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An Assessment of Theoretical Methods for the Calculation of Accurate Structures and S−N Bond Dissociation Energies of *S*-Nitrosothiols (RSNOs)

Cristina Baciu and James W. Gauld*

Department of Chemistry and Biochemistry, University of Windsor, Windsor, Ontario N9B 3P4, Canada

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The ability of conventional electron correlation (MP2 and QCISD) and density functional theory (B3LYP and B3P86) methods to provide accurate and reliable optimized structures, and homolytic S−N bond dissociation energies (BDEs), for a range of *S*-nitrosothiols (RSNOs) has been investigated. It is found that, in general, for any given method the 6-311+G(2df,p) or larger basis set must be used to obtain reliable structures. With a suitably large basis set, the different methods generally give optimized structures in close agreement with each other. However, the B3LYP method consistently overestimates the RS−NO bond length. The trends observed are found to be due in part to the fact that the RS−NO bond does not possess considerable double-bond character as previously suggested, but rather is a long single S−N bond, with the −NO moiety possessing considerable multiple-bond character. The B3P86/6-311+G(2df,p) method consistently gives BDEs in best agreement with values obtained with higher accuracy methods, e.g., CBS-Q, while the B3LYP method increasingly underestimates BDEs with increasing RSNO size. In contrast, for all RSNOs, the QCISD method significantly underestimates BDEs by as much as 55 kJ mol^{-1}. Overall, the B3P86/6-311+G(2df,p) method is found to perform the best of the methods considered for obtaining optimized structures and homolytic S−N BDEs of *S*-nitrosothiols.

1. Introduction

Since 1990, there has been increasing interest in *S*-nitrosothiols (RSNOs), species containing an −SNO functional group, due to the fact that they have been found to be formed in vivo as part of the metabolism of nitric oxide (NO),[1−3] an important biological messenger. In particular, they are thought to be a means of transporting and storing NO within the body.[1−6] Furthermore, they often show many of the same biological properties as NO including vasodilation of arteries and inhibition of platelet aggregation.[5,7−11] Unfortunately, due in part to the fact that they are usually highly reactive, have short lifetimes, and are readily decomposed by heat, light, or Cu$^+$ ions, experimental studies on RSNOs are often quite difficult.[12,13] As a result, our current level of understanding of many of the fundamental properties of this important class of compounds, and their chemistry, is unsatisfactory.

Computational chemistry would seem to offer an attractive alternative approach for investigations on RSNOs, particularly as studies of highly reactive species are generally as straightforward as those of stable long-lived species. However, it can have its own inherent difficulties, not the least of which is determining a reliable and accurate level of theory for investigating chemical properties of interest, e.g., bond dissociation energies.

Recently, several theoretical studies on homolytic S−N bond dissociation energies (BDEs) of RSNOs have appeared in the literature.[4,14−17] In general, they have employed the common approach of performing large single-point or composite method, e.g., G3[18] or CBS,[19] calculations, based on optimized structures obtained at considerably lower levels of theory. More specifically, structures used in these studies have been obtained by using the Hartree−Fock, MP2, or density functional theory (DFT) B3LYP method, in conjunction with a modest basis set, generally 6-31G(d) or smaller. Typically, such levels of theory provide reliable structures for well-behaved species. However, no previous theoretical investigations[4,14−17] have considered their reliability for *S*-nitrosothiols. Indeed, optimized structures of RSNOs obtained by using such methods contain S−N bond lengths that vary considerably, from as short as 1.75 Å[16] to almost 2.05 Å.[16] This range and size is all the more remarkable considering it has been suggested that the RS−NO bond possesses considerable double-bond character.[15,16,20] Hence, it is unclear whether such variable optimized lengths are artifacts of the methods employed, or indicative of the nature of the RS−NO bond. In addition, such significant differences can potentially affect, for example, the reliability of calculated S−N BDEs based on such structures. Indeed, previously calculated S−N BDEs[4,14−17] differ considerably from each other for some particular RSNOs by as much as 40 kJ mol^{-1}.[16] Furthermore, they also differ from the corresponding experimentally determined BDE by more than 30 kJ mol^{-1}.[16] Considering the potential utility of computational chemistry for studying such species, this is an unsatisfactory situation.

The aim of this present study is to assess the ability of a range of commonly employed theoretical methods, in particular DFT methods, to obtain reliable structures and homolytic S−N BDEs of *S*-nitrosothiols. The methods considered are the conventional electron correlation methods MP2 and QCISD and the DFT methods B3LYP and B3P86. A variety of model RSNOs (HSNO, CH_3SNO, C_2H_3SNO, C_2H_5SNO, C_6H_5SNO, and CysSNO (*S*-nitroso-cysteine)) have been used. These were chosen to provide both various sized RSNOs and a range of R groups used in previous experimental and theoretical studies, hence enabling greater comparison.

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* To whom correspondence should be addressed. E-mail: gauld@uwindsor.ca.

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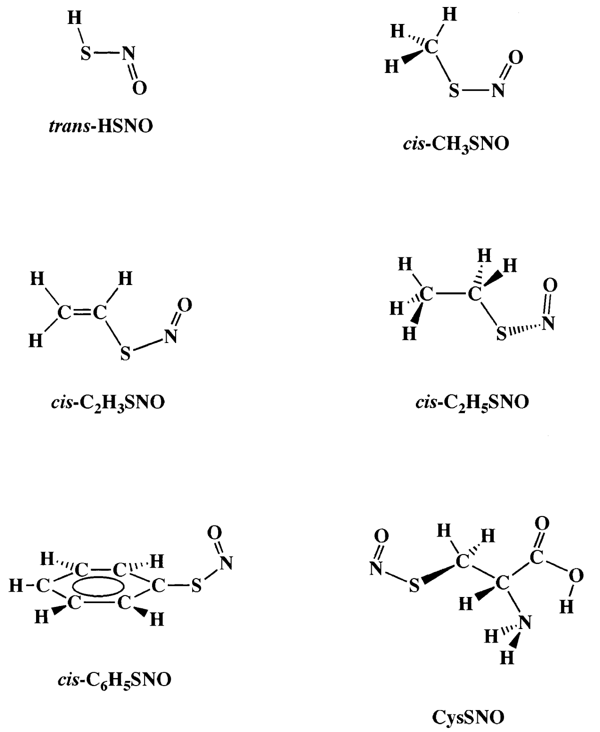

Figure 1. Schematic illustration of the structures of the *S*-nitrosothiols (RSNOs) considered in this present study.

