tution of phenyl for H Figure 3, dotted line), nor is it supported by the lack of analogous effects of phenyl-formethyl substitution in dioxetanes.[13] The latter case however is complicated by postulated reverse reactions, and the symmetry of alkoxy radicals may lessen the geometrical demands for homoconjugation with the aromatic ring. More definitive evidence on this matter would come from electron detachment studies of substituted benzyl alcoholate ions, but these do not appear to have been carried out.

Acknowledgment. This work has been supported by a fellowship to E.M.Q. from the 3M Company.

(13) (a) Richardson, W. H.; Anderegg, J. H.; Price, M. E.; Tappen, W. A.; O'Neal, H. E. *J. Org. Chem.* **1978**, *43*, 2236–2241. (b) Richardson, W. H.; Yelvington, M. B.; O'Neal, H. E. *J. Am. Chem. Soc.* **1972**, *94*, 1619–1623.

Registry No. $(CH_3)_2CHCH_2I$, 513-38-2; *p*-$FC_6H_4CHClCH_3$, 456-16-6; *p*-$ClC_6H_4CHClCH_3$, 20001-65-4; *p*-$BrC_6H_4CHClCH_3$, 20488-10-2; *p*-$CH_3OC_6H_4CHClCH_3$, 1538-89-2; Ph_2CHBr, 776-74-9; *trans*-$C_6H_5CH(CH_3)ON{=}NOCH(CH_3)C_6H_5$, 97012-02-7; *trans*-$C_6H_5CD(CH_3)ON{=}NOCD(CH_3)C_6H_5$, 97012-03-8; *trans*-*c*-$C_6H_{11}ON{=}NOC_6H_{11}$-*c*, 86886-18-2; *trans*-$C_6H_5CH_2ON{=}NOCH_2C_6H_5$, 86886-20-6; *trans*-$CH_3ON{=}NOCH_3$, 86886-15-9; *trans*-$CH_3CH_2ON{=}NOCH_2CH_3$, 91606-80-3; *trans*-$(CH_3)_2CHON{=}NOCH(CH_3)_2$, 86886-16-0; *trans*-$(CH_3)_2CHCH_2ON{=}NOCH_2CH(CH_3)_2$, 97012-04-9; *trans*-*p*-$FC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-F, 97012-05-0; *trans*-*p*-$ClC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-Cl, 97012-06-1; *trans*-*p*-$BrC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-Br, 97012-07-2; *trans*-*p*-$CH_3OC_6H_4CH(CH_3)ON{=}NOCH(CH_3)C_6H_4$-*p*-$OCH_3$, 97012-08-3; *trans*-$(C_6H_5)_2CHON{=}NOCH(C_6H_5)_2$, 97012-10-7; *p*-$FC_6H_4COCH_3$, 403-42-9; *p*-$ClC_6H_4COCH_3$, 99-91-2; *p*-$BrC_6H_4COCH_3$, 99-90-1; *p*-$CH_3OC_6H_4COCH_3$, 100-06-1; *p*-$CH_3OC_6H_4CH(OH)CH_3$, 3319-15-1; 1-tetralol, 529-33-9; 1-tetralyl chloride, 58485-68-0; *trans*-bis(1-tetralyl)hyponitrite, 97012-09-4.

Reactions of the Chlorine Complex of Tetrahydrothiophene

Donald L. Schmidt,* Jerry P. Heeschen, Thomas C. Klingler, and Leslie P. McCarty

The Dow Chemical Company, Midland, Michigan 48640

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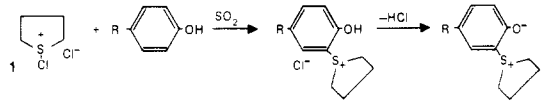
The chlorine complex of tetrahydrothiophene (THT) undergoes the Pummerer reaction to yield not only the expected 2-chloro- and 2,3-dichlorotetrahydrothiophene products but also 1-(2-chlorotetrahydro-3-thienyl)-tetrahydrothiophenium chloride (**10**), which upon hydrolysis yields 1-(tetrahydro-2-hydroxy-3-thienyl)tetrahydrothiophenium chloride **3** and upon elimination of HCl produces 1-(4,5-dihydro-3-thienyl)tetrahydrothiophenium chloride (**2**). The sulfonium **10** was formed by the addition of the chlorine–THT complex to the Pummerer-derived 2,3-dihydrothiophene. The sulfonium formation was monitored in CCl_4, CH_2Cl_2, and liquid SO_2 by proton NMR, and the addition of the complex to cyclohexene, dihydrofuran, styrene, and thiophene was studied. There was a dramatic increase in reactivity of the complex in sulfur dioxide both to addition and substitution type reactions.

Aryl cyclic sulfonium zwitterions are polymerizable monomers[1-3] that are prepared[4] by the reaction of a phenol with the 1:1 complex of chlorine and tetrahydrothiophene **1**. The electrophilic substitution to yield sulfonium goes exclusively para to the phenolic hydroxy. If the para position is blocked, then ortho substitution occurs at a much lower rate. It is interesting that liquid SO_2 is the only solvent that gives a practical reaction rate for ortho substitution to phenols.[4]



zwitterion monomer

The chlorosulfonium salt **1** may be formed by chlorination of tetrahydrothiophene (THT) with chlorine or sulfuryl chloride or from tetrahydrothiophene 1-oxide (THTO) in cold, saturated HCl solutions of methanol[2] or water–methanol.[5]

In the course of preparing large quantities of the zwitterion, we observed that excess **1** and elevated reaction temperatures produced toxic solutions. The toxicity was not related to the THT substitution reaction to phenols but was a result of the unexpected addition of **1** to the Pummerer-derived 2,3-dihydrothiophene to yield bioactive sulfoniums. We report here a subsequent study of the Pummerer rearrangements of **1** and a previously unreported reaction of **1** with alkenes.

Isolation of Sulfoniums. The zwitterion solutions containing the toxic substances were analyzed by high-performance liquid chromatography (HPLC) using a cationic exchange column for separation of the unknown species. Because neuromuscular blockade was the pharmacological property related to toxicity, a bioassay technique reported by Kordaš[6] was used to monitor the HPLC. This method proved both sensitive and semiquantitative. Sufficient material was isolated from the most bioactive HPLC peak for partial characterization. A sample of crystalline material was isolated by picrate precipitation from a solution of zwitterion containing the toxic substance. The chloride salt of this material was identical by bioassay and proton NMR with samples isolated by HPLC.

On the bases of NMR, IR, elemental, and mass spectral analyses this bioactive compound was tentatively assigned structure **2**. Later, chemical considerations confirmed β(3)

(1) Hatch, M. J.; Yoshimine, M.; Schmidt, D. L.; Smith H. B. *J. Am. Chem. Soc.* **1971**, *93*, 4617.
(2) Schmidt, D. L.; Smith, H. B.; Yoshimine, M.; Hatch, M. J. *J. Polym. Sci., A-1* **1972**, *10*, 2951.
(3) Schmidt, D. L. In "Ring-opening Polymerization"; Saequsa, T., Goethals, E., Eds.; American Chemical Society: Washington, DC; 1977; ACS Symposium Series, pp 318.
(4) Klingler, T. C.; Schmidt, D. L.; Jensen, W., Jr.; Urchick, D. U.S. Patent 4 089 877, 1978.
(5) Schmidt, D. L., unpublished results.

(6) Kordaš, M. *Int. J. Neuropharmacol.* **1964**, *3*, 77. The bioassay depended upon the percent depression of an isolated perfused rat phrenic nerve–diaphram (IPD) as described by Kordaš. The toxicity was due to neuromuscular blockage and the potency was quantitated by the percent depression in the contraction of the nerve–diaphragm. After the compounds had been isolated, the potency was compared by the quantity needed for a 25% depression. The LD_{50} in mice was determined by intraperitoneal administration and the measured LD_{50} values were **2a**, 0.83 mg/kg; **3a**, 3.16 mg/kg; and **4a**, 6.81 mg/kg.

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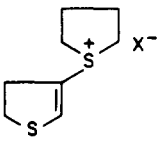
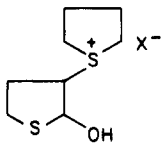


2a, X = Cl^-
2b, X = picrate

THT^+ substitution. When **2a** was heated, ring-opening occured by chloride attack at a ring carbon α to the sulfonium to yield the nonionic species **2R**.

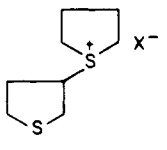
While obtaining larger quantities of **2**, by decomposition of **1** in SO_2, minor product **3** was isolated by fractional



3a, X = Cl^-
3b, X = picrate

crystallization, which had a retention time that matched a bioactive HPLC peak obtained from the original zwitterion solutions. When **1** was decomposed in CH_2Cl_2, **3** became the major product; however, warming appeared to convert **3** to **2**. Since NMR indicated that CHOH methine proton of **3** is vicinal to only one other proton, the hydroxyl was assigned to be in the α(2) position.

