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N−NO Bond Dissociation Energies of *N*-Nitroso Diphenylamine Derivatives (Or Analogues) and Their Radical Anions: Implications for the Effect of Reductive Electron Transfer on N−NO Bond Activation and for the Mechanisms of NO Transfer to Nitranions

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The heterolytic and homolytic N−NO bond dissociation energies [i.e., ΔH_{het}(N−NO) and ΔH_{homo}(N−NO)] of 12 *N*-nitroso-diphenylamine derivatives (**1**−**12**) and two *N*-nitrosoindoles (**13** and **14**) in acetonitrile were determined by titration calorimetry and from a thermodynamic cycle, respectively. Comparison of these two sets of data indicates that homolysis of the N−NO bonds to generate NO$^{\bullet}$ and nitrogen radical is energetically much more favorable (by 23.3−44.8 kcal/mol) than the corresponding heterolysis to generate a pair of ions, giving hints for the driving force and possible mechanism of NO-initiated chemical and biological transformations. The first (N−NO)$^{-\bullet}$ bond dissociation energies [i.e., ΔH(N−NO)$^{-\bullet}$ and $\Delta H'$(N−NO)$^{-\bullet}$] of radical anions **1**$^{-\bullet}$−**14**$^{-\bullet}$ were also derived on the basis of appropriate cycles utilizing the experimentally measured ΔH_{het}(N−NO) and electrochemical data. Comparisons of these two quantities with those of the neutral N−NO bonds indicate a remarkable bond activation upon a possible one-electron transfer to the N−NO bonds, with an average bond-weakening effect of 48.8 ± 0.3 kcal/mol for heterolysis and 22.3 ± 0.3 kcal/mol for homolysis, respectively. The good to excellent linear correlations among the energetics of the related heterolytic processes [ΔH_{het}(N−NO), ΔH(N−NO)$^{-\bullet}$, and pK_a(N−H)] and the related homolytic processes [ΔH_{homo}(N−NO), $\Delta H'$(N−NO)$^{-\bullet}$, and BDE(N−H)] imply that the governing structural factors for these bond scissions are similar. Examples illustrating the use of such bond energetic data jointly with relevant redox potentials for analyzing various mechanistic possibilities for nitrosation of nitranions are presented.

Introduction

The important roles of nitric oxide (NO) in adjusting many physiological functions in life processes have attracted considerable scrutiny over the past decade.[1−11] Although its footprints have indeed been widely detected, the amount of free NO in the human body is generally realized to be very small, a result of the high reactivity of NO as a free radical. Therefore, it should be conceivable that the "stored" NO in its carrier molecules has to go through certain release-and-capture cycles to execute its various biological functions. To understand the mechanistic details of such NO migration, it is obviously desirable to have some quantitative knowledge of the thermodynamic driving forces for Y−NO bond rupture (where Y represents the atom in a carrier to which NO is directly attached). For this purpose, in an earlier work[11a] we have conducted a research on the homolytic and heterolytic Y−NO bond dissociation energies in

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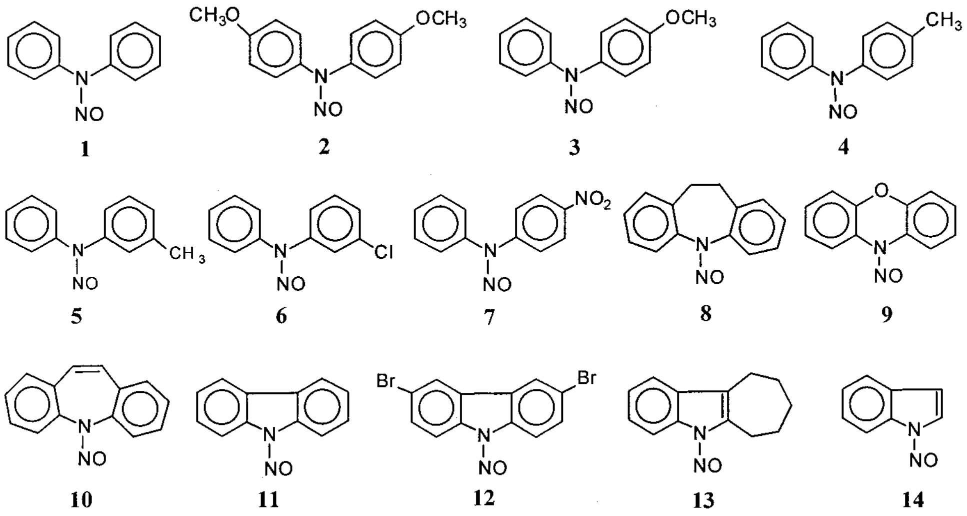
Chart 1