2. Computational Methods

All geometry optimizations were performed with the Gaussian 98 and Gaussian 03 suite of programs.[21] Optimized geometries were obtained by using a variety of methods: the conventional electron-correlation methods MP2 and QCISD, and density functional theory methods. For the DFT methods, Becke's three-parameter hybrid exchange functional[22] as implemented in Gaussian 98,[23] with the Lee−Yang−Parr correlation functional[24] (B3LYP) or with Perdew's nonlocal correlation functionals[25] (B3P86) were employed. All methods were used in combination with basis sets ranging from 6-31G(d) to 6-311++G(3df,3pd), depending on the size of molecule being investigated. Zero-point vibrational energy (ZPVE) corrections were also calculated at these levels of theory, and scaled by an appropriate factor.[26] For each RSNO, S−N homolytic bond dissociation energies were calculated by using a variety of methods, each being corrected with appropriately scaled ZPVEs (see text). Restricted and unrestricted procedures were used for all closed- and open-shell species, respectively. All bond dissociation energies are in kJ mol^{-1} and bond lengths in Å, unless otherwise noted. Optimized geometries obtained for species considered in this present study are given in the Supporting Information (Tables S1 and S2).

3. Results and Discussion

The *S*-nitrosothiols examined in this present study are shown schematically in Figure 1. In all cases, the most significant structural changes occur in the S−N and N−O bond lengths. Thus, the following discussion is limited to these parameters, unless otherwise noted.

Optimized Geometries: HSNO. HSNO, being the smallest *S*-nitrosothiol, was examined with use of the broadest range of methods and basis sets (Table 1). Unlike all other RSNOs presently considered, the lowest energy conformer of HSNO is trans (anti) with the cis (syn) conformer lying just a few kJ mol^{-1} higher in energy. Typically, primary and secondary RSNOs prefer a syn, and tertiary an anti, conformation.[27] For completeness, selected optimized parameters of both conformers are given in Table 1. As the trends observed are essentially the same for both, the following discussion is limited to the trans conformer, unless otherwise noted.

TABLE 1: Selected Optimized Parameters[a] for *trans*- and *cis*-HSNO

		r(S−N)		*r*(H−S)		*r*(N−O)	
method	basis set	trans	cis	trans	cis	trans	cis
MP2	6-31G(d)	1.850	1.827	1.341	1.347	1.205	1.211
	6-31G(d,p)	1.853	1.832	1.331	1.338	1.204	1.209
	6-311G(d,p)	1.891	1.852	1.333	1.340	1.179	1.188
	6-311+G(d,p)	1.850	1.818	1.334	1.342	1.188	1.195
	6-311G(2d,p)	1.929	1.905	1.333	1.339	1.175	1.181
	6-311G(df,p)	1.827	1.794	1.335	1.344	1.186	1.193
	6-311+G(2df,p)	1.826	1.799	1.340	1.348	1.191	1.197
	6-311++G(3df,3pd)	1.810	1.785	1.333	1.341	1.191	1.197
QCISD	6-31G(d)	1.863	1.851	1.346	1.352	1.194	1.197
	6-31G(d,p)	1.864	1.853	1.334	1.339	1.193	1.197
	6-311G(d,p)	1.878	1.860	1.336	1.342	1.175	1.179
	6-311+G(d,p)	1.855	1.838	1.338	1.344	1.179	1.184
	6-311G(2d,p)	1.890	1.878	1.334	1.340	1.174	1.177
	6-311G(df,p)	1.834	1.814	1.338	1.345	1.176	1.180
	6-311+G(2df,p)	1.834	1.818	1.342	1.349	1.179	1.182
	6-311++G(3df,3pd)	1.820	1.804	1.347	1.342	1.179	1.182
B3LYP	6-31G(d)	1.913	1.901	1.349	1.355	1.175	1.178
	6-31G(d,p)	1.914	1.904	1.348	1.353	1.174	1.178
	6-311G(d,p)	1.942	1.928	1.347	1.353	1.160	1.164
	6-311+G(d,p)	1.910	1.894	1.347	1.354	1.166	1.170
	6-311G(2d,p)	1.922	1.909	1.342	1.348	1.163	1.166
	6-311G(df,p)	1.926	1.905	1.347	1.353	1.161	1.165
	6-311+G(2df,p)	1.874	1.857	1.344	1.351	1.169	1.172
	6-311++G(3df,3pd)	1.870	1.852	1.341	1.349	1.168	1.172
B3P86	6-31G(d)	1.881	1.867	1.345	1.352	1.174	1.178
	6-31G(d,p)	1.883	1.870	1.344	1.351	1.174	1.177
	6-311G(d,p)	1.903	1.884	1.344	1.351	1.161	1.165
	6-311+G(d,p)	1.878	1.860	1.345	1.353	1.165	1.169
	6-311G(2d,p)	1.882	1.867	1.340	1.346	1.164	1.167
	6-311G(df,p)	1.887	1.864	1.344	1.351	1.162	1.167
	6-311+G(2df,p)	1.843	1.824	1.342	1.350	1.168	1.173
	6-311++G(3df,3pd)	1.839	1.820	1.340	1.347	1.168	1.172

[a] Bond lengths are in angstroms.

