Synthesis, Stereostructure, Pyramidal Inversion, and Alkylation of 1-Thioniabicyclo[4.4.0]decane Salts[1]

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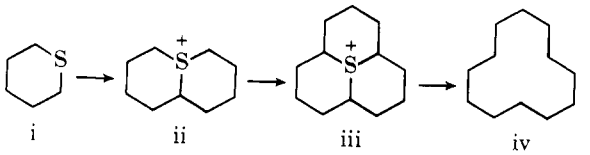
Abstract: Eastman's sulfonium salt, 1-thioniabicyclo[4.4.0]decane tetrafluoroborate, has been prepared by an improved process and shown to be an equimolar mixture (molecular compound) of "trans" and "cis" stereoisomers **1a** and **1b**, each of which has been isolated in pure form. The 6-methoxycarbonyl analogue **9** has also been prepared. Stereostructures have been assigned by a combination of ^{13}C NMR, 360-MHz ^1H NMR, and single-crystal X-ray analysis of salt **9** ($X^- = I^-$). Crystals of **9** are monoclinic, space group $P2_1/n$, $a = 8.890$ (3) Å, $b = 20.120$ (7) Å, $c = 8.150$ (3) Å, $\beta = 110.17$ (4)°, $Z = 4$, $t = 20$ °C, $R = 0.042$ for 1432 X-ray reflections with $F^2 > 2\sigma$. Although stereoisomer **1a** is favored over **1b** by 0.64 kcal mol^{-1} at 110 °C, the 6-methoxycarbonyl analogue **9** prefers the "*cis*" configuration by more than 2.2 kcal mol^{-1} at this temperature. The unexpectedly large effect of the angular substituent is shown to be the result of the small C-S-C bond angles, which cause an angular substituent to have a larger effective size in this system than in decalin. Force-field calculations are presented to support this view. Activation parameters for inversion of salt **1a** are found to be $\Delta H^{\ddagger} = 28.0 \pm 0.9$ kcal mol^{-1} and $\Delta S^{\ddagger} = -3.8 \pm 2.5$ eu in the range 90.07-105.80 °C. Unstabilized sulfonium ylides **15** and **16** have been prepared and their interconversion by pyramidal inversion of sulfur has been investigated; activation parameters for conversion of **15** to **16** are found to be $\Delta H^{\ddagger} = 20.5$ kcal mol^{-1} and $\Delta S^{\ddagger} = 6$ eu. The "cis" ylide **16** is found to be much more stable than the "trans" form **15**, and the effect has been explained in terms of interactions of the vicinal lone pairs on sulfur and carbon. The reactions of ylides **15** and **16** with methyl iodide and acetone have been studied. Three of the four stereoisomeric 2-methyl-1-thioniabicyclo[4.4.0]decanes have been prepared and their stereostructures assigned by ^{13}C NMR. Evidence is adduced that both ylides react with electrophiles in a stereoselective manner. Treatment of salt **1** with *tert*-butyllithium at −72 °C yields the corresponding ylide anions, which undergo stereoselective methylation to provide the 2,10-dimethyl-1-thioniabicyclo[4.4.0]decanes **24** and **25**, stereostructures of which are assigned by ^{13}C NMR. The ring fusion bond of **9** undergoes reductive cleavage, leading to an interesting synthesis of 6-methoxycarbonylthiacyclodecane (**30**).

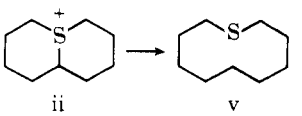
Introduction

The synthesis of multifunctional macrocycles such as the macrolide antibiotics[3] confronts the chemist with two vexing problems: formation of the macrocycle and stereospecific introduction of a number of chiral centers on the conformationally mobile ring. Both these problems can be circumvented if the macrocycle is constructed as the periphery of a rigid polycyclic system of smaller rings. Proper relative chirality may be imparted to the various centers by taking advantage of the rigidity of the intermediate polycycle, after which appropriate bond cleavages will yield the macrocycle. Various versions of this strategy have been studied.[4] In our version of this approach, the macrocycle would be constructed in several steps around a template atom,which would be removed in a final stage. As the template, we selected sulfur, since it could provide activation for carbon-carbon bond formation, and might be more easily removable than other atoms. This approach is illustrated below for the possible synthesis of a simple macrocycle, cyclododecane. The method would be applicable to the



i ii iii iv

synthesis of rings of virtually any size, given the required starting cyclic sulfides, which themselves might be available by carbon-sulfur bond cleavage at the bicyclic stage. However, several fundamental questions must be answered before this approach can be utilized in complex synthesis. First, an efficient annelation[5] technique (e.g., i → ii, ii → iii) must be developed. Second, bicyclic and tricyclic salts such as ii and iii may each exist in two diastereomeric forms. One must know something of their relative stability and ease of interconversion. Third, one must know something of the stereochemistry of alkylation of rigid salts such as ii. Finally, the practicality of working with intermediate salts such as ii and iii must be examined. In this paper, we present the results of our initial steps toward answering some of these questions.



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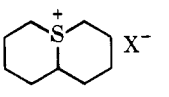
Synthesis of Bicyclic Sulfonium Salts

In 1959, Eastman and Kritchevsky reported the synthesis of salt **1**,[8] which seemed an ideal model for our purposes.



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However, in Eastman's synthesis of **1**, the bicyclic salt is formed by closure of both rings starting with a symmetrical dihydroxythiol. This procedure is not sufficiently general for the purpose we have in mind, which is to construct the two rings consecutively and thus have access to both symmetrical and unsymmetrical bridgehead sulfonium salts. Consequently, we developed the alternate synthesis outlined in Chart I, which produces **1** ($X^- = Br^-$) in 30-40% overall yield. The 6-methoxycarbonyl analogue **9** ($X^- = I^-$) was prepared in 16% overall yield, as outlined in Chart II.

Stereostructure

Bicyclic sulfonium salt **1**, prepared either by Eastman's method[8] or by the method outlined in Chart I, is formed as a 1:1 mixture of stereoisomers **1a** and **1b**, as shown by its ^{13}C NMR spectrum. Thermal equilibration in $CHCl_3$ or CH_2Cl_2

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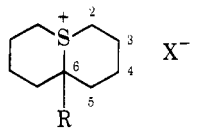
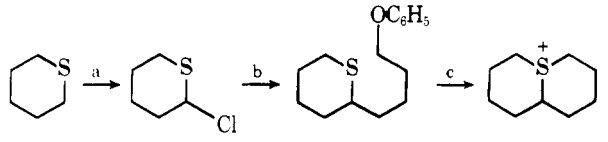
Table I. ^{13}C NMR Chemical Shifts of Salts **1a, 1b,** and **9**[a]



carbon	**1a** (R = H)[b]	**1b** (R = H)[b]	**9** (R = CO_2Me)[c]	$\delta_{1a} - \delta_9$	$\delta_{1b} - \delta_9$
2	38.3	30.7	32.3	+6.0	−1.6
3	23.9	20.0	19.5	+4.4	+0.5
4	23.5	19.9	19.5	+4.0	+0.4
5	30.7	26.1	29.7	+1.0	−3.6
6	53.3	42.6	59.3	−6.0	−16.7
CH_3			54.6		
carbonyl			169.9		

[a] Data are presented in parts per million downfield from internal trimethylsilane. [b] Spectra were determined on ca. 25% solutions in $CDCl_3$. [c] Ca. 5% solution in $CDCl_3$.

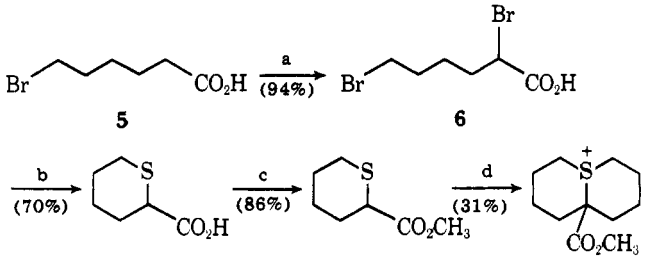
Chart I



2 **3** **4** **1**

a, *N*-chlorosuccinimide, benzene; b, $C_6H_5OCH_2CH_2CH_2CH_2MgCl$; c, HBr, $(CH_3CO)_2O$

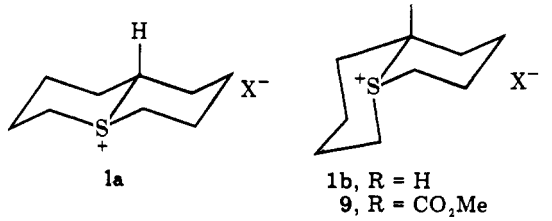
Chart II



5 **6** **7** **8** **9**

a, PCl_3, Br_2; b, 1, $NaHCO_3$, 2, $Na_2S \cdot 9H_2O$; c; CH_3OH, H^+; d, 1, LDA, 2, $ICH_2CH_2CH_2CH_2I$

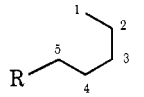
at 110 °C for 24 h affords an equilibrium mixture (70% **1a**, 30% **1b**) from which pure **1a** ($X^- = BF_4^-$) may be obtained by recrystallization. Pure diastereomer **1b** ($X^- = BF_4^-$) is obtained by treating the 1:1 mixture of **1a** and **1b** with *n*-butyllithium in THF at −23 °C, allowing the resulting mixture of ylides to equilibrate for 2 h, then quenching with fluoboric acid. Salt **9** is obtained from the synthesis outlined in Chart II as a single stereoisomer, subsequently shown to have the "*cis*-thioniadecalin" configuration (vide infra).



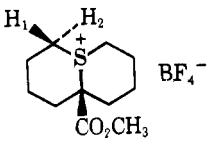
1a **1b**, R = H; **9**, R = CO_2Me

The ^{13}C NMR chemical shifts of salts **1a, 1b,** and **9** ($X^- = BF_4^-$) are tabulated in Table I. Each carbon in sulfonium salt **1a** resonates downfield of the analogous carbon in its less stable stereoisomer **1b,** a situation parallel to that found in *trans*- and *cis*-decalins.[9] The last two columns in Table I are $\Delta\delta$ between stereoisomers **1a** and **1b** and the 6-methoxycarbonyl analogue **9.** For comparison, we list in Table II the ^{13}C NMR chemical shifts for pentane (**10**)[10] and methyl hexanoate (**11**),[11] along with $\Delta\delta$'s for the five corresponding carbons. Comparison of the $\delta_{10} - \delta_{11}$ values in Table II with the $\Delta\delta$ values in Table I clearly indicates that sulfonium salts **1b** and **9** have the same stereostructure. Considering the fact that **1b** and **9** are cyclic structures with only two stable ring conformations each, while **10** and **11** are acyclic, with many possible conformations, the correspondence of $\Delta\delta$'s between the two cases is remarkable.

