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ORIGINAL RESEARCH

Classical and reverse substituent effects in *meta*- and *para*-substituted nitrobenzene derivatives

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Abstract Electron-accepting properties of the nitro group were studied in a series of *meta*- and *para*-X-substituted nitrobenzene derivatives (X = NMe_2, NH_2, OH, OMe, CH_3, H, F, Cl, CF_3, CN, CHO, COMe, $CONH_2$, COOH, COCl, NO_2, NO). For this purpose Hammett-like approaches were applied based on quantum chemistry modeling; the B3LYP/6-311++G(d,p) method was used. The substituent effect (SE) was characterized by the mutually interrelated descriptors: the charge of the substituent active region, cSAR(X), and substituent effect stabilization energy, SESE, as well as substituent constants, σ. Classical SE is realized by dependences of the structural parameters of the nitro group (ONO angle and NO bond lengths) and cSAR(NO_2) on the above mentioned SE descriptors. The reverse substituent effect was clearly documented by a comparison of cSAR(X) values for monosubstituted benzenes, *meta*- and *para*-substituted nitrobenzenes as well as, additionally, for *meta*- and *para*-X-substituted anilines. For *para*-substituted systems the electron-accepting ability of the nitro group increases from cSAR(NO_2) = −0.170 up to −0.284 in dinitrobenzene and nitroaniline, respectively.

Keywords Substituent effects · Electronic structure · Molecular modeling · Substituent effect stabilization energy · Charge of the substituent active region

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Introduction

The nitro group belongs to one of the most electron accepting (EA) substituents and hence it attains an unusual interest as a substituent or a functional group. Firstly, the nitro group is very electronegative (the group electronegativity in the Pauling scale, χ_{NO2}, is equal to 4.00 for a coplanar and 4.19 for a perpendicular orientation with respect to the benzene ring) [1] and as a consequence its strongly inductive effect influences the rest of the substituted molecule. Secondly, this group exhibits a great range of variability of its EA properties [2, 3] with σ_p = 0.78 and σ_p^- = 1.27 which dramatically depends on the kind of a moiety to which the group is attached [4]. A similar situation is with the resonance and field substituent constants σ_R and σ_F equal to 0.16 and 0.62, respectively [3]. The inductive substituent constant [5], σ_I, estimated from acid-base equilibrium constants of substituted acetic acids equals to 0.76. A rotation of NO_2 group around CN bond changes σ_p^- values from 1.27 for a coplanar conformation to 0.70 for the perpendicular one [6], and so the latter is very close to the value to the field parameter [3].

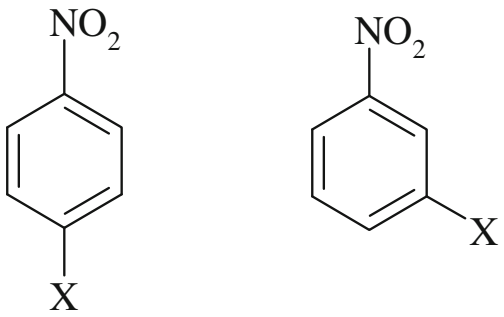
Two comments should be made here. It has to be pointed out, according to a critical compilation by Exner (Table 10.2 in Ref. [2]), that the above mentioned SE characteristics are not the only ones, moreover, they sometimes differ up to 10–20%. A good illustration can be given by the values of σ_p substituent constant for NO_2 group ranging from 0.73 to 0.82 [2]. These deviations are

mostly due to either some experimental errors or/and not exactly equivalent reference series, *i.e.* the intramolecular interactions responsible for the SE have slightly different mechanisms including also medium effects. Additionally, a substituent constant (SC) may depend on the aim of its application. For this purpose either a position of the substituent (*e.g.* *meta*- or *para*-) or, in other cases, the reaction site with strong ED (electron donating) or EA properties is chosen. A good example is a reference reaction for σ_p^- based on the acid-base equilibrium constants of phenol derivatives. In this case the reaction site is the hydroxy group which is a strongly ED functional group. Hence, *e.g.* for EA substituents in the *para*- position the appropriate substituent constants are significantly greater than the "classical" Hammett constants based on benzoic acid dissociation.

