PAPER

Effect of substituents on the stabilities of multiply-substituted carbon-centered radicals†‡

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The bond dissociation energies (BDEs) and radical stabilization energies (RSEs) which result from 166 reactions that lead to carbon-centered radicals of the type $^{•}CH_2X$, $^{•}CHXY$ and $^{•}CXYZ$, where X, Y and Z are any of the fourteen substituents H, F, Cl, NH_2, OH, SH, $CH{=}CH_2$, $C{\equiv}CH$, BH_2, CHO, COOH, CN, CH_3, and CF_3, were calculated using spin-restricted and -unrestricted variants of the double-hybrid B2-PLYP method with the 6-311+G(3df,2p) basis set. The interactions of substituents X, Y, and Z in both the radicals ($^{•}CXYZ$) and in the precursor closed-shell molecules (CHXYZ), as well as the extent of additivity of such interactions, were investigated by calculating radical interaction energies (RIEs), molecule interaction energies (MIEs), and deviations from additivity of RSEs (DARSEs) for a set of 152 reactions that lead to di- ($^{•}CHXY$) and tri- ($^{•}CXYZ$) substituted carbon-centered radicals. The pairwise quantities describing the effects of pairs of substituents in trisubstituted systems, namely pairwise MIEs (PMIEs), pairwise RIEs (PRIEs) and deviations from pairwise additivity of RSEs (DPARSEs), were also calculated for the set of 61 reactions that lead to trisubstituted radicals ($^{•}CXYZ$). Both ROB2-PLYP and UB2-PLYP were found to perform quite well in predicting the quantities related to the stabilities of carbon-centered radicals when compared with available experimental data and with the results obtained from the high-level composite method G3X(MP2)-RAD. Particular selections of substituents or combinations of substituents from the current test set were found to lead to specially stable radicals, increasing the RSEs to a maximum of +68.2 kJ mol^{-1} for monosubstituted radicals $^{•}CH_2X$ (X = CH=CH$_2$), +131.7 kJ mol^{-1} for disubstituted radicals $^{•}CHXY$ (X = NH$_2$, Y = CHO), and +177.1 kJ mol^{-1} for trisubstituted radicals $^{•}CXYZ$ (X = NH2, Y = Z = CHO).

1. Introduction

Carbon-centered radicals are important intermediates in a variety of chemical reactions. Both thermodynamic (stabilization energy) and kinetic (persistence) stabilities[1] of C-centered radicals can be modified to design, manipulate and control the reactions in which they are involved. There are numerous reactions in

synthetic organic chemistry,[2] polymer chemistry,[3] biochemistry[4] and inorganic chemistry,[5] where the effect of substituents on the thermodynamic stabilization or destabilization of C-centered radicals is exploited.

Considerable previous work has been carried out on the effect of substituents on the *thermodynamic* stabilities of carbon-centered radicals,[6] the subject on which the present report will focus. Of particular relevance are experimental,[7,8] and theoretical[9] studies of bond dissociation energies. Additionally, there have been studies concerned with the definition and measurement of radical stability.[10]

A common measure of the effect of a substituent on the thermodynamic stability of a carbon-centered radical is the radical stabilization energy (RSE). For a monosubstituted radical ($^{•}CH_2X$), the RSE is given by the energy change for the hydrogen-atom-transfer reaction:

$$^{•}CH_2X + CH_4 \rightarrow CH_3X + {}^{•}CH_3 \qquad (1)$$
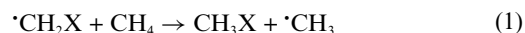
The RSE measures the effect of X on the stability of the radical ($^{•}CH_2X$) relative to its effect in the closed-shell parent (CH$_3$X), with CH$_4$ and $^{•}CH_3$ being included as the reference (unsubstituted) species. Defined in this way, a positive value for the RSE implies a

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† In memory of our dear friend and colleague Athel Beckwith, in recognition of his many outstanding contributions to chemistry.
‡ Electronic supplementary information (ESI) available: Comparison of RSEs calculated for $^{•}CH_2X$ radicals with experimental values (Table S1), calculated ROB2-PLYP and UB2-PLYP (Table S2) and G3X(MP2)-RAD (Table S3) total energies, calculated BDEs, RSEs, RIEs, MIEs, DARSEs, PRIEs, PMIEs and DPARSEs at the UB2-PLYP/6-311+G(3df,2p)//UB3LYP/6-31G(d) level (Table S4) and optimized UB3-LYP/6-31G(d) geometries of molecules (Table S5) and radicals (Table S6). See DOI: 10.1039/c1ob05196b

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net stabilization of the substituted radical $^\bullet CH_2X$ with respect to $^\bullet CH_3$ relative to the same effect in the parent closed-shell species (CH_3X vs. CH_4), while a negative value implies a net destabilization.

The RSE defined by the energy change in reaction 1 can equivalently be regarded as the difference between the homolytic C–H bond dissociation energy (BDE) of methane and CH_3X:

$$RSE(^\bullet CH_2X) = BDE(CH_4) - BDE(CH_3X) \qquad (2)$$

where $BDE(CH_3X)$ is the energy change in the reaction

$$CH_3X \rightarrow {}^\bullet CH_2X + {}^\bullet H \qquad (3)$$

A number of alternatives to the RSE have been proposed as measures of radical stability,[11] and these have recently been critically compared by Coote et al.,[10a] who concluded that, in the case of carbon-centered radicals, the various definitions correlate well with one another, and with calculated spin densities. In the present study, we use RSEs, as these are conceptually the simplest of the various measures. Nevertheless, it is important to keep in mind that RSEs are *relative* quantities and that there is no unambiguous way to define the *absolute* stability of a radical.[10b]

The main purpose of the present study is to improve our understanding of the effect of substituents on the thermodynamic stabilities of trisubstituted carbon-centered radicals ($^\bullet CXYZ$) since these have received limited previous attention in the literature.[6,12] We include, as special cases, the monosubstituted radicals ($^\bullet CH_2X$, i.e., $Y = Z = H$)[9a,13] and disubstituted radicals ($^\bullet CHXY$, i.e., $Z = H$),[2a,b,14] which have been the focus of extensive previous studies. We are particularly interested in examining the stabilizing or destabilizing interactions of substituents both in the closed-shell parents (CHXYZ) and in the product radicals ($^\bullet CXYZ$), and in examining the extent of additivity of such interactions. We introduce new definitions to help us in this endeavor. We also assess the performance of various levels of theory in describing both absolute effects (e.g., BDEs) and relative effects (e.g., RSEs).

2. Analysis of stabilization energies and interaction energies

Following the above introduction, we take as a measure of the combined effect of all substituents on the stability of a general multiply-substituted methyl radical ($^\bullet CXYZ$), relative to their effect in the closed-shell species CHXYZ, the radical stabilization energy (RSE), i.e., the energy change for the reaction:

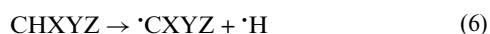$$^\bullet CXYZ + CH_4 \rightarrow CHXYZ + {}^\bullet CH_3 \qquad (4)$$

With this definition, a positive value for the RSE means that, collectively, the substituents stabilize the radical more than they stabilize the closed-shell molecule.

By analogy with eqn (2) and (3) in the introduction, we can write that

$$RSE(^\bullet CXYZ) = BDE(CH_4) - BDE(CHXYZ) \qquad (5)$$

where $BDE(CHXYZ)$ is the energy change for the reaction

$$CHXYZ \rightarrow {}^\bullet CXYZ + {}^\bullet H \qquad (6)$$

For multiply-substituted methyl radicals, it is convenient to introduce some additional quantities. We define the *radical interaction energy* (RIE) for the radical $^\bullet CXYZ$ as the energy of the formal reaction

$$^\bullet CXYZ + 2\,{}^\bullet CH_3 \rightarrow {}^\bullet CH_2X + {}^\bullet CH_2Y + {}^\bullet CH_2Z \qquad (7)$$
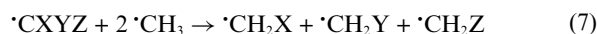
This measures the combined effect of the three substituents in $^\bullet CXYZ$ compared with the sum of their individual effects in the monosubstituted radicals. A positive RIE means that the interaction between the substituents in the multiply-substituted radical is stabilizing, i.e., it is synergistic.

Similarly, the *molecule interaction energy* (MIE) for the molecule CHXYZ is the energy change in the formal reaction

$$CHXYZ + 2\,CH_4 \rightarrow CH_3X + CH_3Y + CH_3Z \qquad (8)$$
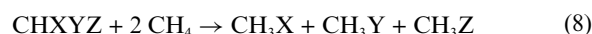
The MIE measures the combined effect of the three substituents in the molecule CHXYZ compared with the sum of their individual effects in the monosubstituted methanes. A positive MIE indicates a stabilizing interaction between the substituents in the multiply-substituted methane.

For di- ($Z = H$) or tri-substituted radicals, it is useful to examine whether the effects of the substituents on the radical stabilization energies reinforce one another (i.e., are synergistic) or whether they oppose one another (i.e., are antagonistic). This is conveniently done by calculating the *deviation from additivity of the radical stabilization energy* (DARSE) for the radical $^\bullet CXYZ$, which is given by

$$DARSE(^\bullet CXYZ) = RSE(^\bullet CXYZ) - RSE(^\bullet CH_2X) - \\ RSE(^\bullet CH_2Y) - RSE(^\bullet CH_2Z) \qquad (9)$$
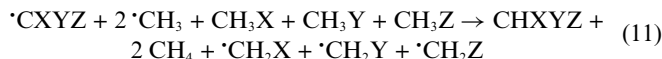
The DARSE values tell us how close the RSEs of multiply-substituted methyl radicals are to the values predicted on the basis of additivity of values for monosubstituted methyl radicals. If RSEs were strictly additive, then the DARSE values would be exactly zero. If the effects of the interactions on the RSEs are synergistic then the DARSE values are positive, whereas if the interactions are antagonistic the DARSE values are negative.
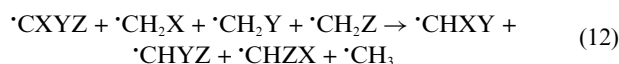
It is easy to show that

$$DARSE(^\bullet CXYZ) = RIE(^\bullet CXYZ) - MIE(CHXYZ) \qquad (10)$$

This indicates that positive DARSE values arise when the interactions in the radical ($^\bullet CXYZ$) are more stabilizing (or less destabilizing) than the interactions in the molecule (CHXYZ).

Both expressions 9 and 10 indicate that DARSE($^\bullet CXYZ$) is given by the energy change for the formal reaction

$$^\bullet CXYZ + 2\,{}^\bullet CH_3 + CH_3X + CH_3Y + CH_3Z \rightarrow CHXYZ + \\ 2\,CH_4 + {}^\bullet CH_2X + {}^\bullet CH_2Y + {}^\bullet CH_2Z \qquad (11)$$
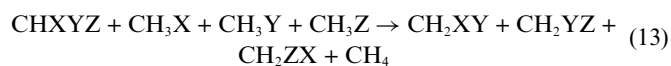
For trisubstituted radicals, it is also useful to examine the *deviations from pairwise additivity*, i.e., to measure how closely the results for trisubstituted radicals can be predicted on the basis of results for disubstituted radicals. In this respect, it is useful to define the *pairwise radical interaction energy* (PRIE) for the radical $^\bullet CXYZ$ as the energy change in the formal reaction

$$^\bullet CXYZ + {}^\bullet CH_2X + {}^\bullet CH_2Y + {}^\bullet CH_2Z \rightarrow {}^\bullet CHXY + \\ {}^\bullet CHYZ + {}^\bullet CHZX + {}^\bullet CH_3 \qquad (12)$$

This compares the interaction of substituents in the radical $^\bullet CXYZ$ with the sum of the interactions in the disubstituted radicals.

Similarly, the *pairwise molecule interaction energy* (PMIE) for the molecule CHXYZ is the energy change in the formal reaction

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$$CHXYZ + CH_3X + CH_3Y + CH_3Z \rightarrow CH_2XY + CH_2YZ + \\ CH_2ZX + CH_4 \quad (13)$$

This compares the interaction of substituents in the molecule CHXYZ with the sum of the pairwise interactions in the disubstituted methanes.

Finally, the deviation from pairwise additivity of the radical stabilization energy (DPARSE) for the radical ˙CXYZ is given by

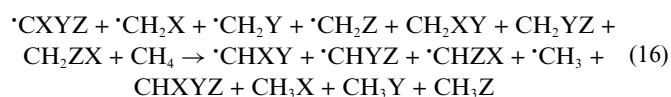$$DPARSE(˙CXYZ) = RSE(˙CXYZ) - RSE(˙CHXY) - \\ RSE(˙CHYZ) - RSE(˙CHZX) + RSE(˙CH_2X) + \quad (14) \\ RSE(˙CH_2Y) + RSE(˙CH_2Z)$$

If RSEs were pairwise additive, then DPARSE(˙CXYZ) would be zero.

It is again easy to show that

$$DPARSE(˙CXYZ) = PRIE(˙CXYZ) - PMIE(CHXYZ) \quad (15)$$

and that DPARSE (˙CXYZ) is the energy change for the formal reaction

$$˙CXYZ + ˙CH_2X + ˙CH_2Y + ˙CH_2Z + CH_2XY + CH_2YZ + \\ CH_2ZX + CH_4 \rightarrow ˙CHXY + ˙CHYZ + ˙CHZX + ˙CH_3 + \quad (16) \\ CHXYZ + CH_3X + CH_3Y + CH_3Z$$

We shall use the various quantities defined in this section to help us in our understanding of the factors that determine the stabilities of carbon-centered radicals.

3. Theoretical methods

Standard *ab initio* molecular orbital theory[15] and density functional theory (DFT)[16] calculations were carried out with the Gaussian 03,[17] Gaussian 09,[18] and Molpro 2002.6[19] computer programs. Geometries and vibrational frequencies were obtained at the B3-LYP/6-31G(d) level (unrestricted version for radicals) and the latter scaled[20] by a factor of 0.9806 to obtain zero-point vibrational energies and by a factor of 0.9989 to obtain thermal corrections to reaction enthalpies. Potential energy scans or conformational searches were carried out both for the parent closed-shell molecules and for the radicals, and were cross-checked with previous structural studies, wherever possible, to find the global minimum structures. In some cases, this involved corrections to predictions of previous studies,[14e] which had used lower levels of theory. Variations in conformational energies were useful in examining the source of stabilizing or destabilizing interactions (*e.g.*, conjugative or hyperconjugative interactions that can be turned on and off by rotation, H-bonding, steric effects *etc.*).

As quantum chemical calculations on open-shell systems pose special problems,[21] the selection of reliable theoretical procedures for the calculation of relative energies constitutes an important aspect of the present study. Several previous studies have aimed to find reliable yet economical methods to study the thermochemistry of radicals.[9] In studies on a test set of 22 monosubstituted methyl radicals,[9b,c,22] we have found that, among contemporary DFT procedures, the restricted-open-shell version of Grimme's double-hybrid B2-PLYP DFT procedure[23] (with incorporation, as in UB2-PLYP, of 53% Hartree–Fock exchange and 27% MP2 correlation based on Kohn–Sham orbitals) performed particularly well when combined with the 6-311+G(3df,2p) basis set. This RB2-PLYP/6-311+G(3df,2p) procedure was found[9c,22] to slightly (but consistently) underestimate the BDEs, giving a mean deviation of −6.9 kJ mol⁻¹ and a mean absolute deviation of 6.9 kJ mol⁻¹ from

values calculated with the high-level W1 method,[24] and −5.3 and 5.4 kJ mol⁻¹ from available experimental BDEs. For RSEs, RB2-PLYP yielded an MAD of 1.9 kJ mol⁻¹ from values calculated with the high-level W1 method,[24] and 2.8 kJ mol⁻¹ from experimentally based RSEs. In a subsequent study,[25] the HF and MP2 mixing parameters for the restricted-open-shell procedure were reoptimized, leading to a method referred to as ROB2-PLYP(59,28), indicating that it has 59% HF exchange and 28% MP2 correlation. As this procedure was found to show improved performance with regard to predicting RSEs, we decided to use it in this study (designating it simply as ROB2-PLYP from here onwards) in association with the 6-311+G(3df,2p) basis set[26] as the primary procedure for single-point energy calculations throughout the present study. Thus, unless otherwise noted, energies in the text refer to ROB2-PLYP/6-311+G(3df,2p)//UB3-LYP/6-31G(d) values.

The BDEs and RSEs for all systems were also calculated with UB2-PLYP/6-311+G(3df,2p)//UB3-LYP/6-31G(d), which we had found to yield predictions of an accuracy comparable to that of (non-optimized) RB2-PLYP.[9b,c] In these calculations, we employed the original B2-PLYP parameters of 53% HF exchange and 27% MP2 correlation. We had found previously[27] that the double-hybrid UDFT procedure is able to benefit from the inclusion of UHF and UMP2 contributions without incurring to the same extent the problems associated with spin contamination as "normal" unrestricted HF and MP2 often do.

Finally, the BDEs and RSEs were calculated for a subset of 106 reactions with the high-level composite procedure G3X(MP2)-RAD,[28] which approximates the URCCSD(T)/G3XLarge level of theory on UB3-LYP/6-31G(2df,p) geometries. This method had previously been found[9] to represent a good compromise between accuracy and affordability for predicting the thermochemistry of monosubstituted radicals (˙CH₂X). The subset of 106 reactions includes the complete set of reactions involving monosubstituted (˙CH₂X)[9b] and trisubstituted (˙CXYZ) radicals, and a selected subset of reactions involving disubstituted (˙CHXY) radicals. The BDEs and RSEs calculated by the RO- and U-B2-PLYP/6-311+G(3df,2p) methods (at UB3-LYP/6-31G(d)-optimized geometries) were compared with the corresponding values predicted by G3X(MP2)-RAD for these sets.

Since our earlier assessment study[9b] was limited to monosubstituted carbon-centered radicals (˙CH₂X), we tested here the performance of the ROB2-PLYP/6-311+G(3df,2p), UB2-PLYP/6-311+G(3df,2p) and G3X(MP2)-RAD methods in predicting radical thermochemistry for di- (˙CHXY) and tri- (˙CXYZ) substituted systems. For this purpose, the BDEs and RSEs calculated at these three levels were compared with the corresponding experimental data for 39 reactions for which experimental data,[7,29,30] are available.

