Restricted Rotation in Benzamidinium Systems

J. S. MCKENNIS AND P. A. S. SMITH*

Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48104

Received May 1, 1972

Variable-temperature nmr examination of N'-phenyl-, N'-benzyl-, N'-ethyl-, and N'-tert-butyl-N,N-dimethylbenzamidine shows the existence of rotational conformers with barriers to rotation about the C-N(CH₃)₂ bond of 12-13 kcal/mol. The corresponding salts have barriers of ca. 20 kcal/mol. Comparison with results of others on N'-acyl-N,N-dimethylbenzamidines shows that the electronic effect is not large. The report (Raison, 1949) of the existence of N,N,N'-trimethyl-N'-phenylbenzamidinium iodide in two forms must be a case of crystalline modifications, for the nmr spectra are identical; the barrier to rotation about the $C-N(CH_s)_2$ bond is about 14 kcal/mol. The coalescence temperature of the nmr signals of the geminal methyl groups in this compound is markedly raised by the addition of anions of oxy acids, as well as by the use of aromatic solvents. Three tetrasubstituted amidinium salts bearing geminal dimethyl groups-N,N-dimethyl-N',N'-dibenzylbenzamidinium iodide, N, N, N'-trimethyl-N'-benzylbenzamidinium iodide, and N, N, N'-trimethyl-N'-benzyl-formamidinium iodide—show magnetic nonequivalence of the geminal methyl groups owing to restricted rotation at lower temperatures, but show no evidence for the existence of different rotational conformations of the more heavily substituted amino group.

Although restricted rotation in amides has been extensively studied,¹ such rotation in amidinium systems has attracted less attention. Rotational barriers about the C-N bond in amidines have been determined by variable-temperature nmr for N,N-dimethylformamidines containing the following substituents on N' (*i.e.*, the imine N): *p*-nitrophenyl ($\Delta G = 15.9$ kcal/mol),² *p*-tolyl ($\Delta G = 14.1$ kcal/mol),² chloromethanesulfonyl ($\Delta G_{418,2^{\circ}K} = 23.3 \text{ kcal/mol}$),³ and tert-butyl ($\Delta G = 11.9 \text{ kcal/mol}$).⁴ Schwenker and Rosswag⁵ reported barriers for a series of N,N-dimethylbenzamidines in which the N' substituents were H, COPh, SO₂Ph, and PO(OPh)₂. They observed a weak correlation between the electronegativity of the N' substituent and the magnitude of the rotational barrier about the central C-N bond, according to the importance of the contribution of dipolar structures that increase the double-bond character of the C-N- $(CH_3)_2$ bond. The effect of differences in electro-

$$\mathrm{RC}^{\mathrm{NY}}_{\mathrm{RC}}$$

negativity was considerably smaller than expected, however, a fact that Jakobsen and Senning have attributed to steric effects³ (see below).

Aromatic solvents have been found to raise the coalescence temperature (but not the rotational barrier²) for several N'-aryl-N,N-dimethylformamidines⁶ by increasing the magnetic nonequivalence, $\Delta \nu$, of the two methyl groups.

Restricted rotation in a few amidinium salts has also been noted.⁶ Barriers have been obtained for acetamidinium chloride (estimated as 9-25 kcal/mol),⁷ N,N-dimethylacetamidinium chloride (21.8 ± 1.0 kcal/mol), and nitrate (21.5 kcal/mol),⁸ and N,N,-N', N'-tetramethylformamidinium perchlorate (17.8) kcal/mol).9

Conformational isomerism of the N substituents in

- (2) D. T. Bertelli and J. T. Gehrig, Tetrahedron Lett., 2481 (1967).
- (3) H. J. Jakobsen and A. Senning, Chem. Commun., 1245 (1968).
- D. L. Harris and K. M. Wellman, *Tetrahedron Lett.*, 5225 (1968).
 G. Schwenker and H. Rosswag, *ibid.*, 2691 (1968).
- (6) J. P. Marsh, Jr., and L. Goodman, ibid., 683 (1967).
- (7) G. S. Hammond and R. C. Neuman, J. Phys. Chem., 67, 1655 (1963).
- (8) R. C. Neuman, Jr., and Y. Jonas, *ibid.*, 75, 3532 (1971).
- (9) J. Rauft and S. Dahne, Helv. Chim. Acta, 47, 1160 (1964).

some N, N'-diaryl- and N-aryl-N'-tert-butylformamidinium trifluoroacetates has been examined, 10 and the existence of only one conformational isomer for N,N'-dimethylacetamidinium chloride has been observed.⁴ A possible example of the existence of stable rotational isomers was reported long ago by Raison,¹¹ who found that N, N, N'-trimethyl-N'-phenylbenzamidinium iodide could be obtained in two states, with distinct melting points. The cause of this phenomenon could not be adequately investigated at that time, when nmr spectroscopy was not available.

In connection with other studies concerning the alkylative behavior of amidines, we have had occasion to prepare a variety of benzamidinium compounds, which provided an opportunity to extend the limited previous studies, and to reexamine the phenomenon reported by Raison and that disputed by Rosswag and Jakobsen and Senning.

Results and Discussion

The nmr spectra of N,N-dimethylbenzamidines bearing an N'-phenyl (Ia), N'-benzyl (Ib), N'-ethyl (Ic), or N'-tert-butyl substituent (Id) showed singlets for the geminal N-methyl protons at ambient temperature (ca. 35°) in methylene chloride. At lower temperatures, however, Ia, Ib, and Ic showed two equally intense singlets for these protons. The rotational barriers (ΔG_{Te}) about the C-N(CH₃)₂ bonds in amidines Ia and Ib at the coalescence temperatures were determined using an approximative method¹²

	NY
PhC	/
	$CH_3)_2$
Ia, $Y =$	Ph OH Ph
	$C_{2}H_{5}$
d, Y =	$C(CH_3)_3$

⁽¹⁰⁾ K. M. Wellman and D. L. Harris, Chem. Commun., 256 (1967).