Small amounts of a third sulfonium (**4**) were obtained when **1** was decomposed in SO_2 followed by addition of water and then allowed to stand at 25 °C. This structure



4a, X = Cl
4b, X = picrate

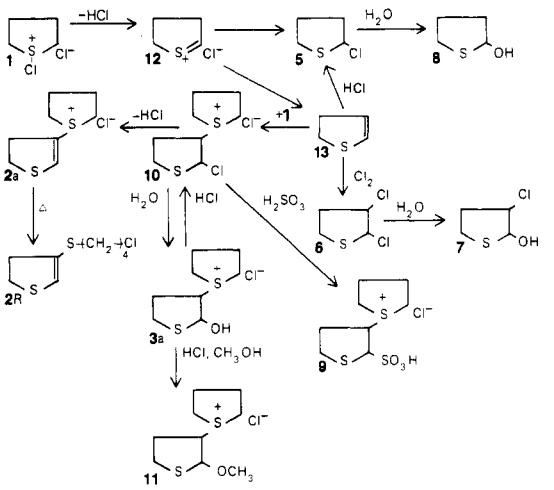
was confirmed by comparison of the mass spectrum and NMR of the isolated material with the authentic compound. The authentic compound was prepared by displacement of the benzenesulfonate ester of 3-hydroxytetrahydrothiophene with THT. The sulfonium **4** was not detected by HPLC in any of the zwitterion solutions which contained toxic substance.

Decomposition Studies in CCl_4, CH_2Cl_2, and SO_2. The decomposition of **1** in CCl_4 gave two phases: a top semisolid, water-soluble phase and a bottom CCl_4 phase. The CCl_4 phase contained 2-chlorotetrahydrothiophene (2-Cl-THT **5**) and *cis*- and *trans*-2,3-dichlorotetrahydrothiophene (2,3-diCl-THT, **6**) in a **5**/**6** ratio of 0.4. The cis isomer has not been reported previously. Addition of D_2O appeared to hydrolyze **6** to 2-hydroxy-3-chlorotetrahydrothiophene (**7**) and **5** to 2-hydroxytetrahydrothiophene (**8**). Addition of D_2O to the water-soluble phase gave **2** and **3** and THTO from hydrolysis of **1**.

When the decomposition of **1** was carried out in CH_2Cl_2 and the solution was extracted with cold D_2O, **3** was observed but little **2** was detected. When the D_2O solution was warmed, **2** became the main product, suggesting that both **2** and **3** came from the same precursor.

The decomposition of **1** in SO_2 was studied by taking D_2O-quenched samples. After 1 h, NMR analysis indicated a species consistent with α-(sulfonic acid)-β-THT^+ substituted THT **9**. After 3 h, the amount of **9** had increased and **2** began to appear. Upon elimination of most of the SO_2 before quenching no **9** could be detected; however, both **3** and **2** were observed. Apparently the formation of

Scheme I



the sulfonic acid **9** requires the presence of a strong H_2SO_3 solution. It appears that **9**, **3**, and **2** were derived from the same precursor.

Finally, the decomposition of **1** in SO_2 was monitored in a sealed NMR tube at −15 °C. The complex **1** was detected initially and slowly decreased with time. After about 6 h, NMR absorptions were detected that were consistent with the cis and trans isomers of the α-chloro β-sulfonium substituted THT structure **10**. Soon after the appearance of **10**, **2** was detected and continued to increase during the decomposition.

Mechanism. NMR studies were performed on HCl solutions of **3** to both determine if **3** could be converted to **10** and to establish chemical shifts of **10**. Adding concentrated HCl to an aqueous solution of **3** produced a weak absorption at 6.18 ppm which was assigned tentatively as the α proton of **10**. The main effect of saturating this solution with HCl gas was the conversion of **3** to **2**. Addition of HCl gas to a methanol solution of **3** at 0 °C caused the complete loss of **3** and the appearance of **10** and the α-methoxy derivative **11**. Both **10** and **11** appeared as major/minor sets of absorptions in methanol–HCl. The predominate isomer of **10** in methanol–HCl had coupled α and β proton absorptions at 6.28 (4.2 Hz) and 4.43 ppm, and the lesser isomer at 6.26 and 4.60 ppm. The major isomer of **11** in methanol–HCl had α and β proton absorptions at 5.41 (d, 4.3 Hz) and 4.19 ppm and a methoxy singlet at 3.30 ppm. The minor isomer of **11** had an α proton absorption at 5.54 ppm but the β proton shift was not established.

Since it was established that **3** has the hydroxyl on the α position and can be converted to **10**, it follows that **10** must have the chlorine on the α position. Similarly, since **3** can be converted to **2**, then **2** must also have the sulfonium in the β position.

From the data available, it appears that the generation of the sulfoniums **10** and **2** is consistent with the mechanism suggested by Wilson and Albert.[7,8] These workers proposed the intermediacy of a sulfocarbonium ion **12** (Scheme I) which either eliminates HCl to yield 2,3-dihydrothiophene (**13**) or is attacked by chloride to yield 2-Cl-THT (**5**). Chlorination of **13** produces 2,3-diCl-THT (**6**). A plausible mechanism for formation of **10** is the addition of the chlorosulfonium salt **1** to **13** to yield **10**. Elimination of HCl from **10** would produce **2** (Scheme I). This is consistent with our observations that **3** is mainly

(7) Wilson, G. E., Jr.; Albert, R. *J. Org. Chem.* **1973**, *38*, 2156.
(8) Wilson, G. E., Jr.; Albert, R. *J. Org. Chem.* **1973**, *38*, 2160.

isolated from low-temperature decomposition conditions and **2** is the major product at higher temperatures. We observed that when 2,3-dihydrothiophene (**13**) was added to a fresh SO_2 solution of **1**, a 2% yield of **2b** was isolated, but under identical conditions in the absence of **13** no **2b** could be isolated. Similar results were obtained by using a CH_2Cl_2 solvent except less sulfonium was obtained. These observations are in agreement with the reaction of **1** with the alkene intermediate **13**.

The isolation of small amounts of the sulfonium **4** from the decomposition of **1** in SO_2–HCl–H_2O also suggests the intermediacy of 2,3-dihydrothiophene (**13**). It is known that sulfides in strong aqueous acids react with alkenes to yield sulfoniums.[10] Thus THT could react under the proper conditions with **13** to yield **4**, although the $\alpha(2)$ sulfonium would be expected to be the favored product. We were unable to prepare **4** under the conditions used by the addition of THT to **13** in acid but obtained only polymer. The conversion of **4** to **10** by the Pummerer reaction using chlorine in CH_2Cl_2 or SO_2 was also unsuccessful.

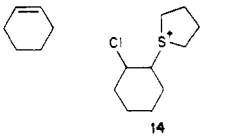
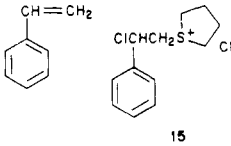
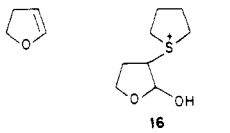
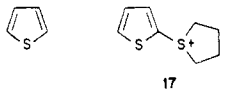
Because of the known reactivity of α-chloro sulfides, it is not surprising that **10** is easily converted either to the α-hydroxy **3** by water or to the α-sulfonic acid **9** by concentrated sulfurous acid. Similarly, **3** reacts with either concentrated HCl to yield **10** or with HCl–CH_3OH to give the methoxy derivative **11**.

We found small amounts of *cis*-2,3-diCl-THT in the reaction mixture, whereas Wilson and Albert[8] detected only the trans isomer on the basis of isolation of the methoxy derivatives. Apparently the ratio of the 2-Cl-THT to 2,3-diCl THT that we measured by NMR also differs from reported values based on conversion to the methoxy derivatives[8] or post addition of trimethylamine.[9]

It appears that the electrophilic addition of **1** to **13** to yield **10** is in competition with the chlorination of **13**. It has also been shown[7] that HCl reacts with **13** to give **5**. Considering these competitive reactions, the reaction of **1** with **13** is probably quite fast. On the basis of decomposition studies, it was difficult to determine if the addition of **1** to **13** was solvent-sensitive. It appears, however, that the dehydrochlorination of **10** to form **2** is solvent-sensitive and this reaction is much slower in CCl_4 and CH_2Cl than in SO_2.

