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Synthesis and Novel Reactivity of Halomethyldimethylsulfonium Salts

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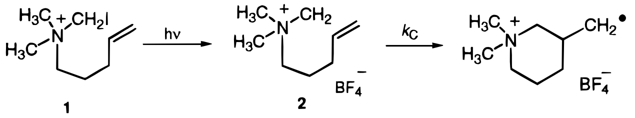
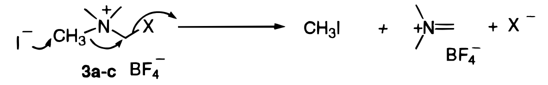
Iodomethyl-, chloromethyl-, and fluoromethyldimethylsulfonium salts, **4b**−**d**, have been synthesized and are observed to be highly reactive molecules that exhibit extraordinary diversity with respect to the nature of their reactivity, undergoing facile direct substitution (S_N2) reactions, but also being highly susceptible to electron-transfer reactions. Cyclic voltametry experiments indicated that the iodomethyldimethylsulfonium compound, **4b**, is a potent electron acceptor, even surpassing the reactivity of perfluoro-*n*-alkyl iodides in that capacity. The iodo- and chloromethyldimethylsulfonium salts, **4b**,**c**, as well as the analogous iodomethyltrimethylammonium salt, **3a**, are shown to be reactive SET acceptors.

In a series of recent papers, it has been shown that halomethyltrialkylammonium salts have quite versatile reactivity, acting as precursors of highly reactive and synthetically useful α-ammoniomethyl distonic radical cations (formed in a variety of free radical chain processes),[1] and undergoing unusual Grob-like nucleophilic substitutions in their reactions with nucleophiles.[2]

Thus, for example, *N*-(4-pentenyl)-*N*,*N*-dimethylammoniomethyl iodide, **1**, in a photoinitiated reaction, was observed to form the respective distonic radical cation, **2**, which cyclized with a rate constant of $1.5 \times 10^6\ s^{-1}$.



The novel reactive nature of trialkylammoniomethyl halides with respect to their reactions with nucleophiles is exemplified by the reaction of bromomethyltrimethylammonium tetrafluoroborate, **3b**, with iodide ion, which was shown to proceed via the following substitution/fragmentation mechanism:



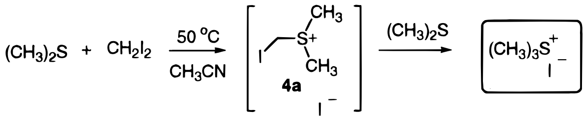
a, X = I; **b**, X = Br; **c**, X = Cl

Sulfonium compounds, because sulfur is a third period element, can exhibit types of reactivity (i.e., ylide chemistry) not normally observed for ammonium compounds, whereas in other instances (i.e., Hoffmann eliminations) they can have a reactivity that is quite similar. It was therefore of interest to compare the reactivity of halomethylsulfonium compounds with those of halomethylammonium compounds in those reaction types above.

Foreshadowing the exceptional reactivity of such compounds was our finding that there was little mention in the literature of halomethyldialkylsulfonium compounds, with the target, prototypical system, iodomethyldimethylsulfonium iodide, being unknown and the bromomethyl analogue having been mentioned but once, reportedly prepared in 0.6% yield in the photochemical reaction of dimethyl sulfide (DMS) with methylene bromide.[3]

Results and Discussion

In an attempt to emulate the easy synthesis of iodomethyltrialkylammonium compounds, the reaction of DMS with methylene iodide was carried out. However, only a trace of the desired iodomethyldimethylsulfonium iodide product (**4a**) could be detected, and the reaction proceeded instead to form trimethylsulfonium iodide (TMSI). Upon closer examination, it was found that with 1 equiv of DMS, the DMS was totally consumed after 2 days, whereas the methylene iodide was only partially consumed, a trace of **4a** was detectable, and the major product was TMSI, along with small amounts of a number of other products, including methyl iodide, iodomethyl methyl sulfide (**5**),[4] and methylthiomethyldimethylsulfonium salt (**6**)[5] (vide infra, Scheme 1). Upon adding a second equivalent of DMS and heating for an additional 4 days, all methylene iodide had been consumed and TMSI was obtained in 96% yield.



It is likely that the formation of trimethylsulfonium iodide proceeded via the intermediacy of the hoped-for iodomethyl compound, **4a**, which, consistent with the substitution/fragmentation process undergone by halomethyl*ammonium* salts, underwent a similar displacement process with DMS acting as nucleophile to give the obtained trimethylsulfonium iodide product.

To test the above hypothesis, an alternative synthesis of **4** was accomplished unambiguously via the procedure

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(1) Rios, L. A.; Dolbier, W. R.; Paredes, R.; Lusztyk, J.; Ingold, K. U.; Jonsson, M. *J. Am. Chem. Soc.* **1996**, *118*, 11313−11314.

(2) Fletcher, M. O.; Zhang, L.; Vu, Q.; Dolbier, W. R., Jr. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1187−1192.

(3) Laird, T.; Williams, H. *J. Chem. Soc.* **1971**, 3471−3474.

(4) Boberg, F.; Winter, G. *Ann. Chem.* **1959**, *621*, 20.

(5) Hansen, D. W.; Olofson, R. A. *Tetrahedron* **1971**, *27*, 4221.

