complexation has a dramatic impact on the kinetics of the epimerization, as the pseudopotential barriers either reduce substantially (e.g., CN) or even vanish, and instead results in a potential sink for the enol intermediate (e.g., CHO and $COCH_3$; see Figure 2). Interestingly, the BH_3 complexation of all cycloadducts are similar and amount to a stabilization of 17–20 kcal/mol (average 17.8 kcal/mol). However, while the stabilizations of all enol intermediates are also similar to each other, the magnitude of stabilization is twice that of the keto cycloadducts, i.e., 35–39 kcal/mol (average 36.9 kcal/mol). It is relevant to note that the exothermicities for epimerizations are hardly effected by BH_3 complexation; the corresponding energy differences are 1.3 → 1.0 kcal/mol for CHO, 3.4 → 3.4 kcal/mol for $COCH_3$, 3.4 → 9.6 kcal/mol for $COOCH_3$, and 1.7 → 1.4 kcal/mol for CN substituted cycloadducts. Consequently, the major influence of Lewis acid catalysis in epimerizations can be generalized as a substantial relative stabilization (16–20 kcal/mol) of the enol intermediates, thereby increasing the epimerization rate.

Acceleration of Diels–Alder reactions on the surface of silica gel and aluminum oxide has been known for some time.[39] In fact, Veselovsky et al. have reported a dramatic acceleration of the Diels–Alder reaction by adsorption on chromatographic adsorbents.[40] Recently, isomerization of (*Z*)-vinylsilanes into the *E* isomer has been described by using silica gel as an additive.[41] Experimentally, we have observed epimerization of some of the Diels–Alder cycloadducts when they were subjected to gas and column chromatography.[18b] Our theoretical calculations indicate that the effect of Lewis acids such as chromatographic adsorbents are limited not only to the cycloaddition reactions but also to the distribution of the reaction products during analysis. Since some of the cycloadducts epimerize rapidly at room temperature, inadvertent alteration of the product distribution of a Diels–Alder reaction by GC and column chromatography, which are routinely used for separation and identification purposes, is possible.

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Registry No. 1, 873-30-3; 2, 766-48-3; 3, 123883-56-7; 4, 123883-57-8; 5, 55169-92-1; 6, 55169-93-2; 7, 123883-58-9; 8, 123883-59-0; 9, 22973-22-4; 10, 7605-51-8; 11, 123883-60-3; 12, 123883-61-4; 13, 57278-90-7; 14, 57278-89-4; 15, 123883-62-5; BH_3, 13283-31-3.

Supplementary Material Available: GAUSSIAN-86 archive entries for the cycloadducts and intermediates (1–15) fully optimized with HF/STO-3G basis set (6 pages). Ordering information is given on any current masthead page.

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Conformational Analysis of 5-Substituted 1,3-Dioxanes. 2. Phenylthio and Cyclohexylthio Groups and Their Sulfinyl and Sulfonyl Derivatives[1]

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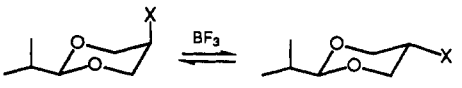
The positions of equilibrium, established by acid catalysis, between diastereomeric *cis*- and *trans*-5-(phenylthio)- (**7**), 5-(phenylsulfinyl)- (**8**), 5-(phenylsulfonyl)- (**9**), 5-(cyclohexylthio)- (**10**), 5-(cyclohexylsulfinyl)- (**11**), and 5-(cyclohexylsulfonyl)-2-*tert*-butyl-1,3-dioxanes (**12**) are reported and compared with published data for the 5-(methylthio)- (**1**), 5-(methylsulfinyl)- (**2**), 5-(methylsulfonyl)- (**3**), 5-(*tert*-butylthio)- (**4**), 5-(*tert*-butylsulfinyl)- (**5**), and 5-(*tert*-butylsulfonyl)-2-isopropyl-1,3-dioxanes (**6**). Although $\Delta G°$ values for sulfides **1**, **4**, and **7** are very similar, there exist significant differences in the conformational behavior of the sulfoxides and the sulfones, which result from the relative steric, electrostatic, and torsional effects arising from each substituent. The information at hand (^1H and ^{13}C NMR spectroscopic data, X-ray crystallographic analysis, etc.) shows that, while sulfone *cis*-**6** has the *S*-*tert*-butyl group outside the ring, with both sulfonyl oxygens above the dioxane ring and eclipsing the endocyclic C–C bonds, the alkyl and aryl substituents in *cis*-**3**, *cis*-**9**, and *cis*-**12** point inside the ring. The phenylsulfonyl-inside rotamer in *cis*-**9** leads to steric and electron/electron repulsion that overcomes the electrostatic attractive interactions between the (negative) endocyclic oxygens and the (positive) sulfur in the sulfonyl group, so that equatorial *trans*-**9** predominates at equilibrium, $\Delta G° = -0.44$ kcal/mol. All sulfoxides place both the sulfinyl oxygen and the substituent outside the dioxane ring.

Introduction

Several years ago, Eliel and co-workers[3] described the conformational equilibria of a large number of 2-isopropyl-5-X-1,3-dioxanes (eq 1).



(1)

Of particular interest was the conformational behavior of the sulfur-containing substituents: while the methylthio group shows a large preference for the equatorial orientation, the methylsulfinyl and the methylsulfonyl derivatives are predominantly axial at equilibrium.

Substitution of a *tert*-butylthio for the methylthio group had no significant effect on the $\Delta G°$ value,[1] whereas the

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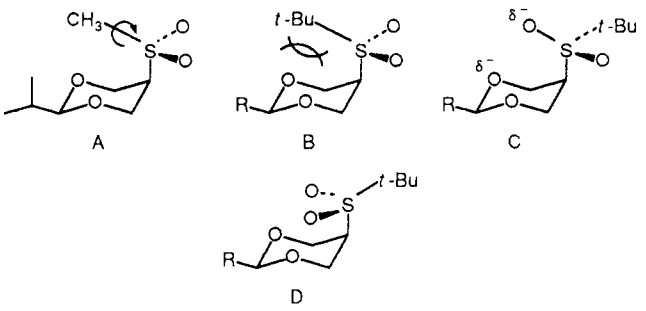
(2) (a) Instituto Politécnico Nacional. (b) University of Arizona.