Undoubtedly, values of SCs depend on the kind of the moiety to which substituents are linked and depend on the selected reference reaction. Therefore, it seems to be valuable to undertake the studies of interrelation between the electron properties of the fixed functional group ("reaction site") Y and the ED or EA properties of the varying substituents X in a general reaction series X-R-Y, where R is a transmitting moiety. The dependence of the properties for a given substituent X on the kind of R-Y was named the **reverse substituent effect** [4], since this works in an opposite direction than the classical SE. In the latter substituents affect properties of Y, whereas in the **reverse SE** various reaction sites cause changes in ED/EA properties of the substituents. This kind of intramolecular interactions is a subject of this paper.

The nitro group is of great significance due to wide applications of nitro-compounds which are very important chemicals, medicines [7], explosives [8, 9] or fertilizers [10]. So it is not surprising a great number of crystal structures deposited in the Cambridge Structural Database [11] (CSD) amounting over 38,000 records, as it has been noted recently [12].

Given such a great interest devoted to compounds with the nitro group it seems to be very advantageous to investigate an impact of the "fixed" nitro group on the properties of substituents X. Additionally, it is very important to use methods which allow to estimate their electron properties independently of reference reactions which rarely can be formulated for any molecular systems containing the nitro group. At present, several known substituent constants are mostly intuitively applied. The aim of this study is to verify the role of the nitro group on electron properties of substituents. For this purpose both the classical and reverse SE are examined for series of *meta*- and *para*-X-substituted nitrobenzene derivatives (Scheme 1) with 16 substituents (X = NMe_2, NH_2, OH, OMe, CH_3, H, F, Cl, CF_3, CN, CHO, COMe, $CONH_2$, COOH, COCl, NO_2, NO).



Scheme 1 General scheme of studied disubstituted benzene derivatives; X = NMe_2, NH_2, OH, OMe, CH_3, H, F, Cl, CF_3, CN, CHO, COMe, $CONH_2$, COOH, COCl, NO_2, NO

Methodology

For all studied structures an optimization without any symmetry constraints was performed with the use of the Gaussian09 program [13]. Three different methods (HF [14], DFT with B3LYP [15, 16] and M06-2X [17] functionals, and MP2 [18]) and three basis sets (6-31+G**, 6-311++G** [19] and aug-cc-pVDZ [20]) were applied for *para*- and *meta*-X-substituted nitrobenzenes to select the best one for the studied problem. To confirm that calculated structures correspond to the minima on the potential energy surface the vibrational frequencies were calculated at the same level of theory.

Similarly to the case of substituted anilines [21], considering the accuracy, sensitivity and computational costs, the B3LYP/6-311++G** method was chosen for all further calculations. The choice was based on the energetic characteristic of the SE – Substituent Effect Stabilization Energy (SESE) and on the comparison of the calculated values with those obtained using MP2/6-311++G** approach (see Table S1 in SI).

Various methods of charge partitioning (NBO [22], AIM [23] and Hirshfeld [24] charges) were used to obtain cSAR values. Natural Bond Orbital (NBO) charges and Hirshfeld's charges were computed in Gaussian program (with the use of NBO 6.0 module [25]). Bader's AIM atomic charges were performed using AIMAll program [26]. In this study only NBO charges were used owing to the good correlation between cSAR(X) values. All calculated cSAR values are shown in Table S2 (SI).

Properties of the substituents were characterized by substituent constants (σ), SESE and cSAR(X) descriptors.

