

ELECTROSTATIC EFFECTS ON IONIZATION EQUILIBRIA: AN MNDO STUDY OF PROTON AND HYDROGEN TRANSFER REACTIONS OF 4-FLUOROBUTYLAMINE

Zdeněk FRIEDL^a and Stanislav BÖHM^b

^a Department of Organic Chemistry,
Slovak Technical University, 812 37 Bratislava and

^b Department of Organic Chemistry,
Prague Institute of Chemical Technology, 166 28 Prague 6

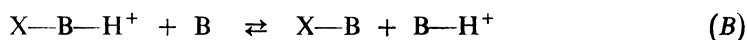
Received February 2, 1989

Accepted April 10, 1989

Dedicated to Professor Otto Exner on the occasion of his 65th birthday.

The relative enthalpies of proton transfer $\delta \Delta H^\circ$ and homolytic bond strengths $\delta DH^\circ(\text{B-H}^+)$ were calculated by the MNDO method for the *sp* and *ap* conformers of 4-fluorobutylamine. The data obtained, along with the experimental gas phase basicities, are compared with the values predicted by the electrostatic theory. It is shown that the substituent polar effects F_D on the basicities of amines are predominantly due to interactions in their protonated forms (X-B-H^+) and/or radical-cations ($\text{X-B}^{+\cdot}$), those in the neutral species (X-B) playing a minor part. A contribution, which is considerably more significant in the *sp* conformer than in the *ap* conformer, arises probably also from substituent effects on the homolytic bond strength $DH^\circ(\text{B-H}^+)$.

Papers in this series¹⁻⁴ have been concerned with electrostatic effects on ionization equilibria, with stress on testing the assumptions and approximations of the theory. For ionization equilibria in the gas phase⁵⁻⁷, Smallwood's formulation of the electrostatic theory⁸ seems to be more appropriate than the generally adopted Kirkwood-Westheimer theory^{9,10}. The reason for this is the vanishing of all solvation terms while the effect of the dipolar substituent X on the isodesmic reactions (A) and (B),



is regarded as the change in the gas phase reaction enthalpy $\delta \Delta H^\circ$.

Provided that the effective relative permittivity ϵ_{eff} is unity in the gas phase, the electrostatic field effect F_D on the equilibria (A) and (B) is expressed by the equation

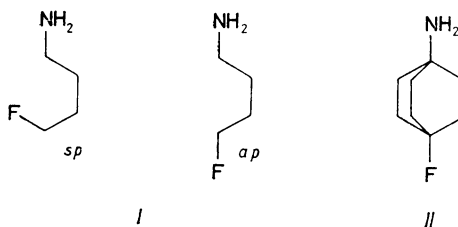
$$\delta \Delta H^\circ \approx \delta \Delta E^\circ = Ze\mu \cos \Theta / r^2 \epsilon_{\text{eff}} (4\pi\epsilon_0), \quad (\text{I})$$

where Z is the charge valence (± 1), e is the charge of the electron, μ is the dipole moment of substituent X , r is the distance between the charge Ze and the centre of the dipole moment μ , and Θ is the angle formed by the vectors r and μ .

Equation (1) implies that the remaining substituent effects have been eliminated by a suitable choice of the system (in particular, that no resonance R_π or steric S_D effects operate). However, previously¹⁻⁴ we pointed to the fact that two fundamental assumptions of the theory, viz. the identity of the homolytic bond strengths in the substituted and unsubstituted acid (base) and the concept of the substituent effect as a direct field effect on the ionizable proton in the neutral acid $X-A-H$ or protonated base $X-B-H^+$, had not been adequately tested.

So far, limited experimental gas phase data of the substituent effects on $DH^0(A-H)$ or $DH^0(B-H^+)$ are available¹¹⁻¹³, and these fail to offer the $\cos \Theta/r^2$ dependence of the F_D effect. Also, few papers discuss simultaneously the alternative action of the F_D effect both in the neutral acids and bases¹⁴⁻¹⁶ ($X-A-H$ and $X-B$) and in the corresponding electrically charged ions^{4,17-19} ($X-A^-$ and $X-B-H^+$).

