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The Radical Stabilization Energy of a Substituted Carbon-Centered Free Radical Depends on Both the Functionality of the Substituent and the Ordinality of the Radical

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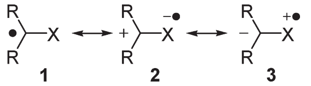

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Chemical intuition suggests that the stabilization of a carbon-centered free radical by a substituent X would be the greatest for a *prim* and least for a more stable *tert* radical because of “saturation”. However, analysis of a comprehensive recent set of bond dissociation energies computed by Coote and co-workers (*Phys. Chem. Chem. Phys.* **2010**, *12*, 9597) and transformed into radical stabilization energies (RSE) suggests that this supposition is often violated. The RSE for a given X depends not only on the nature of X but also on the ordinality (i.e., *prim*, *sec*, or *tert*) of the radical onto which it is substituted. For substituents that stabilize by electron delocalization but also contain electron-withdrawing centers, such as the carbonyl function, the stabilization of $XCMe_2^\bullet$ compared with $HCMe_2\bullet$ is greater than that for $XCH_2\bullet$ compared with $HCH_2\bullet$. However, for substituents that stabilize by lone-pair electron donation, such as N or O centers, the order is strongly reversed. This contrast can be qualitatively rationalized by considering charge-separated VB contributors to the radical structure ($R_2C^+{-}X^{-\bullet}$ and $R_2C^-{-}X^{+\bullet}$) and the contrasting effects of methyl substituents on them. This conclusion is not dependent on the particular definition used for RSE.

Introduction

Practicing free radical chemists have a sense of the relative “stabilities” of carbon-centered radicals (we limit the discussion herein to sp^2-hybridized π-radicals) as these affect reactivity. Several mechanisms of stabilization by substituents placed on an unadorned methyl radical as a reference point are recognized.[1,2] Textbook examples include the following: (1) allyl ≈ benzyl > propargyl > *n*-propyl, which results from stabilizing delocalization of the odd electron into an adjacent π-bond; (2) allyl > acetonyl, which results from tempering such three-center three-electron bonding when the adjacent π-bond terminates in an atom more electronegative than carbon; (3) aminomethyl > hydroxymethyl > ethyl, which results from a stabilizing two-center, three-electron interaction with an adjacent atom that bears a donor lone pair of electrons, the effect being somewhat counterbalanced by destabilizing σ-withdrawal; (4) *tert*-butyl > *sec*-butyl > *iso*-butyl, which results from modestly stabilizing hyperconjugation with an adjacent alkyl group (although the importance of hyperconjugation compared with 1,3-repulsions in determining the stability of alkyl radicals has been the the subject of a recent controversy[3]); and (5) *n*-propyl > 2-fluoroethyl, which results from weak inductive destabilization of the electron-deficient radical center by electronegative groups in the β-position. A “saturation” effect is also recognized; i.e., substitution of a second alkyl or aryl group onto a methyl radical is somewhat less stabilizing than substitution of the first, and a third is less effective still. This trend may however be reversed if a strongly electron-attracting and a strongly electron-donating

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substituent are combined, i.e., the so-called captodative effect as for the α-radical in amino acids.[4] Our purpose here is to highlight and systematize a more subtle, less recognized effect: the extent of stabilization of a radical by a given substituent X depends not only on the nature of X but also on the ordinality (i.e., *prim*, *sec*, or *ter*t) of the radical onto which it is substituted. For example, on the basis of comprehensive recent computational data from Coote, Lin, Beckwith, and Zavitsas (CLBZ),[2] one can conclude that a formyl (-CHO) substituent is significantly more stabilizing when substituted for H-2 in the *iso*-propyl radical than when substituted for H in the methyl radical, whereas the inverse is true for a formyloxy (-OCHO) group.

In spite of the well-known qualitative examples mentioned above, a quantitative definition of radical stabilization energy (RSE) remains elusive, and considerable discussion has re-emerged. Most proposed definitions of RSE incorporate the bond dissociation energy (BDE) of some species R−Y (eq 1).

$$\mathrm{R{-}Y} \rightarrow \mathrm{R\bullet} + \mathrm{Y\bullet}\ \ \mathrm{BDE(R{-}Y)} = \Delta_f H_{298}(\mathrm{R\bullet}) + \Delta_f H_{298}(\mathrm{Y\bullet}) - \Delta_f H_{298}(\mathrm{R{-}Y}) \qquad (1)$$

The difficulty is that structural changes in R for a series of BDE(R−Y) values will affect not only the stability of $R^\bullet$ but also the stability of the R−Y species, so that RSE depends on the nature of the Y group chosen as a reference. For example, the textbook stability order *tert*-alkyl > *sec*-alkyl > *prim*-alkyl > methyl is based on BDE(R−Y) increasing in this order for Y = H or R. However, the apparent stability order is reversed for the very electronegative Y = F. This results because bond strengthening of the R−F bond by its strong dipole, i.e., stabilization by a $R^{\delta+}{-}F^{\delta-}$ contributing structure, is the greatest for the least electronegative *tert*-butyl group and the least for methyl;[5] this effect overwhelms the role of $R^\bullet$.

