

Review Commentary

Conjugation of two functional groups through an unsaturated system

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ABSTRACT: Energies of 51 1-(*E*),4-(*E*)-disubstituted 1,3-butadienes (**1**), 36 1,4-disubstituted benzenes (**2**) and 36 (*E*)-1,2-disubstituted ethenes (**3**) with dipolar substituents were calculated at the B3LYP/6–311 + G(d,p) level and evaluated in terms of isodesmic reactions expressing the interaction of substituents through the conjugated system. The energy of interaction reaches up to 40 kJ mol⁻¹, it is roughly similar in the three series and most regular in the series **1**. While its correlation within the framework of dual substituent parameter analysis lacks physical meaning, it is possible to separate the conjugative (resonance) component by subtracting the inductive component with reference to 1,4-disubstituted bicyclo[2.2.2]octanes **4**. The conjugative interaction is strongly stabilizing for the combination acceptor–donor and destabilizing for two donors; in these cases it is parallel to changes of geometry as they are predicted by the common resonance formulae. Interaction of two acceptors is weak; in addition, there are groups that cannot be classified either as donors or as acceptors. Therefore, one can construct a scale of the resonance ability of donors in conjugation with an acceptor and vice versa, but it is not possible to express the interaction of two donors or of two acceptors on a unified scale for all substituents. The resonance description is certainly appropriate for the typical examples (interaction of NO₂ and NH₂) but should not be generalized to all possible structures. Copyright © 2005 John Wiley & Sons, Ltd.

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KEYWORDS: conjugation; isodesmic reaction; resonance; substituent effect

INTRODUCTION

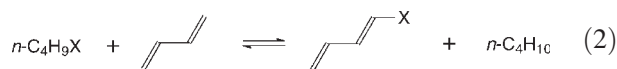
The main shortcoming of the classical theory of resonance has been the lack of a quantitative aspect. Therefore, many attempts have been made to obtain quantitative estimates of the resonance energy and to predict it empirically. A difficult problem is always encountered in defining two systems, one with resonance and the other without resonance, but otherwise as similar as possible. This problem may be attacked more or less successfully but always only with rather rough approximations. One important goal was to arrange various groups, acceptors and donors, into a scale according to their ability to undergo resonance. Three approaches may be distinguished:¹

(a) The simplest possibility is to compare two compounds in which the variable group X is bonded

once to a saturated hydrocarbon residue R¹ and once to an unsaturated residue R². The results were presented as the reaction enthalpy $\Delta_1 H^\circ$ or calculated energy $\Delta_1 E$ of the isodesmic² and homodesmotic³ reaction:



The value of $\Delta_1 E$ may depend on the size of R¹ but is no longer changed with larger alkyls beginning from *n*-butyl.⁴ Hence Eqn (2) was used¹ to obtain better balanced measure of the resonance ability than the previous scales.^{5,6} Nevertheless, it is still not certain whether it expresses only the resonance and does not depend also on polarizability or on other properties.^{1,4–6}



(b) Another approach makes use of another group capable of conjugation, that is, various donors are conjugated with various acceptors.⁷ The problem is whether the conjugative ability of a given group retains its relative value, irrespective of the pertinent

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partner. In this case all groups could be arranged into a common scale.

- (c) The best-known system, connected with the name of Taft,⁸ was based originally on the experimental dissociation constants. Evaluating one resonance constant σ_R requires four dissociation constants: saturated and unsaturated acids, substituted and unsubstituted;^{8,9} on the whole, energies of eight species are involved (acids and anions). The derived resonance constants σ_R are positive for acceptors and negative for donors and were compared on a unified scale. Subsequently, they were correlated with the experimental reactivities in innumerable cases, in combination with the inductive constants σ_I within the framework of the so-called dual substituent parameter (DSP) treatment⁸ [Eqn (3)].

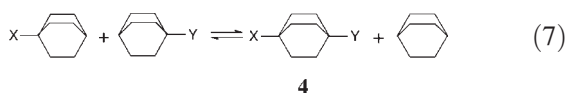
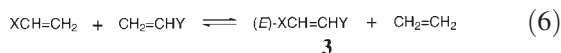
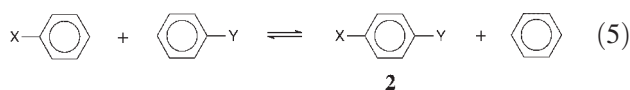
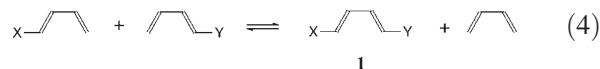
$$\Delta E = \Delta E^\circ + \rho_I \sigma_I + \rho_R \sigma_R^{(0,+,-)} \quad (3)$$

The parameters ρ_I , ρ_R and E° are obtained by multiple regression; the statistical intercept E° is near to the energy of the unsubstituted compound. The symbol $\sigma_R^{(0,+,-)}$ means that one of the three scales may be used, σ_R^0 , σ_R^+ or σ_R^- whichever gives the best fit.

The success was variable. The main problem even in this case is proper choice of a saturated and an unsaturated system: simple subtraction of the inductive effect assumes that it is exactly equal in these two systems. Various possibilities and corrections were much discussed.⁸⁻¹⁰

In all above methods, the calculation is based on the mere difference between one conjugated and one unconjugated system and no direct relation to the theory of resonance and to resonance formulae is evident. Perhaps one could better speak about conjugative interaction and conjugative constants.

In this paper, we return to method (b) above since the previous work in this direction was not satisfactory. Correlation based on experimental enthalpies of formation¹¹ suffered from the small number and low accuracy of these data. Recently, an extensive series of reaction energies was provided, based on quantum chemical calculations,⁷ but they were correlated only with the Taft's σ_R and σ_I ; hence the information obtained was not fully exploited. We used here three models, each having its merits. They are represented by the isodesmic reactions in Eqns (4)–(6).



