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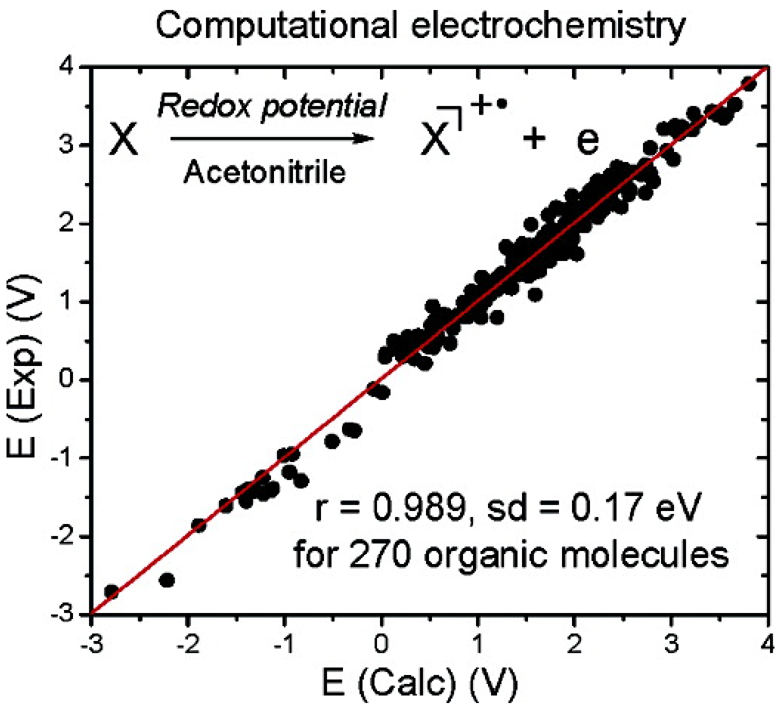

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Quantum-Chemical Predictions of Absolute Standard Redox Potentials of Diverse Organic Molecules and Free Radicals in Acetonitrile

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Abstract: A calibrated B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method was found to be able to predict the gas-phase adiabatic ionization potentials of 160 structurally unrelated organic molecules with a precision of 0.14 eV. A PCM solvation model was benchmarked that could predict the pK_a's of 15 organic acids in acetonitrile with a precision of 1.0 pK_a unit. Combining the above two methods, we developed a generally applicable protocol that could successfully predict the standard redox potentials of 270 structurally unrelated organic molecules in acetonitrile. The standard deviation of the predictions was 0.17 V. The study demonstrated that computational electrochemistry could become a powerful tool for the organic chemical community. It also confirmed that the continuum solvation theory could correctly predict the solvation energies of organic radicals. Finally, with the help of the newly developed protocol we were able to establish a scale of standard redox potentials for diverse types of organic free radicals for the first time. Knowledge about these redox potentials should be of great value for understanding the numerous electron-transfer reactions in organic and bioorganic chemistry.

1. Introduction

The propensity of an organic molecule to donate or accept an electron in solution is measured by its (one-electron) standard redox potential (E°).[1] A sound knowledge about standard redox potentials is fundamental to understanding the innumerable chemical and biological electron-transfer reactions. Thus chemists have developed, and are still developing, a variety of experimental methods to obtain the E° data. At present, the most popular experimental method for measuring E° is cyclic voltammetry.[2] The error of this method is usually as low as 0.01−0.02 V when the redox process is reversible. However, for nonreversible redox reactions the experimental situation is complicated, and accurate E° values are available only via some sophisticated techniques such as pulse radiolysis.[2] Therefore, it is not always easy to obtain reliable experimental E° data. Furthermore, for the species that are highly unstable (e.g., organic radicals), it can be very difficult to measure their standard redox potentials experimentally.

Recognizing the limitations of the experimental methods, some research groups recently tried to develop theoretical approaches to predict the standard redox potentials in solution. A general idea in these studies is to employ a certain theoretical method (i.e., AM1,[3] PM3,[4] DFT[5−9]) to compute the gas-phase ionization energies and then add the solvation energy terms calculated using either an explicit[6] or implicit[3−9] solvation model. The results from these pioneering studies are usually in reasonable agreement with the experiments. However, each of the above studies only considered the redox potentials of a fairly small group of closely related compounds. In some occasions, only the relative E° values between a few structurally related compounds were obtained instead of the absolute values.[8] Thus, it still remains unclear whether one could develop a generally applicable protocol to accurately predict the absolute E° values for a large number of structurally unrelated molecules.

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(1) The standard redox potential refers to standard conditions (i.e., all reactants are 1.0 M or 1 atm pressure, 298 K). Also, in the present study we only considered the single-electron transfer redox potentials. Furthermore, people have defined both the oxidation potentials and reduction potentials by using different orders of half reactions. In the present study, we only considered the redox potential that corresponded to the oxidation of a species. For the reduction of a species, one just needs to consider the oxidation of the corresponding reduced form.

(2) (a) Bard, A. J.; Faulkner, L. R. *Electrochemical Methods: Fundamentals and Applications*; Wiley: New York, 2001. (b) Hamann, C. H.; Hamnett, A.; Vielstich, W. *Electrochemistry*; Wiley-VCH; New York, 1998. (c) *Photochemistry and Radiation Chemistry: Complementary Methods for the Study of Electron Transfer*; Wishart, J. F., Nocera, D. G., Eds.; Advances in Chemistry Series 254; American Chemical Society: Washington, DC, 1998.

(3) Rychnovsky, S. D.; Vaidyanathan, R.; Beauchamp, T.; Lin, R.; Farmer, P. J. *J. Org. Chem.* **1999**, *64*, 6745.

(4) Charles-Nicolas, O.; Lacroix, J. C.; Lacaze, P. C. *J. Chim. Phys.* **1998**, *95*, 1457.

(5) Raymond, K. S.; Grafton, A. K.; Wheeler, R. A. *J. Phys. Chem. B* **1997**, *101*, 623.

(6) (a) Baik, M.-H.; Silverman, J. S.; Yang, I. V.; Ropp, P. A.; Szalai, V. A.; Yang, W. T.; Thorp, H. H. *J. Phys. Chem. B* **2001**, *105*, 6437. (b) Baik, M.-H.; Friesner, R. A. *J. Phys. Chem. A* **2002**, *106*, 7407.

(7) Uudsemaa, M.; Tamm, T. *J. Phys. Chem. A* **2003**, *107*, 9997.

(8) (a) Namazian, M.; Norouzi, P.; Ranjbar, R. *J. Mol. Struct. (THEOCHEM)* **2003**, *625*, 235. (b) Namazian, M. *J. Mol. Struct. (THEOCHEM)* **2003**, *664−665*, 273.

