Amidines. Part 33.[1] Full *ab initio* 3-21G Optimization of the Molecular Structures of Fluoro Derivatives of Formamidine and their Protonation Products. Quantitative Structure–Basicity Relations of Amidines

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ab initio 3-21G geometry optimizations for eight derivatives of formamidine with up to three fluorine substituents, and all corresponding formamidinium cations protonated at the imino nitrogen, show strong conjugation in the amidine system between the C=N double bond and the lone electron pair on the amino nitrogen atom. Substitution with fluorine at each atom of the N=C–N group exerts considerable influence on this conjugation, and as a result the geometry of the molecule can be drastically changed. The introduction of the electron-withdrawing fluorine substituent at the amino nitrogen atom of formamidines leads to a tetrahedral bond arrangement at this atom. For amidines unsubstituted at the amino group and for all protonated systems, co-planarity is predicted by calculation, and all substituents lie in the plane of the N=C–N group.

Calculations of energies of protonations as well as proton transfer between amidines and ammonia show that changes in basicities of amidines caused by substitution at certain sites of the amidine group depend on polar effects of substituents at other sites. This provides an explanation for the observed changes of ρ values caused by substituents at different sites in correlations of experimental pK_a values of amidines with Hammett σ constants. The influence of substitution at both nitrogen atoms on tautomeric equilibria in amidines is discussed.

In the course of studies on structure–basicity relations of amidines it was found[2–6] that the pK_a values of amidines containing a substituted phenyl ring at the carbon atom, the amino nitrogen atom, or the imino nitrogen atom of the amidino group correlate in each case with Hammett substituent σ constants according to equation (1). For each of the three

$$pK_a = pK_a^0 - \rho \cdot \sigma \qquad (1)$$

sites for phenyl substitution on the amidino group, another ρ value is obtained because of different distances from the imino nitrogen atom *i.e.* the centre of protonation.

In addition, it was found that the ρ values obtained for a series of amidines containing variable substituents at the imino nitrogen atom depend, to a considerable degree, on the kind of substituents at the amidino carbon atom.[7–9] Thus it was concluded that the sensitivity of the amidino group to substituent effects at one site depends on the effects of substituents at other sites,[10] and that the pK_a values of amidines containing two substituted phenyl rings did not obey the well-known linear equation (2) but rather equation (3), containing

$$pK_a = pK_a^0 - \rho_1 \cdot \sigma_1 - \rho_2 \cdot \sigma_2 \qquad (2)$$

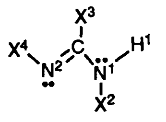
an additional term which takes into account the mutual interaction of the substituents. This equation ensures that if the

$$pK_a = pK_a^0 - \rho_1 \cdot \sigma_1 - \rho_2 \cdot \sigma_2 - \mu \cdot \sigma_1 \cdot \sigma_2 \qquad (3)$$

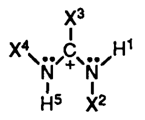
substituent at one of these sites is not varied, a linear correlation [equation (1)] will be obtained. The observed ρ value depends on the σ value of the invariant substituent, and on the term μ representing the mutual interaction of substituents.[11] From several series of *N,N*-dimethylamidines[11,12] it was shown that the ρ value for substitution at the imino nitrogen atom (referred to as ρ_{im}) depends on the effect of substituents at the amidino carbon atom. Recently it was shown[1,13] that the ρ value for substituted phenyl rings at the amino nitrogen atom (referred to as ρ_{am}) also depends on substitution at the amidino carbon atom, and that the ρ_{im} value depends also on substitution at the amino nitrogen atom.

Thus the question arose as to how, and to what extent, simple substituents at each of the three amidino positions interact and affect the influence of substituents at other sites of the amidino group. The aim of this work was to find an explanation of these phenomena on the basis of *ab initio* calculations, using fluorine as a simple substituent for modelling of the electronic behaviour of substituted phenyl rings. For this study, eight formamidines containing the overall electron-withdrawing fluorine substituent at each of the three amidino sites, and in all possible combinations of substitution at more than one site (Figure 1), have been considered with the corresponding products of protonation at the imino nitrogen atoms.

The amidino group gives rise to *Z–E* isomerism with respect to the CN double bond and to conformers (rotamers) due to restricted rotational isomerism at the amide-like CN single bond. Usually, if the substituent X^3 at the amidino carbon is sterically undemanding, the *Z*-orientation of the substituent X^4 at the imino nitrogen with respect to the substituent X^3 at the amidino carbon is calculated to be the most stable[24] and is also observed experimentally.[14] Of the two possible rotamers at the planar amino nitrogen N^1, the one with substituent X^2 in *s-trans* arrangement to X^3 at the carbon is preferred for stereochemical reasons. Therefore, for fluorine-substituted formamidines the most probable stereochemical arrangements (as shown in Figure 1) have been selected to model the stereochemistry of corresponding phenyl-substituted derivatives.



free bases



protonated forms

Compd.	Name	Substituents X^2	X^3	X^4
(1) HHH	Formamidine	H	H	H
(2) FHH	N^2-Fluoroformamidine	H	H	F
(3) HFH	Fluoroformamidine	H	F	H
(4) FFH	(N^2-Fluoro)fluoroformamidine	H	F	F
(5) HHF	(N^1-Fluoro)formamidine	F	H	H
(6) FHF	*N,N'*-Difluoroformamidine	F	H	F
(7) HFF	(N^1-Fluoro)fluoroformamidine	F	F	H
(8) FFF	(*N,N'*-Difluoro)fluoroformamidine	F	F	F
(1p) PHHH	Formamidinium cation	H	H	H
(2p) PFHH	*N*-Fluoroformamidinium cation	H	H	F
(3p) PHFH	Fluoroformamidinium cation	H	F	H
(4p) PFFH	(*N*-Fluoro)fluoroformamidinium cation	H	F	F
(5p) PHHF	*N*-Fluoroformamidinium cation	F	H	H
(6p) PFHF	*N,N'*-Difluoroformamidinium cation	F	H	F
(7p) PHFF	(*N*-Fluoro)fluoroformamidinium cation	F	F	H
(8p) PFFF	(*N,N'*-Difluoro)fluoroformamidinium cation	F	F	F