(3) Kaloustian, M. K.; Dennis, N.; Mager, S.; Evans, S. A.; Alcudia, F.; Eliel, E. L. *J. Am. Chem. Soc.* **1976**, *98*, 956–965.

0022-3263/90/1955-0033$02.50/0

Scheme I



axial preference found in 5-(methylsulfinyl)-1,3-dioxane essentially vanishes in the *tert*-butyl analogue: +0.82 kcal/mol vs +0.10 kcal/mol, respectively, and the most dramatic effect was encountered in the sulfones, where the large preference of the methyl analogue for the axial isomer ($\Delta G°$ = +1.19 kcal/mol) is reversed in the *tert*-butyl derivative **6**, in which the equatorial isomer is more stable ($\Delta G°$ = −1.14 kcal/mol).[1]

Since Eliel and Evans had discovered that 2-isopropyl-5-(methylsulfonyl)-1,3-dioxane (**3**) exists with the methyl group pointing into the ring (structure A, Scheme I),[4] the large $\Delta\Delta G°$ = 2.33 kcal/mol observed between the sulfones **6** and **3** was initially considered to arise from the steric hindrance caused by a *tert*-butyl group still inside the ring (structure B, Scheme I) or by unfavorable electrostatic interactions in conformation C (Scheme I), in which the *tert*-butyl group has turned outward, placing the (negative) ring oxygens close to the (negative) sulfonyl oxygen. However, X-ray crystallographic data showed that structure D (Scheme I) corresponds to the rotamer of minimum energy, at least in the solid state.[1]

This result was rather surprising because chemical intuition might have favored rotamer C, with staggered rather than *eclipsed* S–O/C–C and C–*t*-Bu/C–H bonds. It became of interest then to determine the conformational behavior exhibited by analogous systems, in which groups intermediate in size to methyl and *tert*-butyl have been incorporated. This report describes the conformational study of the 5-phenylthio and 5-cyclohexylthio system, both from the configurational and rotameric points of view.

Results and Discussion

Conformational Analysis. The equilibration of diastereomeric (cis ⇌ trans) dioxanes is readily accomplished by means of BF_3,[5] and the diastereomer ratio (K) was determined by VPC or integration of appropriate signals in the ^{1}H NMR spectra. The free energy difference ($\Delta G° = -RT \ln K$) for *cis*- and *trans*-2-*tert*-butyl-5-phenylthio- and 2-*tert*-butyl-5-cyclohexylthio-1,3-dioxane and their corresponding sulfoxide and sulfone derivatives are summarized in Table I, which includes, for comparison purposes, those for the methyl and *tert*-butyl analogues.

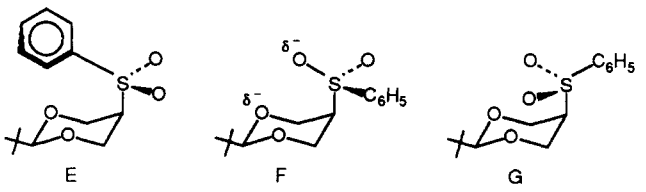
The $\Delta G°$ value for sulfide **7** (X = SC_6H_5) is identical, within the error limits, with those for **1** (X = SCH_3) and **4** (X = S-*t*-Bu); the equilibration *cis*-**10** ⇌ *trans*-**10** could not be achieved because of extensive decomposition, but it is not expected to vary significantly from those in **1**, **4**, and **7**. It seems reasonable that all alkyl and aryl groups point outside the ring, causing similar steric interactions. The finding that $\Delta G°$ for these sulfides is significantly more negative for the dioxanes than for corresponding substituted cyclohexanes provides evidence for a repulsive gauche effect[6] between the endocyclic oxygens and sulfur.

Table I. Conformational Equilibria in 5-Substituted 1,3-Dioxanes (Eq 1)[a]

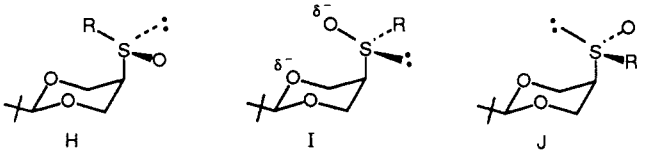
compd	X	$\Delta G°$,[b] kcal/mol	solvt	temp, °C
1	SCH_3[c]	−1.82 ± 0.01	c-C_6H_{12}	26.5
2	$SOCH_3$[c]	+0.82 ± 0.11	$CHCl_3$	54.0
3	SO_2CH_3[c]	+1.19 ± 0.10	$CHCl_3$	50.0
4	S-*t*-Bu[d]	−1.90 ± 0.11	$CHCl_3$	23.0
5	SO-*t*-Bu[d]	+0.10 ± 0.01	$CHCl_3$	23.0
6	SO_2-*t*-Bu[d]	−1.14 ± 0.01	$CHCl_3$	23.0
7	SC_6H_5[e]	−1.93 ± 0.26	$CHCl_3$	25.0
8	SOC_6H_5[e]	+1.59 ± 0.16	$CHCl_3$	25.0
9	$SO_2C_6H_5$[e]	−0.44 ± 0.01	$CHCl_3$	25.0
10	S-c-C_6H_{11}[e]	*f*		
11	SO-c-C_6H_{11}[e]	+0.81 ± 0.05	$CHCl_3$	25.0
12	SO_2-c-C_6H_{11}[e]	0.0 ± 0.01	$CHCl_3$	25.0

[a] In compounds **7**–**12**, *tert*-butyl instead of isopropyl group at C(2). [b] Positive $\Delta G°$ values indicate axial preference. [c] Reference 3. [d] Reference 1. [e] This work. [f] Unreliable measurement due to extensive decomposition.

