RESONANCE ENERGY IN BENZENE DERIVATIVES WITH A VARIABLE FUNCTIONAL GROUP

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Three isodesmic reactions were investigated in which a variable substituent is transferred from a saturated to an unsaturated hydrocarbon residue: ethane → ethene, methane → benzene, ethane → benzene. Their reaction energies could serve as a measure of substituent resonance ability. They were calculated for 31 substituents by the density functional theory (DFT) at the B3LYP/6-311+G(d,p) level, and served as a model for systematic comparison of the DFT energies and experimental enthalpies of formation $\Delta_f H°(298)$. It turned out that calculations at this level are more reliable than experiments; they disagree sometimes with $\Delta_f H°(298)$ measured at different times and in different laboratories but agree better with the values calculated by simple additive scheme. Some particularly suspicious values were pointed out. The DFT reaction energies of the isodesmic reactions, $\Delta_1 E – \Delta_3 E$, were correlated with the standard scales of resonance and with other scales of substituent effects by multiple linear regression and principal component analysis. The three scales are fairly similar to each other (correlation coefficients 0.68–0.83), depend rather strongly on resonance (75% of the variance) but involve still at least one component which could not be explained in terms of common substituent effects. Certainly they do not depend – not even slightly – on the inductive effect, steric effect or polarizability.
Keywords: Arenes; Benzene; Enthalpy of formation; Isodesmic reactions; Resonance energy; Substituent effects; *Ab initio* calculations; DFT.

The concept of resonance has developed in several directions. A long-term program consists in calculating relative resonance ability of various groups (substituents) when they are bonded to a constant system, mostly to a benzene ring bearing still a probe group. The results were expressed in a customary scale of constants denoted σ_R. They were mostly based on equilibrium and rate constants in water or in aqueous solutions[1–3] and should be applied in similar conditions. Their physical meaning can be understood without referring to the concept of resonance, simply as a difference between reactivities of an aromatic and a similar aliphatic derivative[4].

Alternatively, the σ_R constants can be estimated from reactivities in the gas phase[5], from physical properties[6] or from quantum chemical calculations on defined model systems[7,8]. Another approach is calculating the resonance energies. This quantity was defined with some problems mainly for aromatic conjugated systems[9]; for characterizing substituents it can be represented within the framework of isodesmic reactions[10]. We investigated recently two such reactions[11], Eq. (*1*) on the basis of calculated energies and Eq. (*2*) on the basis of experimental enthalpies of formation. Reaction enthalpies of these reactions were attributed mainly to resonance but the two series were not proportional either to each other or to the common scales of σ_R. Before us, Eqs (*1*)–(*3*) were investigated at a lower level of theory and for a smaller number of substituents[12]. Their reaction energies $\Delta_1 E$–$\Delta_3 E$ were claimed[12] to correlate with the inductive and resonance parameters σ_F and σ_R but they need not be necessarily associated with resonance and may be called simply stabilization energies[10,12] or separation energies[13]. Note that Eqs (*1*)–(*3*) are isodesmic[10a] reactions but are not homodesmotic[10d] since one X–C_{sp^3} bond is replaced by a X–C_{sp^2} bond. In our opinion, a homodesmotic reaction cannot be constructed in this case.

$$CH_3CH_2\text{–}X + H_2C=CH_2 \ \rightleftharpoons\ H_2C=CH\text{–}X + C_2H_6 \qquad (1)$$

$$CH_3X + C_6H_6 \ \rightleftharpoons\ C_6H_5X + CH_4 \qquad (2)$$

$$C_2H_5X + C_6H_6 \ \rightleftharpoons\ C_6H_5X + C_2H_6 \qquad (3)$$

In this communication, we used the density functional theory[14] (DFT) to calculate the reaction energies of the reactions in Eqs (*1*)–(*3*) for an extended set of 31 substituents. Importance of a sufficiently large set of substituents was confirmed recently in the calculations of electron densities[8b]. The values of $\Delta_1 E$–$\Delta_3 E$ were exploited for two purposes: Firstly, they were systematically correlated with various scales of resonance effects and with other properties by means of regression analysis and principal component analysis. The main question was whether they could serve as a measure of resonance. Secondly, they offered a good opportunity of comparing calculated and experimental energies; both could be at present of comparable reliability although loaded with errors of different kind.