The molecule of 1*E*,4*E*-disubstituted (*sp*)-1,3-butadiene (1), Eqn (4), is in our opinion most suitable with respect to comparison with saturated reference systems, particularly with 1,4-disubstituted bicyclo[2.2.2]octane 4, Eqn (7), investigated previously by the same theoretical approach.¹² The *para* derivatives of benzene 2 are often used⁵⁻⁹ model compounds but their inherent defect is that the conjugation requires disturbing another conjugated system (crossed conjugation). In the derivatives of ethene 3, the substituents are situated relatively near to each other and substituent effects in such systems are usually less regular. These compounds were included here for comparison only since this reaction has some practical importance.¹³ The reaction enthalpies Δ_4H° to Δ_6H° would only in few cases be available from experimental data,¹⁴ mostly with an insufficient accuracy. We calculated the reaction energies Δ_4E to Δ_6E within the framework of the density functional theory¹⁵ at the B3LYP/6-311 + G(d,p) level, well tried in similar cases.^{1,4,12}

The central problem is whether a general scale of resonance effects is possible at all, i.e. whether the effects retain their relative values when the conjugated partner is changed. In the past, the problem was circumvented by using several scales of resonance constants, discriminated by various superscripts^{8,9} as shown in Eqn (3). This treatment was criticized¹⁶ since the choice of the proper constant was not always unambiguous.¹⁷ To resolve this problem at least for a restricted set of compounds, we choose eight common dipolar substituents (Tables 1–3) and calculated the energies Δ_4E to Δ_6E for all combinations; series Δ_4E was additionally complemented by four further substituents (Table 1). In this way, we could evaluate not only the interaction between an acceptor and a donor (conjugation) but also the interaction between two acceptors or two donors, which has received little attention.^{7,18} The resonance contribution was estimated on the one hand by the traditional procedures and on the other separately for acceptors and donors.

RESULTS AND DISCUSSION

Conformation of the model compounds

Structures of the compounds 1–3 were designed with the intention of restricting the number of possible conformations. In 1 the conformation on the C(2)—C(3) bond is of central importance. We started the calculation with the angle $\tau = \angle \text{C}(1)\text{—C}(2)\text{—C}(3)\text{—C}(4)$ near to 0° but it reached values near 30° in the process of structure optimization. The exact values are listed in Table SI (see Supplementary Material, available in Wiley InterScience). When τ exceeds 30° , the conformation should be denoted *sc*, but we shall make no distinction and discuss all derivatives as near-to-planar (*sp*). Distortion by 30° has little impact on energy, as observed on butadiene mono derivatives.¹

Variable conformation within the substituent itself is possible only with six of our substituents. For our purpose it was sufficient when the disubstituted compounds were in the same conformation as the corresponding mono derivatives.¹ This was fulfilled with all compounds **1**: the COOH group prefers the *sp* conformation on the C—C bond [=O near to C(2)], OH, SH and OCH₃ the *sp* conformation on C—O or on C—S [H or CH₃ near to C(2)]. Exceptionally, these uniform conformations were not the best for all related compounds (Table SI, footnote g), but the energy differences were negligible. In the preferred conformation of the CH₂Cl substituent, the Cl atom is distant from the plane of the double bond. The CF₃ group in the SO₂CF₃ substituent is similarly situated. The same conformations were always found for ethene derivatives **3**.

With some compounds **2**, two conformers are possible even when the conformation of mono derivatives is retained. For instance, the planar molecule of 1,4-dihydroxybenzene can exist either in the C_{2v} or C_{2h} form, and in the non-planar molecule of C₆H₄(CH₂Cl)₂ the Cl atoms can be situated either on the same side or on the opposite sides of the ring plane. Energy differences are negligible; some details are given in the footnotes to Table SI.

Comparison with experimental data

Of the interaction energies Δ_4E to Δ_6E (Tables 1–3), only a few values of Δ_5E can be compared with experiments. The enthalpies Δ_5H° can be derived from the experimental enthalpies of formation¹⁴ $\Delta_fH^\circ(298)$, but their uncertainty is rather high.^{4,6} Recently, Δ_5H° was estimated from combustion data for several derivatives,¹⁸ in good agreement with our Δ_5E values except for 1,4-dinitrobenzene. A more sensitive test was carried out with the gas-phase ionization of substituted benzoic acids¹⁹ and phenols.²⁰ In all cases, tests on experimental data are restricted to compounds that are of little importance in the following correlations.

Interaction energies

Tables 1–3 represent three source matrices: in Tables 2 and 3 the matrices are symmetrical 9 × 9 and full, each with 45 independent entries. Table 1 has been extended by 15 additional compounds with strong substituents [N(CH₃)₂, OCH₃, SH, SO₂CF₃] and now has 60 independent entries. The first problem is the relation between the three scales. Figure 1 reveals a fair correlation of the butadiene series (Δ_4E) with the benzene series (Δ_5E) but a poor correlation with the ethene series (Δ_6E). In both cases, the correlation is spoiled by large deviations of a few substituents: the important cases are noted in Fig. 1. In some of them, we tried to identify the cause of the deviation. For instance, ΔE for the substituents NO₂ and CH₂Cl should be rather close to that for CN and CH₂Cl: this is confirmed for Δ_4E but not for Δ_5E . Several such cases led us to the conclusion that Δ_4E values are more trustworthy than Δ_5E and much more than Δ_6E . We have no explanation for the few deviations of Δ_5E , while the much greater deviations of Δ_6E can be simply classified as a proximity effect. The following correlations were mostly carried out with both Δ_5E and Δ_6E even when we report only the more exact results obtained with Δ_4E .

In classical terms, one can assume that the values of Δ_4E are a result of coincident action of the inductive effect and conjugation (resonance); the latter should be strong when an acceptor group is connected with a donor. Inspection of Tables 1–3 reveals that the substituents are better classified into three groups: acceptors (**A**), strong donors (**D**) and neutral substituents or say weak donors (**N**). The combination **D–A** (framed with double lines in Tables 1–3) brings about strong stabilization, as expected. Destabilization of substituents in the combinations **A–A** (within broken lines in Tables 1–3) can be understood as an inductive effect. Strong destabilization with the combination **D–D** (within full lines in Tables 1–3) is not so obvious and need not be *a priori* expected.