Scheme 1

$$Y^{\ominus} + NO^{\oplus} \underset{\Delta H_{het}}{\overset{\Delta H_{rxn}}{\rightleftharpoons}} Y\text{-}NO \qquad (1)$$

$$\Delta H_{het}(Y\text{-}NO) = -\Delta H_{rxn} \qquad (2)$$

$$Y\text{-}NO \xrightarrow{\Delta H_{het}} Y^{\ominus} + NO^{\oplus} \xrightarrow[-e^{-}]{E_{ox}(Y^{-})} Y^{\bullet} + NO^{\oplus} \xrightarrow[+e^{-}]{E_{1/2}(NO^{+}/NO)} Y^{\bullet} + NO^{\bullet}$$

$$\Delta H_{homo}(Y\text{-}NO) = \Delta H_{het}(Y\text{-}NO) + F[E_{ox}(Y^{-}) - E_{1/2}(NO^{+}/NO)] \qquad (3)$$

acetonitrile (also called "solution-phase $NO^{\bullet}$ and NO^{+} affinities"[12]) as a quantitative model to assess the trend of NO transfer in vivo. The experimental methods there used to determine the bond heterolysis and homolysis energies [i.e., ΔH_{het}(Y−NO) and ΔH_{homo}(Y−NO)] are titration calorimetry and thermochemical cycle (combining heat and electrode potentials), respectively (Scheme 1). The first series of model compounds chosen therein are the N−NO-containing substrates bearing a vicinal *N*-carbonyl group (or its analogues).[11a,b] Later, this approach has been applied to derive the dissociation energies of a series of O−NO bonds in *O*-nitroso carboxylates.[11c] These model compounds, again, bear a vicinal *O*-carbonyl group.

The carbonyl substituent (or its analog) is, of course, not the only known structure capable of activating NO transportation. For example, diphenylamine (DPA) and its derivatives (e.g., diclofenac) are well-known radical scavenger active in many biological transformations.[15] Therefore, it is well conceived that this series of compounds should be good candidates as NO reservoir molecules by virtue of their NO-capturing ability. Indeed, it is evidenced that *N*-nitrosodiphenylamine (NDPA) is readily formed upon treating DPA with NO donor compound and does play a key role as to elevate the total levels of cytochrome P-450 and the activity of NAD(P)H-cytochrome P-450 reductase in vivo,[16] presumably by supplying NO to the neighborhood.

The proven importance of the DPA derivatives in affecting many biological processes spurred us to investigate the energies of N−NO heterolysis and homolysis for this class of model compounds (Chart 1, **1**−**14**). Here we wish to report the first determination of the N−NO bond energies with such a structural feature (i.e., without a carbonyl-type activating group). Further, because reductive electron transfer is known to remarkably reduce bond strength,[17−19] the first series of bond energies of the Y−NO radical anions ($\mathbf{1}^{-\bullet}$−$\mathbf{14}^{-\bullet}$) were also determined in order to release information for the potential roles of bioelectron transfer in activating N−NO bond rupture. Correlation analyses of these bond energy scales in relation to the common structural parameters (σ^{-}, pK_a, BDE) and a model mechanistic analysis of NO-involving reactions utilizing the derived energetic data are also presented and discussed.

Results

The heterolytic N−NO bond dissociation energies [ΔH_{het}(N−NO)] were obtained from the directly measured heats of reaction (ΔH_{rxn}) of NO^{+} with nitranions by

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[12] The corresponding gas-phase nitrosonium (NO^{+}) affinity and C−NO bond dissociation energy (BDE) for many small molecules can be found in refs 13 and 14, respectively.

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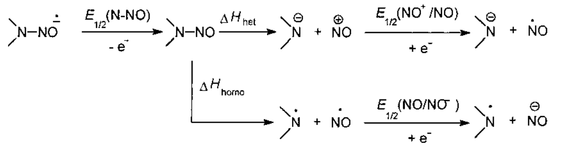
Scheme 2



$$\Delta H(\text{N-NO})^{-\bullet} = \Delta H_{\text{het}}(\text{N-NO}) + F[E_{1/2}(\text{N-NO}) - E_{1/2}(\text{NO}^+/\text{NO})] \qquad (4)$$

$$\Delta H'(\text{N-NO})^{-\bullet} = \Delta H_{\text{homo}}(\text{N-NO}) + F[E_{1/2}(\text{N-NO}) - E_{1/2}(\text{NO}/\text{NO}^-)] \qquad (5)$$

titration calorimetry (see Experimental Section). The homolysis energies (ΔH_{homo}) were derived indirectly from the thermodynamic cycle shown in Scheme 1 by combining heat of heterolysis with appropriate redox potentials (eq 3). The use of an irreversible potential (E_{ox}) in eq 3 may introduce an uncertainty up to about 1 kcal/mol to the ΔH_{homo}(N−NO) data derived, as judged by comparisons of the irreversible and reversible oxidation potentials of largely delocalized anionic species studied previously.[20] Nevertheless, a substantially smaller error margin is expected when the N−NO bond energies are compared in a relative sense, because the degree of electrode irreversibility in nitranion oxidation is quite similar, on the basis of their well-behaved CV traces (wave width all around 55 mV).

The present method (in which the ΔH_{het} values are used in conjunction with redox data to derive the corresponding ΔH_{homo} values) is analogous to that of Arnett for evaluation of the C−C bond energies[22] but differs in that in our method the nitranion takes the place of carbanion and the nitrosonium cation takes the place of carbocation. The solvent used for the measurements is also changed to acetonitrile rather than sulfolane as in the literature cases.[22]

As electron transfer is important in biological and chemical systems and is known to have a substantial effect on activating chemical bonds, the bond dissociation energies of radical anions (**1**$^{-\bullet}$−**14**$^{-\bullet}$) were also estimated to assess the extent of N−NO bond weakening upon a reductive electron transfer. The method, which is analogous to that of Arnett for (C−S)$^{-\bullet}$ bonds,[24] is shown in Scheme 2.