Table II. ^{13}C NMR Chemical Shifts of Pentane and Methyl Hexanoate



carbon	**10** (R = H)[10]	**11** (R = CO_2CH_3)[11]	$\delta_{10} - \delta_{11}$
1	13.7	14.3	−0.7
2	22.6	23.4	−0.8
3	34.5	32.2	+2.3
4	22.6	25.5	−2.9
5	13.7	33.9	−20.2



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Stereostructures for **1a, 1b,** and **9** may confidently be assigned on the basis of the 360-MHz ^1H NMR spectra of the three tetrafluoroborates in D_2O.[12] Pertinent resonances for salts **1a** and **1b** have been discussed elsewhere.[1] For salt **9,** the protons next to sulfur (H_1 and H_2) appear as a complex multiplet in the region around δ 3.5. (J = −13.8, 8.9, 3.3, and 0 Hz) and 3.56 ppm (J = −13.8, 7.0, 3.4, and 0.9 Hz). The higher field resonance was assigned to H_2 in analogy to the results of Barbarella et al.[13] The −13.8-Hz splitting is obviously the geminal constant, while the 3.3- and 3.4-Hz splittings are weighted averages of J_{ae} and J_{ea} with a proton on C_3. The 8.9- and 7.0-Hz splittings are too small for J_{aa} and too large for J_{ae} or J_{ee}, and must be weighted averages of J_{aa} and J_{ee}. Thus, the ^1H NMR results also indicate that this salt has the "*cis*-decalin" configuration **9.**

The cis configuration of **9** was confirmed by determination of the crystal structure of its iodide salt by X-ray diffraction. The crystals of $C_{11}H_{19}IO_2S$ are monoclinic, space group $P2_1/n$, a = 8.890 (3) Å, b = 20.120 (7) Å, c = 8.150 (3) Å, β = 110.17 (4)°, Z = 4, d_{calcd} = 1.661 g/cm^3, d_{obsd} = 1.665 g/cm^3, t = 20 °C. Atomic coordinates are listed in Table III, bond distances in Table IV, and bond angles in Table V.[56] Carbon–hydrogen distances (not listed) range from 0.83 to 1.05 Å with standard deviations of about 0.1 Å, values typical of X-ray diffraction determinations in the absence of correction for the electronic polarization of the hydrogen atom. Other bond lengths are within a standard deviation or two of accepted values for aliphatic compounds. The molecular structure of the cation, shown in Figure 1, has both rings in chair conformations and approximately at a right angle to each other, the same as found for *cis*-decalin in the gas phase by Bastiansen and Hassel.[14] These ions are packed in the crystal as shown in Figure 2. Each iodide ion is surrounded by six cations, and its nearest neighbors are 13 hydrogen atoms at distances ranging

Table III. Atomic Coordinates in 6-Methoxycarbonyl-1-thioniabicyclo[4.4.0]decane Iodide

atom	*x*	*y*	*z*
I	0.145 44 (8)	0.114 72 (3)	0.206 23 (9)
S	0.78 6 (2)	0.2990 (1)	0.2743 (3)
O(1)	−0.2249 (6)	0.3450 (3)	0.2312 (7)
O(2)	−0.1852 (6)	0.4552 (2)	0.2439 (7)
C(1)	0.291 (1)	0.3001 (5)	0.306 (1)
C(2)	0.312 (1)	0.3407 (5)	0.160 (2)
C(3)	0.264 (1)	0.4140 (5)	0.165 (2)
C(4)	0.090 (1)	0.4229 (5)	0.146 (1)
C(5)	0.042 (1)	0.3886 (4)	0.290 (1)
C(6)	0.070 (1)	0.2655 (5)	0.477 (1)
C(7)	0.150 (1)	0.3078 (5)	0.636 (1)
C(8)	0.094 (1)	0.3794 (5)	0.619 (1)
C(9)	0.134 (1)	0.4159 (4)	0.473 (1)
C(10)	−0.139 (1)	0.3929 (4)	0.251 (1)
C(11)	−0.356 (1)	0.4635 (5)	0.213 (2)
H(1)	0.30 (1)	0.254 (4)	0.28 (1)
H(2)	0.34 (1)	0.323 (5)	0.42 (1)
H(3)	0.24 (1)	0.321 (4)	0.05 (1)
H(4)	0.42 (1)	0.340 (5)	0.17 (1)
H(5)	0.33 (1)	0.433 (4)	0.27 (1)
H(6)	0.27 (1)	0.431 (4)	0.07 (1)
H(7)	0.03 (1)	0.402 (4)	0.05 (1)
H(8)	0.06 (1)	0.470 (4)	0.15 (1)
H(9)	0.11 (1)	0.228 (5)	0.48 (1)
H(10)	−0.04 (1)	0.265 (4)	0.45 (1)
H(11)	0.15 (1)	0.281 (5)	0.74 (1)
H(12)	0.25 (1)	0.304 (3)	0.67 (1)
H(13)	0.15 (1)	0.397 (4)	0.72 (1)
H(14)	−0.03 (1)	0.380 (5)	0.60 (1)
H(15)	0.26 (1)	0.416 (4)	0.50 (1)
H(16)	0.11 (1)	0.460 (4)	0.46 (1)
H(17)	−0.38 (1)	0.504 (5)	0.19 (1)
H(18)	−0.42 (1)	0.445 (5)	0.10 (1)
H(19)	−0.37 (1)	0.454 (6)	0.32 (2)

Table IV. Bond Distances (Å)

I-S	3.825 (3)	C(5)-C(9)	1.54 (1)
S-C(1)	1.81 (1)	C(6)-C(7)	1.51 (1)
S-C(6)	1.81 (1)	C(7)-C(8)	1.52 (1)
S-C(5)	1.85 (1)	C(8)-C(9)	1.54 (1)
C(1)-C(2)	1.51 (1)	C(5)-C(10)	1.52 (1)
C(2)-C(3)	1.54 (1)	C(10)-O(1)	1.21 (1)
C(3)-C(4)	1.51 (1)	C(10)-O(2)	1.32 (1)
C(4)-C(5)	1.55 (1)	C(11)-O(2)	1.46 (1)

from 3.1 to 3.8 Å. It has a sulfur atom at 3.82 Å as its closest heavy-atom neighbor. This contact is indicated by a line in Figure 2, and the structure can be regarded as a molecular packing of these ion pairs.[12]

Pyramidal Inversion

The 1:1 mixture of salts **1a** and **1b** ($X^- = BF_4^-$) was thermally equilibrated at 110 °C in several solvents. In each case the "trans" diastereomer **1a** was found to be slightly more stable than the "cis" isomer **1b**, the equilibrium constants being $CHCl_3$, 2.33; CH_2Cl_2, 2.33; THF, 1.50; CH_3CN, 1.70; D_2O, 1.50. Rates of equilibration were determined in CD_2Cl_2 and $CDCl_3$ over the range 90.07–105.80 °C; data are summarized in Table VI. Application of the Eyring equation to these data gives $\Delta H^{\ddagger} = 28.0 \pm 0.9$ kcal mol^{-1} and $\Delta S^{\ddagger} = -3.8 \pm 2.5$ eu. The calculated rate at 100 °C, 4.6×10^{-5} s^{-1}, compares well with that obtained by Fava, 8.1×10^{-5} s^{-1}, for equilibration of 1,3,3-trimethylthianium perchlorate.[15]

The $\Delta G°$ for the equilibrium **1b** ⇌ **1a** is −0.64 kcal mol^{-1} at 110 °C. For comparison, *trans*-decalin is 2.7 kcal mol^{-1} more stable than *cis*-decalin in the range 268–378 °C.[16] The

Table V. Bond Angles (deg)

C(1)-S-C(5)	100.3 (5)	C(4)-C(5)-C(10)	111.5 (7)
C(1)-S-C(6)	104.2 (6)	C(9)-C(5)-C(10)	110.6 (6)
C(5)-S-C(6)	103.6 (5)	S-C(6)-C(7)	114.6 (5)
S-C(1)-C(2)	107.5 (6)	C(6)-C(7)-C(8)	114.5 (8)
C(1)-C(2)-C(3)	112.5 (9)	C(7)-C(8)-C(9)	111.4 (8)
C(2)-C(3)-C(4)	113.2 (9)	C(5)-C(9)-C(8)	113.1 (7)
C(3)-C(4)-C(5)	114.2 (8)	O(1)-C(10)-O(2)	125.4 (6)
S-C(5)-C(4)	106.3 (4)	O(1)-C(10)-C(5)	123.8 (6)
S-C(5)-C(9)	111.5 (4)	O(2)-C(10)-C(5)	110.7 (6)
S-C(5)-C(10)	103.9 (4)	C(10)-O(2)-C(11)	114.2 (7)
C(4)-C(5)-C(9)	112.6 (7)		

Table VI. Rates of Inversion

$$\mathbf{1b} \underset{-k_1}{\overset{k_1}{\rightleftharpoons}} \mathbf{1a}$$

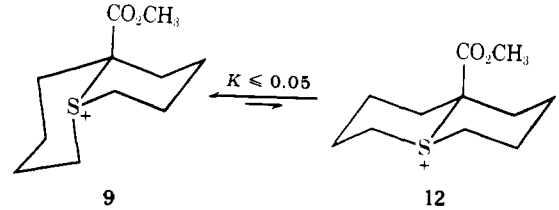
temp, °C	solvent	$10^5 k_1$, s^{-1} [b]	corr coeff
90.07 ± 0.02	CD_2Cl_2	1.57 ± 0.03	0.9983
96.30 ± 0.02	CD_2Cl_2	3.34 ± 0.01	0.9968
104.05 ± 0.02	$CDCl_3$[a]	6.9 ± 0.2	0.9944
105.80 ± 0.02	CD_2Cl_2	8.5 ± 0.1	0.9995

[a] The sulfonium salt partially separates as an oil at this temperature, although it is soluble in $CDCl_3$ at 25 °C. [b] The reverse rate constant (k_{-1}) is equal to $k_1/2.33$.

observed difference in stability has been ascribed to the fact that *cis*-decalin contains three more gauche-butane interactions than the trans isomer.[17] However, Eliel and Willer have recently shown that $\Delta G°$ for SCH_3 in 1-methylthianium salts in small (0.0–0.3 kcal mol^{-1}), suggesting that gauche interactions of the type C-C-S$^+$-C are much smaller than gauche-butane interactions.[18] In salts **1a** and **1b**, the gauche four-atom interactions may be divided into three types (C-C-C-C, C-C-C-S, and C-C-S-C), of which there are 4,4,4 and 5,4,6, respectively. If (for a first approximation) we ignore the C-C-S-C interactions on the basis of the work of Eliel and Willer,[18] then the difference in energy between the "trans" and "cis" diastereomers **1a** and **1b** should be one gauche-butane interaction (0.85 kcal mol^{-1}) plus $\Delta S°$, which should favor diastereomer **1b**, since it has two equivalent chair-chair conformations, while **1a** has only one. For the equilibrium *trans*-decalin ⇌ *cis*-decalin, $\Delta S°$ has been reported to be 0[19] or 0.55 ± 0.3 eu.[16] Thus, at 110 °C, $\Delta G°$ for the equilibrium **1b** ⇌ **1a** should be −0.52 to −0.85 kcal mol^{-1}, in good agreement with the experimental value of −0.64 kcal mol^{-1}.

