

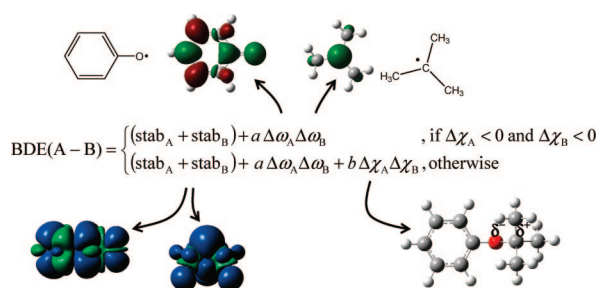
An Intrinsic Radical Stability Scale from the Perspective of Bond Dissociation Enthalpies: A Companion to Radical Electrophilicities

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Bond dissociation enthalpies (BDEs) of a large series of molecules of the type A–B, where a series of radicals A ranging from strongly electrophilic to strongly nucleophilic are coupled with a series of 8 radicals (CH₂OH, CH₃, NF₂, H, OCH₃, OH, SH, and F) also ranging from electrophilic to nucleophilic, are computed and analyzed using chemical concepts emerging from density functional theory, more specifically the electrophilicities of the individual radical fragments A and B. It is shown that, when introducing the concept of relative radical electrophilicity, an (approximately) intrinsic radical stability scale can be developed, which is in good agreement with previously proposed stability scales. For 47 radicals, the intrinsic stability was estimated from computed BDEs of their combinations with the strongly nucleophilic hydroxymethyl radical, the neutral hydrogen atom, and the strongly electrophilic fluorine atom. Finally, the introduction of an extra term containing enhanced Pauling electronegativities in the model improves the agreement between the computed BDEs and the ones estimated from the model, resulting in a mean absolute deviation of 16.4 kJ mol⁻¹. This final model was also tested against 82 experimental values. In this case, a mean absolute deviation of 15.3 kJ mol⁻¹ was found. The obtained sequences for the radical stabilities are rationalized using computed spin densities for the radical systems.

Introduction

All chemical reactions are characterized by the formation and the breaking of chemical bonds. The homolytic bond cleavage of the molecule A–B into the radicals A' and B':



is characterized by the bond dissociation enthalpy (BDE), which measures the strength of the chemical bond between the fragments A and B. The BDE thus constitutes an important

fundamental concept in chemistry. It is defined as the reaction enthalpy at 298 K and 1 atm of the bond dissociation (1) of the molecule A–B in the gas phase:

$$\Delta_f H^{298} = \Delta_f H_{A'}^{298} + \Delta_f H_{B'}^{298} - \Delta_f H_{A-B}^{298} = \text{BDE}(A-B) \quad (2)$$

where $\Delta_f H_A^{298}$, $\Delta_f H_B^{298}$, and $\Delta_f H_{A-B}^{298}$ are the heats of formation of the radicals A and B and the molecule A–B, respectively. Because experimentally the BDEs of complex molecules are sometimes hard to measure,^{1–3} theoretical methods, both

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(semi)empirical^{4–10} and ab initio,^{11–16} are often used to estimate this quantity. High-level ab initio methods in combination with large basis sets and composite methods like G3 or Wn ($n = 1, 2, 3,$ or 4) were found to be very accurate^{17–22} in predicting the values of the BDEs, but cannot be applied to systems of considerable size. However, several studies showed that reasonable accuracy can be obtained with density functional theory (DFT) methods, and this for a wide range of chemical systems and at considerably lower computational cost.^{15,23–26} Next to the accurate computation of BDEs, several studies have considered the investigation of the different factors influencing the magnitude of the BDEs. Toro-Labbé et al. studied bond dissociations in function of the reaction force.²⁷ In another recent study, periodic trends in BDEs were investigated through the electron density of R–X bonds, the electronegativity of the fragment X, the bond length of R–X bonds, etc.²⁸ Other studies^{23,29} showed that the electronegativity of X has an important effect on trends in relative bond dissociation energies for R–X species (R = Me, Et, *i*-Pr, *t*-Bu). Relative BDEs are

quite often used to determine radical stability sequences.^{30–35} The enthalpy change for reactions of the type



is defined as the radical stabilization energy (RSE) for the radical R^{\cdot} and is often applied as a measure of radical stability, relative to the methyl radical. For carbon radicals, this method gives fairly good results in predicting radical stability sequences.^{23,31,33} However, Matsunaga et al.³⁶ argue that thermodynamic quantities, such as radical stabilization energies, cannot depend on the precursor (in this case, the hydrogen atom H^{\cdot}). Indeed, the order of the R^{\cdot} radicals changes when another precursor is used.^{23,29} Matsunaga et al.³⁶ put forward that BDEs are not only affected by the stability of the radicals formed upon homolysis, but also by the electronegativity of the molecular fragments. They considered that this latter effect is not related to the stabilization of the radicals and therefore has to be excluded. They suggest a new definition of radical stability, irrespective of the precursor A^{\cdot} in the molecule AB:

$$RSE(B^{\cdot}) = \frac{1}{2}[BDE(CH_3-CH_3) - BDE(B-B)] \quad (4)$$

In this work, we study BDEs using chemical concepts that are basic quantities in Conceptual DFT^{37–42} such as electrophilicity and electronegativity, as shown by Parr and co-workers.^{43,44} For the latter quantity, the Pauling approach is followed, due to its easy embedding in a thermochemical context. However, the Huheey expression for the interaction energy⁴⁵ between two species was shown to be equivalent to Pauling's extra-ionic resonance energy,⁴⁶ thus bridging both approaches. The study in this work results in an (approximately) intrinsic radical stability scale, which complements our recently introduced scales of radical electrophilicities and nucleophilicities.⁴⁷ Moreover, this scale is in good agreement with the radical stabilities introduced by Matsunaga et al.,³⁶ who proposed a comprehensive scale of this quantity. Several known radical stability sequences are compared to the radical stability scale introduced in this Article and will be rationalized using computed spin densities.

Results and Discussion

For this study, a database of 47 radicals, 12 radicals were added to the list of 35 from a previous study on radical

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electrophilicities,⁴⁷ has been put together, including carbon-, nitrogen-, oxygen-, and sulfur-centered radicals, as well as some halogens, thus comprising a representative set of radicals for applications in organic chemistry. To investigate the influence of electrophilicity and nucleophilicity of the radicals A and B on the BDE of A–B, eight radicals were selected so that the entire range in electrophilicity, from strong nucleophilic to strong electrophilic, is represented. The selection consists of the strongly nucleophilic hydroxymethyl radical (CH₂OH), the medium nucleophilic methyl radical (CH₃), the weakly nucleophilic difluoroamino radical (NF₂), the neutral hydrogen atom (H), the weakly electrophilic methoxy radical (OCH₃), the medium electrophilic hydroxyl (OH) and mercapto (SH) radical, and the strongly electrophilic fluorine atom (F). For each combination of radicals in the two sets (8 versus 47), we have calculated the BDE using a DFT method, chosen on the basis of a small comparative study with experimental data.

