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Computational electrochemistry of diarylnitroxides

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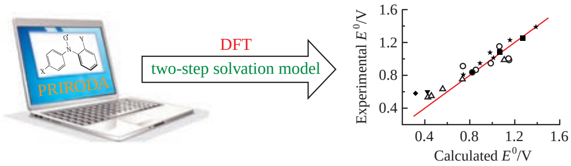
Based on a combination of a gas-phase DFT electronic structure calculation at PBE/L2 level implemented in the highly efficient ‘Priroda’ program package with consecutive fast solvation energy evaluation by continuum solvation model, a liable methodology has been developed for accurate calculation of the standard redox potentials for diarylnitroxides in acetonitrile solution.



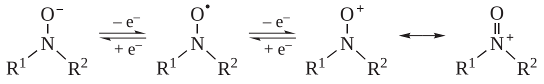
Convenient protocol for computational electrochemistry

Development of new electroactive organic materials as the components of the ‘greener’ electrochemical storage devices based on renewable sources is a topical problem nowadays.[1] Despite huge efforts focused on molecular engineering of the ‘optimal’ stable and technological organic electroactive electrode materials, the majority of ‘all-organic’ batteries are still considered as ‘proof-of-principle’ and have efficiency parameters far below those for inorganic materials.[2,3] To achieve competitive capacities and energy densities, rational design of new types of organic redox active molecules which offer a possibility for fine tuning of an oxidation/reduction potential as well as cycling stability is a challenging problem.

In this context, stable organic radicals which exhibit fast and reversible electron transfer (ET) kinetics are of interest.[4] Application of organic polymers with dialkylnitroxide pendant groups (2,2,6,6-tetramethylpiperidine-1-oxyl, TEMPO) as electroactive cathode material was reported.[5–9]

Diarylnitroxides, contrary to their alkyl counterparts, offer wider possibilities for fine tuning of the properties by variation in their structure and functionalization of the aromatic moiety. Recently, we demonstrated[10] that the optimal structure of diarylnitroxide providing stability of both starting radicals and their redox forms is an unsymmetrical twisted nitroxide containing a *para*-substituent in one ring and a bulky substituent in the *ortho*-position of the second ring which alters the dihedral angle between the *p*-orbital of the nitrogen atom and the aromatic ring thus changing the conjugation degree.

Prior to synthesis, computational estimation of the redox-potential values of target diarylnitroxides should be helpful to choose candidates providing the maximal potential gap ($\Delta E = E_{\mathrm{Ox}} - E_{\mathrm{Red}}$). However, an accuracy of the computations is a crucial point. To provide a valuable alternative to experiment, a proper methodology for prediction of liquid-phase redox potentials should be chosen based on optimal combination of the level of theory and the solvation model. A recent review[11] on computational electrochemistry covers computational protocols which combine quantum mechanical electronic structure with implicit-solvent models and explicit-solvent protocols that employ Monte Carlo or molecular dynamics as well as approaches based on empirical relationships between molecular and electronic structure and electron transfer reactivity. Wide range of the possibilities raises a question: what approach will be the best for each particular type of compounds and solvents?



Scheme 1

Alkylnitroxides can be reversibly oxidized to form the corresponding oxoammonium cations; the resonance structure contributes to their high stability (Scheme 1). On the cathode nitroxide radical is reduced to the aminoxy anion which is commonly insufficiently stable and ET is followed up by a chemical step.[12]

Several publications on reliable computational prediction of alkylnitroxide oxidation potential can be found in literature,[13–17] while calculations of the reduction potential values are rare.[14,15] The semi-empirical AM1 method combined with the SM2 solvation model was used for predicting redox potential of TEMPO and its derivatives.[13] Since then more advanced computational methods were developed. DFT and *ab initio* methods were considered in combination with various basic sets and solvation models; the effect of the level of theory on the accuracy of the redox potential prediction for a number of alkylnitroxides was also studied.[15]

