Gauche/Trans Equilibria of 2,2′-Bi-1,3-dioxepanyl and 2,2′-Bi-1,3-dithiepanyl in Different Media—Theory and Experiment

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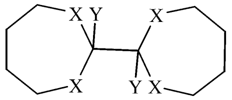
The gauche/trans conformational equilibria of 2,2′-bi-1,3-dioxepanyl **1** and 2,2′-bi-1,3-dithiepanyl **2** dissolved in carbon tetrachloride and benzene are studied through dipole moment determination. Analyses of the relative permittivity data show that both **1** and **2** favor the gauche form at 25 °C. However, X-ray crystallographic determination revealed that **1** and **2** favored the trans conformation in the solid state. Ab initio and DFT calculations were performed to examine the structural features of **1** and **2** and study the effects of solvent on these molecules. The calculated gauche/trans equilibria of **1** and **2** in different media are in good agreement with the experimental findings. CH···X (X = O or S) interactions are important to understand the structures and relative energies of these 1,3-diheteroane systems.

Introduction

In recent years, there has been a growing interest in the interactions involving CH groups and electronegative atoms X.[1,2] These interactions have been found to play an important role in the stabilization of particular conformations of isolated single molecules.[3,4] To elucidate the effect of solvents on CH····X interactions, we have studied the conformations of 2,2′-bi-1,3-dioxolanyls,[5] 2,2′-1,3-dithiolanyls,[5] 2,2′-bi-1,3-dioxanyls,[6] and 2,2′-bi-1,3-dithianyls[6] by dipole moment determination, X-ray crystallography, and density functional calculations. In these studies, we have inferred that the noncovalent CH···X (X = O or S) interactions play an important role in governing their rotational equilibria. For the 2,2′-bi-1,3-dioxolanyl and 2,2′-1,3-dithiolanyl systems, the gauche form is stabilized by two favorable CH···X interactions between the X atom of one five-membered ring and the methylene hydrogen of the adjacent five-membered ring. In the 2,2′-bi-1,3-dioxanyl and 2,2′-bi-1,3-dithianyl systems, the two six-membered rings are too far apart to allow the favorable CH···X interaction in the more stable gauche-ee conformation and thus these compounds prefer the trans conformer in the gas phase. However, the solvent reaction field was found to exert a larger stabilization effect on the less polar trans form such that the gauche/trans equilibrium could be reversed on going from the gas phase to a polar dielectric medium. To gain further insight into the implications of solvent on CH····X interactions, we have investigated, in this work, the conformations of 2,2′-bi-1,3-dioxepanyl **1** and 2,2′-bi-1,3-dithiepanyl **2** (Figure 1) by dipole moment determination, X-ray crystallography, and density functional calculations.

Experimental Procedure

Compounds **1** and **2** were prepared by the acid-catalyzed condensation of glyoxal with 1,4-butanediol or 1,4-butanedithiol.[7] The purities of the compounds were determined by ^{1}H NMR. To our knowledge, compound **2** has not been reported previously and was characterized by elemental analysis, ^{1}H NMR (in CDCl$_3$) and mass spectrometry. **2**: white solid, 22% yield; mp = 71 °C. ^{1}H NMR (300 MHz, CDCl$_3$) δ 4.59 (s, 2H, S−C*H*-S), 3.09−3.03 (m, 4H, SC*H*$_2$), 2.80−2.71 (m, 4H, SC*H*$_2$), 2.02−1.88 (m, 8H, C*H*$_2$C*H*$_2$). MS: *m*/*z* calcd for C$_{10}$H$_{18}$S$_4$: 266.0; found 266.1. Anal. Calcd for C$_{10}$H$_{18}$S$_4$: C, 45.07; H, 6.81; S, 48.12. Found: C, 44.92; H, 6.78; S, 48.17.



1 X = O, Y = H
2 X = S, Y = H

Figure 1. Structures of **1** and **2**.