CALCULATIONS

DFT calculations were performed at the B3LYP/6-311+G(d,p) level according to the original proposal[14] exploiting the Gaussian 94 program[15]. Full geometry optimization and vibrational analysis were carried out in all cases. The minimum-energy conformation was searched for, in questionable cases starting from two or more initial structures. Some indications concerning the geometry of the least-energy conformation are given in Table I together with the pertinent energies. Certain less populated conformations were searched for in all justified cases as explained in the section Conformation. The reaction energies $\Delta_1 E$–$\Delta_3 E$ of the isodesmic reactions, Eqs (*1*)–(*3*), were calculated from the energies if necessary corrected for the presence of higher-energy conformers. Their values are listed in Table II.

Principal component analysis was carried out using a standard program[16].

RESULTS AND DISCUSSION

Conformation

Occurrence of several conformers in equilibrium increases the effective energy over the value calculated for the least-energy conformer and should be taken into account. In the theory of substituent effects, it would be desirable to compare substituents with the same conformation on both sides of the equation; secondary conformers can be neglected. They cannot be neglected in comparison with experiments which relate to the conformer equilibrium at a given temperature. However, the excess energy $\delta E_{ef}(T)$ over the minimum-energy conformer is most often minute. As usual, we took the difference of the calculated energies of two conformers, ΔE, as equal to the difference of Gibbs energies, $\Delta G°(T)$. Then the increase in the effective energy $\delta E_{ef}(298)$ is given by Eq. (*4*).

$$\delta E_{ef}(T) = \Delta E \, e^{-\Delta E/RT}/(1 + e^{-\Delta E/RT}) \qquad (4)$$

This correction becomes negligible in the two limiting cases. When ΔE is small, the conformers possess near energies and can be neglected. This is the case particularly with the conformation of alkyl groups: *e.g.* in the compounds $C_6H_5CH_2CH_3$, $C_6H_5CH(CH_3)_2$ and all derivatives C_2H_5X. When ΔE is greater than say 10 kJ mol^{-1}, the second conformer is virtually absent. This is the case particularly with the groups COOH, COOCH$_3$ and OCOCH$_3$

TABLE I
Calculated energies of monosubstituted benzenes and of reference compounds[a]

| Substituent | C_6H_5X | | E(DFT) | |
	E(DFT)	conformation	CH_3X	C_2H_5X
H	–232.3112375		–40.5339278	–79.8565455
CH_3	–271.6387778	one H sp	–79.8565455	–119.1810828
C_2H_5	–310.9628080	C sp	–119.1810828	–158.5054807
$CH(CH_3)_2$	–350.2862991	one C sp	–158.5064326	–197.8292773
$C(CH_3)_3$	–389.6070228	one C sp	–197.8313933	–237.1526104
$CH=CH_2$	–309.7307574	coplanar	–117.9455761	–157.2696593
$C\equiv CH$	–308.4772460		–116.6927939	–156.0168926
C_6H_5	–463.4227175	C–C–C–C 41°	–271.6387778	–310.962808
CH_2Cl	–731.2607401	C–C–C–Cl 90°	–539.4804665	–578.8049849
CF_3	–569.4608204	one F sp	–377.6865107	–417.0109574
NH_2	–287.6876273	coplanar	–95.8938400	–135.2214503
$N(CH_3)_2$	–366.3140496	coplanar	–174.5276840	–213.8526333
$NHCOCH_3$	–440.3913539	coplanar, C–N–C–O sp	–248.6059340	–287.9331242
	–440.3869020	coplanar, C–N–C–O ap	–248.6019247	–287.928818
OH	–307.5586296	coplanar	–115.7649436	–155.0950566
OCH_3	–346.8675611	coplanar	–155.0770361	–194.4045008
$OCOCH_3$	–460.2556472	C–C–O–C 66°, C–O–C–O sp	–268.4747269	–307.8040789
SH	–630.5252561	coplanar	–438.7432192	–478.0687922
SCH_3	–669.8484213	coplanar	–478.0666923	–517.3919596
F	–331.5801120		–139.7913251	–179.1232936
Cl	–691.9341784		–500.1517384	–539.4804665
Br	–2 805.8538829		–2 614.0741864	–2 653.4020415
CHO	–345.6690693	coplanar	–153.8821476	–156.0168926
$COCH_3$	–385.0016873	coplanar	–193.2181762	–232.5393718
COOH	–420.9481463	coplanar, O–C–O–H sp	–229.1647182	–268.4894844
$COOCH_3$	–460.2581050	coplanar, O–C–O–C sp	–268.4747264	–307.7980136
$CONH_2$	–401.0702582	C–C–C–O 21°	–209.2883302	–248.6128170
$CSNH_2$	–724.0246518	C–C–C–S 34°	–532.2420958	–571.5662668
CN	–324.5777601		–132.7961554	–172.1204347
N=NH	–341.7938025	coplanar E	–150.0076089	–189.3335117
	–341.7829264	coplanar Z	–149.9996287	–189.3245411
NO_2	–436.8746070	coplanar	–245.0915559	–284.4199744
SO_2CH_3	–820.2804020	C–C–S–C 90°	–628.5018165	–667.8279443

