The Synthesis and Hydrolysis of
N-Benzyl-S-methylisothiazolidinium Salts

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Received February 16, 1982

A series of N-benzyl-S-methylisothiazolidinium salts were obtained by iodinic oxidation of the corresponding N-benzyl-3-methylthiopropylamines at neutral pH followed by their isolation as the chloride salts. The parent N-benzyl-3-methylthiopropylamines were prepared by reacting substituted benzaldehydes with 3-methylthiopropylamine and sodium cyanoborohydride. Acid hydrolysis of the isothiazolidinium salts resulted in their quantitative conversion to the corresponding N-benzyl-3-methylsulfenylpropylamines. Although methylsulfenylpropylamine formation also predominated in alkaline solution, a significant fraction was converted to the parent benzaldehyde and presumably, 3-methylthiopropylamine. The latter conversion is believed to involve opening of the isothiazolidine ring via an elimination reaction followed by hydrolysis of the resulting Schiff's base.

The first compound containing an isothiazolidine ring was synthesized by Lavine who was investigating the iodinic oxidation of methionine at neutral pH. Lavine proposed that an intramolecular cyclization reaction occurred between the amine and thioether functional groups of methionine to yield a stable, isolable intermediate which he termed dehydromethionine, (S-methylisothiazolidinium-3-carboxylate) (1). The isothiazolidinium structure of dehydromethionine was verified much later by X-ray diffraction (2).

In a previous investigation, we found that the iodine-induced cyclization reaction proceeds readily from various S-substituted thiopropylamines possessing a primary amine functionality to yield the corresponding, substituted isothiazolidinium salts (3). The resulting isothiazolidin-ium salts were shown to be mixtures of isomers chiral at sulfur. Hydrolysis of the salts in either acidic or alkaline aqueous solution resulted in formation of the corresponding sulfenyl derivatives.

The objective of our present work was to show that the iodine-induced cyclization reaction could be extended to include 3-methylthiopropylamines possessing a secondary amine functionality. We chose to prepare N-benzyl derivatives in order to be able to conveniently follow reactions with an ultraviolet monitor during hplc. The synthesis, characterization and hydrolysis of N-benzyl-S-methyliso-thiazolidinium salts are described in this paper.

The general procedures for the synthesis of the N-benzyl-3-methylthiopropylamines and their oxidative cyclization by iodine to form the respective isothiazolidinium

Figure I
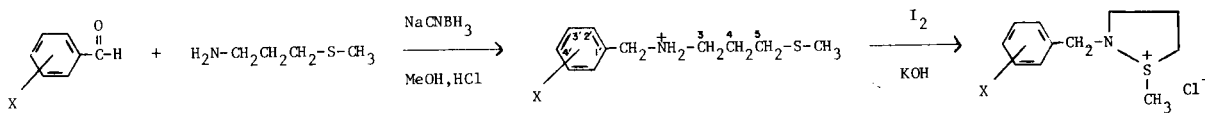
X	N-Benzyl-3-methylthiopropylamine	N-Benzyl-S-methylisothiazolidinium Chloride
H	1	
p-OCH$_3$	2	3
m-OCH$_3$	4	5
p-CH$_3$	6	
m-CH$_3$	7	
p-Cl	8	9
m-Cl	10	11
p-NO$_2$	12	
m-NO$_2$	13	

salts are shown in Figure 1. The synthesis of the N-benzyl-3-methylthiopropylamines proceeds *via* reduction of the intermediate imine formed by reaction of the aldehyde and primary amine. The imine is reduced by sodium cyanoborohydride which, as Borch *et al.* have pointed out is quite effective under mild conditions (4,5). Overall, the N-benzyl-3-methylthiopropylamines were relatively easy to isolate as their crystalline hydrochloride salts and were stable at room temperature.

