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Theoretical Reduction Potentials for Nitrogen Oxides from CBS-QB3 Energetics and (C)PCM Solvation Calculations

Andrew S. Dutton,[†] Jon M. Fukuto,[‡] and Kendall N. Houk*,[†]

Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095-1569, and Department of Pharmacology, University of California, School of Medicine, Center for the Health Sciences, Los Angeles, California 90095-1735

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The complete basis set method, CBS-QB3, is used in combination with two continuum solvation models for aqueous solvation to compute reduction potentials previously determined experimentally for 36 nitrogen oxides and related species of the general formula $H_VC_WN_XO_YCl_Z$. The PCM model led to the correlation E°_{exp} (vs NHE) $= 0.84E^\circ_{\mathrm{calc}} + 0.03$ V with an average error of 0.12 V (2.8 kcal/mol) and a maximum error of 0.32 V (7.4 kcal/mol). The CPCM/UAKS model gave E°_{exp} (vs NHE) $= 0.83E^\circ_{\mathrm{calc}} + 0.11$ V with the same average error. This general method was used to predict reduction potentials (±0.3 V) for nitrogen oxides for which reduction potentials are not known with certainty: NO_2/NO_2^- (0.6 V), NO_3/NO_3^- (1.9 V), $N_2O_3^-/N_2O_3^{2-}$ (0.5 V), $HN_2O_3/HN_2O_3^-$ (0.9 V), HONNO, H^+/HONNOH (1.6 V), 2NO,H^+/HONNO (0.0 V), 2NO/$ONNO^-$ (–0.1 V), $ONNO^-/ONNO^{2-}$ (–0.4 V), HNO,H^+/H_2NO (0.6 V), $H_2NO,H^+/H_2NOH$ (0.9 V), HNO,$2H^+/H_2NOH$ (0.8 V), and HNO/HNO^- (–0.7 V).

Introduction

Electron-transfer reactions are of vital importance in chemistry and biology. The driving force for electron transfer can be determined from reduction potentials. Reduction potentials provide the free energies of the oxidation and reduction processes and are vital to the understanding of reactions in biology. The high reactivity of many nitrogen oxides precludes direct experimental measurement of the reduction potential, and accurate experimental measurement of reactive intermediates is often difficult.[1] Some examples of note in the nitrogen oxide field follow.

Nitric oxide, NO, was reported in the literature to have a reduction potential in the range of 0.39 to −1.0 V vs NHE.[1−8] This broad range was in part a result of the erroneous pK_a of HNO and the misunderstanding of the relevant equilibrium species.[2,9] The one-electron reduction potential for the reduction of NO to NO^- was computed[9] to be −0.8 V vs NHE, in agreement with a previous experimental measurement of −0.81 V vs NHE.[3] This reduction potential indicates that NO will not easily be reduced to NO^- under physiological conditions by simple outer-sphere electron transfer.[3,9] However, the work of Liochev and Fridovich suggests that the reduction of NO to HNO may be biologically accessible under extremely high concentrations of NO.[10] The one-electron reduction potential for the reduction of NO_2 to NO_2^- has a range of 0.89−1.13 V vs NHE in the literature;[11−17] the recently reported value converges on 1.04 V vs NHE.[17]

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* To whom correspondence should be addressed. E-mail: houk@chem.ucla.edu.

[†] Department of Chemistry and Biochemistry.

[‡] Department of Pharmacology.

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Table 1. Standard Reduction Potentials Listed in Order of Decreasing E°_{exp} vs NHE[a]