Reaction with Alkenes. The reactivity of the chlorosulfonium **1** to model alkenes was initiated to determine both the general nature of the reaction and solvent sensitivity. The results of four model reactions carried out under essentially the same conditions and times are shown in Table I. It is evident that **1** adds slowly to cyclohexene to yield **14** and readily with the more reactive styrene to yield **15**. The reaction with 2,3-dihydrofuran gives **16** which is analogous to **3**; **16** did not dehydrochlorinate under the conditions used. Due to its aromatic character, thiophene reacts with **1** by a substitution mechanism to yield the α-sulfonium **17**. Chlorination appears to be competing with the addition reaction and the reaction with cyclohexene gave not only **14** but also considerable 1,2-dichlorocyclohexane. Whether **1** reacts with an alkene to give the dichloro or sulfonium apparently depends upon the electron density of the double bond. It is interesting that the bromine complex[11,12] of dimethyl sulfide in

Table I. Reaction of 1 with Model Compounds

model reactant	product		isolated yield, %	solvent
	**14**	picrate	3.5 none	SO_2 CH_2Cl_2
	**15**		85 9.2	SO_2 CH_2Cl_2
	**16**	picrylsulfonate	19.5 none	SO_2 CH_2Cl_2
	**17**	picrate	15 none	SO_2 CH_2Cl_2

methylene chloride does not add directly to styrene but yields 1-(2-bromo-1-phenylethyl)dimethylsulfonium bromide. This compound is derived by first formation of a three-membered bromonium intermediate followed by nucleophilic attack by dimethyl sulfide at the benzyl carbon. If the bromosulfonium salt added directly to the styrene, then the sulfonium group should be beta to the phenyl and analogous to **15**. It is thus unlikely that the chlorosulfonium **1** reacts with styrene by a three-membered chloronium ion mechanism.

The structure of **15** is supported by the proton NMR of the chloride salt and its ring-opened products **15Ra** and **15Rb**. The NMR of this sulfonium indicates the presence of a phenyl (Ph), THT^+, and a $CHXYCH_2Z$ group. The THT^+ group could be either α or β to the phenyl. Upon heating **15**, a 70/30 mixture of two structures was obtained. The NMR spectrum indicated two SCH_2 triplets, indicating that the THT ring had been opened to yield two types of $S(CH_2)_4Cl$ groups with different $PhCHXCH_2Y$ patterns. Neither product was 1,2-dichloroethylbenzene,[13] whose CH and CH_2 protons are at 4.8 and 3.85 ppm.

Normal substituent effects for chloro and thioalkyl groups allow assignment of the **15R** isomers as shown below. The original sulfonium **15** is assigned as having a β-THT^+, because changing thio sulfur of **15R** to sulfonium of **15** would deshield geminal protons and, to a lesser extent, vicinal protons.

	δ (CH)	δ (CH_2)	structure
15Ra major	5.15	3.21	$PhCHClCH_2S(CH_2)_4Cl$
15Rb minor	4.00	4.00	$PhCH[S(CH_2)_4Cl]CH_2Cl$
15	5.48	3.96	$PhCHClCH_2(THT^+)$

The major isomer **15Ra** was formed by ring-opening via chloride attack at a ring carbon α to the sulfonium. The minor product **15Rb** could be formed by chloride displacement of the THT followed by THT displacement of the benzyl chlorine. The resulting intermediate would then decompose by chloride ring-opening to yield **15Rb**. A more probable mechanism for **15Rb** is the displacement of the benzyl chlorine of **15Ra** by the neighboring sulfur followed by chloride attack on the resulting three-membered sulfonium intermediate.

Table I illustrates the dramatic effect the solvent has on the reactivity of **1** to alkenes. Sulfur dioxide appears

(9) Kruse, C. G.; Poels, E. K.; Jonkers, F. L.; van der Gen, A. *J. Org. Chem.* **1978**, *43*, 3548.
(10) Bosshard, H. *Helv. Chim. Acta* **1972**, *55*, 32. van der Gen, A.; Bosshard, H. *Ibid.* **1972**, *55*, 37.
(11) Chow, Y. L.; Bakker, B. H.; Iwai, K. *J. Chem. Soc., Chem. Commun.* **1980**, 521.
(12) Chow, Y. L.; Bakker, B. H. *Synthesis* **1982**, 648.
(13) Heeschen, J. P., unpublished results.

Table II. Proton NMR Chemical Shifts[a] of THT and 1-Substituted THT Rings

structure	solvent	δ (α)	δ (β)	Δδ
THT	CCl_4	2.73	1.90	0.83
	D_2O/HCl	2.78	1.91	0.87
	SO_2	2.64	1.85	0.79
THT + 0.4HCl	SO_2, −20 °C	2.72	1.90	0.82
THT + $0.5SO_2Cl_2$	SO_2, −20 °C	3.45	2.27	1.18
THT + $1.2SO_2Cl_2$	SO_2, −20 °C	4.20	2.66	1.54
1 (ref 9)	$CDCl_3$, −75 °C	4.20	2.70	1.50
THTO	CCl_4	2.70	2.13	0.57
	D_2O	3.00	2.20	0.80
	D_2O–HCl	3.31	2.30	1.01
THT^+ rings in 2, 3, 16, 17	D_2O or Me_2SO	3.6–3.8	2.2–2.45	1.3–1.4

[a] ppm/Me_4Si. Internal chemical shift reference is Me_4Si in CCl_4 and Me_2SO solution, DSS, or TSP in D_2O solution. The chemical shifts given for THTO and THT^+ are average values, since geminal protons are not equivalent in those moieties.

to increase the reactivity to both addition and substitution reactions above that which would be expected due only to solvent polarity. This is consistent with our observed increase in reactivity of 1 in SO_2 with phenols[4] and the increased rate of formation of 2 in SO_2.

We observed that the rate of decomposition of the chlorosulfonium salt 1 was greatly decreased by the presence of HCl. Hydrogen chloride decreased the amount of isolated 3 and 2, after decomposition of 1 in either CH_2Cl_2 or SO_2, by factors of between 5 and 10.[5] The usual dark Pummerer tars were minimal. The addition of HCl during the preparation of zwitterions decreased the amount of 2 by factors of between 100 and 1000 and also increased the yield of desired product.[4] It is probable that HCl inhibits proton removal from 1 and interferes with the formation of the sulfocarbonium ion 12.

Proton NMR. The tetrahydrothiophenium ring, THT^+, is a key feature of the new structures reported here, and it is important to distinguish this moiety from THT, 1, and THTO, which have potentially similar NMR patterns and which may occur in the various reaction mixtures examined.

Table II presents the chemical shifts and shift differences of the α and β protons of THT, THTO, THT^+, and 1 in pertinent solvents. All α protons of THT and 1 have the same chemical shift and the β protons also have the same shift, due to rapid inversion or planar shape of the ring. For THTO and THT^+, geminal protons are nonequivalent due to the single additional substituent on the pyramidal, noninverting sulfur, and Table II reports the average α and β proton shifts.

The chemical shifts of THT are essentially the same in CCl_4, aqueous acid, SO_2, and SO_2 with HCl, and the shift difference ranges from 0.79 to 0.87 ppm. This small range implies little or no interaction of THT with these solvents or HCl.

Chlorine forms complexes preferentially with THT to make 1 and exchanges rapidly among all THT molecules at temperatures down to −20 °C. The exchange is reported[7] to be slow for 1 in $CDCl_3$ at −75 °C. In the presence of 1.2 mol of chlorine, as SO_2Cl_2, 1 displays a single spectrum with the same shifts as have been reported for the nonexchanging structure in $CDCl_3$ solvent. When only 0.5 mol of chlorine is available, a single time-averaged THT spectrum is observed that shows a rapid exchange of Cl_2 among all THT molecules, and the shift is halfway between that for zero and full complexation. This demonstrates that the Cl_2 association must be almost entirely with THT and not with SO_2.

Tetrahydrothiophene 1-oxide (THTO) displays nonequivalence of geminal protons, resulting in a pattern of the type AA′BB′MM′NN′, with obvious broadening or separation of the α proton absorptions. In contrast to THT, THTO displays a very noticeable solvent effect on chemical shift, going from CCl_4 to water to aqueous acid.

The tetrahydrothiophenium ring, THT^+, also has an AA′BB′MM′NN′ pattern, but not identical with THTO. It appears as complex absorptions of equal area centered at 3.6–3.8 ppm and at 2.2–2.4 ppm. At 60 MHz each region usually has a single maximum and the width varies from 15 Hz (as for THT itself) to 30 Hz. At high resonance frequency, each region usually splits into two complex patterns of equal area. This behavior is characteristic of THT^+ and THTO. The average chemical shift difference between α and β protons is remarkably constant, at 1.3 to 1.4 ppm, despite the strong solvent effects on their absolute values.