For the MP2 method with the smallest basis set used in this study, 6-31G(d), the trans and cis conformers have S−N bond lengths (*r*(S−N)) of 1.850 and 1.827 Å, respectively (Table 1). The inclusion of p-functions on hydrogen (6-31G(d) → 6-31G(d,p)) has minimal affect. Improving the valence description from double- to triple-ζ (6-31G(d,p) → 6-311G(d,p)), however, has a larger affect on the S−N bond, lengthening it by almost 0.04 Å to 1.891 Å. Further augmentation of the basis set by inclusion of diffuse functions on non-hydrogen atoms (6-311G(d,p) → 6-311+G(d,p)) decreases *r*(S−N) by approximately 0.04 Å, while inclusion of a second set of d-functions (6-311G(d,p) → 6-311G(2d,p)) has a similar-sized but opposite affect, i.e., *r*(S−N) increases by almost 0.04 Å. Inclusion of f-functions (6-311G(d,p) → 6-311G(df,p)), however, dramatically shortens the S−N bond by more than 0.06 Å to 1.827 Å. Consequently, at the MP2/6-311+G(2df,p) level, in which these basis set enhancements are combined, the S−N bond (1.826 Å) is shorter relative to that obtained at the MP2/6-311G(d,p) level (1.891 Å), by about 0.06 Å. We note that the length is close to that obtained with the smaller 6-311G(df,p) basis set (1.827 Å). Improving the basis set to 6-311++G(3df,3pd), the largest used in this study, results in only a slight decrease in *r*(S−N) to 1.810 Å.

For the QCISD method, similar trends to those described for the MP2 method are observed (Table 1). However, the size of the changes observed for the *r*(S−N) is now more tempered. For example, including a second set of d-functions (6-311G-

(d,p) → 6-311G(2d,p)) increases r(S−N) by just 0.012 Å, less than half that observed with the MP2 method. Furthermore, including diffuse or f-functions (6-311G(d,p) → 6-311+G(d,p) or 6-311G(df,p)) decreases r(S−N) by about 0.02 and 0.04 Å, respectively, for both conformers. While these are nonnegligible changes, they are smaller than those observed for the MP2 method. At the QCISD/6-311++G(3df,3pd) level, the S−N bond length in *trans*-HSNO is 1.820 Å, close to that obtained with the smaller 6-311+G(2df,p) and 6-311G(df,p) basis sets (both 1.834 Å), see Table 1.

The DFT methods B3LYP and B3P86 exhibit similar basis set affects to each other, which differ from those observed for the conventional MP2 and QCISD methods. With the 6-31G(d) basis set, the B3LYP and B3P86 methods give optimized S−N bond lengths for *trans*-HSNO of 1.913 and 1.881 Å, respectively, longer than obtained at the corresponding MP2 and QCISD levels (Table 1). Increasing the basis set from 6-31G(d) to 6-311G(d,p) lengthens the S−N bond by 0.02−0.03 Å. The B3LYP method exhibits the largest increase, resulting in a quite long S−N bond length of 1.942 Å. Improving the 6-311G(d,p) basis set by including diffuse, and a second set of d- or a set of f-functions results in modest decreases in the optimized values of r(S−N) by 0.016−0.032 Å. When each of these basis set enhancements is combined in the 6-311+G(2df,p) basis set, the B3LYP method still predicts a considerably longer S−N bond length (1.874 Å) than *any* of the other methods. In contrast, the B3P86 method now gives an S−N length of 1.843 Å, in reasonable agreement with the QCISD/6-311+G(2df,p) value of 1.834 Å (see Table 1). Improving the basis set to 6-311++G(3df,3pd) causes only minor decreases in r(S−N) of much less than 0.01 Å. At the B3LYP/6-311++G(3df,3pd) and B3P86/6-311++G(3df,3pd) levels, the S−N bond lengths of *trans*-HSNO are 1.870 and 1.839 Å, respectively. We note that while the agreement between the QCISD and B3P86 methods is slightly worse with this larger basis set, they still agree within 0.02 Å.

Optimized H−S and N−O bond lengths are also included in Table 1. They are noticeably less sensitive to basis set changes than the S−N bond. Indeed, the largest single change observed for all methods occurs in the N−O bond upon going from 6-31G(d,p) to 6-311G(d,p), which shortens by 0.025 Å or less. It is interesting to note, however, that the DFT methods consistently predict slightly shorter N−O distances than the QCISD method, which are shorter than those obtained with the MP2 method, see Table 1.

An explanation for the trends noted above, i.e., sensitivity of r(S−N) to the basis set employed and the requirement for extensive basis sets, e.g., 6-311+G(2df,p), before convergence in its optimized length for a given method is achieved, is suggested by considering the pertinent bonds in $HSNH_2$, HNO, and NO. Formally, $HSNH_2$ contains an S−N single bond[28,29a] and HNO an N−O double bond, while NO has a bond order of 2.5.[29b] Selected optimized parameters of these species obtained with the 6-311+G(2df,p) basis set in conjunction with each method are listed in Table 2. It can be seen that the optimized r(S−N) values for HSNO are all 0.10−0.15 Å greater than those obtained for $HSNH_2$ at the same level of theory. Thus, the S−N bond in HSNO does not possess considerable double bond character as previously thought,[15,16,20] but instead is a long single bond. An explanation for this bond character is suggested by considering the N−O length in HSNO, which is between that of r(N−O) in HNO and NO (cf. Table 1). That is, the −NO moiety in HSNO retains significant multiple-bond character, less than that of NO but enhanced relative to HNO, consequently reducing its participation in the S−N bond, hence its lengthening. The sensitivity of long bonds to the method and basis set employed, i.e., the accuracy of the description of such longer range interactions between moieties, has been noted previously.[30] Thus, the trends noted above are a direct consequence of the long single-bond nature of the RS−NO bond. In addition, the above results suggest that the B3LYP method overestimates the length of such bonds, while the MP2 method is the most sensitive to the description of the orbitals involved, i.e., basis set. We note that a long single RS−NO bond may help explain the experimentally observed high labililty of the NO moiety in RSNOs.