Figure 1. Molecular formulas, conformations, and numbering of the amidines considered in this work [**(2)** (FHH) and **(5)** (HHF) as well as **(4)** (FFH) and **(7)** (HFF) are pairs of tautomers; **(2p)** and **(5p)** as well as **(4p)** and **(7p)** are corresponding conformers].

Because protonation of amidines occurs at the imino nitrogen, with preservation of the stereochemistry of the free base due to allylic conjugation in the amidinium cation, the conformers shown in Figure 1 have been selected for calculations.

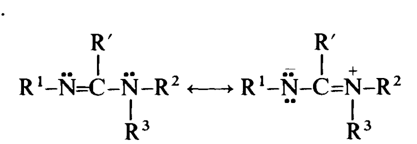
Methods of Calculations.—For the eight amidines and their protonation products (with the stereochemical configurations as shown in Figure 1), single-determinantal *ab initio* SCF Hartree–Fock MO calculations[15–19] with full optimization of molecular structures have been performed. The analytical gradient optimization procedure of Murtagh and Sargent[20] implemented in Pople's GAUSSIAN 82 program,[21] and the split-valence 3-21G basis set[22] have been used in an IBM MVS/XA version on a COMPAREX 7/88 computer.[23] The 3-21G basis set was selected for reasons of economy and to aid comparison with the elaborate calculations of Zielinski *et al.*[24–26] on formamidine and related systems. Use of the STO-3G minimal basis set[27] leads to incorrect CN bond lengths and a tetrahedral geometry for the amino group of formamidine.[28]

Calculated 3-21G bond distances and bond angles are shown in Tables 1 and 2. For formamidine **(1)** and formamidinium cation **(1p)** results of optimizations using the 6-31G basis set[29] which was shown to be best suited for calculations of C–C distances[30] are also included in Tables 1 to 4. Experimental X-ray determinations of the formamidinium cation give 1.282(9) and 1.286(4) Å for the CN bond lengths in the hexachloroferrate(III)[31] and the triformatozincate(II)[32] which are not too far from those calculated, 1.302 and 1.306 Å, in 3-21G and 6-31G basis sets. The experimental NCN angle[32] is 125.6(6)° which corresponds closely to 125.3 and 124.8° calculated with 3-21G and 6-31G basis sets.

Table 3 shows obtained dihedral angles at the amino group of formamidines. For compounds **(1)**–**(4)**, and all protonated molecules, these values are close to 180 and 0°, indicating planarity of the NH_2 group with the rest of the molecule, but in amidines **(5)**–**(8)** with fluorine substitution at the amino nitrogen this group is close to a tetrahedral (*i.e.* non-planar) arrangement. Calculated total energies are given in Table 4.

Results and Discussion

Geometries of the Molecules.—In accordance with classical organic chemistry, the π-electron pair of the CN double bond is conjugated with the lone pair p electrons on the amino nitrogen atom as indicated in equation (4). It was shown[33,34] that the amino nitrogen atom referred to in the literature as the sp^3 nitrogen[35–37] may, at least in some cases, be sp^2 hybridized.



$$R^1-\ddot{N}=\underset{R^3}{\overset{R'}{C}}-\ddot{N}-R^2 \longleftrightarrow R^1-\underset{..}{\overset{-}{N}}-\underset{R^3}{\overset{R'}{C}}=\overset{+}{N}-R^2 \qquad (4)$$

(4a) **(4b)**

It would seem obvious that substituents at both nitrogen atoms have an influence on the extent of conjugation, and that electron-withdrawing substituents at the imino nitrogen atom cause an increase of the conjugation favouring the mesomeric form **(4b)**, whereas at the amino nitrogen atom these cause a decrease of conjugation favouring form **(4a)**. Thus electron-withdrawing substituents at the imino nitrogen should lead to an increase in the length of the formal C=N double bond and decrease the length of the formal C–N single bond[34] and, as known from experimental data,[1–13] decrease the basicity of the amidine. If the acceptor substituent is at the amino nitrogen atom a decrease of conjugation should shorten the C=N double bond and increase the length of the single C–N bond. However it also involves a decrease of amidine basicity, but to a much smaller extent than the same substituent at the imino nitrogen atom, as the observed ρ_{am} value amounts to about one half of that of ρ_{im}.[8]

Table 1. 3-21G calculated bond distances (r_{am} and r_{im} = C–N single and C=N double bonds of amidino group; $\Delta = r_{am} - r_{im}$ = difference of CN bond lengths; X = either H or F).

