to low potency culture filtrates.

Employing 2% *p*-toluenesulfonic acid monohydrate in water saturated *n*-butanol the effect of various salts on the mobilities of streptomycin, dihydrosteptomycin, mannosidostreptomycin, streptothricin and neomycin A sulfates has been studied. Two distinct zones were formed by each of the antibiotics studied in the presence of one or more salts.

KALAMAZOO, MICHIGAN RECEIVED JANUARY 7, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

Ortho Esters, Imidic Esters and Amidines. The Identity of N-Phenyl-N'-*p*-tolylformamidine

BY ROYSTON M. ROBERTS

Walther[1] first reported the preparation of N-phenyl-N'-*p*-tolylformamidine and claimed to have obtained four "isomeric" compounds (m. p.'s. 98°, 102°, 120°, 132°) by various methods. This work was criticized by Wheeler,[2] who claimed that all of Walther's "isomers" were actually mixtures and that the pure compound melted at 103.5–104.5°. However, a short time later, Wheeler and Johnson[3] described two new routes for the preparation of this compound (equations A and B).

$$C_6H_5N{=}CHOEt + H_2NC_7H_7 \rightleftarrows C_6H_5N{=}CH{-}NHC_7H_7 + EtOH \quad (A)$$

$$C_7H_7N{=}CHOEt + H_2NC_6H_5 \rightleftarrows C_7H_7N{=}CH{-}NHC_6H_5 + EtOH \quad (B)$$

The products of the two reactions were said to be identical, m. p. 86°. Although it conflicted with Wheeler's own previous results, this was the work which was accepted and recorded by "Beilstein."

When we set out to prepare this unsymmetrical diarylformamidine, we used the method of Wheeler and Johnson (equation A). To our surprise, we obtained a product which melted sharply at 105–106°. Further investigation of the literature led us to Walther's work and to the earlier paper of Wheeler. Since it was necessary to have a very pure material for our purposes, we studied the conditions of the reaction and the isolation of the product quite carefully. We found that the reaction was greatly affected by a small amount of acid; when a small crystal of aniline hydrochloride was added to a mixture of ethyl N-phenylformimidate and *p*-toluidine at room temperature, a vigorous evolution of heat occurred and the mixture set to a mass of crystals within a few minutes. Products of all such acid-catalyzed reactions were found to melt lower than those from mixtures which had been carefully protected from acid. When very small amounts of acid were used, products were obtained which melted sharply at around 85°, and the melting point was not raised by further recrystallization from petroleum ether or ethanol (the solvents employed by Wheeler and Johnson). We have now shown that the product of the reaction in the absence of acid, which melts at 105–106°, is N-phenyl-N'-*p*-tolylformamidine, and that the product formed in the presence of very small amounts of acid, which melts at about 85°, is a mixture of the unsymmetrical formamidine and the two corresponding symmetrical formamidines, N,N'-diphenylformamidine and N,N'-di-*p*-tolylformamidine. Thus, it seems likely that Wheeler actually had the pure compound in his first work, but in the later work used a reaction which is extremely sensitive to acid-catalyzed disproportionation.

We obtained the same pure "high-melting" product from ethyl N-*p*-tolylformimidate and aniline (equation B) when care was taken to avoid traces of acid. Again, when very small amounts of *p*-toluidine hydrochloride were added to the reaction mixtures, the "low-melting" product was obtained. This "low-melting" product is a very unusual mixture. It melts over a narrow range at around 85° (various preparations after several recrystallizations melted at 83–84°, 84–86°, 85–86°, etc.) and we were not able to raise the melting points of such products by repeated recrystallization from several different solvents. It thus appears to be a eutectic mixture of minimum solubility or, perhaps, a solid solution of the three compounds.

The evidence that the "low-melting" product is a mixture of N-phenyl-N'-*p*-tolylformamidine, N,N'-diphenylformamidine, and N,N'-di-*p*-tolylformamidine, and that the "high-melting" product is pure N-phenyl-N'-*p*-tolylformamidine is: (1) Reactions according to both equations A and B *in the absence of acid* led to the same product, m. p. 105–106°. (2) Reactions according to both equations A and B *in the presence of small amounts of acid* led to products with lower melting points. From both pairs of reactants products were obtained with rather sharp melting points around 85°. (3) Treatment of the "high-melting" product with small amounts of acid in alcohol solution produced the "low-melting" product. (4) The "high-melting" product gave a picrate which melted over a rather narrow range, 174–176°.

