

How the Substituent Effect Influences π -Electron Delocalisation in the Ring of Reactants in the Reaction Defining the Hammett Substituent Constants σ_m and σ_p .

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Dedicated to our friend Professor Marvin Charton in recognition of his outstanding contributions in the area of Physical Organic Chemistry

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Abstract: Application of the geometry (HOMA, EN, GEO) and magnetism based (NICS, NICS(1)) indices of aromaticity to optimised geometry of the ring in 12 meta – and 12 para – substituted benzoic acids and their anions by use of DFT computations at B3LYP/6-311+G(d,p) level has shown a very low substituent effect on the π -electron delocalisation. This resembles (qualitatively) the resistance of benzene (and typical aromatic systems) against reactions leading to the change of π -electron delocalisation.

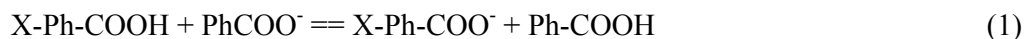
Keywords: Substituent effect, π -electron delocalisation, Hammett substituent constants, *ab initio* calculations.

Introduction

Substituent effect is one of the most frequently used terms in organic chemistry: in the last 7 years every day there appear about 20 papers in which this term is used in the title, in keywords or in the abstract [1]. These effects are most frequently quantified by use of a variety of substituent constants [2]. The idea was introduced by L. P. Hammett in the 30s of the 20th century [3] but till now it has been mainly playing a very important role in the description of the electronic influence of one group in an organic compound on another. Sometimes the substituent effect on the aromatic moiety itself is

important. The most typical case in organic chemistry is the directing effect of substituents [4]. Hence it is understandable to look at the changes in π -electron delocalization in the substituted ring(s). Moreover, the ring in substituted benzene derivatives typical of applying the Hammett treatment is the transmittor of the effect. Thus any knowledge on how this moiety is influenced by substituent effect is a subject of interest.

Recently Exner *et al.* [5] studied energetics of the acid-base equilibria for substituted benzoic acids applying an isodesmic reaction (1):



And then additionally they took into account two other isodesmic reactions (2) and (3):



Energies of these reactions, Δ_1 , Δ_2 , Δ_3 were derived by use of the DFT computation at B3LYP/6-311+G(d,p) level, and also by use of thermochemical data with a good agreement between them. However, none of these energies correlated well with σ_m and σ_p . If the donor para substituents were excluded, then the correlations improved. Moreover, if the two-parameter regression was applied to meta and para substituted series with σ_1 and σ_R as descriptors, the correlations became much better, with the correlation coefficient usually better than 0.96. Undoubtedly, in both reaction series, the meta and para ones, the energies Δ_2 , Δ_3 represent well the non-additivity energy of the intramolecular interactions between the substituents and the functional groups COOH and COO⁻. A question then arises: are these effects related in any way to the changes in π -electron delocalisation in the ring?

It is well known that the substituent effect is associated with an electron delocalisation [2b-e]. The question is how π -electron delocalisation in the ring depends on the substituent effects. In order to answer this question geometries of 25 meta and para substituted benzoic acids and their anions have been used for estimation of π -electron delocalisation parameters: the geometry based HOMA [6], EN and GEO [7] and magnetism based NICS [8] and NICS(1) [9].

Methods

Following the Hellmann-Feynman theorem [10] distribution of electronic density in the molecule determines the forces acting on the nuclei, which in turn, define geometry of the molecule in question. Thus geometry may be a source of reliable information on the electron distribution, and employing appropriate references, may be used for description of π -electron delocalization. Thus aromaticity index HOMA [6, 7] may be used firmly [11] for estimation of π -electron delocalisation except in a few cases like planarized cyclooctatetraene [12] and alike [13]. The extended form of HOMA [7] allows one to get information about the nature of dearomatisation. If dearomatisation is due to an increase of bond alternation, then the GEO index is large; if dearomatisation is due to bond elongation, then the EN term is large. The formula used is:

$$\text{HOMA} = 1 - \left[\alpha (\text{R}_{\text{opt}} - \text{R}_{\text{av}})^2 + \frac{\alpha}{n} \sum (\text{R}_{\text{av}} - \text{R}_i)^2 \right] = 1 - \text{EN} - \text{GEO} \quad (4)$$

where n is the number of bonds taken into the summation; α is a normalisation constant (for CC bonds $\alpha = 257.7$) fixed to give HOMA = 0 for a model non-aromatic system and HOMA=1 for the system

with all bonds equal to the optimal value R_{opt} assumed to be realised for full aromatic systems (when CC bond R_{opt} is equal to 1.388 Å); R_i stands for a running bond length. The magnetism based indices – NICS [8] and NICS(1) [9] are simply a negative value of the absolute shielding estimated in the centre of the ring and 1 Å above it. All data discussed were calculated by use of the DFT computation at B3LYP/6-311+G(d,p) level taken from ref [5].

