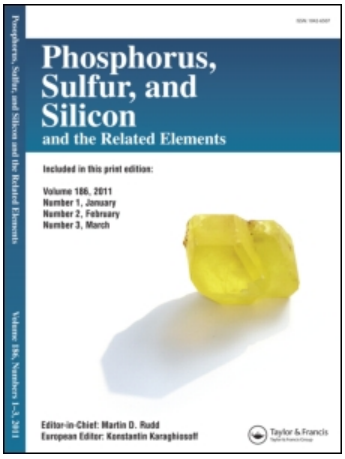

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TRIFLUOROMETHYLTHIOCOPPER CATALYZED OXIRANE RING OPENING

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Trifluoromethylthiocopper has been found to catalyze the opening of the epoxide ring and to furnish not-so-easily accessible novel trifluoromethylthiolated α-hydroxy compounds. This communication presents the mechanism of the formation of the various compounds and their mass spectral data.

Keywords: α-Hydroxy sulfides; free-radical-reactions; oxirane ring cleavage; pseudohalide; trifluoromethylthiocopper

Compounds containing the trifluoromethylthio function exhibit a wide spectrum of biological activity, ranging from antimalarial, fungicidal, insecticidal, virucidal, anti-inflammatory, immune modulatory, antipsychotic, antidopaminergic, anticholinergic, sensory irritation, etc. The trifluoromethylthio function also possesses extremely high lipophilicity,[1] thus facilitating the in vivo absorption and transportation of the compounds containing this moiety.[2] The group's inertness to a variety of chemical reagents permits the parent compounds to exert their pharmacological activity for a prolonged period. The trifluoromethylthio group has been labeled a "pseudohalogen."[3] It has also been described as a highly electronegative group. Thus, this interesting moiety confers a number of useful biological, chemical, and physical properties upon the parent compounds. Hence, it is finding increasing commercial application in the synthesis of pharmaceuticals[2a] and agrochemicals.[4]

However, the introduction of the trifluoromethylthio group into organic compounds entails the use of highly toxic reagents or harsh

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reaction conditions.[5] Unfortunately, there are not too many methods that facilitate the introduction of this group into organic compounds. Of the very limited number of methods available, the popular procedure involves the reaction of halogenated substrates with trifluoromethylthiolated metals such as bis(trifluoromethylthio)-mercury, trifluoromethylthiosilver, and trifluoromethylthiocopper. The first reagent is extremely toxic and corrosive and highly hygroscopic. Until recently the two remaining reagents were prepared and used in situ. Recently, we have developed and described a new method of synthesis of trifluoromethylthiocopper in a highly pure form[6a] and described its X-ray crystallographic structure determination.[6b] In view of properties ascribed to the trifluoromethylthio group, trifluoromethylthiocopper can be regarded as a "soft" metal halide.

Oxiranes comprise an extremely versatile group of intermediates and as such have attracted considerable interest.[7] Because of their ready availability and exceptional reactivity, the epoxides have found a multitude of applications as intermediates in synthetic organic chemistry. The oxirane ring can be opened under almost all conditions: electrophilic, nucleophilic, neutral, gas-phase, thermal, and free-radical conditions (Figure 1).[7a] An excellent review on the preparation and synthetic applications of the oxiranes has appeared.[7f]

Recently there has been considerable interest in the chemo-, regio-, and stereospecific opening of the oxirane ring, for the vicinal halohydrins thus formed from the ring opening serve as versatile intermediates in organic synthesis.[8] Dilithium tetrabromonickelate,[9a] and dilithium tetrachlorocuprate,[9b] both prepared in situ, have been employed as sources of nucleophile bromide and chloride, respectively, in the regioselective cleavage of the oxirane ring under mild reaction conditions. Lithium halides have also been used to regiospecifically open the epoxide ring in the presence of acetic acid[9c] and amberlyst.[9d] The use

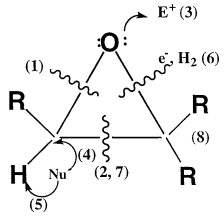

FIGURE 1 Types of oxirane cleavages and reactions. (1, 2) Homolytic cleavages (free radical, photolytic, thermal); (3) electrophilic attack on the ring oxygen; (4) nucleophilic attack on the ring carbon; (5) nucleophilic attack on the ring hydrogen; (6) reactions with electrons and surface reactions; (7) cycloadditions; and (8) reactions of the substituent.

of titanium halides,[10a,b] tin halides,[10c] and aluminum iodide[10b] has also been described. Recently, we reported the microwave-catalyzed oxirane ring opening in the presence of hydrogen dimethylphosphonate.[11] It was considered interesting to test the "pseudohalide" properties of the trifluoromethylthio group and to explore the possibility of synthesizing uniquely substituted α-hydroxy-β-trifluoromethylthio derivatives. Thus, six substrates—namely cyclohexene oxide, 1, 2-epoxybutane, epibromohydrin, exo-epoxy-norbornane, styrene oxide, and phthalimide-N-propyelene oxide—were reacted with trifluoromethylthiocopper, and the cleavage of the oxirane ring was observed in all the cases examined. The results of the reaction of styrene oxide with $CuSCF_3$ have already been reported.[12] This communication presents the results of the remaining five reactions.