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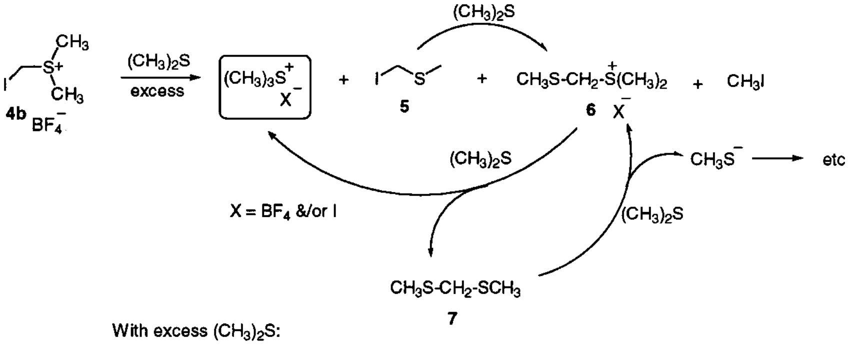
Scheme 1

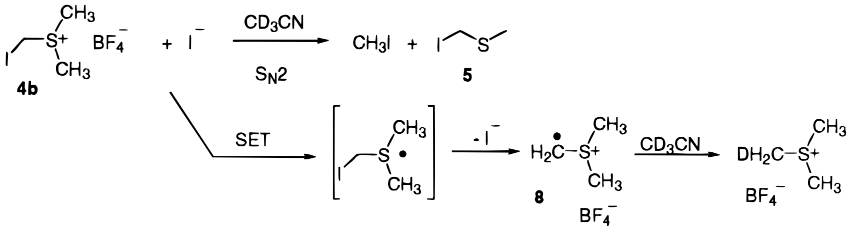


With excess $(CH_3)_2S$:

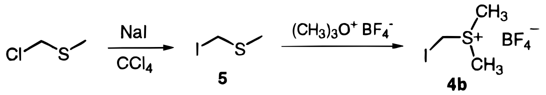
after 2 days at 26 °C: 55% $(CH_3)_3S^+X^-$, 27% **5**, 9% **6**, and 9% CH_3I

after 12 hrs at 60 °C, $(CH_3)_3S^+X^-$ (quant)

Scheme 2



below. Iodomethyl methyl sulfide (**5**) was prepared by the



reaction of chloromethylmethyl sulfide with NaI.[4] Although stable in solution, **5** decomposes rapidly in the neat state, and it therefore was converted, immediately upon isolation, to the desired sulfonium tetrafluoroborate (**4b**) by treatment with trimethyloxonium tetrafluoroborate.

Iodomethyldimethylsulfonium tetrafluoroborate (**4b**) turned out to be a highly reactive molecule. When treated with DMS at room temperature in acetonitrile, it was slowly converted to trimethylsulfonium salt (TMSX) $[(CH_3)_3S^+X^-$ (where X = mixture of BF_4 and I]. Examination of the early stages of the reaction indicated that the reaction proceeded largely as expected, with TMSX along with intermediate coproducts **5**, **6** and methyl iodide being observed. As seen in Scheme 1, by a series of interrelated reactions, and with an excess of DMS, virtually all of **4** should be able to find its way to TMSX. Indeed, the conversion to TMSX was essentially quantitative after 12 h at 60 °C (Scheme 1).

Detection of methyl iodide as a product in the RT reaction indicates that iodide ion (formed inevitably during the course of the processes in Scheme 1) must also be competing with DMS as a nucleophile, perhaps quite effectively. Such CH_3I will, of course, eventually end up as TMSX as a result of its subsequent reaction with DMS.

Consistent with such expectation, the reaction of **4b** with iodide ion occurs readily, with substrate **4b** being largely consumed in 10 min at room temperature in acetonitrile. The reaction was, however, not clean, giving a complex mixture of products comprised mostly of methyl iodide and **5**, but also considerable TMSX, and with small amounts of DMS and methylene iodide also being present (Scheme 2). The competitive formation of TMSX in this reaction, the red color that ensued upon mixing I^- with **4b**, and the poor second-order kinetics of the reaction prevented us from making a desired comparison of the relative S_N2 reactivity of **4b** with that of the analogous iodomethyltrimethylammonium salt (**3a**) and it raised the question of the mechanistic source of TMSX in this reaction. The intervention of a competing SET reaction between I^- and **4b** (with resultant formation of the distonic radical **8**) was confirmed by carrying out the reaction in CD_3CN and then examining the ^2H NMR spectrum of the product mixture, whereby a triplet ($J = 2.1$ Hz) was observed at 3.11 ppm. This peak was attributed to the presence in the product mixture of $(CH_3)_2S^+CH_2D\ X^-$, which would be formed by the abstraction of a deuterium atom from the solvent by the distonic $(CH_3)_2S^+CH_2\bullet$ radical **8**. A quantitative analysis of the H versus D ratio in the obtained TMSX provided a H/D ratio of 27, which indicated a significant 31% incorporation of deuterium into the TMSX product.

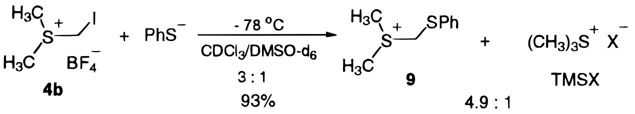
Cyclic Voltametry Experiments. To obtain some estimate of the relative reactivity of **4b** as an SET electron acceptor (in comparison to iodomethyltrimethylammonium analogue, **3a**, and other well-established SET electron acceptors such as perfluoroalkyl iodides), the reduction potentials for **4b**, **3a**, and a number of other related reductants were obtained in acetonitrile by means of cyclic voltametry, using tetrabutylammonium hexafluorophosphate as the supporting electrolyte. Both **4b** and **3a** gave irreversible cyclic voltamagrams, and their extracted cathodic peak potentials, E_{pc}, are summarized in Table 1. It can be seen that the iodomethyldimethylsulfonium salt **4b** is the most easily reduced compound, even more susceptible to reduction than n-perfluoroheptyl iodide. The iodo- and chloromethylmethyl sulfides (i.e., **5**) also exhibit sufficiently low reduction potentials to also be potentially SET reactive.

