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An MNDO study of the electrophilic aromatic substitution on trifluorobenzenes

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Summary. MNDO calculations of trifluorosubstituted benzenes and their protonated intermediates $[Ph-F_3]H^+$ were performed. The results are discussed with respect to changes in geometry, charge distribution and stabilities of the individual intermediates. It appears that the predominant influence which controls the protonation position is the ability of the substituent F to increase both the positive charge and polarities of the carbon bonds situated in the *meta*-position with respect to the substituent, thus directing protonation to the *ortho*- and *para*-positions.

Key words: MNDO – Protonated trifluorobenzenes – Aromatic substitution

Traditionally, substitution effects in electrophilic aromatic substitution are described using a classifying scheme based on the ability of the substituent (of the functional group or atom) to affect the equilibrium and/or rate constants of the reaction. This idea was quantified by Hammett [1, 2] by introducing the σ constants into the linear free energy relations. Later, this equation was modified by Taft [3] who separated the substituent constants into inductive and resonance components.

The use of molecular orbital (MO) theory formalism makes possible the separation of the contributions of the individual σ and π orbitals to the total atomic charge densities, and thus a qualitatively better description of the substituent's effect along the reaction path is possible [4]. As shown by our calculations carried out with variously substituted acetyl compounds, CH_3-CO-R, and their enolic tautomers, both in the neutral and in the ionized state of these systems [5], the substituent constants from the Taft and Hammett equation can also be successfully applied to such nonaromatic systems. Good correlations can be found between these empirical substituent constants and some physicochemical quantities obtained by MO calculations. At the same time it appears that the controlling factor which affects the reaction behaviour is the change of the charge distribution in the reacting molecule caused by the substituent.

Another deeper insight may be obtained from recent studies by Bader [6, 7], dealing with the transferability of atomic properties between various molecular systems as defined by the theory of atoms in a molecular (AIM).

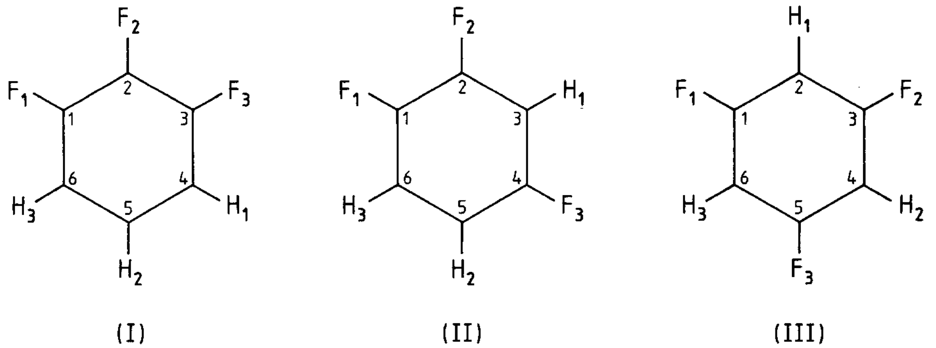
This study is concerned with trifluorosubstituted benzenes and their protonated intermediates $[Ph-F_3]H^+$. These compounds are interesting not only with respect to the investigation of the effect of various positions of the substituents on the course of electrophilic aromatic substitution, but also because of anomalies, following from the character of the substituent F compared with other analogous halogen substituted benzenes, in the mass spectrometric fragmentation under the conditions of chemical ionization (CI). Bearing in mind the possible fragmentation behaviour of such compounds, it is interesting to know the stability of the particular isomers and the energy of intramolecular migration of the hydrogen proton.

The calculations were carried out using an MNDO (minimal neglect of differential overlap) program modified by us for use on an -AT-386/387 personal computer with a standard set of parametres for the particular atoms C, H [9], and F [10]. The geometry was optimized by means of a numerical gradient of internal coordinates of the systems in all degrees of freedom (i.e. irrespective of limitations following from the possible symmetry). For clarity's sake the individual atoms are numbered as in Scheme 1. The mobile hydrogen proton is denoted as H_4 independently of its position.