Nevertheless, implementation of most definitions of RSE thus requires BDE data. A comprehensive collection of experimental data and recommendations is provided by Luo,[6] but there are significant gaps as well as significant experimental scatter in many cases. The ability to compute BDE for moderate-sized species by post-HF ab initio methods has improved rapidly, and computational values may well now be overtaking experimental values in accuracy and internal consistency.[1a,b] Our focus herein was stimulated by a recent computational tour de force by CLBZ[2] who applied the G3(MP2)-RAD method, which has been shown to be quite reliable for radical species,[1b,5d,7] to obtain BDE(R−H), BDE(R−Me), BDE(R−Cl), and BDE(R−R) for all three ordinalities of carbon-centered R groups [*prim* XCH_2-, *sec* XCH(Me)-, and *tert* $XC(Me)_2$-], where X was varied among 64 representative carbon-centered and heteroatom-centered substituents. Hence, the total number of BDE values calculated was 4 × 3 × 64 = 768 (ignoring a few duplicates). The correlation between the computed and experimental BDE values, when available, suggested that the deviations between experiment and computation were typically no greater than the error bars of the experimental data (we add the usual caveat that the computational values refer to the lowest-energy conformer of the radical and a closely related conformer of its precursor, whereas the experimental values represent Boltzmann averages when multiple low-lying conformers are available).

CLBZ applied three different protocols for deriving RSE from these BDE values: (1) the time-honored "standard" method that compares BDE(C−H) values and requires no further parametrization (which we will designate RSE_H), (2) a method championed by Matsunaga, Rogers, and Zavitsas[5b] that begins instead with BDE(R−R) values and corrects for electronegativity differences and steric effects (which was designated RSE_Z), and (3) a method proposed by deVleeschouwer and co-workers[8] that highlights an electrophilicity/nucleophilicity contribution to BDE(A−B) (which was designated RSE_V). CLBZ presented correlations among these RSE scales and discussed some strengths and weaknesses of each. On the basis of a somewhat better correlation of RSE values with the spin density (ρ) at the formal radical-bearing site, which was computed by Mulliken population analysis, they suggested that RSE_H may be superior for "simple carbon-centered" radicals. For the sake of clarity, we first develop our theme based on RSE_H and then show that use of RSE_Z and RSE_V leads to similar qualitative conclusions in this case.

Analysis and Discussion

ΔRSE Effects Based on RSE_H. RSE_H is defined by eq 2 and equals ΔH for the isodesmic hydrogen transfer reaction (eq 3).

$$\mathrm{RSE_H} = \mathrm{BDE(CH_3{-}H)} - \mathrm{BDE(R{-}H)} \qquad (2)$$

$$\mathrm{R\bullet} + \mathrm{H{-}CH_3} \rightarrow \mathrm{R{-}H} + \mathrm{CH_3\bullet} \quad \Delta H = \mathrm{RSE_H} \qquad (3)$$

Although RSE_H thus depends on R−H as well as R•, use of the isodesmic relationship is valuable computationally because of the cancellation of errors.[1a,2] In their Figure 6, CLBZ[2] plotted RSE_H for the 64 members of the *prim* R• = XCH_2• series against X with the X groups arranged such that RSE_H increased monotonically from −8.0 kJ/mol for CF_3 (note that in the nomenclature used, the radical involved here is CF_3CH_2•, not CF_3•) to 0.0 kJ/mol for H (by definition) to 77.3 kJ/mol for CH=C(Me)$_2$. However, when RSE_H for the *sec* R• = XCHMe• or *tert* R• = $XCMe_2$• series was plotted against the X groups maintained in the same order, the plot was not smooth but contained numerous peaks and valleys; e.g., for X = S(O)Me, RSE_H was more than 5 times greater for the *sec* than for the similarly substituted *prim* radical (with both compared to methane), while for X = NHCOMe, RSE_H was actually smaller for the *tert* than for the similarly

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TABLE 1. Positive Values[a] of ΔRSE_H

$\Delta RSE_{H,sec}$ (kJ/mol)		$\Delta RSE_{H,tert}$ (kJ/mol)	
X	value	X	value
S(O)Me	24.6	BH_2	26.9
BH_2	10.6	S(O)Me	22.4
CONHMe	9.1	CHO	14.1
COMe	7.9	CF_2CF_3	10.9
NO_2	6.3	COOH	10.0
CHO	6.2	COMe	8.8
COPh	6.0	COOEt	8.3
COOH	5.6	COOMe	8.3
$CONH_2$	5.1	COO*t*Bu	7.4
COOEt	5.1	$SiMe_3$	6.8
COOMe	5.1	SiH_3	6.7
COO*t*Bu	4.8	NO_2	6.7
CF_2CF_3	4.1	SO_2Me	6.5
$CONMe_2$	4.0	COPh	5.2
		$CONH_2$	4.3

[a] Values of >4.0.

substituted *prim* radical. The authors indeed noted this effect briefly and suggested that the stabilization that accompanies addition of electron-donating methyl substituents at the radical center (increasing ordinality from *prim* to *sec* to *tert*) was enhanced when the resident X was an electron-withdrawing group but was tempered when X was a lone pair/π-donor group; we explore this effect more systematically herein.