TABLE 2: Selected Optimized Parameters[a] for *trans*-$HSNH_2$, HNO, and NO Obtained by Using the 6-311+G(2df,p) Basis Set with Various Methods

	r(S−N)	r(N−O)	
method	$HSNH_2$	HNO	NO
MP2	1.717	1.219	1.137
QCISD	1.721	1.204	1.152
B3LYP	1.724	1.198	1.146
B3P86	1.709	1.193	1.142

[a] Bond lengths are in angstroms.

TABLE 3: Selected Optimized Parameters[a] for *cis*-CH_3SNO

method	basis set	r(S−N)	r(C−S)	r(N−O)
MP2	6-31G(d)	1.811	1.795	1.214
	6-311G(d,p)	1.837	1.789	1.191
	6-311+G(d,p)	1.806	1.791	1.198
	6-311G(2d,p)	1.858	1.797	1.191
	6-311G(df,p)	1.783	1.783	1.196
	6-311+G(2df,p)	1.776	1.790	1.202
	6-311++G(3df,3pd)	1.761	1.784	1.203
QCISD	6-31G(d)	1.834	1.805	1.201
	6-311G(d,p)	1.846	1.801	1.183
	6-311+G(d,p)	1.828	1.804	1.186
	6-311G(2d,p)	1.852	1.809	1.183
	6-311G(df,p)	1.802	1.795	1.184
	6-311+G(2df,p)	1.799	1.801	1.187
B3LYP	6-31G(d)	1.867	1.813	1.187
	6-311G(d,p)	1.887	1.809	1.174
	6-311+G(d,p)	1.861	1.812	1.179
	6-311G(2d,p)	1.864	1.807	1.177
	6-311G(df,p)	1.865	1.808	1.175
	6-311+G(2df,p)	1.821	1.804	1.182
	6-311++G(3df,3pd)	1.814	1.799	1.182
B3P86	6-31G(d)	1.835	1.796	1.186
	6-311G(d,p)	1.848	1.792	1.175
	6-311+G(d,p)	1.829	1.795	1.178
	6-311G(2d,p)	1.827	1.790	1.178
	6-311G(df,p)	1.829	1.791	1.176
	6-311+G(2df,p)	1.793	1.787	1.182
	6-311++G(3df,3pd)	1.787	1.783	1.181

[a] Bond lengths are in angstroms.

Optimized Geometries: CH_3SNO. This next largest alkyl *S*-nitrosothiol was also examined with the broadest range of basis sets, to enable greater comparison with the prototypical RSNO, HSNO. The lowest energy conformer is cis, with one of the methyl hydrogens directed toward the oxygen (see Figure 1). Selected optimized parameters are listed in Table 3.

The same trends upon increasing the basis set for each method are observed as previously described for HSNO. For example, for the MP2 and QCISD methods, inclusion of diffuse or f-functions (6-311G(d,p) → 6-311+G(d,p) or 6-311G(df,p)) causes the S−N bond to shorten by 0.02−0.05 Å, while inclusion of d-functions lengthens it by 0.01−0.02 Å. As for HSNO, the largest changes in r(S−N) for any basis set enhancement occur for the MP2 method. In addition, for both

TABLE 4: Optimized S−N and N−O Bond Lengths[a] for Cis Conformers of CH_2CHSNO, CH_3CH_2SNO, C_6H_5SNO, and CysSNO

		CH_2CHSNO		CH_3CH_2SNO		C_6H_5SNO		CysSNO	
method	basis set	*r*(S−N)	*r*(N−O)	*r*(S−N)	*r*(N−O)	*r*(S−N)	*r*(N−O)	*r*(S−N)	*r*(N−O)
MP2	6-311G(d,p)	1.883	1.184	1.806	1.201	2.097	1.154	1.955	1.170
	6-311G(df,p)	1.800	1.194	1.762	1.204	1.900	1.174	1.791	1.197
	6-311+G(2df,p)	1.803	1.197	1.760	1.210	1.937	1.171	1.795	1.201
QCISD	6-311G(d,p)	1.866	1.180	1.833	1.187	1.906	1.173		
	6-311G(df,p)	1.816	1.181	1.792	1.188				
B3LYP	6-311G(d,p)	1.920	1.169	1.883	1.175	1.966	1.161	1.921	1.167
	6-311+G(2df,p)	1.856	1.176	1.817	1.184	1.887	1.169	1.855	1.174
B3P86	6-311G(d,p)	1.880	1.170	1.846	1.176	1.926	1.161	1.882	1.167
	6-311+G(2df,p)	1.825	1.176	1.792	1.183	1.854	1.169	1.825	1.174

[a] Bond lengths are in angstroms.

of these methods, optimized *r*(S−N) values obtained with the 6-311G(df,p) and 6-311+G(2df,p) basis sets agree within 0.01 Å (see Table 3). For the MP2 method, increasing the basis set further to 6-311++G(3df,3pd) causes only a slight decrease in *r*(S−N). The B3LYP and B3P86 methods again exhibit a more tempered basis set dependence than the MP2 method. For example, improving the 6-311G(d,p) basis set by inclusion of diffuse d- or f-functions results in modest decreases in the optimized *r*(S−N) values of 0.02−0.03 Å (see Table 3). Similar to that noted for HSNO, of the two DFT methods, the largest changes in *r*(S−N) occur with the B3LYP method, which also consistently predicts longer S−N bonds, for a given basis set, than any of the other methods. Increasing the basis set to 6-311++G(3df,3pd) results in only minor shortening of the S−N bonds. It should be noted that optimized S−N bond lengths obtained at the QCISD/6-311+G(2df,p) and B3P86/6-311+G(2df,p) levels are again in close agreement, being 1.799 and 1.793 Å, respectively.

The N−O bond, for all methods, is again quite insensitive to the basis set beyond 6-311G(d,p). The broadest variation occurs for the MP2 method, which also consistently predicts a slightly longer N−O bond than any of the methods. Indeed, the QCISD, B3LYP, and B3P86 methods all give quite similar optimized N−O bond lengths of approximately 1.18 Å, while the MP2 method generally predicts a value close to 1.20 Å (see Table 3).