reaction couple	PCM E°_{calc} (V)	CPCM E°_{calc} (V)	E°_{exp} (V)	PCM E°_{pred} (V)
$H_2N_2O_2 + 2H_3O^+ + 2e^-/N_2 + 4H_2O$	3.04	2.94	2.65	2.58
$O_3 + 2H_3O^+ + 2e^-/^3O_2 + 3H_2O$	2.34	2.29	2.076	2.00
$H_2O_2 + 2H_3O^+ + 2e^-/4H_2O$	2.07	1.99	1.776	1.77
$N_2O + 2H_3O^+ + 2e^-/N_2 + 3H_2O$	2.04	1.98	1.766	1.74
$2HOCl + 2H_3O^+ + e^-/Cl_2 + 4H_2O$	1.97	1.91	1.611	1.68
$2NO + 2H_3O^+ + 2e^-/N_2O + 3H_2O$	1.95	1.91	1.591	1.67
$HO_2 + H_3O + e^-/H_2O_2 + H_2O$	1.64	1.74	1.495	1.41
$HOCl + H_3O^+ + e^-/Cl^- + 2H_2O$	1.69	1.59	1.482	1.45
$2HNO_2 + 4H_3O^+ + 4e^-/N_2O + 7H_2O$	1.54	1.52	1.297	1.32
$ClO_2 + H_3O^+ + e^-/HClO_2 + H_2O$	1.18	1.17	1.277	1.02
$O_3 + H_2O + 2e^-/^3O_2 + 2HO^-$	1.20	0.99	1.24	1.04
$^3O_2 + 4H_3O^+ + 4e^-/6H_2O$	1.55	1.51	1.229	1.33
$N_2O_4 + 2H_3O^+ + 2e^-/2HNO_2 + 2H_2O$	1.33	1.22	1.065	1.15
$N_2O_4 + 4H_3O^+ + 4e^-/2NO + 6H_2O$	1.24	1.18	1.035	1.07
$HNO_2 + H_3O^+ + e^-/NO + 2H_2O$	1.14	1.14	0.983	0.99
$NO_3^- + 4H_3O^+ + 3e^-/NO + 6H_2O$	1.32	1.25	0.957	1.14
$NO_3^- + 3H_3O^+ + 2e^-/HNO_2 + 4H_2O$	1.37	1.30	0.934	1.18
$HO_2^- + H_2O + 2e^-/3HO^-$	1.22	0.81	0.878	1.05
$N_2O_4 + 2e^-/2NO_2^-$	0.65	0.61	0.867	0.58
$2HNO_2 + 4H_3O^+ + 4e^-/H_2N_2O_2 + 6H_2O$	1.04	1.04	0.86	0.90
$^1O_2 + e^-/O_2^-$	0.70	0.76	0.83	0.62
$ClO^- + H_2O + 2e^-/Cl^- + 2HO^-$	1.12	0.86	0.81	0.97
$2NO + H_2O + 2e^-/N_2O + 2HO^-$	0.81	0.62	0.76	0.71
$^3O_2 + 2H_3O^+ + 2e^-/H_2O_2 + 2H_2O$	1.03	1.03	0.695	0.90
$^3O_2 + 2H_2O + 4e^-/4HO^-$	0.41	0.21	0.401	0.37
$(CN)_2 + 2H_3O^+ + 2e^-/2HCN + 2H_2O$	0.27	0.33	0.373	0.26
$2NO_2^- + 3H_2O + 4e^-/N_2O + 6HO^-$	0.18	−0.12	0.15	0.18
$NO_3^- + H_2O + 2e^-/NO_2^- + 2HO^-$	−0.06	−0.30	0.01	−0.02
$^3O_2 + H_2O + 2e^-/HO_2^- + HO^-$	−0.39	−0.38	−0.076	−0.30
$^3O_2 + 2H_2O + 2e^-/H_2O_2 + 2HO^-$	−0.11	−0.27	−0.146	−0.06
$^3O_2 + e^-/O_2^-$	−0.54	−0.48	−0.16	−0.44
$CO_2 + 2H_3O^+ + 2e^-/HCOOH + 2H_2O$	0.11	0.12	−0.199	0.12
$NO_2^- + H_2O + e^-/NO + 2HO^-$	−0.45	−0.84	−0.46	−0.35
$2NO_3^- + 2H_2O + 2e^-/N_2O_4 + 4HO^-$	−0.77	−1.21	−0.85	−0.62
$NO + e^-/^3NO^-$	−1.11	−1.00	−0.81	−0.90
$CO_2 + e^-/CO_2^-$	−2.11	−1.98	−1.8	−1.74

[a] E°_{calc} values were obtained using the method described in the text with the PCM solvation model. E°_{exp} values are the experimentally measured or estimated values from the literature.[3,43–45] E°_{pred} values are the predicted values obtained by using the correlation in Figure 1.