Previously⁴ we tested the two assumptions of the electrostatic theory on the ionization equilibria of the conformers of 5-fluoropentanoic acid. For the same reasons, and also with a view to comparing the ionization equilibria (A) and (B), in this work we test the electrostatic theory further at the semiempirical MNDO level. We have chosen the *sp* and *ap* conformers of 4-fluorobutylamine (structure I)



as model substances enabling us to examine the F_D effect of the C-F dipole with respect to the different geometrical parameters r and Θ in Eq. (1). The MNDO and electrostatic calculations could be compared with experimental data for the structurally related 4-fluorobicyclo[2.2.2]octyl-1-amine (4-F-BCA, structure II), whose gas phase basicity has been measured recently²⁰.

CALCULATIONS AND RESULTS

The quantum chemical calculations were performed at the MNDO level²¹ employing the MNDO and MNDOC computer programs^{22,23}. The standard geometrical parameters²⁴ were used as the starting values for the overall geometry optimization.

During the latter, the planar geometry of the carbon chain was maintained for the two conformers of *I*, and the doublet multiplicity was used for the calculation of the cation-radical.

The calculated enthalpies of formation ΔH_f° for all the above $R-CH_2CH_2CH_2CH_2-X$ structures are given in Table I. The total atomic charges at the nitrogen atoms q_N and the sums of q_H at the hydrogen atoms in the NH_2 , NH_3^+ and $NH_2^{+\bullet}$ groups are given in Table II.

TABLE I

MNDO calculated enthalpies of formation ΔH_f° (kJ mol⁻¹) of substances $R-CH_2CH_2CH_2CH_2-X$ in Eq. (C)

R	X = H		X = F	
	<i>sp</i>	<i>ap</i>	<i>sp</i>	<i>ap</i>
NH ₂	-65.657	-75.670	-238.591	-262.764
NH ₃ ⁺	630.232	619.988	456.979	451.469
NH ₂ ^{+\bullet}	842.167	833.546	662.543	666.541
H	-95.714	-105.553	-267.997	-293.346

TABLE II

MNDO calculated total charges at the nitrogen atoms q_N and sums of total charges at the hydrogen atoms of group R, q_H (both in electrons) of the substances $R-CH_2CH_2CH_2CH_2-X$ in the *sp* (upper rows) and *ap* (lower rows) conformations

R	q_N		q_H	
	X = H	X = F	X = H	X = F
NH ₂	-0.28140	-0.28317	0.18929	0.18980
	-0.28122	-0.27987	0.18900	0.19418
NH ₃ ⁺	0.01128	0.00962	0.64985	0.64842
	0.01089	0.01201	0.65017	0.65655
NH ₂ ^{+\bullet}	-0.04179	-0.04264	0.49304	0.49267
	-0.04560	-0.03988	0.49227	0.49764

Electrostatic Calculations

The relative electrostatic energies $\delta \Delta E^\circ$ were calculated by means of Eq. (I), for which the relative permittivity ϵ_{eff} was put equal to unity and the dipole moment μ was approximated by the difference $\mu_X - \mu_H$. The standard bond moments of $1.0 \cdot 10^{-30}$ and $4.67 \cdot 10^{-30}$ C m were used for the C—H and C—F bonds, respectively²⁵. The geometrical parameters r and θ were calculated from the MNDO optimized atomic coordinates as well as from the standard geometrical parameters²⁴. The nitrogen atom was regarded as the centre of the negative charge in both cases. For the positive charge, two alternatives were considered: in the one, the centre of the positive charge was assumed to lie in the centre of the atomic coordinates of the NH_3^+ ammonium group protons (40 pm far from the nitrogen atom in the extended direction of the C—N bond), whereas in the other²⁶, based on Mulliken's population analysis of the STO-3G calculation of the methylammonium ion, the positive centre was located 20 pm far from the nitrogen atom in the N—C bond direction.

The electrostatic energies $\delta \Delta E^\circ$ for reaction (B) were calculated by means of Eq. (I) using the charge valence $Z = +1$, whereas for the relative electron affinities $\delta \Delta E^\circ(\text{EA})$, the charge valence $Z = -1$ was adopted. This implies that the $\delta \Delta E^\circ$ values express the energy change accompanying the removal of the proton from a molecule of the protonated base X-B-H^+ , whereas the $\delta \Delta E^\circ(\text{EA})$ values predict the energy of electron removal from the electrostatic field for the substituent dipole in the neutral molecule of the base X—B.

