CH_2Cl_2, and dried to afford 4-aminobutyric acid (0.95 g, 92%) identical (IR, ^1H NMR in D_2O solution) with an authentic sample.

1-Octadecanol from Carbonate 14. A solution containing **14** (1.72 g), HOAc (0.6 mL), PPh_3 (0.2 g), and $Pd(PPh_3)_4$ (0.2 g) in CH_2Cl_2 (15 mL) was stirred at 25 °C for 18 h, washed with $NaHCO_3$ solution, dried, and evaporated to yield fairly pure 1-octadecanol containing a small amount of Ph_3P. Recrystallization from methanol gave the pure alcohol: 1.12 g (83%); mp and mmp 58–60 °C.

Registry No. 1, 80127-23-7; **2**, 113-98-4; **4**, 80127-24-8; **5**, 80225-13-4; **6**, 76627-82-2; **6** sulfoxide, 80127-25-9; **7**, 80183-95-5; **12**, 80127-26-0; **14**, 76627-81-1; **15**, 76648-56-1; **16**, 80127-27-1; **17**, 76627-80-0; **18**, 80127-28-2; **19**, 80127-29-3; 1,2-dichloro-2-propene, 78-88-6; allyl bromide, 106-95-6; (*E*)-cinnamyl bromide, 26146-77-0; methyl (*E*)-γ-bromocrotonate, 6000-00-6; 4-aminobutyric acid, 56-12-2; allyl chloroformate, 2937-50-0; 1-aminoadamantane, 768-94-5; cyclododecylamine, 1502-03-0; (6*R*,7*R*)-3-methyl-7-(phenylacetamido)-8-oxo-3-cephem-4-carboxylic acid, 27255-72-7; potassium (6*R*,7*R*)-3-methyl-7-(phenylacetamido)-8-oxo-3-cephem-4-carboxylate, 34708-38-8; 2-ethylhexanoic acid, 149-57-5; 1-adamantamine 2-ethylhexanoate, 80127-30-6; 1-octadecanol, 112-92-5; $Pd(PPh_3)_4$, 14221-01-3.

Stable Thiiranium and Thiirenium Chlorides. Ionization of β-Thioalkyl and β-Thiovinyl Chlorides in Sulfur Dioxide

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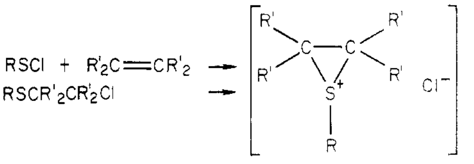
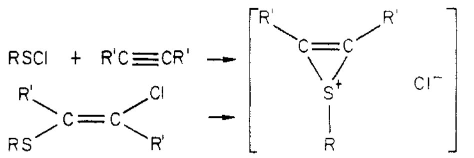
Thiiranium **1** and thiirenium ions **2** have been proposed as intermediates both in the addition of sulfenyl chlorides to double and triple bonds and in the solvolysis of β-thioalkyl and β-thiovinyl chlorides[1] (eq 1 and 2).



(1)

1



(2)

2

Compelling evidence for the presence of these intermediates along the reaction paths of addition[2] and solvolysis[3,4] reactions has been provided by stereochemical[2,3] and kinetic studies.[4] Furthermore we have shown that, in the addition of methanesulfenyl chloride to dialkylacetylenes in sulfur dioxide at low temperature, the corresponding thiirenium chlorides are rapidly formed and may easily be detected by ^1H NMR spectroscopy.[5,6] Stable thiiranium[7,8] and thiirenium salts,[6,9] with the proper counterion, have been isolated: addition of chloride ion to them gives products sterically identical with those obtained from the direct addition of sulfenyl chloride to the corresponding ethylenes or acetylenes.[5,10]

No intermediates, in the form of thiiranium or thiirenium halides, have been detected in the solvolysis reactions, so that the presence of cyclic intermediates is based upon indirect evidence only.

We have already reported that, contrary to the behavior of less heavily substituted thiirenium ions, 1-methyl-2,3-di-*tert*-butylthiirenium chloride (**6**) is stable in sulfur dioxide at room temperature.[6] It may therefore be expected that the corresponding adduct, (*E*)-2,2,5,5-tetramethyl-3-(methylthio)-4-chloro-3-hexene (**4**), might spontaneously ionize in this solvent. We report herein kinetic results for this ionization study, which has been extended, for the sake of comparison, to the reaction of the saturated analogue 2,3-dimethyl-3-(methylthio)-2-chlorobutane (**3**).