Comparative Study with Experiment. Because the emphasis of this Article lies in the description of the bond dissociation enthalpies using chemical concepts and a rather large set of radical combinations will be studied, density functional methods will be used for the theoretical calculation of all BDEs. Feng et al.¹⁵ assessed the performances of DFT methods in the calculation of BDEs, using 161 validated experimental values. They found that the B3LYP, B3P86, and B3PW91 functionals perform reasonably well with standard deviations of about 12.1–18.0 kJ mol⁻¹, but comment that all of the DFT methods underestimate the BDEs in average by 4–17 kJ mol⁻¹. In addition, it was observed that the DFT methods suffer only small basis set effects, except for the heteroatom-hydrogen BDEs. In a study by Izgorodina et al.,²³ it was found that of all DFT methods BMK and KMLYP performed best with mean absolute deviations on the BDEs of 7.4 and 8.1 kJ mol⁻¹, respectively, and an underestimation of about 5 kJ mol⁻¹, but the authors emphasize that these “new generation” functionals can show significant systematic errors in the prediction of relative BDEs. A recent study on the determination of BDEs for a set of hydrocarbons⁴⁸ indicated that again B3P86 and BMK are superior to other DFT functionals in the reproduction of BDEs. Additionally, the influence of the basis set was tested, and it was again found that there is only a slight dependence on the basis set. This good performance of B3P86 and BMK is confirmed by the same authors in an even more recent work.²⁵

In this Article, the B3LYP, B3P86, and BMK functionals with basis set 6-311+G** will be tested against experimental BDEs. For 89 radical combinations, experimental values for the BDEs were found, with uncertainties up to 13 kJ mol⁻¹.^{1–3,49,50} The experimental data set includes 37 bonds of hydrogen with a variety of hetero elements, 23 bonds to CH₃, 15 bonds to OH, 11 bonds to OCH₃, 8 bonds to F, and 4 bonds to SH. The experimental BDEs as well as the theoretically calculated values can be found in Table S1 of the Supporting Information. Table 1 lists the statistical analysis for the three methods, that is, the mean deviation (MD), the mean absolute deviation (MAD), the root-mean-square deviation (rms), and the maximum absolute deviation (MAX).

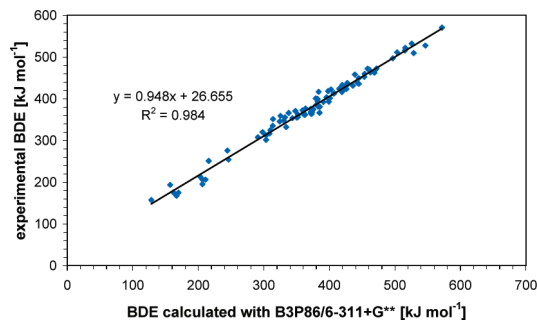


FIGURE 1. Comparison of theoretical and experimental bond dissociation enthalpies for the experimental set of 89 radical combinations (values available in the Supporting Information).

TABLE 1. Mean Deviation (MD), Mean Absolute Deviation (MAD), Root Mean Square Deviation (RMS), and Maximum Deviation (MAX) for the B3LYP, the BMK, and the B3P86 Functional (in kJ mol⁻¹) for the Experimental Set of 89 Radical Combinations

stats	B3LYP	BMK	B3P86
MD	-23.8	-8.7	-7.2
MAD	24.1	11.5	10.5
rms	28.1	14.9	14.2
MAX	57.9	47.0	37.4

The functionals B3P86 and BMK yield reasonable values for the BDEs with an MAD value of 10.5 and 11.5 kJ mol⁻¹, respectively. In accordance with the results of Feng et al.,¹⁵ all DFT methods underestimate the experimental values, with the smallest underestimation (i.e., 7 kJ mol⁻¹) for the B3P86 functional. The largest deviations are observed for the BDEs concerning combinations with the oxygen-centered radicals OH and OCH₃, in accordance with the literature.²³

If only the bond dissociation enthalpies of hydrogen and fluorine bonds are considered, 44 in total, the MAD value in case of the B3P86 method drops to 5.3 kJ mol⁻¹. In Figure 1, the correlation between all experimental and the theoretical BDEs is shown. The correlation coefficient amounts to 0.984. The correlation slope is smaller than unity, which confirms that the method underestimates the experimental values. In the further course of this Article, we will use the B3P86/6-311+G** level of theory for the computation of BDEs (see Table S2 in the Supporting Information).

Correlation of Bond Dissociation Enthalpies with Radical Electrophilicities. As was already mentioned above, bond dissociation enthalpies are linked to radical stability. However, other chemical aspects will also have to be considered, as was suggested already in literature. In a first model, a correlation is investigated between the BDE of a molecule A–B and the global electrophilicity of the radicals A· and B·. Recently, we have established an electrophilicity scale for 35 radicals⁴⁷ within the context of Conceptual DFT,^{37–42,51} classifying them into electrophiles and nucleophiles according to the global electrophilicity index, defined by Parr et al.⁴⁴ (see also the review by Chattaraj et al.⁵²):

$$\omega = \frac{\mu^2}{2\eta} \quad (5)$$

where μ is the electronic chemical potential⁴³ and η is the chemical hardness.⁵³ We now have extended our scale to determine the electrophilic character of the 12 additionally added radicals. Table 2 lists all 47 radicals and their value of the global

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TABLE 2. Global Electrophilicity Index ω , Enhanced Electrophilicity Index $\Delta\omega$ (Relative with Respect to $\omega = 2$), and the Degree of Electrophilic/Nucleophilic Character for the Database of 47 Radicals (B3LYP/6-311+G) (All Values in eV)**

R	ω	$\Delta\omega$	character
C(OH)(CH ₃) ₂	0.581	-1.419	
C(CH ₃) ₃	0.651	-1.349	
CH ₂ OH	0.717	-1.283	strong
CH(CH ₃) ₂	0.720	-1.280	nucleophile
NO	0.876	-1.124	
CH ₂ CH ₃	0.891	-1.109	
CH ₂ CH ₂ CH ₃	0.980	-1.020	
CH ₂ C ₆ H ₄ (OCH ₃)	1.033	-0.967	
CH ₃ C(O)	1.083	-0.917	
CF ₂ CH ₃	1.113	-0.887	
CH ₂ C ₆ H ₄ (CH ₃)	1.157	-0.843	
CH ₂ CHCH ₂	1.161	-0.839	
HC(O)	1.172	-0.828	
CH ₃	1.209	-0.791	moderate
CH ₂ C ₆ H ₅	1.239	-0.761	nucleophile
CHCH ₂	1.252	-0.748	
CH ₂ C ₆ H ₄ (F)	1.265	-0.735	
C ₆ H ₄ (CH ₃)	1.384	-0.616	
C ₆ H ₄ (OCH ₃)	1.398	-0.602	
C ₆ H ₅	1.405	-0.595	
CCl ₃	1.480	-0.520	
C(CN)(CH ₃) ₂	1.495	-0.505	
C ₆ H ₄ (F)	1.579	-0.421	
CF ₃	1.672	-0.328	
NF ₂	1.849	-0.151	weak
C ₆ H ₄ (CN)	1.857	-0.143	nucleophile
NH ₂	1.871	-0.129	
CH ₂ C ₆ H ₄ (CN)	1.878	-0.122	
<i>tert</i> -butoxycarbonylmethyl	1.930	-0.070	
CH ₂ CN	2.003	0.003	neutral
H ^a	2.063	0.063	neutral
OCH ₂ CH ₃	2.114	0.114	
NO ₂	2.118	0.118	
OCH ₃	2.124	0.124	weak
OCH ₂ C(CH ₃) ₃	2.132	0.132	electrophile
SCH ₃	2.206	0.206	
SCH ₂ CH ₃	2.214	0.214	
OC ₆ H ₅	2.236	0.236	
tosyl	2.283	0.283	
phenylsulfonyl	2.358	0.358	moderate
OH	2.462	0.462	electrophile
SH	2.520	0.520	
2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl	3.017	1.017	
Br	3.614	1.614	
Cl	3.772	1.772	strong
F	3.954	1.954	electrophile
CN	4.167	2.167	

^a The electrophilicity of the hydrogen atom was calculated using the B3LYP/6-311++G** level of theory.

electrophilicity index ω . It can be anticipated that the combination of an electrophilic and a nucleophilic radical will have a positive effect on the bond dissociation enthalpy (i.e., resulting in a higher value of the BDE), because an electrophile prefers to attack sites of higher electron density, and, conversely, a nucleophile prefers sites of lower electron density. The stronger is the electrophilic/nucleophilic character of the radicals, the larger is the effect on the BDE. On the other hand, one can expect that two (strong) electrophiles or two (strong) nucleophiles will avoid each other, thus lowering the value of the BDE. Again, the stronger is the electrophilic or nucleophilic character,

the larger is the effect on the BDE. Finally, for all combinations with nearly neutral species, no influence of the electrophilicity index on the BDEs is expected.

