

Water assisted and solvation energies of intramolecular proton transfer process in thioformohydroxamic acid structures

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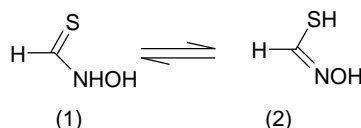
ABSTRACT

A quantum chemistry calculation has been applied in order to investigate the intramolecular proton transfer process in thioformohydroxamic in gas phase and in water. The global isomeric structures, the transfer potential surfaces, the harmonic frequency and transition states geometries of intramolecular proton transfer were calculated at the B3LYP/6-31++G** // B3LYP/6-31G* levels of theory. The free energies, enthalpies of solvation and equilibrium constants are calculated at the same level of theory. The 1Z and 1E are thione forms whereas 2Z and 2E are thiol forms and S1 is the charge-separated structure. The stability order for thioformohydroxamic acid molecules are 2Z>1Z>2E>1E>>>S1. The presence of waters molecules stabilizes the keto-1Z form of the molecules of thioformohydroxamic acid by approximately 2-3 kcal/mol. The thermodynamic and the kinetic parameters reveals that the hydrogen binding with water stabilized both 1Z.2H₂O and 1Z.3H₂O to greater extent than 1E.2H₂O and 1E.3H₂O. The reaction pathways for the interconversion between tautomers were through the transition structures TS1, TS2, TS3 and TS4. The TS3 was involved in the rate-determining step. The ring strain is clearly affecting the activation barrier. Some anionic structures are also examined to look whether the thiohydroxamic acids are O-acid, N-acid or S-acid.

Key Words: Free energy, N-acid, Global isomeric structures, and Potential energy surfaces.

INTRODUCTION

Thiohydroxamic acids like their hydroxamic acid counterparts, play important roles in analytical and biological chemistry, this interesting class of compounds contains a four-atom unit with the diverse atoms Csp², S, N and O. The presence of three electronegative atoms, O1, N and O2 ensures that it has interesting properties [1-3]. In general, thioformohydroxamic acids may exist in the two tautomeric forms, thione (1) or thiol (2).



Despite of these uses, very little is known about their structure, and fewer computational studies have been applied to thioformohydroxamic acid and no theoretical study has been reported for multi-water hydration of thioformohydroxamic acid. The structure and deprotonation of some thiohydroxamic acid derivatives has the subject of several theoretical investigations [4-5]. The aim of this study is to provide a consistent and reliable set of gas-phase and water assisted structures for the thioformohydroxamic acid using B3LYP/6-31G(d)//B3LYP/6-

311++G(d,p) levels of the theory. Additional interests are the molecular geometries, activation barriers, enthalpies and free energy in solution.

MATERIALS AND METHODS

COMPUTATIONAL DETAILS

The calculations were investigated the relative stabilities of the various tautomeric forms of various thiohydroxamic acids, and then studied the reaction paths leading from one to the other. Similar calculations were performed for the thioformohydroxamate anion to decide whether thioformohydroxamic acid is an N-acid, an O-acid or S-acid. The DFT calculations were performed with the B3LYP three parameter density functional, which includes Becke's gradient exchange correction [6] and the Lee–Yang–Parr correlation functional.[7,8] The geometries of all conformers, products and transition states were fully optimized at the B3LYP/6-31G(d) level of theory. This was followed by harmonic frequency calculations at this level; the optimized structures were confirmed to be real minima by frequency calculation (no imaginary frequency). The vibrational frequencies were scaled by a factor of 0.9614 [9]. The zero-point vibrational energy contribution is also considered. Single-point calculations were then performed at the B3LYP/6-31++G(d,p) level for the geometries optimized at the B3LYP/6-31G(d) level. The SCF = Tight option was used in these calculations. Free energy of salvation for 1Z and 1E conformers were calculated using SCRF keyword with Tomasi's polarized continuum (PCM) model [10]. Mon-, di- and tri-water molecules with dielectric constant have been used as a solvent. Calculations were carried out using Gaussian 03 program package [11].

