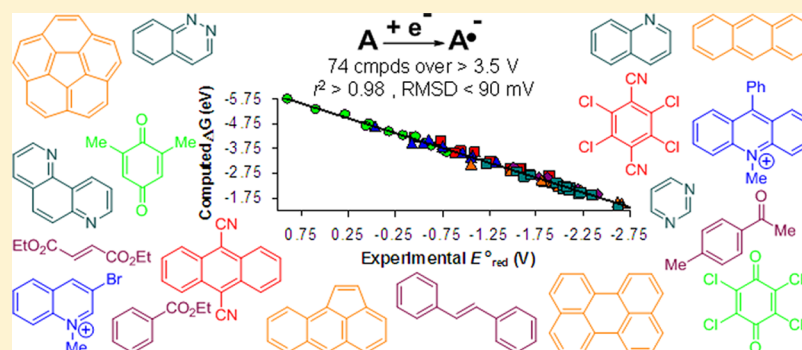


Expanding and Testing a Computational Method for Predicting the Ground State Reduction Potentials of Organic Molecules on the Basis of Empirical Correlation to Experiment

Eugene J. Lynch, Amy L. Speelman, Bryce A. Curry, Charles S. Murillo, and Jason G. Gillmore*

Department of Chemistry, Hope College, 35 E. 12th Street, Holland, Michigan 49423, United States

S Supporting Information

ABSTRACT: A method for predicting the ground state reduction potentials of organic molecules on the basis of the correlation of computed energy differences between the starting S_0 and one-electron-reduced D_0 species with experimental reduction potentials in acetonitrile has been expanded to cover 3.5 V of potential range and 74 compounds across 6 broad families of molecules. Utilizing the conductor-like polarizable continuum model of implicit solvent allows a global correlation that is computationally efficient and has improved accuracy, with $r^2 > 0.98$ in all cases and root mean square deviation errors of < 90 mV (mean absolute deviations < 70 mV) for either B3LYP/6-311+G(d,p) or B3LYP//6-31G(d) with an appropriate choice of radii (UAKS or UA0). The correlations are proven to be robust across a wide range of structures and potentials, including four larger (27–28 heavy atoms) and more conformationally flexible photochromic molecules not used in calibrating the correlation. The method is also proven to be robust to a number of minor student “mistakes” or methodological inconsistencies.

INTRODUCTION

The accurate and efficient calculation of oxidation and reduction potentials of molecules in solution, whether in a relative or an absolute sense, remains an area of active interest,^{1–10} due in part to the relevance of electron transfer reactions to solar energy conversion^{6,9} and other reactions of materials⁵ or biological⁷ relevance. While the calculation of absolute potentials through a thermodynamic cycle is tractable for smaller molecules,^{1–4} simpler calculations are preferable for the larger molecules often of interest to the aforementioned applications. Simpler comparisons of the energies of the molecule of interest and its corresponding one-electron-reduced state can be made. Within a closely related family of molecules over a limited range of potentials, this energy difference (strictly an electron affinity calculation in the gas phase) can directly correlate very well with the absolute reduction potential of the molecule in solution if a suitable implicit or explicit solvent model is used,⁸ though this must be corrected to a relative reduction potential of a reference electrode or secondary standard for direct comparison to experiment. We have previously reported an alternative correlational method for predicting reduction potentials that covers a much more diverse range of structures and reduction potentials, either in the gas phase or in solution (as modeled with dielectric continuum solvent models).⁵

Gas-phase correlations are, as we previously reported, only valid if one wishes to predict a compound within a well-defined and closely related family of structural analogues for which experimental data are available to calibrate the correlation. Generally this is not the case for our research group. Moreover, we have demonstrated that gas-phase correlations benefit more significantly from the diffuse functions of the 6-311+G(d,p) basis set than correlations with implicit solvent, where the 6-31G(d) basis set performs very well. The need to use the larger basis set more than offsets the time savings of neglecting the solvent. Thus, we have chosen to focus our efforts in using, testing, and improving our method of a global correlation using the conductor-like polarizable continuum model (CPCM) with acetonitrile (our electrochemical solvent of choice, and one in which a large body of literature experimental reduction potential data has been taken).

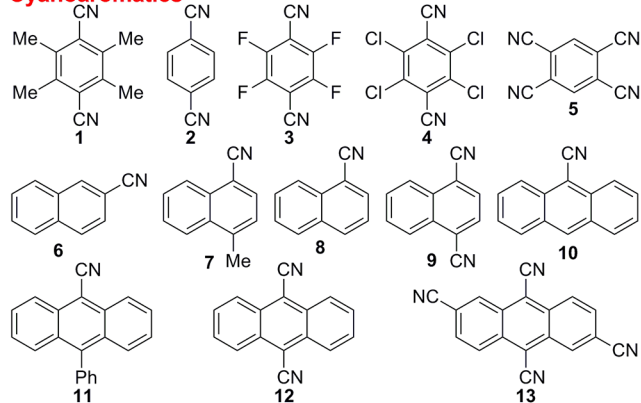
In the course of using our previously published method to predict reduction potentials for some photochromic molecules of interest to our experimental research program, we found that the energy calculations for a few structures, particularly those with

Received: April 27, 2012

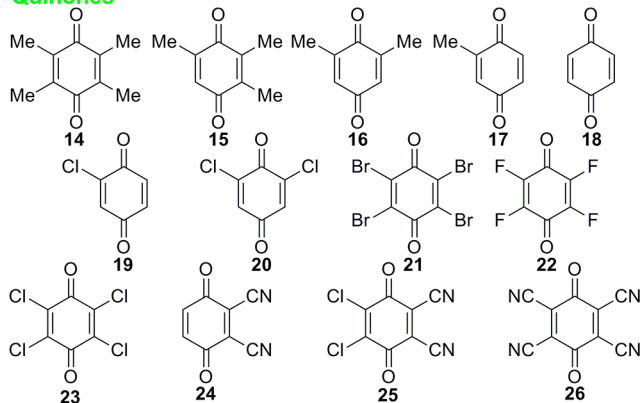
Published: June 23, 2012

the potential for intramolecular hydrogen bonding, failed to converge when the CPCM solvent model was applied with the default (UA0) radii. Calculations on these structures did converge when the alternative UAKS radii parameters were used. Thus we began a systematic investigation, repeating our previously published correlations varying both basis set and CPCM radii parameters for our initial calibrant set, molecules 1–35, spanning three families of conventional photooxidants.