Results and Discussion

Computation of HOMA, EN, GEO, NICS and NICS(1) for 25 *meta*- or *para*- derivatives of benzoic acids and their anions gave the results presented in Tables 1 and 2.

Table 1. Computation of HOMA, EN, GEO, NICS and NICS(1) for 25 *meta*- or *para*- derivatives of benzoic acids.

Entry	Substituent	HOMA	GEO	EN	NICS	NICS1	σ
1	H	0.982	0.004	0.015	-9.73	-11.38	0
2	3-CH ₃	0.978	0.005	0.018	-9.89	-11.36	-0.06
3	3-CH ₃ Cl	0.981	0.003	0.016	-10.17	-11.38	-0.09
4	3-CF ₃	0.985	0.003	0.012	-10.39	-11.54	0.44
5	3-CHO	0.977	0.005	0.019	-9.64	-11.37	0.36
6	3-COOCH ₃	0.980	0.003	0.017	-9.75	-11.35	0.33
7	3-CN	0.976	0.005	0.019	-10.38	-11.54	0.62
8	3-NH ₂	0.973	0.006	0.021	-10.17	-10.70	0
9	3-NO ₂	0.988	0.005	0.007	-10.95	-11.58	0.73
10	3-OH	0.984	0.003	0.013	-11.10	-11.32	0.1
11	3-OCH ₃	0.976	0.008	0.017	-11.05	-11.46	0.11
12	3-F	0.985	0.010	0.005	-11.85	-11.73	0.34
13	3-Cl	0.987	0.005	0.009	-10.75	-11.48	0.37
14	4-CH ₃	0.970	0.008	0.022	-9.62	-11.16	-0.16
15	4-CH ₂ Cl	0.977	0.006	0.017	-10.14	-11.31	0.12
16	4-CF ₃	0.985	0.004	0.012	-10.59	-11.72	0.53
17	4-CHO	0.972	0.011	0.018	-9.98	-11.57	0.43
18	4-COOCH ₃	0.977	0.007	0.016	-10.06	-11.54	0.45
19	4-CN	0.972	0.011	0.018	-10.56	-11.66	0.67
20	4-NH ₂	0.951	0.025	0.024	-9.08	-9.88	-0.62
21	4-NO ₂	0.987	0.005	0.007	-11.23	-11.76	0.78
22	4-OH	0.977	0.010	0.013	-10.27	-10.74	-0.36
23	4-OCH ₃	0.967	0.015	0.018	-10.30	-10.93	-0.29
24	4-F	0.987	0.008	0.005	-11.33	-11.36	0.05
25	4-Cl	0.987	0.004	0.010	-10.50	-11.32	0.22
esd		0.0084	0.0049	0.0052	0.6335	0.4054	0.3548
mean		0.978	0.007	0.015	-10.377	-11.325	0.2028

Table 2. Computation of HOMA, EN, GEO, NICS and NICS(1) for 25 *meta*- or *para*- derivatives of benzoate anions.

Entry	Substituent	HOMA	GEO	EN	NICS	NICS1	σ
1	H	0.978	0.001	0.021	-9.72	-11.50	0
2	3-CH ₃	0.976	0.001	0.022	-9.789	-11.37	-0.06
3	3-CH ₃ Cl	0.975	0.002	0.022	-10.07	-11.74	-0.09
4	3-CF ₃	0.979	0.002	0.019	-10.36	-11.67	0.44
5	3-CHO	0.964	0.009	0.028	-9.42	-11.39	0.36
6	3-COOCH ₃	0.970	0.005	0.025	-9.62	-11.38	0.33
7	3-CN	0.967	0.002	0.026	-10.34	-11.65	0.62
8	3-NH ₂	0.977	0.002	0.022	-10.13	-10.79	0
9	3-NO ₂	0.985	0.002	0.013	-10.73	-11.57	0.73
10	3-OH	0.985	0.002	0.014	-11.05	-11.36	0.1
11	3-OCH ₃	0.983	0.002	0.016	-11.05	-11.55	0.11
12	3-F	0.980	0.013	0.007	-11.85	-11.78	0.34
13	3-Cl	0.986	0.004	0.010	-10.90	-11.59	0.37
14	4-CH ₃	0.977	0.002	0.022	-9.71	-11.31	-0.16
15	4-CH ₂ Cl	0.972	0.005	0.023	-9.99	-11.38	0.12
16	4-CF ₃	0.980	0.003	0.017	-10.35	-11.69	0.53
17	4-CHO	0.956	0.014	0.029	-9.39	-11.40	0.43
18	4-COOCH ₃	0.963	0.010	0.027	-9.55	-11.36	0.45
19	4-CN	0.960	0.013	0.028	-10.29	-11.63	0.67
20	4-NH ₂	0.978	0.001	0.021	-9.95	-10.67	-0.62
21	4-NO ₂	0.978	0.006	0.015	-10.51	-11.48	0.78
22	4-OH	0.984	0.001	0.015	-10.83	-11.23	-0.36
23	4-OCH ₃	0.978	0.003	0.019	-10.88	-11.45	-0.29
24	4-F	0.985	0.008	0.006	-11.66	-11.68	0.05
25	4-Cl	0.987	0.003	0.010	-10.78	-11.53	0.22
esd		0.0085	0.0042	0.0075	0.6659	0.2609	0.3549
mean		0.976	0.005	0.019	-10.357	-11.446	0.202