(9) (a) Winget, P.; Weber, E. J.; Cramer, C. J.; Truhlar, D. G. *Phys. Chem. Chem. Phys.* **2000**, *2*, 1231. (b) Patterson, E. V.; Cramer, C. J.; Truhlar, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 2025. (c) Arnold, W. A.; Winget, P.; Cramer, C. J. *Environ. Sci. Technol.* **2002**, *36*, 3536.

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We recently launched a program to systematically investigate how to utilize the modern quantum-chemical methods to gain useful, quantitative data for realistic, solution-phase organic chemistry. In the first step, we benchmarked a generally applicable protocol to calculate the pK_a values of diverse organic acids in dimethyl sulfoxide with a precision of 1.7−1.8 pK_a units.[10] Herein we wished to develop a first-principle protocol that could be used to predict the absolute standard redox potentials of diverse types of organic molecules. The significance of the study is twofold: (1) to benchmark a generally applicable theoretical tool that could predict the standard redox potentials with reasonable accuracy and (2) to comprehensively test the efficacy of quantum-chemical methods for electrochemistry, which represents one of the few remaining areas of chemistry that has not been successfully modeled by modern ab initio computations.

The focus of the present study was to establish a coherent, simple, and well-defined method to predict the standard redox potentials of diverse organic molecules of substantial size in organic solution. To accomplish this goal, we carefully calibrated the theoretical method for the gas-phase calculations and parametrized the solvation model for the solution-phase calculations. As to the solvent we chose acetonitrile, because acetonitrile is one of the most popular organic solvents for the measurement of redox potentials. To demonstrate that our protocol can be used for diverse types of organic molecules, we extensively searched the literature and compiled more than 270 experimental standard redox potentials.[11] By comparing the theoretical results with the experimental data, we would be able to confidently assess the performance of the theoretical protocol for the redox potential predictions.

Armed with the carefully benchmarked theoretical method, we next tried to establish a scale of standard redox potentials for various organic free radicals. Such a scale of data has been highly desirable for many years in organic and bioorganic chemistry,[12−22] because organic free radicals have been found to participate in a plethora of electron-transfer reactions. Information about the electrochemical properties of these radical reactants or intermediates in solution is of tremendous importance to understanding the reaction mechanisms and kinetics. Unfortunately, as free radicals are usually transient species, their redox potentials are very difficult to measure experimentally. Up to now the $E°$ values of only a few free radicals have been reported,[12−22] and not all of these data are free of flaws. It is truly valuable to have an extensive tabulation of the $E°$ values for organic free radicals. By supplying trustworthy and useful data that are difficult to obtain via the experiments, we also hoped to better demonstrate the value of computational electrochemistry.[6,9]

2. Developing a Reliable Protocol To Calculate Standard Redox Potentials

2.1. Calibrating the Gas-Phase Ionization Potentials. Before computing the standard redox potentials, it is indispensable to calculate the gas-phase adiabatic ionization potentials (IPs), defined as the enthalpy changes of the following reactions in the gas phase at 298 K, 1 atm.

$$\text{Reduced form (g)} \rightarrow \text{Oxidized form (g)} + e^- \text{(g)} \qquad (1)$$

Although high-level theoretical methods such as G3 and CBS-Q can provide very accurate IPs, these methods are too demanding for general applications. The HF and MP2 methods are known to be inappropriate for the IP calculations.[23] Thus, the only choice is to use the density functional theory (DFT) methods to calculate the IPs.

Herein the popular B3LYP density functional was selected to calculate the gas-phase adiabatic ionization potentials. The standard 6-31+G(d) basis set was used for the geometry optimizations and frequency calculations, while the single-point energy calculations were performed with the 6-311++G(2df,2p) basis set. For the molecules that have more than one possible conformation, the conformation with the lowest electronic energy was singled out and used in the ensuing calculations. Each final optimized geometry was confirmed by the B3LYP/6-31+G(d) frequency calculation to be a real minimum on the potential energy surface without any imaginary frequencies. The enthalpy of each species was calculated using the B3LYP/6-311++G(2df,2p) electronic energy and the zero-point vibrational energy and thermal corrections (0 → 298 K) obtained at the B3LYP/6-31+G(d) level (unscaled).

The adiabatic IPs calculated using the above approach are compiled in the Supporting Information. Comparing these theoretical IPs with the available experimental data, we found that the B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method systematically underestimated the adiabatic IPs (Figure 1. Pay attention to the $y = x$ line.). Similar underestimation behavior of the DFT methods in the IP calculations was noted previously by Jursic in his study on alkanes[23] and by Kollman et al. in their study on toluene derivatives.[24]

Despite the underestimation problem, it is found that the B3LYP IPs correlate well with the experimental data, that is:

$$\text{IP (Exptl)} = \text{IP (B3LYP)} + 0.28 \text{ eV} \qquad (2)$$

For 160 structurally unrelated molecules, the correlation coefficient (r) of eq 2 is 0.989 and the standard deviation (sd)

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[10] Fu, Y.; Liu, L.; Li, R.-Q.; Liu, R.; Guo, Q.-X. *J. Am. Chem. Soc.* **2004**, *126*, 814.

[11] Due to the limitation of the computer resources, we only selected the compounds that contain no more than 12 non-hydrogen atoms. Moreover, we only selected the redox potentials corresponding to the one-electron transfer process.

[12] Rao, P. S.; Hayon, E. *J. Am. Chem. Soc.* **1974**, *96*, 1287.

[13] Papaconstantinou, E. *Anal. Chem.* **1975**, *47*, 1592.

[14] (a) Wayner, D. D. M.; Griller, D. *J. Am. Chem. Soc.* **1985**, *107*, 7764. (b) Wayner, D. D. M.; Dannenberg, J. J.; Griller, D. *Chem. Phys. Lett.* **1986**, *131*, 189. (c) Wayner, D. D. M.; McPhee, D. J.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 132. (d) Sim, B. A.; Griller, D.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1989**, *111*, 754. (e) Sim, B. A.; Milne, P. H.; Griller, D.; Wayner, D. D. M. *J. Am. Chem. Soc.* **1990**, *112*, 6635. (f) Wayner, D. D. M.; Sim, B. A.; Dannenberg, J. J. *J. Org. Chem.* **1991**, *56*, 4853. (g) Wayner, D. D. M.; Houmam, A. *Acta Chem. Scand.* **1998**, *52*, 377.

[15] (a) Occhialini, D.; Federsen, S. U.; Lund, H. *Acta Chem. Scand.* **1990**, *44*, 715. (b) Occhialini, D.; Kristensen, J. S.; Daasbjerg, K.; Lund, H. *Acta Chem. Scand.* **1992**, *46*, 474. (c) Occhialini, D.; Daasbjerg, K.; Lund, H. *Acta Chem. Scand.* **1993**, *47*, 1100.