Table 1. Peak potentials for the First Cyclic Voltametric Reduction Wave of Various Halides in Acetonitrile at the Gc Electrode Using Bu_4NBF_4 as the Supporting Electrolyte

substrate	peak potential @ 0.25 V/s (V)
$(CH_3)_3N^+CH_2I\ BF_4^-$ (**3a**)	−1.39
$C_7F_{15}I$	−1.19
CF_3CH_2I	−1.80
$C_6F_{13}CH_2CH_2I$	−2.0
$(CH_3)_3S^+\ SO_3Me^-$	−1.9520[6]
$(CH_3)_2S^+CH_2I\ BF_4^-$ (**4b**)	−0.99
$(CH_3)_2S^+CH_2Cl\ BF_4^-$ (**4c**)	−2.25
CH_3SCH_2I (**5**)	−1.64
CH_3SCH_2Cl	−1.73

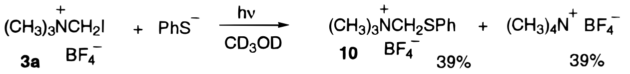
SET Chemistry of 4b and 3a. In view of the results from cyclic voltametry, both **4b** and **3a** should exhibit significant reactivity as electron acceptors in SET processes, such as $S_{RN}1$ reactions, with the former being more reactive. Both presumptions were demonstrated by examination of their relative reactivities with the powerful electron donor, tetrakis(dimethylamino)ethylene (TDAE).[7−10] Whereas, mixing of TDAE with sulfonium salt **4b** led to instant and quantitative conversion to TMSX, ammonium salt **3a** required overnight to accomplish the same.

The reactivity of **4b** and **3a** in an $S_{RN}1$ reaction was also confirmed by looking at their reactions with thiophenoxide ion. Whereas the reaction of PhS^- with ammonium salt **3a** in CD_3OD required UV irradiation to proceed, its reaction with **4b** was rapid and clean at −78 °C. (Reaction at higher temperatures led to secondary reactions between PhS^- and the primary thiophenoxy product, **9**.) It can be seen that H-atom transfer trapping of the intermediate is competitive with the $S_{RN}1$ chain process, which is probably a reflection of the great reactivity of such distonic radical cations.



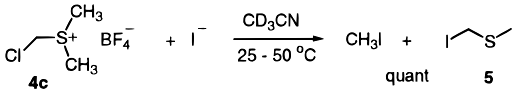
By comparison, the analogous, presumably straightforward S_N2 reaction of TMSI with thiophenoxide was considerably slower, with only 10% reaction being observed after 10 min at room temperature and a quantitative conversion to phenyl methyl sulfide and DMS requiring 12 h.

The photoinduced reaction of ammonio system, **3a**, also led to significant H-transfer reduction product being formed along with the expected $S_{RN}1$ product **10**. Evidence for the intermediacy of the α-ammonio distonic radical cation in this reaction was obtained by examining the ^2H NMR spectrum of the product mixture, which showed a triplet (J = 2.1 Hz) at 3.09 ppm, evidence for deuterium incorporation into the tetramethylammonium salt product.[11]

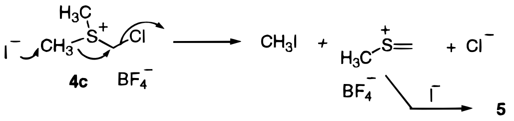


S_N2 Reactivity of Halomethylsulfonium Salts. Although, because of the intervention of SET chemistry, it was not possible to compare the S_N2 reactivity of iodomethylsulfonium salt **4a** with that of the respective iodomethylammonium salt, **3a**, the chloromethylsulfonium salt, **4c**, posed no such problem and exhibited excellent S_N2 behavior in its reaction with iodide ion.

In a manner analogous to that used for synthesis of **4b**, chloromethyldimethylsulfonium tetrafluoroborate, **4c**, was prepared by methylation of chloromethyl methyl sulfide with trimethyloxonium tetrafluoroborate.[12,13] Its reaction with iodide ion[14] at room temperature proceeded cleanly and virtually quantitatively for three half-lives as indicated below.[15] When allowed to react for longer times, the solution became colored and secondary products began to appear. The kinetics of demethylation of **4c** were measured during the first half-life of reaction, and excellent second-order behavior was observed. Rate constants were obtained at five temperatures and are given in Table 2, with the data giving the following activation parameters: $\Delta H^‡ = 8.9 \pm 0.4$ kcal/mol and $\Delta S^‡ = -46.6 \pm 0.7$ cal/deg. These values can be compared with those obtained for the analogous demethylation of iodomethyltrimethylammonium tetrafluoroborate (**3a**): $\Delta H^‡ = 18.3$ kcal/mol and $\Delta S^‡ = -20.8$ cal/deg.[1] Using the activation parameters of **4c** to extrapolate its rate to 101 °C, it can be seen that the chloromethylsulfonium substrate, **4c** ($k = 2.8 \times 10^{-3}$ M^{-1} s^{-1} is 580 times more reactive than the chloromethylammonium substrate, **3c** ($k = 4.8 \times 10^{-6}$ M^{-1} s^{-1}).



