mole) was stirred and heated at 175–210° for one hour. It was poured into water, filtered and dried; wt. 66.8 g. A portion of this crude product was extracted with hot acetone. Recrystallization of the acetone-soluble portion from chloroform showed the crude product to be 36% hexadecylurea, m.p. 105.7–107.0°. The literature gives 106–107°[8] and 108.5°.[5]

Anal. Calcd. for $C_{17}H_{36}N_2O$: C, 71.75; H, 12.75; N, 9.85. Found: C, 72.17; H, 12.36; N, 10.30.

Recrystallization of another portion of crude reaction mixture from chloroform showed it to be 42% 1,3-dihexadecylurea, m.p. 110.7–112.2°.

Anal. Calcd. for $C_{33}H_{68}N_2O$: C, 77.90; H, 13.47; N, 5.51. Found: C, 78.40; H, 13.25; N, 5.93.

1,3-Dioctadecylurea.—A mixture of octadecylamine (59.2 g., 0.22 mole) and urea (6.0 g., 0.10 mole) was stirred and heated for 3 hours at 160–165°. It became homogeneous within an hour and noticeable evolution of ammonia had ceased after 2 hours. The product was recrystallized several times from chloroform to yield 1,3-dioctadecylurea as white flakes, m.p. 113.8–114.7°, having an annoying tendency to develop electrostatic charges. The literature[9] gives the m.p. 112.0–112.5°. The yield of once-recrystallized product was 67%.

Anal. Calcd. for $C_{37}H_{76}N_2O$: C, 78.65; H, 13.56; N, 4.96. Found: C, 79.00; H, 12.61; N, 5.21.

1,3-Didodecylurea and Butyl Dodecylcarbamate.—A mixture of dodecylamine (37.0 g., 0.20 mole), urea (24.0 g., 0.40 mole) and *n*-butyl alcohol (44.4 g., 0.60 mole) was refluxed for 31.5 hours, the temperature rising to 154°. Recrystallization from acetone gave 29.2 g. (74%) of 1,3-didodecylurea, m.p. 100.3–102.5°; m.p., after further recrystallization, 103.3–105.5°.

Anal. Calcd. for $C_{25}H_{52}N_2O$: C, 75.69; H, 13.21; N, 7.06; mol. wt., 397. Found: C, 75.91; H, 13.00; N, 7.32; mol. wt. (benzene b.p.), 412.

The acetone filtrate contained butyl dodecylcarbamate, m.p. 35.2–36.2°. In a subsequent experiment, where equimolar amounts of amine, urea and alcohol were heated at 200°, this compound was obtained in 84% yield.

Anal. Calcd. for $C_{17}H_{35}NO_2$: C, 71.52; H, 12.36; N, 4.91; mol. wt., 285. Found: C, 71.67; H, 12.30; N, 5.37; mol. wt. (benzene b.p.), 292.

(8) S. P. Massie, *Iowa State Coll. J. Sci.*, **21**, 41 (1946).

(9) W. I. Harber, *ibid.*, **15**, 13 (1940).

1,1-Dioctadecylurea.—A mixture of dioctadecylamine (52.1 g., 0.10 mole) and urea (12.0 g., 0.20 mole) was stirred and heated at 160–165° for 5 hours. The molten, two-phase mixture was poured onto ice, filtered, washed with water, and dried; wt. 58.2 g., m.p. 57–64.5°. The literature[9] gives the m.p. 65.0–65.5°. Attempts to shorten the m.p. range by recrystallization from various solvents were not successful. Nevertheless, according to analysis, it was relatively pure.

Anal. Calcd. for $C_{37}H_{76}N_2O$: C, 78.65; H, 13.56; N, 4.96. Found: C, 78.50; H, 13.97; N, 5.38.

1-Dodecylbiuret.—A mixture of dodecylamine (37.0 g., 0.20 mole) and urea (24.0 g., 0.40 mole) was stirred and heated at 170–175° for 4 hours; wt. of crude product 54.5 g. Recrystallization from chloroform showed that this consisted largely of dodecylurea. By recrystallization from ethyl acetate, 1.6 g. of crude 1-dodecylbiuret, m.p. 111.5–120°, was isolated. Further recrystallization from Skelly B–chloroform raised the m.p. to 129–130.5°.

Anal. Calcd. for $C_{14}H_{29}N_3O_2$: C, 61.96; H, 10.77; N, 15.49. Found: C, 61.82; H, 10.79; N, 15.24.