Substituent Effect Stabilization Energy, SESE, was estimated using a homodesmotic reaction [27–30].

$$X{-}R{-}Y + R \rightarrow R{-}X + R{-}Y$$

for which

$$SESE = E(R{-}X) + E(R{-}Y) - E(X{-}R{-}Y) - E(R) \quad (1)$$

SESE values describe the energetic effect of the interaction between substituent X and the reaction site Y, while R is

treated as the transmitting moiety. In our study, Y is the nitro group (NO_2) while R denotes the benzene ring. The greater value of SESE (eq. 1) denotes the higher stabilization energy caused by the substituent effect.

Charge of the Substituent Active Region [31, 32], cSAR(X), is defined as a sum of total charges at all atoms of the substituent X and the charge at the *ipso* carbon atom.

$$\mathrm{cSAR(X)} = q(\mathrm{X}) + q(\mathrm{C_{ipso}}) \quad (2)$$

The nitro group was characterized both by structural (d_{CN}, d_{NO} and a valence angle ONO, φ, see Fig. 1) and electronic [cSAR(NO_2)] parameters.

Results and discussion

The substituent effect in *meta*- and *para*-substituted nitrobenzene derivatives may be considered by means of three ways of understanding this term. Firstly, as a classical description of the changes in properties observed in the nitro group due to the impact of the substituent (classical SE). Secondly, showing mutual dependences between structural and electronic parameters of the NO_2 group resulted from the SE. Finally, as the reverse SE describing changes in EA/ED properties of the substituent resulting from properties of the remainder of the molecule to which it is attached. Subsequent parts of this section are devoted to these issues.

Nevertheless, before going into detailed studies of SEs in *meta*- and *para*-substituted nitrobenzene derivatives by use of classical substituent constants (σ) and quantum chemistry based cSAR(X) [31–33] and SESE [29, 30] characteristics we should determine their mutual interrelations.

The results in Table 1 and Fig. 2 reveal an excellent correlation between SESE and substituent constants for all three cases: for *meta*- and *para*-derivatives as well as for a joint approach the regression lines with $R^2 > 0.933$ are observed. Another two relationships presented by regressions in the Table 1 are also acceptable, but similarly as in the case of aniline derivatives [21] the precision of regressions for *meta*-series is always lower than for the *para*-ones. However, in all three cases slopes, as the absolute values, are greater for *meta*-derivatives than for *para*-systems. This is opposite to those observed for substituted aniline derivatives [21]. A greater sensitivity to the SE from the *meta*-position might be considered as a result of the property of the nitro group as *meta*-directing in the electrophilic substitution. Another possible interpretation could be associated with through space interactions between NO_2 group and substituents, which in *meta*-positions are closer to each other than in the *para*-one.

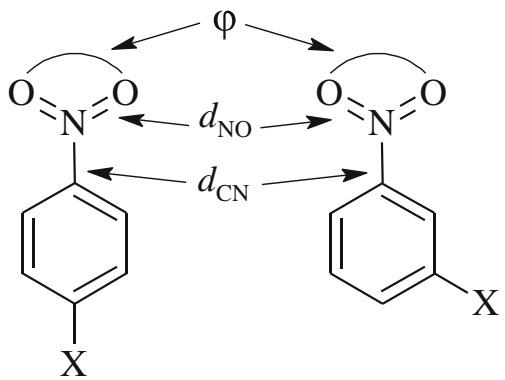


Fig. 1 Structural parameters (d_{CN}, d_{NO} and a valence angle ONO, φ) of the reaction site

The best precision of the linear regression between SESE and classical substituent constants is understandable taking into account that both these SE characteristics include all effects of intramolecular interaction between substituents and the fixed group, NO_2 this case. Both cSAR(X) and cSAR(NO_2) represent local changes in the electron structure and hence describe a slightly different situation.

