Theoretical Study of Intramolecular Hydrogen Transfer in Thioformohydroxamic Acid and Its Aceto and Fluoro-Substituted Derivatives

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Interconversion of five isomeric tautomers of thioformohydroxamic acid and its aceto- and fluoro-substituted derivatives via intramolecular hydrogen transfer was investigated by ab initio theoretical calculation. The transfer potential surfaces, the global isomeric structures, and the transition geometries of intramolecular hydrogen transfer were determined at the MP2/6-31+G** level of calculation. The energy was further analyzed by a single point calculation using MP2/6-31++G**//MP2/6-31+G**. Not counting the unstable charge separating species (S3) which may be an important conformation in the formation of metal complexes, the order of stability of these tautomers was S2Z > S2E > S1Z > S1E, calculated at the MP2 level with zero point energy consideration. The S2Z and S2E are thione forms, whereas S1Z and S1E are thiol forms. The ring structure of the transition state construction dominates the energy barrier of the intramolecular hydrogen transfer, which initiates the interconversion among the five isomeric tautomers. Because the proton attached to the N-atom in the thione form is relatively easy to dissociate, we believe that thioformohydroxamic acid in the dissociating proton in the gas phase is an N-acid. However, in the thiol form it is instead a S-acid rather than an O-acid. Substitution effect (aceto and fluoro derivatives) on the stability of tautomeric structures and intramolecular hydrogen transfer barriers was also examined.

Introduction

Thiohydroxamic acids (RC(═S)NR′OH) play important roles in analytical and biological chemistry and are utilized in the detection and quantitative determination of metals.[1] The chelates of thiohydroxamic acid (R═H, R′ = CH_3) and iron (III) were obtained from bacterial sources and were shown to possess potent antibiotic properties.[2,3] The trischelates of thiohydroxamic acid and Fe^{3+} were believed to participate in bacterial iron transport system.[4] Earlier reports on these trischelates also showed somewhat reduced magnetic moment from the high-spin value,[5,6] even though all known iron-transport compounds are invariably high-spin in nature.[7] It was suggested that they might be showing "spin-crossover" behavior,[8] which drew intense attention.[4] There are two tautomeric forms, thione and thiol, which are analogous to the keto and iminol forms of hydroxamic acid (RC(═O)NHOH). Some experimental studies[9,10] concluded that from the IR spectra thiohydroxamic acids could only exist in the thione form in the solid state and could coexist in both forms in solution. However, no thiol form of NMR spectrum was observed in the solution. Studies also revealed that only the thione form was detected either in the solid state or solution (after the thiohydroxamic acids were fully purified). However, this was not the case for thiophenylacetahydroxamic acid which might exist in the thiol form because there was a clear absorption band observed at 2580 cm^{-1}. This band could be due to the absorption of the S−H band, although Schaumann[11] interpreted it as a strong linear frequency combination of 1343 and 1269 cm^{-1}. The disagreement of the experimental conclusion leaves room for theoretical studies. To the best of our knowledge, there was only one report of ab initio molecular orbital calculation on thiohydroxamic acid by Sekhon,[12] in which only the structures of E and Z thione forms of thioformohydroxamic acid were discussed at the HF/3-21G* level. In this study, we calculated the possible tautomeric structures and energetics of thioformohydroxamic acid (SA) (the thione and thiol forms), the energy hypersurfaces of intramolecular hydrogen transfer between the tautomers, and the substitution effect on the transfer energy barriers. We also discuss whether thioformohydroxamic acid is an N-acid or O-acid in the gas phase, analogous to our previous study[13] for formohydroxamic acid.

Methods of Calculation

The Gaussian 94 set of ab initio computer codes[14] was employed for all calculations. Geometries were optimized with the gradient schemes included therein. To take into account the effect of electron correlation, we employed second-order Moller−Plesset perturbation theory (MP2). The polarized split valence basis set including diffuse function, 6-31+G**, was used. For single point energy calculation, MP2/6-31++G**//MP2/6-31+G** was also employed for stable tautomers of thioformohydroxamic acids, because this level of theory met sufficiently the experimental result of acetohydroxamic acid.[15] In addition, the result of our frequency calculation on thioformohydroxamic acid, listed in Table 1, compared to that from the experiment[11] was quite convincing on this calculation level. Zero-point energy (ZPE) was also considered. When the fully optimized equilibrium structure of each tautomer was determined, the calculation of potential profile for intramolecular hydrogen transfer was carried out. Substitution effect on the energy barrier of intramolecular hydrogen transfer of thioacetohydroxamic acid ($CH_3CSNHOH$) (using a methyl group as an electron-donating group), and thiofluorohydroxamic acid

