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# Some Reactions of *N*-Haloamidines*[1]

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The reactions of a variety of *N*-haloamidines with silver oxide, sodium ethoxide, thiourea derivatives, and phenols are described. In these reactions, *N*-phenyl-*N'*-chlorobenzamidine gave diphenylcarbodiimide, benzimidazole, *N*-amidinobenzamidine and 2,4-diphenylthiadiazole respectively, while the other *N*-haloamidines afforded the corresponding products. The mechanistic implications of these reactions are discussed.

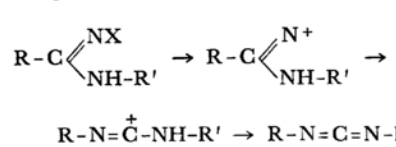
Although *N*-haloamidines had been prepared by Bougault and Robin early in the 1920's from amidine hydrochlorides and sodium hypochlorite,[1] the chemistry of the compounds has not been widely studied. The representative reactions of *N*-haloamidines were the nucleophilic replacement of the halogen atom with the cyanide or isothiocyanate ion,[2] and the oxidation of the iodide ion.[1] Recently, Grenda *et al.*[3] and we[4] have reported that the reaction of *N*-chlorobenzamidine with sodium ethoxide leads to the formation of benzimidazole, probably *via* a nitrene intermediate. These results indicate that the halogen atom of *N*-haloamidines could react in two different ways. In the first type of reaction, the halogen atom of *N*-haloamidines leaves as a halide ion, this reaction can be realized by treating the compounds with such reagents as (a) the silver ion, which has a strong affinity towards the halogen atom, (b) strong nucleophiles, such as cyanide or isothiocyanate ions, which replace the halogen atom directly, and (c) strong bases, such as the ethoxide ion, which takes up first a proton from the amino- or imino group and subsequently eliminates the halide ion. In the second type of reaction, the halogen atom of *N*-haloamidines leaves as a halogen cation, *i. e.*, a positive halogen; this reaction can be realized by the reaction with such reagents as (d) phenols, which readily undergo electrophilic substitution with a positive halogen, and (e) thioamides, which are oxidized with a positive halogen.

This paper will summarize the results obtained so far in our laboratory as to the reaction of *N*-haloamidines with the various kinds of reagents mentioned above.

## Results and Discussion

**Halogenation of Amidines.** Haloamidines have been prepared from amidines and sodium hypochlorite or hypobromite in water.[1] However, the yield of this reaction was not always good, mainly because of the instability of *N*-haloamidines. The process of the separation of haloamidines from the reaction mixture also caused a marked drop of the yield. In this investigation, therefore, the halogenation of amidines was carried out using *t*-butyl hypohalite as a halogenation agent in such organic solvents as chloroform, benzene, or a benzene-ethanol mixture, and the resulting *N*-haloamidines were used for the subsequent reactions without separation. The yields of *N*-haloamidines varied with the structures of the amidines. Aromatic amidines usually gave *N*-haloamidines in good yields, but aliphatic amidines resulted in poor yields. *N*-Substitution with alkyl or aryl group did not affect the yield of the *N*-halogenation, but *N,N'*-disubstitution with two alkyl or two aryl groups completely inhibited the *N*-halogenation.

**Formation of Carbodiimide.** If the chlorine atom of *N*-haloamidine is removed as a chloride ion by the silver cation, the resulting nitrenium cation may react subsequently according to the following scheme to form carbodiimide:



$$R\text{-}C(=NX)\text{-}NH\text{-}R' \rightarrow R\text{-}C(=N^{+})\text{-}NH\text{-}R' \rightarrow R\text{-}N{=}\overset{+}{C}\text{-}NH\text{-}R' \rightarrow R\text{-}N{=}C{=}N\text{-}R'$$

*1 This constitutes Part III of a series entitled "Studies of the Syntheses of Heterocyclic Compounds," by E. Imoto *et al.* It was presented at the 19th Annual Meeting of the Chemical Society of Japan, Yokohama, April, 1966. Part II: T. Takaya, H. Yoshimoto, E. Imoto, This Bulletin **40**, 2844 (1967).