Table III summarizes distinctive proton NMR features of the substituted THT rings, including the chemical shifts of protons at the substitution sites and coupling between them. The positions of substituents Cl, THT^+, and OH on THT rings have been established with good confidence, on the basis of authentic fabrication and/or NMR chemical shift substituent effects and detection of vicinal coupling. In almost all cases the presence of both the cis and trans isomers of a given 2,3-disubstituted structure was supported on the basis that the coupled H(2) and H(3) proton signals appeared in major/minor sets with similar chemical shifts and constant molar ratios of the order of about 5:1.

It is possible to assign configurations and conformations to 3, 4, 5, and 6 by examining the NMR spin–spin coupling constants between vicinal protons on the substituted THT ring. The three-bond coupling between vicinal protons, J(H–C–C–H), is dependent on the dihedral angle between the individual C–H bonds due to rotation about the intervening C–C bond. For tetrahedral carbons a reasonable description of both magnitude and angular dependence is given by the modified Karplus[14] relation, $J(\text{vic}) = 7 - \cos\phi + 5\cos 2\phi$ Hz. Substituents which are strongly electron-withdrawing may reduce the magnitude but not the general angular dependence. Ring inversion is fast on the NMR time scale, so a single time-averaged spectrum is observed. Observed splittings (Experimental Section) were used for this analysis because they are sufficiently close to the true coupling constants to be diagnostic.

The major isomer of 2,3-diCl-THT (6), is assigned as having the chlorine atoms trans and fixed diaxial in a half-chair conformation of the ring. Rotation about all of the C–C bonds is approximately 30° from a planar (eclipsed) conformation. The $J(23)$ value of 1.2 Hz establishes that H(2) and H(3) are 70–110° apart and therefore trans-diequatorial. Protons H(3), H′(4) at δ 2.41, and H(5) at δ 3.23 also are equatorial with respect to their vicinal CH_2 protons, on the basis of individual and summed couplings, and H(4) and H′(5) are axial. The relatively large four-bond coupling of 1.2 Hz between H(2) and the equatorial H′(4) supports the implied planar "W" H–C–C–C–H path between them. This demonstration of trans configuration and diaxial conformation of the major 2,3-diCl-THT isomer confirms the same assertion by others[7,9] on the basis of $J(2,3)$ alone.

The minor isomer of 6 must be *cis*-2,3-diCl-THT. The C(2) chlorine is axial, the C(3) chlorine is equatorial, and the ring is puckered. Vicinal couplings indicate that H(2) and H(3) are cis axial–equatorial. Proton H(3) is most

(14) Becker, E. D. "High Resolution NMR", 2nd ed.; Academic Press: Philadelphia, PA, 1979; p 657.

Table III. Proton NMR Description of 2,3-Disubstituted Tetrahydrothiophenes and Related Structures

structure	substit 2	substit 3	δH(2)	δH(3), ppm	J(2,3), Hz	solvent, remarks
tetrahydrothiophene:						
5	Cl	H	5.68	2.49	1.5	
				2.18	4.5	CCl_4
8	OH	H	5.55	?	<2	CCl_4 from D_2O/CCl_4
6 major (trans)[a]	Cl	Cl	5.55	4.72	1.2	CCl_4
6 minor (cis)[a]	Cl	Cl	5.44	4.37	4.0	CCl_4
7	OH	Cl	5.38	4.4	3.8	D_2O from D_2O/CCl_4* [b]
2-methoxy-3-chloro (trans)	OCH_3	Cl	5.03	4.45	<1	CCl_4, ref 7
3-hydroxy	H	OH	3.2–2.8	4.66	3.4 ave	$CDCl_3$
3-benzenesulfonate	H	OSO_2Ph	3.2–2.7	5.23	3.5 ave	$CDCl_3$
4a	H	THT^+	3.39	4.14	5.8	D_2O
			3.17		5.8	
3a major[a]	OH	THT^+	5.78	4.05	4.3	H_2O
3a minor[a]	OH	THT^+	5.81	4.0	3.3	H_2O
11 major[a]	OCH_3	THT^+	5.41	4.17	4.3	CH_3OH/HCl*
11 minor[a]	OCH_3	THT^+	5.54	n.d.[c]	3.2	CH_3OH/HCl*
9	SO_3H	THT^+	5.17	4.13	2.9	$H_2O/HCl/SO_2$
10 major[a]	Cl	THT^+	6.06	4.16	4.0	SO_2 (dec)
			6.28	4.43	4.2	CH_3OH/HCl
			6.18	n.d.	3.3?	H_2O/HCl
10 minor[a]	Cl	THT^+	5.98	n.d.		SO_2 (dec)
			6.26	4.60	<2	CH_3OH/HCl
tetrahydrofuran:						
16	OH	THT^+	5.54	4.0	4.5	Me_2SO, picryl sulfonate salt
4,5-dihydrothiophene:						
2	H	THT^+	7.60			D_2O, $J(2,4)$ = 1.5 Hz
2R	H	$S(CH_2)_4Cl$	5.98			$CDCl_3$, $J(2,4)$ = 1.8 Hz
thiophene:						
17	THT^+	H		8.00		Me_2SO, picrate $J(3,4/3,5/4,5)$ = 3.8/1.4/5.1 Hz

[a] The major/minor ratio is ca. 5/1 in most cases. [b] The asterisk (*) indicates tentative structure assignment based on limited NMR data in reaction mixtures. [c] n.d. = not detected.

likely to be strongly axial relative to the C(4) H_2 protons, although an eclipsed conformation cannot be excluded.

The chlorine atom of 2-Cl-THT (**5**) is predominantly axial, twisted approximately 30° from elcipsed, and the overall ring conformation is similar to that of *trans*-2,3-diCl-THT above. Protons H(2), H(3), and H(5) are equatorial and H′(3) and H′(5) are axial on the basis of sums of vicinal couplings.

The major isomer of **3** is assigned tentatively as the cis configuration by consideration of vicinal couplings and comparison with $J(2,3)$ of the minor isomer. The sums of J(vic) for the C(5) protons are ~10 and ~18 Hz, after subtracting the geminal coupling from the widths of their absorptions. This significant difference between their sums establishes a fixed staggered conformation about C(4)–C(5). Proton H(3) is eclipsed or fixed axial relative to the protons on C(4) and cannot be equatorial. Coupling constant $J(2,3)$ = 4.3 Hz allows the dihedral angle between H(2) and H(3) to be in the range of 50° to 120°. This limited amount of data permits assignment as either cis-2,3 configuration with the 2-hydroxyl group axial on a half-chair conformation of the ring or trans-2,3 configuration with C(5) out of the plane and cisoid to the hydroxyl group in an envelope conformation of the ring. The cis assignment for the major isomer implies a ring conformation the same as *cis*-2,3-diCl-THT and more easily allows the smaller $J(2,3)$ value of 3.3 Hz for the minor isomer to reflect a dihedral angle closer to 90° in a trans configuration.

The minor isomer of **3** is assigned tentatively as trans configuration. Only the H(2) absorption was detected, so coupling information about other ring protons was not available.

The THT ring of **4** appears to be inverting between puckered half-chair conformations, causing the THT^+ substituent to spend comparable amounts of time axial and equatorial. The couplings $J(2,3)$ and $J(2',3)$ are equal at 5.8 Hz, requiring H(3) to be axial or inverting relative to C(2)H_2, and the sum $J(3,4) + J(3,4')$ = 10.6 Hz requires H(3) to be equatorial or inverting with respect to C(4)H_2. Only an inverting half-chair model satisfies both relations.

Converting **3** to its 2-methoxy (**11**) and 2-chloro (**10**) analogues retains the same $J(2,3)$ values for major and minor products, implying (but not proving) that configuration and conformation are the same. The major isomer of **10** that is formed from **3** also appears to be the major (only detected) isomer of **10** that is formed directly from decomposition of **1** in SO_2, and as such is the precursor to the major isomer of **3**.

Experimental Section

Proton NMR spectra were run at 60 MHz on a Varian EM-360, at 100 MHz on a Varian XL-100 with Digilab NMR-3 data system, at 200 MHz on a Bruker CXP-200, and/or at 360 MHz on a Bruker WM-360 spectrometer. Chemical shift reference in non-aqueous solutions is tetramethyl silane (Me_4Si) and in aqueous solutions is 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propanoic acid, sodium salt (TSP) or 3,3-dimethyl-3-silapropanesulfonic acid, sodium salt (DSS).

The sulfonium structures were separated by HPLC using a standard DuPont Sorbax SCX analytical column and gradient elution with 0.5 M $NaClO_4$ in aqueous 65% acetonitrile containing 0.03M $NaHPO_4$. The zwitterion and **2** were detected at 280 nm and **3** was detected at 235 nm. Total analysis time was 10 min.

