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Relation between resonance energy and substituent resonance effect in *P*-phenols†

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ABSTRACT: Molecular geometries of phenol and its 17 *p*-substituted derivatives were optimized at the B3LYP/6–311+G** level of theory. Three homodesmotic and three isodesmotic reaction schemes were used to estimate aromatic stabilization energies (ASE) and the substituent effect stabilization energy (SESE). Other descriptors of π-electron delocalization (HOMA and NICS, NICS(1) and NICS$(1)_{zz}$) were also estimated. The SESE and ASE values correlated well with one another as well as with substituent constants. Much worse correlations with substituent constants were found for other aromaticity indices. The NICS$(1)_{zz}$ values are the most negative for unsubstituted phenol, indicating its highest aromaticity; that was not the case for NICS(1) and NICS. Copyright © 2005 John Wiley & Sons, Ltd.

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KEYWORDS: substituent effect; substituent constants; aromaticity; π-electron delocalization; NICS; ASE; *ab initio* calculation

INTRODUCTION

The early estimations of aromatic stabilization energy (ASE)[1] are associated with the pioneering work by Pauling and Sherman[2] and by Kistiakowsky *et al.*,[3] leading to the resonance energy of benzene. Despite different methodological approaches they reached exactly the same value for the stabilization energy of the system (36 kcal^{-1} mol^{-1}). Their ideas were extended later to other cyclic π-electron systems,[4] including heterocycles and polycyclic systems. Nowadays, the information about the increased stability of aromatic compounds due to cyclic π-electron delocalization[5] is obtained most often by using the isodesmic and/or homodesmotic reaction formalism.[1,6,7] A disadvantage of the former approach is the large span of estimated stabilization energies for a given system[8–10] (e.g. ~50 kcal for benzene!),[7] which is unacceptable. In turn, if a homodesmotic reaction is carefully chosen for a given set of systems, homogeneous in variation of the structure, the estimated ASE values provide much more consistent information about the stability of the system and extent of π-electron delocalization.[11] Similar to the aromatic stability, the substituent resonance (or mesomeric) effect has long been investigated because it plays an important role in the physicochemical behaviour of substituted species. Qualitatively it appeared early in the 1930s of the 20th century.[12,13] A quantitative way of modelling the substituent effect began with the pioneering works by Hammett[14] and then it was extended in numerous ways.[15–17] Original Hammett constants σ_p and resonance constants R^+, as well as substituent constants σ^+,[18] are well established for a large collection of substituents.[17] The resonance effect depends both on the system to which the substituent is attached and on the choice of the counterpart probe group,[19] therefore a variety of scales of resonance constants are known.[16,17,20] Historically, dipole moments and UV spectra were used to demonstrate the effects of through-conjugation.[21] A recent study on 'resonance energy in benzene and ethene derivatives in the gas phase as a measure of resonance ability of various functional groups' (Ref. 22) did not solve the problem of the relation between resonance energy of the substituted ring and the resonance substituent effects. The isodesmic reactions that were chosen to solve this problem did not represent the resonance energy of the substituted ring but rather the resonance effect of the substituent. Moreover, the energies obtained did not correlate well with the substituent constants. Most probably interactions of the substituents with 'bare' benzene and ethene π-electron systems were too weak not to be perturbed by side-effects such as polarizability or interactions of the X in CH_2X groups with π-electrons of the ring.

The purpose of this report is to analyse the relation between the substituent effect in *p*-substituted phenols

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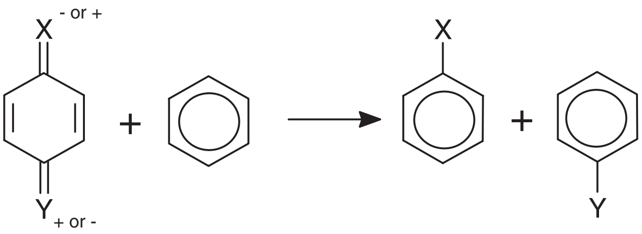
(i.e. systems that served to estimate σ^-) and the aromaticity of the ring. Both of these effects are associated with resonance; in the former case there is a strong resonance effect between the substituents via the benzene ring and in the latter the aromaticity of the ring is associated with the resonance energy (or, more generally, the aromatic stabilization energy). Both of these effects are associated with changes in the stability of the system due to variation in π-electron delocalization.

