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Prediction of Singlet−Triplet Splittings for Aryne Biradicals from ^{1}H Hyperfine Interactions in Aryl Radicals

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Density functional calculations with a polarized double-ζ basis set on simple aryl radicals have predictive utility in the estimation of singlet−triplet energy splittings of corresponding aryne biradicals through a proportionality between isotropic hyperfine couplings for the former species and the splittings for the latter species. This allows rapid estimation of singlet−triplet splittings in large hydrocarbon systems, where direct calculation would be prohibitively costly, and should simplify the design of aryne systems having controlled reactivities as a function of their singlet−triplet state energy splittings.

Didehydroarenes[1−4] ("arynes") are reactive intermediates having two nominally nonbonding σ orbitals; arynes show different degrees of biradical character depending upon the separation distance and relative orientation of those orbitals.[5] The benzynes are archetypal arynes that have a long history of experimental and theoretical investigation.[1−11] Benzynes have become common reagents for organic and organometallic synthesis.[1−4,12−14] *p*-Benzynes formed by Bergman cyclization[15,16] are key intermediates in the mechanisms proposed for the double-stranded cleavage of DNA by enediyne antibiotics.[17−19] Chen and co-workers have recently emphasized that the reactivity of *p*-benzyne type biradicals depends upon the energy splitting between the singlet (S) ground state and triplet (T) excited state; the larger the splitting, the less reactive and more selective the singlet biradical.[20,21] Thus, rational design of more selective enediyne and related antibiotics[22−24] requires a reliable means for estimating S−T splittings in arynes. However, measurement of these quantities is by no means routine,[25] and they are difficult to calculate accurately by ab initio methods,[6−8,11] especially for the larger arynes that may be of interest with respect to drug development. In this Letter, we present a simple computational approach for estimating S−T energy gaps for arynes from a relationship between S−T splittings in the biradicals and the more easily calculated isotropic hyperfine coupling constants in the corresponding aryl monoradicals. We illustrate the method for the 10 isomeric didehydronaphthalenes ("naphthalynes").[4,26−30]

Measurement of the S−T splittings for *o*-, *m*-, and *p*-benzyne was recently accomplished by negative ion photoelectron spectroscopy.[25] All three benzynes have singlet ground states, and as expected,[7,8,11] the S−T gap decreases with increasing number of bonds between the radical centers. Table 1 presents the experimental data together with predictions from two different levels of theory, namely, multireference second-order perturbation theory[31−33] (CASPT2) and density functional theory[34−36] (DFT, specifically BPW91).[37] These theoretical levels are reasonably efficient in terms of demand for computational resources, but neither provides especially satisfactory results. For *o*-benzyne, both levels significantly underestimate the splitting—in the case of CASPT2 this is consistent with its known tendency to overstabilize triplet states relative to singlets, typically by 3−12 kcal/mol in single-center biradicals (e.g., carbenes).[38,39] For *m*-benzyne, the underestimations of the gap are considerably reduced, but predictions from both levels remain outside the experimental error bars. Finally, while CASPT2 *over*estimates the stability of the singlet for *p*-benzyne by 2 kcal/mol, BPW91 erroneously predicts a triplet ground state. This failing of DFT reflects its limitations as a single-determinant model—as the separation between the radical centers increases, nondynamical electron correlation becomes increasingly important for the singlet state, and current functionals are incapable of accurately accounting for this effect.[40]

Calculations at higher levels of theory (e.g., multireference configuration interaction or coupled-cluster approaches including triple excitations) have provided more accurate predictions for the benzynes,[7,8,11] but these approaches are currently impractical for larger systems, such as naphthalynes. Table 1 provides calculated S−T splittings for the naphthalynes at the CASPT2 and BPW91 levels. The expected trends between the two levels based on the benzynes are observed: there is reasonable agreement on the gaps for the 1,2- and 1,3-biradicals, but DFT severely underestimates the singlet stabilities for biradicals with larger separation between the radical sites.

