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## Tautomerism and Regioselectivity of Acylation of 4-Hydroxy-2-mercaptopyridine-*N*-oxide and 2,4-Dimercaptopyridine-*N*-oxide: A Computational Study

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*Relative thermodynamic stability and dipole moments of tautomers of 2-mercapto- (1), 4-hydroxy-2-mercapto- (2), 2,4-dimercapto- (3), 4-hydroxy- (4), and 4-mercapto- (5) pyridine-*N*-oxides were calculated in gas phase at the B3LYP/6-31G(d,p) level of theory. According to the calculations, the general trend in stability of the tautomers follows 2-thiono > 4-thiono/keto > *N*-oxide. A similar trend is observed in monoacetyl (6 and 7) and diacetyl (8 and 9) derivatives of 2 and 3. Therefore, monoacetylation of 2 or 3 is expected to give the 4-acetyl derivatives and diacetylation the 1,4-diacetyl isomers as the thermodynamic products.*

**Keywords** Acetates; derivatives; DFT calculations; 1-hydroxypyridine-2(1*H*)-thione; stability; tautomerism

## INTRODUCTION

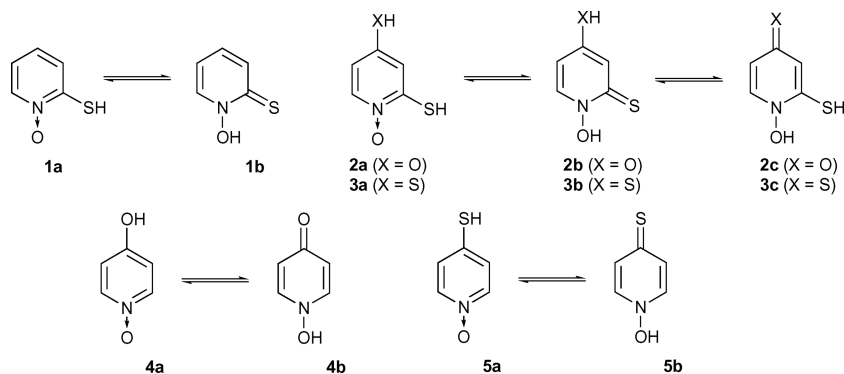
Tautomeric equilibrium between 2-mercaptopyridine-*N*-oxide (**1a**) and *N*-hydroxypyridine-2(1*H*)-thione (**1b**) has been studied experimentally by several research groups.<sup>1–3</sup> Early spectroscopic investigations by IR and UV methods concluded that the thiono form **1b** dominates over the mercapto form **1a** by a factor of  $\sim 10^4$ .<sup>1,2</sup> These findings were corroborated by a single crystal XRD analysis of **1**, which demonstrated **1b** as the solid-state tautomer.<sup>4,5</sup> However, recent UV studies concluded that tautomeric equilibrium for **1** is solvent-dependent: the thiol form

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Dedicated to Professor Marian Mikołajczyk, CBMiM PAN in Łódź, Poland, on the occasion of his 70th birthday.

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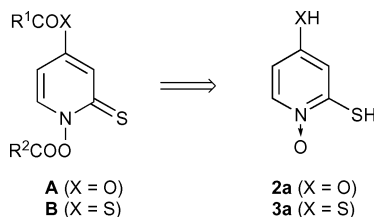


**FIGURE 1** Tautomeric equilibria of pyridine-*N*-oxides **1**–**5**.

**1a** dominates in nonpolar aprotic solvents, while thione **1b** is the main structure in polar and protic solvents (Figure 1).<sup>6</sup>