[16] Abe, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 699.

[17] Hapiot, P.; Konovalov, V. V.; Saveant, J.-M. *J. Am. Chem. Soc.* **1995**, *117*, 1428.

[18] (a) Jonsson, M.; Wayner, D. D. M.; Lusztyk, J. *J. Phys. Chem.* **1996**, *100*, 17539. (b) Jonsson, M.; Kraatz, H. B. *J. Chem. Soc., Perkin Trans. 2* **1997**, 2673.

[19] (a) Larsen, A. G.; Holm, A. H.; Roberson, M.; Daasbjerg, K. *J. Am. Chem. Soc.* **2001**, *123*, 1723. (b) Lund, T.; Wayner, D. D. M.; Jonsson, M.; Larsen, A. G.; Daasbjerg, K. *J. Am. Chem. Soc.* **2001**, *123*, 12590.

[20] Cardinale, A.; Isse, A. A.; Gennaro, A. *Electrochem. Commun.* **2002**, *4*, 767.

[21] Andrieux, C. P.; Pinson, J. *J. Am. Chem. Soc.* **2003**, *125*, 14801.

[22] Grampp, G.; Landgraf, S.; Muresanu, C. *Electrochim. Acta* **2004**, *49*, 537.

[23] Jursic, B. S. *J. Mol. Struct. (THEOCHEM)* **1998**, *452*, 145 and references therein.

[24] Thomas, F.; Kollman, P. A. *J. Phys. Chem.* **1996**, *100*, 2950.

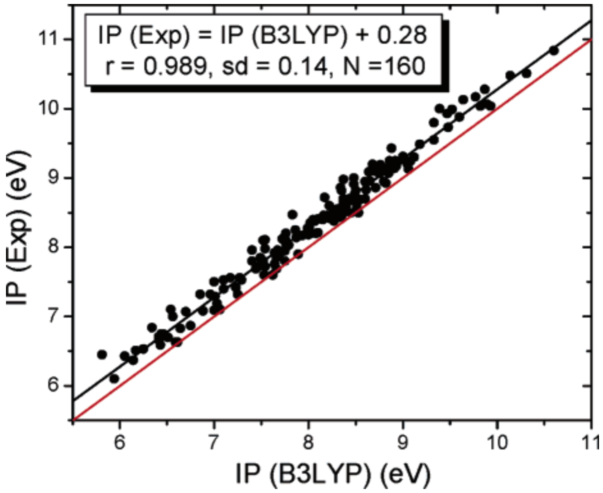

Figure 1. Correlation between the theoretical and experimental adiabatic IPs.

equals 0.14 eV (ca. 3 kcal/mol). It is worth noting that the experimental error for adiabatic IPs is usually 0.05−0.1 eV (i.e., 1−2 kcal/mol). Therefore, by adding 0.28 eV to the B3LYP results one can predict the adiabatic IPs reasonably well.

2.2. Calibrating the Solvation Model. With reliable theoretical gas-phase adiabatic IPs in hand, the next crucial step for the redox potential calculation is the computation of solvation free energies. In the present study, we used the polarized continuum model (PCM) developed by Tomasi and co-workers[25] to calculate the solvation free energies in acetonitrile.

A central idea in the PCM model is the construction of a solvent-inaccessible cavity in which the solute molecule resides.[26,27] In practice, this solvent-inaccessible cavity is built as a union of overlapping spheres centered on the nuclei of atoms or chemical groups. The sphere radii are usually proportional to the atomic radii with a scale factor (f). For aqueous solution, the f value was optimized to be 1.2,[25] while for dimethyl sulfoxide solution f was optimized to be 1.35.[10,28] Nonetheless, for many other solutions including acetonitrile, rigorous optimization of the f value has not been done because of the lack of experimental solvation free energies.

Without a careful optimization (or assessment) of the solvation model for acetonitrile, we were reluctant to blindly apply it to the redox potential calculations. Unfortunately, there are not enough experimental solvation free energies for us to evaluate the PCM model for acetonitrile.[29] At this point, we decided to use the experimental pK_a's of 15 organic acids in acetonitrile to assess the solvation model and to optimize the f value.[30] These 15 experimental pK_a values vary significantly from 15.8 to 27.2 (see the Supporting Information). Thus, it is sensible for us to assess and optimize the solvation model by attempting to calculate these pK_a's theoretically.

To calculate the pK_a's in acetonitrile, we considered the following proton-exchange reaction

$$\mathrm{AH} + {}^{-}\mathrm{CH_2CN} \rightarrow \mathrm{A}^{-} + \mathrm{CH_3CN} \qquad (3)$$

If the free energy change of the above reaction is defined as $\Delta G_{\mathrm{exchange}}$, the p$K_a$ of the acid AH can be calculated by eq 4.[10]

$$\mathrm{p}K_a(\mathrm{HA}) = \mathrm{p}K_a(\mathrm{CH_3CN}) + \frac{\Delta G_{\mathrm{exchange}}}{2.303 \times RT} \qquad (4)$$

It is known from the previous studies that the gas-phase free energy change of eq 3 can be fairly accurately calculated.[10] Thus, whether the theory can reproduce the experimental pK_a's mainly relies on the quality of the solvation energy calculations.

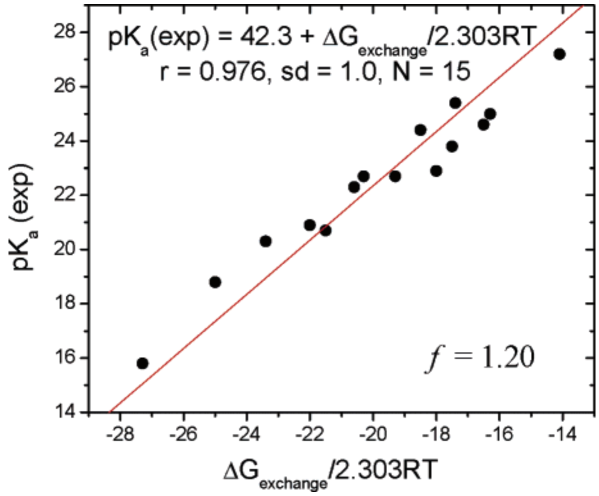

Figure 2. Correlation between the theoretical and experimental pK_a's in acetonitrile.

