

Theoretical studies on the structure of [(1-aza-2-benzimidazol-2-ylprop-1-enyl)amino]aminomethane-1-thione

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Abstract

The tautomerisation and acid-base properties of [(1-aza-2-benzimidazol-2-ylprop-1-enyl)amino]aminomethane-1-thione were studied both in the gas and aqueous phase to elucidate the structure of this compound. The computed data, such as bond lengths, bond angles and dihedral angles, were compared with the experimental X-ray results. Excellent correlations for some properties were observed.

Keywords: Quantum chemical studies, semi-empirical methods, thiosemicarbazones, tautomerism

Introduction

Since thiosemicarbazones possess large numbers of donor atoms they can act as multifunctional types of ligand. p-Delocalization and configurational flexibility allow them to adopt a wide variety of coordination modes¹. Although different coordination modes have been reported, thiosemicarbazones usually act as bidentate ligands through their azomethyne nitrogen and thiocarbonyl sulfur atoms.²⁻⁴ It has been believed that the thiosemicarbazones are efficient on certain biological mechanisms because of their abilities to form complexes with metal cations, by bonding through the sulfur and azomethine nitrogen atoms.⁵ The compounds containing a thiosemicarbazone component have shown a broad spectrum of chemotherapeutic properties, including antimalarial,⁶ antitumour,⁷ antibacterial,⁸ antitrypanosomal,⁹ and antiviral¹⁰ activity. The anticonvulsant,¹¹ antiamebic^{12,13} and antioxidant properties¹⁴ of thiosemicarbazone derivatives should also be mentioned here. Following our work on some other type of ligands,¹⁵⁻¹⁸ we now report our recent work related to the title compound.

Results and Discussion

In the presented work we have attempted to determine some physical parameters, which will help to enlighten the structure and ligand properties of the title compound theoretically. The obtained data are depicted in Table.1.

Tautomerisation

To elucidate the structure and reaction mechanism, such as protonation reaction, it is very important to know some thermodynamic and physical parameters of the investigated compound. Therefore before doing further structural calculations we have searched for the possible tautomeric forms of the title compound **1** (Scheme 2) and the obtained results were evaluated as follows;

Mole fraction. Both AM1 and PM5 calculated mole fraction values are unity indicating the presence of tautomeric form **1** only. Whereas PM3 method indicate the predominance of tautomeric form **2** with a percentage of 97.44 (Table 1).

Tautomeric equilibrium constants. The AM1 and PM5 calculated K_T values (i.e. 4.27×10^{146} and 6.09×10^{89} respectively) supporting the mole fraction method are also indicative of predominance of tautomeric form **1** (Table 2) whereas PM3 calculation results indicate the predominance of form **2**.

Relative Stability (RS)

The calculated RS values were collected in Table 3. The AM1 and PM5 results having negative RS values of -4.92 and -7.30 kcalmol⁻¹ respectively indicate the predominance of amino thion form **1** over the amino thion form **2** as K_T and mole fraction criteria suggest (Tables 1-2). PM3 results however having positive RS value of 2.24 indicates opposite as in the case of K_T and mole fraction approaches.

Similarly, the RS values of -25.72, -27.10 and -28.04 for **3** \rightleftharpoons **1** equilibrium indicate the predominance of form **1** over the form **3** supporting the K_T and mole fraction criteria with all tree methods.