*N*-Oxide **1** is an ambident nucleophile, and its electrophilic substitution may occur either on the S or O atom. Experiments demonstrated that **1** undergoes acylation<sup>7,8</sup> exclusively at the oxygen atom, while the regioselectivity of alkylation<sup>5,8–11</sup> depends on the reaction conditions.<sup>5</sup> Introduction of a hydroxy or a mercapto substituent in the 4 position of **1** complicates the tautomerism and the regioselectivity of electrophilic substitution of 4-hydroxy-2-mercaptopyridine-*N*-oxide (**2a**) and 2,4-dimercaptopyridine-*N*-oxide (**3a**). This is indicated by results obtained for 4-hydroxypyridine-*N*-oxide (**4a**) and 4-mercaptopyridine-*N*-oxide (**5a**), which both show strong preference for the *N*-hydroxy tautomers **4b** and **5b**, respectively. The tautomeric equilibrium of the latter oxide exhibits solvent-dependence similar to that observed for *N*-oxide **1**.<sup>3</sup> In aqueous solutions only the 4-thiono form **5b** has been observed,<sup>1,2</sup> and also this tautomer has been found as the solid-state structure.<sup>12</sup> In contrast, the 4-hydroxy derivative **4a** has a lower tendency to form the keto form **4b**, and in aqueous solutions exists as a mixture of both tautomers **4a** and **4b** in comparable amounts.<sup>13</sup> Of the two disubstituted pyridine *N*-oxides, only the 2,4-dimercapto derivative **3** has been investigated experimentally.<sup>14</sup> Analysis of spectroscopic data for the related methyl derivatives of **3** provided indirect evidence for its preference of the 2-thiono tautomer.<sup>15</sup> Similar tautomeric preference can be expected for the 4-hydroxy-2-mercapto derivative **2**.

We are interested in 4-substituted 2-mercaptopyridine-*N*-oxides **2a** and **3a** and their diacyl derivatives **A** and **B** respectively (Scheme 1). Therefore, we set out to assess the tautomeric equilibria for 4-hydroxy

**SCHEME 1**

and 4-mercapto derivatives **2** and **3** and regioselectivity of their sequential acetylation ( $R^1 = R^2 = \text{Me}$ ) using computational methods.

Here, we first investigate the relative gas phase thermodynamic stability of tautomeric forms of **1**, **4**, and **5** and compare the results with the available experimental data. Subsequently, we calculate the tautomeric equilibria for disubstituted *N*-oxides **2** and **3** and isomeric products of their mono- and diacetylation as a predictor for regioselectivity of sequential substitution of the parent compounds.

## RESULTS AND DISCUSSION

### Mono Substituted Pyridine-*N*-oxides

Analysis of the monosubstituted derivatives of pyridine *N*-oxide **1**, **4**, and **5** provides a good starting point for understanding results for the disubstituted derivatives **2** and **3**.

Gas phase calculations demonstrated that the 2-thiono tautomer **1b** has a higher thermodynamic stability than the 2-mercapto form **1a** by nearly 6 kcal/mol (Table I). This is in qualitative agreement with experimental observations in which the thiono form is preferred in polar solvents.<sup>1,2,6</sup> In contrast, *N*-oxide **5**, an isomer of **1**, prefers the mercapto tautomer **5a** by 4.5 kcal/mol. Considering that the dipole moment of **5b** (7.6 D) is more than twice the dipole moment of **5a** (3.5 D), it can be expected that a polar medium will preferentially stabilize the thiono form and diminish the energy difference between the two tautomers. Therefore, it is possible that 4-thione **5b** will exist in aqueous solutions in significant proportions, as was observed experimentally.<sup>1,2</sup> The 4-hydroxy derivative **4** also prefers the *N*-oxide form **4a** over the keto form **4b** by only 2.4 kcal/mol. This smaller difference in energy observed for tautomers **4** as compared to tautomers **5** is presumably related to a better orbital overlap and, consequently, higher stability of the C=O than the C=S bond. The smaller difference in the molecular dipole moment between the two tautomers of **4** certainly contributes to the smaller energy difference. These results clearly demonstrate the

**TABLE I** Relative Enthalpy of Formation of **1**, **4**, and **5** in Gas Phase and the Molecular Dipole Moment<sup>a</sup>

	<b>a</b>		<b>b</b>	
	$\Delta H$ kcal/mol	$\mu$ D	$\Delta H$ kcal/mol	$\mu$ D
<b>1</b>	5.9	3.6	0.0	5.0
<b>4</b>	0.0	4.6	2.4	6.0
<b>5</b>	0.0	3.5	4.5	7.6

<sup>a</sup>B3LYP/6–31G(d,p) level of theory.