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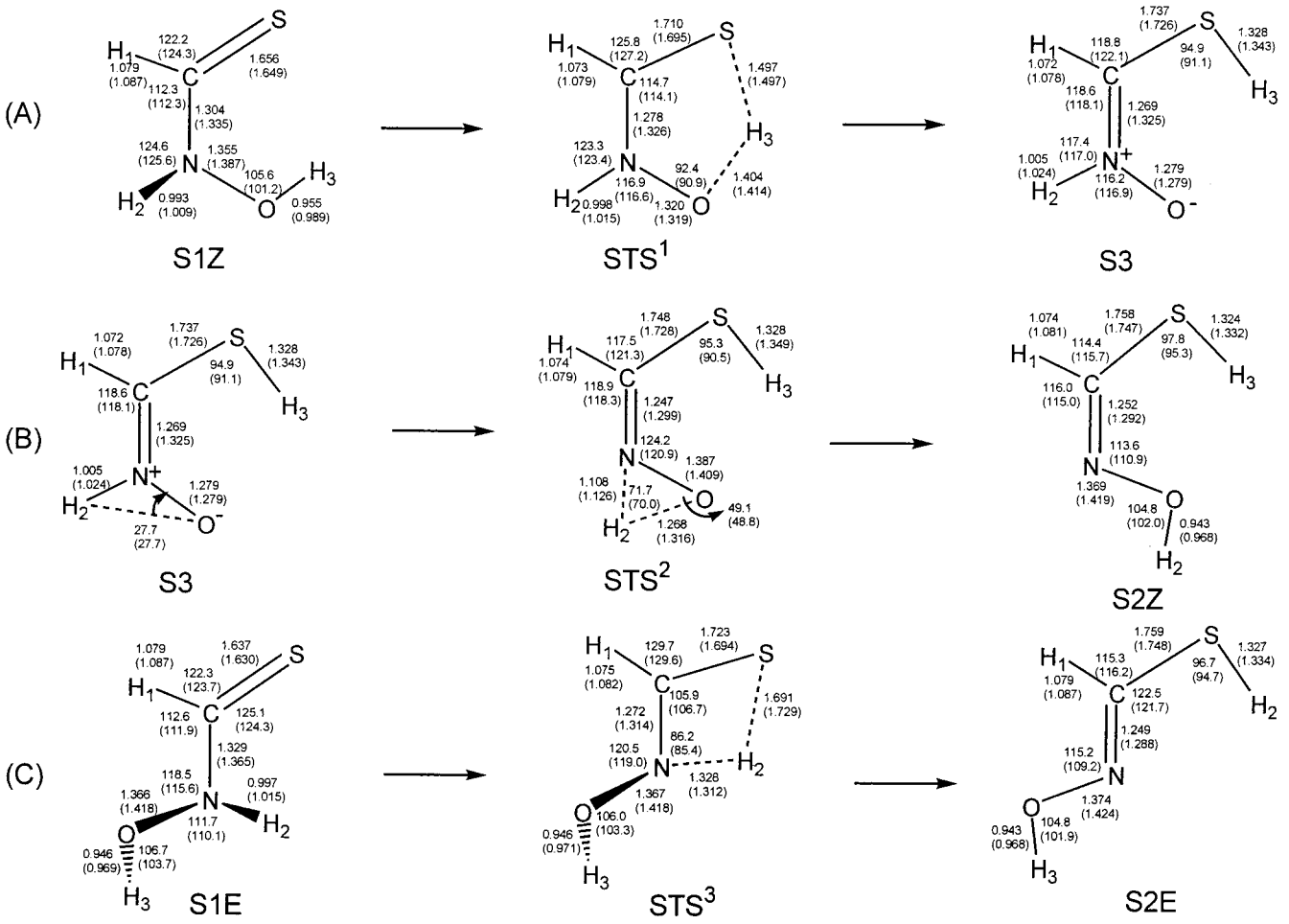

Figure 1. Optimized structures of thioformohydroxamic acid tautomers and their corresponding TS calculation in HF and MP2 levels (bond length in angstroms and angles in degrees). The MP2 data are listed in parentheses.

TABLE 1: Calculated Vibration Normal Modes of Thioformohydroxamic Acid at MP2/6-31+G Level**

normal modes (cm^{-1})	multiplication of scaling factor[a] (cm^{-1})	exp[b] (cm^{-1})
157.3	144.9	
273.4	251.8	
337.1	310.5	
500.4	460.9	
636.8	586.5	
776.6	715.2	
874.1	805.0	
922.9	850.0	
1013.8	933.7	
1332.6	1227.3	
1361.4	1253.8	
1640.1	1510.5	
2833.3	2609.5[c]	2580
3294.9	3034.6	
3859.9	3555.0	

[a] See ref 21. The scaling factor is 0.921 for MP2-fu/6-31G* proposed by Hehre et al. [b] See ref 11. The IR absorption band occurs at 2580 cm^{-1} of thiophenylacetahydroxamic acid. It could be the absorption of S−H band, although Schaumann interpreted it as a strong linear frequency combination of 1343 and 1269 cm^{-1}. [c] The calculated normal mode frequency (mainly S−H band vibration motion) after the multiplication of scaling factor 0.921. The error is about 1%.

(FCSNHOH) (using a fluorine atom as an electron-withdrawing group) was performed as well.

Results and Discussion

The optimized five local minimum isomers, including one charge-separated species, S3, and the three corresponding transition structures (STS) of intramolecular hydrogen transfer are listed in Figure 1. Thione forms are denoted S1 and thiol forms are denoted S2; both have Z and E forms. At MP2/6-31+G** calculation level, S1Z is very near to a planar structure because of the intramolecular hydrogen bonding between S and H_3 atoms, causing S, C, N, O, H_3 (five atoms) to occur almost in one plane. However, S1E is nonplanar because of the typical N atom pyramidal bonding construction. On the other hand, S2Z and S2E are planar, owing to the formation of C═N double bond. The calculated data of bond lengths and bond angles at MP2 and Hartree−Fock (HF) levels do not differ too much except at the double-bond region (C═N and C═S) where the electron distribution is richer, which causes larger electron correlation effect; the result deviates significantly from that of the HF level. From our previous study,[13] the corresponding geometries and parameters of the analogous compound, formohydroxamic acid (HCONHOH, HA), are listed in Figure 2 for comparison. The C═S bond length is longer than that of C═O in HA, yet the C═N bond length is much shorter (about 0.04 Å at HF and 0.02 Å at MP2). The bond length implies that electron resonance effect is more enhanced in the N−C−S bond region than the corresponding N−C−O region in HA. A similar trend was also observed between thioformamide ($HCSNH_2$) and formamide ($HCONH_2$).[16,17]