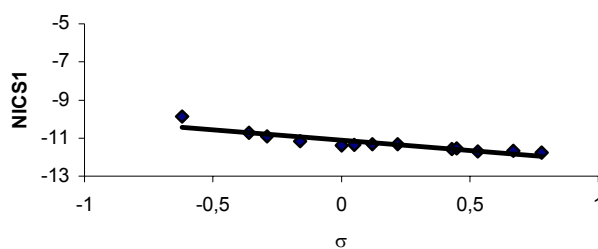
Evidently, the substituent effect on π -electron delocalisation is very small, when HOMA, EN and GEO are used. Comparison of the ranges of variation by means of the ranges themselves (a difference between the maximum and the minimum value) variance as well as interquartile ranges [14] indicates a slightly stronger effect for *para* substituted acids and their anions, than for *meta* systems. Nevertheless the variation of HOMA aromaticity index is within a few percent of the whole scale of HOMA (0.0 for nonaromatic systems, 1.0 for a fully aromatic one). As a rule EN terms are greater than GEO terms. This means that the elongation of bond length is a more important factor than the alternation represented by the GEO term. Also rings in acid molecules are slightly more influenced than those in anions.

Interestingly, the electron donating substituents affect the ring more strongly in acid derivatives, than in the case of anion. This is clearly due to the nature of the reaction site (or the fixed group). In

the first case this is the electron accepting COOH group, whereas in the second case it is the anionic COO⁻ group. Moreover, the carboxylate - group has its own strong local resonance effect and hence its negative charge is weakly involved in the interactions with the π -electron system of the ring.

The NICS and NICS(1) illustrate a similar behaviour, but NICS(1) which is more responsible for π -electron delocalisation [9] varies as a rule less strongly than NICS measured in the center of the ring. This is shown clearly by all parameters of dispersion: the ranges, variance, and the interquartile ranges. Due to very small variation of aromaticity indices in most cases any relationships to substituent constants failed. The only exception is the case of *p*-substituted acids where there exists good correlation between NICS(1) and sigma as shown in Figure 1.

Figure 1 Dependences of σ substituent constants on NICS ($r=-0.905$) for *p*-substituted acids.



The above results may be compared with analogous data for exocyclically substituted fulvene [15] and heptafulvene [16]. In both cases very good correlations with σ_p (and σ_p^- for electron accepting substituents in the case of fulvene and σ_p^+ for the electron donating substituents in the case of heptafulvene, respectively) were observed and the dispersion of the data measured by variance or interquartile ranges was around ten times greater than in the case of *meta* and *para* substituted benzoic acid derivatives and their anions.

It seems reasonable to interpret the above as follows. In the case of benzene derivatives the changes in π -electron delocalisation are mostly possible in the direction of a decrease in aromaticity – and this is not easy to be realized. A π -electron system in aromatic compounds has a tendency to retain its structure, this observation being one of the criteria of a most general definition of aromaticity [17] which states that aromatic are cyclic π -electron systems exhibiting:

- (i) increased stability when compared with acyclic analogues,
- (ii) averaged bond lengths, intermediate between the typical single and double bonds,
- (iii) induction of the π -electron ring current when the system is exposed to external magnetic field and
- (iv) the tendency of the system to retain its π -electron structure in chemical reactions – substitution is privileged over the addition reactions.

Those which fulfill all four criteria (i) – (iv) are defined as fully aromatic compounds [15].

Statistical analysis of polysubstituted benzene derivatives [18] based on molecular geometry of 2045 rings has shown that the variations in HOMA index, taken as mean values of 12 different topological ways of substitution, are in the range between 0.866 and 0.995, which means that the dispersion of HOMA values is much smaller than that observed for individual rings in polycyclic benzoid hydrocarbons (0.271 – 0.862), thus indicating a much stronger effect from the topological location of the ring than the substituent effect.