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(1) Walther, *J. prakt. Chem.*, [2] **55**, 41 (1897); Zwingenberger and Walther, *ibid.*, [2] **57**, 209 (1898).

(2) Wheeler, *Am. Chem. J.*, **19**, 367 (1897).

(3) Wheeler and Johnson, *Ber.*, **32**, 35 (1899).

(5) The "low-melting" product gave a picrate which melted over a wide range (*ca.* 160–190°). Repeated recrystallization of this picrate resulted in isolation of the picrate of N,N'-di-*p*-tolylformamidine. (6) Analysis of the "low-melting" product showed it to have the same proportion of carbon and hydrogen as the "high-melting" product.

N,N'-Diphenylformamidine and N,N'-di-*p*-tolylformamidine have almost identical melting points and solubilities in non-polar solvents, so that isolation of either of these from a mixture is difficult. The melting points and solubilities of the picrates, however, are different enough to allow separation of the less soluble and higher-melting N,N'-di-*p*-tolylformamidine salt. The presence of N,N'-diphenylformamidine in the 85° product is indicated by the elementary analysis, which requires an amount equivalent to the N,N'-di-*p*-tolylformamidine present, and the presence of the unsymmetrical formamidine by the fact that mixtures of only the two symmetrical formamidines melt much higher and over a wide range. In an analogous case all three of the expected diarylformamidines have been isolated. In this case the reaction was between ethyl N-phenylformimidate and *p*-nitroaniline, and the isolation of all three products was possible because of the great difference in melting points and solubility of N,N'-diphenylformamidine, N-phenyl-N'-*p*-nitrophenylformamidine and N,N'-di-*p*-nitrophenylformamidine. We intend to publish the results of the investigation of the reaction of *p*-nitroaniline and other aromatic amines with formimidates separately in the near future.

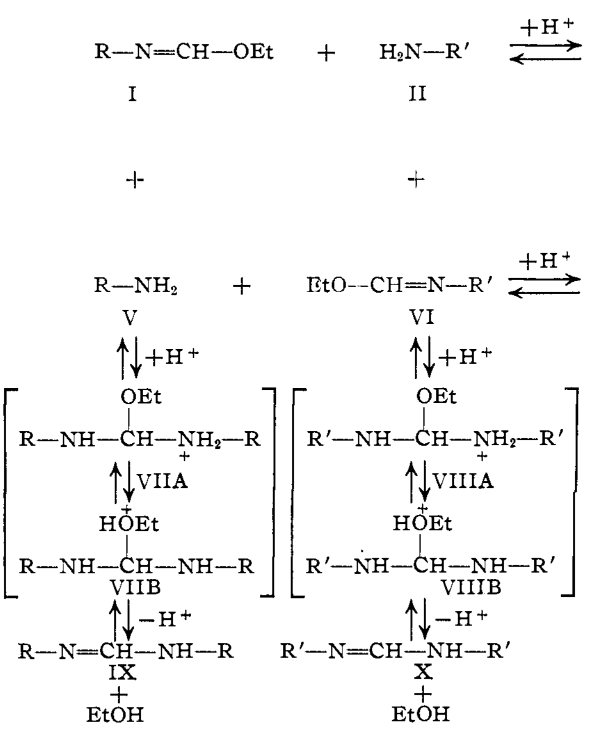
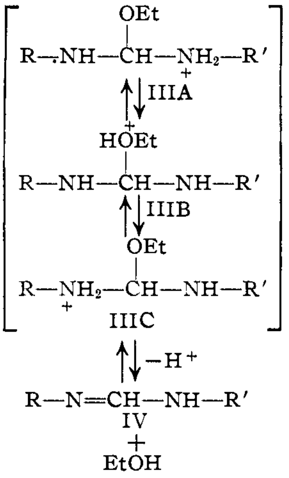


Fig. 1.