Classical substituent effect observed in NO_2 group and its structural units

The classical way of the SE interpretation is based on relating properties of the reaction site (Y) to the substituent constants, σ (X), in the general scheme X-R-Y. In this work, apart from σ constants other descriptors of the SE are used, such as SESE and cSAR(X). In the case of the reaction site (Y = NO_2) the properties taken into consideration are its electronic characteristic by cSAR(NO_2) and structural unit parameters: ONO angle (φ), NO bond lengths (d_{NO}) as well as the length of the linking CN bond (d_{CN}); each of them are subject of the SE from *meta*- and *para*-positions. All statistical data for this kind of interactions are given in Table 2.

As already mentioned, each of three structural parameters (d_{NO}, φ and d_{CN}) is important for the characterization of the nitro group and its interaction with the ring because they describe the nature of the link between NO_2 group and the ring. Changes for the first two structural characteristics are very well described by the Hammett constants and SESE but worse by cSAR(X) as presented in Table 2 and illustrated in Figs S1-S4 (in SI).

It is worth to note that the sensibility of d_{NO} on the SE is again stronger for *para*- than for *meta*-derivatives, contrary to the relation of φ vs. σ presented in Fig. S4. The latter may be associated with the property of the carbon atom in the *meta*-position which is reactive for the electrophilic substitution. What is more, if both series are considered together the obtained relations are characterized by $R^2 > 0.903$. In other words, it can be said that the variability of these parameters seems to be not dependent on the positions of the substituents.

Oppositely to the very good descriptions of d_{NO} and φ angle by σ constants the length of the linking bond d_{CN} does

Table 1 Statistics of mutual correlations between substituent constants (σ), cSAR(X) and SESE: the equation $f(x) = a \cdot x + b$; Δ1 and Δ2 denote $f(x)$ and x ranges of variability, respectively

	R^2	a	b	a_p/a_m	Δ1	$\Delta1_p/\Delta1_m$	Δ2	$\Delta2_p/\Delta2_m$
SESE = $a \cdot \sigma + b$ SESE σ								
m	0.933	−5.962	0.361	0.79	5.55	1.48	0.87	2
p	0.975	−4.686	0.030		8.24		1.74	
m + *p*	0.952	−4.959	0.081					
cSAR(X) = $a \cdot \sigma + b$ cSAR(X) σ								
m	0.726	−0.413	0.089	0.63	0.356	1.11	0.87	2
p	0.919	−0.259	0.039		0.394		1.74	
m + *p*	0.794	−0.292	0.046					
cSAR(X) = $a \cdot$ SESE + b cSAR(X) SESE								
m	0.729	0.067	0.053	0.81	0.356	1.11	5.55	1.48
p	0.913	0.054	0.037		0.394		8.24	
m + *p*	0.820	0.058	0.041					

not give so clear dependence. It is important to note that variations in the CN bond length may serve as an indicator of changes in the resonance effect of the substituted nitrobenzene derivatives for electron donating substituents [34]. This is associated with an appearance of a contribution of the quinoid-like structure in the description of the electron system of the ring. The changes of d_{CN} on σ constants are presented in Fig. S5. The obtained result is very significant. The slopes and the precision of regression lines for *meta*- and *para*-substituted series differ dramatically. The *para*-series has a much higher slope than the *meta*-one (0.017 vs. 0.004) and this is an important observation despite of the low precision of the regression line in the *meta*-series. It indicates a much smaller role of the quinoid structure for *meta*-substituted nitrobenzene derivatives than for the *para*-ones. This is also supported by the variation range of d_{CN} values for *meta*- and *para*-series: 0.005 and 0.029, respectively (Table 2). When we look at these data by means of canonical structures we find that for *para*-substituted systems the quinoid form requires the structure with a single charge separation between the donating substituent and the nitro group, whereas for the *meta*-one a double excitation is needed, which is energetically much less favorable [35].