The magnitude of the S−T splitting, of course, reflects the degree to which spins at the dehydro positions interact with one another. A quite different observable that might be expected to provide information on the degree of this interaction in the biradical is the isotropic hyperfine coupling constant (hfs) to a hydrogen atom *capping a particular site in the corresponding monoradical*, e.g., the hfs value for the para hydrogen in the phenyl radical would constitute a measure of the degree of spin communication between the two radical sites in *p*-benzyne. The utility of focusing on hfs is that it is a one-electron property easily calculated from a doublet wave function,[41,42] and such wave functions for aromatic σ radicals are typically well described by a single determinant.[43] Table 2 lists the BPW91 hfs values calculated for different hydrogen atoms in the phenyl and 1- and 2-naphthyl radicals (there are 17 unique data, the values appear under the benzyne or naphthalyne that would be created were the given hydrogen to be removed from the indicated radical). BPW91 is in excellent agreement with the

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TABLE 1: Computed S−T Splittings (kcal/mol) at the CASPT2 and BPW91 Levels[a]

	benzyne			naphthalyne									
theory	*ortho*	*meta*	*para*	1,2	1,3	1,4	1,5	1,6	1,7	1,8	2,3	2,6	2,7
CASPT2	−30.4	−18.0	−5.8	−32.2	−17.2	−5.6	−7.8	−0.9	−1.6	−0.9	−28.4	−1.8	−2.9
BPW91	−31.3	−19.4	2.0	−33.2	−19.7	1.0	−1.6	25.6	16.9	10.7	−29.6	21.6	10.9
exptl[b]	−37.7 ± 0.7	−21.1 ± 0.4	−3.8 ± 0.5										

[a] S−T splittings from indicated level of theory (cc-pVDZ basis set). Zero-point vibrational energy corrections from BPW91 frequency calculations for both cases. [b] Reference 25.

TABLE 2: Computed Isotropic Hyperfine Splittings (G) at the BPW91/cc-pVDZ Level[a]

	benzyne			naphthalyne									
radical	*ortho*	*meta*	*para*	1,2	1,3	1,4	1,5	1,6	1,7	1,8	2,3	2,6	2,7
phenyl	15.2	5.9	2.1										
1-naphthyl				16.9	5.7	2.2	3.2	−0.2	0.5	−0.3			
2-naphthyl				17.0	5.6			−0.2	0.3		13.7	0.3	0.8
exptl[b]	17.4	5.9	1.9										

[a] Data grouped by benzyne/naphthyne that would be created if the parent radical were dehydrogenated at the position for which hyperfine splitting is reported. [b] Reference 44.