METHODS

The substituent effect stabilization energy (SESE)[23] is the energetic measure of the increase in the stability of a system due to X . . . Y interactions both with the ring and through the ring, which may be accounted for by the homodesmotic reaction (1).



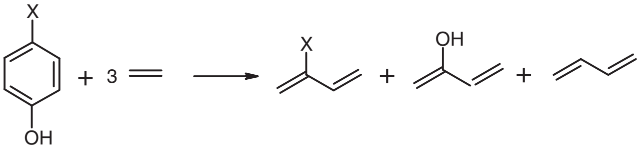
(1)

The changes of aromaticity in monosubstituted derivatives (right-hand side of the equation) are very small[24] because the rings resist well the perturbations leading to changes of π-electron structure. This is well-reflected in a specific reactivity of benzene where substitution dominates over addition; thus, the system tends to re-establish its initial type of structure. Similar to the case of benzene, the electronic structure of monosubstituted derivatives is denoted by a circle. In the case of *p*-disubstituted benzenes [the left-hand side of Eqn (1)] where X and Y belong to opposite groups of substituents (electron-accepting and electron-donating substituent) through-resonance appears, which leads to large modifications in the geometry of the ring[25] towards the quinoid canonical structure formation.[26] This kind of structure therefore is more suitable for use in reaction (1). The through-resonance is an extra (stabilization) effect unobserved in monosubstituted derivatives. Although the interactions between X and Y account mostly for the through resonance effect, the inductive effects should not be considered as completely negligible.[16,27]

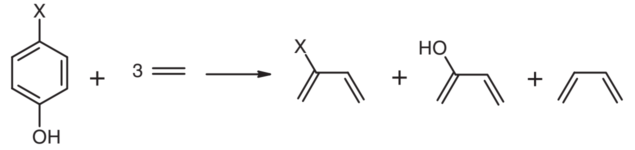
Five reaction schemes were proposed to estimate the extent of aromatic stabilization energies in substituted phenols. Equations (2) and (3) are reactions schemes based on the Dewar and Schmeising approach,[28] which proposed that the stability of an aromatic system should refer to an acyclic analogue, e.g. butadiene-1,3. This evaluation model (ASE 2–3)[29] is probably the most common homodesmotic approach for estimation of the aromatic stabilization of benzene.[30] In the case of substituted species a problem appears with reference systems (substituted butadienes) that have different lowest energy conformations, which in turn makes direct comparisons of the stabilization energies rather difficult. Moreover, the substituents additionally may stabilize the reference systems, and this energetic effect changes from case to case. To overcome this difficulty, reactions (4) and (5) have been proposed. In this case the reference butadiene system is not perturbed because the substitution takes place on the ethene units that are part of the reaction scheme. A disadvantage of the approach is that the reactions are not homodesmotic.

Another reaction scheme, reaction (6), is based on tautomeric equilibria comparisons involving the total energies of two species: a *p*-substituted phenol derivative and its non-aromatic exocyclic isomer. This is a simple modification of the estimation method of aromatic stabilization energy recommended recently by Scheyer and Pühlhoffer.[31] Similar to reactions (4) and (5), this reaction is more isodesmic than homodesmotic but we expect to obtain a minimization of possible errors for the non-cyclic π-electron delocalization effects and creditable results for comparison with other reaction schemes.

The systems with strongly positive ASEs are aromatic whereas those with strongly negative ASE are considered to be anti-aromatic.