RESULTS AND DISCUSSION

Reaction 1: Reaction of Cyclohexene Oxide with Trifluoromethylthiocopper[13]

Refluxing a mixture of cyclohexene oxide (**1**) and trifluoromethylthiocopper (**2**) in freshly distilled dry acetonitrile with stirring overnight under argon, cooling it to room temperature and processing as usual permitted the characterization of five components excluding **1**: (**a**) starting material, (b) 2-fluorocyclohexanol (**3**), (c) 2-chlorocyclohexanol (**4**), (d) 2-(trifluoromethylthio)-cyclohexanol (**5**), (e) cyclopentane aldehyde (**6**), and bis-(1, 2-(trifluoromethylthio)cyclohexane (**7**) (Figure 2). The presence of 2-chlorocyclohexanol (**4**) was attributed to copper (I) chloride accompanying trifluoromethylthiocopper (**2**) as an impurity. When pure trifluoromethylthiocopper (**2**) was used in the above reaction, 2-chlorocyclohexanol (**4**) was not detected.

Various mechanisms such as a four-centered transition state,[14a] without the participation of the radical mechanism,[14b] without the participation of carbonium ions,[14c] and ion-pair–like and carbonium

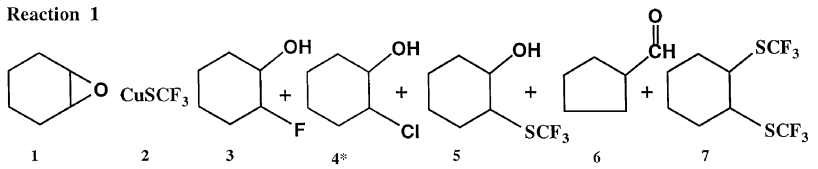

FIGURE 2 Reaction of cyclohexene oxide with $CuSCF_3$. Cu(I)Cl, accompanying as an impurity with activated copper serves as a source of Cl. When purified F_3CSCu was used, this compound was not detected.

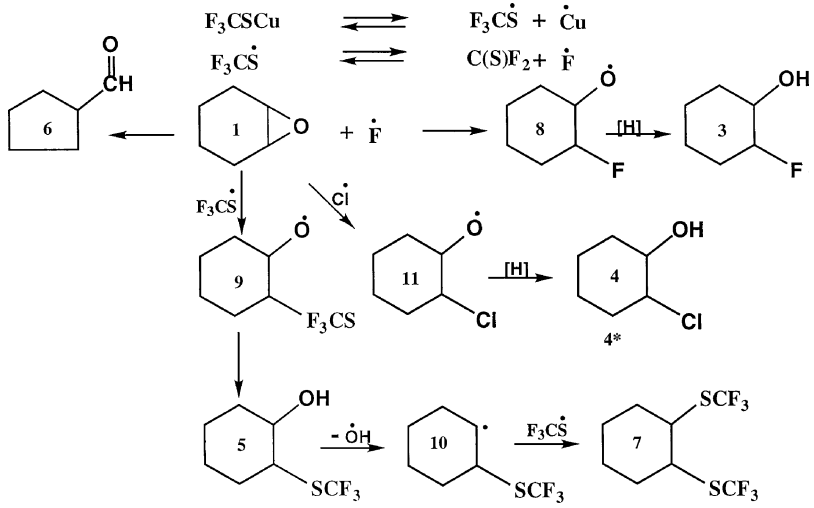

FIGURE 3 Probable mechanism of the formation of compounds.

ion intermediates[14d] have been suggested to explain the formation of the products from the opening of the oxirane ring. Photolysis of ethylene oxide has been reported to furnish "a plethora of products" including methyl radical, butene, etc.[14e] The initial photo-cleavage of the epoxide ring appears to result in a pair of diradicals.[14f] The proposed dissociation of $F_3CS^{\cdot}$ radical into $C(S)F_2$ and $F^{\cdot}$ radical has precedents.[15]

Figure 3 attempts to explain the probable mechanism of the formation of compounds **3–7** from cycloehxene oxide (**1**). 2-Fluorocyclohexanol (**3**) originates from the attack of the substrate (**1**) by $F^{\cdot}$ radical formed from the dissociation of the $F_3CS^{\cdot}$ radical, which itself arises from F_3CSCu (**2**). The intermediate **8** then goes on to abstract hydrogen and to yield **3**. Compound **4** is similarly formed via the attack by the $Cl^{\cdot}$ radical formed from Cu(I)Cl. While the attack by the thiyl radical ($F_3CS^{\cdot}$) on cycloehxene oxide (**1**) results in the intermediate **9**, which in turn abstracts hydrogen and yields 2-(trifluoromethylthio)-1-cyclohexanol (**5**). The loss of the $^{\cdot}OH$ from **5**, followed by the reaction of the intermediate **10** with the $F_3CS^{\cdot}$ radical furnishes bis-(1, 2-(trifluoromethylthio)cyclohexane (**7**). The monothiolated compound (**5**) and the bisthiolated derivative (**7**) could not be completely separated, as they elute very close to each other. This inseparable mixture mostly consists of the monothiolated compound (**5**). The mass spectral fragmentation behavior of compounds cited in the text is given in Table I. The preparation and mass spectra of **3** and **4** have been described.[16a–c]

