. Steinbring performed all of the experimental work described in this paper, although the work was based on certain observations made by Miss Pickering.—H. A.

[2] Dutt, *J. Chem. Soc.*, **123**, 225 (1923).

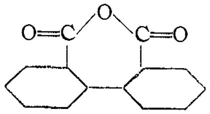
[3] Bischoff and Adkins, This Journal, **45**, 1030 (1923).

[4] Underwood and Kochmann, *ibid.*, **45**, 3071 (1923).

transformation of the anhydride to the isomeric diphenyleneketone-4-carboxylic acid (Formula I) and the possibility that their condensation product was derived from it rather than from the anhydride (Formula II).



I



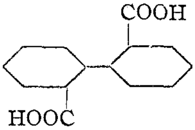
II

In regard to the first of these points it may be said that Bischoff early in his experimental work learned that when the anhydride was condensed with resorcinol at temperatures in the vicinity of those used by Underwood and Kochmann, a non-fluorescent compound was formed, sometimes with the evolution of carbon dioxide. Because of these two facts condensations *were thereafter carried out at a lower temperature. It is obvious that* Underwood and Kochmann did not obtain the same compounds as did the earlier investigators and that their condensation involved fundamental changes in structure that were avoided by Dutt and by Bischoff and Adkins.

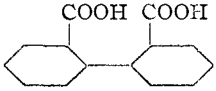
In regard to the second criticism a perusal of the paper from this Laboratory should reveal the fact that it was definitely shown that the condensation product from the anhydride was similar in many properties to that obtained from the ketonic acid but was not identical with it. The establishment of this fact was considered to be one of the most significant things in the experimental work. The two condensation products were differentiated on the basis of the alkali solubility of the acetyl derivatives.

The study of the dipheneins, analogous to the phthaleins, has been continued by the condensation of substituted diphenic anhydrides with resorcinol. Hitherto no substituted diphenic anhydrides have been available, for the nitro and hydroxy acids do not form anhydrides. However, it has been discovered that anhydrides may be prepared from the 4,5- and 2,7-diamino-diphenic acids by the use of acetic anhydride, the amino groups being at the same time acetylated.

Schmidt and Kampf[5] explained the non-formation of anhydrides from the dinitro and dihydroxy diphenic acids as being the result of the nitro or hydroxyl groups causing the carboxyls to take up positions on opposite sides of the rings as illustrated in Formula III rather than on the same side as in diphenic acid, IV.



III



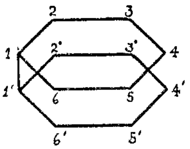
IV

---

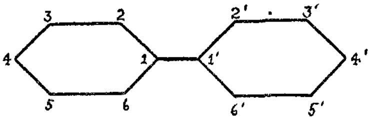
[5] Schmidt and Kampf, *Ber.*, **36**, 3739 (1903).

This hypothesis offers no suggestion of an experimental proof and does not take into consideration the later and rather extensive work upon the configuration of diphenyl derivatives.

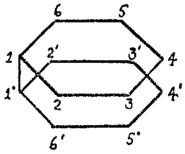
Kauffler[6] advanced the idea that in benzidine the two rings are superimposed as in Formula V, rather than as in the conventional formula VI. Adams, Bullock and Wilson[7] in an interesting discussion in which they give a review of the literature of the subject as well as some illuminating experimental work, think it probable, "that the benzene rings in diphenyl derivatives are in motion with the limiting positions of the two possible Kauffler formulas and the intermediate position of the formula usually assigned to diphenyl."



V



VI



VII

The facts may be explained by supposing first that the position of the rings between the extremes (Formulas V, VI, VII) is determined by the substituents on the ring, and second that this "favored" configuration may be modified by the position of reactive groups in molecules capable of reacting with a group of the diphenyl derivative (as in Adams' work), that is, the relative position of the rings may be altered through the intervention of a second molecule.