RESULTS AND DISCUSSION

There are two thione forms (1Z, 1E), two thiol forms (2Z., 2E) and thiol form with charge-separated structure S1. The anion structures are of three types corresponding to the ionization of a proton from nitrogen, oxygen or sulfur. The 1ZN is an anion formed from the deprotonation of N-H of 1Z structure. Figure 1 and Table 1 Summarized the structures and the bond lengths of the optimized molecules. There are four transition structures (TS1, TS2, TS3 and TS4) located on the potential energy surface. TS3 is located on the reaction coordinate for 2Z to 2E conversion; it is clear that it's the transition state of highest energy in the path and is involved in the rate-determining step. The other transition structures (TS1, TS2, TS4) are involved in the proton transfer between pair of tautomers, 1Z-S1, S1-2Z, and 2E-1E, respectively. Most of the optimized structures were found to be planar. The only non-planar structure was 1E with SCNO angle been the smallest, and thus in this structure the nitrogen adopted a pyramidal orientation. The thiol forms 2Z and 2E are planar due to the formation of C=N double bond.

Table 1: The Selected optimized bond length of the molecules.

| Molecules | C-S | C-N | N-O | O-H | N-H | C-H | S-H |
|-----------|-------|-------|-------|-------|-------|-------|-------|
| 1Z | 1.666 | 1.327 | 1.380 | 0.993 | 1.010 | 1.091 | - |
| S | 1.741 | 1.312 | 1.282 | - | 1.027 | 1.082 | 1.362 |
| 2Z | 1.770 | 1.279 | 1.406 | 0.970 | - | 1.086 | 1.348 |
| 1E | 1.648 | 1.349 | 1.404 | 0.974 | 1.017 | 1.092 | - |
| 2E | 1.765 | 1.276 | 1.412 | 0.970 | - | 1.091 | 1.351 |

The potential energy profile for the intramolecular proton transfer of thioformohydroxamic acid structures is given in Figure 2. The relative energies are listed in Table 2. The calculated total energy at B3LYP/6-311++G(d,p) level of theory showed that the 2Z structure possessed the lowest energy, and the energy values are reported related to 2Z. The stability order are 2Z>1Z>2E>1E>>>S1.

The energy difference among the structures is no greater than 3.62 kcal/mol. If the transformation of 1Z to 2Z were to take place in one step, the only possible path would be the direct transfer of the proton attached to the nitrogen to the sulfur atom. It seems very difficult since the distance between the hydrogen and the sulfur is calculated to be 3.597 Å in the trans position and therefore, there is no sufficient kinetic energy to initiate such direct transfer. Thus interconversion between the thione and thiol form occur via a path (1Z→TS1→S1→TS2→2Z) that has an overall activation barrier of 49.52 kcal/mol. Similar activation barrier for thioformohydroxamic acid has been reported previously at 52.20 kcal/mol [2]. The second path involving the transformation of thiol 2Z structure to thione 1E structures via a path (2Z→TS3→2E→TS4→1E), that has an activation barrier of 34.52 kcal/mol. This is again

comparable to previously reported value (34.50 kcal/mol) [2]. The difference in transition states energies are clearly related to the ring strain of the structure, therefore three-member ring TS2 has higher energy than TS4 and TS1.