To systematize the representation of this effect, we use eq 4 to reflect positive and negative deviations from additivity of substituent effects in the *sec* radical XCHMe• where the methyl group is considered as a second substituent that replaces H on the radical center along with X; eq 5 is the analogue for the *tert* radical $XCMe_2$•.

$$\Delta RSE_{H,sec} = RSE_H(X-CH\bullet-Me) - RSE_H(X-CH\bullet-H) - RSE_H(H-CH\bullet-Me) \quad (4)$$

$$\Delta RSE_{H,tert} = RSE_H(X-C\bullet-Me_2) - RSE_H(X-CH\bullet-H) - RSE_H(H-C\bullet-Me_2) \quad (5)$$

This formulation is commonly used to diagnose captodative effects.[4d] However, for historical reasons, we hesitate to label the effects discussed herein as "captodative" but rather describe positive and negative values of ΔRSE. Chemical intuition based on saturation with increasing stability leads us to expect only negative ΔRSE values; i.e., the effects of X and methyl (or dimethyl) should not be fully additive. Yet of the 64 values each of $\Delta RSE_{H,sec}$ and $\Delta RSE_{H,tert}$ computed by CLBZ, 24 and 22, respectively, were positive. The cases for which RSE_H exceeds an arbitrary cutoff of 4.0 kJ/mol for the *sec* and *tert* ordinalities are compiled in Table 1. Because the computed values of RSE still have an uncertainty of a few kilojoules per mole,[2] we will search for repetitive patterns more than singular values for a specific substituent or radical. In this context, of the 29 total entries in Table 1, 24 represent duplicates that appear on both lists, and for the five singular entries, all appear just slightly farther down the other list.

To portray this effect more pictorially but probably less rigorously (use of a least-squares correlation when the variance along the abscissa is comparable to that along the ordinate), we use separate reference points for each ordinality. For *prim* radicals XCH_2•, we retain $RSE_{H,prim} \equiv RSE_H$; i.e., HCH_2-H remains the reference for XCH_2-H as in eq 2. However, for *sec* radicals XCHMe•, we define $RSE_{H,sec} \equiv BDE(HCH(Me)-H) - BDE(XCH(Me)-H)$; i.e., ethane becomes the reference. For *tert* radicals $XCMe_2$•, we define $RSE_{H,tert} \equiv BDE(HC(Me)_2-H) - BDE(XC(Me)_2-H)$; i.e., H-2 in propane becomes the reference. Note that in these definitions X is "substituted" for H, not Me. This simply causes a linear shift as shown in eqs 6 and 7

$$RSE_{H,sec}(XCHMe\bullet) = RSE_H(XCHMe\bullet) - RSE_H(HCHMe\bullet) = RSE_H(XCHMe\bullet) - 13.5\ \text{kJ/mol} \quad (6)$$

$$RSE_{H,tert}(XCMe_2\bullet) = RSE_H(XCMe_2\bullet) - RSE_H(HCMe_2\bullet) = RSE_H(XCMe_2\bullet) - 23.0\ \text{kJ/mol} \quad (7)$$

where the offsets of 13.5 and 23.0 kJ/mol are the computed RSE_H values for ethyl and *iso*-propyl, respectively. (Note that $\Delta RSE_{H,sec} = RSE_{H,sec} - RSE_{H,prim}$ and $\Delta RSE_{H,tert} = RSE_{H,tert} - RSE_{H,prim}$.) A plot of $RSE_{H,sec}$ versus $RSE_{H,prim}$ is shown in Figure 1. The least-squares correlation gives a slope of 0.89; i.e., on average, the stabilizing effect of X is slightly smaller when substituted on a *sec* than on a *prim* radical center, in agreement with chemical intuition. However, there is considerable scatter, and several points lie either well above or below the correlation line. An analogous plot of $RSE_{H,tert}$ versus $RSE_{H,prim}$ is shown in Figure 2. The correlation slope is lower (0.76), and the deviations, both positive and negative, are larger. In Figure 1, 30 of the 64 entries show positive deviations, and in Figure 2, 26 of the 64 entries show positive deviations. The larger ones for both are compiled in Table 2. Of the 32 entries in Table 2, 26 represent duplicates that appear on both lists, and for the six singular entries, all but one appear just slightly farther down the other list.

The positive values in either portrayal represent the counterintuitive situation for which the substituent X stabilizes a *sec* or *tert* radical more than a *prim* radical, each compared to the parent reference for that ordinality. In other words, X is more stabilizing when it replaces an H in ethane or the 2-H in propane than an H in methane. Again focusing on patterns, we note the strong overlap between the entries in Tables 1 and 2. The X groups in Tables 1 and 2 that recur most often are CHO (four, the maximum), COMe (four), COPh (four), COOH (four), COOMe (four), COOEt (four), COO*t*Bu (four), $CONH_2$ (four), BH_2 (four), NO_2 (four), S(O)Me (four), CONHMe (three), and CF_2CF_3 (three). From Figures 1 and 2, one can see that these X groups are distributed rather smoothly along the $RSE_{H,prim}$ axis. In other words, the ability to preferentially stabilize higher-ordinality radicals covers much of the range of "absolute" stabilizing ability for *prim* radicals. However, the preponderance of carbonyl and related unsaturated structures that allow π-conjugation but also contain an atom more electronegative than carbon is clear.