(2)



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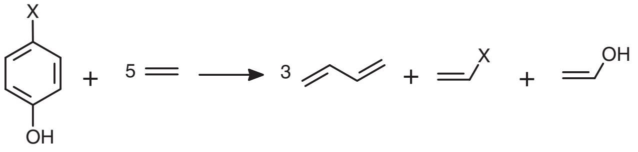

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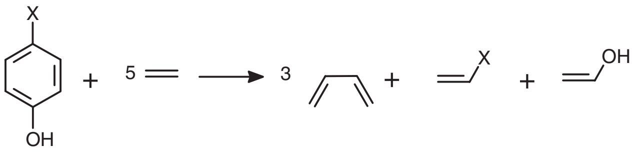

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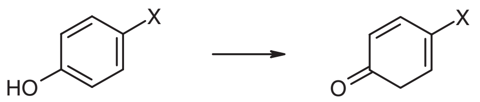


(6)

From the point of view of geometry the extent of π-electron delocalization can be deduced from the bond lengths of the ring (C—C bond lengths) using the Harmonic Oscillator Model of Aromaticity (HOMA).[32] Among many easily accessible quantitative definitions of aromaticity based on the geometric criterion, this approach was suggested to be the most reliable.[33] It is defined as follows[34]

$$\mathrm{HOMA} = 1 - \frac{\alpha}{n}\sum\left(R_{\mathrm{opt}} - R_{\mathrm{i}}\right)^2 \tag{7}$$

where n is the number of bonds taken into the summation; α is a normalization constant (for C—C bonds, $\alpha = 257.7$) fixed to give HOMA = 0 for a model non-aromatic system, e.g. Kekulé structure of benzene,[35] and HOMA = 1 for the system with all bonds equal to the optimal value R_{opt}, assumed to be realized for full aromatic systems (for C—C bonds, $R_{\mathrm{opt}} = 1.388$ Å);[36] and R_{i} stands for a running bond length.

Finally, the nucleus-independent chemical shift (NICS)[37] was used as a descriptor of aromaticity from the magnetic point of view. Originally the NICS has been defined as a negative value of the absolute shielding computed in the ring centre. In this paper it was computed[38] at the ring centre (NICS) and 1 Å above ring centre [NICS(1)].[39] Because the 'out of plane' component of the NICS tensor computed 1 Å above the ring centre (denoted here as NICS(1)$_{zz}$)[40] was found to be a more efficient descriptor of the π structure of the ring,[24b] we also included this characteristic in our analysis. Within the model assumptions the rings with negative values of NICS are qualified as aromatic. The more negative the value of the index, the more aromatic the system is expected to be.

Molecular geometries of phenol and its 17 *p*-substituted derivatives were optimized at the B3LYP/6–311+G** level of theory with the use of the Gaussian 98 program.[38] All the structures corresponded to minima at the B3LYP/6–311+G** level, with no imaginary frequencies. The energies were corrected by the B3LYP/6–311+G** zero-point energies. The GIAO/HF/6–31+G* method was used for the NICS, NICS(1) and NICS(1)$_{zz}$. The HOMA values were also based on B3LYP/6–311+G**-optimized geometries.

RESULTS AND DISCUSSION

Table 1 presents the indices of aromaticity—SESE, ASE [Eqns (2)–(5)] NICS, NICS(1), NICS(1)$_{zz}$ and HOMA—and substituent constants used in the analyses. When SESE values are plotted against the resonance constants σ_p,[17] a reasonably good linear relationship is obtained as shown in Fig. 1. The correlation coefficient of 0.912 illustrates that the experimentally estimated constants are well represented by the SESE values.

A closer analysis of Table 1 shows that the overall range of SESE values is ~4 kcal mol^{-1}. The ranges for ASE values are definitely larger: ~10 kcal mol^{-1} for reactions (2) and (3) and ~5–6 kcal mol^{-1} for reaction schemes (4)–(6). Similarly, the estimated standard

Table 1. Calculated aromaticity indices of *p*-substituted (X) phenols: SESE, ASE(2) and ASE(3) (kcal mol^{-1}); NICS, NICS(1) and NICS(1)$_{zz}$ (ppm); HOMA and substituent constants σ_p