⁽¹⁾ E.g., W. E. Stewart and T. H. Siddall, III, Chem. Rev., 70, 517 (1970).

⁽¹¹⁾ C. G. Raison, J. Chem. Soc., 3319 (1949).

⁽¹²⁾ H. S. Gutowsky and C. H. Holm, J. Chem. Phys., 25, 1228 (1956). Although the use of approximative methods can in some cases lead to considerable error [A. Allerhand, et al., J. Amer. Chem. Soc., 88, 3185 (1966)], the barriers obtained here correlate well with both those in the literature and those calculated using a more exact rate equation (Allerhand, et al.). Recently, the validity of using approximate equations for determining K_c has been discussed [D. Kost, E. H. Carlson, and M. Raban, Chem. Commun., 656 (1971)].

to be ca. 13 and 12 kcal/mol, respectively.¹⁸ These values are compatible with those obtained by Schwenker and Rosswag for N,N-dimethylbenzamidines in which the N' substituents were the more electronegative groups, PhCO (15.2 kcal/mol), PhSO₂ (16.4 kcal/mol), and PO(OPh)₂ (17.6 kcal/mol).⁵

The substantial barriers to rotation in Ia and Ib are of special interest with respect to the controversy over the fact that the barrier in N,N-dimethylbenzamidine (I, Y = H; $\Delta G = 18.2 \text{ kcal/mol}$) is not markedly smaller than that in its benzenesulfonyl derivative (I, Y = PhSO₂), even after a correction of 13 kcal/mol for the estimated role of hydrogen bonding. Jakobsen and Senning³ have proposed that this may not be due to insensitivity to electronic effects, as originally suggested, but to counteracting steric effects resulting from the vastly different spatial requirements of H and $PhSO_2$. However, the spatial requirements of benzyl groups are much closer to those of benzenesulfonyl or benzoyl than to hydrogen, but the electronic effects are very different; thus the small difference in the energy barriers that we have found (about 4 kcal/mol) between Ib, $Y = C_6H_5CH_2$, and I, Y = $C_6H_5SO_2$, confirms that the influence of electronic factors is not large (although it is not so small as had appeared from data involving the ambiguity presented by hydrogen bonding). (The lack of nmr evidence for restricted rotation in Id may be due to too small a value for the magnetic nonequivalence of the methyl groups.¹⁴)

At ambient temperature (ca. 35°), the nmr spectra of the corresponding amidinium salts (IIa = Ia HCl; IIb = Ib HCl; IIc = Ic HCl; IId = Id HI; IIe = I HI, Y = CPh₃) showed two equally intense signals for the N(CH₃)₂ protons. These signals cannot



arise from coupling with NH (if protonation had occurred at the tricoordinate nitrogen), since the two signals persist when the solvent is deuterium oxide.¹⁵ Although the two $-N(CH_8)_2$ absorptions could arise from the presence of a 1:1 mixture of the two rotational isomers, IIIa and IIIb, assuming free rotation about the C-N(CH₃)₂ bond, the persistence of the equal intensity of the NCH₃ absorptions upon varying the size of Y, which should affect the relative population of IIIa and IIIb, argues against this interpretation. Fur-

(15) Similar behavior was observed for the hydrochloride salts of N, N-dimethyl-N'-arylformamidines.⁶

thermore, the spectra of salts IIc and IId showed absorptions attributable to only one type of alkyl group.¹⁶ The preceding observations can be satisfactorily accounted for by restricted rotation about the C-N- $(CH_3)_2$ bond.¹⁷



In protonated amidines, both nitrogens are capable of sharing the positive charge and would be expected to do so¹⁸ if a planar configuration is possible. If the protonated nitrogen does bear substantial charge, the barrier to rotation about the C-NHY bond should be enhanced proportionally to the magnitude of the share. In this regard, it is of interest that none of the ambient-temperature spectra of the protonated benzamidines indicated the existence of the two possible rotational isomers IVa and IVb. Even when the N



substituents were larger than the N' substituent, as in N,N-dibenzyl-N'-methylbenzamidinium chloride, two absorptions were observed for the N substituents and only one for the N' substituent. This circumstance may be a reflection of either a substantially lower rotational barrier about the C-N' bond than about the C-N bond (*i.e.*, C-NHR vs. C-NR₂), corresponding to localization of charge largely on -NR₂, or a higher barrier that fixes the existence of exclusively IVa (or IVb).¹⁹ Space-filling molecular models demonstrate that the Z isomer, IVb, is sterically much more congested than the E isomer, IVa.²⁰ Consequently, if charge delocalization is substantial, the isomer IVa would be expected to predominate.

The barriers to rotation about the C-N bond in the salts IIa, IIb, and IId were determined from variable-temperature spectra in nitrobenzene to be 20.4,

⁽¹³⁾ The low-temperature spectra could alternatively be interpreted in terms of Z and E isomerism about the dicoordinate nitrogen. However, in order to account for the equal intensity of the NCH₄ absorptions, such an interpretation necessities a 1:1 mixture of Z and E isomers for both amidines Ia and Ib, in which the steric bulk of the N' substituent differs considerably; consequently, this alternative interpretation is less attractive. A referee has correctly pointed out that the energy barrier to rotation might be lowered as a consequence of severe crowding, which would raise the energy of the ground state relative to the transition state.

⁽¹⁴⁾ Restricted rotation has been observed in N,N-dimethyl-N'-butyl-formamidine dissolved in aromatic solvents, which presumably increase the magnetic nonequivalence of the geminal N-methyl groups.⁴

⁽¹⁶⁾ The spectrum of the amidinium salt IIb in deuteriochloroform exhibited coupling between the NH proton and the benzyl protons $(J \cong 6 \text{ Hz})$.