Using the Bondi scale of radii,[31−32] we examined different f values (f = 1.10, 1.15, 1.20, 1.25, 1.30, 1.35. See the Supporting Information for details) for the PCM model in the calculation of pK_a's in acetonitrile. Because the pK_a value of CH_3CN in acetonitrile has not been accurately determined (p$K_a(CH_3CN)$ > 33.3[33]), we could only plot the experimental pK_a's against the theoretical results for ($\Delta G_{\mathrm{exchange}}/2.303RT$) at different f values. By fixing the regression slope at 1.00, we found that f = 1.20 gave the best fit with the highest correlation coefficient (r = 0.976) and lowest standard deviation (sd = 1.0 pK_a unit) (Figure 2). It is worth mentioning that the correlation results also suggest that p$K_a(CH_3CN)$ = 42.3.

2.3. Computing Standard Redox Potentials in Acetonitrile. At this point we have established a theoretical protocol that can predict the gas-phase adiabatic IPs with an accuracy of 0.14 eV (ca. 3 kcal/mol). We have also optimized a solvation model that can predict the solution-phase pK_a's with an accuracy of

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(25) (a) Barone, V.; Cossi, M.; Tomasi, J. *J. Chem. Phys.* **1997**, *107*, 3210. (b) Cammi, R.; Mennucci, B.; Tomasi, J. *J. Phys. Chem. A* **1998**, *102*, 870. (c) Cammi, R.; Mennucci, B.; Tomasi, J. *J. Phys. Chem. A* **2000**, *104*, 4690.

(26) Tomasi, J.; Persico, M. *Chem. Rev.* **1994**, *94*, 2027.

(27) (a) Cramer, C. J.; Truhlar, D. G. *Rev. Comput. Chem.* **1995**, *6*, 1. (b) Cramer, C. J.; Truhlar, D. G. *Chem. Rev.* **1999**, *99*, 2161.

(28) Pliego, J. R., Jr.; Riveros, J. M. *Chem. Phys. Lett.* **2002**, *355*, 543.

(29) There are five solvation free energy data for acetonitrile that range from −3.57 to −5.33 kcal/mol (see: Hawkins, G. D.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **1998**, *102*, 3257). It is not sensible to optimize the f value or to evaluate the solvation model using these five similar data.

(30) (a) Stanczyk-Dunaj, M.; Galezowski, W.; Jarczewski, A. *Can. J. Chem.* **2002**, *80*, 1259. (b) Chantooni, M. K., Jr.; Kolthoff, I. M. *J. Phys. Chem.* **1976**, *80*, 1306. (c) Leito, I.; Kaljurand, I.; Koppel, I. A.; Yagupolskii, L. M.; Vlasov, V. M. *J. Org. Chem.* **1998**, *63*, 7863. (d) Kolthoff, I. M.; Chantooni, M. K., Jr.; Bhowmik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23. (e) Chantooni, M. C., Jr.; Kolthoff, I. M. *J. Phys. Chem.* **1975**, *79*, 1176. (f) Ludwig, M.; Pytela, O.; Vecera, M. *Collect. Czech. Chem. Commun.* **1984**, *49*, 2593.

(31) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.

(32) Kolthoff, I. M.; Chantooni, M. K. *J. Phys. Chem.* **1968**, *72*, 2270.

(33) In calculating the entropy change, one needs to include an extra term ($-RT \ln 4 = -0.04$ eV) in addition to the standard thermal entropy terms. This term corresponds to the entropic contribution from the electronic spin degeneracy.

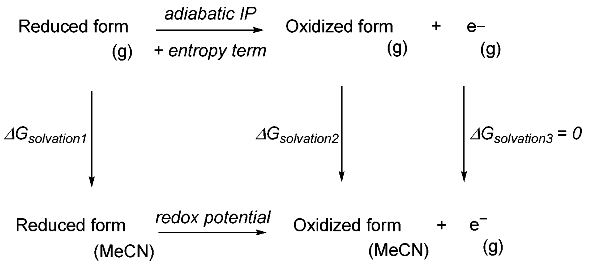

Figure 3. Free energy cycle for the redox reaction in acetonitrile.

1.0 pK_a unit (ca. 1.4 kcal/mol). Now it is time to see whether these theoretical methods can be combined to calculate the standard redox potentials in acetonitrile accurately.

It should be noted that by convention the standard redox potential is defined for half reactions written in the order:

$$E°\text{:}\quad \text{Reduced form} \rightarrow \text{Oxidized form} + e^-\,(g) \tag{5}$$

The value of $E°$ is usually measured relative to a reference electrode, for instance, the normal hydrogen electrode (NHE). The NHE half reaction is $H^+(aq) + e^-\ (g) \rightarrow {}^1/_2H_2(g)$. Thus, the $E°$ value is connected to the standard free energy change of the reaction

$$\Delta G°\text{:}\quad \text{Reduced form} + H^+(aq) \rightarrow \text{Oxidized form} + {}^1/_2H_2(g) \tag{6}$$

in the form of eq 7.

$$E° = \Delta G°/F \tag{7}$$

where F is the Faraday constant equal to 23.06 kcal/mol·V.

From a free energy cycle as shown in Figure 3, one can relate the redox potentials with the gas-phase adiabatic IPs and solvation energies using the following equation:

$$E°\ (\text{versus NHE}) = \text{IP} + \frac{1}{23.06}(-T\Delta S + \Delta G_{\text{solvation2}} - \Delta G_{\text{solvation1}}) - 4.44 \tag{8}$$

In eq 8, IP is the gas-phase adiabatic ionization potential (unit: eV), which equals the gas-phase enthalpy change from the reduced form to the oxidized form plus e^- at 298 K. The second term, $-T\Delta S$ (unit: kcal/mol) is the gas-phase entropy term from the reduced form to the oxidized form plus e^- at 298 K.[33] The next terms, $\Delta G_{\text{solvation1}}$ and $\Delta G_{\text{solvation2}}$ (unit: kcal/mol), correspond to the solvation free energies of the reduced and oxidized forms. The last term, −4.44 (unit: eV), is the free energy change associated with the reference NHE half-reaction (i.e., $H^+(aq) + e^-\ (g) \rightarrow {}^1/_2H_2(g)$).[34]

Using eq 8 it is straightforward to compute the standard redox potential of any organic molecule in acetonitrile from the aforementioned theoretical gas-phase IP (corrected by adding 0.28 eV) and solvation energies ($f = 1.20$). To assess the performance of this protocol, we compiled all the literature experimental standard redox potentials for organic molecules containing no more than 12 non-hydrogen atoms (see the Supporting Information). This compilation provided more than 270 structurally unrelated compounds that included alkanes, alkenes, alkynes, aromatics, alcohols, amines, aldehydes, ketones, ethers, esters, nitro compounds, halogenated compounds, amides, thiols, sulfides, heterocycles, hydrazines, azoalkanes, silanes, and tetrazenes.[35]