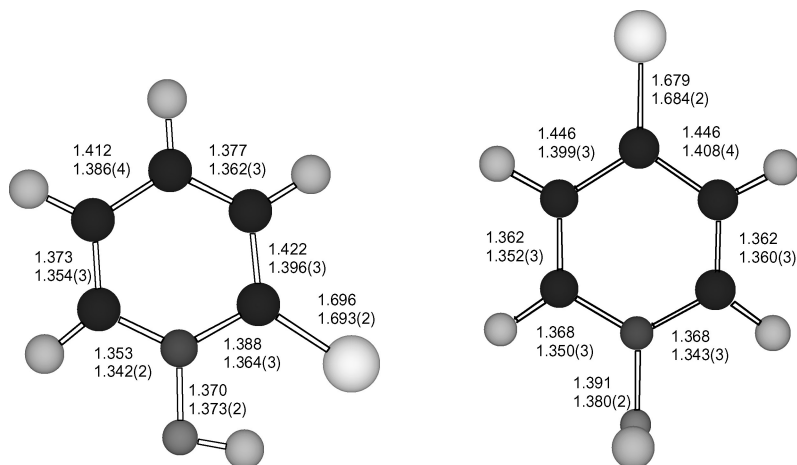
strong preference of the 2-mercapto derivative **1** for the thiono form **1b** even in low polarity environments. In contrast, the 4 substituted derivatives **4** and **5** prefer the *N*-oxide form in low polarity media, but may form the appropriate thiono/keto forms in polar media. Out of the two compounds, 4-hydroxy derivative **4** is more likely to adopt the keto form than the 4-mercapto derivative **5** the thiono form (Table I).

Molecular structures for both tautomers of **1** are planar and stabilized by intramolecular hydrogen bonding S–H $\cdots$ O in **1a** and S $\cdots$ H–O in **1b** (Figure 2). For the 4 substituted derivatives, only the mercapto form **5a** is planar, while in the 4-thiono form **5b** the OH group is orthogonal to the pyridine ring plane (Figure 2). The planar form of **5b** represents a rotational transition state with  $\Delta H^\ddagger = 2.6$  kcal/mol. Similar results were obtained for the 4-hydroxy derivative **4**. A comparison of the two regioisomers shows that the 4-thiono tautomer **5b** is less stable than its 2-thiono isomer **1b** by  $\Delta H = 16.1$  kcal/mol (or 11.6 kcal/mol difference between **5a** and **1b**).

The calculated geometrical parameters for the thiono tautomers of both isomers are in reasonably good agreement with the reported solid-state structures for **1**<sup>4,5</sup> and **5**.<sup>12</sup> A comparison of the calculated and experimental geometrical parameters shows that the theoretical interatomic distances are systematically overestimated by an average of 0.015 Å<sup>4</sup> or 0.020 Å.<sup>5</sup> The exception is the C=S distance, which is calculated within experimental error for both compounds. The most dramatic differences in bond length are observed for the C(4)–C(5) distances (Figure 2).

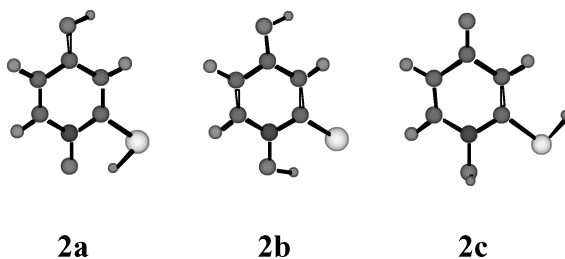
#### 4-Hydroxy-2-mercaptopyridine-*N*-oxide (**2**) and 2,4-Dimercaptopyridine-*N*-oxide (**3**)

There are three tautomeric forms of the 4-hydroxy-2-mercapto and 2,4-dimercapto derivatives **2** and **3** in which no more than one atom at a time acquires formal exocyclic double bond character (Figure 3). Each



**FIGURE 2** Calculated [B3LYP/6–31G(d,p), top] and experimental (bottom) structural parameters for **1b**<sup>4</sup> (left) and **5b**<sup>12</sup> (right). Both structures were optimized at the  $C_s$  symmetry.

of these tautomers has four conformers, which differ in the orientation of the OH and SH hydrogen atoms. A comparison of the B3LYP/6–31G(d)-derived SCF energies for conformers after full geometry optimization without symmetry constraints shows that the most thermodynamically stable conformer has the intramolecular H-bonding  $\text{NO}\cdots\text{H}\cdots\text{S}$  or  $\text{NO}\cdots\text{H}\cdots\text{S}$ . The formation of the intramolecular H-bonding is consistent with the solid state structure of **1**.<sup>4,5</sup> All conformers of tautomers **a** and **b** converge to planar structures with the  $C_s$  point group symmetry. In contrast, the tautomers **2c** and **3c** are nonplanar with the  $\text{C}(2)\text{--N--O--H}$  dihedral angle of  $90^\circ$ .