Compd.	Bond lengths/Å r_{am} $r_{C\text{-}N^1}$	r_{im} $r_{C=N^2}$	$r_{N^1\text{-}H^1}$	$r_{N^1\text{-}X^2}$	$r_{C\text{-}X}$	$r_{N^2\text{-}X^4}$	$r_{N^2\text{-}H^5}$	Δ
(1) HHH	1.364	1.260	0.993	0.997	1.081	1.009	—	0.105
(1) (6-31G)[a]	1.369	1.267	0.990	0.992	1.074	1.008	—	0.102
(2) FHH	1.351	1.271	0.994	0.997	1.070	1.449	—	0.081
(3) HFH	1.349	1.239	0.994	0.994	1.367	1.005	—	0.111
(4) FFH	1.342	1.265	0.995	0.995	1.335	1.435	—	0.077
(5) HHF	1.410	1.245	1.007	1.422	1.079	1.009	—	0.165
(6) FHF	1.391	1.257	1.006	1.421	1.069	1.440	—	0.134
(7) HFF	1.393	1.223	1.005	1.413	1.362	1.006	—	0.170
(8) FFF	1.385	1.250	1.005	1.413	1.332	1.428	—	0.134
(1p) PHHH	1.302	1.302	1.003	1.004	1.071	1.003	1.004	0.000
(1p) (6-31G)[a]	1.306	1.306	0.996	0.998	1.072	0.996	0.998	0.000
(2p) PFHH	1.297	1.301	1.004	1.005	1.071	1.396	1.004	0.004
(3p) PHFH	1.295	1.295	1.006	1.003	1.314	1.006	1.003	0.000
(4p) PFFH	1.292	1.303	1.008	1.004	1.303	1.393	1.004	0.011
(5p) PHHF	1.303	1.291	1.003	1.397	1.071	1.003	1.006	0.011
(6p) PFHF	1.296	1.291	1.005	1.397	1.071	1.393	1.006	0.005
(7p) PHFF	1.303	1.284	1.006	1.393	1.309	1.007	1.006	0.019
(8p) PFFF	1.299	1.292	1.007	1.393	1.299	1.391	1.007	0.007

[a] Calculated values from the 6-31G method for comparison.

As a measure of the conjugation in the amidino group the difference of calculated CN bond distances $\Delta = r_{am} - r_{im}$ as shown in Table 1 may be taken. In the extreme case of the formamidinium cations where bond equalization by conjugation is at a maximum, this value is zero. In the other extreme case, with no conjugation between the two CN bonds, the amino nitrogen atom should be sp^3 hybridized and the bond distances correspond approximately to the C–N single bond in methylamine (experimental r[38] 1.474 Å) and to the isolated C=N double bond in formaldimine (experimental r[39] 1.273 Å) which lead to an experimental estimate of $\Delta_{max} = 0.201$ Å. Calculations in the 3-21G basis set[40] for these compounds yield values of 1.472 and 1.256 Å leading to a 3-21G maximum value of $\Delta_{max} = 0.216$ Å.

This estimation of the CN single bond length may be too large because the carbon atom of the amidine system is not sp^3 but sp^2 hybridized. Zielinski *et al.*[24] calculated for two perpendicularly twisted tetrahedral sp^3 amino groups in formamidine, with the lone pair in the amidine plane, 3-21G bond lengths of 1.434 and 1.435 Å for C–N as well as 1.252 and 1.251 Å for C=N, leading to a more realistic 3-21G estimate for the maximum of a hypothetical unconjugated amidine group Δ_{max} in the range of 0.182 and 0.184 Å. The 3-21G calculated value for planar formamidine as a standard for regular amidine conjugation, from data of Table 1, is 0.105 Å which amounts to about 44% gain in conjugation from the standard of $\Delta_{max} = 0.184$ Å. The experimental Δ for acetamidine[41] with $r_{am} = 1.344$ Å and $r_{im} = 1.298$ Å from X-ray structure determination is 0.046 Å. This is believed to include trends for bond equalization due to H-bridging effects. (For the fluorine substituted compounds studied here, the experimental determinations of molecular geometries are not known, and the calculated geometries strongly depend on applied basis sets, which were studied recently for hydrocarbons.[30] The calculated distances refer to usually experimentally inaccessible r_e values of minima of the energy hypersurface).

Calculated CN distances shown in Table 1 provide support for the above formulated assumptions.

(*a*) An electron-withdrawing fluorine substituent at the imino nitrogen atom causes an increase of the C=N double bond length of 0.011 [**(1)** *vs.* **(2)**] and 0.026 Å [**(3)** *vs.* **(4)**]. It also causes a decrease of the C–N single bond length by 0.013 [**(1)** *vs.* **(2)**] and 0.007 Å [**(3)** *vs.* **(4)**].

(*b*) Fluorine substitution at the amidino carbon in **(3)** leads to a Δ value of 0.111 Å comparable to 0.105 Å of unsubstituted formamidine **(1)**, whereas for those amidines containing fluorine at the imino nitrogen [**(2)** and **(4)**] lower values of 0.081 and 0.077 Å show an increase of conjugation.

(*c*) Fluorine substitution at the amino nitrogen atom leads to non-planarity and causes a decrease of the C=N double bond length of *ca.* 0.015 Å [**(1)** *vs.* **(5)** and **(3)** *vs.* **(7)**], and it causes an increase of the C–N single bond length of *ca.* 0.04 Å [**(1)** *vs.* **(5)** and **(3)** *vs.* **(7)**]. This is an indication of the change of hybridization at amino nitrogen from sp^2 towards sp^3. As a result, the influence on bond lengths due to substitution by a fluorine atom at the amino nitrogen atom is more prominent than that at the imino nitrogen. The Δ values of 0.165 and 0.170 Å for compounds **(5)** and **(7)** clearly indicate that in this case the resonance is considerably decreased.

