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Abstract

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σ-CONSTANTS OF SUBSTITUENTS WITH A TRIFLUOROMETHYL GROUP

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The study of the influence of the trifluoromethyl group on the electronic nature of substituents containing it is a timely problem, since the corresponding compounds are finding ever broader application, for example in the synthesis of dyes and medicinal substances.

One of the methods for describing the quantitative relationship between reactivity and the structure of organic compounds is the application of the Hammett–Taft method (1). This method makes it possible to separate Hammett σ-constants into independent contributions of the inductive effect (σ) and the conjugation effect (σ). The values of σ and σ can be calculated (2) from the rate (or equilibrium) constants for reactions of meta- and para-disubstituted benzenes (K and K).

The redistribution of electron density in the benzene ring caused by a substituent, together with the change in the reactivity of benzene derivatives, leads to a change in the shielding of fluorine nuclei in substituted fluorobenzenes (3). As a result of comparing the chemical shifts of nuclear magnetic resonance (NMR) signals on fluorine nuclei in the meta- and para-positions of the benzene ring (δ and δ) with the constants σ and σ , a fairly good correlation was found (4).

Thus, ^{19}F NMR spectroscopy data can be used to determine the constants σ and σ of substituents in benzene derivatives.

In the present work we used the Hammett–Taft method to clarify the electronic nature of substituents containing the trifluoromethyl group. The constants σ in the Hammett equation $\lg(K/K_0) = \rho\sigma$ for the meta- and para-positions of the substituent were determined from the ionization reaction of benzoic acids. For this reaction the slope of the correlation straight line ρ was taken as 1.535 (5), and the value $pK_a(= -\lg K_0)$ for the unsubstituted acid as 5.71 (6,7). The pK_a values of the benzoic acids were determined by measuring the pH of solutions (in 50% aqueous alcohol) half-neutralized with the aid of an LP-57M type tube potentiometer at 25° (5). The chemical shifts of substituted fluorobenzenes were measured on a YaMR-US-2 spectrometer at a frequency of 19.306 MHz. The values of δ and δ were determined by extrapolating the measured values to zero concentration of the compound under study in n-heptane, which was chosen as an inert solvent (for details see (^{8})). The obtained values of pK_a and δ are given in Table 1. The accuracy of determination is ±(0.01–0.02) and ±(0.05) ppm, respectively.

On comparing the found pK_a values with the values for well-studied substituents (see, for example, (^{5})), one may note that the strength of the acids 1) increases significantly when a methyl group in the corresponding substituent is replaced by a trifluoromethyl group, and 2) with both a meta- and a para-substituent increases in the following series:

$$CH_3CO < CF_3S < CF_3 < CF_3C \equiv C < CN < CH_3SO_2 \leq$$

$$\leq CF_3SO < NO_2 < CF_3SO_2.$$

A more precise conception of the electronic nature of substituents is provided by separate consideration of the inductive effect and the conjugation effect. The constants of these effects, σ_i and σ_c (see Table 1), were calculated from the pK_a data and from chemical shifts. The values ρ_i and α were taken as 1.50 and 0.42, respectively (^{2}). Some discrepancy between σ_i and σ_c calculated from pK_a and from NMR is possibly due to the fact that measurements by these two methods were carried out in different solvents. To characterize the electronic nature of substituents we selected the mean values of σ_i and σ_c as the most probable. It is interesting to note that the mean values obtained for the CF_3 group are very close to values derived on the basis of several series of reactions (0.41 and 0.14, respectively (^{1,2,7})).

