41. *Amidines. Part I. Preparation of Amidines from Cyanides.*

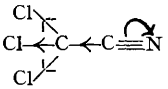
By P. Oxley and W. F. Short.

Amidines and their *N*-monosubstituted derivatives may be prepared by heating the ammonium or alkyl- or aryl-ammonium salt of an aromatic or aliphatic sulphonic acid with a cyanide at 180—300°. α-Naphthamidine and *o*-substituted benzamidines can be prepared in this way.

Although amidines have been obtained by a variety of methods only three are important as methods of preparation. Pinner's method (*Ber.*, 1877, **10**, 1889; " Die Imidoäther," 1892) involves the use of large volumes of anhydrous solvents and cannot be applied to the preparation of *o*-substituted benzamidines or of α-naphthamidines since the corresponding cyanides cannot be converted into imino-ethers. *o*-Ethoxyphenyl cyanide, however, affords an imino-ether in poor yield (Pinner and Dietz, *Ber.*, 1890, **23**, 2942) and a 40% yield of *o*-hydroxybenziminoethyl ether hydrochloride is obtained from *o*-hydroxyphenyl cyanide (Easson and Pyman, *J.*, 1931, 2999). Methods of preparation depending on the production of an imido- or amido-chloride (Gerhardt, *Annalen*, 1858, **108**, 217; Hofmann, *J. pr. Chem.*, 1866, **97**, 267; Klinger, *Annalen*, 1876, **184**, 280; Lossen, Mierau, Kobbert, and Grabowski, *Annalen*, 1891, **265**, 129; v. Pechmann, *Ber.*, 1895, **28**, 2362; 1897, **30**, 1782; Walther and Grossmann, *J. pr. Chem.*, 1908, **78**, 478; Hill and Cox, *J. Amer. Chem. Soc.*, 1926, **48**, 732; Sen and Rây, *J.*, 1926, 646; Pyman and Chew, *J.*, 1927, 2318) frequently afford good yields of amidines when applied to substituted amides of aromatic acids, but anomalous results are usually obtained with the substituted amides of aliphatic acids (Wallach, *Annalen*, 1877, **184**, 1; v. Braun, Jostes, and Heymons, *Ber.*, 1927, **60**, 92; Heymons, *Ber.*, 1932, **65**, 320; v. Braun and Rudolph, *Ber.*, 1934, **67**, 269, 1762; v. Braun, *Angew. Chem.*, 1934, **47**, 611). Walther and Grossmann (*loc. cit.*) showed that aromatic amines react with cyanides in presence of sodium to give sodio-amidines, and unsubstituted amidines may frequently be obtained from cyanides and sodamide or potassamide (Cornell, *J. Amer. Chem. Soc.*, 1928, **50**, 3313; Ziegler, Rohm, and Haas, G.P. 641,125; U.S.P., 2,049,582; Ziegler and Ohlinger, *Annalen*, 1932, **495**, 84; Kirsanov and Polyakova, *Bull. Soc. chim.*, 1936, **3**, 1600; May and Baker, Ewins, Newbery and Ashley, B.P. 538,463; May and Baker, Ewins and Ashley, B.P. 545,708. Cf. Vermillion and Hauser, *J. Org. Chem.*, 1941, **6**, 507). The method is not a general one and good yields are usually obtained only from aromatic cyanides and trisubstituted cyanides, CR$_3$·CN, which cannot yield by-products by reacting in the enimic form. It is stated in almost all the standard text-books of organic chemistry that amidines may be prepared by heating cyanides with ammonium chloride. but this statement appears to be an extrapolation of Bernthsen's discovery (*Annalen*, 1877, **184**, 290; 1878, **192**, 1) that *N*-aryl- and *NN*-diaryl-amidines may be prepared by heating a cyanide with the hydrochloride of a primary aromatic amine or of diphenylamine. (See also Walther and Grossmann, *loc. cit.*; Scholl, *Monatsh.*, 1918, **39**, 238.) Bernthsen expressly stated that amidines could not be obtained from cyanides and ammonium chloride. Very small yields of amidines have subsequently been obtained by heating acetamide with ammonium nitrate and liquid ammonia (Fichter, *Z. Elektrochem.*, 1912, **18**, 651; *Verh. Naturf. Ges. Basel*, 1913, **23**, 221) and from cyanides by heating under pressure with ammonium chloride and liquid ammonia (Cornell, *loc. cit.*).