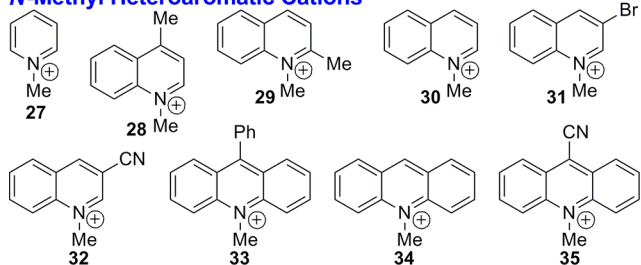
Cyanoaromatics



Quinones



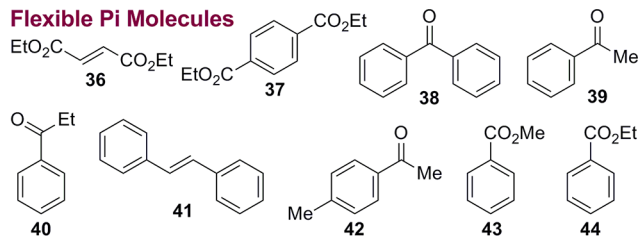
N-Methyl Heteroaromatic Cations



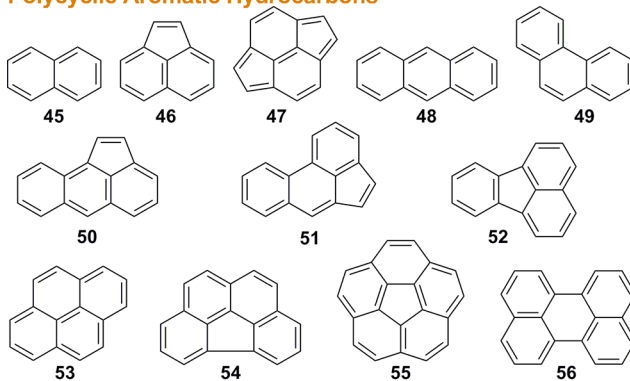
Simultaneously, we sought to test (and ultimately expand) our global correlation with a more diverse range of structures covering a wider range of reduction potentials than we had previously reported. Thus, we found experimental literature reduction potentials for 39 additional molecules (36–74) from three additional broad families, including molecules with more “flexible” π systems, polycyclic aromatic hydrocarbons (PAHs), and heterocyclic amines, and proceeded to compute the necessary geometries and energies for these molecules as well. Compounds 36–74 span a total of 1.6 V, including an additional 0.7 V beyond the 2.8 V window spanned by compounds 1–35 that we had previously reported.

Finally, in engaging novice high school and two-year community college students in this computational endeavor, it

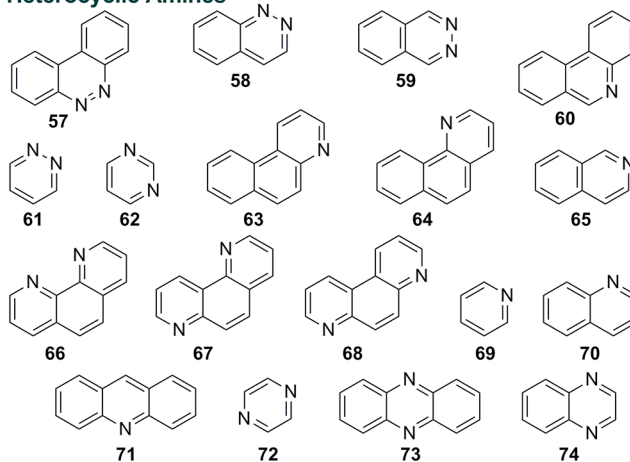
Flexible Pi Molecules



Polycyclic Aromatic Hydrocarbons



Heterocyclic Amines



became clear that occasional inconsistencies of method and parameters were occurring. While we faithfully repeated and corrected these anomalous calculations, we also seized these occurrences as opportunities to further test the robustness of our method, specifically developed for use by non-experts, to endure these minor variations.

COMPUTATIONAL DETAILS

The procedures we followed were analogous to those we previously reported.⁵ All calculations were carried out with the *Gaussian03* software package,¹¹ implemented through the *WebMO* graphical user interface.¹² Structures were drawn in the *WebMO* interface, and preliminary optimizations were performed using that program’s “comprehensive cleanup with mechanics” tool, prior to queuing gas-phase geometry optimizations on the cluster using density functional theory on *Gaussian03* with the B3LYP hybrid functional^{13–15} and either the MIDI!^{16,17} or 6-31G(d) basis set. The optimal geometry of the S_0 state was used as the starting point for the geometry optimization of the corresponding D_0 state. Solution-phase molecular energies of the S_0 and D_0 species were computed on *Gaussian03* with the B3LYP hybrid functional and either the 6-31G(d) or 6-311+G(d,p) basis sets. Implicit acetonitrile solvent ($\epsilon = 36.64$)¹¹ for these single-point energy calculations was implemented using the conductor-like polarizable continuum model (CPCM),^{18,19} with either the default (in *Gaussian03*) UA0 or alternative UAKS radii parameters.