In CH_3SNO, for all methods in combination with the 6-311+G(2df,p) basis set or larger, the S−N bond is predicted to be significantly longer than in $HSNH_2$ while concomitantly the N−O bond length lies midway between that of HNO and NO (cf. Table 2). Thus, while the CH_3S−NO bond is shorter than that in HSNO (cf. Table 1), it is still a lengthened S−N single bond, again with considerable multiple-bond character in the −NO moiety.

Optimized Geometries: CH_2CHSNO, CH_3CH_2SNO, C_6H_5SNO, and CysSNO. Optimized S−N and N−O bond lengths for all four species are given in Table 4. Due to their larger size, a reduced range of basis sets and methods was used.

In general, similar trends are observed as previously described for HSNO and CH_3SNO. For example, for the conventional MP2 and QCISD methods, inclusion of f-functions (6-311G(d,p) → 6-311G(df,p)) significantly shortens the S−N bond with a concomitant, though less dramatic, lengthening of the N−O bond. In addition, increasing the basis set further at the MP2 level to 6-311+G(2df,p) results in only quite minor changes in the optimized bond lengths. A notable exception to this occurs for C_6H_5SNO, where *r*(S−N) increases by almost 0.04 Å (see Table 4). However, the MP2 method appears to have considerable difficulty describing the interaction between the aromatic (C_6H_5S) system and the NO moiety, ultimately causing it to overestimate *r*(S−N). This is indicated by the fact that at the MP2/6-311G(d,p) level, the optimized S−N bond length is very long at 2.097 Å, while at the QCISD/6-311G(d,p) level it is 1.906 Å, 0.191 Å shorter. In comparison, at the same levels of theory, the corresponding differences obtained for the other RSNOs are all less than 0.03 Å (cf. Tables 1 and 3). It should also be noted that the N−O bond length is 1.154 Å at the MP2/6-311G(d,p) level, markedly shorter than the value obtained for *any* other RSNO at *any* level of theory.

For the DFT methods, substantial decreases in the optimized *r*(S−N) values, with smaller concomitant increases in the *r*(N−O) values also occur upon increasing the basis set from 6-311G(d,p) to 6-311+G(2df,p). In general, structures obtained at the B3P86/6-311+G(2df,p) level are again in better agreement with those obtained with the QCISD/6-311G(df,p) and MP2/6-311+G(2df,p) methods, than are those obtained at the B3LYP/6-311+G(2df,p) level, which again generally predicts longer S−N bonds than the other methods. The exception to this occurs for C_6H_5SNO; however, this is most likely due to overestimation of the C_6H_5S−NO bond length by the MP2 method, as noted above.

As for HSNO and CH_3SNO, comparison with the appropriate bond lengths of $HSNH_2$, HNO, and NO clearly illustrates the long single-bond nature of the RS−NO bond and multiple-bond character of the −NO group, in each of the above RSNOs (cf. Table 2).

Homolytic S−N BDEs: HSNO and CH_3SNO. Calculated S−N BDEs of *trans*-HSNO and *cis*-CH_3SNO are listed in Table 5. Both exhibit very similar basis set dependencies. For all methods, improving the basis set from 6-311G(d,p) to 6-311+G(2df,p) increases the calculated BDEs. The largest increases of approximately 30 and 20 kJ $mol^{-1}$are observed for the MP2 and QCISD methods, respectively, while those observed for the B3LYP and B3P86 methods are just 10 kJ mol^{-1} or less. Improving the basis set further, 6-311+G(2df,p) to 6-311++G(3df,3pd), results in only minor changes in the calculated BDEs. For a suitably large basis set, e.g., 6-311+G(2df,p) or larger, values obtained with the MP2 and B3P86 methods are in close agreement, agreeing within 5 kJ mol^{-1} (see Table 5). The corresponding values calculated with the B3LYP method are lower by 15−20 kJ mol^{-1}. Surprisingly, however, S−N BDEs calculated by using the QCISD method with any basis set are significantly lower than those obtained with use of any other method by 30−50 kJ mol^{-1}. Thus, while the QCISD method appears to provide reliable structures, it grossly underestimates the strength of the long single S−N bond.

Of the methods previously used to calculate S−N BDEs, the CBS-Q and G3 methods have the highest expected reliability and accuracy. We note that the CBS-QB3 method is of similar accuracy. In general, however, for the RSNOs in this present

TABLE 5: Calculated[a] Homolytic S−N BDEs of *trans*-HSNO and *cis*-CH_3SNO (kJ mol^{-1})

method	HSNO	CH_3SNO
MP2/6-311G(d,p)	101.3	113.4
MP2/6-311+G(2df,p)	130.8	142.5
MP2/6-311++G(3df,3pd)	130.4	144.6
QCISD/6-311G(d,p)	65.0	75.9
QCISD/6-311+G(2df,p)	84.1	92.0
QCISD/6-311++G(3df,3pd)[b]	85.4	
B3LYP/6-311G(d,p)	109.1	112.8
B3LYP/6-311+G(2df,p)	116.8	121.0
B3LYP/6-311++G(3df,3pd)	116.8	121.7
B3P86/6-311G(d,p)	126.1	132.2
B3P86/6-311+G(2df,p)	135.5	142.2
B3P86/6-311++G(3df,3pd)	135.4	142.9
B3LYP/6-31G(d)[16]	120.9	123.8
B3LYP/6-311++G(2df,p)//B3LYP/6-31G(d)[16]	121.8	124.3
ROMP2/6-311++G(d,p)//B3LYP/6-31G(d)[16]	85.4	94.1
CBS-4M[16]	137.2	143.9
CBS-QB3[14]	122.2[a]	135.6
CBS-Q[16]	128.9	141.0
G3[16]	120.9	131.8

[a] From this current study, unless otherwise noted. [b] ZPVE calculated at the QCISD/6-311G(d,p) level, scaled by 0.96.