Conclusions

As a general conclusion it may be stated that similarly to the resistance of benzene (and most typical aromatic systems) in chemical reactions to change its π -electron structure, i.e. to maintain the π -electron delocalisation, the substituent effect as a kind of perturbation meets similar resistance to change the π -electron delocalisation in the ring.

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References and Notes

1. Institute for Scientific Information, Philadelphia (1996-2004). Retrieved in February 2004.
2. (a) Exner, O. In *Correlation Analysis in Chemistry*; Plenum Press: New York, **1978**; Chap. 10, p. 439; (b) Charton, M. *Progr. Phys. Org. Chem.* **1981**, *13*, 119; (c) Fujio, M.; McIver, R.T.; Taft, R.W. *J. Am. Chem. Soc.* **1981**, *103*, 4017-4029; (d) Charton, M. *Progr. Phys. Org. Chem.* **1987**, *16*, 287-315; (e) Hansch, C.; Leo, A.; Taft, R.W. *Chem. Rev.* **1991**, *91*, 165-195; (f) Shorter, J. *Pure Appl. Chem.* **1994**, *66*, 2451-2468; (g) Shorter, J. *Pure Appl. Chem.* **1997**, *69*, 2497-2510.
3. Hammett, L. P. *Physical Organic Chemistry*; McGraw – Hill: New York, **1940**.
4. (a) Stock, L.M.; Brown, H.C. *Adv. Phys. Org. Chem.* **1963**, *1*, 36-154; (b) Bunce, E.; Norris, A.R.; Russel, K.E. *Quart. Rev.* **1968**, *XXII*, 123-146; (c) Hoggett, J.G.; Moodie, R.B.; Penton, R.B.; Schofield, K. *Nitration and Aromatic Reactivity*; Cambridge University Press: Cambridge, U.K., **1971**; (d) Taylor, R. *Electrophilic Aromatic Substitution*; Wiley: New York, **1990**.
5. Exner, O.; Böhm, S. *J. Org. Chem.* **2002**, *67*, 6320-6327.
6. (a) Kruszewski, J.; Krygowski, T.M. *Tetrahedron Lett.* **1972**, 3839-3842; (b) Krygowski, T.M. *J. Chem. Inf. Comput. Sci.* **1993**, *33*, 70-78.
7. Krygowski, T.M.; Cyrański, M. *Tetrahedron* **1996**, *52*, 1713-1722.
8. Schleyer, P.v.R.; Maerker, C.; Dransfeld, H.; Jiao, H.; Hommes, N. J. R. v. E. *J. Am. Chem. Soc.* **1996**, *118*, 6317.
9. Schleyer, P.v.R.; Monoharar, M.; Wang, Z.; Kiran, B.; Jiao, H.; Puchta, R.; Hommess, N.J.R.v.E. *Org. Lett.* **2001**, *3*, 2465-2468.
10. (a) Hellmann, H. *Einführung in die Quantenchemie*; Franz Deuticke: Leipzig, **1937**; (b) Feynman, R.P. *Phys. Rev.* **1939**, *56*, 340.
11. Schleyer, P.v.R. *Chem. Rev.* **2001**, *101*, 1115-1117.

12. Krygowski, T.M.; Pindelska, E.; Cyrański, M.K.; Häfelinger, G. *Chem. Phys. Lett.* **2002**, *359*, 158-162.
13. Fowler, P.W.; Havenith, R.W.A.; Jenneskens, L.W.; Soncini, A.; Steiner, E. *Angew. Chem.* **2002**, *41*, 1558-1560.
14. Czerminski, J.; Iwasiewicz A.; Paszek Z.; Sikorski A. *Statistical Methods in Applied Chemistry*; PWN and Elsevier: Warsaw and Amsterdam, **1990**.
15. Stępień, B. T.; Krygowski, T. M.; Cyrański, M. K. *J. Org. Chem.* **2002**, *67*, 5987-5992.
16. Stępień, B. T.; Krygowski, T. M.; Cyrański, M. K. *J. Phys. Org. Chem.*, **2003**, *16*, 426-430.
17. (a) Krygowski, T.M.; Cyrański, M.K.; Czarnocki, Z.; Häfelinger, G.; Katritzky A.R. *Tetrahedron* **2000**, *56*, 1783-1796; (b) Cyrański, M.K., Krygowski T.M., Katritzky A.R., Schleyer P.v.R. *J. Org. Chem.* **2002**, *67*, 1333-1338.
18. Cyrański, M.; Krygowski, T. M. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 1142-1145.