Oxidation and reduction potentials within 40 mV (3.9 kJ mol^{-1}) of experimental values were found using G3(MP2)-RAD//B3LYP/6–31G(d) gas-phase energies and PCM solvation calculations at the B3LYP/6-31G(d) level. The accuracy estimation was performed using relatively broad set of experimental oxidation potentials (seven TEMPOs with different substituents) and only two reduction potentials (measured for TEMPO and 4-hydroxy-TEMPO). The better accuracy was achieved in ref. 14: mean absolute deviation from experimental values of 16 mV was obtained. The high level *ab initio* methodology [UAKS-PCM/B3LYP/6-31G(d)//G3(MP2)-RAD] was used to establish trends in the values of oxidation potentials of cyclic dialkylnitroxides. The alteration of the N-containing skeleton (pyrrolidine, piperidine, isoindoline, *etc.*) as well as the introduction of different substituents were performed within 120 alkylnitroxide radicals, the major part of which are hypothetical species that have not been synthesized yet. The plot of calculated *vs.* experimental standard oxidation potentials was presented for a test set of 13 nitroxides which are of similar type and do not contain aromatic moiety. Sufficiently good correlation between the experimental redox potentials and the DFT-computed adiabatic ionization energies accounting for solvation (using polarizable continuum model) between nitroxyl radicals and oxoammonium species was obtained[16] for azaadamantane-type and azabicyclo-type nitroxyl radicals.

Though an excellent agreement between the calculated and experimental oxidation potentials was achieved for alkylnitroxides, an extraordinary discrepancy (mean absolute deviation up to 0.60 V) was observed for azaphenalene class of nitroxide which contain alkylnitroxide ring fused to an aromatic system with different substituents,[17] implying that some influence of aromatics is not considered in the theoretical calculations. Theoretical study of diarylnitroxides has not been performed yet and it is not evident that the approaches elaborated for alkylnitroxides will be equally valid for aryl derivatives. This work was aimed at the elaboration of the appropriate low-cost computational methodology of reliable predicting oxidation potential values for diarylnitroxides.

DFT calculations were carried out with the 'PRIRODA' quantum chemistry program;[18,19] the gradient-corrected exchange-correlation Perdew, Burke and Ernzerhof (PBE) functional[20] was used for calculations. The special basic sets (L-basic sets[21]) developed for the 'Priroda' program package were applied.[18] The program is known to be efficient and reliable for DFT and *ab initio* electronic structure calculations of large molecular systems as well as their spectral characteristics. However, solvation effect is not implemented in the program package. Meanwhile, consideration of the solvation effect is an extremely important issue in computational prediction of redox potential values in solution.

Solvation contributions to the redox potentials are commonly treated in three different ways.[11] The most widely used methods consider solvent as a continuous dielectric medium characterized by macroscopic properties and, in some cases, by microscopic properties such as polarizability of the solvent molecules and an effective solvent radius (PCM/CPCM). Another approach is based on atomistical treatment of the solvent (molecular dynamic methods). The third group of protocols relies on empirical or semi-empirical correlations of redox potentials and some other quantities (which may be either experimental or calculated ones). In the present study, an alternative two-step procedure for evaluation of solvation free energy which has been proposed in 2005[22] was combined with the fast gas phase DFT calculations in the 'Priroda' program (PBE/L2). Contrary to the other implicit solvent model-based methods, solvation impact is neglected in the initially calculated wave function and only at the second step solvation energy is evaluated by solving Poisson–Boltzmann equations for atomic charges system derived from vacuum state wave function. Merz–Kollman atomic charges are used within the calculation for the best fit of the molecular electrostatic potential. In ref. 22 it was stated that this two-step procedure provides sufficiently better results as compared to commonly applied one-step protocol. The advantage of the two-step procedure arises from mitigation of the so called 'electron leakage effect', which is inherent to the wave function calculation in a dielectric medium. This effect is especially significant for highly polarizable molecules such as long π-conjugated systems[22] and should be taken into account in estimation of solvation impact for computations of standard oxidation potentials of diarylnitroxides.

To establish the reliability of the approach, oxidation potentials for a number of previously investigated alkylnitroxides were re-estimated first. Alkylnitroxides of various types were selected, including aliphatic nitroxides with fused or attached aromatic rings, for which the significant deviation of the previously obtained calculated data from the experimental values was observed.

The computational procedure employed consists of the following steps: calculation of the adiabatic ionization energy[†] of the standard redox compound (TEMPO) and the test compound in the given solvent followed by evaluation of the standard redox potential *versus* a chosen reference electrode.