Among all five isomers, S3 is calculated to be the least stable and its energy is much higher than that of the others (the relative energies are listed in the upper part of Table 2). The C═N double bond in S3 is more than 0.03 Å (MP2) longer than the corresponding thiol forms of S2Z and S2E, yet the N−O bond

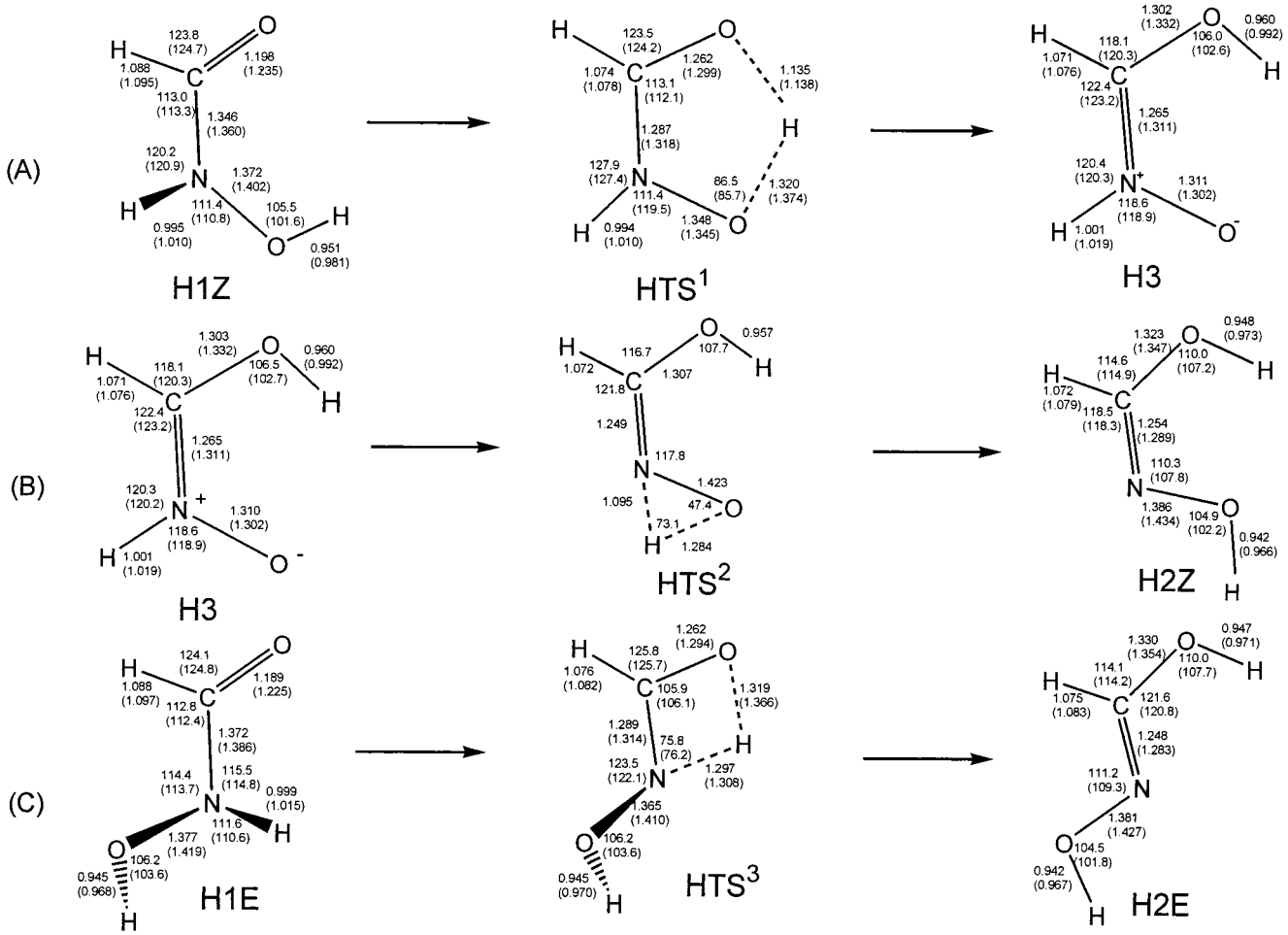

Figure 2. Optimized structures of formohydroxamic acid (HA tautomers and their corresponding TS in HF and MP2 levels (bond length in angstroms and angles in degrees). The MP2 data are listed in parentheses.

TABLE 2: Calculated Total Energies,[a] ZPE,[a] and Relative Energies[b] of the Tautomers of Thioformohydroxamic Acid (SA), Thioacetohydroxamic Acid (SMA), Thiofluorohydroxamic Acid (SFA) and Their Transition Structures