Dipole Moment Determination. The dipole moment data for compounds **1** and **2** are shown in Table 1. Benzene and carbon tetrachloride were carefully distilled and dried before use. Three concentration dependencies, namely those of the relative permittivities, densities, and refractive indices ($\alpha\epsilon_1$, βd_1, and γn_1^2) were determined for each solvent at three temperatures. The sample temperature was controlled within ±0.5 °C by circulating thermostated water around the dielectric cell. Relative permittivity was measured with a heterodyne-beat meter[8] and densities and refractive indices by standard procedures.[9] The physical constants required for the relative permittivity have been given previously.[10,11] With use of the least-squares method, the experimental values of the slope $\alpha\epsilon_1$, βd_1, and γn_1^2 (given by eq 1) at infinite dilutions of the compounds (w_2 denoting the solute weight fraction) and the respective molar polarization, refraction and dipole moments were calculated.

$$\alpha\epsilon_1 = \left(\frac{\delta\Delta\epsilon}{\delta w_2}\right)_{w_2\to 0} \quad \beta d_1 = \left(\frac{\delta\Delta d}{\delta w_2}\right)_{w_2\to 0} \quad \gamma {n_1}^2 = \left(\frac{\delta\Delta n^2}{\delta w_2}\right)_{w_2\to 0} \tag{1}$$

By measuring the dielectric effects in extremely dilute solutions of the compounds, we may interpret our system as consisting of isolated molecules immersed in a well-defined environment. The dipole moments were determined using the method of LeFevre and Vines.[9,12]

Crystallography. Single crystals of **1** and **2** were obtained from hexane solutions. A Siemens SMART CCD system cooled

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TABLE 1: Molar Polarization, Refractions, and Dipole Moments at Infinite Dilution of Compounds 1 and 2 (1D = 3.337 × 10^{-30} cm)

T/°C	solvent	concn range ($10^5 w_2$)	$\alpha\epsilon_1$	β	γ	P_2/ cm^3	R_D[a]/ cm^3	μ[b]/D
a. 2,2′-Bi-1,3-dioxepanyl **1** (R_D = 51.56 cm^3)[c]								
7	CCl$_4$	170−520	3.58	−0.373		124.7		1.80 ± 0.01
25	CCl$_4$	180−480	3.18	−0.375	0.108	119.1	53.68	1.78 ± 0.01
45	CCl$_4$	180−430	2.85	−0.366		114.6		1.77 ± 0.01
7	benzene	160−460	1.86	0.133		127.7		1.84 ± 0.01
25	benzene	160−340	1.75	0.190	0.002	122.4	55.45	1.83 ± 0.01
45	benzene	140−320	1.42	0.152		115.1		1.78 ± 0.02
b. 2,2′- Bi-1,3-dithiepanyl **2** (R_D = 76.12 cm^3)[c]								
7	CCl$_4$	140−260	4.35	−0.213		177.7		2.12 ± 0.01
25	CCl$_4$	70−180	3.92	−0.193	0.432	169.0	75.42	2.09 ± 0.01
45	CCl$_4$	70−170	2.88	−0.091		138.3		1.72 ± 0.02
7	benzene	100−310	2.97	0.278		208.9		2.44 ± 0.01
25	benzene	115−310	2.69	0.285	0.095	200.0	75.30	2.42 ± 0.01
45	benzene	210−310	1.88	0.582		136.4		1.72 ± 0.01

[a] R_D determined from refractive indices measured with a refractometer equipped with a sodium D lamp. [b] $P_D = 1.05R_D$. Errors were calculated based on the method described by Topping.[17] [c] R_D computed from bond refractions for the sodium D line.[18]