TABLE I Mass Spectral Fragmentation of Compounds Cited in the Narrative

1. Mass spectral fragmentation of 2-Fluorocyclohexanol (**3**, r. t. = min, 9.1%); M^+ = 118; 99 (M—F); 85 (99-CH_2); 83 (C_5H_7O); 80 (C_6H_8); 75 (M—C_2H_3O); 72 (C_4H_5F); 69 (C_4H_5O); 59 (C_3H_4F); 57 (C_3H_5O, or C_4H_9 100%); and 55 (C_4H_7 or C_3H_3O).
2. Mass spectral fragmentation of 2-Chlorocyclohexanol (**4**, r. t. = min, 0.6%); M^+ = 134 [^{35}Cl; (136: ^{37}Cl)]; 116 (M—H_2O); 98 (M—HCl); 88 (116-C_2H_4); 83 (98-CH_3); 80 (98-H_2O); 62 (C_2H_3Cl); 57 (C_4H_7 or C_3H_5O, 100%); and 55 (C_4H_7).
3. Mass spectral fragmentation of 2-Trifluoromethylthiocyclohexanol (**5**, r. t. = min, 36.3%); M^+ = 200; 180 (M—HF); 154 ($C_5H_5F_3S$); 131 (M—CF_3); 113 (131-H_2O); 101 (SCF_3); 98 (M—$HSCF_3$); 85 (113-C_2H_4), 81 (C_5H_5O or 98-OH); 69 (CF_3); 57 (C_3H_5O or C_4H_9, 100%); 55 (C_4H_7); and 45 (CSH).
4. Mass spectral fragmentation of Cyclopentanecarboxylaldehyde (**6**, r. t. = min, 0.3%); M^+ = 98.
5. Mass spectral fragmentation of Bis-1, 2-Trifluoromethylthiocyclohexane (**7**, r. t. = min, 0.3%); M^+ = 300.
6. Mass spectral fragmentation of 1-(Trifluoromethylthio)-2-butanol (**13**, r. t. = 1.02 min, 72.9%); M^+ = 174; 141 (M—H_2O—C_2H_4); 125 (C_3F_3S); 115 (CF_3SCH_2); 101 (SCF_3); 87 (C_4H_7S); 82 (CSF_2); 69 (CF_3); 63 (CSF); 59 (C_2H_3S, 100%); 55 (C_4H_7); 50 (CSF_2); and 45 (CSH).
7. Mass spectral fragmentation of 2-(Trifluoromethylthio)-butanol (**14**, r. t. = 1.08 min, 13.0%); M^+ = 174; 143 (M—CH_2OH); 115 (CH_2SCF_3 or 143-C_2H_4); 105 (M—CF_3); 91 (105-CH_2, 100%); 87 (105-H_2O); 75 (C_3H_7S); 61 (75-CH_2); 58 (C_3H_6O); 55 (C_4H_7); 51 (SF); and 45 (CSH).
8. Mass spectral fragmentation of bis-1, 1-(Trifluoromethylthio)butane (**18**, r. t. = 3.11 min, 0.8%); M^+ = 258 (not seen); 244 (M—CH_2); 115 (CH_2SCF_3); 101 (SCF_3); 87 (C_4H_3S); 71 (87-CH_2); 59 (C_2H_3S); 57 (C_2HS); 56 (C_4H_8); 55 (C_4H_7, 100%); and 45 (CSH).
9. Mass spectral fragmentation of 1-(Trifluoromethylthio)butane (**19**, r. t. = 1.50 min, 2.5 %); M^+ = 158 (not seen); 144 (M—CH_2); 115 (CH_2SCF_3); 101 (SCF_3); 87 (C_4H_7S); 71 (87-CH_2); 57 (M—SCF_3); 56 (C_4H_8); 55 (C_4H_7, 100%); and 45 (CSH).
10. Mass spectral fragmentation of bis-1, 3-(Trifluoromethylthio)-2-propanol (**25**, r. t. = 2.03 min, 19.8%); M^+ = 260 (100%); 242 (M—H_2O); 191 (M—CF_3); 173 ($C_4H_4F_3S_2$); 158 (M—$HSCF_3$); 144 ($C_3H_3F_3OS$); and 126 (144-H_2O).
11. Mass spectral fragmentation of bis-2, 3-(Trifluoromethylthio)bromopropane (**26***, r. t. = 2.2 min,%); M^+ = 322; 242 (M—HBr); 180 ($BrSCF_3$, ^{81}Br also seen); 141 ($C_4H_4F_3S$); 125 (C_2SCF_3); 115 0(CH_2SCF_3); 73 (C_3H_5S); 69 (CF_3); 59 (C_2H_3S, 100%); 47 (SCH_3); and 45 (CSH).
12. Mass spectral fragmentation of 3 -Bromo-2-(Trifluoromethylthio)propanol (**27***, r. t. = 2.21 min, 57.2 %); M^+ = 238 (^{81}Br also seen); 219 (M—F); 158 (M—HBr); 145 (M—CH_2Br); 123 (M—CH_2SCF_3, 100%); 116 (CH_3SCF_3); 107 ($BrCH_2CH_2$); 101 (SCF_3); 93 (CH_2Br); 82 (CSF_2); 69 (CF_3); 63 (CSF); 59 (C_2H_3S); 47 (SCH_3); and 45 (CSH).
13. Mass spectral fragmentation of Bis-1, 3–(Trifluoromethylthio)propene (**28**, r. t. = 8.58 min, 11.3%); M^+ = 242; 204 (M—2F); 173 (M—CF_3); 141 (M—SCF_3); 115 (CH_2SCF_3, 100%); 69 (CF_3); 63 (CSF); 59 (C_2H_3S); and 45 (CSH).
14. Mass spectral fragmentation of Bis-2, 3-(Trifluoromethylthio)propanol (**29**, r. t. = 3.05 min, 2.9%); M = 260 (not seen); 243 (M—OH); 173 ($C_4H_4F_3S_2$); 159 (M—SCF_3); 141 ($C_4H_4F_3S$); 115 (CH_2SCF_3, 100%); 69 (CF_3); 63 (CSF); 59 (C_2H_3S); and 45 (CSH).