The non-formation of anhydrides from the nitro and hydroxy acids is due, on the basis of Kauffler's and of Adams' work, either to the fact that in these diphenyl derivatives the two rings are extended as in Formula VI or else the rings are superimposed, but in such a way that the carboxyls are not adjacent to each other. (Such an arrangement would be found in Formula V or VII depending on whether the carboxyls were in the 2,2′- or in the 2,6′-positions.) The second hypothesis would be feasible if the non-formation of anhydrides occurred only in compounds unsymmetrically substituted with respect to the major axis of the rings. But since the nitro groups in the 4,4′-position prevent the formation of the anhydride as well as when they are in other positions it seems rather certain that the non-formation of the anhydrides is due to the fact that in the dinitro and dihydroxy acids the rings are extended as in the conventional formula, while in the amino or benzidine type of acids the rings are superimposed.

One would then hazard the opinion that the nitro-carboxylic benzidines that did not form anhydrides would not manifest the reactions that Kauf-

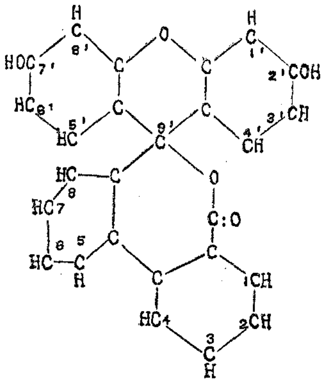
---

[6] Kauffler, *Ann.*, **351,** 156 (1907); *Ber.*, **46,** 3250 (1907).

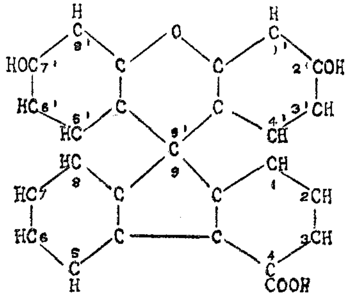
[7] Adams, Bullock and Wilson, THIS JOURNAL, **45,** 521 (1923).

fler, and Adams, Bullock and Wilson found to take place between benzidine and phthalic anhydride or terephthal aldehyde or isophthal aldehyde and that such benzidines when tetrazotized would couple with almost equal facility at both diazo groups.

The N-diacetyl-diamino-diphenic anhydrides have been condensed with resorcinol to form the corresponding disubstituted dipheneins. The simplest diphenein to be derived from resorcinol is represented in Formula VIII. The isomeric condensation product derived from the keto-carboxyl acid produced by the rearrangement of the anhydride prior to condensation is represented in Formula IX. Both have been previously prepared.[2,3]

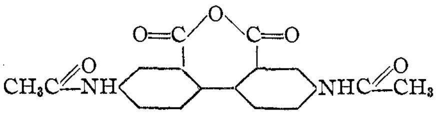


VIII

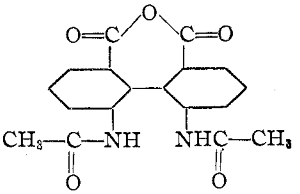


IX

It has been found that when the 2,7-anhydride (Formula X)—resorcinol condensation is carried out at temperatures much above 110°, rearrangement takes place and the product has the —NHCOCH$_3$ groups in the 2 and 7 positions of Formula IX. This is evidenced by the fact that the acetyl derivative of the condensation product is soluble in sodium carbonate solution, due to the presence of the free carboxyl group. When, however, the condensation is carried out at 110° in an electrically-heated oven, rearrangement does not take place and the true diphenein is obtained in which the —NHCOCH$_3$ groups are in the 2 and 7 positions of Formula VIII. The acetyl derivative of the true diphenein is insoluble in solutions of sodium carbonate since there is no free carboxyl group in this type of compound.



X

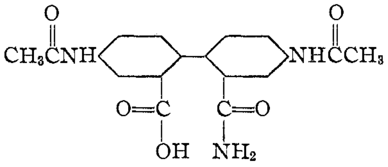


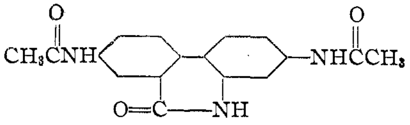
XI

When the anhydride of the diphenic acid having acetyl amino groups in the 4,5-positions (Formula XI) is condensed with resorcinol, rearrangement to form the ketonic acid is impossible so that there can be no question but that from this anhydride a diphenein is obtained in which —$NHCOCH_3$ groups are in Positions 4 and 5 of Formula VIII. This is borne out by the fact that the acetyl derivative is insoluble in a sodium carbonate solution.