The optimized geometries of three possible neutral structures (I–III) (1,2,3-trifluorobenzene, 1,2,4-trifluorobenzene and 1,3,5-trifluorobenzene) and the partial charges on the individual atoms do not differ significantly. All three systems are planar and have essentially identical delocalized system of π-electrons; the lengths of the individual C–C bonds vary slightly ($r_{CC} = 140.3-143.7$ pm). No significant changes depending on the different substituent position can be observed in the C–F ($r_{CF} = 132.2$ pm) and C–H ($r_{CH} = 109$ pm) bonds. For obvious reasons, electron densities based on Mulliken's population analysis predict negative fluorine atoms ($q_F = -160$ me), slightly positive hydrogen atoms ($q_H = 90$ me) and alternating charges on the carbon skeleton with a comparatively high polarity of individual C–C bonds.

The change to the respective radical cations is connected with reduced delocalization of the π-system and increased polarization of the individual bonds. Marked changes in the bond lengths are observed, though the planarity of the carbon skeleton remains unchanged.

In 1,2,3-trifluorobenzene (I), the C_1-C_2 and C_2-C_3 bonds ($\Delta r_{CC} = 5.2$ pm) are extended and the C_3-C_4 and C_1-C_6 bonds ($\Delta r_{CC} = -2.3$ pm) become



Scheme 1.

shorter, due to the distinctly higher positive charge on the carbon atoms C_1-C_3 ($\Delta q_{C_{1(3)}} = 54$ me, $\Delta q_{C_2} = 215$ me), and thus to the stronger coulombic repulsion between these atoms and the slight increase in the negative charge on the carbon atoms C_4, C_6 ($\Delta q_{C_{4(6)}} = 5$ me). The fluorine atoms remain negative, in spite of the total positive charge of the radical cation ($q_{F_{1(6)}} = -86$ me $q_{F_2} = -24$ me). The positive charge on the hydrogen atoms H_1-H_3 ($\Delta q_{H_{1(3)}} = 63$ me, $\Delta q_{H_2} = 59$ me) also becomes markedly higher.

Similarly, in the 1,2,4-trifluorobenzene radical cation (II), the C_1-C_2 ($\Delta r_{CC} = 7.2$ pm) and C_4-C_5 ($\Delta r_{CC} = 4.5$ pm) bonds become longer, along with a strong increase in the positive charge on the carbons C_1 ($q_{C_1} = 318$ me), C_2 ($q_{C_2} = 242$ me), and C_4 ($q_{C_4} = 356$ me). The same happens with the 1,3,5-trifluorobenzene radical cation (III), where the C_{3v} symmetry is perturbed and the C_1-C_2 is extended by $\Delta r_{CC} = 4.8$ pm, with the corresponding extension of the C_4-C_5 bond by $\Delta r_{CC} = 4.6$ pm).

Table 1 presents the results of optimized geometries of all $[Ph-F_3]H^+$ arenium ion intermediates. These structures also preserve the planarity of the carbon skeleton, with only the hydrogen proton H_4 and the corresponding atom of the original trifluorobenzene protruding from this plane at an angle of c. 109° ($r_{CH} = 112.5$ pm). The lengths of the individual C–H bonds, and the bond angles are not tabulated, because they do not deviate from 109.2 pm and 120° in any significant way. The structures of the arenium ion are labelled similarly to Scheme 1, where the Arabic numeral always denotes the position in which the proton is bound.