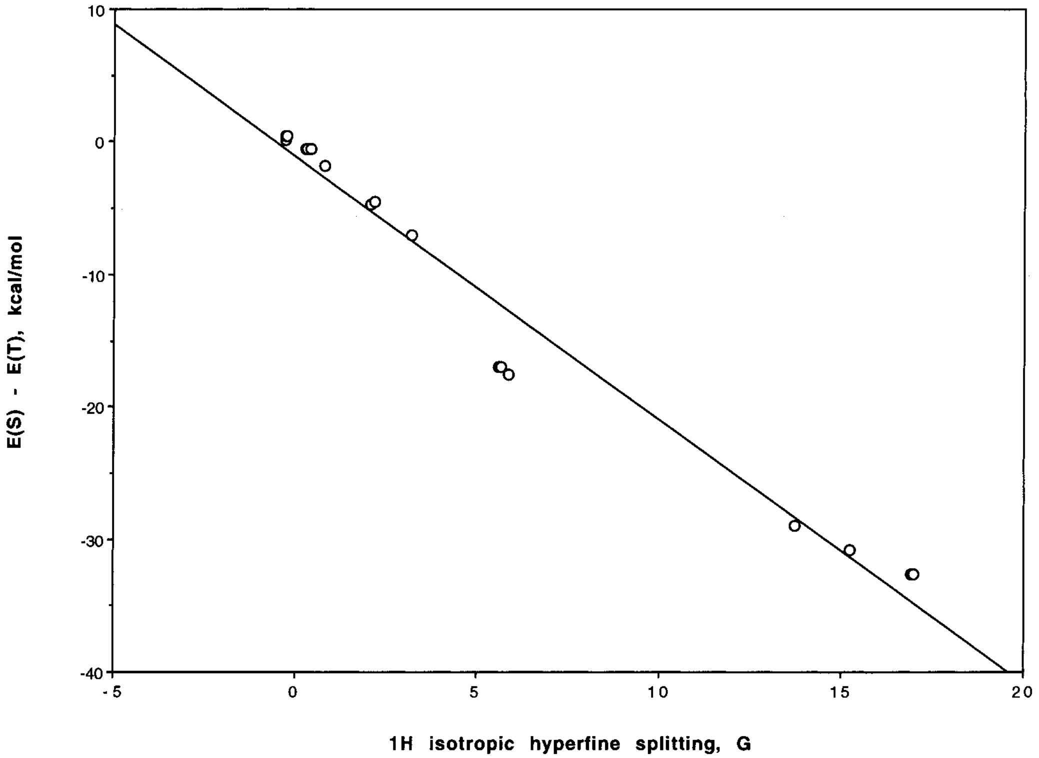

Figure 1. CASPT2 aryne S−T gaps (electronic energy only) vs BPW91 hfs for phenyl and naphthyl radicals. See Table 2 for correspondence of data.

measured[44] hfs values for the phenyl radical; indeed, DFT has been shown to provide very accurate hfs predictions in many different molecules.[39,45−49]

Figure 1 shows that there is indeed a strong correlation between the magnitude of the CASPT2-predicted benzyne and naphthyne S−T gaps and the DFT-predicted hfs values in the phenyl and naphthyl radicals. The nearly linear fit ($R^2 = 0.97$) for all 17 data points is in part fortuitous. Geometries of the arynes and corresponding radicals optimized at the CAS level are quite similar when the two radical centers in the aryne do not interact strongly (as measured by either a small S−T gap or a small hfs value). However, in the 1,3-arynes there is moderate distortion in the singlets from bonding overlap between the two radical centers, and that distortion becomes quite large in th 1,2-arynes, where the singlets have a formal triple bond. Since geometry distortion may significantly alter the spin−spin interaction, we expect correlation between S−T gaps and hfs values to be least accurate for the 1,2-arynes (rightmost cluster of points in Figure 1), improved for the 1,3-arynes (middle cluster), and most accurate for the remaining more remotely coupled arynes. Furthermore, Figure 1 does *not* include the zero-point vibrational energy differences between the spin states (since one would not expect hfs values to provide any measure of this quantity). All of these caveats aside, it is clear that there is a quantitatively meaningful relationship between S−T splitting and hfs. This relationship is *not* simply founded on each of these properties becoming smaller with greater separation between aryne centers; there is poor correlation between either observable and the relevant C−C distance ($R^2 = 0.70$ and 0.74 for hfs and S−T splitting, respectively) with scatter being largest for long-range separations where hfs and S−T splittings appear to be similarly sensitive to critical through-bond couplings.

This analysis provides a useful, efficient method for semiquantitative estimation of S−T splittings, limited in this case

TABLE 3: Corrected S−T Splittings (kcal/mol) for Naphthalynes from Two Methods

	naphthalyne									
method	1,2	1,3	1,4	1,5	1,6	1,7	1,8	2,3	2,6	2,7
CASPT2[a]	−39.5	−20.3	−3.5	−5.8	1.2	0.5	1.2	−35.7	0.2	−0.8
^{1}H hfs[b]										
1-naphthyl	−41.8	−20.3	−4.0	−5.9	0.4	−0.8	0.5			
2-naphthyl	−42.0	−20.1			0.5	−0.5		−33.9	−0.6	−1.5
best estimate (average)	**−41.1**	**−20.2**	**−3.8**	**−5.8**	**0.7**	**−0.3**	**0.8**	**−34.8**	**−0.2**	**−1.2**

[a] S−T splittings corrected based on benzynes (see text). [b] S−T splittings calculated from hfs values based on benzynes (see text).

