1.55 (s, 3 H) (singlet overlaps doublet), 1.7–2.1 (m, 1 H), 5.2 (m, 1 H); ^{13}C NMR δ 142 (s), 121 (s), 36 (t), 20 (s), 18 (s), 17 (s).

Oxidation of (*E*)-(*R*)-4-Deuterio-3-methyl-2-pentene. In a 10-mL flask, 185 mL (1.67 mmol) of SeO_2 was dissolved in 5 mL of *tert*-butyl alcohol. When all of the solid had dissolved, 500 μL (350 mg, 4.17 mmol) of *E* deuterio olefin [98/2 *E*/*Z*; $[\alpha]_D$ −0.91 (*c* 35, *tert*-butyl alcohol)]. The reaction was monitored by VPC. After 24 h the yield as estimated by VPC was 30%, of which 87% was the desired secondary alcohol and less than 2% was the corresponding ketone. The remaining 11% of the product was unidentified, but it is probably the result of oxidation at CH_3. Further VPC analysis revealed that the allylic alcohol was 97% *E* and 3% *Z*.

At this point the reaction mixture was poured into water and extracted with ether. The water was then saturated with salt and extracted again. The ether extracts were dried with K_2CO_3, and the ether was removed by distillation and worked up as previously indicated, $[\alpha]_D$ −0.33. (The product was not purified by preparative VPC since dehydration was noted under preparative conditions.)

Analysis of the Allylic Alcohol. Proton NMR was used to determine the deuterium content of the product. This was done by comparison of the integrals for the singlet quartet signals due to the vinyl and methine protons. The methine quartet was overlapped by a singlet, probably due to the primary alcohol derived from oxidation at methyl. Addition of approximately 5–10 mol % of $Pr(fod)_3$ shift reagent cleanly separated the two peaks.

Integration of the shifted spectrum led to a measure for the isotope effect of 4.0 ± 0.25. Bulb-to-bulb distillation separated the product from the shift reagent.

MTPA Ester of the Allylic Alcohol. The alcohol was dissolved in 2.0 mL of carbon tetrachloride and 2.0 mL of dry pyridine. To this was added 350 μL of (+)-methoxy(trifluoromethyl)phenylacetyl chloride, $[\alpha]_D^{20}$ +132.9 [*c* 7.5, CCl_4 (obtained from H. S. Mosher and co-workers)]. A precipitate formed immediately upon addition of the acid chloride. After stirring at room temperature overnight, 180 μL of (dimethylamino)propylamine was added to remove excess acid chloride and any anhydride formed during the reaction. This mixture was stirred for 90 min and then diluted with ether. The ether solution was washed twice with cold 5% HCl, once with saturated Na_2CO_3, and once with brine. The ether was then dried with $MgSO_4$. Following removal of the ether on the rotary evaporator, CCl_4 was added and the solution reconcentrated. When proton NMR revealed the presence of MTPA anhydride (extra methoxy peak upfield from the ester methoxy peak), the product was redissolved in 5 mL of CCl_4 and treated with 50 μL of (dimethylamino)propylamine for 1 h, followed by a repetition of the workup above. NMR δ 1.5–1.8 (m, 9 H), 3.55 (br s, 3 H), 5.5 (q, 1.3 H), 7.5 (m, 5 H).

Analysis of the MTPA Esters. Three separate NMR analyses of the diastereomeric MTPA esters were undertaken. Carbon-13 spectra were taken at 25.1 MHz by using a 30–45° pulse with a 0.8-s acquisition time and a 1.2-s pulse delay. While several peaks showed broadening due to the presence of diastereomers, only the carbinol carbon (at about 76 ppm downfield from Me_4Si) clearly showed a doublet due to the existence of diastereomers. Examination of the spectrum allowed an estimate of 3.0 to be made for the *R*(H)/*S*(H) ratio. Only carbons bearing hydrogen are observed in this spectrum because the deuterium-bearing carbon signals are reduced in intensity (no NOE) and split into triplets.

Analysis of the fluorine-19 spectrum taken at 56 MHz showed an overlapping doublet. Addition of $Eu(fod)_3$ shifted both peaks upfield and split them farther apart so that they were base-line separated after about 20 mol % of shift reagent had been added. Integration of the shifted spectrum led to a value of 2.0 ± 0.1 for the *S*/*R* ratio.

Addition of more $Eu(fod)_3$ up to about 40–50 mol % also separated the diastereomeric methoxy group signals in the proton NMR spectrum. Data from this integrated spectrum supported the fluorine-19 results.

Oxidation of (*Z*)-4-Deuterio-3-methyl-2-pentene. In a 10-mL flask, 183 mg (1.67 mmol) of SeO_2 was dissolved in 5 mL of *tert*-butyl alcohol as before. To this was added 485 μL (348 mg, 4.14 mmol) of *Z* olefin that VPC analysis showed was 5% low boiling point impurity, 94% *Z* olefin, 1% *E* olefin, $[\alpha]_D$ +0.66. After 48 h, the yield of the oxidation as assayed by VPC was 27%, of which 78% was secondary alcohol, 2% was ketone, and 17% was due to oxidation at methyl. The alcohol was shown to be 95% *E* and less than 4% *Z*. The product was worked up as before. Integration of the $Pr(fod)_3$-shifted proton spectrum gave an isotope effect of 3.8 ± 0.4. The alcohol was recovered by bulb-to-bulb distillation and converted to the (+)-MTPA ester as before. Shift studies using $Eu(fod)_3$ gave an *R*/*S* ratio of 2.1 ± 0.2 and an estimate of the *S*(H)/*R*(H) ratio of 3.7.

Acknowledgment. This work was supported by the National Science Foundation by Grants MPS-73-05049A01 (to Stanford University) and CHE 75-17816/CHE 77-12744 (to Case Western Reserve University).

Registry No. **1**, 616-12-6; **1**-*d*, 71927-52-1; **2**, 922-62-3; **2**-*d*, 71927-53-2; **3**, 24652-51-5; **4**, 64683-06-3; **5**, 1567-73-3; **6**, 6622-76-0; **7**, 69432-94-6; **8**, 71831-22-6; **8** mesylate, 71831-23-7; **9**, 71831-24-8; **10**, 1787-45-7; **11**, 513-35-9; **12**, 687-47-8; **12** mesylate, 63696-99-1; **13**, 71831-25-9; **14**, 71831-27-1; 2-ethyl-1-butene, 760-21-4; (*E*)-1,1-dideuterio-2-(trideuteriomethyl)-2-buten-1-ol, 71831-28-2; (*E*)-2-methyl-2-buten-1-ol, 497-02-9; ethyl iodide, 75-03-6; 2-butanone, 78-93-3.