	HF[b,c]	MP2[b,d]	MP2[a]	ZPE[a] (0.921)	MP2+ZPE[a] (0.921)
S1Z	0.2(1.9)	2.2(3.9)	−566.99187	0.04422	−566.94765
S1E	0.4(2.1)	4.3(6.3)	−566.98862	0.04477	−566.94385
S2Z	0.0(0.0)	0.0(0.0)	−566.99541	0.04157	−566.95384
S2E	2.1(1.6)	3.8(3.5)	−566.98930	0.04111	−566.94819
S3	18.7(19.0)	10.8(11.2)	−566.97815	0.04216	−566.93599
STS^1	27.8(26.5)	14.3(13.4)	−566.97264	0.04008	−566.93256
STS^2	72.0(68.3)	54.7(51.4)	−566.90827	0.03629	−566.87198
STS^3	51.5(49.3)	40.1(38.2)	−566.93149	0.03854	−566.89295
SM1Z	−0.6(1.1)	2.1(3.6)	−606.1852	0.07004	−606.11516
$SMTS^1$	25.7(24.4)	13.7(12.9)	−606.16678	0.06639	−606.10039
SM3	18.6(19.0)	11.3(11.8)	−606.17052	0.06840	−606.10212
$SMTS^2$	71.0(67.3)	53.9(50.7)	−606.10275	0.06264	−606.04011
SM2Z	0.0(0.0)	0.0(0.0)	−606.18859	0.06769	−606.1209
SM1E	0.4(2.3)	4.3(6.6)	−606.18172	0.07134	−606.11038
$SMTS^3$	47.8(45.7)	37.5(35.8)	−606.12881	0.06504	−606.06377
SM2E	2.4(2.2)	3.6(3.6)	−606.18288	0.06768	−606.1152
SF1Z	−3.2(−1.8)	−2.5(−0.6)	−666.01587	0.03666	−665.97921
$SFTS^1$	28.7(27.3)	17.2(16.6)	−665.98444	0.03269	−665.95175
SF3	22.3(22.4)	16.0(16.4)	−665.98637	0.03433	−665.95204
$SFTS^2$	72.9(69.0)	56.9(54.0)	−665.92121	0.02903	−665.89218
SF2Z	0.0(0.0)	0.0(0.0)	−666.01186	0.03364	−665.97822
SF1E	−3.6(−1.6)	−1.9(0.5)	−666.01497	0.03749	−665.97748
$SFTS^3$	50.0(48.2)	38.9(37.6)	−665.94989	0.03152	−665.91837
SF2E	1.8(1.7)	3.2(3.3)	−666.00682	0.03387	−665.97295

[a] The calculated total energies at MP2/6-31++G**//MP2/6-31+G**, ZPE (zero-point energy) multiplied by the scaling factor 0.921, and that of MP2 + ZPE(×0921) are in the third, fourth, and fifth column of the table, respectively. All units are in au. [b] The relative energies (in kcal/mol) at the first and second column of the table are reported with respect to S2Z for SA tautomers (upper part of the table), SM2Z for SMA tautomers (middle part), and SF2Z for SFA tautomers (lower part), respectively, including their transition structures. The energies in parentheses are corrected for computed ZPE. [c] The energies are calculated with full optimized methods at HF/6-31+G** level. [d] Energies are calculated at MP2/6-31++G**//MP2/6-31+G**.

is much shorter (about 0.14 Å), because of the distinct charge separation in the S3 form. It is still not known if S3 is the possible conformation in the metal complexes formed. Further study needs to be carried out. At HF level, S2Z is calculated to be the most stable, and the energy values reported are relative to S2Z. The energy differences among these isomers are no

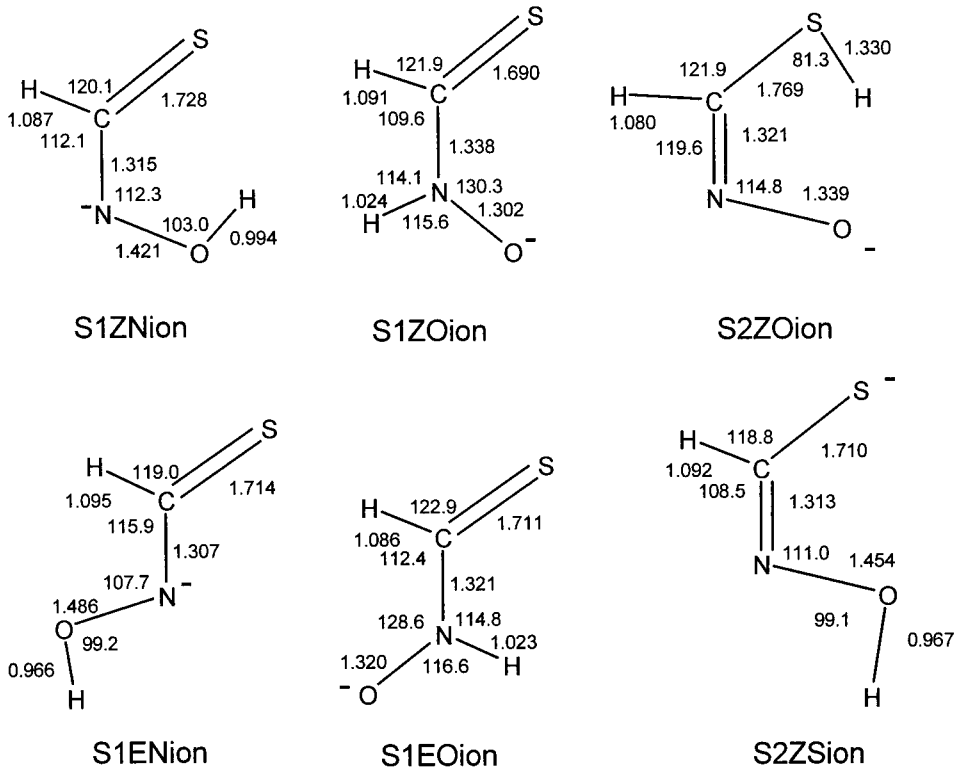

Figure 3. Optimized structures of six anions of thioformohydroxamic acid in the MP2 levels (bond length in angstroms and angles in degrees).