The iodinic oxidation to form the isothiazolidinium salts proceeded readily from the parent N-benzyl-3-methyl-thiopropylamines accompanied by the complete disappearance of iodine within two hours. Quantitative conversion of the 3-methylthiopropylamines to the respective isothiazolidinium salts was indicated by hplc. However, the isothiazolidinium salts were difficult to isolate by fractional crystallization, leading to 30-40% yields, and poor crystallizability hampered further purification. This problem had previously been encountered with a series of S-substituted isothiazolidinium salts (3). In spite of this difficulty, the *para* and *meta* methoxy and chloro derivatives were isolated and their proposed structures were supported by elemental analyses and nmr. The *p*-methoxy derivative, **3**, was the easiest to isolate followed by the *p*-chloro derivative, **9**. Additionally, as described below, some of the respective N-benzyl-3-methylsulfenylpropylamines were isolated and characterized to further indicate that iodinic oxidation of the N-benzyl-3-methylthiopropylamines at neutral *p*H proceeds to the isothiazolidinium salts rather than the 3-methylsulfenylpropylamines. The isothiazolidinium salts were clearly resolved from their respective thioether and methylsulfenyl counterparts by hplc.

Inconclusive elemental analyses were obtained for both of the isolated N-methylbenzyl-S-methylisothiazolidinium salts; however, nmr and hplc provided no evidence of contaminants and the positions of the eluted peaks on high pressure liquid chromatograms were consistent with those of other well-characterized, isothiazolidinium salts. The elemental analyses were consistent with some water of hydration being present and the samples were observed to be hygroscopic. Isolation and characterization of either of the N-nitrobenzyl-S-methylisothiazolidinium salts was not achieved. We observed that greater than expected quantities of iodine and potassium hydroxide were required during the oxidative cyclization of the N-nitrobenzyl-3-methylthiopropylamines, **12** and **13**.

Proton and ^{13}C-nmr spectra were consistent with the proposed structures of the thioethers and isothiazolidinium salts. When comparing the nmr spectral data of the N-benzyl-S-methylisothiazolidinium salts to their parent 3-methylthiopropylamines, a downfield shift was observed for both the S-methyl and C-5 hydrogens and carbon atoms. This downfield shift is consistent with the deshielding effect of the positively-charged azasulfonium center present within the isothiazolidinium salts. Likewise, the proton nmr signals representing the C-3, C-4 and C-5 hydrogens of the isothiazolidinium salts are complicated as expected for a ring system in which none of the ring hydrogens are equivalent. Similar findings were made when comparing the nmr spectra of dehydromethionine and methionine (3).

The 3-methylsulfenylpropylamines were generated in solution by acid hydrolysis of the corresponding isothiazolidinium salts, which were, in turn, formed in solution

Figure II
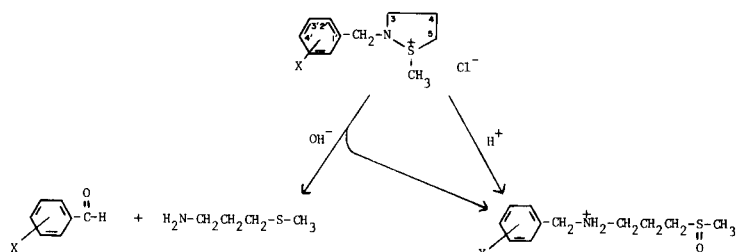
X	N-Benzyl-3-methylsulfenylpropylamine Hydrochloride
H	14
p-OCH₃	15
m-OCH₃	16
p-CH₃	17
p-Cl	18

by iodinic oxidation of the respective *N*-benzyl-3-methyl-thiopropylamines. Methylsulfenylpropylamine formation is illustrated in Figure 2. After acid hydrolysis of the isothiazolidinium salts, the methylsulfenylpropylamines were isolated in crystalline form. Several of these had the expected elemental composition according to elemental analyses and are listed in the experimental section. The other methylsulfenylpropylamines analyzed low for carbon, nitrogen and sulfur and we suspect this was due to water since these methylsulfenylpropylamines (including the *p*-chloro derivative) appeared to be pure by hplc.