In the presence of acid, we believe that the formation of a diarylformamidine from a formimidate and an aromatic amine takes the course: I + II → IIIA → IIIB → IV (Fig. 1). The same reaction product may be obtained from the opposite pair of reactants V and VI, via IIIC and IIIB. Since a mobile equilibrium should exist between IIIA, IIIB, and IIIC, it may be expected that V and VI would soon be present in a reaction mixture which contained I and II at the outset, and *vice versa*. Possibility then exists of reaction of I with V to give IX (via VIIA and VIIB) and of II with VI to give X (via VIIIA and VIIIB). This scheme is supported by a number of further observations. When ethyl N-phenylformimidate was treated with excess *p*-toluidine in ether solution in the presence of catalytic amounts of *p*-toluidine hydrochloride, N,N'-di-*p*-tolylformamidine was isolated. Similarly, ethyl N-*p*-tolylformimidate was treated with excess aniline and N,N'-diphenylformamidine was obtained. When N-phenyl-N'-*p*-tolylformamidine (m. p. 105°) was treated with ethanol and excess *p*-toluidine, N,N'-di-*p*-tolylformamidine was isolated. Heating equimolar amounts of N,N'-diphenylformamidine, N,N'-di-*p*-tolylformamidine, and ethanol in the presence of acid catalyst gave a product melting at 85° which gave no depression when mixed with the "low-melting" product from the reaction of ethyl N-phenylformimidate with *p*-toluidine in the presence of acid.



Recently the author published a note[4] on the preparation of formimidates from ethyl orthoformate and aromatic amines or diarylformamidines in the presence of acid catalysts. The mechanism of the reaction was not discussed in detail because it was considered to be intimately related to the present work, which was in progress, and it was thought that a more unified treatment of the relationships between orthoformates, formimidates, and formamidines could be presented here. These relationships are outlined in Fig. 2. The steps shown for the conversion of an orthoformate to a formimidate (X → XVI) are entirely analogous to those proposed by Winstein and Buckles[5] for the related process of acid catalyzed hydrolysis of an

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[4] Roberts, THIS JOURNAL, **71**, 3848 (1949).

[5] Winstein and Buckles, *ibid.*, **65**, 613 (1943).

orthoester. The conversion of a formimidate to a formamidine is considered to take place by a continuation of the same process of replacement of –OR by –NHR. The final product of such replacements might be expected to be an orthoformamide (XXII), which indeed was reported ,by some workers to be the type of product obtained from the reaction of ethyl orthoformate with aromatic amines,[6] but these products have now conclusively been shown to be formamidines.[7] The isolation of a formamidine is probably due to the stabilization of its conjugate acid by resonance.[7b,8]

It will be seen that XVI → XV → XVII → XVIII → XIX → XX of Fig. 2 corresponds to I → IV, I → IX, and VI → X of Fig. 1. The preparation of ethyl N-phenylformimidate from ethyl orthoformate and aniline is considered to proceed as shown by X → XVI in the presence of acid catalysts. The preparation of the formimidate from N,N'-diphenylformamidine and ethyl orthoformate may also be illustrated by this scheme.[9] The first step is X → XII + ethanol. The ethanol then reacts with the formamidine conjugate acid (XIX) which is converted to one mole of XVI and aniline. The aniline reacts with XII to produce a second mole of XVI, so that the over-all reaction is that which was given in the note[4] and also by Claisen[10]

$$C_6H_5N{=}CHNHC_6H_5 + HC(OC_2H_5)_3 \longrightarrow 2C_6H_5N{=}CHOC_2H_5 + C_2H_5OH$$

In order to explain the reactions of orthoformates and formimidates with aromatic amines in the absence of acid, different mechanisms from those outlined in Figs. 1 and 2 must be assumed to operate, for when acid is excluded ethyl orthoformate reacts with aniline to produce only N,N'-diphenylformamidine, and no ethyl N-phenylformimidate can be isolated even though excess orthoformate is used. Likewise, ethyl N-phenylformimidate reacts with *p*-toluidine to produce the pure unsymmetrical formamidine.

Acknowledgment.—The author gratefully acknowledges the assistance of Mr. Robert H. DeWolfe, who carried out some of the experiments, and a grant from the University of Texas Research Institute which made this assistance possible.