1,3-Dioctadecylbiuret.—A mixture of octadecylamine (53.8 g., 0.20 mole) and urea (12.0 g., 0.20 mole) was heated at 150–160° for 4 hours. Then, over a period of 2 hours, the temperature was raised to 195–200°. The mixture was heated at 195–200° for 6 hours; at the end of this time the evolution of ammonia had ceased. The weight of crude product was 59.2 g., consisting mostly of 1,3-dioctadecylurea. However, recrystallization from chloroform yielded 16.1 g. of crude 1,3-dioctadecylbiuret, m.p. 90–94°. Further recrystallization from Skelly B and pyridine–acetonitrile raised the m.p. to 96.5–98.5°. The material shows a strong tendency to develop electrostatic charges.

Anal. Calcd. for $C_{38}H_{77}N_3O_2$: C, 75.06; H, 12.77; N, 6.91. Found: C, 75.07; H, 12.29; N, 6.80.

1,5-Dioctadecylbiuret.—A mixture of octadecylamine (53.8 g., 0.20 mole), urea (12.0 g., 0.20 mole) and ethylene glycol (6.5 g., 0.105 mole) was stirred and heated at 120–130° for 6 hours. It was homogeneous after the first 2 hours. Recrystallization from chloroform–acetone gave 47.3 g. of crude product, m.p. 98–101°. Further recrystallization from chloroform raised the m.p. to 104.5–105.5°.

Anal. Calcd. for $C_{38}H_{77}N_3O_2$: C, 75.06; H, 12.77; N, 6.91. Found: C, 75.05; H, 12.61; N, 7.35.

This compound was also obtained in good yield by heating octadecylamine and urea for 3 hours at 162–172°.

Minneapolis 13, Minnesota

The Conversion of Formamides into Formamidines[1]

By H. George Mandel[2] and Arthur J. Hill

N,N'-Diarylformamidines have been prepared by the interaction of substituted formanilides with anilines in the presence of phosphorus pentachloride, in chloroform medium. The homodisubstituted amidines were obtained in yields up to 70%. Heterosubstituted amidines could be prepared by two different routes but usually were contaminated with the corresponding homodisubstituted compounds. Ethoxy-, carbethoxy-, amino- and nitro derivatives of diphenylformamidine were prepared. The nitroamidines could be reduced to the corresponding amino compounds. Trisubstituted formamidines were synthesized by different routes and alkyl–aryl amidines were obtained. Neither dialkyl nor alkyl–aryl disubstituted formamidines could be prepared.

The structural relationship of formamidines to the imidazole ring, which forms a portion of the histamine molecule, suggested that these compounds might possess antihistaminic or other biological activity. The synthesis of a number of substituted derivatives of these compounds was therefore investigated.

The application of the phosphorus halide method for the synthesis of amidines from amines and amides has been previously reported by Hill and Rabinowitz.[3] In their study of homologs of phenacaine, $CH_3C\underset{\diagdown NHC_6H_4OC_2H_5}{\overset{\diagup NC_6H_4OC_2H_5}{}}$, these investigators prepared several amidines in which the methyl group had been replaced with other alkyl radicals. The method was extended by Hill and Cox[4] to hetero-

(3) A. J. Hill and I. Rabinowitz, This Journal, **48**, 732 (1926).

(4) A. J. Hill and M. V. Cox, *ibid.*, **48**, 3214 (1926).

TABLE I

N,N'-DIARYLFORMAMIDINES HC$\begin{cases} NC_6H_4X \\ NHC_6H_4Y \end{cases}$

X	Y	M.p., °C.	Substituent on amine reactant	Yield, %	Formula	Nitrogen, % Calcd.	Found
H	H	140–141	X	66	$C_{13}H_{12}N_2$	14.29	14.10
p-CO₂C₂H₅	p-CO₂C₂H₅	192–193	X	69	$C_{19}H_{20}N_2O_4$	8.24	8.12
p-OC₂H₅	p-OC₂H₅	114–115.5	X	62	$C_{17}H_{20}N_2O_2$	9.86	9.72
H	p-CO₂C₂H₅	112–114ᵃ	X 8 / Y 11		$C_{16}H_{16}N_2O_2$	10.44	10.25
p-OC₂H₅	p-CO₂C₂H₅	143–145ᵃ	X 54 / Y 32		$C_{18}H_{20}N_2O_3$	8.92	9.02
p-NO₂	p-NO₂	239–240	X	10	$C_{13}H_{10}N_4O_4$	19.59	19.84
m-NO₂	m-NO₂	201–203	X	65	$C_{13}H_{10}N_4O_4$	19.59	19.77
o-NO₂	o-NO₂	160–161ᵇ	X	70	$C_{13}H_{10}N_4O_4$	19.59	19.33
H	p-NO₂	185–186	Y	6	$C_{13}H_{11}N_3O_2$	17.42	17.47
H	m-NO₂	138–139	Y	56	$C_{13}H_{11}N_3O_2$	17.42	17.39
p-CO₂C₂H₅	m-NO₂	208–209	Y	14	$C_{16}H_{15}N_3O_4$	13.41	13.17