The validity of the present approach to indirectly derive the desired bond energetic data by mixing enthalpies with free energy terms (i.e., redox potentials) through a cycle relies largely on the closeness of the approximation to equate ΔH_{ET} with ΔG_{ET}. Otherwise, ΔS_{ET} must be taken into account and be corrected for. While there is no fundamental reason the entropy effect of electron transfer should be negligible, Arnett was able to show that the temperature coefficients of redox potentials of both the resonance-stabilized anions and cations they studied that resemble ours were indeed very small,[22] giving confidence in the present method.

Table 1. Heterolytic Dissociation Energies of the N−NO Bonds in Compounds 1−14 and Redox Potentials of the Relevant Species in CH$_3$CN at 25 °C

compound	ΔH_{het}(N−NO)^a (kcal/mol)	E_{ox}(N$^-$)^b (V vs Fc$^+$/Fc)	E_{red} (N−NO)^b (V vs Fc$^+$/Fc)
1	62.0 ± 0.1	−0.846	−1.261
2	65.8 ± 0.2	−1.082	−1.274
3	63.5 ± 0.2	−0.964	−1.270
4	62.5 ± 0.4	−0.917	−1.262
5	62.4 ± 0.3	−0.876	−1.261
6	60.2 ± 0.4	−0.701	−1.259
7	50.2 ± 0.3	−0.260	−1.221
8	63.4 ± 0.1	−0.893	−1.266
9	57.5 ± 0.2	−1.040	−1.241
10	62.8 ± 0.4	−1.029	−1.261
11	55.1 ± 0.4	−0.336	−1.249
12	51.6 ± 0.3	−0.148	−1.243
13	57.7 ± 0.3	−0.351	−1.259
14	56.5 ± 0.3	−0.342	−1.256

[a] The N−NO bond heterolysis energies (ΔH_{het}) in compounds **1**−**14** were measured by titration calorimetry in CH$_3$CN at 25 °C. [b] Measured by cyclic voltametry (CV) in CH$_3$CN at 25 °C. Reproducibility = 0.005 V.

The directly measured heats of N−NO heterolysis and the redox potentials of both the parent compounds **1**−**14** and the corresponding nitranions **1**$^-$−**14**$^-$ in acetonitrile are given in Table 1. The three sets of N−NO bond energy data indirectly derived from eqs 3−5 [i.e., ΔH_{homo}(N−NO), ΔH(N−NO)$^{-\bullet}$, and $\Delta H'$(N−NO)$^{-\bullet}$], together with ΔH_{het} values, are tabulated in Table 2. The literature N−H bond energies (i.e., pK_a's and BDEs) are also compiled therewith for comparison. The four sets of N−NO bond energetic data here obtained provide the first opportunity for quantitatively comparing the relative ease of N−NO bond cleavage for the model compounds of interest in different oxidation states. Such comparisons may serve as useful guide for understanding the basic principles governing the driving forces and directions of NO release and capture in both chemical and biological systems and for predicting the possible mechanisms of NO-related transformations.

Discussion

Heterolytic and Homolytic N−NO Bond Dissociation Energies. In a sharp contrast to the familiar R−H bonds, whose heterolysis is always easier than homolysis in solution phase, the data in Table 2 show that the ΔH_{het}(N−NO)s obtained in the present work are, instead, all found to be substantially greater than the corresponding ΔH_{homo}(N−NO)s ($\Delta\Delta H$ ranging from 23.6 to 44.9 kcal/mol), indicating that the N−NO bonds would much favor generating NO$^\bullet$ rather than NO$^+$ or NO$^-$. A comparison of the present N−NO energetic data with those in the earlier work[11a] demonstrates that the ΔH_{het}/ΔH_{homo} gaps of the DPA derivatives are, generally, considerably larger than those of the *N*-carbonyl (or its analog)-bearing N−NO compounds. This suggests that the DPA compounds are both better NO$^+$ receptors and better NO$^\bullet$ donors, a feature believed to be important for modeling the NO transfer vehicles in vivo.[24] Further comparison of these two sets of data against the changes of their molecular structures shows that the energy gap between ΔH_{het} and ΔH_{homo} gets broader for an EDG (electron-donating group)-bearing DPA and narrower for an EWG (electron-withdrawing group)-bearing DPA (within se-

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(20) The agreements between the irreversible oxidation potentials of delocalized carbanion obtained from conventional cyclic voltammetry (CV) and the corresponding reversible potentials obtained from either the fast-scan CV[21] or the second-harmonic ac voltammetry[22] were generally observed to be within 50 mV.[21]