Charge-separated VB structures **2** and **3** contribute to the stability of radical **1**. The electron-withdrawing character of the X groups in Tables 1 and 2 will enhance the contribution of **2**. In this circumstance, additional stabilization can then be realized when R = H is replaced with the more

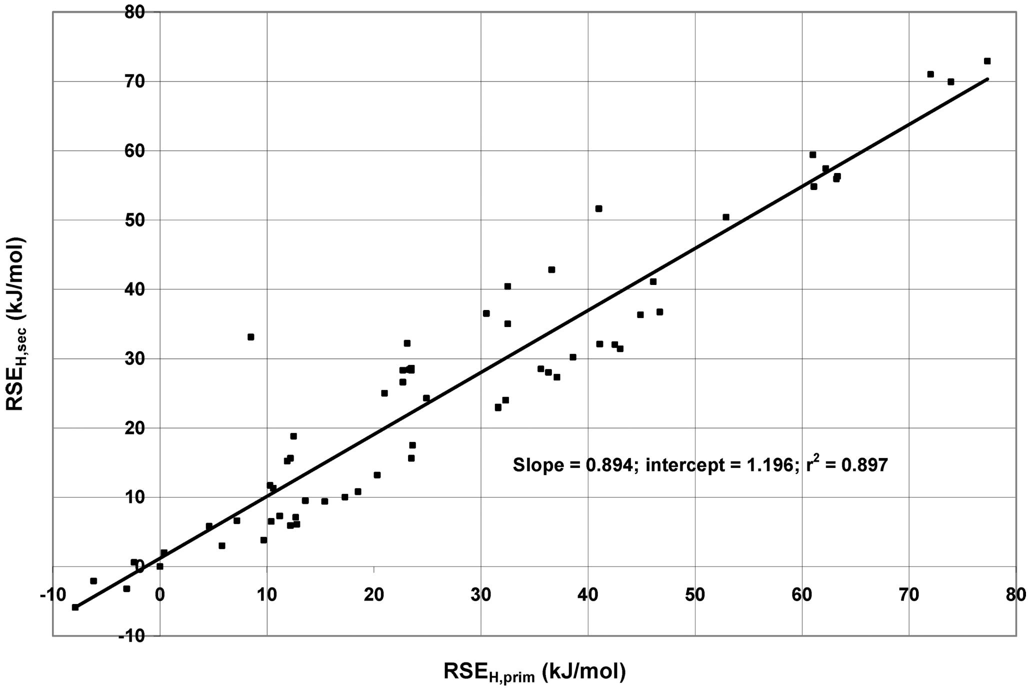

FIGURE 1. RSE$_{H,sec}$ vs RSE$_{H,prim}$.

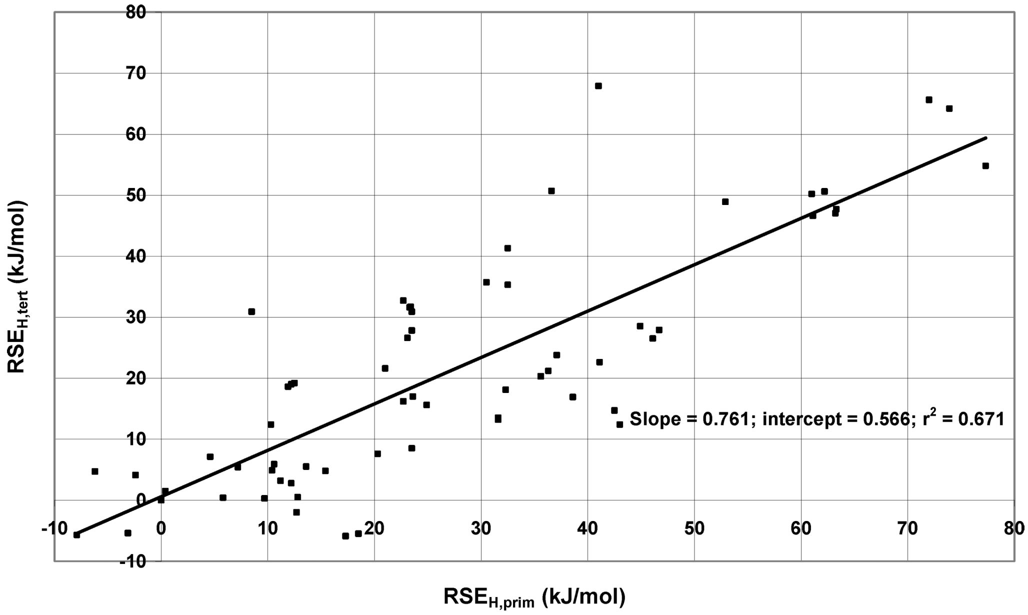

FIGURE 2. RSE$_{H,tert}$ vs RSE$_{H,prim}$.