Table 1. Correlations of Computed D_0-S_0 Energy Difference with Experimental Reduction Potential for Compounds 1–35 Varying Basis Set and CPCM Radii

correlation	B3LYP/	CPCM radii	slope m (eV/V)	y -intercept b (eV)	r^2	rmsd ^a residual (V)	MAD ^b residual (V)	x -intercept ^c (V)
1	6-31G(d)	UA0	-1.1220	-4.2335	0.9861	0.0835	0.0635	-3.7733
2	6-31G(d)	UAKS	-1.1513	-4.2606	0.9730	0.1170	0.1001	-3.7006
3	6-311+G(d,p)	UA0	-1.1214	-4.6193	0.9730	0.1171	0.0953	-4.1192
4	6-311+G(d,p)	UAKS	-1.1495	-4.6838	0.9846	0.0878	0.0705	-4.0746

^aRoot mean square deviation, taken from individual residuals for each compound as predicted by each trend line (as reported in the Supporting Information). ^bMean average deviation, taken from individual residuals for each compound as predicted by each trend line (as reported in the Supporting Information). ^cThe computed x -intercept ($=-b/m$) corresponds to the reference electrode potential correction (SCE = NHE + 0.24 V = -4.12 V)²⁰ and any systematic inaccuracies of the computational model employed.

While it is strictly necessary to set the criterion SCF=tight with the larger basis set with diffuse functions,¹ this criterion was inadvertently also used in all single-point energy calculations (except for the control experiment so noted). For consistency we also generally disabled symmetry in all calculations of both geometry and energy (as any time savings due to leaving symmetry enabled was minimal in our experience).

RESULTS AND DISCUSSION

We began this work by re-examining our previously reported correlations of the computed energy differences between the one-electron-reduced D_0 and initial S_0 of compounds 1–35 with their literature reduction potentials at two different basis sets and with two different CPCM radii. Though the calculations were repeated from the beginning, the results for the UA0 radii are essentially identical with those we have reported previously. The correlations, along with four different measures of goodness of fit, are reported in Table 1. In addition to r^2 and root mean square deviation (rmsd) residuals, which we have previously used to assess the goodness of our correlations, we now also include mean absolute deviation (MAD) residuals for comparison to other work⁸ in the field. Finally, in an ideal model, if the calculated D_0-S_0 energy difference, essentially an electron affinity calculated in a dielectric continuum solvent model rather than in the gas phase, truly was “equivalent to” a reduction potential, the x -intercept ($=-b/m$) should correspond to the reference potential of the reference electrode, and the slope should be unity. For the larger basis set, our method does come close on both these metrics. However, we find it both more useful and more precise to use the correlation rather than the calculated energy difference itself directly.

As we reported previously, the larger basis set with diffuse functions appears unnecessary to giving good predictive ability (indeed for the UA0 radii the errors are lower for 6-31G(d) than for 6-311+G(d,p)) from this method that includes implicit solvent. However it is clear that not including diffuse functions introduces a systemic error that is accounted for in the correlation but is manifested in the deviation of the x intercept away from the -4.12 V reference potential of the saturated calomel electrode (SCE) to which the experimental data are directly or indirectly referenced. This systemic deviation in intercept appears to be due to the overestimation of the energy of the anion when diffuse functions are not included (both S_0 and D_0 are more negative in 6-311+G(d,p) than in 6-31G(d), but the difference is larger for D_0 than S_0 and thus the difference between S_0 and D_0 increases with diffuse functions, shifting the intercept accordingly). Nevertheless, the method is equally predictive and more computationally efficient if the smaller basis set is used. Interestingly, it appears that the default UA0 radii for CPCM pair best with the smaller 6-31G(d) basis set, while the alternative UAKS radii for CPCM pair better with the larger 6-311+G(d,p)

basis set, allowing equally good predictive abilities if the “appropriate” radii are chosen for each basis set.

Next, to further test our method, we computed D_0-S_0 energy differences (Table 2) for 39 additional compounds (36–74) of known experimental reduction potential, falling largely outside the range of potentials spanned by compounds 1–35 used to create the four different correlations (Table 1), at the four different combinations of basis set and CPCM radii. Applying the appropriate correlation from Table 1, we were able to predict the reduction potentials of compounds 36–74 and compare them to the experimental data available in the literature. The results of these predictions (notably made on compounds not included in the correlation itself) are reported in Table 3. As expected, in all cases the r^2 value of the correlation of experimental reduction potential with the potential predicted from the computed D_0-S_0 energy difference on the basis of a correlation not including these molecules is less than the r^2 value for the correlation at that same level of theory reported in Table 1, though still reasonably good (0.94–0.96 vs 0.97–0.99). Likewise, the rmsd and MAD residuals are generally larger (except, oddly, in the case of 6-311+G(d,p) with the UA0 radii) but still respectable. Importantly, there does seem to be some evidence here that the larger basis set can perhaps achieve greater predictive results when the compound one is computing is not a member of the calibrant set (as is typically the case when actually applying our methodology to unknown molecules). Interestingly, the UA0 radii continue to pair well with 6-31G(d), but which radii are better for the larger 6-311+G(d,p) basis set is less clear in this test.

New correlations based only upon molecules 36–74 are possible and are reported in the Supporting Information. However, the most valuable way to utilize the new data regarding these three additional families of molecules is to incorporate them into a single larger correlation of all 74 compounds. These correlations (5–8) are reported in Table 4. Clearly the expansion of the correlations to all 74 compounds yields meaningful improvements in r^2 and rmsd and MAD residuals in three out of four cases (all but 6-31G(d) with UA0 radii), improving the predictive ability and giving increased confidence to predictions of reduction potentials outside our initial window of potentials of the first 35 calibrant molecules. However, it is also clear that the correlations do move slightly further from a slope of unity and an x -intercept equal to the -4.12 V reference potential of SCE. The model is thus accommodating other systemic errors of the method in the slope and intercept terms of the correlation. Far from being disheartening, we find this encouraging that while the computed “electron affinity” in a dielectric continuum implicit solvent model is not itself a perfect analogue for solution reduction potential, it correlates extremely well and has good predictive abilities over a wide range of potentials with systemic errors