The results obtained clearly indicated that the combination of the 'Priroda' program (PBE/L2) with the two-step procedure for estimation of solvation impact gives much better accuracy for the selected compounds with naphthyl and phenyl moieties than previously used computational procedures. Comparison of experimental oxidation potential values for a number of previously investigated alkylnitroxides with the obtained theoretical values is shown in Figure 1 (previously[17] obtained theoretical data for the same compounds are also included for comparison). The accuracy provided by the proposed protocol is of the same order and in some cases even better than that of reported data obtained using generally used PCM/CPCM approach combined with the high level DFT or *ab initio* electronic structure method.

Computational determination of the redox potentials for diarylnitroxides has not been done so far since the experimental values were scarce. Our recent research allowed us to broaden the scope of the stable diarylnitroxides[10,27–29] making possible reliable comparison of calculated *vs.* experimental redox potential values and an accuracy estimation. Experimental oxidation potential values for previously known diarylnitroxides as well as for aryl–alkyl derivatives were taken from literature. One can see that theoretical and experimental results obtained for arylnitroxides are relatively close (Table 1). A mean average deviation of 33 mV (0.7 kcal mol^{-1}) from the experimental data is observed for both aryl and alkyl derivatives (see Figure 1). Thus, 'Priroda' DFT package combined with the two-step procedure for evaluation of the solvation free energy is an appropriate low-cost method for calculation of standard potentials for one-electron oxidation of nitroxides (of dialkyl, diaryl and aryl–alkyl type) to the corresponding oxoammonium cations.

Since DFT computation of the electrochemical potentials using aforementioned protocol agrees with the experiment, it provides a toolset for the predictive design of new diarylnitroxides. However, molecular design strategy for diaryl nitroxides should be based not only on structure–reactivity relationships which allow one to predict oxidation and reduction potential values. Stability and side reactions are crucial points, which puts additional limitations on the rational molecular design of diarylnitroxides. Thus, it is necessary to consider a special scope of the substituents (in particular, they should not have α-hydrogen atoms and other

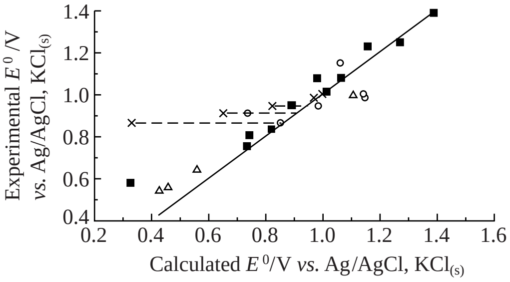


Figure 1 Experimental oxidation potentials *vs.* calculated values. Filled signs correspond to arylnitroxides (see Table 1 for details). Alkylnitroxides (empty signs): empty triangles correspond to experimental values taken from ref. 16, empty circles stand for values from ref. 17. Crosses correspond to theoretically obtained values taken from ref. 17.

[†] For calculation of the adiabatic ionization energy, the following procedure was applied: gas-phase structure optimization of an oxidized and reduced form of the compound; calculation of the thermal contributions to Gibbs energy (in ideal gas, rigid rotor, harmonic oscillator approximations) at PBE/L1 level of theory; gas-phase single point calculation for the oxidized and reduced forms of the compound at PBE/L2 level; calculation of Merz–Kollman charges for the oxidized and reduced forms (in Multiwfn program, http://sobereva.com/multiwfn/); evaluation of solvation energies for the oxidized and reduced forms of the compound by solving Poisson–Boltzmann equation for a found charge system in a given solvent (in APBS program, http://www.poissonboltzmann.org/).

Table 1 Calculated and experimental values of oxidation potentials of some arylnitroxides $R^1R^2N–O^•$.