(Continued on next page)

TABLE I Mass Spectral Fragmentation of Compounds Cited in the Narrative (Continued)

15. Mass spectral fragmentation of [(3-(Trifluoromethylthio)propyl)(3-hydroxypropyl)-ether (**30**, r. t. = 5.23 min, 3.1%); $M^+ = 218$; 174 (M—C_2H_4O); 141 ($C_4H_4F_3S$); 115 (CH_2SCF_3); 105 (174-CF_3); 82 (CSF_2); 75 ($C_3H_7O_2$); 73 (C_3H_5S); 69 (CF_3); 59 (C_2H_3S); and 45 (CSH, 100%).
16. 2-(Trifluoromethylthio)-3-norborneol (**50**, r. t. = 8.03 min, 3.1%); $M^+ = 212$; 194 (M—H_2O); 166 (194-C_2H_4); 143 (M—CF_3); 125 (143-H_2O); (110 (M—$HSCF_3$, 100%); 93 (110-OH); 81 (C_2H_7); 69 (CF_3); 67 (C_5H_7); 55 (C_4H_7); and 45 (CSH).
17. N-(epoxypropyl)phthalimide (**66**, r. t. = 11.08 min, 85.0%); $M^+ = 203$ (204; MS-CI-mode); 185 (M—H_2O); 174 (M—CHO); 160 (M—C_2H_3O, 100%); 146 [$C_6H_4(CO)_2N$]; 133 [$C_6H_4(C_2HO_2)$]; 117 (133-O); 104 M—CNO-C_3H_5O); 90 [C_6H_4N]; 76 (C_6H_4); 56 (C_3H_4O); and 50 (C_4H_2).
18. N-(3-hydroxy-2-fluoropropyl)phthalimide (**67**, r. t. = 15.20 min, 1.4%); $M^+ = 22.3$ (not seen in EI-mode, 224; MS-CI-mode); 203 (M—HF); 190 (M—CH_2F); 172 (190-H_2O); 160 (M—C_2H_4FO, 100% 133 (160-HCN); 117 (133-O); 104 (C_7H_4O); 77 (C_6H_5); and 50 (C_4H_2).
19. N-(2-hydroxy-3-trifluoromethylthiopropyl)phthalimide (**69A**, r. t. = 17.05 min, 9.3%); $M^+ = 305$ (not seen in EI-mode; 306, MS-CI-mode); 287 (M—H_2O); 218 (287-CF_3); 204 (M—SCF_3); 190 (M—CH_2SCF_3, 100%); 160 (M—$C_2H_4O.SCF_3$); 133 (160-HCN); 117 (133-O); 104 (C_7H_4O); 82 (CSF_2); 77 (C_6H_5); 69 (CF_3); 59 (C_2H_3S); and 50 (CF_2).
20. N-(2-hydroxy-3-trifluoromethylthiopropyl)phthalimide (**69B**, r. t. = 17.21 min, 1.2%); $M^+ = 305$ (not seen in EI-mode; 306, MS-CI-mode); 190 (M—CH_2SCF_3, 100%); 172 (190-H_2O); 160 (M—$C_2H_4O.SCF_3$); 133 (160-HCN); 104 (C_7H_4O); 90 (C_6H_4N); 76 (C_6H_4); and 50 (CF_2).
21. N-(3-hydroxy-2-trifluoromethylthiopropyl)phthalimide (**68**, r. t. = 17.26 min, 2.6%); $M^+ = 305$ (not seen in EI-mode; 306, MS-CI-mode); 204 (M—SCF_3); 190 (M—CH_2SCF_3); 160 (M—$C_2H_4OSCF_3$); 117 [$CH_3S^+(H)SCF_3$, 100%]; 105 (C_7H_5O); 101 (SCF_3); 89 (C_3H_5OS); 76 (C_6H_4); 59 (C_2H_3S); and 50 (CF_2).

*Ellute close together and could not be separated; combined yields 19.8%.