TABLE 2: Crystallographic Data

compound	**1**	**2**
formula weight	202.24	266.48
wavelength (Å)	0.71073 (Mo Kα)	
crystal system	monoclinic	monoclinic
space group	$P2(1)/n$	$P2(1)/c$
unit cell dimensions		
a (Å)	4.3818(3)	8.617(3)
b (Å)	11.5391(8)	5.4343(18)
c (Å)	10.0669(7)	13.344(4)
β (deg)	92.7900(10)	98.018(8)
volume (Å^3)	508.40(6)	618.8(4)
Z, calculated density (g cm^{-3})	2, 1.321	2, 1.430
μ (mm^{-1})	0.101	0.729
F(000)	220	284
reflections collected/ unique	4002/1441	4249/1495
refinement method	full-matrix least-squares on F^2	
no. of parameters	100	64
goodness-of-fit on F^2	1.091	1.077
R1, wR2 (all data)	0.0589, 0.1637	0.0407, 0.0958

to 223 K in a stream of cold N$_2$ gas was used for the data collection. Data were collected using three ω-scans on each crystal over a 180° range at a fixed φ value of 54.74° with 0.30° scan width and 5-s count time per frame and a crystal-to-detector distance of 5.04 cm. Data were corrected for Lorentz and polarization effects with the SMART suite of programs[13] and for the absorption effects with SADABS.[14] Structural solution and refinement were carried out with the SHELXTL programs.[15] Further crystallographic data and details of the structure determination for the compounds are given in Table 2.

Results and Discussion

Dipole Moment Determination. *A. 2,2′-Bi-1,3-dioxepanyl **1***. Analysis of the data in Table 1 shows that the dipole moment of this compound decreases with increasing temperatures in both carbon tetrachloride and benzene solutions, indicating that the gauche conformer is more stable than the trans and is higher in population in these solvents. To analyze the dipole moment data more fully, it is necessary to estimate the dipole moment of the gauche conformer. One approach is the Lennard-Jones-Pike method of analysis,[16] which uses eq 2 to evaluate ΔE and μ_g by superimposing a theoretical curve of ln $F(x)$ versus ln x onto an experimental curve of ln μ_{obs}^2 against ln(1/T). Application of this analysis to our dipole moment data in carbon tetrachloride yields a ΔG ($G_g - G_t$) value of −7.03 kJ mol^{-1} and a gauche conformer dipole moment (μ_g) of 1.89 D. Assuming that the trans conformer dipole moment, $\mu_t = 0$ D and μ_g is independent of temperature, an estimate of the gauche-conformer population (x%) in solution can be made from eq 3, which on substituting the observed moment and μ_g values yield a population of 89% gauche and 11% trans at 25 °C.

$$\overline{\mu^2} - \mu_t^{\,2} = (\mu_g^{\,2} - \mu_t^{\,2})\,F(x)$$

where $\overline{\mu^2}$ is the mean square dipole moment,

$$F(x) = \frac{2e^{-x}}{1 + 2e^{-x}} \quad \text{and} \quad x = \frac{\Delta E}{RT} \tag{2}$$

$$x = \frac{100\,\mu_{obs}^{\,2}}{\mu_g^{\,2}} \tag{3}$$

The experimental data for benzene solutions show that the dipole moment results are very similar to those for carbon tetrachloride solution. Lennard-Jones-Pike analysis[16] of the dipole moment data in benzene gives a μ_g value of 2.01 D and ΔG value of −5.53 kJ mol^{-1}. This corresponds to a composition of 83% gauche and 17% trans at 25 °C. Comparison of the gauche population of **1** with that of 2,2′-bi-1,3-dioxolanyl (gauche population in carbon tetrachloride and benzene are 19 and 9%, respectively)[8] and 2,2′-bi-1,3-dioxanyl (gauche population in carbon tetrachloride and benzene are 25 and 19%, respectively)[6] shows an increase in the gauche population as the ring size increases.