electron-donating R = Me, the stabilizing effect of alkylation on carbenium ions of course being well-known. Hence, the radicals that profit from structure **2** appear to be those that lead to positive values of ΔRSE. As a specific example, consider the preponderant X = carbonyl group. VB contributor **5** is the normal focus to explain the stabilization of **4**. However, the positive ΔRSE values suggest an additional nontrivial contribution from **6**. Analogues of **6** are easily visualized for X = S(O)Me, NO_2, CN, and SO_2Me. The analogue for X = CF_2CF_3 may involve negative hyperconjugation.[9]

The large RSE values for X = BH_2 (**7**), even for RSE$_{prim}$, have usually been interpreted[1b,10] as a stabilizing two-center one-electron interaction between the radical orbital on carbon and the unoccupied p-type orbital on the boron atom; i.e., the embodiment of **2** in this case would be **8** (CLBZ[2] noted, however, that the decreases in the calculated ρ for X = BH_2 were smaller than expected from the large increases in RSE values, and they suggested that this nonparallel behavior may result instead from σ-donation from the BH_2 group

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TABLE 2. Positive Deviations[a] of RSE_H from the *sec-prim* and *tert-prim* Correlation Lines[b]

$RSE_{H,sec}$ vs $RSE_{H,prim}$		$RSE_{H,tert}$ vs $RSE_{H,prim}$	
X	deviation	X	deviation
S(O)Me	24.3	BH_2	36.1
BH_2	13.7	S(O)Me	23.9
CONHMe	10.4	CHO	22.3
COMe	10.1	COMe	16.0
CHO	8.9	COOH	14.9
COPh	8.0	COOEt	13.3
COOH	6.8	COOMe	13.3
NO_2	6.4	COO*t*Bu	12.5
$CONH_2$	6.4	COPh	11.9
COOEt	6.4	$CH{=}CH_2$	10.3
COOMe	6.4	CN	10.0
COO*t*Bu	6.1	$CONH_2$	9.4
$CH{=}CH_2$	5.4	$SiMe_3$	9.2
$CONEt_2$	5.1	NO_2	9.1
$CONMe_2$	5.0	SiH_3	9.0
		CF_2CF_3	8.8
		CONHMe	8.5

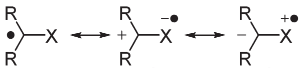
[a] Values of > 5.0 for $RSE_{H,sec}$ vs $RSE_{H,prim}$ and > 8.5 for $RSE_{H,tert}$ vs $RSE_{H,prim}$. [b] RSE values in kilojoules per mole.

TABLE 3. Negative Values[a] of ΔRSE_H

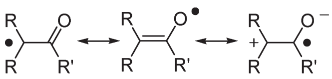
$\Delta RSE_{H,sec}$ (kJ/mol)		$\Delta RSE_{H,tert}$ (kJ/mol)	
X	value	X	value
NHCOMe	−11.6	NHCOMe	−30.6
NHCHO	−10.5	NHCHO	−27.8
NHMe	−10.0	OCOMe	−24.0
SCH_2CO_2Me	−9.8	OCHO	−23.2
SMe	−9.0	$CH{=}CMe_2$	−22.5
OMe	−8.7	SCH_2Ph	−21.7
NH_2	−8.6	NMe_2	−19.6
OEt	−8.6	NHMe	−18.8
SCH_2Ph	−8.4	SMe	−18.5
SH	−8.3	OMe	−18.4
OH	−8.3	OEt	−18.1
c-Pr	−7.9	NH_2	−16.5
OCOMe	−7.7		

[a] Values of less than −7.5 for $\Delta RSE_{H,sec}$ and less than −16.5 for $\Delta RSE_{H,tert}$.

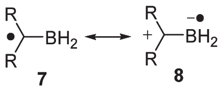
to the electron-deficient radical center without delocalizing spin).



1 **2** **3**



4 **5** **6**



7 **8**

For the other extreme, the most negative values of $\Delta RSE_{H,sec}$ and $\Delta RSE_{H,tert}$ are compiled in Table 3. Of the 25 entries, 18 represent duplicates on both lists, and of the seven singular entries, all appear just slightly farther up the other list. From the alternate presentation from Figures 1 and 2, the most negative cases are compiled in Table 4. Of the 28 entries, 20 represent duplicates on both lists, and of the eight singular entries, all appear just slightly farther up the other list.