X	SESE	ASE(2)	ASE(3)	ASE(4)	ASE(5)	ASE(6)	HOMA	NICS	NICS(1)	NICS(1)$_{zz}$	σ_p
—NO	2.0	28.0	36.5	25.2	35.5	18.6	0.963	−9.9	−10.4	−26.4	0.91
—NO$_2$	1.2	28.8	34.3	25.6	36.0	20.2	0.985	−11.2	−10.9	−27.0	0.78
—CN	0.8	24.9	34.1	24.6	35.0	19.9	0.970	−11.0	−11.1	−28.1	0.66
—COCl	1.8	29.0	35.4	25.7	36.0	21.0	0.964	−10.3	−10.7	−26.7	0.61
—COCH$_3$	1.3	28.4	34.2	24.9	35.2	19.9	0.973	−10.3	−10.8	−27.5	0.5
—COOCH$_3$	1.2	28.3	34.8	25.6	35.9	19.0	0.978	−10.4	−10.8	−27.4	0.45
—COOH	1.3	28.4	34.9	25.7	36.0	19.5	0.976	−10.3	−10.7	−27.4	0.45
—CHO	1.4	27.0	33.7	25.2	35.5	20.6	0.971	−10.2	−10.8	−27.6	0.42
—CONH$_2$	0.9	26.5	33.4	24.9	35.2	19.1	0.980	−10.6	−11.1	−28.1	0.36
—CCH	0.3	24.3	33.3	23.6	33.9	18.3	0.960	−11.0	−11.0	−28.1	0.23
—Cl	−0.6	22.3	31.0	22.8	33.2	17.9	0.993	−11.7	−11.2	−28.5	0.23
—F	−1.3	20.5	29.5	23.0	33.4	17.4	0.992	−12.8	−11.6	−29.4	0.06
—H	0.0	22.4	32.1	23.7	34.0	17.4	0.989	−10.8	−11.3	−29.9	0.00
—Ph	0.0	24.9	33.6	22.1	32.4	17.7	0.977	−10.4	−10.6	−28.0	−0.01
—CH$_3$	−0.4	22.4	31.4	22.5	32.8	16.4	0.983	−10.9	−11.1	−29.0	−0.17
—OCH$_3$	−1.6	19.4	28.0	21.5	31.8	14.9	0.986	−12.2	−11.5	−29.1	−0.27
—NH$_2$	−2.0	20.7	29.1	20.5	30.8	16.4	0.983	−11.4	−10.8	−27.7	−0.66
—OH	−1.7	20.0	29.0	22.4	32.7	17.6	0.992	−12.3	−11.4	−28.8	−0.37
Mean	0.26	24.8	32.7	23.9	34.2	18.4	0.979	−11.0	−11.0	−28.0	—
SD	1.27	3.39	2.48	1.63	1.63	1.63	0.01	0.82	0.33	0.94	—
Variance	1.62	11.49	6.14	2.65	2.65	2.65	0.0001	0.67	0.11	0.89	—