The above presented relationship is also observed when cSAR(X) or SESE are used as SE characteristics. However, for the dependence of d_{CN} on SESE, shown in Fig. 3, the difference between changeability of d_{CN} for all *meta*-derivatives is small, for the *para*-ones with SESE <0 is clearly stronger, whereas the slope for all other points (SESE ≥0, the green line in Fig. 3) is much higher and equals to −0.0055.

This finding is a significant support for the interpretation of the role of the resonance effect on the CN bond lengths. A similar picture is found when we plot cSAR(NO_2) against cSAR(X) (Fig. S6). The slopes of cSAR(Y) *vs*. cSAR(X) may be used as a measure of an intensity of the communication between X and Y [36]. The more negative value the stronger interaction between X and Y. In Fig. S6 we have three different situations: a very weak interaction for *meta*-series (the slope = −0.014), in *para*-series a moderate interaction for EA substituents (the slope = −0.246) and a very strong interaction for ED substituents with the slope = −0.755.

In all presented above cases the regressions for *para*-series are more precise than for the *meta*-ones, and almost in all the cases slopes (as absolute values) are greater for *para*-series.

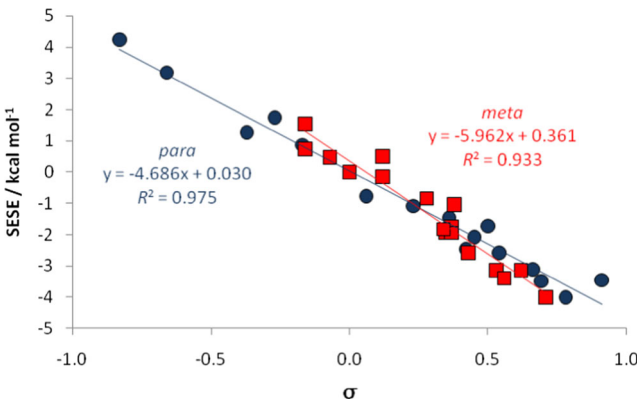


Fig. 2 Regressions SESE = $a \cdot \sigma + b$ for *meta*- and *para*-series; for a joint set of data: y = −4.959 · x + 0.081 with $R^2 = 0.952$

Substituent effect observed in changes of structural units of NO_2 group

As documented earlier [21], the substituent effect may be observed by mutual correlations between changes of various structural parameters of the reaction site (the NO_2 group in the discussed case) and its link to the ring, the CN bond length. In some cases there are good mutual correlations between these kind of structural parameters. The relation of ONO angle vs. CN bond length is presented in Fig. S7. Two trends of regression lines are observed. The line for *para*- substituted systems has a high

Table 2 Classical model for the description of substituent effects: the equation $f(x) = a \cdot x + b$, Δ means the range of f(x) variability; d_{CN} and d_{NO} are given in Å, φ in deg and SESE in kcal/mol