Scheme II



Scheme III



On purely steric grounds, one would expect a larger equatorial preference ($-\Delta G°$) for the corresponding sulfoxide **8** and still larger for sulfone **9**; this is, in fact, the case in the (methylthio)-, (methylsulfinyl)-, and (methylsulfonyl)cyclohexane series where polar effects are absent.[7] It is found, however, that equilibrium *cis*-**8** ⇌ *trans*-**8** strongly favors the axial isomer ($\Delta G°$ = +1.59 kcal/mol), more so than in **5** (+0.82 kcal/mol). The stabilizing effect operative in *cis*-**8** can be rationalized in terms of an electrostatic attraction between the endocyclic oxygens (partial negative charge) and the partially positive sulfinyl sulfur,[3,4] the more electron-withdrawing phenyl group[8] leading to a stronger attractive interaction in axial **8** relative to axial **2** ($\Delta G°$ = +0.82 kcal/mol) owing to the increased positive charge at sulfur in the former.

The conformational equilibria of sulfoxides **2** (X = $SOCH_3$) and **11** (X = SO-c-C_6H_{11}) are very similar: $\Delta G°$ = +0.82 and +0.81 kcal/mol, respectively. This result argues against the predominance of rotamers H (Scheme III) since the different steric requirements of methyl and cyclohexyl would give rise to a significant difference in $\Delta G°$. The observed axial preference also does not fit with

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(7) (a) Jensen, F. R.; Bushweller, C. M.; Beck, B. H. *J. Am. Chem. Soc.* **1969**, *91*, 344–351. (b) Eliel, E. L.; Kandasamy, D. *J. Org. Chem.* **1976**, *41*, 3899–3904.
(8) See, for example: Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper & Row: New York, 1981; pp 271–272.

Table II. 250-MHz ^{1}H NMR Chemical Shifts (ppm) for *cis*- and *trans*-7–12 at Ambient Temperature in $CDCl_3$[a]

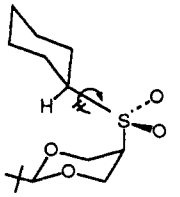
proton	*cis*-7	*trans*-7	*cis*-8	*trans*-8	*cis*-9	*trans*-9	*trans*-10	*cis*-11	*trans*-11	*cis*-12	*trans*-12
H(2)	4.17	4.04	4.22	4.04	3.91	4.01	4.04	4.20	4.10	4.09	4.08
H(4ax)	4.07	3.52	4.08	3.96	4.09	3.92	3.42	4.04	4.09	4.11	4.00
H(4eq)	4.19	4.24	4.86[b]	4.25	4.80	4.28	4.18	4.64[b]	4.36	4.66	4.38
H(5)	3.10	3.39	2.49	3.03	2.92	3.50	2.99	2.66	3.09	2.66	3.54
H(6ax)	4.07	3.52	3.89	3.96	4.09	3.92	3.42	4.13	3.98	4.11	4.00
H(6eq)	4.19	4.24	3.76	3.96	4.80	4.28	4.18	4.13	4.21	4.66	4.38
t-Bu	0.96	0.88	0.94	0.86	0.49	0.86	0.89	0.91	0.90	0.92	0.90
H(1′)							2.69	2.65	2.65	3.37	2.76

[a] *cis*-10 was not available in pure state. [b] Syn to S=O bond.

conformation I (Scheme III) in view of the $O^{\delta-}/O^{\delta-}$ repulsive interaction involved here. The most stable rotamer must therefore be structure J, in which both the S–O bond and the alkyl groups are outside the ring. This argument will be discussed further below.

As for sulfone **9**, its equatorial predominance ($\Delta G°$ = –0.44 kcal/mol) reflects nevertheless an attractive interaction operative in **9**-axial, since it is less negative than $\Delta G°$ in **7** ($\Delta G°$ = –1.93 kcal/mol) despite the increase in steric bulk. Two explanations suggested themselves to account for the contrasting behavior of **9** and **3** (–0.44 and +1.19 kcal/mol, respectively): (1) An axial sulfonyl group with the phenyl ligand inside the ring (structure E, Scheme II) would lead to significant electron/electron repulsion between the oxygen lone pairs and the π electrons on the aromatic ring, causing the axial isomer to be destabilized. (2) The conformations with the phenyl group turned outward (structures F or G, Scheme II) place the (negative) ring oxygens close to the (negative) sulfonyl oxygen(s), leading again to an unfavorable electrostatic interaction. We consider that rotamer G does not contribute significantly because it could be expected that it would give rise to the same repulsive electrostatic interactions encountered in the *tert*-butylsulfonyl analogue **6** ($\Delta G°$ = –1.14 kcal/mol[1]), the observed $\Delta G°$ = –0.44 kcal/mol being substantially smaller.

Sulfone **12** does not show a preference for either the axial or the equatorial form; $\Delta G° \simeq 0$. This behavior is intermediate to those exhibited by methyl sulfone **3** ($\Delta G°$ = +1.19 kcal/mol) and *tert*-butyl sulfone **6** ($\Delta G°$ = –1.14 kcal/mol). A predominance of an eclipsed rotamer analogous to G (Scheme II) is not likely for *cis*-**12** since the repulsive electrostatic interaction among (negative) oxygens would then be about as significant as in *cis*-**6**. A distinction between the cyclohexyl analogues of E and F (Scheme II) will be based on ^{1}H and ^{13}C NMR spectroscopic evidence (next section). Nevertheless, it is interesting that $\Delta\Delta G°$ for **3** and **12** is ca. 1.2 kcal/mol, which could arise, at least in part, from an entropic effect in structure E: whereas the *S*-methyl group in *cis*-**3** seems capable of rotation in structure A (Scheme I), inspection of Dreiding models indicates that rotation in the cyclohexyl analogue is restricted, owing to the steric bulk of the two rings in the molecule.[9]