Our analysis had the main goal of separating the resonance component. Three approaches were attempted: (a) common DSP analysis, (b) correlation based only on

Table 1. Interaction energies of substituents in 1(*E*),4(*E*)-disubstituted 1,3-butadienes **1**, Eqn (4) (kJ mol⁻¹)

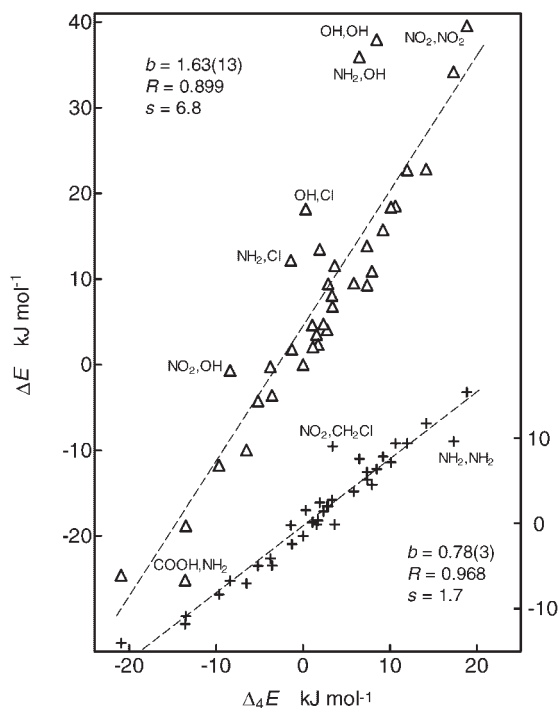
	H	CN	CF ₃	COOH	NO ₂	SO ₂ CF ₃	NH ₂	OH	Cl	CH ₂ Cl
H	0	0	0	0	0	0	0	0	0	0
CN	0	10.62	9.18	7.36	14.13		-13.50	-5.20	3.32	2.75
CF ₃	0	9.18	7.34	7.91	11.97		-9.68	-3.76	2.87	2.33
COOH	0	7.36	7.91	5.83	10.10		-13.58	-6.52	1.55	1.72
NO ₂	0	14.13	11.97	10.10	18.82	21.07	-20.94	-8.41	3.62	3.37
NH ₂	0	-13.50	-9.68	-13.58	-20.94	-23.59	17.29	6.47	-1.42	-3.57
N(CH ₃) ₂	0	-16.42	-11.74	-16.34	-24.64	-28.34	11.39			
OH	0	-5.20	-3.76	-6.52	-8.41	-9.86	6.47	8.45	0.31	-1.29
OCH ₃	0				-10.75	-12.76	10.71			
SH	0				-6.10	-7.07	2.05			
Cl	0	3.32	2.87	1.55	3.62		-1.42	0.31	1.91	1.04
CH ₂ Cl	0	2.75	2.33	1.72	3.37		-3.57	-1.29	1.04	1.12

Table 2. Interaction energies of substituents in 1,4-disubstituted benzenes **2**, Eqn (5) (kJ mol^{-1})

	H	CN	CF ₃	COOH	NO ₂	NH ₂	OH	Cl	CH ₂ Cl
H	0	0	0	0	0	0	0	0	0
CN	0	10.82	9.27	6.58	13.16	-9.36	-3.51	4.22	3.50
CF ₃	0	9.27	7.47	6.01	10.82	-6.83	-2.64	3.46	2.88
COOH	0	6.58	6.01	5.21	8.61	-10.29	-5.54	1.35	1.82
NO ₂	0	13.16	10.82	8.61	16.79	-12.50	-5.22	4.73	10.48
NH ₂	0	-9.36	-6.83	-10.29	-12.50	11.04	9.00	1.26	-3.45
OH	0	-3.51	-2.64	-5.54	-5.22	9.00	7.82	3.01	-0.93
Cl	0	4.22	3.46	1.35	4.73	1.26	3.01	3.91	1.61
CH ₂ Cl	0	3.50	2.88	1.82	10.48	-3.45	-0.93	1.61	0.59

Table 3. Interaction energies of substituents in 1,2-(*E*)-disubstituted ethenes **3**, Eqn (6) (kJ mol^{-1})

	H	CN	CF ₃	COOH	NO ₂	NH ₂	OH	Cl	CH ₂ Cl
H	0	0	0	0	0	0	0	0	0
CN	0	18.53	15.75	9.30	22.83	-18.81	-4.22	8.08	4.09
CF ₃	0	15.75	13.86	10.90	22.73	-11.75	-0.24	9.45	4.74
COOH	0	9.30	10.90	9.51	18.38	-25.16	-9.97	3.52	2.36
NO ₂	0	22.83	22.73	18.38	39.55	-24.57	-0.67	11.58	6.79
NH ₂	0	-18.81	-11.75	-25.16	-24.57	34.19	35.95	12.19	-3.58
OH	0	-4.22	-0.24	-9.97	-0.67	35.95	37.96	18.17	1.79
Cl	0	8.08	9.45	3.52	11.58	12.19	18.17	13.47	4.63
CH ₂ Cl	0	4.09	4.74	2.36	6.79	-3.58	1.79	4.63	2.09

**Figure 1.** Energy of interaction of two substituents in 1(*E*),4(*E*)-disubstituted 1,3-butadienes **1**, Eqn (4) (*x*-axis) vs interaction in 1,4-disubstituted benzenes **2**, Eqn (5) (*y*-axis, plus symbols) and 1,2-disubstituted (*E*)-ethenes **3**, Eqn (6) (*y*-axis, triangles). The substituents are indicated at some deviating points

the values of Δ_4E and (c) comparison with saturated compounds. The results are presented in the next three sections.