No isomerization of salt **9** ($X^- = BF_4^-$) was observed by ^{13}C NMR on heating at 110 °C for 72 h (conditions under which **1a**/**1b** are completely equilibrated). With the assumption that the NMR detection limit is ≤5% of isomer **12**, $\Delta G°_{9 \rightarrow 12}$ exceeds 2.2 kcal mol^{-1}.

An alternative explanation for the failure of **9** to undergo thermal isomerization might invoke an unusually high inversion barrier caused by the methoxycarbonyl group. However, it has been found that $\Delta G^{\ddagger}$'s for pyramidal inversion of ethylmethylphenacylsulfonium perchlorate and benzylethylmethylsulfonium perchlorate at 100 °C are 27.3 and 26.9 kcal mol^{-1}, respectively.[20] In order to provide a further check on



9 **12**

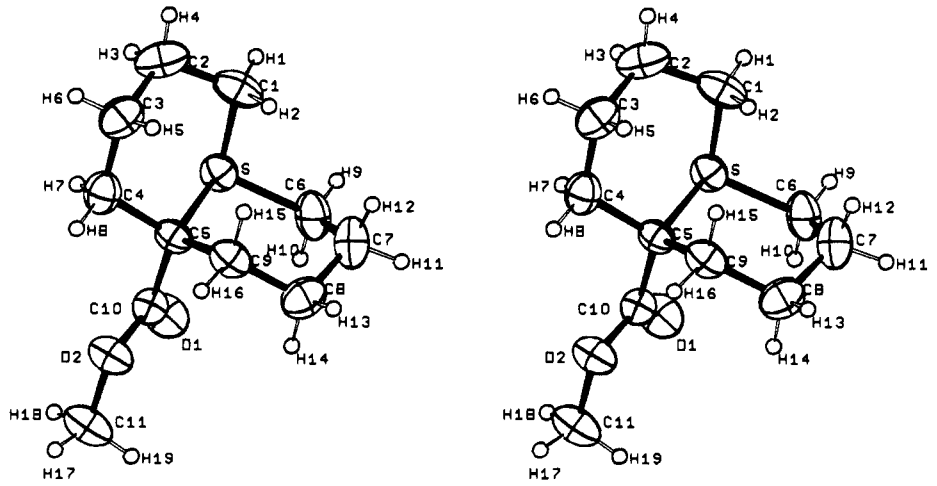


Figure 1. Stereodrawing (ORTEP) of the bicyclic sulfonium cation **9.** Hydrogen atoms are drawn with fictitious spherical thermal parameters of 0.5 Å^2.

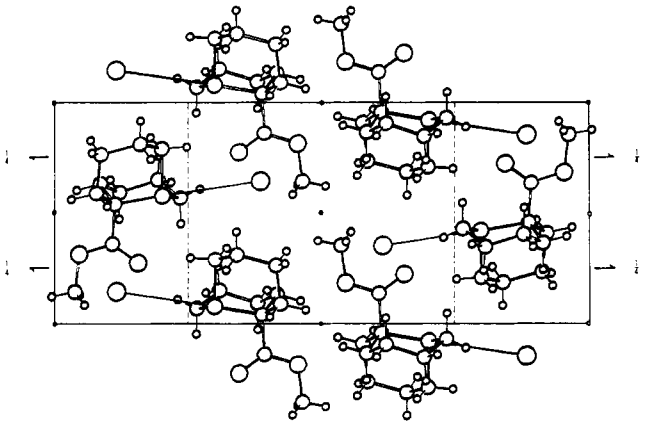
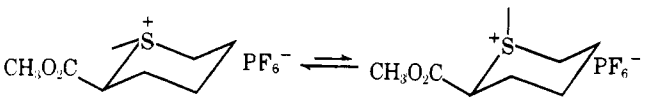


Figure 2. The unit cell, viewed along the *c* axis. The long axis is *b*. A line connects each iodide ion with its nearest sulfur neighbor.

this point, we heated a 9:1 mixture of thianium salts **13** and **14** at 110 °C in 1:1 acetone-d_6/$CDCl_3$; after 10 h an equilibrium



13 **14**

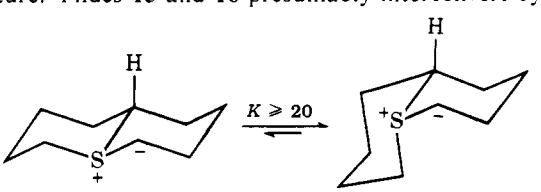
mixture (7:3, unchanged by further heating) resulted. Thus, it would seem that the barrier for inversion of salt **9** should be comparable to that for inversion of salt **1a,** and that **9** is indeed substantially more stable than **12.**

If it is accepted that **9** is more than 2.2 kcal mol^{-1} more stable than **12,** then replacement of angular hydrogen by methoxycarbonyl disfavors the *trans*-1-thioniabicyclo[4.4.0]decane configuration by at least 2.2 + 0.6 = 2.8 kcal mol^{-1}, relative to the cis configuration. A similar phenomenon is observed with the decalins. While *trans*-decalin is 2.7 kcal mol^{-1} more stable than is *cis*-decalin, 9-methyl-*trans*-decalin is estimated to be only 0.3 kcal mol^{-1} more stable than 9-methyl-*cis*-decalin at 250 °C.[21,22] The effect has been ascribed to the fact that replacement of the C_9 H by CH_3 adds four new gauche-butane interactions in the trans isomer and only two in the cis isomer.[21] The same explanation may be offered for the effect of substitution at C_6 in compound **1.** However, the *A* value for the methoxycarbonyl group on a cyclohexane ring is only 1.3 kcal mol^{-1}.[24] Even allowing for the possibility that the *A* value for a tertiary methoxycarbonyl is as high as 1.55 kcal mol^{-1},[25] the group seems to be exerting too large an effect in destabilizing isomer **9** by at least 2.8 kcal mol^{-1}.

The reason for this larger than expected apparent "size" of an angular substituent in the thioniadecalin system originates in the small C-S-C bond angles (100-104°; see Table V). This has the effect of tilting the axial bonds at C_2 and C_{10} toward that at C_6, thus increasing 1:3 diaxial interactions. This question was addressed by carrying out molecular mechanics calculations on **1a, 1b,** and their 6-methyl analogues using the Allinger 1973 force field.[26] Preliminary calculations were performed on 1-methylthianium ion (for which an X-ray structure is known[27]) and eight pairs of diastereomeric *S*-methylthianium ions (for which equilibrium constants have been determined[18]). Using Allinger's equilibrium C-S^+-C bond angle of 94.3°, it was found that the computed bond angles in 1-methylthianium ion are about 4° too small and that the stability of the equatorial *S*-methyl diastereomers is overestimated by 0.9-1.2 kcal mol^{-1}. By employing an equilibrium C-S^+-C angle of 101°, we were able to adequately reproduce the bond distances (within 0.02 Å), bond angles (within 1°), and torsion angles (within 3°). Furthermore, the Alliger program reproduces the experimental enthalpies of equilibration for the eight pairs of diastereomeric *S*-methylthianium ions by 0.15 ± 0.2 kcal mol^{-1}, with the computed stability of equatorial *S*-methyl groups still being slightly exaggerated. The force field predicts trans isomer **1a** to be 0.84 kcal mol^{-1} more stable than cis isomer **1b** (compared to the experimental value of 0.64 kcal mol^{-1}). On the other hand, the 6-methyl derivative of **1b** is predicted to be 2.8 kcal mol^{-1} more stable than its trans counterpart.[28]

Pyramidal Inversion of Unstabilized Sulfonium Ylides

As mentioned earlier, pure diastereomer **1b** may be obtained by forming the sulfonium ylide from the 1:1 mixture of salts **1a** and **1b** (X^- = BF_4^-) with *n*-butyllithium in THF at −23 °C, followed by a fluoboric acid quench after 2 hr this temperature. Ylides **15** and **16** presumably interconvert by py-



15 **16**

ramidal inversion at sulfur, with diastereomer **16** being at least 1.5 kcal mol^{-1} more stable than **15.** We propose that lone pair-lon pair interaction[29] is responsible for the preponderance of cis ylide **16.** Bernardi et al. have recently reported ab initio calculations of $^+SH_2CH_2^-$ which show a minimum energy

Table VII. Values of θ (deg) for Structures **15a–16d**

	15a	15b	16a	16b	16c	16d
θ^a	50	170	46	168	50	75
θ^b			44	176	51	76

[a] Dihedral angle between the axes of the lone pairs, measured from Dreiding scale stereomodels.[31] [b] Dihedral angles calculated between the sulfur lone pair and the appropriate C–H bonds calculated from the atomic coordinates of salt **9**. The lone-pair axis was assumed to pass through the midpoint of the triangle described by C_1, C_5, and C_6 (crystallographic numbering).

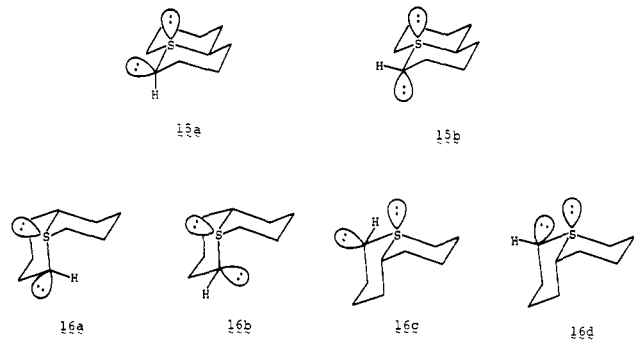


Figure 3. Possible conformations of ylides **15** and **16**.

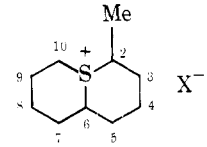
structure for the ylide when the lone pairs on carbon and sulfur are orthogonal, with maxima at lone pair–lone pair dihedral angles of 0 and 180° (11.0 and 7.6 kcal mol^{-1}, respectively).[30] If we assume that both sulfur and the carbanion are pyramidal, then there are two stereochemical possibilities for ylide **15** (**15a,b**) and four for ylide **16** (**16a–d**) which must be considered (Figure 3). Using Dreiding scale models[31] and assuming a perfect tetrahedral geometry for the carbanion, one may estimate θ, the dihedral angle between the axes of the two lone pairs in structures **15a,b** and **16a–d**; values are summarized in Table VII, along with the dihedral angles calculated from the atomic coordinates of salt **9**. Clearly, structure **16d** allows the lone pairs to approach orthogonality with the least structural reorganization.[32] Attempts to obtain experimental evidence for the relative disposition of the lone pairs in ylide **16** by deuteration were unsuccessful. Best results were obtained by inverse quench of the equilibrated ylide mixture with DCl in ether or D_2SO_4 in CH_3OD, but even under these conditions a mixture of 15% d_2, 70% d_1, and 15% d_0 products was obtained.