K

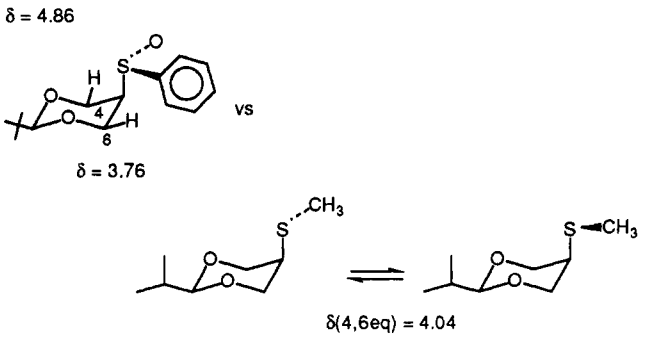
(9) Free rotation around the S–c-C_6H_{11} bond seems likely in equatorial *trans*-**12**, but perhaps only one rotamer (structure K, see text) is possible in *cis*-**12**.

It should be noted that the discussion presented above for the conformational behavior of **7–12** refers to 5-substituted 1,3-dioxanes in which the anchoring group is a *tert*-butyl group, whereas the analogous **1–6** contain an isopropyl group instead. For the present work we chose the 2-*tert*-butyl substituent because it was anticipated that these derivatives could provide crystalline materials, in case X-ray diffraction analysis would prove to be required. In addition, ^{1}H NMR spectra are somewhat simpler with a *tert*-butyl group relative to an isopropyl group. Of course, both the isopropyl and *tert*-butyl groups at C(2) in 1,3-dioxanes are quite effective as conformational anchoring groups.[5]

Because comparison of the NMR data for the 2-*tert*-butyl substituted **4–6** and their 2-isopropyl analogues are practically identical,[1] we do not expect significant differences in the conformational behavior of **7–12** relative to the corresponding 2-isopropyl derivatives. Nevertheless, as one referee has pointed out, a rigorous comparison of the conformational equilibria in both series would be pertinent.

Rotamer Population in Sulfoxides 8 and 11 and in Sulfones 9 and 12. ^{1}H and ^{13}C NMR Spectra. Table II lists the chemical shifts observed for the hydrogen atoms in sulfides **7** and **10**, sulfoxides **8** and **11**, and sulfones **9** and **12**, in $CDCl_3$ at 250 MHz and ambient temperature.

The very large chemical shift difference between H(4eq) and H(6eq), 1.10 ppm, supports rotamer J (Scheme III)



for sulfoxide *cis*-**8** in view of the known downfield proton shift induced by a *syn*-S=O group to H(4eq),[10] working in combination with an induced shielding effect by the aromatic ring on the proton over its plane, H(6eq).[11] Taking the δ(4,6eq) = 4.04 ppm in *cis*-2-isopropyl-5-(methylthio)-1,3-dioxane[3] as reference, it seems that H-(4eq) gets deshielded by ca. 0.8 ppm, while H(6eq) is shielded by ca. 0.3 ppm.

A sizeable $\Delta\delta$(4eq/6eq) is also observed in the corresponding cyclohexyl sulfoxide **11**, 0.51 ppm (Table II); this spectroscopic behavior is quite similar to that observed in

(10) Johnson, C. R.; Siegl, W. O. *J. Am. Chem. Soc.* **1969**, *91*, 2796–2797, and references therein.

(11) See, for example: Becker, E. D. *High Resolution NMR*, 2nd ed.; Academic Press: New York, 1980; pp 73–74.

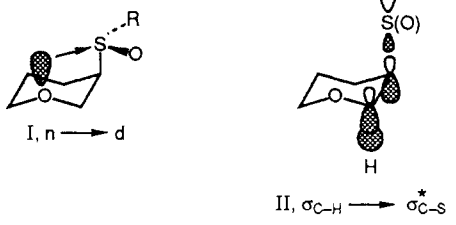
Table III. ^{13}C NMR Data (ppm) for *cis*- and *trans*-7–12 at Ambient Termperature in $CDCl_3$[c]

C	*cis*-7	*trans*-7	*cis*-8	*trans*-8	*cis*-9	*trans*-9	*trans*-10	*cis*-11	*trans*-11	*cis*-12	*trans*-12
C(2)	108.09	107.57	108.26	107.48	108.39	107.74	107.38	108.00	107.70	108.57	107.79
C(4)	70.08	70.90	64.06[a]	63.84[b]	64.92	65.10	71.76	64.06[b]	64.36[a]	64.97	65.05
C(5)	44.81	41.09	65.27[a]	55.60	60.63	57.34	37.13	53.48	48.19	59.98	51.31
C(6)	70.08	70.90	64.49[a]	65.83	64.92	65.10	71.76	64.83	66.35[a]	64.97	65.05
$C(CH_3)_3$	35.06	34.72	35.19	34.72	34.54	34.76	34.61	35.11	34.85	34.98	34.80
$C(CH_3)_3$	24.57	24.70	24.44	24.54	24.05	24.53	24.69	24.44	24.66	24.62	24.62
C(1′)							43.46	55.47	56.56	61.11	61.07
C(ipso)	135.78	*d*	142.98	140.38	139.42	137.65					
C(ortho)	131.62	132.45	125.47	124.04	128.98	128.33					
C(meta)	128.98	129.02	129.28	129.33	129.85	129.50					
C(para)	126.90	127.60	131.71	131.36	133.57	134.31					

[a] These values may be interchanged. [b] Carbon syn to S=O bond. [c] *cis*-10 was not available in pure form. [d] Not observed; possibly overlapped with C(ortho) at 132.45 ppm.

cis-5 ($\Delta\delta$(4eq/6eq) = 0.60 ppm), for which rotamer J (Scheme III) has been deduced.[1] Structures H and I seem to be significantly higher in energy relative to J, since the proton NMR spectra of *cis*-11 [particularly $\Delta\delta$(4eq/6eq)] did not vary in the temperature range −80 to +33 °C, suggesting that the rotamer population is not significantly altered by the large change in temperature.