The trifluoromethyl group is a meta-directing group in electrophilic substitution in the aromatic ring and has a positive σ_c, characteristic of substituents of the second kind (^{1,2}). The substituent CF_3O is para-directing and has a negative σ_c, characteristic of substituents of the first kind (^{1,2}). The substituent CF_3SO is also meta-directing and, in its constants σ_i and σ_c, is very close to CN and CH_3SO_2. In this connection it is interesting to note that replacement of the hydrogen atoms by fluorine in CH_3SO is equivalent to oxidation of the latter to the CH_3SO_2 group. The substituent CF_3SO_2 proved to be the strongest electron-acceptor group among those known at present. In its inductive effect, CF_3SO_2 approaches substituents existing in the ionic state, of the type $\overset{+}{N}R_3$. The substituent $CF_3CH{=}CH$ can be placed after iodine in the halogen series; however, its peculiarity is the very small magnitude of the conjugation effect. As was to be expected, the group $CF_3C{\equiv}C$ is more electron-accepting than $CF_3CH{=}CH$ and, in its σ_i and σ_c, like CF_3, approaches COOR and $COCH_3$. The perfluoropropenyl group is similar to $CF_3C{\equiv}C$. The substituents $CF_3CH{=}CH$, $CF_3C{\equiv}C$, and $CF_3CF{=}CF$ differ sharply in their directing influence from CF_3. On nitration of the corresponding benzene derivatives, about 50% para-nitro isomers are isolated, whereas benzotrifluoride is nitrated only in the meta position. The corresponding analogy is observed when comparing the directing influence of the substituents CH=CHX and X, where X = NO_2, COOH, SO_2Cl. Such behavior of these substituents is usually explained (^{9}) by a partial displacement, under the influence of a strong electrophilic agent, of the π electrons of the double or triple bond of the side chain toward the benzene ring and by the formation in the transition state of more stable ortho- or para-substituted carbocations as compared with meta-substituted ones. In the case of the $CF_3CF{=}CF$ group, the unshared electron pairs of fluorine bonded to the β-carbon atom may possibly participate in such conjugation.

It should be pointed out that the values of σ_i and σ_c for the substituents CF_3S and CF_3 show a striking similarity. In addition, these substituents exhibit a very close exaltation of the constant σ_i on passing from benzoic acids to aniline derivatives (0.13 and 0.12, respectively (^{10})). Meanwhile, upon nitration of phenyl trifluoromethyl sulfide, in contrast to benzotrifluoride, only the ortho and para isomers are formed (^{11}). This anomalous behavior apparently can be explained as follows. In the ground state there is competition between two oppositely directed effects, namely: 1) displacement of the unshared electron pair of sulfur toward the benzene ring and 2) displacement of this pair toward the fluorine atoms of the CF_3 group; the latter overrides the negative conjugation effect of the sulfur atom (σ_c for SCH_3 is equal to -0.24). As a result, the electron-acceptor strength of the sulfur atom increases, which in turn causes (as Sheppard first noted (^{10}), and as was shown later in studies of dipole moments by A. E. Lutsky, L. M. Yagupolsky, and E. M. Obukhova) a displacement of the π-electron cloud of the benzene ring toward the free d orbitals of sulfur with the formation of a positive charge in the ortho and para positions. However, upon attack by a strong

of the electrophilic agent (NO_2^+), under its influence a redistribution of electron density occurs with participation of the unshared electron pair of sulfur, and a positive charge appears on sulfur in the transition state. In this case nitration of trifluoromethyl sulfide proceeds in the ortho or para positions. It is possible that, under the action of a weaker electrophilic agent, redistribution of electron density in the transition state will play a subordinate role, and a significant amount of the meta isomer will be formed.

Table 1

Constants of σ-substituents containing a trifluoromethyl group

Substituent	Meta position, pK_a^m ($-\lg K_m$)	Meta position, σ_m	Meta position, δ_m (ppm)	Para position, pK_a^p ($-\lg K_p$)	Para position, σ_p	Para position, δ_p (ppm)	σ_i-constant by pK_a	σ_i-constant by NMR	σ_i-constant mean	σ_c-constant by pK_a	σ_c-constant by NMR	σ_c-constant mean
CF_3	5,11 (*)	0,39	−2,1 (*)	4,96	0,49	−5,1 (*)	0,33	0,43	0,38	0,17	0,10	0,14
CF_3O	5,17	0,35	−3,21	5,22	0,32	−2,41	0,40	0,60	0,50	−0,07	−0,18	−0,13
CF_3S	5,16	0,36	−2,55	5,01	0,46	−4,10	0,30	0,50	0,40	0,17	0,06	0,12
CF_3SO	4,74	0,63	−3,60	4,65	0,69	−7,47	0,60	0,67	0,64	0,11	0,13	0,12
CF_3SO_2	4,54	0,76	−4,57	4,24	0,96	−13,70	0,64	0,83	0,74	0,34	0,31	0,33
$CF_3-CH=CH$ (trans)*	5,38	0,12	−0,75	5,40	0,20	−3,00	0,23	0,21	0,22	−0,03	0,07	0,02
$CF_3C\equiv C$	5,08	0,41	−1,56	4,93	0,51	−6,25	0,35	0,34	0,35	0,17	0,16	0,17
$CF_3SO_2CH=CH$ (trans)*	–	–	−1,59**	–	–	−8,97	–	0,34	–	–	0,25	–
$CF_3CF=CF$ (trans)*	–	–	−1,45	–	–	−5,58	–	0,32	–	–	0,14	–
$FC_6H_4(CF_2)_2$	–	–	−1,24**	–	–	−4,09	–	0,29	–	–	0,10	–

* The trans orientation was established from NMR spectra.
** Extrapolation was carried out in dichloroethane.