Results

The reactions of the adducts **3** and **4** in sulfur dioxide were followed by ^1H NMR spectroscopy. In agreement with expectation, vinyl chloride **4** ionizes to 1-methyl-2,3-di-*tert*-butylthiirenium chloride (**6**) at a measurable rate at room temperature ($t_{1/2}$ at 25 °C ≃ 90 min). The conversion of alkyl chloride **3** to pentamethylthiiranium chloride **5** is much faster and was to be followed at lower temperature ($t_{1/2}$ at −60 °C ≃ 5 min). The signals of thiiranium chloride **5** (δ 2.39, methyl bound to sulfur; δ 1.97 and 1.93, ring carbon methyls) and thiirenium chloride **6** (δ 2.61, methyl bound to sulfur; δ 1.53, *tert*-butyls) were identified through comparison with those of the hexachloroantimonate salts of the same cations.[6,8] The ionization of **3** was followed by measuring the integrated intensities of the α-Cl methyls in **3** and the sulfur methyl in **5**, which are relatively isolated. For the ionization of **4** the *tert*-butyl resonances of **4** and **6** have been monitored.

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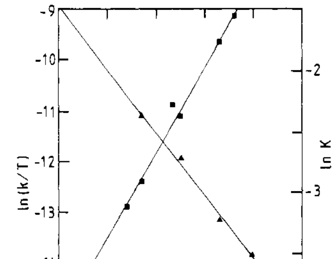


Figure 1. van't Hoff (■) and Eyring (▲) plots for the solvolysis of β-thioalkyl chloride **3** to pentamethylthiiranium chloride (**5**) in sulfur dioxide.

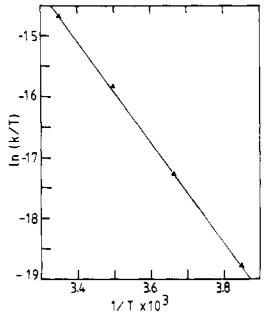
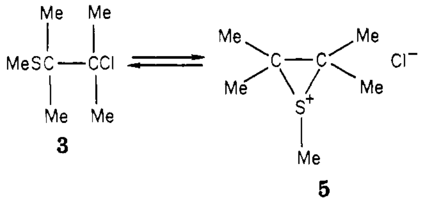
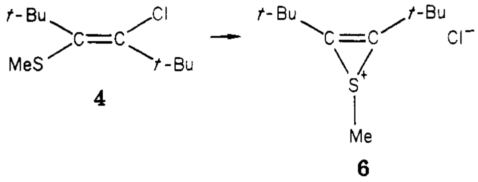


Figure 2. Eyring plot for the solvolysis of β-thiovinyl chloride **4** to 1-methyl-2,3-di-*tert*-butylthiirenium chloride (**6**) in sulfur dioxide.

It turned out that the ionization of **4** to thiirenium chloride **6** is quantitative, whereas **3** and thiiranium chloride **4** are in equilibrium (eq 3 and 4).



(3)



(4)

The constant for the equilibrium shown in eq 3 was measured at different temperatures (between −40 and −70 °C), and from a van't Hoff fit the following parameters were obtained for the ionization of thiiranium chloride: $\Delta H^\circ = -7.0$ kcal mol^{-1}, $\Delta S^\circ = -37$ cal mol^{-1} deg^{-1}.

In the same manner the kinetics of the ionizations of **3** and **4** were followed in the proper temperature range (between −53 and −73 °C for **3**; between 25.2 and −13.2 °C for **4**). The experimental data fit nicely into equations describing respectively a first-order reaction in equilibrium with a second-order one and an irreversible first-order reaction. The rate constants fit into the Eyring equation and the following activation parameters were obtained: for ionization to thiiranium chloride, $\Delta H^\ddagger = 12.2$ kcal mol^{-1}, $\Delta S^\ddagger = -13$ cal mol^{-1} deg^{-1}; for ionization to thiirenium chloride, $\Delta H^\ddagger = 16.5$ kcal mol^{-1}, $\Delta S^\ddagger = -21$ cal mol^{-1} deg^{-1}.

Results of equilibrium and kinetics measurements are shown in Figures 1 and 2.

Discussion

For the ionizations under investigation a monotonic decrease of entropy is observed in going from reagents to transition states and (in one case) from transition state to the ionic product. The entropy change is to be associated with specific solvation of chloride ion by sulfur dioxide, a solvent with Lewis acid characteristics. This may explain why covalent β-thio-substituted chlorides **3** and **4** solvolize in sulfur dioxide, giving *stable* ionic chlorides **5** and **6**;[11] in fact, a more correct, although approximate, description of the anion may be $Cl(SO_2)_n^-$.[12]

Furthermore, di-*tert*-butylthiirenium chloride **6** seems more stable with respect to the precursor than pentamethylthiiranium chloride (**5**). This finding is surprising if we consider the great number of thiiranium salts isolated[7,8] with different substituents at carbon or sulfur, while only two thiirenium salts stable at room temperature have been so far reported.[6,9] The latter are characterized by the presence of bulky substituents at the ring carbons.