Table 1. Semi empiric calculated thermodynamic and physical parameters

Compound	Heat of formation ΔH_f (kcal mol ⁻¹)	Enthalpy ΔH (cal mol ⁻¹)	Entropy ΔS (cal mol ⁻¹)	Free energy of formation ΔG_f^a (kcal mol ⁻¹)	Gibbs free energy ΔG^b (kcal mol ⁻¹)	Mol fractions of tautomers(f) ^c	$\delta\Delta G_{(WA)}$ (kcal mol ⁻¹) ^d	Mol fractions of tautomers	$\delta\Delta G_{(WA)}$ (kcal mol ⁻¹)	HOMO	LUMO
AM1											
1	127.616	8987.464	117.540	92.589	-26.039	1.000		1.000		-8.647	-
2	132.542	8786.899	115.371	98.161	-25.594	3.975E-05	92.589	3.975E-05	-26.039	-8.029	-
3	153.337	9174.301	119.800	117.637	-26.526	4.251E-19		4.251E-19		-8.492	-
4	98.937	9626.930	126.079	61.365	-27.945					-4.194	2.516
5	77.097	9496.360	123.670	40.243	-27.357					-4.095	2.696
6	297.673	9514.919	122.691	261.111	-27.047					-	-
7	287.012	9709.989	124.532	249.901	-27.401					-	-
8	264.415	9883.864	128.537	226.111	-28.420					12.429	5.615
9	271.710	9539.510	121.354	235.547	-26.624					-11.643	-4.870
H ₂ O	-59.251	2369.362	45.087	-72.687	-11.067					-11.548	-5.143
H ₃ O ⁺	143.461	2379.918	46.195	129.695	-11.386						
PM3											
1	110.193	10126.690	127.802	72.108	-27.958	2.564E-02		2.564E-02		-8.802	-1.198
2	107.952	10166.316	127.509	69.954	-27.831	9.744E-01	70.010	9.744E-01	-27.835	-8.285	-0.957
3	137.296	9220.795	119.568	101.665	-26.410	5.374E-24		5.374E-24		-8.803	-5.588
4	76.589	9490.046	123.622	39.750	-27.349					-4.329	1.877
5	48.578	10000.066	128.073	10.412	-28.166					-4.260	2.405
6	282.067	10375.512	129.605	243.445	-28.247					-11.218	-5.962
7	273.631	10419.007	129.662	234.992	-28.220					-12.324	-5.792
8	249.050	10276.136	128.917	210.633	-28.141					-11.677	-5.160
9	252.257	10489.034	132.068	212.901	-28.867					-11.525	-5.331
H ₂ O	-53.433	2369.867	44.987	-66.839	-11.036						
H ₃ O ⁺	159.066	2378.813	46.037	145.347	-11.340						
PM5											
1	96.029	9738.215	123.530	59.217	-27.074	1.000		1.000		-8.761	-0.922
2	103.333	9615.116	121.230	67.206	-26.511	1.382E-06	59.217	1.382E-06	-27.074	-8.017	-1.336
3	124.065	9297.506	119.639	88.413	-26.355	3.857E-22		3.857E-22		-8.913	-5.931
4	62.510	8492.687	112.261	29.056	-24.961					-4.414	2.257
5	34.572	10018.341	127.917	-3.547	-28.101					-4.529	2.488
6	263.132	9727.691	124.042	226.167	-27.237					-11.294	-5.517
7	255.269	10305.580	129.898	216.559	-28.404					-12.323	-5.658
8	237.255	9908.522	123.407	200.480	-26.867					-11.738	-4.920
9	249.417	9848.928	122.156	213.015	-26.554					-11.555	-5.425
H ₂ O	-53.697	2371.296	44.943	-67.090	-11.022						
H ₃ O ⁺	138.066	2452.756	46.164	124.309	-11.304						

^a $\Delta G_f = \Delta H_f - T\Delta S$, ^b $\Delta G = \Delta H - T\Delta S$, ^c $N_1=1/(1+K_{T(2)}+K_{T(3)})$, $N_2= K_{T(2)}/(1+K_{T(2)}+K_{T(3)})$, $N_3= K_{T(3)}/(1+K_{T(2)}+K_{T(3)})$, $K_T=e^{-(\delta\Delta G/RT)}$, ^dWeighted average of $K_{T(2)}$ and $K_{T(3)}$ tautomer forms $\delta\Delta G_{(WA)}=(N_1\times\Delta G_1+ N_2\times\Delta G_2+ N_3\times\Delta G_3)$.

Table 2. Semi empirical calculated tautomeric equilibrium constants for molecule [(1-Aza-2-benzimidazol-2-ylprop-1-enyl)amino]aminomethane-1-thione molecule

Tautomeric equilibrium	$\delta\Delta G_f^a$ (kcal mol ⁻¹)	$K_{T(f)}^b$	$pK_{T(f)}^c$	$\delta\Delta G^d$ (kcal mol ⁻¹)	K_T^e	pK_T^f
AM1						
2K1-1	5.572	8.189E-05	4.087E+00	-199.919	4.270E+146	-1.466E+02
3K2-1	25.048	4.252E-19	1.837E+01	186.164	2.872E-137	1.365E+02
PM3						
2K1-1	-2.154	3.801E+01	-1.580E+00	39.713	7.456E-30	2.913E+01
3K2-1	29.557	2.096E-22	2.168E+01	-903.441		
PM5						
2K1-1	7.989	1.382E-06	5.860E+00	-122.414	6.088E+89	-8.978E+01
3K2-1	29.196	3.857E-22	2.141E+01	-439.549		

^a $\delta\Delta G_f = \Delta G_{f(K)} - \Delta G_{f(I)}$, ^b $K_{Tf} = e^{(-\delta\Delta G_f/RT)}$, $R = 1,987 \times 10^{-3}$ kcal/mol^oK and $T = 298$ °K, ^c $pK_{T(f)} = -\log K_{T(f)}$, ^d $\delta\Delta G = \Delta G_{(K)} - \Delta G_{(I)}$, ^e $K_T = e^{(-\delta\Delta G_f/RT)}$, $R = 1,987 \times 10^{-3}$ kcal/mol^oK and $T = 298$ °K, ^f $pK_T = -\log K_T$