The following model is a first attempt to break down the BDE into parts that incorporate the chemical concepts radical stability and electrophilicity:

$$\text{model 1: BDE(A-B)} = (\text{stab}_A + \text{stab}_B) + a\Delta\omega_A\Delta\omega_B \quad (6)$$

The first two terms correspond to the stabilities of the radical fragments A (stab_A) and B (stab_B). The more stable is the radical, the lower is the contribution to the BDE. The second contribution involves a special form of the electrophilicities of the radical fragments A and B, incorporating the enhanced electrophilicity index $\Delta\omega$. This index can be retrieved from Table 2 for all 47 radicals and is defined as the difference between the electrophilicity index ω and the borderline between electrophilicity and nucleophilicity for radicals, which is at 2 eV:⁴⁷ $\Delta\omega = \omega - 2$.

Nucleophilic radicals are therefore represented by a negative value of $\Delta\omega$, while the enhanced electrophilicity index acquires a positive value for electrophilic radicals. For neutral species, $\Delta\omega$ obtains a value of zero. If we now look closer to the second contribution in eq 6, $a\Delta\omega_A\Delta\omega_B$, it can be expected that the parameter a is negative to get a positive contribution when A is a nucleophile and B an electrophile (or vice versa) and a negative contribution in case that both radicals are either electrophilic or nucleophilic. The latter effect cannot be taken into account if one would use the difference in electrophilicities of the radical fragments. In total, 48 parameters have to be estimated, the coefficient a and 47 stabilities. The training set, which will be used to fit the model, consists of the BDEs for the combinations of the strongly nucleophilic CH₂OH radical, the neutral hydrogen atom, and the strongly electrophilic fluorine atom with the entire database of 47 radicals (138 values in total). As such, the whole range in electrophilicity is taken into account and different chemical environments are represented, forming the basis for an (approximately) intrinsic scale of radical stabilities. Furthermore, the theoretical BDEs for the hydrogen and fluorine bonds agree well with the experimental values as mentioned in the previous section. Also, one can expect that, in these cases, the influence of the steric and resonance effects will be small, although the latter could play some role in the case of the fluorine, when this atom is coupled to groups exhibiting electron-withdrawing resonance effects. We have minimized the residual sum of squares (RSSQ), which corresponds to the squared difference between the BDEs predicted by the model (\hat{y}_i) and the theoretical BDEs obtained with the B3P86/6-311+G** level of theory (y_i):

$$\text{RSSQ} = \sum_i (y_i - \hat{y}_i)^2 \quad (7)$$

As a result, the stabilities of all radicals were obtained (Figure 2). The estimated radical stabilities and parameter a , which has a value of $-29.26 \text{ kJ mol}^{-1} \text{ eV}^{-2}$, were then used to predict the BDEs of the remaining radical combinations. Table 3 lists the statistical analysis of the linear regression for all radical combinations with the training set (CH₂OH, H, and F), the test set (CH₃, NF₂, OCH₃, OH, and SH), and both sets together. It has to be mentioned that, due to the approach followed in the construction of this model, the number of data points available to estimate the stability of the CH₂OH, H, and F radicals is larger than that for the other radicals in the scale. As a result,

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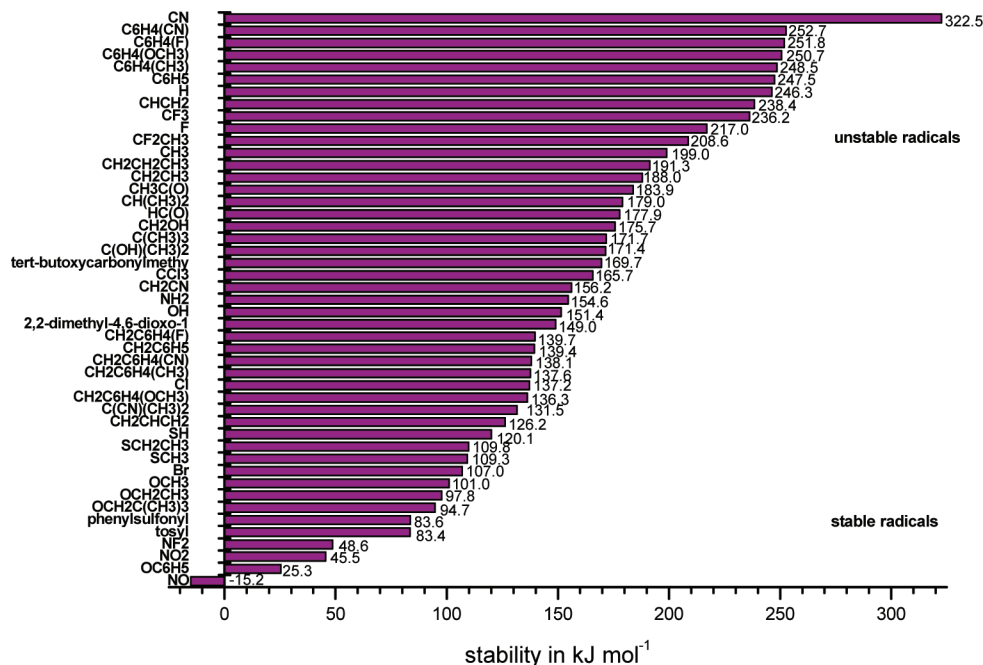


FIGURE 2. Radical stability scale, obtained from model 1, for the entire database of 47 radicals.

TABLE 3. Mean Deviation (MD), Mean Absolute Deviation (MAD), Root Mean Square Deviation (RMS), and Maximum Deviation (MAX) between the Theoretical BDEs (B3P86) and the BDEs Obtained with Model 1 for the Training Set (CH₂OH, H, and F), the Test Set (CH₃, NF₂, OCH₃, OH, and SH), and Both Sets Together (in kJ mol⁻¹) (See Table S3 in the Supporting Information)

stats	training set	test set	training set + test set
MD	0.7	-3.0	-1.7
MAD	33.9	29.7	30.6
rms	48.7	40.0	42.3
MAX	178.8	145.8	178.8

care has to be taken statistically, when considering the absolute magnitude of the stabilities of these radicals. However, the trends in the radical stabilities, in which our main interest lies, will remain unchanged.

The mean absolute deviation amounts to 30.6 kJ mol⁻¹. In some cases, the estimated BDE is twice the value of the theoretical BDE. For instance, the theoretical value for the F–F bond dissociation is about 143 kJ mol⁻¹, while the model predicts a value of 322 kJ mol⁻¹ (see MAX in Table 3). Notice that the deviations for the test set are slightly below the ones for the training set, indicating that, although the model is not perfect, it is representative for all radical combinations. We can therefore already state that the sequence in radical stabilities is realistic (Figure 2). Indeed, several known trends are reproduced. For instance, increasing alkylation raises the stability of the radical, which can be seen in the following sequences: *tert*-butyl > *i*-propyl > ethyl > methyl; OCH₂C(CH₃)₃ > OCH₂CH₃ > OCH₃ > OH; etc. For the specific case of alkanes, Gronert proposed an alternative interpretation of C–H bond strengths based on 1,3 repulsive steric interactions.⁵⁴ Another example is that the benzyl and the allyl radical are indeed found to be more stable than *tert*-butyl, while the vinyl and phenyl radical demonstrate less stability than the methyl radical.

