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Conformational Mobility of Thianthrene-5-oxide

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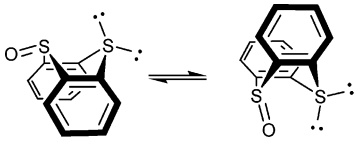
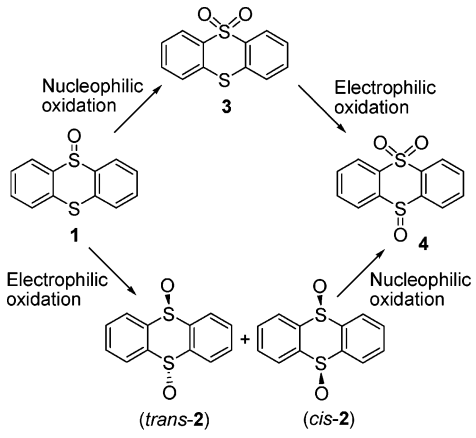


Data on the apparent dipole moment of thianthrene-5-oxide (**1**) and ^{1}H NMR spectra in different solvents support the conformational mobility of **1**, which flaps between two limit boat conformations with the sulfinyl group in pseudoequatorial and pseudoaxial positions, respectively. The conformational equilibrium of **1** occurs too fast for the ^{1}H NMR (500 MHz) time-scale even at −130 °C, and the equilibrium constant has not been determined. The apparent dipole moments of **1** in *n*-hexane and 1,4-dioxane and the ^{1}H NMR spectra of **1** and the model compounds *cis*- and *trans*-thianthrene-5,10-dioxides (**2**) and thianthrene (**5**) in different solvents and at various temperatures confirm that the relative position of the conformational equilibrium of **1** is solvent-dependent, and more polar solvents favor the conformation with the sulfoxide group in the pseudoaxial position (**1**$_{ax}$). Variable-temperature ^{1}H NMR spectra have established the interconversion barrier of *trans*-**2** and confirmed that the conformational equilibrium of *cis*-**2** is strongly displaced toward the conformation with both sulfinyl groups in the pseudoequatorial position. The ^{1}H NMR data support the transannular interaction of the functional groups in **1** and *trans*-**2**.

Introduction

Thianthrene-5-oxide (**1**) was introduced[1] in 1984 as a general mechanistic probe for determining the electrophilic or nucleophilic character of a given oxidant. Thus, electrophilic oxidants should prefer to react with the sulfide moiety of **1** to yield disulfoxide **2**, while nucleophilic oxidants should preferably react at the sulfoxide sites of **1** and **2** to give sulfones SSO_2 (**3**) and $SOSO_2$ (**4**), respectively (Scheme 1). Oxidants are classified as either electrophilic or nucleophilic according to the value χ_{SO}, which is defined by the ratio of oxidation at the SO site to total oxidation. Thianthrene-5-oxide (**1**) has been used extensively to determine the electronic nature of many classes of oxidants such as peroxometal complexes,[2] metalloporphyrin catalysts,[3] hemoprotein-oxidizing species,[4] heteropolyoxometalate oxidants,[5] dimethylphenylsilylhydrotrioxide,[6] dialkylperoxonium intermediates,[7]

SCHEME 1. Thianthrene-5-oxide Mechanistic Probe



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carbonyl oxides,[1] peracids,[8] dioxiranes,[9] and several metal oxidants.[10]

This mechanistic probe has been introduced and applied with the assumption[1] that the thianthrene-5-oxide molecule (**1**) exists in solution in a single geometry folded along the axis defined by the sulfur atoms and the pseudoequatorial oxygen atom. However, in a recent density functional study, Deubel[11] found a moderate energy barrier for conformational ring inversion of thianthrene-5-oxide (**1**) and suggested that this could affect the chemo- and stereoselectivity of the oxidation reaction.

Early findings[12] on dipole moment and UV and IR spectroscopic measurements in solution showed that thianthrene and its dioxides were conformationally flexible in solution and switched between two boat-type limit conformations about the line joining the sulfur atoms. Although UV and IR analyses of thianthrene-5-oxide (**1**) and theoretical calculations[13] have pointed out the conformational mobility of this molecule in solution, there have been no previous systematic studies on this substrate.

In our study[14] on the oxidation of sulfides with dioxiranes, we found a clear discrepancy between the results obtained with simple sulfides and thianthrene-5-oxide (**1**). This prompted us to further examine the conformational flexibility of this mechanistic probe in solution, since this could allow transannular interaction between the reaction intermediates and the second functional group present in the molecule.[14a] This interaction could divert the course of the reaction and cause the probe to behave abnormally in these oxidation reactions.

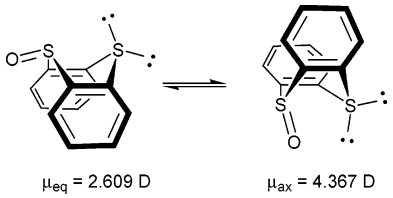

FIGURE 1. Conformational equilibrium of **1**.

We report here the apparent dipole moment and low-temperature ^{1}H NMR measurements of thianthrene-5-oxide (**1**) in different solvents. The results provide evidence for the conformational mobility of **1** in solution, and the relative populations of pseudoequatorial and pseudoaxial conformers are solvent- and temperature-dependent. The conformational equilibrium of **1** occurs too fast for the ^{1}H NMR time-scale, and the equilibrium constant has not been determined quantitatively. Variable-temperature spectra in different solvents have allowed us to establish the energy barrier for the conformational interchange of *trans*-**2** and also the strong displacement of the conformational equilibrium of *cis*-**2** toward the pseudoequatorial conformer. The ^{1}H NMR data also indicate transannular interactions between the functional groups of thianthrene-5-oxide (**1**) and *trans*-**2**.