⁽¹⁷⁾ The hydrochloride of N-benzyl-N-methyl-N'-phenylbenzamidine also exhibits hindered rotation at ambient temperature, as evinced by two NCH₃ and two NCH₂Ph absorptions in which the high- and low-field NCH₃ signals are correlated by relative intensities with the low- and high-field NCH₂Ph signals, respectively. If there were free rotation about the $C-N(CH_3)CH_2Ph$ bond, the methyl and benzyl protons in either of the rotamers would be expected to be shifted in the same direction. Accordingly, the high-field methyl and benzyl protons would correspond to one isomer and the low-field protons to the other.

⁽¹⁸⁾ J. Sandstrom [J. Phys. Chem., 71, 2318 (1967)] using MO methods has calculated the delocalization energy in a positively charged amidinium system to be 0.632β .

⁽¹⁹⁾ R. Kwok and P. Prane [J. Org. Chem., 32, 738 (1967)] have concluded from ambient-temperature spectra that the positive charge in the hydrochloride of N-ethyl-N'-methyl-N-phenylbenzamidine is localized on the nitrogen bearing the ethyl and phenyl groups. However, a fixed conformation about the C-NHCH₃ bond would be consistent with their data.

⁽²⁰⁾ For a discussion of the Z and E nomenclature see J. E. Blackwood, et al., J. Amer. Chem. Soc., 90, 509 (1968); J. E. Blackwood, et al., J. Chem. Soc., 8, 30 (1968).

20.1, and 19.7 kcal/mol,²¹ respectively. That the N' substituent has very little effect on the barrier is presumably due to dominance of steric effects. As expected, these barriers are higher than those in the free bases and are comparable to the reported barrier in N,N-dimethylacetamidinium chloride ($E_{act} = 21.8$ kcal/mol)⁸ (and also to those in simple N,N-dimethylbenzamides).²²

Quaternary amidinium salts (N,N,N',N' tetrasubstituted) are of interest because they lack a proton substituent, with its small size, great mobility, and capacity for hydrogen bonding. At ambient temperature in deuteriochloroform and methylene chloride, the nmr spectra of N, N, N'-trimethyl-N'-phenylbenzamidinium iodide (Va) in either of the two forms reported by Raison¹¹ and tetrafluoroborate (Vb) were identical and consisted of two NCH₃ absorptions (relative intensity 1:2), corresponding to the methyl protons on the phenyl-substituted nitrogen and those on the other nitrogen, respectively.²³ At lower temperatures the spectra showed two broad peaks (ca. 1:1) corresponding to the geminal N-methyl groups; the other methyl peak was also broadened, but remained a singlet at temperatures as low as -50° . The estimated rotational barriers were approximately 14 and 15 kcal/mol, respectively. These results show that the two forms of Va obtained by Raison must have been different crystalline modifications, rather than different rotational conformations.

PhC
$$\bigvee_{i=1}^{N(CH_3)Ph} X^{-}$$

N(CH₃)₂
Va, X = I
b, X = BF₄

The ambient-temperature spectra of Va and Vb were dramatically influenced by changes in the medium The addition of trifluoroacetic, trichloroacetic. fluorosulfonic, nitric, or formic acid to deuteriochloroform solutions of these salts, or dissolution of the salts in any of the liquid acids, caused the absorption corresponding to the geminal N-methyl protons to separate into two absorptions of equal intensity ($\Delta \nu \cong$ 6 Hz). On the other hand, no effect on the spectra was observed when glacial acetic, HCl-saturated glacial acetic, DMSO-acetic, concentrated hydrochloric, 48% hydriodic, p-toluenesulfonic, or dilute sulfuric acid was added. Phosphoric acid caused only broadening of the $N(CH_3)_2$ peak. The nmr spectra (CDCl₃) of the trifluoroacetate or the nitrate, prepared in situ from silver trifluoroacetate and nitrate and the amidinium iodide, were virtually identical with that observed for the iodide plus trifluoroacetic or nitric acid. The perchlorate, prepared similarly, showed a very closely spaced doublet. It is evident that the nature of the anion, rather than the acidity of the medium, causes the splitting, and the cause cannot be the presence of free base, which Neuman and Jones⁸ found to be the cause of anomalous behavior of N,N-dimethylacetamidinium salts.

The spectrum of the amidinium iodide (Va) in trifluoroacetic acid and in formic acid was examined at higher temperatures. The two methyl groups coalesced at 63° (CF₃CO₂H) and 54° (HCO₂H) and the free energies of the exchange processes based upon $\Delta \nu_{\infty} = 9$ and 6 Hz, respectively, were estimated to be 17 kcal/mol.²⁴ consistent with restricted rotation as the cause. Other amidinium salts, e.g., VI, VII, and VIII, showed equivalent geminal N-methyl groups in the presence of various oxy acids, but the foregoing anion effect would not have been observed if the coalescence temperature, even though raised, remained below ambient (ca. 35°). Neuman and Jones have reported⁸ a higher $\Delta \nu_{\infty}$ for N,N-dimethylacetamidinium nitrate (5.17 Hz, 38°) than for the chloride (1.8 Hz, 37.8°); the values of E_a (21.3 ± 0.3 and 22.8 ± 0.7) and ΔG (21.5 and 21.8 kcal/mol at 25°) for rotation about the central C-N bond were very similar. The foregoing effect seems to be associated with the presence of bidentate anions, and is presumably a result of differences in association or solvation.²⁵

Aromatic media also affect the spectrum; at ambient temperature (ca. 35°) the amidinium iodide in $CDCl_3-C_6H_6$ (ca. 1:5) showed a doublet ($\Delta \nu = 5$ Hz) corresponding to the geminal N-methyl groups. The effect of aromatic solvent and the anion may arise in part from an enhancement of the rotational barrier or, alternatively, solely from increased magnetic nonequivalence $(\Delta \nu)$ of the geminal N-methyl groups. The aromatic solvent effect observed for rotation in N'-aryl-N,N-dimethylformamidines stems solely from an increase in $\Delta \nu$, since the free energies of activation are affected negligibly. Interestingly, however, the enthalpy and entropy of activation for rotation in the N'-p-nitrophenyl derivative are considerably enhanced. With regard to the benzamidinium salts, stronger association of the aromatic solvent with the positively charged substrate may affect the free energy as well as the enthalpy and entropy of activation.