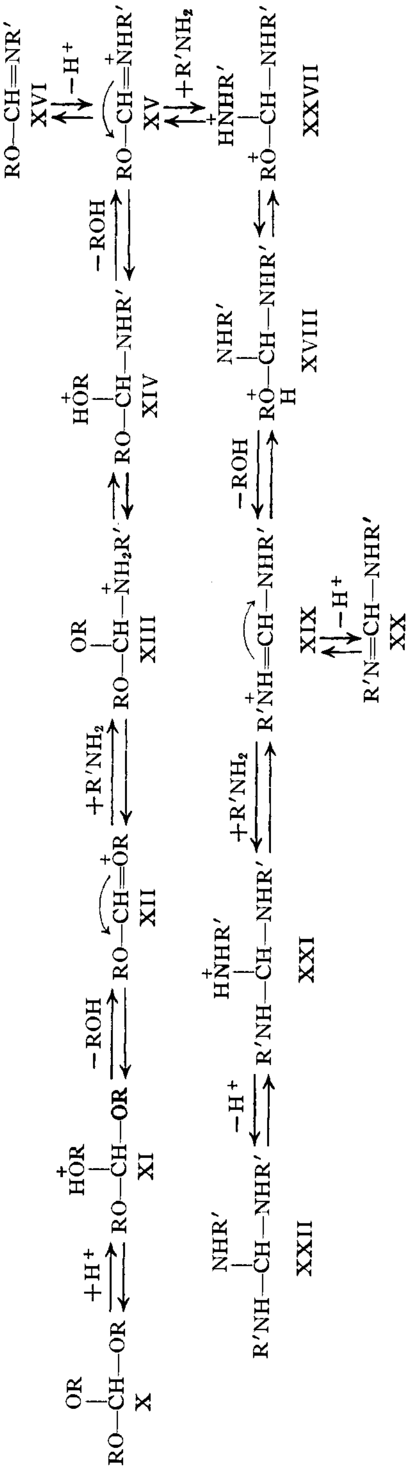

Fig. 2.

Experimental[11]

N-Phenyl-N'-*p*-tolylformamidine. A. From Ethyl N-Phenylformimidate and *p*-Toluidine.—In all experiments where it was desired to exclude acid, each piece of apparatus used was washed with ammonium hydroxide solu-

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(6) (a) Giacolone, *Gazz. chim. ital.*, **62**, 577 (1932); (b) Lewis, Krupp, Tieckelmann and Post, *J. Org. Chem.*, **12**, 303 (1947).

(7) (a) Backer and Wanmaker, *Rec. trav. chim.*, **67**, 257 (1948); **68**, 247 (1949); (b) Knott and Jeffreys, *J. Org. Chem.*, **14**, 879 (1949).

(8) Wheland, "The Theory of Resonance," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 180.

(9) Knott and Jeffreys[7b] outlined possible reaction paths for the reactions of orthoformates and formamidines, some of which are analogous to those of Figs. 1 and 2, except that the function of hydrogen ion was not indicated. The mechanism proposed by them for the formation of formimidate from an orthoformate and a formamidine was very different from the one described here, however, and since it implied no dependence on acid catalysis, it does not fit the facts as well.

(10) Claisen, *Ann.*, **287**, 362 (1895).

(11) All melting points are corrected. Microanalyses by Clark Microanalytical Laboratory, Urbana, Illinois.

tion and carefully dried. Equimolar amounts of the reactants were allowed to react, (a) at room temperature in a closed flask, (b) at room temperature with a slow stream of dry nitrogen bubbling through the mixture, (c) at 100°, and (d) at room temperature in ether solution. In all cases the products were identical. An example of procedure (b) is given here and of (d) in the section below where a similar experiment including acid is compared.

One-tenth molar quantities of ethyl N-phenylformimidate,[4] b. p. 118–119° (40 mm.), and *p*-toluidine (recrystallized) were mixed, and dry nitrogen was bubbled through the liquid at a slow rate. Crystals began to form in the reaction mixture after about four hours; it was a solid mass in a short time. After the closed flask had remained two days at room temperature, the crystalline product was ground in a mortar with petroleum ether (b. p. 60–68°; this solvent, "Skellysolve B," was the petroleum fraction used in all the experiments unless otherwise noted). The crystals were collected on a filter and washed with more solvent; 16.5 g. was obtained, m. p. 102–103.8°. After three recrystallizations from a mixture of petroleum ether and absolute ethanol (9:1 by volume), the product had a constant melting point of 105–106°, and crystallized in the form of small thick prisms.

Anal. Calcd. for $C_{14}H_{14}N_2$: C, 79.96; H, 6.71; N, 13.33. Found: C, 80.07; H, 6.61; N, 13.61.

The crystallization behavior of this compound is very interesting. When it was crystallized from petroleum ether, the crystals were so strongly charged with electricity that the mixture could not be filtered due to the tenacity with which the crystals stuck to the bottom and sides of the flask. The addition of a small amount of ethanol to the petroleum ether prevented this behavior and also aided in the purification of the formamidine. The ability of the substance to crystallize in two habits noticed by Wheeler was also observed by us. If warm petroleum ether solutions (with or without ethanol) were cooled rapidly, long thin needles were usually produced; if allowed to stand in the solvent, the needles were converted into thick highly refractive prisms, which could also be produced directly in the same solutions by more gradual cooling. The prisms were never obtained, however, unless the product was rather pure (melting point over 100°); the "low-melting" products (85°) were always obtained in the form of fine cottony needles.