Protonic and Conformational Equilibria of 1,3-Dithiaalkanes and Their Congeners in Highly Acidic Media

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Disulfides of the structure $CH_3S(CH_2)_nSCH_3$ are fully diprotonated in FSO_3H when $n = 2$ or 3 but are only monoprotonated when $n = 1$. These compounds were examined as models for cyclic disulfides. The ^{13}C resonances of 1,3-dithiane in FSO_3H have been assigned by comparison with isotopic modifications containing deuterium in the 2, 5, or 4/6 positions. The same deuterated modifications permit a more complete assignment of the ^{1}H spectra. In FSO_3H, there are approximately equal amounts of a monoprotonated form of 1,3-dithiane and of a second form that is probably the ring-opened sulfonium ion or a decomposition product therefrom. Similar phenomena are observed in 1,3-diselenane, 1,3,5-trithiane, 1,3-dithiolane, and other saturated group 6 heterocycles.

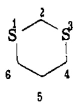
Protonation of dithiaalkanes in which the sulfur atoms are separated by one or more carbon atoms (eq 1) leads to a number of kinetic and conformational consequences. First, protonation can occur on one or both sulfur atoms,

0022-3263/79/1944-4689$01.00/0

$$\mathrm{RS(CH_2)_nSR} \xrightarrow{\mathrm{H^+}} \mathrm{R\overset{+}{S}(H)(CH_2)_nSR} \xrightarrow{\mathrm{H^+}} \mathrm{R\overset{+}{S}(H)(CH_2)_n\overset{+}{S}(H)R} \quad (1)$$

depending on the acidity of the medium and on the specific characteristics of the substrate. Second, the rate of exchange of the proton on sulfur can be rapid or slow on the NMR time scale, depending on the temperature of observation and again on the specific characteristics of the substrate. Chemical shifts and coupling constants are averaged when the exchange rate is rapid. Third, the proton on sulfur in cyclic dithiaalkanes can have conformational properties such as axial or equatorial location in six-membered rings. Fourth, the structure of 1,3-dithiane appears to have protonation properties that are peculiar to the cyclic system.[2]

We have recently discussed the results of the protonation of 1,3-dithiane (1) in fluorosulfonic acid (FSO_3H) in



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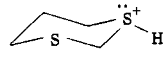

1-e

terms of the above four principles.[2] Monoprotonation was predominant, but a number of resonances from a second species were present. Exchange of the sulfur proton with the medium was very rapid at +70 °C. By 0 °C, exchange was slow enough that conformational biasing occurred, with the result that geminal axial/equatorial protons produced separate resonances. The monoprotonated species was mainly equatorial SH (1-e). The most unusual observation was that at +70 °C, proton exchange was rapid enough to average all geminal nonequivalencies but was still slow enough to retain separate identities at the 4 and 6 positions. We explained this latter observation as resulting from exclusive reprotonation at the same sulfur atom after exchange with the medium. A possible mechanism for such a process is maintenance of hydrogen bonds between the substrate and the solvent throughout the exchange process, so that the exchanging proton is not lost to the greater medium. We termed this phenomenon "selective kinetic equalization of chemical shifts", since axial/equatorial chemical shifts were averaged but the 4- and 6-positions were not.[2]

Because of the ramifications of these observations in a number of fields, including dynamic NMR spectroscopy, conformational analysis, disulfide chemistry, and hydrogen bonding, we have broadened this study on three fronts. (1) We have studied the protonation of acyclic disulfides in order to determine what kinetic properties are specific to the ring structure. (2) In order to clarify the identity of a number of ^1H and ^{13}C resonances from 1,3-dithiane in FSO_3H,[2] we have prepared an extensive series of deuterated modifications of 1. Examination of these simplified spectra enables us to assign most of these resonances. (3) In order to determine the scope of these observations, we have also studied the protonic and conformational equilibria in FSO_3H for numerous other heterocycles, including five- and six-membered 1,3-dithia-, dioxa-, and diselenaalkanes. We report these three areas of research in this paper.

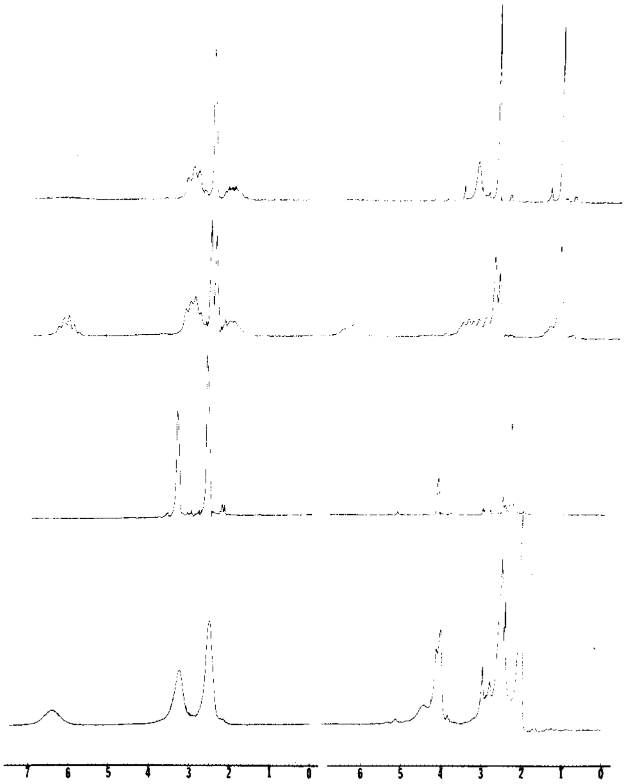

Figure 1. The 60-MHz ^1H spectra in FSO_3H/SO_2 of (upper left pair) 1,3-di(methylthio)propane (2) at −10 and −40 °C, (upper right pair) 2,2-dimethyl-1,3-di(methylthio)propane (3) at −15 and −45 °C, (lower left pair) 1,2-di(methylthio)ethane (4) at −10 and −60 °C, and (lower right pair) di(methylthio)methane (5) at −10 and −60 °C.