It should be pointed out that substitution at the amidino carbon atom has no influence on the difference of the bond lengths, however it definitely has an effect on their absolute values. Substitution by fluorine at the amidino carbon atom causes a decrease of both bond lengths by 0.015 Å [**(1)** *vs.* **(3)**] and 0.010 Å [**(2)** *vs.* **(4)**] for the C–N single bond and 0.021 Å [**(1)** *vs.* **(3)**] and 0.024 Å [**(2)** *vs.* **(4)**] for the C=N double bond. This effect is easily understandable by application of Walsh rules:[42] the electron-attracting substituent fluorine causes an increase of p-character in its bond to carbon which leads to an increase of s-character in both bonds to nitrogen and consequent shortening. Another observable effect is that the bond angle [W(NCN)] at carbon opens appreciably to about 127° in **(3)** and **(7)** (see Table 2).

Krygowski *et al.*[43] recently showed that for X-ray solid-state structures of eight free-amidine bases, a shortening of the C–N single bond is related to a lengthening of the C=N double bond as described by equation (5).

$$R_{C=N} = 2.059 - 0.567 \cdot R_{C-N} \qquad (5)$$

Table 2. 3-21G calculated bond angles (X = either H or F).

Compd.	Angle/° H^1–N^1–C W(CNH^1)	X^2–N^2–C W(CNX^2)	N^1–C–N^2 W(NCN)	X^3–C–N^1 W(NCX^3)	X^4–N^2–C W(CNX^4)	H^5–N^2–C W(CNH^5)
(**1**) HHH	122.2	118.5	122.4	112.5	114.7	—
(**1**) (6-31G)[a]	122.1	118.8	122.2	113.6	115.4	—
(**2**) FHH	121.0	120.2	122.0	116.8	105.3	—
(**3**) HFH	120.5	118.9	126.8	109.9	116.8	—
(**4**) FFH	119.8	119.9	122.9	112.8	108.0	—
(**5**) HHF	115.4	110.4	123.8	109.2	115.3	—
(**6**) FHF	116.4	110.1	122.8	114.0	105.6	—
(**7**) HFF	116.1	109.8	127.8	106.7	118.1	—
(**8**) FFF	116.4	109.5	123.9	110.0	107.9	—
(**1p**) PHHH	120.9	123.0	125.3	117.3	120.9	123.0
(**1p**) (6-31G)[a]	120.7	123.2	124.8	117.6	120.7	123.2
(**2p**) PFHH	120.2	123.7	125.3	119.4	114.0	132.9
(**3p**) PHFH	119.6	123.2	127.5	116.3	123.2	127.5
(**4p**) PFFH	119.2	123.8	125.4	117.6	115.0	131.0
(**5p**) PHHF	131.2	115.2	123.5	116.2	121.5	121.1
(**6p**) PFHF	131.1	114.7	123.2	118.6	114.5	130.9
(**7p**) PHFF	130.0	114.2	125.4	115.2	120.3	121.3
(**8p**) PFFF	129.9	113.7	123.4	116.9	114.9	129.5

[a] Calculated values from the 6-31G method for comparison.

Our 3-21G calculated bond lengths together with data of Zielinski[24–26] yield similar results [presented in equation (6)] for 12 data points, with a correlation coefficient $r = 0.945$ and a standard deviation e.s.d. = 0.005. The data points for fluorine substituents on amidino carbon [(**3**) and (**7**)] are, owing to the aforementioned operation of Walsh rules, far off the correlation line and have been omitted.

$$r_{C=N} = 1.930 - 0.488 \cdot r_{C-N} \qquad (6)$$

In the protonated forms of the amidinium cations (**1p**)–(**8p**), which are optimized to planarity, both CN bond distances are nearly equalised and, as an effect of the fluorine substitution, slightly shortened. The Δ values are all *ca.* zero. Closer inspection of Table 1 shows that in the cases of asymmetric substitution with fluorine either in a synperiplanar [(**5p**) and (**7p**)] or antiperiplanar conformation [(**2p**) and (**4p**)], the CN bond bearing the fluorine substituent is elongated and the other one is shortened.

For cationic species, Krygowski's correlations of experimental data[43] indicated that substituents at the amidino carbon atom cause simultaneously an increase or decrease of both CN bond distances, thus a positive slope of a statistically poor linear regression is obtained. Our 3-21G calculated CN bond lengths of protonated amidines (nine data points with inclusion of the calculated CN distance of 1.309 Å for acetamidinium cation[28]) yield the regression equation (7) with $r = 0.479$ and esd = 0.007 which is statistically poor due to too small differentiations of bond lengths, but it does show a positive slope indicating simultaneous variation of bond lengths.

$$r_{C=N} = 0.197 + 0.844 \cdot r_{C-N} \qquad (7)$$

Configuration and Conformation.—Planarity of the molecules (which was not assumed as a constraint by input geometry) is best shown by the dihedral angles H^1–N^1–C–N^2 and X^2–N^1–C–N^2. As is readily seen in Table 3, unsubstituted formamidine and derivatives containing the fluorine substituent at the imino nitrogen or at the amidino carbon atom [(**1**)–(**4**)] have planar conformations.

Fluoro-substituted formamidines (**5**)–(**8**) containing a fluorine substituent at the amino nitrogen atom are calculated to be non-planar. The values of dihedral angles H^1–N^1–C–N^2 of Table 3 are in the range of 131 to 140° and dihedral angles F^2–N^1–C–N^2 are between 11 and 18° for compounds (**5**)–(**8**). These values leave no doubt that the configuration on the amino nitrogen atom in these amidines is close to tetrahedral, and the fluorine atom is slightly off the plane of the amidine group. Further evidence is provided by the values of the valence bond angles H^1–N^1–C (*ca.* 116°), as well as the values of angles F^2–N^1–C (*ca.* 110°), and an inner group angle H^1–N^1–F^2 of *ca.* 116° as shown in Table 2. Observed values indicate that these angles are also affected by fluorine substitution of the amidino carbon atom.