The ^{13}C NMR data for sulfoxide *cis*-8 are presented in Table III. An interesting observation is the following: C(ortho) and C(para) are slightly *downfield* in the (axial) cis isomer relative to *trans*-8. An opposite trend is observed for the axial and equatorial 2-(diphenylphosphinoyl)-1,3-dithianes, in which an electron-transfer interaction from sulfur to phosphorus (3p → 3d) was proposed in the axial isomer.[12,13] The lack of any upfield shifts in the aromatic carbons, C(ortho,para), for the axial sulfoxide *cis*-8, which would suggest electronic enrichment at the adjacent sulfur, may argue against a $n_O \rightarrow d_S$ stabilizing orbital interaction (I) in gauche $OCH_2CH_2S(O)$ segments[14] or a $\sigma_{C-H} \rightarrow \sigma^*_{C-S(O)}$ stereoelectronic stabilizing factor (II) in axial 8.[15]



Seen in this light, the argument based on the electrostatic attraction between the electron-deficient sulfur in the sulfinyl group and the endocyclic oxygens, as proposed by Eliel and co-workers,[3,6] may best account for the stability of axial 8.

Two spectroscopic observations from the ^1H NMR spectra of *cis*-9 and *cis*-12 demonstrate that the aryl and alkyl substituents on the axial sulfonyl groups are oriented *above* the 1,3-dioxane ring. Indeed, the *tert*-butyl signal in *cis*-9 appears at 0.49 ppm, significantly more upfield than any of the *tert*-butyl groups ($\delta \sim$ 0.9–1.0 ppm) in all the other compounds (*cis*- or *trans*-7–12; Table II). This is a strong argument in support of structure E (Scheme II), where the phenyl group has an induced shielding effect on the *tert*-butyl group at C(2).[11]

On the other hand, whereas the methine proton on the cyclohexyl group, H(1′), in sulfone *trans*-12 appears at δ 2.76 ppm, the cis isomer shows that proton at δ 3.37 ppm. This sizeable deshielding effect is not observed in the axial sulfoxide, *cis*-11, where the cyclohexane ring is outside the dioxane ring and is only likely in structure K (see above). In this respect, it is of interest to note that this apparent downfield shift provoked by the endocyclic oxygens ($\Delta\delta$ = 0.61 ppm) is ca. 3 times stronger than the one observed in *cis*-3 ($\Delta\delta$ = 0.22 ppm),[3,16] where the methyl group is also above the dioxane ring but where each of the protons spends only one-third of the time in the deshielding region; by contrast, rotation around the S–C(1′) bond is prevented in K, holding the methine proton in the deshielding region.

In summary, it is concluded from this spectroscopic analysis that the axial sulfoxides (*cis*-8 and *cis*-11) adopt staggered conformations in which the aryl and alkyl substituents point outside the ring, whereas in the axial sulfones (*cis*-9 and *cis*-12) the sulfonyl substituents are oriented above the dioxane ring (also in a staggered conformation), giving rise to steric and/or electronic repulsion, which is nevertheless of lesser magnitude than the electrostatic repulsion between (negative) oxygens in conformations F and G (Scheme II).

Experimental Section

General Information. Melting points were obtained in a Mel-Temp and/or Electrothermal melting point apparatus with an open capillary tube.

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

Proton NMR spectra were recorded on Varian EM-360 (60 MHz), Varian EM-390 (90 MHz), or Bruker WM-250 (250 MHz) spectrometers. ^{13}C NMR spectra were recorded on a JEOL FX-90Q (22.49 MHz) instrument operated in pulsed Fourier transform mode and locked on solvent deuterium.

Preparation of the 5-Substituted 1,3-Dioxanes. The preparation of *cis*- and *trans*-5-(phenylthio)- (*cis*-7 and *trans*-7), *cis*- and *trans*-5-(phenylsulfinyl)- (*cis*-8 and *trans*-8), *cis*- and *trans*-5-(phenylsulfonyl)- (*cis*-9 and *trans*-9), *cis*- and *trans*-5-(cyclohexylthio)- (*cis*-10 and *trans*-10), *cis*- and *trans*-5(cyclohexylsulfinyl)- (*cis*-11 and *trans*-11), and *cis*- and *trans*-5-(cyclohexylsulfonyl)-2-*tert*-butyl-1,3-dioxanes (*cis*-12 and *trans*-12) was carried out according to the procedure of Eliel et al.[3,6] with C_6H_5SK and c-$C_6H_{11}SK$ instead of CH_3SH. (See also Scheme V in ref 1.)

Diethyl (Phenylthio)malonate. Potassium hydroxide (5.18 g, 93 mmol) was dissolved in 25 mL of absolute ethanol, phenyl mercaptan (9.5 mL, 93 mmol) was added, and the mercaptide solution was poured dropwise into a solution of diethyl chloro-

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malonate (18 g, 93 mmol) in 15 mL of ethanol. Potassium chloride precipitated immediately. The suspension was stirred at room temperature for 12 h, diluted with water (200 mL), and extracted with ether (3 × 100 mL). The ethereal extracts were combined, dried ($MgSO_4$), and concentrated to dryness (rotary evaporator) to afford a yellow oil, which was distilled (bp 152–154 °C/1.2 mmHg) to afford a colorless material: 14.0 g, 56.5%; ^1H NMR ($CDCl_3$, 60 MHz) δ 1.23 (t, J = 7.2 Hz, 6 H), 4.2 (q, J = 7.2 Hz, 4 H), 4.41 (s, 1 H), 7.1–7.8 (m, 5 H).