For two molecules, allyl fluoride and allyl chloride, the BDEs obtained with G3X(MP2)-RAD differed from the currently recommended values[7] by more than 10 kJ mol⁻¹. They were therefore further examined using the high-level W1 procedure[24] to see whether theory or experiment was more likely to be at fault.

4. Results and discussion

Bond dissociation energies (BDEs) and radical stabilization energies (RSEs) were calculated at the ROB2-PLYP/6-311+G(3df,2p) and UB2-PLYP/6-311+G(3df,2p) levels for relevant species

involved in the 166 reactions that lead to carbon-centered radicals of the type $^\bullet CH_2X$, $^\bullet CHXY$ and $^\bullet CXYZ$, where X, Y and Z are any of the fourteen substituents H, F, Cl, NH_2, OH, SH, $CH{=}CH_2$, $C{\equiv}CH$, BH_2, CHO, COOH, CN, CH_3, and CF_3. Radical interaction energies (RIEs), molecule interaction energies (MIEs), and deviations from additivity of RSEs (DARSEs) were also calculated with ROB2-PLYP for the set of 152 reactions that lead to di- ($^\bullet CHXY$) and tri- ($^\bullet CXYZ$) substituted carbon-centered radicals.[31] The pairwise quantities, namely PMIEs, PRIEs and DPARSEs, were calculated for the set of 61 reactions that lead to trisubstituted radicals ($^\bullet CXYZ$).

The substituents can be classified as:

(1) π-donor, σ-acceptor ($\pi_d\sigma_a$):NH_2, F, Cl, OH, and SH.

(2) π-acceptor, σ-donor ($\pi_a\sigma_d$): BH_2.

(3) π-acceptor, σ-acceptor ($\pi_a\sigma_a$): CHO, COOH, and CN.

(4) π-acceptor or π-donor (π_a/π_d): $CH{=}CH_2$ and $C{\equiv}CH$. These substituents may either be π-donors or π-acceptors depending on their environment.

(5) Hyperconjugative donor or hyperconjugative acceptor (hc_d/hc_a): CH_3. This group can also be a weak σ-donor or σ-acceptor, depending on the environment.

(6) σ-acceptor and hyperconjugative acceptor ($\sigma_a hc_a$): CF_3.

To facilitate comparison, it is convenient to divide the test set consisting of 166 systems into five groups:

(A) {π_d}: This set (2–29) consists of systems mono-, di- or tri-substituted by π-donors.

(B) {π_a}: This set (30–66) consists of systems mono-, di- or tri-substituted by π-acceptors. The systems with (π_a/π_d) substituents are included here.

(C) {$\pi_d\pi_a Z$}: This set (67–127) consists of di- and tri-substituted systems in which one of the substituents (X) is a π-donor, a second substituent (Y) is a π-acceptor, and Z varies.

(D) {CQ_3}: This set (128–134) consists of systems mono-, di- or tri-substituted with CH_3 and/or CF_3.

(E) {X-CQ_3}: This set (135–166) consists of di- and tri-substituted systems where X varies and where the Y (for $^\bullet CHXY$) or Z (for $^\bullet CXYZ$) substituents are either CH_3 or CF_3.

4.1. Comparison of methods

A comprehensive and critical compilation of experimental BDE data has been published by Luo.[7] Table 1 compares the BDEs and RSEs calculated at the ROB2-PLYP, UB2-PLYP and G3X(MP2)-RAD levels for the 39 reactions for which recommended experimental BDEs are available.[7] For a small number of molecules (see below), we use alternative experimental BDEs,[29] as recommended in ref. 9b.

The largest differences between theoretical and experimental BDEs in Table 1 (approximately 20 kJ mol⁻¹) occur for allyl fluoride and allyl chloride. In order to check whether it is likely to be theory or experiment that is at fault in these comparisons, we have also calculated the BDEs for these two molecules using the high-level W1 procedure. The W1 values of the BDEs for allyl fluoride and allyl chloride are 349.2 and 349.9 kJ mol⁻¹, respectively, while the related RSEs are 83.1 and 82.4 kJ mol⁻¹, which provides support for the predictions of our other theoretical methods. In the light of the close agreement between theoretical and experimental BDEs for the other systems, and noting the limitations often encountered in experimental determinations of bond dissociation energies,[7] we

recommend a re-evaluation of the experimental BDEs for allyl fluoride and allyl chloride.

Table 1 shows that the G3X(MP2)-RAD BDEs compare reasonably well with the experimental BDEs, with an MAD of 3.6 kJ mol⁻¹. ROB2-PLYP seems to consistently underestimate the BDEs when compared with experimental values, and as a result the mean deviation (MD = −7.4 kJ mol⁻¹) and the mean absolute deviation (MAD = 7.5 kJ mol⁻¹) have almost the same magnitudes. The underestimation of BDEs is somewhat greater for UB2-PLYP (MD = −11.8 kJ mol⁻¹, MAD = 11.8 kJ mol⁻¹).

The isodesmic reaction that defines the radical stabilization energies (eqn (4)) offers the prospect for some cancellation of errors. As a consequence, methods that perform less well in predicting BDEs might still produce acceptable radical stabilization energies. This is the case for ROB2-PLYP and UB2-PLYP, for which the RSEs have an MAD from the experimental values of 3.5 and 3.9 kJ mol⁻¹, respectively. However, G3X(MP2)-RAD shows a slightly larger MAD for RSEs (3.9 kJ mol⁻¹) than for BDEs (3.6 kJ mol⁻¹).

In addition to comparing the theoretical BDEs and RSEs with the corresponding experimental values, we also compare the RSEs calculated at the ROB2-PLYP and UB2-PLYP levels with the corresponding G3X(MP2)-RAD values, to enable a broader comparison. It can be seen from the correlation graph given in Fig. 1 that the ROB2-PLYP and G3X(MP2)-RAD trends in RSEs are in good accord, with a correlation equation y = 1.0795x + 3.2503, showing an R^2 value of 0.9921. For UB2-PLYP the corresponding equation is y = 1.0707x + 4.6257, also with an R^2 value of 0.9921. Both ROB2-PLYP and UB2-PLYP consistently overestimate the RSEs of mono-, di- and tri-substituted radicals, with mean deviations of 9.2 and 10.0 kJ mol⁻¹ from G3X(MP2)-RAD values. Interestingly, the mean deviation in the ROB2-PLYP RSEs from the G3X(MP2)-RAD values increases as we go from mono- (2.1 kJ mol⁻¹) to di- (5.7 kJ mol⁻¹), to tri- (12.6 kJ mol⁻¹) substituted radicals.
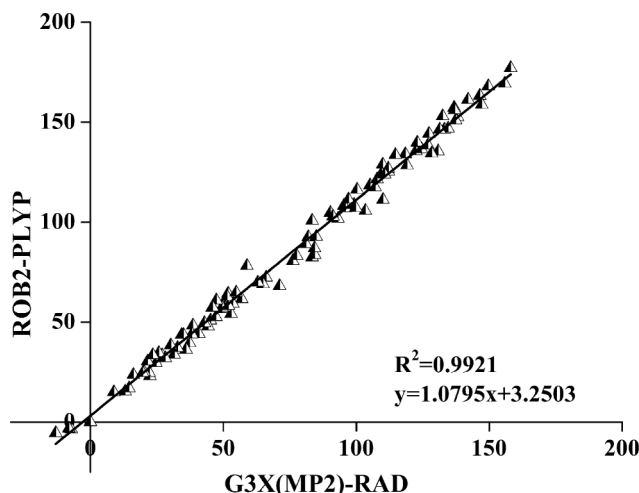

Fig. 1 Correlation of ROB2-PLYP and G3X(MP2)-RAD radical stabilization energies (kJ mol⁻¹).

4.2. Effect of substituents on radical stability

Table 2 lists the bond dissociation energies (BDEs, reaction 6) and the radical stabilization energies (RSEs, reaction 4) for the 166

Table 1 Comparison of calculated bond dissociation energies (BDEs) for CHXYZ → ˙CXYZ +˙H and radical stabilization energies (RSEs) for ˙CXYZ with experimental values (0 K, kJ mol^{-1})

X	Y	Z	BDE				RSE			
			ROB2-PLYP[a]	UB2-PLYP[a]	G3X(MP2)-RAD	Expt.[b]	ROB2-PLYP[a]	UB2-PLYP[a]	G3X(MP2)-RAD	Expt.[b]
H	H	H	426.6	423.5	429.1[c]	432.5 ± 0.4				
NH$_2$	H	H	375.7	371.4	383.9[c]	386.7 ± 8.4	50.9	52.1	45.2[c]	45.8 ± 8.4
OH	H	H	390.5	386.3	396.6[c]	395.8 ± 0.6	36.1	37.2	32.5[c]	36.7 ± 0.6
F	H	H	411.2	407.3	416.0[c]	417.3 ± 4.2	15.4	16.2	13.1[c]	15.2 ± 4.2
CH$_3$	H	H	409.6	405.8	414.5[c]	413.0 ± 1.3	17.0	17.7	14.5[c]	19.5 ± 1.3
CF$_3$	H	H	430.2	427.4	436.3[c]	439.3 ± 4.5	−3.6	−3.8	−7.2[c]	−6.8 ± 4.5
SH	H	H	387.1	382.0	391.8[c]	386.1 ± 8.4	39.5	41.5	37.3[c]	46.4 ± 8.4
Cl	H	H	403.6	399.0	406.7[c]	411.3 ± 2.3	23.0	24.5	22.4[c]	21.2 ± 2.3
CHCH$_2$	H	H	358.4	351.7	358.0[c]	363.5 ± 3.0	68.2	71.9	71.1[c]	69.0 ± 3.0
CCH	H	H	372.5	367.2	376.2[c]	377.5 ± 4.2[d]	54.1	56.3	52.9[c]	55.0 ± 4.2[d]
CHO	H	H	390.3	386.7	393.1[c]	392.7[e,f]	36.3	36.8	36.0[c]	39.8[e,f]
COOH	H	H	401.9	397.9	406.9[c]	407.7 ± 3.3[g]	24.7	25.6	22.1[c]	24.8 ± 3.3[g]
CN	H	H	392.8	389.0	397.6[c]	399.5 ± 4.2	33.8	34.5	31.5[c]	33.0 ± 4.2
CH$_3$	CH$_3$	H	397.0	392.6	404.4	406.7 ± 2.9	29.6	30.8	24.7[c]	25.8 ± 2.9
CH$_3$	NH$_2$	H	369.1	364.7	378.5	370.4 ± 8.4	57.5	58.7	50.6	62.1 ± 8.4
F	CHCH$_2$	H	344.2	337.0	345.7	364.8 ± 4.6[h]	82.4	86.5	83.4	67.7 ± 4.6[h]
Cl	CHCH$_2$	H	342.9	337.0	344.7	365.1 ± 4.6[h]	83.7	86.5	84.4	67.4 ± 4.6[h]
CH$_3$	CCH	H	357.6	352.4	364.1	365.6[f]	69.0	71.0	64.9	66.9[f]
CH$_3$	CHCH$_2$	H	346.0	339.7	353.0	351.8[f]	80.6	83.8	76.1	80.7[f]
CH$_3$	CHO	H	365.0	361.2	372.1	378.1[f]	61.6	62.2	57.0	54.4[f]
CH$_3$	Cl	H	394.5	389.9	400.9	399.4 ± 1.5	32.1	33.6	28.2	33.1 ± 1.5
CH$_3$	CN	H	374.0	370.0	381.8	386.4 ± 12.6[i]	52.6	53.4	47.2	46.1 ± 12.6[i]
CH$_3$	F	H	401.4	397.3	408.9	404.2 ± 8.4	25.2	26.2	20.1	28.3 ± 8.4
CH$_3$	OH	H	382.6	378.3	391.0	394.8 ± 4.2	44.0	45.1	38.1	37.7 ± 4.2
CHCH$_2$	CHCH$_2$	H	315.4	309.6	319.1	315.0[f]	111.2	113.9	110.0	117.5[f]
Cl	CF$_3$	H	403.0	397.7	412.9	418.8 ± 6.3	23.6	25.8	16.2	13.7 ± 6.3
Cl	Cl	H	389.5	384.9	396.3	394.2 ± 2.0	37.1	38.6	32.8	38.3 ± 2.0
CN	CN	H	356.8	354.3	366.1	360.5[f]	69.8	69.2	63.0	72.0[f]
COOH	Cl	H	367.3	362.4	375.5	375.0[f]	59.3	61.1	53.6	57.5[f]
COOH	CN	H	368.4	365.1	377.1	385.0[f]	58.2	58.4	52.0	47.4[f]
COOH	COOH	H	378.7	374.3	384.8	394.3[f]	47.9	49.2	44.2	38.2[f]
COOH	NH$_2$	H	318.3	313.7	333.7	323.5[f]	108.3	109.8	95.3	109[f]
F	F	H	411.6	408.0	420.3	425.7 ± 4.2	15.0	15.5	8.8	6.8 ± 4.2
NH$_2$	CN	H	334.1	330.1	347.2	348.8[f]	92.5	93.3	81.9	83.7[f]
OH	CHCH$_2$	H	320.9	314.9	325.6	335.1 ± 7.5	105.7	108.6	103.5	97.4 ± 7.5
F	Cl	H	402.0	397.8	409.4	415.6 ± 10.0	24.6	25.6	19.7	16.9 ± 10.0
F	F	F	431.9	428.3	442.2	440.2 ± 4.2	−5.3	−4.8	−13.1	−7.7 ± 4.2
CH$_3$	CH$_3$	CH$_3$	388.2	383.6	398.8	392.4 ± 2.9	38.4	39.9	30.2	40.1 ± 2.9
Cl	Cl	Cl	377.0	372.7	386.2	386.3 ± 2.5	49.6	50.8	42.9	46.2 ± 2.5
MD[f,h,i,j]			−7.4	−11.8	−1.0		1.6	2.9	−2.5	
MAD[f,h,i,j]			7.5	11.8	3.6		3.5	3.9	3.9	

[a] Calculated using the 6-311+G(3df,2p) basis set. [b] BDEs and RSEs at 0 K calculated using experimental BDEs at 298 K from ref. 7, unless otherwise noted, with the thermal back-corrections to 0 K obtained at the (scaled) UB3-LYP/6-31G(d) level. [c] BDEs and RSEs taken from ref. 9b. [d] Calculated using the experimental BDE for propyne reported by Tsang.[29] [e] Calculated using the experimental BDE for acetaldehyde reported by Cumming and Kebarle.[29] [f] Species without experimental error bars are not included in the statistics. [g] Calculated using the experimental BDE for acetic acid reported by Lagoa *et al.*;[29] [h] BDEs of allyl fluoride and allyl chloride are excluded from the statistics. [i] Species with experimental uncertainties greater than ±10 kJ mol^{-1} are not included in the statistics. [j] MD and MAD are the mean deviation and mean absolute deviation, respectively, from experimental values.

reactions that lead to mono-, di- and trisubstituted carbon-centered radicals. Also given are the radical interaction energies (RIEs), the molecule interaction energies (MIEs), and the deviations from additivity of the RSEs (DARSEs), calculated as the energy changes for reactions 7 and 8, and from eqn (9), respectively, for the set of 91 reactions that lead to disubstituted radicals ˙CHXY and the 61 reactions that lead to trisubstituted radicals ˙CXYZ. For the latter, Table 2 also gives the pairwise quantities, namely the pairwise molecule interaction energies (PMIEs), pairwise radical interaction energies (PRIEs) and deviations from pairwise interaction energies (DPARSEs), calculated for the energy changes for reactions 12 and 13, and from eqn (14),

respectively. The relative energies have all been calculated at the ROB2-PLYP level. RSEs calculated at the UB2-PLYP level for the entire set of reactions and those calculated at the G3X(MP2)-RAD level for a subset of 106 reactions are also included in square brackets and in parentheses, respectively, in Table 2. In the following sections, we will often use the nomenclature (X,Y,Z) to describe the CHXYZ/˙CXYZ system. For example, (NH$_2$,NH$_2$,NH$_2$) would refer to the dissociation reaction involving the molecule CH(NH$_2$)$_3$ and the radical ˙C(NH$_2$)$_3$.

