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Theoretical Study of the Structures, Conformations, and Spectroscopic Properties of 2-Formylthiophene-*N*-acetylhydrazone and 2-Thiophenecarboxaldehyde-2-thienylhydrazone

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ABSTRACT: *2-Formylthiophene-N-acetylhydrazone (Hait) and 2-thiophenecarboxaldehyde-2-thienylhydrazone (Htit) in the cis and trans conformations were investigated in the gas-phase by density functional method using B3LYP as the functional set and 6-311++G(d,p) as the basis set. The cis and trans structures were fully optimized in the* C_1 *and* C_s *symmetries. Transition states were also modeled for the cis–trans isomerization of the title compounds and the barriers to internal rotation were calculated. This work reports the structural, energetics, and spectroscopic parameters of all the optimized geometries. Some of the structural parameters are in good agreement with experimental literature data. The computed parameters for these compounds are also in good agreement with a related molecule, namely, acetohydrazide. For both Hait and Htit, the trans conformers are more stable than the cis conformers and the energy barriers are larger compared with the energy differences between the cis and trans conformers. This accounts for Hait and Htit existing mostly in the trans conformation.* Heteroatom Chem 20:144–150, 2009; DOI 10.1002/hc.20526

INTRODUCTION

Thienyl hydrazones are important class of compounds due to their coordinating ability [1] and antineoplastic activity [2]. Thienyl hydrazones can exhibit conformational isomerism [3,4], leading to the cis and trans conformers. Cis–trans isomerization is known to play significant role in biochemical processes [5] and one of them involves the mechanism of vision [6]. A brief overview of the literature of thienyl hydrazones has been useful to set the objectives of this work. Karabatsos et al. [7] observed that the reactions of aliphatic aldehydes with 2.4-dinitrophenylhydrazine lead to the cis hydrazones, but on prolonged standing, the solutions resulted in cis–trans equilibrations that are catalyzed by an acid. They observed that the cis conformer is thermodynamically more stable than the trans conformer. Berge [8] described the synthesis of eighteen 2-pyridylhydrazone and 2-quinolylhydrazone compounds containing either 2-thiophene or 2-furan derivatives. More recently, Concistrè et al. [9] obtained the structure and conformations of 2-thiophenecarboxaldehyde

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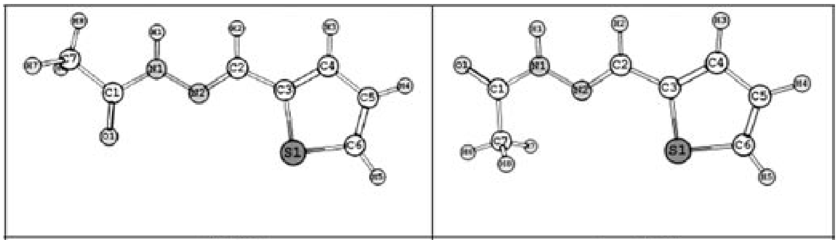
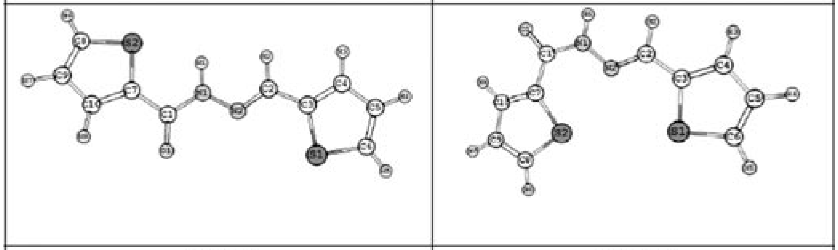


cis-Hait *trans*-Hait



cis-Htit *trans*-Htit

FIGURE 1 The cis and trans conformers of 2-formylthiophene-*N*-acetylhydrazone (Hait) and 2-thiophenecarboxaldehyde-2-thienylhydrazone (Htit).