The nmr data are consistent with the structures proposed for the 3-methylsulfenylpropylamines. When comparing spectra for each methylsulfenylpropylamine with its corresponding thioether, a downfield shift is observed in the proton and ^{13}C nmr spectra for both the *S*-methyl- and C-5 hydrogen and carbon atoms. This is consistent with the deshielding effect of the electron-withdrawing oxygen of the methylsulfenyl group. Likewise, the broad singlet at 10 ppm representing the amine hydrogen disappears on formation of the isothiazolidinium salt from the parent *N*-benzyl-3-methylthiopropylamine, but is seen to reappear upon formation of the 3-methylsulfenylpropylamine.

Isothiazolidinium salts are relatively stable in solution at neutral *p*H; however, the lability of these compounds is greatly increased upon addition of acid or base. For example, dehydromethionine is quantitatively hydrolyzed to methionine sulfoxide upon addition of acid or base (1). Thus, in order to quantitate methylsulfenylpropylamine formation and elucidate any pathway other than simple hydrolysis, we investigated by hplc the reactions of the *N*-benzyl-*S*-methylisothiazolidinium salts upon acid and base treatment.

The products obtained upon acid and base treatment of the isothiazolidinium salts are illustrated in Figure 2. High pressure liquid chromatography was used to separate the isothiazolidinium salt, sulfoxide and parent benzaldehyde carrying the same aromatic substitutent. Under the conditions used, standards were eluted in the order of parent benzaldehyde, methylsulfenylpropylamine, isothiazolidinium salt and thioether. Mixtures of the standards were completely resolved.

Acid treatment of the various isothiazolidinium salts led to methylsulfenylpropylamine formation in quantitative yields. No other products were detected in hplc studies of the products from hydrolysis of *N*-*p*-methoxybenzyl-*S*-methylisothiazolidinium chloride, **3**, or *N*-*p*-chlorobenzyl-*S*-methylisothiazolidinium chloride, **9**. Those methylsulfenylpropylamines isolated in sufficient quantity and purity to permit characterization were found to be clearly differentiated from their parent isothiazolidinium salts by nmr, hplc, elemental analysis and melting point.

Treatment with base, however, resulted in hydrolysis

proceeding by two pathways. One pathway produced methylsulfenylpropylamine and the other, the parent benzaldehyde. For example, base treatment of compound **3** led to an 82% conversion of **3** to the methylsulfenyl-propylamine, **15**, and an 18% conversion to *p*-anisaldehyde. Base treatment of compound **9** yielded similar values of 80% conversion to the methylsulfenylpropyl-amine, **18**, and 20% to *p*-chlorobenzaldehyde. Thus methylsulfenylpropylamine formation was found to proceed to the greater extent upon base treatment, probably *via* nucleophilic attack by hydroxide ion on sulfur (6). 3-Methylthiopropylamine is presumed to form in equimolar amounts to the parent benzaldehyde during the base treatment of these isothiazolidinium salts.

A mechanism for the base-catalyzed conversion of the *N*-benzyl-*S*-methylisothiazolidinium salts to form the parent benzaldehydes and 3-methylthiopropylamine is proposed in Figure 3. Abstraction of a benzylic proton

Figure III
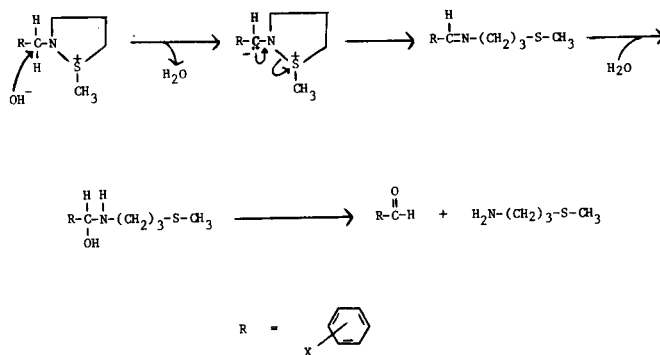
leads to opening of the ring and formation of a Schiff's base which subsequently hydrolyzes to form the parent benzaldehyde and 3-methylthiopropylamine. The products are, indeed, the reactants used to synthesize the *N*-benzyl-3-methylthiopropylamines.