In fact, the different stability toward chloride ion may be ascribed to simple steric factors. First, because of the pyramidal arrangement of the sulfur atom,[7b,8] the methyl groups in pentamethylthiiranium ion **5** are obliged to occupy a situation of greatest steric repulsion, while in the case of β-thioalkyl chloride **3** they can minimize their mutual repulsion by assuming the staggered conformation. As for the unsaturated analogues, the absolute conformation of di-*tert*-butylthiirenium ion **6**, known from X-ray analysis,[13] suggests a steric repulsion between methyl and *tert*-butyl groups not greater than that which can be expected in the precursor β-thiovinyl chloride **4**.

Furthermore, the anti stereospecificity observed in the addition and solvolysis reactions 1 and 2 requires the in-plane attack of the nucleophile to the ring carbons of the intermediates **1** and **2**.[9,14] This attack is relatively easy on thiiranium ion **5**, where methyl substituents are under and above the plane containing the ring and the nucleophile, but it is strongly hindered on thiirenium ion **6**, where the bulky *tert*-butyl substituents, the molecular ring, and the chloride ion lie in the same plane.[15] This is even more so when the nucleophile is the species suggested above, $Cl(SO_2)_n^-$, which is itself noticeably bulky. With nonbulky substituents, thiirenium ions **2** are less stable: trimethylthiirenium ion is easily attacked by chloride ion also in sulfur dioxide to give the corresponding covalent compound.[6] Electron-releasing properties of carbon substituents may also contribute to the stability of thiirenium ions.

A final piece of discussion shall be devoted to the activation parameters. The activation enthalpy for the ionization of vinyl chloride **4** is significantly greater than that found for the ionization of the saturated chloride **3**. This circumstance reflects the greater strength of a C_{sp^2}–Cl bond with respect to that of a C_{sp^3}–Cl bond. Activation entropies, being more subject to error, should be considered

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(11) The stability of cations **5** and **6** as such is to be attributed to the bridging of sulfur atom: *tert*-butyl chloride kept 7 days in sulfur dioxide at 75 °C does not show any activity. Because ethanolysis of the same compound was observed under much milder conditions [Cooper, K. A.; Hughes, E. D.; Ingold, C. K.; MacNulty, B. J. *J. Chem. Soc.* **1948**, 2038], we think that solvolysis to *tert*-butyl cation and chloride does occur but that the equilibrium is shifted toward the covalent compound.

(12) The enthalpy of solvation of Cl$^-$ ion by two SO_2 molecules (from high-pressure mass spectroscopy measurements) is −34.1 kcal mol^{-1}: Keese, R. G.; Castleman, A. W., Jr. *J. Am. Chem. Soc.* **1980**, *102*, 1446.

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in their sign and order of magnitude only; these parameters suggest again the importance of the solvent sulfur dioxide in the cleavage of the C–Cl bond.

Experimental Section

NMR Experiments. Equilibria and kinetics were measured with a FT Bruker WP-60 instrument equipped with a BNC-28 microcomputer and a variable-temperature unit. Faster kinetics were first recorded as FID's in different sections of the computer memory and Fourier transformed at the end. The samples were prepared by condensing a measured quantity of sulfur dioxide in a NMR tube containing a weighed amount of covalent chloride 3 or 4. For high-temperature experiments the tubes were sealed.

Materials. Sulfur dioxide and 2,3-dimethyl-2-butene (tetramethylethylene) are commercial products. Methanesulfenyl chloride[16] and 2,2,5,5-tetramethyl-3-hexyne (di-*tert*-butylacetylene)[17] were prepared according to published procedures.

2,3-Dimethyl-3-(methylthio)-2-chlorobutane (3). To an ice-cooled and stirred dichloromethane solution of tetramethylethylene (in slight excess) is added methanesulfenyl chloride in the same solvent dropwise. After 5 min at 0 °C and 10 min at room temperature, the solvent and excess olefin are removed under vacuum; a yellow oil is obtained: 97% yield; bp 74–78 °C (20 mmHg). Because of product sensitivity to moisture, a bad elemental analysis was obtained; before use the alcohol formed is to be removed under vacuum: NMR ($CDCl_3$) [SO_2, −60 °C] δ 2.14 [2.05], SMe; 1.74 [1.73], CMe_2Cl; 1.46 [1.42], CMe_2S.