TABLE 1 Bond Lengths and Bond Angles of the Optimized Cis, Transition State, and Trans Conformers of 2-Formylthiophene-*N*-acetylhydrazone

	Cis		*Transition State Structure, Theoretical*	*Trans*	
	This Work	*Literature [3]*		*This Work*	*Literature [3]*
			Bond length (Å)		
S1—C3	1.747	1.713(2)	1.747	1.748	1.712(2)
S1—C6	1.731	1.700(3)	1.733	1.732	1.704(3)
C6—C5	1.368	1.340(4)	1.367	1.367	1.335(4)
C5—C4	1.420	1.407(5)	1.422	1.421	1.415(5)
C4—C3	1.378	1.389(3)	1.377	1.378	1.361(4)
C3—C2	1.444	1.447(3)	1.447	1.444	1.453(3)
C2—N2	1.282	1.274(3)	1.280	1.284	1.269(3)
N2—N1	1.357	1.373(4)	1.378	1.355	1.385(2)
N1—C1	1.389	1.358(3)	1.473	1.385	1.340(3)
C1—C7	1.519	1.488(4)	1.500	1.509	1.501(3)
C1—O1	1.209	1.229(3)	1.199	1.217	1.221(3)
N1—H1	1.016	0.84(3)	1.024	1.019	0.840(3)
C2—H2	1.098	0.88(5)	1.097	1.096	0.980(3)
			Bond angle (°)		
C3—S1—C6	91.1	91.6(1)	91.3	91.3	91.6(1)
S1—C6—C5	112.3	112.7(2)	112.2	112.2	112.4(2)
C6—C5—C4	112.4	113.0(3)	112.5	112.5	112.4(2)
C5—C4—C3	113.2	111.8(3)	113.3	113.3	112.7(2)
C4—C3—S1	110.8	110.9(2)	110.8	110.8	110.8(2)
C4—C3—C2	126.5	127.2(2)	126.6	126.5	127.2(2)
C3—C2—N2	122.3	121.2(2)	122.4	122.3	121.0(2)
C2—N2—N1	117.3	115.0(2)	118.2	117.8	115.0(2)
N2—N1—C1	121.6	121.2(2)	111.7	123.1	120.9(2)
C7—C1—O1	122.9	122.9(2)	125.3	124.4	122.2(2)
S1—C3—C2	122.6	121.9(2)	122.6	122.7	121.9(2)
N1—C1—O1	123.5	120.6(4)	121.6	119.1	123.7(2)
C7—C1—N1	113.6	119.4(2)	113.1	116.6	123.7(2)
N2—N1—H1	119.3	118.0(2)	113.9	121	120.0(2)
C1—N1—H1	119.1	121.0(2)	110.0	115.9	119.0(2)
C3—C2—H2	115.8	121.0(2)	116.0	116.0	120.0(2)
N2—C2—H2	122.0	117.0(2)	121.7	121.7	119.0(2)

from partially averaged dipolar couplings. Domiano et al. [3] studied the restricted rotation in 2-formylthiophene-*N*-acetylhydrazone (Hait) using X-ray data and infrared spectrum analysis. Battaglia et al. [4] reported the structural and spectroscopic properties of Hait and 2-thiophenecarboxaldehyde-2-thienylhydrazone (Htit). They reported that the trans conformer, *E*-configuration with respect to the C=N double bond, is more predominant. In view of the importance of these compounds, the present work aims to study the title compounds by theoretical methods so as to obtain the energy differences between the cis and trans conformers and a more important parameter, difficult to obtain experimentally, the barriers of rotation. In this decade, several theoretical studies [10–14] have been conducted targeting those compounds that are analogous to Hait and Htit to have more understanding about the relative stabilities of the conformers. We hereby report the findings of our research work.