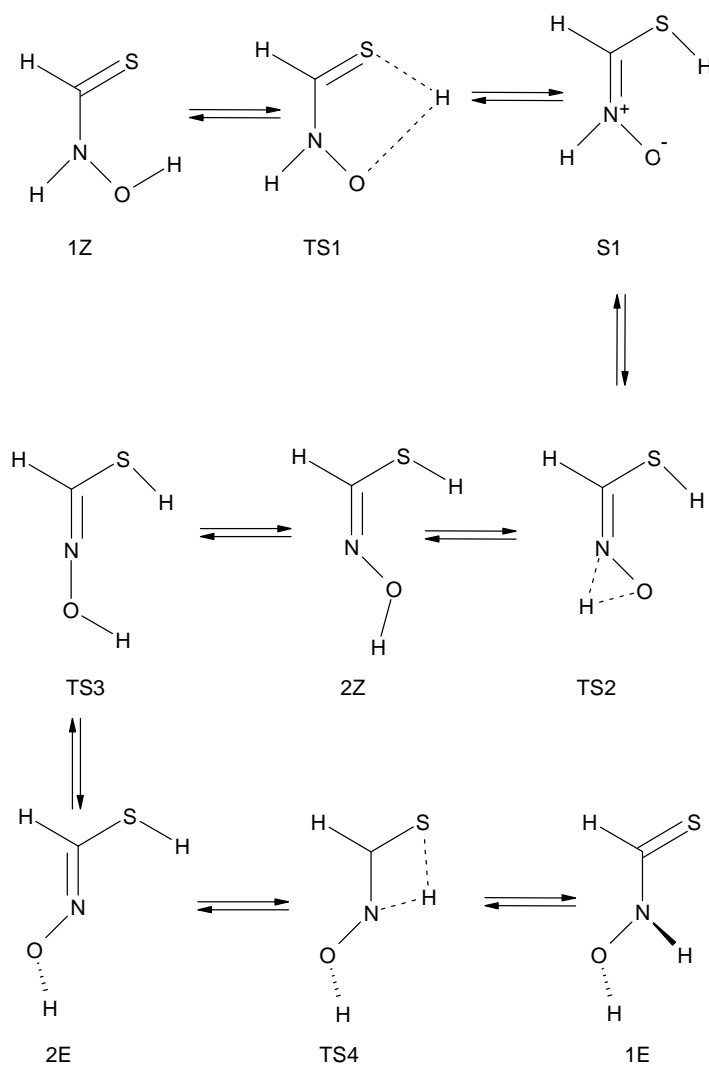


Fig. 1. The structures of thioformohydroxamic acid and the transition states interconnecting them.

| Table 2: The relative energy of the molecules in kcal/mol. | |
|--|------------|
| Structure | Relative E |
| Z1 | 0.423 |
| TS1 | 10.75 |
| CS | 9.67 |
| TS2 | 49.52 |
| Z2 | 0.00 |
| TS3 | 51.19 |
| E2 | 3.09 |
| TS4 | 34.52 |
| E1 | 3.62 |
| Z1N | 326.65 |
| Z1O | 341.43 |
| E1N | 335.45 |
| E1O | 335.03 |
| E2S | 335.46 |
| E2O | 356.67 |