The rate of isomerization of trans ylide **15** to cis ylide **16** was measured in tetrahydrofuran at −23 and −32 °C; activation parameters were found to be $\Delta H^{\ddagger}$ = 20.5 kcal mol^{-1} and $\Delta S^{\ddagger}$ = 6 eu. Activation parameters for pyramidal inversion of an unstabilized sulfonium ylide have not been previously reported. Trost and Hammen have demonstrated that the ylide derived from optically active 1-adamantylallylethylsulfonium salt undergoes [2,3]-sigmatropic rearrangement with at least 94% transfer of chirality from sulfur to carbon.[35a] This experiment demonstrates that the activation energy for [2,3]-sigmatropic rearrangement of an allylsulfonium ylide is lower than that for pyramidal inversion at sulfur in such an ylide. Our results, in conjunction with those obtained by Trost and Hammen, would seem to place an upper limit of $\Delta G^{\ddagger}$ = 19 kcal mol^{-1} at −35 °C, the temperature at which the rearrangement experiment was carried out.[35b]

Alkylation of Ylides 15 and 16

Since one of our main goals in this study was to obtain information regarding the stereochemistry of alkylation of bicyclic sulfonium ylides, we examined the methylation of ylides **15** and **16**. We first formed a mixture of the ylides by slow addition of *n*-butyllithium to a 1:1 mixture of salts **1a** and **1b** in THF at −72 °C, and allowed the ylides to react with methyl iodide at −72 °C. After conversion to tetrafluoroborate salts, ^{13}C NMR spectroscopy showed the product formed under these conditions to consist mainly of two isomers, subsequently shown to be **17** and **18**, present in nearly equal amount. When this mixture is heated at 110 °C in $CHCl_3$, the amount of isomer **18** increases, while that of isomer **17** decreases. Pure isomer **18** (X^- = picrate) may be obtained by recrystallization of the picrate salts. When the ylide mixture is equilibrated at −23 °C for 2 h, then methylated at −72 °C, the alkylation product consists of isomer **17** and a new isomer (**19**) in a ratio of 3:2; isomer **18** is not produced under these conditions.

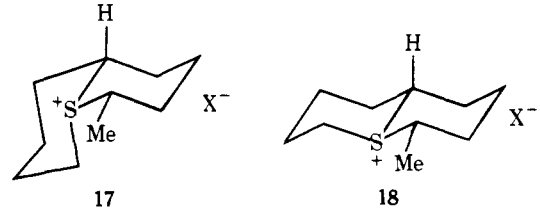
Table VIII. ^{13}C NMR Chemical Shifts of Salts **17**, **18**, and **19**[a]

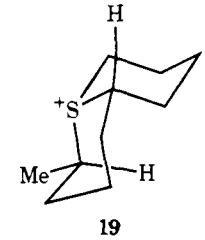


carbon	18	$\delta_{18} - \delta_{1a}$	17	19
2	49.6	11.0	45.3	38.6
3	35.9	12.0	26.1	31.5
4	23.8[b]	0.3	23.3	18.5
5	30.9[c]	0.2	22.1	28.4
6	53.4	0.0	44.7	43.9
7	30.9[c]	0.2	29.2	(24.5)[d]
8	23.8[b]	0.3	16.8	(23.6)[d]
9	23.8[b]	−0.1	22.9	(21.5)[d]
10	33.3	−5.3	22.7	30.7
CH_3	17.4		17.7	18.0

[a] Spectra were determined on ca. 5% solutions of the picrates in $CDCl_3$; data are presented in parts per million downfield from internal Me_4Si. [b] Triple intensity peak. [c] Double intensity peak. [d] These assignments are uncertain.

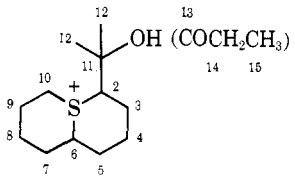
Thermal equilibration of this mixture affords a 3:2 mixture of isomers **18** and **19**.





Stereostructures were assigned to salts **17**, **18**, and **19** on the basis of their ^{13}C NMR spectra, which are tabulated in Table VIII. First, it is clear that isomer **18** has the *trans*-1-thioniabicyclo[4.4.0]decane structure, from the values of $\Delta\delta$ given in the second column of Table VIII. The equatorial disposition of the methyl group is shown by the fact that C_{10} is shifted upfield (γ-gauche interaction),[36] while C_4 and C_6 resonate at nearly the same frequency as in salt **1a**. The large shifts of C_2 and C_3 result from the expected α and β effects.[36] Since isomer **17** is converted to isomer **18** by pyramidal inversion of sulfur,

Table IX. ^{13}C NMR Chemical Shift of Salts **21, 22,** and **23**[a]



carbon	21a	21b	22a	22b	23b
2	66.7	61.9	63.4	60.4	55.0
3	24.4	19.5	*d*	19.3	24.2
4	23.9[b]	*c*	*d*	*e*	16.9
5	31.5[b]	23.4[b]	30.4	*e*	34.1
6	54.6	44.6	54.3	45.0	44.6
7	31.0[b]	29.9	31.0	30.1	*c*
8	23.9[b]	17.6	*d*	18.6	*c*
9	23.7[b]	23.5[b]	*d*	*e*	21.8
10	42.6	*c*	37.8	25.4	35.3
11	73.5	72.1	84.2	82.5	84.4
12	27.8, 28.3	27.5, 28.9	27.6, 29.3	26.8, 27.5	28.0, 28.3
13			151.4	151.8	151.5
14			63.0	63.4	62.6
15			13.5	13.5	13.5

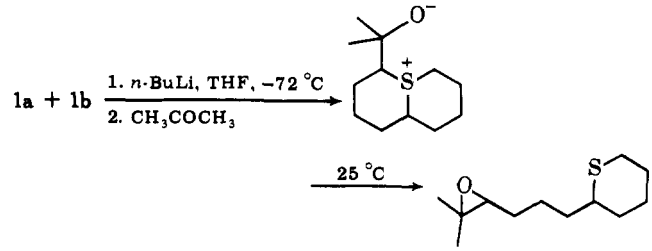
[a] Spectra were determined on ca. 5% solutions of the tetrafluoroborate salts in $CDCl_3$; data are presented in parts per million downfield from internal Me_4Si. [b] These assignments are considered to be slightly uncertain. [c] Resonance not found; assumed to coincide with another peak. [d] These resonances could be either 20.1 or 23.0; the 23.0 peak is large enough for at least three carbons. [e] Could be either 22.8 or 23.9.

it must have the stereostructure indicated, and, since isomer **19** is produced after equilibration of the ylides to the "cis" form, it must be the remaining cis isomer, as indicated. Assignment of resonaces to **17** and **19** was made on the basis of consideration of the number of α, β, and γ-gauche interactions in these isomers, relative to the spectrum of the parent salt **1b.** The chemical shifts of the various carbons in isomers **17** and **19** do not correspond as closely to those in the parent unmethylated salt **1b,** mainly owing to the fact that **1b** has two equivalent conformations, while **17** and **19** probably exist primarily in the conformation in which the methyl is equatorial, with a resultant change in the number of effective γ-gauche interactions.[37]

The stereochemistry of these methylations is of interest. When methylation is carried out without allowing the ylide mixture to warm above −70 °C, the equatorial methylated salts **17** and **18** are produced in a ratio close to that of the starting salts **1a** and **1b.** Furthermore, these products are precisely those expected for replacement of the proton most nearly orthogonal to the lone pair in each isomer (**1a** and **1b**).[38] It is noteworthy that isomer **19** is not produced in this reaction, although it *is* produced after the ylides are allowed to equilibrate. These results are consistent with the hypothesis that **15a** is the kinetic ylide derived from **1a, 16d** is the kinetic ylide derived from **1b,** and that these ylides do not undergo stereomutation, either at sulfur *or at carbon* at −72 °C. Upon warming to −23 °C for 2 h prior to methylation, the ylides equilibrate by pyramidal inversion at both sulfur and carbon, giving a mixture of ylides **16d** and either **16a** or **16c** (which are chair–chair conformers).

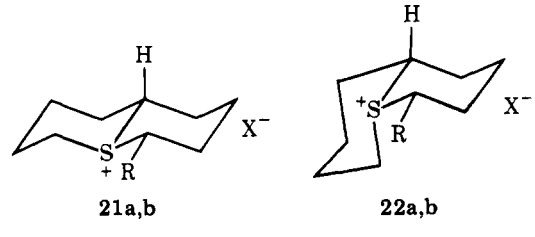
The foregoing hypothesis demands that $\Delta G^{\ddagger}$ for pyramidal inversion of the carbanion exceed $\Delta G^{\ddagger}$ for methylation (or reaction with acetone, vide infra). Calculations of the inversion barrier for methyl anion range from 1.7 to 25.2 kcal mol^{-1},[40] with the most sophisticated calculations giving a value of 9.9 kcal mol^{-1}.[41] However, the adjacent sulfonium group should raise the barrier,[42] although the magnitude of this effect is unknown.[43]

The reactions of ylides **15** and **16** with acetone are qualitatively similar to the methylations. If the intermediate zwitterion is allowed to warm to room temperature, epoxy sulfide **20** is produced. However, the zwitterion can be trapped by

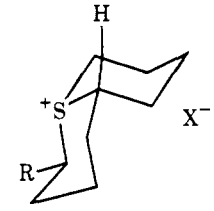


20

quenching at −72 °C with fluoboric acid or ethyl chloroformate. When the zwitterion is quenched with HBF_4, salts **21a** and **22a** are produced in roughly equal amounts. A trace of the other cis isomer **23a** may be seen in the ^{13}C NMR spectrum of the crude product. Pure salt **22a** ($X^- = BF_4^-$) may be isolated by recrystallization of the product. Thermal equilibration ($CDCl_3$, 110 °C, 5 h) of the crude product provides essentially pure trans salt **21a.** When the zwitterion is trapped with ethyl chloroformate, an equimolar mixture of carbonates **21b** and **22b** is produced. When the ylide mixture is allowed to thermally equilibrate at −23 °C before formation of the zwitterion at −72 °C, which is then trapped with ethyl chloroformate, cis sulfonium salts **22b** and **23b** are produced in a ratio of 3:1.