$N(CH_2Ph)_2$		$N(CH_3)CH_2P$	h	N(CH ₃)CH ₂ P	h
PhC, +	I_	$PhC_{1}^{\prime\prime}$ +	Ι-	HC +	Ι-
$N(CH_3)_2$		$N(CH_3)_2$		$N(CH_3)_2$	
VI		VII		VIII	

The low-temperature spectra of salts VI-VIII demonstrate the importance of steric effects upon the conformation of the amidinium system. Restricted rotation about the $C-N(CH_3)_2$ bond was observed in each compound by the nonequivalence of the signals of the two *N*-methyl groups. Hindrance to rotation about the other carbon-nitrogen bond was not observed even at -50° . These observations can be interpreted to imply that the positive charge is borne predominantly by the nitrogen bearing the two *N*-

⁽²¹⁾ These barriers, determined from the coalescence temperatures, agreed well with those calculated using eq 12, A. Allerhand, et al., ref 12. (22) I. M. Iseiterse, T. F. Kennerger, and D. G. Hurtherse, T. F. Kennerger, and D. G. Hurtherse, T. F. Kennerger, and M. S. Kennerger, and Ken

⁽²²⁾ L. M. Jackman, T. E. Kavanagh, and R. C. Haddon, Org. Magn. Resonance, 1, 109 (1969).

⁽²³⁾ This assignment is supported by the spectra of the deuteriomethylated iodides, N,N-dimethyl-N'-(methyl- d_3)-N'-phenylbenzamidinium and N,N'-dimethyl-N'-(methyl- d_3)-N-phenylbenzamidinium iodide, prepared by deuteriomethylation of N,N-dimethyl-N'-phenylbenzamidine and N,N'-dimethyl-N-phenylbenzamidine, respectively.

⁽²⁴⁾ Although examination of spectra at temperatures below ambient may reveal larger frequency differences $(\Delta \nu)$ and thus smaller rotational barriers, in order to obtain a calculated barrier less than 17 kcal/mol for the trifluoroacetate, the limiting frequency difference $(\Delta \nu_{\infty})$ would have to be >31 Hz. The highly polar acids used as solvents may, of course, influence the magnitude of the barrier.

⁽²⁵⁾ R. C. Neuman, Jr., and V. Jonas, J. Phys. Chem., 75, 3550 (1971), have observed a difference in the degree of ion pairing between amidinium chloride and nitrate.

methyl groups, an explanation that requires that the geminal methyl groups lie in the N-C-N plane but that the C-N-C plane formed by the larger substituents on the other nitrogen be twisted substantially out of the N-C-N plane. An alternative explanation, applicable only to VII and VIII, is that the N-C-N and both C-N-C planes may be coplanar, but that the configuration of the $-N(CH_3)CH_2Ph$ moiety is fixed with the benzyl group exo, owing to its bulk. A configuration with both C-N-C planes parallel, but partially twisted out of the N-C-N plane, capable of conformational inversion by concerted conrotatory motion, is inconsistent with our observations.

A tentative assignment of the position (endo or exo) of the methyl groups in the protonated amidines can be made on the basis of the spectrum of the hydrochlo $ride \quad of \quad N-benzyl-N-methyl-N'-phenylbenzamidine.$ The ambient-temperature spectrum of the salt in deuteriochloroform reveals the existence of two rotational isomers in a ratio of ca. 3.8:1.26 The rotamer in lower concentration possesses the higher field methyl signal and the lower field benzyl signal. If this rotamer is that in which the bulkier group (benzyl) is endo, then the high- and low-field geminal N-methyl signals for the protonated amidines can be assigned to the exo- and endo-methyl groups, respectively.²⁷ In all of the protonated amidines studied, the lower field methyl signal has a larger width at half-height than does the higher field methyl signal (the larger signal width of the endo-methyl can perhaps be attributed to selective long-range coupling with the NH proton).

Curiously, in the quaternary amidinium salts studied here, the width of the low-field methyl signal appears to be smaller than that for the high-field methyl signal. At low temperatures, the spectra of the N,N,N'trimethylbenzamidinium salts contain three methyl signals (ca. 1:1:1), in which the signal corresponding to the N'-methyl groups and the high-field N-methyl signal are wider than the low-field N-methyl signal. Extrapolation from the assumed correlation between signal width and position in the protonated amidines would suggest that in the methylated amidinium salts, the high-field N-methyl signal corresponds to the endo methyl group. Since these assignments are based purely on signal width and steric arguments, however, they must at present be viewed with caution.²⁸

As the temperature is lowered from 0 to -60° , both the N'-methyl signal and the high-field N-methyl signal broaden considerably and to the same extent. This line broadening is similar to that observed by Dewar²⁹ for the methyl signals of bis(dimethylamino)phenylborane and is consistent with the above assignment, assuming the N'-methyl group to be endo.