1-(4,5-Dihydro-3-thienyl)tetrahydrothiophenium Picrate (2b). A solution of 86 g (0.97 mol) of THT over dry nitrogen was cooled to −40 °C and 350 g of SO_2 was condensed through a dry ice condenser. To this solution was added 130 g (0.96 mol) of SO_2Cl_2 slowly at −20 °C. The solution was refluxed at −8 to −10 °C for 4 h and then 100 mL of SO_2 was removed under vacuum. Water, 200 mL, was slowly added, the remaining SO_2 was removed under vacuum, and the resulting solution was extracted 3 times with 100-mL portions of *n*-hexanol. After cooling with an ice bath, solid LiOH was added to adjust the pH to 7. Lithium picrate solution was immediately added until a maximum precipitate was obtained. After filtration and washing with water, the solid was

recrystallized from acetone–water to yield after drying 21.5 g (5.6%) of **2b**.

A 16% yield of **2b** was obtained by using a 0.92/0.93 THT to SO_2Cl_2 molar ratio and allowing the temperature to rise to −5 °C: 100-MHz ^1H NMR (Me_2SO-d_6) δ 8.59 (2 H, s, picrate), 7.78 [1 H, t, J = 1.6 Hz, C(2)H], 3.52 [2 H, t, J = 8.9 Hz, C(5)H_2], 3.09 [2 H, td, J = 8.9 Hz, J' = 1.6 Hz, C(4) H_2], 3.62 (4 H, m, width 15 Hz, THT^+ α H), 2.20 (4 H, m, width 15 Hz, THT^+ β H), decoupling 7.78 ppm collapses the 1.6-Hz splitting at 3.09 ppm. Apparent coupling constants, equal to average observed mutual splittings, are $J(2,4)$, $J(2,4')$ = 1.6 Hz, $J(4,5) + J(4,5') = J(4',5) + J(4',5')$ = 17.8 Hz. Anal. Calcd for $C_{14}H_{15}N_3O_7S_2$: C, 41.89; H, 3.77; N, 10.47. Found: C, 41.60; H, 3.90; N, 10.20.

1-(4,5-Dihydro-3-thienyl)tetrahydrothiophenium Chloride (2a). The picrate **2b**, 4 g, was exchanged with Dowex 2 × 8 resin (Cl^- form) in methanol. After removal of solvent under vacuum, the solid was recrystallized from ethanol to yield, after drying, 1.2 g (52%): 60-MHz ^1H NMR (D_2O) δ 7.60 (1 H, t, J = 1.5 Hz), 3.5 (6 H, m), 3.0 (2 H, m, half of A_2B_2), 2.3 (4 H, m, width 16 Hz); 360-MHz ^1H NMR (strongly acidic D_2O extracts decomposition experiments) δ 7.62 (1 H, t, J = 1.5 Hz), 3.56 (2 H, interference), 3.09 (2 H, t, J = 9.1 Hz), 3.65 (4 H, m, THT^+ α), 2.36 (2 H, m, THT^+ β), 2.27 (2 H, m, THT^+ β) (Apparent coupling constants, equal to average observed splittings, are $J(2,4) = J(2,4')$ = 1.5 Hz, $J(4,5) + J(4,5') = J(4',5) + J(4',5')$ = 18.2 Hz); direct probe electron impact mass spectrum, parent m/e 208 (1 Cl), 118, 117, 91 (1 Cl), 85 (These mass spectra are attributed to structures which result from facile rearrangement of the original chloride salt in the mass spectrometer.); IR (KBr pellet) 3060 and 1548 cm^{-1} (C=C), 3004 (asymmetric CH_2 stretch for -$CH_2S^+CH_2$-), 815 (C–S stretch of -C=CS). Anal. Calcd for $C_8H_{13}ClS_2 \cdot 1.2H_2O$: C, 41.71; H, 6.74; Cl, 15.40. Found: C, 41.55; H, 6.51; Cl, 15.50.

Thermal Rearrangement Product of 2a To Yield 4-[(4-Chlorobutyl)thio]-2,3-dihydrothiophene (2R). The chloride salt **2a** was heated to 120 °C to produce a water-insoluble but chloroform-soluble solid. The mass spectrum was identical with that of the unmelted salt: 60-MHz ^1H NMR ($CDCl_3$) δ 5.98 (1 H, t, J = 1.8 Hz), 3.7–3.1 (4 H, m), 2.8 (4 H, "t"m, "J" = 8 Hz), 1.85 (4 H, m).

Isolation of 2b from a Zwitterion Solution Containing Toxin. A 500-g zwitterion (that contained toxin) 30% solution was concentrated under vacuum to about 50% solids. Concentrated HCl was added while cooling with ice. The resulting crystalline zwitterion salt was removed and the mother liquor was concentrated under vacuum. After cooling, more salt was removed and the pH of the final mother liquor was adjusted with LiOH to 10. Lithium picrate was added to the solution and after 3 days at 2 °C 0.3 g of **2b** was isolated.

1-(Tetrahydro-2-hydroxy-3-thienyl)tetrahydrothiophenium Picrate (3b). A solution of CH_2Cl_2 (200 mL) and 97 g (1.10 mol) of THT was cooled to −5 °C and 71 g (1.0 mol) of chlorine was introduced. After 6 h, 250 mL of H_2O was added. The water phase was extracted 3 times with hexanol and the pH was adjusted to 7.0 with lithium hydroxide. Addition of lithium picrate solution gave after filtration and water washing 20.0 g (4.7%) of **3b** that was about 90% pure by NMR. Crystallization from water acetone gave a pure sample: 100-MHz ^1H NMR (Me_2SO-d_6) δ 8.59 (2 H, s, picrate), 6.92 (1 H, d, J = 5.8 Hz, OH), 5.67 [1 H, t, J = 5.2 Hz, C(2) H], 3.94 [1 H, ddd, J = 11.6 Hz, J' = 6.2 Hz, J'' = 4.4 Hz, C(3) H], 3.60 (4 H, complex, width 20 Hz, THT^+ α), 2.4–3.5 (complex, partially obscured by solvent), 2.23 (4 H, complex, width 15 Hz, THT^+ β H) (Decoupling at 6.92 collapses 5.67 to a 4.4-Hz doublet. Decoupling 5.67 collapses the 4.4-Hz splitting at 3.94 ppm. Adding D_2O caused 6.92 to disappear and collapsed 5.67 to a doublet. Apparent coupling constants, equal to average mutual observed splittings, are J(2-OH) = 5.8 Hz, $J(2,3)$ = 4.4 Hz, $J(3,4;3,4')$ = (11.6, 6.2) or (6.2, 11.4) Hz; 100-MHz ^1H NMR (acetone-d_6/reference acetone-d_5 2.10) δ 8.74 (2 H, s, picrate), 5.93 [1 H, d, J = 4.5 Hz, C(2)H], 4.30 [1 H, ddd, J = 11.5 Hz, J' = 6.0 Hz, J'' = 4.5 Hz, C(3)H], 3.95 (4 H, complex, width 25 Hz, THT^+ α), 3.4 (2 H, m), 2.5 (4 H, complex, width 15 Hz, THT^+ β), remainder obscured. Apparent coupling constants, equal to the observed splittings, are $J(2,3)$ = 4.5 Hz, $J(34,34')$ = (11.5, 6.0) or (6.0, 11.5) Hz;

Anal. Calcd for $C_{14}H_{17}N_3O_8S_2$: C, 40.09; H, 4.09; N, 10.02. Found: C, 39.9; H, 4.20; N, 9.83.

1-(Tetrahydro-2-hydroxy-3-thienyl)tetrahydrothiophenium Chloride (3a). The chloride salt was obtained by ion exchange as described above but could not be isolated in crystalline form: 360-MHz ^1H NMR (CH_3OH), major isomer, δ 6.98 [1 H, b, C(2) OH], 5.84 [1 H, b, C(2) H], 4.22 [1 H, m, width 22.1 Hz, C(3) H], 3.84 (>4 H, c, including THT^+ α), 3.11 (1 H, c), 2.78 (1 H, c), 2.45 (>4 H, c, including THT^+ β); minor isomer, δ 6.85 [1 H, b, C(2) OH], 5.88 (1 H, b, C(2) H), remainder obscured. After standing in CH_3OH solution 3 days, the OH absorptions at 6.98 and 6.85 ppm disappeared and the C(2)H absorptions at 5.84 and 5.88 ppm collapsed to doublets (4.4 and 3.9 Hz, respectively). This sample also contained **2**: 360-MHz ^1H NMR (H_2O/reference dioxane 3.75 ppm) major isomer δ 5.78 [1 H, d, J = 4.3 Hz, C(2) H], 4.05 [1 H, m, sum = 22.6 Hz, C(3) H], 3.72 (ca. 4–5 H, c, width 50 Hz, including THT^+ α), 3.29 [1 H, m, sum = 20.2 Hz, C(5) H], 3.06 [1 H, m, sum = 27.9 Hz, C(5) H′ or C(4) H], 2.71 [1 H, m, sum = 29.8 Hz, C(4) H′], 2.37 (4 H, m, THT^+ β). Apparent coupling constants, equal to the average observed mutual splittings, are $J(2,3)$ = 4.3 Hz, $J(3,4) + J(3,4')$ = 18.3 Hz; minor isomer δ 5.81 [d, J = 3.3 Hz, C(2) H], remainder obscured. Sample also contains **2**. Molar ratio major isomer:minor isomer:**2** = 5:1:2 in both CH_3OH and H_2O solution. Electron impact mass spectrum, m/e 226 (1 Cl) weak, 208 (1 Cl), 131, 118, 117, 91, 85.