21a,b **22a,b**

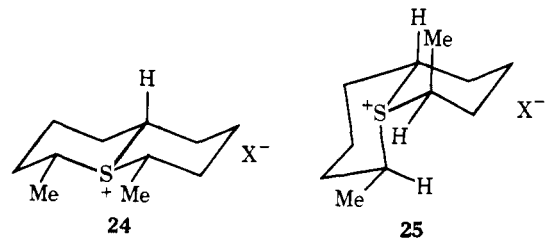


23a,b

a, R = $C(CH_3)_2OH$ b, R = $C(CH_3)_2OCOC_2H_5$

Stereostructures were assigned to salts **21–23** on the basis of arguments analogous to those used for assignments of methylated salts **17–19.**[37] Table IX summarizes the ^{13}C NMR chemical shifts.

We have also briefly examined the formation and alkylation of sulfonium ylide anions. When the 1:1 mixture of salts **1a** and **1b** is treated with 2.5–3.0 equiv of *tert*-butyllithium in THF under careful conditions so that the temperature is maintained at −76 ± 2 °C, and the resulting solution then treated with excess methyl iodide, an equimolar mixture of salts **24** and **25** (X^- = picrate) is isolated in 12% yield. If the ylide anion solution is kept at −65 to −70 °C for 1 h before methylation, the

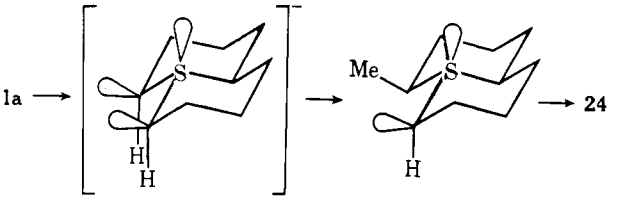


24 **25**

sole product is salt **25,** isolated in 12% yield. Attempted thermal equilibration of the 1:1 mixture of **24** and **25** ($CHCl_3$, 110 °C, 10 h) produces no change in composition.

The ^{13}C NMR chemical shifts of salts **24** and **25** are summarized in Table X. The correspondence in chemical shifts between isomer **24** and the analogous resonances in salts **18** (Table VIII) and **1a** (Table I) is striking and clearly supports the assigned stereostructure. The alternative *trans*-1-thioniabicyclo[4.4.0]decane structure having one methyl axial is ruled out by symmetry (11 resonances would result). The alternative *trans*-1-thioniabicyclo[4.4.0]decane structure having one methyl axial is ruled out by symmetry (11 resonances would result). The "trans" salt having both methyls axial is eliminated by the lack of γ-gauche shifts on C_4 and C_6, and also because this isomer would thermally equilibrate to "cis" isomer **25.** Isomer **25** is assigned the indicated stereostructure first on symmetry grounds. Since this isomer has two equivalent conformations, the molecule has average C_s symmetry and should show only six resonances, as is observed. The alternative structure having both methyls equatorial would show 11 resonances. The isomer having both methyls trans to the angular hydrogen would also show average C_s symmetry, but should thermally equilibrate to isomer **24.** The spectrum of **25** may be most profitably compared to that of its parent unmethylated salt **1b,** since both exist as a mixture of two enantiomeric chair–chair conformers. In addition to the expected large downfield shifts of C_2 and C_3 (α and β effects), C_4 experiences a moderate upfield shift in **25,** resulting from the fact that this carbon experiences a new γ-gauche interaction in one of its two conformations. The γ-gauche effect expected on C_6 is not observed, perhaps because of the greater length of the C_2–S and C_6–S bonds.

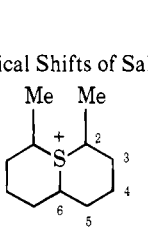
Although the isolated yields in the alkylations leading to **24** and **25** are low, we feel that the results are significant since dimethylated isomers **24** and **25** are the only sulfonium salts isolated; no starting material or monomethylated material may be detected in the crude product by ^{13}C NMR spectroscopy. The results definitely suggest that ylide anion undergoes stereomutation at sulfur with a considerably lower barrier than that for ylide **15.**[43] It also seems that the stabel structure of this species is one having a *cis*-1-thioniabicyclo[4.4.0]decane structure, as in the case of the ylide itself. The most reasonable hypothesis is that the "trans" salt **1a** gives an ylide anion **26** in which both carbanion lone pairs are gauche to the sulfur lone pair; after the first methylation, the product ylide **27** is formed.



26 27

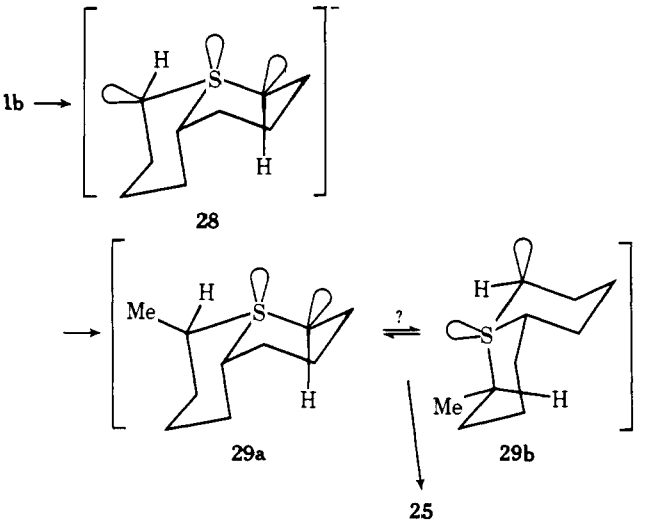
The cis salt **1b** might afford ylide anion **28,** which would probably react first on the more basic carbon lone pair (e.g., the one having the most unfavorable interaction with the sulfur lone pair) to give **29,** which might exist either in conformation **29a** or **29b,** depending on whether the unfavorable lone-pair interactions in **29b** or the axial methyl group in **29a** are more important. Of course, since the precursors of products **24** and **25** are not neutral species, they may exist as ion pairs or aggregates, or may even by C-lithiated ylides. Finally, we should point out that these reaction intermediates are apparently the first known sulfonium ylide anions, although analogous species derived from ammonium and phosphonium salts have been previously described.[44] Dianions derived from sulfones[45] and nitroalkanes[46] have also been studied.

Table X. ^{13}C NMR Chemical Shifts of Salts **24** and **25**[a]



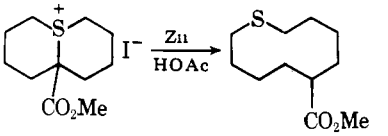
carbon	24	$\delta_{24} - \delta_{1a}$	25	$\delta_{25} - \delta_{1b}$
2	50.2	11.6	41.0	10.3
3	34.9	11.0	28.4	8.4
4	23.7	0.2	17.2	−2.7
5	31.0	0.3	26.5	0.4
6	53.9	0.5	42.2	−0.4
CH_3	20.5		18.0	

[a] Spectra were determined on ca. 5% solutions of the picrate salts in $CDCl_3$; data are presented in parts per million downfield from internal Me_4Si.



Conversion of Salt 9 to 6-Methoxycarbonylthiacyclodecane

In the Introduction, we considered the possibility that the sulfur-template approach might be employed to synthesize cyclic sulfides with ring sizes not conveniently accessible by direct cyclization. Bicyclic salt **9** provided us with an excellent opportunity to test this hypothesis. In fact, treatment of **9** with zinc dust in refluxing acetic acid affords the ten-membered cyclic sulfide **30** in 96% yield, thus establishing the feasibility of this approach to large-ring sulfides.



9 30

Conclusions

The present study has provided answers to a number of our original questions regarding the feasibility of a sulfur template approach to macrocycles. Bicyclic sulfonium salts *can* be prepared and their ylides alkylated stereoselectively. At this point, yields are not exceptional, but additional research may remedy this problem. The greatest obstacle we have encountered thus far stems from the difficulty with handling the sulfonium salts (they are usually produced as oils, often highly hygroscopic), and with separating mixtures of salts. In the future, use of ion-exchange or reverse-phase high-pressure liquid chromatography may alleviate these problems.

Experimental Section

The ^1H NMR spectra were determined on a Varian T-60 NMR spectrometer or on a Bruker HXS-360 (Stanford Magnetic Resonance Laboratory). The ^{13}C NMR spectra were measured at 25.14 MHz with a Nicolet TT-23 spectrometer. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane (Me_4Si) or sodium trimethylsilylpropionate (TSP). Significant ^1H NMR data are tabulated in order (number of protons, multiplicity, proton assignment). Infrared spectra were determined on a Perkin-Elmer 137 infrared spectrophotometer. Mass spectra were obtained with Atlas MS-12 and Consolidated 12-110B mass spectrometers. Melting points (Pyrex capillary) and boiling points are uncorrected. Microanalyses were performed by the College of Chemistry Microanalytical Laboratory, University of California, Berkeley. Ether solvents were distilled from $LiAlH_4$ or sodium/benzophenone prior to use. All reactions involving ylides were performed under a nitrigen atmosphere.

4-Chloro-1-phenoxybutane. To a solution of 120 g (3.0 mol) of sodium hydroxide dissolved in 1 L of water is added 282 g (3.0 mol) of phenol. To this solution is added 381 g (3.0 mol) of 1,4-dichlorobutane. The heterogeneous mixture is refluxed until it becomes nearly neutral (several days). Ether (300-500 mL) is added and the aqueous layer is separated and extracted again with 500 mL of ether. The combined ether extracts are washed with 5% sodium hydroxide and saturated brine and dried with $MgSO_4$. The solvent is evaporated in vacuo and the residue is distilled through a 30-cm Vigreux column to yield 390 g (77%) of pure chloro ether (bp 86-87 °C, 0.5 Torr): IR (neat) 1600, 1580, 1500, 1460, 1250 cm^{-1}; ^1H NMR (CCl_4) δ 1.78 (4 H, m), 3.38 (2 H, t, J = 6 Hz), 3.78 (2 H, t, J = 6 Hz), 6.80 (3 H, m), 7.02 (2 H, m). Anal. ($C_{10}H_{13}ClO$) C, H, Cl.

2-(4-Phenoxybutyl)pentamethylene sulfide (4) is prepared by the method of Tuleen and Bennett.[47] In a 2-L flask, 25 g (1.0 g-atom) of magnesium turnings is stirred under nitrogen with 250 mL of dry ether. A solution of 174 g (0.95 mol) of 4-chloro-1-phenoxybutane in 300 mL of dry ether is added dropwise so as to maintain a gentle reflux. The reaction mixture is refluxed for an additional 1 h after the addition of chloride is complete. In a 500-mL inversion addition flask is placed 48.5 g (475 mmol) of pentamethylene sulfide in 250 mL of benzene. The solution is cooled to 10 °C and 63.0 g (475 mmol) of *N*-chlorosuccinimide (NCS) is added in portions so as to maintain the temperature below 20 °C. The mixture is stirred for an additional 1 h after the final addition of NCS and is then filtered into the Grignard reaction mixture at a rate so as to keep the temperature between 10 and 15 °C. After the mixture is stirred overnight at room temperature, CO_2 is bubbled through the reaction mixture to remove excess Grignard reagent, and a 10% HCl solution is added dropwise. The aqueous layer is separated and extracted with ether. The combined ether layers are washed with 10% NaOH and saturated brine and dried over potassium carbonate. Removal of the solvents gives crude sulfide **4**, which is used without further purification. In a similar reaction, a sample was purified by distillation (bp 145-150 °C, 0.2 Torr): ^1H NMR (CCl_4) δ 1.6 (12 H, m), 2.6 (3 H, m), 3.90 (2 H, t, J = 6 Hz, OCH_2), 6.8 (3 H, m), 7.0 (2 H, m). Anal. ($C_{15}H_{22}OS$) C, H.