TABLE 3: The Calculated Intramolecular Hydrogen Transfer Barriers[a] of Formohydroxamic Acid (HA), Thioformohydroxamic Acid (SA), Thioacetohydroxamic Acid (SMA), and Thiofluorohydroxamic Acid (SFA) (in kcal/mol)

		HF[b]	MP2[c]	Δr (Å)[e]
HA	(A)	27.2	15.9	0.393
	(B)	71.2	58.6[d]	0.342[f]
	(C)	62.8	46.1	0.293
SA	(A)	27.6(24.6)	12.1(9.5)	0.425
	(B)	72.0(68.3)	54.7(51.4)	0.348
	(C)	51.1(47.2)	35.8(31.9)	0.297
SMA	(A)	26.3(23.3)	11.6(9.3)	
	(B)	71.0(67.3)	53.9(50.7)	
	(C)	47.4(43.4)	33.2(29.2)	
SFA	(A)	31.9(29.1)	19.7(17.2)	
	(B)	72.9(69.0)	56.9(54.0)	
	(C)	53.6(49.8)	40.8(37.1)	

[a] The barrier is calculated for the energy difference between TS and the stable tautomer in each hydrogen transfer process. The barrier in parentheses is corrected for computed ZPE. [b] The energies are calculated with full optimized methods using 6-31+G** basis sets. [c] Energies are calculated at MP2/6-31++G**//MP2/6-31+G**, except where noted. [d] Energy is calculated at MP2/6-31++G**//HF/6-31+G**. [e] The distance for the migration of proton from the stable tautomer to the TS state in each step calculated at MP2/6-31+G**, except where noted. [f] Calculated at HF/6-31+G**.

TABLE 4: Relative Energies[a] of the Anions of the Tautomers of Thioformohydroxamic Acid (in kcal/mol)

anion	HF[b]	MP2[c]
S1ZNion	0.0	0.0
S1ZOion	20.5	18.0
S1ENion	7.9	11.2
S1EOion	11.1	12.0
S2ZOion	33.2	23.4[d]
S2ZSion	8.5	10.3

[a] All energies are reported with respect to S1ZNion. [b] The energies are calculated by full optimized methods using 6-31+G** basis set. [c] Energies are calculated at MP2/6-31++G**//MP2/6-31+G**. [d] Fixed S−H bond length at 1.330 Å (the equilibrium bond length at the optimized construction).

greater than 2.1 kcal/mol and further decrease to 0.5 kcal/mol among S2Z, S1Z, and S1E. The stability order is S2Z > S1Z > S1E > S2E. Little difference appears when ZPE calculation is considered, except that S1E becomes less stable than S2Z by 0.5 kcal/mol. The energy differences among the isomers are still no greater than 2.1 kcal/mol. In contrast, the energy differences become much larger and increase up to 6.3 kcal/mol when ZPE is considered at MP2 level. S2Z is still the most stable, yet the stability order changes. When ZPE is considered, the stability order is S2Z > S2E > S1Z > S1E; S1E becomes the least stable. Obviously, the calculation levels and ZPE calibration shift the stability order a bit for these isomers. It is interesting to note that according to our calculated MP2 result, the thiol forms (S2Z and S2E) are more stable than the thione forms (S1Z and S1E). This outcome is exactly the opposite of the calculated result of the HA counterparts, in which the keto forms (1Z and 1E) are more stable than the enol forms (2Z and 2E). The main reason is the weak bonding of C═S double bond in the thione form. Gonzalez[18] reported a similar finding in his discussion of stability in the organic compounds containing C═S double bond. The thiol form (especially S2Z) also contains weak hydrogen bonding, S−H···O, which further stabilizes the compound. Isomeric tautomers of thiohydroxamic acid can be formed through intramolecular hydrogen transfer starting from S1Z, via three successive paths (labeled (A), (B), and (C)). The calculated transfer barriers of thioformohydroxamic acid together with formohydroxamic acid in parallel transfer processes are listed in Table 3. In both cases, process (A) has the lowest energy barrier, because it is carried out via a five-membered ring TS construction, which has the lowest ring-strain. The next higher energy barrier is process (C), through a four-membered ring, and process (B) is the highest energy barrier, a three-membered ring. At the HF level, the energy barriers of SA are only a bit larger than that of HA for both (A) and (B) processes (0.4−0.8 kcal/mol), while that of (C) process is substantially smaller (11.7 kcal/mol) than HA. At