The results of this and a previous investigation (3) indicate that, in general, 3-methylthiopropylamines possessing either a primary or secondary amine functionality will rapidly cyclize to yield isothiazolidinium salts when oxidized with iodine at neutral *p*H. Oxidation of simple thioethers by iodine normally produces the sulfoxides. However, in the case of 3-methylthiopropylamines, intramolecular attack by the favorably located amine nitrogen appears to preclude attack by water even when the reactions are carried out in a predominantly aqueous medium. Analyses by hplc of product mixtures obtained for a variety of *N*-benzyl-3-methylthiopropylamines reacted with iodine indicate that only a very minor amount of methylsulfenyl-propylamine is formed when the reactions are carried out at neutral *p*H. The isothiazolidinium salts are labile to hydrolysis under acidic and alkaline conditions.

The isothiazolidinium salts reported here can be viewed as containing the azasulfonium linkage (or protonated sulfilimine) within a ring structure. These derivatives appear to be much more stable than acyclic, azasulfonium salts and sulfilimines reported previously (6) which, in general, have had strongly electron-withdrawing groups bound to the nitrogen and/or sulfur. Stabilization of labile bonds by incorporation into a ring of optimal size has been frequently observed. Thus, the oxidative cyclization of 3-methylthiopropylamines by iodine provides examples where the reaction course at sulfur is altered by participation of the neighboring amine, and the products of the reaction, the isothiazolidinium salts, are stabilized by incorporation of the azasulfonium functionality into a ring structure.

EXPERIMENTAL

Dowex-1 chloride ion exchange resin was obtained from Sigma Chemical Co. Sodium cyanoborohydride and all aldehyde derivatives were obtained from Aldrich and used without further purification. Dimethyl-d_6 sulfoxide (99.9 atom%) and deuteriochloroform (99.8 atom%) each containing 1% tetramethylsilane were obtained from Aldrich. 3-Methylthiopropylamine was obtained from Eastman.

Elemental analyses for carbon, hydrogen, nitrogen and sulfur were conducted by Galbraith Laboratories, Inc., Knoxville, Tennessee. Hygroscopic samples were stored under vacuum during shipment. Melting points were taken on a Fisher-Johns melting point apparatus. Proton nmr spectra were obtained on a Varian EM-390 90 MHz nmr spectrometer. The ^{13}C-nmr spectra were obtained at 15 MHz on a JEOL FX-60 Fourier transform nmr spectrometer. The N-benzyl-3-methylthiopropylamines, isothiazolidinium salts and 3-methylsulfenylpropylamines were dissolved in deuteriochloroform or d_6-dimethylsulfoxide at concentrations of 15-20 mg/ml and 75 mg/ml for proton nmr and ^{13}C nmr, respectively. Chemical shifts were determined relative to the methyl substituents of tetramethylsilane.

High pressure liquid chromatography was used extensively as a tool for following the progress of reactions, verifying the purity of compounds and differentiating between N-benzyl derivatives carrying the same aromatic substituent. The chromatographic behavior of N-p-methoxybenzyl-3-methylthiopropylamine hydrochloride and its derivatives were representative of the compounds reported here. The order of elution and the elution volumes were: p-anisaldehyde (8.50 ml), N-p-methoxybenzyl-3-methylsulfenylpropylamine hydrochloride (10.58 ml), N-p-methoxybenzyl-S-methylisothiazolidinium chloride (13.70 ml) and N-p-methoxybenzyl-3-methylthiopropylamine hydrochloride (26.0 ml). The instrument used was a Beckman Model 100A high pressure liquid chromatograph equipped with a Beckman Model 153 uv detector (254 nm), an Altex 210 injection valve and an Altex 25 cm × 4.6 mm Ultrasphere-ODS silica column (5 micron particle size). Elution peaks were recorded on a Varian Model 9176 recorder. The solvent for chromatography was 50:50 (v/v) methanol:50mM heptane sulfonic acid (sodium salt) in water. Twenty microliters of a mixture was injected via a 1 ml syringe and chromatographed at a flow rate of 1 ml/minute.

General Procedure for Synthesis of the N-Benzyl-3-methylthiopropylamines.