In Figure 3, we compare the radical stabilities obtained by this model (model 1) with the radical stabilities of Matsunaga

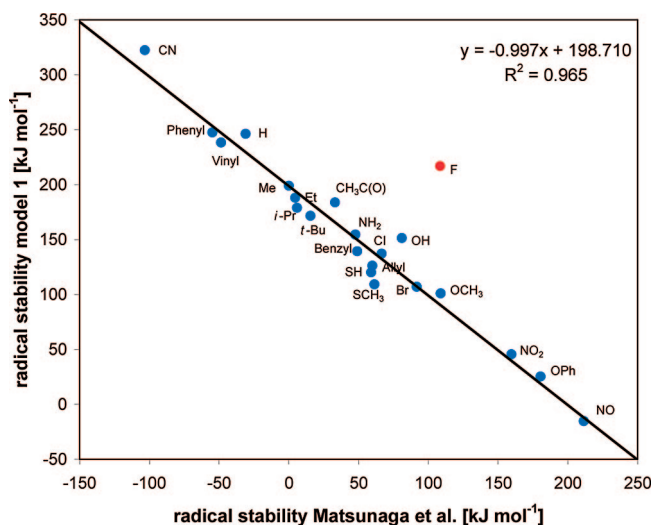


FIGURE 3. Comparison of the radical stabilities obtained from model 1 with the stabilities listed in the paper of Matsunaga et al.³⁶

et al.³⁶ for the 22 radicals that are listed in both works. Note that fluorine is not included in the linear regression of Figure 3. As can be seen, the radical stabilities, resulting from the model that only uses the enhanced electrophilicities of the radicals, are in good agreement with this scale.

When comparing the expression of the stability of A from model 1

$$\text{stab}_A = \frac{1}{2} \text{BDE}(A-A) - \frac{1}{2} a \Delta \omega_A^2 \quad (8)$$

with the definition of the RSE of A (eq 4) by Matsunaga et al., it can be seen that the radical stability is proportional to 0.5 BDE(A–A) (and thus proportional to the stability expression obtained by Matsunaga et al.), but for the electrophilicity term. This means that for weak electrophilic or nucleophilic radicals A, the correlation between the radical stability and BDE(A–A) will be very good. However, some deviations occur, for

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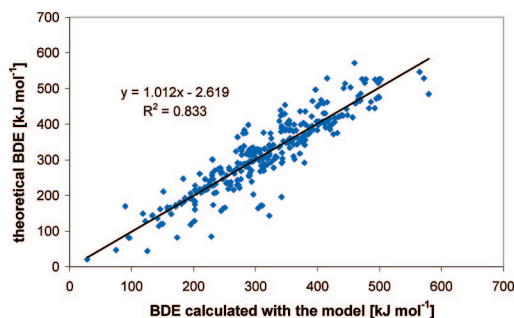


FIGURE 4. Comparison of theoretical BDEs and BDEs obtained with model 1, incorporating the stability and the electrophilicity of the radical fragments for the entire set (training set + test set) of 348 radical combinations.

TABLE 4. Pauling Electronegativities χ and the Enhanced Pauling Electronegativities $\Delta\chi$ (Relative with Respect to the Reference Value +3) for All Chemical Elements from Our Database

element	χ	$\Delta\chi$
H	2.20	-0.80
C	2.60	-0.40
N	3.05	0.05
O	3.50	0.50
F	4.00	1.00
S	2.60	-0.40
Cl	3.15	0.15
Br	2.85	-0.15

example, in the case of F_2 , due to the high electrophilicity of the fluorine atom, which makes the contribution of the enhanced electrophilicity term become more important.

Figure 4 depicts the comparison of the BDEs obtained with the model and the theoretical BDEs for all radical combinations (348 in total). The correlation coefficient has a value of 0.83, which indicates that 83% of the magnitude of the BDEs is accounted for by the radical stabilities and the global electrophilicities of the radical fragments. In the next section, we will show that the inclusion of the Pauling electronegativity for atoms in an additional term will clearly improve the agreement with the computed bond dissociation enthalpies.

Correlation with Radical Electrophilicity and Pauling Electronegativity. To improve the quantitative agreement of model 1 with the computed BDEs, we extend the model with a contribution that reflects the strength of the bond A–B. A simple chemical property that probably suits best this aim is the Pauling electronegativity for atoms, which describes the ability of an atom to attract electrons in a covalent bond. Pauling^{55,56} introduced the concept to explain why the bond between two atoms A and B is stronger than the average of the strengths of A–A and B–B. Pauling's electronegativity scale was constructed using a large set of bond dissociation enthalpies and by applying the following formula:

$$\chi_A - \chi_B = (\text{eV})^{-\frac{1}{2}} \sqrt{\text{BDE}(A-B) - \frac{\text{BDE}(A-A) + \text{BDE}(B-B)}{2}} \quad (9)$$

The electronegativity of the fluorine atom was chosen as a reference and set to a value of 4.0. The Pauling electronegativity values for the atoms in our database are listed in Table 4. Ochterski et al.⁵⁷ adjusted the Pauling equation by introducing empirical polarizability parameters α , which were determined by performing a least-squares fit on BDEs, to attenuate better the energetic effect of differences in electronegativities:

$$\text{BDE}(A-B) = \sqrt{\text{BDE}(A-A)\text{BDE}(B-B)} + |2.883(\chi_A - \chi_B)|^{(\alpha_A + \alpha_B)} \text{kcal mol}^{-1} \quad (10)$$

In analogy to model 1, we make a difference between the strong and the weak electronegative atoms. Therefore, we introduce the so-called enhanced Pauling electronegativity values (Table 4), which can be obtained simply as $\Delta\chi = \chi - 3$. If the element has an electronegativity larger than the fictive boundary of 3, which is approximately the medium value between the lowest and the highest Pauling electronegativity in our database, it is regarded as strongly electronegative. Otherwise, the chemical element is considered weakly electronegative. As mentioned before, the bond between two different atoms becomes stronger when the electronegativity difference between those atoms increases. So if a strong and a weak electronegative atom are connected, a raising effect on the BDE is expected. On the other hand, if the directly bonded atoms are both strongly electronegative, a lowering effect on the BDEs is noticed. One example is the unexpectedly weak bond in F_2 , which has been discussed upon many times in the literature.^{56,58–61} In a recent study,⁶² it was concluded that in systems consisting of a bond between two strongly electronegative atoms, as is the case for F_2 and for instance HO–OH, the charge is highly located at the nuclei and not within the internuclear region. This effect has to be accounted for somehow in the expression, and this is not possible by simply taking the difference of the Pauling electronegativities on the radical centers. We conjecture that the combination of two weakly electronegative atoms will not influence the magnitude of the BDE.

Our first model will thus be extended with a term, combining the enhanced Pauling electronegativity of the radical centers of the two radical fragments: $b \Delta\chi_A \Delta\chi_B$. To have a positive contribution to the BDEs when a weakly and a strongly electronegative radical center are connected and a negative contribution when both radical centers are strongly electronegative, the parameter b should have a negative sign. As mentioned before, combining two weakly electronegative atoms will have no effect on the magnitude of the BDE, and therefore the local term is put to zero in this case. The new and final model (model 2) has the following form:

model 2:

$$\text{BDE}(A-B) = \begin{cases} (\text{stab}_A + \text{stab}_B) + a\Delta\omega_A\Delta\omega_B, & \text{if } \Delta\chi_A < 0 \text{ and } \Delta\chi_B < 0 \\ (\text{stab}_A + \text{stab}_B) + a\Delta\omega_A\Delta\omega_B + b\Delta\chi_A\Delta\chi_B, & \text{otherwise} \end{cases} \quad (11)$$

Note that when both $\Delta\chi_A$ and $\Delta\chi_B$ are less than zero, this model is the same as model 1, thus involving only electrophilicities of the radicals A and B.