study it gives values that lie between those obtained with the G3 and CBS-Q methods. Thus, for simplicity, it is omitted from the following discussion, unless otherwise noted. From Table 5 it can be seen that the G3 method predicts BDEs that are about 10 kJ mol^{-1} lower than obtained with the CBS-Q method. As a result, S−N BDEs obtained by using the MP2 and B3P86 methods with the 6-311+G(2df,p) basis set or larger are within 5 kJ mol^{-1} or less of those obtained by using the CBS-Q method. However, BDEs obtained with the B3LYP method and 6-311+G(2df,p) basis set or larger give the best agreement with those obtained by using the G3 method, being just 10 kJ mol^{-1} or less lower. As the QCISD method underestimates the S−N BDE of HSNO and CH_3SNO, it gives poorest agreement with most of the previously calculated values, in particular those obtained with the CBS-Q and G3 methods, being approximately 35−50 kJ mol^{-1} too low.[14,16] We note that BDEs calculated at the QCISD/6-311+G(2df,p) level are close to those obtained[16] with the mixed MP2/6-311++G(d,p)//B3LYP6-31G(d) method. However, these values are likely to be erroneously low, due in part to the fact that structures obtained with the B3LYP method possess considerably longer S−N bonds than obtained with the MP2 method (cf. Tables 1 and 3).

Homolytic S−N BDEs: CH_2CHSNO, CH_3CH_2SNO, C_6H_5SNO, and CysSNO. Calculated and experimental, where available, values for these RSNOs are listed in Table 6. In general, similar trends as previously described for HSNO and CH_3SNO are observed. For instance, improving the basis set from 6-311G(d,p) to 6-311+G(2df,p) for any method increases the calculated S−N BDEs. The largest increases, approximately 25−30 kJ mol^{-1}, are again observed for the MP2 method while, in contrast, the DFT methods exhibit smaller increases of just 14.4 kJ mol^{-1} or less. In addition, the QCISD method again drastically underestimates RS−NO BDEs. For example, for CH_3CH_2SNO the BDE obtained at the QCISD/6-311G(d,p) level is 55.3 kJ mol^{-1} lower than that obtained at the B3P86/6-311G(d,p) level, which is itself in good agreement with the previously calculated[16] G3 value (see Table 6).

Unlike HSNO and CH_3SNO, however, of all of the methods considered, the B3P86/6-311+G(2df,p) level gives closest agreement with values obtained at *both* the G3/G3(MP2) *and* CBS-Q levels, the differences being less than 10 and 5 kJ mol^{-1}, respectively. For the 6-311+G(2df,p) basis set, the B3LYP values are all approximately 20−25 kJ mol^{-1} less than the corresponding B3P86 values. Consequently, the B3LYP/6-311+G(2df,p) level no longer gives comparable agreement with the higher accuracy composite methods, as observed for HSNO and CH_3SNO. Indeed, values calculated at this level are lower than the corresponding G3/G3(MP2) and CBS-Q values by 11−26 kJ mol^{-1}, the difference increasing with increasing size of the RSNO (see Table 6). The B3P86/6-311+G(2df,p) and MP2/6-311+G(2df,p) S−N BDEs are now only in close agreement for CH_3CH_2SNO and CysSNO, i.e., those containing saturated R groups. In contrast, for CH_2CHSNO and C_6H_5SNO, the MP2/6-311+G(2df,p) values are 28 and 105 kJ mol^{-1} higher, respectively, than the corresponding values obtained at the B3P86/6-311+G(2df,p) level. This is due to high spin contamination of the underlying Hartree−Fock wave function for $CH_2CHS^{\bullet}$ and $C_6H_5S^{\bullet}$, with $\langle S^2 \rangle$ values of 0.94 and 1.20, respectively. Thus, erroneously high energies, and consequently S−N BDEs, are obtained. In contrast, spin contamination in all other $RS^{\bullet}$ radicals at the same level of theory was much lower, 0.75−0.78. We note that the QCISD method also experienced high spin contamination for these radicals. However, due in part to its explicit consideration of single and double excitations, it is less affected.

From Tables 5 and 6 it can be seen that the B3P86/6-311+G(2df,p) BDEs of the saturated RSNOs (HSNO, CH_3SNO, CH_3CH_2SNO, CysSNO) are all within 10 kJ mol^{-1}. In contrast, the corresponding BDEs of the conjugated RSNOs CH_2CHSNO and C_6H_5SNO, while in close agreement with each other (see Table 6), are 29−37 kJ mol^{-1} lower. This is due to stabilization of the sulfur radical by the π-system of the adjacent R group.[32]

From Table 6, it can be seen that the various CBS and G3 style methods give homolytic S−N BDEs that are generally in reasonable agreement with each other, and furthermore are in reasonable agreement with those obtained at the B3P86/6-311+G(2df,p) method. This is despite the fact that they are all based upon different optimized structures. However, due to the "elongated single-bond" nature of the RS−NO bond, it can be expected that the potential energy surface for homolytic dissociation is relatively flat. Hence, differences in optimized structures will not have as great an energetic consequence as is generally the case with more typical covalent single and double bonds, *as long as* an appropriate level of theory is chosen for obtaining the relative energies of interest, e.g., not QCISD or B3LYP.

The experimentally[4] determined S−N BDE of C_6H_5SNO is also listed in Table 6. It should be noted, however, that it was not directly measured but rather was estimated by using a series of related thermochemical values. The present results suggest that it may be a lower estimate of the gas-phase S−N BDE of C_6H_5SNO.

4. Conclusions

The reliability and accuracy of the conventional electron correlation methods MP2 and QCISD, and the density functional theory methods B3LYP and B3P86, to obtain optimized structures and homolytic S−N BDEs of a range of *S*-nitrosothiols, has been investigated.