ᵃ Identical m.p.'s for either route of preparation, no depression on admixture. ᵇ Zwingenberger and von Walther[6] have reported 124–125°. It is likely that their product had decomposed to o-nitroformanilide, m.p. 122–123°.

substituted amidines, where the N-substituents, usually ester-containing groups such as C_6H_4-$CO_2C_2H_5$, differed from each other. Segool,[5] using a similar procedure, has prepared various homologs of phenacaine in which the alpha carbon was tertiary.

For the present investigations, the applicability of the phosphorus halide method for the synthesis of formamidines was examined

$$HCONHR + R'NH_2 \xrightarrow{PCl_5} HC\begin{cases} NR \\ NHR' \end{cases}$$
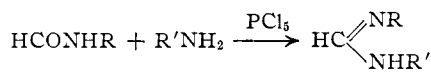
Results and Discussion

The formamides were prepared directly by the condensation of formic acid and the corresponding amine. Previous methods of synthesis, where available, were employed.

Disubstituted Formamidines.—Various N,N'-diarylformamidines (Table I) were then prepared by the interaction of phosphorus pentachloride in a chloroform medium upon an R-substituted formamide and an R'-substituted amine.

Dialiphatic or aliphatic–aromatic N,N'-disubstituted formamidines were not formed during the reaction, as indicated by (1) the failure of the reaction products upon hydrolysis to reduce mercuric chloride to the insoluble mercurous chloride, whereas formamidines upon hydrolysis readily effect this reduction; and (2) the formation of the picrate and chloroplatinate of the starting aliphatic amine instead of the usual formation of the insoluble salts of a formamidine with these reagents.

Synthesis.—As a general procedure for the synthesis of formamidines, the formanilide was slowly added to a solution of phosphorus pentachloride in chloroform, cooled to 0°. The aniline derivative was then introduced. After refluxing the resulting mixture, the formamidine hydrochloride was obtained by filtration and was converted to the base.

In order to obtain maximum yields in the conversion of formamides into formamidines, the reaction between aniline and formanilide in the presence of a chlorinating agent was studied in detail. Phos-

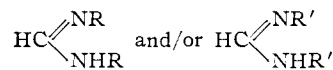(5) H. D. Segool, Dissertation, Yale University, 1938.

phorus pentachloride consistently gave a higher yield of the desired amidine than did thionyl chloride or phosphorus trichloride. The substitution of chloroform for benzene, which had been used as solvent by previous workers,[3–5] was found to be most advantageous. The formamidine was produced with fewer by-products and in a higher yield. The lower reflux temperature of chloroform solutions diminished the formation of undesirable by-products.

Treatment of the formamidine hydrochloride with aqueous ammonia converted any excess aniline hydrochloride into the water-insoluble oily base which coated the solid amidine hydrochloride. Complete neutralization was therefore prevented, and the aqueous medium slowly decomposed the water-unstable amidine hydrochloride. On the other hand, during neutralization in an anhydrous medium, as with sodium ethylate in alcohol, the excess aniline remained in the alcohol solution, allowing for better contact between the amidine hydrochloride and the neutralizing solution. A quantitative conversion of the hydrochloride to the free base was achieved by this procedure.