The character of the bonds (and their changes), as a function of the position of protonation, is similar in all the molecules under investigation. The length of the C–C bonds where one C is protonated is extended to 149.4–156.9 pm, i.e. to the value of an almost single bond. At the same time, the corresponding C–C–C angle decreases to 114°–116°. The C–C bond adjacent to this bond is reduced to 136.3–139.8 pm, i.e. to a length close to the value of the classical double bond. Generally, it may be stated that the C–C bonds originating in the protonated carbon atom in $[Ph-F_3]H^+$ arenium ions become alternatively shorter and longer. Changes in the lengths of the individual C–C bonds are followed by

Table 1. Optimized bond lengths (r in pm) for variously substituted arenium cations $[Ph-F_3]H^+$

	$r_{C_{12}}$	$r_{C_{23}}$	$r_{C_{34}}$	$r_{C_{45}}$	$r_{C_{56}}$	$r_{C_{61}}$	r_{F_1}	r_{F_2}	r_{F_3}
I-1	156.6	142.6	143.1	143.0	137.2	153.4	134.3	129.4	131.8
I-2	156.6	156.6	139.6	142.0	142.0	139.8	129.9	134.1	129.9
I-4	145.8	141.9	152.0	149.9	137.2	145.0	129.6	131.7	130.0
I-5	146.9	146.7	139.1	149.4	149.5	139.3	131.8	129.3	131.8
II-1	156.9	139.8	143.8	146.2	136.3	153.4	134.3	129.7	129.6
II-2	156.9	153.0	138.4	146.2	140.2	141.3	129.3	134.3	131.9
II-3	141.8	151.9	152.2	140.7	141.0	144.1	131.7	130.2	130.1
II-4	147.7	138.6	153.5	153.5	137.2	144.6	129.2	131.8	134.6
II-5	148.2	142.5	141.2	152.5	149.8	138.2	131.7	129.7	129.9
II-6	143.4	142.1	144.8	139.5	149.4	152.0	129.7	131.8	131.8
III-1	153.0	139.6	144.3	144.3	139.6	153.0	134.6	131.9	131.9
III-2	152.6	152.6	139.5	144.2	144.2	139.5	130.4	130.4	129.8

changes in the π-bond order (p^{π}). Here, shorter bonds (e.g. $r_{C_{56}} = 136.3$ pm of II–1) have the corresponding high p^{π} values ($p^{\pi}_{C_{56}} = 0.851$), while in the case of longer bonds the p^{π} value approaches zero ($p^{\pi}_{C_{12}} = 0.135$ of II-1 corresponds to $r_{C_{12}} = 156.9$ pm).

As has been stated by Bader [7], on the basis of *ab initio* calculations of monosubstituted benzenes, the properties of the particular C–C bonds do not depend very much on the type of the substituent, but are predominantly determiend by their position with respect to the protonated carbon atom. This holds not only for their lengths, but also for the polarization and charge distributions.

The atomic charges of the neutral systems (I–III) are not tabulated, but relatively high positive charges were found on the carbon atoms C_1 ($q_{C_2(C_3)} = 150$ me), C_2 ($qC_2 = 93$ me), C_3 in (I), C_1 ($q_{C_1} = 111$ me), C_2 ($p_{C_2} = 150$ me), C_4 ($q_{C_4} = 163$ me) in (II) or C_1, C_3, C_5 ($q_{C_1(C_3,C_5)}$) $= 201$ me in (III). This is caused by the above mentioned negative charge of the substituent F atoms (q_F from -151 me to -169 me in (I–II)). These charges ensue from the character of fluorine which is a strong σ-acceptor. With respect to electrophilic substitution (protonation), the decisive role is then played by the F substituent which directs the highest negative charge to carbon atom C_4 ($q_{C_4} = -78$ me) in (I), to carbon atoms C_3 ($q_{C_3} = -100$ me) and C_5 ($q_{C_5} = -77$ me) in (II) and, logically, to carbon atom C_2 ($q_{C_2} = -136$ me) in the system (III), i.e. to the *ortho- para*-positions. This is in line with the finding that the controlling and activating ability of a substituent X is generally determined by the position of the positive charge with respect to X in the resonance structure which may be drawn for the transition state or for the intermediate [11, 12].