The pairs of protonated compounds (**2p**) and (**5p**), and (**4p**) and (**7p**), are the two possible conformers of *N*-fluoro-substituted formamidinium and fluoroformamidinium cations, respectively. The total energies in Table 4 indicate that in the protonated form the more stable isomer is that with the fluorine substituent at nitrogen in the synperiplanar orientation with respect to the second nitrogen atom.

Basicities of Amidines.—It seems evident that the basicity of amidines expressed as pK_a values are related to corresponding protonation energies, *i.e.* the difference between 3-21G calculated total energies of pairs of protonated and unprotonated amidines which are shown in Table 4. For scaling, calculated basicities relative to ammonia are obtained as energies of the reaction equation (8) of proton transfer

$$\text{am} + NH_4^+ \underset{}{\overset{K}{\rightleftharpoons}} \text{amH}^+ + NH_3 \qquad (8)$$

between ammonia and amidines in the gas phase at 0 K. The corresponding values are shown in the last column of Table 4. If $\Delta E < 0$ the protonated amidine is predicted to be a weaker acid than NH_4^+, or *vice versa* the corresponding amidine is a stronger base than NH_3. These values do not contain any contributions from zero-point vibrations or any entropy effects, but often in solution changes in entropy parallel those in enthalpy.[44]

Table 3. 3-21G calculated valence and dihedral angles at amino nitrogen (X = H or F).

	Angle/°					
Compd.	H^1-N^1-X^2	H^5-N^2-X^4	H^1-N^1-C-N^2 DH1	X^2-N^1-C-N^2 DX2	N^1-C-N^2-X^4 DX4	N^1-C-N^2-H^5 DH5
(1) HHH	119.3	—	179.96	−0.01	—	—
(1) (6-31G)[a]	119.1	—	180.0[b]	0.0[b]	—	—
(2) FHH	118.7	—	179.2	0.6	—	—
(3) HFH	120.6	—	179.4	0.5	—	—
(4) FFH	120.2	—	179.3	0.6	—	—
(5) HHF	105.3	—	130.8	11.6	—	—
(6) FHF	106.2	—	131.4	10.6	—	—
(7) HFF	110.6	—	140.0	17.6	—	—
(8) FFF	108.2	—	138.0	14.9	—	—
(1p) PHHH	116.2	116.2	179.96	−0.01	179.96	−0.01
(1p) (6-31G)[a]	116.1	116.1	180.0[b]	0.0[b]	180.0[b]	0.0[b]
(2p) PFHH	116.1	113.1	179.4	−0.6	179.5	−0.7
(3p) PHFH	117.3	117.3	180.1	−0.1	180.1	−0.1
(4p) PFFH	117.0	114.0	180.0[b]	0.0[b]	180.0[b]	0.0[b]
(5p) PHHF	113.7	117.4	179.5	0.04	179.96	−0.08
(6p) PFHF	114.3	114.7	180.0[b]	0.0[b]	180.0[b]	0.0[b]
(7p) PHFF	115.9	118.3	180.0[b]	0.0[b]	180.0[b]	0.0[b]
(8p) PFFF	116.3	115.6	179.1	0.4	179.5	0.7

[a] Calculated values from the 6-31G method for comparison. [b] Dihedral angles fixed to planarity.

Table 4. 3-21G calculated total energies and protonation energies.

				Protonation energies $(U - P)$		
Compd.	Unprotonated amidines (U) Hartree	Compd.	Protonated amidines (P) Hartree	Hartree	kcal mol^{-1}	Basicities relativetoNH$_3$ ΔE/kcal mol^{-1}
(1) HHH	−148.237 77	**(1p)**	−148.643 51	−0.405 74	−254.6	−28.3
(1) HHH	−148.237 77[a]	**(1p)**	−148.643 51[a]	−0.405 74	−254.6	−28.3
(1) 6-31G[e]	−149.011 46	**(1p)**	−149.410 73	−0.399 27	−250.6	—
(2) FHH	−246.500 86	**(2p)**	−246.850 27	−0.349 41	−219.3	7.1
(3) HFH	−246.580 21	**(3p)**	−246.958 35	−0.378 14	−237.3	−11.0
(4) FFH	−344.823 36	**(4p)**	−345.154 95	−0.331 59	−208.1	18.2
(5) HHF	−246.468 63	**(5p)**	−246.856 13	−0.387 50	−243.2	−16.8
(6) FHF	−344.726 34	**(6p)**	−345.059 46	−0.333 13	−209.0	17.3
(7) HFF	−344.803 16	**(7p)**	−345.162 98	−0.359 82	−225.8	0.5
(8) FFF	−443.041 06	**(8p)**	−443.356 92	−0.315 86	−198.2	28.1
NH_3	−55.872 20[b]	NH_4^+	−56.232 86[b]	−0.360 66	−226.3	0.0
$MeNH_2$	−94.681 70[c]	$MeNH_3^+$	−95.059 34[d]	−0.377 64	−237.0	−10.7
$EtNH_2$	−133.503 68[d]	$EtNH_3^+$	−133.886 40[d]	−0.382 72	−240.2	−13.8
FCH_2NH_2	−193.014 74[d]	$FCH_2NH_3^+$	−193.358 00[d]	−0.343 26	−215.4	10.9
FCH_2– –CH_2NH_2	−231.821 56[d]	FCH_2– –$CH_2NH_3^+$	−232.187 15[d]	−0.375 59	−235.6	−9.4

[a] Values taken from ref. 24 show the high degree of agreement with our calculations. [b] Taken from ref. 40. [c] Taken from ref. 40; ref. 49 obviously contains a misprint of the total energy of methylamine (given: −94.681 07). [d] Taken from ref. 49. [e] Calculated values from the 6-31G method for comparison.