[a] In a.u., calculated at a B3LYP/6-311+G(d,p) level.

TABLE II
Reaction energies of isodesmic reactions, Eqs (1)–(3)^a

Substituent	$\Delta_1 E_{calc.}$ ^{b}	$\Delta_2 E_{calc.}$	$\Delta_2 H_{exp.}$	$\Delta_3 E_{calc.}$	$\Delta_3 H_{exp.}$	$b^{(2)d}$
H	0	0	0	0	0	0
CH$_3$	–12.3	–12.9	–23.2	–7.9	–12.8	0.07
C$_2$H$_5$	–11.8	–11.6	–23.6	–6.9	–11.1	0.13
CH(CH$_3$)$_2$	–14.9	–6.7	–18.8	–6.1	–8.4	0.18
C(CH$_3$)$_3$	–15.0	4.4	–15.6	0.7	–5.4	0.19
CH=CH$_2$	–28.6	–20.7	–30.5	–16.8	–19.3	–0.03
C≡CH	–20.5	–18.7	–15.6	–14.9	–4.7	0.21
C$_6$H$_5$	–20.4	–17.4	–25.6	–13.7	–14.8	0.14
CH$_2$Cl	–6.4	–7.8	–26.2	–2.8	–17.8	–0.19
CF$_3$	6.1	7.9	–11.9	12.7		0.22
NH$_2$	–33.1	–43.3	–47.4	–30.1	–33.7	–0.06
N(CH$_3$)$_2$	–33.6	–23.8	–33.2	–17.7		–0.01
NHCOCH$_3$	–29.2^c	–21.3		–9.3		0.28
OH	–32.8	–43.0	–52.8	–23.3	–28.4	0.05
OCH$_3$	–17.6	–34.7	–40.8	–22.0	–18.3	0.18
OCOCH$_3$	1.5	–9.5	–27.1	8.2	–2.8	0.37
SH	–13.8	–12.4	–19.0	–4.6	–5.1	–0.03
SCH$_3$	–14.7	–11.6	–21.1	–4.6	–8.4	0.08
F	–12.3	–30.1	–19.0	–5.6	–20.2	0.21
Cl	–7.0	–13.5	–21.1	2.6	–0.1	0.21
Br	–0.3	–6.3	–16.0	7.5	1.8	0.28
CHO	–24.0	–25.2	–28.9	–22.1	–17.6	0.42
COCH$_3$	–19.9	–16.3	–27.1	–20.0	–15.1	0.51
COOH	–12.0	–16.1	–20.8	–10.4	–9.0	0.45
COOCH$_3$	–13.6	–15.9	–35.3	–14.2	–61.7	0.79
CONH$_2$	–16.2^c	–12.1		–7.2		0.38
CSNH$_2$	–17.1^c	–13.8		–9.7		0.29
CN	–11.4	–11.3	–12.6	–6.9	+0.6	–0.07
N=NH	–10.1^c	–23.3		–14.7		0.13
NO$_2$	–2.7	–15.1	–15.6	0.2	+2.8	–0.15
SO$_2$CH$_3$	–0.3^c	–3.3	–22.7	5.9	–11.8	0.54