The Heterodisubstituted Formamidines.—The phosphorus halide method of synthesis of amidines possessed the advantage that in addition to the homodisubstituted amidines, heterodisubstituted amidines could be prepared. These latter compounds were synthesized by two routes, depending on whether (1) HCONHR and R'NH₂ or (2) HCONHR' and RNH₂ were the reactants. In either case the identical product was obtained, confirming the tauterism

$$HC\begin{cases} NR \\ NHR' \end{cases} \rightleftarrows HC\begin{cases} NHR \\ NR' \end{cases}$$
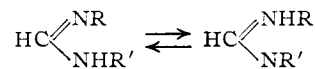
Frequently in these reactions the homodisubstituted formamidines

$$HC\begin{cases} NR \\ NHR \end{cases} \text{ and/or } HC\begin{cases} NR' \\ NHR' \end{cases}$$

were isolated from the reaction mixture, together with the desired heterodisubstituted formamidine,

Table II

N,N'-Diarylaminoformamidine Hydrochlorides HC⟨NC₆H₄X / NHC₆H₄Y⟩·ZHCl

$$HC{\underset{NHC_6H_4Y}{\overset{NC_6H_4X}{\Big\langle}}}\cdot ZHCl$$

X	Y	Z	Method	Yield, %	Formula	Nitrogen, % Calcd.	Found	Chlorine, % Calcd.	Found
p-NH₂	p-NH₂	3	A	98	C₁₃H₁₇N₄Cl₃	16.71	16.51	31.75	31.50
m-NH₂	m-NH₂	3	A	99	C₁₃H₁₇N₄Cl₃	16.71	16.54	31.75	31.56
o-NH₂	o-NH₂	3	A	41	C₁₃H₁₇N₄Cl₃	16.71	16.62	31.75	31.54
H	m-NH₂	2	A	95	C₁₃H₁₅N₃O₂	14.80	14.88	25.00	24.82
p-CO₂C₂H₅	m-NH₂	2	A	61	C₁₆H₁₉N₃O₂Cl₂	11.85	11.68	19.91	19.61
H	m-NH₂	2	B	53	C₁₃H₁₅N₃Cl₂	14.80	15.00	25.00	25.01
H	p-N(C₂H₅)₂	2	B	56	C₁₇H₂₃N₃Cl₂	12.35	12.48	20.90	21.00
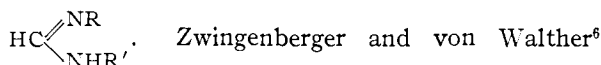
$HC{\overset{NR}{\underset{NHR'}{\Big\langle}}}$. Zwingenberger and von Walther[6] had concluded that the heterosubstituted formamidines produced by the interaction of formanilide and p-toluidine, or p-methylformanilide and aniline, in the presence of a chlorinating agent, were isomers. The demonstration by Wheeler[7] that these products were identical but were contaminated with other amidines to different extents are confirmed by the present results. The contamination with the homodisubstituted derivatives has also been observed independently by Roberts,[8] who used the ortho-ester procedure for amidine synthesis.
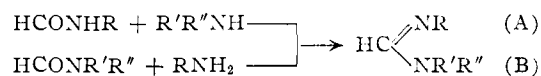
In the preparation of heterosubstituted diarylformamidines as presented in this work, several observations were made from which certain generalizations could be drawn. When R or R' represented p-carbethoxyphenyl, the relatively insoluble N,N'-di-p-carbethoxyphenylformamidine (I) was always produced. When R represented p-carbethoxyphenyl, and R' represented o- or p-nitrophenyl, only I could be isolated (yields of 20–30%) whereas with R' = m-nitrophenyl, under similar conditions, the desired heterosubstituted amidine N-p-carbethoxyphenyl-N'-m-nitrophenylformamidine, resulted. The reaction between formanilide and p-nitroaniline produced the expected heterosubstituted amidine together with N,N'-di-p-nitrophenylformamidine. With the o-isomer, however, the only compound isolated was the N,N'-di-o-nitrophenylformamidine (35% yield). Diphenylformamidine was not isolated as a by-product. In the case of the reaction of m-nitroaniline with formanilide the heterosubstituted amidine N'-m-nitrophenyl-N'-phenylformamidine was formed in good yield. When an aliphatic amine was reacted with p-carbethoxyformanilide, I was formed exclusively. The aliphatic amines used in these reactions were benzyl-, cyclohexyl-, n-butyl-, n-octyl- and n-octadecylamine.

The separation of the heterosubstituted amidine from the contaminating homosubstituted derivatives by the usual procedures such as recrystallization, adsorption chromatography and vacuum sublimation was unsuccessful. Fractional precipitation, however, was highly effective in separating the formamidines. For this procedure, the mixture was dissolved in acetone at room temperature, and water was added dropwise until a precipi-

tate formed. The alternate removal of the precipitate by centrifugation and the addition of more water to the supernatant solution provided various fractions of precipitates which could be easily grouped and combined according to their melting points. The pooled products were further subjected to repeated fractional precipitations until material of constant melting point was obtained. The analytical data showed that good separations had been effected.