All the substituents considered in the present work contain a trifluoromethyl group. In order to obtain an idea of the nature of the influence of the CF_3 group on the substituent containing it, we compared the inductive effects and conjugation effects of these substituents and of the corresponding substituents with a methyl group. In Fig. 1 the values of the constants σ_i for substituents with the CF_3 group are plotted on the ordinate axis, and those for the corresponding substituents with the CH_3 group on the abscissa axis. As a result it was found that the degree of increase in electron-acceptor strength upon replacing the CH_3 group by CF_3 is directly related to the number of bonds n separating the trifluoromethyl group and the benzene ring. Since all the straight lines in Fig. 1 were drawn with the same slope of 45°, the points of intersection with the ordinate axis correspond to the increment of the inductive effect $\Delta\sigma_i$ introduced by the CF_3 group. At $n = 2$, the inductive increment of the trifluoromethyl group (0,19) decreases in comparison with $n = 1$ ($\Delta\sigma_i = 0,46$) by approximately a factor of 2.4, which is in agreement with the coefficient 1/2.78 for attenuation of the inductive effect of group X upon transmission through a methylene group (^{1}). For $n = 3$ and 4 the values of $\Delta\sigma_i$ are respectively 0,13 and 0,07. The values found for the increments of the inductive influence of the CF_3 group make it possible to estimate the constants σ_i for unstudied substituents with a trifluoromethyl group, if σ_i is known for the corresponding substituents with a methyl group. For example, for $COCF_3$, $NHCOCF_3$, and $N(CH_3)(CF_3)$, values of 0,47,

Fig. 1 and Fig. 2

Figure 1: Fig. 1 and Fig. 2

0,39, and 0,29, respectively, should be expected. The observed correlation of inductive effects, including both saturated and unsaturated intermediate atoms and groups of atoms, represents additional evidence that the constant σ_i reflects the influence of the substituent on the redistribution of electron density, which is transmitted mainly through the system of σ-bonds (^{1}).

In comparing the conjugation effect, the data at our disposal were limited to substituents with $n = 1$ and 2. Correlation

of the constants σ_c of substituents with a trifluoromethyl group and the corresponding substituents with a methyl group is shown in Fig. 2 and corresponds to the relation

$$\sigma_c^{\mathrm{X-CF_3}} = 0.8\sigma_c^{\mathrm{X-CH_3}} + 0.2. \tag{5}$$

The dependence found shows that the conjugation effect of the CF_3 group, when transmitted through a heteroatom (oxygen, sulfur), practically does not die out. Hence it may be concluded that the contribution of the form with the trifluoromethyl group

Fig. 1. Dependence between the induction constants σ_i of substituents containing a trifluoromethyl group and the corresponding substituents with a methyl group. Points on the graph:
1–CF_3 and CH_3; 2–CF_3CH_2 and CH_3CH_2;
3–CF_3O and CH_3O; 4–CF_3S and CH_3S;
5–CF_3SO and CH_3SO; 6–CF_3SO_2 and CH_3SO_2;
7–$CF_3(CH_2)_2$ and $CH_3(CH_2)_2$; 8–$CF_3CH{=}CH$ and $CH_3CH{=}CH$;
9–$CF_3C{\equiv}C$ and $CH_3C{\equiv}C$; 10–$CH_3(CH_2)_3$ and $CH_3(CH_2)_3$.

Fig. 2. Dependence between the conjugation constants σ_c of substituents containing a trifluoromethyl group and the corresponding substituents with a methyl group. The point designations are the same as in Fig. 1.

in the form $= CF_2F^-$ remains approximately constant for the substituents considered. This state of the CF_3 group is due to partial transfer of electrons of an unshared pair (or π-electrons) of the neighboring atom to the antibonding orbital of the C–F bond [12,13]. In the case of substituents with a negative conjugation effect, replacement of the CH_3 group by CF_3 leads to its complete or partial compensation, and for substituents with a positive conjugation effect, to its enhancement. From equation (5) it appears possible to estimate the constants σ_c for substituents with a CF_3 group if σ_c is known for the corresponding substituents with a methyl group. For $COCF_3$ one should expect σ_c to be close to 0.3, and for $N(CH_3)(CF_3)$, to -0.2.

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