Acyclic Dithiaalkanes

Sulfides and mercaptans protonate in FSO_3H to give the expected spectra of the corresponding sulfonium salts.[3] We have examined the dithiaalkanes **2–5** in order to es-

$CH_3SCH_2CH_2CH_2SCH_3$ **2**
$CH_3SCH_2C(CH_3)_2CH_2SCH_3$ **3**
$CH_3SCH_2CH_2SCH_3$ **4**
$CH_3SCH_2SCH_3$ **5**

tablish the role of the second sulfur atom in the absence of the conformational requirements imposed by cyclic compounds such as 1. As before, we examined the substrates in FSO_3H and in FSO_3H/SO_2 and found no significant difference between the two media. We include SO_2 when spectra below about 0 °C are needed.

In 1,3-di(methylthio)propane (2) three carbon atoms separate the two sulfurs. The ^1H spectrum of the compound without solvent contains an unsplit singlet for the thiomethyl protons and a second order $AA'B_2B_2'$ pair of multiplets (1/2) for the three methylene groups. At −10 °C in FSO_3H/SO_2, the spectrum is very similar, although somewhat broadened (Figure 1, top left). At and above this temperature, exchange of the proton with the medium is rapid on the NMR time scale. As the temperature is lowered, the methyl singlet broadens and splits into a doublet at −40 °C. At the same time, the resonance of the S proton appears at about δ 6 as a sextet. Proton exchange is sufficiently slow to permit the coupling ($J \sim 8$ Hz) to

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(1) (a) This work was supported by the National Science Foundation (Grant Nos. CHE77-08384 and CHE79-05542) and by the donors of the Petroleum Research Fund, administered by the American Chemical Society; (b) Petroleum Research Fund Postdoctoral Fellow, 1977–78, on leave of absence from the Institute of Drug Research, Pharmaceutical Faculty of the Medical Academy, Lódź, Poland.

(2) Lambert, J. B.; Vulgaris, E.; Featherman, S. I.; Majchrzak, M. *J. Am. Chem. Soc.* **1978**, *100*, 3269–3274.

(3) Olah, G. A.; O'Brien, D. H.; Pittman, C. U., Jr., *J. Am. Chem. Soc.* **1967**, *89*, 2996–3001.

be observed between the proton on sulfur and the five adjacent protons. Double irradiation of the S proton resonance causes the methyl doublet to collapse to a singlet. The activation energy for proton exchange is about 13 kcal mol^{-1}. The low and high temperature extremes are shown in Figure 1 (upper left pair). All spectral changes for the acyclic dithiaalkanes **2–5** are completely reversible. Integration of the S proton resonance demonstrates that the molecule is essentially all diprotonated. Although *dl* and meso forms are possible in the diprotonated substrate, the spectrum clearly shows only one diastereoisomer or (more likely) two with superimposed resonances.

In order to clarify any changes in the methylene resonances, we also examined 2,2-dimethyl-1,3-di(methylthio)propane (**3**). Its spectrum in CCl_4 contains the expected three singlets. Similarly, at -15 °C in FSO_3H/SO_2, there are three singlets, indicative of rapid proton exchange. Lowering the temperature to -45 °C produces no change in the geminal dimethyl resonance. The *S*-methyl resonance splits into a doublet, the methylene resonance splits into an octet, and a sextet appears for the S proton at about δ 6.8. The high and low temperature spectra are given in Figure 1 (upper right pair). The situation is the same as that for **2**. At low temperatures, S proton exchange is sufficiently slow to permit observation of the vicinal HSCH couplings. In addition, the chirality of the $-CH_2\ddot{S}^{+}HCH_3$ group conveys nonequivalence to the adjacent methylene protons. A four-peak AB spectrum is split into eight by the vicinal coupling to the S proton. Irradiation of the S proton resonance collapses the methyl doublet to a singlet and the methylene octet to an AB quartet (J = 12 Hz). There is no sign of separate peaks from diastereomers. The activation energy to proton exchange again is about 13 kcal mol^{-1}. Integration of the S proton resonance shows that this species also is diprotonated.

Examination of these two di(methylthio)propanes shows that two sulfur atoms separated by three carbons act essentially independently. The solvent FSO_3H/SO_2 protonates both sulfur atoms, thereby creating chiral centers. Proton exchange with the medium is fast at -10 °C, with an activation energy of about 13 kcal mol^{-1}.

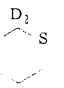
In 1,2-di(methylthio)ethane (**4**), the sulfur atoms are now separated by two carbons, and any interaction between the two charged centers should be larger than that in **2** and **3**. The neat spectrum and the -10 °C FSO_3H/SO_2 spectrum contain a 3/2 pair of singlets. As the temperature is lowered in FSO_3H/SO_2, these peaks broaden, and the S proton resonance appears at about δ 6.4. No fine structure from HSCH coupling is observed, even at -70 °C. The medium may be too viscous to permit observation of the coupling at -60 °C. Proton exchange here has a slightly lower activation energy (no more than 12 kcal mol^{-1}) than that in the (methylthio)propanes, **2** and **3**. The high and low temperature spectra are given in Figure 1 (lower left pair). Integration clearly shows that the molecule is diprotonated, so that sulfurs separated by two carbon atoms act essentially independently. The breadth of the peaks obscures any diastereomeric differences.

Di(methylthio)methane (**5**) provides the best acyclic model for 1,3-dithiane (**1**), since the two sulfurs are separated by only a single carbon. The neat spectrum and the FSO_3H/SO_2 spectrum at -10 °C contain the expected 3/1 pair of singlets. As the temperature is lowered in FSO_3H/SO_2 to -60 °C, the methyl singlet splits into at least two peaks (unfortunately obscured by some small impurity peaks), the methylene singlet splits into at least a doublet, and the S proton resonance appears at δ 4.4. Differences from the previously discussed spectra of **2–4** are threefold. (1) The S proton resonance (identified in FSO_3D) integrates to unity, so that the molecule is only monoprotonated. (2) The splitting between the two methyl peaks is about 30 Hz, far too large to be a coupling. Consequently, there must be two types of methyls, one attached to the protonated sulfur and the other attached to the unprotonated sulfur. As in **4**, the HSCH coupling is not observable. (3) The S proton resonates at almost 2 ppm higher field than in the other cases. The high and low temperature spectra are given in Figure 1 (lower right pair). The activation energy for proton exchange is about 12 kcal mol^{-1}.