A picrate of the product was prepared by dissolving equal parts of the formamidine and picric acid in thirty parts of absolute ethanol and pouring together the two hot solutions. Fine yellow needles of the salt separated from the hot solution, m. p. 172–176°, sintering about 168°; recrystallized from glacial acetic acid or dry benzene, it melted at 176–177.5° (rapid temperature rise); 174–176° (slow temperature rise).

Anal. Calcd. for $C_{20}H_{17}O_7N_5$: C, 54.67; H, 3.90. Found: C, 55.23; H, 3.98.

Recrystallization from ethanol is not recommended because disproportionation takes place in the hot acid solution; a sample melting originally at 173–176° after twenty minutes in refluxing ethanol melted *ca.* 162–200°.

The formamidine was recovered from the salt by suspending it in chloroform and adding concentrated ammonium hydroxide. The chloroform layer was extracted repeatedly with ammonium hydroxide portions until the latter were no longer colored. The dried chloroform solution was evaporated to yield colorless crystals, m. p. 103.5–104.5°; mixing with the original N-phenyl-N′-*p*-tolylformamidine did not depress the melting point of the recovered material.

B. **From Ethyl N-*p*-Tolylformimidate and Aniline.**—A mixture of 0.05 mole of ethyl N-*p*-tolylformimidate,[4] b. p. 132–134° (40 mm.), and 0.05 mole of aniline (redistilled) was treated as above. After one recrystallization from petroleum ether, the product melted at 100.5–102.5°. Several further recrystallizations from petroleum ether, ethanol, and mixtures of the two brought the melting point to 104–105°.

Products obtained from these reactants (equation B) were shown to be identical with those obtained from the other pair (equation A) by the mixture melting point method.

The picrate of this product was also prepared. It had the same melting point as one prepared from the product of reaction A; a mixture of the two melted at the same point.

Reaction of Ethyl N-Phenylformimidate with *p*-Toluidine in the Presence of Acid.—To a homogeneous mixture of 0.02 mole of each of these compounds at room temperature was added a small crystal of aniline hydrochloride. The mixture became hot; after thirteen minutes crystallization began and was complete two minutes later. The product was allowed to stand in a desiccator one hour. Hot petroleum ether (20 ml.) was then added and the solution was allowed to cool at room temperature; 2.5 g. of crystals separated and were collected on a filter. The crystals melted between 85 and 92°. The filtrate from these was cooled to 0° and a second crop of crystals was collected, 0.8 g., m. p. 84.5–85.5°.

A second batch of the reactants (0.02 mole each) was heated in an oil-bath at 110° for three or four minutes. No visible change occurred; the addition of a small crystal of aniline hydrochloride produced immediate evolution of ethanol. The heating was continued for a few minutes after the bubbling ceased; when the mixture cooled, it crystallized to a solid mass, m. p. 82.5–92.5°. This product was separated by means of petroleum ether into two fractions: 0.5 g., m. p. 93–97°, and 2.9 g., m. p. 83–93°. Recrystallization of the former from methanol gave a small amount of product melting at 98–100°. The lower-melting fraction was suspended in petroleum ether at room temperature, the insoluble material was collected on a filter, and the filtrate was cooled in ice to yield white needles, m. p. 81–82.5°.

An experiment in which a 50 mole per cent. excess of formimidate was used gave a crude product which melted at 84–96°. One in which a 100 mole per cent. excess of *p*-toluidine was used gave a product melting at 101–114°. These results should be compared with those described below, obtained when a 600 mole per cent. excess of one of the reactants was used.

Reaction of Ethyl N-*p*-Tolylformimidate with Aniline in the Presence of Acid.—The first batch of ethyl N-*p*-tolylformimidate (prepared from N,N′-di-*p*-tolylformamidine, ethyl orthoformate and a small amount of *p*-toluidine hydrochloride) apparently contained traces of the acid catalyst, because when it was treated with aniline in four different experiments in which great care was taken to exclude acid, products melting at 84–95°, 82–84°, 86–97°, and 80–95°, respectively, were obtained. In later syntheses of ethyl N-*p*-tolylformimidate, precautions were taken to prevent contamination of the product by the catalyst and subsequent reactions with aniline yielded the pure unsymmetrical formamidine as described above. A product which had been shown to be acid-free in this way was used in the following experiment:

One-tenth molar amounts of the two reactants were mixed and 1×10^{-4} mole of *p*-toluidine hydrochloride was added. The flask was cooled in a water-bath to dissipate the heat produced by the addition of the catalyst, and 20 ml. of anhydrous ether was added. The flask was stoppered and allowed to stand at room temperature forty-eight hours; the ether was then removed under reduced pressure. The solid residue was recrystallized from 100 ml. of petroleum ether; white needles, m.p. 82–83° were obtained. These were recrystallized twice from a mixture (20:1 by volume) of petroleum ether and absolute ethanol. The melting point of the product was 84–85°, and a third recrystallization did not raise it further.