The relative electrostatic energies $\delta \Delta E^\circ$ and electron affinities $\delta \Delta E^\circ(\text{EA})$ calculated based on the optimized MNDO and standard geometrical parameters are given in Table III.

DISCUSSION

The applicability of the semiempirical MNDO method to the study of substituent effects²⁷⁻²⁹ has been tested before⁴ on the structurally related *ap* 4-F-pentanoic acid and 4-F-bicyclo[2.2.2]octane-1-carboxylic acid (4-F-BCO). The MNDO and the more recently published^{30,31} *ab initio* STO-3G ionization energies are compared with the experimental value for 4-F-BCO (ref.⁷) in Table IV. The MNDO method can be claimed to offer substituent effect estimates that are at least as good as those obtained from STO-3G calculations in the minimal basis set and without geometry optimization.

From this point of view, the consistency of the calculated and experimental data in Table V can be regarded as satisfactory.

The good agreement of the $\delta \Delta H^\circ$ value of the *ap* conformer of I with the *ab initio* STO-3G calculation³² and, in particular, with the experimental $\delta \Delta G^\circ$ energy of 4-F-BCA (structure II) indicates that the MNDO method describes adequately also

the F_D effect⁴ on the gas phase basicity ($-18.6 \text{ kJ mol}^{-1}$ vs $-24.3 \text{ kJ mol}^{-1}$; $\delta \Delta S^\circ \approx 0$, refs^{5,33}).

The electrostatic theory and MNDO calculations are mutually compared in Tables III and V. Now the question arises as to whether the $\delta \Delta E^\circ(\text{EA})$ energies are a more appropriate approximation of the gas phase basicities than the classical $\delta \Delta E^\circ$ values^{6,8,14}. The data in Tables III and V demonstrate that both the $\delta \Delta E^\circ$ and $\delta \Delta E^\circ(\text{EA})$ energies predict correctly the $\delta \Delta H^\circ$ value of the *ap* conformer of *I* but they overestimate the reverse substituent effect in the *sp* conformer by an order of magnitude (6.8 kJ mol^{-1} vs 0.3 kJ mol^{-1}). No improvement is achieved by using

TABLE III

Relative electrostatic energies $\delta \Delta E^\circ$ and electron affinities $\delta \Delta E^\circ(\text{EA})$ (kJ mol^{-1}) of 4-F-butylamine *I*

Conformation	$\delta \Delta E^\circ$		$\delta \Delta E^\circ(\text{EA})$	
	<i>a</i>	<i>b</i>	<i>a</i>	<i>b</i>
	MNDO	Std.	MNDO	Std.
<i>sp</i>	6.8	22.5	-6.8	-27.6
	8.7 ^c	14.6 ^c	—	—
<i>ap</i>	-15.4	-18.8	18.3	22.2
	-19.4 ^c	-24.2 ^c	—	—

^a Geometrical parameters Θ and r calculated from MNDO optimized atomic coordinates; ^b values of Θ and r calculated from standard geometrical parameters²⁴; ^c positive charge located 20 pm far from the nitrogen atom in the N-C bond direction²⁶.

TABLE IV

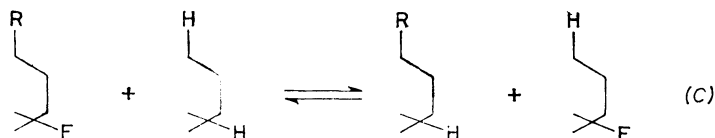
Comparison of MNDO and STO-3G relative energies $\delta \Delta H^\circ$ (kJ mol^{-1}) for reaction (A)

Acid	$\delta \Delta H^\circ$		
	MNDO ^a	STO-3G ^b	Experimental
5-F-Pentanoic (<i>ap</i>)	-16.2	-13.8	—
4-F-BCO	-16.7	-13.3, -14.6 ^c	-23.4 ^d

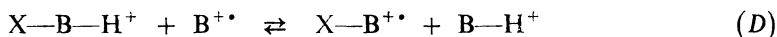
^a Overall geometry optimization⁴; ^b in the minimal basis set and without geometry optimization³⁰; ^c ref.³¹; ^d $\delta \Delta G^\circ$ value⁷.

the alternative location of the positive charge as outlined above, and quite unreasonable values are obtained when using the standard geometries. In this situation, the $\delta \Delta H^\circ$ energy of the *ap* conformer of *I* is most reliably approximated by the $\delta \Delta E^\circ(\text{EA})$ MNDO energy (18.3 kJ mol^{-1}).