The spectral evidence is clear, that a separation of only one carbon atom between the two sulfurs generates sufficient Coulombic repulsion that only monoprotonation takes place. Furthermore, rapid exchange of the S proton causes complete exchange of the methyl resonances, so that only a singlet is observed at -10 °C (in contrast to the analogous case for 1,3-dithiane). When the separation of sulfur atoms is larger, the molecules are diprotonated.

Deuterated Modifications of 1,3-Dithiane

Our examination of 1,3-dithiane in FSO_3H left a number of questions unanswered.[2] Among these, two were foremost. (1) In addition to the peaks for the monoprotonated 1,3-dithiane, a full set of ^1H resonances was observed for a second species, which we termed an impurity or the "open chain isomer". What is the actual nature of this species? (2) The ^{13}C spectrum was temperature independent, but none of the peaks could be assigned. What are the ^{13}C assignments? To answer both of these questions, we had recourse to a series of deuterated modifications of 1,3-dithiane (**6–10**).



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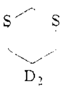

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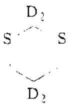

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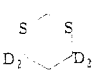

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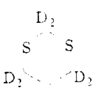

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The assignment of the ^{13}C peaks followed directly from the disappearance of peaks to which deuterium was attached, because of the greatly altered relaxation times. Thus in the fully protonated version, peaks were observed at 63.0, 55.7, 51.1, 50.1, 46.7, 39.6, 32.5, and 25.8 ppm. In 2-deuterated materials (**6**, **8**, and **10**), the peaks at 55.7 and 51.1 dropped out, so that these resonances come from the 2-carbons in the two respective species in solution. In 5-deuterated materials (**7** and **8**), the peaks at 39.6 and 25.8 dropped out, so that these resonances come from the 5-carbons. Finally, in 4,6-deuterated materials (**9** and **10**), the peaks at 63.0, 50.1, 46.7, and 32.5 dropped out, so that these resonances come from the 4- and 6-carbons. For each carbon there are two resonances, corresponding to the monoprotonated species and the second species. Furthermore, for the 4- and 6-carbons, there are four total resonances, two for each of the species. Thus the 4- and 6-carbons must be nonequivalent in both species. This observation corroborates our earlier observation that the 4- and 6-methylene protons remain nonequivalent.[2] The concentrations of the two species in solution appear to be very similar, so that assignment of the ^{13}C peaks to the respective species is not possible from intensity considerations.

As mentioned before, the ^{13}C spectrum is totally independent of temperature over the same range (−60 to +70 °C) that registers enormous alterations in the ^1H spectrum. The dynamic processes therefore cannot alter the overall symmetry of the carbon skeleton. These observations are consistent with ring reversal equilibria, since this processs averages axial and equatorial ^1H resonances but has no effect on the carbon skeleton. Protonic equilibria also would cause no change, provided that the protons depart from and return to the same sulfur.

For the ^1H spectra, the most revealing deuterated modifications were **8** and **9**, which respectively isolate the resonances of the 4- and 6-protons and the 2- and 5-protons. The remaining modifications were confirming but duplicative. We will discuss and illustrate the spectra only of **8** and **9** (Figures 2 and 3). For these derivatives and all others, including the fully undeuterated form, we observed that protonation appears to occur slowly on the laboratory time scale below −60 °C. In fact, the ^1H spectrum of 1,3-dithiane mixed with FSO_3H/SO_2 at this temperature is identical with that of unprotonated material.[4] As the temperature is raised, these resonances slowly disappear and are replaced by the set of resonances discussed in the previous paper.[2] By −20 °C, the replacement is complete and irreversible. Lowering the temperature again to −60 °C does not regenerate the unprotonated 1,3-dithiane resonances. These observations result from the very low basicity of the dithiane substrate. It is noteworthy that the resonances from monoprotonated substrate and the "open chain" material develop simultaneously under these conditions.

The spectra from modification **9** (4,6-deuterated) are given in Figure 2. There are two singlets, respectively at about δ 2.0 and 2.7, that must come from the 5-protons. They remain unsplit over the entire temperature range from +50 to −50 °C. The intensities are essentially equal, so that the monoprotonated species and the other species must be in about equal concentrations. The resonances from the 2-protons are more complex. The high temperature singlet at δ 4.8 from the 2-protons in the monoprotonated species becomes a very clear AB quartet by 0 °C. Slowing of proton exchange brings about a biased equilibrium. Since sulfur inversion is certainly slow at 0 °C,[5a] the 2-axial and 2-equatorial protons must give distinct resonances, with the appropriate geminal coupling. We have made similar observations in numerous other systems.[5b] This AB quartet remains unchanged at lower temperatures.

The analogous resonances from the second species in solution are more complex. At the high temperature extreme (60 °C), there are at least three peaks close to the 2-proton (monoprotonated) singlet and possibly a fourth under this singlet. All of these resonances pass through a coalescence at about 35 °C, with the monoprotonated singlet proceeding to the AB quartet and the other peaks resharpening also at 0 °C. In the 60-MHz spectrum, three small resonances are visible at lower field than the AB quartet. Clearly, the integration of these peaks is insufficient, so that additional peaks must be obscured by the