Cyclopentane aldehyde (**6**) arises from a simple epoxide–carbonyl rearrangement. There are precedents for such rearrangements.[7f,16d] The mass spectrum of **6** has been reported.[16e] Acyclic oxiranes on treatment with organocuprates yield allylic alcohols and carbonyl compounds.[16d,h,f,g]

Reaction 2: Reaction of 1, 2-Epoxybutane (12) with Trifluoromethylthiocopper (2)[13]

With a view to examine the regiospecificity of the terminal oxirane ring opening with trifluoromethylthiocopper (**2**), a stoichiometric mixture of 1, 2-butene oxide (**12**) and trifluoromethylthiocopper (**2**) in dry toluene was heated at 100–110°C for 14 h. The processing of the reaction mixture indicated the presence of seven compounds. The two

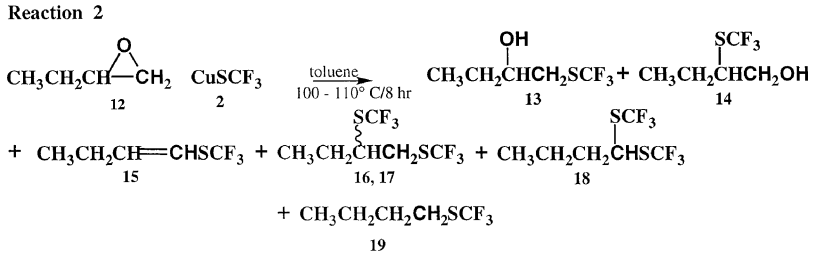

FIGURE 4 Reaction of 1, 2-epoxybutane.

major components were identified as 1-trifluoromethylthio-2-butanol (**13**, 72.9%) and 2-trifluoro-methylthiobutanol (**14**, 13.0%), respectively. The third compound was characterized as 1-tri-fluoromethylthio-1-butene (**15**, 5.0%) (Figure 4). Among the four additional minor components present in the reaction product are three isomers with the same molecular weight ($M^+ = 268$), occurring in 2.0–2.5% yields. They split off the F_3CS moiety to give the peak corresponding to m/e = 157 in their mass spectra. These compounds have been identified as bis-1, 2-trifluoromethylthiobutanes (isomers, **16** and **17**) and bis-1, 1-(trifluoromethylthio)butane (**18**). The remaining compound present in trace amounts was identified as 1-(trifluoromethylthio)-butane (**19**).

The reaction of 1, 2-epoxybutane (**12**) with F_3CSCu (**2**) gives products arising from various reactions such as dehydration, migration of neighboring hydrogen, etc. There is nothing unusual about their formation. The two major compounds arise from the attack of the thiyl radical on C_1- and C_2-carbons, while the third results from the dehydration of one of the two compounds. Thus, the attack on the C_1-carbon of the substrate gives intermediate **20**, which simply absorbs hydrogen and forms 1-trifluoromethylthio-2-butanol (**13**) (Figure 5). On the other hand, if the attack takes place at the C_2-carbon, then it would lead to the intermediate **21**, which then can be expected to form 2-trifluoromethylthio-1-butanol (**14**) via hydrogen abstraction. Indeed, this is what was seen. Finally, the elimination of H_2O from **13** furnishes 1-trifluoromethylthio-1-butene (**15**).

The loss of the hydroxyl radical from **13**, (Figure 5), leads to the intermediate **22**, which has two options available to it. Firstly, it reacts with the thiyl ($F_3CS^{\bullet}$) radical to yield a pair of isomeric compounds, **16** and **17**. Secondly, the C_1-hydrogen from the intermediate **22** migrates to the C_2 position to form the radical **23**, which joins with the thiyl radical to furnish compound **18**. Finally, compound **19** can be rationalized to arise from the same intermediate, namely **23**, via hydrogen abstraction.

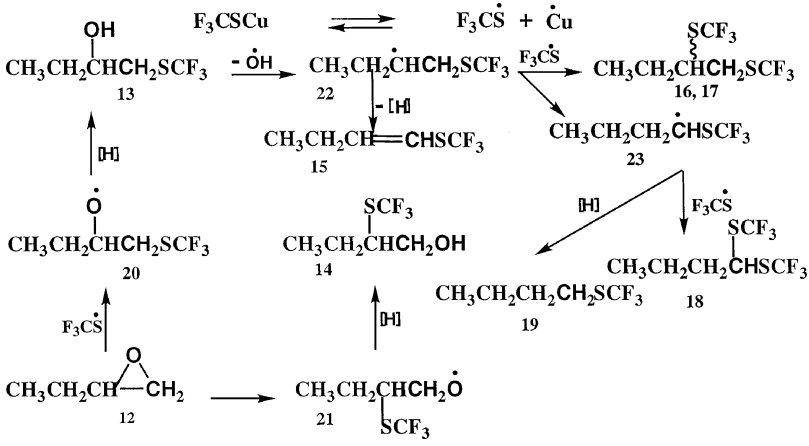

FIGURE 5 Mechanism of formation of compounds from 1, 2-epoxybutane.