by the accuracy of the CASPT2/cc-pVDZ level of theory that is being correlated. In principle, of course, what one would like to correlate is predicted hfs values against *experimental* S−T splittings.[50] With only three experimental aryne splittings available, such an approach is of questionable statistical relevance. Nevertheless, if we take advantage of the experimental data available for the benzynes, we can attempt to scale the results from both theoretical approaches (CASPT2 computed S−T gaps and the correlation between BPW91 hfs and S−T gaps) and see how they compare. Table 3 provides "corrected" S−T gaps as predicted by each method. CASPT2 splittings for 1,2-, 1,3- and more distantly coupled naphthalynes are corrected simply by adding the deviations found for this level compared to experiment for *o*-, *m*-, and *p*-benzyne, respectively. The gaps calculated from BPW91 use the proportionalities of the experimental gaps to the computed hfs values for the benzynes as multipliers for the naphthalyne hfs values. Again, the 1,2-, 1,3-, and more distant cases are all three treated separately (multiplication factors of −2.47, −3.60, and −1.83 kcal mol^{-1} G^{-1}, respectively). These two different approaches give remarkably similar predictions, which lends credibility to the results. In the absence of sufficient experimental data, we see no reason yet to prefer one method over the other, so Table 3 simply provides the average of all computed S−T gaps as our "best estimate".

A number of chemically interesting trends are apparent in Table 3. For instance, the S−T gap is much larger for 1,2-naphthalyne compared to 2,3-naphthalyne. As discussed by Ford,[51] this derives from the bond alternation already present in naphthalene, where there is increased bond order between positions 1 and 2 compared to 2 and 3. In addition, the 1,6- and 1,8-naphthalynes are predicted to be ground-state triplets. This is a plausible spin state for these species since, in the absence of through-space and through-σ-bond interactions, polarization of the π system favors opposite spins on sites separated by an even number of centers (including adjacent centers) and parallel spin on sites separated by an odd number of centers, as are the 1,6- and 1,8-positions.[5] A framework larger than that offered by *m*-benzyne is required to observe this preference for the triplet since in that species (and 1,3-naphthalyne), even though the radical sites are separated by an odd number (1) of carbons, there is rear-lobe overlap between the two nonbonding σ orbitals.

Other aspects of the naphthalynes will be discussed elsewhere.[52] In concluding, however, we emphasize that the result of greatest *practical* importance here is that a very cheap calculation, namely, a density functional calculation with a polarized double-ζ basis set on a simple radical, has predictive utility in the estimation of singlet−triplet energy splittings through the proportionality of those splittings to isotropic hyperfine couplings. Moreover, if the experimental hyperfine couplings can be resolved, one has a relatively simple *laboratory* method for estimating S−T gaps in aryne systems. The computational method, in any case, should allow rapid evaluation of larger hydrocarbon systems where the size of the π space would otherwise be prohibitively large for multireference methodologies incorporating all π orbitals. Systems containing heteroatoms will also likely be amenable to this approach, although initial benchmarking against experiment and/or higher levels of theory is necessary. This should simplify the design of aryne systems having controlled reactivities as a function of their singlet−triplet state energy splittings.

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(42) Isotropic ^{1}H hyperfine coupling constants in the naphthyl radicals are calculated as $a_{\mathrm{H}} = (8\pi/3)gg_{\mathrm{H}}\beta\beta_{\mathrm{H}}\rho(\mathrm{H})$, where g is the electronic g factor, β is the Bohr magnetron, g_{H} and β_{H} are the corresponding values for ^{1}H, and ρ(H) is the Fermi contact integral that measures the unpaired spin density at the hydrogen nucleus. The Fermi contact integral is evaluated from $\rho(\mathrm{H}) = \sum_{\mu\nu} P^{\alpha-\beta}\phi_\mu(\mathbf{R}_{\mathrm{H}})\ \phi_\nu(\mathbf{R}_{\mathrm{H}})$, where $\mathbf{P}^{\alpha-\beta}$ is the BPW91/cc-pVDZ one-electron spin density matrix, the summation runs over basis functions ϕ, and evaluation of the overlap between basis functions ϕ_μ and ϕ_ν is only at the hydrogen nuclear position, $\mathbf{R}_{\mathrm{H}}$.

(43) The Hartree−Fock (HF) level might also be indicated for single-reference calculations; however, since it fails to account for electron correlation, this level rarely provides accurate hfs predictions (see ref 41). Moreover, HF wave functions for aryl radicals can suffer from high degrees of spin contamination, making them poor reference configurations for post-HF methods that *do* account for correlation. These considerations make DFT the preferred method for the systems considered here.

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