All of these condensation products are fluorescent, although not so markedly as is fluorescein. Their solutions in alkali are cherry-red to brownish-red. They dye silk and wool to give rather pleasing shades of pink and grayish-purple. The colors apparently are quite fast to washing and light.

In further study of the phenanthridone series,[8] a member of that series has been prepared. The 2,7-N-diacetyl-diamino-diphenic anhydride has been converted into the corresponding amic acid (Formula XII), which has been treated with sodium hypobromite to give the amino-carboxylic acid. This latter compound immediately loses water forming the 2,7-N-diacetyl-diamino-9(10)-phenanthridone (Formula XIII).


XII


XIII

Experimental Part

Phenanthraquinone,[8] 2,7- and 4,5-dinitro-phenanthraquinone,[9] and the 2,7- and 4,5-dinitro-diphenic acids[10] were prepared as previously described. The yields and melting points of these compounds in the order given above were: 58%, m. p. 202°; 40%, m. p. 303°; 40%, m. p. 216°; 90%, m. p. 253°; 93%, m. p. 298°.

2,7-Diamino-diphenic Acid.—In attempting to prepare this compound Hummel[11] obtained colored products that were obviously impure. In using his method similar products were obtained in this Laboratory. An improved method has been devised which gives pure white compounds having melting points above those previously found. To a mixture of 22 g. of the dinitro acid and a solution of 100 g. of stannous chloride in 100 cc. of water, in a 500cc. round-bottom flask under a reflux condenser, was slowly added 116 cc. of 37% hydrochloric acid through the condenser, and the flask agitated and if necessary warmed in order to start the reaction. After the reaction was almost complete the solution was boiled for 10 minutes or until the acid had disappeared. The reaction mixture was evaporated nearly to dryness, and the residue dissolved in a liter of water. Hydrogen sulfide was then introduced until further precipitation of tin sulfides did not occur on dilution of the mixture. After filtration, the solution and wash-

---

[8] Oyster and Adkins, THIS JOURNAL, **43,** 208 (1921).

[9] Schmidt and Kampf, *Ber.*, **36,** 3739 (1903).

[10] Schultz, *Ann.*, **196,** 26 (1878).

[11] Hummel, *Ann.*, **193,** 132 (1878).

ings were evaporated to about 100 cc.; upon cooling, the hydrochloride of the amino acid crystallized in fine, white needles; yield av., 16.5 g.

Anal. Calc. for $C_{14}H_{12}O_4N.2HCl$: N, 8.11. Found: 8.01, 8.07.

The free 2,7-diamino acid, m. p. 265°, was obtained by treating the dry hydrochloride with a dilute solution of ammonia and carefully neutralizing with acetic acid. Hummel gives the melting point as 250–251°.

Anal. Calc. for $C_{14}H_{12}O_4N_2$: N, 10.29. Found: 10.2.

2,7-N-Diacetyl-diamino-diphenic Anhydride.—Twenty-six g. of the hydrochloride of the 2,7-diamino-diphenic acid was refluxed with 150 cc. of acetic anhydride for an hour, and as this liquid cooled 25 g. of the acetylated anhydride separated in fine, white needles. The compound did not melt and was insoluble in hydrochloric acid and in a cold solution of sodium hydroxide.

Anal. Calc. for $C_{18}H_{14}O_5N_2$: N, 8.27. Found: 8.16.

2,7-N-Diacetyl-diamino-diphenamic Acid.—Ten g. of the anhydride was refluxed for 30 minutes with 50 cc. of ammonium hydroxide (d., 0.90). The cold solution was made *just* acid with acetic acid and the sides of the beaker were rubbed with a glass rod, whereupon the amic acid separated in fine white crystals. These are soluble in dil. alkali and in acetic acid.

Anal. Calc. for $C_{18}H_{17}O_5N_3$: N, 11.83. Found: 11.76.