Anal. Calcd. for $C_{14}H_{14}N_2$: C, 79.96; H, 6.71. Calcd. for $C_{15}H_{16}N_2$: C, 80.32; H, 7.19. Calcd. for $C_{13}H_{12}N_2$: C, 79.56; H, 6.17. Found: C, 79.94; H, 6.49.

On the basis of composition the product could be (1) pure N-phenyl-N′-*p*-tolylformamidine, (2) a mixture of **equal amounts of N,N′-diphenylformamidine and** N,N′-

di-*p*-tolylformamidine, or (3) a mixture of the unsymmetrical compound with equal amounts of the two symmetrical compounds. Other data indicate that it is a mixture, and since an equimolar mixture of the two symmetrical compounds melts at 104–110°, this "low-melting" product must contain all three diarylformamidines.

A picrate prepared from this product as described above melted at *ca.* 162–190°.

Reactions in Ether Solution According to Equations A and B with and without Acid Present.—This experiment represents an attempt to repeat the work of Wheeler and Johnson.[3] The amount of reactants reported by them (0.024 mole) and 5 ml. of anhydrous ether were placed in two glass-stoppered flasks which had been rinsed with ammonium hydroxide solution and dried. Duplicate reaction mixtures were prepared and to these was added 2.4×10^{-4} mole of the hydrochloride of the respective aromatic amine present. The four flasks were stoppered and allowed to stand at room temperature for forty-eight hours. The ether was then removed under reduced pressure. The melting points of the crude crystalline products were

Equation A reactants, acid absent; 100–102.5°
Equation B reactants, acid absent; 98–100.5°
Equation A reactants, acid present; 81–82.5°
Equation B reactants, acid present; 81–82.5°

The two high-melting products were recrystallized three times from petroleum ether; the melting points were then A, 102.5–103.8°, B, 100.5–102.2°; mixture, 101.0–103.5°.

Another similar experiment was carried out which differed from A, acid present, only by the fact that the amount of toluidine hydrochloride was cut by one-tenth so that there was 0.001 mole acid per mole of reactants. The crude product was recrystallized three times from petroleum ether; 2.05 g. of needles was obtained, m. p. 83.5–84.3°.

Other Acid-catalyzed Reactions

N-Phenyl-N'-*p*-tolylformamidine with Ethanol.—Test-tube experiments showed that when N-phenyl-N'-*p*-tolylformamidine was heated for twenty minutes at 70–75° in absolute ethanol containing a little *p*-toluenesulfonic acid, the melting point was lowered from 105–106° to 81–83°, while N,N'-diphenylformamidine was recovered unchanged after similar treatment for two hours. In order to characterize the mixture produced from N-phenyl-N'-*p*-tolylformamidine by this treatment, a 0.1-mole sample, m. p. 103–104°, was heated for twenty minutes at the boiling point in 55 ml. of absolute ethanol containing 1×10^{-3} mole of *p*-toluenesulfonic acid. The solution was cooled in an ice-bath, and a mass of fine white needles was collected; 10.9 g., m. p. 81–83°. A small amount of this product recrystallized from petroleum ether melted at 83–84°.

A 7.0-g. sample of the product was dissolved in ethanol and treated with picric acid to give 13.0 g. of yellow needles, m. p. 155–190°. This mixed picrate was fractionally crystallized from dry benzene and benzene-chloroform mixtures to yield eventually 0.71 g. of crystals, m. p. 220–221°. These were shown to be N,N'-di-*p*-tolylformamidine picrate. The melting point was undepressed by mixture with an authentic sample of this picrate, m. p. 222–223° (lit.,[2] 211°; the melting or decomposition point is somewhat dependent on the rate of heating).

Anal. Calcd. for $C_{21}H_{19}O_7N_5$: C, 55.63; H, 4.22. Found: C, 55.85; H, 4.11.