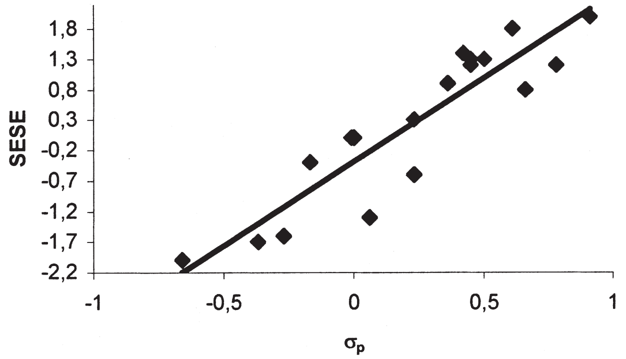
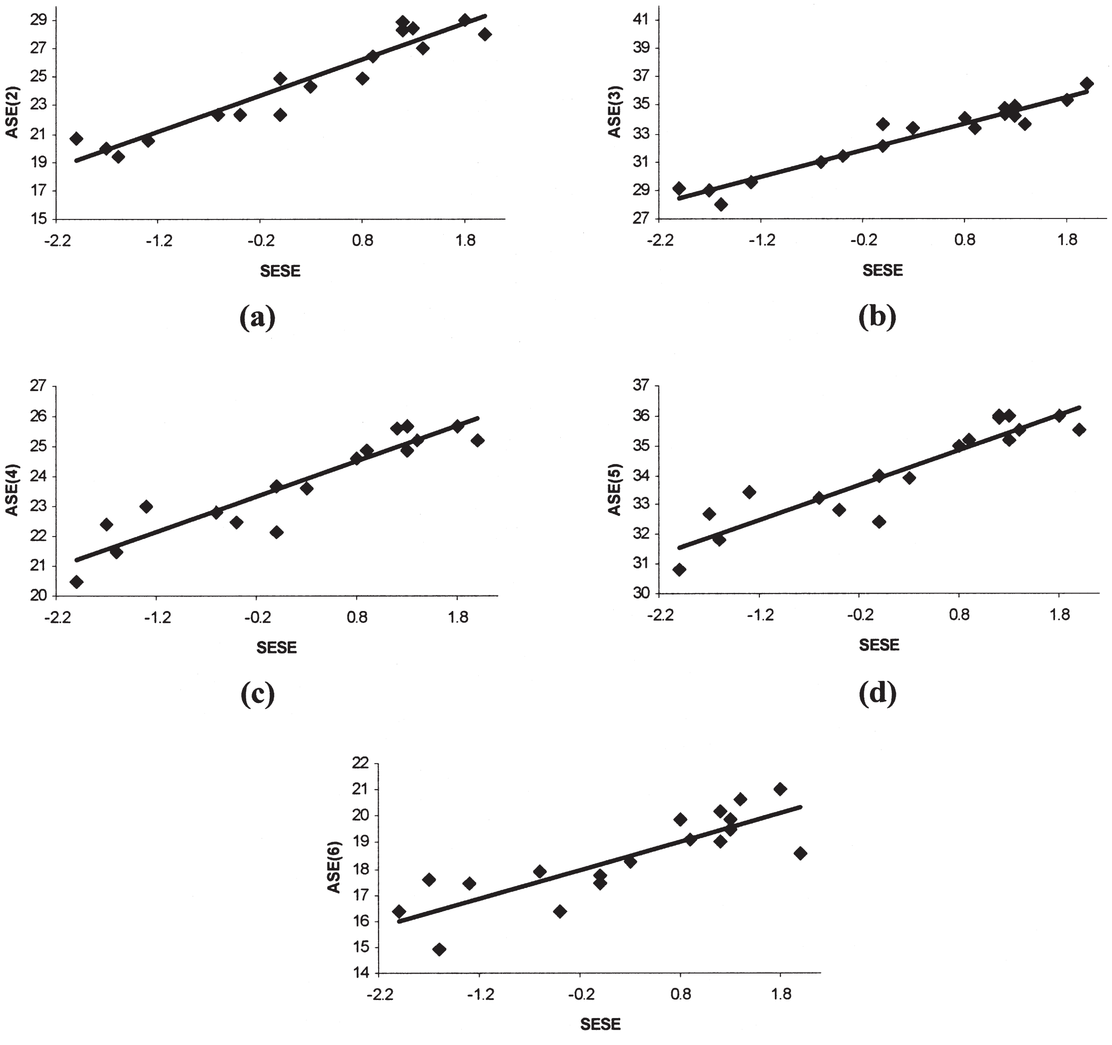


Figure 1. The SESE values plotted against values

deviations for the ASE are usually larger than those for the SESE. This means that despite the moderate energetic effect of non-additivity of substituents, they may lead to quite substantial modifications of the π-electron structure of the ring. Importantly, from the aromatic stabilization energy criterion, this kind of interaction between substituents does not necessarily lead to a lowering in the stability of the systems. In many cases (mostly for the electron-attracting substituents) the ASE values are larger than for benzene.

Comparison of ASE with SESE values leads to the answer to the title problem. Figure 2 shows the dependences of the ASE [Eqns (2)–(6)] on the SESE values. They all present a tendency towards a linear relationship, and the quality of correlation (as justified by correlation coefficients) depends to some extent on the kind of reaction. The best correlation was found between SESE and ASE(3), with a correlation coefficient of 0.968; the worst one was between SESE and ASE(6). This indicates some kind of a relationship between the resonance energy (ASE) and the resonance effects (SESE). An analysis of the regression coefficient of the former correlation [Eqn (5)] leads to the



(a) **(b)**

(c) **(d)**

(e)

Figure 2. The SESE values plotted against values of: (a) ASE(2) [correlation coefficient (cc) = 0.955]; (b) ASE(3) (cc = 0.968); (c) ASE(4) (cc = 0.924); (d) ASE(5) (cc = 0.920); (e) ASE(6) (cc = 0.836)

conclusion that the substituent effect on ASE is almost twice as large as that observed for SESE.

$$\mathrm{ASE}(3) = 1.89\,\mathrm{SESE} + 32.20 \qquad (8)$$

Becasue on the left-hand side of all reactions the substituent effects are the same, the substituent effects on the right-hand side of the reactions have to be weaker for SESE [reaction (1)] than for the ASE estimation [reactions (2)–(6)]. This might be associated with the well-known fact that olefines exhibit π-electron delocalization much more weakly[41] and hence the substituent effect on the π-system is also weaker.