4.2.1. Monosubstituted systems. As already mentioned, the stabilization of monosubstituted carbon-centered radicals by

Table 2 Calculated bond dissociation energies (BDEs), radical stabilization energies (RSEs), molecule interaction energies (MIEs), radical interaction energies (RIEs), deviations from additivity of RSEs (DARSEs), pairwise MIEs (PMIEs), pairwise RIEs (PRIEs), and deviations from pairwise additivity of RSEs (DPARSEs) (0 K, kJ mol^{-1}) for the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$, $\{CQ_3\}$, and $\{X-CQ_3\}$ sets

Set	#	X	Y	Z	BDE^a	RSE^{a,b}	MIE^a	RIE^a	DARSE^a	PMIE^a	PRIE^a	DPARSE^a
	1	H	H	H	426.6	0.0 [0.0] (0.0)						
$\{\pi_d\}$	2	F	H	H	411.2	15.4 [16.2] (13.1)						
	3	Cl	H	H	403.6	23.0 [24.5] (22.4)						
	4	NH$_2$	H	H	375.7	50.9 [52.1] (45.2)						
	5	OH	H	H	390.5	36.1 [37.2] (32.5)						
	6	SH	H	H	387.1	39.5 [41.5] (37.3)						
	7	F	F	H	411.6	15.0 [15.5] (8.8)	52.9	37.1	−15.8			
	8	Cl	F	H	402.0	24.6 [25.6] (19.7)	20.6	6.8	−13.8			
	9	NH$_2$	F	H	403.1	23.5 [24.3]	64.0	21.2	−42.8			
	10	OH	F	H	398.4	28.2 [28.8]	61.9	38.5	−23.3			
	11	SH	F	H	393.5	33.1 [34.7]	21.6	−0.2	−21.9			
	12	Cl	Cl	H	389.5	37.1 [38.6] (32.8)	2.9	−6.1	−8.9			
	13	NH$_2$	Cl	H	390.3	36.3 [36.8]	44.4	6.8	−37.6			
	14	OH	Cl	H	387.8	38.8 [39.6]	34.7	14.4	−20.3			
	15	SH	Cl	H	379.4	47.2 [48.9]	9.6	−5.7	−15.4			
	16	NH$_2$	NH$_2$	H	369.2	57.4 [58.3] (49.5)	39.3	−5.1	−44.4			
	17	OH	NH$_2$	H	383.5	43.1 [44.1]	51.5	7.6	−43.9			
	18	SH	NH$_2$	H	359.8	66.8 [68.1]	24.0	0.4	−23.6			
	19	OH	OH	H	389.6	37.0 [37.7]	63.7	28.4	−35.3			
	20	SH	OH	H	382.6	44.0 [45.4]	29.2	−2.5	−31.7			
	21	SH	SH	H	367.8	58.8 [60.7]	11.4	−8.9	−20.3			
	22	F	F	F	431.9	−5.3 [−4.8] (−13.1)	135.1	83.5	−51.6	−23.7	−27.9	−4.2
	23	Cl	Cl	Cl	377.0	49.6 [50.8] (42.9)	0.2	−19.2	−19.4	−8.5	−1.1	7.4
	24	NH$_2$	NH$_2$	NH$_2$	369.2	57.4 [58.9] (46.0)	96.1	0.8	−95.3	−21.8	16.0	37.8
	25	OH	OH	OH	382.9	43.7 [44.6] (35.0)	137.2	72.4	−64.7	−53.9	−12.8	41.2
	26	SH	SH	SH	343.4	83.2 [85.2] (77.6)	19.9	−15.6	−35.5	−14.3	11.2	25.5
	27	NH$_2$	F	OH	393.0	33.6 [34.6] (23.5)	135.4	66.5	−68.9	−41.9	−0.8	41.1
	28	SH	NH$_2$	NH$_2$	361.7	64.9 [66.6] (54.8)	69.6	−6.8	−76.4	−17.8	−2.6	15.1
	29	SH	SH	NH$_2$	348.4	78.2 [79.6] (58.9)	44.9	−6.9	−51.8	−14.5	1.2	15.8
$\{\pi_a\}$	30	BH$_2$	H	H	382.6	44.0 [43.2] (40.9)						
	31	CHO	H	H	390.3	36.3 [36.8] (36.0)						
	32	CN	H	H	392.8	33.8 [34.5] (31.5)						
	33	COOH	H	H	401.9	24.7 [25.6] (22.1)						
	34	CHCH$_2$	H	H	358.4	68.2 [71.9] (71.1)						
	35	CCH	H	H	372.5	54.1 [56.3] (52.9)						
	36	BH$_2$	BH$_2$	H	370.0	56.6 [57.2] (49.5)	16.3	−15.1	−31.4			
	37	BH$_2$	CHO	H	366.5	60.1 [59])	9.4	−10.8	−20.2			
	38	BH$_2$	CN	H	355.9	70.7 [70.4]	4.2	−2.9	−7.1			
	39	BH$_2$	COOH	H	378.5	48.1 [48.4]	8.1	−12.5	−20.7			
	40	CHO	CHO	H	362.5	64.1 [62.9]	−4.7	−13.1	−8.5			
	41	CHO	CN	H	358.7	67.9 [67.2]	−10.4	−12.6	−2.1			
	42	CHO	COOH	H	370.9	55.7 [55.8]	−3.0	−8.3	−5.3			
	43	CN	CN	H	356.8	69.8 [69.2] (63.0)	−34.6	−32.3	2.3			
	44	CN	COOH	H	368.4	58.2 [58.4] (52.0)	−17.0	−17.3	−0.3			
	45	COOH	COOH	H	378.7	47.9 [49.2] (44.2)	−7.1	−8.6	−1.5			
	46	CHCH$_2$	BH$_2$	H	315.3	111.3 [112.8]	4.5	3.6	−0.9			
	47	CHCH$_2$	CHO	H	319.8	106.8 [108.3]	5.5	7.8	2.3			
	48	CHCH$_2$	CN	H	329.6	97.0 [99.3]	2.8	−2.1	−4.9			
	49	CHCH$_2$	COOH	H	334.9	91.7 [94.1]	3.8	2.7	−1.1			
	50	CHCH$_2$	CHCH$_2$	H	315.4	111.2 [113.9] (110.0)	8.4	−16.7	−25.1			
	51	CHCH$_2$	CCH	H	316.3	110.3 [112.8]	4.2	−7.7	−12.0			
	52	CCH	BH$_2$	H	325.8	100.8 [101]	1.0	3.6	2.6			
	53	CCH	CHO	H	335.1	91.5 [91.8]	−0.5	0.5	1.0			
	54	CCH	CN	H	338.0	88.6 [89.1]	−17.2	−16.5	0.7			
	55	CCH	COOH	H	343.4	83.2 [84.5]	−8.8	−4.4	4.3			
	56	CCH	CCH	H	324.0	102.6 [103.7]	−9.9	−15.5	−5.7			
	57	BH$_2$	BH$_2$	BH$_2$	369.4	57.2 [58.4] (45.7)	60.1	−14.8	−74.9	11.3	30.6	19.4
	58	CHO	CHO	CHO	339.6	87.0 [82.9] (84.3)	−8.3	−30.2	−22.0	5.7	9.2	3.5
	59	CN	CN	CN	319.5	107.1 [104.7] (95.9)	−95.2	−89.3	5.8	8.6	7.4	−1.1
	60	CHCH$_2$	CHCH$_2$	CHCH$_2$	291.1	135.5 [135.9] (130.8)	18.1	−50.9	−69.0	−7.3	−0.9	6.4
	61	CCH	CCH	CCH	279.7	146.9 [146.9] (134.6)	−27.7	−43.2	−15.5	1.9	3.4	1.5
	62	CHO	CHO	CN	337.6	89.0 [86.2] (81.0)	−20.5	−37.9	−17.4	5.0	0.4	−4.6
	63	CHCH$_2$	BH$_2$	BH$_2$	319.5	107.1 [107.7] (99.8)	24.6	−24.5	−49.1	−0.7	−16.5	−15.8
	64	CHCH$_2$	BH$_2$	CHCH$_2$	292.2	134.4 [134.3] (128.4)	20.7	−25.3	−46.0	3.2	−15.9	−19.0
	65	CCH	CCH	CN	290.1	136.5 [136.1] (124.5)	−40.4	−45.9	−5.5	3.8	2.6	−1.3
	66	CCH	CHO	CN	309.1	117.5 [116.2] (107.1)	−25.3	−32.1	−6.7	2.8	−3.5	−6.3

Table 2 (*Contd.*)

Set	#	X	Y	Z	BDE[a]	RSE[a,b]	MIE[a]	RIE[a]	DARSE[a]	PMIE[a]	PRIE[a]	DPARSE[a]
{$\pi_d\pi_a$Z}	67	F	BH$_2$	H	341.6	85.0 [85.5]	5.4	31.0	25.6			
	68	F	CHO	H	364.2	62.4 [63.4]	7.2	17.9	10.7			
	69	F	CN	H	376.3	50.3 [51.3]	−13.2	−12.1	1.1			
	70	F	COOH	H	376.4	50.2 [52]	−0.7	9.3	10.1			
	71	F	CHCH$_2$	H	344.2	82.4 [86.5] (83.4)	19.0	17.8	−1.2			
	72	F	CCH	H	361.3	65.3 [67.6]	2.4	−1.9	−4.3			
	73	Cl	BH$_2$	H	345.2	81.4 [82.5]	5.5	19.9	14.4			
	74	Cl	CHO	H	359.1	67.5 [68.2]	2.7	10.9	8.2			
	75	Cl	CN	H	366.0	60.6 [61.1]	−16.7	−12.8	3.8			
	76	Cl	COOH	H	367.3	59.3 [61.1] (53.6)	−8.3	3.2	11.5			
	77	Cl	CHCH$_2$	H	342.9	83.7 [86.5] (84.4)	14.4	6.9	−7.5			
	78	Cl	CCH	H	352.7	73.9 [75.4]	−2.0	−5.2	−3.2			
	79	NH$_2$	BH$_2$	H	308.2	118.4 [119.2] (105.1)	44.1	67.6	23.5			
	80	NH$_2$	CHO	H	294.9	131.7 [132.3])	18.4	62.9	44.5			
	81	NH$_2$	CN	H	334.1	92.5 [93.3] (81.9)	8.2	16.1	7.9			
	82	NH$_2$	COOH	H	318.3	108.3 [109.8] (95.3)	17.6	50.3	32.7			
	83	NH$_2$	CHCH$_2$	H	308.7	117.9 [120.2]	16.0	14.8	−1.2			
	84	NH$_2$	CCH	H	326.6	100.0 [101.6])	11.0	6.0	−5.0			
	85	OH	BH$_2$	H	298.1	128.5 [129.4])	5.4	53.7	48.3			
	86	OH	CHO	H	319.0	107.6 [108.2])	24.3	59.4	35.2			
	87	OH	CN	H	348.9	77.7 [78.6]	−0.7	7.1	7.8			
	88	OH	COOH	H	339.1	87.5 [89.3]	20.9	47.6	26.6			
	89	OH	CHCH$_2$	H	320.9	105.7 [108.6] (103.5)	18.7	20.1	1.4			
	90	OH	CCH	H	334.9	91.7 [93.6]	8.2	9.6	1.4			
	91	SH	BH$_2$	H	335.0	91.6 [92.3]	31.1	39.2	8.0			
	92	SH	CHO	H	325.2	101.4 [102.1])	9.6	35.2	25.5			
	93	SH	CN	H	346.3	80.3 [80.9]	−5.6	1.3	6.9			
	94	SH	COOH	H	336.4	90.2 [92.2]	1.6	27.6	25.9			
	95	SH	CHCH$_2$	H	334.8	91.8 [94.7]	15.0	−0.9	−15.9			
	96	SH	CCH	H	336.1	90.5 [91.8]	2.4	−0.7	−3.2			
	97	NH$_2$	BH$_2$	OH	275.6	151.0 [151.4] (137.4)	92.5	112.4	20.0	−8.5	−16.4	−7.9
	98	NH$_2$	BH$_2$	F	291.0	135.6 [136.2] (122.5)	75.8	101.1	25.3	−37.6	−18.7	18.9
	99	NH$_2$	BH$_2$	NH$_2$	280.3	146.3 [146.7] (133.2)	92.1	92.5	0.4	−35.4	−37.6	−2.2
	100	NH$_2$	BH$_2$	CHO	302.1	124.5 [124.7] (109.5)	93.5	86.7	−6.8	21.7	−32.9	−54.6
	101	NH$_2$	BH$_2$	COOH	315.2	111.4 [112.4] (97.1)	85.8	77.6	−8.2	16.0	−27.7	−43.7
	102	NH$_2$	BH$_2$	BH$_2$	325.9	100.7 [101] (83.4)	104.6	66.3	−38.2	0.1	−53.7	−53.8
	103	NH$_2$	BH$_2$	CN	302.0	124.6 [124.8] (109.)	60.1	56.0	−4.1	3.6	−24.8	−28.4
	104	NH$_2$	BH$_2$	CCH	292.5	134.1 [134.4] (118.4)	65.5	50.5	−15.0	9.4	−26.7	−36.1
	105	NH$_2$	BH$_2$	CHCH$_2$	288.0	138.6 [138.5] (126.9)	70.5	45.9	−24.5	5.9	−40.0	−45.9
	106	NH$_2$	CHO	OH	273.6	153.0 [153.3] (132.)	68.8	98.5	29.7	−25.2	−31.4	−6.1
	107	NH$_2$	CHO	F	310.3	116.3 [116.2] (100.3)	64.4	78.0	13.7	−25.2	−24.0	1.2
	108	NH$_2$	CHO	NH$_2$	269.3	157.3 [157.5] (136.8)	58.1	77.3	19.2	−17.9	−43.4	−25.5
	109	NH$_2$	CHO	CHO	249.5	177.1 [177.0] (158.1)	30.3	83.8	53.6	−1.8	−28.8	−27.1
	110	NH$_2$	CHO	COOH	270.6	156.0 [156.2] (137.0)	33.3	77.4	44.1	0.2	−27.5	−27.8
	111	NH$_2$	CHO	CN	265.3	161.3 [161.5] (142.1)	7.1	47.4	40.3	−9.1	−19.0	−9.9
	112	NH$_2$	CHO	CCH	258.6	168.0 [168.3] (149.7)	20.4	47.0	26.7	−8.5	−22.4	−13.9
	113	NH$_2$	CHO	CHCH$_2$	263.4	163.2 [163.6] (146.5)	31.5	39.4	7.9	−8.3	−46.2	−37.9
	114	OH	BH$_2$	OH	257.3	169.3 [168] (155.9)	58.3	111.3	53.0	−16.3	−24.6	−8.3
	115	OH	BH$_2$	BH$_2$	299.8	126.8 [125.7] (112.0)	35.5	38.1	2.6	8.4	−54.2	−62.6
	116	OH	BH$_2$	CCH	267.9	158.8 [157.5] (147.3)	10.8	35.2	24.5	−3.8	−31.7	−27.9
	117	OH	CHO	OH	293.0	133.6 [133.5] (114.7)	75.9	100.9	25.0	−36.3	−46.3	−10.0
	118	OH	CHO	CHO	302.7	123.9 [123.2] (110.7)	36.2	51.3	15.2	−7.7	−54.4	−46.7
	119	OH	CHO	CCH	280.2	146.4 [146.6] (131.3)	24.0	43.8	19.8	−7.9	−25.7	−17.9
	120	F	BH$_2$	F	298.2	128.4 [129.3] (119.1)	32.7	86.2	53.5	−31.0	−12.8	18.2
	121	F	BH$_2$	BH$_2$	333.8	92.8 [92.6] (85.0)	25.3	14.6	−10.7	−1.7	−32.1	−30.4
	122	F	BH$_2$	CN	318.0	108.7 [108.7] (99.2)	−9.9	5.5	15.4	−6.2	−10.4	−4.2
	123	NH$_2$	CCH	NH$_2$	305.1	121.5 [121.8] (107.8)	41.5	7.0	−34.5	−19.7	0.2	19.9
	124	NH$_2$	CCH	CCH	274.0	152.6 [153.2] (138.1)	−0.4	−7.0	−6.6	−12.5	−3.4	9.1
	125	F	CHO	CCH	323.8	102.8 [102.8] (91.3)	5.0	2.0	−3.0	−4.1	−14.5	−10.4
	126	NH$_2$	CN	F	363.9	62.7 [63.3] (51.5)	48.4	11.0	−37.3	−10.6	−14.2	−3.6
	127	NH$_2$	CN	CN	286.8	139.8 [139.9] (122.9)	−29.5	−8.1	21.4	−11.4	−8.1	3.3
{CQ$_3$}	128	CH$_3$	H	H	409.6	17.0 [17.7] (14.5)						
	129	CF$_3$	H	H	430.2	−3.6 [−3.8] (−7.2)						
	130	CH$_3$	CH$_3$	H	397.0	29.6 [30.8] (24.7)	10.6	6.3	−4.3			
	131	CF$_3$	CF$_3$	H	429.7	−3.1 [−1.3] (−8.1)	−20.6	−16.5	4.1			
	132	CF$_3$	CH$_3$	H	411.5	15.1 [16.6] (8.8)	12.6	14.3	1.6			
	133	CH$_3$	CH$_3$	CH$_3$	388.2	38.4 [39.9] (30.2)	27.8	15.3	−12.5	−4.0	−3.6	0.4
	134	CF$_3$	CF$_3$	CF$_3$	422.5	4.1 [6.6]	−66.0	−51.1	14.8	−4.3	−1.7	2.5

Table 2 *(Contd.)*

Set	#	X	Y	Z	BDE[a]	RSE[a,b]	MIE[a]	RIE[a]	DARSE[a]	PMIE[a]	PRIE[a]	DPARSE[a]
{X – CQ$_3$}	135	F	CH$_3$	H	401.4	25.2 [26.2] (20.1)	27.7	20.5	−7.2			
	136	Cl	CH$_3$	H	394.5	32.1 [33.6] (28.2)	20.4	12.5	−7.9			
	137	NH$_2$	CH$_3$	H	369.1	57.5 [58.7] (50.6)	18.0	7.6	−10.4			
	138	OH	CH$_3$	H	382.6	44.0 [45.1] (38.1)	23.9	14.7	−9.2			
	139	SH	CH$_3$	H	378.0	48.6 [50.5]	13.0	5.0	−8.0			
	140	F	CF$_3$	H	414.9	11.7 [13.3]	−3.1	−3.2	−0.1			
	141	Cl	CF$_3$	H	403.0	23.6 [25.8] (16.2)	−7.9	−3.7	4.2			
	142	NH$_2$	CF$_3$	H	378.2	48.4 [50.9] (38.5)	17.7	18.8	1.1			
	143	OH	CF$_3$	H	391.0	35.6 [37.8]	9.9	12.9	3.0			
	144	SH	CF$_3$	H	385.4	41.2 [44.0]	1.0	6.3	5.3			
	145	NH$_2$	F	CH$_3$	396.2	30.4 [31.3] (21.5)	96.9	44.1	−52.9	−12.7	−5.2	7.4
	146	NH$_2$	NH$_2$	CF$_3$	362.2	64.4 [66.8] (51.7)	55.3	21.5	−33.8	−19.4	−11.1	8.3
	147	NH$_2$	CF$_3$	CF$_3$	365.6	61.0 [64] (47.4)	−0.3	17.0	17.3	−15.1	−4.2	10.9
	148	BH$_2$	CH$_3$	H	354.2	72.4 [72.3] (66.1)	1.2	12.7	11.4			
	149	CHO	CH$_3$	H	365.0	61.6 [62.2] (57.0)	11.9	20.3	8.3			
	150	CN	CH$_3$	H	374.0	52.6 [53.4] (47.2)	8.9	10.8	1.9			
	151	COOH	CH$_3$	H	373.1	53.5 [54.7]	7.2	19.0	11.8			
	152	CHCH$_2$	CH$_3$	H	346.0	80.6 [83.8] (76.1)	9.7	5.2	−4.6			
	153	CCH	CH$_3$	H	357.6	69.0 [71.0] (64.9)	8.6	6.5	−2.2			
	154	BH$_2$	CF$_3$	H	393.0	33.6 [33.7] (26.9)	5.9	−1.0	−6.9			
	155	CHO	CF$_3$	H	401.5	25.1 [25.7]	−8.6	−16.2	−7.6			
	156	CN	CF$_3$	H	394.7	31.9 [32.8]	−21.1	−19.4	1.8			
	157	COOH	CF$_3$	H	404.5	22.1 [23.5]	−14.9	−14.0	1.0			
	158	CHCH$_2$	CF$_3$	H	358.4	68.2 [72.1]	6.0	9.7	3.7			
	159	CCH	CF$_3$	H	372.6	54.0 [56.3]	−6.9	−3.5	3.4			
	160	BH$_2$	CN	CH$_3$	324.8	101.8 [101.5] (93.2)	5.2	12.3	7.0	−9.1	−8.3	0.8
	161	BH$_2$	BH$_2$	CF$_3$	383.0	43.6 [45.1] (34.3)	24.3	−16.5	−40.8	−3.8	0.5	4.4
	162	BH$_2$	CF$_3$	CF$_3$	392.0	34.6 [36.0] (25.7)	−19.4	−21.7	−2.3	−10.7	−3.3	7.4
	163	NH$_2$	BH$_2$	CH$_3$	301.2	125.4 [126.0] (112.1)	65.7	79.2	13.5	2.4	−8.7	−11.1
	164	NH$_2$	CHO	CH$_3$	282.3	144.3 [144.7] (127.4)	39.3	79.4	40.1	−8.9	−11.4	−2.5
	165	NH$_2$	BH$_2$	CF$_3$	322.0	104.7 [113.6] (90.3)	58.5	71.8	13.3	−9.2	−13.7	−4.4
	166	NH$_2$	CHO	CF$_3$	297.7	128.9 [130.2] (109.9)	14.4	59.7	45.3	−13.0	−5.8	7.2

[a] Calculated at the ROB2-PLYP/6-311+G(3df,2p)//UB3-LYP/6-31G(d) level. [b] RSEs calculated with UB2-PLYP/6-311+G(3df,2p) and G3X(MP2)-RAD are respectively given in square brackets and in parentheses.

an adjacent substituent has been discussed in detail in several papers.[6,9a,13] We confirm that our results are consistent with those of the earlier studies.