A 1:3:2 molar ratio of 3-methylthiopropylamine:aldehyde:sodium cyanoborohydride was reacted in 150 ml of methanol. Since the reaction was exothermic, the reaction vessel was cooled in ice prior to and during the reaction until the pH had stabilized after which the ice bath was removed. The pH was kept between 6 and 8 with 4M hydrogen chloride in methanol. After several hours, 100 ml of 1M potassium hydroxide were added to the reaction mixture and methanol was removed by rotary evaporation. The remaining aqueous mixture was extracted with three, 100 ml portions of ether. The combined ether fractions were dried with anhydrous magnesium sulfate and filtered gravimetrically. Anhydrous hydrogen chloride gas was bubbled through the ether mixture to produce a solid and/or oil.

Crystallization of the product in the oil or solid was readily accomplished by dissolving the product in acetonitrile, decolorizing with charcoal, filtering and cooling to 4°. Recrystallization was carried out in acetonitrile until reproducible melting points could be obtained for each compound. Crystals were collected by vacuum filtration and dried under vacuum. Yields of the N-benzyl-3-methylthiopropylamines varied between 30-50%.

General Procedure for Synthesis of the N-Benzyl-S-methylisothiazolidinium Salts.

The N-benzyl-S-methylisothiazolidinium salts were synthesized by iodinic oxidation of the respective parent, N-benzyl-3-methylthiopropylamines. Three mmoles of the thioether dissolved in 50 ml of methanol or 1:1 (v/v) methanol:water were reacted at room temperature with 3 mmoles molecular iodine dissolved in methanol (added dropwise). One molar potassium hydroxide was added dropwise to maintain the pH between 7.0 and 7.5. When the iodine color was nearly gone (1-2 hours), the product mixture was chromatographed on a 10 ml bed volume of Dowex-1 chloride which had been packed in a 10 ml plastic syringe and washed successively with 30 ml each of water, methanol, 1M hydrochloric acid and methanol. The reaction mixture was chromatographed in methanol at a flow rate of approximately 3 ml/minute. This afforded exchange of the iodide for the chloride anion which, in turn, facilitated crystallization. The resultant eluate, which was colorless or nearly so, was then adjusted to neutral pH. After rotary evaporation to remove all solvent, the residue was taken up in dry ethanol and filtered under vacuum to remove potassium chloride. Subsequently, the ethanol was quantitatively removed by rotary evaporation and drying with small portions of acetone. The resultant residue was dissolved in acetone or ethanol and cooled. Often scratching the side of the vessel with a glass rod, cooling in the freezer at -20° and/or adding ether to the cloud point was necessary to induce crystallization. Crystals were collected by vacuum filtration and immediately dried under vacuum. Yields for these white-colored compounds ranged from 30-40% and were increased by working rapidly through the purification procedure.

General Procedure for Synthesis of the N-Benzyl-3-methylsulfenylpropylamine Salts.

The N-benzyl-S-methylisothiazolidinium chloride, either dissolved from crystalline form or generated in solution by iodinic oxidation of the respective N-benzyl-3-methylthiopropylamine, was reacted with 5 ml of 0.50M hydrochloric acid. The solvent was removed by rotary evaporation and the sulfoxide was crystallized from the resultant residue by dissolving in either ethanol or acetone and adding ether to the cloud point. Recrystallization was carried out using the same procedure. Yields for the crystallized, dried, white-colored sulfoxide salts ranged from 80-90%.

Procedures for the Acid and Base Treatment of the N-Benzyl-S-methylisothiazolidinium Salts.