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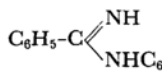
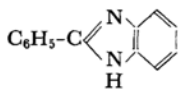
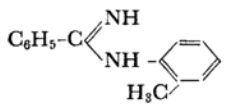
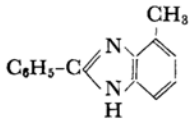
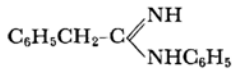
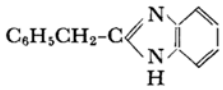
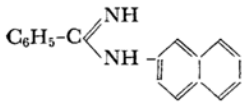
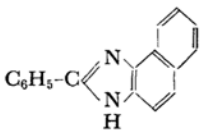
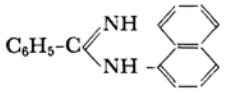
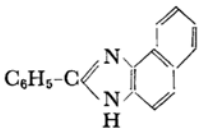
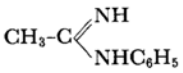
1) P. Robin, *Compt. rend.*, **173**, 1805 (1921); *ibid.*, **177**, 1304 (1923); J. Bougault and P. Robin, *Compt. rend.*, **171**, 38 (1920).

2) J. Goerdeler and D. Loevenich, *Chem. Ber.*, **86**, 890 (1953).

3) V. J. Grenda, R. E. Jones, G. Gale and M. Sletzinger, *J. Org. Chem.*, **30**, 259 (1965).

4) E. Haruki, T. Inaike and E. Imoto, This Bulletin, **38**, 1805 (1965).

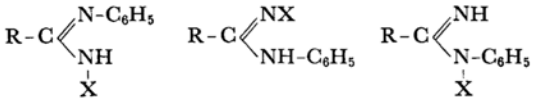
Table 1. Formation of benzimidazole derivatives from *N*-haloamidine

| Amidine | Reaction product | Yield % | Mp °C | Analysis C% | Analysis H% | Analysis N% |
|---|---|---|---|---|---|---|
|  |  | 87 | 289—290 | 80.20 (90.38) | 5.17 (5.19) | 14.65 (14.24) |
|  |  | 76 | 247—248 | 80.96 (80.74) | 5.67 (5.81) | 13.32 (13.45) |
|  |  | 36 | 183—184 | 80.77 (80.74) | 5.60 (5.81) | 13.62 (13.45) |
|  |  | 64 | 215—216 | 83.55 (83.58) | 4.87 (4.95) | 11.52 (11.47) |
|  |  | 24 | 215—216 | 83.65 (83.58) | 5.01 (4.95) | 11.50 (11.47) |
|  | Polymeric product | — | — | — | — | — |

The figures in parentheses are calculated values for the corresponding benzimidazoles.

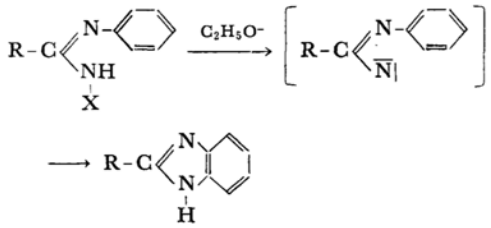
In accordance with this expectation, the reaction of *N*-chlorobenzamidine with silver oxide gave the corresponding diphenyl carbodiimide.

**Formation of Benzimidazoles.**[3] *N*-Phenylhaloamidines may exist in an equilibrium of three tautomeric forms, A, B and C:



(A) (B) (C)

When R is an aryl, the most favorable strcture is presumed to be A because of the great conjugation ability between the aryl and phenyl groups across the carbon nitrogen double bond. When R is an alkyl, however, the most of favorable structure could not be determined analogously. Furthermore, the hydrogen atom attached to the chloroimino group of the A structure is supposed to be fairly acidic, and it could be removed readily by a strong base. The resulting anion may spontaneously release a chloride ion to form a nitrene. The nitrene thus produced probably attacks the adjacent benzene nucleus to give a benzimidazole ring, as is illustrated in the following scheme. The same mechanism has been suggested by Grenda



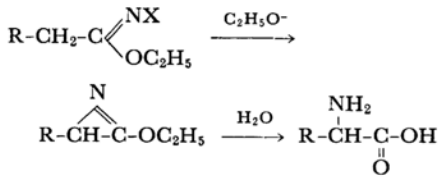
*et al.* in the benzimidazole formation from *N*-chloroamidines. Such a nitrene intermediate has also been proposed by Smith and Leon[5] in the pyrolysis of 1,5-diphenyltetrazole to give benzimidazole and *N,N'*-diphenylcarbodiimide.

When aromatic *N*-arylhaloamidines were treated with sodium ethoxide in ethanol, the expected benzimidazoles were obtained in good yields, as Table 1 shows. However, aliphatic *N*-arylhaloamidines such as *N*-phenyl-*N'*-chloroacetamidine did not form the expected 2-methylbenzimidazole, but only a resinous material.