^{a} In kJ mol^{-1}, based on the calculation at the B3LYP/6-311+G(d,p) level unless otherwise noted. ^{b} Based on the calculations at the MP2/6-31G(d,p) level; ref.[11]. ^{c} This work, MP2/6-31G(d,p) level. ^{d} Second component scores of PCA, orthogonal to the resonance component.

whose stable *sp* conformation on the C(O)–O bond is known both from experiments and calculations. Hence, the second conformer was not taken into consideration in Table I. There remained few intermediate cases. A relatively stable conformer was found in the case of the substituent $NHCOCH_3$ on the C–N bond: the *sp* conformation is preferred in all cases but the energies of the ap conformer are also given in Table I. Nevertheless, the population of this conformer is less than 1% and its presence is not manifested in the values of Δ_2E and Δ_3E. Conformation on the bond C_{ar}–X was examined particularly with the molecules $C_6H_5NHCOCH_3$ and $C_6H_5OCOCH_3$ since the former was found to be planar and the latter nonplanar with a torsion angle of 66° (Table I). Detailed examination has not revealed any secondary energy minimum in either case. In the case of phenyl acetate, the energy barrier (in planar form) is only 2.8 kJ mol^{-1}; the most stable conformation agrees well with the experimental results obtained under different conditions[17] (54–65°). In the case of acetanilide, the barrier in the perpendicular form is 11.7 kJ mol^{-1}; planar or nearly planar conformation was assumed[18] both from calculations and from ^{1}H NMR spectra.

Similar problems arise when several configurations are possible. This is the case only with the substituent N=NH but with no consequences for the total energy: the *E* isomer is preferred (Table I), whereas the *Z* isomer is populated to less than 0.01%. In any case, the highest possible value of $\Delta E_{ef}(298)$ according to Eq. (*4*) is 0.63 kJ mol^{-1} (for $\Delta E = 2.9$). This value is immaterial for comparison with any experimental quantity (see the next section).

Comparison of Experimental and Calculated Energies

In Table II, columns 2, 3 and 5, we have three sets of calculated reaction energies, $\Delta_{1-3}E$(DFT) of the isodesmic reactions (Eqs (*1*)–(*3*)). They should express more or less the resonance ability of the given substituents. Irrespective of possible interpretation, these values offer an opportunity of comparing the DFT energies with experimental reaction enthalpies $\Delta_2H°(298)$ and $\Delta_3H°(298)$ (Table II, columns 4 and 6) which have been obtained from known enthalpies of formation[19] $\Delta_fH°(298)$. Recent systematic comparison[20] of calculated and experimental enthalpies used calculations at a lower level than in this work (B3LYP/6-31G(d)) but supplemented by calculation of thermal enthalpies by statistical thermodynamics. However, the main difference against the present work was in using empirical correction terms for bonds of different type; in this way, the calculated enthalpies

of formation were obtained explicitly[20]. In our opinion, the isodesmic reactions offer a better opportunity for comparison since several empirical and statistical terms cancel and even some thermodynamic terms may cancel at least partly[21]. However, correlations of our calculated energies with experiments revealed bad fit with some marked deviations; even correlations between the two experimental values $\Delta_2 H°$ and $\Delta_3 H°$ showed some outliers, difficult to explain. We examined the suspicious enthalpies of formation both in the original literature and by means of the additive scheme of Domalski and Hearing[19a]. This scheme is based on a set of group values (increments) for a given atom or atom group with respect to the nearest neighbors. The agreement with experiment is given[19a] as better than 4 kJ mol^{-1} in 67% of all compounds, better than 8 kJ mol^{-1} in 83%. In the case of our simple derivatives, the lower limit should be reached. Reliability of any additive scheme depends on the number of variable increments and/or special correction terms, further on the validity range[22]. This scheme is very detailed and has been derived from all available data of organic compounds[19a]. When an experimental value does not agree with this scheme, it means essentially that it does not conform with the experiments on similar compounds. An example is given in Fig. 1, where the calculated energies $\Delta_2 E$ and experimental $\Delta_2 H°(298)$ pertinent to Eq. (*2*) are plotted. Of the evi-
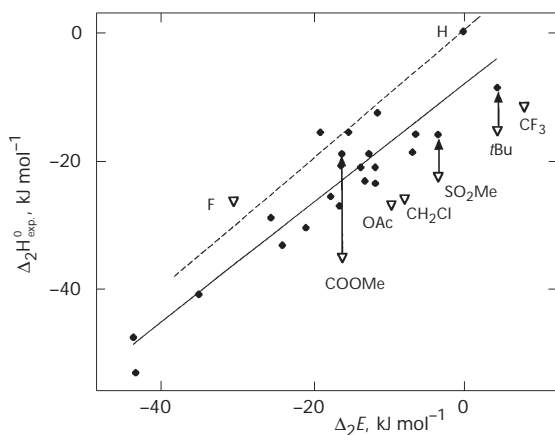