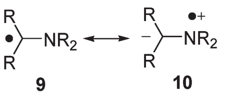
TABLE 4. Negative Deviations[a] of RSE_H from the *sec-prim* and *tert-prim* Correlation Lines[b]

$RSE_{H,sec}$ vs $RSE_{H,prim}$		$RSE_{H,tert}$ vs $RSE_{H,prim}$	
X	deviation	X	deviation
NHCOMe	−8.2	NHCOMe	−20.9
NHCHO	−7.2	OCOMe	−20.1
SCH_2CO_2Me	−7.1	OCHO	−19.6
OCOMe	−6.9	NHCHO	−18.2
OCHO	−6.7	SCH_2Ph	−13.0
c-Pr	−6.6	OCF_3	−12.2
OMe	−6.5	OMe	−11.4
F	−6.5	OEt	−11.1
OEt	−6.4	*c*-Pr	−9.9
NHMe	−6.2	F	−9.8
Et	−6.2	SMe	−9.2
Cl	−6.1	NMe_2	−9.1
OH	−6.1	Cl	−8.4
CH_2OH	−6.1	NHMe	−8.2

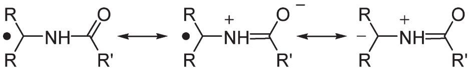
[a] Values of less than −6.0 for $RSE_{H,sec}$ vs $RSE_{H,prim}$ and less than −8.0 for $RSE_{H,tert}$ vs $RSE_{H,prim}$. [b] Values in kilojoules per mole.

The negative values in either portrayal represent the more intuitive situation in which the substituent X stabilizes a *sec* or *tert* radical less than a *prim* radical, each again compared to a parent reference for that ordinality. For example, the $\Delta RSE_{H,sec}$ and $\Delta RSE_{H,tert}$ values for X = Me are −4.1 and −8.1 kJ/mol, respectively. The values in Tables 3 and 4 represent the most negative ones. There is again strong overlap between the entries in these two tables. The X groups in Tables 3 and 4 that recur most often are NHCHO (four, the maximum), NHCOMe (four), NHMe (four), OCOMe (four), OMe (four), OEt (four), OCHO (three), SMe (three), SCH_2Ph (three), *c*-Pr (three), SCH_2CO_2Me (two), NH_2 (two), NMe_2 (two), OH (two), Cl (two), and F (two). In Figures 1 and 2, one can see that these X groups are also distributed rather smoothly along the $RSE_{H,prim}$ axis. In other words, the ability to preferentially stabilize lower-ordinality radicals again covers much of the range of "absolute" stabilizing ability for *prim* radicals. However, the preponderance of groups with an electron-donating lone pair on N, S, or O is clear.

The stabilizing effect of an adjacent atom with an electron-donating lone pair is typically pictured by VB contributor **3**. In contrast to **2**, **3** should be destabilized by the change from R = H to R = Me, consistent with the well-known destabilizing effect of alkylation on carbanions. For example, for X = NRR′ as a representative case, we would have a significant contribution from **10** to the stabilization of **9**. For X = NHCOR, a variety of resonance contributors **11**−**13** can be considered for the amide group, with **13** again placing negative charge at the radical center (little attention has been paid to theoretical description of four-center five-electron structures such as **11**−**13**).



9 **10**



11 **12** **13**

In simplest terms then, it would appear that those radicals that are stabilized by the transfer of charge away from the formal radical center have positive ΔRSE values while those that are stabilized by the transfer of charge in the reverse direction have negative ΔRSE values.

ΔRSE Effects Based on RSE_Z. The RSE_Z approach[5b] uses the Pauling electronegativity concept[11] to account for the incremental increase in BDE of an unsymmetrical A−B species that results from the $A^{\delta+}{-}B^{\delta-}$ resonance contributor. RSE_Z is defined in eq 8

$$RSE_Z = \frac{1}{2}[BDE(Me-Me) - BDE(R-R)^*] \qquad (8)$$

where BDE(R−R)* is a hypothetical BDE of the R−R species corrected for strain (and other "special effects") and the ethane reference is assumed to be strain-free. This approach builds on the observations of Rüchardt and Beckhaus[12] that BDE(R−R), determined from homolysis rates, can be significantly decreased by relief of internal steric strain from bulky R groups. The two required parameters for each radical, BDE(R−R)* and χ_R, are derived from the modified Pauling equation (eq 9)

$$BDE(A-B) = \frac{1}{2}[BDE(A-A)^* + BDE(B-B)^*] + 96(\chi_A - \chi_B)^2 \text{ kJ/mol} \qquad (9)$$

by solving two simultaneous equations for an arbitrarily selected R−X (with "small" X) along with R−Me:

$$BDE(R-X) = \frac{1}{2}[BDE(R-R)^* + BDE(X-X)] + 96(\chi_R - \chi_X)^2$$

and

$$BDE(R-Me) = \frac{1}{2}[BDE(R-R)^* + BDE(Me-Me)] + 96(\chi_R - \chi_{Me})^2$$

where it is assumed that R−X, R−Me, X−X, and Me−Me species are strain-free. Inserting (in this case the computed) BDE values for R−X, R−Me, X−X, and Me−Me species and known values for χ_X and χ_{Me} allows us to solve for these parameters. In the original work,[5b] X = OH was used, but CLBZ[2] used X = Cl and reported values of χ_R (with χ_{Cl} = 3.18 and χ_{Me} = 2.52) and BDE(R−R)* as well as RSE_Z(R•). Quite reasonably, χ for alkyl radicals decreases with increasing ordinality.