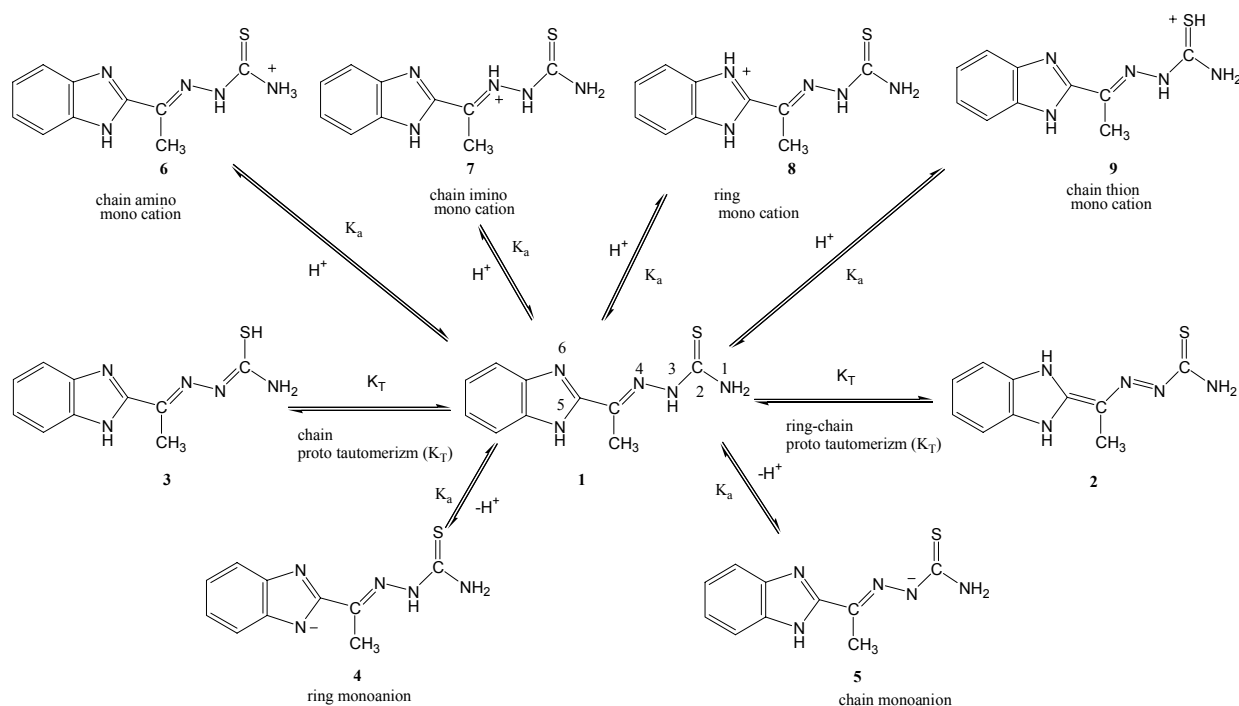
Table 3. Semi empiric calculated relative stabilities (RS) for [(1-Aza-2-benzimidazol-2-yl)prop-1-enyl)amino]aminomethane-1-thione molecule

Process	RS ^a		
	AM1	PM3	PM5
2-1	-4.926	2.241	-7.304
3-1	-25.721	-27.103	-28.036
4-1	28.679	33.604	33.519
5-1	50.519	61.615	61.457
6-1	-170.057	-171.874	-167.103
7-1	-159.396	-163.438	-159.240
8-1	-136.799	-138.857	-141.226
9-1	-144.094	-142.064	-153.388

^aRS= ΔH_f (tautomer, neutral form)- ΔH_f (ionic form), the minus sign indicates the predominance of the product.

Acidity constants

The next step to study the structure and reactivity of this biologically active molecule is to evaluate the calculated acidity constants. The possible protonation pathway for the parent compound **1** and its tautomeric forms **2** and **3** are described in Scheme 2. The calculated acidity constants are depicted in Table 4. Since the tautomeric form of **1** was found to be predominant the deprotonation equilibrium of form **1** will be discussed here.



Scheme 2. Possible tautomerisation and protonation patterns for [(1-Aza-2-benzimidazol-2-yl)prop-1-enyl]amino]aminomethane-1-thione molecule.