**FIGURE 3** Molecular models for tautomers of **2** obtained by geometry optimization at the B3LYP/6–31G(d,p) level of theory.

**TABLE II** Relative Enthalpy of Formation of **2** and **3** in Gas Phase and Molecular Dipole Moment<sup>a</sup>

	<b>a</b>		<b>b</b>		<b>c</b>	
	$\Delta H$ kcal/mol	$\mu$ D	$\Delta H$ kcal/mol	$\mu$ D	$\Delta H$ kcal/mol	$\mu$ D
<b>2</b>	7.8	4.0	0.0	4.4	17.2	5.2
<b>3</b>	7.0	3.0	0.0	4.1	17.2	6.8

<sup>a</sup>B3LYP/6-31G(d,p) level of theory. For structures **2**, see Figure 3.

The most stable conformers of each tautomer were optimized using appropriate symmetry constraints, and their thermodynamic parameters were calculated at the B3LYP/6-31G(d,p) level of theory. The computational data were used to calculate the relative stability of each tautomer, and the results are shown in Table II.

Computational results show that the 2-thiones **2b** and **3b** are most stable among the tautomers, while the 4-keto and 4-thiono forms **2c** and **3c** are the least stable. Interestingly, molecular dipole moment values for the *N*-oxides **2a** and **3a** are smaller than those of the 2-thiono forms. This suggests that the polarity of the two tautomers does not increase the relative energy of the 2-thiono form relative to the *N*-oxide in gas phase. In polar solvents, however, the *N*-oxide form will be less stabilized than the 2-thiono form, and the difference in their thermodynamic stability is expected to increase.

The observed order of stability of the tautomers in both series **b** > **a** > **c** is consistent with that found for the monosubstituted derivatives: **1b** > **1a** > **5b**.

## Monoacetyl Derivatives

Monoacetylation of **2** and **3** leads to three tautomeric pairs of regioisomers **6a–6f** and **7a–7f**, respectively (Figure 4). In both series, the most thermodynamically stable regioisomer is acetylated at the 4 position, with the 2-thione tautomer (**6b** and **7b**) being more stable than the thiol (**6a** and **7a**) by about 6 kcal/mol (Table II). The 1-acetyloxy-2-thione derivative **6c** is less stable than **6b**, also by about 6 kcal/mol. In contrast, structure **7c**, the 1-acetyloxy derivative of **3**, is only 1.5 kcal/mol less stable than the 4-acetylthio isomer. A comparison of the two tautomers **c** and **d** demonstrates again the significance of the 2-thiono form over the 4-thiono/keto form in the structure stabilization; the former is about 9 kcal/mol more stable than the latter in both series of compounds. Thermodynamically least stable are the 2-acetylthio

derivatives **e** and **f**, which is consistent with the results for the parent compounds **1** and **3**.

Two of the six structures in series **6** converged at the planar geometry ( $C_s$ ), while all six structures for **7** are non-planar. The acetyloxy group at the 1 position in structures **c** and **d** is nearly orthogonal to the ring plane. This is consistent with the solid state structure for 1-(4-*t*-butylcyclohexanecarbonyloxy)pyridine-2(1*H*)-thione, a close analog of **6c** and **7c**, and ascribed to the repulsion of the electron pairs of the N and O atoms.<sup>8</sup> The 2-AcS group in structures **6e** and **7e** is coplanar with the ring, while in **6f** and **7f** the N-C(2)-S-C(=O) dihedral angle is 58°. A similar lack of co-planarity of the AcS group with the ring is found for **6a** and **6b** in which the C(3)-C(4)-S-C(=O) dihedral angle is 128° and 136°, respectively.