1-Thioniabicyclo[4.4.0]decane Bromide (1, X^- = Br^-). To 300 mL of acetic anhydride, cooled with an ice bath, is added 300 mL of 48% HBr. The crude sulfide **4** is added slowly, while cooling with an ice bath. This reaction mixture is refluxed for 6-10 h, and is then cooled and extracted with benzene (2 × 250 mL). The aqueous layer is evaporated in vacuo to near dryness and triturated with THF. Recrystallization from THF/ethanol yields an off-white product (30-40%). An analytical sample is obtained by an additional recrystallization: mp 264-265 °C dec (lit.[8] mp 266-267 °C); ^1H NMR (D_2O, external Me_4Si) δ 1.5-2.2 (12 H, m), 2.8-3.6 (5 H, m); ($CDCl_3$) δ 1.7-2.4 (12 H, m), 3.8-4.6 (5 H, m); ^{13}C NMR ($CDCl_3$) trans δ 23.3 (double intensity), 30.5, 38.0, 50.8; cis δ 19.6, 19.9, 26.0, 31.5, 42.5. Anal. ($C_9H_{17}BrS$) C, H, Br, S.

1-Thioniabicyclo[4.4.0]decane Tetrafluoroborate (1, X^- = BF_4^-): Method A. To a solution of 5.5 mL (50 mmol) of trimethyl orthoformate in 6 mL of dry methylene chloride, cooled to −72 °C, is added 7.3 mL (56 mmol) of boron trifluoride etherate, and the resulting mixture is stirred at −72 °C for 0.5 h and at 0 °C for 0.5 h. To the dimethoxycarbonium tetrafluoroborate reaction mixture is added 3.88 g (16.4 mmol) of sulfonium bromide **1**. After the mixture is stirred overnight at room temperature, several milliliters of ethanol are added and the mixture is stirred for 1 h. Removal of the solvents and trituration with ether give is **1** (X^- = BF_4^-) in quantitative yield. Recrystallization from ethanol yields 3.41 g (85%) of pure salt, mp 174-175 °C.

Method B. To a cold solution of 125 mL of acetic acid and 125 mL of 48% fluoboric acid is added crude 2-(4-phenoxybutyl)pentamethylene sulfide (**4**), prepared from 245 mmol of pentamethylene sulfide. This mixture is refluxed for 4 days, and is then cooled and neutralized with sodium hydroxide. The resulting mixture is extracted three times with ether. The water is removed in vacuo and the sulfonium salt is removed from the sodium tetrafluoroborate by extraction with methylene chloride. Removal of the solvent and trituration with THF yields 10 g (17%) of sulfonium salt **1** (X^- = BF_4^-): ^1H NMR (360 MHz, 1% in D_2O) trans δ 1.67 (4 H, m), 1.85 (2 H, br d, J = 14 Hz), 1.97 (2 H, br d, J = 15 Hz), 2.12 (2 H, br d, J = 15 Hz), 2.31 (2 H, br d, J = 15 Hz), 3.16 (2 H, ddd, J = −11.8, 13.3, 2.5 Hz), 3.27 (1 H, tt, J = 11.9, 2.3 Hz), 3.56 (2 H, dd, J = −11.8, 2.3 Hz); cis δ 1.60 (2 H, m), 1.94 (6 H, m), 2.13 (4 H, m), 3.23 (2 H, ddd, J = −13.9, 3.3 Hz), 3.48 (2 H, dddd, J = −13, 7, 3.4, 0.9 Hz), 3.69 (1 H, tt, J = 7.8, 3.9 Hz); ^{13}C NMR ($CDCl_3$) trans 23.5, 23.9, 30.7, 38.3, 53.3; cis 19.9, 20.0, 26.1, 30.7, 42.6. Anal. ($C_9H_{17}BF_4S$) C, H, S.

Thermal Equilibration of 1-Thioniabicyclo[4.4.0]decane Tetrafluoroborate (1). A solution of 495 mg of salt **1** (1:1 mixture of **1a**/**1b**) dissolved in 10 mL of $CDCl_3$ (or ethanol-free $CHCl_3$) was heated at 110 °C (sealed tube) for 21 h to give a 70:30 mixture of **1a**/**1b**. The ratios were determined by 360-MHz ^1H NMR (by comparing the resonance at δ 3.69 of the cis isomer to the resonance at δ 2.31 of the trans isomer) and ^{13}C NMR (by comparing resonances of **1a** to the corresponding resonances of **1b** and using the average of the values obtained). Further heating did not change this ratio. Salt **1** was equilibrated in other solvents in the same manner and the ratios were determined by ^{13}C NMR. Pure trans salt (**1a**) is obtained by dissolving the equilibrated salt (**1a**/**1b** = 7:3) in a minimum amount of hot ethanol. THF is added and the solution is allowed to cool. The 1:1 mixture of **1a** and **1b** preciptates and is removed by filtration. The filtrate is evaporated to dryness and the process repeated. After three crystallizations of the molecular compound **1a**/**1b**, the concentrated filtrate (ca. 25% yield) is pure **1a**, as shown by its ^{13}C NMR spectrum. The pure salt is obtained as a clear glass; we have not attempted to crystallize it.

2,6-Dibromohexanoic acid (6) was prepared in 94% yield by Hell-Volhard-Zelinsky bromination of bromo acid **5**[48] after the method of Clarke and Taylor:[49] mp 45-47 °C (lit.[50] oil at room temperature); ^1H NMR (CCl_4) δ 1.6-2.4 (6 H, m), 3.42 (2 H, t, J = 7 Hz), 4.25 (1 H, t, J = 7 Hz), 12.1 (1 H, s). Anal. ($C_6H_{10}Br_2O_2$) C, H, Br.

2-Carboxypentamethylene Sulfide (7). A mixture of 14 g (164 mmol) of $NaHCO_3$, 45 g (164 mmol) of 2,6-dibromohexanoic acid, and 40 g (167 mmol) of finely ground $Na_2S{\cdot}9H_2O$ in 200 mL of water is kept at room temperature for 20 h. Concentrated HCl (40 mL) is added and the squeous mixture is extracted with ether. The extract is dried and evaporated to yield 16.5 g (70%) of crude acid **7**, which may be used in the subsequent esterification. The analytical sample was obtained by distillation (bp 103-105 °C, 1 Torr): IR (neat) ν_{max} 3000 (broad), 1710 cm^{-1}; ^1H NMR (CCl_4) δ 1.6-2.2 (6 H, m), 2.7 (2 H, m), 3.62 (1 H, dd, J = 4 and 6 Hz), 12.0 (1 H, s). Anal. ($C_6H_{10}O_2S$) C, H, S.

2-Methoxycarbonylpentamethylene Sulfide (8). A solution of 16.5 g (113 mmol) of crude acid **7** and 1 mL of concentrated H_2SO_4 in 100 mL of CH_3OH is stirred overnight. Sodium carbonate is added and the CH_3OH removed under vacuum. The residue is taken up in ether, washed with aqueous Na_2CO_3 and saturated brine, and then dried. Removal of the solvent affords an oil which is distilled under vacuum to obtain pure ester **8** (15.4 g, 86%): IR (neat) ν_{max} 1740 cm^{-1}; ^1H NMR (CCl_4) δ 1.8-2.2 (6 H, m), 2.7 (2 H, m), 3.45 (1 H, dd, J = 4 and 6 Hz), 3.70 (3 H, s). Anal. ($C_7H_{12}O_2S$) C, H, S.

6-Methoxycarbonyl-1-thioniabicyclo[4.4.0]decane Iodide (9). To a solution of 11.2 mL (78 mmol) of diisopropylamine in 100 mL of dry tetrahydrofuran, cooled to 0 °C, is added 78 mmol of a solution of *n*-butyllithium in hexane. After 30 min at room temperature, the lithium diisopropylamide solution is cooled to −76 °C in a bath of dry ice/acetone and 12.5 g (78 mmol) of ester **8** is added. The cold enolate solution is added to a solution of 12 mL (90 mmol) of 1,4-diiodobutane in 50 mL of dry tetrahydrofuran, which has been precooled to −76 °C. After 3 h at −76 °C and 2 h at room temperature, the solvent and diisopropylamine are removed under vacuum and the residue is partitioned between ether and water. The ether layer is separated and the aqueous layer extracted again with ether. The combined ether extracts

are quickly dried by filtration through a column of anhydrous $MgSO_4$ and then refluxed for 3 days. The resulting salt is removed by filtration and the mother liquors are again refluxed for 3 days, yielding more insoluble salt. The combined salts are recrystallized from ethanol to obtain 8.64 g (31%) of analytically pure **9**: mp 144–145 °C; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.6–3.0 (12 H, m), 3.8–6.2 (m), 3.95 (s); ^{13}C NMR ($CDCl_3$) δ 19.0, 29.5, 32.9, 54.2, 58.7, 169.4. Anal. ($C_{11}H_{19}IO_2S$) C, H, S, I.

The fluoborate salt (mp 121–122 °C) is prepared by adding 1 equiv of $AgBF_4$ to a methylene chloride solution of the iodide salt (100%): IR ($CHCl_3$) ν_{max} 1740, 1050 cm^{-1}; ^{1}H NMR (360 MHz, D_2O, external Me_4Si) δ 1.68 (2 H, m), 1.94 (4 H, m), 2.18 (4 H, m), 2.48 (2 H, ddd, J = 15, 9, and 2.5 Hz), 3.48 (2 H, ddd, J = 13.8, 8.9, and 3.3 Hz), 3.56 (2 H, dddd, J = 13.8, 7.0, 3.4, and 0.9 Hz), 3.95 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 19.5, 29.7, 32.3, 54.6, 59.3, 169.9. Anal. ($C_{11}H_{19}BF_4O_2S$) C, H.

6-Methoxycarbonylthiacyclodecane (30). Zinc dust (3.5 g) is added to a solution of 426 mg (1.24 mmol) of salt **9** ($X^- = I^-$) in 20 mL of acetic acid. The heterogeneous mixture is refluxed for 20 h, and is then diluted with 100 mL of water. The excess zinc is removed by filtration and the filtrate is extracted with ether (4 × 50 mL). The combined ether extracts are washed with saturated $NaHCO_3$ solution until the washings are neutral and then with saturated brine. After drying, the ether is removed under vacuum and the resulting oily product is purified by bulb-to-bulb distillation. In this way, 257 mg (96%) of analytically pure **30** is obtained: IR (neat) ν_{max} 1740 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.4–2.0 (13 H, m), 2.3–2.8 (5 H, m), 3.58 (3 H, s). Anal. ($C_{11}H_{20}O_2S$) C, H. HRMS: Found, 216.1189.