COMPUTATIONAL METHOD

The cis and trans conformers of the title compounds are studied in C_1 and C_s symmetries and their atom labels are illustrated in Fig. 1. The transition state structures for both Hait and Htit are obtained by rotating about C1—N1 such that H1—N1—C1—O1 dihedral angle is 90°. The optimized equilibrium structures, atomization energies, highest occupied molecular orbital (HOMO)–lowest occupied molecular orbital (LUMO) gaps, uncorrected harmonic frequencies, infrared intensities, Raman activities, and NMR of Hait and Htit are computed by density functional method. The closed-shell singlets are used for all computations. For all atoms, B3LYP is used as the functional set and 6-311++G(d,p) as the basis set. Frequency computations are used to confirm the nature of the stationary points. All computations are performed with the Gaussian 03W [15] package. The compounds are subjected to normal coordinate analysis for the assignment of some of the computed vibrational frequencies and GaussView 3.09 [16] has been used for visualizing the conformers.

RESULTS AND DISCUSSION

TABLE 2 Bond Lengths and Bond Angles of the Optimized Cis, Transition State, and Trans Conformers of 2-Thiophenecarboxaldehyde-2-thienylhydrazone

	Cis	*Transition State Structure*	*Trans*
		Bond length (Å)	
S1—C3	1.747	1.748	1.748
S1—C6	1.731	1.734	1.732
C6—C5	1.368	1.670	1.368
C5—C4	1.420	1.422	1.420
C4—C3	1.378	1.377	1.378
C3—C2	1.444	1.446	1.443
C2—N2	1.282	1.282	1.284
N2—N1	1.355	1.370	1.351
N1—C1	1.389	1.468	1.385
C1—C7	1.487	1.469	1.477
C1—O1	1.213	1.205	1.223
N1—H1	1.017	1.020	1.019
C2—H2	1.098	1.096	1.096
		Bond angles (°)	
C3—S1—C6	91.1	91.3	91.2
S1—C6—C5	112.4	112.2	112.2
C6—C5—C4	112.4	112.5	112.4
C5—C4—C3	113.2	113.3	113.3
C4—C3—S1	110.9	110.8	110.8
C4—C3—C2	126.5	126.6	126.1
C3—C2—N2	122.1	122.2	123.0
C2—N2—N1	117.2	118.3	117.7
N2—N1—C1	121.1	113.9	124.9
C7—C1—O1	121.9	122.5	121.7
S1—C3—C2	122.6	122.6	123.2
N1—C1—O1	123.6	120.0	118.0
C7—C1—N1	114.5	117.5	120.4
N2—N1—H1	119.2	116.3	120.9
C1—N1—H1	119.6	114.4	114.2
C3—C2—H2	115.9	116.1	115.8
N2—C2—H2	122.0	121.7	121.3

Tables 1 and 2 report the bond lengths and bond angles of the optimized cis, transition state, and trans conformers of Hait and Htit. These parameters have been obtained experimentally for Hait by X-ray analysis, and they are also included in the Table 1 for comparison. It is interesting to note that data from this theoretical work and those reported experimentally compare satisfactorily. To be more precise, the minimum deviation in bond length is 0.020 Å and the maximum deviation is 0.218 Å, whereas the minimum deviation in bond angle is 7.1° and the maximum deviation is 2.8°. The average dihedral angle of the thiophene rings in Htit is 8.7° and those between the ring planes and that of the atom chain connecting them is 7.1° for the first and 0.07° for the second ring, respectively. These are supported by experimental dihedral angles reported to be 6.1°, 3.3°, and 4.1° respectively [4].