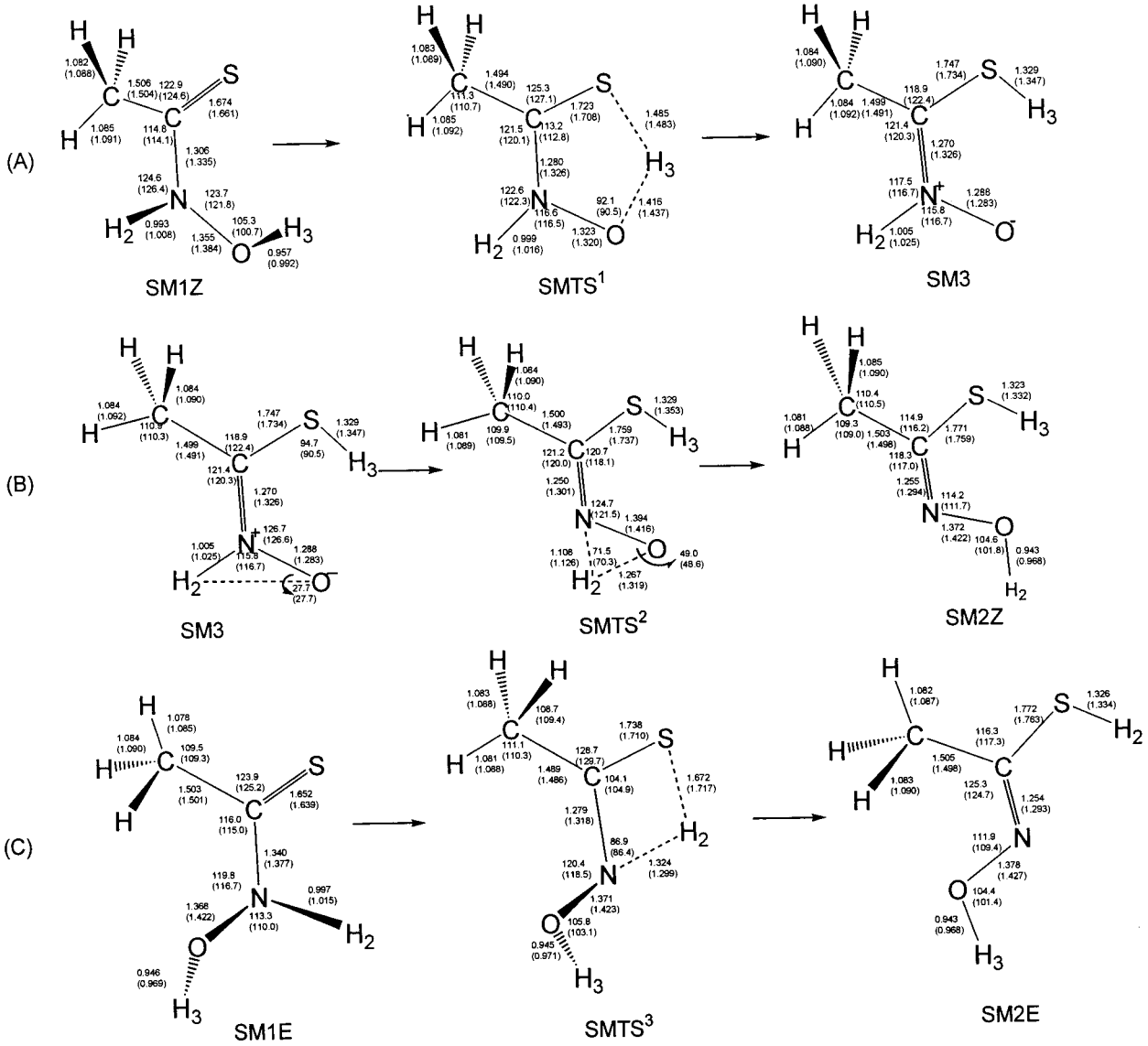

Figure 4. Optimized structures of thioacetohydroxamic acid tautomers and their corresponding TS in HF and MP2 levels (bond length in angstroms and angles in degrees). The MP2 data are listed in parentheses.

the MP2 level, the energy barriers of SA are also smaller in the three processes by 3.9, 1.1, and 10.3 kcal/mol, respectively. The (C) process still decreases the most. Earlier studies[19,20] indicated that when intramolecular hydrogen transfer took place, four factors would determine the size of the barrier: (1) the bonding energy of the hydrogen to the heavy atom, (2) the protonation energy of the target heavy atom, (3) the distance that the transferred hydrogen traveled (Δr), and (4) the ring strain of the transition state construction. As shown in the last column of Table 3, Δr represents the distance that the hydrogen traveled from the original stable structure to the transition state construction. We found no significant relation between Δr and the energy barrier in this system. For instance, in path (A), Δr is much greater than in path (C), yet the energy barrier in (A) is much smaller than that in path (C) in both SA and HA. The barrier is strictly correlated to the construction of the transition state. In Figures 1 and 2, the $\angle$C−N−H angle of transition state STS[3] of SA in path (C) is much greater than that of TS[3] of HA in the parallel path (85.4° vs 76.2°). It largely releases the ring-strain of the transition construction in STS[3] and therefore the energy barrier decreases substantially (46.1 vs 35.8 kcal/mol). A similar argument can be applied to the process (A) in the angle $\angle$N−O−H_3 of transition state constructions in SA and HA (90.9° vs 85.7°). However, the release of the ring-strain ratio due to the larger angle in the transition state of path (A) is smaller than that in path (C), because the transition structure of path (A) is a five-membered ring which has smaller ring-strain than a four-membered ring in path (C). Therefore, the decrease of the barrier in path (A) is not as much as that in path (C) (3.8 vs 10.3 kcal/mol). The calculated deprotonation energy of SA is smaller than that of HA (326.1 vs 339.6 kcal/mol) and it adds more to lower the energy barrier in SA.

The issue of whether the formohydroxamic acid (HA) is an O-acid or an N-acid has been debated for a long time. In our previous study,[13] we addressed our conclusion on this issue based on the fact that whether it is an N-acid or O-acid depends on which hydrogen atom (attached to the N atom or the O_2 atom) can be more easily dissociated. For that reason, we supported that HA was an N-acid rather than an O-acid in the gas phase. Analogous interpretation is applicable to the thioformohydroxamic acid (SA). The calculated relative energies for the hydrogen dissociated anions either from the N or O atom of SA are listed in Table 4. The name S1ZNion indicates that the anion is being formed by proton dissociation from the N atom of S1Z tautomer, and that of S1ZOion is from the O atom of S1Z. The corresponding structures are also shown in Figure