*B. 2,2′-bi-1,3-dithiepanyl **2***. The large dipole moments in carbon tetrachloride and benzene suggest that the polar gauche conformer must be present in high proportion in these solvents. Table 1 shows that the dipole moments obtained in both carbon tetrachloride and benzene solutions decrease with increasing temperatures, indicating that, like in **1**, the gauche conformer is more stable than the trans and is higher in population in these solvents. Application of the Lennard-Jones-Pike analysis[16] to our dipole moment data yields ΔG values of −5.21 and −4.86 kJ mol^{-1} in carbon tetrachloride and benzene, respectively. The μ_g and percentage of gauche population at 25 °C were found to be 2.33 D and 80% in carbon tetrachloride and 2.74 D and 78% in benzene. It appears that the solvent effect on **2** is weaker than that in **1**. This could plausibly be attributed to the increased size of the sulfur atom and the increased carbon−sulfur bond length (C−S = 1.81 Å in **2**; C−O = 1.41 Å in **1**), which causes a smaller 1,3-transannular nonbonded interaction in **2**, thus resulting in a decrease in the flexibility of the 1,3-dithiepane ring.

Solid-State Structure. Figures 2 and 3 depict the structures and define the atomic numbering of **1** and **2** respectively. X-ray crystal structure analyses of **1** and **2** show that both molecules exist in the trans conformation in the solid state. Both the 1,3-dioxepane and 1,3-dithiepane rings in **1** and **2**, respectively, adopt a twist-chair conformation.

Theoretical Calculations. Standard ab initio and density functional calculations were carried out using the GAUSSIAN 98 series of programs.[19] Geometry optimizations were performed

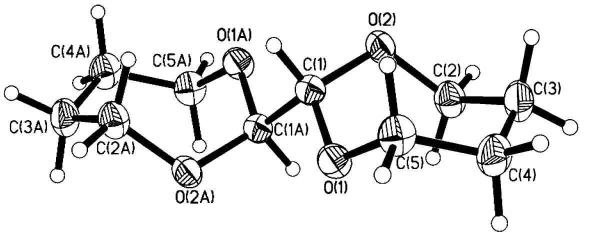


Figure 2. Thermal ellipsoid diagram of **1**.

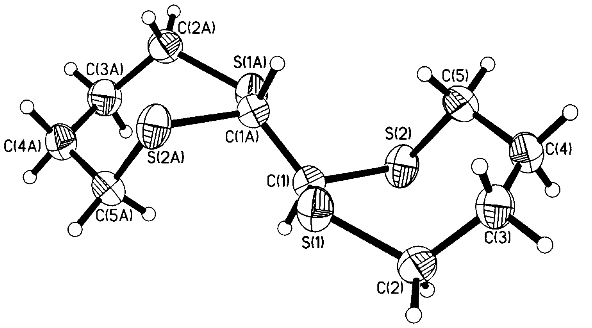


Figure 3. Thermal ellipsoid diagram of **2**.

TABLE 3: Calculated Relative Energies[a] (kJ mol^{-1}) of the Conformers of 1,3-Dioxepane and 1,3-Dithiepane

conformer	1,3-dioxepane (X = O)	1,3-dithiepane (X = S)
TC1	0.0	0.4
TC2	12.2	0.0
TC3	10.4	9.3
TC4	10.8	1.6
TB1	13.5	*b*
TB2	*b*	3.8
C	1.2	10.0
B	19.3	18.7

[a] G3(MP2) level. [b] Does not exist at the MP2/6-31G* level; it collapses to the most stable twist-boat form.

at the B3LYP[20] level using the split-valence polarized 6-31G* basis set. Higher level relative energies were computed at the MP2/6-311+G(2d,p) level based on the B3LYP/6-31G* optimized geometries and include the zero-point energy (ZPE) correction (B3LYP/6-31G* value, scaled by a factor of 0.9804).[21] The structures and relative energies of 1,3-dioxepane and 1,3-dithiepane were examined at the G3(MP2) theory.[22] For solvent-effect calculations, we have employed the Onsager's self-consistent reaction field (SCRF) theory[23] and the self-consistent isodensity surface-polarized continuum model (SCIPCM).[24] Geometry optimizations were performed using the SCRF method at the B3LYP/6-31G* level and the higher level single-point energy calculations were carried out with the SCIPCM method at the B3LYP/6-311+G(2d,p) level. The free energy differences (ΔG) were computed from the equation $\Delta G_T = \Delta H_T - T\Delta S$, where ΔS is the entropy change and $\Delta H_T = \Delta H_0 + (H_T - H_0)$.