Monosubstituted radicals ($^\cdot$CH$_2$X) with π-donor substituents ($π_d$) generally show positive RSEs (Table 2). Because the radical center is electron-deficient, the π-donor substituents play a dual role of stabilizing the radical center through a three-electron interaction between the lone pair on X and the odd electron, and destabilizing it through an electron-withdrawing inductive effect. The RSEs increase in the order, F < Cl < OH < SH < NH$_2$, *i.e.*, with increasing π-donor abilities and decreasing electronegativities of the substituents (X), two effects that reinforce one another in RSEs. The largest RSE of 50.9 kJ mol^{-1} among the π-donors (or the smallest BDE of 375.7 kJ mol^{-1}) occurs for X = NH$_2$, *i.e.*, aminomethyl radical.

Monosubstituted radicals with π-acceptor substituents ($π_a$) also show positive RSEs. The π-acceptor substituents generally stabilize the radical center by delocalization of the unpaired electron. The BH$_2$ substituent is more effective in this regard than CHO, presumably because the former is also a σ-donor while the latter is a σ-acceptor. The CH=CH$_2$ substituent, which we have classified as $π_d/π_a$, is particularly effective. Thus, the largest RSE for a monosubstituted radical of 68.2 kJ mol^{-1} (or the smallest BDE of 358.4 kJ mol^{-1}) occurs for X = CH=CH$_2$, *i.e.*, the allyl radical.

The ethyl radical shows a positive RSE of +17.0 kJ mol^{-1}, which may be attributed to the hyperconjugation offered by the methyl group. In contrast, the trifluoroethyl radical shows a negative RSE of −3.6 kJ mol^{-1}, which may be attributed to the strong electron-withdrawing effect of the trifluoromethyl group.

In summary, we confirm that monosubstituted carbon-centered radicals can be stabilized both by π-electron donors and π-electron acceptors, whereas they are destabilized by strongly electron-withdrawing substituents (CF$_3$). The smallest BDE (358.4 kJ mol^{-1}) and the largest RSE (68.2 kJ mol^{-1}) among the monosubstituted systems of the current test set occur for propene and the allyl radical, respectively, which is unsurprising in view of the substantial resonance stabilization that the allyl radical enjoys.

4.2.2. Multiply-substituted systems. It is impractical to try to rationalize the RSEs, DARSEs, MIEs and RIEs of each and every system in Table 2. Instead, we approach the task in two stages. In section 4.2.2, we discuss the overall trends in the RSEs, RIEs, MIEs and DARSEs of the multiply-substituted systems of the $\{π_d\}$, $\{π_a\}$, $\{π_dπ_aZ\}$, $\{CQ_3\}$ and $\{X\text{-}CQ_3\}$ sets, without focusing on individual systems. We also examine the pairwise quantities, namely PRIEs, PMIEs and DPARSEs. In section 4.2.3, we will investigate the RSEs and the DARSEs of a selection of representative specific systems from the various sets under study, with the help of RIEs and MIEs.

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4.2.2.1. Radical stabilization energies. RSEs are positive for most of the multiply-substitued radicals in this study. A comparison of Fig. 2(a) and 2(b) shows that the trends in the RSEs of di- and tri-substituted radicals for the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$ and $\{CQ_3\}$ sets are quite similar. For both ˙CHXY and ˙CXYZ, the $\{\pi_d\pi_aZ\}$ and $\{\pi_a\}$ radicals generally show larger RSEs than the $\{\pi_d\}$ and $\{CQ_3\}$ radicals. The largest RSEs occur within the $\{\pi_d\pi_aZ\}$ set, with (NH₂,CHO,H) and (NH₂,CHO,CHO) showing RSEs of 131.7 kJ mol⁻¹ and 177.1 kJ mol⁻¹, respectively.

In the $\{\pi_d\}$ set, the combinations of SH and/or NH₂ are found to lead to larger RSEs than other substituents (consistent with results for the monosubstituted radicals). The largest RSEs among the di- and tri-substituted radicals occur respectively for (SH,NH₂,H) (66.8 kJ mol⁻¹) and (SH,SH,SH) (83.2 kJ mol⁻¹) (highlighted in Fig. 2(a) and 2(b), respectively).

In the $\{\pi_a\}$ set, the RSEs are larger for the π_a/π_d substituents than for the $\pi_a\sigma_a$ substituents, and these in turn are larger than for the $\pi_a\sigma_d$ substituents. The largest RSEs occur for the divinyl- (CHCH₂,CHCH₂,H) (111.2 kJ mol⁻¹)[32] and triethynyl-(CCH,CCH,CCH) (146.9 kJ mol⁻¹) methyl radicals, respectively, among di- and tri-substituted radicals (highlighted in Fig. 2(a) and 2(b)). This does not support a recent suggestion[33] that tricyanomethane might have one of the weakest C–H bonds for a closed-shell neutral organic molecule. Indeed the BDE for CH(C≡CH)₃ is lower than that for CH(CN)₃ by more than 40 kJ mol⁻¹ (Table 2).

The very large RSEs in the $\{\pi_d\pi_aZ\}$ set confirm the advantage of simultaneously having a π-donor and a π-acceptor at a carbon radical center. In fact, the extra stabilization provided to a carbon-centered radical by the captodative effect has been known and extensively studied for many years.[2a,d,4b,k,14,34] Among the disubstituted radicals of this set, (NH₂,CHO,H), where a very strong π-donor and a very strong π-acceptor combine, shows the highest RSE of 131.7 kJ mol⁻¹ (highlighted in Fig. 2(a)). It is then of interest to examine the influence of a third substituent (Z) on the RSE of a captodatively-stabilized ˙CHXY radical. Table 2 shows that for most series of this set, (*viz*, (NH₂,BH₂,Z), (OH,BH₂,Z), (F,BH₂,Z) and (OH,CHO,Z)), relatively larger RSEs occur when Z is a π_a/π_d substituent or a π-donor. However, for the (NH₂,CHO,Z) series, this trend is somewhat altered owing to the possibility of additional stabilizing interactions (see sections 4.2.3.6 and 4.2.3.7).

The largest RSE among $\{\pi_d\pi_aZ\}$ of 177.1 kJ mol⁻¹ occurs for (NH₂, CHO, CHO), highlighted in Fig. 2(b)).

As can be seen from Fig. 2(a) and 2(b), the RSEs for the $\{CQ_3\}$ set are much smaller than those for the other sets. Among the di- and tri-substituted radicals of this set, the largest RSEs of 29.6 and 38.4 kJ mol⁻¹ are found for the isopropyl (CH₃,CH₃,H) and the *tert*-butyl (CH₃,CH₃,CH₃) radicals (highlighted in Fig. 2(a) and 2(b)), respectively. It is notable that while monosubstitution by the CF₃ substituent gives rise to a negative RSE (of −3.6 kJ mol⁻¹), the RSEs are less negative (−3.1 kJ mol⁻¹ for (CF₃,CF₃,H)) and positive (+4.1 kJ mol⁻¹ for (CF₃,CF₃,CF₃)) in the doubly- or triply-substituted systems, respectively.

The fifth set $\{X\text{-}CQ_3\}$ is treated separately from the rest of the radicals because the pattern of RSEs is only minimally altered by replacing H by CQ₃. *i.e.*, the trends in the RSEs of this set are more or less determined by the nature of X for (X,CQ₃,H) and by the nature of X and Y for (X,Y,CQ₃). This set therefore does not need detailed discussion. As can be seen from Fig. 3, adding CH₃ as a second substituent for disubstituted radicals of this set is found to consistently increase the RSEs, whereas adding CF₃ as a second substituent is found to either minimally change or slightly decrease the RSEs. A similar pattern of behavior is observed for trisubstituted radicals of this set (see Table 2). We note that our results are consistent with the finding of Coote *et al.*[10a,35] that inclusion of the methyl group as a second or third substituent generally tends to stabilize the radicals, and this stabilization is enhanced when X is a π-accepting group (particularly BH₂) but is less significant if X is a π-donor group.

Another important general point that emerges from comparing the RSEs of mono-, di-, and tri-substituted radicals is that increasing the degree of substitution almost always leads to larger RSEs for C-centered radicals. The only exception to this trend occurs for the F-series of radicals where the RSE decreases as we go from the mono- (15.4 kJ mol⁻¹) to di- (15.0 kJ mol⁻¹) to trifluoromethyl radical (−5.3 kJ mol⁻¹), which has previously been reported by Zhang.[36] However, it is notable that, for those systems showing extra stabilization, the extent of this depends on the nature of X, Y and Z. Fig. 4 displays the mean RSEs of ˙CH₂X, ˙CHXY and ˙CXYZ for the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$ and $\{CQ_3\}$ sets, and shows that as we go from mono- to di- to tri-substituted radicals, the increase in the mean RSEs is largest in the $\{\pi_d\pi_aZ\}$ set.
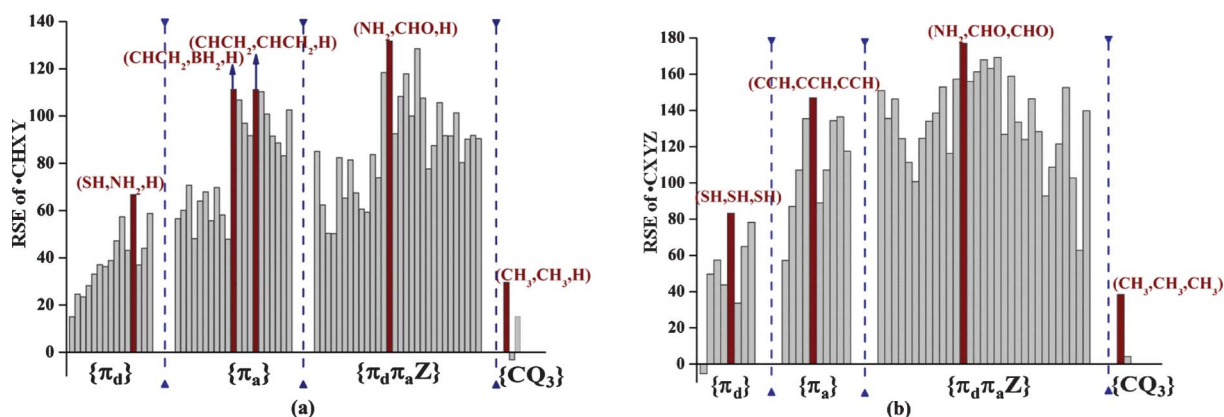

Fig. 2 Calculated radical stabilization energies (RSEs in kJ mol⁻¹) for (a) disubstituted radicals (˙CHXY) and (b) trisubstituted radicals (˙CXYZ) in the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$ and $\{CQ_3\}$ sets.

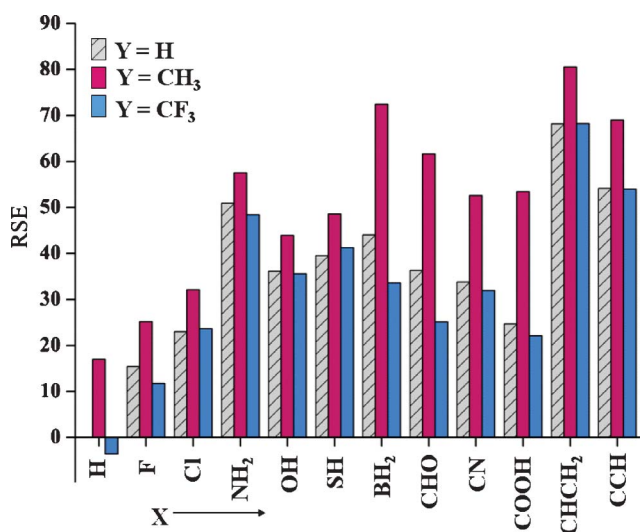**Fig. 3** Comparison of RSEs (kJ mol⁻¹) for ˙CHXY radicals in the {X-CQ₃} set, with Y = H, CH₃ or CF₃.

Fig. 4 Comparison of mean RSEs in kJ mol⁻¹ for mono-, di-, and tri-substituted radicals for the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d \pi_a Z\}$ and $\{CQ_3\}$ sets.

4.2.2.2. Radical interaction energies. As already mentioned, the RSEs of multiply-substituted methyl radicals include non-negligible contributions from interactions in the precursor substituted methanes.[14f] It is advantageous therefore to examine radical interaction energies (RIEs),[14a,f] which refer to the radicals alone. The RIEs compare the energies of multiply-substituted methyl radicals with those of the individual singly-substituted methyl radicals (eqn (7)), and thus quantitatively measure the extra stabilization or destabilization resulting from the interaction of the substituents.

Fig. 5(a) and 5(b) display the RIEs of the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d \pi_a Z\}$ and $\{CQ_3\}$ sets for di- and tri-substituted radicals, respectively. A comparison of these figures indicates that, as in the case of the RSEs, the trends in the RIEs are very similar for the ˙CHXY and ˙CXYZ radicals. The RIEs, whether positive or negative, are again generally larger in magnitude for trisubstituted radicals, than for disubstituted radicals. For both ˙CHXY and ˙CXYZ, the $\{\pi_d \pi_a Z\}$ set generally shows positive RIEs, whereas the $\{\pi_a\}$ set shows negative RIEs. RIEs of the $\{\pi_d\}$ set show both positive and

negative values. In the $\{CQ_3\}$ set, RIEs are negative for radicals multiply-substituted with CF₃ groups but positive for radicals multiply-substituted with CH₃ groups.

In the $\{\pi_d\}$ set, it is notable (Table 2) that RIEs are generally positive for radicals with substituents involving first-row elements, (roughly in the order F > OH > NH₂), with (OH,F,H) and (F,F,F) having the largest positive RIEs of 38.5 and 83.5 kJ mol⁻¹, respectively, among di- and tri-substituted radicals. The RIEs are generally less positive or are negative for radicals with substituents involving second-row elements, with (SH,SH,H) and (Cl,Cl,Cl) showing the largest negative RIEs of −8.9 and −19.2 kJ mol⁻¹ among the two classes of radicals, respectively (see highlighted bars in Fig. 5(a) and 5(b)).

In the $\{\pi_a\}$ set, consistent with the findings of Leroy *et al.*[14f] and Song *et al.*[14a] for disubstituted radicals, RIEs are generally negative, with radicals involving $\pi_a \sigma_a$ substituents showing relatively larger negative RIEs. The largest negative RIEs occur for the dicyano- (−32.3 kJ mol⁻¹) and the tricyano-methyl radical (−89.3 kJ mol⁻¹) among the di- and tri-substituted radicals,
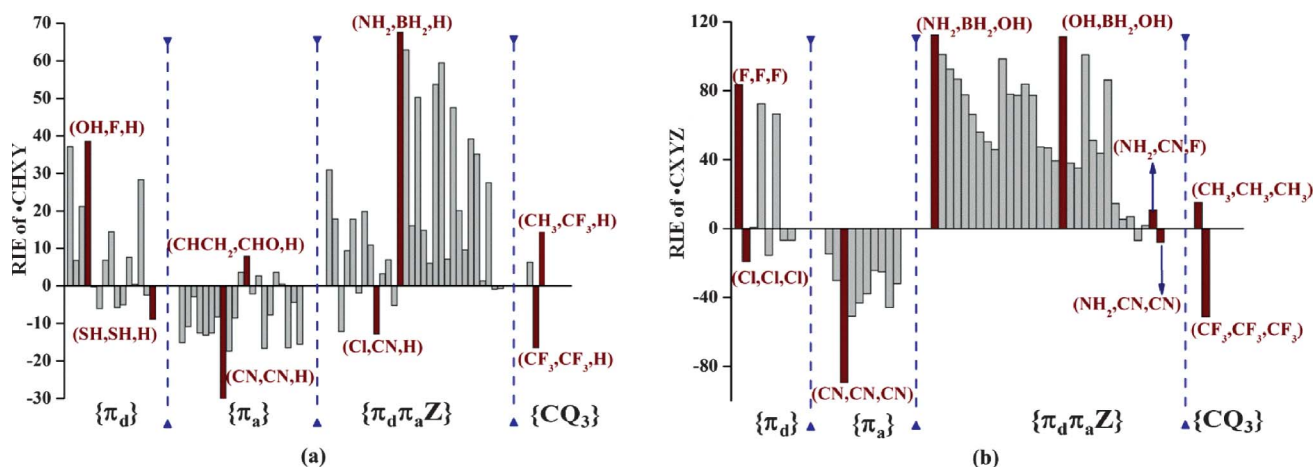
Fig. 5 Calculated radical interaction energies (RIEs, kJ mol⁻¹) for (a) disubstituted radicals (˙CHXY) and (b) trisubstituted radicals (˙CXYZ) in the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d \pi_a Z\}$ and $\{CQ_3\}$ sets.