X-ray Diffraction. Crystals of the iodide of **9** were found as plates and needles. The plate-like crystals seemed less perfect, and Weissenberg photographs indicated many to be multiple crystals. The needles appeared to be single under the microscope with optical extinction approximately parallel with the long direction (c axis). One of these (0.174 × 0.070 × 0.030 mm) was glued to a glass fiber for examination by Weissenberg and diffractometer technique. Cell dimensions were determined from setting angles for 12 reflections (2θ in the range 25–32°) with a Picker FACS-I diffractometer with Mo Kα radiation (λ 0.709 26 Å for Kα_1). Intensity data were measured by θ–2θ scans (2θ from 0.5° below Kα_1 to 0.5° above Kα_2) with 10-s background counts (20 s at some of the higher angles) near each end of the scan. Three standard reflections, indicated a linear decrease in intensity of 10% in the course of the measurements, and a compensating correction was applied. Absorption corrections (μ = 22.99 cm^{-1}) were calculated using dimensions of the crystal which were adjusted to minimize the variation of intensity with azimuthal angle for several test reflections. The corrections ranged from 1.07 to 1.18. Measurements were made of 5499 reflections not excluded by the space group in the hemisphere $\pm h, +k, \pm l$; the maximum 2θ was 50°. Averaging of equivalent reflections yielded 2426 unique ones, of which 1432 with $F^2 > 2\sigma$ were used in the least-squares refinement.

The structure was solved by the heavy-atom method. A Patterson function revealed the position of the iodine atom. Other nonhydrogen atoms were found in a ΔF map. After some refinement by least squares, another ΔF map revealed the hydrogen atoms. With isotropic thermal parameters for hydrogen and anisotropic ones for other atoms, refinement reduced $R = \sum|\Delta F|/\sum|F_0|$ to 0.042 for 1432 reflections stronger than 2σ and 0.089 including zero-weighted data; $R_w = [\sum w(\Delta F)^2/\sum wF_0^2]^{1/2} = 0.042$. The goodness of fit was 0.97. Scattering factors for spherical hydrogen from Stewart, Davidson, and Simpson[51] and for other atoms from Doyle and Turner[52] and dispersion corrections from Cromer and Liberman[53] were used. Calculations were made with the CDC-7600 computer and programs listed elsewhere.[54]

Kinetics of Equilibration of 1-Thioniabicyclo[4.4.0]decane Tetrafluoroborate (1). The 1:1 mixture of **1a** and **1b** was dissolved in deuteriochloroform or deuteriomethylene chloride (0.33–0.57 g/mL). The solution was sealed in an NMR tube, which was placed in a constant-temperature bath (±0.02 °C) and periodically cooled to room temperature to analyze the isomer ratio by ^{13}C NMR. Several values were corroborated by 360-MHz ^{1}H NMR, and analyses by the two methods corresponded within 2–3%. Rate constants were obtained using the equation

$$\ln[1 - F_t(1 + 1/K)] - \ln[1 - (F_t)_0(1 + 1/K)] = -(k_1 + k_{-1})t$$

where F_t is the mole fraction of trans salt **1a**, $(F_t)_0$ is the initial mole fraction of **1a** (0.50), and K is the equilibrium constant (2.33 ± 0.03).

Table XI

temp, °C	% **1a**	time, h
−23	34.9	0
	20.1	1.0
	12.3	2.0
−33	50.0	0
	33.0	4
	28.8	5

Data were analyzed by plotting $\ln[1 + F_t(1 + 1/K)]$ vs. time; the negative slope of the resulting line is the sum of the rate constants k_1 and k_{-1}. Results are summarized in Table VI.

2-Methoxycarbonyl-1-methylthianium Hexafluorophosphate (13 + 14). A mixture of 2.94 g (14.3 mmol) of trimethyloxonium hexafluorophosphate (Aldrich Chemical Co., Inc.) and 2.52 g (15.7 mmol) of 2-methoxycarbonylpentamethylene sulfide in 10 mL of dry ether is stirred for 7 h at room temperature. Filtration of the mixture gives a 9:1 mixture of **13** and **14** in quantitative yield. Recrystallization from ethanol provides an analytical sample: mp 102–104 °C; ^{1}H NMR (D_2O/Me_2SO-d_6, internal TSP) δ 1.8–2.6 (6 H, m), 2.86 (minor, s, $^+SCH_3$), 3.00 (major, 3 H, s, $^+SCH_3$), 3.2–3.8 (2 H, m), 3.84 (3 H, s, OCH_3). Anal. ($C_8H_{15}F_6O_2PS$) C, H.

A sample of the 9:1 mixture of **13** and **14** was dissolved in a 1:1 mixture of acetone-d_6 and $CDCl_3$ and heated in a sealed NMR tube for 10 h at 110 °C. After this period of time, the ratio of **13**/**14** was 7:3; further heating at 110 °C for 62 h did not alter this ratio.

Kinetics of Inversion of Ylide 15. In three separate flasks were placed a 1:1 mixture of sulfonium salts **1a** and **1b** and sufficient dry THF to make a 0.34 (±0.01) M solution. The solutions were cooled to −72 °C (internal temperature) and a slight excess (5%) of n-butyllithium was added simultaneously to each flask over a 15-min period. By this slow addition there was no noticeable temperature rise. The reaction mixtures were stirred for 1 h at −70 °C to ensure complete formation of the ylide. The three flasks were placed in the constant-temperature bath (±1 °C) and allowed to warm to the desired temperature. When the internal temperature reached that of the constant-temperature bath, one reaction mixture was quenched by addition of aqueous fluoboric acid for an initial ratio (t = 0). The remaining two reaction flasks were kept at constant temperature and quenched after an appropriate amount of time. The solvents were removed in vacuo and the isomer ratios were determined by comparing the ^{13}C resonances of the trans isomer to the corresponding ^{13}C resonances of the cis isomer. Data are tabulated in Table XI. Rate constants were determined in the same manner as that used for equilibration of salt **1a** (vide supra).

2-Methyl-1-thioniabicyclo[4.4.0]decane Salts (17, 18, 19). To a slurry of 102.6 mg (0.420 mmol) of 1-thioniabicyclo[4.4.0]decane tetrafluoroborate (**1a**/**1b** = 1:1) in 1 mL of dry THF, cooled to −72 °C, is added a 10% excess of n-butyllithium. After the mixture is stirred for 1.5 h at −72 °C, 0.5 mL (8 mmol) of methyl iodide is added, giving an immediate precipitate. The reaction mixture is allowed to stir at −72 °C for 0.5 h, then allowed to warm to room temperature over a 1-h period. The solvents are removed and chloroform is added. After filtration, the chloroform is evaporated to obtain 106.9 mg (85–99%, mixture of iodide and tetrafluoroborate salts) of a mixture of salts **17** and **18**, shown by ^{13}C NMR to be present in an approximate equimolar ratio. ^{1}H NMR ($CDCl_3$) δ 1.58 (minor, 3 H, d, J = 6.8 Hz, CH_3), 1.65 (major, 3 H, d, J = 6.6 Hz, CH_3), 1.5–2.8 (12 H, m), 3.5–4.8 (5 H, m). The product was converted to the picrate[8] for analysis. Anal. ($C_{16}H_{21}N_3O_7S$) C, H, N.

Isomer 18. In a similar alkylation, employing 4.08 mmol of salt **1**, the reaction mixture was filtered and a hot solution of 1 g of picric acid in 75 mL of water was added. Filtration yielded 383.4 mg (24%) of a mixture of **17** and **18** (mp 155–159 °C). The solvents were removed from the filtrate and the resulting oil was redissolved in THF and treated with hot aqueous picric acid as above to obtain 180.0 mg (11%) of pure salt **18**: ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.50 (3 H, d, J = 6.6 Hz, CH_3), 1.6 (2 H, m), 1.9 (5 H, m), 2.2 (3 H, m), 2.32 (1 H, d, J = 15 Hz), 2.44 (1 H, br d, J = 10 Hz), 3.45 (1 H, dd, J = −11.5, 2.3 Hz), 3.94 (1 H, ddd, J = −11.5, 12.5, 3 Hz), 4.04 (1 H, tt, J = 12.5, 2 Hz), 4.25 (qdd, J = 12, 6.5, 3 Hz); ^{13}C NMR ($CDCl_3$) δ 53.4, 49.6, 35.9, 33.3, 30.9 (double intensity), 23.8 (triple intensity), 17.4.

Isomers 17 and 19. A slurry of 189.9 mg (0.778 mmol) of salt **1** (X^-

= BF_4^-, **1a/1b** = 1:1) in 2 mL of dry THF is cooled to −23 °C. *n*-Butyllithium (20% excess) is added and the mixture is stirred for 2 h at −23 °C. The ylide solution is cooled to −76 °C and 1 mL (16 mmol) of methyl iodide is added. After several hours of stirring, approximately 5 mmol of dimethoxycarbonium tetrafluoroborate[55] is added and the mixture is stirred at room temperature for 4 h. A few milliliters of methanol is added and the mixture is stirred for 1 h. The solvents are removed and the product is triturated with THF and filtered. The lithium salts are removed by adding chloroform and filtering. ^{13}C NMR (D_2O, external Me_4Si): major isomer (60%) δ 45.1, 44.6, 28.8, 25.4, 22.9 (double intensity), 21.5 (double intensity), 17.3, 16.0; minor isomer (40%) δ 43.8, 38.4, 31.0, 30.7, 28.0, 23.8, 22.3 (double intensity), 18.1, 17.3.

The product is converted to the picrate by adding a hot picric acid solution containing a 10–20% excess of picric acid. ^{13}C NMR ($CDCl_3$): major isomer δ 45.3, 44.7, 29.2, 26.1, 23.3, 22.9, 22.7, 22.1, 17.7, 16.8; minor isomer δ 43.9, 38.6, 31.5, 30.7, 28.4, 24.5 (?), 23.6 (?), 21.5 (?), 18.5, 18.0.

The foregoing mixture of tetrafluoroborate salts **17** and **19** is dissolved in $CHCl_3$ and heated at 110 °C (sealed tube) for 4 days. The solvent is removed and the product analyzed by ^{13}C NMR. The ^{13}C NMR resonances of the major isomer are nearly identical with those of salt **18** (X^- = picrate). ^{13}C NMR ($CDCl_3$): major isomer (60%) δ 53.5, 49.9, 35.9, 32.7, 31.1, 30.3, 23.8, 23.5, 23.3, 16.9; minor isomer (40%) δ 43.6, 38.2, 31.1, 28.4, 24.3, 21.5, 18.4, 17.7.