Relatively little is known about the conformational effects of the seven-membered rings dioxepane and dithiepane. Experimentally, Dell'erba et al. have investigated the free jet millimeterwave absorption spectrum of 1,3-dioxepane.[25] The authors suggested that the most stable conformation is a twist-chair structure with C_2 symmetry. The only computational study of 1,3-dioxepane corresponds to the force field calculations by Hendrickson.[26] As with cycloheptane and oxepane,[27-29] there are four possible structures of 1,3-dioxepane and 1,3-dithiepane: chair (**C**), boat (**B**), twisted-chair (**TC**), and twisted-boat (**TB**). Here, we have employed the high-level G3(MP2) theory to investigate the relative stability of their conformations. For both 1,3-dioxepane and 1,3-dithiepane, the twist-chair form is found to be the preferred structure. The chair and boat forms (C_s symmetry, Scheme 1) are not stable equilibrium structures on the MP2/6-31G* potential energy surface. They correspond to transition states for pseudorotation of the twist-chair and twist-boat forms, respectively. For the twist-chair and twist-boat structures, there are several conformations arising from the different positions of 1,3-heteroatom substitution of the seven-membered rings. One may generate all possible forms by considering 1,3-heteroatom substitution of cycloheptane (C_2 symmetry): **TC1**, **TC2**, **TC3**, and **TC4** for the twist-chair structure and **TB1**, **TB2**, **TB3**, and **TB4** for the twist-boat structure (see Scheme 1). The **TC1** conformation, with two oxygen atoms adjacent to the unique apical carbon atom, is calculated to be the lowest energy structure for 1,3-dioxepane. Our computed (MP2/6-31G*) rotational constants ($A = 3523.9$, $B = 3186.5$, $C = 1916.6$ MHz) are in very good accord with the observed values in the gas phase ($A = 3565.8$, $B = 3193.5$, $C = 1936.3$ MHz). Interestingly, the sulfur analogue, 1,3-dithiepane, prefers the **TC2** twist-chair conformation (Table 3). The **TC1** conformation lies just 0.4 kJ mol^{-1} above **TC2**. The predicted dipole moments (MP2/6-31G*) of the most stable twist-chair forms of 1,3-dioxepane and 1,3-dithiepane are 0.98 and 2.26 D, respectively. Other twist-chair conformers are found to lie significantly higher in energy than the global minimum for 1,3-dioxepane (Table 3). Of the four possible twist-boat forms, only one stable form is found in both cases. 1,3-Dioxepane favors the **TB1** form, while 1,3-dithiepane prefers the **TB2** form. It thus appears that the sulfur system favors a structure with the sulfur atom located at the apical atom for both the twist-chair and twist-boat forms. This finding may be rationalized in terms of the fact that sulfur can accommodate a smaller bond angle better than oxygen at the apical position.

SCHEME 1: Conformations of 1,3-Diheteroanes

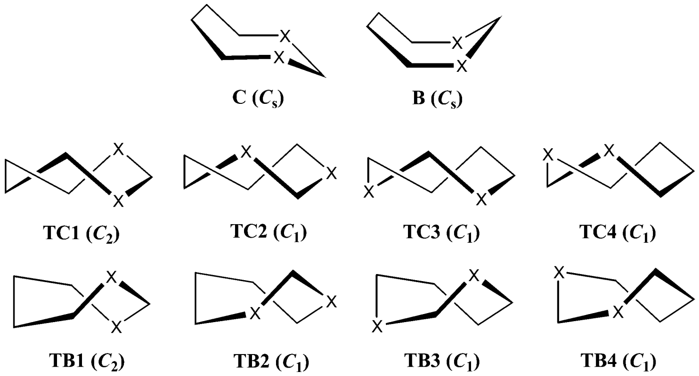


TABLE 4: Calculated Dipole Moments[a] (μ, D) and Relative Energies[b] (ΔE_0, ΔH_{298} and ΔG_{298}, in kJ mol^{-1})