2,3-Dihydrothiophene (13). 2-(Benzoyloxy)tetrahydrothiophene was pyrolized as reported by Sosnovsky[15] except the product was isolated under high vacuum in a trap cooled with liquid nitrogen. The 60-MHz proton NMR spectrum agreed with published data.[7]

3-Hydroxytetrahydrothiophene. 3-Thiophanone (Frinton) (105 g, 1.03 mol) in 225 mL of CH_3OH was cooled in an ice bath and 20 g (0.528 mol) of $NaBH_4$ in 150 mL of water was added. After standing 3 days, HCl was added to pH 6 and the product was extracted with diethyl ether. The ethereal extract was dried (Na_2SO_4), concentrated, and distilled, giving 61.0 g (57%) of the alcohol: bp 57–58 of (0.9 mm) (*J. Chem. Soc.* **1960**, 2649, 52 °C/0.12 mm); ^1H NMR ($CDCl_3$) δ 4.66 [1 H, pentet, J = 3.4 Hz, C(3) H], 3.2–2.8 (4 H, complex), 2.52 [1 H, s, C(3) OH], 2.2–1.6 (2 H, complex).

Tetrahydrothiophen-3-yl Benzenesulfonate. A solution of 50 g (0.48 mol) of 3-hydroxytetrahydrothiophene in 500 mL of pyridine was cooled to −30 °C and 108.8 g (0.616 mol) of benzenesulfonyl chloride was added slowly. The solution was warmed to 0 °C and after 24 h. 4 mL of water was added with stirring. The solution was added to 2 L of crushed ice and 150 mL of H_2SO_4 and then the mixture was extracted with chloroform. The chloroform extract was extracted 3 times with water and dried (Na_2SO_4), and the solvent was removed, giving 101.4 g (86%) of mp 34–35 °C: 60-MHz ^1H NMR ($CDCl_3$) δ 8.0–7.5 (5 H, phenyl), 5.23 [1 H, pentet, J = 3.5 Hz, C(3) H], 3.2–2.7 (4 H, complex), 2.6–1.7 (2 H, complex). Anal. Calcd for $C_{10}H_{12}O_3S$: C, 49.16; H, 4.95. Found: C, 49.30; H, 5.10.

1-(Tetrahydro-3-thienyl)tetrahydrothiophenium Picrate (4b). A solution of 10 g (0.041 mol) of tetrahydrothiophen-3-yl benzenesulfonate in 100 mL THT and 20 mL of water was heated to 75 °C for 5 days. Chloroform (50 mL) was added and the solution was extracted 3 times with water. The water was removed under vacuum to yield 10 g of syrup. Addition of a solution of lithium picrate gave 15.2 g (92%) of **4b**. Anal. Calcd for $C_{14}H_{17}N_3O_7S_2$: C, 41.68; N, 4.25; N, 10.42. Found: C, 41.71: H, 4.24; N, 10.41.

Isolation of 4 from the Decomposition of 1. Small amounts of a third sulfonium were obtained when an SO_2 solution of **1** was held at −5 °C for 4 h, water was added, and the solution was allowed to stand at 25 °C. The resulting dark liquid was loaded on a cation column of Dowex 50^+ resin and eluted with 6 N HCl. From this solution a material was isolated by HPLC with NMR and mass spectra analyses consistent with structure **4**.

1-(Tetrahydro-3-thienyl)tetrahydrothiophenium Chloride (4a). The picrate **4b** was exchanged to the chloride by using the described method: 100-MHz ^1H NMR (D_2O) δ 4.14 [1 H, pentet, sum = 22.4 Hz, C(3) H], 3.41 [1 H, dd, J = 12.4 Hz, J' = 5.8 Hz, C(2) H], 3.15 [1 H, dd, J = 12.4 Hz, J' = 5.8 Hz, C(2)H′], 3.12 [2 H, t, J = 7 Hz, C(5) H_2], 2.8–2.4 [2 H, complex, C(4) H_2].

(15) Sosnovsky, G. *Tetrahedron* **1962**, *18*, 903.

Decoupling at 4.14 collapses 3.6–3.0 ppm to an AB quartet at δ 3.40 and 3.20 with J(AB) = 13 Hz and collapses much structure at 2.8–2.4 ppm. Decoupling at 2.5 ppm collapses partially the patterns at 4.14 and 3.12 ppm. Analysis of the absorptions at 3.41 and 3.15 ppm as AB of ABX:C(2)H = 3.39 ppm, C(2)H′ = 3.17 ppm, J(2,2′) = 12.4 Hz, J(2,3) = 5.8 Hz, J(2′,3) = 5.8 Hz. Other apparent coupling constants as observed splittings: J(3,4) + J(3,4′) = 10.6 Hz, J(4,5) + J(4,5′) = J(4′,5) + J(4′,5′) = 14 Hz. Direct probe electron impact mass spectrum; parent m/e 210 (1 Cl). Anal. Calcd for $C_8H_{15}ClS_2 \cdot 0.69H_2O$: C, 43.06; H, 7.40; Cl, 15.89. Found: C, 43.15; H, 7.25; Cl, 16.30.

2-Chlorotetrahydrothiophene (5) and 2,3-Dichlorotetrahydrothiophene (6). Most of the CCl_4-soluble decomposition products were **5** and **6**. Their room-temperature NMR spectra were analyzed and assigned, without separation, via selective decoupling experiments on the neat CCl_4 phase from the decomposition of **1** in CCl_4. 2-Cl-THT (**5**): 360-MHz ^{1}H NMR (CCl_4 with *trans*-**6** and *cis*-**6**) δ 5.68 [1 H, dd, J = 4.5 Hz, J' = 1.5 Hz, C(2)H], 3.19 [1 H, ddd, J = 10.0 Hz, J' = 6.8 Hz, J'' = 2.7 Hz, C(5)H], 2.90 [1 H, td, J = 9.7 Hz, J' = 7.3 Hz, C(5)H′], 2.49 [1 H, dm, J = 12.5 Hz, J' sum = 8 Hz, C(3) H], 2.28 [2 H, complex including a d, J = 10–12 Hz, C(4) H_2], 2.18 [1 H, dddd, J = 12.3 Hz, J' = 12.0 Hz, J'' = 6.1 Hz, J''' = 4.6 Hz, C(3) H′]. (Decoupling 5.68 partially collapses 2.49 and 2.18. The following doublets form AB intensity patterns: 12.3–12.5 Hz at 2.49 and 2.18, 10–12 Hz at 2.28 and 2.18. Apparent coupling constants, equal to the average observed mutual splittings, are J(2,3) = 1.5 Hz, J(2,3′) = 4.5 Hz, J(3,3′) = 12.4 Hz, J(3,4) + J(3,4′) ~ 6.5 Hz, J(3′,4) = 6.1 Hz, J(3′,4′) = 12.0 Hz, J(4,5) = 2.7 Hz, J(4,5′) = 9.7 Hz, J(4′,5), = 6.8 Hz, J(4′,5′) = 7.3 Hz, J(5,5′) = 9.8 Hz. The relative signs were not determined.