The picrate obtained by fractional crystallization was decomposed with ammonium hydroxide solution as described above, and N,N'-di-*p*-tolylformamidine was obtained, m. p. 138–140.5°, mixed with authentic material without depression. The melting point of a mixture of the product with N,N'-diphenylformamidine was 105–117°.

N,N'-Diphenylformamidine and N,N'-Di-*p*-tolylformamidine with Ethanol.—A mixture of N,N'-diphenylformamidine (0.05 mole), N,N'-di-*p*-tolylformamidine (0.05 mole), absolute ethanol (0.10 mole), aniline hydrochloride (5×10^{-5} mole) and dry benzene (20 ml.) was heated in an oil-bath at 70–75° for one hour in a flask equipped with a reflux condenser and protected from moisture by a calcium chloride tube. Ethanol and benzene were removed by distillation, first at atmospheric pressure, finally under reduced pressure. The solid residue was melted and recrystallized from 125 ml. of petroleum ether to yield 15.8 g. of colorless needles, m. p. 81.5–83°. Attempts were made to fractionate this product from petroleum ether and from ethyl ether with no success. Crystallization from isopropyl alcohol and then from petroleum ether–ethanol (9:1 by volume) raised the melting point to 84–85°, but no higher. This product was compared by the mixture melting point method with one (m. p. 82–83°) from the acid-catalyzed reaction of ethyl N-phenylformimidate with *p*-toluidine; no depression resulted.

Ethyl N-Phenylformimidate with Excess *p*-Toluidine.—In a glass-stoppered flask were placed ethyl N-phenylformimidate (0.02 mole), *p*-toluidine (0.12 mole), *p*-toluidine hydrochloride (2×10^{-5} mole) and 10 ml. of anhydrous ether. The mixture was left at room temperature for sixteen hours. The ether was removed under reduced pressure leaving a mixture of liquid and crystals. A small amount of petroleum ether was added, and the crystals were collected on a filter and washed with more solvent; they weighed 0.90 g. and melted at 135–136.8°, sintering from 119°. By adding petroleum ether and cooling, two additional crops of crystals were obtained from the filtrate before the excess *p*-toluidine began to crystallize. The three crops of crystals were combined and recrystallized from a mixture of petroleum ether and dry benzene, giving 1.04 g. of prisms, m. p. 137–139°. The melting point was raised to 139–140.2° by one further recrystallization, and the product was shown to be N,N'-di-*p*-tolylformamidine by the mixture melting point method.

Ethyl N-*p*-Tolylformimidate with Excess Aniline.—This experiment was carried out on the same scale and exactly as above, except that the crystalline product was filtered from the excess amine directly without first adding petroleum ether; it weighed 0.78 g., m. p. 123–131°. Recrystallizing twice from petroleum ether–benzene and twice from petroleum ether–ethanol gave N,N'-diphenylformamidine in the form of colorless needles, m. p. 137.5–139°; mixed with authentic material, undepressed; mixed with N,N'-di-*p*-tolylformamidine, m. p. 108–115°.

N-Phenyl-N'-*p*-tolylformamidine with Excess *p*-Toluidine.—A 0.02-mole sample of the formamidine (m. p. 102.6–104.4°), 0.02 mole of absolute ethanol, 0.10 mole of *p*-toluidine, 2×10^{-5} mole of *p*-toluidine hydrochloride, and 10 ml. of anhydrous ether were allowed to stand at room temperature in a stoppered flask for sixteen hours. The ether was removed and the crystals which separated were collected and washed on a filter with petroleum ether: 2.18 g. was obtained, m. p. 134–137°. These were recrystallized twice from petroleum ether–benzene to yield 1.20 g. of N,N'-di-*p*-tolylformamidine, m. p. 139–140°, identified as before.

Summary

1. Pure N-phenyl-N'-*p*-tolylformamidine has been shown to melt at 105–106°, not at 86° as previously reported.

2. The product melting at 86°, reported by Wheeler and Johnson to be N-phenyl-N'-*p*-tolylformamidine, has been shown to be a mixture of this compound, N,N'-diphenylformamidine and N,N'-di-*p*-tolylformamidine, produced by acid-catalyzed disproportionation.

3. A mechanism has been proposed to account for this disproportionation. Several other reactions expected on the basis of this mechanism have been tested and observed to support it.

4. A general scheme for the mechanism of acid catalyzed reactions of ortho esters, imidic esters, and amidines has been outlined and the relationships of these three types of compounds have been pointed out in terms of this scheme.