The reaction of *N*-phenyl-*N*(or *N'*)-chlorophenylacetamidine with ethoxide ions was also investigated. If this haloamidine exists predominantly in the B structure, ethoxide ions may

5) P. A. S. Smith and E. Leon, *J. Am. Chem. Soc.*, **80**, 4647 (1958).

remove a proton from the $\alpha$-methylene group rather than from the NH group. In such a case, an $\alpha$-aminocarboxylic amide may be produced *via* the following processes, similar to the formation of the $\alpha$-aminocarboxylic ester from imino ether[6]:



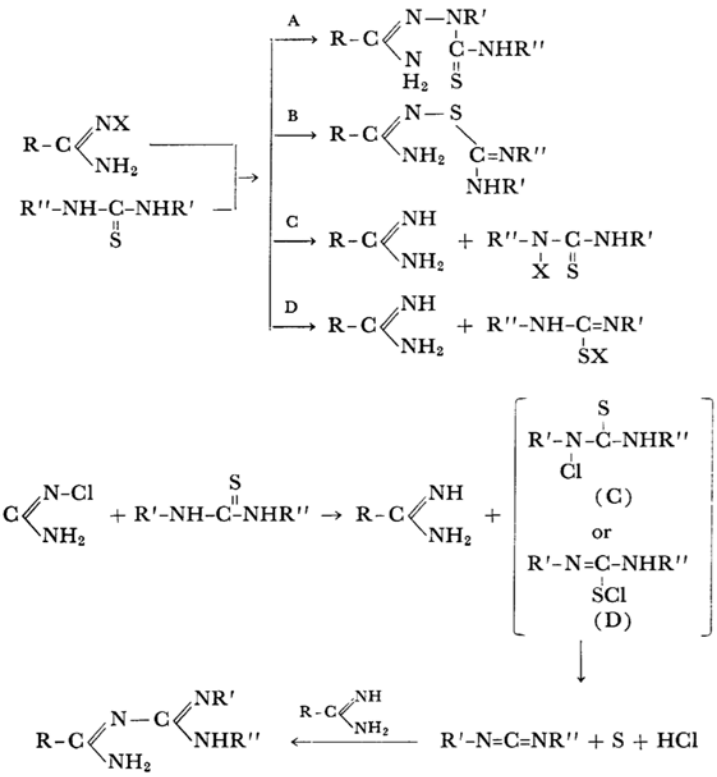
However, our expectation was pot realized; instead 2-benzylbenzimidazole was obtained in a 36% yield, as shown in Table 1. These results show that the hydrogen atom of the $\alpha$-methylene group in *N*-phenyl-*N*(or *N'*)-chlorophenylacetamidine is not removed by ethoxide ions in ethanol; this amidine exists predominantly in the structure A.

**Reaction of *N*-Bromobenzamidine with Phenol.** *N*-Bromobenzamidine reacted with phenol in carbon tetrachloride to yield benzamidinium tribromophenolate. Similarly, *p*-hydroxybenzaldehyde yielded benzamidinium 2,6-dibromo-4-formylphenolate.

We also attempted a direct amination of phenol with *N*-haloamidines in the presence of aluminum chloride in nitrobenzene or carbon disulfide, and also in the presence of boron trifluoride etherate in ether. The direct amination of phenol was unsuccessful; only halophenol was obtained.

**Reactions of Thioureas with Haloamidines.** The reactions of *N*-haloamidines with thioureas are supposed to proceed though the following four processes. Routes A and B are a nucleophilic attack of the nitrogen or the sulfur atom of thioureas on the chloroamino (or chlorimino) group of haloamidines, followed by cyclization to give 1,2,4-thiadiazoles or 1,2,4-triazoles. On the other hand, routes C and D may result in the halogenation of the amino or sulfhydryl group of thiourea by the positive chlorine produced from *N*-haloamidines. Such halogenation has been proposed by Goerdeler *et al.*[7] as the first step in the formation of isothiazoles from $\beta$-iminothioamides and iodine in pyridine or in other solvents.

The experiments showed that the reaction of thiourea with *N*-chlorobenzamidine in ethanol or in water at room temperature affords *N*-amidinobenzamidine, which is then converted to *N*-cyanobenzamidine by treating it with sodium ethoxide in ethanol or to benzamide by refluxing it



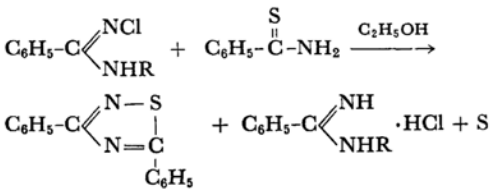
6) H. E. Baumgarten, J. E. Dirkes, J. M. Petersen and D. C. Wolf, *ibid.*, **82**, 4422 (1960); H. E. Baumgarten, J. E. Petersen and R. L. Zey, *J. Org. Chem.*, **31**, 3708 (1966).