The correlation analysis also reveals fair dependences between the aromatic stabilization energies and the Hammett substituent constants σ_p. The best of them were found for ASE(4) and ASE(5), as quantified by the correlation coefficients of 0.904 and 0.910, respectively.

Interestingly, only qualitative correlations were found between the geometric and magnetic descriptors of π-electron delocalization HOMA, NICS, NICS(1) and NICS$(1)_{zz}$ values on the Hammett σ_p. Figure 3 presents these dependences. The large scatter may be due to the much smaller variation in magnitudes of these indices compared with the variation of ASE. In the case where the range of variations is significantly smaller, the worse dependences on substituent effect descriptors may be due to a possible greater influence on the aromaticity indices resulting from some side-effects.

The hydroxy group of substituted phenols is not a strong electron-donating substituent. In the case of *p*-substituted benzyl cations the dependences of aromaticity indices on σ_p^+ were found to be much more indicative.[19] This is obviously due to the fact that the CH_2^+ substituent interacts very strongly with the counterpart substituents and hence the level of noice is relatively low. This allowed stronger effects on π-electron delocalization to be observed.

Finally, an important remark should be made that, among the three kinds of NICS, NICS$(1)_{zz}$ is the only one for which the value for unsubstituted phenol is most negative, i.e. represents the case of the highest aromaticity. This is similar to the case for monosubstituted benzene derivatives,[24b] for which the unsubstituted ring is most aromatic only when NICS$(1)_{zz}$ is used.

CONCLUSIONS

It may be concluded that the resonance energy (ASE values) of *p*-substituted phenol derivatives correlates well with the substituent effect stabilization energy (SESE values). The resistance of the system against breaking a cyclic π-electron delocalization is correlated with the measure of the non-additivity in energy due to the substituents interacting through the ring.