***trans*-2,3-diCl-THT (*trans*-6)**: 360-MHz ^{1}H NMR (CCl_4) with *cis*-**6** and **5**) δ 5.55 [1 H, t, J = 1.4 Hz, C(2) H], 4.72 [1 H, ddd, J = 4.0 Hz, J' = 1.6 Hz, J'' = 1.1 Hz, C(3) H], 3.30 [1 H, ddd, J = 10.6 Hz, J' = 10.2 Hz, J'' = 6.1 Hz, C(5) H], 3.23 [1 H, ddd, J = 10.1 Hz, J' = 7.9 Hz, J'' = 1.6 Hz, C(5) H′], 2.70 [1 H, dddd, J = 13.7 Hz, J' = 10.9 Hz, J'' = 8.0 Hz, J''' = 3.9 Hz, C(4) H], 2.41 [1 H, ddq, J = 13.8 Hz, J' = 6.1 Hz, J'' = 1.4 Hz average, C(4) H′]. Decoupling 5.55 ppm sharpened 4.71 and 2.41. Decoupling 4.71 partially collapses 5.55, 2.70, and 2.41. Decoupling 3.25 partially collapses 2.70 and 2.41. Decoupling 2.70 partially collapses 4.72, 3.25 region, and 2.41. The following pairs of doublets form AB intensity patterns: 10.6–10.9 Hz at 3.30 and 2.70, 10.1–10.2 Hz at 3.30 and 3.23, 7.9–8.0 Hz at 3.23 and 2.70, 13.7–13.8 Hz at 2.70 and 2.41. The apparent coupling constants, equal to average observed mutual splittings, are J(2,3) = 1.2 Hz, J(2,4′) = 1.6 Hz, J(3,4) = 4.0 Hz, J(3,4′) = 1.6 Hz, J(4,4′) = 13.8 Hz, J(4,5) = 10.8 Hz, J(4,5′) = 8.0 Hz, J(4′,5) = 6.1 Hz, J(4′,5′) = 1.6 Hz, J(5,5′) = 10.2 Hz. Relative signs of the couplings were not determined.

***cis*-2,3-diCl-THT (*cis*-6)**: 360-MHz ^{1}H NMR (CCl_4 with **5** and *trans*-**6**) δ 5.44 [1 H, d, J = 4.0 Hz, C(2) H], 4.37 [1 H, ddd, J = 11.4 Hz, J' = 6.4 Hz, J'' = 4.2 Hz, C(3) H], the remaining protons are obscured by **5** and *trans*-**6**. Decoupling 5.44 collapses 4.37 to dd, J = 11.4 Hz, J' = 6.4 Hz. Apparent coupling constants, equal to mutual observed splittings, are J(2,3) = 4.1 Hz, J(3,4) = 11.4 Hz, J(3,4′) = 6.4 Hz. Relative signs were not determined.

Decomposition of 1 in CCl_4. The decomposition of **1** in CCl_4 at 0 °C for 1 h gave two phases: a top semisolid phase and a bottom CCl_4 phase. The CCl_4 phase contained **5** and **6** in a **5**/**6** ratio of 0.4 plus a small amount of THT. Both the cis and trans isomers of **6** were detected in a trans/cis ratio of about 20. Extraction of the CCl_4 phase with D_2O appeared to hydrolyze **5** and **6** to materials having aldehyde CHO absorptions at 9.75 and 9.55 ppm and another absorption at 4.4 ppm. The D_2O solution also showed coupled strong proton absorptions at 5.48 and 5.56 ppm and weak coupled absorptions at 5.38 and 4.4 ppm, probably due to **7** formed by the hydrolysis of **6**. Absorptions at 5.55 ppm were consistent with H(2) of **8** formed by hydrolysis of **5**.

Addition of D_2O–CCl_4 to the top, water-soluble phase gave an acidic D_2O solution containing **2**, **3**, **8**, and THTO. The ratio of the major to minor isomers of **3** was 4. The CCl_4 from the D_2O–CCl_4 addition contained THT and materials similar to materials obtained by D_2O extraction of the original CCl_4 phase.

Decomposition of 1 in CH_2Cl_2. The decomposition of **1** was carried out in CH_2Cl_2 at −10 °C for 6 h. Tetraethylammonium chloride was added to the solution as a quantitative reference since the methyl protons absorb clear of interference at 1.25 ppm. The resulting cold, homogeneous solution was mixed with D_2O and the D_2O phase, which was acidic, was analyzed by proton NMR after extraction with CCl_4. There was considerable THTO and the yield of **3** was about 5%. Under the reaction conditions very little **2** was detected. When the CH_2Cl_2 reaction solution was warmed to ambient temperature, the amount of **3** decreased and **2** became the main product.

Decomposition of 1 in Liquid SO_2. The decomposition of **1** was studied in liquid SO_2 at −15 °C by taking samples with time and quenching the cold solutions with D_2O–CCl_4. After vacuum removal of the SO_2 the samples were monitored by NMR. Tetraethylammonium chloride was used as an internal quantitative reference. After 1 h at −15 °C, the D_2O phase contained THTO and a small amount of coupled α,β proton absorptions at 5.15 and 4.13 ppm. The NMR of this material was consistent with an α-(sulfonic acid)-β-THT$^+$ substituted THT, **9**. This tentative NMR interpretation is based on the lesser deshielding effect of the sulfonic acid group relative to the hydroxyl group of **3**. After 3 h the amount of **9** had increased and **2** began to appear. After 10 h, the yields based on the internal standard were 5% **9** and 5% **2**. Upon elimination of most of the SO_2 before quenching, by warming to 10 °C, no **9** could be detected. However, a yield of 8% of **3** and 12% of **2** was observed. The CCl_4 phase from the D_2O–CCl_4 quench contained hydrolysis products of **5** and **6**. When the SO_2 solution of **1** was warmed to 0 °C for 3 h, the anhydrous CCl_4 extract of the SO_2 solution contained a 2-Cl-THT/2,3-diCl-THT ratio of 0.42 and the trans to cis ratio of 2,3-diCl-THT was 14.

Decomposition of 1 Monitored by NMR. The decomposition of **1** in SO_2 was monitored by NMR in sealed tubes at −15 °C. The complex **1** in SO_2 had α and β proton shifts of 4.20 and 2.77 ppm and these absorptions decreased with time. After 1.8 h, HCl was detected followed at 5.8 h by coupled α,β proton absorptions at 6.06 and 4.16 ppm which increased with time. Small coupled absorptions at 5.98 and 4.16 ppm later became apparent and they maintained a constant proportion to the absorptions at 6.06 and 4.16 ppm. These chemical shifts are consistent with the cis and trans isomers of the structure **10**. The J(2,3) couplings of these two isomers are 4.0 Hz for the major isomer and less than 4.0 Hz (unresolved) for the lesser isomer. In contrast to the cis and trans isomers of **6**, the major isomer of **10** exhibited larger J(2,3) coupling. Soon after the appearance of **10**, the sulfonium **2** was detected and continued to increase during the decomposition. Other unidentified products developed absorptions at 5.33, 5.14, and 4.8 ppm. The latter absorptions were probably from the dark tars commonly formed by the Pummerer reaction. Absorptions at 4.8 ppm and greater are consistent with α hydrogens geminal to strongly electron-withdrawing α substituents, based on substitution chemical shift effects observed for **3**, **4**, **5**, and **6**. Not much **5** and **6** was detected by NMR; they may have phased out of solution. After 12.5 h at −15 °C, about 64% of the complex **1** still remained; however, it decomposed after warming to room temperature.

1-(2-Chlorocyclohexyl)tetrahydrothiophenium Picrate (14). To 95 g of SO_2 and 20 g (0.23 mol) of THT at −30 °C was added 28.3 g (0.21 mol) of SO_2Cl_2 followed by 17.8 g (0.217 mol) of cyclohexene. After 30 min at −5 °C, 30 mL of H_2O was added and the SO_2 was removed. The bottom phase (15.1 g, 0.099 mol) was mostly 1,2-dichlorocyclohexane as identified by NMR comparison with authentic compound. The water phase was extracted twice with CH_2Cl_2 and adjusted to pH 7 with lithium hydroxide, and lithium picrate was added to give 3.3 g (3.5%) of **14**: 100-MHz ^{1}H NMR (Me_2SO-d_6) δ 8.62 (2 H, s, picrate), 4.49 [1 H, td, J = 10.0 Hz, J' = 4.2 Hz, C(2) H], 3.97 [1 H, td, J = 10.0 Hz, J' = 3.7 Hz, C(1) H], 3.72 (4 H, m, width 15 Hz, THT$^+$ α H), 2.17 (4 H, m, width 15 Hz, THT$^+$ β H), 2.2 (2 H, m), 2.1–1.3 (6 H, complex); 25-MHz ^{13}C NMR (Me_2SO-d_6) δ 141.9 and 125.1 (picrate), 59.9 [C(1)], 44.2, 43.8, 38.2, 36.4, 29.0, 28.6, 25.8, 24.0, 23.8. Anal. Calcd for $C_{16}H_{20}ClN_3O_7S$: C, 44.29; H, 4.65; N, 9.69. Found: C, 44.00; H, 4.64; N, 9.84.