Gladwin et al. recently proposed a mechanism by which nitrite may be converted to NO via hemoglobin in red blood cells to explain the observed vasodilative property of nitrite;[18] the NO_2^-,H_2O/NO,$2HO^-$ reaction couple has a reduction pontential of −0.46 V (Table 1). A range from 1.9 to 2.6 V vs NHE has been reported for the one-electron reduction of NO_3 to NO_3^-;[12,14,19–21] although there has not been agreement on the exact value for this reduction potential, Stanbury suggests using 2.5 V vs NHE.[1]

Angeli's salt, $N_2O_3^{2-}$, is used as a donor of HNO for the investigation of HNO biology and chemistry. Angeli's salt decomposes in a pH-dependent manner releasing HNO in the pH range of 10−4 and releasing NO in the pH range of 4 and below.[22,23] Recently, there have been reports in the literature casting doubt on the use of Angeli's salt as an HNO donor under aerobic conditions; it has been observed that peroxynitrite, $ONOO^-$, is formed from the decomposition of Angeli's salt in the presence of oxygen.[24,25] A proposed mechanism for the formation of $ONOO^-$ from Angeli's salt is the reduction of NO, a potential product from Angeli's salt decomposition, to NO^-; O_2 and NO^- react at near diffusion control with a rate constant of 2.7×10^9 M^{-1} s^{-1}.[2,24,25] This mechanism seems unlikely because the computed and measured reduction potentials of the reduction of NO to NO^- imply that reduction is difficult, and therefore it is unlikely that NO^- would be generated using the above mechanism under physiological conditions. There is another possible explanation for the formation of $ONOO^-$. The direct oxidation of Angeli's salt with O_2 could yield nitrite, NO, and superoxide; the fast reaction of NO and superoxide ($k = 1.9 \times 10^{10}$ M^{-1} s^{-1}) would then generate $ONOO^-$.[26] Knowledge of the redox chemistry of Angeli's salt would allow for the evaluation of the possible reduction of O_2 by Angeli's salt. However, reduction potentials for Angeli's salt have not been reported experimentally.

Lymar and co-workers have recently reported reduction potentials for the hyponitrite radical, HONNO, which is formed from the reaction of NO with HNO.[27] They report reduction potentials for $2NO/ONNO^-$, $ONNO^-/ONNO^{2-}$, 2NO,H^+/ONNOH, and ONNOH,H^+/HONNOH to be −0.38, 0.96, −0.06, and 1.75 V, respectively (vs NHE).[27] These reduction potentials imply that the hyponitrite radical can be both a reductant and an oxidant.

Ab initio and density functional methods have been used previously to predict reduction potentials for a variety of species that are important in chemistry and biology.[9,28–34] B3LYP,[35] a widely used density functional, has been used for the geometry optimization and energy calculations to predict the reduction potentials of *p*-benzoquinonones[28] in water using a free energy perturbation method for the aqueous solvation calculation, and it has also been used to predict values for a series of redox active organic molecules, metallocenes, and complexes of the type $[M(bpy)_3]^x$ (M =

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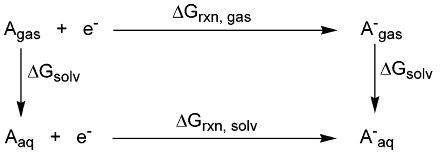
Scheme 1. Free Energy Cycle for Computation of the Free Energy Change of a Reduction in Solution from the Computed Gas-Phase Free Energy Change and the Free Energies of Solvation