2-(Phenylthio)-1,3-propanediol. A solution of diethyl (phenylthio)malonate (12.0 g, 45 mmol) in 40 mL of anhydrous ether was added dropwise to a suspension of lithium aluminum hydride (3.42 g, 90 mmol) in 60 mL of anhydrous ether under a nitrogen atmosphere, at −78 °C. The resulting mixture was allowed to reach ambient temperature and was stirred at this temperature overnight. The resulting suspension was refluxed for 15 h and then stirred at room temperature for 12 h. The reaction mixture was then diluted with n-hexane and treated carefully with 100 mL of H_2O to destroy the excess $LiAlH_4$. The lithium salts present were dissolved with 10% aqueous H_2SO_4, which was added only as necessary. Treatment then with 100 mL of 10% aqueous NaOH was followed by extraction with ether (3 × 100 mL); the usual workup procedure afforded 6.2 g (75.3%) of a viscous oil, bp 142 °C/2 mmHg; ^1H NMR ($CDCl_3$, 90 MHz) δ 3.07 (b s, 2 H), 3.35 (p, J = 6 Hz, 1 H), 3.80 (d, J = 6 Hz, 4 H), 7.16–7.70 (m, 5 H); ^{13}C NMR ($CDCl_3$, 22.49 MHz) δ 52.96, 62.97, 127.64, 129.20, 132.45, 133.10; MS, m/e 184 (M^+), 135, 109, 75.

***cis*- and *trans*-2-*tert*-Butyl-5-(phenylthio)-1,3-dioxanes (*cis*- and *trans*-7).** A solution of 5 g (27 mmol) of 2-(phenylthio)-1,3-propanediol, 2.37 g (27.5 mmol) of pivalaldehyde, and a few crystals of p-toluenesulfonic acid in ca. 80 mL of benzene was refluxed for 13 h until ca. 0.50 mL of water was removed (Dean–Stark trap). The resulting solution was washed with 10% aqueous KOH (25 mL) and 80 mL of water, dried ($MgSO_4$), and concentrated (rotary evaporator) to afford 6.6 g (97% yield) of a solid material that was shown by vapor-phase chromatography (on a 7 ft × $^1/_8$ in. 20% FFAP column on Chromosorb W 60/80 mesh, at 175 °C) to consist of 2.2% of *cis*-7 and 97.8% *trans*-7. Separation of this mixture was achieved by flash chromatography[17] (petroleum ether/ethyl acetate, 99:1) to afford 3.8 g (55.8% yield) of *trans*-7 and 0.09 g (1.3% yield) of *cis*-7. Trans isomer: mp 83–84 °C; ^1H NMR spectrum in Table II; ^{13}C NMR spectrum in Table III; IR (KBr) 3320 (Ar H), 2975 and 2850 (C–H), 1640 and 1540 (C=C), 1365 [$(CH_3)_3C$], 1130 and 1080 (C–O), 625 cm^{-1} (C–S); MS, m/e 252 (M^+), 195, 149, 123, 109, 57, 43.

Anal. Calcd for $C_{14}H_{20}SO_2$: C, 66.63; H, 7.99. Found: C, 66.79; H, 7.70.

Cis isomer: mp 76–77 °C; ^1H NMR spectrum in Table II; ^{13}C NMR spectrum in Table III; IR (KBr) 3300 (Ar H), 2940 and 2850 (C–H), 1640 and 1540 (C=C), 1400 [$(CH_3)_3C$] 1140, 1040 and 1025 (C–O), 610 (C–S); MS, m/e 252 (M^+), 195, 149, 123, 109, 77, 57, 43.

***trans*-2-*tert*-Butyl-5-(phenylsulfinyl)-1,3-dioxane (*trans*-8).** A solution of 1.44 g (8 mmol) of m-chloroperoxybenzoic acid in 15 mL of dichloromethane was added dropwise to a cold solution (−20 °C) of *trans*-2-*tert*-butyl-5-(phenylthio)-1,3-dioxane (2.0 g, 7.9 mmol) in 25 mL of dichloromethane. The reaction mixture was stirred at this temperature for 1 h and at room temperature overnight. The solution was then washed with saturated aqueous sodium bicarbonate (25 mL) and water (25 mL), dried ($MgSO_4$), and concentrated (rotary evaporator) to afford 2.0 g of the crude sulfoxide containing 3–4% of the sulfone. Final purification was accomplished by flash chromatography[17] (n-hexane/ethyl acetate, 80:20) to afford 1.4 g (65.7% yield) of the desired product, mp 75–77 °C; ^1H NMR spectrum in Table II; ^{13}C NMR spectrum in Table III; IR (KBr) 3300 (Ar H), 2960, 2940 and 2860 (C–H), 1640 and 1540 (C=C), 1370 [$(CH_3)_3C$], 1140 and 1090 (C–O), 1040 cm^{-1} (S=O).

Anal. Calcd for $C_{14}H_{20}SO_3$: C, 62.66; H, 7.51. Found: C, 62.89; H, 7.38.

***cis*-2-*tert*-Butyl-5-(phenylsulfinyl)-1,3-dioxane (*cis*-8).** This compound was obtained from the chemical equilibration of its diastereomer, *trans*-8. A solution of *trans*-2-*tert*-butyl-5-(phenylsulfinyl)-1,3-dioxane (0.6 g, 2.24 mmol) was dissolved in 21 mL of chloroform, and the resultant mixture treated with 0.33 g (2.24 mmol) of boron trifluoride etherate. The solution was stirred at 25 °C for 5 days, neutralized with 10% aqueous $NaHCO_3$, washed with 10 mL of water, dried ($MgSO_4$), and concentrated. The solid obtained (0.57 g, 97.8%) was shown by ^1H NMR to consist of a 93.2:6.8 mixture of the cis and trans diastereomers, respectively. Separation was accomplished by flash chromatography[17] (n-hexane/ethyl acetate 85:15) to afford 0.51 g (85.6% yield) of *cis*-8 as white crystals, mp 100–102 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 3300 (Ar H), 2940 and 2860 (C–H), 1640 and 1540 (C=C), 1365 [$(CH_3)_3C$], 1140 and 1055 (C–O), 1040 cm^{-1} (S=O); MS, m/e 268 (M^+), 211, 143, 125, 77, 57, 43.