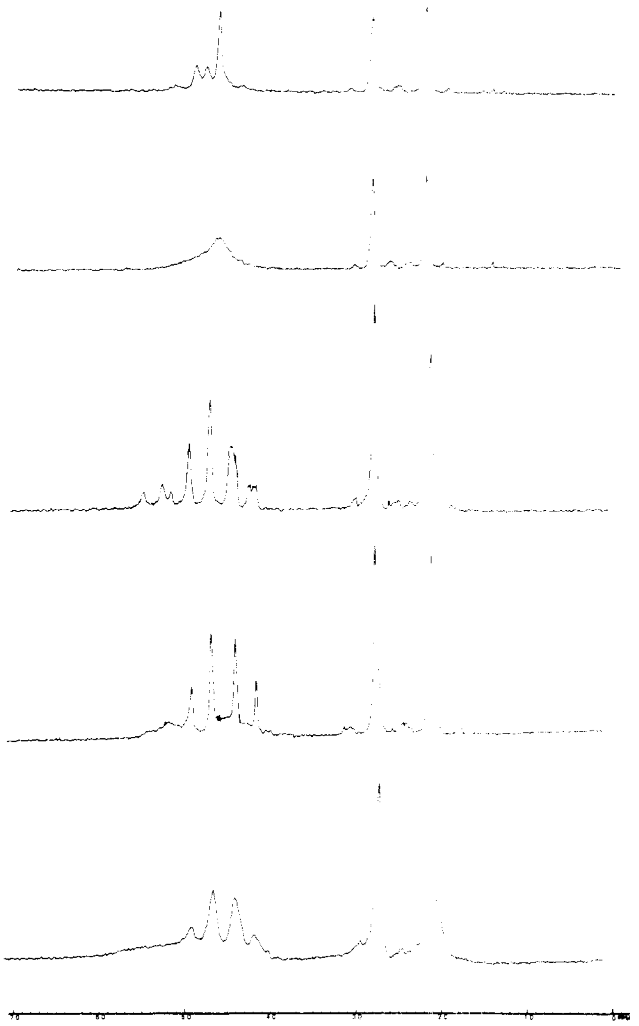

Figure 2. The 60-MHz ^1H spectrum of 1,3-dithiane-*4,4,6,6-d*$_4$ (**9**) in FSO_3H/SO_2 as a function of temperature: (bottom to top) −40, −20, 0, 34, and 50 °C.

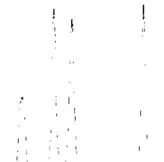

Figure 3. The 60-MHz ^1H spectrum of 1,3-dithiane-*2,2,5,5-d*$_4$ (**8**) in FSO_3H/SO_2 at −10 (bottom) and 50 (top) °C.

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(4) A referee has suggested that the −60 °C material is the monoprotonated material and that both of the other materials are unspecified decomposition products. However, we recover up to 50% of 1,3-dithiane at room temperature, and the low temperature material is completely gone after several minutes at −40 °C or almost instantaneously at −10 °C. No 1,3-dithiane would have been recovered if the −60 °C material was monoprotonated and had decomposed at higher temperatures. Furthermore, each resonance at −60 °C superimposes perfectly on its unprotonated analogue in $CDCl_3$. Protonation should have introduced new couplings, altered the magnitudes of old couplings, or changed second order effects, as we observed on protonation of **2**–**5**. Third, the ^1H chemical shifts of the resonances assigned to the monoprotonated species show remarkable agreement with those of the methylated analogue, 1-methylthianium salts, as pointed out in ref 2. Finally, the spectral changes seen in Figure 2 are best explained by a ring structure.

(5) (a) Lambert, J. B. *Top. Stereochem.* 1971, *6*, 19–105. Slow inversion about trivalent sulfur is well substantiated in other systems, such as 1-methylthianium iodide[2] and thiane 1-oxide.[5b] (b) Lambert, J. B.; Keske, R. G.; Weary, D. K. *J. Am. Chem. Soc.* 1967, *89*, 5921–5924.

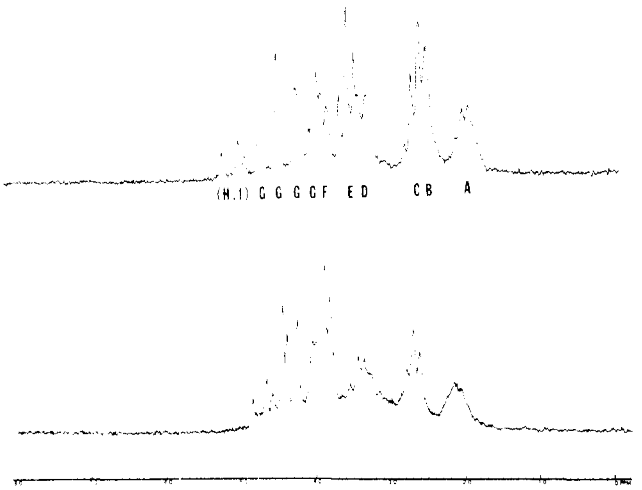


Figure 4. The 60-MHz ^1H spectra of 1,3-dithiane (1) (top) in FSO_3H at 0 °C and 1,3-diselenane (14) (bottom) in FSO_3H at 20 °C.

AB quartet. Indeed, the 270-MHz spectrum reveals several other peaks within the AB quartet. Interestingly, these three lowest field peaks pass through a second coalescence at about -30 °C, while the AB quartet remains quite sharp.

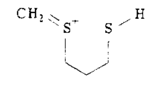
In our original interpretation,[2] we assigned some of these peaks (15%) to a diprotonated species. It is clear from the rather clean spectrum at 0 °C that there simply are no other ring resonances to go with the previously assigned diprotonated 2-proton resonances. Whereas we had discussed the undeuterated spectrum in terms of three species,[2] monoprotonated, diprotonated, and "open chain", it is apparent that there are only two major species in solution, as is clearly indicated by the ^{13}C spectrum and by only two peaks from the 5-protons. What we had assigned to the diprotonated form must in fact be attributed to the same species that we designated "open chain". We had assigned peaks A, B, D, and G to the monoprotonated form, peaks C, E, F, and H to the "open chain" form, and I to the diprotonated form.[2] In fact, peaks C, E, F, H, and I must all belong to the "open chain" species, and resonances H and I both correspond to the 2 protons. (See Figure 4 for the lettering system.)

It is extremely significant that the 2-protons of the second species do not coalesce to a singlet at +60 °C, as would be demanded of any simple diprotonated species. This observation is critical in any structural assignment for the second species.

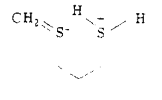
Figure 3 shows the spectra for 8, in which only the 4- and 6-protons remain. At +70 °C, there are four singlets. Thus the 4- and 6-protons, like the 4- and 6-carbons, are nonequivalent at fast proton exchange in both the monoprotonated form and the second species. As the temperature is lowered, the two higher field singlets, assigned to the monoprotonated form, become AB quartets. The slowing of proton exchange, as mentioned above, results in a biased equilibrium, in which axial and equatorial protons are nonequivalent. Thus in the deuterated derivative, the 4- and 6-protons have the same pattern as the 2-protons for the monoprotonated species, except that the AB chemical shift difference is somewhat smaller. The two lower field peaks are nearly independent of temperature, as expected for an open chain structure lacking axial/equatorial locations. The δ 4.0 singlet remains unchanged (this peak was a multiplet in the undeuterated material, which was temperature independent even at 100 and 270 MHz[2]). The resonance at lowest field is much broader, but there is no coalescence at higher temperatures, so that a ring structure is not needed.