The large negative entropies of activation observed for both **3a** and **4c** would appear to be characteristic of the synchronous substitution/fragmentation mechanism that has been demonstrated for the halomethylammonium salts, **3a**−**c**.[16,17]



Nevertheless, it was decided to have a look at the relative reactivity of the analogous *fluoro*methylsulfonium salt in its reaction with I^-. Fluoromethyldimethylsulfonium tetrafluoroborate, **4d**, was synthesized as

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(6) Colichman, E. L.; Love, D. L. *J. Org. Chem.* **1953**, *18*, 40.

(7) Brisco, M. W.; Chambers, R. D.; Mullins, S. J.; Nakamura, T.; Vaughan, J. F. S.; Drakesmith, F. G. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3115.

(8) Wiberg, N. *Angew. Chem.* **1968**, *20*, 809.

(9) Pawelke, G. *J. Fluorine Chem.* **1991**, *52*, 229.

(10) Carpenter, W. *J. Org. Chem.* **1966**, *31*, 789.

(11) Products **9** and **10** were both synthesized by alternative routes to confirm their identity as products in the reactions of PhS^- with **4a** and **3a**, respectively (see Experimental Section).

(12) Bohme, H.; Krack, W. *Ann. Chem.* **1977**, 51.

(13) Kaczmarczyk, G.; Jonczyk, A. *Synlett* **1997**, 921.

(14) Benzyltrimethylammonium iodide was used as the iodide source because of its solubility characteristics and because it was found to be stable for 24 h at 70 °C in acetonitrile.

(15) Chloromethylsulfonium compound, **4c**, is also reactive, but less so than **4b**, in the SET reaction with PhS^-, and it gives a similar product profile.

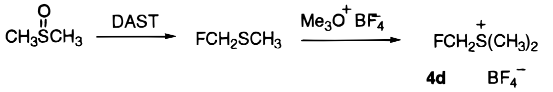
(16) For example, a much less negative entropy ($\Delta H^‡ = 24.8$ kcal/mol and $\Delta S^‡ = -5$ cal/deg) has been reported for the demethylation of *p*-chlorophenyldimethylsulfonium perchlorate by hydroxide ion, a process that produces noncharged products.

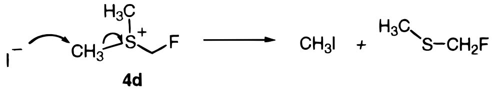
(17) Coward, J. K.; Sweet, W. D. *J. Org. Chem.* **1971**, *36*, 2337.

Table 2. Rate Constants for the Reaction of Chloromethyldimethylsulfonium Tetrafluoroborate (4c) in CD_3CN

temp/°C	25	30	35	40	50
$k/10^{-4}M^{-1}\,s^{-1}$	1.08(0.03)	1.33(0.03)	1.84(0.08)	2.23(0.05)	3.57(0.10)

shown below, and, somewhat surprisingly, it underwent reaction with iodide ion with a rate constant [$k = 4.41 \times 10^{-3}$ $M^{-1}\,s^{-1}$ at 30 °C] that was *33 times larger* than that of the chloromethylsulfonium salt, **4c**. Obviously, and most probably because of the much larger entropic demand for formation of F^- ion, the reaction of **4d** is *not* proceeding via the substitution/elimination mechanism that is characteristic of halomethylammonium salts, **3a**–**c**, but rather via a simple S_N2 process that is enhanced by the beneficial inductive effect of the fluorine substituent on the sulfide leaving group ability. Although, based on these kinetic results, it is a safe conclusion that the reaction of **4d** is proceeding via a simple S_N2 mechanism, one cannot, without additional studies, reach a similar, definitive conclusion about the pathway utilized by the *chloro*methyl compound, **4c**. However, based on the large negative $\Delta S^{\ddagger}$ of this reaction, we would favor it proceeding via the substitution/fragmentation mechanism.





Conclusions

Halomethyldimethylsulfonium salts, **4b**–**d**, have been synthesized and are observed to be highly reactive molecules that exhibit extraordinary diversity with respect to the nature of their reactivity, undergoing facile direct substitution (S_N2) reactions, but also being highly susceptible to electron-transfer reactions. Regarding the latter, electrochemical analysis has indicated that the iodomethyldimethylsulfonium compound, **4b**, is a potent electron acceptor, even surpassing the reactivity of perfluoro-*n*-alkyl iodides in that capacity. Consistent with their powerful electron-accepting ability, the iodo- and chloromethyldimethylsulfonium salts, **4b**,**c**, have been found to be reactive substrates in $S_{RN}1$ reactions.

Experimental Section

The cyclic voltametry experiments were performed in acetonitrile solution containing 0.1 M of substrate and 0.1 M tetrabutylammonium hexafluorophosphate (Bu_4NBF_4) under nitrogen. Investigations were carried out in an electrolytic cell using glassy carbon working and platinum counter electrodes. An Ag/AgCl electrode served as a reference electrode. Cyclic voltammetric curves were recorded with electrochemical system BAS CV-27 potentiostat. The reduction potential was corrected to the reduction potential vs SCE by adding ferrocene as a reference.

Reaction of Dimethyl Sulfide with Diiodomethane. Into a 50 mL three-neck round-bottomed flask was added diiodomethane (5.36 g, 0.02 mol), dimethyl sulfide (1.24 g, 0.02mol) and acetonitrile (15 mL). The reaction mixture was heated at 50 °C. A white solid was formed during the reaction, which is trimethylsulfonium salt, TMSI. After 3 days, ^1H NMR spectra revealed that the DMS had been consumed. From the spectra, the main product was TMSI along with small amount of **4a**, **5**, iodomethane, and methylthiomethydimethylsulfonium salt. An additional 1 equiv of DMS (1.24 g, 0.02 mol) was added, and the reaction mixture continued to heat at 50 °C. After 4 days, the ^1H NMR showed that the diiodomethane had been consumed. Solvent and volatile materials were evaporated, and the resultant solid was recrystallized from ethanol to obtain white crystalline TMSI (3.9 g, 96%, based on diiodomethane): ^1H NMR (DMSO-d_6) δ 2.90 (s, 9H); ^{13}C NMR, δ 26.10 ppm.