The DSP analysis

Correlation of experimental data with the DSP equation⁸ [Eqn (3)] may be regarded as a standard procedure; differences are only in the choice of σ_R constants (σ_R^0 , σ_R^+ or σ_R^-). We correlated the reaction energies Δ_4E [Eqn (4)], always with a constant group Y and variable X, that is, eight series with Y = CN, CF₃, COOH, NO₂, NH₂, OH, Cl and CH₂Cl. With the best values⁹ of σ_I and σ_R that are available, we obtained a satisfactory fit, with correlation coefficients *R* from 0.951 to 0.988 and standard deviations *s* from 0.4 to 3.0 kJ mol^{-1} . However, some results are unacceptable since they have no physical meaning. From the three examples given below, the values of $\Delta_4E(\text{NO}_2)$, that is, Eqn (4) with the constant substituent Y = NO₂, gave meaningful results [Eqn (8)]. The positive regression coefficients ρ_I and ρ_R mean that the molecule is destabilized when both X and Y are electron attracting by any mechanism.

$$\Delta_4E(\text{NO}_2) = 0.7 \pm 1.4 + (21.0 \pm 3.0)\sigma_I + (30.2 \pm 1.7)\sigma_R$$

$$R = 0.9931, s = 1.9 \text{ kJ mol}^{-1}, N = 13$$

(8)

$$\Delta_4E(\text{NH}_2) = -1.7 \pm 3.2 - (21.5 \pm 6.9)\sigma_{\text{I}} - (23.6 \pm 3.9)\sigma_{\text{R}}$$

$$R = 0.950, s = 4.3 \text{ kJ mol}^{-1}, N = 13$$
(9)

$$\Delta_4E(\text{COO}^-) = -2.3 \pm 4.5 - (70 \pm 11)\sigma_{\text{I}} - (38 \pm 7)\sigma_{\text{R}}$$

$$R = 0.974, s = 6.2 \text{ kJ mol}^{-1}, N = 9$$
(10)

In the series $\Delta_4E(\text{NH}_2)$ with the constant substituent $Y = \text{NH}_2$, the negative value of ρ_{R} in Eqn (9) means that acceptor substituents X are stabilizing and donors destabilizing, but there is a large defect in the negative value of ρ_{I} . This would mean that two electron-attracting substituents are stabilizing, in contrast to the broad experimental evidence. A similarly unacceptable result was obtained also for the series $\Delta_4E(\text{OH})$: ρ_{I} is negative but smaller in absolute value (-5.2 ± 2.4). In the series $\Delta_4E(\text{Cl})$, ρ_{R} is positive classifying Cl as acceptor, at variance with the structure but the effects are small and Cl cannot be classed either as acceptor or donor.

These examples show the danger inherent in DSP and similar treatments of data by multiple regression. In many cases physically impossible regression coefficients were claimed; often the statistical significance of all terms was not tested. The algorithm of the multiple regression allows an increase in one term at the cost of another, particularly when the number of data is small and/or the explanatory variables are dependent on each other [this is not the case in Eqn (9)]. Improvement of the correlation can be still attempted by trying alternative values of σ_{R} : for instance, the correlation in Eqn (8) may be slightly improved ($R = 0.993$, $s = 1.9 \text{ kJ mol}^{-1}$) by introducing⁹ σ_{R}^{\pm} instead of σ_{R} . However, the fundamental difficulty is not removed.

Recently, the DSP equation was extended to substitution by two equivalent substituents and Eqn (11) was derived:⁷

$$\Delta E = \Delta E^{\circ} + \rho_{\text{I}}\sigma_{\text{I}}(\text{X})\sigma_{\text{I}}(\text{Y}) + \rho_{\text{R}}\sigma_{\text{R}}(\text{X})\sigma_{\text{R}}(\text{Y})$$

$$+ \rho_{\text{in}}[\sigma_{\text{I}}(\text{X})\sigma_{\text{R}}(\text{Y}) + \sigma_{\text{R}}(\text{X})\sigma_{\text{I}}(\text{Y})]$$
(11)

For our 51 compounds, we obtained a good correlation with $R = 0.975$ and $s = 2.6 \text{ kJ mol}^{-1}$, but the physical meaning is not clear. The interaction term with ρ_{in} is not a small correction but is sometimes the largest; in many cases the small final result arises by compensation of fairly large terms. However, the main weakness again lies in the significance of individual terms. This can be shown on an artificial example: The interaction energies Δ_7E of bicyclo[2.2.2]octanes **4** [Eqn (7)] were correlated with Eqn (11), although any resonance effect is *a priori* impossible. The term with $\sigma_{\text{R}}(\text{X})\sigma_{\text{R}}(\text{Y})$ was absent but the interaction term was highly significant at

$\alpha < 0.001$ ($\rho_{\text{I}} = 24.6 \pm 1.5$, $\rho_{\text{in}} = 3.4 \pm 0.7$, $R = 0.950$, $s = 1.0 \text{ kJ mol}^{-1}$). In our opinion, Eqn (11) should be further tested but it will be difficult to provide a sufficiently large data set.

Internal correlations

Correlation of the values of Δ_4E themselves, without assistance from any explanatory variable, was attempted by principal component analysis (PCA). This was based on an 8×9 data matrix (completely filled columns and lines in Table 1). The data were not standardized since otherwise the irregular series would have a deciding effect. With two latent variables, 99.4% of the variability was explained; improvement against DSP was highly significant. However, we found no physical meaning of the latent variables and no relation to common scales of substituent effects. In particular, no latent variable or their linear combination was correlated with σ_{I} , not even approximately ($R = 0.692$).

We searched also for similarities of particular series, i.e. of two series of Δ_4E with different substituents Y . There is a close proportionality of the interaction of two donors with variable acceptors or vice versa, for instance of $\Delta_4E(\text{OH})$ and $\Delta_4E(\text{NH}_2)$ (variable acceptors, $R = 0.9911$) or of $\Delta_4E(\text{NO}_2)$ and $\Delta_4E(\text{SO}_2\text{CF}_3)$ (variable donors, $R = 0.9997$), but there is no correlation with the weak substituents or when acceptors are compared with donors.