From the energetic point of view it is of interest that due to ionization there occur marked shifts in the stabilities (heat of formations (ΔH_f)) of the individual isomers. If neutral systems differed only by 0.3 kcal/mol in the series

$$\mathrm{I} \succ \mathrm{II} \succ \mathrm{III} \qquad (1)$$

then in the ionized state the 1,2,4-trifluorobenzene radical cation (II) is the most stable, and the differences in the stability values of the individual radical cations are higher by an order of magnitude (4.88 or 2.11 kcal/mol) in the series

$$\mathrm{II} \succ \mathrm{I} \succ \mathrm{III} \qquad (2)$$

The stabilities of the individual protonated trifluorobenzenes given in Table 2 show a still larger scatter of the calculated (ΔH_f) values. If these values are related to the enthalpies calculated for the individual corresponding radical cations (I–III), we obtain, by analogy with the proton affinities, the relative stabilities of the arenium ions ($\Delta(\Delta H_f)$). From these values too, one can see that in the aromatic substitution on the trifluorobenzenes investigated in this study, the *ortho-* and *para*-directing effect of the substituents F is clearly operative. Furthermore, vertical ionization potentials calculated by using the Koopmann's theorem are also given in Table 2.

To accomplish the energy balance, we modelled the reaction path of migration of the hydrogen proton along the carbon skeleton of the benzene ring. Figure 1 schematically represents the procedure used in the calculation of geometries and energies of intramolecular migration. Since following the trajectory of the hydrogen proton from one carbon atom to the next is not trivial, and the use of the cartesian coordinates involves changes in three variables (which in

Table 2. Heat of formation, ΔH_f, and relative stabilities of substituted benzenes [Ph–F_3] (I–III) and their radical cations in comparison with those of arenium ions [Ph–F_3]H^+

System	ΔH_f [kcal/mol]	ΔH_f^+ [kcal/mol]	$\Delta(\Delta H_f)^a$ [kcal/mol]	IP [eV]
I	−115.28	106.70	0.0	10.065
II	−115.67	101.82	0.0	9.834
III	−115.90	108.81	0.0	10.140
I-1	—	111.37	4.67	15.647
I-2	—	95.79	−10.91	15.658
I-4	—	87.79	−18.91	15.601
I-5	—	94.24	−10.46	15.776
II-1	—	93.97	−7.85	16.093
II-2	—	101.57	−0.25	15.597
II-3	—	88.69	−13.13	15.288
II-4	—	101.63	−0.19	16.062
II-5	—	87.17	−14.65	15.671
II-6	—	94.68	−7.14	13.398
III-1	—	110.83	2.02	15.876
III-2	—	82.00	−26.81	15.709

[a] $\Delta(\Delta H_f)$ denotes relative stability compared with the unprotonated system; the negative value means that the arenium ion is more stable than the corresponding radical cation

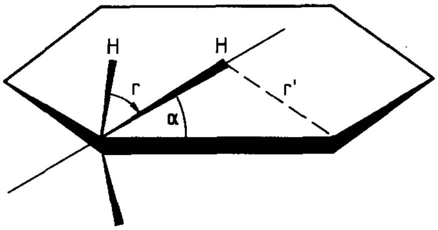


Fig. 1. Principle of modelling the minimum energy reaction path for migration of the proton (or fluorine) through a bridged transition structure

turn raises the number of necessary calculations) inner coordinates were used. The valency angle α allows the reaction path of minimal energy to be followed as a function of only one variable. All the other degrees of freedom (including the bond length $C{-}H_4$ and the respective torsional angle) were optimized during variation of the angle α.

Variation of the angle α in steps of 10° gave energy profiles of reactions (3)

$$[\text{I-5}][\text{I-4}] \rightarrow [\text{I-1}] \rightarrow [\text{I-2}] \tag{3}$$

as illustrated in Fig. 2 for the isomerization 1,2,3-trifluoro-5H-benzene cation [1-5] → 1,2,3-trifluoro-4H benzene cation [I-4]. The structures of the saddle points were subsequently optimized in order to reach more exact energy values. The heat of formation and ensuing the activation energies ΔE, along with the total profile of the energy hypersurface, are summarized in Fig. 3.