FIG. 1

Plot of calculated reaction energies $\Delta_2 E$ and experimental reaction enthalpies $\Delta_2 H°(298)$ of the isodesmic reaction, Eq. (*2*); suspected experimental values are noted by ∇, their possible corrections carried out according to the additive scheme (ref.[19a]) are shown by arrows. Full line is the regression line after eliminating the outliers, broken line corresponds to $\Delta_2 H°(298) = \Delta_2 E$

dent outliers at least three can be attributed to uncertainties in the experimental[23] $\Delta_f H°(298)$. The deviation of the substituent *tert*-butyl is due to $\Delta_f H°(298)$ of *tert*-butylbenzene: experimental[23a] –22.6 kJ mol^{-1}, calculated from group contributions[19a] –15.8 kJ mol^{-1}. Similar differences were found for methyl benzoate (all values in kJ mol^{-1}): experimental[23b] –287.9, calculated[19a] –271.6, and for methyl phenyl sulfone, experimental[23c] –253.4, calculated[19a] –246.8. We are of the opinion that these experimental $\Delta_f H°(298)$ should be reinvestigated, in any case they are not reliable. When we preferred the calculated[19a] values to the experimental ones[23], we got the corrections shown in Fig. 1 by arrows: the improvement is evident. Compounds containing fluorine deserve a particular mention. Due to the paucity of experimental data, the pertinent group values were calculated each on the basis of few compounds; in the case of compounds CH_3F and $C_6H_5CF_3$, the group value was estimated just from this one compound and any comparison with the calculated value is not possible. In addition, the experimental data are less accurate and even the DFT calculations might be somewhat less reliable.

When the outliers in Fig. 1, including the two fluoro derivatives, are eliminated, the standard deviation from the regression line (full line in Fig. 1) is 4.6 kJ mol^{-1}. This value corresponds well to the assumed uncertainties in $\Delta_f H°$. On the other hand, there is an evident shift in the sense that calculated values are less negative and the point for hydrogen deviates from the regression, see the broken line in Fig. 1. With Eq. (*3*) we obtained very similar results since the problem is mostly in the compound C_6H_5X; details will not be discussed. The general shift might be attributed to a common shortcoming in calculating ΔE instead of $\Delta H°(298)$ while the scatter of individual points might be caused from a great part by experimental errors.

Experimental values of $\Delta_f H°$ were tentatively classified into four categories according to their estimated accuracy[19b]. Most our compounds belong to class 3 with the "average error" less than 10 kJ mol^{-1}, but *tert*-butylbenzene belongs to class 4 (less than 30 kJ mol^{-1}). This classification may appear as too pessimistic but it draws correctly attention to certain suspicious values. The actual reliability is certainly better, particularly in the relative values when similar compounds are compared, investigated by the same method and in the same laboratory. On the other hand, the accuracy given in the original literature, sometimes better than 1 kJ mol^{-1}, might be often overestimated.

On selected examples we have also checked whether the agreement between calculated and experimental values cannot be improved by more so-

phisticated calculations. The resulting $\Delta_2 E$ obtained for two substituents at the B3LYP/6-311+G(3df,2pd)//B3LYP/6-311+G(d,p) level differed only by few tenths of kJ mol^{-1} from data of Table II. Also calculation of the sum of electronic and thermal enthalpies, $\Delta H^\circ(298)$, by statistical thermodynamics[15] did not improve the agreement with experiment. Some previous experience with this technique was also merely negative[11].