A number of new methods for the preparation of substituted and unsubstituted amidines of the open chain, cyclic, and semicyclic type will be described in this series of memoirs, and we now record the preparation of amidines and their *N*-monosubstituted derivatives by heating the ammonium or alkyl- or aryl-ammonium salt of an aromatic or aliphatic sulphonic acid with a cyanide at a suitable temperature within the range 180—300°.

There is no record of the production of an amidine by the addition of ammonia or an amine to an unsubstituted cyanide,* but the introduction of certain polar atoms or groups stimulates the cyano-group so that addition occurs. Thus, Curtis and Nickell (*J. Amer. Chem. Soc.*, 1913, **35**, 887) found that amidines are produced by the addition of diethylamine, di-*n*-propylamine, or benzylamine to ethyl cyanotartronate, (CO$_2$Et)$_2$C(OH)·CN, and trichloromethyl cyanide adds ammonia and amines at low temperatures to give trichloroacetamidine and its derivatives (I.G., G.P. 671,785). It seems evident that in these compounds the kationoid properties of the unsaturated carbon of the cyano-group are enhanced by the inductive effect of the substituents and a similar activation doubtless accounts for the enhanced reactivity of trichloromethyl cyanide in the Hoesch reaction and for the alkaline hydrolysis of chloral and trichloroacetic acid. We suggest that the additive capacity of the cyano-group may also be



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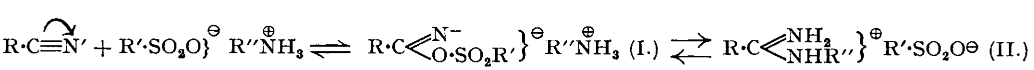
* The statement that *N*-*o*-chlorophenylbenzamidine is obtained in 75% yield by heating phenyl cyanide and *o*-chloroaniline at 180° (Walther and Grossmann, *loc. cit.*, p. 491) is probably due to a typographical error, since repetition of the experiment failed to yield any amidine. The amine hydrochloride was probably used as in all other cases reported in the paper.

enhanced by an " imported " stimulus and that the reaction between a cyanide and a salt of a sulphonic acid may be represented as follows :—



$$\mathrm{R{\cdot}C{\equiv}N' + R'{\cdot}SO_2O\}^{\ominus}\ R''\overset{\oplus}{N}H_3 \rightleftharpoons R{\cdot}C{\lessdot}\begin{matrix}N^-\\ O{\cdot}SO_2R'\end{matrix}\}^{\ominus} R''\overset{\oplus}{N}H_3\ (I.) \rightleftarrows R{\cdot}C{\lessdot}\begin{matrix}NH_2\\ NHR''\end{matrix}\}^{\oplus} R'{\cdot}SO_2O^{\ominus}\ (II.)}$$

The salient features are the production of (i) a complex anion (cf. I) capable of degrading the ammonium ion (cf. the decomposition of ammonium nitrite), probably by hydrogen bond formation between the nitrogen atoms, (ii) the amidine salt of a strong acid. An alternative mechanism postulating the dissociation of the ammonium salt and ammonolysis of the intermediate, $\mathrm{R{\cdot}C(:NH){\cdot}O{\cdot}SO_2R'}$, is unacceptable since no ammonia is liberated during the reaction and the intermediate would not be stable at the temperature employed (see Part II). An equilibrium is established between *p*-cyanophenyl methyl sulphone, ammonium benzenesulphonate, and the benzenesulphonate of *p*-amidinophenyl methyl sulphone, and the constituents are readily isolated in this case owing to the absence of by-products. The equilibrium constants have been determined at 250—255° and at 258—260° by isolating the amidine produced from mixtures of the cyanide with the ammonium salt (Table I); the experimental errors involved are too large to allow the heat of reaction to be calculated.

TABLE I.

Temp.	250—255°		258—260° (*a*)	
Mols. of $\mathrm{Ph{\cdot}SO_3NH_4}$.	Yield of amidine, %.	Equilibrium constant.	Yield of amidine, %.	Equilibrium constant.
1·0	48	2·70	47·5 (*b*)	2·64
1·5	55	2·49	56·9	2·73
2·0	61	2·69	61·3 (*c*)	2·73
2·5	—	—	63·5	2·67
3·0 (*d*)	64	2·53	64·0	2·53

Notes.—(*a*) We are indebted to Dr. M. W. Partridge for the determinations at 258—260°.
(*b*) 47% of the amidine salt remains when the salt is heated at 260° for 2 hours.
(*c*) The value 60·2% is obtained when the equilibrium is approached from the other side.
(*d*) Mixtures containing more than 3·0 mols. of ammonium salt are not homogeneous.
Equilibrium is attained in 2 hours in all cases.