7) J. Goerdeler and H. W. Phland, *Chem. Ber.*, **94**, 2950 (1961); *ibid.*, **96**, 596 (1963); J. Goerdeler and W. Miltler, *ibid.*, **96**, 944 (1963); J. Goerdeler and H. Horn, *ibid.*, **96**, 1551 (1963).

with sodium hydroxide in water for a long period of time. The *N*-cyanobenzamidine thus obtained was identical with that prepared from *N*-chlorobenzamidine and sodium cyanide in every respect. However, when the reaction between thiourea and *N*-chlorobenzamidine was carried out in the presence of sodium ethoxide in ethanol or of potassium hydroxide in water, *N*-cyanobenzamidine was obtained directly. These *N*-(*N'*-substituted amidine)benzamidines could not be converted to *N*-cyanobenzamidine by treating them with sodium ethoxide.

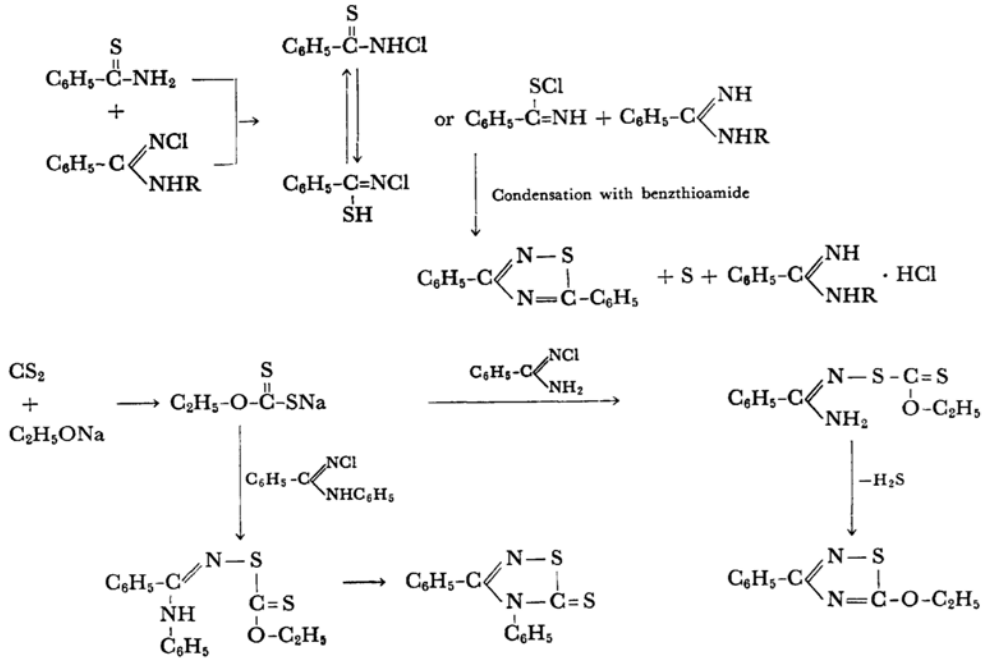
These results indicate that the process of the formation of *N*-amidinobenzamidines may proceed through the intermediate C or D, followed by the elimination of elemental sulfur and hydrogen chloride to form carbodiimide, to which the addition of amidine then takes place.

**Formation of Thiadiazoles.** The reaction of benzthioamide with *N*-chlorobenzamidine or *N*-chloro-*N'*-phenylbenzamidine in ethanol at room temperature for 5 hr afforded 3,5-diphenyl-1,2,4-thiadiazole, together with the amidine hydrochloride and elemental sulfur.



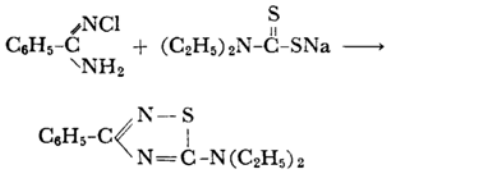
In this reaction *N*-haloamidines act as oxidizing agents on benzthioamide, as is shown in the following scheme. It is interesting to note that thiadiazoles have previously been obtained upon the oxidation of thioamides with halogen.[8]