For base treatment of N-p-methoxybenzyl-S-methylisothiazolidinium chloride, 50 microliters of a 5.0 mg/ml solution of this isothiazolidinium salt was mixed with 50 microliters of 0.10M potassium hydroxide. After standing 15 minutes, the solution was neutralized with 50 microliters of 0.10M hydrochloric acid and diluted to a final volume of 650 microliters with the solvent used for hplc. Acid hydrolysis of the methoxy derivatives was performed exactly as above except the order of potassium hydroxide and hydrochloric acid addition was switched. For base treatment of N-p-chlorobenzyl-S-methylisothiazolidinium chloride, 100 microliters of a 20.0 mg/ml solution of this isothiazolidinium salt was mixed with 100 microliters of 0.40M potassium hydroxide and 50 microliters methanol (to insure complete dissolution of reactants). After standing 15 minutes,

the reaction mixture was neutralized with 100 microliters of 0.40*M* hydrochloric acid and diluted to 1100 microliters with the solvent used for hplc. Acid hydrolysis of the chloro derivative, **9**, was performed exactly as stated above except the order of addition of potassium hydroxide and hydrochloric acid was switched. High pressure liquid chromatography runs for both the acid and base hydrolyses and standards were made in quadruplicate or triplicate. The chart paper from hplc analysis was xeroxed and each peak was carefully cut out and weighed on an analytical balance.

N-Benzyl-3-methylthiopropylamine Hydrochloride.

Compound **1** had mp 206°; ^{1}H nmr (deuteriochloroform): δ 1.7-2.4 (quin, 2H), 2.08 (s, 3H), 2.4-2.7 (t, 2H), 2.8-3.1 (t, 2H), 4.1 (s, 2H), 7.2-7.8 (m, 5H), 10.0 (broad singlet, 1.5H).

Anal. Calcd. for $C_{11}H_{18}ClNS$: C, 57.00; H, 7.84; N, 6.04; S, 13.83. Found: C, 57.32; H, 7.95; N, 5.90; S, 14.13.

N-*p*-Methoxybenzyl-3-methylthiopropylamine Hydrochloride.

Compound **2** had mp 190°; ^{1}H nmr (deuteriochloroform): δ 1.9-2.3 (quin, 2H), 2.08 (s, 3H), 2.4-2.7 (t, 2H), 2.7-3.1 (t, 2H), 3.75 (s, 3H), 3.95 (s, 2H), 6.8-7.0 (d, 2H), 7.4-7.7 (d, 2H), 9.9 (broad singlet, 2H); ^{13}C nmr (d_6-dimethylsulfoxide): δ 14.36 (S-CH$_3$), 49.32 (C-3), 24.56 (C-4), 30.08 (C-5), 44.90 (benzyl), 55.23 (OCH$_3$), 123.84 (C-1'), 131.64 (C-2'), 113.90 (C-3'), 159.64 (C-4').

Anal. Calcd. for $C_{12}H_{20}ClNOS$: C, 55.05; H, 7.70; N, 5.35; S, 12.25. Found: C, 55.31; H, 7.88; N, 5.46; S, 12.31.

N-*p*-Methoxybenzyl-*S*-methylisothiazolidinium Chloride.

Compound **3** had mp 142°; ^{1}H nmr (deuteriochloroform): δ 2.3-2.7 (m, 2H), 2.8 (s, 3H), 3.0 (s, 3H), 3.4-3.9 (m, 2H), 4.0-4.7 (m, 4H), 6.7-7.1 (d, 2H), 7.1-7.5 (d, 2H); ^{13}C nmr (d_6-dimethylsulfoxide): δ 54.58 (S-CH$_3$), 55.52 (C-3), 24.79 (C-4), 29.21 (C-5), 48.41 (benzyl), 55.13 (OCH$_3$), 128.22 (C-1'), 130.30 (C-2'), 114.06 (C-3'), 159.22 (C-4').

Anal. Calcd. for $C_{12}H_{18}ClNOS$: C, 55.48; H, 6.98; N, 5.39; S, 12.34. Found: C, 55.58; H, 6.71; N, 5.39; S, 12.25.

N-*m*-Methoxybenzyl-3-methylthiopropylamine Hydrochloride.

Compound **4** had mp 116°; ^{1}H nmr (deuteriochloroform): δ 1.9-2.4 (quin, 2H), 2.08 (s, 3H), 2.4-2.7 (t, 2H), 2.8-3.1 (t, 2H), 3.8 (s, 3H), 4.03 (s, 2H), 6.8-7.5 (m, 4H), 10.05 (broad singlet, 2H).