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respectively (highlighted in Fig. 5(a) and 5(b), see also section 4.2.3.4). However, it is notable that, among disubstituted radicals, RIEs are positive for those radicals where the X groups have relatively higher-lying HOMOs (CH=CH$_2$) and the Y groups have relatively lower-lying LUMOs (BH$_2$ or CHO), *i.e.*, where there is a possibility for captodative stabilization[2a,d,34] (highlighted in Fig. 5(a)).

In the $\{\pi_d\pi_aZ\}$ set, RIEs are mostly positive, with few exceptions, again reflecting captodative stabilization.[2a,d,34] For the disubstituted radicals,[14a,f] larger RIEs occur when X is a better π-donor (*e.g.*, NH$_2$) and Y is a better π-acceptor (*e.g.*, BH$_2$ or CHO), with the largest RIE of 67.6 kJ mol^{-1} occurring for (NH$_2$,BH$_2$,H) (highlighted in Fig. 5(a)). Negative RIEs occur for very few cases, specifically when X and Y are less good π-donors and π-acceptors, respectively (*e.g.*, the largest negative RIE of −12.8 kJ mol^{-1} occurs for (Cl,CN,H), highlighted in Fig. 5(a)).

Consistent with this trend, the RIEs of ˙CXYZ radicals in the $\{\pi_d\pi_aZ\}$ set are also larger when X is a better π-donor and Y is a better π-acceptor, with very large RIEs of 112.4 and 111.3 kJ mol^{-1} occurring for (NH$_2$,BH$_2$,OH) and (OH,BH$_2$,OH), respectively (highlighted in Fig. 5(b)). An interesting trend in the RIEs is that, for fixed X and Y, RIEs are relatively larger when Z is a π-donor. This is illustrated in Fig. 6 for the (NH$_2$,BH$_2$,Z) series, where the RIEs change by up to approximately 70 kJ mol^{-1} with variation in Z. It is interesting to note at this point that, for the (NH$_2$,CN,Z) series, the RIE is positive (11.0 kJ mol^{-1}) when Z is a π-donor (F) and negative (−8.1 kJ mol^{-1}) when Z is a π-acceptor (CN) (highlighted in Fig. 5(b)). The (NH$_2$,CHO,Z) series shows small modifications to this general trend (see sections 4.2.3.6 and 4.2.3.7).
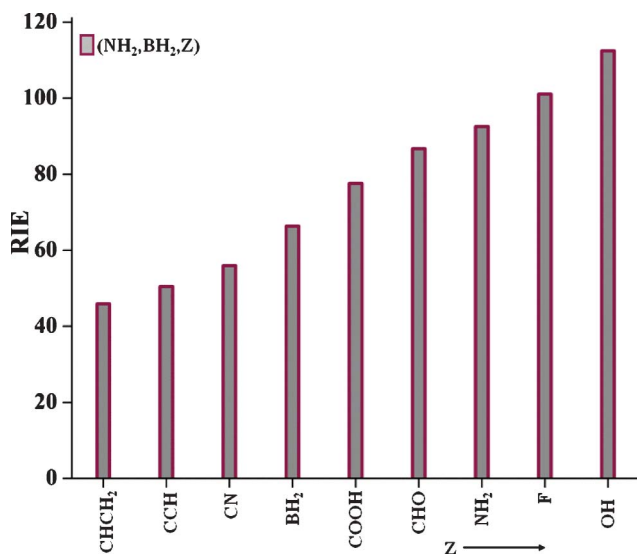
Fig. 6 Radical interaction energies (RIEs, kJ mol^{-1}) for radicals in the (NH$_2$,BH$_2$,Z) series.

In the $\{CQ_3\}$ set, CF$_3$ is found to destabilize the radicals, as reflected in the negative RIEs of −16.5 and −51.1 kJ mol^{-1} for the bis- and tris(trifluoromethyl) radicals (*i.e.*, (CF$_3$,CF$_3$,H) and (CF$_3$,CF$_3$,CF$_3$)), respectively, whereas CH$_3$ is found to stabilize the radicals, as reflected in the positive RIEs of 6.3 and 15.3 kJ mol^{-1} for the isopropyl and the *tert*-butyl radicals (*i.e.*, (CH$_3$,CH$_3$,H) and (CH$_3$,CH$_3$,CH$_3$)), respectively (highlighted in Fig. 5(a) and

5(b)). However, it is notable that the destabilization resulting from multiple substitution by CF$_3$ is much greater than the stabilization resulting from multiple substitution by CH$_3$.

In the $\{X$-$CQ_3\}$ set, RIEs are consistently positive for ˙CHXY when the second substituent (Y) is CH$_3$ and mostly negative when the second substituent is CF$_3$, as can be seen from Fig. 7. However, because CF$_3$ is a hyperconjugative acceptor, exceptional cases of positive RIEs occur when the X groups are strong π-donors (NH$_2$, OH, or SH) or π_d/π_a substituents with high-lying HOMOs (CH=CH$_2$), as a result of captodative stabilization.
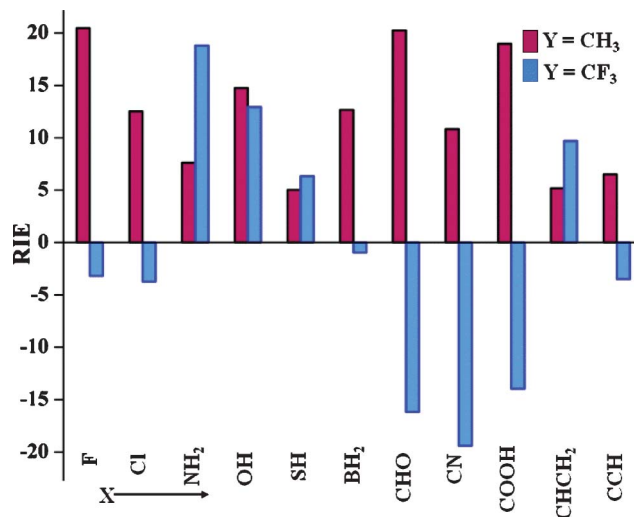
Fig. 7 Radical interaction energies (RIEs, kJ mol^{-1}) for ˙CHXY radicals in the $\{X$-$CQ_3\}$ set for Y = CH$_3$ and CF$_3$.

For the ˙CXYZ radicals of the $\{X$-$CQ_3\}$ set, the behavior is similar to that of ˙CHXY, with the RIEs being consistently positive (and more positive than when Z = H) when the third substituent is CH$_3$. Moreover, the trends in the RIEs are dominated by the interactions between X and Y. However, CF$_3$, is not as inconspicuous a partner as CH$_3$ in that the RIEs not only depend on the interactions of X and Y, but also depend on the interactions of CF$_3$ with both X and Y, and hence a uniform trend or a generalization for radicals of the type (X,Y,CF$_3$) cannot be easily drawn.

4.2.2.3. Molecule interaction energies (MIEs). Molecular interaction energies, as defined by eqn (8), have been extensively used in previous studies of geminal substituent effects.[15a,37] MIEs compare the energies of multiply-substituted methanes with those of the corresponding singly-substituted methanes, and thus quantitatively measure the extra stabilization or destabilization associated with the interaction of the substituents.

Fig. 8(a) and 8(b) show the MIEs in the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$ and $\{CQ_3\}$ sets for di- and tri-substituted methanes, respectively. A comparison of these figures indicates that the trends in MIEs are again very similar for the CH$_2$XY and CXYZ molecules. However, MIEs (as is the case for RIEs), whether positive or negative, are generally larger in magnitude for trisubstituted than for disubstituted methanes.

In general, for both di- and tri-substituted methanes, MIEs are consistently positive in the $\{\pi_d\}$ set and mostly positive in the $\{\pi_d\pi_aZ\}$ set, with the former showing larger MIEs than the latter. MIEs in the $\{\pi_a\}$ set show both positive and negative values. In
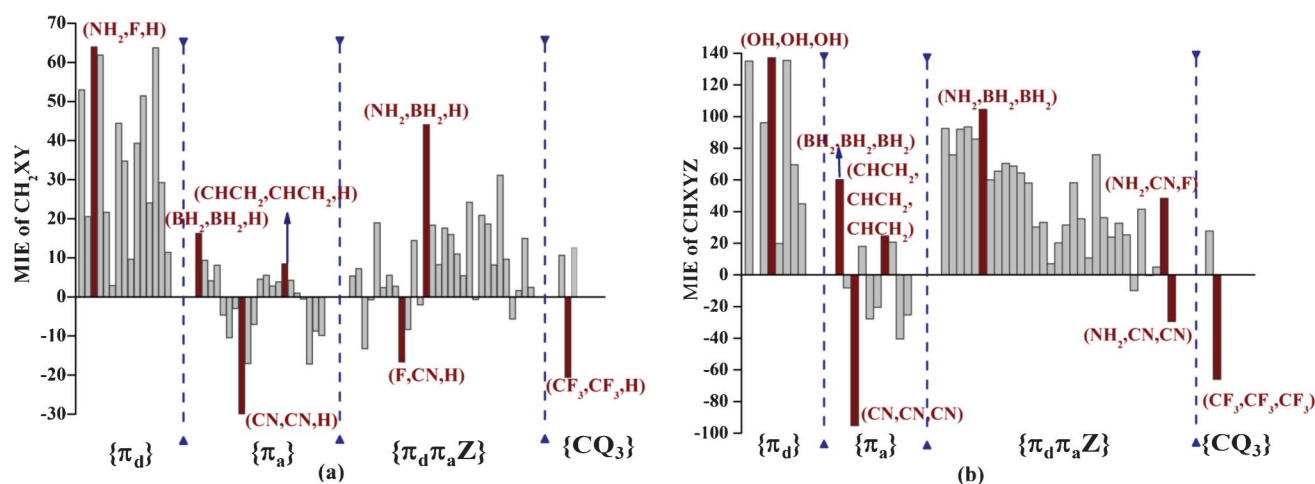
Fig. 8 Molecule interaction energies (MIEs, kJ mol^{-1}) for (a) disubstituted (CH$_2$XY) and (b) trisubstituted (CHXYZ) methanes in the {π_d}, {π_a}, {$\pi_d\pi_a$Z} and {CQ$_3$} sets.

the {CQ$_3$} set, MIEs are negative for molecules that are multiply-substituted with CF$_3$ groups but positive for molecules multiply-substituted with CH$_3$ groups.

We next discuss in more detail how MIEs vary among the various sets of molecules.

In the {π_d} set, larger positive MIEs occur for methanes substituted with π-donors involving first-row elements, with (NH$_2$,F,H) and (OH,OH,OH) showing the largest positive MIEs of 64.0 and 137.2 kJ mol^{-1}, respectively, among the di- and tri-substituted methanes (highlighted in Fig. 8(a) and 8(b)). MIEs are comparatively smaller for methanes solely substituted with π-donors involving second-row elements, with di- and tri-chloromethane showing the lowest MIEs of 2.9 and 0.2 kJ mol^{-1} among CH$_2$XY and CHXYZ, respectively. This matches the earlier findings of Schleyer and others.[37a,38]

In the {π_a} set, for both di- and tri-substituted methanes, MIEs are negative[37d] for those substituted only with $\pi_a\sigma_a$ substituents, with di- and tri-cyanomethane showing the largest negative MIEs of −34.6 and −95.2 kJ mol^{-1}, respectively (highlighted in Fig. 8(a) and 8(b), see also section 4.2.3.4). MIEs are positive for methanes in which at least one of the substituents is a $\pi_a\sigma_d$ (BH$_2$) or a π_a/π_d (CH=CH$_2$) group. It can be seen from Fig. 8(a) and 8(b) that (BH$_2$,BH$_2$,H) (16.3 kJ mol^{-1}) and (BH$_2$,BH$_2$,BH$_2$) (60.1 kJ mol^{-1}) show quite large positive MIEs. However, MIEs are negative for methanes substituted by ethynyl (C≡CH) groups.

In the {$\pi_d\pi_a$Z} set, MIEs are generally positive for most multiply-substituted methanes, with the largest positive MIEs of 44.1 and 104.6 kJ mol^{-1} occurring for (NH$_2$,BH$_2$,H) and (NH$_2$,BH$_2$,BH$_2$), respectively, among the di- and tri-substituted methanes. Apart from these, it is notable that MIEs are relatively larger when Z is a π-donor than when Z is a π-acceptor. This is consistent with the larger positive MIEs of the molecules with two π-donors and the less positive or negative MIEs of molecules with two π-acceptors. The relatively large positive MIE of (NH$_2$,CN,F) (48.4 kJ mol^{-1}) and negative MIE of (NH$_2$,CN,CN) (−29.5 kJ mol^{-1}) illustrate this (highlighted in Fig. 8).

In the {CQ$_3$} set, the CF$_3$ group is found to interact un-favorably with other CF$_3$ groups in CF$_3$-substituted methanes, as reflected in the negative MIEs of −20.6 and −66.0 kJ mol^{-1}

for bis- and tris(trifluoromethyl)methane (*i.e.*, (CF$_3$,CF$_3$,H) and (CF$_3$,CF$_3$,CF$_3$)), respectively, whereas CH$_3$ is found to interact favorably with other CH$_3$ groups in CH$_3$-substituted methanes, as reflected in the positive MIEs of 10.6 and 27.8 kJ mol^{-1} for propane and isobutane (*i.e.*, (CH$_3$,CH$_3$,H) and (CH$_3$,CH$_3$,CH$_3$)), respectively. However, consistent with the trend in RIEs, desta-bilization resulting from multiple substitution by CF$_3$ is much greater than stabilization resulting from multiple substitution by CH$_3$.

In the {X-CQ$_3$} set, MIEs are positive for disubstituted methanes CH$_2$XY when the second substituent Y is CH$_3$ and mostly negative when Y is CF$_3$, as can be seen from Fig. 9. However, in the latter cases positive MIEs occur when X is a strong π-donor (NH$_2$, OH, or SH) or a π_d/π_a substituent (CH=CH$_2$) or a $\pi_a\sigma_d$ substituent (BH$_2$).
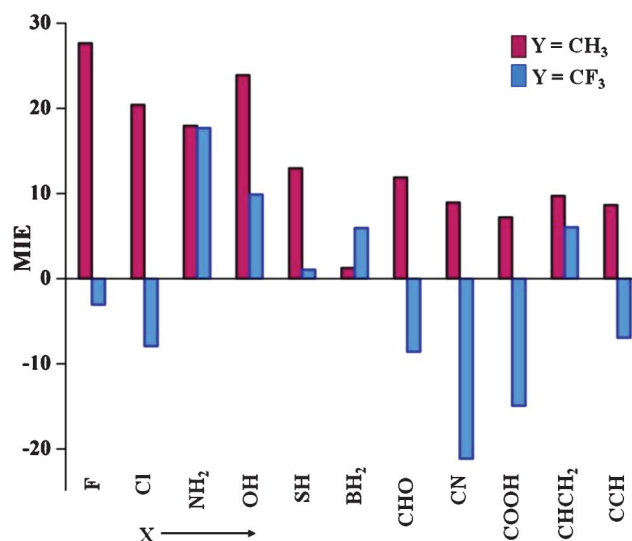

Fig. 9 Molecule interaction energies (MIEs, kJ mol^{-1}) for CH$_2$XY in the {X-CQ$_3$} set for Y = CH$_3$ and CF$_3$.

For the trisubstituted methanes CHXYZ of this set, the MIEs are consistently positive (and more positive than when Z = H)

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Org. Biomol. Chem., 2011, **9**, 3636–3657 | 3647

when the third substituent Z is CH_3. Moreover the trends in MIEs are dominated by the interactions between X and Y. However, when the third substituent is CF_3, such a uniform trend cannot be seen, as was the case for RIEs.

4.2.2.4. Deviations from additivity of radical stabilization energies (DARSEs). DARSE values[14d,f,h] tell us how close the RSEs of multiply-substituted methyl radicals are to the values predicted on the basis of additivity of RSEs of the monosubstituted methyl radicals (eqn (9)), *i.e.*, whether the RSEs of multiply-substituted radicals are strictly additive (DARSE = 0), synergistic (positive DARSE), or antagonistic (negative DARSE). According to eqn (10), DARSE values are positive if the interactions between the substituents in the multiply-substituted radicals are more favorable (or less unfavorable) than those in the corresponding parent closed-shell molecules, and *vice versa*.

Fig. 10(a) and 10(b) show plots of the DARSEs in the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$ and $\{CQ_3\}$ sets for ˙CHXY and ˙CXYZ, respectively. A comparison of these figures indicates that the trends in DARSEs are very similar for both di- and tri-substituted methyl radicals. However, DARSEs (as is the case of RIEs and MIEs), whether positive or negative, are generally larger in magnitude for trisubstituted than for disubstituted radicals.

We see that the radicals in the $\{\pi_d\}$ and $\{\pi_a\}$ sets generally show negative DARSE values whereas those in the $\{\pi_d\pi_aZ\}$ set generally shows positive DARSE values, which matches with earlier findings of Leroy *et al.*[14f] and Song *et al.*[14a] for disubstituted radicals. In the $\{CQ_3\}$ set, while multiple substitution with CF_3 leads to positive DARSEs, similar substitution by CH_3 leads to negative DARSEs.

Next we discuss in more detail how DARSEs vary among the various sets of radicals.

In the $\{\pi_d\}$ set, DARSE values are consistently negative, with diaminomethyl (*i.e.*, (NH_2,NH_2,H)) and triaminomethyl (*i.e.*, (NH_2,NH_2,NH_2)) radicals showing the largest negative DARSEs of −44.4 and −95.3 kJ mol^{−1} among the di- and tri-substituted radicals, respectively.