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Table 2. Heterolytic and Homolytic Dissociation Energies of N−NO Bonds in Compounds 1−14 and Their Radical Anions and of the Corresponding N−H Bonds at 25 °C[a]

compound	ΔH_{het}(N−NO)[b] (kcal/mol)	ΔH_{homo}(N−NO)[b] (kcal/mol)	ΔH(N−NO$^{-\bullet}$)[c] (kcal/mol)	$\Delta H'$(N−NO$^{-\bullet}$)[d] (kcal/mol)	pK_a[e] (DMSO)	BDE[f] (kcal/mol)
1	62.0	22.6	13.2	0.2	24.9[5]	87.7
2	65.8	21.0	16.5	−1.8	26.7	84.4
3	63.5	21.4	14.3	−1.3	25.8	85.8
4	62.5	21.4	13.5	−1.1	25.5	87.1
5	62.4	22.3	13.4	−0.2	25.3	87.8
6	60.2	24.1	11.3	1.7	23.0	88.6
7	50.2	24.3	2.1	2.8	16.8[5]	90.6
8	63.4	22.9	14.5	0.3	25.5	87.2
9	57.5	13.6	9.0	−8.4	21.66	80.0
10	62.8	19.2	13.8	−3.3	26.1	84.8
11	55.1	27.4	6.4	5.2	19.9	93.0
12	51.6	28.3	3.0	6.3	17.1[5]	93.8
13	57.7	29.7	8.8	7.3		
14	56.5	28.7	7.6	6.3	20.9[4]	94.1

[a] The N−NO bond energies and the N−H bond energies were obtained in acetonitrile and DMSO, respectively. Energy unit is kcal mol^{-1}. [b,c,d] From eqs 3, 4, and 5, respectively, taking $E_{1/2}$(NO$^+$/NO) = 0.863 V and $E_{1/2}$(NO/NO$^-$) = −0.287 V (vs Fc$^+$/Fc).[11b] Estimated uncertainties are 2 kcal mol^{-1}. [e] From early work (Bordwell, F. G.; Zhang, X.-M.; Cheng, J.-P. *J. Org. Chem.* **1991**, *56*, 3216). [f] Calculated by equation: BDE = 1.364pK_a + E_{ox}(N$^-$) + 73.6; equation from Cheng, J.-P.; Zhao, Y.; Haun, Z. *Sci. China Ser. B* **1995**, *38*, 1417.

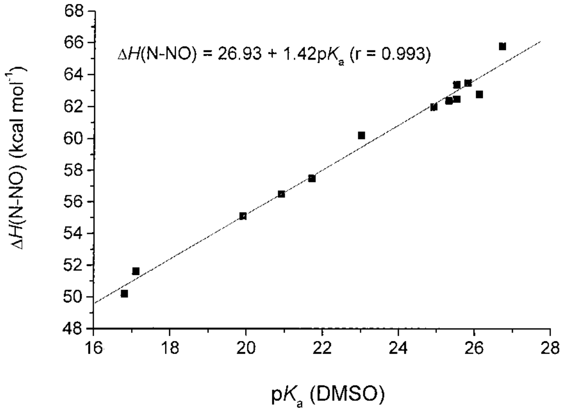

Figure 1. Correlation of the heats of heterolysis of N−NO bonds in compounds **1**−**12** and **14** with the corresponding pK_a's of their parent N−H molecules.

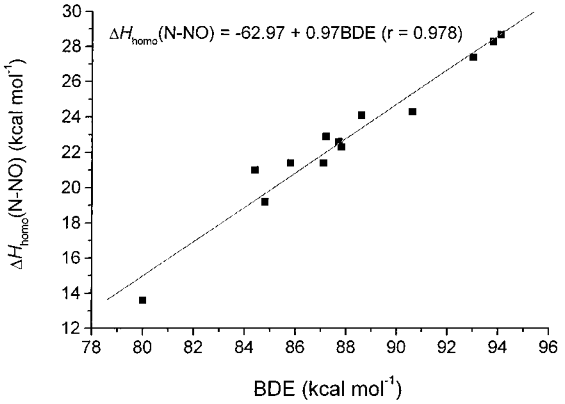

Figure 2. Correlation of the heats of homolysis of N−NO bonds in compounds **1**−**12** and **14** with the corresponding BDE (N−H) of their parent N−H molecules.

ries). This is because EDGs tend to stabilize the nitrogen radical but destabilize the nitranion (causing an decrease in ΔH_{homo} and an increase in ΔH_{het}, respectively), whereas the effect of EWGs is just the opposite. The greater stability of NO relative to that of NO$^+$ in acetonitrile also contributes to the lower ΔH_{homo} value [as judged from $E_{1/2}$(NO$^+$/NO) of 0.863 V, NO is almost 20 kcal/mol more stable than NO$^+$].[11a] The general suggestion that NO$^\bullet$ (rather than NO$^+$) as the major form play key roles in many chemical[25] and biological[26] systems is in line with the relative ease of N−NO homolysis versus heterolysis observed in the present work.

The N−NO bond heterolysis covers an energy range of 50.2−65.8 kcal/mol. The ΔH_{het} of the N−NO bonds was found to correlate linearly with the pK_a of the corresponding N−H acids in DMSO[27] (Figure 1r = 0.993). Similar linear correspondence was also observed in an earlier work on the ΔH_{het} of *N*-nitrosoureas.[11a] The much higher energy required for heterolytically breaking N−NO bonds as compared to N−H bonds ($\Delta\Delta H_{het}$ = 28.1 ± 0.6 kcal/mol, Table 2) may be attributed mainly to the substantially lower stability of nitrosonium ion compared to that of proton in solution.