Fe, Ru, Os; $x = 3, 2, 1, 0, -1$; bpy = 2,2′-bipyridine) in water, acetonitrile, dimethylformamide, and dichloromethane using a continuum solvation model.[31] The majority of reports use density functional theory for the geometry optimization in the gas phase followed by a method that includes extensive treatment of electron correlation energy to compute the free energy of the optimized structure in the gas phase.[9,29,30,32−34] A solvation model is then used to compute the free energy of solvation of the oxidant and reductant. The free energy cycle shown in Scheme 1 is used to compute the free energy change for the reaction couple in water. Using the Nernst equation, $\Delta G_{\mathrm{rxn,solv}} = -nFE°$, where n is the number of electrons transferred and F is Faraday's constant, 23.06 kcal $\mathrm{mol^{-1}\ V^{-1}}$, the reduction potential can be calculated. Friesner and Baik plotted the computed reduction potentials, $E°_{\mathrm{calc}}$, versus the experimental reduction potentials, $E°_{\mathrm{exp}}$, for a series of reductions and demonstrated an excellent correlation.[31]

Here, we report computations with CBS-QB3 for gas-phase free energies and PCM or CPCM for aqueous solvation energies. The one-electron reduction potentials for the NO_2/NO_2^- and NO_3/NO_3^- reaction couples have been evaluated and revised. The reduction potentials reported by Lymar and co-workers for hyponitrite radicals, as well as for HNO to the iminoxyl radical, H_2NO, and hydroxylamine, H_2NOH, were investigated theoretically. Finally, the reduction potentials for Angeli's salt have been computed in order to test the plausibility of oxidation by O_2 via outer-sphere electron transfer.

Computational Details

All structures were optimized and their energies computed using the procedures of the complete basis method developed by Petersson and co-workers, CBS-QB3,[36] a series of calculations that generally gives gas-phase energies with an average error of ±1 kcal/mol as compared to experimentally measured values for the G3 data set. The Gaussian 98 program was used.[37] Free energies are given at 298 K. Aqueous solvation energies were calculated as single points on the B3LYP/6-311+G(d) gas-phase optimized geometries using a 6-311+G(d) basis set and default parameters in the polarizable continuum model,[38] PCM, implemented in Gaussian 98. Aqueous solvation energies were also calculated using the conductor-like polarizable continuum model,[39] CPCM, implemented in Gaussian 03, with the United Atom Kohn Sham cavity model, UAKS.[40] For the polarizable continuum-based solvation models of water, the CPCM method using UAKS cavities implemented in Gaussian 03 has been shown to be more accurate, with a mean absolute deviation of 3.0 kcal/mol for a test set of 70 molecules, than PCM, which had a mean absolute deviation of 11.3 kcal/mol for the same test set, for computing the solvation energy of a range of charged and uncharged species.[41] The solvation energies were applied to the CBS-QB3 optimized gas-phase energies along with a 1.9 kcal/mol conversion factor for changing from the gas phase (1 atm) to the solution phase (1 M). The calculation of the change in free energy, including solvation, for the balanced reduction reactions yields $\Delta G_{\mathrm{rxn,solv}}$, as shown in Scheme 1. The Nernst equation, $\Delta G_{\mathrm{rxn,solv}} = -nFE°$, relates $\Delta G_{\mathrm{rxn,solv}}$ to the reduction potential $E°$ where n is the number of electrons transferred and F is the Faraday constant. The reduction potential determined in this manner is an absolute reduction potential, $E°_{\mathrm{abs}}$, because it has not been referenced to a standard electrode. By subtracting 4.43 V, the absolute reduction potential estimated for the NHE,[42] we obtained the calculated reduction potential, $E°_{\mathrm{calc}}$, for the standard conditions of 298 K, 1 atm, and 1 M H^+ vs NHE. This procedure was carried out on 36 experimentally known reduction potentials. The reaction couples are given in Table 1.[3,43−45] $E°_{\mathrm{calc}}$ is plotted versus $E°_{\mathrm{exp}}$ in Figures 1 and 2. Correlations between the theoretically and experimentally determined values are shown in Figure 1 for the PCM solvation model and in Figure 2 for the CPCM solvation model. All of the values reported in the subsequent tables and discussed in the text were obtained using the PCM solvation model because the maximum deviation from the experimental values is less for these data.