The molecules of Table 4, in order of decreasing basicity are as follows:

(1) > **(5)** > $EtNH_2$ > **(3)** > $MeNH_2$ > $FCH_2CH_2NH_2$ > NH_3 > **(7)** > **(2)** > FCH_2NH_2 > **(6)** > **(4)** > **(8)**

Unsubstituted formamidine **(1)** is the most basic compound of this series. Fluorine substitution in each case reduces the basicity. The smallest effect is shown by substitution at amino nitrogen **(5)** because the protonation occurs far away at the imino nitrogen of the amidino group. Fluorine substitution at the amidino carbon **(3)** leads to a basicity comparable to methylamine. Numerically, this change in basicity from **(1)** to **(3)** by 17.32 kcal mol^{-1} * is close to the calculated change of 21.6 kcal mol^{-1} from methylamine to fluoromethylamine. Two fluorine atoms at both amino-N and carbon [compound **(7)**] leads to basicity in the range of NH_3. Substitution by fluorine at the imino nitrogen [compound **(2)**] shows the most pronounced substituent effect due to the attachment to the centre of protonation. The other compounds show basicities lower than NH_3 decreasing from **(6)** over **(4)** to **(8)**.

Relation of Protonation Energies to Hammett ρ Values.—Figure 2 shows the inter-relation of substituted amidines **(1)**–**(8)** applied for the discussion of mutual interaction of fluorine substituents. As we consider only two substituents hydrogen and fluorine at three different sites of substitution, the difference

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* 1 cal = 4.184 J.

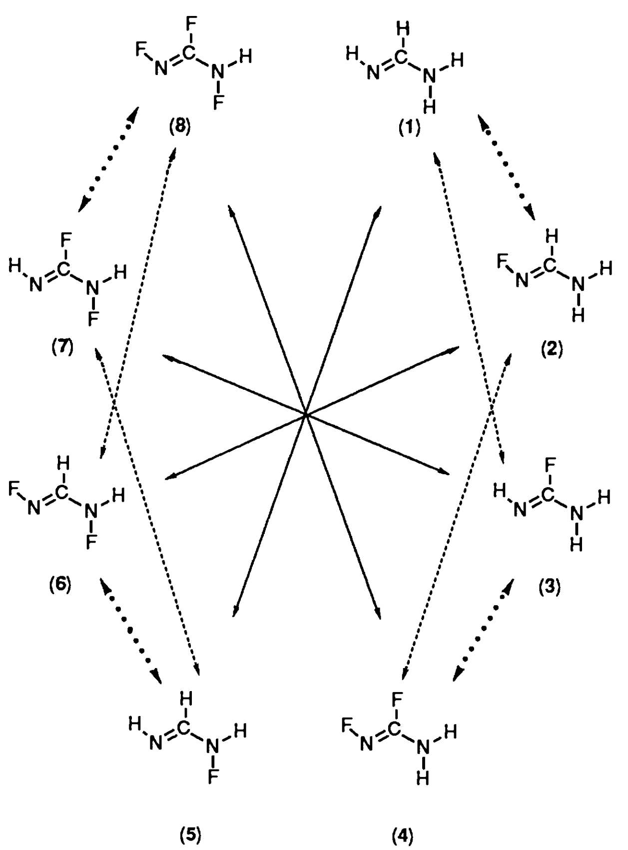

Figure 2. Selection of pairs of molecules for estimation of influences of fluorine substitution at various sites of formamidine on ρ values (. . . . , ρ_{im}; – – – –, ρ_C; ——, ρ_{am}).

Table 5. Influence of substitution by fluorine at various sites of the amidine group to simulate ρ values of the Hammett equation, (1).

Marker subst.	Influence of second subst. at	Based on compds.	Differences in energies of proton transfer kcal mol^{-1}	δ
ρ_{im}	none	(1) *vs.* (2)	35.351	0.0
	N_{am}	(5) *vs.* (6)	34.121	−1.230
	C	(3) *vs.* (4)	29.210	−6.141
	N_{am} + C	(7) *vs.* (8)	27.585	−7.766
ρ_C	none	(1) *vs.* (3)	17.323	0.0
	N_{am}	(5) *vs.* (7)	17.373	0.050
	N_{im}	(2) *vs.* (4)	11.182	−6.141
	N_{im} + N_{am}	(6) *vs.* (8)	10.837	−6.486
ρ_{am}	none	(1) *vs* (5)	11.447	0.0
	C	(3) *vs.* (7)	11.497	0.050
	N_{im}	(2) *vs.* (6)	10.217	−1.230
	N_{im} + C	(4) *vs.* (8)	9.872	−1.575

between σ values of the two substituents is in each case the same. Therefore all calculated differences in protonation energies (or proton transfer energies) should reflect changes in ρ values for a hypothetical two-point Hammett treatment. Numerical values are shown in Table 5. [The experimentally determined ρ values[1,7–13] are obtained for *meta-* and *para-*substituted phenyl substituents which are too large for *ab initio* calculations. However, in our discussion we neglect difficulties with fluorine as a substituent bound directly to two different nitrogens and the carbon atom which may give rise to different σ-acceptor and π-donor contributions, *i.e.* different σ-constants. We also neglect difficulties of basis set balance for fluorine relative to carbon and nitrogen as well as effects due to the change of hybridization to non-planar sp^3 nitrogen in compounds (**4**) to (**8**).]