For examining this problem, three types of isodesmic reaction (C),



where *R* is an ammonium group NH_3^+ , an amine group NH_2 or a cation-radical $\text{NH}_2^{+\bullet}$, were considered for both the *sp* and *ap* conformers of *I*. The substituent effect on the basicity $\delta \Delta H^\circ$ is given by the change in the energy of reaction (B), which is identical with the difference in the $\delta \Delta H^\circ_c$ energies in reaction (C) for the NH_3^+ and NH_2 groups. Similarly the substituent effects on the homolytic bond strength $\delta DH^\circ(\text{B-H}^\bullet)$ are given by the change in the energy of reaction (D),



while reaction (E) expresses the substituent effects on the electron affinity of the cation-radical $\delta \text{EA}(\text{B}^{+\bullet})$:

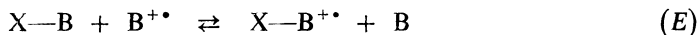


TABLE V

Relative energies $\delta \Delta H^\circ$ (kJ mol^{-1}) for reaction (B) and total atomic charges of 4-F-butylamine (I) for $\text{R} = \text{NH}_3^+$, NH_2 and $\text{NH}_2^{+\bullet}$, respectively

Amine	$\delta \Delta H^\circ$		$\delta q_{\text{N}}^a \cdot 10^{-3}, e$			$\delta q_{\text{H}}^b \cdot 10^{-3}, e$		
	MNDO	STO-3G	NH_3^+	NH_2	$\text{NH}_2^{+\bullet}$	NH_3^+	NH_2	$\text{NH}_2^{+\bullet}$
<i>Isp</i>	0.3	—	-1.66	-1.77	-0.85	-0.48	0.26	-0.18
<i>Iap</i>	-18.6	-14.8 ^c	1.12	1.35	5.72	2.13	2.59	2.68
4-F-BCA	—	-15.9 ^{c,d}	—	—	—	—	—	—

^a $q_{\text{N}}(\text{X}) - q_{\text{N}}(\text{H})$ difference; ^b $[q_{\text{H}}(\text{X}) - q_{\text{H}}(\text{H})]/n$ difference ($n = 3, 2$ and 2 , respectively); ^c in the minimal basis set and without geometry optimization^{26,32}; ^d experimental $\delta \Delta G^\circ$ value is $-24.3 \text{ kJ mol}^{-1}$ (ref.²⁰).

The substituent effects on the gas phase basicity then are given, with regard to reactions (B), (D) and (E), by the equation

$$\delta \Delta H^\circ = \delta DH^\circ(\text{B-H}^+) - \delta EA(\text{B}^{+\bullet}). \quad (2)$$

The MNDO calculated $\delta \Delta H^\circ_C$ energies, the homolytic bond strengths $\delta DH^\circ(\text{B-H}^+)$ and the electron affinities $\delta EA(\text{B}^{+\bullet})$ are given in Table VI. Comparison of the data demonstrates that the substituent effect on $\delta \Delta H^\circ$ is mainly due to interactions in the molecules carrying positive charges^{4,6,15-19}, hence, in the cations X-B-H^+ and cation-radicals $\text{X-B}^{+\bullet}$, while the neutral bases X-B contribute a minor part. The high difference in the $\delta \Delta H^\circ_C$ energies for the *sp* conformer of *I* for $\text{R} = \text{NH}_3^+$ (1.0 kJ mol^{-1}) vs $\text{R} = \text{NH}_2^+$ (7.3 kJ mol^{-1}) as compared to the *ap* conformer cannot be explained satisfactorily in terms of the electrostatic theory. A possible cause, however, may be in a failure of the MNDO method itself, viz. in an overestimation of the short-range interaction of the C-F dipole in the *sp* cation-radical.