DARSEs are also negative for most radicals of the $\{\pi_a\}$ set, although less negative than those in the $\{\pi_d\}$ set. The largest negative DARSE values among ˙CHXY and ˙CXYZ occur for the (BH_2,BH_2,H) (−31.4 kJ mol^{−1}) and (BH_2,BH_2,BH_2)

(−74.9 kJ mol^{−1}) systems (highlighted in Fig. 10(a) and 10(b), see section 4.2.3.3). It is notable that divinylmethyl (*i.e.*, $CHCH_2,CHCH_2,H$) (−25.1 kJ mol^{−1}) and trivinylmethyl (*i.e.*, $CHCH_2,CHCH_2,CHCH_2$) (−69.0 kJ mol^{−1}) radicals also show quite large negative DARSEs, as highlighted in Fig. 10(a) and 10(b) (see section 4.2.3.5). Additionally, several radicals of the $\{\pi_a\}$ set, *e.g.*, (CN,CN,H) and (CN,CN,CN) (highlighted in Fig. 10(a) and 10(b), see also section 4.2.3.4), show small positive DARSEs.

In the $\{\pi_d\pi_aZ\}$ set, the largest positive DARSE value among the ˙CHXY radicals occurs for (OH,BH_2,H) (48.3 kJ mol^{−1}). Large positive DARSEs of 44.5 and 53.5 kJ mol^{−1} also occur for (NH_2,CHO,H) and (F,BH_2,F), respectively, in di- and tri-substituted radicals. It is notable from Fig. 10(a) and 10(b) that, as we go from di- to tri-substituted radicals, the increase in the positive DARSEs for $\{\pi_d\pi_aZ\}$ is not as significant as the increases in the negative DARSEs for the $\{\pi_d\}$ and $\{\pi_a\}$ sets. There are a number of trisubstituted radicals in the $\{\pi_d\pi_aZ\}$ set that show negative DARSEs. Additionally the DARSEs are consistently negative for ˙CHXY when Y is a π_d/π_a substituent.

In the $\{CQ_3\}$ set, the bis- and tris-(trifluoromethyl) radicals show positive DARSEs of 4.1 and 14.8 kJ mol^{−1}, respectively (see section 4.2.3.8), whereas the isopropyl and *tert*-butyl radicals show negative DARSEs of −4.3 and −12.5 kJ mol^{−1}, respectively.

Given that the DARSE values are equal to the difference between the RIEs and MIEs, it is of interest to examine whether they are generally dominated by the interactions in the radicals (RIEs) or in the parent methanes (MIEs). This is illustrated for the case of trisubstituted systems in Fig. 11.

Negative DARSEs for the $\{\pi_d\}$ set, can be seen to arise from larger favorable interactions in molecules (indicated by large positive MIEs) than in radicals (relatively less positive RIEs (*e.g.*, (F,F,F), see section 4.2.3.2) or negative RIEs). On the other hand, the generally negative DARSEs for the $\{\pi_a\}$ set primarily arise from the less favorable interactions in radicals than in their parents.

The large positive DARSEs in the $\{\pi_d\pi_aZ\}$ set, can be attributed to the larger stabilization in the radicals than in the molecules. However, there are a few cases where the DARSEs are negative, despite the positive RIEs, and these arise because of larger positive MIEs, for example, for several systems in the (NH_2,BH_2,Z) series
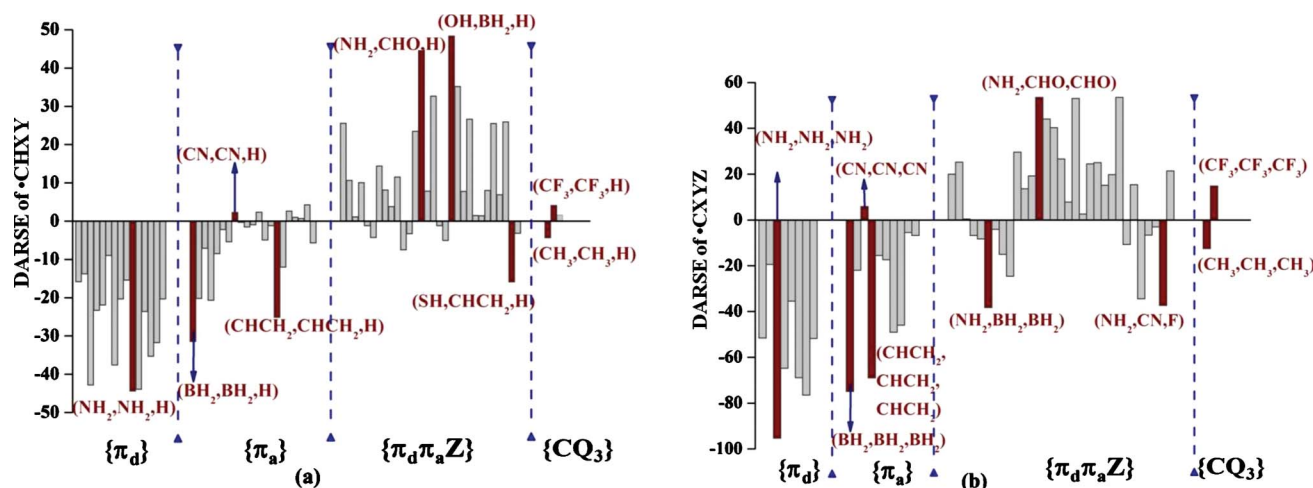

Fig. 10 Calculated deviations from additivity of RSEs (DARSEs, kJ mol^{−1}) in (a) disubstituted (˙CHXY) and (b) trisubstituted (˙CXYZ) methyl radicals in the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$ and $\{CQ_3\}$ sets.
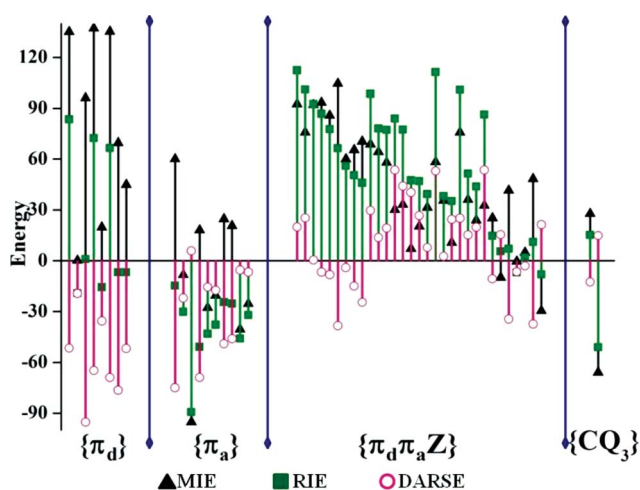
Fig. 11 Trends in DARSEs, MIEs and RIEs of trisubstituted systems (kJ mol⁻¹) in the $\{\pi_d\}$, $\{\pi_a\}$, $\{\pi_d\pi_aZ\}$ and $\{CQ_3\}$ sets.

(see section 4.2.3.6). Finally, it is interesting to note that positive DARSEs can alternatively arise if there are unfavorable interactions in the radicals but they are smaller than the unfavorable interactions in the parent molecules. This occurs, for example, for the ˙C(CF₃)₃ radical of the $\{CQ_3\}$ set.

As can be seen from Fig. 12, DARSEs for the ˙CHXY radicals of the $\{X\text{-}CQ_3\}$ set are positive when π-donors or π_d/π_a groups (X) are coupled with CF₃ (Y) and negative when they are coupled with CH₃ (Y). Conversely, DARSEs are either less positive or negative when π-acceptors are coupled with CF₃ and positive when they are coupled with CH₃.

For ˙CXYZ radicals of the $\{X\text{-}CQ_3\}$ set, DARSEs are found to generally depend on the nature of the X and Y substituents. For instance, among radicals with Z = CH₃, the largest positive DARSE occurs for (NH₂,CHO,CH₃) (40.1 kJ mol⁻¹) while the largest negative DARSE occurs for (NH₂,F,CH₃) (−52.9 kJ mol⁻¹), which is consistent with the large positive and negative DARSEs of (NH₂,CHO,H) and (NH₂,F,H), respectively. Similarly, among
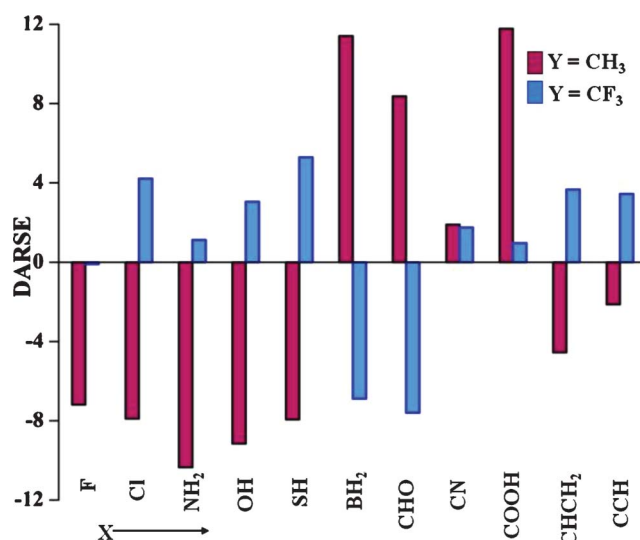
Fig. 12 Deviations from additivity of RSEs (DARSEs, kJ mol⁻¹) for ˙CHXY radicals in the $\{X\text{-}CQ_3\}$ set with Y = CH₃ and CF₃.

radicals with Z = CF₃, the largest positive DARSE occurs for (NH₂,CHO,CF₃) (45.3 kJ mol⁻¹) and the largest negative DARSE for (BH₂,BH₂,CF₃) (−40.8 kJ mol⁻¹).

4.2.2.5. Deviations from pairwise additivity of the RSEs (DPARSEs). DPARSEs were calculated in order to examine whether they could prove useful in predicting the relative stabilities of trisubstituted radicals, as they take into account pairwise interactions in both disubstituted radicals and disubstituted methanes (see eqn (14)). In other words, when we try to predict the RSE of a trisubstituted radical by adding the RSEs of monosubstituted radicals, we take the interactions one at a time (DARSEs). If RSEs were additive (DARSE = 0), we could accurately predict the RSEs of trisubstituted radicals from the RSEs of the corresponding monosubstituted radicals. Since the DARSEs are not negligible (they vary from −95.3 to +53.6 kJ mol⁻¹), because of synergistic or antagonistic interactions between the substituents in the radicals
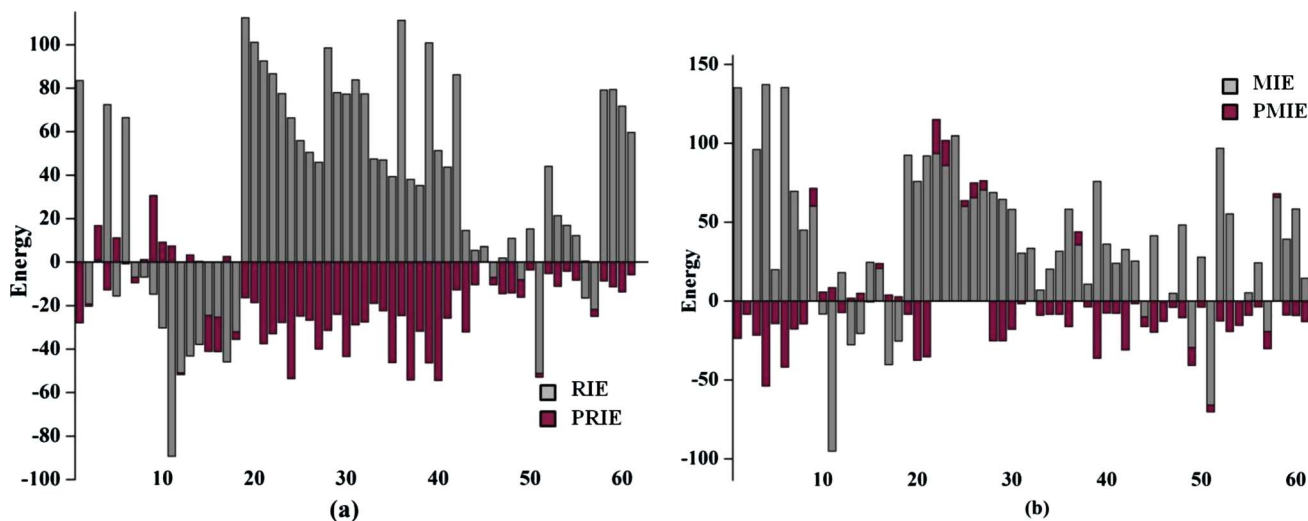
Fig. 13 (a) Calculated radical interaction energies (RIEs) and pairwise radical interaction energies (PRIEs) in trisubstituted radicals (˙CXYZ), and (b) calculated molecule interaction energies (MIEs) and pairwise molecule interaction energies (PMIEs) in trisubstituted methanes (CHXYZ) (for 61 species, kJ mol⁻¹).

and/or closed-shell molecules, we wished to examine whether, if we take account of the interactions two at a time, the relative stabilities of trisubstituted radicals might be better predicted from the RSEs of the corresponding disubstituted radicals, and hence have introduced DPARSEs. The DPARSE values of trisubstituted radicals are included in Table 2. Although the DPARSE values are generally smaller than DARSE values, they are not small in absolute terms, ranging from −62.6 to +41.2 kJ mol⁻¹.

The magnitudes of the DPARSE values can be explained using the trends in the pairwise radical interaction energies (PRIEs) and pairwise molecule interaction energies (PMIEs) (eqn (12) and 13). From Fig. 13(a) and 13(b), it is clear that the PRIE and PMIE values, although smaller in magnitude than the RIEs and MIEs, respectively, show opposing trends to these quantities. The sign-reversal of PMIEs and PRIES suggests that addition of pairwise interaction energies will overestimate both the stabilizing and destabilizing effects in the trisubstituted systems.

Fig. 14 displays the trends in DARSE and DPARSE values for trisubstituted radicals. DPARSE values generally show opposite signs to the DARSEs yet, unlike PMIEs and PRIEs, DPARSEs are not always smaller in magnitude than the DARSE values. It would therefore appear that a pairwise additivity assumption would not be useful in predicting the RSEs of trisubstituted systems, at least not for the current test set.
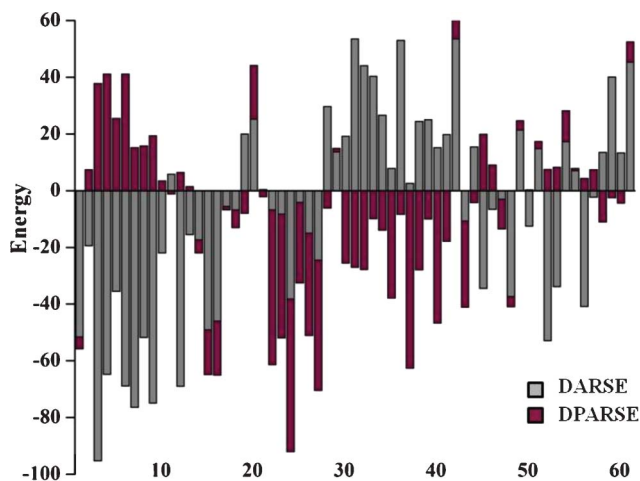
Fig. 14 Comparison of calculated deviations from additivity in RSEs (DARSEs) and deviations from pairwise additivity in RSEs (DPARSEs) (for 61 reactions, kJ mol⁻¹).

4.2.3. Analysis of trends in RSEs and DARSEs. As already noted, it is impractical to try to rationalize the factors affecting the stabilities of each and every system in Table 2. Instead, having examined the broad picture in section 4.2.2, in this section, we investigate the radical stabilization energies (RSEs) of a few representative examples from the various sets under study. For multiply-substituted systems, we do so with the help of calculated deviations from additivity of RSEs (DARSEs), radical interaction energies (RIEs) and molecule interaction energies (MIEs). As a first step, we discuss the principal interactions that influence the thermodynamic stabilities of substituted radicals and molecules.

The interactions that stabilize or destabilize monosubstituted carbon-centered radicals[6,9a,13] ($^{\bullet}CH_2X$) include (a) inductive effects that are stabilizing if X is electropositive (*e.g.*, $^{\bullet}CH_2BH_2$) and

destabilizing if X is electronegative (*e.g.*, $^{\bullet}CH_2CF_3$), (b) lone-pair donation when X is a π-donor (*e.g.*, $^{\bullet}CH_2NH_2$), corresponding to the three-electron stabilizing interaction between the unpaired electron at the radical center and a nonbonding pair of electrons on the heteroatom, (c) conjugation, involving stabilization by delocalization of the unpaired electron into an adjacent π-system (*e.g.*, $^{\bullet}CH_2$–$CH{=}CH_2$), and (d) hyperconjugation, involving stabilization by delocalization of the unpaired electron to adjacent σ- or σ^*-orbitals (*e.g.*, $^{\bullet}CH_2CH_3$).

In multiply-substituted radicals, additional stabilizing or destabilizing effects may be operative, and these are indicated by positive or negative RIEs. Most prominent among them is captodative stabilization,[2a,d,4b,14,34] in radicals substituted with both a π-donor and a π-acceptor (*e.g.*, $^{\bullet}CH(NH_2)(BH_2)$, see section 4.2.3.6). Next there is conjugation saturation, which can lead to less-than-additive stabilization (*e.g.*, $^{\bullet}C(NH_2)_3$, $^{\bullet}C(BH_2)_3$, and $^{\bullet}C(CH{=}CH_2)_3$, see sections 4.2.3.1, 4.2.3.3 and 4.2.3.5) because the interactions between substituents need to be "shared".[14f] On the other hand, hydrogen-bonding interactions between the substituents (*e.g.*, $^{\bullet}C(NH_2)(CHO)_2$, see section 4.2.3.7) can contribute to enhanced stabilization. Electrostatic effects,[39,40] whether favorable (*e.g.*, $^{\bullet}C(BH_2)_3$, see section 4.2.3.3) or unfavorable (*e.g.*, $^{\bullet}C(CF_3)_3$, see section 4.2.3.8) should be amplified with the number of substituents. Finally, hyperconjugative interactions between substituents (*e.g.*, $^{\bullet}CHFNH_2$)) have been found to influence both the structures and stabilities of disubstituted radicals.[41]

Next, we discuss the principal interactions that influence the stabilities or instabilities of the precursor substituted methanes. In discussing RSEs in monosubstituted systems, one usually focuses on the effect of substituents on the radicals, implicitly assuming that this effect dominates the RSE, which is consistent with arguments presented by Coote *et al.*[10a] However, in multiply-substituted systems, interactions between the substituents in the closed-shell methanes can be substantial and therefore cannot be ignored.