Table 2. Experimental Reduction Potentials and Calculated D_0-S_0 Energy Differences for 36–74

compd	exptl		calcd D_0-S_0 energy diff (eV)			
	lit. E_{red}^0 (V) ^a	ref	6-31G(d)		6-311+G(d,p)	
			UA0	UAKS	UA0	UAKS
36	-1.5	21	-2.345	-2.230	-2.733	-2.648
37	-1.78	21	-2.491	-2.466	-2.909	-2.933
38	-1.86	21	-3.045	-3.043	-3.552	-3.608
39	-2.1	21	-3.302	-3.303	-3.430	-3.648
40	-2.15	21	-3.595	-3.700	-3.941	-4.093
41	-2.2	21	-1.920	-1.833	-2.352	-2.309
42	-2.2	21	-1.990	-1.881	-2.419	-2.353
43	-2.22	21	-2.040	-1.946	-2.480	-2.432
44	-2.4	21	-2.806	-2.777	-3.201	-3.218
45	-2.66	22	-2.538	-2.461	-2.934	-2.898
46	-1.8	22	-2.571	-2.476	-2.961	-2.909
47	-1.06	22	-3.179	-3.147	-3.552	-3.562
48	-2.1	22	-3.745	-3.832	-4.076	-4.206
49	-2.62	22	-3.282	-3.121	-3.739	-3.595
50	-1.47	22	-3.387	-3.232	-3.867	-3.733
51	-1.81	22	-3.478	-3.330	-3.981	-3.861
52	-1.92	22	-3.570	-3.436	-4.090	-3.991
53	-2.22	22	-3.764	-3.656	-4.320	-4.254
54	-1.84	22	-3.893	-3.770	-4.368	-4.289
55	-1.99	22	-4.108	-3.993	-4.526	-4.456
56	-1.81	22	-4.329	-4.214	-4.691	-4.629
57	-1.554	23	-4.153	-4.069	-4.774	-4.742
58	-1.686	23	-4.367	-4.263	-4.706	-4.644
59	-1.976	23	-4.650	-4.662	-5.074	-5.125
60	-2.118	23	-4.927	-4.947	-5.278	-5.337
61	-2.12	23	-5.173	-5.301	-5.562	-5.729
62	-2.34	23	-2.659	-2.894	-3.002	-3.239
63	-2.14	23	-3.013	-3.170	-3.313	-3.478
64	-2.208	23	-2.971	-3.125	-3.252	-3.412
65	-2.22	23	-3.098	-3.301	-3.405	-3.615
66	-2.042	23 ^b	-3.361	-3.557	-3.647	-3.859
67	-2.092	23	-3.545	-3.810	-3.831	-4.112
68	-2.044	23	-3.527	-3.673	-3.814	-3.974
69	-2.636	23 ^b	-3.481	-3.662	-3.769	-3.961
70	-2.105	23	-4.184	-4.382	-4.458	-4.672
71	-1.62	23	-2.628	-2.486	-3.125	-3.013
72	-2.08	23	-2.279	-2.133	-2.736	-2.623
73	-1.227	23	-2.100	-2.068	-2.596	-2.615
74	-1.702	23	-1.804	-1.612	-2.387	-2.232

^aVs SCE in CH_3CN (or corrected to vs SCE according to refs 20 and 24 for those not reported vs SCE in the primary reference).

^bReconfirmed experimentally in our laboratory.

largely accounted for in the fitting parameters of slope and intercept.

Figure 1 contains the plots from which correlations 1–8 in Tables 1 and 4 were constructed. Graphically it is easy to see the greater divergence that occurs for calibrations based on UAKS radii than those based on UA0 radii when the correlation is expanded from calibrants 1–35 to include all molecules 1–74 and the greater range of potentials these molecules span.

We have applied our method to the prediction of the reduction potentials of several larger and more complicated photochromic molecules of interest to our research group, perimidinespirohexadienones (PSHDs, 75 and 76)^{25,26} being prototypical among them. The data in Table 5 indicate that all eight correlations do a fairly good job predicting the reduction potentials of these

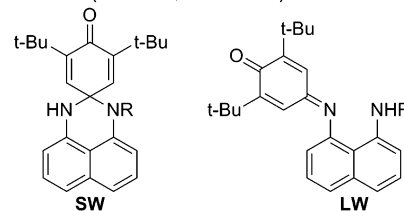
Table 3. Using Correlations 1–4 from Table 1 (Based on Compounds 1–35) To Predict the Reduction Potentials of Compounds 36–74

B3LYP/	CPCM radii	r^2	rmsd ^a residual (V)	MAD ^b residual (V)
6-31G(d)	UA0	0.9402	0.1324	0.1032
6-31G(d)	UAKS	0.9514	0.1918	0.1769
6-311+G(d,p)	UA0	0.9423	0.0842	0.0633
6-311+G(d,p)	UAKS	0.9570	0.1154	0.0987

^aRoot mean square deviation, taken from individual residuals for each compound as predicted by each trend line (as reported in the Supporting Information). ^bMean average deviation, taken from individual residuals for each compound as predicted by each trend line (as reported in the Supporting Information).

4 photochrome structures, with rmsd errors on these compounds less than the rmsd errors of the original correlations. In some cases the predicted errors are smaller than the errors in the experimental data. In this small sample set the correlations (1–4) based on the initial 35 calibrants outperform those based on all 74 calibrant molecules (correlations 5–8), but this trend does not hold when we examine additional photochromes, which we will report in the future.²⁷ These first four photochromes provide proof of principle that these calculations can be useful in guiding us to more reducible analogues of the PSHDs as synthetic targets; we have also found them vital to understanding the more complicated systems we are now investigating.

PSHDs (75 R=H; 76 R=Me)



As these photochromes are the largest molecules we have examined with this computational methodology, they provide the best test for the computational efficiency of our method. Gas-phase geometries of S_0 or D_0 calculated at B3LYP/6-31G(d) on a single 2.60 GHz AMD Opteron-252 processor (with 8 GB RAM and 250 GB HD) took 12–32 h, while MIDI! geometries were typically slightly faster (8–30 h). CPCM single-point energies took 7–22 h at 6-311+G(d,p) and only about 1 h (40–100 min) at 6-31G(d), for either UA0 or UAKS radii. UAKS generally took about 10% longer. At 6-311+G(d,p), D_0 states generally took about 2 times longer (ca. 20 h) than the corresponding S_0 state of the same molecule (ca. 10 h); the difference was slightly less pronounced at 6-31G(d). All calculations on calibrants 1–74 were considerably faster due to their smaller size, generally similar to the times reported in our previous work.⁵