Again, a least-squares fit has been performed, but now 49 parameters needed to be estimated: 47 radical stabilities and 2 coefficients a and b . The same training set (CH_2OH , H, and F) and test set (CH_3 , NF_2 , OCH_3 , OH, and SH) were used, the central idea again being the combination of the radicals A with the radicals B ranging from strongly electrophilic to strongly nucleophilic to design an (approximately) intrinsic stability scale

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TABLE 5. Mean Deviation (MD), Mean Absolute Deviation (MAD), Root Mean Square Deviation (RMS), and Maximum Deviation (MAX) between the Theoretical BDEs and the BDEs Obtained with Model 2 for the Training Set (CH₂OH, H, and F), the Test Set (CH₃, NF₂, OCH₃, OH, and SH), and Both Sets Together (in kJ mol⁻¹) (see Tables S4 and S5 in the Supporting Information)

stats	training set	test set	training set + test set
MD	-0.1	7.1	4.5
MAD	13.2	18.3	16.4
rms	18.3	25.1	22.9
MAX	56.7	70.5	70.5

to serve as a companion to the radical electrophilicity scale. The following values were obtained for the two coefficients: $a = -12.88 \text{ kJ mol}^{-1} \text{ eV}^{-2}$ and $b = -216.50 \text{ kJ mol}^{-1}$. In Table 5, the statistical analysis of the linear regression for all radical combinations with the training set, the test set, and both sets together can be found. In comparison to the agreement with the computed BDEs is much improved. The mean absolute deviation for the complete set drops from 30.6 kJ mol^{-1} for model 1 to a value of 16.4 kJ mol^{-1} for the definitive model. Especially the BDEs for the combinations with the carbon-centered radicals CH₃ and CH₂OH are well-described by the model, with an MAD of only 7.5 kJ mol^{-1} .

Again, the combinations with the oxygen-centered radicals OCH₃ and OH show the largest deviations (MAD of 24.2 kJ mol^{-1}). For 19 radical combinations, of which 16 contain at least one oxygen-centered radical, a deviation larger than 50 kJ mol^{-1} is found. For 8 of these 19 combinations, experimental BDEs are known, and for 5 of them the experimental and theoretical BDEs differ by more than 10 kJ mol^{-1} (even up to 37 kJ mol^{-1}). Therefore, it seems plausible that the large deviations between the theoretical BDEs and the ones obtained with the model can be traced back to the inadequacy of the B3P86 functional and DFT methods in general to reproduce very accurately BDEs of oxygen bonds.²³

The stability of the coefficients and the radical stabilities obtained with this model was also tested. The addition or removal of a radical to the database has no effect on the values of the parameters. Using a different radical in the training set, that is, other than CH₂OH, H, and F, has only a small effect on the parameters. For instance, the coefficient a varies from -12.9 to $-16.1 \text{ kJ mol}^{-1} \text{ eV}^{-2}$ for six different test sets. Remark, however, that at least one electrophilic and one nucleophilic radical should be included in the test set to be representative and that the inclusion of radicals for which the theoretical BDEs deviate strongly from the experimental values should be avoided.

Figure 5 depicts the correlation between the theoretical BDEs and the BDEs obtained with model 2. The correlation coefficient amounts to 0.958. Remark that the BDEs obtained with this model slightly overestimate the theoretical values (a mean deviation of 4.5 kJ mol^{-1} and a correlation slope above unity); this could indicate a good agreement between the model and experiment, because the theoretical values obtained with B3P86 underestimate the experimental BDEs.

Next, a comparison of the BDE values obtained by this second model with the experimental values is made; these quantities are listed in Table 6. Table 7 shows the results of the statistical analysis. For the complete experimental set of 89 radical combinations, a mean absolute deviation of 19.6 kJ mol^{-1} is found between the experimental values and the values predicted by our final model 2. If those BDEs are eliminated that differ by more than 55 kJ mol^{-1} as compared to the theoretical BDEs

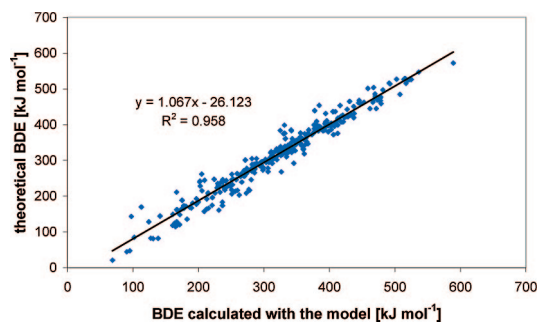


FIGURE 5. Comparison of theoretical BDEs and BDEs obtained with our definitive model, incorporating the stability, the electrophilicity, and the local Pauling electronegativity of the radical fragments for the entire set (training set + test set) of 348 radical combinations.

(7 in total), the MAD value reduces to 15.3 kJ mol^{-1} . This is a very good result, with respect to the MAD value of 9.8 kJ mol^{-1} for the comparison between the theoretical B3P86 and experimental BDEs of the reduced set of 82 radical combinations. Furthermore, the experimental BDEs are underestimated less by the BDEs obtained with the model than by the B3P86 values. Figure 6 depicts the correlation of the model with experiment; R^2 decreases 3% to 0.952, but the correlation slope of 0.985 is very close to unity. We can therefore conclude that fairly accurate bond dissociation enthalpies can be achieved from this model. It should again be mentioned that both of our models only relate the BDEs with the electrophilicities and electronegativities of the radical fragments and that the effect of resonance is not included. This effect will result in stronger bonds between the radical fragments than predicted by the model. Examples include the BDEs of compounds consisting of combinations of groups exhibiting strong electron-withdrawing and electron-releasing resonance effects, such as CH₃C(O)-OH, HC(O)-OH, and C₆H₅-OH.

Finally, we have investigated the weight of each property on the magnitude of the BDEs. The major contributions are due to the radical stabilities, even up to 100% for the H-CH₂CN bond. When two strong electrophilic and/or nucleophilic radicals are combined, the electrophilicity contribution increases to about 15%. The term involving the Pauling electronegativity on the radical centers is numerically more important with maximum contributions of 60% for the F-F bond and 50% for the F-OC₆H₅ bond. However, it turns out to be mandatory that both the electrophilicity term and the Pauling electronegativity term are included in our model to get the most reliable radical stability scale. This stability scale can thus be considered to be a companion to our computed radical electrophilicities.

Radical Stability Scale. In Figure 7 are listed the radical stabilities, from the most stable radical NO (i.e., the smallest value at the bottom of Figure 7) to the least stable fragment CN. Note that the stability of NO is now slightly positive, as compared to the negative value obtained from model 1. In the literature, the BDE of ON-NO is found to be negative with respect to two ground-state NO molecules. A similar finding concerning the BDE of O₂NO-ONO₂ has been discussed earlier.^{63,64} However, even with a positive value for the radical stability, a negative BDE can be obtained, due to the (negative) contributions of the electrophilicity and electronegativity term.