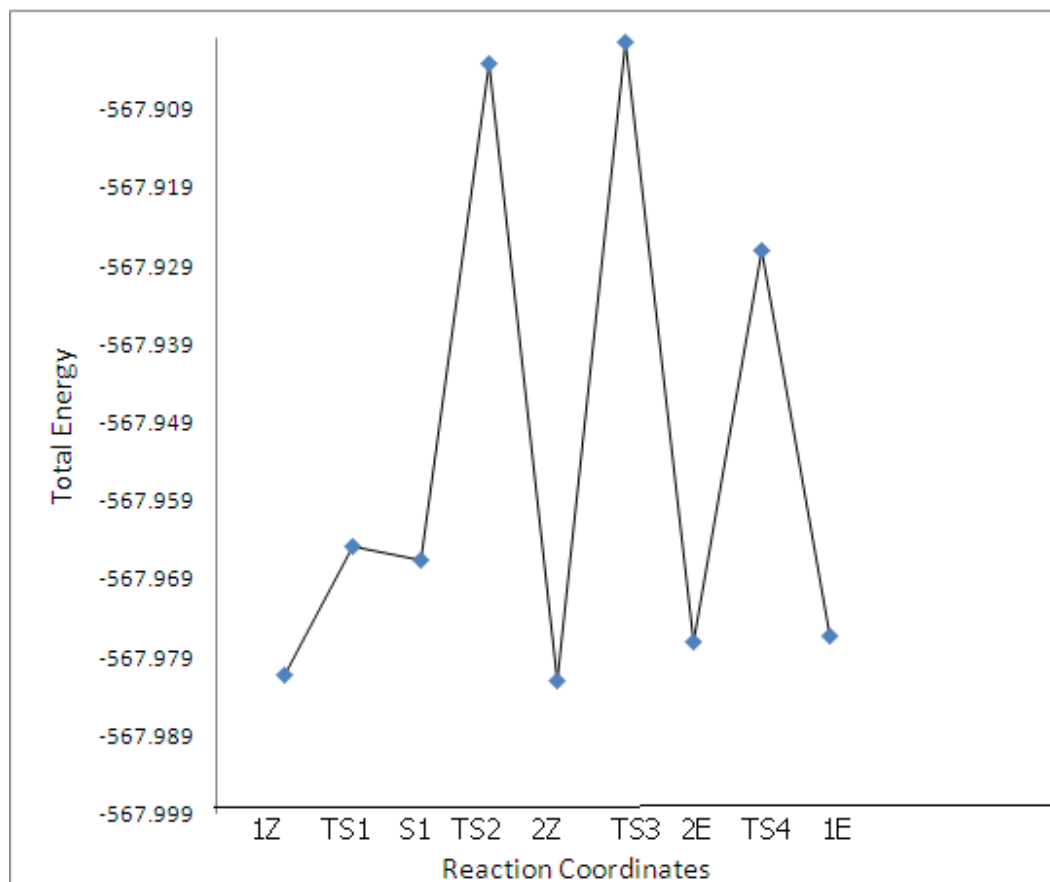


Fig. 2. Schematic energy profile for the proton transfer in thioformohydroxamic acid.

Solvation effect

The free energy of solvation for 1Z and 1E conformers were calculated using $n\text{H}_2\text{O}$ ($n = 1, 2$ and 3) molecules as a solvent. The selected optimized geometries of the hydrated molecules are listed in Table 3. The major purpose from considering solvent effect is simulation of real system and determination of the differences between the gas phase and solvent systems. The total energies, enthalpies and free energies of the calculated molecules are listed in Table 4 and Figure 3.

Table 4: The total energy (E_t), free energies (G) and enthalpies (H); energies in solution (E_{soln}) and total free energies in solution (G_{soln}) all are in Hartree/particle and in atomic unit.

| | E_{soln} | G_{soln} | E_t | G | H |
|---------|-------------------|-------------------|-------------|-------------|-------------|
| Z1.1H2O | -644.592804 | -644.586200 | -644.512491 | -644.392980 | -644.353948 |
| Z1.2H2O | -721.072086 | -721.062245 | -720.943220 | -720.802154 | -720.756321 |
| Z1.3H2O | -797.540790 | -797.529422 | -797.387319 | -797.209173 | -797.158231 |
| E1.1H2O | -644.589810 | -644.582680 | -644.509675 | -644.390539 | -644.350734 |
| E1.2H2O | -721.065267 | -721.055136 | -720.935553 | -720.795288 | -720.748086 |
| E1.3H2O | -797.528439 | -797.516547 | -797.363023 | -797.202805 | -797.147557 |
| H2O | - | - | -76.436831 | -76.406115 | -76.384014 |
| 2H2O | - | - | -152.876309 | -152.810430 | -152.777325 |
| 3H2O | - | - | -229.326217 | -229.221723 | -229.185745 |