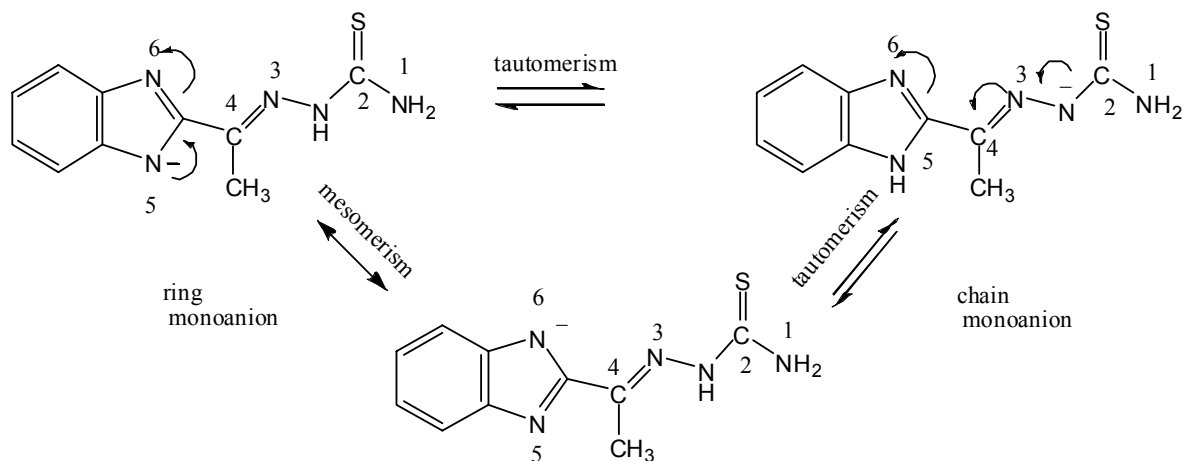
Table 4. Semi empiric calculated acid dissociation constants (i.e. acidity constant) for deprotonation and protonation for [(1-Aza-2-benzimidazol-2-yl)prop-1-enyl]amino]aminomethane-1-thione molecule

Deprotonation equilibrium	$\Delta\Delta G_f^a$	$pK_a(f)^b$	$\Delta\delta G^c$	pK_a^d	$\delta\Delta G_{f(WA)}^e$	$pK_{a(f)(WA)}^f$	$\Delta\delta G_{(WA)}^g$	$pK_{a(WA)}^h$
AM1								
1(BH ₂)-4(BH ⁻)	171.158	125.513	-2.225	-1.632	171.157	125.512	-1.985	-1.456
1(BH ₂)-5(BH ⁻)	150.036	110.024	-1.637	-1.200	150.035	110.023	-1.397	-1.024
PM3								
1(BH ₂)-4(BH ⁻)	179.828	131.871	27.654	20.279	181.926	133.409	27.540	20.196
1(BH ₂)-5(BH ⁻)	150.490	110.357	27.654	20.279	152.588	111.895	27.540	20.196
PM5								
1(BH ₂)-4(BH ⁻)	161.238	118.239	26.792	19.647	161.238	118.239	26.516	19.445
1(BH ₂)-5(BH ⁻)	128.635	94.330	26.792	19.647	128.635	94.330	26.516	19.445
Protonation equilibrium	$\delta\Delta G_f^i$	$pK_a(f)^j$	$\Delta\delta G^k$	pK_a^l	$\delta\Delta G_{f(WA)}^m$	$pK_{a(f)(WA)}^n$	$\Delta\delta G_{(WA)}^o$	$pK_{a(WA)}^p$
AM1								
1(B)-6(BH ⁺)	33.860	24.830	0.689	0.505	33.861	24.831	0.449	0.329
1(B)-7(BH ⁺)	45.070	33.051	1.043	0.765	45.071	33.051	0.803	0.589

1(B)-8(BH ⁺)	68.860	50.496	2.062	1.512	68.861	50.497	1.822	1.336
1(B)-9(BH ⁺)	59.424	43.577	0.266	0.195	59.425	43.577	0.026	0.019
PM3								
1(B)-6(BH ⁺)	40.849	29.955	-0.015	-0.011	38.751	28.417	0.099	0.073
1(B)-7(BH ⁺)	49.302	36.154	-0.042	-0.031	47.204	34.616	0.072	0.053
1(B)-8(BH ⁺)	73.661	54.017	-0.121	-0.089	71.563	52.478	-0.007	-0.005
1(B)-9(BH ⁺)	71.393	52.354	0.605	0.444	69.295	50.815	0.719	0.527
PM5								
1(B)-6(BH ⁺)	24.449	17.929	-0.119	-0.087	24.449	17.929	0.157	0.115
1(B)-7(BH ⁺)	34.057	24.975	1.048	0.769	34.057	24.975	1.324	0.971
1(B)-8(BH ⁺)	50.136	36.766	-0.489	-0.359	50.136	36.766	-0.213	-0.156
1(B)-9(BH ⁺)	37.601	27.573	-0.802	-0.588	37.601	27.573	-0.526	-0.386