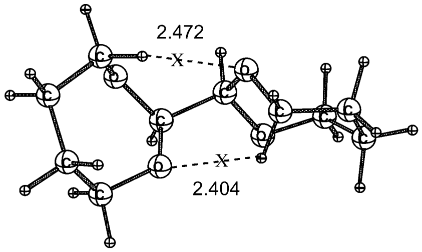
				ΔG_{298}[c]		
species	μ	ΔE_0	ΔH_{298}	$\epsilon = 1.0$	$\epsilon = 2.0$[d]	$\epsilon = 40.0$[d]
			1			
trans	0.00	0.0	0.0	0.0	0.0	0.0
gauche	1.33	−9.3	−9.6	−7.3	−4.8	−1.8
			2			
trans	0.00	0.0	0.0	0.0	0.0	0.0
gauche	1.64	−3.3	−3.5	−1.6	−0.8	−0.5

[a] Gas-phase B3LYP/6-311+G**//B3LYP/6-31G* values. [b] Based on MP2/6-311+G(2d,p)//B3-LYP/6-31G*+ZPE level. [c] $\Delta G_{298} = \Delta H_{298} - 298^*\Delta S$. [d] $\Delta G_{\text{solution}} = \Delta G_{\text{gas-phase}} - \Delta G_{\text{solvent}}$, where $\Delta G_{\text{solvent}}$ was calculated at the SCIPCM-B3LYP/6-311+G(2d,p) level.

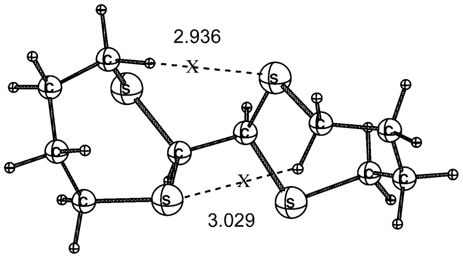
For instance, the CXC bond angles of the **TC2** form in 1,3-dioxepane and 1,3-dithiepane are 116.7° and 101.8°, respectively.

In light of the conformational behavior of the seven-membered rings 1,3-dioxepane and 1,3-dithiepane, one may anticipate that there are many possible conformations of **1** and **2** arising from various combinations of the monomer ring moieties. Furthermore, there are three possible arrangements of the two rings for certain trans and gauche conformers, resulting in six possible conformations, namely, trans-ee, trans-ea, trans-aa, gauche-ee, gauche-ea, and gauche-aa. Thus, there are many plausible conformations to be considered in order to establish the global energy minimum. To this end, we have first examined systematically all the possible conformations at the HF/3-21G level. These calculations confirmed that the twisted-chair forms of the seven-membered rings prevail. Subsequently, only the lower energy conformations were further examined at the higher level of theory. Table 4 summarizes the energies of the most favorable trans and gauche conformations of **1** and **2**. In agreement with the solution results, the gauche form is the preferred conformation in both cases. Our computed gas-phase gauche/trans free energy differences at 298 K (ΔG_{298}) for **1** and **2** are −7.3 and −1.6 kJ mol^{-1}, respectively. These trans and gauche forms of **1** and **2** adopt the **TC1** twist-chair form in the seven-membered rings, which is in accord with the observation conformation in their X-ray structures. The calculated HCCH torsional angles of the gauche forms of **1** and **2** are 71.0° and 62.0°, respectively. It is important to note that the B3LYP method slightly underestimates the stability of the gauche conformations based on some benchmark calculations at the MP4 and CCSD levels. Thus, MP2 theory was employed to evaluate the gauche/trans relative energies.