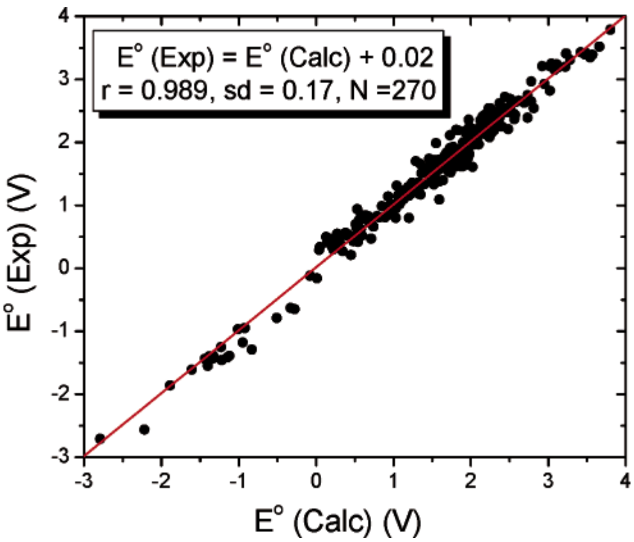

Figure 4. Correlation between the theoretical and experimental standard redox potentials in acetonitrile.

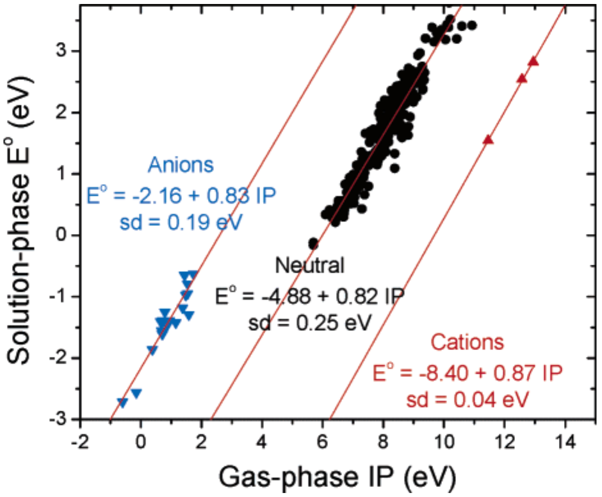

Figure 5. Correlation between the gas-phase adiabatic ionization potentials (theoretical values) and experimental standard redox potentials in acetonitrile.

The correlation between the experimental and theoretical standard redox potentials is shown in Figure 4. From Figure 4 it can be seen that the slope and intercept of the correlation are 1.00 and 0.02 V, respectively, indicating that there is almost no systematic error in the predictions. The correlation coefficient (r) is 0.989. The standard deviation between the experimental and theoretical standard redox potentials is 0.17 V (e.g., 4 kcal/mol) for 270 structurally unrelated compounds. Although this standard deviation is higher than the reported experimental error (0.01−0.02 V) of cyclic voltammetry, it is worth noting that not all of the experimental redox potentials were measured under rigorously reversible reaction conditions. In fact, for most cases the experimental errors are reported to be around 0.1 V.

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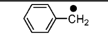
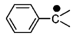
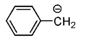
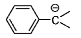
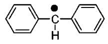
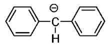
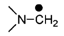
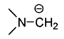
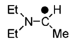
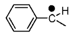
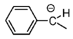
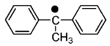
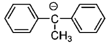
(34) Trasatti, S. *Pure Appl. Chem.* **1986**, *58*, 955.

(35) Not all the redox potentials are reported relative to NHE. Nevertheless, it is not hard to convert one scale of redox potentials to the other by using the relative potentials of different electrodes. For instance, SCE versus NHE = +0.24 V and Ag|Ag$^+$ (0.1 M) versus NHE = +0.57 V.

Table 1. Experimental and Theoretical Adiabatic Ionization Potentials (IPs, eV) and Standard Redox Potentials (E°, V) in Acetonitrile for Organic Free Radicals

Species (As reduced form)	IP (exp.)	IP (calc)[a]	E^0 (exp) *vs.* NHE	E^0 (calc) *vs.* NHE	Ref.
	7.24 ± 0.01	7.48	0.97	0.96	14a
	6.6	6.71	0.40	0.48	14c
	0.91 ± 0.01	1.16	-1.21	-1.31	14a
	0.79 ± 0.11	1.00	-1.49	-1.57	14c
	7.3 ± 0.1	6.74	0.59	0.63	14a
	1.36 ± 0.10	1.71	-0.90	-0.88	14a
	5.7	5.91	-0.79	-0.85	14b
	-	0.00	-1.76	-1.82	14c
	-	5.21	-0.88	-1.24	14b
	6.9	6.99	0.61	0.58	14c
	0.81 ± 0.13	1.05	-1.34	-1.31	14c
	-	6.49	0.47	0.43	14c
	-	1.51	-1.10	-1.16	14c
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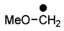
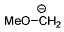
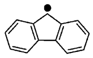
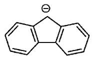
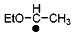
	6.94	7.38	0.00	0.35	14c
	-0.02 ± 0.10	0.18	-1.06	-1.48	14c
	7.07	7.16	1.00	1.01	14c
	1.87 ± 0.01	2.07	-0.52	-0.48	14c
	-	6.45	-0.21	-0.23	14c
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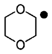
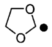
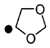
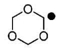
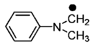
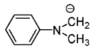
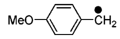
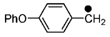
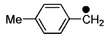
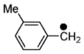
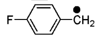
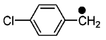
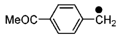
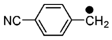
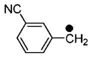
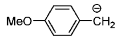
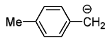
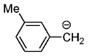
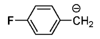
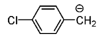
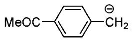
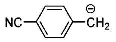
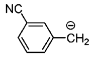
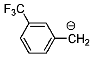
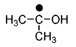
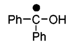
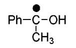
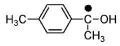
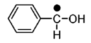
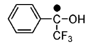
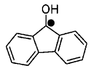
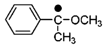
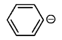
	-	6.74	0.16	-0.04	14c
	-	6.21	0.55	(-0.62)	14c
	-	7.10	-0.10	0.17	14c
	-	6.38	0.44	(-0.66)	14c
	-	5.95	-0.61	-0.46	14c
	-	0.50	-1.79	-1.71	14c
	6.8 ± 0.1	6.72	0.50	0.50	14e
	-	6.69	0.69	0.80	14e
	6.96 ± 0.02	7.13	0.75	0.85	14e
	7.12 ± 0.02	7.31	0.94	0.98	14e
	-	7.43	0.97	0.92	14e
	-	7.43	1.04	0.97	14e
	-	7.70	1.14	1.22	14e
	-	8.02	1.32	1.36	14e
	-	8.03	1.35	1.28	14e
	-	0.99	-1.51	-1.50	14d
	0.84 ± 0.14	1.07	-1.38	-1.42	14d
	0.88 ± 0.14	1.15	-1.26	-1.30	14d
	0.94 ± 0.01	1.19	-1.26	-1.34	14d
	-	1.42	-1.16	-1.29	14d
	-	2.03	-0.47	-0.75	14d
	-	2.11	-0.53	-0.78	14d
	-	1.82	-0.87	-1.05	14d
	-	1.64	-0.96	-0.92	17
	-	6.47	-0.37	-0.46	19b
	-	6.22	-0.01	0.10	19b
	-	6.34	0.00	0.01	19b
	-	6.13	-0.22	-0.13	19b
	-	6.65	-0.06	0.17	19b
	-	7.21	0.55	0.79	19b
	-	6.61	0.62	0.46	19b
	-	6.07	0.15	-0.20	19b
	1.10 ± 0.01	1.33	-0.29	-0.60	21