AUSTIN, TEXAS RECEIVED DECEMBER 21, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF TEXAS]

The Molecular Association of Diarylformamidines

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The structure of the compounds produced by the reaction of aromatic amines with ethyl orthoformate, which had long been considered to be N,N′-diarylformamidines (I), was questioned by Post[1] who pointed out that elementary analysis data fitted equally well orthoformamide structures (II). Apparent evidence for the latter structure soon came from Post's laboratory in the form of cryoscopic molecular weight data.[2] The identification of these compounds with the orthoformamide structure was quickly challenged by Backer and Wanmaker,[3] however, who showed that the analyses of salts of the bases corresponded to formamidine structures, and more recently by Knott and Jeffreys,[4] who presented further conclusive proof that these compounds are indeed formamidines. Before the paper of Knott and Jeffreys appeared, we had reached the same conclusion based on some of the same experimental data; e. g., the formation of diarylformamidines in high yields from N-arylformimidates and aromatic amines,[5] and we had begun an investigation of the results reported by Lewis, Krupp, Tieckelmann and Post.[2] We thought that the high molecular weight values reported by these workers might be due to molecular association in solution, and we proposed two tests to show if this were the case: (1) determination of the neutralization equivalent of the hydrochloride of one of these bases by direct titration, and (2) cryoscopic molecular weight determinations *at different concentrations*.

$$\underset{\text{I}}{\mathrm{RN{=}CHNHR}} \qquad\qquad \underset{\text{II}}{\mathrm{(RNH)_3CH}}$$

The neutralization equivalent of the base hydrochloride should be independent of the degree of association and should show the formula weight of the molecule associated with one equivalent of hydrogen chloride. Lewis, *et al.*, claimed that titration of the product from aniline and ethyl orthoformate was impossible because it dissolved in hydrochloric acid very slowly. However, we found that the hydrochloride may be prepared readily by passing dry hydrogen chloride into a benzene solution of the base; the salt is reasonably soluble in water and may be titrated with sodium hydroxide to a sharp end-point. The neutralization equivalents found in three titrations were all within 1% of the calculated value for N,N′-diphenylformamidine hydrochloride.

Knott and Jeffreys[4] reported Rast molecular weight determinations which checked fairly well for N,N′-diphenylformamidine, and they suggested that the high values of Lewis, *et al.*, must be due to association, possibly to a dimeric structure. Hunter and Marriott,[6] in their extensive survey of compounds which exhibit molecular association through hydrogen bonds, investigated several N,N′-diarylacetamidines and found them to be only slightly associated in naphthalene at its freezing temperature. However, it might be expected that more association would occur at the lower freezing temperature of benzene, the cryoscopic solvent used by Lewis, *et al.* The molecular weights reported by them for the product from aniline and ethyl orthoformate were 293 ± 6 and 267 ± 3 (using 4.9 as the cryoscopic constant). The first value is very close to the formula weight of $(C_6H_5NH)_3CH$ (289); the concentration in this experiment was 1.76 g. solute/100 g. solvent. The concentration in the other experiment was not specified. The other compounds investigated by these workers were those derived from *o*-, *m*- and *p*-chloroaniline; the molecular weights found were 392 ± 4, 393 ± 4 and 393 ± 4, respectively (calculated for $(ClC_6H_4NH)_3CH$, 393), and no data regarding concentration were given.

We have now determined the apparent molecular weight of N,N′-diphenylformamidine, N,N′-di-*o*-chlorophenylformamidine and N,N′-di-*p*-chlorophenylformamidine in benzene and in naphthalene at various concentrations. The results are collected in Tables I and II and are presented graphically in Figs. 1 and 2. The formula weights of the compounds are given after the names.

The slight solubility of the chlorine-containing compounds in benzene at its freezing temperature severely limits their investigation in this solvent; at concentrations slightly higher than those in Table I, crystallization of solute occurred.

The data indicate that N,N′-diphenylformamidine and N,N′-di-*p*-chlorophenylformamidine are

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[1] H. W. Post, "The Chemistry of the Aliphatic Orthoesters," Reinhold Publishing Corp., New York, N. Y., 1943, p. 92.

[2] Lewis, Krupp, Tieckelmann and Post, *J. Org. Chem.*, **12**, 303 (1947).

[3] Backer and Wanmaker, *Rec. trav. chim.*, **67**, 257 (1948); **68**, 247 (1949).

[4] Knott and Jeffreys, *J. Org. Chem.*, **14**, 879 (1949).

[5] Roberts, THIS JOURNAL, **72**, 3603 (1950).

[6] Hunter and Marriott, *J. Chem. Soc.*, 777 (1941).