Table 3 reports the dipole moments, rotational constants, energies, and rotational barriers of the title compounds. The cis conformers are more polar than the trans conformers for both Hait and Htit, and this can be explained in terms of more opposing dipoles in the trans conformers. The rotational constants are in the order $I_a > I_b \approx I_c$. An analysis of the table indicates that the trans conformer is more stable for both Hait and Htit and the barrier of rotation is larger than the energy difference between the

TABLE 3 Dipole Moments, Rotational Constants, Energies, and Rotational Barriers of 2-Formylthiophene-*N*-acetylhydrazone (Hait) and 2-Thiophenecarboxaldehyde-2-thienylhydrazone (Htit)

	Hait			*Htit*		
	Cis	*Transition State Structure*	*Trans*	*Cis*	*Transition State Structure*	*Trans*
DM (debye)	5.276	2.693	4.341	4.732	4.706	3.950
A (GHz)	3.327	2.941	3.151	1.834	1.015	1.047
B (GHz)	0.388	0.396	0.400	0.167	0.230	0.257
C (GHz)	0.348	1.414	0.356	0.154	0.212	0.207
Energy (hartree)	−854.598055	−854.574772	−854.605127	−1,367.142339	−1,367.119451	−1,367.147941
Enthalpy (hartree)	−854.444419	−854.422841	−854.451374	−1,366.966495	−1,366.945251	−1,366.971922
Free energy (hartree)	−854.495172	−854.471231	−854.501374	−1,367.024361	−1,367.001417	−1,367.029124
Atomization energy (kJ/mol)	10,329.99	10,268.86	10,348.56	10,486.63	10,426.53	10,501.33
Homo–Lumo gap (kJ/mol)	409.50	416.35	404.22	386.92	340.71	389.36
η (kJ/mol)	204.75	208.18	202.11	193.46	170.36	194.68
μ (kJ/mol)	−389.72	−366.13	−397.63	−398.85	−398.83	−406.09
ΔE (kJ/mol)		18.57			14.71	
ΔH (kJ/mol) (298.15 K)		18.26			14.25	
ΔG (kJ/mol) (298.15 K)		16.28			12.51	
Barrier of rotation (kJ/mol)		79.70			74.80	

conformers. The large barrier of rotation indicates the high preference for the trans conformer, and it is found that for both Hait and Htit, the percentage of the trans conformer is more that 99%. However, this is not found experimentally for Htit, for which it is reported that the population of the trans conformer is 80%. The barrier of rotation for the simplest related molecule, acetohydrazide, has been computed to be 108.7 kJ/mol [11].

In Kohn-Sham's density functional framework [17], two parameters, namely, μ and η, can be calculated by HOMO and LUMO energies as:

$$\mu \cong \frac{1}{2}(E_{\mathrm{LUMO}} + E_{\mathrm{HOMO}}) \tag{1}$$

$$\eta \cong \frac{1}{2}(E_{\mathrm{LUMO}} - E_{\mathrm{HOMO}}) \tag{2}$$

These parameters and HOMO–LUMO gaps are reported in Table 3.

The significances of μ and η are that μ is related to charge transfer processes and η is related to chemical hardness. In this case, the values of μ indicate that charge transfer processes are more predominant for Htit than for Hait. This leads to stabilization through hyperconjugative interactions. The values of η indicate that hardness decreases from Hait to Htit. Furthermore, a decrease in the HOMO–LUMO gap of these conformers indicates a decrease in the kinetic stability. The HOMO and LUMO surfaces for the conformers of Hait and Htit are illustrated in Figs. 2a and 2b.

Table 4 summarizes the computed ^{1}H NMR, ^{14}N NMR, ^{13}C NMR, and ^{17}O NMR data (ppm) of the atoms about which rotation is considered for the cis–trans isomerization of the conformers of Hait and Htit. An analysis of the chemical shifts indicates that all the shifts, except for hydrogen (H_1), are more downfield for all the atoms in the Hait conformers than in Htit. This is not in agreement with the electron-donating methyl group attached to C_1. However, these may be interpreted in terms of the electronic effects of the methyl group and

TABLE 4 ^{1}H NMR, ^{14}N NMR, ^{13}C NMR, and ^{17}O NMR (ppm) of the Cis, Transition State, and Trans Conformers of 2-Formylthiophene-*N*-acetylhydrazone (Hait) and 2-Thiophenecarboxaldehyde-2-thienylhydrazone (Htit)[a]