Anal. Calcd. for $C_{12}H_{20}ClNOS$: C, 55.05; H, 7.70; N, 5.35; S, 12.25. Found: C, 54.88; H, 7.76; N, 5.49; S, 11.95.

N-*m*-Methoxybenzyl-*S*-methylisothiazolidinium Chloride.

Compound **5** had mp 120°.
Anal. Calcd. for $C_{12}H_{18}ClNOS$: C, 55.48; H, 6.98; N, 5.39; S, 12.34. Found: C, 54.74; H, 7.25; N, 5.29; S, 11.93.

N-*p*-Methylbenzyl-3-methylthiopropylamine Hydrochloride.

Compound **6** had mp 207°; ^{1}H nmr (deuteriochloroform): δ 1.9-2.4 (quin, 2H), 2.08 (s, 3H), 2.29 (s, 3H), 2.4-2.7 (t, 2H), 2.7-3.1 (t, 2H), 3.97 (s, 2H), 7.1-7.3 (d, 2H), 7.4-7.6 (d, 2H), 9.9 (broad singlet, 1H).

Anal. Calcd. for $C_{12}H_{20}ClNS$: C, 58.63; H, 8.20; N, 5.70; S, 13.04. Found: C, 58.80; H, 8.56; N, 5.78; S, 12.76.

N-*m*-Methylbenzyl-3-methylthiopropylamine Hydrochloride.

Compound **7** had mp 171°; ^{1}H nmr (deuteriochloroform): δ 1.9-2.4 (quin, 2H), 2.08 (s, 3H), 2.4-2.7 (t, 2H), 2.8-3.1 (t, 2H), 4.07 (s, 3H), 7.2-7.8 (m, 4H), 10.0 (broad singlet, 2H).

Anal. Calcd. for $C_{12}H_{20}ClNS$: C, 58.63; H, 8.20; N, 5.70; S, 13.04. Found: C, 58.80; H, 8.56; N, 5.78; S, 12.76.

N-*p*-Chlorobenzyl-3-methylthiopropylamine Hydrochloride.

Compound **8** had mp 212°; ^{1}H nmr (deuteriochloroform): δ 1.9-2.3 (quin, 2H), 2.08 (s, 3H), 2.4-2.7 (t, 2H), 2.8-3.1 (t, 2H), 4.03 (s, 2H), 7.3-7.5 (d, 2H), 7.5-7.7 (d, 2H), 10.05 (broad singlet, 2H).

Anal. Calcd. for $C_{11}H_{17}Cl_2NS$: C, 49.44; H, 6.79; N, 5.24; S, 12.00. Found: C, 49.92; H, 6.60; N, 5.24; S, 11.66.

N-*p*-Chlorobenzyl-*S*-methylisothiazolidinium Chloride.

Compound **9** had mp 124°.
Anal. Calcd. for $C_{11}H_{15}Cl_2NS$: C, 50.00; H, 5.72; N, 5.30; S, 12.14. Found: C, 49.87; H, 5.86; N, 5.15; S, 11.89.

N-*m*-Chlorobenzyl-3-methylthiopropylamine Hydrochloride.

Compound **10** had mp 189°; ^{1}H nmr (deuteriochloroform): δ 1.7-2.2 (quin, 2H), 2.05 (s, 3H), 2.4-2.8 (t, 2H), 2.8-3.2 (t, 2H), 4.11 (s, 2H), 7.3-7.9 (m, 4H), 9.8 (broad singlet, 1.5H).

Anal. Calcd. for $C_{11}H_{17}Cl_2NS$: C, 49.44; H, 6.79; N, 5.24; S, 12.00. Found: C, 49.61; H, 6.48; N, 5.21; S, 12.06.

N-*m*--Chlorobenzyl-*S*-methylisothiazolidinium Chloride.

Compound **11** had mp 123°.
Anal. Calcd. for $C_{11}H_{15}Cl_2NS$: C, 50.00; H, 5.72; N, 5.30; S, 12.14. Found: C, 49.94; H, 5.82; N, 5.28; S, 11.98.

N-*p*-Nitrobenzyl-3-methylthiopropylamine Hydrochloride.