Positive (*e.g.*, CH(BH2)₃, see section 4.2.3.2) and negative[42] (*e.g.*, CH(NH₂)₃, see section 4.2.3.1) hyperconjugative interactions between vicinal bonds,[43] 1,3-interactions (*e.g.*, NH₂CH₂BH₂, see section 4.2.3.6), and intramolecular hydrogen bonding (*e.g.*, NH₂CH₂CHO, see section 4.2.3.7), all of which can be modulated through bond rotations, influence the structures of multiply-substituted methanes,[44,37e] and should also play an important role in enhancing their stabilities (and thereby contribute positively to the MIEs). Additionally, the stabilities of multiply-substituted methanes are found to be affected by attractive (*e.g.*, CHF₃, see section 4.2.3.2) or repulsive (*e.g.*, CH(CN)₃, see section 4.2.3.4) coulombic interactions.[37b,45]

In addition to the electronic factors mentioned above, repulsive steric interactions[46] should facilitate C–H bond dissociation as we go from mono- to di- to tri-substituted methanes.

4.2.3.1. NH₂-series. NH₂ is the strongest π-donor among the substituents that we have examined. Such π-donor substituents generally play a dual role of stabilizing the adjacent radical center through three-electron interaction between the lone pair and the odd electron, and destabilizing it through an electron-withdrawing inductive effect.[39,40] NH₂, with a relatively high-lying HOMO and with a relatively low electronegativity compared with the other π-donors, leads to the highest RSE of 50.9 kJ mol⁻¹ among the monosubstituted radicals in the {π_d} set.

However, substitution at the C-radical center with additional NH_2 groups does not significantly change the RSE, which increases only marginally by 6.5 kJ mol⁻¹ as we go from the mono- to the di-aminomethyl radical, and does not increase at all when one includes a third NH_2 group. Indeed, the largest negative DARSEs of −44.4 and −95.3 kJ mol⁻¹ among the ˙CHXY and ˙CXYZ radicals occur for the di- and the tri-aminomethyl radicals, respectively (Fig. 10). Let us look at the RIEs and MIEs of these species to try to explain these trends.

RIE values are comparatively small for ˙$CH(NH_2)_2$ (−5.1 kJ mol⁻¹) and ˙$C(NH_2)_3$ (0.8 kJ mol⁻¹). The negative RIE indicates an unfavorable interaction of the NH_2 groups in ˙$CH(NH_2)_2$. This is consistent with conjugation saturation, as demonstrated in Fig. 15, $i.e.$, the donor NH_2 group interacts with an electron-deficient ˙C center, and leads to the electron-deficient center being less electron-deficient than it was initially (Fig. 15(a)). Consequently, the interaction of the modified 2p(˙C) SOMO with the second NH_2 donor group will be less favorable (Fig. 15(b)). Although, conjugation saturation and thereby destabilization is expected to increase further if another amino group is added, this is not seen for ˙$C(NH_2)_3$ (RIE = 0.8 kJ mol⁻¹).
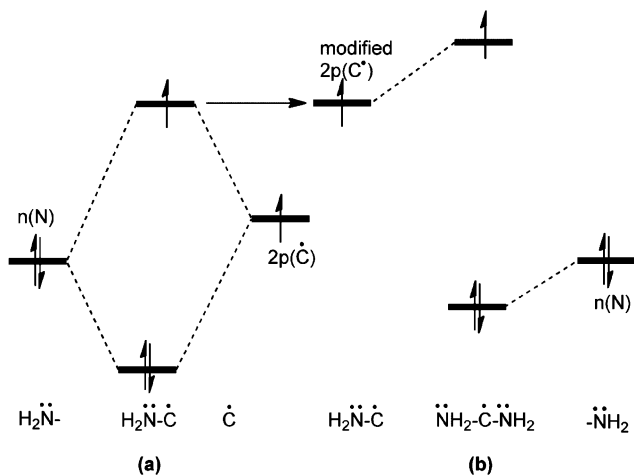
Fig. 15 Orbital interaction diagram showing saturation of conjugation effects in ˙$CH(NH_2)_2$.

Unlike the case of the radicals, strongly stabilizing interactions exist in di- and tri-aminomethane, as indicated by the very large MIEs of 39.3 and 96.1 kJ mol⁻¹. These can mainly be attributed to two electronic effects. One of them arises because a methylene carbon connected to an electronegative X (NH_2^i in Fig. 14) carries an increased positive charge compared with the situation for X = H. This in turn leads to a stronger coulombic attraction to the second electronegative Y (NH_2^{ii} in Fig. 16). Introduction of yet another electronegative substituent Z (NH_2^{iii}) further increases the stabilization. The second effect is the hyperconjugative interaction between a lone pair on the NH_2 group and the vicinal σ*(CH_2–NH_2) orbital of the adjacent NH_2 groups in diaminomethane (Fig. 16(a)), sometimes referred to as the generalized anomeric effect. Negative hyperconjugation of this type also prevails in triaminomethane (Fig. 16(b)).

In summary, the relatively small RSEs and the large negative DARSEs of the di- and tri-aminomethyl radicals can be attributed to the large stabilizing interactions in $CH_2(NH_2)_2$ and $CH(NH_2)_3$,
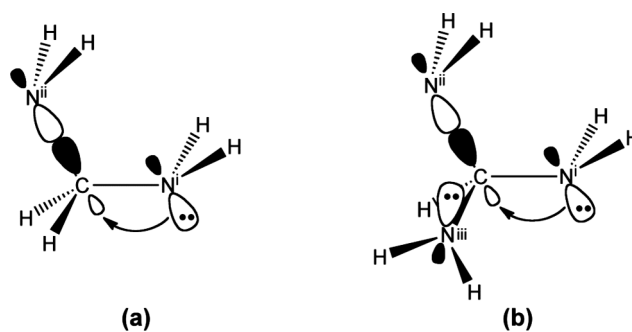

Fig. 16 (a) The lone pair of NH_2^i hyperconjugates with the σ*(CH_2–NH_2^{ii}) orbital in $CH_2(NH_2)_2$. An analogous interaction (which is not shown) also occurs between the lone pair of NH_2^{ii} and σ*(CH_2–NH_2^i). (b) Very similar hyperconjugative interactions prevail between N^i and N^{ii} in $CH(NH_2)_3$, but the orientation of the lone pair of NH_2^{iii} indicates that its involvement in hyperconjugation is minimal.

rather than to the unfavorable interactions in ˙$CH(NH_2)_2$ and ˙$C(NH_2)_3$.

4.2.3.2. F-series. Discussion of the {π_d} set would be incomplete if only the NH_2-series were considered because, although the RSEs, the DARSEs and the MIEs of most of the other systems in the {π_d} set show trends similar to those for the NH_2-series, there are several instances, like the F-series, where the RIEs are large positive numbers, unlike those for the NH_2-series. Hence a brief comment on the RIEs of the F-series is warranted. Let us compare the RIE of ˙CF_3 ($i.e.$, (F,F,F)) which shows the largest positive RIE of 83.5 kJ mol⁻¹, with that of ˙$C(NH_2)_3$ ($i.e.$, (NH_2,NH_2,NH_2)) (0.8 kJ mol⁻¹). Two factors appear to be primarily responsible for this large difference. In the first place, for radicals disubstituted with π-donors, π-conjugation has been found to compete with negative hyperconjugative interactions between the substituents, which is one of the reasons why the radical center becomes pyramidal.[47] Conformational analyses in the present study indicate a similar effect for trisubstituted radicals within the {π_d} set. The spatial arrangement of the lone pairs that would allow both normal π-conjugation and negative hyperconjugative interactions is more difficult to achieve for NH_2 in ˙$C(NH_2)_3$, thus stabilization by the latter is almost absent. On the other hand, in the case of ˙CF_3, the fact that F has three orthogonal lone pairs that have no directional constraint leads to a greater prospect for simultaneous stabilization of the radical *via* conjugative and hyperconjugative interactions. Secondly, as Song has suggested,[14a] a stronger conjugation between the first donor group and the radical center should lead to a more significant saturation effect. Because NH_2 is a stronger π-donor than F, the conjugation saturation should thus be more pronounced for multiple substitution with NH_2 than with F, making the RIE of ˙$C(NH_2)_3$ less positive than that of ˙CF_3.

4.2.3.3. BH₂-series. BH_2, being a π acceptor, stabilizes the radical by a two-center-one-electron interaction (Fig. 17(a)). Because BH_2 is a σ donor, it further stabilizes the radical by coulombic interaction. Thus, monosubstitution with BH_2 leads to a significant positive RSE of 44.0 kJ mol⁻¹. However, the RSEs of ˙$CH(BH_2)_2$ (56.6 kJ mol⁻¹) and ˙$C(BH_2)_3$ (57.2 kJ mol⁻¹) indicate that there is only a small additional net stabilizing benefit for carbon-centered radicals from multiple substitution with BH_2. Let
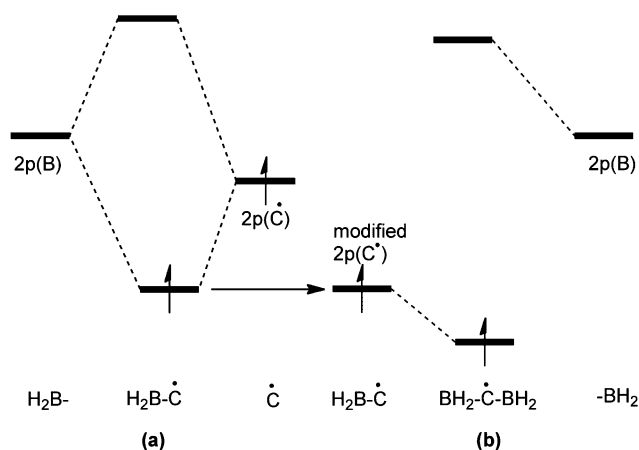
Fig. 17 Orbital interaction diagram showing saturation of conjugation effects in ·CH(BH$_2$)$_2$.

Fig. 18 (a) σ(BH$_2^{ii}$–CH$_2$) hyperconjugates with 2p(B^i) in CH$_2$(BH$_2$)$_2$. A similar interaction (which is not shown) occurs between σ(BH$_2^i$–CH$_2$) and 2p(B^{ii}). (b) CH(BH$_2$)$_3$ has C_{3v} symmetry and the three 2p(B) orbitals interact equally with the neighboring σ(BH$_2$–CH$_2$) orbitals.

us look at the RIEs and MIEs of these species to try to understand these trends.

·CH$_2$BH$_2$ has a planar structure whereas the multiply-substituted radicals, ·CH(BH$_2$)$_2$ and ·C(BH$_2$)$_3$, are pyramidal. The preferred geometries of the latter suggest that, as in the case of the multiply-substituted radicals of the {π$_d$} set, π-conjugation competes with the hyperconjugation between σ(B–C) and the formally vacant 2p(B) orbital at the second BH$_2$. Despite these stabilizing hyperconjugative interactions between the substituents and despite the increasing coulombic stabilization with substitution associated with the σ-donating ability of BH$_2$, the RIEs are negative for both ·CH(BH$_2$)$_2$ (−15.1 kJ mol^{-1}) and ·C(BH$_2$)$_3$ (−14.8 kJ mol^{-1}). The negative RIEs is likely to be a consequence of conjugation saturation, *i.e.*, the formally vacant 2p(B) orbital interacts with the 2p(·C) orbital to lower the energy of the latter, as shown in Fig. 17(a). Consequently, the interaction of the modified 2p(·C) orbital with the second 2p(B) orbital is diminished owing to the increased energy difference between the interacting orbitals, as shown in Fig. 17(b).

In the case of the CH$_2$(BH$_2$)$_2$ and CH(BH$_2$)$_3$ molecules, the MIEs have relatively large positive values: 16.3 kJ mol^{-1} for the former and 60.1 kJ mol^{-1} for the latter. This can mainly be attributed to two effects. Firstly, because B is electropositive, the methylene carbon carries a partial negative charge. This in turn leads to a stronger coulombic attraction to the second and third BH$_2$ groups. Secondly, the favorable hyperconjugative interaction in CH$_2$(BH$_2$)$_2$ (Fig. 18(a)) corresponds to donation from the σ(BH$_2$–CH$_2$) orbital of the second BH$_2$ to the formally vacant 2p(B) orbital of the first BH$_2$ substituent, leading to a relatively large positive MIE of 16.3 kJ mol^{-1}. When there are three BH$_2$ substituents, hyperconjugation is enhanced and thus CH(BH$_2$)$_3$ shows a large positive MIE of 60.1 kJ mol^{-1} (Fig. 18(b)).

To summarize, the minimal increase in RSEs with multiple substitution by BH$_2$ and the large negative DARSE values can mainly be attributed to the relatively large stabilization of the parent molecules and, to a lesser degree, destabilization of the corresponding radicals.

4.2.3.4. CN-series. CN is a π-acceptor–σ-acceptor substituent that simultaneously stabilizes the radical center by electron delocalization of the unpaired electron (owing to its π-accepting ability) and destabilizes the radical by electron withdrawal (owing
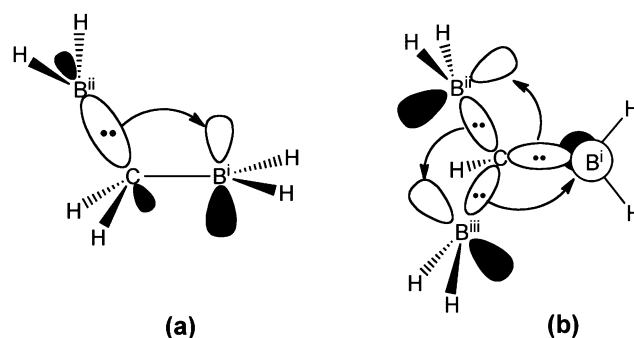
to its σ-accepting nature). Monosubstitution with CN results in an RSE of 33.8 kJ mol^{-1}. The RSEs are found to increase progressively to 69.8 kJ mol^{-1} for the dicyano- and 107.1 kJ mol^{-1} for the tricyano-methyl radical.

Although the additional π-systems offer the prospect for extended electron delocalization of the unpaired electron in the radicals ·CH(CN)$_2$ and ·C(CN)$_3$, conjugation saturation[14f] (similar to that in the BH$_2$-series) together with an electrostatic destabilizing effect contribute to making the RIEs negative. In fact, the largest negative RIEs among di- and tri-substituted systems occur respectively for ·CH(CN)$_2$ (−32.3 kJ mol^{-1}) and ·C(CN)$_3$ (−89.3 kJ mol^{-1}).

Similarly, the large negative MIEs of CH$_2$(CN)$_2$ (−34.6 kJ mol^{-1}) and CH(CN)$_3$ (−95.2 kJ mol^{-1}) indicate significant destabilizing interactions. Wiberg *et al.*[45] have pointed out the unfavorable electrostatic interactions in these molecules. Thus, although CN is a σ-withdrawing substituent, the carbon at the point of attachment to the methylene group is positively charged (unlike F or NH$_2$), owing to the presence of the electronegative nitrogen in CN. The central carbon also acquires a positive charge as a result of substitution. Thus there is coulombic repulsion between the central carbon and the cyano carbon, which results in destabilization. Equivalently, the destabilization can be attributed to unfavorable interactions between the local dipoles of the CN groups.

The large RIEs and MIEs almost cancel, and this leads to small positive DARSE values (2.3 and 5.8 kJ mol^{-1}, respectively, for ·CH(CN)$_2$ and ·C(CN)$_3$). Thus it turns out that the positive DARSE values for these systems arise not because of favorable synergistic interactions in the radicals (which would be the superficial interpretation) but because the interactions in the radicals are less unfavorable than those in the closed-shell molecules.

4.2.3.5. CH=CH$_2$-series. We have already noted in section 4.2.1 that monosubstitution of a methyl radical with the π$_d$/π$_a$ substituent CH=CH$_2$ leads to the largest RSE of 68.2 kJ mol^{-1}, which can be related to the resonance stabilization of the allyl radical. Consistent with this, ·CH(CH=CH$_2$)$_2$ and ·C(CH=CH$_2$)$_3$ also show quite large RSEs of 111.2 and 135.5 kJ mol^{-1}, respectively.

RIEs of the multiply-substituted radicals of the CH=CH$_2$-series are negative, *viz*, −16.7 kJ mol^{-1} for the disubstituted and −50.9 kJ mol^{-1} for the trisubstituted radical. The RSEs are less negative than those in the CN-series because CH=CH$_2$ lacks the heteroatom that gives rise to the positive terminal carbon or the

bond dipole moments in the CN-series, and hence there is no significant coulombic repulsion. On the other hand, the RIEs are more negative than those in the BH₂-series because, unlike BH₂, CH=CH₂ does not benefit from electrostatic stabilization in the radical. The main reason for the negative RIEs appears to be the conjugation saturation effect.

MIEs of the multiply-substituted molecules of the CH=CH₂-series are positive. In a similar manner to the RIEs, the MIEs of divinyl- (8.4 kJ mol⁻¹) and trivinyl- (18.1 kJ mol⁻¹) methane are neither near the positive extreme shown by those of the BH₂-series nor near the negative extreme shown by those of the CN-series. This can be attributed to the hyperconjugative stabilizing interactions being weaker than in the former and the electrostatic destabilizing interactions being weaker than in the latter.

Although the DARSE values are negative for the multiply-substituted radicals of the CH=CH₂-series, it can be seen that CH=CH₂ is a more effective substituent for stabilizing mono-, di- or tri-substituted C-centered radicals than any of the other substituents among the $\{\pi_a\}$ set.

4.2.3.6. (NH₂,BH₂,Z)-series. The disubstituted radical of this series (Z = H) shows a large RSE of 118.4 kJ mol⁻¹. In the case of the trisubstituted radicals, (NH₂,BH₂,OH) shows the highest RSE of 151.0 kJ mol⁻¹. As discussed in section 4.2.2.1, the RSEs of the (NH₂,BH₂,Z) series are generally larger when Z is a π-donor substituent. RSEs are also large when Z is a π_d/π_a substituent but relatively smaller when Z is a π_a substituent.