	$f(x)$	x	R^2	a	b	a_p/a_m	Δ	Δ_p/Δ_m
	cSAR(NO2)	σ						
m			0.354	0.021	−0.191	4.19	0.033	4.73
p			0.943	0.090	−0.221		0.156	
m + *p*			0.792	0.077	−0.213			
	d_{CN}	σ						
m			0.465	0.004	1.482	4.71	0.005	5.95
p			0.917	0.017	1.475		0.029	
m + *p*			0.765	0.015	1.477			
	d_{NO}	σ						
m			0.910	−0.003	1.225	1.31	0.003	2.48
p			0.939	−0.004	1.226		0.008	
m + *p*			0.903	−0.004	1.225			
	φ	σ						
m			0.939	0.912	124.602	0.77	0.876	1.41
p			0.966	0.702	124.625		1.236	
m + *p*			0.943	0.751	124.631			
	$cSAR(NO_2)$	cSAR(X)						
m			0.036	−0.014	−0.186	23.16	0.033	4.73
p			0.919	−0.329	−0.207		0.156	
m + *p*			0.501	−0.187	−0.199			
	d_{CN}	cSAR(X)						
m			0.219	−0.005	1.482	12.07	0.005	6.00
p			0.885	−0.062	1.477		0.029	
m + *p*			0.510	−0.037	1.479			
	d_{NO}	cSAR(X)						
m			0.618	0.006	1.224	2.75	0.003	2.48
p			0.877	0.015	1.223		0.008	
m + *p*			0.683	0.011	1.224			
	φ	cSAR(X)						
m			0.715	−1.643	124.801	1.54	0.876	1.41
p			0.919	−2.536	124.734		1.236	
m + *p*			0.817	−2.136	124.761			
	$cSAR(NO_2)$	SESE						
m			0.379	−0.004	−0.190	5.28	0.033	4.73
p			0.945	−0.019	−0.220		0.156	
m + *p*			0.723	−0.014	−0.210			
	d_{CN}	SESE						
m			0.497	−0.001	1.482	5.95	0.005	6.00
p			0.928	−0.004	1.475		0.029	
m + *p*			0.690	−0.003	1.477			
	d_{NO}	SESE						
m			0.962	0.0006	1.224	1.67	0.003	2.48
p			0.963	0.0009	1.225		0.008	
m + *p*			0.898	0.0008	1.225			
	φ	SESE						
m			0.987	−0.151	124.659	0.99	0.876	1.41
p			0.994	−0.150	124.629		1.236	
m + *p*			0.990	−0.151	124.644			

precision (R^2 = 0.950) whereas that for the *meta* ones does not show any correlation (R^2 = 0.489). While the ranges of φ and d_{CN} values for *para*- derivatives are large they are more narrow for the *meta*- ones, particularly for

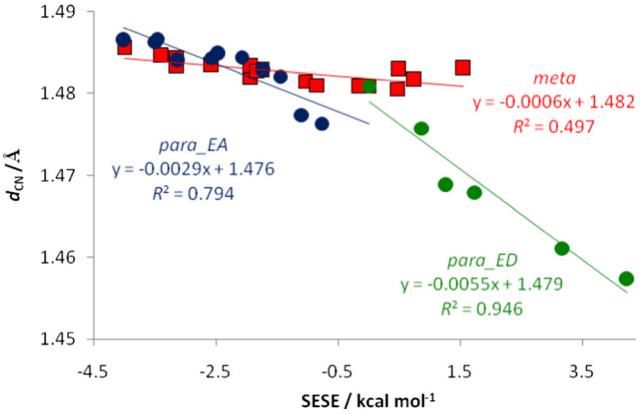


Fig. 3 Regression lines for d_{CN} plotted against SESE for *meta*- and *para*-nitrobenzene derivatives. The green regression line illustrates the relation for ED substituents and X = H (SESE ≥0)

d_{CN}. The latter would suggest a weaker influence of the resonance effect.

The correlation is even better between d_{NO} and φ angle (Fig. S8). For all considered relations (for *meta*-, *para*- and the joint data set) R^2 is greater than 0.920.

The reverse substituent effect

As documented recently [4, 21], changes in EA/ED properties of a substituent X in dependence of the kind and nature of the substituted species may be well described by cSAR(X). Table 3 presents cSAR(X) values for *meta*- and *para*-substituted nitrobenzene derivatives and, for comparison, for monosubstituted benzenes. To show significance of the reverse SE cSAR(X) values for nitro and amino groups in appropriate aniline derivatives are added [21] (Table 3, italics).

The most indicative observation is that the difference between cSAR(X) for *meta*- and *para*-values are different for EA substituents and for ED ones. The EA substituents in *meta*-derivatives have, as a rule, a stronger electron attracting power (cSAR(X) values are more negative) than the *para*-ones, whereas the ED substituents are stronger donating from *para*- than from *meta*-positions. The opposite trends have been documented for aniline series [21], illustrated by values of cSAR(X) for nitro- and amino-aniline derivatives (Table 3).