Considering first the case of substitution at imino-N (ρ_{im}), comparison of compounds (**1**) and (**2**) leads to the most pronounced decrease in basicity of 35.35 kcal mol^{-1}. Additional substitution at amino-N shown by comparison of (**5**) and (**6**) leads to a value of 34.1 kcal mol^{-1}, and a second substitution at amidino-C from comparison of (**3**) and (**4**) yields only 29.2 kcal mol^{-1} for the stabilization energy. The combined action of both fluorine substituents from comparison of (**7**) and (**8**) leads to 27.6 kcal mol^{-1}. The differences of these values are shown in Table 5 as δ values. These show a small effect of −1.2 kcal mol^{-1} for the second substitution at N_{am} and a larger effect of −6.1 kcal mol^{-1} for the second substitution at amidino-C. The combined effect with −7.8 deviates from additivity by 0.4 kcal mol^{-1}. Corresponding values in Table 5 for substitution at the amidino carbon (ρ_C) from comparison of (**1**) and (**3**) yield 17.3 kcal mol^{-1} stabilization energy and substitution at the amino-N (ρ_{am}) from compounds (**1**) *vs.* (**5**) leads to only an 11.4 kcal mol^{-1} decrease of basicity.

The δ values indicate that the strongest influence is exerted if one of the substituents is at the amidino carbon atom and the second at the imino nitrogen atom. This influence is much lower if the substituents are at both nitrogens. However, if one of the substituents is at the amino nitrogen atom and the second at the amidino carbon atom, the δ value is very low and has the opposite sign. This means that a substituent at the amidino carbon causing an increase of the ρ_{im} value may cause a decrease of the ρ_{am} value. This conclusion provides good support for the same assumption drawn on the unexpected relation between substitution at the amidino carbon atom and observed ρ values for symmetrically *N,N'*-disubstituted amidines.[4,5]

The results we obtained are in good agreement with earlier conclusions based on experimental results. Calculated differences between protonation energies are highest for substitution at the imino nitrogen atom, lower for that at the amidino carbon, and lowest for substitution at the amino nitrogen atom. The differences δ between protonation energies indicate that, in accordance with equation (3), as a result of substitution at the second site the observed ρ value is changed by the same value, which depends only on the polar effect of the substituent, and which in the empirical relation [equation (3)] is represented by the term $\mu \cdot \sigma_1 \cdot \sigma_2$.

Tautomerization.—Two pairs of compounds studied here are tautomeric forms; compounds (**2**) and (**5**) are tautomers of *N*-fluoroformamidine whereas (**4**) and (**7**) are tautomers of (*N*-fluoro)fluoroformamidine.

It can be assumed that the differences in total energies between both tautomers are related to equilibrium constants. If there is no difference between total energies (*e.g.* in the case when both tautomeric forms are identical) than the equilibrium constant is equal to unity.

For the tautomers in equation (9) the calculated difference

$$\underset{\textbf{(2)}}{\mathrm{FN{=}CH{=}NH_2}} \rightleftharpoons \underset{\textbf{(5)}}{\mathrm{FNH{-}CH{=}NH}} \qquad (9)$$

in total energies is 20.2 kcal mol^{-1}, and for the tautomers in equation (10) the difference is 12.7 kcal mol^{-1}. These data

$$\underset{\textbf{(4)}}{\mathrm{FN{=}CF{-}NH_2}} \rightleftharpoons \underset{\textbf{(7)}}{\mathrm{FNH{-}CF{=}NH}} \qquad (10)$$

indicate that the tautomeric equilibrium is shifted towards the tautomer containing the electron-withdrawing substituent at the imino nitrogen atom. This is in accord with an earlier conclusion[46] that the less basic tautomer predominates in the equilibrium mixture of tautomers.

In the case of fluoroformamidine the difference between total energies of both tautomers is lower than in the case of formamidine. This provides further support for an earlier assumption, based on the dependence of the ρ-values, that a substituent at the amidino carbon atom exerts an influence on tautomeric equilibrium, causing considerable differences in the values of equilibrium constants for various amidines identically substituted at both nitrogen atoms. Fluoroformamidine is a weaker base than formamidine. Obtained results indicate that in this case the equilibrium constant is closer to unity. Thus the general conclusion may be drawn that the more basic the amidine the larger the difference between the energy of the two tautomeric forms, and in consequence the higher should be the difference between concentrations of tautomers. This may provide an explanation why some authors have claimed[47,48] that amidines exist in one tautomeric form only, as this concerned strongly basic amidines with substituents of considerably different polar effects at the two nitrogen atoms.