The observation of distinct 4 and 6 ^1H and ^{13}C resonances for the second species, not obvious for the undeuterated material,[2] eliminates a simple diprotonated form as being the second species. In the cis diprotonated form, the 4- and 6-positions are equivalent by symmetry, and in the trans form they are equivalent because of rapid ring reversal above 0 °C. Thus no resonances are reasonably assigned to a diprotonated form. Experiments in which the concentration of 1,3-dithiane was varied corroborated this conclusion, since the spectrum was relatively insensitive until the ratio of FSO_3H to substrate approached about 3/1. The absence of diprotonated 1,3-dithiane is in agreement with the observations for di(methylthio)methane (**5**), in which the two sulfurs also are separated by only one carbon.

If the second species is not diprotonated material, we must stay with our original suggestion[2] that it is an open chain form such as **11**-H^+ or **11**-$2H^+$ or a solvolysis product



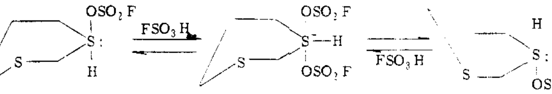
11-H^+



11-$2H^+$

from **11**. The $CH_2{=}$, SH, or $^+SH_2$ resonances would have to fall in the low field area in the vicinity of δ 5. Examination of this region at 270 MHz for the 4,6-deuterated modification (**9**) indeed revealed the requisite resonances, with the AB quartet of **1**-H^+ superimposed symmetrically thereon. The ^{13}C resonance of the $CH_2{=}S^+$ functionality (the "2"-carbon) must be assigned either to δ 51.1 or 55.7, from spectra of **6**, **8**, and **10**. Although there is no empirical information on the expected ^{13}C shift of $CH_2{=}S^+$, these numbers seem low, i.e., too high field. Either our expectations are unrealistic or the open chain material is a solvolysis product of **11** with the $CH_2{=}S^+$ group no longer intact. In **11** or its solvolysis products, the 4- and 6-protons and -carbons are nonequivalent, as demanded by the ^1H and ^{13}C spectra. The high temperature rate process could be C=S rotation rather than unbiasing of a ring conformation. We have observed with reasonable certainty the open chain material analogous to **11** for the dinitrogen heterocycle 1,3-dimethyldiazolidine.[6] Other authors have observed the open chain form of 2,2-dimethyl-1,3-oxathiolane in FSO_3H/SbF_5.[7]

We will close this section with some further comments about the structure of the monoprotonated material. In order to exchange the axial and equatorial protons (the "top" and "bottom" of the molecule) without interchanging the 4 and 6 positions (the "left" and "right" sides of the molecule), we postulated that deprotonation/reprotonation must always occur at the same sulfur atom.[2] An alternative explanation is given in eq 2. If the sulfur species is present



(2)

as a sulfurane, in which the fluorosulfonate anion is bound to the protonated sulfur atom, geminal axial and equatorial protons would be nonequivalent. Nucleophilic displacement of fluorosulfonate by another fluorosulfonate would pass through an intermediate or transition state of the form illustrated in the middle of eq 2. In this high-energy form, the axial and equatorial protons are equivalent (ring

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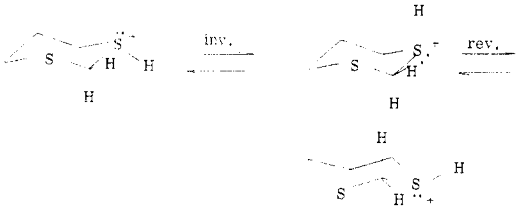
(6) Lambert, J. B.; Majchrzak, M. W. *J. Am. Chem. Soc.* **1979**, *101*, 1048–1049.

(7) Guinot, F.; Lamaty, G.; Munsch, H. *Bull. Soc. Chim. Fr.* **1971**, 541–546.

reversal is rapid at these temperatures), but the two sulfur atoms and hence the 4- and 6-positions remain distinct.

The simplest explanation for axial/equatorial exchange without 4/6 exchange would be inversion about the protonated sulfur without proton exchange (eq 3). In con-



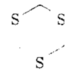
(3)

junction with even more rapid ring reversal, sulfur inversion is formally consistent with the spectral changes. Sulfur inversion, however, is known to have a much higher barrier than that observed for the 1,3-dithiane process[2] (14.8 kcal/mol). The sulfonium salt $(CH_3)(C_2H_5)(C_6H_5CH_2)S^+ClO_4^-$ has a $\Delta G^{\ddagger}$ of 26.6 kcal mol^{-1}.[8] 1-Methylthianium salts do not invert on the NMR time scale.[5] The calculated barrier for $H_3S{:}^+$ is 29–30 kcal/mol.[9] Although secondary sulfonium salts ($R_2HS{:}^+$) might be expected to invert more slowly than tertiary salts ($R_3S{:}^+$), the difference observed in amines is small. Evidence for the above proton exchange mechanism rather than sulfur inversion is found in the analogous experiments with protonated thiane, $(CH_2)_5S^+H$.[5] The AB quartet for the 2-, 6-protons collapses to an A_2 singlet (as in 1,3-dithiane) at the same rate as the HSCH coupling disappears. Only proton exchange, rather than sulfur inversion, can explain these observations, since inversion does not wash out couplings.

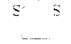
We have offered three explanations for the "selective equalization of chemical shifts" in protonated 1,3-dithianes, selective reprotonation,[2] fluorosulfonate exchange on a sulfurane, and sulfur inversion. All three mechanisms are unprecedented and at present cannot be distinguished on the basis of the spectral changes. In addition to clarification of the process responsible for the spectral changes observed for protonated 1,3-dithiane (Figure 2), there are other questions still not fully answered. What is the structure of the second species? Why does 1,3-dithiane protonate so slowly at −60 °C? What is the cause of the differences between 1,3-dithiane and its acyclic analogue 5? Where are the SH resonances and why are the HSCH couplings not observed? We hope that further experimentation will help bring answers to these questions.

