ELECTROSTATIC EFFECTS IN IONIZATION EQUILIBRIA: AN AM1 STUDY OF REVERSED SUBSTITUENT EFFECT IN 5-FLUOROBICYCLO[3.3.3]UNDECANE-1-CARBOXYLIC ACID

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Relative proton transfer enthalpies $\delta\ \Delta H^0$ of *sp* and *ap* conformers of 5-fluorobicyclo[3.3.3]undecane-1-carboxylic acid have been calculated by the AM1 method and the results were compared with the prediction of the electrostatic theory. It is shown that the great reversed substituent effect in the *sp* conformer ($\delta\ \Delta H^0 = 32.1$ kJ mol^{-1}) is substantially overestimated largely due to sterical Baeyer strain and non-bonded interactions.

The most promising approach to test the electrostatic field effect on the proton transfer reaction (*A*)

$$\text{X–A–H} \quad + \quad \text{A}^- \rightleftharpoons \quad \text{X–A}^- \quad + \quad \text{A–H} \qquad (A)$$

focused an attention on the substituent angle θ involved in Eq. (*1*)

$$\delta\ \Delta H^0 \approx \delta\ \Delta E^0 = Z\,\boldsymbol{e}\,\mu\cos\theta/\boldsymbol{r}^2\varepsilon_{\mathrm{eff}}(4\pi\varepsilon_0)\ , \qquad (1)$$

but not in any equation of the alternative topological “sigma-inductive” theory[1,2]. Equation (*1*) holds for a dipolar substituent with the point dipole μ in the distance $\boldsymbol{r}$ from the charged reaction center of charge valence Z (+1), and θ is the angle of the two vectors μ and $\boldsymbol{r}$.

Apparently it would be sufficient to synthesize two acids with the same topology but rather different geometry so that the electron-withdrawing substituent could generate a dipole that would oppose the ionization (reversed field effect).

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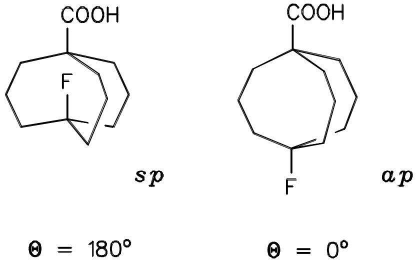
The use of conformers of 5-substituted bicyclo[3.3.3]undecane-1-carboxylic acid (5-X–BCU) was originally proposed by Roberts and Carboni[3] but, in accordance with the expected barrier to their syntheses, the conformers of suggested 5-Cl–BCU were never prepared.

For the reasons mentioned above, we decided to investigate the "ideal" 5-X–BCU model system at least at an AM1 semiempirical quantum chemical level. The *sp* and *ap* conformers of 5-fluorobicyclo[3.3.3]undecane-1-carboxylic acid (*I*) were chosen while the applicability of AM1 method for the isodesmic proton transfer reactions has been established recently[4].

CALCULATIONS AND RESULTS

The quantum chemical calculations were performed at the semiempirical AM1 level[5] by using the MOPAC (ref.[6]) program. The standard geometric parameters[7] were used as a starting value for the restricted geometry optimization assuming the C_{3v} symmetry of bicyclic skeleton of the basic hydrocarbons (R, X = H, see Table I). From these starting geometries all the remaining structures were calculated with the total geometry optimization. The calculated enthalpies of formation $\delta\,\Delta H_f^0$ for all 1-R-5-X-bicyclo[3.3.3]undecanes are given in Table I and selected interatomic distances and bond angles are given in Table II.



I

The AM1 relative proton transfer enthalpies $\delta\,\Delta H^0$ for reaction (*A*) and the interaction energies for isodesmic reaction (*B*) $\delta\,\Delta H_B^0$, where R is carboxyl COOH and/or carboxylate COO^- group, are given in Table III.

The relative electrostatic energies $\delta\,\Delta E^0$ were calculated[1] from Eq. (*1*) using $\varepsilon_{ef} = 1$ and introducing the difference $\mu_X - \mu_H$ for μ. Standard bond moments[8] were used (in 10^{-30} C m): C–H, −1.0 and C–F, 4.67, respectively.

The geometry parameters $\boldsymbol{r}$ and $\cos\theta$ were calculated from the AM1 optimized atomic coordinates considering an orientation of the $\boldsymbol{r}$ vector from the carboxyl proton to the point dipole $C\rightarrow F$. The negative charge on the carboxylate anion was localized in the middle of the linkage of the carboxylate oxygens. The electrostatic energies

$\delta\,\Delta E^0$ were calculated taking charge valence $Z = +1$, while in the case of relative electron affinities $\delta\,\Delta E^0$(EA) the charge valence was taken as $Z = -1$. The relative electrostatic energies $\delta\,\Delta E^0$ and electron affinities $\delta\,\Delta E^0$(EA) are given in Table III.

TABLE I
AM1 calculated enthalpies of formation ΔH_f^0 the 1-R-substituted 5-X-bicyclo[3.3.3]undecane conformers shown in Eq. (*B*) (in kJ mol^{-1})

X	Conformation	R		
		COOH	COO^-	H
H	*sp*	–324.131	–401.919	26.466
	ap	–523.548	–592.618	–172.188
F	*sp*	186.342	140.611	556.135
	ap	–777.316	–859.825	–427.230

TABLE II
Selected AM1 interatomic distances and bond angles in conformers of 5-F–BCU (*I*)

Atoms	*I sp*	*I ap*	4-F–BCO[a]
	Interatomic distance, pm		
C1–C2	164.4	153.2	156.8
C2–C3	160.7	151.1	154.8
C1–F	189.1	479.2	400.7
	Bond angle, °		
C1–C2–C3	125.7	118.6	110.3
C2–C3–C4	127.0	118.7	110.6

[a] MNDO optimized geometry parameters for 4-F-bicyclo[2.2.2]octane-1-carboxylic acid (ref.[9]).