Results and Discussion

Thianthrene-5-oxide (**1**) can be depicted in two equilibrating boat-type limit conformations with the oxygen atom placed either in a pseudoequatorial ($\mathbf{1}_{eq}'$) or pseudoaxial ($\mathbf{1}_{ax}'$) position (Figure 1). Switching between these limit conformations occurs through a planar form by flapping of the aromatic rings.

The sulfoxide moiety in conformation $\mathbf{1}_{eq}'$ is flanked by aromatic *peri*-C−H bonds, which allows electrostatic interactions between the oxygen and hydrogen atoms. In conformation $\mathbf{1}_{ax}'$, electronic repulsion exists between the pseudoaxial sulfoxide group and the cis electron lone-pair of the sulfide-type opposite sulfur atom. Theoretical calculations[11] show the existence of two potential energy minima that correspond to these conformations, where $\mathbf{1}_{eq}'$ is 3.8−6.8 kcal mol^{-1} more stable than $\mathbf{1}_{ax}'$. The theoretical predicted[11] activation energy for the ring inversion of **1** is 3.8−7.4 kcal mol^{-1}. MOPAC PM3 semiempirical calculations give values of 2.609 and 4.367 D for the dipole moments of $\mathbf{1}_{eq}'$ and $\mathbf{1}_{ax}'$, respectively. In the following sections, we report the results of our analysis of the conformational equilibrium of **1** by means of dipole moments and ^{1}H NMR spectra in different solvents at different temperatures.

Dipole Moment. The apparent molecular polarization at infinite dilution ($P_{2\infty}$), molecular refraction (R_D), dipole moment (μ_2), polarizabilities (α), and partial molar volumes (V_2^0) of **1** were determined in *n*-hexane and 1,4-dioxane solutions following reported methods[15] based on measurements of the dielectric permittivity, density, and refractive index at 25 °C. The apparent dielectric constant

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TABLE 1. Polarization Data and Dipole Moments of Thianthrene-5-oxide (1) in *n*-Hexane and 1,4-Dioxane[a]

magnitude	hexane	1,4-dioxane
α	2.58 ± 0.07	6.7 ± 0.3
β	-0.7 ± 0.1	-0.29 ± 0.02
γ	0.3 ± 0.1	-0.2 ± 0.1
$(d\epsilon_{1,2}/dY_2)_{Y_2=0}$	0.91 ± 0.05	1.5 ± 0.1
$P_{2\infty}$ ($cm^3\ mol^{-1}$)	228 ± 13	303 ± 13
R_D ($cm^3\ mol^{-1}$)	64 ± 5	26 ± 4
V_2^0 ($cm^3\ mol^{-1}$)	197 ± 10	158 ± 6
ϵ_2'	6.5 ± 0.3	12 ± 1
n_{2IR}	1.6 ± 0.3	1.3 ± 0.1
dipole moment[b] (D)	2.8 ± 0.3	3.7 ± 0.1
dipole moment[c] (D)	2.8 ± 0.1	3.7 ± 0.1
dipole moment[d] (D)	2.8 ± 0.5	4.0 ± 0.5

[a] Averages of at least four independent runs. [b]From the method of Lange,[16a] Errera,[16b] and Williams.[16c] [c]From the method of Guggenheim−Smith.[16h−j] [d]From the method of Onsanger−Kirkwood.[16k,l]

(ϵ_2') and the refraction index extrapolated in the IR region (n_{IR}) were estimated for the solute. The apparent dipole moments were determined by the method of Lange,[16a] Errera,[16b] and Williams and co-workers,[16c−g] the approach of Guggenheim−Smith,[16h−j] and the more complex equation obtained from the Onsanger−Kirkwood liquid theory.[16k,l] For a detailed description of the method used, see the Experimental Section. The results are shown in Table 1.

The relative increase in molecular polarization ($P_{2\infty}$) and the strong decrease in the magnitudes of molecular refraction (R_D) and partial molar volume (V_2^0) observed on going from *n*-hexane to 1,4-dioxane reflect structural changes in the solute promoted by the differences in the electrical field associated with each solvent. In *n*-hexane, the absence of interactions and external electric fields results in poor solvation and induces the solute molecules to chiefly adopt conformation $\mathbf{1}_{eq}'$, with the oxygen atom in the pseudoequatorial position. The strong external interactions or fields exerted by 1,4-dioxane allow better solvation and stabilize conformation $\mathbf{1}_{ax}'$, with the oxygen atom in the pseudoaxial position. Thus, in the less-polar solvent, we found lower values for polarization and the average dipole moment and a higher value for the molar volume. These results support the conformational flexibility of thianthrene-5-oxide (**1**) and also the solvent-dependence of the conformational equilibrium.

The experimental method used yields an average dipole moment μ given by eq 1:

$$\mu = (\Sigma_i n_i \mu_i^2)^{1/2} \quad (1)$$

where n_i is the molar fraction of each conformer and μ_i is the corresponding dipole moment.[17] Substitution in eq 1 of the μ_i values calculated for conformers $\mathbf{1}_{eq}'$ and $\mathbf{1}_{ax}'$ and the average experimental dipole moment μ measured in each solvent allows us to estimate that the molar fraction of $\mathbf{1}_{ax}'$ at equilibrium is 31% in *n*-hexane and 67% in 1,4-dioxane. Accordingly, the population of the flagpole conformer $\mathbf{1}_{ax}'$ at equilibrium is expected to increase with an increase in the polarity of the solvent.

^{1}H NMR. ^{1}H NMR spectroscopy could presumably be used to determine the equilibrium population of conformers $\mathbf{1}_{eq}'$ and $\mathbf{1}_{ax}'$ in solution provided that the rate of interconversion is slow enough to observe two sets of signals for the *peri* hydrogen atoms adjacent to the sulfoxide group. However, the ^{1}H NMR spectra (500 MHz) of SSO (**1**) measured in CD_2Cl_2, toluene-d_8, THF-d_8, and THF-d_8:diethyl ether-d_{10} from 25 to −130 °C showed only averaged signals of variable chemical shifts, indicating that, as predicted by theoretical calculations,[11] this process is too fast for the NMR time-scale and that it is not possible to determine the equilibrium constant (Figures 2 and S14 (Supporting Information)).