[a] Calculated by the B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method and corrected by adding 0.28 eV to the DFT results. Experimental gas-phase adiabatic ionization potentials are taken from NIST Standard Reference Database 69, March 1998 Release: *NIST Chemistry WebBook* (data compiled by J. E. Bartmess).

Therefore, the theoretical protocol is modestly successful for predicting the standard redox potentials.

At this point, we need to mention that not all of the theoretical predictions are in reasonable agreement with the experiment. For propene, 2-methyl-propene, 1-butene, 2-butene, 1-pentene, 1-octene, and 2-octene, the experimental standard redox potentials[36] (versus NHE) are 3.21, 3.16, 3.17, 2.72, 3.25, 3.21, and 2.74 V, but the theoretical values are 2.73, 2.33, 2.82, 2.32, 2.81, 2.61, and 2.24 V, respectively. The deviation between the experiment and the theory is about 0.5−0.8 V (i.e., 11−18 kcal/mol). Furthermore, for propane-1-thiol and butane-1-thiol the experimental standard redox potentials are 1.71 and 1.91 V versus NHE,[37] but the theoretical predictions are 2.37 and 2.48 V, respectively. The cause of these dramatic deviations remains to be clarified.

2.4. Correlation between Ionization Potentials and Redox Potentials. No one has compiled as many standard redox potentials in acetonitrile previously. Therefore, we have a unique opportunity to reliably reinvestigate one important subject related to the redox potentials, i.e., the correlation between gas-phase ionization potentials and solution-phase standard redox potentials. This correlation has been proposed and used by many authors in either explaining the experimental data or predicting unknown redox potentials.[38,39] We were interested in this

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(36) (a) Fleischmann, M.; Pletcher, D. *Tetrahedron Lett.* **1968**, *60*, 6255. (b) Clark, D. B.; Fleischmann, M.; Pletcher, D. *J. Electroanal. Chem. Interfacial Electrochem.* **1973**, *42*, 133.

(37) Loveland, J. W.; Dimeler, G. R. *Anal. Chem.* **1961**, *33*, 1196.

(38) Miller, L. L.; Nordblom, G. D.; Mayeda, E. A. *J. Org. Chem.* **1972**, *37*, 916.

(39) Recent examples: (a) Dhiman, A.; Becker, J. Y.; Minge, O.; Schmidbaur, H.; Muller, T. *Organometallics* **2004**, *23*, 1636. (b) Ue, M.; Murakami, A.; Nakamura, S. *J. Am. Chem. Soc.* **2002**, *149*, 1572.

correlation because it could reveal some important information about the solvation effect on redox potentials. Thus we plotted the theoretical gas-phase adiabatic IPs against the experimental redox potentials in Figure 5.

From Figure 5 it is clear that the gas-phase IPs cannot have a unified correlation with the solution-phase redox potentials for all of the compounds. Nevertheless, after we separated the compounds into three groups, i.e., anions (20 members), neutral compounds (247 members), and cations (3 members), we obtained three nice correlation lines. Surprisingly, the slopes of these three lines (0.83, 0.82, and 0.87) are fairly close to each other, although their intercepts (−2.16, −4.88, and −8.40 V) are dramatically different. Therefore, in each group the standard redox potentials are correlated with the IPs, but molecules with different total charges cannot be put together for such a correlation.

It is obvious that the different intercepts (i.e., −2.16, −4.88, and −8.40 V) are caused by the different solvation effects experienced by the anions, neutral molecules, and cations in acetonitrile. Furthermore, the slopes (ca. 0.85) of the correlations indicate that about 15% of the gas-phase ionization potentials are offset by the solvation in the solution-phase redox processes. Both of the above two effects are nicely reproduced by the PCM solvation model. Thus the redox potentials of anions, neutral molecules, and cations can be successfully predicted by a single quantum-chemical method.

At this instant we should mention that, although the continuum solvation model has been shown to be successful for various types of closed-shell molecules, it has never been extensively tested for open-shell species (e.g., radicals) against solid experimental data in the past. Since the redox potential calculations require accurate computation of the solvation energies of the open-shell species, the results from the present study should represent one of the first confirmations for the validity of the continuum solvation model for open-shell species. Such a confirmation is important, because we expect steady growth in the application of computational methods to studies of the solution-phase chemistry of various open-shell speices.

3. Standard Redox Potentials of Organic Free Radicals in Acetonitrile

To test the usefulness of the above theoretical protocol, we utilized it to study the standard redox potentials of organic free radicals in acetonitrile.[40] These redox potential data are of particular importance in mechanistic organic chemistry because free radicals are the intermediates of a plethora of electron-transfer reactions. Although considerable efforts have been devoted to the determination of the redox potentials of free radicals, up to now chemists have only measured the standard redox potentials of a few relatively stable free radicals (e.g., benzyl radicals).[12−22]

3.1. Comparing the Predictions with Available Experimental Data. Before predicting the unknown redox potentials, we first utilized the theoretical protocol developed in section 2 to calculate the standard redox potentials of free radicals that had been experimentally measured. The results are summarized in Table 1. It is worth noting that both the oxidation from carbon anions to carbon radicals and the oxidation from carbon radicals to carbon cations were considered in the present work.

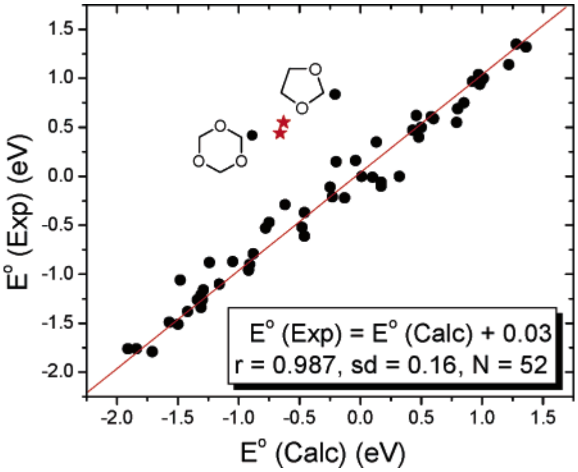

Figure 6. Correlation between the theoretical and experimental redox potentials in acetonitrile for organic free radicals.