We conclude this section by an opinion that the experimental values of $\Delta_f H^\circ(298)$ are in general not sufficiently precise to allow efficient testing of calculated energies. On the contrary, the calculations appear to be more reliable at the present state of development. This statement should be specified in two respects. Firstly, its main reason is that some experimental values are loaded with big errors that cannot be easily revealed; many other values might be reliable. Secondly, it is certainly valid for simpler structures but need not apply to molecules with a strong tension and/or strong steric hindrance. Our set of compounds did not contain such compounds but very differing structures were included, both aliphatic and aromatic. Our comparison with experiments, carried out within the framework of isodesmic reactions, is in our opinion more efficient than that of Allinger *et al.*[20] which is restricted to a class of very similar compounds and uses empirical corrections. The fit given[20] (2.0 kJ mol^{-1}) seems hardly reliable since it is smaller than the experimental uncertainty. The treatment is evidently overparametrized. Our analysis that follows is based on the calculated energies of isodesmic reactions, $\Delta_1 E$–$\Delta_3 E$.

Reaction Energies of Isodesmic Reactions

The reaction energies $\Delta_1 E$–$\Delta_3 E$ of Eqs (*1*)–(*3*) are certainly controlled mainly by the resonance of substituents X with the ethenyl or phenyl group, although it has been proven in the previous work[11] that other factors may be operating. For instance the substituents CH_2Hal and $CH_2SO_2CH_3$ showed large values of $\Delta_2 E$ explained by homoconjugation in compounds $C_6H_5CH_2X$. In our set of compounds, only the CH_2Cl substituent is present, in which the effect is weak and can be neglected in the whole context. We believed that deviations of some other substituents may be assigned to experimental errors and that the pattern will be simplified when we restrict ourselves in this paper only to calculated values. This has not been confirmed. Already preliminary calculations have shown that mutual correlations between $\Delta_1 E$, $\Delta_2 E$ and $\Delta_3 E$ are relatively weak (Table III, lines 1–3); they also correlate rather weakly with the standard substituent constants σ_R. The latter correlation is associated with two problems. Firstly, choice of this

standard was not quite evident; we chose the values derived by Charton[3a] from carefully selected reactivities in aqueous solution; essential were pK values of 4-substituted benzoic acids in water. However, the choice of the standard scale is not critical: with other scales, the correlations are little different. Secondly and more important, resonance of both donor and acceptor groups causes negative values of $\Delta_1 E$–$\Delta_3 E$ while the pertinent σ_R values are negative for donors and positive for acceptors. Hence we carried out correlation with the absolute values $|\sigma_R|$, Table III, lines 4–6. The correlation is poor, although there is some relation in the highest values, *viz.* for substituents NH_2, NMe_2, OH. Previously, we unraveled this problem[11] by assigning signs to ΔE in agreement with the sign of σ_R; the apparent fit was better. The heart of the problem is in different behavior of acceptor and donor substituents[24,25]. While the donor groups form a series with graduated resonance ability and control most regularities observed, the acceptor groups form merely a cluster with very similar properties; their resonance ability is in many cases close to zero[24]. This is shown in Fig. 2. Some general dependence on the resonance of the donor group is evident but certain outliers can be also observed. The acceptor groups do not contribute to this de-

TABLE III
Correlations of the energies of the isodesmic reactions, $\Delta_1 E$–$\Delta_3 E$, with various substituent parameters

No.	Response function	Explanatory variables	b^a	R^b	SD^b	f^b
1	$\Delta_1 E$	$\Delta_2 E$	0.61(12)	0.677	7.8	29
2	$\Delta_1 E$	$\Delta_3 E$	0.80(11)	0.792	6.5	29
3	$\Delta_3 E$	$\Delta_2 E$	0.73(9)	0.827	5.9	29
4	$\Delta_1 E$	$|\sigma_R|$ ref.[3a]	–27(7)	0.578	8.7	29
5	$\Delta_2 E$	$|\sigma_R|$ ref.[3a]	–34(8)	0.648	9.0	29
6	$\Delta_3 E$	$|\sigma_R|$ ref.[3a]	–20(8)	0.426	9.5	29
7	$\Delta_2 E$	$|\sigma_R|$ σ_I	–34(8) –4(9)	0.648	9.2	28
8	$\Delta_2 E$ don.	σ_R σ_I	37(9) –6(13)	0.739	9.2	17
9	$\Delta_2 E$ acc.	σ_R σ_I	–11(78) 22(21)	0.359	9.5	8
10	$\Delta_1 E$	$|\sigma_R|$ σ_I υ σ_χ σ_α	–31(7) 16(8) 15(8) –6(8) 25(9)	0.751	7.6	25