Since experimental $\delta \Delta H^\circ$ and $\delta EA(\text{B}^{+\bullet})$ data, which might enable the $\delta DH^\circ(\text{B-H}^+)$ energies to be obtained³⁵, are unavailable, we calculated the $\delta DH^\circ(\text{B-H}^+)$ energies of reaction (D) at the MNDO level⁴; the values are given in Tables III, V and VI. The electron affinities $\delta EA(\text{B}^{+\bullet})$ are consistent with the dominant role of the substituent effect both in the *sp* and *ap* cation-radicals of *I*, whereas the relative homolytic bond strengths $\delta DH^\circ(\text{B-H}^+)$ for the two conformers differ considerably (-6.4 and 1.5 kJ mol^{-1} , respectively) (Table VI). As mentioned above, the reliability of the MNDO method for the calculation of ΔH°_f of the cation-radicals $\text{X-B}^{+\bullet}$ may not be very high. An alternative approach to the calculation of the electron affinities consists of the use of the MNDO ionization potentials (IP), i.e. the negative HOMO energies of the neutral bases X-B . The

TABLE VI

MNDO calculated energies $\delta \Delta H^\circ_C$ for reaction (C), relative homolytic bond strengths $\delta DH^\circ(\text{B-H}^+)$ for reaction (D) and relative electron affinities $\delta EA(\text{B}^{+\bullet})$ for reaction (E) (in kJ mol^{-1})

R	$\delta \Delta H^\circ_C$		$\delta DH^\circ(\text{B-H}^+)$		$\delta EA(\text{B}^{+\bullet})$	
	<i>sp</i>	<i>ap</i>	<i>sp</i>	<i>ap</i>	<i>sp</i>	<i>ap</i>
NH_3^+	1.0	-19.3	-6.4	1.5	-6.7	20.1
NH_2	0.7	-0.7	-2.4 ^a	1.2 ^a	-2.7 ^b	19.8 ^b
NH_2^+	7.3	-20.8	-	-	-	-

^a Calculated from Eq. (2); ^b calculated as $\text{IP}(\text{X-B}) - \text{IP}(\text{B})$.

$\delta EA(B^{+*})$ values calculated as

$$\delta EA(B^{+*}) = \delta IP = IP(B-X) - IP(B) \quad (3)$$

can be considered a more reliable estimate of the substituent effects in the case treated. The δIP values and the $\delta DH^{\circ}(B-H^+)$ energies calculated from Eq. (2) are given in Table VI. The more pronounced decrease in $\delta DH^{\circ}(B-H^+)$ for the *sp* conformer (-2.4 kJ mol^{-1}) is made up for by the $\delta EA(B^{+*})$ energy, so that the resulting $\delta \Delta H^{\circ}$ value is mere 0.3 kJ mol^{-1} (Table V). Irrespective of the absolute values of $\delta DH^{\circ}(B-H^+)$, the general trend of the F_D effect on reaction (D) is well-understandable: the lower the polarity of the N—H bond, the lower the homolytic bond strength. In Table V, this dependence is presented in a more illustrative way in terms of the relative atomic charges δq_H , documenting a higher increase in the electron density at the ammonium group of the *sp* conformer of I.

In the classical electrostatic theory the relative homolytic bond strengths are either put equal to zero^{1,8} or neglected altogether^{9,10,34}. If, however, the ionization reactions (A) and (B) are treated in solution rather than in the gas phase, the magnitude of $\delta DH^{\circ}(B-H^+)$ becomes more significant since the solvent effect will bring about lowering particularly in the $\delta EA(B^{+*})$ term in Eq. (2), whereupon the $\delta \Delta H^{\circ}$ value will decrease. For instance, the solvent attenuation factor⁶ $SAF(aq) = \rho_F(\text{gas})/\rho_F(aq)$ for the methylammonium, 4-X-quinuclidinium and 4-X-pyridinium cations attains values⁶ about 2.5.

In summary, it can be concluded that for the acidities (A) studied previously⁴ as well as for the basicities (B) discussed in this work, the homolytic bond strengths may not compensate and can affect proton transfer reactions both in the gas and liquid phases.