Although the correlation of RSE_Z values with RSE_H values shown by CLBZ[2] was quite good (r^2 = 0.895) with a near-unit slope, they did not emphasize that RSE_Z was systematically offset to much lower values; i.e., $RSE_Z = 0.967 \times RSE_H - 15.80$. Thus, the intercept is decidedly nonzero, and the RSE_Z value for a given radical is on average 16 kJ/mol lower than its RSE_H. If the total RSE_Z values are again partitioned into $R_{Z,prim}$, $R_{Z,sec}$, and $R_{Z,tert}$ as described above, the disparity between the scales, based on the intercepts of the correlations, can be seen to be the greatest for the former and the least for the latter:

$$RSE_{Z,prim} = 0.963(RSE_{Z,prim}) - 11.03 \quad (r^2 = 0.90)$$

$$RSE_{Z,sec} = 1.039(RSE_{H,sec}) - 9.00 \quad (r^2 = 0.95)$$

$$RSE_{Z,tert} = 1.092(RSE_{H,tert}) - 3.22 \quad (r^2 = 0.92)$$

This pattern, when coupled with parallel definitions of ΔRSE_Z, leads to the correlations

$$\Delta RSE_{Z,sec} = 0.673(\Delta RSE_{H,sec}) + 3.48 \quad (r^2 = 0.54)$$

$$\Delta RSE_{Z,tert} = 0.676(\Delta RSE_{H,tert}) + 8.85 \quad (r^2 = 0.60)$$

Most ΔRSE_Z values will be larger than ΔRSE_H (see Tables S-1−S-4 of the Supporting Information), and indeed, 35 of the 64 values of $\Delta RSE_{H,sec}$ and 37 of the 64 values of $\Delta RSE_{H,tert}$ were positive.

The most positive and negative values of ΔRSE_Z are collected in Tables S-1−S-4 of the Supporting Information, and the major deviations from the $RSE_{Z,sec}$ versus $RSE_{Z,prim}$ and $RSE_{Z,tert}$ versus $RSE_{Z,prim}$ correlations (not shown) are collected in Tables S-5−S-8 of the Supporting Information. The functionalities of X that emerge are structurally very similar to those derived from RSE_H. Hence, while the two scales give quite different absolute values of radical stability, the trend for electron-attracting groups to give positive ΔRSE values and for electron-donating groups to give negative ΔRSE values is the same for both scales.

ΔRSE Effects Based on $RSE_{V'}$. Rather than being tied to a reference BDE, the RSE_V approach[8] builds up BDE(A−B) from the sum of individual RSE_V values for each radical A• and B•, augmented by one or two polar correction terms dependent on their electrophilicity and electronegativity, as defined in eq 10

$$BDE(A-B) = RSE_V(A\bullet) + RSE_V(B\bullet) + a[\Delta\omega(A\bullet)][\Delta\omega(B\bullet)] + b[\Delta\chi(A\bullet)][\Delta\chi(B\bullet)] \qquad (10)$$

where the last term is omitted (b = 0) if $\Delta\chi$(A•) and $\Delta\chi$(B•) are both negative, as is true for most carbon-centered radicals. The parameter ω is the global electrophilicity index of the radical from Conceptual DFT[13] and depends on the electronic chemical potential μ and the chemical hardness η according to eq 11

$$\omega = \mu^2/\eta = (IP+EA)^2/8(IP-EA) \quad \text{(eV units)} \qquad (11)$$

These can be evaluated from the experimental or calculated vertical ionization potential (IP) and electronic affinity (EA) of the radical in question. For example, the values of ω for the carbon-centered radicals being considered herein, as derived from the computed IP and EA values of CLBZ,[2] range from 0.55 for the very nucleophilic 2-hydroxy-2-propyl radical to 2.59 for the very electrophilic nitromethyl radical (these computations were conducted at a lower DFT level of theory). De Vleeschouwer and co-workers[8] therefore introduced a shifted "enhanced electrophilicity index" ($\Delta\omega \equiv \omega - 2$) such that the product $a[\Delta\omega(A\bullet)][\Delta\omega(B\bullet)]$ will make a positive contribution to BDE(A−B) for the combination of a very electrophilic and very nucleophilic radical when $a < 0$. Analogously, an "enhanced Pauling electronegativity" ($\Delta\chi \equiv \chi - 3$) was introduced so that when

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[11] Pauling, L. *J. Am. Chem. Soc.* **1932**, *54*, 3570.

[12] (a) Rüchardt, C.; Beckhaus, H.-D. *Angew. Chem., Int. Ed.* **1980**, *19*, 429. (b) Rüchardt, C.; Beckhaus, H.-D. *Top. Curr. Chem.* **1985**, *130*, 1.

[13] Geerlings, P.; De Proft, F.; Langenaeker, W. *Chem. Rev.* **2003**, *103*, 1793.

the electronegativity term is used for very electronegative radicals, the product $b[\Delta\chi(\mathrm{A}\bullet)][\Delta\chi(\mathrm{B}\bullet)]$ makes a positive contribution when $b < 0$.