The equilibrium constants of hydrated reactions were calculated from Gibbs free energies using $\Delta G = -RT \ln K_{\text{eq}}$. The equilibrium constant at 298.15 K of the hydration reactions are listed in Table 5, all the hydration reactions showed a very small equilibrium constant values which means that the reactions at this temperature favor the reactants. The $1\text{E} + 3\text{H}_2\text{O}$ reaction is quantitative and has the largest value (1.6). The Gibbs free energy difference

(ΔG) between hydrated conformers at B3LYP/6-311++G(d,p) level of theory lie between -3.266 and 0.286 kcal/mol Table 5. From the free energies of various 1Z and 1E molecules in aqueous solution it was found that the values for 1Z.H₂O, 1Z.2H₂O and 1Z.3H₂O are -0.217, -3.266 and -0.584 kcal/mol, whereas the values for 1E.H₂O, 1E.2H₂O and 1E.3H₂O are -1.811, -2.083 and 0.286 kcal/mol respectively at 298.15 K and 1 atmosphere pressure. Therefore, the 1Z form becomes more favored in aqueous solution, in agreement with experimental finding [12]. The 1Z.nH₂O was found to be more stable than 1E.nH₂O by 1.77, 4.81 and 15.25 kcal/mol assigned for mono-, di- and tri-hydrated molecules respectively. Thus, 1Z becomes more strongly favored in aqueous solution. The calculated enthalpies for hydration process in which mono- di- and tri-water molecules are added; the enthalpies of 1Z are -10.37, -16.05 and -11.97 kcal/mol attributed for mono-, di- and tri-hydrated molecules respectively. The calculated enthalpies for 1E.nH₂O are -11.49, -14.03 and -8.41 kcal/mol. Thus, hydrogen binding with water stabilized both 1Z.2H₂O and 1Z.3H₂O to greater extent than 1E.2H₂O and 1E.3H₂O. The enthalpies were estimated by adding the thermal corrections to the energy to account for translational, vibrational and rotational motion at 298.15 K and 1 atmosphere pressure.

Table 5: Free energies, enthalpies and equilibrium constants for the hydration reactions.

| The reaction | ΔG | ΔH | Keq |
|---|------------|------------|----------|
| 1Z + H ₂ O → 1Z.H ₂ O | -0.217115 | -10.37 | 6.94E-31 |
| 1Z + 2H ₂ O → 1Z.2H ₂ O | -3.2661375 | -16.05 | 4.06E-33 |
| 1Z + 3H ₂ O → 1Z.3H ₂ O | -0.5842025 | -11.97 | 3.73E-31 |
| 1E + H ₂ O → 1E.H ₂ O | -1.810965 | 5.95 | 4.72E-32 |
| 1E + 2H ₂ O → 1E.2H ₂ O | -2.0833 | 3.41 | 2.98E-32 |
| 1E + 3H ₂ O → 1E.3H ₂ O | 0.28614 | 9.03 | 1.60 |