This method for the preparation of amidines has been widely applied and the results are shown in Table II. The influence of temperature, time of reaction, and proportion of reactants on the yield of amidine has not been thoroughly examined in all cases, so that the yields recorded in Table II are not necessarily the highest obtainable. It will be noted that primary aromatic amines afford either a *N*-mono- or a *NN'*-di-arylamidine as main product, so that the amine sulphonates behave in the same way as the hydrochlorides (Bernthsen, *loc. cit.*). The ammonium salts of a variety of sulphonic acids may be employed and in some cases the use of a salt of an alkanesulphonic acid is advantageous owing to the lower m. p. and the greater solubility of the cyanide in the melt. The fact that ammonium chloride gives very low yields of amidines even under special conditions is doubtless connected with its infusibility and its inability to yield homogeneous mixtures with cyanides. The use of other ammonium salts and of other nitrogen compounds in the preparation of amidines will be described in later communications. The formation of amidines from phenyl cyanides is usually promoted by groups which act as electron-sinks (*p*-$\mathrm{MeSO_2}$·, *p*-Br, *p*-$\mathrm{NO_2}$) and is retarded by those which act as electron-sources. This may mean that amidine formation is analogous to the production of cyanohydrins (Lapworth), but an electron displacement which accelerates the formation of (I) will retard its rearrangement to (II) at a higher temperature. In the absence of a detailed physico-chemical investigation, it is impossible to decide which is the rate-determining stage of the reaction. The observation that, in general, amidine formation is more complete with the salts of weak bases agrees with the reaction mechanism suggested, since the corresponding ammonium ion will be more prone to degradation.

This method of producing amidines is applicable to α-naphthyl cyanide and *o*-substituted phenyl cyanides, thus rendering accessible amidines not easily made by other methods, and can be used in the preparation of monoamidines from dicyanides. It has the advantage of being a one-stage process which can be operated without employing a solvent. Unchanged cyanide and excess of the ammonium salt are readily separated and recovered from the reaction product. Substances which may be regarded as potential sources of cyanides under the conditions of the reaction may be used in place of cyanides, but the yield of amidine is usually lower owing to side reactions. Thus, benzamide and ammonium benzenesulphonate (1·1 mol.) afford benzamidine benzenesulphonate (4%) when heated at 250° for 3 hours.

EXPERIMENTAL.*

The cyanide and the salt of the sulphonic acid are heated, preferably with stirring, under the conditions specified in Table II; the use of sealed tubes is unnecessary except in the case of volatile cyanides such as phenyl cyanide. A homogeneous melt is usually produced at the outset but, in a few cases, the mixture only becomes homogeneous as the reaction proceeds. The isolation of the amidine salt and liberation of the free amidine are effected by known methods. The amidine benzenesulphonates in general are less soluble in cold water than the corresponding hydrochlorides, and it is often possible to extract unchanged cyanide from the reaction product with acetone or ether and then separate the residual

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* See also Boots Pure Drug Co. Ltd., Oxley and Short, B.P. 573,266 (27.1.1944).

TABLE II.