^a $\delta\Delta G_{f(BH_2)} = [\Delta G_{f(BH^-)} + \Delta G_{f(H_3O^+)}] - [\Delta G_{f(BH_2)} + \Delta G_{f(H_2O)}]$, ^b $pK_{a(f)(BH_2)} = \delta\Delta G_{f(BH_2)} / (2,303RT)$, $R=1,987 \times 10^{-3} \text{ kcal mol}^{-1} \text{ K}^{-1}$ and $T=298 \text{ K}$, ^c $\delta\Delta G_{(BH_2)} = [\Delta G_{(BH^-)} + \Delta G_{(H_3O^+)}] - [\Delta G_{(BH_2)} + \Delta G_{(H_2O)}]$, ^d $pK_{a(BH_2)} = \delta\Delta G_{(BH_2)} / (2,303RT)$, ^e $\delta\Delta G_{f(WA)(BH_2)} = [\Delta G_{f(BH^-)} + \Delta G_{f(H_3O^+)}] - [\Delta G_{f(BH_2)} + \Delta G_{f(H_2O)}]$, ^f $pK_{a(f)(WA)(BH_2)} = \delta\Delta G_{f(WA)(BH_2)} / (2,303RT)$, $R=1,987 \times 10^{-3} \text{ kcal mol}^{-1} \text{ K}^{-1}$ and $T=298 \text{ K}$, ^g $\delta\Delta G_{(WA)(BH_2)} = [\Delta G_{(BH^-)} + \Delta G_{(H_3O^+)}] - [\Delta G_{(BH_2)} + \Delta G_{(H_2O)}]$, ^h $pK_{a(WA)(BH_2)} = \delta\Delta G_{(BH_2)} / (2,303RT)$, ⁱ $\delta\Delta G_{f(BH^+)} = [\Delta G_{f(B)} + \Delta G_{f(H_3O^+)}] - [\Delta G_{f(BH^+)} + \Delta G_{f(H_2O)}]$, ^j $pK_{a(f)(BH^+)} = \delta\Delta G_{f(BH^+)} / (2,303RT)$, $R=1,987 \times 10^{-3} \text{ kcal mol}^{-1} \text{ K}^{-1}$ and $T=298 \text{ K}$, ^k $\delta\Delta G_{(BH^+)} = [\Delta G_{(B)} + \Delta G_{(H_3O^+)}] - [\Delta G_{(BH^+)} + \Delta G_{(H_2O)}]$, ^l $pK_{a(BH^+)} = \delta\Delta G_{(BH^+)} / (2,303RT)$, $R=1,987 \times 10^{-3} \text{ kcal mol}^{-1} \text{ K}^{-1}$ and $T=298 \text{ K}$, ^m $\delta\Delta G_{f(WA)(BH^+)} = [\Delta G_{f(B)} + \Delta G_{f(H_3O^+)}] - [\Delta G_{f(BH^+)} + \Delta G_{f(H_2O)}]$, ⁿ $pK_{a(f)(WA)(BH^+)} = \delta\Delta G_{f(WA)(BH^+)} / (2,303RT)$, $R=1,987 \times 10^{-3} \text{ kcal mol}^{-1} \text{ K}^{-1}$ and $T=298 \text{ K}$, ^o $\delta\Delta G_{(WA)(BH^+)} = [\Delta G_{(B)} + \Delta G_{(H_3O^+)}] - [\Delta G_{(BH^+)} + \Delta G_{(H_2O)}]$, ^p $pK_{a(WA)(BH^+)} = \delta\Delta G_{(WA)(BH^+)} / (2,303RT)$, $R=1,987 \times 10^{-3} \text{ kcal mol}^{-1} \text{ K}^{-1}$ and $T=298 \text{ K}$

Deprotonation pK_a values. There are two acidic NH protons in molecule **1**. The first NH is placed in the chain (i.e. 3NH) and the second NH is in the imidazole ring (i.e. 5NH). When one of the protons of the two NH groups is removed the following two mesomeric and a tautomeric form of the anion become feasible; and both ring and chain anions may rearrange into the same form (Scheme 1). The formed minus charge is stabilized better on 6N atom because of the aromaticity of the imidazole ring. Therefore, the closeness of the pK_a values for **1** \rightleftharpoons **4** and **1** \rightleftharpoons **5** deprotonation equilibrium is expected. The PM3 and PM5 calculated pK_a values of 20.28 and 19.65 (Table 4) are acceptable results. If we consider the effect of substituent at 2C these results are comparable with experimentally obtained pK_a value of 12.75 for deprotonation of benzimidazole²⁴.



Scheme 1. Possible deprotonation patterns for [(1-Aza-2-benzimidazol-2-ylprop-1-enyl) amino]aminomethane-1-thione molecule.

Protonation pK_a values. The protonation acidity constant of benzimidazole molecule was reported as 5.56²⁵ and none of the calculated pK_a value is close to that value. However, if we consider the electronic and steric effect of the big substituted group located at 2C position we can suggest a reaction path for the first protonation of molecule **1**. The AM1 calculated pK_a values of 1.51 and 1.34 suggest a ring protonation via **1** \rightleftharpoons **8** equilibrium. Whereas the PM5 calculated pK_a value of 17.30 suggest firstly a transformation into tautomeric form of **2** then deprotonation from the ring proton via **1** \rightleftharpoons **8** equilibrium.

Proton affinities (PA). The gas phase calculated proton affinities for molecule **1** were depicted in Table 5. For 5N anion (molecule **4**) proton affinities were found to be bigger than that of 3N anion (molecule **5**) with all methods. So we can say protonation on 5N anion **4** should be easier than that of 3N anion **5**. The reverse argument is applicable for deprotonation.