Compound **12** had mp 162°; ^{1}H nmr (d_6-dimethylsulfoxide): δ 1.7-2.2 (quin, 2H), 2.03 (s, 3H), 2.4-2.7 (t, 2H), 2.7-3.2 (t, 2H), 4.29 (s, 3H), 7.8-8.1 (d, 2H), 8.1-8.4 (d, 2H), 9.9 (broad singlet, 1.5H).

Anal. Calcd. for $C_{11}H_{11}ClN_2O_2S$: C, 47.73; H, 6.19; N, 10.12; S, 11.58. Found: C, 47.84; H, 6.16; N, 10.09; S, 11.39.

N-*m*-Nitrobenzyl-3-methylthiopropylamine Hydrochloride.

Compound **13** had mp 179°; ^{1}H nmr (d_6-dimethylsulfoxide): δ 1.7-2.3 (quin, 2H), 2.08 (s, 3H), 2.4-2.7 (t, 2H), 2.8-3.2 (t, 2H), 4.32 (s, 2H), 7.6-8.7 (m, 4H), 9.9 (broad singlet, 1.5H).

Anal. Calcd. for $C_{11}H_{11}ClN_2O_2S$: C, 47.73; H, 6.19; N, 10.12; S, 11.58. Found: C, 47.83; H, 6.11; N, 10.12; S, 11.28.

N-Benzyl-3-methylsulfenylpropylamine Hydrochloride.

Compound **14** had mp 171°; ^{1}H nmr (d_6-dimethylsulfoxide): δ 2.0-2.4 (quin, 2H), 2.55 (s, 3H), 2.7-3.2 (m, 4H), 4.12 (s, 2H), 7.3-7.7 (m, 5H), 9.72 (broad singlet, 1H).

Anal. Calcd. for $C_{11}H_{18}ClNOS$: C, 53.32; H, 7.32; N, 5.65; S, 12.94. Found: C, 53.25; H, 7.42; N, 5.61; S, 12.84.

N-*p*-Methoxybenzyl-3-methylsulfenylpropylamine Hydrochloride.

Compound **15** had mp 179°; ^{1}H nmr (deuteriochloroform): δ 2.3-2.7 (quin, 2H), 2.6 (s, 3H), 2.7-3.2 (m, 4H), 3.76 (s, 3H), 4.03 (s, 2H), 6.8-7.0 (d, 2H), 7.4-7.6 (d, 2H), 10.0 (broad singlet, 2H); ^{13}C nmr (d_6-dimethylsulfoxide): δ 37.88 (s-CH$_3$), 49.57 (C-3), 19.10 (C-4), 55.55 (OCH$_3$), 128.91 (C-1'), 124.23 (C-2'), 115.00 (C-3'), 159.19 (C-4').

Anal. Calcd. for $C_{12}H_{20}ClNO_2S$: C, 51.88; H, 7.26; N, 5.04; S, 11.54. Found: C, 51.77; H, 7.40; N, 5.03; S, 11.26.

N-*m*-Methoxybenzyl-3-methylsulfenylpropylamine Hydrochloride.

Compound **16** had mp 92°.
Anal. Calcd. for $C_{12}H_{20}ClNO_2S$: C, 51.88; H, 7.26; N, 5.04; S, 11.54. Found: C, 51.60; H, 7.50; N, 5.04; S, 11.36.

N-*p*-Methylbenzyl-3-methylsulfenylpropylamine Hydrochloride.

Compound **17** had mp 183°.
Anal. Calcd. for $C_{12}H_{20}ClNOS$: C, 55.05; H, 7.70; N, 5.35; S, 12.25. Found: C, 54.97; H, 7.80; N, 5.28; S, 12.02.

N-*p*-Chlorobenzyl-3-methylsulfenylpropylamine Hydrochloride.

Compound **18** had mp 182°; ^{1}H nmr (deuteriochloroform): δ 2.0-2.4 (quin, 2H), 2.58 (s, 3H), 2.7-3.2 (m, 4H), 4.23 (s, 2H), 7.4-7.8 (m, 4H), 9.8 (broad singlet, 1.5H).

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