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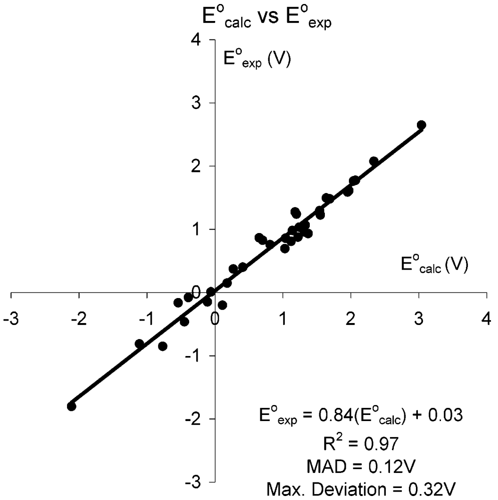

Figure 1. Plot of 36 standard experimental reduction potentials[3,43−45] versus the calculated reduction potentials using the PCM solvation model. The equation of the fitted straight line and statistics are shown in the figure.

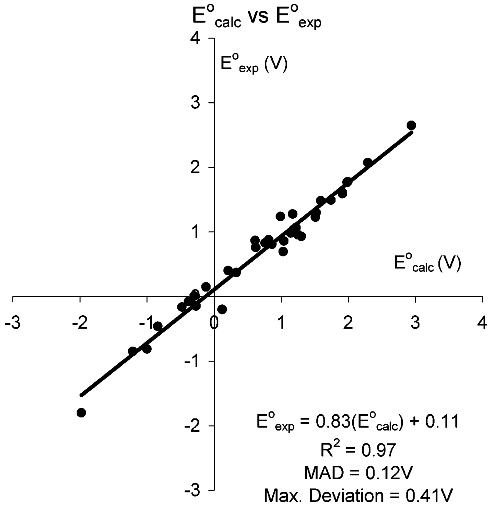

Figure 2. Plot of 36 standard experimental reduction potentials[3,43−45] versus the calculated reduction potentials using the CPCM solvation model. The equation of the fitted straight line and statistics are shown in the figure.

Results and Discussion

For both the PCM solvation model, Figure 1, and the CPCM/UAKS solvation model, Figure 2, the correlation coefficient was found to be $R^2 = 0.97$. The CPCM/UAKS solvation model provided the equation E°_{exp} (vs NHE) = $0.83E^\circ_{\mathrm{calc}} + 0.11$ V. The mean absolute deviation from this correlation is 0.12 V with a maximum deviation of 0.41 V for the $CO_2,2H_2O^+/HCOOH,2H_2O$ reaction couple. The PCM solvation model produces the equation E°_{exp} (vs NHE) = $0.84E^\circ_{\mathrm{calc}}) + 0.03$ V. The mean absolute deviation is 0.12 V with a maximum deviation of 0.32 V for the same reaction couple. The slopes for both correlations are very similar, approximately 0.84. The slopes are 16% less than the ideal value of 1. The origin of this difference is not known and is the subject of ongoing investigation. An error in the solvation energy of H_2O likely contributes to this error. Almost all of the values with positive reduction potentials involve H_2O as a product, while most of the reduction potentials below zero involve H_2O as a reactant. Therefore, the solvation energy of H_2O influences the slope of the line. The experimentally determined solvation energy for water is -6.32 ± 0.05 kcal/mol[46] which is overestimated by PCM and CPCM, −8.0 and −7.5 kcal/mol, respectively. This overestimation results in a lower calculated free energy of the products for reactions involving the conversion of H_3O^+ to H_2O. The converse occurs for reactions involving OH^- where the computed free energy of the reactants will be overestimated resulting in an underestimated reduction potential. The use of the experimental solvation energy of water with the PCM solvation energies of all other species yields a correlation of computed and experimental reduction potentials of E°_{exp} (vs NHE) = $0.9E^\circ_{\mathrm{calc}} + 0.0$ V (data not shown). The solvation energies of H_3O^+ and OH^- are known with less accuracy. Values of −110.2 and −105, respectively, have been reported in the literature.[47] The use of these experimentally derived solvation energies for H_3O^+ and OH^-, −110.2 and −105, respectively, did not improve the correlation. In the discussion that follows, the reduction potentials are obtained from the theoretical values using PCM solvation energies for all species, including water. The reduction potentials computed for the other nitrogen oxide systems, where experimental values are either unknown or not known with certainty, were not used in the correlations reported in Figures 1 and 2 and are given in Tables 2−4.