Estimation of the resonance energy

Although the dependence of Δ_4E on the inductive effect was not proven, we made an attempt to separate the resonance effect by the traditional treatment,^{8,9} i.e. by subtracting the inductive effect determined from bicyclo[2.2.2]octane derivatives¹² **4** in Eqn (7). The problem is that the inductive effects in Eqns (7) and (4) need not be of the same intensity. The resonance component $\Delta_{12}E$ is then given by Eqn (12), where λ is not far from unity but unknown exactly.

$$\Delta_{12}E = \Delta_4E - \lambda\Delta_7E$$
(12)

It is generally not possible to define two systems, one conjugated and the other saturated, in which the inductive effects would be *a priori* equal. The problem has already been encountered when interpreting the solution reactivities^{10a} and has been discussed extensively, mainly on benzene derivatives.^{8-10,21,22} In Eqn (12), λ must be greater than unity since the substituent effects in **1** are 1.3 times greater than in **2** (Fig. 1, plot at the bottom) and **2** were always accepted as comparable to **4**. Fortunately, the choice of λ is of little consequence for the values of $\Delta_{12}E$, as shown in Fig. 2. When Δ_4E values are plotted

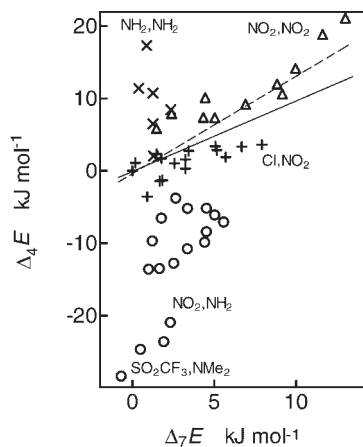


Figure 2. Energy of interaction Δ_4E of the two substituents in 1(*E*),4(*E*)-disubstituted 1,3-butadienes **1**, Eqn (4), vs interaction Δ_7E of the same substituents in 1,4-disubstituted bicyclo[2.2.2]octanes **4**, Eqn (7). Circles, substituents acceptor and strong donor; crosses, two donors; triangles, two acceptors; plus symbols, neutral substituents or weak donors. The substituents are indicated at some typical compounds. The full line has a slope of 1.0 and the broken line 1.3

against Δ_7E , the compounds without resonance should be situated near the straight line $y = \lambda x$ and for the other compounds the resonance energy $\Delta_{12}E$ is given by the (positive or negative) distance from this line. Figure 2 reveals that the choice of $\lambda = 1$ or 1.3 makes little difference: the acceptor–donor interaction is strongly stabilizing and the donor–donor interaction strongly destabilizing. The choice of λ may affect the interaction of two acceptors: some $\Delta_{12}E$ may become negligible. However, this result is acceptable and will be confirmed (see the next section).

The values of $\Delta_{12}E$ calculated with $\lambda = 1.3$ are listed in Table 4. In the qualitative sense, there is no great difference compared with Table 1; certain regularities are seen more clearly. The acceptor–donor interaction is always stabilizing (the area limited by double lines in

Table 4), the donor–donor interaction destabilizing (heavy lines) and the acceptor–acceptor interaction slightly destabilizing or virtually zero (broken lines). The Cl and CH_2Cl substituents behave towards acceptors as weak donors and towards donors as weak acceptors (like $\text{CH}=\text{CH}_2$ and similar groups²³). The central question is now whether $\Delta_{12}E$ values are proportional in all series. According to our results, this is not fulfilled generally with acceptable accuracy. PCA of $\Delta_{12}E$ carried out with the same data matrix as above with Δ_4E is deciding. The DSP theory would require that one component were sufficient corresponding to the term $\rho_R\sigma_R$. However, one component explained only 91.6% of the variance and two components 98.6%. Detailed analysis revealed a close correlation in a subset when one substituent was an acceptor and the other a strong donor. In Fig. 3, several series are directly compared. For the combination donor–acceptor, the correlation is very close (open circles). The accuracy is lowered when the Cl and CH_2Cl substituents are included. For the combinations acceptor–acceptor and donor–donor (open and closed triangles, respectively) large deviations are observed. We carried out PCA on a small 5×4 data matrix, restricted to the combinations acceptor–donor. One component gave 99.87% of the explained variance and allowed $\Delta_{12}E$ to be expressed by an empirical equation of the common type:

$$\begin{aligned} \Delta_{12}E &= 57.71 \sigma_D \sigma_A + 0.028 \\ R &= 0.9988, s = 0.35 \text{ kJ mol}^{-1}, N = 20 \\ R &= 0.9968, s = 0.65 \text{ kJ mol}^{-1}, N = 28 \\ R &= 0.947, s = 4.5 \text{ kJ mol}^{-1}, N = 52 \end{aligned} \quad (13)$$

We used the symbols σ_D and σ_A in order to stress that the equation is valid only for the combination of a donor and an acceptor substituent. Nevertheless, their scaling was carried out to express also the other combinations of substituents with the highest possible accuracy. The variable range of validity is evident from the statistics

Table 4. Estimated resonance energies in 1(*E*),4(*E*)-disubstituted 1,3-butadienes **1**, Eqn (12) (kJ mol^{-1})

	H	CN	CF ₃	CO ₂ H	NO ₂	SO ₂ CF ₃	NH ₂	OH	Cl	CH ₂ Cl
H	0	0	0	0	0	0	0	0	0	0
CN	0	-1.28	0.21	1.73	1.18		-15.63	-9.57	-5.35	-1.69
CF ₃	0	0.21	0.81	4.80	0.49		-11.25	-7.20	-3.82	0.42
COOH	0	1.73	4.80	3.93	4.33		-14.85	-4.09	-2.65	-0.59
NO ₂	0	1.18	0.49	4.33	3.72	4.15	-23.93	-14.27	-6.66	-3.20
NH ₂	0	-15.63	-11.25	-14.85	-23.93	-26.06	16.17	4.85	-3.57	-4.75
N(CH ₃) ₂	0	-16.87	-10.41	-15.75	-25.26	-27.42	10.90			
OH	0	-9.57	-7.20	-8.79	-14.27	-15.59	4.85	5.41	-3.89	-3.67
OCH ₃	0				-15.10	-16.02	9.09			
SH	0				-12.62	-14.30	0.39			
Cl	0	-5.35	-3.82	-2.65	-6.66		-3.57	-3.89	-5.48	-2.28
CH ₂ Cl	0	-1.69	0.42	-0.59	-3.20		-4.75	-3.67	-2.28	0.90