In summary, restricted rotation about the formal C-N single bond in amidines appears generally to have a lower barrier than in amidinium salts, and lower than in amides. It is more sensitive to steric than to

(27) Presumably, the anisotropic effect of the benzene nucleus is at least in part responsible for the upfield position of the protons of the exo group. Hammond and Neuman' observed that in the spectrum of N,N'-dimethylacetamidinium chloride, the protons of the exo groups were down-field relative to the protons of the endo groups.

(28) The need for such caution is dramatically illustrated and advocated by Frucht, Lewin, and Bovey [*Tetrahedron Lett.*, 3707 (1970)].

(29) M. J. S. Dewar and R. Rona, J. Amer. Chem. Soc., 91, 2259 (1969).

electronic effects. There is no evidence for the separate existence at ambient temperatures of rotational isomers of amidines or amidinium salts, and the RR'N moiety has an overwhelming preference for the conformation with the bulkier group in the exo orientation.

Experimental Section

General Procedures.—Nuclear magnetic resonance spectra were recorded using a Varian A-60 spectrometer; chemical shifts are referred to tetramethylsilane as internal standard unless otherwise stated. The temperatures recorded for the variabletemperature spectra were determined by calibration with the spectra of ethylene glycol and methanol as recommended by Varian³⁰ and, accordingly, are accurate to 2°. All of the nmr solutions used in the variable-temperature studies were 1 M.

The rotational barriers were calculated using the approximative equation $k_{\text{Te}} = (\pi/\sqrt{2})\Delta\nu$ and the Eyring equation.¹² The pertinent data are given in Tables I and II.

TABLE I

C-N(CH₈)₂ ROTATIONAL BARRIERS IN BENZAMIDINES AND THEIR HYDROHALIDES

 $PhC(=\!\!=\!\!NX)N(CH_3)_2$

			Coales-		
		$\Delta \nu$, Hz	cence	$\Delta G_{T_{c}}$,	
		(temp,	temp	kcal/	Sol-
Compd	х	°C)	$(T_{\rm c}), \ ^{\circ}{\rm C}$	mol	vent ^a
Ia	\mathbf{Ph}	24(-55)	-16	13.0	$\mathrm{CH}_{2}\mathrm{Cl}_{2}$
$IIa(Ia \cdot HCl)$		$47 ~(\simeq 35)$	135	20.4^{b}	$PhNO_2$
\mathbf{Ib}	$PhCH_2$	33(-55)	-40	12.0	$\mathrm{CH}_{2}\mathrm{Cl}_{2}$
IIb (Ib·HCl)		$47 (\sim 35)$	130	20.4	$PhNO_2$
Ic	$\mathrm{CH_{3}CH_{2}}$		~ -55		$\mathrm{CH}_2\mathrm{Cl}_2$
IIc (Ic·HCl)		$36 (\sim 35)$			$PhNO_2$
Id	$(CH_3)_{3}C$		< -70		CH_2Cl_2
IId (Id·HCl)		$44(\sim\!35)$	120	19.7	$\mathrm{C_2H_2Cl_4}$

^a All concentrations were 1 M. ^b $E_a = 20.8$ kcal/mol; log A = 13; $\Delta H^{\pm} = 20.0$ kcal/mol [calculated using eq 12, A. Allerhand, et al., J. Amer. Chem. Soc., 88, 3185 (1966)].

The preparative data for the benzamidines and their salts are given in Tables III and IV. The benzamidines were prepared by the treatment of N-substituted benzimidoyl chlorides³¹ with amines. In some cases, disubstituted amidines prepared in this manner were subsequently methylated with methyl iodide to afford the desired trisubstituted amidines. The preparations of N'-benzyl-N,N-dimethylbenzamidine (Ib), N-methyl-N'-tertbutylbenzamidine (IX), and N,N-dimethyl-N'-tert-butylbenzamidine (Id) are illustrative.

The hydrochloride salts were prepared from the amidine and hydrogen chloride; the preparation of N-benzyl-N-methyl-N'-phenylbenzamidinium chloride is illustrative. Hydrochlorides which were quite hygroscopic (see Table III) were prepared in situ by bubbling anhydrous hydrogen chloride through nitrobenzene solutions $(1 \ M)$ of the amidines. The solutions were degassed with nitrogen prior to nmr examination.

N'-Benzyl-N, N-dimethylbenzamidine (Ib).—To an ice-cooled, stirred solution of 11.9 g (0.052 mol) of N-benzylbenzimidoyl chloride³¹ in 200 ml of benzene was gradually added 40 ml of a benzene solution of dimethylamine (*ca.* 20% by volume). The resulting solution was allowed to assume room temperature and was stirred for 20 hr. During this period a white precipitate formed. The reaction mixture was treated with an additional 10 ml of the dimethylamine solution, refluxed on a steam bath for 20 min, and then left to stand at room temperature overnight. Dimethylamine hydrochloride (4.2 g) was removed by filtration and washed with ether. The filtrate and ether washings were combined and concentrated *in vacuo* to afford 11.7 g of a pale yellow liquid. N'-Benzyl-N, N-dimethylbenzamidine was obtained in a total yield of 8.7 g (70%) as two fractions by distillation under reduced pressure: fraction A, wt 0.6 g, bp 152–154° (1–1.25 mm), *n*²⁷D 1.5785; fraction B, wt 8.1 g, bp 154° (1.5

⁽²⁶⁾ This ratio represents an equilibrium mixture, since approximately the same ratio was obtained when the nmr sample was heated to induce coalescence and then allowed to cool.

^{(30) &}quot;Varian Variable Temperature Accessory Manual," 87-202-006.
(31) (a) J. v. Braun and W. Pimpernelle, Ber., 67, 1218 (1934); (b) I. Ugi, F. Beck, and U. Fetzer, Chem. Ber., 95, 126 (1962).