Anal. Calcd for $C_{14}H_{20}SO_3$: C, 62.66; H, 7.51. Found: C, 62.65; H, 7.48.

***trans*-2-*tert*-Butyl-5-(phenylsulfonyl)-1,3-dioxane (*trans*-9).** To a well-stirred mixture of 0.10 g (0.35 mmol) of *trans*-2-*tert*-butyl-5-(phenylthio)-1,3-dioxane (*trans*-7) in 1.05 mL of $CH_3CO_2H/(CH_3CO)_2O$ (1:1) was added 0.34 mL of 30% H_2O_2. The resulting solution was stirred for 6 h at room temperature, diluted with 4 mL of water, and extracted with three 5-mL portions of $CHCl_3/CH_2Cl_2$ (1:1). The combined organic extracts were washed with saturated $NaHCO_3$ and then with water, dried with $MgSO_4$, and concentrated to afford the crude product in quantitative yield. Recrystallization from n-hexane afforded 98 mg (89% yield) of *trans*-9 as white crystals with mp 110–112 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 3300 (Ar H), 2950 and 2870 (C–H), 1640 and 1540 (C=C), 1365 [$(CH_3)_3C$], 1320 and 1150 (S=O), 1090 and 1075 cm^{-1} (C–O); MS, m/e 284 (M^+), 227, 141, 125, 77, 57, 43.

Anal. Calcd for $C_{14}H_{20}SO_4$: C, 59.13; H, 7.09. Found: C, 59.42; H, 7.16.

***cis*-2-*tert*-Butyl-5-(phenylsulfonyl)-1,3-dioxane (*cis*-9).** A solution of *cis*-2-*tert*-butyl-5-(phenylsulfinyl)-1,3-dioxane (0.15 g, 0.56 mmol) in 10 mL of chloroform was treated with 0.106 g (0.62 mmol) of m-chloroperoxybenzoic acid in 15 mL of chloroform, and the resulting mixture was stirred for 12 h at room temperature. The solution was then washed with saturated aqueous sodium bicarbonate (15 mL) and water (15 mL), dried ($MgSO_4$), and concentrated (rotary evaporator) to give the crude product, which was purified on a preparative chromatographic plate (n-hexane/ethyl acetate, 80:20) to afford 0.13 g (81.8% yield) of pure *cis*-9, mp 158–159 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 3300 (Ar H), 2940 and 2850 (C–H), 1640 and 1525 (C=C), 1365 [$(CH_3)_3C$], 1280 and 1150 (SO_2), 1075 and 1060 cm^{-1} (C–O); MS, m/e 284 (M^+), 227, 141, 125, 77, 57, 43.

Diethyl (Cyclohexylthio)malonate. The same procedure described for the preparation of diethyl (phenylthio)malonate (see above) was followed, with 21.46 g (185 mmol) of cyclohexyl mercaptan and 36.0 g (185 mmol) of diethyl chloromalonate. The crude product was distilled at reduced pressure (bp 165 °C/2 mmHg) to give 25.0 g (50.0% yield) of a colorless oil: ^1H NMR (CCl_4, 60 MHz) δ 0.87–2.27 (m, 10 H), 1.28 (t, J = 7.2 Hz, 6 H), 2.33–3.2 (m, 1 H), 4.05 (s, 1 H), 4.22 (q, J = 7.2 Hz, 4 H).

2-(Cyclohexylthio)-1,3-propanediol. The procedure used in the preparation of 2-(phenylthio)-1,3-propanediol was followed, with 24 g (0.09 mol) of diethyl (cyclohexylthio)malonate and 6.66 g (0.18 mol) of lithium aluminum hydride. The crude product (14.4 g, 86.7% yield) was recrystallized from cold benzene to afford 10.3 g (62.0% yield) of the desired product, mp 51–53 °C; ^1H NMR ($CDCl_3$, 60 MHz) δ 0.9–2.33 (m, 10 H), 2.48–3.15 (m, 1 H), 2.95 (p, J = 6.0 Hz, 1 H), 3.38 (t, J = 5.6 Hz, 2 H), 3.85 (t, J = 6.0 Hz, 4 H); ^{13}C NMR ($CDCl_3$, 22.49 MHz) δ 25.61, 26.05, 34.28, 43.69, 48.24, 63.49; IR (KBr) 3300 (OH), 2925 and 2850 (C–H), 1025 cm^{-1} (C–O); MS, m/e 190 (M^+), 115, 83, 75, 56, 41.

Anal. Calcd for $C_9H_{18}SO_2$: C, 56.80; H, 9.53. Found: C, 56.60; H, 9.64.

***trans*-2-*tert*-Butyl-5-(cyclohexylthio)-1,3-dioxane (*trans*-10).** 2-(Cyclohexylthio)-1,3-propanediol (5.5 g, 29 mmol) and pivalaldehyde (2.53 g, 29.4 mmol) were allowed to react according to the procedure described in the preparation of 7. The crude product was purified by flash chromatography[17] (n-hexane) to afford 4.88 g (65% yield) of crystalline *trans*-10, mp 47–49 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 2950 and 2900 (C–H), 1450 (c-C_6H_{11}), 1360 [$(CH_3)_3C$], 1142 and 1090 (C–O),

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625 (C-S); MS, *m/e* 258 (M^+), 201, 83, 73, 57, 41.

***trans*-2-*tert*-Butyl-5-(cyclohexylsulfinyl)-1,3-dioxane (*trans*-11).** The procedure was similar to that described in the preparation of *trans*-8, with 3.0 g (12 mmol) of *trans*-2-*tert*-butyl-5-(cyclohexylthio)-1,3-dioxane and 2.1 g (12.2 mmol) of *m*-chloroperoxybenzoic acid. The crude product was purified by flash chromatography (*n*-hexane/ethyl acetate, 85:15), to give 2.5 g (78.6% yield) of pure *trans*-11, mp 131-132 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 2948 and 2850 (C-H), 1450 (c-C_6H_{11}), 1375 [$(CH_3)_3C$], 1142 and 1095 (C-O), 1040 cm^{-1} (S=O); MS, *m/e* 217 (M^+ - 57), 131, 83, 57, 41.