The chemical shifts of the ^{1}H NMR signals corresponding to a rapidly equilibrating population of conformers under different conditions of solvent and/or temperature can evidence the effect of these factors on the relative position of the conformational equilibrium. Assuming that the shielding of the *peri* hydrogen atoms adjacent to the sulfoxide group depends on the spatial orientation of the sulfinyl oxygen atom, the relative $\mathbf{1}_{eq}'/\mathbf{1}_{ax}'$ ratio could be estimated provided that the shielding effects exerted by the sulfoxide in the pseudoequatorial or pseudoaxial position are known. Since the conformational equilibrium of thianthrene-5-oxide (**1**) does not become slow at the NMR time-scale, we considered the structurally related thianthrene (**5**) and *cis*- and *trans*-thianthrene-5,10-dioxides (**2**) as references to estimate the effects of the spatial orientation of the sulfoxide moiety, the solvent, and the temperature on the chemical shifts of the *peri* hydrogen atoms. With this information in hand, it may be possible to interpret the displacement of the ^{1}H NMR signals of thianthrene-5-oxide (**1**) under different conditions of solvent and temperature.

Previous ^{1}H NMR studies have examined the effects of temperature and aromatic solvent-induced shift (ASIS)[18] on a series of related tricyclic diaryl sulfides and sulfoxides with the sulfur atom in the *meso* position[19] such as 9-substituted thioxanthene derivatives. However, to the best of our knowledge, there have been only two reports[12c,f] on the ^{1}H NMR analysis of the conformational equilibrium of **1**, thianthrene-5,10-dioxides (**2**), and thianthrene (**5**). The absence of data on **1** and our model compounds **2** and **5** prompted us to obtain variable-temperature ^{1}H NMR spectra for these systems in different solvents.

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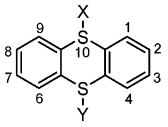
TABLE 2. ^{1}H NMR (500 MHz) Resonances δ_H (in ppm) of 1, *cis*-2, *trans*-2, and 5 in Different Solvents and at Various Temperatures



1, X= :, Y= =O
cis-**2**, X=Y= =$O_{ax/eq}$
trans-**2**, X= =O_{eq}, Y= =O_{ax}
5, X= Y= :

compd	solvent	T (°C)	δH^1	δH^4	δH^2	δH^3
1	CD_2Cl_2	25	7.63	7.87	7.54	7.42
		−100	7.54	7.72	7.47	7.35
cis-**2**	CD_2Cl_2	25	8.07		7.76	
		−100	7.99		7.75	
trans-**2**	CD_2Cl_2	25	8.12		7.71	
		−100	8.14	8.02	7.74	7.64
5	CD_2Cl_2	25	7.54		7.3	
		−100	7.51		7.29	
1	toluene-d_8	25	7.11	7.91	6.96	6.79
		−100	6.99	8.17	6.84	6.68
cis-**2**	toluene-d_8	25	7.8		6.86	
		−100	7.83		6.57	
trans-**2**	toluene-d_8	25	7.55		6.75	
		−100	8.03	6.68	6.49	6.38
5	toluene-d_8	25	7.21		6.8	
		−100	7.13		6.65	
1	THF-d_8	25	7.71	7.91	7.63	7.5
		−100	7.89	7.91	7.75	7.64
cis-**2**	THF-d_8	25	8.05		7.78	
		−100	8.07		7.9	
trans-**2**	THF-d_8	25	8.13		7.71	
		−100	8.26	8.21	7.89	7.81
5	THF-d_8	25	7.52		7.29	
		−100	7.65		7.42	

The ^{1}H NMR spectra at 500 MHz of samples of thianthrene **5**, *cis*-**2**, and *trans*-**2** dissolved in CD_2Cl_2, toluene-d_8, THF-d_8, and 3:2 THF-d_8/Et_2O-d_{10} were measured from 25 to −130 °C. The ^{1}H NMR data of **1**, *cis*-**2**, *trans*-**2**, and **5** at 25 and −100 °C are summarized in Table 2 (data for 3:2 THF-d_8/Et_2O-d_{10} are collected in Table S1 in Supporting Information). Figures 3 and 4 show the variable-temperature ^{1}H NMR spectra in CD_2Cl_2 for *trans*-**2** and *cis*-**2**, respectively. The NMR spectra measured for all of these compounds in CD_2Cl_2, toluene-d_8, THF-d_8, and 3:2 THF-d_8/Et_2O-d_{10} are depicted in Figures S1−S17 (Supporting Information).

The variable-temperature ^{1}H NMR spectra in CD_2Cl_2 showed that at low temperatures, the conformational equilibration of *trans*-**2** became slow on the NMR time-scale and the AA′XX′ spin system observed at 25 °C evolved into a first-order one formed by four anisochronous protons (Figure 3). To the best of our knowledge,

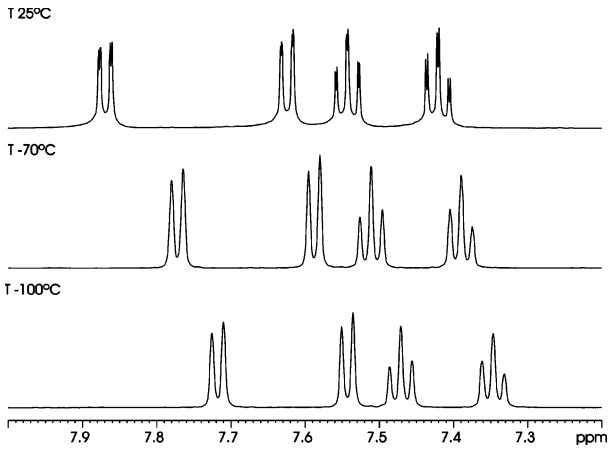


FIGURE 2. Temperature dependence of the ^{1}H NMR (500 MHz) spectra of **1** in CD_2Cl_2.