Several stability trends concerning radicals are known in literature. A first acknowledged fact is that increasing alkylation raises the stability of the radical. This is reproduced for several sequences, as shown in Figure 8. Secondly, radicals that are

TABLE 6. The BDE of 49 Radicals in Combination with a Set of 8 Radicals, Calculated with the Final Model 2, as well as the Experimental Values, Given in Bold (For References, See Table S1 in the Supporting Information) in kJ mol^{-1}

A	CH ₂ OH	CH ₃	NF ₂	H	OCH ₃	OH	SH	F
C(OH)(CH ₃) ₂	311.7	341.7	233.0	402.5	321.8	376.9	281.6	469.5
C(CH ₃) ₃	312.8	342.4	233.0	381.0 402.4	321.6	376.5	281.1	467.7
CH ₂ OH	317.9	366.1 347.1	237.2	403.8 406.4	351.5	400.8	284.7	470.1
CH(CH ₃) ₂	321.0	350.1	240.2	401.8 409.4	328.6	383.1	287.7	473.0
NO	161.2	370.7 189.4	69.0	412.5 251.2	359.0	399.6		462.8 205.0
CH ₂ CH ₃	332.2	167.4 360.3	248.9	195.4 417.6	174.9	206.3	294.9	477.1
CH ₂ CH ₂ CH ₃	336.6	372.4 364.1	252.0	423.0 420.5	355.6	393.3	297.2	477.8
CH ₂ C ₆ H ₄ (OCH ₃)	282.2	309.4	196.9	423.3 365.2	284.1	337.3	241.6	421.2
CH ₃ C(O)	330.4	357.3	244.4	364.7 412.5	331.4	384.4	288.6	467.3
CF ₂ CH ₃	355.6	353.5 382.2	269.1	374.0 437.2	418.4	459.8		511.3 491.2
CH ₂ C ₆ H ₄ (CH ₃)	285.1	311.5	198.0	416.3 366.0	356.0	408.8	313.1	522.2 418.9
CH ₂ CHCH ₂	273.8	300.1	186.6	368.0 354.5	273.3	326.0	230.2	407.4
HC(O)	325.6	320.1 351.9	238.2	361.9 406.2	325.0	377.5	281.7	458.7
CH ₃	347.1	354.8 373.2	259.2	368.6 427.0	345.8	398.2	302.4	478.7
CH ₂ C ₆ H ₅	287.9	376.0 313.7	199.5	438.9 367.3	348.1	385.3	312.5	472.0
CHCH ₂	387.0	324.7 412.8	298.5	375.3 466.2	286.0	338.3	242.5	418.3
CH ₂ C ₆ H ₄ (F)	288.6	424.3 314.3	199.8	463.2 367.5	385.0	437.2	341.3	516.9
C ₆ H ₄ (CH ₃)	398.8	423.8	308.4	367.5	286.2	338.4	242.6	417.9
C ₆ H ₄ (OCH ₃)	401.2	426.1	310.6	475.7	394.4	446.0	350.1	523.2
C ₆ H ₅	398.1	422.9	307.4	477.9	396.5	448.1	352.2	525.0
CCl ₃	317.2	433.0 341.5	225.4	474.6	393.3	444.8	348.9	521.6
C(CN)(CH ₃) ₂	283.2	307.5	191.2	472.4 392.4	422.6	470.3	361.9	532.2
C ₆ H ₄ (F)	404.5	428.2	311.2	392.5 358.2	311.0	362.2	266.2	437.5
CF ₃	390.1	413.2	295.5	361.9 478.0	276.8	327.9	231.9	402.9
NF ₂	237.2	259.2	130.8	478.0	396.5	447.3	351.2	520.7
C ₆ H ₄ (CN)	409.0	430.9	311.6	462.0	380.4	430.8	334.7	502.4
NH ₂	343.5	365.3	236.7	449.5 310.4	171.3	220.9	177.7	240.4
CH ₂ C ₆ H ₄ (CN)	294.6	316.4	197.0	316.7 477.7	395.9	445.5	349.2	513.6
<i>tert</i> -butoxycarbonylmethyl	326.8	348.3	228.4	416.2	277.1	326.7	283.4	345.7
CH ₂ CN	314.3	356.5 335.3	214.8	452.7 394.3	312.5	361.7	265.4	428.4
H	406.4	332.2 427.0	310.4	392.9 380.4	298.6	347.6	251.2	412.8
OCH ₂ CH ₃	322.2	392.9 342.5	168.1	363.8 471.5	432.9	481.6	341.9	589.0
NO ₂	237.5	438.9 257.8	127.2	316.7 436.0	436.0	497.0	381.6	570.5
OCH ₃	325.6	437.7 345.8	171.3	437.7 429.7	163.8	212.3	256.5	178.0
OCH ₂ C(CH ₃) ₃	319.4	437.7 339.6	165.0	306.0	166.7	215.2	171.7	229.5
SCH ₃	269.9	428.0 289.7	167.5	306.0	175.7 166.9	206.7	259.6	180.9
SCH ₂ CH ₃	270.5	193.7 290.2	168.0	432.9	166.9	215.4	259.6	180.9
OC ₆ H ₅	251.2	365.3 270.7	95.3	436.0 426.6	157.3	157.3	209.0	174.3
tosyl	245.0	428.0 264.2	141.4	428.0 332.6	250.5	298.6	202.1	360.0
		307.9		365.3				
		307.9		365.3				
		376.8		376.8				
		306.3		306.3				

TABLE 6. Continued

A	CH ₂ OH	CH ₃	NF ₂	H	OCH ₃	OH	SH	F
phenylsulfonyl	246.2	264.9	141.5	306.1	224.0	271.4	174.8	329.9
OH	380.1	398.2	220.9	481.6	215.4	262.4	306.3	221.3
		385.3		497.0		213.0		
SH	284.7	302.4	177.7	341.9	259.6	306.3	209.5	361.6
		312.5		381.6			276.0	
2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl	319.8	334.4	205.5	368.4	285.7	330.3	233.1	376.0
Br	303.3	314.1	177.6	341.5	231.4	273.3	202.8	280.5
		301.7		366.5				
Cl	357.1	366.9	212.9	405.5	236.8	278.1	252.9	249.8
				431.6		251.0		
F	470.1	478.7	240.4	589.0	180.9	221.3	361.6	97.5
		472.0		570.5				
CN	507.6	514.9	376.6	536.2	452.7	492.3	394.2	515.9
		509.6		527.6				

TABLE 7. Mean Deviation (MD), Mean Absolute Deviation (MAD), Root Mean Square Deviation (RMS), and Maximum Deviation (MAX) between the Experimental BDEs and the BDEs Obtained with Our Definitive Model for the Complete Experimental Set (in kJ mol⁻¹) and the Set Without the Strong Deviations

stats	complete experimental set (89 values)	experimental set without the strong deviations (82 values)
MD	-9.1	-5.9
MAD	19.6	15.3
rms	28.1	20.6
MAX	91.8	66.5

able to delocalize the unpaired electron over an aromatic ring are found to be very stable, even more stable than *tert*-butyl. This is the case for the phenoxy radical and all *p*-substituted benzyl radicals. Other radicals, like for instance tosyl, phenylsulfonyl, 2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl, and the allyl radical show several resonance forms as well. The spin distribution over the radical is a good indicator to see whether the radical shows any resonance behavior. Figure 9 depicts the spin density on the heavy atoms of the aforementioned radicals, all obtained using the Natural Population Analysis. The spin density on the radical center varies from 0.36 for tosyl and phenylsulfonyl over 0.7 for the *p*-benzyl radicals to 0.88 for *tert*-butoxycarbonylmethyl. On the other hand, the phenyl radicals do not display these resonance effects, because the unpaired electron cannot be delocalized over the ring. The spin density on the radical center is consequently very close to unity (Figure 10). Hence, all of the *p*-substituted phenyl radicals are found to be very unstable. The same reasoning applies to the

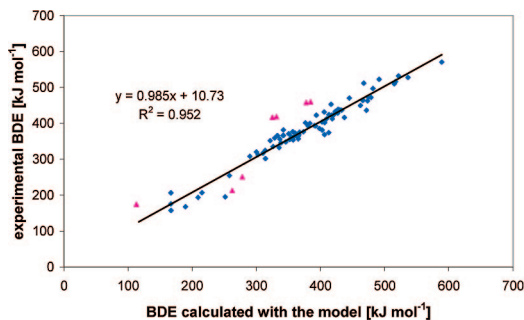


FIGURE 6. Comparison of experimental BDEs and BDEs obtained with model 2 for the complete experimental set (89 values); 7 BDEs obtained with model 2 (see the red \blacktriangle), which deviated more than 55 kJ mol⁻¹ from the theoretical BDEs were not included in the correlation analysis and equation.

vinyl radical. Vinyl and phenyl radicals are σ -type radicals that are in general localized at the site from which the hydrogen was removed, while benzyl radicals are π -type radicals that are stabilized due to resonance stabilization.