^{a} Regression coefficients with standard deviations in parentheses. ^{b} Correlation coefficient R, standard deviation from the regression SD, and degrees of freedom f, respectively.

pendence. Their values of $\Delta_1 E - \Delta_3 E$ are not zero but are almost constant and need not be due to resonance. When we made the correlations in Table III, lines 4–6 only with donor groups ($f = 19$), the results were almost unchanged (not given).

It has been thus proven that other factors than resonance are operative in the values of $\Delta_1 E - \Delta_3 E$. We tried to identify them by two statistical approaches: multiple linear regression (MLR) and principal component analysis (PCA). MLR was carried out with $|\sigma_R|$ and with the following additional explanatory variables: the inductive (localized) substituent constant σ_I derived from acidities of substituted acetic acids in water[3a], exalted resonance constants[3b], polarizability constants σ_α calculated with a quantum chemical model[5,8a], calculated[8a] electronegativity constants σ_χ, steric constants υ estimated from standard geometries[26], and some other sets of steric constants. The result was completely negative: no factor was revealed on which $\Delta_1 E - \Delta_3 E$ would depend even slightly. Of the many correlations performed, we report in Table III only few examples. Particular attention was given to correlations with σ_R and σ_I known as Dual Substituent Parameter treatment[1,2]. Greenberg and Stevenson[12] claimed a correlation of $\Delta_1 E - \Delta_3 E$ (calculated at a 4-31G level) with σ_R and σ_I. Since they used simple σ_R rather than their absolute values $|\sigma_R|$, they were obliged to correlate donor and acceptor substituents separately. Some correlations included only 4 items and were not significant: although R varied from 0.38 to 0.996, the regression
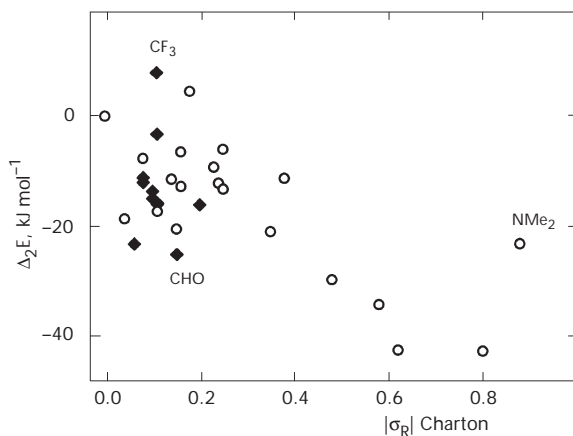

FIG. 2
Dependence of the reaction energy $\Delta_2 E$ of the isodesmic reaction, Eq. (*2*), on the absolute values of standard resonance constants $|\sigma_R|$ (ref.[3a]); ○ donor substituents, ◆ acceptor substituents

coefficients at σ_I were strongly variable and sometimes very small – their significance was not tested. We carried out correlations with σ_I and $|\sigma_R|$ and found no dependence on σ_I. An example is given (Table III, line 7) with Δ_2E for which the best fits were claimed[12]; results with Δ_1E or Δ_3E were not better. Separate correlations of donors and acceptors were not better, particularly for the acceptors (Table III, lines 8 and 9). The results reported[12] can be thus explained only by a small number of data. Common misuse of DSP treatment was criticized from a general point of view[27].

Further MLR with more explanatory variables, particularly with steric constants υ, polarizability constants and electronegativities did not reveal any significant explanatory variable. From many attempts, one example is given in Table III, line 10. As far as we know, the only factor describing interaction in neutral molecules that could possibly explain even the differences between Δ_2E and Δ_3E is the constant φ of Istomin and Palm[28]. However, we have not found any relation of our data to these constants, this was hindered also by the small number of available values.