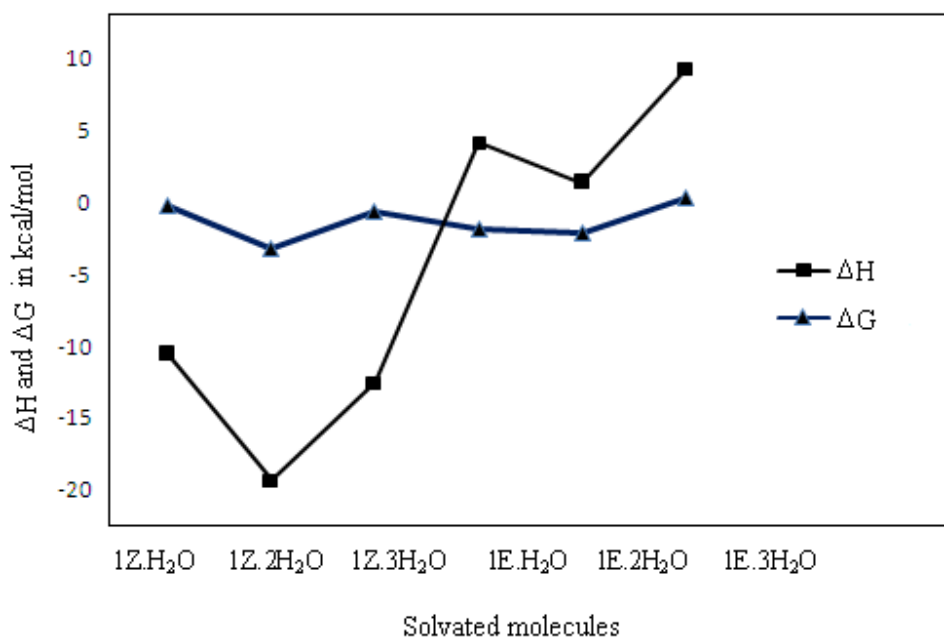


Figure 3: The enthalpies (ΔH) and the free energies of solvation (ΔG) for the hydration reactions.

Frequencies study

The computed vibrational frequencies are listed in Table 6. The computed infrared spectra of 1Z and 2Z tautomers are given in Figure 4,5. The calculated infrared spectra are in agreement with the assignments of the experimental infrared spectra for thiohydroxamic acids in carbon tetrachloride solutions [13]. They reported the S-H frequency at 2600 cm⁻¹ along with three bands in the higher region over 3200 cm⁻¹. The four bands were found to be sensitive to deuteration suggesting that they all corresponding to a hydrogen involvement. The DFT calculations showed that the νO-H of 1Z is shifted to lower frequency in comparison with 2Z form which has been attributed to intramolecular hydrogen bonding. The results for the other structures showed no different trend.

Table 6: The calculated vibrational frequencies in cm^{-1} for 1Z, 2Z, 1E and 2E molecules

| 1Z | 2Z | 1E | 2E |
|------------|------------|------------|------------|
| cm-1 | cm-1 | cm-1 | cm-1 |
| 221 | 213 | 159 | 236 |
| 248 | 244 | 289 | 272 |
| 391 | 356 | 365 | 314 |
| 467 | 501 | 455 | 360 |
| 661 | 602 | 602 | 439 |
| 847 | 704 | 896 | 780 |
| 884 | 824 | 988 | 888 |
| 988 | 908 | 1008 | 909 |
| 1234 | 944 | 1260 | 985 |
| 1384 | 1287 | 1283 | 1239 |
| 1422 | 1335 | 1376 | 1370 |
| 1554 | 1622 | 1467 | 1620 |
| 3029 (C-H) | 2598 (S-H) | 3020 (C-H) | 2589 (S-H) |
| 3231 (O-H) | 3098 (C-H) | 3408 (N-H) | 3036 (C-H) |
| 3511 (N-H) | 3619 (O-H) | 3543 (O-H) | 3612 (O-H) |

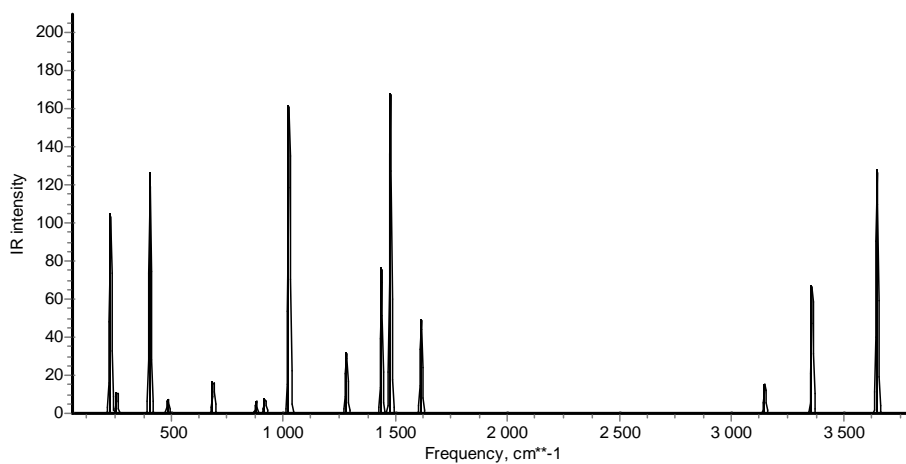


Fig. 4. Computed infrared spectrum of the 1Z structure.