2,7-N-Diacetyl-diamino-9(10)-phenanthridine.—Five g. of the amic acid was dissolved in 25 cc. of a 10% solution of sodium hydroxide. A solution of 2.35 g. of bromine in 25 cc. of a 10% sodium hydroxide solution was then added and the mixture allowed to stand for a half hour. The excess of hypobromite was removed with a cubic centimeter of a saturated solution of sodium bisulfite. Four g. of the phenanthridine was obtained by precipitation with a solution of hydrochloric acid. It was recrystallized from acetic acid. The compound does not melt, but darkens at 350°, is insoluble in water, hydrochloric acid and sodium hydroxide solution, and is only slightly soluble in boiling alcohol or nitrobenzene.

Anal. Calc. for $C_{17}H_{15}O_3N_3$: N, 13.55. Found: 13.42.

The Hydrochloride of 2,7-Tetrazonium-diphenic Acid; 2,7-Dihydroxy-diphenic Acid.—Twenty g. of the hydrochloride of the 2,7-diamino-diphenic acid was dissolved in 75 cc. of water and 16 cc. of a 37% solution of hydrochloric acid added. The compound was tetrazotized with a slight excess of a 40% sodium nitrite solution at a temperature below 3°. After a short time fine, pure white crystals of the tetrazonium salt separated. The compound turned yellow after exposure to the air for an hour or two. The moist crystals were dissolved in 150 cc. of water and hydrolyzed in a boiling water-bath for an hour. The solution was then concentrated to about 25 cc., and as it cooled 12 g. (72% of the calculated quantity) of the hydroxy acid separated. This product was dissolved in 20 cc. of hot water, the solution boiled with charcoal, filtered and cooled. Pure white crystals, m. p., 278°, were obtained.

Anal. Calc. for $C_{14}H_{10}O_6$: C, 61.3; H, 3.65. Found: C, 61.2; H, 3.96.

The phenolic acid condensed with phthalic anhydride to give a compound that showed a blue color with purple fluorescence when dissolved in alkali. The color was red in an acid solution. The phenolic acid was also condensed with a substituted diphenic anhydride but no colored compound was obtained.[11] Schmidt and Scholl[12] describe the 2,7-dihydroxy acid as a yellow compound melting at 271–272°. They did not obtain an insoluble tetrazonium salt and evidently did not obtain a pure phenol.

---

[12] Schmidt and Scholl, *Ber.*, **38**, 3769 (1905).

4,5-Diamino-diphenic Acid Hydrochloride.—The method used in the preparation of the 2,7-isomer was not satisfactory because the hydrochloride of the 4,5-compound is much less soluble in water. The method was modified as follows. A mixture of 20 g. of the 4,5-dinitro-diphenic acid, 22 g. of tin, 100 cc. of concd. hydrochloric acid and 100 cc. of water was refluxed for an hour. As this cooled, the impure 4,5-hydrochloride separated and was purified by solution in 10% sodium hydroxide solution and precipitation with hydrochloric acid. The product was then recrystallized from *boiling* water; yield, 15–16 g.

The free 4,5-diamino acid was prepared in the same manner as its 2,7-isomer and was found to be similar to it in properties. It melts with decomposition at 312–313° and is soluble in hot water, in acids and in alkalies.

Anal. Calc. for $C_{14}H_{12}O_4N_2$: N_2, 10.3. Found: 10.31, 10.40.

4,5-N-Diacetyl-diamino-diphenic Anhydride.—This compound was prepared in the same manner as the 2,7-compound. It was found to be much less stable. Mere exposure to moisture for some days converted it to 4,5-*N*-diacetyl-diamino-diphenic acid. The compound was heated to 150° for eight hours to drive off traces of moisture.

Anal. Calc. for $C_{18}H_{14}O_5N_2$: N, 8.29. Found: 8.28, 8.25.