The authors wish to thank Professor Robert W. Taft (University of California, Irvine) for providing them with gas phase basicity data of 4-X-bicyclo[2.2.2]octyl-1-amines, and Professor William F. Reynolds (University of Toronto) for discussions stimulating the orientation of this work.

REFERENCES

1. Exner O., Friedl Z.: Collect. Czech. Chem. Commun. **43**, 3227 (1978).
2. Friedl Z., Hapala J., Exner O.: Collect. Czech. Chem. Commun. **44**, 2928 (1979).
3. Kalfus K., Friedl Z., Exner O.: Collect. Czech. Chem. Commun. **49**, 179 (1984).
4. Friedl Z.: Can. J. Chem. **63**, 1068 (1985).
5. Kebarle P.: Annu. Rev. Phys. Chem. **28**, 445 (1977).
6. Taft R. W.: Prog. Phys. Org. Chem. **14**, 247 (1983).
7. Taft R. W., Topsom R. D.: Prog. Phys. Org. Chem. **16**, 1 (1987).
8. Smallwood H. M.: J. Am. Chem. Soc. **54**, 3048 (1932).
9. Kirkwood J. G., Westheimer F. H.: J. Chem. Phys. **6**, 506 (1938).

10. Westheimer F. H., Kirkwood J. G.: *J. Chem. Phys.* **6**, 513 (1938).
11. Staley R. H., Taagepera M., Henderson W. G., Koppel I., Beauchamp J. L., Taft R. W.: *J. Am. Chem. Soc.* **99**, 326 (1977).
12. Cumming J. B., Kebarle P.: *Can. J. Chem.* **56**, 1 (1978).
13. Bartmess J. E., McIver R. T. in: *Gas Phase Ion Chemistry* (M. T. Bowers, Ed.), Vol. 2, p. 87. Academic Press, New York 1979.
14. Ehrenson S.: *Prog. Phys. Org. Chem.* **2**, 195 (1964).
15. Siggel M. R., Thomas T. D.: *J. Am. Chem. Soc.* **108**, 4360 (1986).
16. Thomas T. D., Carroll T. X., Siggel M. R. F.: *J. Org. Chem.* **53**, 1812 (1988).
17. Pross A., Radom L., Taft R. W.: *J. Org. Chem.* **45**, 818 (1980).
18. Yoder C. S., Yoder C. H.: *J. Am. Chem. Soc.* **102**, 1245 (1980).
19. Exner O.: *J. Org. Chem.* **53**, 1810 (1988).
20. Koppel I., Mishima M., Taft R. W.: Unpublished results.
21. Dewar M. J. S., Thiel W.: *J. Am. Chem. Soc.* **99**, 4899 (1977); **99**, 4907 (1977).
22. Thiel W.: *QCPE 11*, 353 (1978).
23. Thiel W.: *QCPE 15*, 438 (1983).
24. Pople J. A., Gordon M.: *J. Am. Chem. Soc.* **89**, 4253 (1967).
25. Exner O. in: *Dipole Moments in Organic Chemistry*, p. 33. Thieme, Stuttgart 1975.
26. Topsom R. D.: *J. Am. Chem. Soc.* **103**, 39 (1981).
27. Dewar M. J. S.: *J. Mol. Struct.* **100**, 41 (1983).
28. DeBruijn S.: *Int. J. Quant. Chem.* **25**, 367 (1984).
29. Topsom R. D.: *Prog. Phys. Org. Chem.* **16**, 125 (1987).
30. Marriott S., Topsom R. D.: *J. Am. Chem. Soc.* **107**, 2253 (1985).
31. Inamoto N., Masuda S., Niwa J.: *Bull. Chem. Soc. Jpn.* **58**, 158 (1985).
32. Topsom R. D.: *Tetrahedron Lett.* **21**, 403 (1980).
33. Aue D. H., Bowers M. T. in: *Gas Phase Ion Chemistry* (M. T. Bowers, Ed.), Vol. 2, p. 1. Academic Press, New York 1979.
34. Reynolds W. F.: *Prog. Phys. Org. Chem.* **14**, 165 (1983).
35. Janousek B. K., Brauman J. I. in: *Gas Phase Ion Chemistry* (M. T. Bowers, Ed.), Vol. 2, p. 53. Academic Press, New York 1979.

Translated by P. Adámek.