	Hait	*Htit*
	Cis	
H_1	7.48	7.97
N_1	200.56	194.30
C_1	164.77	157.44
O_1	430.93	399.77
	Transition state	
H_1	5.00	6.11
N_1	179.53	172.48
C_1	191.61	170.92
O_1	607.90	552.60
	Trans	
H_1	7.47	7.52
N_1	204.14	199.66
C_1	174.27	163.09
O_1	429.57	375.84

[a] References are TMS (6-311+G(2d,p)), NH_3 (6-311+G(2d,p)), TMS (6-311+G(2d,p)), and H_2O (6-311+G(2d,p)) for ^{1}H NMR, ^{14}N NMR, ^{13}C NMR, and ^{17}O NMR, respectively. All these chemical shifts are computed with B3LYP as the functional set.

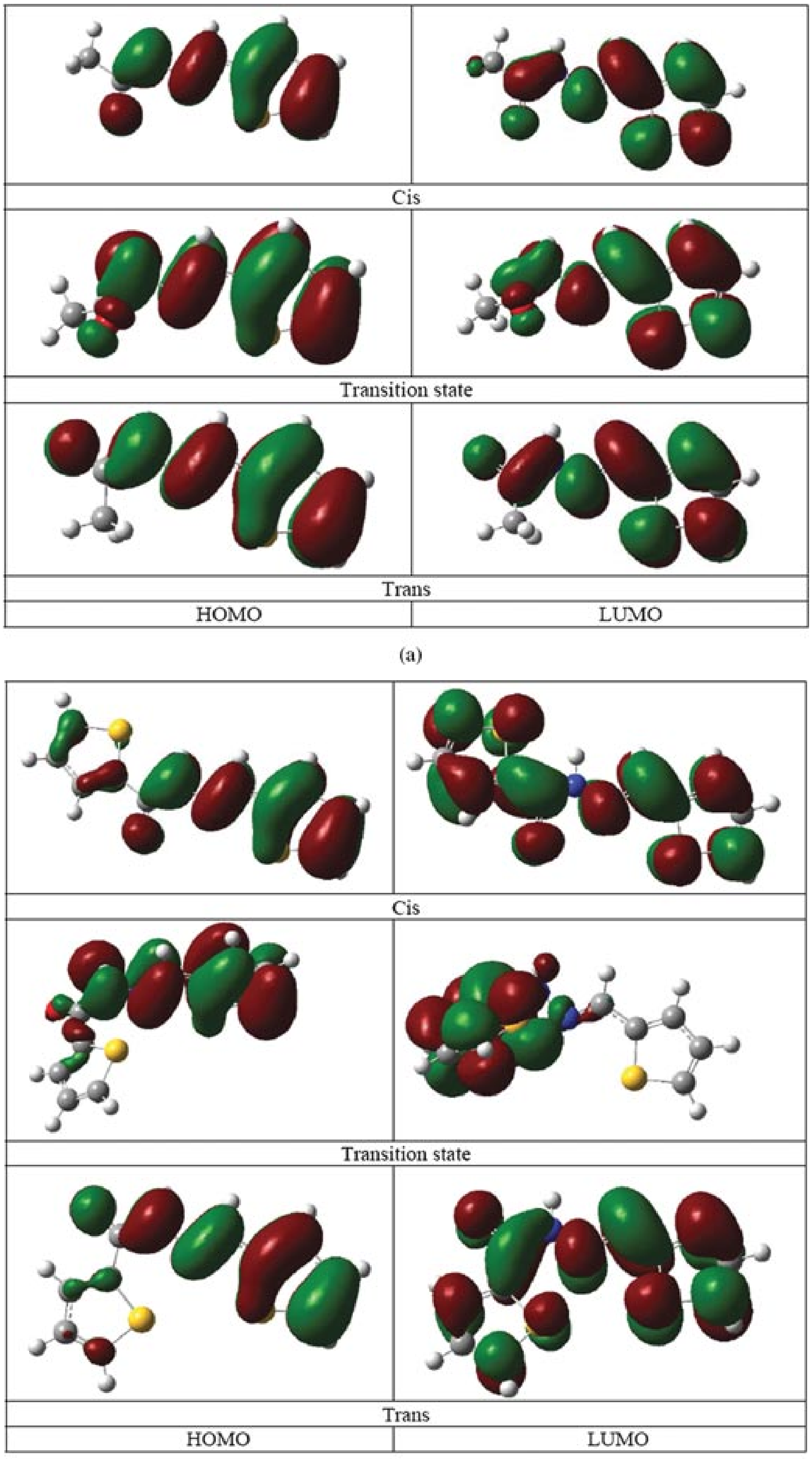


FIGURE 2 Highest occupied molecular orbital (HOMO) and lowest occupied molecular orbital (LUMO) surfaces of (a) 2-formylthiophene-*N*-acetylhydrazone (Hait) and (b) 2-2-thiophenecarboxaldehyde-2-thienylhydrazone (Htit).

TABLE 5 Stretching Frequencies of the Bonds in the Amide Linkage of 2-Formylthiophene-*N*-acetylhydrazone (Hait) and 2-Thiophenecarboxaldehyde-2-thienylhydrazone (Htit)

	Cis		*Transition State*		*Trans*	
	Infrared Frequency (cm^{-1})	*Intensity (km/mol)*	*Infrared Frequency (cm^{-1})*	*Intensity (km/mol)*	*Infrared Frequency (cm^{-1})*	*Intensity (km/mol)*
			Hait			
$C=O$	1782.7 (1650)[a]	397.6	1822.6	219.3	1759.0 (1650)[a]	668.5
$N-H$	3499.3	6.3	3389.7	3.4	3479.1	4.0
$C-N$	1228.4	329.0	1199.7	251.2	1317.0	383.7
			Htit			
$C=O$	1750.4 (1670)[b]	309.7	1769.3	388.3	1707.4 (1670)[b]	601.5
$N-H$	3485.5	6.8	3435.9	1.7	3483.5	10.0
$C-N$	1219.3	353.6	1208.7	126.8	1322.5	412.6

[a] Ref. [3].
[b] Ref. [4].

thiophene rings and the planarity of the trans conformers only. Moreover, as no experimental NMR data are available for the title compounds, acetohydrazide has been used for comparison. Experimentally, it is found that in $CDCl_3$, the hydrogen atom (H_1) and the carbon atom (C_1) of the amide group have chemical shift values of 7.95 and 171.23 ppm, respectively [18]. As a result, the calculated NMR shifts employing B3LYP/6-311++G(d,p) theory level are consistent with these experimental values.

Raw harmonic vibrational frequencies and their intensities have been computed for the conformers of Hait and Htit. Table 5 reports only the stretching frequencies of the bonds in the amide linkage about which rotation occurs for cis–trans isomerization because many of the vibrations are extensively coupled. Some literature experimental wave numbers are also included for the title compounds for comparison. In the simplest related molecule such as acetohydrazide, experimentally [18], the $C=O$ stretching vibration commonly referred as amide I is observed at 1667 cm^{-1}, the $N-H$ stretching is observed at 3450 cm^{-1}, and the $C-N$ stretching is observed at 1314 cm^{-1}. Therefore, it is interesting to note the close similarity between the observed experimental values and the computed unscaled frequencies.

CONCLUSION

This paper reports a theoretical gas-phase study of the structures, energetics, and spectroscopic parameters of the cis and trans conformers of Hait and Htit. The transition state resulting from cis–trans isomerization has also been modeled. Some of the results compare satisfactorily with available literature results for Hait conformers. The interesting aspect of this work is that the trans conformers are more stable for both Hait and Htit. Furthermore, the energy barrier, a parameter that is more difficult to obtain experimentally, is larger than the energy difference between the cis and trans conformers. This accounts for the trans conformers being almost exclusive for both Hait and Htit.

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