Plotting the theoretical redox potentials against the experimental data, we obtained a nice correlation (Figure 6). The slope and intercept of the correlations are 1.00 and 0.03 V, respectively, indicating that there is almost no systematic error for the predictions. The correlation coefficient (r) is as high as 0.987, and the standard deviation for 52 redox couples is as low as 0.16 V. Thus the theoretical protocol is satisfactory for the calculation of standard redox potentials of organic free radicals. Nevertheless, there are two cases for which the theory does not agree with the experiment. They correspond to the oxidations of 1,3-dioxolane and 1,3,5-trioxane radicals to the corresponding cations (Figure 6).[14]

3.2. A Scale of Standard Redox Potentials for Organic Free Radicals. Having confirmed the reliability of the theoretical method for a number of free radicals, we next utilized the same method to calculate the standard redox potentials of various types of organic free radicals. These include the alkyl radicals, α-amino radicals, α-alkoxyl radicals, α-carbonyl radicals, captodative radicals, alkenyl radicals, alkynyl radicals, aromatic radicals, and carbonyl radicals. For each type, we selected a few representative examples. Both the oxidation of free radicals to carbon cations and the oxidation of carbon anions to free radicals were considered. The results are shown in Table 2.

To better illustrate the calculation results, we showed the predicted standard redox potentials graphically in Figure 7. From Figure 7 it can be seen that the aromatic carbon radicals have the highest standard redox potentials, around ∼+1.5 to +3.0 V (versus NHE). They are followed by alkynyl (ca. +2.4 V), alkyl (∼+0.5 to +2.5 V), and α-carbonyl radicals (∼+1.2 to +2.3 V). The standard redox potentials of alkenyl and captodative radicals are about 1.0 V. The standard redox potentials of carbonyl radicals are about 0.6 V. The standard redox potentials of α-alkoxyl radicals are about ∼−0.5 to +0.8 eV. The standard redox potentials of α-amino radicals are about ∼−1.5 to +0.5 V. Thus, depending on the substituents, the standard redox potentials of carbon-centered free radicals range from −1.5 to +3.0 V.

Compared to the radicals, the standard redox potentials for the carbon anions follow a different trend. The highest standard redox potentials are observed for the alkynyl anions (ca. +1.4

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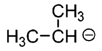
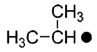
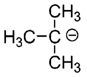
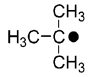
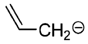
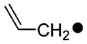
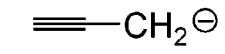
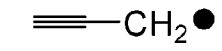
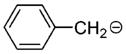
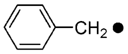
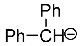
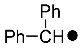
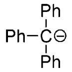
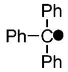
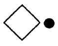
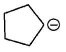
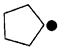
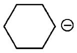
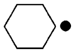
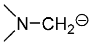
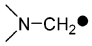
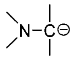
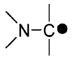
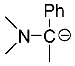
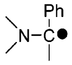
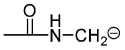
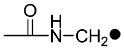
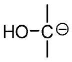
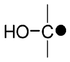
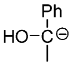
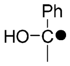
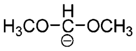
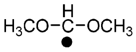
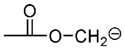
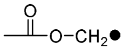
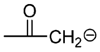
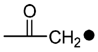
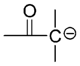
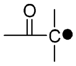
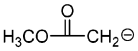
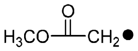
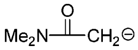
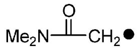
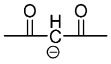
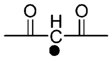
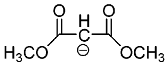
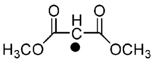
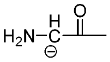
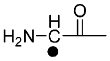
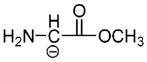
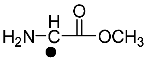
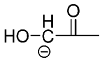
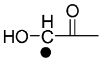
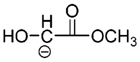
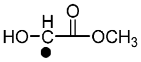
[40] Only the carbon-centered free radicals are considered in the present study.

Table 2. Adiabatic Ionization Potentials (IP, eV) and Standard Redox Potentials ($E°$, V) of Organic Free Radicals in Acetonitrile Predicted by the Method Developed in the Present Study

Species (As reduced form)	IP	E^0 *vs.* NHE	Species (As reduced form)	IP	E^0 *vs.* NHE
		Alkyl radicals			
$CH_3^{\ominus}$	0.36	-0.98	$CH_3^{\bullet}$	10.23	2.54
$H_3C{-}CH_2^{\ominus}$	0.06	-1.55	$H_3C{-}CH_2^{\bullet}$	8.49	1.23
	0.06	-1.81		7.65	0.65
	0.22	-1.88		7.03	0.17
	0.79	-1.11		8.42	1.42
	1.23	-0.64		9.00	2.00
	1.16	-1.31		7.48	0.96
	1.71	-0.88		6.74	0.63
	1.77	-0.99		6.32	0.45
	0.62	-1.05		7.05	0.05
	0.20	-1.69		7.78	0.83
	0.11	-1.84		7.41	0.57
	0.32	-1.76		7.30	0.63
		α-Amino radicals			
$H_2N{-}CH_2^{\ominus}$	-0.26	-1.80	$H_2N{-}CH_2^{\bullet}$	6.69	-0.66
	0.00	-1.82		5.91	-0.85
	0.18	-1.86		5.10	-1.47
	1.00	-1.53		5.40	-0.82
	0.75	-1.45		7.26	0.36
		α-Alkoxyl radicals			
$HO{-}CH_2^{\ominus}$	0.07	-1.55	$HO{-}CH_2^{\bullet}$	7.97	0.49
	0.13	-1.81		6.50	-0.42
	0.87	-1.59		6.45	0.02
$H_3CO{-}CH_2^{\ominus}$	0.18	-1.48	$H_3CO{-}CH_2^{\bullet}$	7.38	0.35
	0.40	-1.37		6.07	-0.64
	0.86	-1.21		7.55	0.85
		α-Carbonyl radicals			
	2.04	0.04		8.70	1.94
	1.59	-0.58		8.00	1.49
	1.96	0.01		8.87	2.09
	1.79	-0.34		7.55	1.17