Contrarily, the dramatically higher stability of the NO$^\bullet$ radical relative to the H$^\bullet$ radical, on the other hand, causes a huge weakening effect on the N−NO bonds. The N−NO bond strength is reduced by an average of 65.2 ± 0.8 kcal/mol compared to the BDEs of the corresponding N−H bonds (Table 2). The trend of ΔH_{homo}(N−NO) variation as induced by structural changes follows a pattern similar to that of the N−H bonds, as seen from the fair correlation (r = 0.977) between the BDEs of these two different types of bonds (Figure 2).

Bond Dissociation Energies of (N−NO)$^{-\bullet}$ Radical Anions; Effect of Reductive Electron Transfer on N−NO Bond Activation. Electron transfer is a widely occurring process in chemical and biological reactions and is known to have a strong influence on activating chemical bonds. One way to quantitate such effect, taking one-electron reduction of N−NO bond as an example, is to allow the strengths of both the R$_2$N−NO and (R$_2$N−NO)$^{-\bullet}$ bonds to be measured and to take the energy difference as the index. Unfortunately, quantities of this kind were estimated only in a few cases for some (C−

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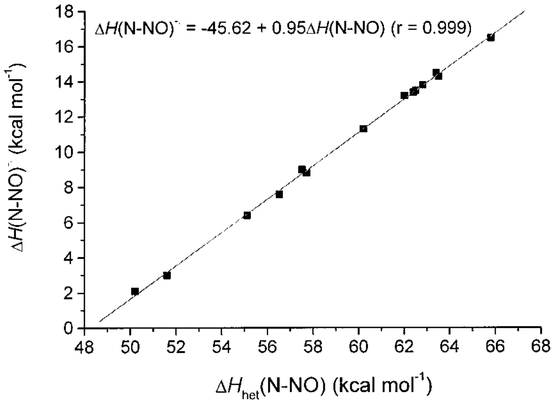

Figure 3. Correlation of $\Delta H(\mathrm{N-NO})^{-\bullet}$ with $\Delta H_{\mathrm{het}}(\mathrm{N-NO})$ (kcal/mol) for compounds **1**−**14**.

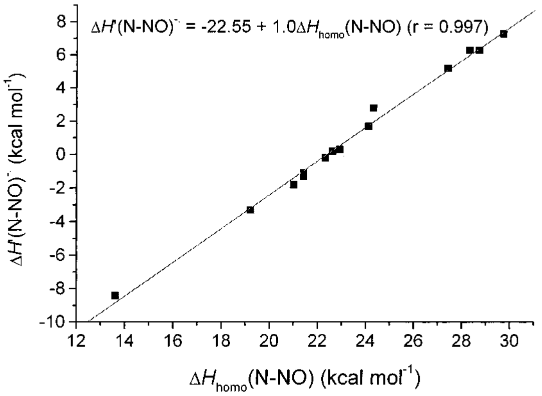

Figure 4. Correlation of $\Delta H'(\mathrm{N-NO})^{-\bullet}$ with $\Delta H_{\mathrm{homo}}(\mathrm{N-NO})$ (kcal/mol) for compounds **1**$^{-\bullet}$−**14**$^{-\bullet}$.

C)$^{-\bullet}$,[19a] (C−H)$^{-\bullet}$,[28] and (C−X)$^{-\bullet}$ bonds,[17b,18] and no such data for any (N−N)$^{-\bullet}$ bonds have yet been reported because of the high instability of radical anions. This knowledge is important, however, because NO-carriers such as the ones with *S*-nitroso residue, known as the key structure for NO transportation in vivo,[29] are believed to undergo rapid (S−NO)$^{-\bullet}$ bond dissociation upon one-electron reduction.[6] In the present work, we present the first series of (Y−NO)$^{-\bullet}$ bond energy data for **1**$^{-\bullet}$−**14**$^{-\bullet}$ as shown in Table 2, in which $\Delta H(\mathrm{N-NO})^{-\bullet}$ denotes the energy required for an NO-generating decomposition whereas $\Delta H'(\mathrm{N-NO})^{-\bullet}$ for an NO$^-$-generating decomposition (Scheme 2).