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References

1 Part 32. J. Oszczapowicz, W. Krawczyk, and M. Kumińska, unpublished results.
2 H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.
3 L. L. Popova, I. D. Sadekov, and V. I. Minkin, *Reakts. Sposobn. Org. Soedin.* (*Tartu*), 1968, **5**, 651; 1968, **5**, 682; 1969, **6**, 47.
4 B. V. Passet, G. N. Kulbitskii, N. A. Kalashnikova, and T. I. Voropaeva, *Zh. Org. Khim.*, 1972, **8**, 1246.
5 J. Vaes, F. Faubert, and Th. Zeegers-Huyskens, *Can. J. Chem.*, 1975, **53**, 604.
6 M. J. Cook, A. R. Katritzky, and S. Nadji, *J. Chem. Soc., Perkin Trans. 2*, 1976, 211.
7 J. Oszczapowicz, J. Osek, and R. Orlinski, *Pol. J. Chem.*, 1980, **54**, 1191.
8 J. Oszczapowicz, E. Raczynska, and R. Orlinski, *Pol. J. Chem.*, 1981, **55**, 2031.
9 E. Raczyńska, J. Oszczapowicz, and M. Walczak, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1087.
10 J. Oszczapowicz and E. Raczyńska, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1087.
11 J. Oszczapowicz and K. Ciszkowski, *J. Chem. Soc., Perkin Trans. 2*, 1987, 663.
12 J. Oszczapowicz and W.. Krawczyk, *J. Chem. Soc., Perkin Trans. 2*, 1989, 21.
13 J. Oszczapowicz, W. Krawczyk, and P. Łyzwiński, *J. Chem. Soc., Perkin Trans. 2*, 1990, 311.
14 G. Gilli and V. Bertolasi, *J. Am. Chem. Soc.*, 1979, **101**, 7704.
15 I. G. Csizmadia, 'Theory and Practice of MO Calculations on Organic Molecules,' Elsevier, Amsterdam, 1976.
16 P. Carsky and M. Urban, '*ab initio* Calculations. Lecture Notes in Chemistry,' vol. 16, Springer, Berlin, 1980.
17 A. Szabo and N. S. Ostlund, 'Modern Quantum Chemistry. Introduction to Advanced Electron Structure Theory,' MacMillan, New York, 1982.
18 W. J. Hehre, L. Radom, P. v. R. Schleyer, and J. A. Pople, '*ab initio* Molecular Orbital Theory,' Wiley, London, 1986.
19 C. E. Dykstra, '*ab initio* Calculations of the Structures and Properties of Molecules,' Elsevier, Amsterdam, 1988.
20 B. A. Murtagh and R. W. H. Sargent, *Comput. J.*, 1970, **13**, 185.
21 J. S. Binkley, M. J. Frisch, D. J. DeFrees, K. Raghavachari, R. A. Whiteside, H. B. Schlegel, E. M. Fluder, and J. A. Pople, 'GAUSSIAN 82,' Carnegie–Mellon Quantum Chemistry Publishing Unit, Pittsburgh PA, 1984.
22 J. S. Binkley, J. A. Pople, and W. J. Hehre, *J. Am. Chem. Soc.*, 1980, **102**, 939.
23 Calculations at the 'Zentrum für Datenverarbeitung der Universität Tübingen.'
24 T. J. Zielinski, M. R. Peterson, I. G. Csizmadia, and R. Rein, *J. Comput. Chem.*, 1982, **3**, 62.
25 T. J. Zielinski, R. A. Poirer, M. R. Peterson, and I. G. Csizmadia, *J. Comput. Chem.*, 1983, **4**, 419.
26 T. J. Zielinski and R. A. Poirer, *J. Comput. Chem.*, 1984, **5**, 466.
27 W. J. Hehre, R. F. Stewart, and J. A. Pople, *J. Chem. Phys.*, 1969, **51**, 2657.
28 G. Ritter, unpublished work.
29 W. J. Hehere, R. Ditchfield, and J. A. Pople, *J. Chem. Phys.*, 1972, **56**, 2257.
30 G. Häfelinger, C. U. Regelmann, T. M. Krygowski, and K. Wozniak, *J. Comput. Chem.*, 1989, **10**, 329.
31 U. Demant, E. Conradi, U. Müller, and K. Dehnicke, *Z. Naturforsch., Teil B*, 1985, **40**, 443.
32 R. Norrestam, *Acta Crystallogr., Sect. C*, 1984, **40**, 297.
33 R. Mierzecki, J. Oszczapowicz, and G. Kozakowski, *Pol. J. Chem.*, 1979, **53**, 1139.
34 J. W. Krajewski, Z. Urbanzcyk-Lipkowska, P. Gluzinski, I. Busko-Oszczapowicz, J. Oszczapowicz, J. Bleidelis, and A. Kemme, *Pol. J. Chem.*, 1981, **55**, 1015.
35 R. Mecke and W. Kutzelnigg, *Spectrochim. Acta*, 1960, **16**, 1216.
36 Z. B. Kiro, Yu. Terenin, L. N. Nikolenko, and B. I. Stepanov, *Zh. Org. Khim.*, 1972, **8**, 2573.
37 H. Goncalves and A. Secches, *Bull. Soc. Chim. Fr.*, 1970, 2589.
38 P. Pulay and F. Török, *J. Mol. Struct.*, 1975, **29**, 239.
39 K. Pearson and F. J. Lovas, *J. Chem. Phys.*, 1977, **66**, 4149.
40 R. A. Whiteside, M. J. Frisch, and J. A. Pople, Carnegie–Mellon Quantum Chemistry Archive, Department of Chemistry, Carnegie–Mellon University, Pittsburgh, 3rd edn., 1983.
41 R. Norrestam, S. Mertz, and I. Crossland, *Acta Crystallogr., Sect. C*, 1983, **39**, 1554.
42 H. A. Bent, *Chem. Rev.*, 1961, **61**, 275; T. M. Krygowski, *J. Chem. Res.* (*S*), 1984, 234.
43 R. Anulewicz, T. M. Krygowski, and B. Pniewska, *J. Cryst. Spectrosc. Res.*, 1987, **17**, 661; T. M. Krygowski, R. Anulewicz, and S. Grabowski, *ibid.*, in the press.
44 O. Exner, *Prog. Phys. Org. Chem.*, 1973, **10**, 411.
45 J. Oszczapowicz, and K. Ciszkowski, *J. Chem. Res.*, in the press.
46 E. Raczyńska and J. Oszczapowicz, *Tetrahedron*, 1985, **41**, 5175.
47 J. C. Grivas and A. Taurins, *Can. J. Chem.*, 1959, **37**, 795.
48 J. C. Grivas and A. Taurins, *Can. J. Chem.*, 1961, **37**, 414.
49 T. Silvestro, R. D. Topsom, C. W. Bock, and R. W. Taft, *J. Mol. Struct.* (*Theochem.*), 1989, **184**, 33.

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