TABLE II C-N(CH₈)₂ Rotational Barriers in Quaternary Benzamidinium Salts [PhC(NXCH₃)NYZ] +An⁻

				-			
Compd	x	Y	z	νΔ, Hz (temp, °C)	Coalescence temp (T_c) , °C	ΔG_{Tc} , kcal/mol	$Solvent^a$
Va (Ia CH ₃ I)	\mathbf{Ph}	CH_3	CH_3	15(-60)	1	14.2	CH_2Cl_2
Va (Ia CH ₃ I)				$9 (\sim 35)$	63	17.8	$CF_{3}CO_{2}H$
Va (Ia CH ₃ I)				$6 (\sim 35)$	54	17.5	HCO₂H
Vb (Ia CH ₃ BF ₄)				17(-45)	31	15.6	CH_2Cl_2
VI (XI CH ₃ I)	CH_{3}	$PhCH_2$	$PhCH_2$	23(-50)	31	15.5	$\mathrm{CH}_{2}\mathrm{C}^{1}_{2}$
VII (Ib CH ₃ I)	\mathbf{PhCH}_{2}	CH_{3}	CH_3		< -40		$\mathrm{CH}_{2}\mathrm{Cl}_{2}$

^a All concentrations 1 M.

TABLE III BENZAMIDINES AND THEIR HYDROHALIDES^a

	x-		Che	emical shifts, τ^{b}		Z	Bp, °C (mm)	Mp, °C	Yield, %
Iac	Ph		CH_3	7.05	CH_3	7.05		71-72 ^d	87
IIa (Ia HCl)				$6.4(6.06)^{\circ}$		$7.0(6.83)^{s}$		f	
Ib	$PhCH_2$	5.89	CH_3	7.23	CH_3	7.23	152 - 154(1.25)	-	70
IIb (Ib HCl)		5.85		$6.47(6.13)^d$		$7.20(6.90)^{e}$		f	
Ico	$CH_{3}CH_{2}$	7.09	CH_3	7.30	CH_3	7.30	$78(2)^{g}$		100
IIc (Ic HCl)				6.5		7.1		f	
Id ^h	(CH₃)₃C	9.03	CH_3	7.35	CH_3	7.35	50(0.1-0.05)		75
IId $(Id HI)^i$		8.68		6.27		7.05		202 - 203	93
IIe $(X CH_3I)^i$	$Ph_{3}C$		CH_3	6.15	CH_3	7.0		146 - 148	56
\mathbf{IX}^k	(CH ₃) ₃ C	8.62	Η	6.2	CH_3	7.20	63-66(0.5)		66
\mathbf{X}^k	$\mathbf{Ph}_{3}\mathbf{C}$		H	7.8	$\mathbf{CH}_{\mathfrak{s}}$	7.8		135 - 136	56
XI^k	CH_3	7.21	$PhCH_2$	5.70	$PhCH_2$	5.70		71-72	79

^a All new compounds gave satisfactory elemental analysis; boiling and melting points are uncorrected. ^b All values refer to chemical shifts in CHCl₃. ^c Prepared from dimethylamine and the appropriate N-substituted benzimidoyl chloride. ^d Reported mp 73-74°: H. von Peckmann, *Ber.*, **28**, 2362 (1895). ^e Chemical shift in PhNO₂. ^f These compounds were hygroscopic and consequently were prepared *in situ*. ^g Reported bp 130° (12 mm): P. Oxley and W. F. Short, *J. Chem. Soc.*, 382 (1947). ^h Prepared from *N*-methyl-*N'-tert*-butylbenzamidine and methyl iodide. ⁱ Prepared by treatment of IX with methyl iodide. ^j Prepared by treatment of X with methyl iodide. ^k Prepared from the appropriate amine and *N*-methylbenzimidoyl chloride.

TABLE IV

QUATERNARY AMIDINIUM SALTS^a

[RC	(NXY)N(($\mathcal{J}\mathbf{H}_{3})_{2}$	TAn T

\sim Chemical shifts, τ^b						Yield,	
	R	~~~-X-~~~	Y-		(CH ₃) ₂	Mp, °C	%
Va (Ia CH ₃ I)	\mathbf{Ph}	Ph	CH_3	6.45	6.85	142–143 ,	97
						180-181°	
Vb (Ia CH ₃ BF ₄)	\mathbf{Ph}	Ph	CH_3	6.56	7.0	103-104	85
VI (XI CH ₃ I)	\mathbf{Ph}	$PhCH_2$ 5.65	\mathbf{PhCH}_{2}	5.65	6.55	153 - 153.5	79
VII (Ib CH ₃ I)	\mathbf{Ph}	$PhCH_2$ 5.42	CH_3	6.79	6.69	119 - 120	85
VIII ^d	н	PhCH ₂ 5.06	CH_3	7.7	6.54	148 - 149	96

^a All new compounds gave satisfactory elemental analyses, and melting points are uncorrected. ^b Chemical shifts in CDCl₃. ^c Reported^{11,32} mp 144-145, 180-182°. ^d An⁻ = I⁻; prepared by treatment of N'-benzyl-N,N-dimethylformamidine³⁴ with methyl iodide.

mm), $n^{27}D$ 1.5813. Spectral and elemental analyses were performed on fraction B: ir (neat) 1600 (C=C or C=N) and 1620 cm⁻¹ (C=N); nmr (CDCl₃) τ 2.92 (m, 10, aromatic), 5.89 (s, 2, NCH₂Ph), and 7.23 [s, 6, N(CH₃)₂].