Amidine.	Ammonium or amine benzene-sulphonate mols.	Reaction		Yield of amidine, %.	Amidine benzenesulphonate.			
		Temp.	Time, hrs.		M. p.	Formula.	Found, N, %.	Re-quired.
(1) Benzamidine	4·0	270—280°	20	66	175—175·5°	—	—	—
(2) *N*-Phenylbenzamidine	1·0	270	0·25	81·5	—	—	—	—
(3) *NN*-Diphenylbenzamidine	1·0	200—210	0·33	29	243	$C_{25}H_{22}O_3N_2S$	6·55	6·5
(4) *N*-*p*-Tolylbenzamidine	1·0	240	0·17	84	184	—	—	—
(5) *NN'*-Di-*p*-tolylbenzamidine	2·5	270	1·0	86	217	—	—	—
(6) *N*-*p*-Nitrophenylbenzamidine	1·1	240	0·25	30	258 (decomp.)	$C_{19}H_{17}O_5N_3S$	10·7	10·5
(7) 4-*Bromobenzamidine*	1·0	250—260	2·0	52	257	$C_{13}H_{13}O_3N_2BrS$	8·1	7·8
(8) 4-Methoxybenzamidine	1·0	260—270	1·0	18	212	$C_{14}H_{16}O_4N_2S$	9·15	9·1
(9) 4-Amidinophenyl methyl sulphide	1·2	270	1·0	49	—	—	—	—
(10) 4-Amidinophenyl methyl sulphone	2·5	258—260	2·0	63·5	253	$C_{14}H_{16}O_5N_2S_2$	8·0	7·9
(11) *N*-Ethyl-4-amidinophenyl methyl sulphone	1·0	275—280	1·3	41	—	—	—	—
(12) *p*-Sulphonamidobenzamidine	1·4	250—255	2·0	67	—	—	—	—
(13) *N*-4'-Sulphonamidophenyl-4-sulphonamidobenzamidine	1·0	230	0·5	45	—	—	—	—
(14) *o*-Nitrobenzamidine	1·9	250	2·5	12·5	213·5	$C_{13}H_{13}O_5N_3S$	13·2	13·0
(15) *m*-Nitrobenzamidine	1·06	245—250	2·0	34·5	203·5	—	—	—
(16) *p*-Nitrobenzamidine	1·06	255—260	2·0	43·5	258·5	—	—	—
(17) α-Naphthamidine	1·7	260—270	2·0	29	210—211	$C_{17}H_{16}O_3N_2S$	8·7	8·5
(18) β-Naphthamidine	2·2	250	2·0	25	203	—	—	—
(19) 2-Amidinopyridine	1·4	265—270	1·25	49	145·5	$C_{12}H_{13}O_3N_3S$	15·2	15·05
(20) 3-Amidinopyridine	1·2	250—255	4·5	18	185—185·5	$C_{12}H_{13}O_3N_3S$	15·0, 15·0	15·05
(21) Phenylacetamidine	1·33	260—270	3·0	54·5	186—186·5	—	—	—
(22) *N*-*o*-Chlorophenylphenylacetamidine	1·0	230—235	0·5	100	—	—	—	—
(23) *N*-Methylphenylacetamidine	1·1	240—280	1·0	57	—	—	—	—
(24) *N*-Benzylphenylacetamidine	1·1	245—295	1·0	62	131	—	—	—
(25) *N*-*p*-Tolylphenylacetamidine	1·0	240	0·17	73	—	—	—	—
(26) αγ-Diamidinopropane	2·0	235—240	1·0	50	197	$C_{17}H_{24}O_6N_4S_2$	12·55	12·6
(27) 1 : 11-Diamidinoundecane	4·0	260—265	3·0	—	—	—	—	—
(28) α-4-Amidinophenoxy-β-4'-cyanophenoxyethane	1·0	260	2·0	22	239—239·5	$C_{22}H_{21}O_5N_3S$	10·2	9·6
(29) 4 : 4'-Diamidino-αβ-diphenoxyethane	3·0	260	3·0	57	>270	$C_{28}H_{30}O_8N_4S_2$	10·0	9·1
(30) 4 : 4'-Diamidino-αγ-diphenoxypropane	4·0	260—270	2·75	39	236—237	$C_{29}H_{32}O_8N_4S_2$	8·9	8·9
(31) 4 : 4'-Diamidinostilbene	6·0	275—280	2·0	47	—	—	—	—
(32) 4 : 4'-Diamidinodiphenyl sulphone	4·6	270	1·0	57	—	—	—	—
(33) 4-Amidino-4'-cyanodiphenyl disulphoxide	4·0	245—250	2·0	50	245—247	$C_{20}H_{17}O_5N_3S_3$	8·95	8·85

Notes.—(1) Rouiller (*Amer. Chem. J.*, 1912, **47**, 483) states that the benzenesulphonate has m. p. 173°. The picrate had m. p. 238—239° (Found: N, 20·2. Calc. for $C_{13}H_{11}O_7N_5$: N, 20·1%); Dieckmann (*Ber.*, 1892, **25**, 547) gives m. p. 228°. The trichloroacetate had m. p. 126° decomp. (Pinner, "Imidoäther") records m. p. 127° (decomp.).

(2) The amidine had m. p. 116° (Brunner, Seeger, and Dittrich, *Monatsh.*, 1924, **45**, 69, give m. p. 113·5°) and the hydrochloride, m. p. 231° (Lossen, *Annalen*, 1891, **265**, 138, gives m. p. 224°). *NN'*-Diphenylbenzamidine (15%), m. p. 147° (Busch and Falco, *Ber.*, 1910, **43**, 2559, record m. p. 144°), was simultaneously formed.