**Reaction of Carbon Disulfide with *N*-Haloamidines.** The reaction of carbon disulfide with *N*-haloamidines was also investigated, although the structures of the products have not yet been completely determined. Carbon disulfide reacted with *N*-chlorobenzamidine in the presence of sodium ethoxide in an ethanol-benzene mixture at the reflux temperature to yield an oily material (bp 109—111°C/0.6 mmHg), while no reaction occurred in the absence of sodium ethoxide. The oily material obtained was assumed to be 3-phenyl-5-ethoxy-1,2,4-thiadiazole from the results of elemental analysis and from its absorption characteristics in the infrared spectrum (1520, 1430, 1330, 1300, and 1250 $cm^{-1}$). This compound may be formed from *N*-chlorobenzamidine and sodium ethyl xantate. That is, the reaction of *N*-chlorobenzamidine and sodium ethyl xantate may produce first an unstable intermediate, benzthioamidoxime ethyl thiocarbonate, and then this intermediate might cyclize, eliminating hydrogen sulfide, to produce the product. The eliminated hydrogen sulfide may be oxidized with *N*-chlorobenzamidine to sulfur. Carbon disulfide also reacted with *N*-chloro-*N'*-phenylbenzamidine to afford crystals with a mp of 146—156°C, the




8) A. W. Hoffmann and S. Gabriel, *Ber.*, **25**, 1586 (1892); S. Ishikawa, *Chem. Abstr.*, **22**, 1581 (1928); **19**, 3087 (1925); G. C. Charkravarti, *J. Chem. Soc.*, **123**, 964 (1923).

structure of which seemed to be 3,4-diphenyldihydro-1,2,4-thiadiazole-5-thione. When sodium *N,N'*-diethyl dithiocarbamate was used in the above reaction instead of sodium ethyl xantate, the product obtained seemed to be 3-phenyl-5-diethylamino-1,2,4-thiadiazole.



**Reaction of *N*-Haloamidines with Acylating Agents.** 1,2,4-Oxadiazoles have been prepared by the acylation of amidoxime, followed by a cyclization between the amino group and the ethoxycarbonyl carbon atom. Thus, it could be expected that 1,2,4-oxadiazole can also be produced from *N*-haloamidine and an acylating agent *via* the following processes.

However, even when a mixture of *N*-chlorobenzamidine and acetic anhydride was heated under reflux for 2 hr, the product was the unexpected 2-methyl-4,6-diphenyl-*s*-triazine, which was identified by a comparison of its mp and infrared spectrum with those of an authentic sample.[9] When a solution of *N*-chlorobenzamidine and benzoyl chloride in benzene was heated under reflux for 5 hr, the products were 2,4,6-triphenyl-*s*-triazine and *N*-benzoylbenzamide. In this case the expected 1,2,4-oxadiazole derivative was not obtained.

## Experimental

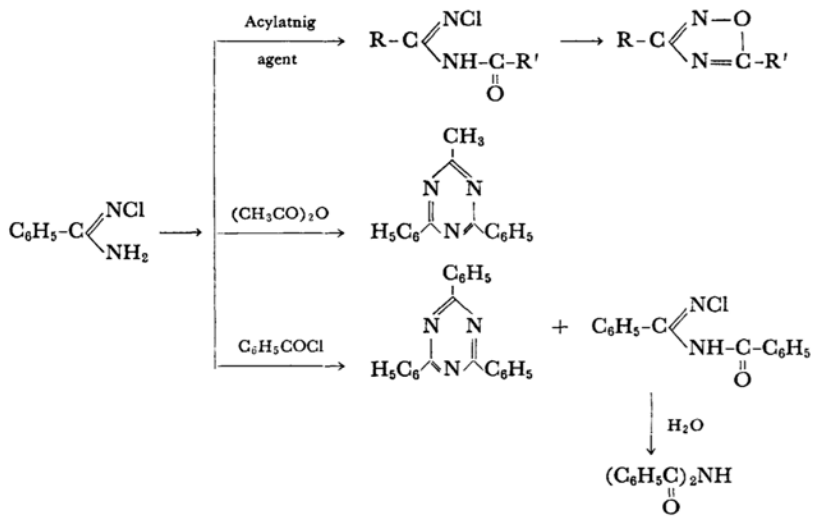
**Amidines.** *N*-Phenylbenzamidine,[10] mp 110—112°C, *N*-phenylphenylacetamidine,[10] mp 137—139°C, *N*-(α-naphthyl)benzamidine,[11] mp 140—142°C, and *N*-(β-naphthyl)benzamidine,[12] mp 153—155°C, were prepared from the corresponding amine hydrochlorides and nitriles by a method similar to that described in the literature. *N*-Methyl-*N'*-phenylbenzamidine,[13] mp 126—130°C, was prepared from the *N*-phenylbenziminochloride and methyl amine hydrochloride. Benzamidine hydrochloride, mp 167—169°C, *N*-butylbenzamidine hydrochloride, mp 188—190°C, *N, N*-pentamethylenebenzamidine hydrochloride, mp 204—207°C, and *N, N*-pentamethylenephenylacetamidine hydrochloride, mp 218—220°C, were prepared from the corresponding iminoethers and amines by Pinner's method.[14]

Free amidines were obtained by extracting a solution of the respective amidine hydrochloride in 30% sodium hydroxide with chloroform and by then removing the solvent.