A simple comparison of the $\Delta H(\mathrm{N-NO})^{-\bullet}$ and ΔH_{het}(N−NO) data immediately indicates that breaking an (N−NO)$^{-\bullet}$ bond requires remarkably less energy than breaking a neutral N−NO bond of the same structure. The effect of one-electron addition on N−NO bond activation is, surprisingly, observed to be quite independent of either a vicinal or a remote structural variation in diarylamine, as seen from the nearly constant energy difference of 48.8 ± 0.3 kcal/mol (i.e., $\Delta\Delta H$, cf. Table 2). The constant bond-activation effect can be understood, however, if one considers the relationship of these two energetic quantities in eq 4 with an almost constant redox potential of the *N*-nitroso compounds (see Table 1). The insensitivity of $E_{\mathrm{red}}(\mathrm{N-NO})$ to the changes of either remote substituent or vicinal structure suggests that the NO moiety serve as the sink of electrons for all *N*-nitroso compounds **1**−**14**, probably as a result of the favorable driving force for the follow-up (N−NO)$^{-\bullet}$ bond rupture (see $\Delta H^{-\bullet}$ data in Table 2). In fact, the $\Delta H(\mathrm{N-NO})^{-\bullet}$ values estimated in this work are as low as 2.1−16.5 kcal/mol, which indeed indicate a spontaneous bond dissociation at room temperature. The nearly constant $E_{\mathrm{red}}(\mathrm{N-NO})$ leads to an excellent linear correspondence of the $\Delta H(\mathrm{N-NO})^{-\bullet}$ with $\Delta H_{\mathrm{het}}(\mathrm{N-NO})$ ($r = 0.9994$) as expected (Figure 3). Similarly, there exist good correlation of the $\Delta H(\mathrm{N-NO})^{-\bullet}$ values with pK_a's ($r = 0.9939$) and with σ^- values ($r = 0.9938$) (within the DPA family). All these suggest that the factors governing the nitranion-generating N−NO dissociation, no matter for neutrals or for anion radicals, should function in a quite similar manner.

Effect of one-electron addition on weaking the N−NO bond can also be examined by comparing the $\Delta H'(\mathrm{N-NO})^{-\bullet}$ data (−8.4 to 7.3 kcal/mol) with N−NO homolysis energies (ΔH_{homo}) in Table 2 (see Figure 4). Inspection of these data demonstrates that the homolytic N−NO bond dissociation is further activated upon one-electron reduction by 22.3 ± 0.3 kcal/mol and therefore can spontaneously take place. Linear free energy relationship among the energetics of the nitrogen-radical-generating processes also holds well for these systems [$\Delta H'(\mathrm{N-NO})^{-\bullet}$ versus $\Delta H_{\mathrm{homo}}(\mathrm{N-NO})$, ($r = 0.997$); $\Delta H'(\mathrm{N-NO})^{-\bullet}$ versus BDE ($r = 0.9873$)]. It is also noted by comparing the $\Delta H^{-\bullet}$ and $\Delta H^{-\bullet\prime}$ data in Table 2 that in most cases the nitrogen-radical-generating N−NO dissociation (to release NO$^-$) in acetonitrile is energetically favored over the nitranion-generating N−NO dissociation (to release NO) presumably as a result of the better solvation of NO$^-$ relative to that of NO$^\bullet$. The NO$^-$ anion is also known as a physiologically active species in living body.[30]

Worthy of pointing out also is that all the *N*-nitroso substrates studied in this work can be considered as fairly good electron acceptor because their reduction potentials (−1.22 to −1.27 V vs Fc$^{+\bullet}$/Fc, Table 1) are in the vicinity of those of the typical electron acceptors such as CBr$_4$ and CHI$_3$ ($E_{\mathrm{red}} = -1.25$ and -1.29 V vs Fc$^+$/Fc, respectively).[17b] The reductive electron transfer may be also assisted by the follow-up reactions of radical anions (see data in Table 2). Although the actual biological environment may make a substantial difference, the NO-bearing DPAs can still be likely good candidates in many cases for modeling both electron and NO reservoir molecules in vivo.[15,16]

Application of Driving-Force Analysis on Differentiating Mechanistic Possibilities As Exemplified by Nitrosation of Nitranions. In a preceding paper on this issue,[31] we showed that nitrosation of dibromocarbazolide ion (**4**$^-$) by NO proceeded first by electrophilic combination of NO with N$^-$ to yield an N−NO$^{-\bullet}$ radical anion, which then transferred an electron to NO to wind up the reaction. Now this work has been extended to include all of the 14 structurally related

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Scheme 3

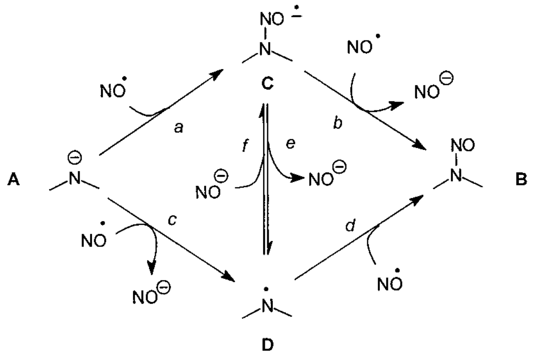


Table 3. Energetics (kcal mol^{-1}) of Each Mechanistic Step Shown in Schemes 3 and 4[a]

	ΔH				
substrate	**a**[b]	**b**[c]	**c**[d]	**d**[e]	**e**[f]
			Group I		
1	−13.2	−22.4	−13.0	−22.6	0.2
2	−16.5	−22.8	−18.3	−21.0	−1.8
3	−14.3	−22.7	−15.6	−21.4	−1.3
4	−13.5	−22.5	−14.6	−21.4	−1.1
5	−13.4	−22.5	−13.6	−22.3	−0.2
6	−11.3	−22.4	−9.6	−24.1	1.7
7	−2.1	−19.9	0.7	−22.6	2.8
8	−14.5	−22.6	−14.2	−22.9	0.3
			Group II		
9	−9.0	−22.0	−17.4	−13.6	−8.4
10	−13.8	−22.5	−17.1	−19.2	−3.3
			Group III		
11	−6.4	−22.0	−1.2	−27.2	5.2
12	−3.0	−22.0	3.3	−28.3	6.3
13	−8.8	−22.4	−1.5	−29.7	7.3
14	−7.6	−22.4	−1.3	−28.7	6.3

[a] All values were derived in CH_3CN at 25 °C in kcal/mol. [b] From eq 6. [c] From eq 7. [d] From eq 8. [e] From eq 9. [f] From eq 10.