(3) A mixture of diphenylamine, benzenesulphonic acid, and phenyl cyanide was employed. The amidine had m. p. 113—113·5° (Brunner, Seeger, and Dittrich, *loc. cit.*, give m. p. 112°) and the nitrate, 220° (decomp.) (Bernthsen, *Annalen*, 1878, **192**, 13, gives m. p. 213—215° (decomp.)).

(4) The amidine had m. p. 100·5—101° (Bernthsen, *Annalen*, 1876, **184**, 355, gives 99—99·5°).

(5) Prepared from *p*-toluidine benzenesulphonate. *N*-*p*-Tolylbenzamidine benzenesulphonate was simultaneously obtained in 4% yield. *NN'*-Di-*p*-tolylbenzamidine had m. p. 131—132° (Bernthsen, *loc. cit.*, gives m. p. 131°), and the hydrochloride, m. p. 240—241° (decomp.)).

(6) The amidine had m. p. 168°; Barber (*J.*, 1943, 103) records m. p. 167—168°.

(7) The *amidine* had m. p. 159° (decomp.) (Found: N, 13·6. $C_7H_7N_2Br$ requires N, 14·1%) and the *picrate*, 272° (decomp.) (Found: N, 16·1. $C_{13}H_{10}O_7N_5Br$ requires N, 16·4%). Andrewes, King, and Walker (*Proc. Roy. Soc.*, 1946, *B*, **133**, 20) describe the hydrochloride, m. p. 264—265°.

(8) *p*-Methoxybenzamidine had m. p. 119° (Found: N, 18·5. Calc. for $C_8H_{10}ON_2$: N, 18·7%). Lossen and Grabowsky (*Annalen*, 1897, **297**, 385) record m. p. 112°. The *picrate* had m. p. 213° (Found: N, 18·4. $C_{14}H_{13}O_8N_5$ requires N, 18·5%).

(9) Prepared by Dr. A. Koebner. The hydrochloride had m. p. 218—220° (Found: N, 13·7. Calc. for $C_8H_{11}N_2ClS$: N, 13·8%). Fuller, Tonkin, and Walker (*J.*, 1945, 633) record m. p. 218—219°.

(10) The hydrochloride had m. p. 294° (Found: N, 11·9; Cl, 15·1. Calc. for $C_8H_{11}O_2N_2ClS$: N, 11·9; Cl, 15·1%) in agreement with Fuller, Tonkin, and Walker (*loc. cit.*). Andrewes, King, and Walker (*loc. cit.*) record m. p. 288—289°.

(11) Prepared from ethylamine benzenesulphonate. The *picrate* had m. p. 155·5—156° (Found: N, 15·4. $C_{16}H_{17}O_9N_5S$ requires N, 15·4%) and the *toluene*-p-*sulphonate*, m. p. 242° (Found: C, 51·15; H, 5·6; N, 7·2 $C_{17}H_{22}O_5N_2S_2$ requires C, 51·25; H, 5·6; N, 7·0%).

(12) The free base, m. p. 223° (decomp.), and the hydrochloride hemihydrate, m. p. 250—252°, did not depress the m. p.'s of specimens prepared as described by Levene, Pyman, and Boots Pure Drug Co. (B.P. 544,836 of 1941). Delaby and Harispe (*Bull. Soc. chim.*, 1943, **10**, 580) state that the base and anhydrous hydrochloride melt at 251° and 242° respectively; Andrewes, King, and Walker (*loc. cit.*) give m. p. 228° decomp. as the m. p. of the base and 250—251° as that of the hydrochloride hemihydrate. Ammonium methane-, toluene-*p*-, *m*- and *p*-nitrobenzene-, naphthalene-α- and naphthalene-β-sulphonates were also used in the preparation of this amidine.

(13) The amidine had m. p. >270°; the *hydrochloride*, m. p. 288·5° (decomp.), was hydrated (Found, on sample dried at 100°: N, 14·3. $C_{13}H_{15}O_4N_4ClS_2$, requires N, 14·3%).

(14) The *picrate* had m. p. 232—233° (decomp.) (Found: N, 21·3. $C_{13}H_{10}O_9N_6$ requires 21·3%).

(15) Rouiller (*loc. cit.*, p. 491) records m. p. 198—200° for the benzenesulphonate.

(16) Rouiller (*loc. cit.*) states that the benzenesulphonate has m. p. 250°. The *picrate* melts at 240° (Found: N, 21·5. $C_{13}H_{10}O_9N_6$ requires N, 21·3%).