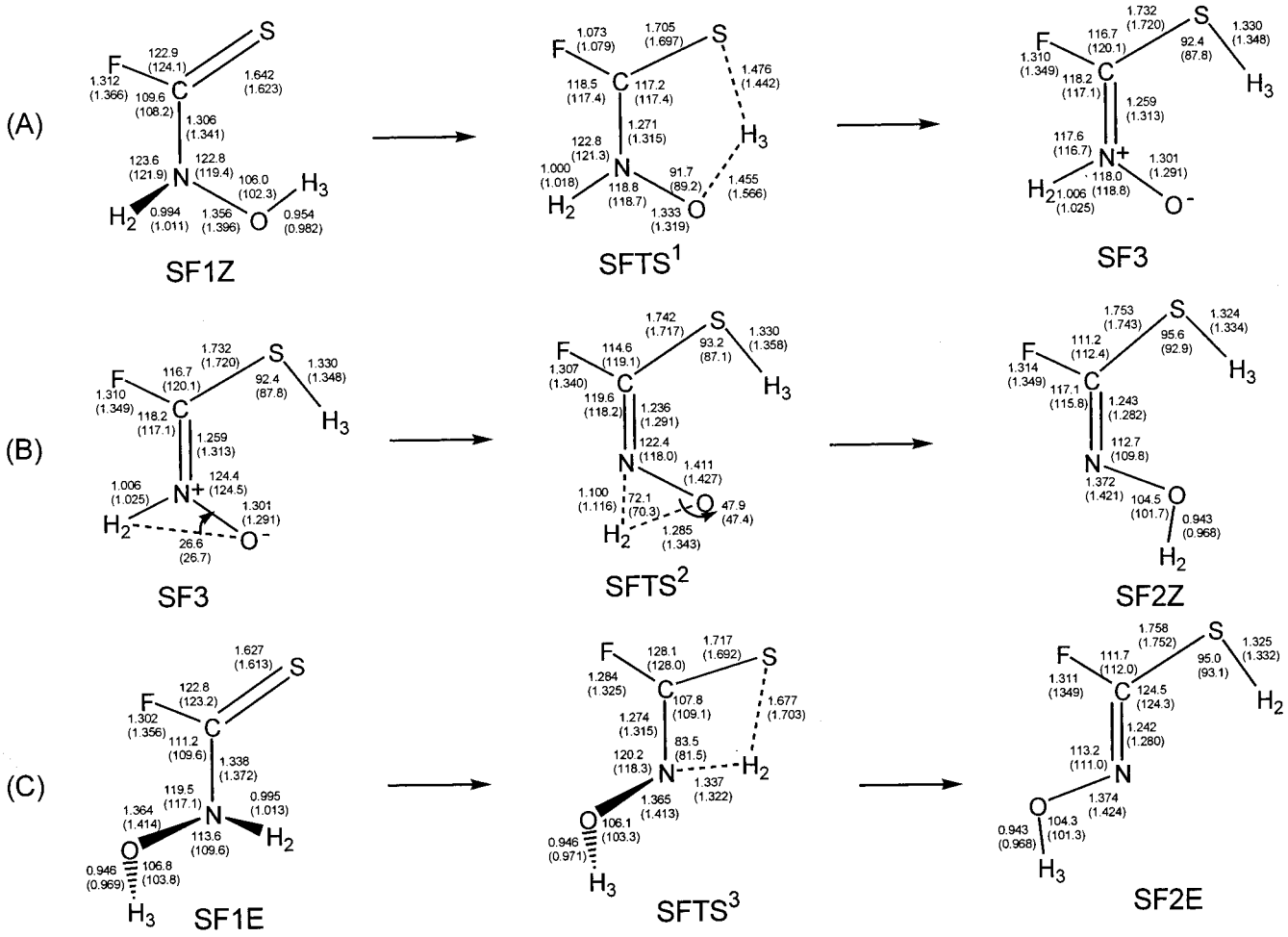

Figure 5. Optimized structures of thiofluorohydroxamic acid tautomers and their corresponding TS in HF and MP2 levels (bond length in angstroms and angles in degrees). The MP2 data are listed in parentheses.

3. As shown in Table 4, S1ZNion is the most stable anion at either level of calculation (at least lowered by 10 kcal/mol). If the proton dissociated from the N atom to form an anion, an electron resonance effect would develop within N−C−S bonds and release the instability of the two unshared electron pairs on the N atom. In contrast, if the proton dissociated from the O atom, there would not be any electron resonance effect developed to lower the system; instead, the originally existing intramolecular H-bonding would disappear, and hence increase the instability of the forming anion. The fact that S1ENion is less stable than S1ZNion could be due to the absence of intramolecular H-bonding, whereas S1ZOion being less stable than S1EOion could result from the charge-repelling effect between the S and O^- atom in the same side. In addition, from our study of intramolecular hydrogen transfer in process (A), with a much smaller barrier, 12.1 kcal/mol (MP2), we realize that the proton on the O atom is likely to be confined and delocalized between S and O atoms; therefore, it is not easily dissociated. In contrast, because the proton on the N atom is less likely to experience intramolecular hydrogen transfer (S1Z → S1E → STS^3 → S2E → S2Z, a much more complicated reaction), it is relatively easy to dissociate. As a consequence, we support the theory that thioformohydroxamic acid (SA) is an N-acid in the gas phase. A similar argument can be applied for the thiol form of S2Z tautomer. The calculated proton-dissociated anions (S2ZOion and S2ZSion) are also listed in the last part of Table 4. The MP2 level of calculation showed that S2ZSion is much more stable than the S2ZOion. We concluded that the existing thiol form (S2Z) would be a S-acid rather than an O-acid in the gas phase.