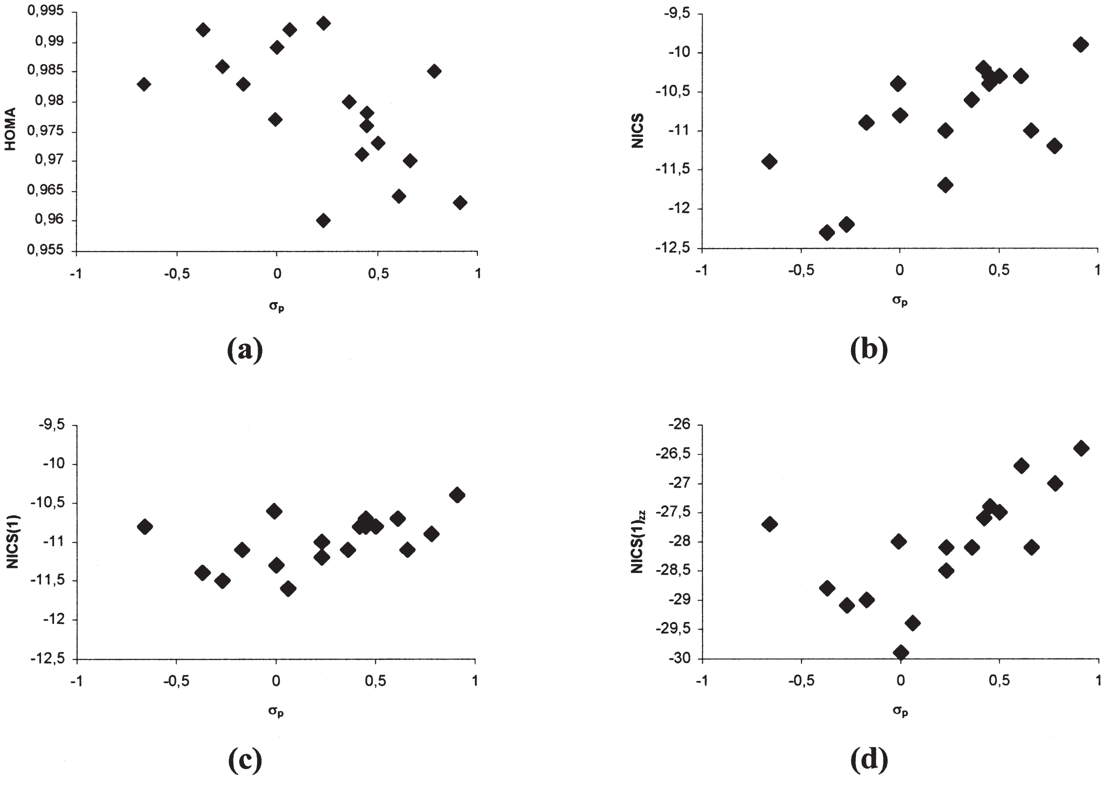


Figure 3. The scatter plots of HOMA (a), NICS (b), NICS(1) (c) and NICS$(1)_{zz}$ (d) values vs. σ_p

Supplementary material

Total energies, zero-point energies and the Cartesian coordinates at B3LYP/6–311+G** for all analysed systems are available in *Wiley Interscience*.