Similarly proton affinity values for molecule **1** states that the biggest PA values which were calculated with AM1, PM3 and PM5 methods belong to amino group. Therefore, the first protonation should take place at NH_2 and, as was stated under the other headings, the protonation pattern is **1** \rightleftharpoons **6** for molecule **1**.

Nucleophilicity. The calculated nucleophilicity values are collected in Table 6. The results with all methods are indicative of the biggest nucleophilicity of molecule **1**. This result supports the greatest basicity of (i.e. greater pK_a values) molecule **1** compared to the other tautomers (i.e. molecules **2** and **3**) and even than that of anions (i.e. molecules **4** and **5**).

Table 5. The proton affinities, PA values, for molecule [(1-Aza-2-benzimidazol-2-yl)prop-1-enyl]amino]aminomethane-1-thione molecule

Process	PA ^a		
	AM1	PM3	PM5
1-4(proton loss) ^a	-174.033	-178.895	-158.244
1-5(proton loss) ^a	-152.193	-150.884	-130.306
1-6(proton gain) ^c	32.655	40.625	24.66
1-7(proton gain) ^c	43.316	49.061	32.523
1-8(proton gain) ^c	65.913	73.642	50.537
1-9(proton gain) ^c	58.618	70.435	38.375

^aPA=[$\Delta H_f(\text{BH}_2)+\Delta H_f(\text{H}_2\text{O}) - \Delta H_f(\text{BH}^-)+\Delta H_f(\text{H}_3\text{O}^+)$], ^bPA=[$\Delta H_f(\text{BH}^-)+\Delta H_f(\text{H}_2\text{O}) - \Delta H_f(\text{B}^{2-})+\Delta H_f(\text{H}_3\text{O}^+)$], ^cPA=[$\Delta H_f(\text{B})+\Delta H_f(\text{H}_3\text{O}^+) - \Delta H_f(\text{BH}^+)+\Delta H_f(\text{H}_2\text{O})$]

Table 6. Calculated nucleophilicities for studied molecules

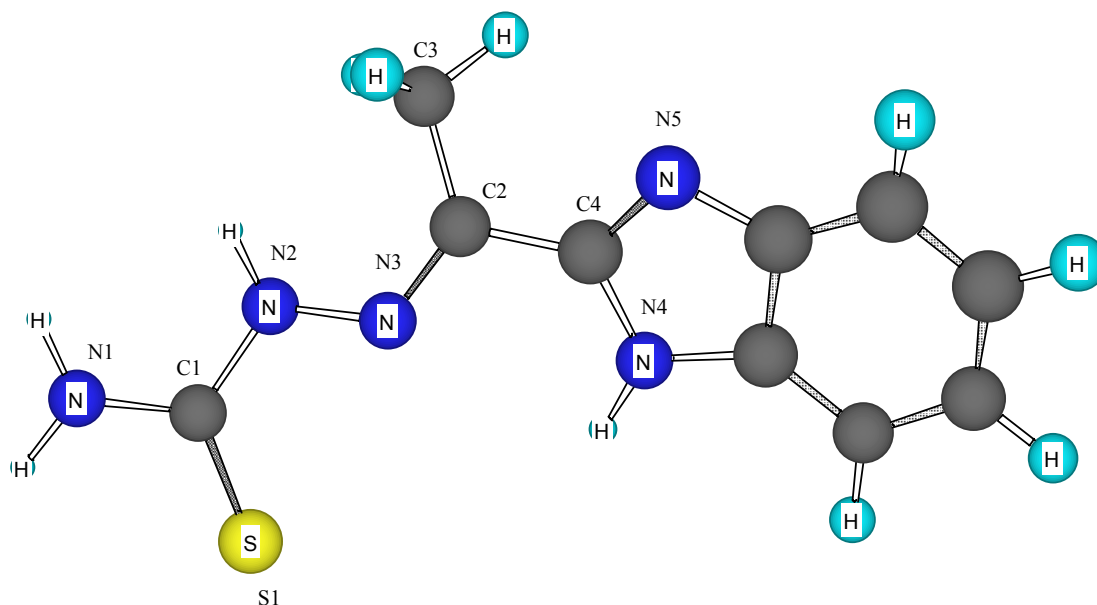
Molecules	(η) nucleophilicity ^a		
	AM1	PM3	PM5
1	-7.964	-7.604	-7.839
2	-7.099	-7.328	-6.681
3	-2.901	-3.215	-2.982
4	-6.710	-6.206	-6.671
5	-6.791	-6.665	-7.017
6	-5.839	-5.256	-5.777
7	-6.814	-6.532	-6.665
8	-6.773	-6.517	-6.818
9	-6.405	-6.194	-6.130

^a η =HOMO-LUMO

Structure elucidation via correlation

Knowledge of the predominant tautomeric form and some physical parameters will make the elucidation of the structure of the title compound easier. The best way to do this will be searching the correlation between calculated and experimental results.