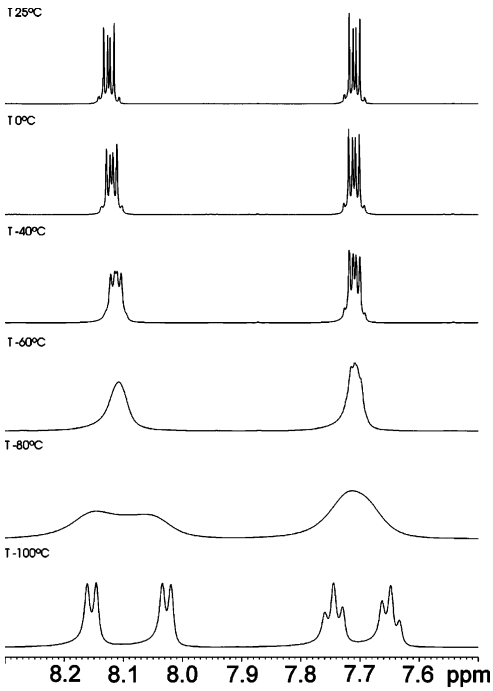


FIGURE 3. Temperature-dependence of the ^{1}H NMR (500 MHz) spectra of *trans*-**2** in CD_2Cl_2.

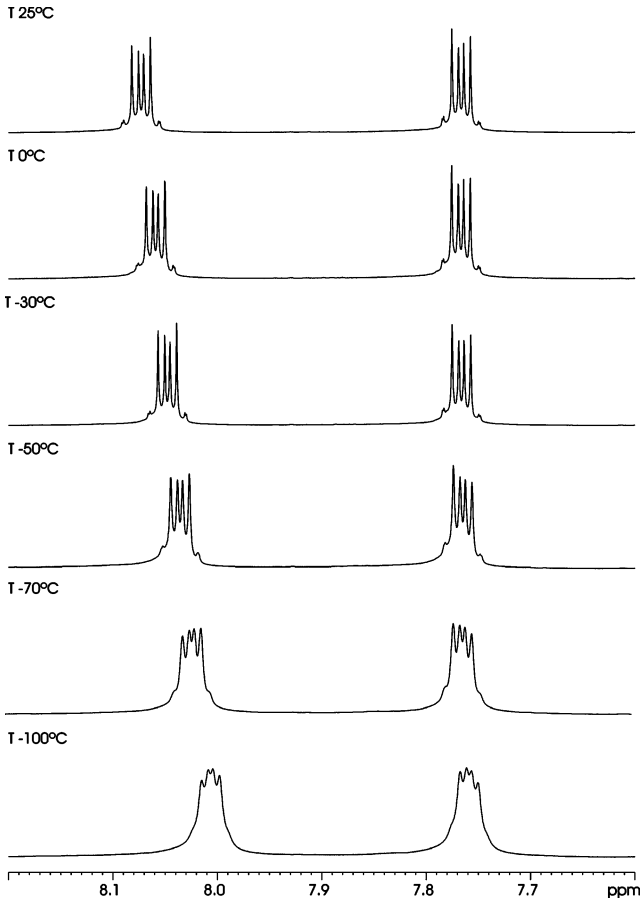


FIGURE 4. Variable-temperature ^{1}H NMR spectra (500 MHz) of *cis*-**2** measured in CD_2Cl_2.

this is the first time that this phenomenon has been observed for *trans*-**2**. Coalescence of the *peri* protons takes place at −60 °C. Since the separation between $H^{4,6}/H^{1,9}$ measured at −100 °C is 60 Hz, the activation energy for the conformational inversion at the coalescence temperature is $\Delta G^{\ddagger} = 10.2$ kcal mol^{-1}, which agrees very well with the calculated value[11] of 9.7 kcal mol^{-1}. The known diamagnetic anisotropy effect of the sulfinyl moiety[12c,20] enables us to assign the doublets at δ 8.14 ($^3J = 7.4$ Hz) and 8.02 ($^3J = 7.4$ Hz) ppm to the $H^{1,9}$ and $H^{4,6}$ hydrogen atoms adjacent to the pseudoequatorial and pseudoaxial sulfinyl groups, respectively. The triplets at δ 7.74 ($^3J =$ 7.4 Hz) and 7.64 ($^3J = 7.4$ Hz) ppm were assigned to the $H^{2,8}$ and $H^{3,7}$ hydrogen atoms, respectively, via a COSY experiment (Figure S5).

trans-**2** also showed a slow conformational equilibration on the NMR time-scale in toluene-d_8, THF-d_8, and 3:2 THF-d_8/Et_2O-d_{10} (Figures S8, S12, and S16), with a coalescence temperature of −60 °C and activation energies of 9.2, 10.6, and 9.9 kcal mol^{-1}, respectively (Table S2). In toluene-d_8 at −100 °C, $H^{1,9}$ and $H^{4,6}$ exhibit an extremely large chemical shift difference of 675 Hz ($\Delta\nu(H^{1,9} - H^{4,6})_{(-100°C)} = 675$ Hz). The most deshielded doublet was assigned to $H^{1,9}$ in the proximity of the pseudoequatorial sulfinyl group (δ 8.03 ppm, $^3J = 6.7$ Hz) (Table 2).