Reaction 3: Reaction of Epibromohydrin (3-Bromo-1, 2-epoxypropane) (24) with Trifluoromethylthiocopper (2)[13]

This reaction was carried out in a manner analogous to that described above except that 1, 2-butene oxide (**12**) was replaced with 1-bromo-2, 3-epoxypropane or epibromohydrin (**24**). Compound **24** has three potential sites of reaction, namely the bromine and the two carbon atoms of the oxirane ring. In principle, the free radicals should be able to attack all three sites. Though this seems to be a somewhat complicated process, this is what was indeed observed. Thus, the GC -MS (gas chromatographic-mass spectral) analysis of the reaction mixture permitted the characterization of the six compounds (Figure 6): (1) Bis-1, 3-(trifluoromethylthio)-2-propanol (**25**); (2) Bis-2, 3-(trifluoromethylthio)-1-bromopropane (**26**); (3) 2-(trifluormethylthio)-

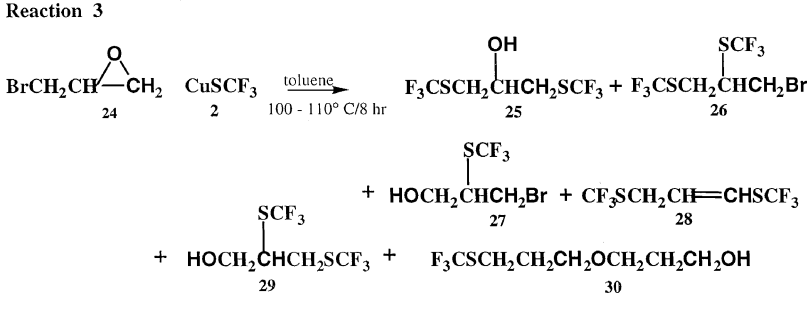

FIGURE 6 Reaction of epibromohydrin.

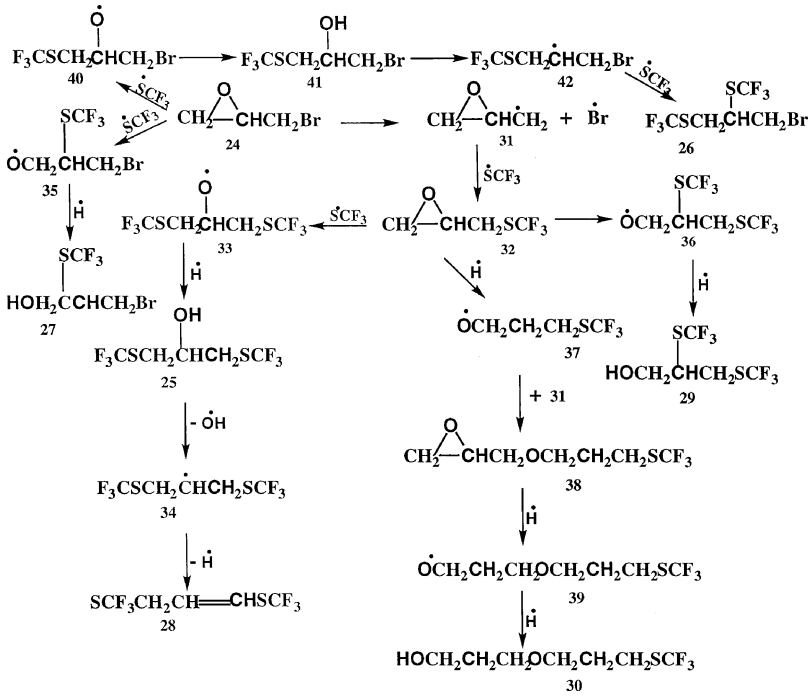

FIGURE 7 Compounds formed from epibromohydrin.

3-bromopropanol (**27**); (4) Bis-1, 3-(trifluoro-methylthio)-1-propene (**28**); (5) Bis-2, 3-(trifluoromethylthio)-1-propanol (**29**); and (6) [3-(trifluoromethylthio)propyl]-[(3-hydroxypropyl)] ether (**30**) (cf. Figure 6).

Figure 7 endeavors to rationalize the formation of the six compounds, **25–30**. The splitting up of $Br^{\cdot}$ from **24** results in the intermediate **31**, which reacts with the $F_3CS^{\cdot}$ to form intermediate **32**. A second attack by the same radical on **32** followed by hydrogen abstraction leads to bis-1, 3-(trifluoromethylthio)-2-propanol (**25**) via **33**. Compound **25** undergoes dehydration and furnishes bis-1, 3-(trifluoromethylthio)propene (**28**) via **34**. If the attack occurs at the C_2-carbon of **24**, then that would lead to the intermediate radical **35**, which after hydrogen abstraction yields compound **27**. The intermediate **32**, in addition to serving as the source of compounds **25** and **28**, has two more pathways open to it. Attack by the $F_3CS^{\cdot}$ on C_2-carbon gives radical **36**, which goes on to abstract hydrogen and to yield compound **29**. Instead, when the C_2-carbon of **32** gets attacked by $H^{\cdot}$ it would result in the intermediate **37**, which combines with **31** to give **38**.

Just as in the case of **32**, the oxirane ring of **38** becomes cleaved by hydrogen to yield **39**, which then abstracts hydrogen and forms [3-(trifluoromethylthio)propyl]-[(3-hydroxypropyl)] ether (**30**). The attack by the $F_3CS^{\cdot}$ radical on the C_1-carbon of **24** gives **40**, which forms **41** after hydrogen abstraction, and **41** in turn splits off hydroxyl radical to form radical **42**. The latter subsequently joins with the $F_3CS^{\cdot}$ to furnish bis-2, 3-(trifluoromethylthio)-1-bromopropane (**26**) (cf. Figure 7).