***N*-Haloamidines.** *N*-Bromobenzamidine was prepared from benzamidine hydrochloride and sodium hypobromite in water, according to the method reported in the literature;[15] it had a mp of 80—81°C after recrystallization from carbon tetrachloride.

*N*-Chloroamidines were prepared from amidines and *t*-butyl hypochlorite in organic solvents, such as chloroform, benzene, ligroin or a benzene-ethanol mixture, at 0—10°C. Among these solvents, chloroform gave the best results. The following is a typical experiment for the preparation of *N*-chloroamidines.

To a solution of *N*-phenylbenzamidine (78 g, 0.40 mol) in chloroform (300 ml) *t*-butyl hypochlorite (50 g, 0.46 mol) was added, drop by drop, at 0—10°C over



9) A. Pinner, *Ber.*, **17**, 2512 (1884); **25**, 1624 (1892).
10) A. Bernthsen, *Ann.*, **184**, 348 (1877).
11) A. Bernthsen and H. Trompetter, *Ber.*, **11**, 1756 (1878).
12) B. River and Ch. Shneider, *Helv. Chim. Acta*, **3**, 132 (1920).
13) C. Gerhsrt, *Ann.*, **108**, 219 (1858).
14) A. Pinner, "Organic Synthesis," Coll. I, John Wiley and Sons, New York, (1956), p. 5.
15) J. Goerdeller and D. Loevenich, *Chem. Ber.*, **86**, 890 (1953); J. Goerdeller and H. Haubrich, *ibid.*, **93**, 397 (1960).

30 min; then the mixture was stirred at the same temperature for 3 hr. The solvent was removed by distillation under reduced pressure at room temperature, and the residue, a brown solid, was recrystallized from ligroin, mp 126—128°C. The yield of *N*-chloro-*N'*-phenylbenzamidine was 46 g (50%).

Found: C, 67.37; H, 4.88; N, 12.08%. Calcd for $C_{13}H_{12}N_2Cl$: C, 67.68; H, 4.81; N, 12.14%.

The other *N*-haloamidines were prepared by a method similar to that described above and were used for the subsequent reactions without separation.

**Preparation of Carbodiimide. Diphenylcarbodiimide.** A suspension of *N*-chloro-*N*(or *N'*)-phenylbenzamidine (2.3 g, 0.01 mol) and silver oxide (5.0 g, 0.02 mol) in ligroin was heated at reflux for 2 hr. After the precipitate had been removed by filtration, the filtrate was distilled under reduced pressure to give a fraction with a bp of 140—144°C (14 mmHg) (1.6 g), which was identified as diphenylcarbodiimide by a comparison of its infrared spectrum with that of an authentic sample prepared from *N,N'*-diphenylthiourea. The distillate (1.9 g) was dissolved in methanol (10 m*l*), mixed with 10 m*l* of 6 N hydrochloric acid, and then boiled for 30 min. After cooling, the solid which was precipitated, *N,N'*-diphenylurea showed no depression of its melting point (229—230°C) upon a mixed-melting-point determination with an authentic *N,N'*-diphenylurea.

**2-Substituted Benzimidazoles and 2-Phenylnaphtho[1',2'-*d*]imidazole.** To 3.9 g (0.02 mol) of *N*-phenylbenzamidine in 15 m*l* of dry benzene and 15 m*l* of absolute ethanol, 2.3 g of *t*-butyl hypochlorite were added at −5—0°C. After the mixture had been stirred at the same temperature for 2 hr, sodium (0.9 g, 0.039 mol) in 10 m*l* of absolute ethanol was added, and then the mixture was refluxed for 3 hr. When the mixture was cooled and poured into ice water, brown precipitates were obtained. Recrystallization from aqueous ethanol gave 3.1 g (80%) of a pure product, mp 289—290°C. This compound was identified with 2-phenylbenzimidazole by means of infrared and ultraviolet spectroscopic measurements, and by a mixed-melting-point test with an authentic sample which had been prepared according to the method described in the literature.[16] By the same procedure, *N*-(*o*-tolyl)-benzamidine was converted to 4-methyl-2-phenylbenzimidazole in a 76% yield, and *N*-phenylphenylacetamidine, to 2-benzylbenzimidazole in a 35% yield. However, an attempt to convert *N*-phenylacetamidine to 2-methylbenzimidazole was unsuccessful. Both *N*-(α-naphthyl)benzamidine and *N*-(β-naphthyl)benzamidine afforded the same product, 2-phenylnaphtho-[1',2'-*d*]-imidazole, in 24% and 64% yields respecti-vely.