For all methods considered, optimized S−N bond lengths are found to be highly dependent on the basis set being employed. In particular, the MP2 method is found to be the most sensitive to the basis set being used, with the other methods exhibiting more tempered affects. In general, to obtain convergence in the *r*(S−N) values of RSNO for a given method, the 6-311+G-

TABLE 6: Comparison of Calculated[a] and Experimental Homolytic S−N BDEs of *cis*-CH_2CHSNO, *cis*-CH_3CH_2SNO, *cis*-C_6H_5SNO, and *cis*-CysSNO (kJ mol^{-1})

method	CH_2CHSNO	CH_3CH_2SNO	C_6H_5SNO	CysSNO
MP2/6-311G(d,p)	107.3	115.9	185.5	126.6
MP2/6-311+G(2df,p)	133.0	146.0	211.3	146.5[b]
QCISD/6-311G(d,p)[b]	53.5	75.9	70.1	
B3LYP/6-311G(d,p)	78.9	111.1	78.3	109.3
B3LYP/6-311+G(2df,p)	85.2	118.6	86.9	117.0
B3P86/6-311G(d,p)	97.1	131.2	95.9	126.9
B3P86/6-311+G(2df,p)	105.4	139.6	106.6	141.3
B3LYP/6-31G(d)[16]	84.3[a]	121.8	85.4	115.5[a]
B3LYP/6-31+G(d)[4]	82.6[a]	116.9[a]	84.5	123.5[a]
B3LYP/6-311++G(d,p)//B3LYP/6-31G(d)[16]	80.2[a]	128.9	88.3	119.6[a]
ROMP2/6-311++G(d,p)//B3LYP/6-31G(d)[16]	65.0[a]	101.3	77.0	102.2[a]
ROMP2/6-31G(2df,p)//ROMP2/6-31G(d)[17]				129.9
CBS-4M[16]	98.6[a]	143.9	115.9	147.0[a]
CBS-QB3[14]	97.5	133.9	103.9[a]	138.8[a]
CBS-Q[16]	101.8[a]	139.3	111.3	142.6[a]
G3[16]	96.6[a]	131.8	106.3	137.4[a,c]
exptl[4]			81.2	

[a] From this current study, unless otherwise noted. [b] Scaled ZPVE obtained at the MP2/6-311G(d,p) level used. [c] Values calculated by using the modified G3 method, G3(MP2) [ref 31].

(2df,p) or larger basis set is required. For the conventional MP2 and QCISD methods, however, reliable structures can be obtained with the smaller, less computationally expensive, 6-311G(df,p) basis set. When suitably large basis sets are used, the MP2, QCISD, and B3P86 methods generally give optimized structures that are in close agreement with each other, particularly the QCISD and B3P86 methods. In contrast, the B3LYP method typically overestimates RS−NO bond lengths compared to the above methods. However, for N−O bond lengths, the MP2 method typically predicts longer RSN−O bonds than the other methods, which generally give lengths in good agreement with each other. In the case of C_6H_5SNO, the MP2 method fails to correctly predict the S−N bond length, with any of the basis sets used.

These observed basis set and method dependencies are found to be due to the fact that the S−N bond in RSNOs *does not* possess considerable double-bond character as previously suggested, but that it is in fact a long single S−N bond. Conversely, the −NO moiety within RSNOs is found to retain considerable multiple-bond character, between that of a formal N−O double bond in HNO and the N−O bond (bond order 2.5) of isolated NO. Thus, of the methods considered, the DFT method B3LYP overestimates the distance of such long-bond interactions, while the MP2 method is most sensitive to the description of the molecular orbitals involved. In contrast, for obtaining optimized structures possessing such long bonds, the DFT method B3P86 exhibits similar reliability and accuracy to that of the highest conventional electron correlation method used in this study, QCISD.

In general, to achieve convergence in the calculated homolytic RS−NO bond dissociation energy for a given method, the 6-311+G(2df,p) or larger basis set must be used. For all RSNOs considered in this present study, the QCISD method, regardless of the basis set employed, severely underestimates the strength of the RS−NO bond, predicting BDEs that are considerably lower than any other methods by as much as 55 kJ mol^{-1}. When the R group in the RSNO is not aromatic or conjugated, the MP2/6-311+G(2df,p) method gives values in reasonable agreement with those obtained with the B3P86/6-311+G(2df,p) and CBS-Q methods. When the R group is unsaturated or aromatic, however, it significantly overestimates BDEs due to spin contamination.

For the small *S*-nitrosothiols HSNO and CH_3SNO, S−N BDEs calculated at the B3LYP/6-311+G(2df,p) level give the best agreement of all methods with those calculated by using the high accuracy G3 method. However, as the size of the RSNO increases, the B3LYP method increasingly underestimates the S−N BDEs, i.e., predicts values that become increasingly lower than the corresponding values obtained at the G3/G3(MP2) and CBS-Q levels. In contrast, for small *S*-nitrosothiols, the B3P86/6-311+G(2df,p) method predicts BDEs in good agreement with those values calculated by using the CBS-Q method. However, as the size of the RSNO increases, it continues to give the best agreement with the CBS-Q calculated values and furthermore, now also gives the best agreement with those values obtained at the G3/G3(MP2) level. In addition, the absolute differences remain essentially constant as the size of the *S*-nitrosothiol increases.

Due to the elongated single-bond nature of the RS−NO bond, hence relatively flat potential energy surface for homolytic bond dissociation, reasonable homolytic S−N BDEs can be calculated by using optimized structures with different (within reason) S−N bond lengths. This will hold as long as an appropriate method is chosen, e.g., G3, CBS, or B3P86/6-311+G(2df,p) but not QCISD or B3LYP, for obtaining the necessary relative energies. Of course, the more accurate the structure used with, for example, the G3 method, the more reliable and accurate the calculated values will be.

Overall, the B3P86/6-311+G(2df,p) method represents the best compromise between computational cost and accuracy for obtaining reliable structures *and* homolytic S−N bond dissociation energies of *S*-nitrosothiols, particularly with increasing size of the RSNO.

It is noted that the structures and BDEs of RSNOs, in particular C_6H_5SNO, can also be thought of in terms of resonance structures, i.e., $[C_6H_5S]^+[NO]^- \leftrightarrow [C_6H_5SNO] \leftrightarrow [C_6H_5S]^-[NO]^+$. However, atomic charges from a Mulliken Population Analysis of C_6H_5SNO suggest that contributions due to ionic structures are comparatively small; the −NO moiety exhibits atomic charges close to those calculated for isolated NO. More detailed studies are currently in progress.