Chloromethyl Dimethylsulfonium Tetrafluoroborate, 4c. Into a suspension of trimethyloxonium tetrafluoroborate (0.8 g, 5.4 mmol) in methylene chloride (10 mL) was added chloromethyl methyl sulfide (0.5 g, 5.2 mmol) under dry nitrogen. The reaction mixture was stirred for 3 h at room temperature. The reaction mixture was separated to two layers. The solvent was decanted, and the residue was recrystallized in ethanol to give 0.5 g (51%) of a white solid, **4c**:[12] ^1H NMR (CD_3CN), δ 2.87 (s, 6H), 5.13 (s, 2H); ^{19}F NMR, δ −151.13; ^{13}C NMR, δ 23.38, 50.82. LSIMS (POS) Calcd. for C_3H_8ClS: 111.0035; found: 111.0031.

Reaction of Chloromethyldimethylsulfonium Tetrafluoroborate, 4c, with Iodide Ion. In a NMR tube, chloromethyldimethylsulfoniumtetrafluoroborate (19 mg, 0.1 mmol) was dissolved in acetonitrile-d_3 (0.7 mL). Benzyltrimethylammonium iodide (28 mg, 0.1 mmol) was added to the solution. The reaction progress was monitored by ^1H NMR spectroscopy. During the first three half-lives of **4c** (about 6 h), the reaction gave cleanly iodomethane and iodomethyl methyl sulfide, **5**. Over a longer period, the reaction mixture became red, and other materials were formed, in particular TMSX. After a week, the reaction had become dark red and gave a complicated product mixture, but the major product was TMSX. It was therefore possible to measure the kinetics of demethylation of **4c** during the first three half-lives of its reaction.

Iodomethyl Methyl Sulfide, 5. Into a 25-mL, three-necked, round-bottomed flask, equipped with a solid additional funnel, chloromethyl methyl sulfide (4.9 g) was dissolved in CCl_4 (10 mL), and then the reaction mixture was cooled in an ice bath. The fine powder of NaI (7.1 g) was added slowly to the reaction mixture, so that the reaction temperature was maintained under 20 °C. After addition, the reaction mixture was stirred for 6 h at room temperature. The solid was filtered and washed with CCl_4. The filtrate was distilled at reduced pressure, during which the oil bath temperature was kept below 75 °C. After removal of solvent, the residue was distilled at 12 mmHg to obtain 6.7 g (70%) of **5** as a light yellow liquid: bp 52–54 °C/12 mmHg; ^1H NMR ($CDCl_3$), δ 2.21 (s, 3H), 4.37 (s, 2H); ^{13}C NMR, δ 11.58, 18.78.

Iodomethyldimethylsulfonium Tetrafluoroborate, 4b. Into a suspension of trimethyloxonium tetrafluoroborate (0.8 g, 5.4 mmol) in methylene chloride (10 mL) was added 1 g (5.2 mmol) of **5** under dry nitrogen. The reaction mixture was stirred for 3 h at room temperature. The reaction mixture was separated to two layers. The solvent was decanted, and the residue was recrystallized in ethanol to give white solid at −5 °C. The white solid became a viscous oil at room temperature, and although it was stable in the refrigerator, it slowly decomposed at room temperature. The reaction gave 0.78 g (52%) of **4b**: ^1H NMR (CD_3CN), δ 2.81 (s, 6H), 4.59 (s, 2H); ^{19}F NMR, δ −149.53 (s); ^{13}C NMR, δ 3.13, 27.70; LSI MS (POS) Calcd for C_3H_8IS: 202.9391; found: 202.9392.

Reaction of 4b with Iodide Ion (at room temperature). Into an NMR tube, iodomethyldimethylsulfonium tetrafluoroborate, **4b**, (0.029 g; 0.1 mmol) was dissolved in acetonitrile (0.7 mL). Sodium iodide (0.015 g, 0.1 mmol) or benzyltrimethylammonium iodide (0.028 g, 0.1 mmol) was added to the solution, and it immediately became light red. The proton NMR spectrum of the reaction mixture revealed that the most of the starting material had been consumed. Carefully examining the NMR spectrum, several compounds could be identified based on their chemical shifts: mainly methyl iodide, **5**, and TMSX, along with small amounts of DMS and diiodomethane. Also, a small peak at 9.62 ppm indicated the formation of the intermediate methylmethylenesulfonium cation. There were also some other unidentified materials. This experiment was repeated several times, and the NMR spectra were not consistent each time.

A ^{2}H NMR spectrum of the reaction mixture showed a triplet at 3.11 ppm with the coupling constant of 2.1 Hz, indicating formation of $(CH_3)_2S^+CH_2D$ salt. Using toluene as an quantitative internal standard for the protons and CD_2Cl_2 as a quantitative internal standard for the deuterium of $(CH_3)_2S^+$-CH_2D, a ratio of 27 was obtained for H vs D in this obtained TMSX. This indicates a 31% incorporation of deuterium into TMSX by deuterium atom abstraction from CD_3CN.

Reaction of 4b with Iodide Ion (at 70 °C). A similar reaction mixture was heated at 70 °C for 5 h, and the ^{1}H and ^{13}C NMR spectra revealed the major (60%) product to be TMSX.