Diarylaminoformamidines.—Some of the nitroamidines prepared by these methods were reduced catalytically to yield the corresponding aminoformamidines (method A, Table II). These aminoformamidines could be prepared also by the direct interaction of phosphorus pentachloride upon formanilide and a phenylenediamine derivative (method B, Table II) indicating that only one of the amino groups of the diamine had reacted in the synthesis.

Trisubstituted Formamidines.—Two routes of synthesis were possible for the synthesis of trisubstituted formamidines, as shown in the transformations

$$\left.\begin{array}{l} HCONHR + R'R''NH \longrightarrow \\ HCONR'R'' + RNH_2 \longrightarrow \end{array}\right\} \longrightarrow HC{\overset{NR}{\underset{NR'R''}{\Big\langle}}} \quad \begin{array}{l}(A)\\(B)\end{array}$$

Reaction (B) provided the better yield of the desired amidine. A tendency toward the formation of homodiarylformamidines was observed during the preparation of trisubstituted formamidines when route (A) was employed. This by-product formation has been noted also during the synthesis of heterodisubstituted formamidines.

With formanilide and N-methylaniline as reactants in the phosphorus pentachloride reaction (reaction A) some diphenylformamidine (II), together with the desired N,N'-diphenyl-N'-methylformamidine (III), was detected among the products. In the converse procedure in which N-methylformanilide was treated with aniline (reaction B), the resulting trisubstituted amidine (III) was not contaminated with by-product II. Similarly, with formanilide and di-n-butylamine as reactants (route A), II was again produced as a by-product, whereas di-n-butylformamide with aniline (route B) gave only the desired trisubstituted amidine, N-phenyl-N',N'-di-n-butylformamidine (IV).

It is probable that, in the synthesis of the heterodisubstituted and the trisubstituted formamidines, the direct formation of a formamidine from a formanilide, which may occur even in the absence of an added amine, is responsible for the for-

(6) O. Zwingenberger and R. von Walther, J. prakt. Chem., [2] 57, 209 (1898).

(7) H. L. Wheeler, Am. Chem. J., 19, 367 (1897).

(8) R. M. Roberts, This Journal, 72, 3603 (1950).

mation of the homodisubstituted derivatives in the reaction mixture. The presence of diphenylformamidine, II, as a by-product in the above synthesis of a trisubstituted product might be explained as a product of the interaction of formanilide with phosphorus pentachloride. This reaction has been shown to take place, with the concomitant release of carbon monoxide.

Prototypes of the synthetic methods employed for each of the above reactions are described in the Experimental Part. The preparation of dialiphatic formamidines by amine interchange with diarylformamidines in a sealed tube resulted in very low yields.

Formamidines hydrolyze slowly in the presence of moisture, and organic solvents containing even traces of water are unsuitable as recrystallization media. At 100° the amidine in aqueous solution is easily degraded into formanilide and aniline. In hot dilute acid or base the formanilide is further broken down to aniline and formic acid. The hydrochlorides of formamidines, which may be easily prepared, are more stable than the bases and, when dry, may be stored indefinitely in a desiccator.

Experimental[9]

Formamides.—The formamides used in these investigations were prepared as previously reported.[10-17]

n-Octylformamide.—A mixture of 6.0 ml. (0.14 mole) of 90% formic acid and 5.0 ml. (0.031 mole) of *n*-octylamine was refluxed for 30 minutes. Water and excess formic acid were removed by distillation, and the residual *n*-octylformamide was distilled; yield 3.4 g., 70%, b.p. 289–291°, [*n*]^{25}D 1.4475, d^{25} 0.90.

Anal. Calcd. for C$_9$H$_{19}$NO: N, 8.91. Found: N, 8.76.

Di-*n*-butylformamide.—A mixture of 12 ml. (0.29 mole) of 90% formic acid and 34 ml. (0.20 mole) of freshly distilled di-*n*-butylamine was refluxed for 45 minutes. Water and excess formic acid were removed by distillation, and the residual di-*n*-butylformamide was distilled; yield 24.1 g., 77%, b.p. 244–246°, n^{25}D 1.4416, d^{25} 0.88.

Anal. Calcd. for C$_9$H$_{19}$NO: N, 8.91. Found: N, 8.82.