(17) α-Naphthamidine had m. p. 154° and its picrate m. p. 226·5°; Ponzio and Zanardi-Lamberti (*Gazzetta*, 1923, **53**, 818) record 154° and 223° respectively.

(18) β-Naphthamidine had m. p. 136° (Lossen and Grabowski, *Annalen*, 1897, **297**, 381, give m. p. 145°, and Kirsanov and Polvakova, *Bull. Soc. chim.*, 1936, **3**, 1606, give m. p. 133—136°); the picrate melted at 247°; Ponzio and Zanardi-Lamberti (*loc. cit.*), give m. p. 240°.

(19) The picrate had m. p. 207·5—208°.

(20) Barber and Slack (*J. Amer. Chem. Soc.*, 1944, **66**, 1607) have prepared nicotinamidine hydrochloride, m. p. 190°, by the Pinner method, and Andrewes, King, and Walker (*loc. cit.*) record m. p. 189—190°.

(21) Rouiller (*loc. cit.*, p. 492) records m. p. 182—183° for the benzenesulphonate.

(22) The amidine had m. p. 111·5—112° (Found: N, 11·55. Calc. for $C_{14}H_{13}N_2Cl$: N, 11·45%). The *picrate* had m. p. 153—153·5° (Found: N, 14·75. $C_{20}H_{16}O_7N_5Cl$ requires N, 14·8%).

(23) The free base was an oil; the *Reineckate* separated from 30% aqueous acetone in plates, m. p. *ca.* 137° (Found: SCN, 49·6, 49·7. $C_{13}H_{19}N_8S_4Cr$ requires SCN, 49·7%).

(24) In agreement with Neber and Uber (*Annalen*, 1928, **467**, 52) the free base had m. p. 93°. These authors give benzenesulphonate, m. p. 127—130°.

(25) The free base had m. p. 119°; Bernthsen (*Annalen*, 1876, **184**, 346) gives m. p. 118—119°.

(26) Preparation by Dr. J. Cymerman. The *di-picrate* had m. p. 235° (Found: N, 23·4. $C_{17}H_{18}O_{14}N_{10}$ requires N, 23·9%).

(27) The yield of crude amidine was good but purification losses were high. The picrate, m. p. 190—192°, did not depress the m. p. of a specimen prepared as described by King, Lourie, and Yorke (*Lancet*, 1937, **233**, 1360).

(28) The *picrate* had m. p. 202° (Found: N, 16·4. $C_{22}H_{18}O_9N_6$ requires N, 16·5%).

(29) The free base had m. p. 228° (decomp.) and the *picrate*, m. p. >270° (Found: N, 18·3. $C_{28}H_{24}O_{16}N_4$ requires N, 18·5%). May and Baker, Ewins, Barber, Newbery, Ashley and Self (B.P. 507,565; *J.*, 1942, 110) record 231—232° (decomp.) and 234—235° (decomp.) as the m. p. of the free base.

(30) Preparation by Dr. M. W. Partridge. The amidine has been prepared by May and Baker, Ewins, *et al.* (*loc. cit.*).

(31) Preparation by Mr. S. W. Stroud. The dihydrochloride had m. p. >360° after drying at 60° under reduced pressure (Found: N, 16·5. Calc. for $C_{16}H_{16}N_4,2HCl$: N, 16·6%). This amidine has been described by May and Baker, Ewins and Ashley (B.P. 510,097; *J.*, 1942, 110).

(32) Preparation by Dr. A. Koebner. The dihydrochloride, m. p. 300—302°, did not depress the m. p. of a specimen prepared as described by Ashley, *et al.* (*loc. cit.*, p. 110).

(33) Preparation by Dr. J. Cymerman.

mixture of amidine and ammonium salts by crystallisation from water or alcohol. The sulphonic acid salts of the substituted amidines are often sparingly soluble in water and, since they do not crystallise readily from aqueous solutions, it is often preferable to employ alcohol as solvent. Alternatively, the free amidine may be liberated by the addition of ammonia or 5N-sodium hydroxide to an aqueous or alcoholic solution or suspension of the salt. The free base is collected by filtration or in a suitable solvent (*e.g.*, chloroform) and may then be separated from unchanged cyanide by solution in hydrochloric acid. Aqueous solutions of the sulphonic acid salts of ammonia and amidines frequently dissolve considerable amounts of cyanides which are almost insoluble in water.

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[*Received, August* 25*th*, 1945.]