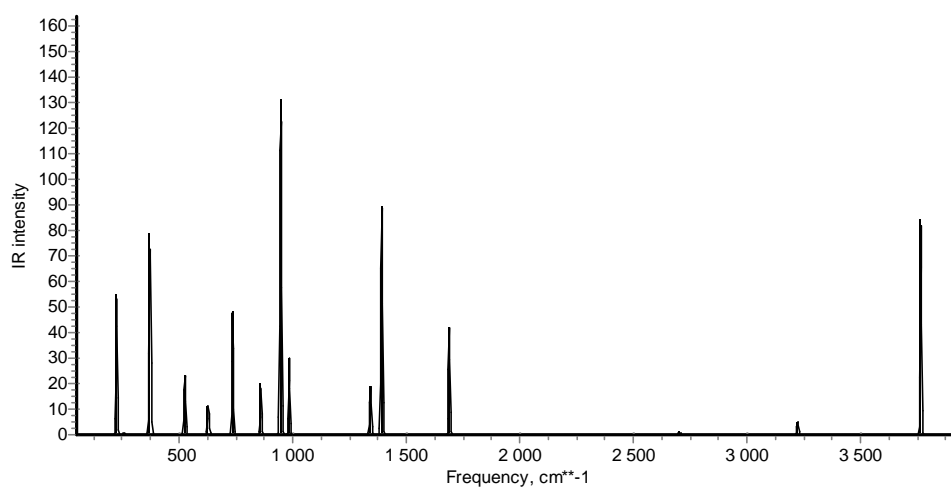


Fig. 5. Computed infrared spectrum of the 2Z structure

Anion study

The question of whether thioformohydroxamic acid is an O-acid, N-acid or S-acid has been examined, Table 2, showed the relative energies and the structures of the anions under consideration. The previous study on formohydroxamic acid revealed that it is N-acid [1]. Analogous interpretation is applicable to the thioformohydroxamic acid. The name 1ZN indicates that the anion is being formed by proton dissociation from the N atom of 1Z structure and so on. 1ZN is the most stable anion at B3LYP/6-311++G(d,p) level of theory. For 1ZN clearly there is electron resonance effect within N-C-S bonds and release the instability of the two unshared electron pair on the N atom. In contrast 1ZO structure has no electron resonance effect to lower the system; instead the originally existing intramolecular hydrogen bonding would disappear and hence increase the instability of 1ZO. Therefore, the 1Z and 1E tautomer are an N-acid, 2E is a S-acid, since 2ES has lower energy than 2EO.

CONCLUSION

The calculations revealed that both thione 1Z and thiol 2Z tautomers are stable in the gas phase. The existences of the forms are in agreement with the experimental infrared finding. Because of the low intensity of S-H band it is difficult to distinguish between the two forms. The stability order for thioformohydroxamic acid tautomers are $2Z > 1Z > 2E > 1E > > S1$. The transition states energies are affected by the ring strain. TS3 is located on the reaction coordinate for 2Z to 2E conversion; it is clear that TS3 has the highest energy in the path and is involved in the rate-determining step. The thermodynamic and the kinetic parameters reveals that the hydrogen binding with water stabilized both 1Z.2H₂O and 1Z.3H₂O to greater extent than 1E.2H₂O and 1E.3H₂O. The 1Z and 1E tautomer are an N-acid, 2E is a S-acid, since 2ES has lower energy than 2EO. The calculated vibrational frequencies are in an excellent agreement with the assignments of the experimental infrared spectra for thioformohydroxamic acid.

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