## Diacetyl Derivatives

Introduction of the second acetyl group to **6** and **7** leads to three possible isomers in each resulting series **8** and **9**, respectively (Figure 5). Analysis of the thermodynamic data shows that the most stable isomers are the 1,4-diacetylated derivatives **8b** and **9b**. The 2,4-diacetyl derivatives, **8a** and **9a**, are less stable by 9 and 7.9 kcal/mol, respectively, even though their molecular dipole moments are lowest in the series (Table IV). The dipole moments of the 1,2-diacetyl derivatives are about twice as large as those for the 1,4-isomers, which coincides with their lowest thermodynamic stability. Interestingly, there is only a small difference in the calculated enthalpy of formation (0.9 kcal/mol) between the 2,4- and 1,2-diacetyl derivatives **9a** and **9c** in gas phase. Given the nearly three times bigger dipole moment for the latter, the relative stability of the two isomers may reverse in polar media.

Analysis of the geometry of the optimized structures shows that only **8a** is essentially planar with the CH<sub>3</sub> group of the 2-AcS substituent rotated away from the molecular plane by 12°. In all other structures, one or both carbonyl groups are not coplanar with the ring. For instance, in **9a** and **9b**, the C(3)-C(4)-S-C(=O) dihedral angle is 126° and 138°, respectively, similar to that observed in **6a** and **6b** (vide supra).

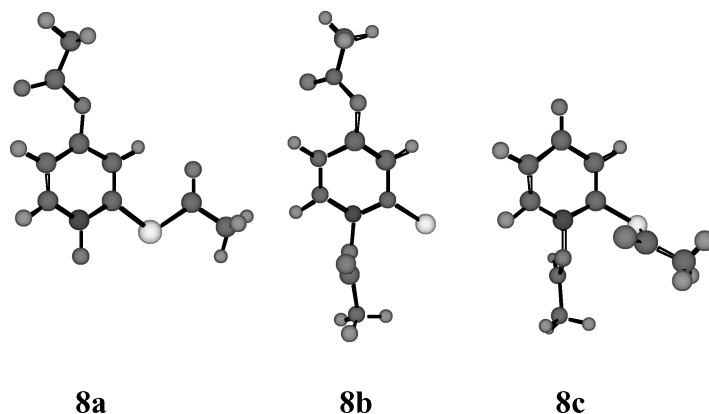
## CONCLUSIONS

Gas phase calculations showed that the 2-mercapto isomers are more thermodynamically stable than the 4-mercapto isomers. This is evident from the comparison of enthalpy of formation for pairs **1** and **5** (Table I) and also **7a** and **7e** (Table III). Analysis of the data demonstrates



<sup>a</sup>B3LYP/6-31G(d,p) level of theory. For structures **6**, see Figure 4.





**FIGURE 5** Molecular models for regioisomers of **8** obtained by geometry optimization at the B3LYP/6–31G(d,p) level of theory.

that in general, the 2-mercapto derivatives have much higher tendency to exist in the 2-thiono tautomers, than the 4-mercapto isomers in the 4-thiono forms or 4-hydroxy analogs in the 4-keto forms. For instance, tautomerization of the 2-mercapto group in **3a** is exothermic by 7 kcal/mol, while the formation of 4-thiono form **3c** is endothermic by about 10 kcal/mol (Table II). Also in esters **7**, the 2-thiono form of **7a** is more stable by nearly 6 kcal/mol, while the tautomerization of the 4-mercapto isomer **7e** is endothermic by 1.5 kcal/mol (Table III). Similar results were obtained for the 4-hydroxy analogues **6**.

The observed order of stability does not follow the trend in the molecular dipole moment of the tautomers. Nevertheless, the lower tendency of the 4-mercapto group as compared to the 2-mercapto group to tautomerize coincides with the larger increase of the molecular dipole moment in the former. For instance, tautomerization of the 4-SH group in **3a** increases the dipole moment by 225% in **3c**, while the dipole moment

**TABLE IV** Relative Enthalpy of Formation of **8** and **9** in Gas Phase and Molecular Dipole Moment<sup>a</sup>

	<b>a</b>		<b>b</b>		<b>c</b>	
	$\Delta H$ kcal/mol	$\mu$ D	$\Delta H$ kcal/mol	$\mu$ D	$\Delta H$ kcal/mol	$\mu$ D
<b>8</b>	9.0	3.7	0.0	3.9	13.0	7.9
<b>9</b>	7.9	3.3	0.0	4.5	8.8	9.5

<sup>a</sup>B3LYP/6-31G(d,p) level of theory. For structures **8**, see Figure 5.