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Supporting Information Available: Optimized geometries for all species in the present study (Tables S1 and S2). This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) Fujimori, K.; Nakajima, T. *Rev. Heteroatom Chem*. **2000**, *22*, 181.

(2) Williams, D. L. H. *Acc. Chem. Res*. **1999**, *32*, 869.

(3) Feldman, P. L.; Griffith, O. W.; Stuehr, D. J. *Chem. Eng. News* **1993**, *Dec 20*, 26.

(4) Lü, J. M.; Wittbrodt, J. M.; Wang, K.; Wen, Z.; Schlegel, B. H.; Wang, P. G.; Cheng, J. P. *J. Am. Chem. Soc*. **2001**, *123*, 2903.

(5) Al-Sa'Doni, H.; Ferro, A. *Clin. Sci.* **2000**, *98*, 507.

(6) de Belder, A. J.; MacAllister, R.; Radomski, M. W.; Moncada, S.; Valence, P. J. *Cardiovasc. Res.* **1994**, *28*, 691.

(7) Azuma, H.; Ishikawa, M.; Sekizaki, S. *Br. J. Pharmacol*. **1986**, *88*, 411.

(8) Furlong, B.; Henderson, A. H.; Lewis, M. J.; Smith, J. A. *Br. J. Pharmacol*. **1987**, *90*, 687.

(9) Radomski, M. W.; Palmer, R. M. J.; Moncada, S. *Br. J. Pharmacol*. **1987**, *92*, 636.

(10) Radomski, M. W.; Palmer, R. M. J.; Moncada, S. *Biochem. Biophys. Res. Commun*. **1987**, *148*, 1482.

(11) Radomski, M. W.; Palmer, R. M. J.; Moncada, S. *Lancet ii* **1987**, 1057.

(12) Lipton, A. J.; Johnson, M. A.; Macdonald, T.; Lieberman, M. W.; Gozal, D.; Gaston, B. *Nature* **2001**, *413*, 171.

(13) Lipton, A. S. *Nature* **2001**, *413*, 118.

(14) Bartberger, M. D.; Mannion, J. D.; Powell, S. C.; Stamler, J. S.; Houk, K. N.; Toone, E. J. *J. Am. Chem. Soc*. **2001**, *123*, 8868.

(15) Bartberger, M. D.; Houk, K. N.; Powell, S. C.; Mannion, J. D.; Lo, K. Y.; Stamler, J. S.; Toone, E. J. *J. Am. Chem. Soc*. **2000**, *122*, 5889.

(16) Fu, Y.; Mou, Y.; Lin, B.-L.; Liu, L.; Guo, Q.-X. *J. Phys. Chem. A.* **2002**, *106*, 12386.

(17) de Oliveira, M. G.; Shishido, S. M.; Seabra, A. B.; Morgon, N. H. *J. Phys. Chem. A* **2002,** *106*, 8963.

(18) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1998**, *109*, 7764.

(19) See, for example: (a) Montgomery, J. A., Jr.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A. *J. Chem. Phys.* **1999**, *110*, 2822. (b) Montgomery, J. A., Jr.; Frisch, M. J.; Ochterski, J. W.; Petersson, G. A. *J. Chem. Phys.* **2000**, *112*, 6532 and references, therein.

(20) Wang, P. G.; Xian, M.; Tang, X.; Wu, X.; Wen, Z.; Cai, T.; Janczuk, A. J. *Chem. Rev.* **2002**, *102*, 1091.

(21) (a) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Salvador, P.; Dannenberg, J. J.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98*, Revision A.11.1; Gaussian, Inc.: Pittsburgh, PA, 2001. (b) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A. J.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T. A.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B. G.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, Revision A.1; Gaussian Inc.: Pittsburgh, PA, 2003.

(22) Becke, A. D. *J. Chem. Phys*. **1993**, *98*, 1372.

(23) Stephens, P. J.; Devlin, F. J.; Frisch, M. J.; Chabalowski, C. F. *J. Phys. Chem*. **1994**, *98*, 11623.

(24) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev*. B **1988**, *37*, 785.

(25) (a) Perdew, J. P. *Phys. Rev*. B **1986**, *33*, 8822. (b) Perdew, J. P. *Phys. Rev*. B **1986**, *34*, 7406.

(26) MP2/6-311G(d,p) ZPVEs were scaled by 0.9496 [taken from the following: Scott, A. P.; Radom, L. *J. Phys. Chem*. **1996**, *100*, 16502]; QCISD/6-311G(d,p) ZPVEs were scaled by 0.96; B3LYP/6-311G(d,p) and B3P86/6-311G(d,p) ZPVEs were scaled by 0.97.

(27) Grossi, L.; Montevecchi, P. C.; Strazzari, S. *J. Am. Chem. Soc.* **2001**, *123*, 4853.

(28) This is also indicated by the fact that values of r(S−N) in species with S−N bonds possessing double-bond character, e.g., polythiazyl [$(SN)_x$], are much less than r(S−N) in $HSNH_2$ (see ref 29a).

(29) Cotton, F. A.; Wilkinson, G.; Murillo, C. A.; Bochmann, M. *Advanced Inorganic Chemistry*, 6th ed.; John Wiley & Sons: New York, 1999: (a) p 511, (b) p 326.

(30) See, for example: Gauld, J. W.; Radom, L. *Chem. Phys. Lett*. **1997**, *275*, 28.

(31) Curtiss, L. A.; Redfern, P. C.; Raghavachari, K.; Rassolov, V.; Pople, J. A. *J. Chem. Phys.* **1999**, *110*, 4703.

(32) Henry, D. J.; Parkinson, C. J.; Mayer, P. M.; Radom, L. *J. Phys. Chem*. A **2001**, *105*, 6750.