Other Heterocyclic Systems

In order to assess the generality of these phenomena, we have also examined the spectra of a number of other heterocycles in FSO_3H (12–19).



12



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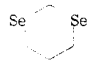

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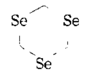

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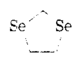

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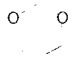

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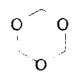

18

19

1,3,5-Trithiane (12) gives an 11-peak spectrum on treatment with FSO_3H. Its approximate mirror symmetry about the central peak is consistent with a protonated form, but a greater delineation cannot be made. The spectrum undergoes no appreciable change on lowering the temperature to −40 °C, but it undergoes irreversible changes on heating to +80 °C. The absence of any reversible kinetic process makes further interpretation valueless.

1,3-Dithiolane (13) in FSO_3H gives a complex but reproducible spectrum that is consistent with monoprotonation. A quartet (2-proton) is located at about δ 4.3 and a multiplet (4- and 5-proton) at 3.2. The multiplet nature of the latter resonance is consistent with protonation on one sulfur only, which would give an ABCD multiplet. The spectrum remains unchanged down to below −40 °C, and irreversible processes occur above 35 °C.

1,3-Diselenane (14) gives a 60-MHz spectrum in FSO_3H that is remarkably similar to the 1,3-dithiane spectrum (Figure 4). The multiplet at δ 3.2 comes from the 5-protons in a monoprotonated form and those at 3.7 and 4.4 from the 4- and 6-protons. The four peaks at 5.05, 5.25, 5.45, and 5.65 are an AB quartet from the 2-protons (J = 12 Hz). The remaining peaks are from the analogous "second species", which may be slightly less abundant than for 1,3-dithiane. This spectrum is unchanged down to below −40 °C and up to 50 °C. Irreversible changes occur above that temperature. The AB quartet from the 2-protons has not begun to coalesce at 50 °C, so that the exchange process that interconverts axial and equatorial protons is slower than that for 1,3-dithiane. Deuteration at the 5-position erases the resonance at δ 3.2 and collapses that at 3.7 to a singlet. The resonance at 4.4 becomes an AB quartet (J = 12 Hz) with a very small chemical shift difference, and the resonances in the 5.2–5.9 region remain unchanged, as expected for the 2-protons. The large triplet at 4.9 sharpens to a broad singlet. These observations confirm the presence of two species, one most likely the monoprotonated form and the other the open chain isomer. Parallelism with 1,3-dithiane is striking, except that the proton exchange process is still slow on the NMR time scale at the point that irreversible decomposition takes place.

The spectrum of 1,3,5-triselenane (15) is quite similar to that of the trithiane. There are many lines, displayed approximately symmetrically about a center point. No changes take place between −10 and +70 °C. Although decomposition is slow, there is no sign of rapid proton exchange, which would change the spectrum to a singlet (complete exchange with solvent) or to a 2/1 doublet (exchange with maintenance of left/right nonequivalence).

1,3-Diselenolane (16) gives an extremely complex spectrum that is stable from −40 to +40 °C. The form of the spectrum is consistent with monoprotonation. Decomposition occurs at higher temperatures.

1,3-Dioxane (17) gives a spectrum up to 0 °C that is essentially the same as that of the free base, with chemical shift perturbations. Either protonation has not occurred (unlikely) or the protonated form(s) exhibits rapid and complete exchange with the medium. Decomposition occurs at higher temperatures.

1,3,5-Trioxane (18) gives three nearly equal intensity singlets below 0 °C and irreversible decomposition at higher temperatures. No interpretation is possible.

1,3-Dioxolane (19) decomposes immediately on treatment with FSO_3H.

Thus the examination of numerous other heterocycles yields little important new information. The selenium heterocycles behave rather similar to the sulfur com-

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[8] Darwish, D.; Hui, S. H.; Tomilson, R. *J. Am. Chem. Soc.* **1968**, *90*, 5631–5632.

[9] Rauk, A.; Andose, J. D.; Frick, W. G.; Tang, R.; Mislow, K. *J. Am. Chem. Soc.* **1971**, *93*, 6507–6515.

pounds. The oxygen forms are more labile. Decomposition of the selenium heterocycles and the alternative sulfur heterocycles occurs irreversibly at high temperatures, so that selective nonequivalence is not observed. The specific behavior of 1,3-diselenane is quite similar to that of 1,3-dithiane, except with the absence of high-temperature coalescence of the AB quartet from the 2-protons.

Conclusions

Open-chain disulfides react in a straightforward fashion in FSO_3H to give independent protonation of both sulfurs when they are separated by two or more carbons but of only one sulfur when they are separated by one carbon. Coulombic repulsion suffices to explain these results. In 1,3-dithiane the sulfurs are also separated by one carbon atom, and half of the peaks in FSO_3H can be attributed to a monoprotonated form. The remaining half of the peaks are best attributed to an open-chain isomer rather than to a diprotonated form. The high-temperature spectral changes are consistent with selective reprotonation, sulfurane exchange, or sulfur inversion. The ^1H spectrum of 1,3-diselenane and of 1,3-dithiolane shows very similar properties in FSO_3H to that of 1,3-dithiane.

Experimental Section

Proton magnetic resonance spectra were obtained at 60 MHz on a Perkin-Elmer R20B spectrometer. Carbon-13 magnetic resonance spectra were obtained at 20 MHz on a Varian CFT20 spectrometer. Temperatures were calibrated with the methanol standard (^1H).

1,3-Di(methylthio)propane (2) and **1,2-di(methylthio)ethane** (4) were prepared by treatment of the corresponding dibromide with methylmercaptan and sodium ethoxide in ethanol at 80 °C, with respective yields of 78 and 46%.

2,2-Dimethyl-1,3-di(methylthio)propane (3) was prepared by treatment of 1,3-dibromo-2,2-dimethylpropane with methylmercaptan and sodium ethoxide in ethanol at 140 °C: 75% yield; bp 96–98 °C (20 mm); NMR (neat) δ 0.9 (s, 6, CH_3C), 2.0 (s, 6, CH_3S), 2.4 (s, 4, CH_2). Anal. Calcd for $C_7H_{16}S_2$: C, 51.16; H, 9.81; S, 39.02. Found: C, 51.23; H, 9.60; S, 37.96.