The reduction potential for the one-electron reduction of NO_2 to NO_2^- is predicted to be 0.6 ± 0.3 V vs NHE. This result is significantly lower than the reported experimentally derived reduction potentials, 0.89−1.13 V vs NHE, and predicts NO_2 to be a weaker oxidant.[11−17] The predicted value for the NO_2/NO_2^- reduction potential is less oxidizing than expected given the experimentally observed reaction of NO_2 with thiols, such as cysteine.[48] The experimentally determined reduction potential[48] for cysteine, $RS,H^+/RSH$ is 0.9 V, and therefore, our predicted value appears to have an error of 0.3 V, the maximum error expected. The principal difficulty in experimentally measuring this reduction potential arises from the bimolecular disproportionation of NO_2 in solution.[1] The predicted reduction potential for the NO_3/NO_3^- reaction couple is 1.9 ± 0.3 V vs NHE. This predicted reduction potential matches the value reported by Endicott, but is on the low end of the values cited in the literature, 1.9−2.6 V.[1,12,14,19−21]

With the surge of importance of NO and HNO in biology, Lymar and co-workers have recently reported reduction potentials for the hyponitrite radical, HONNO, a product of the reaction between HNO and NO.[27] Theoretically computed reduction potentials, shown in Table 2, for the one-electron reduction reaction couples of $2NO/ONNO^-$, $2NO,H^+/HONNO$, and $HONNO,H^+/HONNOH$ agree well with the reported experimental values: -0.1 ± 0.3 V computed compared to −0.38 V measured, 0.0 ± 0.3 V computed compared to −0.06 V measured, and 1.6 ± 0.3 V computed compared to 1.75 V measured, respectively, all vs NHE.

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Table 2. Computed and Experimental Reduction Potentials for Hyponitrite Radical vs NHE

reaction couple	E°_{pred} (V)	E°_{exp} (V)
$2NO + e^-/ONNO^-$	-0.1 ± 0.3	-0.38^b
$ONNO^- + e^-/ONNO^{2-}$	-0.4 ± 0.3	0.96^b
$2NO + H_3O^+ + e^-/HONNO + H_2O$	0.0 ± 0.3	-0.06^b
$HONNO + H_3O + e^-/HONNOH + H_2O$	1.6 ± 0.3	1.75^b
$NO + e^-/{}^3NO^-$	-0.9 ± 0.3	-0.81^a

[a] From ref 3. [b] From ref 27.

Table 3. Computed and Experimental Reduction Potentials for HNO and H_2NO vs NHE

reaction couple	E°_{pred} (V)	E°_{exp} (V)
$HNO + H_3O^+ + e^-/H_2NO + H_2O$	0.6 ± 0.3	
$H_2NO + H_3O^+ + e^-/H_2NOH + H_2O$	0.9 ± 0.3	
$HNO + 2H_3O^+ + 2e^-/H_2NOH + 2H_2O$	0.8 ± 0.3	0.7^b
$HNO + e^-/HNO^-$	-0.7 ± 0.3	
${}^3O_2 + e^-/O_2^-$	-0.4 ± 0.3	-0.33^a
${}^3O_2 + H_3O^+ + e^-/HO_2 + H_2O$	-0.3 ± 0.3	-0.076^c

[a] From ref 1. [b] From ref 2. [c] From ref 3.