The LW isomers of 75 and 76 and related photochromes also have a readily accessible second reduction potential, which we have also determined experimentally. Attempts to use the computed energy difference between the doubly reduced dianion (S_0 or T_0) and the singly reduced D_0 anion radical with any of the eight correlations we developed and calibrated for predicting first reduction potentials (from D_0 anion radical and S_0 neutral computed energy differences) unfortunately but unsurprisingly fail to yield an accurate prediction of these second reduction potentials. Presumably, a new correlation of second reduction

Table 4. Correlations of Computed D_0-S_0 Energy Difference with Experimental Reduction Potential for Compounds 1–74 Varying Basis Set and CPCM Radii

correlation	B3LYP/	CPCM radii	slope m (eV/V)	y -intercept b (eV)	r^2	rmsd ^a residual (V)	MAD ^b residual (V)	x -intercept ^c (V)
5	6-31G(d)	UA0	-1.1751	-4.2519	0.9887	0.0880	0.0662	-3.6184
6	6-31G(d)	UAKS	-1.2461	-4.2887	0.9840	0.1050	0.0825	-3.4416
7	6-311+G(d,p)	UA0	-1.1242	-4.6167	0.9852	0.1007	0.0796	-4.1068
8	6-311+G(d,p)	UAKS	-1.1930	-4.6903	0.9889	0.0829	0.0629	-3.9314

^aRoot mean square deviation, taken from individual residuals for each compound as predicted by each trend line (as reported in the Supporting Information). ^bMean average deviation, taken from individual residuals for each compound as predicted by each trend line (as reported in the Supporting Information). ^cComputed x -intercept ($= -b/m$) corresponds to the reference electrode potential correction (SCE = NHE + 0.24 V = -4.12 V),²⁰ and any systematic inaccuracies of the computational model employed.

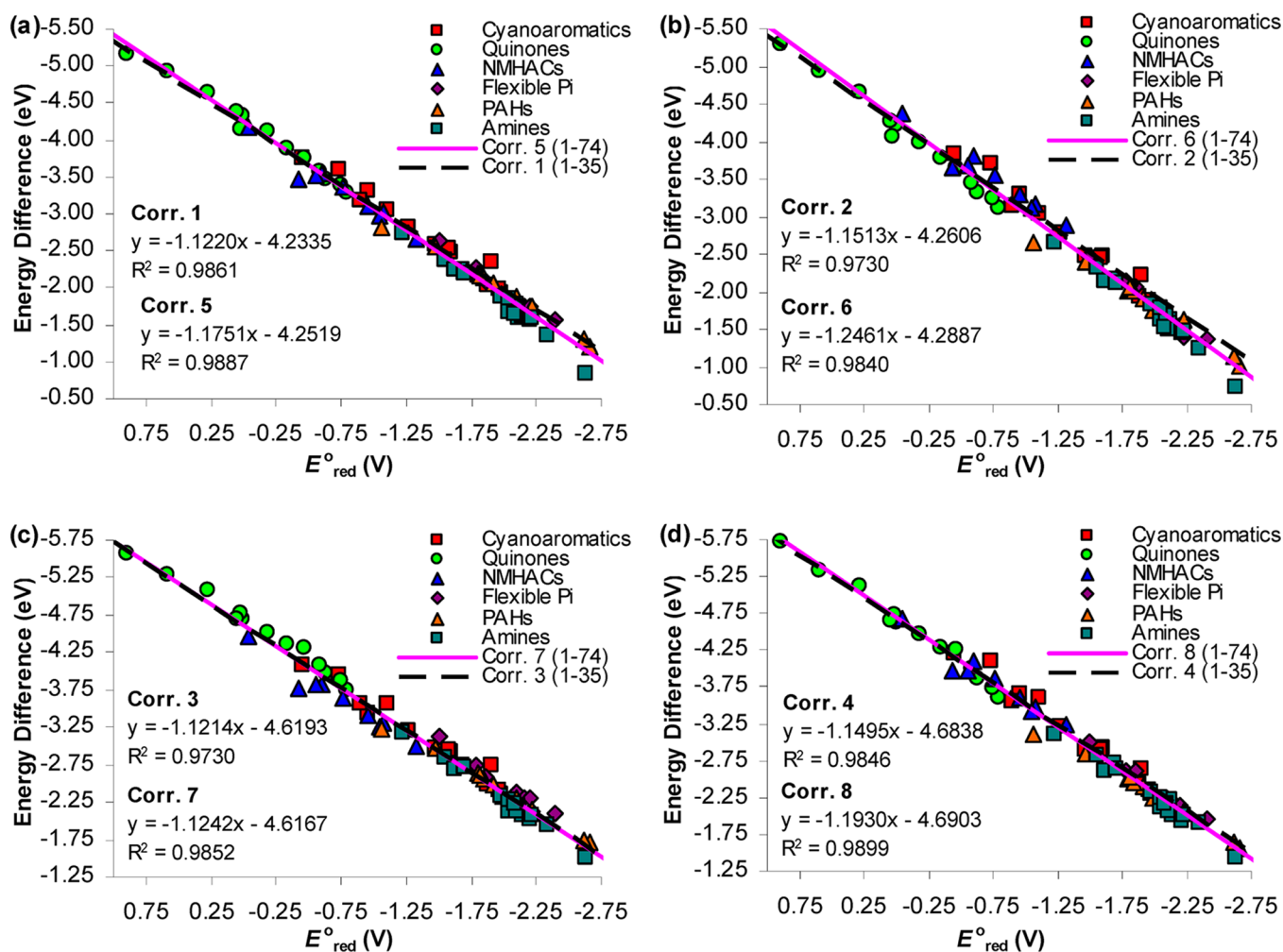


Figure 1. Plots of computed D_0-S_0 energy differences vs experimental reduction potential, varying basis set and CPCM radii: (a) 6-31G(d)/UA0; (b) 6-31G(d)/UAKS; (c) 6-311+G(d,p)/UA0; (d) 6-311+G(d,p)/UAKS. Dashed black lines represent correlations based on the initial calibrant set 1–35; solid pink lines represent correlations based on all molecules 1–74. Correlation numbers match those used in the text and Tables 1 and 3.

potentials could be developed if a sufficient range of second reduction potentials could be obtained experimentally to calibrate a correlation, though we have no immediate plans to pursue this further.