In a recent study, the substituent effect on the stability of *p*-substituted benzyl radicals was investigated by Singh et al.⁶⁵ They proposed the following order of radical stability, derived from proton hyperfine couplings obtained from electron paramagnetic resonance (EPR):⁶⁶ CN > OCH₃ > CH₃ > H. This sequence is confirmed by our radical stability scale. Singh et al. put forward that the calculated bond dissociation enthalpy of *p*-substituted toluenes depends solely on radical stabilization. This is in complete agreement with our model, because the electrophilicity term does not contribute much to the BDEs of these toluenes, considering the “neutral” character of the hydrogen atom.

The next example is the stability of the acetyl and formyl radical. The electronegative oxygen, bonded to the radical center, increases the positive charge on the carbon, which results in an extra stabilization of the radical.⁶⁷ It is suggested in the literature⁶⁸ that these two radicals are even more stable than the *tert*-butyl radical. Our stability scale does not reproduce this, probably because with our definitive model the obtained BDEs of both radicals in their bond with H and F show rather large deviations from the theoretical values: $\Delta\text{BDE}(\text{CH}_3\text{C}(\text{O})-\text{H}) = 37 \text{ kJ mol}^{-1}$; $\Delta\text{BDE}(\text{CH}_3\text{C}(\text{O})-\text{F}) = -36 \text{ kJ mol}^{-1}$; $\Delta\text{BDE}(\text{HC}(\text{O})-\text{H}) = 34 \text{ kJ mol}^{-1}$; and $\Delta\text{BDE}(\text{HC}(\text{O})-\text{F}) = -42 \text{ kJ mol}^{-1}$. Another aspect is the polarizability of an atom or a molecule. The tendency of the electron cloud of an atom to be distorted in the presence of an external electric field will possibly have an effect on the stability of the system. This is confirmed by the following sequences: SH is more stable than OH, and Br is more stable than Cl, which is again found to be more stable than F.

We finally compare the radical stabilities again with those obtained by Matsunaga et al.³⁶ As can be seen from Figure 11,

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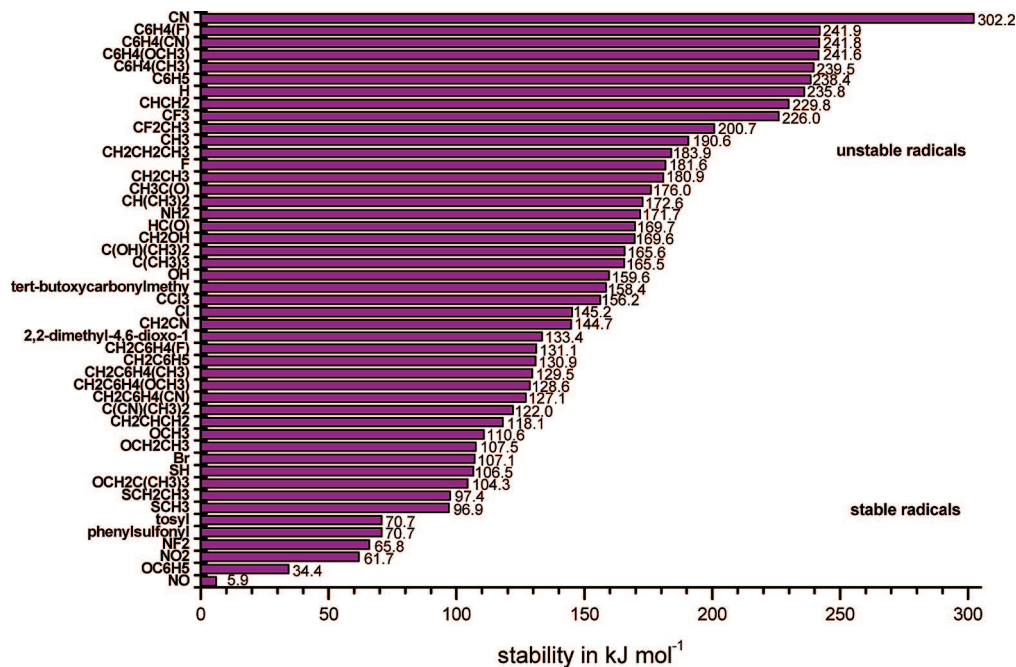


FIGURE 7. Radical stability scale, obtained from model 2, for the entire database of 47 radicals.

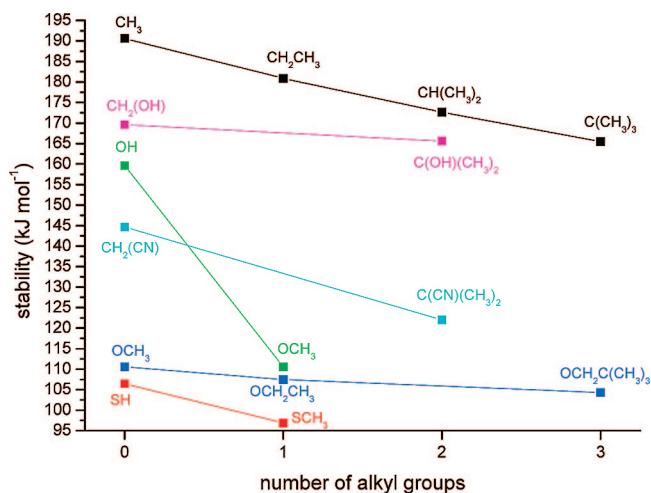


FIGURE 8. Increasing alkylation raises the stability of the radical.

the agreement between the two scales is very good, although somewhat less good than that with model 1.

In a recent contribution,⁶⁹ it was shown that the definition of a useful measure of intrinsic radical stability is both possible and desirable, as a tool to give chemical explanations. As a rough initial definition of this concept, these authors proposed “a measure of the general propensity of a radical to react across a range of different chemical environments”. In this sense, our scale can be considered to be approximately intrinsic, as combinations of the radicals with different chemical environments (i.e., combination with a neutral, electrophilic, and nucleophilic radical and combination of low–low, high–low, and high–high values of the electronegativity of the connecting atoms) were considered. In our approach, steric interactions and resonance effects between A and B are ignored; however, the chosen A-radicals, that is, CH₂OH, and especially H and F, are not very bulky, so the magnitude of the steric effects is expected

to be low. Consequently, since we determined the radical stabilities for combinations of A and B where the steric interaction is expected to be low, it can be anticipated that this approach will yield reliable radical stabilities. As for the resonance effects, they indeed could play a role in the combinations of fluorine with groups exhibiting electron-accepting resonance effects and thus have an influence on the determination of some radical stabilities. We thus have constructed a radical stability scale that complements our previously established electrophilicity scale, which was extended to new radical systems in this work.

This ultimately means that, starting from our models, we can obtain an estimate of the intrinsic stability of any radical R by the computation of a bond dissociation enthalpy of the radical with, for example, H, that is, the BDE of R–H, which will not be influenced by steric and resonance effects, and the computation of the electrophilicity of R, which can be performed from first principles and which is an important quantity when studying the reactivity of R. This approach could then be applied not only to common radicals, but also to transition states of radical reactions and biradical systems.