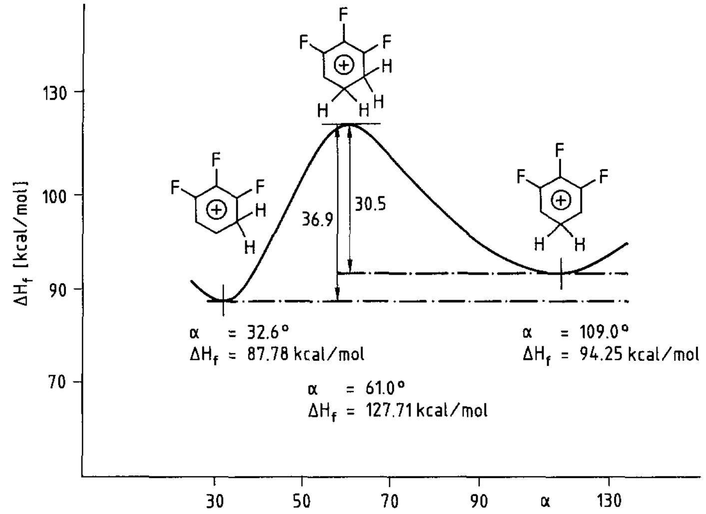


Fig. 2. Energy profile of intramolecular migration of the proton by variation of the angle α in the sense of reaction (3)

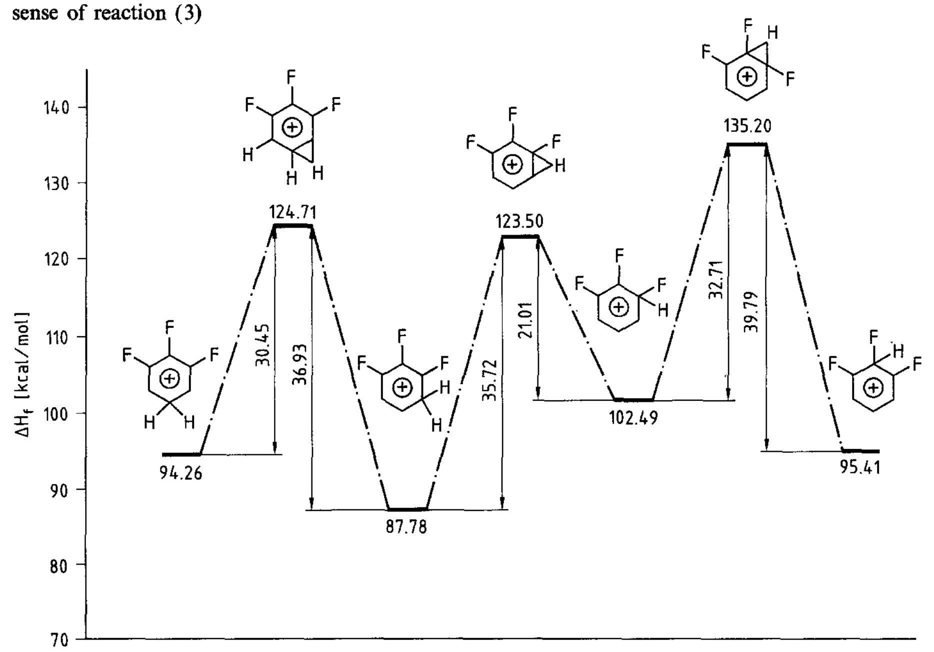


Fig. 3. The MNDO calculated profile of migration of the hydrogen atom in the protonated 1,2,3-trifluorobenzene cation

It is somewhat surprising that the energy barrier value of the I-1 → I-2 transition (23.71 kcal/mol) is comparable with the other ΔE values. Generally, it may be stated that these calculated thermodynamic data are in a good agreement with the energy values obtained by McLafferty for the isomerization path $[CH_3-C_6H_4-Y]$ for Y = F, Br, I [13].

The activation energy values of the individual rearrangements (3), together with the stability values of arenium ions (I-I)–(I-5) in the gas phase, sugggest a comparatively free migration of the proton. This is also corroborated by mass spectrometric experiments involving isotropically labelled compounds.

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