**Reaction with Thiourea and Thiourea Derivatives. *N*-Amidinobenzamidine.** Thiourea (1.5 g, 0.020 mol) was added, portion by portion, to a solution of *N*-chlorobenzamidine (3.1 g, 0.020 mol) in 20 m*l* of absolute ethanol. An exothermic reaction started immediately, and sulfur soon began to precipitate. The reaction mixture was then kept overnight at room temperature. After separating the precipitated sulfur (0.38 g, 0.012 mol) by filtration, the filtrate was concentrated by distillation. The residual viscous liquid crystallized upon the addition of a small amount of ether. The *N*-amidinobenzamidine hydrochloride thus obtained 3.2 g (81%) was very hygroscopic and was used for the subsequent reactions without further purification.

***N*-Cyanobenzamidine.** A mixture of *N*-amidinobenzamidine hydrochloride (2.5 g, 0.013 mol) and metallic sodium (0.4 g, 0.017 mol) in 10 m*l* of absolute ethanol was kept overnight at room temperature. After the ethanol had then been removed from the reaction mixture by distillation, the addition of a small amount of water to the residue gave crude *N*-cyanobenzamidine, which was recrystallized from an ethanol-benzene mixture (4 : 1). The yield was 0.92 g (50%); mp 142—143°C. The *N*-cyanobenzamidine thus obtained was identified by a comparison of its infrared spectrum and melting point with those of an authentic sample which had been prepared by the method described in the literature.[14] A mixed-melting-point test with the authentic sample showed no depression.

**Direct Preparation of *N*-Cyanobenzamidine from Thiourea and *N*-Chlorobenzamidine.** To a suspension of thiourea (1.5 g, 0.02 mol) in 10 m*l* of ethanol, there was added, drop by drop, a solution of sodium (1.5 g, 0.065 mol) in 15 m*l* of ethanol, and then a solution of *N*-chlorobenzamidine (3.1 g, 0.02 mol) in 20 m*l* of ethanol. The reaction mixture immediately became turbid and sodium chloride precipitated out. After being allowed to stand overnight at room temperature, the reaction mixture was filtered and the precipitate was washed with water to give 0.47 g of sulfur. The filtrate was distilled under reduced pressure to remove the solvent. The viscous residue solidified upon the addition of a small amount of water. Recrystallization from a benzene-ethanol mixture, gave 1.8 g of *N*-cyanobenzamidine mp 142—143°C.

***N*-(*N,N'*-Diphenylamidino)benzamidine and *N*-(*N*-Phenylamidino)benzamidine.** A solution of *N*-chlorobenzamidine (3.1 g, 0.02 mol) in 20 m*l* of ethanol was added, drop by drop, to a solution of sodium (0.5 g, 0.022 mol) and *N,N'*-diphenylthiourea (4.0 g, 0.02 mol) in 20 m*l* of ethanol, after which the mixture was heated at reflux for 5 min. After it had been filtrated while hot to remove the sodium chloride, the filtrate gave, on cooling, crude *N*-(*N,N'*-diphenylamidino)-benzamidine which was recrystallized from ligroin, mp 134—135°C. The yield was 3.8 g (60%).

Found: C, 76.21; H, 5.44; N, 18.05%. Calcd for $C_{20}H_{18}N_4$: C, 76.40; H, 5.77; N, 17.82%.

*N*-(*N*-Phenylamidino)benzamidine was prepared by the same procedure as that of *N*-(*N,N'*-diphenylamidino)benzamidine.

Found: C, 70.37; H, 5.87; N, 23.83%. Calcd for $C_{14}H_{14}N_4$: C, 70.56; H, 5.92; N, 23.51%.

**3,5-Diphenyl-1,2,4-thiadiazole.** *N*-Chlorobenzamidine (3.1 g, 0.02 mol) was added in one portion to a solution of benzthioamide (2.7 g, 0.02 mol) in 20 m*l* of ethanol. The reaction mixture soon became turbid. When the exothermic reaction ceased and the reaction mixture was cooled to room temperature, colorless needle crystals gradually precipitate out. After standing for 5 hr, the precipitate was collected by filtration and recrystallized three times from an ethanol-water (4 : 1) mixture, mp 89—90°C. The 3,5-diphenyl-1,2,4-thiadiazole obtained was identified by a comparison of its infrared spectrum and melting point with those of an

16) B. A. Porai-Koshits, O. F. Ginzburg and L. S. Eflos, *J. Gen. Chem. (U. S. S. R.)*, **17**, 1768 (1947).

authentic sample synthesized from benzthioamide and benzthioperimidic acid by the method described in the literature.[17] A mixed-melting-point determination of the compound with the authentic sample showed no depression. The filtrate was concentrated under reduced pressure and the residual solid was washed with ether to obtain crude hydrated benzamidine hydrochloride with a mp of 75—85°C. The reaction between benzthioamide and *N*-chloro-*N'*-phenylbenzamidine was carried out as described above to give 3,5-diphenyl-1,2,4-thiadiazole, mp 87—89°C, after recrystallization from an ethanol-water mixture. The yield was 78%.