The extra stabilization when the carbon at the radical center is disubstituted with a strong acceptor (like BH₂) and a strong donor (like NH₂) has been known for many years. This extra stabilization

has been explained with the help of orbital interaction diagrams[14b] such as those shown in Fig. 19(a) and 19(b). The lone pair of electrons on NH₂ interacts with the 2p(·C) orbital, raising the energy of the latter as shown in Fig. 19(a). There is then enhanced interaction between the modified 2p(·C) with the 2p(B) as shown in Fig. 19(b), which has been coined the captodative effect. This leads to a large positive RIE of 67.6 kJ mol⁻¹ for (NH₂,BH₂,H).

In the case of trisubstituted radicals of this series, as has been discussed in section 4.2.2.2, the RIEs are larger when the third substituent is a π-donor than when it is a π-acceptor. This can be rationalized using the orbital interaction diagrams presented in Fig. 19(c) and 19(d), respectively, for the situation when the third substituent is a π-donor (NH₂) or a π-acceptor (BH₂). The second modified 2p(C·) of NH₂CH·BH₂ interacts more efficiently with the NH₂-lone pair orbital in (c), and less efficiently with the 2p(B) orbital in (d), because of the decreased and increased energy gaps, respectively, between the interacting orbitals. We refer to the former extra stabilizing effect as the *capto**di**dative effect.* Additionally, it is interesting to note that, among the π-accepting Z substituents, RIEs are larger for those radicals for which there are additional stabilizing hydrogen-bonding interactions (*e.g.*, when Z = CHO or COOH).

When it comes to the substituted methanes of this series, the MIEs are found to be quite large, owing to the stabilizing 1,3-interactions consistently present. As shown in Fig. 20, 1,3-interactions between NH₂ and BH₂ groups in these molecules go beyond a simple hyperconjugative interaction and end up with something approaching a dative bond. Additional stabilizing interactions such as positive hyperconjugation (when Z = BH₂,
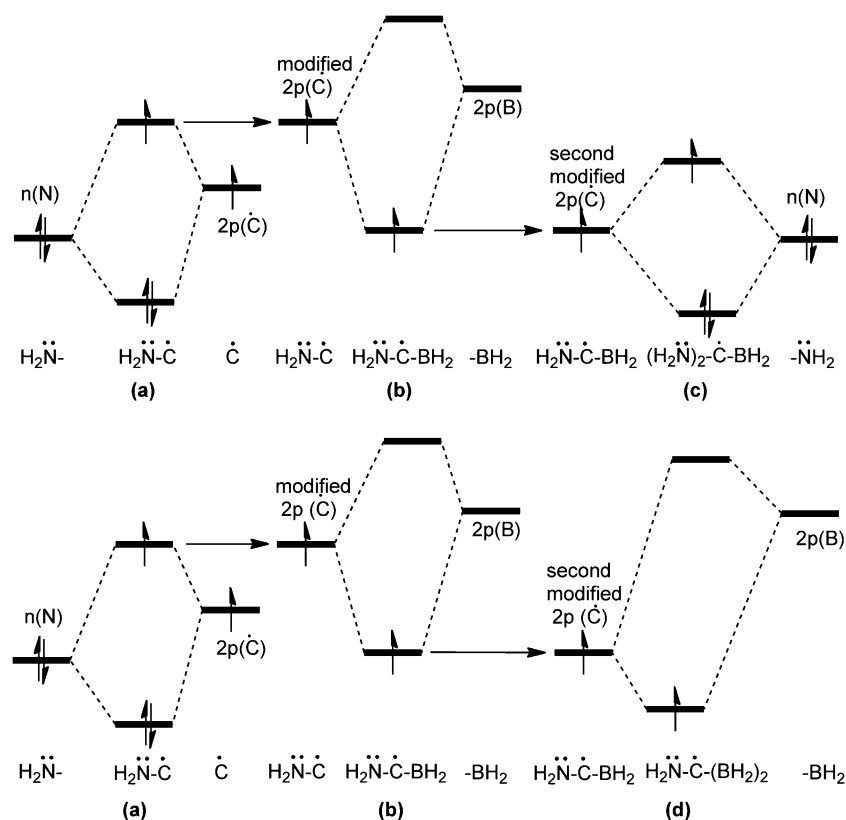

Fig. 19 Orbital interaction diagrams for (NH₂,BH₂,NH₂) and (NH₂,BH₂,BH₂).
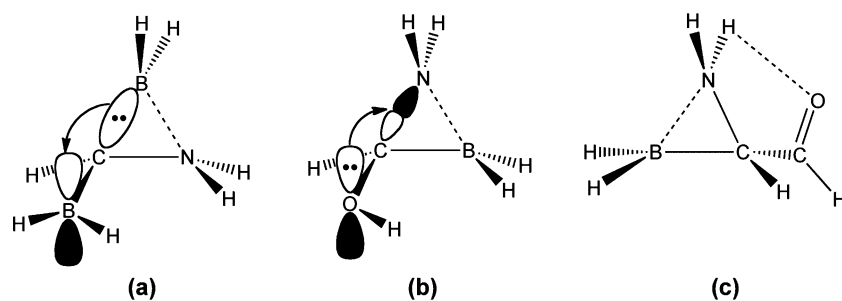
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Fig. 20 1,3-Interactions between the NH_2 and BH_2 groups are present in all the molecules of the (NH_2,BH_2,Z)-series. (a) Additional positive hyperconjugative interaction between the $\sigma(B–C)$ and $2p(B)$ orbitals in (NH_2,BH_2,BH_2). (b) Additional negative hyperconjugative interaction between the $n(OH)$ and $\sigma^*(C–N)$ orbitals in (NH_2,BH_2,OH). (c) Additional H-bonding interaction in (NH_2,BH_2,CHO).

Fig. 20(a), negative hyperconjugation when Z = F, OH or NH_2 (Fig. 20(b)), and hydrogen bonding (when Z = CHO or COOH, Fig. 20(c)) lead to relatively larger MIEs for the respective molecules, with (NH_2,BH_2,BH_2) showing the largest MIE of 104.6 kJ mol^{-1} in the entire series.

In summary, despite the larger MIE values, DARSEs are positive in those radicals in this series where Z is a π-donor. We attribute this primarily to the larger positive RIEs associated with the captodidative effect. We note that captodidative stabilization can also be seen in the series (OH,BH_2,Z), (OH,CHO,Z), (F,BH_2,Z), and (NH_2,CCH,Z).

4.2.3.7. (NH_2,CHO,Z)-series. It is interesting to note that, despite the larger RIEs of the (NH_2,BH_2,Z)-series, the (NH_2,CHO,Z)-series shows larger RSEs. Two reasons may be put forward for this observation. Firstly, the stabilization of the closed-shell parents (reflected in the MIE values) of the (NH_2,CHO,Z)-series is relatively low compared with that for the (NH_2,BH_2,Z)-series. Secondly, there is additional stabilization (and hence larger RIEs) offered by H-bonding in the (NH_2,CHO,Z)-series.

As in the case for the (NH_2,BH_2,Z)-series, the RIEs are quite large for the captodatively-stabilized radicals of the (NH_2,CHO,Z)-series. In fact, the RIE values for (NH_2,CHO,CHO) and $(NH_2,CHO,COOH)$ are as large as those of the captodatively-stabilized radicals of the (NH_2,CHO,Z)-series. This can be attributed to the extra stabilization provided by double H-bonding in these radicals, as shown in Fig. 21.
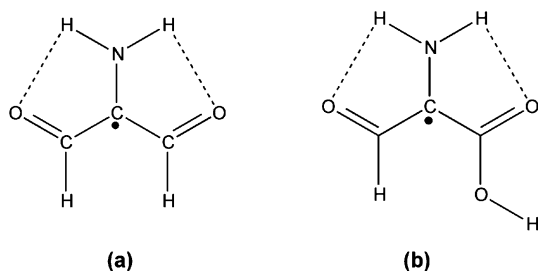

Fig. 21 Hydrogen-bonding interactions in the (NH_2,CHO,CHO) and $(NH_2,CHO,COOH)$ radicals.

Thus, the relatively smaller stabilization of the parent molecule (MIE = 30.3 kJ mol^{-1}) and the larger additional stabilization of the radical (RIE = 83.8 kJ mol^{-1}) lead to (NH_2,CHO,CHO) having very high RSE and DARSE values of 177.1 and +53.6 kJ mol^{-1}, respectively.

4.2.3.8. CF_3-series. Because the trifluoromethyl group is strongly electron-withdrawing, it destabilizes the carbon-centered radical on monosubstitution (RSE = −3.6 kJ mol^{-1}). However, with the introduction of additional CF_3 groups, the RSEs become less negative for $\cdot CH(CF_3)_2$ (−3.1 kJ mol^{-1}), and even positive for $\cdot C(CF_3)_3$ (+4.1 kJ mol^{-1}), as discussed in section 4.2.2.1.

Let us analyze the RIE and MIE values for multiply-substituted species of this series to explain this trend. The RIEs of $\cdot CH(CF_3)_2$ (−16.5 kJ mol^{-1}) and $\cdot C(CF_3)_3$ (−51.1 kJ mol^{-1}) have large negative values as the increasing number of CF_3 groups continues to deplete the electron density at the radical center. At the same time, the precursor molecules are increasingly destabilized by coulombic interactions, as indicated by large negative MIEs for $CH_2(CF_3)_2$ (−20.6 kJ mol^{-1}) and for $CH(CF_3)_3$ (−66.0 kJ mol^{-1}). It is interesting that multiple substitution with CF_3 groups has a destabilizing effect similar to that of CN (see section 4.2.3.4).[45] Thus, despite the large destabilization in the multiply-substituted radicals, the bond dissociation is facilitated because of the larger destabilization in the molecules. It is also notable that the DARSEs are positive, as in the case of the CN-series, because the interaction in the radical is less unfavorable than that in the closed-shell molecule.

5.   Conclusions

We have defined a number of quantities that allow us to analyze the stabilities of singly-, doubly-, and triply-substituted carbon-centered radicals. We have used these quantities to probe the interactions of substituents in both the substituted methyl radicals ($\cdot CXYZ$) and in the precursor closed-shell methane derivatives (CHXYZ), and have investigated the extent to which these interactions are additive. Additionally, we have assessed the performance of the restricted and unrestricted double-hybrid B2-PLYP methods, with the 6-311+G(3df,2p) basis set, in predicting quantities related to the stabilities of the carbon-centered radicals, through comparisons with available experimental data and with the results obtained from the high-level composite method G3X(MP2)-RAD. The test set consisting of 166 systems was subdivided into five smaller sets *viz*, (1) the $\{\pi_d\}$ set consisting of systems substituted by π-donors, (2) the $\{\pi_a\}$ set consisting of systems substituted by π-acceptors (including $CH{=}CH_2$ and $C{\equiv}CH$), (3) the $\{\pi_d\pi_aZ\}$ set consisting of systems in which one of the substituents (X) is a π-donor, a second substituent (Y) is a π-acceptor, with varying Z, (4) the $\{CQ_3\}$ set consisting of systems substituted with CH_3 and/or CF_3, and (5) the $\{X\text{-}CQ_3\}$

set consisting of systems in which X varies and where the Y (for •CHXY) or Z (for •CXYZ) substituents are either CH_3 or CF_3. The following important conclusions emerge from our study:

(1) The G3X(MP2)-RAD method produces bond dissociation energies (BDEs) and radical stabilization energies (RSEs) in good agreement with experimental values, with mean absolute deviations (MADs) from experiment for 39 reactions for which experimental data are available of 3.6 (BDEs) and 3.9 (RSEs) kJ mol^{-1}.

(2) The ROB2-PLYP method when used with the 6-311+G(3df,2p) basis set consistently underestimates the BDEs of carbon-centered radicals, with a mean deviation (mean absolute deviation) from experiment of −7.4 (7.5) kJ mol^{-1}. However, it gives significantly improved RSEs, with an MAD of 3.5 kJ mol^{-1}. The corresponding MAD values for the UB2-PLYP method are 11.8 (BDEs) and 3.9 (RSEs) kJ mol^{-1}.

(3) For a larger test set of 106 systems, ROB2-PLYP and UB2-PLYP consistently overestimate RSEs compared with G3X(MP2)-RAD values, with MDs of +9.2 and +10.0 kJ mol^{-1}, respectively.

(4) We recommend re-evaluation of experimental C–H BDEs for allyl fluoride and allyl chloride, on the basis of the significant disagreement between the current experimental values and the theoretical values obtained with the G3X(MP2)-RAD and high-level W1 procedures. Our current best estimates for the BDEs at 0 K are 349.2 (allyl fluoride) and 349.9 (allyl chloride) kJ mol^{-1}.

(5) *Monosubstitution* of radicals leads mostly to positive RSEs, particularly for substituents that are predominantly π-donors, π-acceptors or σ-donors. However, monosubstitution with the σ-accepting CF_3 group is unfavorable, leading to a negative RSE of −3.6 kJ mol^{-1}. The largest RSE among monosubstituted systems (+68.2 kJ mol^{-1}) is brought about by the vinyl (CH=CH$_2$) substituent.

(6) *Disubstitution* is generally found to decrease BDEs (or increase RSEs), the extent depending on the nature of X and Y. Disubstitution with a π-donor–π-acceptor combination of substituents is confirmed to be most effective, leading to captodative stabilization. Disubstitution with two π-acceptors is also favorable. The increase in the RSEs with increasing substitution is less pronounced for π-donor–π-donor combinations. Among the disubstituted systems studied, the largest RSE is found for H_2N•CHCHO (+131.7 kJ mol^{-1}). The only disubstituted radical examined that shows a negative RSE is •CH(CF$_3$)$_2$ (−3.1 kJ mol^{-1}).

(7) *Trisubstitution* is found generally to further decrease the BDEs (and increase the RSEs). Consistent with the trends in disubstituted radicals, trisubstitution with π-acceptors leads to larger RSEs than trisubstitution with π-donors. The largest RSE among the {π$_a$} set occurs for •C(C≡CH)$_3$ (+146.9 kJ mol^{-1}) while the largest RSE among the {π$_d$} set occurs for •C(SH)$_3$ (+83.2 kJ mol^{-1}). Trisubstituted radicals of the {π$_d$π$_a$Z} set show the largest RSEs overall, with H_2N•C(CHO)2 at the top (+177.1 kJ mol^{-1}).

(8) Radical interaction energies (RIEs) and molecule interaction energies (MIEs) were calculated for the di- and tri-substituted systems in order to help in the analysis of the RSEs. They are defined such that positive values correspond to a stabilizing interaction of the substituents. Deviations from additivity of the RSEs (DARSEs) were also calculated to probe whether the effects of two or three substituents are synergistic (positive DARSE) or antagonistic (negative DARSE). If RSEs were strictly additive,

then the DARSE values would be zero. The DARSE value may also be obtained as the difference between the RIE and the MIE, so that a positive DARSE arises when the interactions of the substituents in a radical are more favorable (or less unfavorable) than in the parent methane derivative.

(9) RIEs are generally positive for radicals in the {π$_d$π$_a$Z} set, confirming that the captodative stabilization associated with the combination of π$_d$ and π$_a$ substituents is the major effect that stabilizes radicals. They are generally negative for radicals in the {π$_a$} set. The {π$_d$} set shows mixed trends. RIEs are found to be generally enhanced when Z in the {π$_d$π$_a$Z} set is a π-donor. We call this a *capto**di**dative* effect. The interactions, whether stabilizing or destabilizing, are found to be enhanced on going from di- to tri-substituted radicals, *i.e.*, positive RIEs become more positive and negative RIEs become more negative for trisubstituted compared with disubstituted radicals.

(10) Among the various sets of multiply-substituted methanes examined, the {π$_d$} set shows the largest positive MIEs. The molecules of the {π$_d$π$_a$Z} set also generally give positive MIEs. Multiple substitution is less favorable for the {π$_a$} set, as indicated by negative MIEs. The intramolecular interactions, whether they are stabilizing or destabilizing, again increase as we go from di- to tri-substituted methanes. The largest positive MIE is found for CH(OH)$_3$, (+137.2 kJ mol^{-1}) while the largest negative MIE is found for CH(CN)$_3$ (−95.2 kJ mol^{-1}).

(11) A positive DARSE value is often taken as an indication of synergistic effects in multiply-substituted radicals. Indeed, the large positive DARSEs in the {π$_d$π$_a$Z} set can mainly be attributed to the large positive RIEs for the radicals of this set. The largest positive DARSE is found for H_2N•C(CHO)$_2$ (+53.6 kJ mol^{-1}). Positive DARSEs can alternatively arise if there are antagonistic interactions in the radical but they are smaller than the antagonistic interactions in the parent molecules. This occurs, for example, in the •C(CN)$_3$ radical of the {π$_a$} set, and for the •C(CF$_3$)$_3$ radical of the {CQ$_3$} set.

(12) A negative DARSE value is often taken as an indication of antagonistic interactions (*e.g.*, saturation) in radicals. Alternatively, it might arise from larger synergistic effects in molecules than in radicals. Indeed, it is important to note that the negative DARSEs of the {π$_d$} set are primarily associated with the large positive MIEs of the parent methane rather than to negative RIEs. The largest negative DARSE is found in the {π$_d$} set for •C(NH$_2$)$_3$ (−95.3 kJ mol^{-1}).

(13) More generally, variations in the thermodynamic stability of radicals with respect to C–H dissociation should not be solely attributed to the radicals. Interactions in the parent closed-shell molecules can also contribute to the enhancement or diminution of the C–H BDEs. Indeed, for the systems examined in the present study, the variation in the interaction energies associated with multiple substitution in the radicals is actually smaller than that in the closed-shell molecules, as shown by the range of RIEs (−89.3 to +112.4 kJ mol^{-1}) compared with MIEs (−95.2 to +137.2 kJ mol^{-1}).

(14) Deviations from pairwise additivity in RSEs (DPARSEs) are found to be non-negligible, indicating that the RSEs of trisubstituted radicals cannot be reliably predicted simply by taking into account the pairwise interactions in disubstituted molecules and radicals. We find that pairwise additivity generally leads to an overestimation of both the stabilizing and destabilizing interactions

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Acknowledgements

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