Reaction of 4b with DMS at 60 °C. 4b (0.52 g, 1.8 mmol) was dissolved in acetonitrile (5 mL). DMS (0.3 g, 4.8 mmol) was added, and the reaction mixture was heated at 60 °C overnight. The solvent was evaporated, and the residue was recrystallized from ethanol to obtain white solid 0.30 g (94%). The ^{1}H and ^{13}C NMR spectra revealed that the solid was TMSX.

Reaction of 4b with DMS (at room temperature). A similar mixture was prepared and allowed to stand at room temperature. The ^{1}H NMR spectrum was immediately recorded and showed only starting materials. The reaction progress was observed for 2 days. It was observed that the **4b** had been consumed after 2 days, with the reaction mixture showing the presence of several products including TMSX, **5**, methyl iodide, and methylthiomethyldimethylsulfonium salt, **6**,[5] with the ratio of theses compounds being 12:2:2:6.

Reaction of 4c with DMS. In an NMR tube, **4c** (20 mg, 0.1 mmoml) was dissolved in acetonitrile-d_3 (0.7 mL), and the tube was sealed with a rubber septum. DMS (6.2 mg, 0.1 mmol) was added into the reaction mixture by a syringe. The ^{1}H NMR spectrum was recorded and showed that only starting materials were present. After standing at room temperature for 2 days, the ^{1}H NMR showed that no reaction had occurred. The reaction mixture was heated at 80 °C, and the reaction progress was observed for 3 days by ^{1}H NMR spectroscopy. The **4c** had been consumed after 30 h, with the reaction mixture showing the presence of several products, including TMSX, chloromethyl methyl sulfide, and methylthiomethyldimethylsulfonium salt. After 3 days, the major product was TMSX (>90%), with a small amount of chloromethyl methyl sulfide, and methylthiomethyldimethylsulfonium compound still being present.

Reaction of 4b with Sodium Thiophenoxide. At −78 °C. In an NMR tube, **4b** (0.0361 g, 0.12 mmol) was dissolved in 3:1 of $CDCl_3$ and DMSO-d_6 (0.5 mL). The NMR tube was cooled to −78 °C with dry ice/acetone. After 10 min, a solution of sodium thiophenoxide (0.0164 g, 0.12 mmol) in 3:1 of $CDCl_3$/DMSO-d_6 (0.5 mL) was added to the NMR tube at −78 °C. The NMR tube was shaken to mix the two solutions, and it was maintained at −78 °C for 30 min. The ^{1}H NMR spectrum was then taken, and it showed the reaction to be finished. The main products were phenylthiomethyldimethylsulfonium salt, **9**, for which the NMR ratio of methylene group (5.08 ppm) to dimethyl group (2.91 ppm) was 1 to 3, and TMSX (ratio of products = 4.9:1) (92%). The other 8% of the products were the secondary reaction products that are seen to dominate when the reaction is run at 0 °C or higher.

Room-Temperature Reaction. A similar reaction mixture was prepared, and after 10 min, the ^{1}H NMR spectrum of the mixture showed that all **4b** was gone. The reaction mixture contained several products, including **9**, along with phenylthiomethyl methyl sulfide (1:3 of CH_2 (4.19 ppm): CH_3 (2.46 ppm)), diphenylthiomethane (4.64 ppm), DMS (2.04 ppm), TMSX (2.90 ppm), and phenyl methyl sulfide (2.15 ppm). The ratio of these compounds was 4.7:2:1:1:0.5:1.

When excess of sodium thiophenoxide was added to the reaction mixture, the reaction gave mainly phenylthiomethyl methyl sulfide, phenyl methyl sulfide, and dimethyl sulfide along with some diphenylthiomethane.

Phenylthiomethyl Methyl Sulfide. **Synthesis of Authentic Product.** Into a 25 mL round-bottom flask equipped with stirrer, thermometer, and reflux condenser was added a solution containing 0.82 g of sodium methoxide (15.2 mmol) in 10 mL of absolute methanol. While maintaining the solution at 25−30 °C, 1.67 g (15.2 mmol) of thiophenol in 4 mL of absolute methanol was added. Thereto, at 25 °C, 1.47 (15.2 mmol) of chloromethyl methyl sulfide in 4 mL of absolute methanol was added to reaction mixture with stirring. The reaction mixture was warmed to 35 °C and stirred for 3 h. The solvent was evaporated, in vacuo, and then hexane was added. The hexane solution was washed with brine, and after removal of solvent, the residue was purified by column chromatography (hexane) to obtain a liquid 2.3 g (88%): ^{1}H NMR ($CDCl_3$), δ 1.24 (s, 3H), 4.01 (s, 2H), 7.21−7.40 (m, 3H), 7.31 (d, J = 6.6 Hz, 2H); ^{13}C NMR, δ 15.33, 40.56, 127.12, 129.11, 130.79, 135.31; HRMS (EI) Calcd for $C_8H_{10}S_2$: 170.0224; found: 170.0223.

Phenylthiomethyldimethylsulfonium Tetrafluoborate, 9. Into a suspension of trimethyloxonium tetrafluoroborate (0.35 g, 2.4 mmol) in methylene chloride (10 mL) was added phenylthiomethyl methyl sulfide (0.4 g, 2.4 mmol) under dry nitrogen at −78 °C. The reaction mixture was warmed to room temperature and stirred for 3 h. The reaction mixture separated into two layers. The solvent was decanted, and the residue was recrystallized from ethyl acetate to give a white solid 0.42 g (70%): ^{1}H NMR (DMSO-d_6), δ 2.79 (s, 6H), 4.68 (s, 2H), 7.42−7.48 (m, 3H), 7.56−7.65 (m, 2H); ^{13}C NMR, δ 24.09, 46.69, 128.57, 129.72, 130.83, 131.08; LSI MS POS calcd for $C_9H_{13}S_2^+$: 185.0459; found: 185.0460.