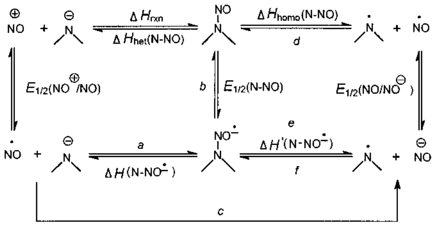
nitranions ($\mathbf{1^-}$−$\mathbf{14^-}$) with a much broader energetic range, to allow a more general mechanistic spectrum to be outlined on the basis of a detailed analysis on the energetics of each feasible elementary steps. The general mechanism diagram of nitrosation is depicted in Scheme 3. The energies related therein can be evaluated on the basis of appropriate cycles shown in Scheme 4 using the respective eqs 6−10.[31] The data derived are summarized in Table 3.

The most eye-catching feature of the data in Table 3 is that the energy changes of all the elementary steps (**a**−**g**) are either exothermic or only slightly endothermic, indicating that nitrosation of these nitranions would readily take place and quickly go to completion. The experimentally observed clean and rapid reactions in this work (see Experimental Section) and in an earlier study[31] do in fact support this expectation based on the energetic analysis.

The energetic characteristics of these 14 reactions are not all exactly the same, however. The grouping suggested in Table 3 was based on their thermodynamic similarity of the reactions. For group III (i.e., **11**−**14**), the driving forces of the electrophilic combination step (**a**) are all greater than those of the competing electron-transfer step (**c**), and the driving forces of another electron-transfer step (**b**) are all greater than those of the alternative path (**e**). Therefore, the **a**,**b** mechanism can be proposed for these reactions. As an example of this group of reactions, the nitrosation of compound **4** with NO was investigated by a detailed energetic and product analysis that indeed supports the proposed mechanism.[31]

The thermodynamic feature of the group II reactions (i.e., **9** and **10**) is quite different from the one described above. It is clear that the driving forces of the direct electron transfer to NO (step **c**) and that of the follow-up radical coupling (step **d**) are both energetically more favorable than those of the potentially competing alternative routes (**a**) and (**f**). Therefore, the **c**,**d** mechanism would be most suitable for these reactions. As for group III, because the two possible initiating steps (i.e., **a** and **c**) are energetically very close to each other, and the energetics of their corresponding follow-up reactions (**b**) and (**d**) are also similar, it is expected that no single mechanism could be dominant for these reactions. In other words, the reaction mechanism would most likely be a balanced combination of the two extremes. Though the scope of the present research limited us from a scrupulous experimental confirmation of all the mechanisms for these 14 reactions, the similar energetic analysis for differentiating the mechanistic possibilities of NAD(P)H model reactions was indeed widely supported by experimental observation,[32] giving confidence to the analytical strategy herein applied. Therefore, we believe that the mechanistic guidelines suggested here should be of value in analyzing or predicting the mechanisms of some relevant NO-related transformations.

Scheme 4



Steps:

a: $\Delta H_a = -\Delta H_{het}(\text{N-NO}^{\cdot-}) = -\Delta H_{het}(\text{N-NO}) - F[E_{1/2}(\text{N-NO}) - E_{1/2}(\text{NO}^+/\text{NO})]$ (6)

b: $\Delta H_b = -F[E_{1/2}(\text{NO}/\text{NO}^-) - E_{1/2}(\text{N-NO})]$ (7)

c: $\Delta H_c = -F[E_{1/2}(\text{NO}/\text{NO}^-) - E_{ox}(\text{N}^-)]$ (8)

d: $\Delta H_d = -\Delta H_{homo}(\text{N-NO}) = -\Delta H_{het}(\text{N-NO}) + F[E_{1/2}(\text{NO}^+/\text{NO}) - E_{ox}(\text{N}^-)]$ (9)

e: $\Delta H_e = \Delta H_{homo}(\text{N-NO}^{\cdot-}) = \Delta H_{homo}(\text{N-NO}) + F[E_{1/2}(\text{N-NO}) - E_{1/2}(\text{NO}/\text{NO}^-)]$ (10)

Conclusion

Four sets of N−NO bond dissociation energies of 14 *N*-nitroso diphenylamine derivatives (or the analogues) (**1**−**14**) and their radical anions ($\mathbf{1}^{-\bullet}$−$\mathbf{14}^{-\bullet}$) were first determined in solution. It can be concluded that (i) homolysis of the N−NO bonds is more likely to take place than the corresponding heterolysis in solution; (ii) the large $\Delta H_{het}/\Delta H_{homo}$ gaps of the DPA (and analogue) derivatives indicate that they are good models for NO reservoir molecules; (iii) one-electron reduction has a remarkable and almost constant effect on N−NO bond activation for both homolysis (by 22.3 ± 0.3 kcal) and heterolysis (by 48.8 ± 0.3 kcal); (iv) good linear free energy relationship holds for the energetics of the nitranion-generating decompositions [i.e., ΔH_{het}(N−NO), ΔH(N−NO)$^{-\bullet}$, and pK_a] and of the decompositions generating a nitrogen radical [i.e., ΔH_{homo}(N−NO), $\Delta H'$(N−NO)$^{-\bullet}$, and BDE], suggesting that the governing factor for these bond scissions be similar; and (v) the analysis on the driving forces for each elementary process (Scheme 3) can provide informative guidelines for differentiating various mechanistic possibilities.