Bond lengths. The correlation attempt to reveal out the relation between the experimental and computed bond lengths have indicated that the best correlation was observed by PM5 calculations (i.e. $R^2 = 0.9871$). The slope of the regression line however is a little away from the unity (i.e. $m = 1.447$) indicating that no one to one correspondence is present. In the bond length calculations for N1-C1, S1-C1 and C2-C4, however, the AM1 method was found to perform better (Table 7).



Scheme 3. [(1-Aza-2-benzimidazol-2-yl)prop-1-enyl]amino]aminomethane-1-thione molecule (Chem3D Draw)

Table 7. The Gas phase selected bond distances, angles and dihedral angles (T=298 K) in CAChe Work system Pro Version 6.1 program

Bond Lengths (Å)	AM1	%(a)	m	R ²	PM3	%(b)	m	R ²	PM5	%(c)	m	R ²	Exp.
N1-C1	1.382	5.335			1.418	8.079			1.384	5.488			1.312(6)
S1-C1	1.600	5.716			1.622	4.420			1.602	5.598			1.697(4)
C1-N2	1.422	5.255			1.435	6.218			1.421	5.181			1.351(5)
N2-N3	1.326	2.999	1.3039	0.8679	1.384	1.244	1.3620	0.8869	1.389	1.609	1.4470	0.9871	1.367(4)
N3-C2	1.317	2.411			1.307	1.633			1.307	1.633			1.286(5)
C2-C3	1.496	0.268			1.498	0.402			1.496	0.268			1.492(6)
C2-C4	1.484	0.815			1.466	0.408			1.474	0.136			1.472(5)
Bond Angles (°)													
S1-C1-N1	120.269	2.458	(a)	(a)	121.032	1.839	(a)	(a)	119.648	2.962	(a)	(a)	123.300(3)
S1-C1-N2	125.003	4.868	(b)	(b)	128.224	7.570	(b)	(b)	126.769	6.350	(b)	(b)	119.200(3)
N1-C1-N2	114.727	2.360			110.744	5.750			113.558	3.355			117.500(4)
C1-N2-N3	120.526	2.227			118.419	0.440			114.180	3.155			117.900(4)
N2-N3-C2	121.969	2.495			122.061	2.572			120.489	1.251			119.000(4)

N3-C2-C3	128.803	1.181			125.369	1.517			129.277	1.553			127.300(4)
N3-C2-C4	116.354	3.059			117.112	3.731			114.512	1.428			112.900(4)
C3-C2-C4	114.841	4.139			117.519	1.904			116.209	2.997			119.800(3)
C2-C4-N4	121.162	3.302			123.640	1.325			121.730	2.849			125.300(4)
C2-C4-N5	126.469	3.578			126.553	3.647			126.353	3.483			122.100(3)
N4-C4-N5	112.369	0.205			109.738	2.542			111.917	0.607			112.600(3)
Dihedral Angles (°)													
N1-C1-N2-N3	179.875	131.667			164.461	895.933			166.305	773.000			1.500(6)
S1-C1-N2-N3	0.091	0.792	0.9732	0.9999	15.554	7.900	1.0604	0.9940	15.514	7.877	1.0421	0.9948	177.900(3)
C1-N2-N3-C2	179.909	1.072			164.345	7.671			169.568	4.737			178.000(4)
N2-N3-C2-C3	0.033	98.059			3.220	89.412			4.486	163.882			1.700(7)
C3-C2-C4-N4	0.042	98.688			1.747	45.406			1.536	52.000			3.200(7)
C3-C2-C4-N5	179.966	1.618	0.9732	0.9999	174.929	1.226	0.9732	0.9999	178.459	0.767	0.9732	0.9999	177.100(5)
N3-C2-C4-N4	179.984	1.859			178.449	0.990			178.038	0.757			176.700(4)
N3-C2-C4-N5	0.008	99.733			4.875	62.500			1.997	33.433			3.000(6)

% (a) $(|AM1-Exp. | / Exp.) \times 100$; % (b) $(|PM3-Exp. | / Exp.) \times 100$; % (c) $(|PM5-Exp. | / Exp.) \times 100$.

Angles. The correlation attempts of experimental and computed bond angles however not successful as bond lengths. The best regression constant R^2 was 0.573 with a slope m of 0.6109 with PM5 method and we can say that it is not a successful attempt so as the other methods (i.e. AM1 and PM3 methods indicate R^2 values of 0.5194 and 0.5002 respectively) (Table 7).