NCH₂Ph), and 7.23 [s, 6, N(CH₃)₂]. Anal. Calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.76. Found: C, 80.77; H, 7.66; N, 11.84. N'-Methyl-N-tert-butylbenzamidine (IX).—To an ice-cooled,

 $N'\text{-}\mathbf{Methyl}\text{-}N\text{-}tert\text{-}\mathbf{butyl}\mathbf{benzamidine}$ (IX).—To an ice-cooled, stirred solution of 20.0 g (0.13 mol) of N-methylbenzimidoyl chloride^{31b} in 90 ml of benzene was gradually added 19.0 g (0.26 mol) of recently distilled *tert*-butylamine. After the addition was completed, the reaction mixture was allowed to assume room temperature and was then refluxed on a steam bath for 5 hr. The resulting mixture was cooled to room temperature, filtered to remove the white, crystalline precipitate (wt 14.8 g, mp 298–299°), and concentrated. Vacuum distillation of the residual yellow oil afforded 16.4 g (66%) of a colorless liquid: bp 63–66° (0.5 mm); ir (neat) 1365 and 1395 (*tert*-butyl), 1605, 1620 (C=N), and 3425 cm⁻¹ (NH); nmr (CDCl₃) τ 2.62–2.95 (m, 5, aromatic), 6.2 (b s, 1, NH), 7.20 (s, 3, NCH₃), and 8.62 (s, 9, *tert*-butyl).

Anal. Calcd for $C_{12}H_{18}N_2$: C, 75.74; H, 9.53; N, 14.72. Found: C, 75.70; H, 9.56; N, 14.80. N,N-Dimethyl-N'-tert-butylbenzamidine (Id) and N,N-Dimethyl-N'-tert-butylbenzamidinium Iodide (IId).—To a solution of 15.0 g (0.08 mol) of N-methyl-N'-tert-butylbenzamidine (IX) in 45 ml of benzene was added 22.4 g (0.16 mol) of methyl iodide. The mixture was allowed to stand at room temperature for 12 min, then heated at 50° for 4 hr, and was finally left at room temperature overnight. The cream-colored hydriodide (IId) was collected by filtration, washed with benzene, and air dried: yield 24.8 g; mp 191-192.5° (crude), 202-203° after two recrystallizations from 95% ethanol; nmr (CDCl₈) τ 2.48 (s, 5, aromatic), 6.27 (s, 3, NCH₈), 7.05 (s, 3, NCH₈), and 8.68 (s, 9, tert-butyl).

Anal. Calcd for $C_{18}H_{21}N_2$: C, 47.00; H, 6.38; N, 8.43. Found: C, 47.08; H, 6.39; N, 8.52.

A stirred, ice-cooled, aqueous suspension of 22 g of the salt IId was made alkaline with aqueous sodium hydroxide and then extracted with ether until all of the solid material had disappeared and the ether extracts left no oil upon evaporation. The combined extracts were dried (Na₂CO₃) and evaporated to give 12.2 g (75% overall, based on 24.8 g of crude hydroiodide) of a colorless liquid. An analytical sample of compound Id was obtained from two distillations under reduced pressure: bp 50° (0.1–0.5 mm); ir (neat) 1360 and 1390 (tert-butyl), 1605 and 1625 cm⁻¹ (C=N); nmr (CDCl₃) τ 2.67–30.7 (m, 5, aromatic), 7.35 [s, 6, N(CH₃)₂], and 9.03 (s, 9, tert-butyl).

Anal. Calcd for $C_{13}H_{20}N_2$: C, 76.42; H, 9.87; N, 13.71. Found: C, 76.21; H, 9.87; N, 13.67.

The picrate salt was prepared in methanol from the purified amidine, mp $174-175.5^{\circ}$ (after two recrystallizations from methanol).

Anal. Calcd for C₁₉H₂₀N₃·C₆H₃N₃O₇: C, 52.65; H, 5.35; N, 16.16. Found: C, 52.70; H, 5.29; N, 16.04. *N*-Benzyl-*N*-methyl-*N'*-phenylbenzamidinium Chloride.—*N*-

N-Benzyl-N-methyl-N'-phenylbenzamidinium Chloride.—N-Benzyl-N-methyl-N'-phenylbenzamidine (10 g) in 300 ml of ether (dried over sodium) was treated with anhydrous hydrogen chloride. The resultant gummy, pale-yellow precipitate was collected by filtration, washed with ether, and recrystallized once from chloroform-ethyl acetate to afford 5.6 g of N-benzyl-N-methyl-N'-phenylbenzamidinium chloride as a white, crystalline solid, mp 204-205° [lit.¹¹ mp 206-207° (corrected)]. The nmr spectrum possessed two sets of N-methyl and N-benzyl absorptions at τ 6.3 and 7.0 and at 4.4 and 5.4, respectively, with the relative intensities 5.7:1.5:1:3.8, corresponding to two rotational isomers in a ratio of ca. 3.8:1. N,N,N'-Trimethyl-N'-phenylbenzamidinium iodide (Va) was

N, N, N'-Trimethyl-N'-phenylbenzamidinium iodide (Va) was prepared according to the method of Pyman.³² As reported by Raison,¹¹ two different melting points (142–143°, 180–181°) were obtained, depending upon the reaction conditions. The infrared and nmr spectra of the two differently melting forms were identical. In the nmr spectrum (CDCl₃) there were N-methyl absorptions at τ 6.45 [s, 3, N(CH₃)Ph] and 6.85 [s, 6, N(CH₃)₂].

to use at V of S (s), s), $N(CH_3)H$ if and 0.55 (s), 0, $N(SH_3)_2$]. N, N, N'-Trimethyl-N'-phenylbenzamidinium tetrafluoroborate (Vb) was prepared in 85% yield by alkylation of either N, N-dimethyl-N'-phenyl- or N, N'-dimethyl-N-phenylbenzamidine in methylene chloride with trimethyloxonium tetrafluoroborate.³⁸ The salt was purified by recrystallization from chloroform-ethyl acetate (ca. 1:5): mp 103-104°; nmr (CDCl₃) τ 2.45 (m, 10, aromatic), 6.56 [s, 3, N(CH₃)Ph], and 7.0 [s, 6, N(CH₃)₂].