Condensation of 2,7-N-Diacetyl-diamino-diphenic Anhydride with Resorcinol.—Five g. each of the 2,7-anhydride, resorcinol and zinc chloride were well mixed and heated with occasional stirring for 25–30 hours at 110° in a well-regulated oven. As the melt cooled, a red glass formed which was treated with boiling water to dissolve the zinc chloride. This operation softened the glass which was then easily worked up into a sticky mass. The water was then poured off and the residue several times dissolved in 5% sodium hydroxide solution and precipitated with hydrochloric acid to purify it from zinc oxide. The light red precipitate so obtained was then extracted with ethyl alcohol and the solution filtered. The alcoholic filtrate was evaporated to dryness and the residue heated at 125° in an oven for several hours to drive off the last traces of water and alcohol. The solutions of the compound in dilute alkali were reddish-brown and showed a green fluorescence, which was lost when concentrated alkali was used or when the dilute alkali solution was boiled.

Anal. Calc. for $C_{30}H_{22}O_7N_2$: N, 5.36. Found: 5.37, 5.32.

Three g. of the condensation product described above was acetylated by boiling for two hours with acetic anhydride. A dark red, slimy solid was obtained upon pouring the mixture into water. This was washed with water several times and dried at 100°. Two g. of a dark red, brittle solid resulted which was insoluble in sodium carbonate solution but very slowly soluble in cold, dil. sodium hydroxide and more readily soluble in a boiling solution. The cold alkali does not become colored until it stands for 20–30 minutes in contact with the product. After 10 to 12 hours complete solution takes place yielding a dark, reddish-brown liquid which exhibits green fluorescence upon dilution.

This condensation was also carried out at 150–180°. The products obtained also gave reddish-brown, fluorescent solutions with alkalies but their acetylated derivatives were soluble in sodium carbonate solution and in cold sodium hydroxide solution. About twenty condensations were made at different temperatures from 110° to 180°. The results were essentially as outlined in the two experiments described above.

A sample of the acetylation product obtained from a condensation at 160–170° was purified by dissolving it in alcohol and precipitating by the addition of water, dried and analyzed.

Anal. Calc. for $C_{50}H_{32}O_{12}N_2$: N, 4.03. Found: 3.98.

Condensation of 4,5-N-Diacetyl-diamino-diphenic Anhydride with Resorcinol.—The condensations were carried out as with the 2,7-isomer at 110° and a similar fluorescent product was obtained. The acetylation product also was found to be insoluble in sodium carbonate solution but slowly soluble in cold sodium hydroxide solution on long standing and more rapidly soluble in the boiling solution.

Bromination of a Diphenein.—A condensation product derived from the 2,7-anhydride, which had been formed at 135–150° was brominated as in the preparation of eosin. The product gave a cherry-red solution in alkali. Acids precipitated a red, amorphous powder which contained four bromine atoms to the molecule.

Anal. Calc. for $C_{30}H_{18}O_7N_2Br_4$: Br, 38.1. Found: 37.3.

The analysis checks the calculated amount exactly if one assumes that the compound was monohydrated, as has been found previously for similar compounds.

Summary

1. It has been shown that anhydrides of substituted diphenic acids may be prepared if —$NHCOCH_3$ groups are in the 2,7- or 4,5-positions of the acid although it has not been possible to prepare such anhydrides when the substituents are nitro or hydroxy groups.

2. The formation or non-formation of anhydrides is apparently dependent upon whether the substituents cause the diphenyl rings to be superimposed or extended. The rings are apparently superimposed in the case of diphenic acid and of the amino derivatives of diphenyl but are extended in the case of the nitro or hydroxy derivatives.

3. Substituted dipheneins have been prepared at 110° from substituted diphenic anhydrides and resorcinol. These dipheneins have the —$NHCOCH_3$ groups in the 2,7- and in the 4,5-positions. When the condensation was carried out at higher temperatures with the anhydride of the acid substituted in the 2,7-positions, rearrangement took place with the formation of a derivative of fluorenone.

4. A substituted diphenamic acid and a phenanthridone have been prepared.

5. Improved methods of preparation and corrected physical constants of certain amino and hydroxyl derivatives of diphenic acid have been given.

6. Certain apparently erroneous statements in Underwood and Kochmann's recent paper on diphenyl derivatives have been pointed out.

Madison, Wisconsin