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REFERENCES

1. Minkin VI, Glukhovtsev MN, Simkin BYa. *Aromaticity and Antyaromaticity, Electronic and Structural Aspects*. Wiley: New York, 1994.
2. Pauling L, Sherman J. *J. Chem. Phys*. 1933; **1**: 606.
3. Kistiakowsky GB, Ruhoff JR, Smith HA, Vaughan WE. *J. Am. Chem. Soc*. 1936; **58**: 146–153.
4. Wheland GW. *The Theory of Resonance and its Application to Organic Chemistry*. Wiley: New York, 1947.
5. Pauling L. *The Nature of Chemical Bond and the Structure of Molecules in Crystals* (3rd edn). Cornell University Press: Ithaca, 1960.
6. (a) George P, Trachtman M, Bock CW, Brett AM. *Theor. Chim. Acta* 1975; **38**: 121; (b) George P, Trachtman M, Brett AM, Bock CW. *J. Chem. Soc., Perkin Trans. 2* 1977: 1036–1047.
7. Krygowski TM, Cyrański MK. *Chem. Rev*. 2001; **101**: 1385–1419.
8. Krygowski TM, Cyrański MK, Czarnocki Z, Häfelinger G, Katritzky AR. *Tetrahedron* 2000; **56**: 1783–1796.
9. Cyrański MK, Krygowski TM, Katritzky AR, Schleyer PvR. *J. Org. Chem*. 2002; **67**: 1333–1338.
10. Cyrański MK, Schleyer PvR, Krygowski TM, Jiao H, Hohlneicher G. *Tetrahedron* 2003; **59**: 1657–1665.
11. Kovacević B, Barić D, Maksić ZB, Muller T. *Chem. Phys. Chem*. 2004; **5**: 1352–1364.
12. Robinson R. *Two Lectures on an 'Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions'*. Institute of Chemistry of Great Britain and Ireland: London, 1932.
13. (a) Ingold CK. *J. Chem Soc*. 1933: 1120; (b) Ingold CK. *Chem. Rev*. 1934; **15**: 225–274.
14. Hammett LP. *Physical Organic Chemistry* (2nd edn). Mc-Graw-Hill: New York, 1970.
15. Jaffe HH. *Chem. Rev*. 1953; **53**: 191–261.
16. Charton M. *Progr. Phys. Org. Chem*. 1981; **13**: 119–251.
17. Hansch C, Leo A, Taft RW. *Chem. Rev*. 1991; **91**: 165–195.
18. Hansch C, Leo A. *Substituent Constants for Correlation Analysis in Chemistry and Biology*. Wiley: New York, 1979.
19. Morao I, Hilier IH. *Tetrahedron Lett*. 2001; **42**: 4429–4431.
20. Bromilow L, Brownlee RTC, Craik DJ, Sadek M, Taft RW. *J. Org. Chem*. 1980; **45**: 2429–2438.
21. Exner O, Krygowski TM. *Chem. Soc. Rev*. 1996: 71–75.
22. Exner O, Böhm S. *J. Chem. Soc. Perkin 2* 2000; 1994–1999.
23. (a) Pross A, Radom L, Taft RW. *J. Org. Chem*. 1980; **45**: 818–826; (b) Hehre WJ, Radom l, Schleyer PvR, Pople JA. *Ab initio Molecular Orbital Theory*. Wiley: Chichester, 1986; 364 ff.
24. (a) Krygowski TM, Stępień BT. *Pol. J. Chem*. 2004; **78**: 2213–2217; (b) Krygowski TM, Ejsmont K, Stępień BT, Cyrański MK, Poater J, Sola M. *J. Org. Chem*. 2004; **69**: 6634–6640.
25. Krygowski TM, Maurin J. *J. Chem. Soc. Perkin Trans. 2* 1989; 695–698.
26. Hiberty PC, Ohanessian G. *J. Am. Chem. Soc*. 1984; **106**: 6963–6968.
27. (a) Exner O, Böhm S. *Chem. Eur. J*. 2002; **8**: 5147–5152; (b) Wiberg KB. *J. Org. Chem*. 2002; **67**: 4787–4794.
28. Dewar MJS, Schmeising HN. *Tetrahedron* 1959; **5**: 166–178.
29. (a) Dewar JMS, Gleicher GJ. *J. Am. Chem. Soc*. 1965; **87**: 692–696; (b) Dewar MJS, DeLlano C. *J. Am. Chem. Soc*. 1969; **91**: 789–795; (c) Haddon RC, Raghavachari K. *J. Am. Chem. Soc*. 1985; **107**: 289–298; (d) Schleyer PvR, Jiao H, Hommes NJRvE, Malkin VG, Malkina O. *J. Am. Chem. Soc*. 1997; **119**: 12669–12670.
30. Maksic ZB, Baric D, Petanjek I. *J. Phys. Chem. A* 2000; **104**: 10873–10881.
31. Schleyer PvR, Pühlhoffer F. *Org. Lett*. 2002; **4**: 2873–2876.
32. Kruszewski J, Krygowski TM. *Tetrahedron Lett*. 1972; 3839–3842.
33. Schleyer PvR. *Chem. Rev*. 2001; **101**: 1115–1117.
34. Krygowski TM. *J. Chem. Inf. Comput. Sci*. 1993; **33**: 70–78.
35. Julg A, François Ph. *Theor. Chim. Acta* 1967; **7**: 249.
36. Krygowski TM, Cyrański MK. *Tetrahedron* 1996; **52**: 10255–10264.
37. Schleyer PvR, Maerker C, Dransfeld A, Jiao H, Hommes NJRvE. *J. Am. Chem. Soc*. 1996; **118**: 6317–6318.
38. Frisch MJ, Trucks GW, Schlegel HB, Gill PMW, Johnson BG, Robb MA, Cheesman JR, Keith T, Peterson GA, Montgomery JA, Raghavachari K, Al-Laham MA, Zakrzewski VG, Ortiz JV, Foresman JB, Cioslowski J, Stefanov BB, Nanayakkara A, Challacombe M, Peng CY, Ayala PY, Chen W, Wong MW, Andres JL, Replogle ES, Gomperts R, Martin RL, Fox DJ, Binkley JS, Defrees DJ, Baker J, Stewart JP, Head-Gordon M, Gonzales C, Pople JA. *Gaussian 98*. Gaussian: Pittsburgh, PA, 1998.
39. Schleyer PvR, Manoharan M, Wang Z-X, Kiran B, Jiao H, Puchta R, Hommes NJRvE. *Org. Lett*. 2001; **3**: 2465–2468.
40. Corminboeuf C, Heine T, Seifert G, Schleyer PvR, Weber J. *Phys. Chem. Chem. Phys*. 2004; **6**: 273–276.
41. Hess BA, Schaad LJ. *J. Am. Chem. Soc*. 1971; **93**: 2413–2416.