Finally, we have made several different attempts to test and demonstrate the robustness of our model to the minor variations in exact methodology that can easily creep into computational protocols over time, particularly when training novice undergraduate, community college, and high school students in their execution. One such opportunity was found when we inadvertently used the *Gaussian* convergence keyword SCF=tight for all our single-point energies regardless of basis set throughout

this study, when this is only necessary for the 6-311+G(d,p) basis set with diffuse functions. We went back and repeated one entire correlation (see Supporting Information) of molecules 1–35 without this keyword for the 6-31G(d)/CPCM(UA0) correlation. The slopes, x - and y -intercepts, and r^2 values for this correlation all changed by less than 0.1%, while rmsd and MAD increased by less than 1%. The maximum change in any given prediction was 4.1 mV, and the average change was 1.0 mV. Moreover, if the SCF=tight energy differences were used to predict reduction potentials in the correlation created without this criterion, the rmsd and MAD errors both remained unchanged to the fourth decimal place (at 0.0835 and 0.0635 V, respectively). Likewise,

Table 5. Comparison of Experimental Reduction Potentials of PSHD Photochromes to Those Predicted Using Correlations 1–8

cmpd	exptl E_{red}° (V vs SCE) ^a	predicted E_{red}° (V vs SCE), based on correlation ^b							
		corr 1 (±0.084)	corr 2 (±0.117)	corr 3 (±0.117)	corr 4 (±0.088)	corr 5 (±0.088)	corr 6 (±0.105)	corr 7 (±0.101)	corr 8 (±0.083)
75 SW	-1.744 (±0.020)	-1.836	-1.813	-1.835	-1.846	-1.759	-1.698	-1.830	-1.784
75 LW	-0.939 (±0.028)	-0.947	-0.946	-0.980	-1.012	-0.877	-0.897	-0.950	-0.980
76 SW	-1.689 (±0.013)	-1.683	-1.664	-1.706	-1.720	-1.607	-1.560	-1.695	-1.663
76 LW	-0.919 (±0.028)	-0.935	-0.935	-0.972	-1.004	-0.856	-0.886	-0.931	-0.973
rmsd ^c	0.023	0.047	0.015	0.035	0.024	0.123	0.043	0.101	0.038

^aReversible ground state reduction potential E_{red}° for LW isomers and half-peak potential $E_{\text{red}}^{1/2}$ for irreversible reduction of SW isomers, in dry acetonitrile containing 0.1 M tetrabutylammonium hexafluorophosphate electrolyte, normalized to ferrocene/ferrocenium, and corrected to vs SCE.^{20,24} ^b± root mean square deviation error of the correlation (from Tables 1 and 2) indicated in parentheses with each correlation number. ^cRoot mean square deviation of the experimental (from error bars) or predicted (relative to experimental) reduction potentials for these four photochromic structures.

if the energy differences found without SCF=tight were used in the correlation created with the SCF=tight criterion (corr 1), the rmsd and MAD errors again remained unchanged at the fourth decimal place (at 0.0840 and 0.0640 V, respectively). The maximum changes in any given predicted reduction potential in either of these uses of data across correlations was 1.5 mV, and the average change was only 0.5 mV. Clearly the method is robust with respect to this casual mistake in convergence criteria in *Gaussian*.

Next, we found that at times we had been inconsistent in our application of symmetry (it was our default to disable symmetry) in our geometry optimizations and single-point energies. We therefore reexamined several molecules of a range of sizes and symmetries with and without disabling symmetry for gas-phase geometry optimizations. Then we computed the single-point energies (with CPCM solvent using both UA0 or UAKS radii with both basis sets of interest) on all these geometries, again both with and without disabling symmetry. We then determined the maximum impact any of the resulting differences made by symmetry could have on a predicted reduction potential. The molecules we studied most exhaustively were dicyanobenzene **2**, acanthrylene **50**, and a new photochrome we will report in the future. For highly symmetric **2**, the largest computed energy difference in this experiment was 28 neV, corresponding to a difference in predicted reduction potential of less than 44 nV. For the less symmetric **50**, the largest computed energy difference was 3.5 μeV for a difference in predicted reduction potential of less than 3.0 μV . Finally for a highly unsymmetric photochromic LW, the largest computed energy difference was 4.9 meV for a difference in predicted reduction potential of less than 3.0 mV. It is not clear that disabled symmetry is even responsible for these differences, as it is possible that slightly different minima were found for each geometry. Rather, these results set an upper bound on the error introduced by the application of symmetry. These errors are at least 1 order and potentially several orders of magnitude less than the error of our method and therefore are of no practical consequence.

Other variables that occurred in our calculations were the application of different basis sets to the geometry optimizations. Our group has at times used MIDI! and 6-31G(d) interchangeably for gas-phase geometry optimizations. A similar analysis of the few molecules for which we had CPCM single-point energies computed at the same level of theory for both MIDI! and 6-31G(d) geometries showed a maximum computed energy difference of 7 meV and a maximum difference in predicted reduction potential of 2 mV, more than a factor of 40 less than our current error bars. Thus, we believe it is safe to use our

correlations and our methods on any set of good reasonable gas-phase geometries regardless of specific basis set used. Similarly small differences were found regardless of whether *Gaussian03* or *QChem 3.0*²⁸ was used for the gas-phase geometry optimizations.

During the course of our work, all of which was conducted using *Gaussian03*,¹¹ we did work briefly on another cluster running a different revision (B.05 vs D.01) of the software. We found that the difference in any given energy was often nil but occasionally as high as 1.5 meV. The maximum difference in predicted reduction potential was only 0.2 mV. We wanted to confirm that it was acceptable to move this project to *Gaussian09* in the future. Thus, we also compared *Gaussian03* (revision D.01) to *Gaussian09* (revision A.02)²⁹ and found even smaller energy differences of at most 1.1 meV, though in this case the largest difference in predicted reduction potential was 0.3 mV. We find it curious that different revisions or editions most often gave absolutely no difference in energy all the way to the final decimal place (nHartree = 27 neV), as should be expected, but sometimes varied by up to a millielectronVolt even for identical input files, with no obvious pattern, presumably due to finite convergence criteria. Nevertheless, this level of consistency is within our error bars by well more than 1 order of magnitude, and thus our method and correlation should be robust to version and revision of *Gaussian* used, at least with respect to those specifically tested.