DISCUSSION

Table III compares the AM1 calculated proton transfer enthalpies $\delta\,\Delta H^0$ with electrostatic energies $\delta\,\Delta E^0$, electron affinities $\delta\,\Delta E^0$(EA), and interaction energies $\delta\,\Delta H^0_\mathrm{B}$ of the isodesmic reaction (*B*)

$$\text{R–BCU–X} \quad + \quad \text{BCU} \rightleftharpoons \text{R–BCU} \quad + \quad \text{X–BCU}\,, \qquad (B)$$

where BCU means bicyclo[3.3.3]undecane and R is COOH or COO^- group. For conformer *I ap* a good agreement to 1.1 kJ mol^{-1} can be seen for $\delta\,\Delta E^0$(EA) energy, which is considered as a more reliable measure of the electrostatic field effect[9–11]. The interaction energies $\delta\,\Delta H^0_\mathrm{B}$ than confirm that the substituent effect originates almost exclusively from the electrostatic interaction in the charged carboxylate anion.

For the second conformer *I sp* both $\delta\,\Delta H^0$ and $\delta\,\Delta E^0$, $\delta\,\Delta E^0$(EA), and $\delta\,\Delta H^0_\mathrm{B}$ energies predict the reversed substituent effect (i.e., positive sign of $\delta\,\Delta H^0$). However, the agreement is considerably poorer (up to 18.7 kJ mol^{-1} greater $\delta\,\Delta H^0$ than $\delta\,\Delta E^0$(EA)). The poor agreement here is not a question of failure of the AM1 method and apparently still other interactions in *I sp* must occur.

As noted previously[1–3] there is an assumption that especially the *sp* conformer of 5-X–BCU derivatives will be considerably sterically overcrowded. Indeed, interatomic distances and bond angles in Table II confirm the noticeable sterical strain. Comparing both geometrical parameters of *I sp* with *I ap* and 4-F–BCO acid[9] in Table II, it can be seen apparent distorsion especially of C1–C2–C3 bond angle (difference from standard value of 109.5° is up to 17° in comparison with 0.8° for 4-F–BCO). As regards the bond lengths in *I sp* (Table II) these are considerably in excess of 154 pm and are equal to the longest unbridged C–C single bond length (164 pm) reported[12] in sterically over-

TABLE III
Relative proton transfer enthalpies $\delta\,\Delta H^0$, isodesmic interaction energies $\delta\,\Delta H^0_\mathrm{B}$, electrostatic energies $\delta\,\Delta E^0$, and electron affinities $\delta\,\Delta E^0$(EA) of investigated conformers of the acid *I* (in kJ mol^{-1})

Energy	*I sp*	*I ap*
$\delta\,\Delta H^0$	32.1	–13.4
$\delta\,\Delta H^0_\mathrm{B}$ (COOH)[a]	19.2	–1.3
$\delta\,\Delta H^0_\mathrm{B}$ (COO^-)[b]	–12.9	12.1
$\delta\,\Delta E^{0,c}$	10.5	–9.8
$\delta\,\Delta E^0$ (EA)[c]	–13.4	12.3

[a] Interaction energy of reaction (*B*) where R = COOH; [b] interaction energy of reaction (*B*) where R = COO^-; [c] geometry parameters cos θ and *r* calculated from AM1 optimized atomic coordinates.

crowded 5,6-dibutyl-5,6-diphenyldecane. In addition the interatomic distance C1–F between fluoro substituent and opposite bridgehead carbon atom inside the molecule is very short (189 pm) and thus certain non-bonded interactions and/or transannular strain will probably occur.

Summarizing the present evidence, we can state that *I sp* conformer of 5-F–BCU describes qualitatively the reversed electrostatic field effect which is, however, substantially overestimated due to sterical Baeyer strain and non-bonded interactions.

REFERENCES

1. Exner O., Friedl Z.: Prog. Phys. Org. Chem. *19*, 259 (1993).
2. Bowden K., Grubbs E. J.: Prog. Phys. Org. Chem. *19*, 183 (1993).
3. Roberts J. D., Carboni R. A.: J. Am. Chem. Soc. *77*, 5554 (1955).
4. Dewar M. J. S., Dieter K. M.: J. Am. Chem. Soc. *108*, 8075 (1986); Voest R., Francois J.-P., Martin J. M. L., Mullens J., Yperman J., Van Poucke L. C.: J. Comput. Chem. *10*, 449 (1989); *11*, 269 (1990); Luque F. J., Orozco M.: Chem. Phys. Lett. *168*, 269 (1990); Ferenczy G. G., Reynolds C. A., Richards W. G.: J. Comput. Chem. *11*, 159 (1990).
5. Dewar M. J. S., Zoebisch E. G., Healy E. F., Stewart J. J. P.: J. Am. Chem. Soc. *107*, 3902 (1985).
6. Stewart J. J. P.: QCPE Bull. *5*, 133 (1985).
7. Marriott S., Topsom R. D.: Theochem, J. Mol. Struct. *110*, 337 (1984).
8. Exner O.: *Dipole Moments in Organic Chemistry*, p. 33. Thieme, Stuttgart 1975.
9. Friedl Z.: Can. J. Chem. *63*, 1068 (1985).
10. Friedl Z., Bohm S.: Collect. Czech. Chem. Commun. *55*, 1 (1990).
11. Friedl Z., Bohm S.: Collect. Czech. Chem. Commun. *55*, 2880 (1990).
12. Topsom R. D.: Prog. Phys. Org. Chem. *16*, 85 (1987).

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