1-(2-Chloro-2-phenylethyl)tetrahydrothiophenium Chloride (15). Preparation in SO_2. To 70 g of SO_2 and 20 g (0.23 mol) of THT at −30 °C was added 26.7 g (0.20 mol) of SO_2Cl_2 followed by slow addition of 18.1 g (0.17 mol) of styrene. After

30 min at −15 °C, about 60% of the SO_2 was removed. The liquid was stirred into diethyl ether, the ether was decanted, and acetone was added to yield upon filtration 29 g (85%) of **15**.

Preparation of 15 in CH_2Cl_2. To 70 g of CH_2Cl_2 and 20 g (0.23 mol) of THT at −30 °C was added 14 g (0.40 mol) of chlorine followed by addition of 18.1 g (0.17 mol) of styrene. After 30 min, the solution was stirred into ether, the ether was decanted, and acetone was added to give 4.2 g (9.2%) of **15**: 60-MHz ^{1}H NMR (D_2O) δ 7.5 (5 H, b, phenyl), 5.48 [1 H, t, J = 7 Hz, C(2) H], 3.96 [2 H, AB of ABX, J(AB) = 13 Hz, C(1) H2], 3.4 (4 H, m, width 20 Hz, THT^+ α H), 2.14 (4 H, m, width 14 Hz, THT^+ β H); 60-MHz ^{1}H NMR (CF_3COOH) δ 7.5 (5 H, b, phenyl), 5.45 (1 H, t, J = 7 Hz), 3.85 (2 H, t, J = 7 Hz), 3.55 (4 H, m, width 25 Hz), 2.36 (4 H, m, width 15 Hz). Anal. Calcd for $C_{12}H_{16}Cl_2S$: C, 54.76; H, 6.13; Cl, 26.94. Found: C, 54.80; H, 6.25; Cl, 25.80.

[2-Chloro-1-[(4-chlorobutyl)thio]ethyl]benzene (15Rb) and [1-Chloro-2-[(4-chlorobutyl)thio]ethyl]benzene (15Ra). The chloride salt **15** was heated gently in a test tube to 120 °C, causing it to melt and resolidify to a water-insoluble and acetone-soluble product: 60-MHz ^{1}H NMR (acetone-d_6) δ 7.35 (5 H, m, phenyl), 5.15 (0.7 H, t, J = 7.5 Hz), 4.00 (0.7 H, ABC pattern), 3.53 (2 H, t, J = 8 Hz), 3.21 (1.3 H, d, J = 7.5 Hz), 2.80 (0.4 H, t, J = 8 Hz), 2.50 (2 H, t, J = 8 Hz), 1.8 (4 H, m width 20 Hz).

1-(2-Hydroxytetrahydro-3-furanyl)tetrahydrothiophenium Picrylsulfonate (16). To 70 g of SO_2 and 20 g (0.23 mol) of THT at −30 °C was added 26.7 g (0.20 mol) of SO_2Cl_2 followed by addition of 14 g (0.20 mol) of 2,3-dihydrofuran. After 30 min at −15 °C about $^2/_3$ of the SO_2 was removed under vacuum, 50 mL of water was added, and the remaining SO_2 was removed. The aqueous solution was extracted with CH_2Cl_2 and picrylsulfonic acid was added, giving 18.2 g (19.5%) of **16**: 60-MHz ^{1}H NMR (Me_2SO-d_6) δ 8.82 (2 H, s, picrylsulfonate), 7.45 [1 H, d, J = 4 Hz, C(2) OH], 5.54, [1 H, t, J = 4 Hz, C(2) H], 3.98 [3 H, m, incl J = 0.6 Hz, C(3) H and C(5) H_2], 3.5 (4 H, m, width 15 Hz, THT^+ α), 2.18 [6 H, m, width 20 Hz, C(4) H_2 and THT^+ β]. Smaller absorptions at δ 7.7, 4.6, and 3 are attributed to another component. Adding D_2O caused the δ 7.45 signal to disappear and that at 5.54 to collapse to a 4.5 Hz d. Anal. Calcd for $C_{14}H_{17}N_3O_{11}S_2$: C, 35.97; H, 3.67; N, 8.99. Found: C, 36.24; H, 3.54; N, 8.96.

1-(2-Thienyl)tetrahydrothiophenium Picrate (17). To 75 g of SO_2 and 16 g (0.18 mol) of THT at −30 °C was added 21.7 g (0.16 mol) of SO_2Cl_2 followed by 13.96 g (0.16 mol) of thiophene. After 30 min at −5 °C 30 mL of H_2O was added and the SO_2 was removed. After extraction twice with both chloroform and hexanol, the material was converted to the picrate by the usual manner to give 9.3 g (14.6%) of **17**: 100-MHz ^{1}H NMR (Me_2SO-d_6) δ 8.61 (2 H, s, picrate), 8.22 [1 H, dd, J = 5.1 Hz, J' = 1.4 Hz, C(5) H], 8.00, [1 H, dd, J = 3.8 Hz, J' = 1.4 Hz, C(3) H], 7.34 [1 H, dd, J = 5.1 Hz, J' = 3.8 Hz, C(4) H], 3.88 (4 H, m, width 60 Hz, THT^+ α), 2.39 (4 H, m, width 18 Hz, THT^+ β). Coupling constants among thiophene ring protons: J(3,4) = 3.8 Hz, J(3,5) = 1.4 Hz, J(4,5) = 5.1 Hz. Placement of the THT^+ ring at the 2-position on the thiophene ring is established by similarity of the thiophene ring proton–proton coupling constants to the corresponding values reported[16] for unsubstituted thiophene, J(3,4) = 3.50 Hz, J(2,4;3,5) = 1.04 Hz, J(2,3;4,5) = 4.90 Hz, J(2,5) = 2.84 Hz. Anal. Calcd for $C_{14}H_{13}O_7N_3S_2$: C, 42.10; H, 3.28; N, 10.52. Found: C, 41.8; H, 3.33; N, 10.54.

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(16) Brügel, W. "Handbook of NMR Spectral Parameters"; Heyden and Sons Inc.: Philadelphia, 1979; Vol. 3, pp 657.

Dioxiranes: Synthesis and Reactions of Methyldioxiranes

Robert W. Murray* and Ramasubbu Jeyaraman

Department of Chemistry, University of Missouri—St. Louis, St. Louis, Missouri 63121

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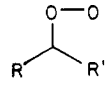
The peroxymonosulfate–acetone system produces dimethyldioxirane under conditions permitting distillation of the dioxirane from the synthesis vessel. The same conditions were used to prepare other methyldioxiranes. Solutions of dimethyldioxirane prepared in this manner were used to study its chemical and spectroscopic properties. The caroate–acetone system was also used to study the chemistry of in situ generated dimethyldioxirane.

Introduction

Dioxiranes (1) members of the smallest cyclic peroxide system, are isomeric with carbonyl oxides **2**, one of the



2

1a, R = R' = H
1b, R = R' = CF_3
1c, R = CF_3, R' = CF_2Cl
1d, R = R' = CH_3
1e, R = CH_3, R' = CH_3CH_2
1f, R = CH_3, R' = $CH_3CH_2CH_2$
1g, R = CH_3, R' = $CH_3CH_2CH_2CH_2$
1h, R = R' = CH_3CH_2

peroxidic intermediates involved in the ozonolysis process. Dioxirane **1a**, produced via ozonolysis of ethylene, has been characterized by both mass spectral and microwave methods.[1-3] In two cases, **1b** and **1c**, it has been reported[4] that dioxiranes have been isolated and characterized by physical and chemical methods. In these cases the dioxiranes were synthesized by oxidation of the corresponding dilithioalkoxides.

Dioxiranes have been postulated as intermediates in reactions involving peracids.[5-10] Edwards, Curci, and

(1) Lovas, F. J.; Suenram, R. D. *Chem. Phys. Lett.* **1977**, *51*, 453–456.
(2) Martinez, R. I.; Huie, R. E.; Herron, J. T. *Chem. Phys. Lett.* **1977**, *51*, 457–459.
(3) Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* **1978**, *100*, 5117–5122.
(4) Talbott, R. I., Thompson, P. G. U.S. Patent 3 632 606, 1972.
(5) Edwards, J. O.; Pater, R. H.; Curci, R.; DiFuria, F. *Photochem. Photobiol.* **1979**, *30*, 63–70.
(6) Montgomery, R. E. *J. Am. Chem. Soc.* **1974**, *96*, 7820–7821.
(7) Gallopo, A. R.; Edwards, J. O. *J. Org. Chem.* **1981**, *46*, 1684–1688.
(8) Cicala, G.; Curci, R.; Fiorentino, M.; Laricciuta, O. *J. Org. Chem.* **1982**, *47*, 2670–2673.

0022-3263/85/1950-2847$01.50/0