Finally, the failure of some of our photochromes (analogues of **75** and **76** with an OH group capable of intramolecular hydrogen bonding to an imine N) to converge when performing CPCM calculations with the default UA0 radii was a motivating factor in establishing the UAKS correlations (which despite also being a united atom topological model like UA0, without explicit spheres for hydrogen,^{11,29} fortuitously converged our photochromes). Now that we have those data, we can compare the errors that arise when the UA0 correlation is applied to a UAKS energy difference and vice versa. When the UA0 radii correlation is applied to the energy differences computed for compounds **1**–**74** using UAKS radii, the rmsd error increases from 0.0880 to 0.1333 V (a 51% increase) for 6-31G(d) and from 0.1007 to 0.1035 V (a 3% increase) for 6-311+G(d,p). Similarly, when our new UAKS correlation is applied to predict reduction potentials from the energy differences computed for **1**–**74** using UA0 radii, the rmsd error increases from 0.1050 to 0.1080 V (a 3% increase) for 6-31G(d) and from 0.0829 to 0.1079 V for 6-311+G(d,p) (a 30% increase). While the MAD errors are (by definition) lower than the rmsd errors, the relative increases in MAD are greater than in rmsd in all cases. In all these

misapplications of correlation based on CPCM radii the largest individual change in predicted reduction potential is 142 mV, while the average change is 54 mV. These are smaller than the corresponding largest residual and mean average deviation, respectively, for most of our methods. Thus, while certainly not optimal, if radii parameters need to be adjusted to allow a calculation to converge for a given molecule of interest, it is likely still possible to apply our correlations without establishing a full new correlation for the new radii parameters.

CONCLUSIONS

We have tested and improved our previous correlation⁵ and demonstrated its robustness and utility for computationally predicting the first ground-state reduction potentials of a wide range of organic molecules spanning over 3.5 V of the potential window across several families of conjugated organic molecules with a variety of functional groups, including larger, more complicated, and more flexible molecules than were used to form the calibration. Furthermore, the method is robust and tolerant to a range of modest “mistakes” and variations in computational methodology and is thus suitable for non-expert users. Good global correlations over a wide potential window are now available for CPCM implemented with either the default UA0 or alternative UAKS radii parameters, with the B3LYP functional using either the 6-31G(d) or 6-311+G(d,p) basis set.

We have demonstrated that either of these radii models for CPCM work well in our application, and to date we have been able to get all molecules of interest to our research group (included herein or not) to converge and give good results with at least one of these two radii models. UA0 uses the united atom topological model applied on atomic radii of the UFF force field for heavy atoms, while hydrogens are enclosed in the sphere of the heavy atom to which they are bonded.^{11,29} UAKS meanwhile uses the same united atom topological model applied on atomic radii optimized for the PBE0 hybrid functional³⁰ (PBE1PBE in *Gaussian09*) and the 6-31G(d) basis set.^{11,29} In neither case are explicit spheres for hydrogen atoms specified, nor have we done so on an individual basis. The convergence of some of our intramolecularly hydrogen bonded photochrome species with UAKS radii that failed to converge with UA0 is likely fortuitous—others may find one or the other radii better suited to their needs. However, explicit spheres for all or individual hydrogens are an option and may be particularly worthwhile in molecules where a hydrogen may be too far from any heavy atom or too close to more than one. As we move to *Gaussian09*²⁹ in the future, we will likely explore using the UFF radii, which is now the default for CPCM and which does include explicit hydrogens. A useful discussion of radii in CPCM calculations was recently published,³¹ after this currently reported work was completed. This may prove helpful to us or others using a similar methodology in the future.

Finally, we maintain that correlational or “relative” methods such as ours, while perhaps less elegant, maintain an advantage over “absolute” methods in that systematic deviations in the computational approach can be accounted for in slope and intercept terms. Nor is correction of experimental data (obtained relative to an electrode) to an absolute scale required. Thus, we feel our methods are complementary to others in the literature and provide a useful alternative to both novice and experienced users of computation alike.

EXPERIMENTAL SECTION

Compounds **75** and **76** (in their SW form) were prepared as previously reported.^{25,26} Reduction potentials of the SW and LW isomers of each were determined in at least triplicate by cyclic voltammetry with a glassy-carbon working electrode, platinum-wire counter electrode, and a non-aqueous Ag/AgNO₃ reference electrode, in argon-purged solutions of dry HPLC grade acetonitrile containing 0.1 M tetrabutylammonium hexafluorophosphate electrolyte and 1–3 mM analyte. Results were normalized to ferrocene/ferrocenium by back-to-back experiments and then corrected to vs SCE.^{20,24} LW isomers could be obtained by photolyzing the SW solution under argon with the 405 nm line of a 350 W mercury arc lamp or electrogenerated by repeated CV scans of the SW solution.²⁵ The reported potentials are the reversible ground state reduction potentials (E_{red}°) for LW isomers and the half-peak potentials ($E_{\text{red}}^{1/2}$) for irreversible reduction of SW isomers.

