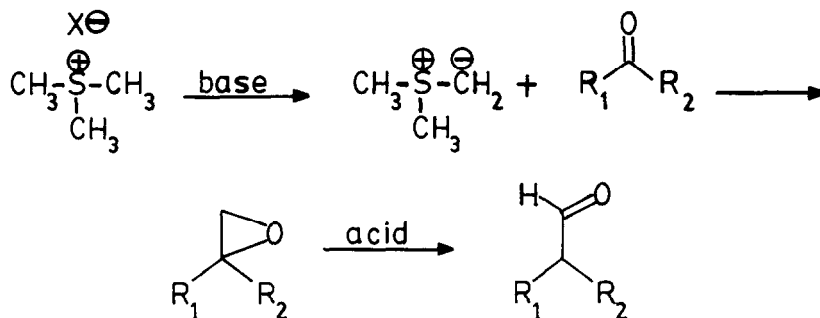


THE PREPARATION OF TRIMETHYLSULFONIUM CHLORIDE  
FROM METHYL CHLOROFORMATE AND DIMETHYL SULFIDE

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**Abstract:** Trimethylsulfonium chloride is conveniently prepared in one step by reacting dimethyl sulfide with methyl chloroformate.

Our interest in trimethylsulfonium chloride stemmed from a need to obtain  $\alpha$ -alkyl aldehydes. The synthetic approach that proved to be most effective for the target aldehydes was the rearrangement of oxiranes,<sup>1</sup> which were in turn prepared from ketones and dimethylsulfonium methylide.<sup>2,3,4</sup>



To generate dimethylsulfonium methylide in situ, we evaluated several trimethylsulfonium salts as precursors.

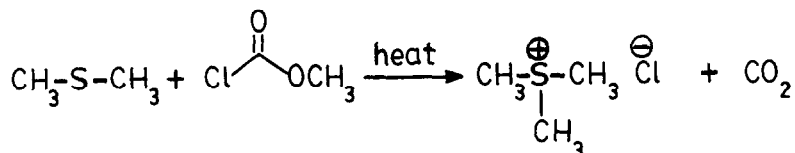
While trimethylsulfonium iodide<sup>5</sup> gave excellent yields of oxiranes with bases such as sodium hydride, poor yields and long reaction times were found with NaOH or KOH. Similar results were obtained with trimethylsulfonium methylsulfate.<sup>4</sup> Bases such as NaOH and KOH are desirable since they offer advantages of safety and economy for large scale preparations.

Rosenberger found that in aqueous NaOH the counter ion of the trimethylsulfonium salt played an important role in ylide formation, with the chloride being more reactive than the bromide, and the iodide being unreactive. We confirmed that the trimethylsulfonium chloride salt was effective in obtaining our target oxiranes with NaOH.

Having established the above advantage of having chloride as the counter ion, we sought a convenient method to prepare trimethylsulfonium chloride.

One of the standard methods of preparation is the reaction of dimethyl sulfide with methyl chloride in methanol, which gives excellent yields (92%),<sup>1,6</sup> but uses methyl chloride, a highly toxic, highly diffusive (bp  $-23.7^\circ\text{C}$ ) reagent. Another preparation, using trimethylsulfonium iodide and ion exchange, is expensive and tedious.<sup>7</sup>

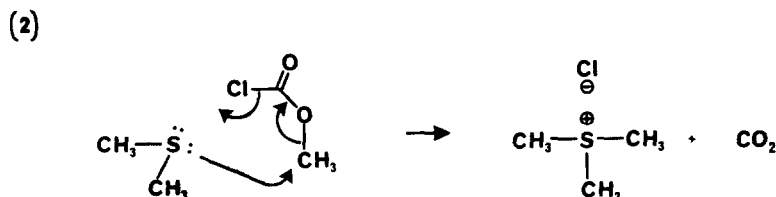
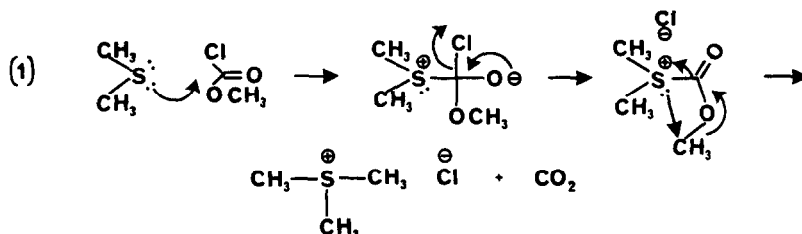
We have found that reacting dimethyl sulfide with methyl chloroformate cleanly gives trimethylsulfonium chloride in good yields (73%).