Reaction of 9 with Sodium Thiophenoxide. To demonstrate the secondary reaction chemistry of **9** with thiophenoxide, the following reaction was studied. In a NMR tube, **9** (0.0272 g, 0.1 mmol) and sodium thiophenoxide (0.0132 g, 0.1 mmol) were dissolved in DMSO-d_6 (0.7 mL). After 10 min, the ^{1}H NMR spectrum showed that starting material was gone. The reaction mixture contained several products, including phenylthiomethyl methyl sulfide, phenyl methyl sulfide, bis(phenylthio)methane, and DMS. The ratio of these compounds was 2.9:2.9:1:1.

Reaction of TMSI with Sodium Thiophenoxide. In an NMR tube, TMSI (0.0204 g, 0.1 mmol) and sodium thiophenoxide (0.0132 g, 0.1 mmol) were dissolved in DMSO-d_6 (0.7 mL). After 10 min, the ^{1}H NMR spectrum showed that 10% of starting material had been consumed. After overnight, the reaction quantitatively gave phenyl methyl sulfide and DMS.

Fluoromethyldimethylsulfonium Tetrafluoroborate, 4d. The following procedure for the preparation was modified based on a literature procedure.[18] In a three-neck round-bottomed flask, in which one of necks was connected to a trap cooled to −78 °C, a solution of dimethyl sulfoxide (0.4 g, 5 mmol) in methylene chloride (5 mL) was added. To the above solution was added DAST (1 g, 6.2 mmol) under nitrogen, and the mixture was stirred at room temperature. The progress of the reaction was monitored by the appearance in the ^{1}H NMR of the CH_2F product signal (doublet, J_{HF} = 53.2 Hz) centered at δ 5.41. After 28 h, the NMR spectrum showed the completion of reaction (disappearance of DMSO), but there was nothing in the trap. The products remained in solution, as indicated by the NMR spectrum which indicated the presence of the desired product: fluoromethyl methyl sulfide: ^{1}H NMR ($CDCl_3$), δ 2.25 (d, J = 2.7 Hz, 3H), 5.41 (d, J = 53.2 Hz, 2H); ^{19}F NMR, δ −188.56 (t, J = 53.2 Hz, 1F).

The solution was distilled into a flask containing trimethyloxonium tetrafluoroborate (0.5 g), and the resulting mixture was sealed and stirred overnight at room temperature. The solvents were evaporated, and the residue was recrystallized

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(18) McCarthy, J. R.; Peet, N. P.; Le Tourneau, M. E.; Ingasekaran, M. J. *J. Am. Chem. Soc.* **1985**, *107*, 735.

from ethanol to obtain a white solid (0.2 g). The NMR spectra confirmed the solid to be the product, **4d**, which contained a small amount of non-fluorine-containing impurity: Fluoromethyldimethylsulfonium tetrafluoroborate, **4d**: ^{1}H NMR (CD_3CN), δ 2.87 (d, $J = 1.0$ Hz, 6H), 5.83 (d, $J = 45.9$ Hz, 2H); ^{19}F NMR, δ −146.50 (s, 4F); −222.99 (t, $J = 45.9$ Hz, 1F).

Reaction of 4d with Iodide. Into an NMR tube, a solution of the crude **4d** in CD_3CN was added, and the ^{19}F NMR spectrum showed the characteristic triplet of **4d** at δ −222.99. A slight excess of tetrabutylammonium iodide was added at room temperature, and the reaction mixture was monitored over a period of 1 h. The ^{19}F NMR spectrum revealed that the peak intensity of **4d** decreased gradually and that the peak of fluoromethyl methyl sulfide (δ −188.56) appeared and gradually increased in intensity. The reaction was complete in 10 h with the fluoromethyl of **4d** being totally (and quantitatively) converted to that of fluoromethyl methyl sulfide. The kinetic study will be described subsequently (vide infra).

Reaction of 4b with Tetrakis(dimethylamino)ethylene (TDAE). In an NMR tube, **4b** (0.029 g, 0.1 mmol) was dissolved in dimethylformamide-d_6 (0.7 mL). Nitrogen was bubbled to the system, and it was closed with a rubber cap. TDAE (0.040 g, 0.2 mmol) was added to the mixture, and it turned red. The ^{1}H NMR spectrum showed that the starting materials were totally consumed after 5 min. TMSX was formed in quantitative yield based on its ^{1}H NMR spectrum.

Reaction of 3a with TDAE. In an NMR tube, **3a** (0.032 g, 0.11 mmol) was dissolved in dimethylformamide-d_6 (0.7 mL). Nitrogen was bubbled to the system, and it was closed with a rubber cap. TDAE (0.040 g, 0.2 mmol) was added to the mixture. The reaction mixture turned to red color, and it was kept overnight at room temperature. A white solid was formed in the NMR tube. The solvent was decanted and the solid washed with ether and dried by vaccum to give tetramethylammonium tetrafluoroborate (0.008 g) as confirmed by ^{1}H and ^{13}C NMR spectra. The yield was quantitative.