Entry	Nitroxides $R^1R^2N–O^•$		Calculated[a] E^0/V *vs.* Ag/AgCl, $KCl_{(s)}$	Experimental $E_{1/2}$/V *vs.* Ag/AgCl, $KCl_{(s)}$
	R^1	R^2		
1	4-$(PhMe_2C)C_6H_4$	4-$(PhMe_2C)C_6H_4$	0.820	0.836[23]
2	4-$MeOC_6H_4$	4-$MeOC_6H_4$	0.325	0.580[24]
3	4-$Bu^tC_6H_4$	4-$Bu^tC_6H_4$	0.742	0.807[10]
4	4-$Bu^tC_6H_4$	4-$CF_3C_6H_4$	1.013	1.015[10]
5	2-$Bu^tC_6H_4$	4-$Bu^tC_6H_4$	0.889	0.952[10]
6	2-$CF_3C_6H_4$	4-$CF_3C_6H_4$	1.388	1.391[10]
7	2-$Bu^tC_6H_4$	4-$CF_3C_6H_4$	1.157	1.230[10]
8	2-$CF_3C_6H_4$	4-$Bu^tC_6H_4$	0.979	1.079[10]
9	Bu^t	4-$Bu^tC_6H_4$	0.733	0.755[25]
10	Bu^t	2-pyridyl	1.064	1.08[26]
11	Bu^t	4-trifluoromethyl-pyridin-2-yl	1.270	1.25[26]

[a] PBE/L2 + two-step solvation model.

easily leaving groups) as well as their determined location (the *para*-position of the conjugated phenyl ring should be blocked).[30] From this point of view, hypothetical structures which might be perspective combine pyridyl and aryl moieties directly attached to the NO radical center. Based on the principles of the rational molecular design of diarylnitroxides,[27] CF_3 and Bu^t substituents in *ortho*- and *para*-positions in the phenyl ring were chosen. The nitrogen atom in the *N*-4-pyridyl moiety might be expected to impede side reactions *via* 4-position; hence, the unsubstituted pyridyl moiety can be applied. This type of nitroxides has not been reported yet. The only work concerns *N*-pyridyl, *N*-*tert*-butylnitroxides which were obtained as intermediates *via* electrochemical oxidation of the corresponding hydroxyl amines with subsequent one-electron reduction.[26]

Estimation of the oxidation potential values was performed using our above approach which was demonstrated to be suitable for accurate prediction of the redox potentials (Table 2). As one can see, trends in the oxidation potentials within a family of substituted *N*-aryl-*N*-(4-pyridyl)nitroxides are in line with the electron donating and withdrawing ability of the substituents in the phenyl ring. As expected, donor substituents facilitate oxidation. The effects are much more pronounced as compared to aliphatic nitroxide series.[15] The effect of the *ortho*-substituted ring is in agreement with the torsion angle value.[27] It is sufficiently higher for Bu^t than for CF_3 group providing greater difference in the oxidation potentials between the *ortho*- and *para*-isomers in the former case (244 and 80 mV, see Table 2).

In conclusion, a combination of the ‘Priroda’ program package at the PBE/L2 level of theory with continuum solvation model (in the form of the two-step procedure) provides a low-cost and reliable methodology for calculation of the standard redox potentials for nitroxides in acetonitrile solution. A mean absolute deviation from the experimental values is 33 mV. Importantly, the proposed protocol provides sufficiently good agreement with the experimental data for both alkyl and aryl derivatives. It is of note that, though the approach is relatively simple, it gives in some cases (when aromatic moiety is one or two sp^3 carbons removed from the NO group) even better results than previously used approaches. Computational electrochemistry for diarylnitroxides has not been done before. DFT prediction of oxidation potential values for currently unknown hypothetical *N*-aryl-*N*-(4-pyridyl) nitroxides was performed providing guidelines for the predictive design of new nitroxides. The possibility to perform gas phase calculations utilizing accurate quantum chemical methods separately to solvation effect (provided by the above two-step procedure) is beneficial in terms of resources saving. The results obtained can be further combined with the required reaction conditions providing estimations of the potential values in a variety of solvents without repeating time-consuming high level electronic structure calculations. We believe that the treatment of solvation described may be useful for correcting gas-phase calculations of other type reaction energies thus providing better agreement between theoretical investigation and experiment.

Table 2 DFT predicted oxidation potentials for *N*-aryl-*N*-(4-pyridyl)-nitroxides.

Aryl in ArPyN–O$^•$	E^0_{ox}/V *vs.* Ag/AgCl, $KCl_{(s)}$
2-$Bu^tC_6H_4$	1.338
4-$Bu^tC_6H_4$	1.094
2-$CF_3C_6H_4$	1.532
4-$CF_3C_6H_4$	1.452

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