2-(4-Epoxy-5-methylhexyl)thiane (20). A slurry of 93.3 mg (0.382 mmol) of 1-thioniabicyclo[4.4.0]decane tetrafluoroborate in 1 mL of dry THF is cooled to −72 °C. A 20% excess of *n*-butyllithium is added and the solution is stirred for 1 h at −72 °C. To the ylide solution is added 1 mL (14 mmol) of purified acetone. The reaction mixture is allowed to slowly warm up to room temperature and is added to 100 mL of water. After extraction with ether (2 × 100 mL), the organic layers are combined and washed with a saturated salt solution, then dried over K_2CO_3. Removal of the solvents and bulb-to-bulb distillation yields 48.4 mg (59%) of sulfide **20.** ^1H NMR (CCl_4) δ 1.22 (3 H, s, CH_3), 1.25 (3 H, s, CH_3), 1.2–2.3 (12 H, m), 2.4–2.8 (3 H, m). Anal. ($C_{12}H_{22}OS$) C, H.

2-(2-Hydroxyisopropyl)-1-thioniabicyclo[4.4.0]decane Tetrafluoroborate (21a, 22a). To a slurry of 758.3 mg (3.11 mmol) of **1** in 5 mL of dry THF, cooled to −72 °C, is added a 20% excess of *n*-butyllithium. After stirring for 1 h at −72 °C, a large excess of acetone is added and the solution is stirred for 4 min; the reaction is then quenched by addition of aqueous fluoboric acid. The solvents are removed and the salt is dried in vacuo overnight. Chloroform is added and the lithium salts are filtered. The $CHCl_3$ is removed and the product is dissolved in THF, leaving behind 24.0 mg (0.10 mmol) of starting material. Evaporation of solvent yields an equimolar mixture of **21a** and **22a.** ^{13}C NMR ($CDCl_3$): **21a,** δ 73.5, 66.7, 54.6, 42.6, 31.5, 31.0, 28.3, 27.8, 24.4, 23.9 (double intensity), 23.7; **22a,** δ 72.1, 61.9, 44.6, 29.9 (?), 28.9 (?), 27.5 (?), 23.5, 23.4, 19.5, 17.6. Crystallization of this mixture from THF yields 303.2 mg (32%) of analytically pure **22a:** mp 178.5–179.0 °C; ^1H NMR ($CDCl_3$) δ 1.32 (3 H, s, CH_3), 1.45 (3 H, s, CH_3), 1.4–2.6 (13 H, m), 3.4–4.3 (4 H, m). Anal. ($C_{12}H_{23}BF_4OS$) C, H.

A solution of 189 mg of the 1:1 mixture of salts **21a** and **22a** (X^- = BF_4^-) is dissolved in $CDCl_3$ and heated at 110 °C (sealed NMR tube) for 5 h. The ^{13}C NMR spectrum showed that isomer **22a** had disappeared. ^{13}C NMR ($CDCl_3$) δ 73.6, 66.7, 54.5, 42.5, 31.7, 31.3, 28.3, 28.1, 24.6, 23.9 (triple intensity).

2-(2-Oxyethoxycarbonylisopropyl)-1-thioniabicyclo[4.4.0]decane Tetrafluoroborate (21b, 22b, 23b). Method A. To a flask containing 219.3 mg (0.897 mmol) of salt **1** (X^- = BF_4^-) and 3 mL of dry THF, cooled to −72 °C, is added an equivalent amount of *n*-butyllithium. The reaction mixture is stirred at −72 °C for 2 h, at which time 0.75 mL (10 mmol) of acetone is added. After stirring for 5 min, 1 mL (10 mmol) of ethyl chloroformate (distilled from potassium carbonate) is added. The solution is allowed to stir for 0.5 h at −72 °C, then allowed to warm to room temperature. The resulting salt is dissolved in water and extracted with ether. The water is removed at reduced pressure. Chloroform is added and any undissolved material is removed by filtration. Removal of the $CHCl_3$ yields 261.5 mg (78% as BF_4^-, 90% as Cl^-) of product. The product was converted to the tetrafluoroborate by ion exchange and recrystallized from THF to give analytically pure carbonate: mp 155–157 °C; ^1H NMR (360 MHz, $CDCl_3$) δ 1.28 (3 H, m, CH_3), 1.62 (3 H, s, CH_3, major isomer), 1.67 (3 H, s, CH_3, minor isomer), 1.70 (3 H, s, CH_3, minor isomer), 1.72 (3 H, s, CH_3, major isomer), 1.8–2.0 (6 H, m), 2.0–2.4 (6 H, m), 3.16 (1 H, m, minor isomer), 3.57 (1 H, broad t, J = 13 Hz, minor isomer), 3.83 (1 H, m), 4.13 (3 H, m), 4.35 (1 H, broad d, J = 12 Hz, major isomer); ^{13}C NMR ($CDCl_3$) **21b** δ 151.4, 84.2, 63.4, 63.0, 54.3, 37.8, 27.6, 26.0, 24.1, 23.0, 20.1; **22b** δ 151.8, 82.5, 63.4, 60.4, 45.0, 30.1, 27.5, 26.8, 25.4, 23.9, 23.3, 22.8, 19.3, 18.6, 13.5; **23b** δ 151.5, 84.4, 62.6, 55.0, 44.6, 35.3, 34.1, 28.3, 28.0, 24.2, 21.8, 16.9. Anal. ($C_{15}H_{27}BF_4O_3S$) C, H.

Method B. A slurry of 891.0 mg (3.65 mmol) of salt **1** (X^- = BF_4^-) in 5 mL of dry THF is cooled to −23 °C. *n*-Butyllithium (10% excess) is added and the mixture is stirred for 2 h keeping the temperature between −20 and −23 °C. The reaction mixture is cooled to −72 °C and 2.7 mL (37 mmol) of acetone is added. After 5 min of stirring at −72 °C, 0.4 mL (4 mmol) of ethyl chloroformate is added; the solution is stirred for 0.5 h and allowed to warm to room temperature. The solvents are removed at reduced pressure and CH_2Cl_2 is added. Any material that does not dissolve is removed by filtration. The CH_2Cl_2 is evaporated and the product is triturated with ether. The product is dried in vacuo to yield 880 mg (65–75%): IR ($CHCl_3$) ν_{max} 1730, 1000–1100 cm^{-1}; ^{13}C NMR ($CDCl_3$), **22b** (75%) δ 151.8, 82.5, 63.4, 60.4, 45.0, 30.1, 29.2, 27.5, 26.8, 25.4, 23.9, 23.3, 22.8, 13.5; **23b** (25%) δ 151.5, 84.4, 62.6, 55.0, 44.6, 35.3, 34.1, 28.3, 28.0, 25.7, 21.8, 18.6, 16.9.

1,10-Dimethyl-1-thioniabicyclo[4.4.0]decane Picrate (24 + 25). Method A. To a slurry of 212.4 mg (0.870 mmol) of salt **1** (X^- = BF_4^-) in 2 mL of dry THF, cooled to −76 °C, is slowly added 3 equiv of *tert*-butyllithium. After the mixture is stirred for 1 h at −76 °C, 2 mL (32 mmol) of methyl iodide is added and the mixture is stirred for 0.5 h at −72 °C. The solvents are evaporated and the crude product is converted to the picrate to yield 42.4 mg (12%) of dimethyl isomers **24** and **25:** ^1H NMR (D_2O, external Me_4Si, 60 MHz) δ 1.54 (d, J = 7 Hz, CH_3), 1.60 (d, J = 6 Hz, CH_3), 1.5–2.4 (m), 3.5–4.2 (m); ^1H NMR (360 MHz, D_2O) δ 1.54 (3 H, d, J = 7.0 Hz, CH_3), 1.60 (3 H, d, J = 6.5 Hz, CH_3), 1.6–2.3 (12 H, m), 3.46 (1 H, m), 3.78 (1 H, m), 3.88 (1 H, tt, J = 7.8, 3.9 Hz), 3.95 (1 H, t, J = 7 Hz); ^{13}C NMR ($CDCl_3$) **24** δ 53.9, 50.2, 34.9, 31.0, 23.7, 20.5; **25** 42.4, 41.0, 28.4, 26.5, 18.0, 17.2. Anal. ($C_{17}H_{23}N_3O_7S$) C, H, N.

Method B. A slurry of 281.3 mg (1.15 mmol) of salt **1** (X^- = BF_4^-) in 2 mL of dry THF is cooled to −72 °C and 3 equiv of *tert*-butyllithium is added. After the mixture is stirred at −65 to −70 °C for 1 h, an excess (2 mL) of methyl iodide is added and the mixture is stirred for 15 min. Several drops of 48% fluoboric acid is added and the solvents are removed. A hot picric acid solution is added to yield 58.8 mg (12%) of salt **24:** ^{13}C NMR ($CDCl_3$) δ 42.2, 41.0, 28.4, 26.5, 18.0, 17.2.

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Supplementary Material Available: Tables of thermal parameters and structure factors for compound **9;** 360-MHz ^1H NMR spectra of compounds **1a, 1b,** and **9** (14 pages). Ordering information is given on any current masthead page.

References and Notes

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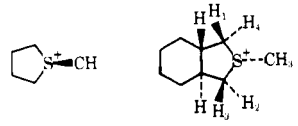
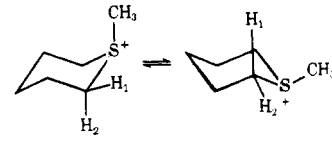


vi vii

The relative rates of deprotonation of the four ring protons in vii are H_1, 1; H_2, 700; H_3, ca. 90; H_4, ca. 90.[34b] Because the NMR signals of H_3 and H_4 overlap, separate exchange rates were not determined, although it is asserted that they appear to exchange at about the same rate. Examination of a scale model of vii[31] reveals the relevant dihedral angles to be H_1, 5°; H_2, 100°; H_3, 20°; H_4, 125°. Thus, it is clear that H_2 should exchange most rapidly and H_1 least rapidly, with H_3 and H_4 being of intermediate acidity. Since Fava and co-workers have shown that the more flexible salt vi exists in a conformation with maximum puckering at C_3–C_4 and minimum puckering at C_2–S–C_5,[34a] the same argument may be used to explain the enhanced acidity of the protons syn to methyl in this salt. Furthermore, this argument serves to explain why H_2 in vii and the syn protons in vi are more acidic than either ring proton in salt viii.[33a] For compound viii, which may



viiia viiib

exist in conformations viiia and viiib ($\Delta G° = 0.0$ kcal mol^{-1}),[33b] estimated dihedral angles for the C_1–H and C_2–H bonds are 55, 60° and 55, 175°, respectively. Experimental dihedral angles for the analogous 4-*tert*-butyl salts[33b] are 51, 64° and 57, 175°, respectively.

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