Photo SET Reaction of 3a with Sodium Thiophenoxide. In an NMR tube, **3a** (0.0202 g) and sodium thiophenoxide (0.0092 g) was dissolved in methanol-d_4 (0.7 mL). The solution was degassed (freeze and thaw) three times, sealed with rubber septum under nitrogen, and photolyzed using a Rayonet reactor for 10 h at 26 °C. A white solid was formed, and the ^{1}H NMR showed that the starting material had been consumed. The methanol was evaporated to obtain a crude product. DMSO-d_6 (0.7 mL) was added to dissolve the solid. The reaction gave tetramethylammonium tetrafluoroborate (0.0045 g, 39%) and phenylthiomethyltrimethylammonium tetrafluoborate, **10** (0.0074 g, 39%). The structures were confirmed by comparison with authentically samples. Diphenyl disulfide could also be isolated from the reaction. A ^{2}H NMR spectrum of the tetramethylammonium tetrafluoroborate product showed a triplet at 3.09 ppm with coupling constant 2.1 Hz.

Another NMR tube containing the same reaction mixture was left at room temperature for 20 h. A ^{1}H NMR spectrum showed no reaction at all.

In a control experiment, **3a** alone (0.0202 g) was dissolved in methanol-d_4 (0.7 mL). The solution was degassed (freeze and thaw) three times, sealed with rubber septa under nitrogen, and photolyzed using a Rayonet reactor for 20 h at 26 °C. After that, the ^{1}H NMR spectrum showed that 95% of **3a** remained.

Dimethylaminomethylphenyl Sulfide. A three-necked, 100 mL round-bottomed flask was fitted with a 25 mL pressure-equalizing addition funnel, spiral condenser, ice bath, and magnetic stirrer. Into the flask was added 40% dimethylamine solution (22 mL, 0.17 mol). Thiophenol (20.5 mL, 0.2 mol) was added to the cooled amine in over 30 min. To the resulting mixture was added 37% formaldehyde solution in water (14.1 g, 0.173 mol). The reaction mixture was heated at room temperature for 30 min before raising the temperature to 80 °C where it was heated for 2 h. The reaction mixture was cooled to room temperature and extracted with diethyl ether (25 mL × 3). The combined ether extract was dried with anhydrous sodium sulfate. After filtering the drying agent, the ether was removed by rotary evaporation. The residue was then fractionally distilled through a 2 in. vigreux column at 53−55 °C at 0.15 mmHg. The compound was obtained in 78% yield: ^{1}H NMR ($CDCl_3$), δ 2.29 (s, 6H), 4.45 (s, 2H), 7.33 (m, 5H); ^{13}C NMR, δ 42.37, 68.63, 126.84, 128.77, 131.41, 137.88; HRMS (LSIMS POS calcd for $C_9H_{14}NS$ (M + 1): 168.0847, found: 168.0847.

Phenylthiomethyltrimethylammonium Iodide. In a 10 mL round-bottom flask was placed dimethylaminomethyl phenyl sulfide (0,56 g, 3 mmol), methyl iodide (0.85 g, 6 mmol), and acetonitrile (5 mL). The reaction mixture was stirred at room temperature for 17 h. The crude product was filtered from the reaction mixture through a glass frit and recrystallized from absolute ethanol. The title compound was obtained as a white solid in 20% yield: mp 152−153 °C, ^{1}H NMR (DMSO-d_6), δ 3.07 (s, 6H), 5.11 (s, 2H), 7.44 (m, 3H), 7.70 (d, $J = 6.6$ Hz, 2H); ^{13}C NMR, δ 51.20, 69.32, 128.51, 129.66, 131.18, 132.08; HRMS (LSIMS POS) calcd for $C_{10}H_{16}NS$: 182.1004; found: 182.1002.

General Procedure for Determination of Rates of Demethylation of Sulfonium Salts. (a) Kinetics for the Demethylation of Chloromethyldimethylsulfonium Tetrafluoroborate, 4c. A solution of 0.0167 mmol of **4c** and 0.0167 mmol of benzyltrimethylammonium iodide in 0.7 mL acetonitrile-d_3 was made in the NMR tube. The tubes were heated in a Varian VXR 300 spectrometer which was calibrated using neat ethylene glycol as a reference. The disappearance of the salt with respect to time was monitored by proton NMR, with the reactions being generally followed for one half-life. The proton signal for the methyl peak of benzyltrimethylammonium iodide at δ 3.03 was used as an internal standard. Second-order rate constants were obtained by applying the usual rate equation for a situation where the reactants are equal or unequal in concentration (eq 1).

$$1/(a_0 - x) = kt + 1/a_0 \text{ or } \ln[1 + a_0/a] = a_0kt + \ln 2 \quad (1)$$

The second-order rate constants were obtained by plotting the reciprocal of the concentration (NMR intensity) of the salt with respect to time in seconds, with the rate of demethylation being obtained from the slope of the plot. Arrhenius parameters were determined by plotting the logarithms of these second-order rate constants against the reciprocals of the temperatures in K. Eyring parameters were determined by plotting ln(k/T) vs $1/T$. Tables of kinetic data for **4c** may be found in the Supporting Information.

(b) Kinetics of Demethylation of Fluoromethyldimethylsulfonium Tetrafluoroborate, 4d. The kinetic experiment for the demethylation of **4d** was run at 30 °C in CD_3CN. The peak intensity of **4d** was recorded relative to the peak intensity of internal standard α,α,α-trifluorotoluene. In this experiment, an excess of tetrabutylammonium iodide was used to ensure pseudo-first-order conditions.

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Supporting Information Available: Supporting Information. NMR spectra of **4b**−**d**, **5**, **9**, and **10**, tables of kinetic data, and cyclic voltamagrams. This material is available free of charge via the Internet at http://pubs.acs.org.

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