Anal. Calcd for $C_{14}H_{26}SO_3$: C, 61.28; H, 9.55. Found: C, 61.45; H, 9.35.

***cis*-2-*tert*-Butyl-5-(cyclohexylsulfinyl)-1,3-dioxane (*cis*-11).** The cis isomer was prepared from the chemical equilibration of *trans*-11, as described for *cis*-8 (see above). *trans*-2-*tert*-Butyl-5-[cyclohexylsulfinyl)-1,3-dioxane (1.4 g, 5.11 mmol) and boron trifluoride etherate (0.77 g, 5.11 mmol) gave a cis/trans mixture shown by ^1H NMR as 78:22, respectively. Separation by flash chromatography[17] (*n*-hexane/ethyl acetate, 70:30) afforded 1.0 g (71.4% yield) of the desired cis diastereomer, mp 146-147 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 2930 and 2850 (C-H), 1440 (c-C_6H_{11}), 1375 [$(CH_3)_3C$], 1147 and 1050 (C-O), 1031 cm^{-1} (S=O); MS, *m/e* 274 (M^+), 217, 87, 83, 57, 41.

Anal. Calcd for $C_{14}H_{26}SO_3$: C, 61.28; H, 9.55. Found: C, 61.31; H, 9.57.

***trans*-2-*tert*-Butyl-5-(cyclohexylsulfonyl)-1,3-dioxane (*trans*-12).** This compound was prepared following the same procedure described for *trans*-9 (see above), with 0.31 g (1.2 mmol) of *trans*-2-*tert*-butyl-5-(cyclohexylthio)-1,3-dioxane (*trans*-10) and 1.2 mL of 30% H_2O_2. The crude product was recrystallized from *n*-hexane to give 0.29 g (82.9% yield) of the desired product, mp 175-176 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 2946 and 2851 (C-H), 1440 (c-C_6H_{11}), 1375 [$(CH_3)_3C$], 1310 and 1140 (SO_2), 1130, 1100 and 1050 cm^{-1} (C-O); MS, *m/e* 233 (M^+ - 57), 151, 83, 57, 41.

Anal. Calcd for $C_{14}H_{26}SO_4$: C, 57.90; H, 9.02. Found: C, 57.87; H, 9.01.

***cis*-2-*tert*-Butyl-5-(cyclohexylsulfonyl)-1,3-dioxane (*cis*-12).** The oxidation of 0.15 g (0.55 mmol) of *cis*-2-*tert*-butyl-5-(cyclohexylsulfinyl)-1,3-dioxane (*cis*-11) was achieved with 0.10 g (0.57 mmol) of *m*-chloroperoxybenzoic acid, according to the procedure described in the preparation of *cis*-9. The crude product obtained was purified by preparative TLC (*n*-hexane/ethyl acetate, 55:45) to give 0.12 (75.5% yield) of crystalline, pure *cis*-12, mp 138-139 °C; ^1H NMR in Table II; ^{13}C NMR in Table III; IR (KBr) 2994 and 2860 (C-H), 1460 (c-C_6H_{11}), 1380 [$(CH_3)_3C$], 1305 and 1167 (SO_2), 1138 and 1033 cm^{-1} (C-O); MS, *m/e* 233 (M^+ - 57), 151, 83, 57, 41.

Equilibrations and Analysis. Equilibrium was approached from both sides; boron trifluoride etherate was the catalyst: ca. 30 mg of the dioxane was placed in a 20-mL ampule and dissolved in 10 mL of chloroform before the addition of two to three drops of the catalyst. The ampule was sealed and submerged in a constant-temperature bath (Precision Circulating System, GCA Corp.) until equilibrium was reached. Quenching was effected by pouring the equilibrating solution into aqueous sodium bicarbonate. The dioxanes were then extracted with chloroform, dried, and evaporated, and the progress of the equilibration was conveniently monitored by ^1H NMR spectroscopy. Quantitative product analysis was carried out by vapor-phase chromatography (on a 7 ft × $^1/_8$ in. 20% FFAP column on Chromosorb W 60-80 mesh, at 175 °C) except in the case of the (nonvolatile) sulfoxides and sulfones where a less accurate analysis was obtained by integration of appropriate peaks in the ^1H NMR spectrum (e.g., H_5). In the case of the sulfoxides 8 and 11, the analysis was effected in the presence of $Eu(fod)_3$ to ensure adequate separation of the *tert*-butyl peaks used in the analysis.

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Gas-Phase Basicity of N^1,N^1-Dimethyl-N^2-phenylformamidines

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Gas-phase basicities (GB) for a series of N^1,N^1-dimethyl-N^2-phenylformamidines (FDMP) are determined in proton-transfer equilibria measured in ion cyclotron resonance experiments. The effects of substituents on the GB values are studied. The measured GB values are compared with Brønsted basicities in H_2O and the hydrogen-bonding basicities in CCl_4. These comparisons explain the various substituent effects on the protonation (deprotonation) and the formation of hydrogen bonding complexes in FDMP.

Introduction

Investigations on the effects of substituents on the gas-phase basicities of amidines are not reported in the literature, and to our knowledge, this is the first paper that addresses this question. A series of para-substituted N^1,N^1-dimethyl-N^2-phenylformamidines (FDMP), compounds 1-6 have been synthesized, and their GB values determined in proton-transfer equilibrium reactions carried out in an ICR spectrometer. All the compounds have the same *E* stereochemical structure.[1,2]

$Me_2N—CH=NC_6H_4X$ (FDMP)

1, X = 4-NO_2; 2, X = 4-CN; 3, X = 4-COMe

4, X = 4-Br; 5, X = H; 6, X = 4-Me

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