Computational Details

All calculations were performed within the Kohn–Sham framework, using the Gaussian 03 software package.⁷⁰ Geometries of all molecules and related radical species were optimized at the B3LYP/6-311+G** level of theory.^{71–73} Subsequent frequency calculations at the same level provided the thermal corrections to the enthalpy. Next, single-point energies on the optimized structures of the radicals and originating molecules were performed, using the three DFT-functionals B3LYP, B3P86, and BMK with basis set 6-311+G**.^{74,75}

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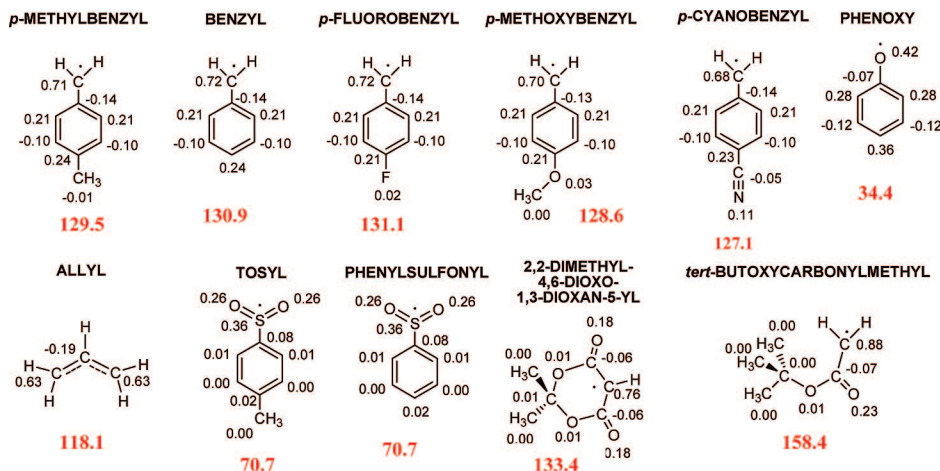


FIGURE 9. Spin density on the heavy atoms of some radicals for which delocalization of the unpaired electron is possible, using the NPA method, together with the values for the stability (in kJ mol^{-1}).

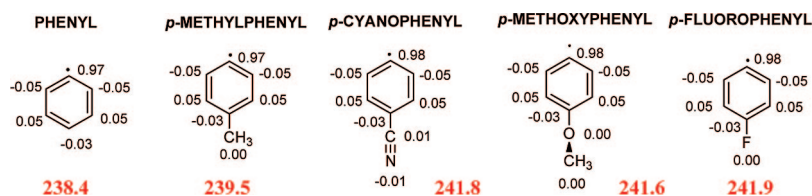


FIGURE 10. Spin density on the heavy atoms of the *p*-substituted phenyl radicals, using the NPA method: no delocalization of the unpaired electron possible, together with the values for the stability (in kJ mol^{-1}).

To calculate the electrophilicity index, the electronic chemical potential and the chemical hardness have to be known (cfr. eq 5). For an *N*-electron system with external potential $v(\mathbf{r})$ and total energy E , the electronic chemical potential μ , that is, the negative of the electronegativity χ , is defined as the partial derivative of the energy to the number of electrons at constant external potential:^{4,3}

$$\mu = -\chi = \left(\frac{\partial E}{\partial N} \right)_{v(\mathbf{r})} \approx -\frac{I+A}{2} \quad (12)$$

where I and A are the vertical ionization energy and electron affinity, respectively. These two quantities were calculated, again using the B3LYP/6-311+G**method. Parr and Pearson⁵³ proposed the following definition for the chemical hardness η , differentiating the chemical potential to the number of electrons, again at constant external potential:

$$\eta = \left(\frac{\partial^2 E}{\partial N^2} \right)_{v(\mathbf{r})} \approx I - A \quad (13)$$

For the computation of the spin densities, atomic populations were obtained with the NPA-method,^{76–78} again using Becke's hybrid three-parameter functional B3LYP with basis set 6-311+G**.

Conclusion

In this Article, we studied the magnitude of bond dissociation enthalpies (BDEs) using the chemical concepts of electrophilicity and electronegativity. In a first model, the BDEs are investigated exploiting the global electrophilicity of the radical fragments. For 47 radicals, the (approximately) intrinsic stability was estimated from computed BDEs of their combinations with

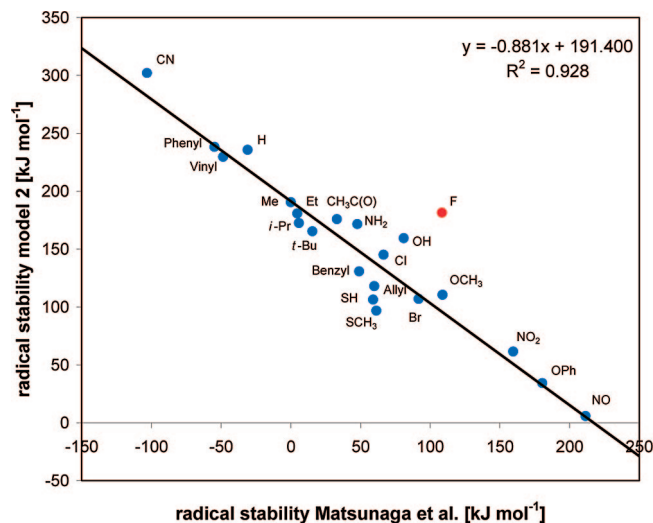


FIGURE 11. Comparison of the radical stabilities obtained from model 2 with the stabilities listed in the paper of Matsunaga et al.³⁶

the strongly nucleophilic hydroxymethyl radical, the neutral hydrogen atom, and the strongly electrophilic fluorine atom. This model accounts for 83% of the magnitude of the BDEs and yields radical stabilities that are already in good agreement with previously acknowledged trends for this quantity and with the scale of Matsunaga et al. Subsequently, to push the quantitative agreement of the model with computed and experimental values of the BDEs, it was extended with a term, involving the Pauling electronegativity of the radical centers of the fragments. This additional term again improves the model, now explaining 96% of the magnitude of the BDEs; the computed BDEs and the BDEs predicted by this model show a mean absolute deviation of 16.4 kJ mol^{-1} . Next, the model was also tested against the reduced set of 82 experimental values. In this case, a mean

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absolute deviation of 15.3 kJ mol^{-1} is found. The correlation slope of 0.985 is very close to unity, and the standard deviation has a value of 10.7 kJ mol^{-1} . If the weight of each property on the magnitude of the BDEs is considered, we observe that the major contributions are generally due to the stability term. Despite the fact that the local Pauling term is about 4 times more important than the global electrophilicity term, both terms have to be included in the model to get, in our view, the most reliable radical stability scale. Several acknowledged radical stability sequences, for example, increasing alkylation, are reproduced by our intrinsic radical stability scale, and also this model yields intrinsic values that are in good agreement with the previously proposed scale of Matsunaga et al. Other sequences were analyzed through the computation of the spin densities in the radicals. Radicals that are able to delocalize the unpaired electron are indeed found to be very stable. In addition, our model provides the possibility to compute radical stabilities for other radicals, on the basis of the computation of only the global electrophilicity of the new radical fragment and 1 BDE. It might, however, be advisable to estimate the radical stability using three BDEs (e.g., by combining the radical with a (strongly) nucleophilic, a neutral (e.g., hydrogen), and a (strongly) electrophilic radical) to guarantee that the influence of different chemical environments is properly taken into

account. These stabilities then complement our recently established radical electrophilicity scale so that we now have available a compatible and internally consistent radical electrophilicity and stability scale that can be of importance in the study of radical reactions.

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Supporting Information Available: Chemical structures of the radicals, table of the experimental and theoretical (B3LYP, B3P86, and BMK) BDEs for the experimental database, table of the theoretical (B3P86) BDEs for the complete set of radical combinations, table of the BDEs, calculated with models 1 and 2, and table of the differences in BDE between the B3P86 method and model 2. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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