Di(methylthio)methane (5) was prepared by the condensation of formalin in concentrated HCl with methyl mercaptan, in a 65% yield.

Deuterated derivatives of 1,3-dithiane (6–10) were obtained by cyclization of the appropriately deuterated propane-1,3-dithiol with dimethoxymethane in the presence of BF_3 etherate, with a typical yield of 75%.[10] The labeled dithiols came from treatment of the labeled 1,3-dibromopropane with H_2O, thiourea, and ethylenediamine.[11] 1,3-Dibromopropane-*2,2-d*$_2$, needed for preparation of 7 and 8, came from exchange of the methylene protons in dimethyl malonate, reduction of the malonate with $LiAlH_4$, and treatment of the diol with PBr_3.[12] 1,3-Dibromopropane-*1,1,3,3-d*$_4$, needed for 9 and 10, was prepared by reduction of dimethyl malonate with $LiAlD_4$ and treatment of the diol with PBr_3.[13] Exchange of the 2-protons with deuterium in 6, 8, and 10 was carried out according to the Seebach procedure[14] by treatment of the dithiane with butyllithium and D_2O in tetrahydrofuran.

1,3,5-Trithiane (12), **1,3-dioxane** (17), **1,3,5-trioxane** (18), and **1,3-dioxolane** (19) are commercially available materials.

1,3-Dithiolane (13) was prepared by the condensation of ethane-1,2-dithiol with paraformaldehyde in the presence of p-toluenesulfonic acid, with a 72% yield.[15]

1,3-Diselenane (14) was prepared by the condensation of propane-1,3-diselenol with formaldehyde (36% aqueous solution) in the presence of concentrated HCl, with a yield of 27%.[16] The propanediselenol was obtained by the Birch reduction of propane-1,3-diselenocyanate, which in turn came from treatment of 1,3-dibromopropane with KSeCN.

1,3-Diselenane-*5,5-d*$_2$ came ultimately from 1,3-dibromopropane-*2,2-d*$_2$.[11]

1,3,5-Triselenane (15) was prepared by condensation of formaldehyde (36% aqueous solution) with Al_2Se_3 in the presence of concentrated HCl in 23% yield.[16]

Ethane-1,2-diselenol was prepared by a procedure analogous to that of propane-1,3-diselenol[17] from the Birch reduction of ethane-1,2-diselenocyanate. The latter was obtained from 1,2-dibromoethane on treatment with KSeCN. The yield of the diselenol was 46%: bp 70–71 °C (15 mm); NMR (CS_2) δ 0.8 (m, 2, SeH), 3.0 (m, 4, CH_2). Anal. Calcd for $C_2H_6Se_2$: C, 12.77; H, 3.21. Found: C, 13.08; H, 3.19.

1,3-Diselenolane (16) was prepared by the condensation of ethane-1,2-diselenol (3.6 g, 0.019 mol) with paraformaldehyde (0.57 g, 0.019 mol) in the presence of p-toluenesulfonic acid (0.5 g, 0.0029 mol). The reactants were heated under reflux for 4 h with a Dean–Stark trap. The reaction mixture was then washed with 1 N $NaCO_3$ (5 × 20 mL) and with H_2O (5 × 20 mL). The organic portion was concentrated and the residue distilled to give 2.1 g (55%) of the product: bp 99–100 °C (15 mm); NMR (CS_2) δ 3.4 (s, 4, CH_2CH_2), 3.85 (s, 2, $SeCH_2Se$). Anal. Calcd for $C_3H_6Se_2$: C, 18.02; H, 3.02. Found: C, 18.05; H, 3.11.

Protonation. For ^1H spectra, about 50 mg of the substrate was placed in a 5-mm NMR tube, 0.3 mL of FSO_3H was pipetted in, and about an equal volume of SO_2 was condensed in with cooling. The respective amounts for the ^{13}C spectra were 300 mg of substrate and 1.2 mL of FSO_3H in an 8-mm tube. Solutions were also prepared by mixing the materials at −78 °C and taking spectra at −60 °C without warming the sample. For the acyclic compounds 2–5, the spectrum was independent of the mode of preparation. For 1,3-dithiane, the −60 °C spectrum appeared to be largely from unreacted starting material that only protonated on warming to −40 °C and above.[4] For quenching, 100-mg samples of 1,3-dithiane were mixed with FSO_3H at 25, 0, and −50 °C for 1 h, poured onto ice, and filtered. A small amount of nonmelting white solid, nearly insoluble in $CHCl_3$ and giving no ^1H spectrum, was produced. The filtrate was neutralized with saturated aqueous Na_2CO_3 solution and extracted with $CHCl_3$. The dried (Na_2SO_4) extract was evaporated to give (at all three temperatures) 60–65 mg of a yellowish solid (mp 45–48 °C; 1,3-dithiane melts at 53–55 °C) that gave a ^1H spectrum in $CDCl_3$ identical with that of 1,3-dithiane without impurity peaks. The product may be contaminated to some extent with the insoluble material, so that the actual recovered yield is less than 60–65%. Extraction with ethyl ether instead of $CHCl_3$ produced much lower recovery. Chloroform extraction without neutralization also produced a lower recovery (35%).

Registry No. 2, 24949-35-7; **3**, 71870-73-0; **4**, 6628-18-8; **5**, 1618-26-4; **6**, 71870-74-1; **7**, 71870-75-2; **8**, 71870-76-3; **9**, 71870-77-4; **10**, 71870-78-5; **12**, 291-21-4; **13**, 4829-04-3; **14**, 22714-00-7; **15**, 291-25-8; **16**, 23636-54-6; **17**, 505-22-6; **18**, 110-88-3; **19**, 646-06-0; 1,3-dibromopropane, 109-64-8; 1,2-dibromoethane, 106-93-4; methylmercaptan, 74-93-1; 1,3-dibromo-2,2-dimethylpropane, 5434-27-5; 1,3-dibromopropane-*2,2-d*$_2$, 38645-15-7; 1,3-dibromopropane-*1,1,3,3-d*$_4$, 64528-94-5; ethane-1,2-dithiol; propane-1,3-diselenol, 59637-44-4; propane 1,3-diselenocyanate, 7314-77-4; ethane-1,2-diselenol, 56742-33-7; 1,2-dibromoethane 1,2-diselenocyanate, 71870-79-6; paraformaldehyde, 30525-89-4.

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