Table 3 cSAR(X) values for *para*- and *meta*-X-nitrobenzenes as well as for X-benzene (mono) derivatives, and the differences between cSAR(X) for *meta*- and *para*-nitrobenzenes as well as for X-nitrobenzene and X-benzene derivatives, ΔcSAR(X)

X	σ_p[a]	σ_m[a]	*para* cSAR(X)	*meta* cSAR(X)	mono cSAR(X)	*para* ΔcSAR(X)	*meta* ΔcSAR(X)	$\Delta cSAR(X)_{m\text{-}p}$
NO	0.91	0.62	−0.131	−0.152	−0.190	0.059	0.038	−0.021
NO_2	0.78	0.71	−0.170	−0.168	−0.202	0.032	0.034	0.002
			−0.284[b]	*−0.184*[b]		*−0.082*	*0.018*	*0.100*
COCl	0.69	0.53	−0.175	−0.193	−0.237	0.062	0.044	−0.018
CN	0.66	0.56	−0.152	−0.171	−0.202	0.050	0.031	−0.019
CF_3	0.54	0.43	−0.112	−0.129	−0.154	0.042	0.025	−0.017
COMe	0.50	0.38	−0.090	−0.113	−0.152	0.062	0.039	−0.023
COOH	0.45	0.37	−0.128	−0.149	−0.186	0.058	0.037	−0.021
CHO	0.42	0.35	−0.114	−0.136	−0.172	0.058	0.036	−0.022
$CONH_2$	0.36	0.28	−0.066	−0.087	−0.122	0.056	0.035	−0.021
Cl	0.23	0.37	0.016	−0.010	−0.036	0.052	0.026	−0.026
F	0.06	0.34	0.100	0.075	0.054	0.046	0.021	−0.025
H	0.00	0.00	0.042	0.019	0.000	0.042	0.019	−0.023
CH_3	−0.17	−0.07	0.060	0.031	0.006	0.054	0.025	−0.029
OMe	−0.27	0.12	0.168	0.126	0.102	0.066	0.024	−0.042
OH	−0.37	0.12	0.162	0.129	0.105	0.057	0.024	−0.033
NH_2	−0.66	−0.16	0.186	0.163	0.132	0.054	0.031	−0.023
			0.080[c]	*0.129*[c]		*−0.052*	*−0.003*	*0.049*
NMe_2	−0.83	−0.16	0.219	0.163	0.137	0.082	0.026	−0.056
Average	0.19	0.28	−0.011	−0.035	−0.066	0.055	0.030	−0.024
Range	1.74	0.87	0.394	0.356	0.374	0.050	0.025	0.058
Esd	0.51	0.26	0.138	0.125	0.134	0.011	0.007	0.012

[a] Values substituent constants taken from Ref. [3]

[b] Values obtained for *para*- and *meta*-NO_2-C_6H_4-NH_2, respectively, taken from Ref. [21]

[c] Values obtained for *para*- and *meta*-NH_2-C_6H_4-NH_2, respectively, taken from Ref. [21]

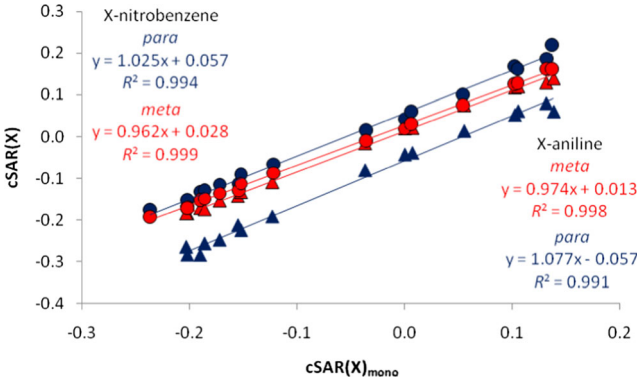


Fig. 4 Relations between cSAR(X) values for *meta*- and *para*-substituted nitrobenzene and aniline derivatives and cSAR(X) for monosubstituted benzenes; circles and triangles denote nitrobenzene and aniline systems, respectively; data for aniline systems are taken from Ref. [21]