Anal. Calcd for $C_{16}H_{19}N_2BF_4$: C, 58.92; H, 5.87; N, 8.59. Found: C, 58.91; H, 5.95; N, 8.61. N',N'-Dibenzyl-N,N-dimethylbenzamidinium Iodide (VI).--

A mixture of 2.0 g (6.4 mmol) of N,N-dibenzyl-N'-methylbenzamidine (XI), 1.8 g (ca. 12.8 mmol) of methyl iodide, and 3 ml of benzene was heated at 55° for 2.5 hr and then allowed to stand for 4 hr at room temperature. Concentration of the mixture in vacuo afforded a pale yellow, viscous solid, which was thoroughly digested with ether. The insoluble N,N-dibenzyl-N',N'-dimethylbenzamidinium iodide was collected by filtration, washed with more ether, and dried in air, yield 2.3 g (79%), mp The nmr spectrum of the crude material contained 149-152°. two broad absorptions at τ 5.65 and 6.55 (relative intensities ca. 2:3, respectively) in addition to aromatic absorption and weak absorptions corresponding apparently to traces of the substrate amidine and the hydroiodide salt. Attempted recrystallizations from common solvents and solvent mixtures, such as ethanolwater, chloroform-ligroin, chloroform-ether, chloroform-ethyl acetate, and acetonitrile-ethyl acetate, afforded only oils. An analytical sample was finally obtained as off-white crystals, mp 153-153.5°, by repeated trituration with hot ethyl acetate.

Anal. Caled for $C_{23}H_{25}N_2I$: C, 59.47; H, 5.67; N, 6.30. Found: C, 59.63; H, 5.57; N, 6.17.

N'-Benzyl-N, N, N'-trimethylbenzamidinium Iodide (VII).-A mixture of 1.0 g (4.2 mmol) of N'-benzyl-N,N-dimethylbenzamidine (Ib), 0.3 g of methyl iodide (dried over sodium carbonate), and 5 ml of acetonitrile (dried by distillation from phosphorus pentoxide) was refluxed for 7 hr (gradual darkening). The addition of 25 ml of anhydrous ether to the cooled reaction mixture precipitated a dark orange oil which settled to the bottom of the reaction vessel. Decantation followed by trituration of the oil with one 25-ml and three 15-ml portions of boiling ether afforded a light orange, viscous mass. The mass was taken up in 5 ml of chloroform (dried by passage through alumina), and 25 ml of ethyl acetate (similarly dried) was added. After 5 min, a white solid began to precipitate. The mixture was allowed to stand for 0.5^{-} hr and then cooled in an ice bath. The white precipitate, N'-benzyl-N', N, N-trimethylbenzamidinium iodide, was collected by filtration, washed with ethyl acetate, and dried in air: yield 1.35 g (85%); mp 117-118°; nmr (CDCl₃) τ ca. 2.5 (m, 10, aromatic), 5.42 [s, 2, N(CH₃)CH₂Ph], 6.69 [s, 6, N(CH₃)₂], and 6.79 [s, 3, N(CH₃)CH₂Ph].

An analytical sample, mp 119–120°, was prepared by recrystallization from chloroform-ethyl acetate mixtures.

Anal. Caled for $C_{17}H_{21}N_2I$: C, 53.69; H, 5.57; N, 7.36. Found: C, 53.58; H, 5.57; N, 7.43. *N*-Benzyl-*N*,*N*,*N'*-trimethylformamidinium Iodide (VIII).—

N-Benzyl-*N*, *N*, *N'*-trimethylformamidinium Iodide (VIII).— A mixture of 0.5 g (3.1 mmol) of *N'*-benzyl-*N*, *N*-dimethylformamidine,³⁴ 1.3 g (ca. 9.2 mmol) of methyl iodide, and 4 ml of acetonitrile was maintained at 60° for 6 hr and then was refluxed for 1 hr. Upon cooling to room temperature, a white solid precipitated. It was collected by filtration and washed with anhydrous ether, yield 0.7 g, mp 147–148°. The filtrate and ether washings were combined and concentrated to a yellow oil. Addition of a small amount of ether precipitated white crystals, which were collected and washed with ether, yield 0.2 g, mp 146–148°. The total yield of *N'*-benzyl-*N*, *N*, *N'*-trimethylformamidinium iodide was 0.9 g (96%). Recrystallization from 95% ethanol gave white crystals: mp 148–149°; nmr (CDCl₃) τ 2.55 (m, 5, aromatic), 5.06 [s, 2, N(CH₃)CH₂Ph], 6.54 [b s, 6, N(CH₃)₂], and 7.7 (s, 3, N(CH₃)CH₂Ph].

Anal. Caled for $C_{11}H_{17}N_{2}I$: C, 43.43; H, 5.64; N, 9.21. Found: C, 43.34; H, 5.67; N, 9.40.

Registry No.—Ia, 2397-36-6; Ib, 36529-77-8; Ic, 36529-78-9; Id, 36529-79-0; Id picrate, 36529-80-3; IIa, 36488-79-6; IIb, 36529-81-4; IIc, 36476-55-8; IId, 36476-56-9; IIe, 36476-57-0; Va, 36476-58-1; Vb, 36476-59-2; VI, 36476-60-5; VII, 36476-61-6; VIII, 36476-62-7; IX, 36476-63-8; X, 36476-64-9; XI, 36476-65-0.

Acknowledgment.—The authors are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for financial support of this work.

(34) H. Bredereck, et al., Chem. Ber., 92, 837 (1959).

⁽³²⁾ F. L. Pyman, J. Chem. Soc., 123, 3359 (1923).

⁽³³⁾ H. Meerwein, Org. Syn., 46, 120 (1966).