Substitution Effect. We extend our investigation to the structure stabilities and the potential energy profiles of hydrogen transfer under the influence of substitution with a typical electron-donating group (CH_3) and an electron-withdrawing group (fluorine atom) on the SA system. The isomeric tautomers of thioacetohydroxamic acid ($CH_3CSNHOH$), SMA, and thiofluorohydroxamic acid (FCSNHOH), SFA, are shown in Figures 4 and 5, respectively. The corresponding intramolecular hydrogen transfer processes (labeled (A), (B), and (C)), transition structures, and the geometric parameters are also illustrated. The calculated data of bond lengths and angles at the HF and MP2 levels (listed in the parentheses) do not differ too much except at the double bond (C═S, C═N) and the C−F bond regions where the electron charge density is larger. The calculated total energies and relative energies of the isomeric tautomers of SMA and SFA, along with the corresponding transition structures with respect to SM2Z and SF2Z, are listed in the middle and the lower parts of Table 2, respectively. The stability trend of SMA tautomers is similar to that of SA, with SM2Z the most and SM1E the least stable construction. However, in the fluoro-substituted system, the stability order changes. SF1Z is the most stable and SF2E is the least stable at either level of calculations. Note that the fluoro-substituted thione form is more stable than the thiol form, which is the opposite of the stability of the corresponding SA and SMA tautomers. The reason for less stable thione forms in SA and SMA could be due to the larger

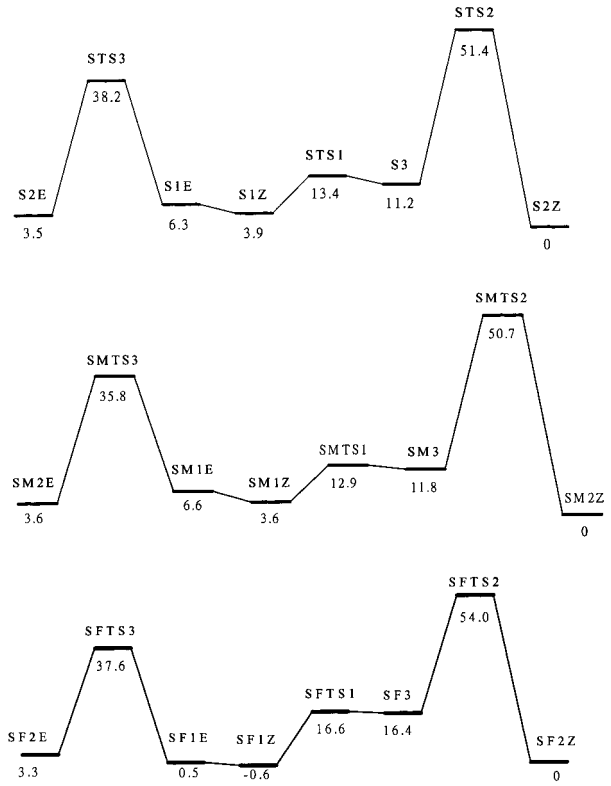

Figure 6. Schematic diagram of potential energy surfaces describing intramolecular hydrogen transfer, connecting structures from S2E to S2Z, SM2E to SM2Z, and SF2E to SF2Z, respectively. The values are calculated at the MP2/6-31++G**//MP2/6-31+G** level.

charge density centered on the carbon atom of the C═S bond, which can be seen from the abnormal long C═S bond length (1.65 Å, compared to 1.20 Å of C═O bond) in SA and SMA. In contrast, the fluoro-substituted thione form resolves this instability. The strong electron negativity of the fluorine atom withdraws charges from the electron-rich carbon atom and stabilizes the thione form. In addition, there also exists intramolecular H-bonding between F and H_2 atoms in SF1Z, which further solidifies the structure. The calculated intramolecular hydrogen transfer barriers of SA, SMA, and SFA of the three processes are listed in Table 3. Clearly, the electron-donating substituent (CH_3) reduces the barriers a small amount, while that of the electron-withdrawing counterpart (F) enlarges the barrier significantly in all three processes. The schematic diagram of the potential surfaces describing intramolecular hydrogen transfer for SA and other two substituted derivatives is also depicted in Figure 6. It clearly shows the substitution effect on the change of energy barriers in the parallel processes. At the HF level, the mean for the barrier reduction is around 2 kcal/mol, but it is only 1.3 kcal/mol at MP2. However, the mean for raising the barrier is around 2.6 kcal/mol at HF, and increases to 4.9 kcal/mol at MP2. These results are in good agreement with our previous study[19] in the substituted aldehyde systems.

Summary

Thioformohydroxamic acid is the simplest form of thiohydroxamic acids, yet experimental data are scarcely available. The theoretical calculation results become important. Among the five calculated isomeric tautomers, S2Z, a thiol form with weak intramolecular hydrogen bonding, is the most stable. The corresponding thione form, S1E, is about 6 kcal/mol higher in energy (MP2, with ZPE). A similar result was obtained for the methyl-substituted counterparts (SMA), which are in contrast to the analogous structure of formohydroxamic acid where the keto form is more stable than the iminol form. In contrast, in the fluoro-substituted species the thione form, SF1Z, is the lowest tautomer, about 0.7 kcal/mol (MP2, with ZPE) less than the corresponding thiol form, SF2Z. A further decrease of energy (−1.3 kcal/mol) was obtained at a G2(MP2) level of calculation. The energy barrier for the interconversion of the tautomers through intramolecular hydrogen transfer is strongly related to the ring structure of the transition state. The smaller the member ring, the higher the ring-strain and the larger the barrier. The proposed three processes of intramolecular hydrogen transfer all have lower energy barriers in SA than the parallel processes of HA counterparts. The barrier in (C) process decreases the most (about 10 kcal/mol) because the extent of the release of the ring-strain in the transition structure of SA in this process is the largest. Substitution effect on the transfer barriers clearly appears and agrees well with the prediction of electron-releasing or -withdrawing nature of the substituents when compared with the nonsubstituted counterparts (SA). The evidence of the calculated stability order of the proton-dissociated anions, as well as the energy barriers of the intramolecular hydrogen transfer via the discussed processes, leads us to believe that thioformohydroxamic acid is an N-acid rather than an O-acid in the gas phase. Also, it is a S-acid rather than an O-acid in the thiol conformations.

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