The variable-temperature ^{1}H NMR spectra of *cis*-**2** in CD_2Cl_2, toluene-d_8, THF-d_8, and 3:2 THF-d_8/Et_2O-d_{10} (Figure 4 and Figures S2, S7, S11, and S15) exhibited an AA′XX′ spin system from 25 to −130 °C. This lack of variation in the multiplicity pattern of *cis*-**2** could be attributed to interconversion between conformers *cis*-$\mathbf{2}_{ax}'$ and *cis*-$\mathbf{2}_{eq}'$ that is still rapid on the NMR time-scale. However, considering that the energy barrier calculated[11] for this interconversion is 13.5 kcal mol^{-1} (3.8 kcal mol^{-1} higher than that predicted for *trans*-**2**) and that the *cis*-$\mathbf{2}_{eq}'$ conformer is 1.9−3.6 kcal mol^{-1} more stable[11] than the *cis*-$\mathbf{2}_{ax}'$, the presence of only one set of AA′XX′ signals in the ^{1}H NMR spectrum of *cis*-**2** at −100 °C indicates that the conformational equilibrium is highly shifted toward the *cis*-$\mathbf{2}_{eq}'$ conformer in all of the solvents investigated. This conclusion agrees well with those drawn by other authors on the basis of IR and UV spectra and dipole moment measurements.[12]

The ^{1}H NMR chemical shifts of the different hydrogen atoms in SSO (**1**), *cis*-**2**, *trans*-**2**, and **5** depend on the solvent and the temperature. The chemical shifts under different conditions and the displacement of the signals on going from CD_2Cl_2 or THF-d_8 to toluene-d_8 at −100 °C and with a decrease in temperature from 25 to −100 °C are shown in Tables 3 and 4, respectively.

The most salient feature of the ASIS study is the strong deshielding observed for the $H^{4,6}$ hydrogens of **1** adjacent to the sulfinyl group on going from the polar solvents CD_2Cl_2 and THF-d_8 to toluene-d_8, in clear contrast to the consistent upfield shielding observed for all the signals of structurally related thianthrene (**5**) and its disulfoxides (**2**) (Table 3). A comparison of the spectra in CD_2Cl_2 and toluene-d_8 (Table 3) shows that the aromatic solvent shields the signals corresponding to **1**, *cis*-**2**, *trans*-**2**, and **5** to different degrees ranging between 80 and 670 Hz, except that of the $H^{4,6}$ of **1**, which is *deshielded* by −225 Hz. The same trend is observed on going from THF-d_8 to toluene-d_8 (Table 3). In this case, the signal of $H^{4,6}$ in **1** is *deshielded* by −130 Hz, while the rest of the signals are shielded by 115−765 Hz.

TABLE 3. Effect of the Solvent on the Proton Resonances of 1, *cis*-2, *trans*-2, and 5 at − 100 °C[a]

solvent	compd	$\Delta\nu H^1$	$\Delta\nu H^4$	$\Delta\nu H^2$	$\Delta\nu H^3$
CD_2Cl_2 to toluene-d_8	**1**	275	−225	315	335
	cis-**2**	80	80	590	590
	trans-**2**	55	670	625	630
	5	190	190	320	320
THF-d_8 to toluene-d_8	**1**	450	−130	455	480
	cis-**2**	120	120	665	665
	trans-**2**	115	765	700	715
	5	260	260	385	385

[a] $\Delta\nu H = [\nu H_{(solvent)} - \nu H_{(toluene)}]$ in Hz.

TABLE 4. Effect of Temperature on the Proton Resonances of 1, *cis*-2, *trans*-2, and 5[a]

solvent	compd	$\overline{\Delta\nu H^1}$	$\overline{\Delta\nu H^4}$	$\overline{\Delta\nu H^2}$	$\overline{\Delta\nu H^3}$
CD_2Cl_2	**1**	45	75	35	35
	cis-**2**	40	40	5	5
	trans-**2**	20	20	10	10
	5	15	15	5	5
toluene-d_8	**1**	60	−130	60	55
	cis-**2**	−15	−15	145	145
	trans-**2**	98	98	157	157
	5	40	40	75	75
THF-d_8	**1**	−90	0	−60	−70
	cis-**2**	−10	−10	−70	−70
	trans-**2**	−52	−52	−70	−70
	5	−65	−65	−65	−65

[a] $\overline{\Delta\nu H} = [\bar{\nu} H_{(25\ °C)} - \bar{\nu} H_{(-100\ °C)}]$ in Hz.

These results point out the existence of a superimposed deshielding factor that affects the hydrogen atoms *peri* to the sulfinyl group of **1**, which overwhelms the upfield shift due to the aromatic solvent. The ^{1}H NMR data on *trans*-**2** and *cis*-**2** and the known diamagnetic anisotropy of the sulfoxide group establish that the chemical shifts of the hydrogen atoms adjacent to a pseudoequatorial sulfinyl group appear at lower fields than those adjacent to a pseudoaxial sulfinyl group, and this difference is 675 Hz for *trans*-**2** in toluene-d_8 (Table 2). Therefore, the downfield displacement of the signal for $H^{4,6}$ of **1** from 7.72 and 7.91 ppm in CD_2Cl_2 and THF-d_8, respectively, to 8.17 ppm in toluene-d_8, despite the intense shielding effect of the aromatic solvent observed on the *peri* hydrogen atoms of *trans*-**2** and *cis*-**2**, can be attributed to an increased contribution of the conformer with the sulfoxide group in the pseudoequatorial position ($\mathbf{1}_{eq}'$) to the average signal of $H^{4,6}$ in toluene-d_8 ($\mu = 0.30$ D) with respect to that in the polar solvents CD_2Cl_2 ($\mu = 1.56$ D) and THF-d_8 ($\mu = 1.74$ D). Thus, the results suggest that the conformational equilibrium of **1** is shifted toward the conformer with the sulfoxide group in a pseudoaxial position ($\mathbf{1}_{ax}'$) in polar solvents and toward the conformer with a pseudoequatorial sulfoxide group ($\mathbf{1}_{eq}'$) in nonpolar solvents, according to the dipole moment of each conformer, which agrees well with the observed apparent dipole moment data. The hydrogen atoms $H^{2,8}$ of *trans*-**2**, in the *meta* position with respect to a pseudoequatorial sulfinyl group, also appear at higher chemical shifts than

(20) (a) Pritchard, J. G.; Lauterbur, P. C. *J. Am. Chem. Soc.* **1961**, *83*, 2105. (b) Tanaka, S.; Sugihara, Y.; Sakamoto, A.; Ishii, A.; Nakayama, J. *J. Am. Chem. Soc.* **2003**, *125*, 9024 and references therein.