The $\mathrm{RSE_V}$ approach does not explicitly address strain effects. In practice, not only coefficients a and b but also all the individual empirical $\mathrm{RSE_V(R\bullet)}$ values need to be fitted from a large judiciously chosen training data set. For the sake of consistency, we use the "refit" values from CLBZ[2] based on their computed BDE values (the *prim*, *sec*, and *tert* radical sets were fit separately), whereas the original study[8] had used DFT methods. Because the $\mathrm{RSE_V}$ values are large numbers that decrease with increasing radical stability, to facilitate comparison with $\mathrm{RSE_H}$ and $\mathrm{RSE_Z}$, we convert them to an inverted scale:

$$\begin{aligned}\mathrm{RSE_{V'}(R\bullet)} &= \mathrm{RSE_V(Me\bullet)} - \mathrm{RSE_V(R\bullet)}\\ &= 185.7 - \mathrm{RSE_V(R\bullet)}\end{aligned}$$

Although the correlation of $\mathrm{RSE_{V'}}$ with $\mathrm{RSE_H}$ shown by CLBZ[2] was again quite good ($r^2 = 0.952$), $\mathrm{RSE_{V'}}$ was also systematically offset to lower values than $\mathrm{RSE_H}$, i.e., $\mathrm{RSE_{V'}} = 0.958 \times \mathrm{RSE_H} - 10.61$, although less so than $\mathrm{RSE_Z}$. If the total $\mathrm{RSE_{V'}}$ values are partitioned into $R_{\mathrm{V}',prim}$, $R_{\mathrm{V}',sec}$, and $R_{\mathrm{V}',tert}$ as described above, the disparity between the scales, based on the intercepts of the correlations, can again be seen to be the greatest for the former and the least for the latter:

$$\mathrm{RSE}_{\mathrm{V}',prim} = 0.956(\mathrm{RSE}_{\mathrm{H},prim}) - 7.61 \quad (r^2 = 0.95)$$

$$\mathrm{RSE}_{\mathrm{V}',sec} = 1.013(\mathrm{RSE}_{\mathrm{H},sec}) - 5.58 \quad (r^2 = 0.97)$$

$$\mathrm{RSE}_{\mathrm{V}',tert} = 1.033(\mathrm{RSE}_{\mathrm{H},tert}) - 1.47 \quad (r^2 = 0.97)$$

This pattern, when coupled with parallel definitions of $\Delta\mathrm{RSE_{V'}}$, leads to the correlations

$$\Delta\mathrm{RSE}_{\mathrm{V}',sec} = 0.775(\Delta\mathrm{RSE}_{\mathrm{H},sec}) + 3.17 \quad (r^2 = 0.78)$$

$$\Delta\mathrm{RSE}_{\mathrm{V}',tert} = 0.750(\Delta\mathrm{RSE}_{\mathrm{H},tert}) + 6.56 \quad (r^2 = 0.83)$$

Most $\Delta\mathrm{RSE_{V'}}$ values will lie between $\Delta\mathrm{RSE_Z}$ and $\Delta\mathrm{RSE_H}$ (see Tables S-1–S-4 of the Supporting Information), and indeed, 31 of the 64 values of $\Delta\mathrm{RSE}_{\mathrm{H},sec}$ and 29 of the 64 values of $\Delta\mathrm{RSE}_{\mathrm{H},tert}$ were positive.

The most positive and negative values of $\Delta\mathrm{RSE_{V'}}$ are also collected in Tables S-1–S-4 of the Supporting Information, and the major deviations from the $\mathrm{RSE}_{\mathrm{V}',sec}$ versus $\mathrm{RSE}_{\mathrm{V}',prim}$ and $\mathrm{RSE}_{\mathrm{V}',tert}$ versus $\mathrm{RSE}_{\mathrm{V}',prim}$ correlations (not shown) are collected in Tables S-5–S-8 of the Supporting Information. Again, the functionalities of X that emerge are structurally very similar to those derived from $\mathrm{RSE_H}$, and the same trend for electron-attracting groups to give positive ΔRSE values and for electron-donating groups to give negative ΔRSE values is seen.

Conclusion

In summary, the RSE for a given X depends on both the nature of X and the ordinality of the radical onto which it is substituted. For substituents that stabilize by electron delocalization but also contain electron-withdrawing centers, the general pattern is the counterintuitive $\mathrm{RSE}_{tert} > \mathrm{RSE}_{sec} > \mathrm{RSE}_{prim}$. However, for substituents that stabilize by lone-pair electron donation, the order is strongly reversed. This contrast can be grossly rationalized by considering charge-separated VB contributors **2** and **3** and the contrasting effect of methyl substituents on them. When **2** is the dominant ionic contributor, as dictated by the nature of X, added methyl substituents are particularly stabilizing and $\Delta\mathrm{RSE} > 0$. However, when X favors **3**, the effect of added methyl substituents is reversed and $\Delta\mathrm{RSE} < 0$. This qualitative dichotomy is not dependent on the definition used for RSE.

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Supporting Information Available: Tables S-1–S-8 are the analogues to Tables 1–4 for $\mathrm{RSE_Z}$ and $\mathrm{RSE_{V'}}$ as well as $\mathrm{RSE_H}$. This material is available free of charge via the Internet at http://pubs.acs.org.