However, there is considerable disagreement for the $ONNO^-/ONNO^{2-}$ reaction couple with a computed reduction potential of -0.4 ± 0.3 V compared to the value of 0.96 V vs NHE cited by Lymar et al.[27] The computed value is considerably lower than the measured value indicating that $ONNO^-$ should be a poor oxidant. The experimental value indicates that $ONNO^-$ is a good oxidant. The theoretically derived reduction potentials predict that it is easier to reduce nitric oxide to form $ONNO^-$ than to reduce $ONNO^-$ to form $ONNO^{2-}$. This seem reasonable because the addition of an electron into $ONNO^-$ involves unfavorable electrostatics and the electron enters the same π^* orbital as in formation of $N_2O_2^-$. The experimentally determined reduction potential for $ONNO^-$ is difficult to obtain and derived by using experimentally determined pK_a's to approximate the free energies of the species involved.[27] The one-electron reduction potential for NO to ${}^3NO^-$ is shown in Table 2 for reference.[3]

The reduction potentials predicted for the basic and acidic one-electron reduction of HNO are shown in Table 3 along with the corresponding one-electron reduction potentials for oxygen for comparison. The reduction potential of HNO in acid agrees with the experimental work of Shafirovich and Lymar.[2] The computed value of 0.8 ± 0.3 V vs NHE for the two-electron reduction reaction couple of $HNO,2H^+/H_2NOH$ agrees well with the estimated value of ~0.7 V vs NHE determined by Shafirovich and Lymar.[2] These results predict that HNO is easily reduced in 1 M acid, 0.3 ± 0.3 V vs NHE, and in neutral solutions, 0.2 ± 0.3 V vs NHE. In basic solutions, reduction of HNO to HNO^- is predicted to be less facile than reduction of O_2.

Table 4. Computed Reduction Potentials for $N_2O_3^-$ and HN_2O_3 vs NHE

reaction couple	E°_{pred} (V)
$N_2O_3^- + e^-/N_2O_3^{2-}$	0.5 ± 0.3
$HN_2O_3 + e^-/HN_2O_3^-$	0.9 ± 0.3

The reduction potential of Angeli's salt was predicted since the fate of Angeli's salt during aerobic decomposition is still under debate in the literature.[49] The theoretically predicted reduction potentials, shown in Table 4, predict that Angeli's salt, as either the dianion or the protonated monoanion, will not react in an outer-sphere electron-transfer process with O_2. $ONOO^-$ is formed from the reaction of NO with O_2^- from the redox reaction of Angeli's salt with O_2. It cannot occur via the direct oxidation of Angeli's salt via electron transfer, which is in agreement with the mechanisms proposed in the literature.[24,25,49]

Conclusions

Computational predictions of the reduction potentials of reactive nitrogen oxides have been described. The maximum error of the predictions is 0.3 V. The weakest link in the calculations is the computed solvation energies. Calculations incorporating explicit water molecules during the optimization might yield more accurate results.[50]

The reduction potentials for the NO_3/NO_3^- and NO_2/NO_2^- reaction couples are predicted to be 1.9 ± 0.3 and 0.6 ± 0.3 V, respectively. The computed reduction potentials for the hyponitrite radicals agree with Lymar and co-worker's experimentally determined reduction potentials (Table 2) except for the one-electron reduction of $ONNO^-$ to $ONNO^{2-}$.[27] The reactive biological species HNO is predicted to have reduction potentials of 0.6 and 0.8 V for one- and two-electron reductions, respectively. Angeli's salt, $N_2O_3^{2-}$, is predicted to be a poor reductant with a computed reduction potential of 0.5 ± 0.3 V for the $N_2O_3^-/N_2O_3^{2-}$ reaction couple. The protonated form is expected to be a worse reductant with a computed reduction potential of 0.9 ± 0.3 V for the $HN_2O_3/\ HN_2O_3^-$ reaction couple.

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Supporting Information Available: Cartesian coordinates of the CBS-QB3 structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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