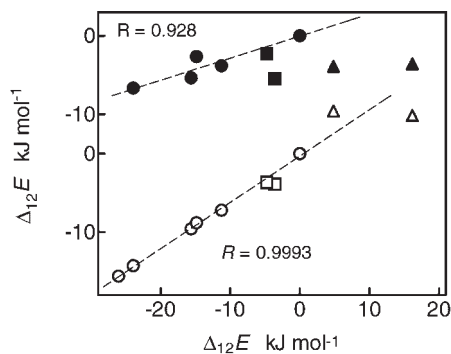


Figure 3. Comparison of estimated resonance interaction energies $\Delta_{12}E$ of the two substituents in 1(E),4(E)-disubstituted 1,3-butadienes **1**; plotted are always two series with two constant substituents Y: x-axis, Y = NH₂; y-axis, at the top Y = Cl, at the bottom Y = OH. Open and closed circles, acceptor substituents X; open and closed squares, X = Cl or CH₂Cl, open and closed triangles, donor substituents X. The correlation coefficients relate to the subgroups open and closed circles

accompanying Eqn (13). They confirm generally what was observed with the examples in Fig. 3: Eqn (13) holds with very high accuracy for the combinations acceptor-donor [CN, CF₃, COOH, NO₂, SO₂CF₃ with NH₂, N(CH₃)₂, OH, OCH₃, SH]; this accuracy is much lowered on adding the 'weak' substituents Cl and CH₂Cl (second line with 28 compounds). Equation (13) does not hold for all combinations of substituents (third line; the individual deviations may reach up to 20 kJ mol⁻¹).

The constants σ_D and σ_A are given in Table 5. We do not intend to introduce a new scale of resonance constants in addition to all scales already published. Our intention was merely to show that a unified scale is not possible and would have no physical meaning. Remarkably, there is a similarity of σ_D to the constants⁹ σ_R^+ and of σ_A to σ_R^- when properly scaled (Table 5, columns 4 and 5), but the two scales cannot be merged together. We conclude that the resonance ability can be evaluated on a scale for donors and on another scale for acceptors. Interaction of

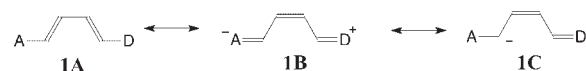
Table 5. Resonance constants obtained with Eqn (12) from the energies of 1(E),4(E)-disubstituted 1,3-butadienes **1**, separately for donor and acceptor groups

Substituent	σ_D	σ_A	$\sigma_R^+/1.5$	$1.5\sigma_R^-$
H	0	0	0	0
NH ₂	-0.728		-0.73	
N(CH ₃) ₂	-0.765		-0.81	
OH	-0.438		-0.43	
OCH ₃	-0.453		-0.44	
SH	-0.391		-0.37	
Cl	-0.212		-0.14	
CH ₂ Cl	-0.045		-0.08	
CN		0.377		0.39
CF ₃		0.248		0.18
COOH		0.356		0.47
NO ₂		0.571		0.56
SO ₂ CF ₃		0.621		0.83

two groups of the same category cannot be empirically predicted from the same scale: the strong interaction of two donors is different from the weak interaction of two acceptors. There still remain groups that do not belong to either donors or acceptors.

Resonance formulae and geometric parameters

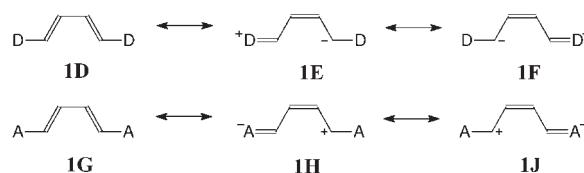
Until now, we understood the term resonance effect in the same sense as Taft in the DSP theory:⁸ a simple difference between the effects in a conjugated and a saturated compound. This definition is evident from Eqn (12). However, the classical resonance theory goes further in describing the structure by contribution of resonance formulae. A molecule of **1** with a donor and an acceptor substituent is described by the formulae **1A** ↔ **1B**, which predict that resonance makes the C(2)—C(3) bond shorter and the dihedral angle $\tau\angle C(1)—C(2)—C(3)—C(4)$ smaller.



For comparison with resonance energies, we derived from the bond lengths l_{23} the relative values Δl_{23} according to Eqn (14). These values are due only to mutual interaction of the two groups X and Y and are equal to zero for all mono derivatives, similarly as Δ_4E or $\Delta_{12}E$.

$$\Delta l_{23} = l_{23}(X, Y) - l_{23}(X, H) - l_{23}(H, Y) + l_{23}(H, H) \quad (14)$$

The two measures of resonance, $\Delta_{12}E$ and Δl_{23} are compared in Fig. 4. There is a good correlation for all combinations of substituents. In the case of two donors, **1D**, one can imagine that they can be conjugated either one or the other (**1E** or **1F**), hence the resonance is weakened.