Species (As reduced form)	IP	E^0 *vs.* NHE	Species (As reduced form)	IP	E^0 *vs.* NHE
		α-Carbonyl radicals			
	3.09	0.76		8.84	2.18
	3.16	0.83		8.65	2.23
		Captodative radicals			
	1.19	-0.98		7.44	0.54
	1.12	-1.02		7.23	0.37
	1.54	-0.50		8.47	1.46
	1.36	-0.71		8.27	1.37
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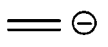
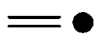
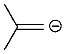
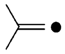
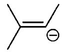
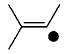
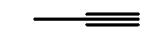
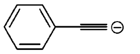
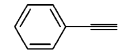
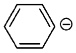
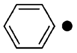
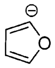
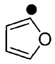
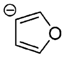
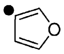
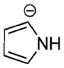
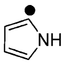
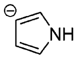
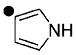
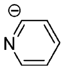
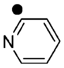
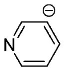
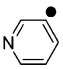
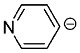
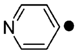
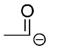
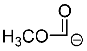
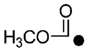
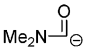
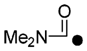
	0.96	-0.61		8.97	1.63
	1.01	-0.77		7.31	0.46
	0.79	-1.15		7.22	0.55
		Alkynyl radicals			
	3.04	1.35		9.04	1.98
	3.34	1.38		9.33	2.60
		Aromatic radicals			
	1.33	-0.60		8.51	1.80
	2.13	0.33		9.79	2.85
	1.91	0.08		9.90	2.99
	1.86	0.01		9.04	2.18
	1.40	-0.29		9.10	2.28
	1.07	-0.75		8.07	1.41
	1.68	-0.32		8.59	1.92
	1.71	-0.35		8.74	1.97
		Carbonyl radicals			
	0.74	-1.07		7.41	0.24
	1.66	-0.26		7.79	0.79
	0.93	-0.93		7.03	0.29

V). They are followed by α-carbonyl (∼−0.6 to +0.7 V) and aromatic (∼−0.8 to +0.2 V) anions. Carbonyl anions and captodative anions have similar standard redox potentials (∼−1.0 to −0.5 V). The standard redox potentials of alkenyl anions are around −1.0 V. The standard redox potentials of α-alkoxyl and α-amino anions are about ∼−2.0 to −1.5 V. The standard redox potentials of alkyl anions range from −2.0 to −0.7 V.

4. Summary

The ability to accurately predict the standard redox potential for a given molecule in the solution phase is highly desirable.

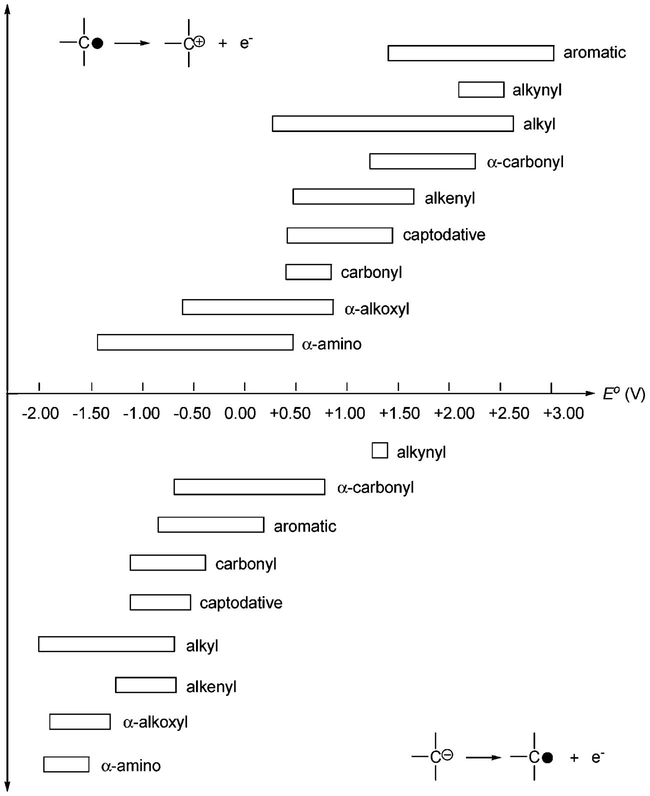


Figure 7. Standard redox potentials of various types of organic free radicals in acetonitrile.

Identifying key electronic features that dictate the redox potential on a molecular level is of substantial importance and might facilitate the derivation of rational strategies for tuning the redox properties of catalysts and provide a unique pathway to discovering novel redox-active systems with desired chemical behavior. In the present study, we carefully benchmarked a generally applicable theoretical protocol for the prediction of standard redox potentials in acetonitrile. This protocol was utilized to calculate the standard redox potentials of 270 structurally unrelated organic molecules, and it was demonstrated to have a precision of 0.17 V.

The primary value of the study is that it provides the chemical community a calibrated protocol for the prediction of standard redox potentials. Second, the study demonstrates that it is time for computational electrochemistry[6,9] to become a powerful tool for organic chemistry research. Furthermore, the study comprehensively tests the validity of the continuum solvation theory for the organic radical species. It demonstrates that this great theoretical model can successfully predict the solvation energies of organic radicals. Finally, with the help of the newly developed protocol we are able to establish a scale of standard redox potentials for diverse types of organic free radicals for the first time. Knowledge about these redox potentials is of great value for understanding the numerous electron-transfer reactions in organic and bioorganic chemistry.

5. Computational Methodology

All of the theoretical calculations were conducted using the Gaussian 98 and 03 programs.[41,42] The gas-phase calculations were conducted using the standard B3LYP/6-311++G(2df,2p)//B3LYP/6-31+G(d) method. The PCM solvation model was used in its original dielectric formulation (D-PCM) developed by Tomasi and co-workers[25,26] to calculate the solvation free energies in acetonitrile. The gas-phase geometry was utilized for all the solution-phase calculations, as it was demonstrated that the change of geometry by the solvation effect was usually not significant.[27] All the PCM calculations were performed at B3LYP/6-31+G(d,p) level (version = MATRIX INVERSION, cavity = PENTAKISDODECAHEDRA, Icomp = 4, TSNUM = 60, TSARE = 0.4, radii = bondi, alpha = ~1.10−1.35).

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Supporting Information Available: Experimental and theoretical adiabatic ionization potentials and standard redox potentials for more than 270 compounds. Experimental and theoretical pK_a values for 15 organic acids. Complete citations for refs 41 and 42. This material is available free of charge via the Internet at http://pubs.acs.org.

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(41) Frisch, M. J. et al. *Gaussian 98*, revision A.7; Gaussian, Inc.: Pittsburgh, PA, 1998.
(42) Frisch, M. J. et al. *Gaussian 03*, revision B.04; Gaussian, Inc.: Pittsburgh, PA, 2003.