N,N'-Diphenylformamidine.—Formanilide (2.4 g., 0.020 mole) was added in small portions to a cooled solution of phosphorus pentachloride (4.8 g., 0.023 mole) in 20 ml. of chloroform. On cessation of the reaction a chloroform solution of 1.9 ml. (0.020 mole) of freshly distilled aniline was added. A precipitate formed immediately. The mixture was refluxed with agitation for 2.5 hours, then cooled in an ice-bath and filtered. The solid material was washed with cold acetone and dried *in vacuo*. The product was converted to the free amidine base by adding it to a solution of sodium ethylate in ethanol. The reaction mixture was cooled in an ice-bath, filtered,[18] and the precipitated amidine washed with cold ethanol and dried. The precipitate, containing inorganic salts, was extracted with acetone, and the combined acetone extracts were poured into water. The white amidine which precipitated at once was collected by filtration, washed with cold water and dried. It was purified

(9) All melting points are corrected.

(10) F. K. Kleine, *Z. physiol. Chem.*, **22**, 327 (1897).

(11) S. E. Cairncross and M. T. Bogert, *Collection Czech. Chem. Communs.*, **8**, 57 (1936).

(12) E. Wedekind and E. Froehlich, *Ber.*, **40**, 1002 (1907).

(13) W. J. Comstock and H. L. Wheeler, *Am. Chem. J.*, **13**, 516 (1891).

(14) H. Huebner, *Ann.*, **209**, 369 (1881).

(15) O. C. Dermer and J. King, *J. Org. Chem.*, **8**, 168 (1943).

(16) B. A. Hunter, *Iowa State Coll. J. Sci.*, **15**, 223 (1941).

(17) G. T. Morgan and W. R. Grist, *J. Chem. Soc.*, **113**, 690 (1918).

(18) For the more alcohol-soluble amidines, the alcohol solution was diluted directly with acetone. After removal of the inorganic material by centrifugation the supernatant solution containing the amidine was precipitated with water, and the amidine was filtered off.

by fractional precipitation from acetone–water mixtures; yield 2.6 g., 66%, m.p. 140–141°.

N,N'-Diphenylformamidine Hydrochloride.—Diphenylformamidine was dissolved in acetone, and a solution of dry hydrogen chloride gas in anhydrous acetone was added dropwise to precipitate the amidine hydrochloride. When the reaction was complete the solid was filtered off and was washed with anhydrous acetone. The amidine hydrochloride was formed in 96% yield and was analytically pure, m.p. 256–258°.

Anal. Calcd. for C$_{13}$H$_{13}$N$_2$Cl: N, 12.08. Found: N, 11.88.

N,N'-Di-*p*-aminophenylformamidine Trihydrochloride. (Method A).—Di-*p*-nitrophenylformamidine (2.1 g.) suspended in 100 ml. of purified dioxane was hydrogenated in a shaker hydrogenator in the presence of Adams platinum oxide catalyst under a pressure of four atmospheres of hydrogen. After four hours of hydrogenation the catalyst was filtered off and the filtrate was diluted with acetone. A solution of hydrogen chloride in acetone was added dropwise until precipitation was complete. The amidine hydrochloride was filtered off, washed with dry acetone, and allowed to dry *in vacuo;* yield 2.4 g., 98%. It was extremely hygroscopic and readily oxidizable. It was stored in sealed ampules under an atmosphere of dry nitrogen. Neither a picrate nor a chloroplatinate could be prepared from this amidine.

N-Phenyl-N'-*m*-aminophenylformamidine Dihydrochloride (Method B).—A solution of phosphorus pentachloride (2.5 g., 0.012 mole), formanilide (1.2 g., 0.010 mole) and *m*-phenylenediamine (1.1 g., 0.010 mole) in 40 ml. of chloroform was refluxed for three hours. The amidine hydrochloride was collected by filtration, washed with cold anhydrous acetone and dried *in vacuo;* yield 1.5 g., 53%. The light tan powder was stored in sealed ampules under an atmosphere of dry nitrogen. Neither a picrate nor a chloroplatinate could be isolated.