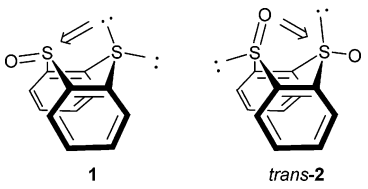


FIGURE 5. Transannular interactions.

those of $H^{3,7}$ in the *meta* position with respect to a pseudoaxial group. However, in this case, the difference between the chemical shifts in toluene-d_8 is only 55 Hz, and consequently the displacement of the conformational equilibrium of **1** toward the conformer $\mathbf{1}_{eq}'$ cannot overcome the shielding derived from the aromatic solvent.

The chemical shift of the $H^{4,6}$ hydrogen atoms of **1** in toluene-d_8 at −100 °C ($\delta H^{4,6}$ 8.17 ppm) is higher than those corresponding to the *peri* hydrogen atoms of *cis*-**2** ($\delta H^{4,6}$ 7.83 ppm) and $H^{1,9}$ of *trans*-**2** ($\delta H^{1,9}$ 8.03 ppm), which are adjacent to a sulfoxide group in a pseudoequatorial position. This observation suggests that thianthrene-5-oxide (**1**) with the sulfinyl group in a pseudoequatorial position is the preferred conformation in the nonpolar solvent toluene-d_8 but also indicates that there is some type of interaction between the functional groups of **1**. Thus, the stronger deshielding of the *peri* hydrogen atoms exerted by the sulfinyl group in **1** compared to that exerted by the pseudoequatorial sulfinyl group of *cis*-**2** and *trans*-**2** could be interpreted in terms of an electron donation from the sulfide group to the pseudoequatorial sulfoxide in **1**, which results in a higher electron population in the S−O bond and a stronger diamagnetic effect. This electron donation could be the result of the resonant electron-releasing effect of the sulfide group (in the *ortho* position with respect to the sulfoxide group) or alternatively could be due to through-space transannular interaction between both functional groups (Figure 5).

A topological analysis[11] of the electron density of **1** indicates the feasibility of this transannular interaction in $\mathbf{1}_{eq}'$, since the area of charge depletion of the sulfoxide group points toward the transannular electron density of the sulfide moiety. Conversely, the region of charge depletion of the flagpole sulfoxide group of $\mathbf{1}_{ax}'$ points inward to the free concave space of the folded molecule and is far from aligning with the electron density regions of the transannular sulfide group.

Concerning the interaction between the functional groups in these systems, the data in Table 2 also show that, for all of the solvents and at −100 °C, the hydrogen atoms $H^{1,9}$ of *cis*-**2** appear at higher fields than those of *trans*-**2** even though they are adjacent to a pseudoequatorial sulfinyl group in both isomers. These results indicate that in *trans*-**2**, the pseudoaxial sulfinyl group boosts the diamagnetic anisotropic effect of the transannular pseudoequatorial sulfinyl group with respect to that in *cis*-**2**, where both oxygen atoms are in a pseudoequatorial position. This effect is analogous to that mentioned above for **1** and could be attributed to a through-space transannular electron donation from the pseudoaxial oxygen atom to the opposite electron-deficient sulfinyl group (Figure 5). The increase in electron density at the pseudoequatorial sulfinyl group would enhance its diamagnetic effect. Interaction between the functional groups of the thianthrene derivatives **1** and *trans*-**2** has also been proposed[2a] on the basis of the lower energy requirement for the UV excitation of the flagpole sulfinyl group of *trans*-**2** and $\mathbf{1}_{ax}'$ and also of the relative rate of oxidation[2a] of **1**, *cis*-**2**, *trans*-**2**, and **5** with the oxo-diperoxomolybdenum complex MoO_5·HMPT, which was found to depend on the relative orientation of the sulfinyl groups.

On the other hand, the data in Table 2 show that in the polar solvents CD_2Cl_2 and THF-d_8, the chemical shifts of the $H^{4,6}$ hydrogen atoms of **1** ($\delta H^{4,6}$ 7.72 ppm in CD_2Cl_2 and $\delta H^{4,6}$ 7.91 ppm in THF-d_8) are lower than those found for the $H^{4,6}$ hydrogen atoms *peri* to the pseudoaxial sulfinyl group of *trans*-**2** ($\delta H^{4,6}$ 8.02 ppm in CD_2Cl_2 and $\delta H^{4,6}$ 8.21 ppm in THF-d_8). This difference is consistent with the lack of a second electron-withdrawing sulfoxide group in **1**; however, it may also indicate that the conformation with the sulfinyl group in a pseudoaxial position comprises a significant population in these polar solvents since the deshielding exerted by a pseudoequatorial sulfoxide group is more intense in **1** than in disulfoxides **2**, as seen above.

The data in Table 3 show that the lowest shielding effect of the aromatic solvent corresponds to the hydrogens *peri* to a sulfinyl group in a pseudoequatorial position, while the highest shielding corresponds to the hydrogen *peri* to a sulfinyl group in a pseudoaxial position. Thus, the data show upfield shifts of 80 and 55 Hz upon moving from CD_2Cl_2 to toluene-d_8 for *cis*-**2** and the $H^{1,9}$ hydrogen atoms of *trans*-**2**, respectively, and upfield shifts of 120 and 115 Hz upon moving from THF-d_8 to toluene-d_8 for *cis*-**2** and the $H^{1,9}$ hydrogen atoms of *trans*-**2**. The upfield shifts for the $H^{4,6}$ hydrogen atoms of *trans*-**2** are 670 and 765 Hz upon moving from CD_2Cl_2 and THF-d_8 to toluene-d_8, respectively.