**Reaction of Carbon Disulfide with *N*-Chlorobenzamidine.** To a solution of carbon disulfide (1.5 g, 0.02 mol) and *N*-chlorobenzamidine (3.1 g, 0.02 mol) in 15 m*l* of ethanol, there was added a solution of sodium ethoxide prepared from sodium (0.46 g, 0.02 mol) and 10 m*l* of ethanol. The reaction mixture was heated gradually. An exothermic reaction occurred suddenly and the temperature rose to 60°C and boiled spontaneously. After having been heated for 1 hr, the reddish-colored reaction mixture was cooled and the precipitated crystals of sodium chloride were collected by filtration. The filtrate was concentrated under reduced pressure to remove the solvent and then distilled to give two fractions: (1) bp 95—109°C/0.6 mmHg, (0.4 g, $n_D^{23}$ 1.5830), and (2) bp 109—111°C/0.6 mmHg (1.2 g, $n_D^{23}$ 1.6042). The second fraction, the main product, was soluble in ether, ethanol, and glacial acetic acid, but was insoluble in water, 2 N hydrochloric acid, and 2 N sodium hydroxide.

Found: C, 58.12; H, 4.71; N, 13.67%. Calcd for $C_{10}H_{10}ON_2S$: C, 58.23; H, 4.89; N, 13.58%.

The structure of this compound was assumed to be 3-phenyl-5-ethoxy-1,2,4-thiadiazole on the basis of its infrared spectrum (1580, 1520, 1335, and 1300 $cm^{-1}$).

**Reaction with Acetic Anhydride.** A solution of *N*-chlorobenzamidine (3.1 g, 0.02 mol) in acetic anhydride (6.1 g, 0.06 mol) was refluxed for 2 hr. After cooling, the precipitate was collected by filtration, washed with a small amount of cold 95% aqueous ethanol, and then recrystallized three times from ethanol to give 1.4 g of 2-methyl-4,6-diphenyl-*s*-triazine, mp 108.5—109.5°C, which had the same melting point and infrared spectrum as an authentic sample; the melting point showed no depression upon a mixed-melting-point determination with an authentic sample.[9]

**Reaction with Benzoyl Chloride.** A solution of *N*-chlorobenzamidine (3.1 g, 0.02 mol) and benzoyl chloride (2.8 g, 0.02 mol) in 20 m*l* of benzene was refluxed for 5 hr. After the solution had been cooled and a small amount of the precipitates by removed filtration, the filtrate was evaporated and the residual solid was recrystallized from ethanol. The needles obtained were 2,4,6-triphenyltriazine (0.30 g, mp 225—230°C). The precipitates obtained upon the addition of water to the mother liquor were recrystallized from ligroin. The needles obtained were *N*-benzoylbenzamide (1.7 g, mp 145—146°C).

**Bromination of Phenols with *N*-Bromobenzamidine.** A solution of phenol (0.4 g, 0.004 mol) and *N*-bromobenzamidine (2.6 g, 0.013 mol) in carbon tetrachloride was refluxed for 10 min. Upon the cooling of the mixture, crystals (0.90 g, mp 116—122°C) were obtained. The same compound, benzamidinium tribromophenolate, was obtained by the addition of tribromophenol to a solution of benzamidine in ethanol, followed by the removal of the ethanol and washing with chloroform. The benzamidinium tribromophenolate thus obtained (0.9 g, 0.0027 mol) was heated for a little while together with 7 m*l* of 2 N hydrochloric acid, and cooled to give tribromophenol (0.4 g, 0.0012 mol).

*p*-Oxybenzaldehyde reacted similarly with *N*-bromobenzamidine in carbon tetrachloride to produce benzamidinium 2,6-dibromo-4-formylphenolate, mp 143—144°C. The salt obtained was treated with an acidic solution of 2,4-dinitrophenylhydrazine to yield 2,4-dinitrophenylhydrazone of 3,5-dibromo-4-hydroxybenzaldehyde, which was identified by a comparison of its melting point and infrared spectrum with those of an authentic sample.

17) R. Kitamura, *Yakugaku Zasshi. (J. Pharm. Soc. Japan)*, **58**, 809 (1938).