ASSOCIATED CONTENT

Supporting Information

Three Excel workbooks (the first for correlations based on **1–35** alone, the second for correlations based on **36–74** alone, and the third for correlations based on all calibrant molecules **1–74**), each with separate tabbed worksheets for each basis set and radii combination, providing additional graphs and correlations by family of molecules as well as all correlations reported herein including misapplication of data to the “wrong” correlation, and including complete data of the individual computed S_0 and D_0 energies for each molecule at each level of theory, along with the resulting energy differences and the literature reduction potentials to which they were correlated. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

*E-mail: gillmore@hope.edu.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was funded by an NSF CAREER award (CHE-0952768) and a Camille & Henry Dreyfus Foundation Start-up Award (SU-04-040). E.J.L. (home institution College of the Canyons, Santa Clarita, CA) was supported by an NSF REU SITE award (CHE-0851194) to Hope College. High school students B.A.C. and C.S.M. (Holland High School, Holland, MI) were supported by the Research Experiences Across Cultures at Hope (REACH) program funded by a Howard Hughes Medical Institute grant to Hope College. Computations were conducted on the Midwest Undergraduate Computational Chemistry Consortium (MU3C) cluster, supported by NSF MRI grants CHE-0520704 and CHE-1039925, housed in the Hope College Computational Science & Modeling Laboratory. Support from CSM Laboratory director Prof. Brent P. Krueger and staff Mr. Paul Van Allsburg is also gratefully acknowledged. Several helpful reviewer comments are also gratefully acknowledged.

REFERENCES

- (1) Cramer, C. J. *Essentials of Computational Chemistry: Theories and Models*, 2nd ed.; Wiley: Chichester, West Sussex, England, 2004.
- (2) Winget, P.; Weber, E. J.; Cramer, C. J.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2000**, *2*, 1231.
- (3) Baik, M.-H.; Friesner, R. A. *J. Phys. Chem. A* **2002**, *106*, 7407.
- (4) Schmidt am Busch, M.; Knapp, E.-W. *J. Am. Chem. Soc.* **2005**, *127*, 15730.
- (5) Speelman, A. L.; Gillmore, J. G. *J. Phys. Chem. A* **2008**, *112*, 5684.

- (6) Paoprasert, P.; Laaser, J. E.; Xiong, W.; Franking, R. A.; Hamers, R. J.; Zanni, M. T.; Schmidt, J. R.; Gopalan, P. *J. Phys. Chem. C* **2010**, *114*, 9898.
- (7) Tugsuz, T. *J. Phys. Chem. B* **2010**, *114*, 17092.
- (8) Davis, A. P.; Fry, A. J. *J. Phys. Chem. A* **2010**, *114*, 12299.
- (9) Häussler, M.; King, S. P.; Eng, M. P.; Haque, S. A.; Bilic, A.; Watkins, S. E.; Wilson, G. J.; Chen, M.; Scully, A. D. *J. Photochem. Photobiol. A* **2011**, *220*, 102.
- (10) Wang, L.-P.; Van Voorhis, T. *J. Chem. Theory Comput.* **2012**, *8*, 610.
- (11) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision D.01*, Gaussian, Inc., Wallingford, CT, 2004.
- (12) Schmidt, J. R.; Polik, W. F. *WebMO Pro, v. 9.1*, and *WebMO Enterprise, v. 10.1*; WebMO LLC, Holland, MI, 2009 and 2010; available from <http://www.webmo.net> (last accessed April 2012).
- (13) Becke, A. D. *J. Chem. Phys.* **1996**, *104*, 1040.
- (14) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.
- (15) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
- (16) Easton, R. E.; Giesen, D. J.; Welch, A.; Cramer, C. J.; Truhlar, D. G. *Theor. Chim. Acta* **1996**, *93*, 281.
- (17) Li, J.; Cramer, C. J.; Truhlar, D. G. *Theor. Chem. Acc.* **1998**, *99*, 192.
- (18) Barone, V.; Cossi, M. *J. Phys. Chem. A* **1998**, *102*, 1995.
- (19) Cossi, M.; Rega, N.; Scalmani, G.; Barone, V. *J. Comput. Chem.* **2003**, *24*, 669.
- (20) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications*, 2nd ed.; Wiley: New York, 2000.
- (21) Fukuzumi, S.; Koumitsu, S.; Hironaka, K.; Tanaka, T. *J. Am. Chem. Soc.* **1987**, *109*, 305.
- (22) Koper, C.; Sarobe, M.; Jenneskens, L. W. *Phys. Chem. Chem. Phys.* **2004**, *6*, 319.
- (23) Millefiori, S. *J. Heterocycl. Chem.* **1970**, *7*, 145.
- (24) Pavlishchuk, V. V.; Addison, A. W. *Inorg. Chim. Acta* **2000**, *298*, 97.
- (25) Minkin, V. I.; Komissarov, V. N.; Kharlanov, V. A. Perimidinespirocyclohexadienones. In *Organic Photochromic and Thermochemical Compounds*; Crano, J. C., Guglielmetti, R. J., Eds.; Plenum Press: New York, 1999, Vol. 1, pp 315–340.
- (26) Moerdyk, J. P.; Speelman, A. L.; Kuper, K. E.; Heiberger, B. R.; TerLouw, R. P.; Zeller, D. J.; Radler, A. J.; Gillmore, J. G. *J. Photochem. Photobiol. A* **2009**, *205*, 84.
- (27) Sluiter, K. B.; Moerdyk, J. P.; Speelman, A. L.; Lynch, E. J.; Gillmore, J. G. Manuscript in preparation.
- (28) Shao, Y.; Fusti-Molnar, L.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; Levchenko, S. V.; O'Neill, D. P.; Distasio, R. A., Jr.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Van Voorhis, T.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Dachsel, H.; Doerksen, R. J.; Dreuw, A.; Dunietz, B. D.; Dutoi, A. D.; Furlani, T. R.; Gwaltney, S. R.; Heyden, A.; Hirata, S.; Hsu, C.-P.; Kedziora, G.; Khalliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W.; Lotan, I.; Nair, N.; Peters, B.; Proynov, E. I.; Pieniazek, P. A.; Rhee, Y. M.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; Woodcock, H. L., III; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; Schaefer, H. F., III; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3172.
- (29) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09, Revision A.02*; Gaussian, Inc., Wallingford, CT, 2009.
- (30) Adamo, C.; Barone, V. *J. Chem. Phys.* **1999**, *110*, 6158.
- (31) Tao, J.-Y.; Mu, W.-H.; Chass, G. A.; Tang, T.-H.; Fang, D.-C. *Int. J. Quantum Chem.* **2012**, DOI: 10.1002/qua.24065.