How do we account for the preference of the sterically unfavorable gauche form in **1** and **2**? Careful inspection of their calculated geometries indicates that there are two sets of close CH···X (X = O or S) contact (Figure 4). These nonbonding H···X distances in the gauche forms are significantly less than the sum of their van der Waals atomic radii. We may explain these short contact distances in terms of the intramolecular CH···O and CH···S hydrogen bonds between the CH proton of one ring and the electronegative O (or S) atom of the adjacent ring. High-pressure Raman-scattering CH vibrational frequency shift studies by Ben-Amotz and co-workers have provided evidence for the formation of CH···X hydrogen bonds.[30] Recent studies have clearly established that these weaker CH···X hydrogen bonds play an important role in the understanding of various areas of organic, biochemical, and material chemistry.[31] The presence of the CH···X interactions in the gauche conformers of **1** and **2** is confirmed by the critical bond analysis based on Bader's theory of atoms in molecules (AIM).[32] The CH···X hydrogen bonds are characterized by a maximum electron density path between the two bonding H and X atoms and the associated properties of the bond critical point (bcp). The electron density (ρ) and Laplacian of electron density ($\nabla^2\rho$) values calculated for the bond critical points of these two gauche conformers are similar to those of a characteristic hydrogen bond.[33] In addition, there is a significant increase of net charge of the CH proton (by 0.004−0.008 e). In summary, we attribute the preference of the gauche conformation in **1** and **2** to the presence of favorable intramolecular CH···X hydrogen bonds. The larger calculated gauche/trans free energy difference in **1** can be explained by the fact that the CH···O interaction is stronger than the sulfur analogue. Similar finding of gauche preference has been reported for the five-membered-ring analogues, namely, bi-1,3-dioxolanyl and bi-1,3-dithiolanyl.[5]



gauche-**1**



gauche-**2**

Figure 4. Calculated (B3LYP/6-31G*) geometries of the gauche forms of **1** and **2** showing the CH···X (X = O or S) hydrogen bonds. The H···O and H···S distances are given in Å and X denotes the bond critical point. The $\nabla^2\rho$ values at the bond critical point are 0.044 and 0.038 for gauche-**1** and 0.026 and 0.020 for gauche-**2**.

Last, we investigated the influence of a dielectric medium on the gauche/trans equilibria of **1** and **2**. The trans forms of **1** and **2** have a zero dipole moment, but a significant dipole moment is predicted for the gauche conformations (Table 4). The computed dipole moments are higher than the observed values. However, it is important to note that the observed dipole moment may not correspond to the lowest energy gauche form. Other low-lying gauche conformations with a lower dipole moment may also contribute to the observed value. In our earlier studies of 1,3-diheteroanes,[5,6] we have inferred that the quadrupole moments of bi-1,3-diheteroanes may also play a crucial role in stabilizing the solute in a dielectric medium. Thus, it is important to consider not only the dipole moment but also the higher moments in predicting the solvent effect on rotational equilibria of the systems studied in this paper. To this end, we have calculated the solvent effects of **1** and **2** using the SCIPCM method. As with the five-membered ring analogues,[5] the trans forms in **1** and **2** are predicted to have a larger solvent stabilization than the corresponding polar gauche forms. This results in a smaller energy difference in the presence of a dielectric medium of $\epsilon = 2$ (represents nonpolar) and 40 (polar) (Table 4). However, the differential solvation effect is not sufficient to reverse the gauche/trans rotational equilibria in solution phases. In conclusion, the gauche forms of **1** and **2** are predicted to be the predominant conformer in the isolated state and in solutions. In both cases, the adjacent rings are sufficiently close that it is stabilized by CH···O or CH···S hydrogen bonds (Figure 4). Perhaps, one may attribute the observation of the trans form in the solid state to crystal packing effect.

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Supporting Information Available: Additional experimental details and crystallographic information files for compounds **1** and **2**. This material is available free of charge via the Internet at http://pub.acs.org.

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