These results contrast with the aromatic solvent-induced shifts (ASISs) reported[19b] for a series of 9-alkyl derivatives of thioxanthene-S-oxide. In these substrates, the change from $DCCl_3$ to C_6D_6 induces an upfield shift of the *peri* protons of substrates with a pseudoaxial sulfoxide group but a downfield shift for *peri* protons of systems with a pseudoequatorial sulfoxide group. Although these data were obtained[19b] on conformationally flexible systems, the conclusions were drawn without considering that the polarity of the solvent could modify the relative position of the conformational equilibrium of the solute and thus contribute to the displacement of the chemical shifts. The conformational equilibria in our model systems *trans*-**2** and **5** are degenerate, and consequently the present results regarding the ASIS effect should not be contaminated by any superimposed shift arising from its displacement. The same applies for the model system *cis*-**2**, since in this case the conformational equilibrium is strongly shifted toward the conformer *cis*-$\mathbf{2}_{eq}'$ in all of the solvents.

Finally, the data show that the shielding effect of the aromatic solvent toluene-d_8 at −100 °C on the signals corresponding to the $H^{2,8}$ and $H^{3,7}$ hydrogen atoms is stronger for the disulfoxides (**2**) than for thianthrene (**5**) and thianthrene-5-oxide (**1**). This could be related to the increased electron acceptor ability of the aromatic rings in the more oxidized derivatives, which favors the charge-transfer interactions with the aromatic solvent.

The effects of the temperature on the chemical shifts of **1**, *cis*-**2**, *trans*-**2**, and **5** in different solvents are shown

in Table 4. The ^{1}H NMR data in CD_2Cl_2 at 25 °C and −100 °C show a consistent upfield shift for all of the hydrogen atoms of the model compounds. The hydrogen atoms *peri* to the sulfinyl group shift upfield 40 Hz in *cis*-**2** ($\overline{\Delta\nu H}^{4,6}_{(25\text{ to }-100\text{ °C})}$ = 40 Hz and 20 Hz in *trans*-**2** ($\overline{\Delta\nu H}^{4,6}_{(25\text{ to }-100\text{ °C})}$ = 20 Hz), indicating that the shielding effects derived from changes in the solvent with a decrease in the temperature are more intense for hydrogen atoms adjacent to a pseudoequatorial sulfinyl group than for those adjacent to a pseudoaxial sulfinyl group. However, the data for **1** show upfield shifts for all of the signals that are significantly more intense than those found for the model compounds; the highest value corresponds to the $\overline{H}^{4,6}$ hydrogen atoms in **1** and is shifted upfield 75 Hz ($\overline{\Delta\nu H}^{4,6}_{(25\text{ to }-100\text{ °C})}$ = 75 Hz). Since the upfield shifts of the signals observed for the model compounds **2** and **5** with a decrease of the temperature do not account for the displacements observed in **1**, there must be another factor that further shields the averaged ^{1}H NMR signals of **1**. The ^{1}H NMR data for *trans*-**2** in CD_2Cl_2 (Table 2) indicate that the hydrogen atoms *peri* and *meta* to a pseudoaxial sulfinyl group are more shielded than those corresponding to a pseudoequatorial sulfinyl group ($\delta H^{1,9} - \delta H^{4,6}$ = 0.12 ppm, $\delta H^{2,8} - \delta H^{3,7}$ = 0.10 ppm). Therefore, the effect of the temperature on the chemical shifts of **1** can be interpreted as the sum of the shielding effects derived from changes in the solvation and anisotropy of the solvent and the displacement of the conformational equilibrium of **1** toward the conformer with the sulfoxide group in a pseudoaxial position (**1**$'_{ax}$) with a decrease in temperature.

The same trend is observed in THF-d_8. In this case, a decrease in temperature promotes a consistent downfield shift for all of the signals of compounds **1**, *cis*-**2**, *trans*-**2**, and **5** *except* for those of the $H^{4,6}$ hydrogen atoms of thianthrene-5-oxide (**1**), which are not affected by the change in temperature. In this case, the deshielding effect due to the solvent at low temperature is balanced by the shielding effect resulting from displacement of the conformational equilibrium of **1** toward the conformer with the sulfoxide group in a pseudoaxial position (**1**$'_{ax}$) with a decrease in temperature. In THF-d_8, the differences between the chemical shifts corresponding to the hydrogen atoms *peri* and *meta* to pseudoaxial and pseudoequatorial sulfinyl groups ($\bar{\nu}H^{1,9} - \bar{\nu}H^{4,6}$ = 0,05 ppm, $\bar{\nu}H^{2,8} - \bar{\nu}H^{3,7}$ = 0.07 ppm) are not as intense as those in CD_2Cl_2.

The data for toluene-d_8 indicates an opposite trend, consistent with the nonpolar nature of this solvent. Thus, on going from 25 to −100 °C, the signals corresponding to the hydrogen atoms *peri* to the sulfinyl groups of *cis*-**2** and **1** shift downfield −15 and −130 Hz, respectively, while the rest of the signals shift upfield 40−158 Hz. The 98 Hz upfield shift of the $H^{4,6}$ and $H^{1,9}$ hydrogen atoms of *trans*-**2** corresponds to the averaged contributions of the pseudoequatorial and pseudoaxial sulfinyl groups. Considering that the hydrogen atoms *peri* to the pseudoequatorial sulfinyl group of *cis*-**2** shift downfield −15 Hz, we can estimate that the hydrogen atoms *peri* to the pseudoaxial sulfinyl group in *trans*-**2** contribute an upfield shift of ca. 200 Hz to this average. The higher value of the downfield shift of the $H^{4,6}$ hydrogen atoms in **1** (−130 Hz) with respect to that of *cis*-**2** (−15 Hz) indicates that some additional deshielding factor contributes to the observed displacement of the signal. The difference in chemical shifts between the hydrogen atoms *peri* to pseudoequatorial and pseudoaxial sulfinyl groups, where the former is more deshielded than the latter, indicates displacement of the conformational equilibrium of **1** toward the conformation with a pseudoequatorial sulfinyl group (**1**$'_{eq}$) with a decrease in temperature.