(*E*)-2,2,5,5-Tetramethyl-3-(methylthio)-4-chloro-3-hexene (4). With the same procedure, methanesulfenyl chloride is added to an equimolar amount of di-*tert*-butylacetylene. After 1 h the solution is washed with sodium carbonate in water and water to neutrality. The solution is dried and the solvent removed at low pressure; a yellow oil is obtained: 96% yield; bp 110–120 °C (15 mmHg); NMR ($CDCl_3$) [SO_2, −50 °C] δ 2.18 [2.25], SMe; 1.48 and 1.41 [1.45 and 1.37], *tert*-butyls.

Anal. Calcd for $C_{11}H_{21}ClS$: C, 59.85; H, 9.6. Found: C, 59.65; H, 9.5.

Registry No. 3, 77483-47-7; 4, 63720-34-3; 5, 79899-49-3; 6, 63720-33-2; tetramethylethylene, 563-79-1; methanesulfenyl chloride, 5813-48-9; di-*tert*-butylacetylene, 17530-24-4.

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Studies in the Heterocyclic Series. 22. New Chemistry of Azaphenothiazine and Its Precursors

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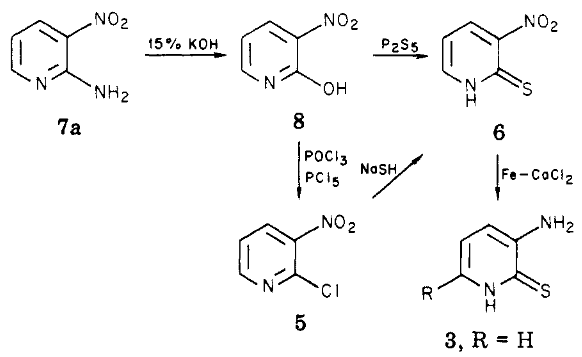
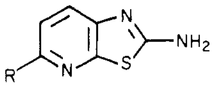
Received April 28, 1981

In continuation of our studies on triazaphenothiazines,[2-5] we now report the synthesis of the parent 1,4,6-triaza compound **1a**. The route used involved the condensation of 2,3-dichloropyrazine (**2**) with 3-aminopyridine-2(1*H*)-thione (**3**, R = H).

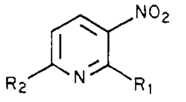
Scheme I



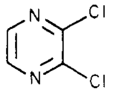
The key intermediate **3** (R = H) has been previously prepared[6,7] by the reaction of 3-amino-2-chloropyridine (**4**) with sodium hydrosulfide. Since the synthesis of **4** from nicotinamide has been found hazardous,[7] an alternative route to **3** (R = H) was developed by conversion of 2-chloro-3-nitropyridine (**5**) to the thione **6** and reduction with iron in the presence of calcium chlorides (Scheme I). The reagent is very convenient and permits facile isolation of the amine **3** in high yield. 3-Amino-6-methoxypyridine-2(1*H*)-thione (**3**, R = OCH_3) and the 6-chloro analogue (**3**, R = Cl) were obtained by the Fe–$CaCl_2$ reduction of the nitro compounds **7b** and **7c** followed by thiocyanation and alkaline hydrolysis of the intermediate thiazolo[5,4-*b*]pyridines (**9**).[8]



9, R = OCH_3; Cl

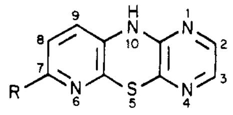


7a, R_1 = NH_2; R_2 = H
b, R_1 = H; R_2 = OCH_3
c, R_1 = H; R_2 = Cl

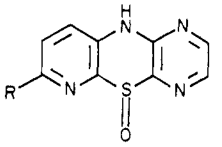


2

The reaction of an alkaline solution of the aminopyridinethiones with 2,3-dichloropyrazine (**2**) in propylene glycol or DMF gave greenish yellow solids whose composition and spectral properties were consistent for the 1,4,6-triazaphenothiazines **1** (R = H, OCH_3, Cl).



1a, R = H
b, R = OCH_3
c, R = Cl



10a, R = H
b, R = OCH_3
c, R = Cl

These 1,4,6-triazaphenothiazines were also converted to their 5-sulfoxides by the action of mixed concentrated nitric and sulfuric acids.

Experimental Section

General Methods. Melting points were determined with a Fisher-Johns apparatus and are uncorrected. UV and visible spectra were recorded on a Pye Unicam SP 8000 spectrophotometer using matched 1-cm quartz cells. The solvent was methanol, and the absorption maxima are always given in nanometers; the figures in parentheses are ε values. IR spectra were obtained on a Perkin-Elmer Model 137 spectrophotometer using potassium bromide disks unless otherwise stated. ^1H NMR

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