Experimental Section

All reagents were of commercial quality from freshly opened containers or were purified before use. Reagent grade acetonitrile was refluxed over $KMnO_4$ and K_2CO_3 for several hours and was doubly distilled over P_2O_5 under argon before use. The commercial tetrabutylammonium hexafluorophosphate (Bu_4NPF_6, Aldrich) was recrystallized from CH_2Cl_2 and was vacuum-dried at 110 °C overnight before preparation of supporting electrolyte. The nitrosating reagent $NO^+ClO_4^-$ was prepared by a literature method.[33] All of the precursor diphenylamine and indole compounds were either Aldich products or gifts from Prof. Arnett or were prepared previously in this laboratory. Compounds **1**−**14** generated from nitrosation of the corresponding nitranions by NO or NO^+ were confirmed by comparison with the authentic samples specially prepared. Redox potentials were obtained by CV on a BAS-100B electrochemical analyzer. The heats of reaction of NO^+ with nitranions were determined on a Tronac 458 titration calorimeter.

Titration Calorimetry. Reaction of NO^+ ($NO^+ClO_4^-$) with nitranions (K^+ as counterion) in dry CH_3CN was rapid and clean, giving coupling product in nearly quantitative yield. The reaction heat (ΔH_{rxn}) was measured at 25 °C by a standard procedure similar to that of Arnett.[22] The performance of the calorimeter was checked by measuring the standard heat of neutralization of an aqueous solution of sodium hydroxide with a standard aqueous HCl solution. The MeCN solution of $NO^+ClO_4^-$ (0.1 M) was prepared inside the argon-filled drybox with an analytical balance and volumetric flask before each calorimetric run. The calibrated motor-driven buret, filled with 2 mL of NO^+ solution, and the reaction vessel, containing about 40 mL of nitranion solution (in excess), were connected to the calorimeter insert assembly. A dry argon atmosphere was maintained at the top of the reaction vessel to protect anions from unexpected reaction. The heat of dilution of nitrosonium perchlorate was small enough to be neglected for heat of reaction measurements. The reported ΔH_{rxn} is the average value of two or three independent runs, which consisted of up to six titrations with the same stock solution.

General Procedure for Preparation of Anions. The method of E. M. Arnett et al.[22] was followed: The anion precursor (0.2 mmol) was dissolved in 40 mL of dry acetonitrile, and then a slightly excess amount of KH was added. The mixture was stirred at room temperature for about 20 min, and then filtered directly into the reaction vessel. All operations were carried out in an argon-filled VAC drybox.

Measurement of Redox Potentials. All electrochemical experiments were carried out by CV (sweep rate, 100 mV/s) using a BAS-100B electrochemical apparatus in dry CH_3CN solution under an argon atmosphere as described previously.[34] *n*-Bu_4NPF_6 (0.1 M) was employed as the supporting electrolyte. A standard three-electrode cell consists of a glassy carbon disk as working electrode, a platinum wire as counter electrode, and 0.1 M $AgNO_3$/Ag (in 0.1 M Bu_4NPF_6−MeCN) as reference electrode. All sample solutions were 1.5 mM. The ferrocenium/ferrocene redox couple (Fc^+/Fc) was taken as the internal standard. The reproducibility of the potentials (iR compensated) was usually ≤5 mV for ionic species and ≤10 mV for neutral species.

Preparation of NO Gas. NO gas was produced by reaction of $NaNO_2$ with sulfuric acid in the absence of oxygen and was purified by passing through 10% $NaOH_{aq}$ to remove higher oxides of nitrogen and finally through a solid NaOH dry tube to remove water.[35]

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Supporting Information Available: Correlation of the heats of heterolysis of N−NO bonds in compounds $\mathbf{1}^{-\bullet}$−$\mathbf{12}^{-\bullet}$ and $\mathbf{14}^{-\bullet}$ with the corresponding pK_a's of their parent N−H molecules, correlation of the heats of homolysis of N−NO bonds in compounds $\mathbf{1}^{-\bullet}$−$\mathbf{12}^{-\bullet}$ and $\mathbf{14}^{-\bullet}$ with the corresponding BDE (N−H) of their parent N−H molecules, and correlations of the heats of heterolysis of N−NO bonds in compounds **1**−**4** and **7** and the heats of $NO^\bullet$-generating dissociation of radical anions $\mathbf{1}^{-\bullet}$−$\mathbf{4}^{-\bullet}$ and $\mathbf{7}^{-\bullet}$ against the Hammett constants of the *para*-substituents. This material is available free of charge via the Internet at http://pubs.acs.org.

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