Attempted Preparation of N,N'-Di-*n*-octylformamidine.—A solution of N-*n*-octylformamide (1.6 g., 0.010 mole), *n*-octylamine (1.3 g., 0.010 mole) and phosphorus pentachloride (2.5 g., 0.012 mole) in 50 ml. of chloroform was refluxed for two hours. No precipitate formed, and the yellow-colored solution had become deep red. On removal of the chloroform the brown residue was diluted with acetone. A white, acetone-insoluble material was obtained which was identified as *n*-octylamine hydrochloride. It melted at 198°, and the mixed m.p. with an authentic sample of *n*-octylamine hydrochloride was not depressed. The test for the formyl group was negative. Chloroplatinates were prepared from the acetone solution of the original reaction mixture and from alcohol solutions of the isolated solid and of *n*-octylamine. All three derivatives melted at 215–220° with decomposition and showed no depression of the m.p. on admixture.

N,N'-Diphenyl-N'-methylformamidine (III).—A solution of formanilide (7.2 g., 0.060 mole), N-methylaniline (6.4 ml., 0.060 mole) and phosphorus pentachloride (15 g., 0.072 mole) in 70 ml. of chloroform was refluxed for 3 hours. No precipitate formed. Upon cooling, the solution was diluted with anhydrous ether and the precipitated amidine hydrochloride was removed by filtration, washed with ether, and neutralized with sodium hydroxide. The base was extracted with ether, and the ether solution was dried over sodium sulfate and was evaporated. The residual yellow oil distilled at 213–217° (17 mm.). The residue exhibited a strong odor of isonitrile. Upon cooling, the partially solidified distillate was treated with ligroin and the mixture was centrifuged. The solid phase, upon crystallization from hot ligroin, weighed 1.2 g. (20%), m.p. 139–140°, and on admixture with an authentic sample of diphenylformamidine showed no depression of the melting point. The supernatant solution was distilled to remove the ligroin. Redistillation of the residue at 215–217° (17 mm.) provided the trisubstituted amidine[19]; yield 5.3 g., 36%, n^{25}D 1.6469.

In the converse reaction, the interaction of N-methylformanilide, freshly distilled aniline and phosphorus pentachloride in chloroform solution produced the desired amidine in 74% yield using the procedure as described for IV below.

(19) H. L. Wheeler and T. B. Johnson, *Am. Chem. J.*, **20**, 853 (1898).

The amidine **hydrochloride** was prepared by the dropwise addition of a solution of hydrogen chloride in dry acetone to an acetone solution of the base. The hydrochloride melted at 228–230°.

Anal. Calcd. for $C_{14}H_{15}N_2Cl$: Cl, 14.45; N, 11.35. Found: Cl, 14.46; N, 11.48.

The chloroplatinate derivative was prepared by the addition of an alcohol solution of chloroplatinic acid to an aqueous solution of the amidine hydrochloride. Golden-yellow crystals with a characteristic double melting point were isolated, m.p. 139–141°, 196–198°.

Anal. Calcd. for $C_{28}H_{30}N_4PtCl_6\cdot3H_2O$: Pt, 22.10; H_2O, 6.12. Found: Pt, 22.00; H_2O, 5.84.

N-Phenyl-N',N'-di-n-butylformamidine (IV).—A solution of 8.9 ml. (0.050 mole) of N-di-n-butylformamide, 4.7 ml. (0.050 mole) of freshly distilled aniline and 15 g. (0.072 mole) of phosphorus pentachloride in 50 ml. of chloroform was refluxed for three hours. Upon cooling ether was added until two phases separated. The mixture was extracted with several portions of water until the aqueous extract was free of chloride. The combined aqueous extracts, containing the amidine hydrochloride, were then made alkaline with sodium hydroxide, and the amidine was extracted with ether. After drying the ether solution over sodium sulfate and removing the ether, the residual oil distilled at 190–192° (16 mm.); yield 6.2 g., 54%, $n^{25}D$ 1.5364.

Anal. Calcd. for $C_{15}H_{24}N_2$: N, 12.06. Found: N, 11.87.

In the converse procedure, the interaction of di-n-butyl-amine, formanilide and phosphorus pentachloride in chloroform solution produced the desired amidine in 8% yield. N,N'-Diphenylformamidine (II) was isolated from the reaction product in 8% yield.

The amidine **hydrochloride** was prepared by the addition of a solution of hydrogen chloride in anhydrous ether to an ether solution of the amidine. A colorless sirup was obtained which could not be crystallized.

Anal. Calcd. for $C_{15}H_{25}N_2Cl$: N, 10.45; Cl, 13.25. Found: N, 10.13; Cl, 12.65.

The **chloroplatinate** derivative was obtained by the addition of chloroplatinic acid to an alcohol solution of the amidine. Golden-yellow needles were isolated, m.p. 216–218° dec.