Reaction 4: Reaction of Exo-Epoxynorbornane (43) with Trifluoromethylthiocopper (2)[13]

To examine whether the oxirane ring attached to a sterically hindered and somewhat rigid system such as the bicyclo[2.2.1]heptane would behave analogously as the acyclic and cyclic oxiranes do under similar experimental conditions, exo-epoxynorbornane (**43**) was reacted with trifluoromethylthiocopper (**2**) and found to furnish (1) norboranone (**44**), (2) 3-cyclohexenyl aldehyde (**45**), and (3) 2-(trifluoromethylthio)-1-norborneol (**46**; Figure 8).

The reaction of norbornene oxide with $CuSCF_3$ furnishes four compounds: (1) the substrate (**43**, $M^+ = 110$, r.t. = 3.44 min, 90.1%), (2) 3-cyclohexene aldehyde (**45**, $M^+ = 110$, r.t. = 4.20 min, 4.8%), (4) norbornanone, (**44**, $M^+ = 110$, r.t. = 4.07 min, 2.1%), and (4) 3-(trifluoromethylthio)-2-norbornanol (**46**, $M^+ = 212$, r.t. = 8.3 min, 3.1%). In principle the epoxide **43** can open to form the radical intermediates **47** and **48** on reacting with the thiyl radical, and then upon hydrogen abstraction would lead to either of the two compounds, or both compounds, **46** and **49.** Since only one compound containing the F_3CS-group is present, it is reasonable to assume that this compound must have been formed from the reaction of exo-epoxynorbornane (**43**) with trifluoromethylthiocopper (**2**). Its formation can be explained via the opening of the oxirane ring by the thiyl radical to form the intermediate **47**. For steric reasons, the attack appears to occur from below to form the said intermediate. The latter then abstracts hydrogen to give compound **46**. It is conceivable that the alternate mode of oxirane ring opening would result in compound **49** via **48**. The formation of 3-cyclohexene carboxaldehyde (**45**), and norbornanone (**44**)

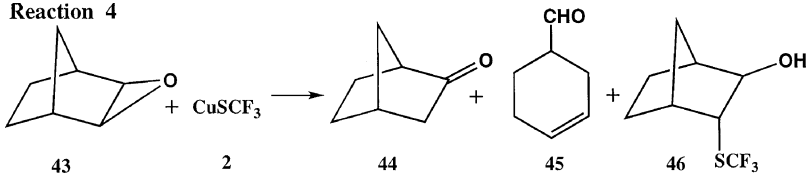

FIGURE 8 Reaction of exo-epoxynorbornane.

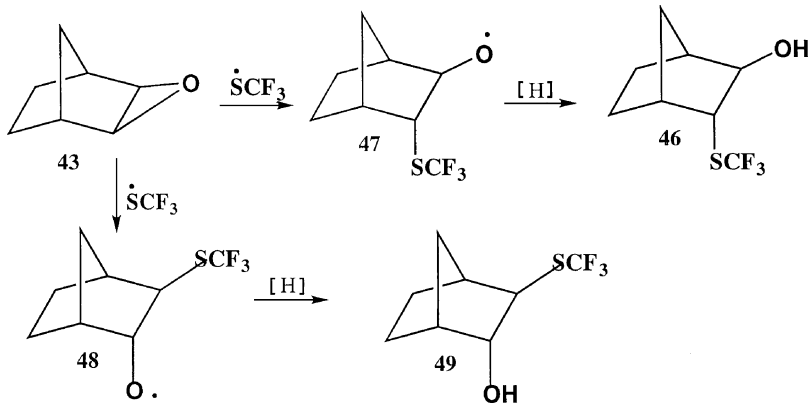

FIGURE 9 Formation of products from exo-epoxynorbornane.

can be attributed to the rearrangement of the substrate on the G.C. column.[17a–b] The mass spectra of expoxynorbornane (**43**), 3-cyclohexene aldehyde (**45**), and norbornanone (**44**) have been described.[17a]

Sulfenyl chlorides (R_aSCl) are known add to the carbon–carbon multiple bonds, and the product formation is usually ascribed to the participation of the cyclic sulfonium ion intermediates.[18] It was considered interesting to compare the results of the above reaction with the results of the same substrate (**43**) with trifluoromethylsulfenyl chloride (**50**). Accordingly, this reaction was carried out using dry pentane as a solvent at $-80^{\circ}C$. The processing of the reaction product showed the presence of 16 compounds (**45** and **51**–**66**). Of the 16 compounds, 7 compounds (**53**–**59**) are derived from the solvent, namely pentane via free-radical reactions; two (**51** and **52**) are formed from trifluoromethylsulfenyl chloride (**50**) itself, while compounds **60**–**65** and **45** have their origin in epoxy-norbornane **43** (Figure 10). The formation of these compounds has been rationalized and explained using free-radical reaction processes.[19]

Reaction 5: Reaction of Phthalimide-N-2, 3-Propylene Oxide (66) with Trifluoromethylthiocopper (2)[20]

With the expectation of synthesizing amines containing the trifluoromethylthio function, the reaction of phthalimide-N-(2, 3-propylene oxide) (**66**) with trifluoromethylthiocopper (**2**) was explored and found to furnish five compounds (Figure 11), namely (1) phthalimide-N-2-fluoro-3-propanol (**67**), (2) phthalimide-N-2-trifluoromethylthio-3-propanol (**68**), (3) isomers phthalimide-N-3-trifluoromethylthio-2-propanol (**69A** and **69B**), and (4) an as-yet unidentified compound.