The theory of resonance makes no distinction between donors and acceptors and would predict the same effect also for acceptors (equations **1G–1J**). However, this was not observed: Both $\Delta_{12}E$ and Δl_{23} display only small values, almost within the errors of the whole approach (Fig. 4, plus symbols). The great quantitative difference between the conjugation of acceptors and donors was claimed already on the basis of solution reactivities^{10a} and supported by various arguments.^{10,24} Figure 4 gives a simple proof based directly on observable quantities. Weak to negligible resonance of acceptors was considered even in conjugated compounds such as **1A** assuming that

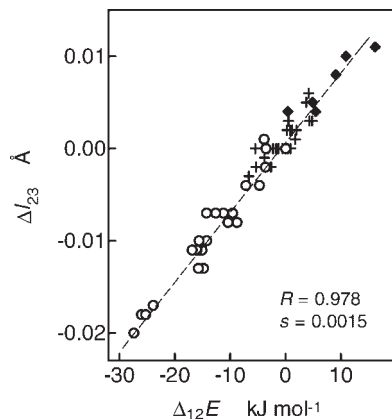


Figure 4. Comparison of two measures of resonance: increase of the bond length Δl_{23} of the C(2)—C(3) bond in 1(*E*),4(*E*)-disubstituted 1,3-butadienes **1** [Eqn (14)] plotted vs the estimated resonance energy $\Delta_{12}E$ [Eqn (12)] of the same compound. Diamonds, derivatives with two strong donors; circles, with one strong donor; and plus symbols, with acceptor substituents and/or weak donors

only the donor group is conjugated and its resonance is strengthened by the inductive effect of the acceptor group.²⁵ This may be pictured by **1C**. A test can be based on the length of the A—C(1) bond, which is shortened in **1B** but not in **1C**. Then the C—N bond in various nitro derivatives should be little dependent on the donor present, in contrast to various amino derivatives where it should depend on the acceptor present. Selected bond lengths presented in Table SIII (Supplementary Material) do not support this assumption, hence the importance of **1C** has not been proven.

Additional information was searched for in the bond lengths of the C=C double bonds. According to the resonance formula for **1B**, the two bonds C(1)=C(2) and C(3)=C(4) in one molecule should be affected equally. Even when the effect of hybridization at the C(1) and C(4) atoms is taken into account, these bonds should be equal for instance in 1-nitro-4-aminobutadiene. This is not the case; generally, the double bonds adjacent to a donor are much more lengthened than those at an acceptor. In addition, there are specific effects, for instance the small effect of OH and relatively strong effect of CN. This all shows on the one hand the restricted ability of resonance formulae to predict the geometric parameters and on the other the qualitative differences between groups of various structures.

Figure 4 can serve as an additional proof of the physical meaning of the resonance energy $\Delta_{12}E$ and of the approximate value of the coefficient λ . When the relative bond lengths Δl_{23} were plotted against the original interaction energies Δ_4E (Fig. 5), a linear dependence as in Fig. 4 was not obtained: derivatives with and without a donor group behave differently, the latter being controlled mainly by the inductive effect.

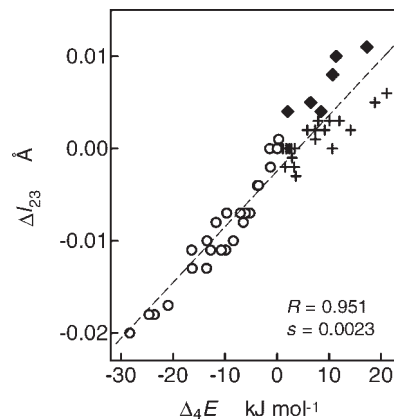


Figure 5. Increase of the bond length Δl_{23} of the C(2)—C(3) bond in 1(*E*),4(*E*)-disubstituted 1,3-butadienes **1** [Eqn (14)] plotted vs the interaction energy Δ_4E of the same compounds. Symbols as in Fig. 4

We attempted also to draw similar conclusions from the dihedral angle τ . The relative values $\Delta\tau$ were derived similarly to Δl_{23} in Eqn (14). When they were plotted against $\Delta_{12}E$ (not shown), it turned out that they are influenced also by some unknown factors. There was a rough proportionality of $\Delta\tau$ and $\Delta_{12}E$ controlled by the strong donors, but some compounds with COOH and NO₂ substituents deviated since they are almost planar (τ near to zero). Different effects of resonance on energy and on geometry are known,¹ and $\Delta\tau$ is perhaps too sensitive to structural changes since the torsional barrier is low.

CONCLUSIONS

In our opinion, resonance is a simple, merely qualitative concept, valid in typical cases, that should not be too much generalized or refined. Conjugation of a donor and an acceptor group through a conjugated system is an evident fact and can be quantified in terms of both energy and geometry: the results are concordant. There are, however, differences between the conjugation of donors and acceptors. Any scale of resonance constants should be better divided into two scales: one for donors describing their conjugation with an acceptor and the other for acceptors when they are conjugated with a donor. Mutual interactions of two donors or of two acceptors cannot be expressed using the same scale.

In principle, similar but weaker objections have already been raised^{12b} against the concept of the inductive effect. This principle is valid and quantitatively defined in typical examples, that is, for the interaction with charged or strongly polar groups; in other cases the effect is not only weak but also less regular.^{12b} The experimental proofs of both inductive and resonance effects were

mostly presented as linear correlations, controlled essentially by the end-points; it was almost never proven that they are valid even for the weak effects in the middle region.

CALCULATIONS

The DFT calculations were performed at the B3LYP/6-311+G(d,p) level with the Gaussian 03 program.²⁶ Previously we attempted to improve this model to the B3LYP/AUG-cc-VTZ//B3LYP/6-311+G(d,p) level, but it turned out that it was necessary to compute at the tight convergence;⁴ the results were then little different from those at the B3LYP/6-311+G(d,p) level. For this reason, we used the latter level even in this work.

Full energy optimization and vibrational analysis were carried out for all molecules. The minimum-energy conformations were searched for starting from two or more initial structures with different conformations within the functional group. The conformation on the C(2)—C(3) bond of **1** was *a priori* chosen as near to *sp*. The calculation started with a dihedral angle τ near to 0° and this was allowed to take the optimum value. The final values of τ are given in Table SI (Supplementary Material).

The energies of **1**, **2** and **3** are given in Table SI together with some geometric parameters, energies of additional compounds of the series **4** are given in Table SII and additional geometry parameters of selected compounds **1** are given in Table SIII. The reaction energies $\Delta_4E-\Delta_6E$ of the isodesmic reactions Eqns (4)–(6) are given in Tables 1, 2 and 3, respectively.