Dihedral angles. The correlation attempts of dihedral angles were revealed that the best correlation was observed by AM1 calculations (i.e. $R^2=0.9871$ and $m=0.9732$). The slope is about unity and regression is about unity that means it may safely be used to predict dihedral angles of such a big molecules which contains sulphur and nitrogen heteroatoms (Table 7). PM3 and PM5 methods also produce similar results, which can be used in a predictive manner to eliminate the time and expenditure of elaborate X-ray analysis.

Table 8. The Gas phase selected bond distances, angles and dihedral angles (T=298 K) in Spartan 04 V1.0.3 program

Bond Lengths (Å)	6-31G** ^a	%(d)	m	R ²	B3LYP/6-31G* ^b	%(e)	m	R ²	Exp.
N1-C1	1.327	1.143			1.345	2.515			1.312(6)
S1-C1	1.683	0.825			1.679	1.061			1.697(4)
C1-N2	1.348	0.222			1.369	1.332			1.351(5)
N2-N3	1.345	1.609	0.9843	0.9871	1.360	0.512	1.0865	0.9916	1.367(4)
N3-C2	1.265	1.633			1.302	1.244			1.286(5)
C2-C3	1.507	1.005			1.508	1.072			1.492(6)
C2-C4	1.481	0.611			1.474	0.136			1.472(5)
Bond Angles (°)									
S1-C1-N1	122.970	0.268			123.720	0.268			123.300(3)
S1-C1-N2	119.930	0.612	(a) -0.6747	(a) 0.8897	119.690	0.612	(a) 0.8945	(a) 0.9485	119.200(3)
N1-C1-N2	117.090	0.349	(b) 0.6439	(b) 0.6987	116.560	0.800	(b) 5.4413	(b) 0.9977	117.500(4)
C1-N2-N3	121.170	2.774			123.850	2.774			117.900(4)
N2-N3-C2	121.460	2.067			117.460	2.067			119.000(4)
N3-C2-C3	117.560	7.651			118.790	7.651			127.300(4)
N3-C2-C4	124.350	10.142			121.880	10.142			112.900(4)
C3-C2-C4	118.080	1.436			119.320	1.436			119.800(3)
C2-C4-N4	122.510	2.227			124.200	2.227			125.300(4)
C2-C4-N5	125.120	2.473			123.530	2.473			122.100(3)
N4-C4-N5	112.330	0.240			111.980	0.240			112.600(3)
Dihedral Angles (°)									
N1-C1-N2-N3	1.610	7.333			0.470	7.333			1.500(6)
S1-C1-N2-N3	177.620	0.157			178.780	0.157			177.900(3)
C1-N2-N3-C2	173.940	2.281			161.440	2.281			178.000(4)
N2-N3-C2-C3	179.990	10487.647	1.029	0.999	174.350	10487.647	1.2955	0.9043	1.700(7)
C3-C2-C4-N4	7.070	120.938			49.450	120.938			3.200(7)
C3-C2-C4-N5	175.540	0.881			137.320	0.881			177.100(5)
N3-C2-C4-N4	171.57	2.903			131.620	2.903			176.700(4)
N3-C2-C4-N5	5.820	94.000			41.610	94.000			3.000(6)

% (d) (|6-31G** -Exp. | /Exp.)x100, % (e) (|B3LYP -Exp. | /Exp.)x100. ^aGas phase, RHF,6-31G**, ^bGas phase, DFT (RHF,B3LYP/6-31G*).

Experimental Section

General Procedures. A slightly modified procedure from the literature was applied to prepare the thiosemicarbazone derivatives.¹⁹ To achieve this a mixture of 2-acetylbenzimidazole (5 mmol), thiosemicarbazide (5 mmol) and acetic acid (1 mL) in ethanol (50 mL) was refluxed for six hours. The raw product precipitated in cooled solution was filtered and recrystallised from ethanol: yield: 70-80 %; mp 230-231 °C. The structure elucidation was done by X-ray method and reported elsewhere.²⁰

Quantum chemical calculations were carried out at the Restricted Hartree–Fock level using AM1, PM3, and PM5 semi-empirical SCF-MO methods in the CAChe Work system Pro Version 6.1 program²¹ and Restricted Hartree–Fock level using 6-31G** and DFT in B3LYP 6-31G* *ab initio* methods in the Spartan²², implemented on an Intel Pentium Pro.400 MHz computer. Initial estimates for the geometries its structures were obtained by a molecular mechanics program (CS Chemoffice Pro for Windows)²³, followed by full optimization of all geometrical variables (bond lengths, bond angles and dihedral angles), without any symmetry constraint, using the semi-empirical AM1, PM3, and PM5 quantum chemical methods in the CAChe Work system Pro Version 6.1 and Spartan 04 V1.0.3 programs.

Conclusions

It seems that quantum chemical calculation can safely be used in structure elucidation of big molecules such as [(1-aza-2-benzimidazol-2-yl)prop-1-enyl]amino]aminomethane-1-thione and this kind of calculations should be performed as a prediction of possible synthesis and the stability of the predictive product. In order words it is an economical predictive approach for elaborate synthesis.

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