Let us assume monosubstituted benzene derivatives as a reference system. Then the differences of cSAR(X) values for di-substituted (X-R-Y) and monosubstituted systems (Y = H), ΔcSAR(X), show in a numerical way how far the properties of substituent X may vary depending on the chemical nature of R-Y. These differences both for *meta*- and *para*-nitrobenzenes are positive. Therefore, the EA substituents characterize weaker attracting power and the ED stronger donating power than found for monosubstituted derivatives. The ranges of ΔcSAR(X) variations are for *meta*-substituted series half of that for the *para*-ones, similarly as in the case of the ranges of σ_p and σ_m constants variation.

It can be said that this study is devoted to the nitro group, therefore, let us look at its properties as a substituent. In nitrobenzene systems its EA power decreases, both for *para*- and *meta*-positions, by ca. 16% with respect to the observed in Ph-NO_2. When the amino group is the reaction site (aniline derivatives) the EA power of NO_2 increases significantly (up to 41%) for *para*-position and decreases (down to 9%) for the *meta*-one. In nitrobenzene systems the nitro group (the reaction site) strongly affects properties of ED substituents. In the case of the amino substituent – its ED power increases both for *para*- and *meta*- positions (by 41% and 24%, respectively, with respect to the observed in Ph-NH_2). The opposite changes of the ED power of NH_2 have been found for aniline systems (a decrease by 39% and 2%, respectively).

The above data present a clear documentation that, the EA/ED ability of the substituent strongly depend on the character of the reaction site. The application of cSAR parameter allows, in principle, to estimate the reverse SE in a quantitative way for any reaction site chosen. Additionally, a comparison of EA/ED properties of substituents in *meta*- and *para*-substituted nitrobenzene as well as in aniline derivatives in relation to the monosubstituted benzene derivatives is illustrated in Fig. 4. In this case differences in intramolecular interactions for nitrobenzene and aniline substituted derivatives with respect to monosubstituted systems can be discussed.

First, it is important to stress that in all cases correlations are very good with $R^2 > 0.99$. Secondly, presented data illustrate nicely the reverse SE. Finally, as results from the slopes of the presented relationships (Fig. 4) in *para*-series the intermolecular interaction of substituents with the fixed group (Y = NO_2 or NH_2) is stronger than in the Y = H substituted system, whereas for the *meta*- ones is oppositely.

Conclusions

All used characteristics of the SE: the Hammett σ constants, cSAR(X) and SESE are mutually correlated with higher determination coefficients for *para*-substituted derivatives than for the *meta*-ones. The best mutual correlation is for SESE *vs*. σ relationships since both characteristics take into account all interactions existing in the substituted systems, whereas cSAR(X) represent rather local EA/ED properties of the substituent.

Structural characteristics of the nitro group such as ONO angle or NO bond lengths fulfill well dependences between themselves as well as on the SE characteristics. Moreover, only insignificant differences between *meta*- and *para*-substituted derivatives are observed. Contrary to these, the dependences of CN bond length on all SE characteristics should be considered separately for ED substituents in *para*-position due to their much stronger interaction than all other data. This is due to the resonance effect and hence an appearance of the quinoid-like structure.

The reverse substituent effect is confirmed by showing the significant difference between cSAR(X) in *para*- and *meta*-located substituents. Comparison with cSAR(X) for monosubstituted benzene derivatives reveals much stronger electron attraction/donation in *para*-substituted derivatives than in *meta*-ones.

In summary, we can state that the application of the cSAR approach allows to estimate ED/EA properties of substituents independently of the system to which the substituent is attached. What is more, this is a handy way to quantify the reverse substituent effect.

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