of the 2-thiono form **3b** is bigger only by 35%. For ester **7e**, the dipole moment increases over three times in the 4-thiono form **7f**. Overall, molecular polarity is expected to play a role in the relative stabilities of the isomers and tautomers, and the thermodynamic preference observed in the gas phase may change in highly polar media in favor of more polar species. It is also possible that protic solvents such as alcohol and water will affect further the tautomeric equilibrium. Therefore, future computational analysis of these tautomeric systems will require a solvation model such as the COSMO.<sup>16</sup>

The observed strong thermodynamic preference for the 2-thiono form governs the stability of the acetyl regioisomers. Thus, the 4-substituted isomers are most stable among the monoacetyl derivatives **6** and **7**, and 1,4-diacetyl derivatives **8b** and **9b** with the 2-thione group are the most stable among the diacetyl derivatives (Table IV). Therefore, it can be expected that in non-polar solvents, the introduction of the acyl groups will lead to the formation of 1,4-diacetylated compounds. Calculations show that 4-acetyloxy derivative **6b** is separated from the next most stable regioisomer 1-acetyloxy **6c** by a comfortable margin of 5.6 kcal/mol, while the same difference for the sulfur analogs **7b** and **7c** is only 1.5 kcal/mol. Therefore, monoacylation of **3** may lead to a mixture of 1 and 4 substituted products **7b** and **7c**, respectively. The ratio of the two products can presumably be controlled with the polarity of the solvent, temperature, and the base.

Overall, computational results suggest that it is possible to selectively introduce two different acyl groups in position 4 and subsequently in position 1 to form compounds of structures **A** or **B**.

## COMPUTATIONAL DETAILS

Quantum-mechanical calculations were carried out with the B3LYP/6-31G(d,p) method using the Gaussian 98 package.<sup>17</sup> Geometry optimizations were undertaken using appropriate symmetry constraints and default convergence limits. Vibrational frequencies were used to characterize the nature of the stationary points and to obtain thermodynamic parameters at standard conditions (298.15 K and 1.0 atm). Zero-point energy (ZPE) corrections were scaled by 0.9806.<sup>18</sup>

## REFERENCES

- [1] A. R. Katritzky and R. A. Jones, *J. Chem. Soc.*, 2947 (1960).
- [2] R. A. Jones and A. R. Katritzky, *J. Chem. Soc.*, 2937 (1960).
- [3] B. M. Aveline and R. W. Redmond, *J. Am. Chem. Soc.*, **121**, 9977 (1999).
- [4] A. Bond and W. Jones, *Acta Cryst. C*, **C55**, 1536 (1999).

- [5] J. Hartung, R. Kneuer, M. Schwarz, I. Svoboda, and H. Fuess, *Eur. J. Org. Chem.*, **97** (1999).
- [6] B. M. Aveline, I. E. Kochevar, and R. W. Redmond, *J. Am. Chem. Soc.*, **118**, 10113 (1996).
- [7] D. H. R. Barton, D. Crich, and W. B. Motherwell, *Tetrahedron*, **41**, 3901 (1985).
- [8] J. Hartung, M. Hiller, M. Schwarz, I. Svoboda, and H. Fuess, *Liebigs Ann.*, 2091 (1996).
- [9] A. L. J. Beckwith and B. P. Hay, *J. Am. Chem. Soc.*, **110**, 4415 (1988).
- [10] A. L. J. Beckwith and B. P. Hay, *J. Am. Chem. Soc.*, **111**, 230 (1989).
- [11] B. P. Hay and A. L. J. Beckwith, *J. Org. Chem.*, **53**, 4330 (1988).
- [12] J. Hartung, I. Svoboda, and M. T. Duarte, *Acta Cryst. C*, **C53**, 1631 (1997).
- [13] J. N. Gardner and A. R. Katritzky, *J. Chem. Soc.*, 4375 (1957).
- [14] A. Puszko and Z. Talik, *Polish J. Chem.*, **65**, 377 (1991).
- [15] A. Puszko, *Polish J. Chem.*, **68**, 657 (1994).
- [16] G. B. Bacskay and J. R. Reimers, in *Encyclopedia of Computational Chemistry*, P. v. R. Schleyer, Ed. (Wiley, New York, 1998), Vol. 4, pp. 2620–2632, and references therein.
- [17] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian 98, Revision A.7, Gaussian, Inc., Pittsburgh, PA, 1998.
- [18] A. P. Scott and L. Radom, *J. Phys. Chem.*, **100**, 16502 (1996).