In a cursory examination of the scope of this reaction, a number of sulfides were evaluated with ethyl and methyl chloroformate. The results are reported in Table I.

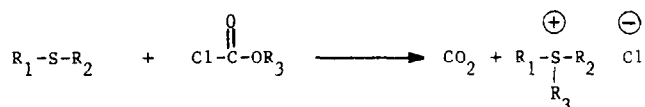
Several observations are noteworthy. With the exception of dimethyl sulfide, the acyclic sulfides tested were unreactive, possibly due to steric hinderance. Ethyl chloroformate was unreactive, even with dimethylsulfide. Again, this may be due to steric bulk. Tetrahydrothiophene did give the methyl sulfonium chloride salt, possibly because tetrahydrothiophene is less hindered and more nucleophilic than diethyl sulfide.



Two possible mechanisms for the reaction are shown below:



A representative preparation of trimethylsulfonium chloride is as follows: into a 195 ml pressure bottle was added 6.20g (0.1 mol) dimethylsulfide and 4.75g (0.05 mol) methyl chloroformate (Aldrich). The sealed bottle was heated at 80°C in an oil bath. After 4 hours the pressure bottle was cooled to -78°C and the seal opened. The bottle was immediately warmed to 20-25°C in a water bath to expell the dissolved CO<sub>2</sub>.<sup>9</sup> The bottle was sealed and heated for another 22 hours. The bottle was cooled to -78°C and opened. After warming to 20-25°C, the white crystals were washed twice in the bottle with 15 ml dry THF. The white crystals were dried for 4 hours at 0.1 torr, yielding 4.13g (73.5% yield) of trimethylsulfonium chloride (Temp. 192°C).

Table I  
The Preparation of Sulfonium Salts from Sulfides<sup>a</sup>



Sulfide R <sub>1</sub> , R <sub>2</sub>	Chloroformate R <sub>3</sub>	Temp. °C	Time, hrs	Yield
-CH <sub>3</sub> , -CH <sub>3</sub>	-CH <sub>3</sub>	60°	30	43.7%
-CH <sub>3</sub> , -CH <sub>3</sub>	-CH <sub>3</sub>	80°	7	50.0%
-CH <sub>3</sub> , -CH <sub>3</sub>	-CH <sub>3</sub>	80°	26	73.5% <sup>c</sup>
-CH <sub>3</sub> , -CH <sub>3</sub>	-CH <sub>2</sub> CH <sub>3</sub>	80°	48	negligible
-CH <sub>3</sub> , -CH <sub>2</sub> CH <sub>3</sub> <sup>d</sup>	-CH <sub>3</sub>	80°	25	"
	-CH <sub>3</sub>	80°	47	"
	-CH <sub>3</sub>	60°	30	43.7% <sup>e</sup>
"	-CH <sub>3</sub>	80°	26	37.7%
"	-CH <sub>3</sub>	100°	27	0
-CH <sub>3</sub> , -CH <sub>2</sub> CH=CH <sub>2</sub>	-CH <sub>3</sub>	80°	47	negligible
-CH <sub>3</sub> , -CH <sub>2</sub> CN	-CH <sub>3</sub>	80°	47	"
-CH <sub>3</sub> , -CH(CH <sub>3</sub> )COCH <sub>3</sub>	-CH <sub>3</sub>	80°	48	"

a) Heated in an oil bath 0.1 moles sulfide<sup>b</sup> and 0.05 moles chloroformate in a pressure bottle.

b) The excess sulfide was used as a solvent.

c) M.p. = 192° (literature<sup>7</sup>, m.p. not given); NMR (D<sub>2</sub>O) δ 2.88(s).

d) A repeat experiment in acetonitrile was also unsuccessful.

e) M.p. = 171-174°C (literature<sup>8</sup>, M.p. 192-3°);

elemental analysis C<sub>5</sub>H<sub>11</sub>SCl (138.66).

Theory: C = 43.31%, H = 8.00%, S = 23.12%, Cl = 25.57%;

Observed: C = 43.40%, H = 8.17%, S = 23.12%, Cl = 25.19%;

NMR (D<sub>2</sub>O) δ 2.40 (m,4H), 2.8 (s,3H), 3.5 (m,4H).

The reaction of methyl chloroformate and dimethyl sulfide is a convenient one-pot, one-step preparation of trimethylsulfonium chloride.

Extension of this reaction to the preparation of quaternary ammonium and quaternary phosphonium salts are being investigated in our laboratory.

#### References and Notes

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- 9) Without removing some of the CO<sub>2</sub>, the pressure build-up occasionally caused the bottle sealing gasket to fail.

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