Anal. Calcd. for $C_{30}H_{50}N_4PtCl_6$: Pt, 22.30. Found: Pt, 22.42.

N-Phenyl-N-methyl-N'-n-butylformamidine.—A solution of 7.9 ml. (0.060 mole) of N-methylformanilide, 6.0 ml. (0.060 mole) of freshly distilled n-butylamine and 15 g. (0.072 mole) of phosphorus pentachloride in 50 ml. of chloroform was refluxed for three hours. The amidine was isolated by the procedure described for IV and distilled at 149–151° (18 mm.); yield 6.5 g., 56%, $n^{25}D$ 1.5490.

The amidine **hydrochloride**, prepared from ether solution by the usual procedure, yielded white needles, m.p. 123–124°.

Anal. Calcd. for $C_{12}H_{19}N_2Cl$: N, 12.40; Cl, 15.72. Found: N, 12.30; Cl, 15.79.

The **chloroplatinate** derivative obtained from aqueous solution by the usual procedure, yielded yellow needles, m.p. 179–181°.

Anal. Calcd. for $C_{24}H_{38}N_4PtCl_6$: Pt, 24.70. Found: Pt, 24.50.

Amine Interchange.—A mixture of diphenylformamidine (3.6 g., 0.018 mole), n-butylamine hydrobromide (2.8 g., 0.018 mole) and n-butylamine (7.2 ml., 0.074 mole) was heated in a sealed tube at 105° for 45 hours. After cooling, the reaction mixture was removed and shaken with 100 ml. of anhydrous ether. The brown oil which separated from the solution was washed with anhydrous ether and treated with sodium ethylate in ethanol in order to convert the oily hydrobromide into the free base. The insoluble inorganic constituents of the mixture were removed by centrifugation. Ethanol and butylamine were removed by distillation at 20 mm. N,N'-Di-n-butylformamidine was isolated from the residue by distillation at 85–95° (1.5 mm.); yield 0.15 g., 5%.

The chloroplatinate derivative was prepared in the usual procedure, m.p. 118–119°.

Anal. Calcd. for $C_{18}H_{42}N_4PtCl_6$: Pt, 27.05. Found: Pt, 27.25.

Qualitative Test for Formamidines.—Approximately 1 g. of formamidine was refluxed with 10 ml. of an 8% solution of sodium hydroxide for 10 hours. When cool, the mixture was extracted with ether, and the water phase, after acidification with dilute hydrochloric acid, was filtered to remove any silica. It was then neutralized by the addition of a few crystals of sodium carbonate and heated to boiling with 3 ml. of a 5% solution of mercuric chloride. The formation of a heavy white precipitate of mercurous chloride, insoluble in mineral acid, served as a test for the detection of the formyl group. A negative test precluded the presence of formamidines in the material examined.

Detection of Carbon Monoxide.—The synthesis of diphenylformamidine was carried out in the usual manner except that no aniline was added prior to refluxing the reaction mixture. After 15 minutes of refluxing, the system was evacuated and the gases from the reaction vessel were bubbled through a solution of sodium hydroxide to trap hydrogen chloride. Carbon monoxide was absorbed by an iodine pentoxide preparation (Carbon Monoxide Detector, Mine Safety Appliance Co., Pittsburgh, Pa.). A green color, characteristically produced by carbon monoxide, was persistently obtained.

Hydrolysis of Formamidines.—A suspension of 1.0 g. of N,N'-diphenylformamidine in water or in a dilute hydrochloric acid solution was refluxed on the steam-bath for 18 hours. The chilled reaction mixture was neutralized with sodium bicarbonate, extracted with ether and the combined ether extracts dried over sodium sulfate. The ether was evaporated, and the residue treated with a slight excess of acetic anhydride. The product, acetanilide, was crystallized from boiling water, collected by filtration and dried *in vacuo.*

In water diphenylformamidine under the above conditions yielded 33% of acetanilide although formanilide gave no acetanilide. In dilute hydrochloride acid diphenylformamidine yielded 65% and formanilide 71% of acetanilide, while under the same conditions aniline gave 69%.

Formanilide, the other product of hydrolysis of diphenylformamidine, was obtained by first removing the aniline by steam distillation, and then seeding the residual red oil with crystals of formanilide. The compound crystallized and melted without depression with an authentic sample of formanilide, m.p. 47–48°.

New Haven, Conn.