In contrast, Purcell and Berschied proposed[12e] that *cis*-**2** is a mixture of two equilibrating conformers in a solution of 1,1,2,2-tetrachloroethane and chloroform on the basis of the temperature independence of the difference $\delta H^{peri} - \delta H^{meta}$ for the proton resonances of **5** and *trans*-**2** from −20 to 160 °C. However, in our study, from 25 to −100 °C the values of $\nu H^{peri} - \nu H^{meta}$ in CD_2Cl_2, toluene-d_8, and THF-d_8 change by 10, −35, and 0 Hz and by 5, −370, and 25 Hz for **5** and *trans*-**2**, respectively (Table 2). The shifts of the signals observed may be attributed to changes in the solvation and anisotropy of the solvent with a decrease in temperature.

The effect of the temperature on the relative position of conformational equilibrium is related to the change in entropy, where lower temperatures favor a more ordered system. The change in entropy of the conformational equilibrium is related to the organization of the solvent molecules in the solvation sphere induced by each conformer.[21] The conformer with the higher dipole moment would exert a stronger effect on the dipolar solvent molecules than the conformer with a lower dipole moment. Accordingly, the conformer of **1** with a pseudoaxial sulfinyl group (**1**$'_{ax}$) would be better solvated (more ordered) in polar solvents than its pseudoequatorial analogue, the change in entropy of the equilibrium would be negative (Figure 1), and a decrease in temperature would displace the equilibrium to the right side (Figure 1). Conversely, the less polar conformer would interact better with the molecules of nonpolar solvents than the conformer with a higher dipole moment. In this case, the conformer of **1** with a pseudoequatorial sulfinyl group (**1**$'_{eq}$) would be better solvated (more ordered) in the nonpolar aromatic solvent than the pseudoaxial conformer, the change in entropy of the equilibrium would be positive, and a decrease in temperature would shift the conformational equilibrium to the left side (Figure 1). These considerations are consistent with the experimental results, which support a shift of the conformational equilibrium toward the conformer that is better solvated in each solvent.

Conclusion

The data on the apparent dipole moment of **1** in different solvents and the ^{1}H NMR spectra of **1** and model compounds *cis*-**2**, *trans*-**2**, and **5** under different conditions of solvent and temperature support the rapid conformational equilibrium of **1**, which flaps between two limit boat conformations with the sulfoxide group in a pseudoaxial or pseudoequatorial position, respectively (Figure 1). The conformational equilibrium of **1** occurs too fast for the ^{1}H NMR time-scale even at −130 °C; however, the experimental data support the notion that

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the relative populations of the conformers depend on the solvent and the more polar conformer $\mathbf{1}'_{ax}$ is favored by more polar solvents. Furthermore, ^{1}H NMR data have revealed transannular interaction between the functional groups of **1** and *trans*-**2**. Any application of thianthrene-5-oxide (**1**) as a mechanistic probe should not disregard these distinctive features of this molecule to avoid misleading interpretations.

Experimental Section

General. Solvents and reagents were purified by standard procedures.[22] Thianthrene-5-oxide (**1**) was prepared by the oxidation of thianthrene (**5**) with *meta*-chloroperbenzoic acid.[2a] *trans*-Thianthrene-5,10-dioxide (*trans*-**2**) and *cis*-thianthrene-5,10-dioxide (*cis*-**2**) were prepared following reported procedures.[2a]

n-Hexane (Scharlau) and 1,4-dioxane (Merck), which were used for measurements of dielectric permittivity, density, and refractive index, were purified by two rounds of fractional distillation. The solvents were dried over sodium wire before use. The measured densities, refractive indices, and dielectric constants at 25.0 °C for *n*-hexane and 1,4-dioxane were 0.6551 ± 0.0004 and 1.0285 ± 0.0005 g cm^{-3}, 1.3722 ± 0.0005 and 1.4201 ± 0.0007, and 1.8518 ± 0.0006 and 2.2087 ± 0.0006, respectively. Dielectric constants were measured in a W. T. W. Model DM 01 dipolometer (frequency 2 MHz) using a thermostated DFL1 precalibrated cell. Refractive indices were measured for the D_{II} sodium line (5896 Å) on a Pulfrich-type refractometer from Bellingham and Stanley. A rapid flow of water was conducted through the heating block supporting the prism to maintain the temperature to within ±0.05 °C. The solution was preheated before the measurements were performed. The densities were determined using a pycnometer with a graduated neck that was previously calibrated with highly pure water.

^{1}H NMR experiments were performed on two spectrometers working at proton frequencies of 300.13 and 500.13 MHz. Two 5 mm probe heads were used, a QNPZ probe (^{1}H, ^{13}C, ^{15}N, ^{31}P) and a direct triple probe ^{1}H/^{31}P, BB (^{31}P − ^{109}Ag) for the 300.13 and 500.13 MHz instruments, respectively. Pulse widths for the 90° pulses were 8.8 (−2 dB)/300.13 MHz and 9.2 (−4 dB)/500.13 MHz. The figures in brackets correspond to the attenuation levels applied. Tetramethylsilane was used as an internal standard for reference purposes. Temperature calibration was achieved through the method of van Geet.[23]

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Supporting Information Available: ^{1}H NMR data (500.13 MHz) and variable-temperature spectra for compounds **1**, *cis*-**2**, *trans*-**2**, and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

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