More objective results, although also negative, were obtained from PCA. We prepared a data matrix of the dimensions 8 descriptors × 31 objects (substituents). The descriptors included the three reaction energies (Δ_1E, Δ_2E and Δ_3E) and five scales designed to describe the more or less pure resonance effect. We chose the following scales of constants σ_R, independently determined: from solution reactivities (Charton[3a]), from IR intensities[6], from ^{19}F NMR shifts[2], and from π-electron densities in substituted ethenes[6c,8a] or in substituted benzenes[8b]. All σ_R values were input as absolute values. When we designed this data matrix, we assumed that the five latter descriptors would be closely related and would serve as reference to reveal an additional factor or factors present in $\Delta_1E–\Delta_3E$. This assumption was confirmed by the correlation matrix. The five σ_R descriptors correlated with each other giving rather high correlation coefficients R from 0.885 to 0.953, although the correlation of absolute values is worse than that of original values with ± signs. Also the three energy values revealed some correlations with each other as found already in MLR ($R = 0.677$ to 0.827) while the correlations between the two groups were very weak with negative R (–0.380 to –0.723). PCA was carried out first with the data matrix reduced to five $|\sigma_R|$ sets: one component explained 93.5% of the total variance. PCA of the whole data matrix revealed two components explaining 74.8 and 16.1% of the variance, respectively. Third component was insignificant. All σ_R sets depend virtually on the first component (loadings greater than 0.902 for the first component and smaller than 0.297 for the second), while the ΔE sets depend on both. The strongest dependence on the resonance compo-

nent (loading –0.847) and the weakest dependence on the second component (loading 0.340) were observed in the case of $\Delta_2 E$. For $\Delta_3 E$ the reverse is true (loadings –0.693 and 0.682, respectively). All this is in agreement with the idea that all σ_R scales describe essentially the same factor, say resonance. Since the five scales are completely independent, both in principle and in the underlying experiments, the present analysis brings a very strong support that the principle of resonance and its scaling has some basis in the real world. The energies of isodesmic reactions, $\Delta_1 E$–$\Delta_3 E$ are controlled by the same factor only partly, the second controlling factor, most important in $\Delta_3 E$ and least important in $\Delta_2 E$, has no relation to resonance. In order to get more information about this factor, we tried an orthogonal rotation of components in such a way that the first component $b^{(1)}$ should be most closely related to the single component b^o obtained from the restricted $|\sigma_R|$ matrix. After rotation, this first component should represent the resonance, the second component $b^{(2)}$ the unknown factor, relieved of resonance contribution as far as possible. It turned out that rotation only by a very small angle was required: the component scores $b^{(2)}$ remain virtually unchanged. Their values are listed in Table II, last column; they were normalized to get $b^{(2)} = 0$ for hydrogen, the scaling being arbitrary. We have not revealed any physical or structural property in these values; it seems merely that their function is compensating for great deviations of particular substituents. In any case, the $b^{(2)}$ scores should not be viewed as a new "substituent constant"; for this reason we have not denoted them by any particular letter.

Similarly to MLR, also PCA gave almost the same results when the data matrix was restricted only to donor substituents. While separation of donors and acceptors was evident, we did not find additional grouping of substituents with the claimed[29] unfavorable consequences for the statistical treatment.

CONCLUSIONS

The isodesmic reactions, Eqs (*1*)–(*3*), have served here also as a tool for comparing calculated and experimental energies and testing the density functional theory. In our opinion, the test using isodesmic reactions is more correct than introducing empirical parameters[20] and capable of being applied to various compounds. Our equations included saturated aliphatic, unsaturated aliphatic and aromatic derivatives and a great variety of functional groups. Hence they may furnish a significant test. The conclusion is that calculated energies are more reliable than experimental enthalpies

based on combustion experiments since the latter can be relatively often loaded with unpredictable big errors.

As a measure of resonance, Eqs (*1*)–(*3*) are not suitable since the pertinent reaction energies are controlled, besides by resonance, also by other factors which cannot be simply described in terms of structure. The concept of resonance is not denied by this fact; in our opinion, it is strongly supported by close dependence of resonance constants derived independently from different compounds and from different properties.

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