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REFERENCES

- Böhm S, Exner O. *J. Mol. Struct. (Theochem)* 2005; **722**: 125–131.
- (a) Pross A, Radom L, Taft RW. *J. Org. Chem.* 1980; **45**: 818–826; (b) Exner O. *Org. React. (Tartu)* 1995; **29**: 1–6.
- George P, Trachtman M, Bock CW, Brett AM. *J. Chem. Soc., Perkin Trans. 2* 1976; 1222–1227.
- Exner O, Böhm S. *J. Comput. Chem.* 2004; **25**: 1979–1986.
- (a) Hehre WJ, Radom L, Pople RA. *J. Am. Chem. Soc.* 1972; **94**: 1496–1504; (b) Greenberg A, Stevenson TA. *J. Am. Chem. Soc.* 1985; **107**: 3488–3494; (c) Helal MR. *J. Mol. Struct. (Theochem)* 2000; **528**: 255–261.
- (a) Exner O, Böhm S. *J. Chem. Soc., Perkin Trans. 2* 2000; 1994–1999; (b) Exner O, Böhm S. *Collect. Czech. Chem. Commun.* 2001; **66**: 1623–1637.
- Liu L, Fu Y, Liu R, Li R-Q, Guo Q-X. *J. Chem. Inf. Comput. Sci.* 2004; **44**: 652–657.
- (a) Ehrenson S, Brownlee RTC, Taft RW. *Prog. Phys. Org. Chem.* 1973; **10**: 1–80; (b) Hansch C, Leo A, Taft RW. *Chem. Rev.* 1991; **91**: 165–195; (c) Taft RW, Topsom RD. *Prog. Phys. Org. Chem.* 1987; **16**: 1–83.
- Charton M. *Prog. Phys. Org. Chem.* 1981; **13**: 119–251.
- (a) Exner O. *Collect. Czech. Chem. Commun.* 1966; **31**: 65–89; (b) Decouzon M, Exner O, Gal J-F, Maria P-C. *J. Phys. Org. Chem.* 1994; **7**: 511–517; (c) Exner O. *J. Phys. Org. Chem.* 1999; **12**: 265–274.
- Exner O. *Prog. Phys. Org. Chem.* 1990; **18**: 129–161.
- (a) Exner O, Böhm S. *Chem. Eur. J.* 2002; **8**: 5147–5152; (b) Exner O, Böhm S. *J. Phys. Org. Chem.* 2004; **17**: 124–130.
- (a) Kopečný J, Kurc L, Červený L. *Chem. Listy* 2004; **98**: 246–253; (b) Spronk R, Mol JC, *Appl. Catal.* 1991; **70**: 295–306.
- (a) Domalski ES, Hearing ED. *J. Phys. Chem. Ref. Data* 1993; **22**: 805–1159; (b) Bureš M, Holub R, Leitner J, Voňka P. *Termochemické Veličiny Organických Sloučenin (Thermochemical Quantities of Organic Compounds)*. Institute of Chemical Technology: Prague, 1987.
- (a) Becke AD. *Phys. Rev. A* 1988; **38**: 3098–3100; (b) Lee C, Yang W, Parr RG. *Phys. Rev. B* 1988; **37**: 785–789.
- Exner O, Böhm S. *Phys. Chem. Chem. Phys.* 2004; **6**: 3864–3871.
- Exner O. *Correlation Analysis of Chemical Data*. Plenum Press: New York, 1988; 150.
- Roux MV, Jiménez P, Dávalos JZ, Temprado M, Liebman JF. *J. Chem. Thermodyn.* 2003; **35**: 803–811.
- Exner O, Böhm S. *J. Org. Chem.* 2002; **67**: 6320–6327.
- Wiberg KB. *J. Org. Chem.* 2003; **68**: 875–882.
- (a) Palm VA, *Osnovy Kolichestvennoi Teorii Organicheskikh Reaktsii*. Khimiya: Leningrad, 1967; Chapt. IX-2; (b) Tsuno Y, Sawada M, Fujii T, Yukawa Y. *Bull. Chem. Soc. Jpn.* 1979; **52**: 3033–3042; (c) Adcock W, Dewar MJS, Gupta BD. *J. Am. Chem. Soc.* 1973; **95**: 7353–7358; (d) Vorpapel ER, Streitwieser A Jr, Alexandratos SD. *J. Am. Chem. Soc.* 1981; **103**: 3777–3781; (e) Segurado MAP, Reis JCR, de Oliveira JDG. *J. Chem. Soc., Perkin Trans. 2* 2002; 323–328.
- S. Böhm S, Exner O. *J. Mol. Struct. (Theochem)* 2004; **682**: 171–177.
- Zhang K-C, Fu Y, Lin B-L, L. Liu L, Cheng Y-H, Guo Q-X. *J. Mol. Struct. (Theochem)* 2003; **625**: 199–205.
- (a) Hoefnagel AJ, Oosterbeek W, Wepster BM. *J. Org. Chem.* 1984; **49**: 1993–1997; (b) Alunni S, Clementi S, Ebert C, Linda P, Musumarra G, Edlund U, Sjöström M, Wold S. *Gazz. Chim. Ital.* 1986; **116**: 679–682.
- (a) Hiberty PC, Ohanessian G. *J. Am. Chem. Soc.* 1984; **106**: 6963–6968; (b) Krygowski TM, Maurin J. *J. Chem. Soc., Perkin Trans. 2* 1989, 695–698.
- Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Montgomery JA Jr, Vreven T, Kudin KN, Burant JC, Millam JM, Iyengar SS, Tomasi J, Barone V, Mennucci B, Cossi M, Scalmani G, Rega N, Petersson GA, Nakatsuji H, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Klene M, Li X, Knox JE, Hratchian HP, Cross JB, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Ayala PY, Morokuma K, Voth GA, Salvador P, Dannenberg JJ, Zakrzewski VG, Dapprich S, Daniels AD, Strain MC, Farkas O, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Ortiz JV, Cui Q, Baboul AG, Clifford S, Cioslowski J, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Challacombe M, Gill PMW, Johnson B, Chen W, Wong MW, Gonzalez C, Pople JA. *Gaussian 03, Revision B.03*. Gaussian: Pittsburgh, PA, 2003.