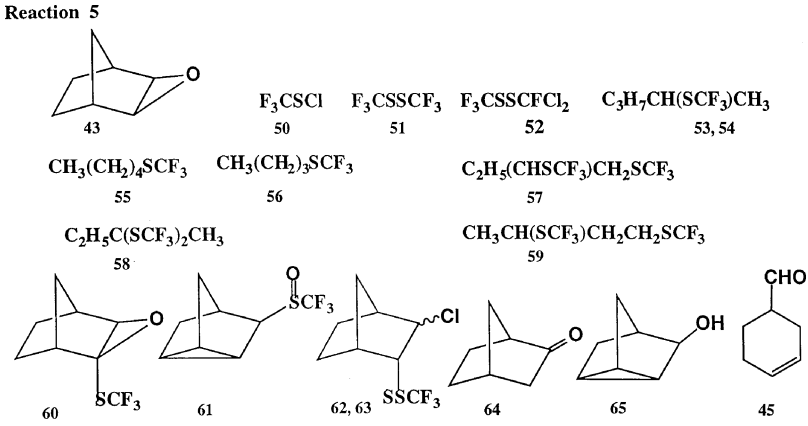

FIGURE 10 Reaction of epoxynorbornane with trifluoromethylsulfenyl chloride.

The abovementioned compounds arise from the free-radical reactions, and their formation follows the expected pathway (cf. Figure 12). The unidentified compound also has the phthalimide moiety.

To begin with, trifluoromethylthiocopper (**2**) fragments form the thiyl radical, which then dissociates to give thiocarbonyl difluoride and fluorine radical. The latter then goes on to react with the diradical (**70**) formed from the substrate to yield the intermediate (**71**), which in turn abstracts hydrogen to give compound **67**. In a similar manner, compounds **68** and **69** arise from the initial attack by the thiyl radical and via the intermediates **72** and **74**, respectively (Figure 12). The implied diradical formation from the epoxide entity has been suggested previously.[14f]

The mass spectral breakdown of the phthalimide derivatives has been discussed.[21a] The mass spectrum of phthalimide-N-2, 3-propylene oxide has been reported.[21b] Cyclic amides have been stated to lose CO_2

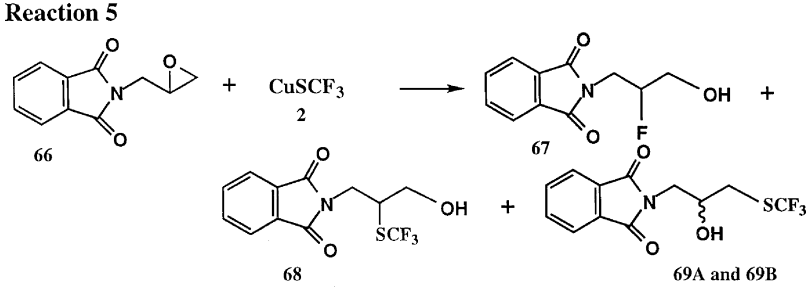

FIGURE 11 Reaction of phthalimide-N-propylene oxide.

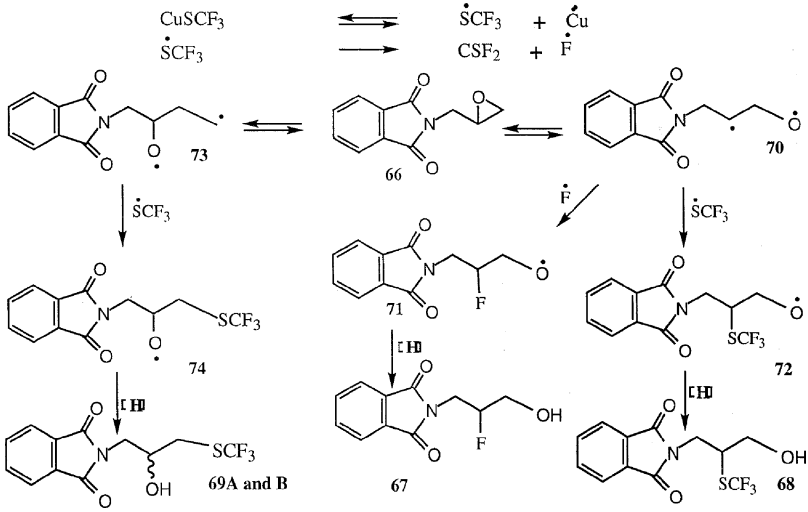

FIGURE 12 Products from phthalimide-N-(2, 3-propylene oxide).

via skeletal rearrangement, and the migration of hydrogen attached to nitrogen has been observed.[21a] The compounds cited above follow a similar mass spectral breakdown behavior, and the presence of the phthalimide entity bereft of the side chain is seen in their mass spectra.

EXPERIMENTAL

Mass spectra were obtained using a Finnigan TSQ-7000 GC/MS/MS equipped with a 30 m × 0.25 mm. i.d. DB-5 capillary column (J and W Scientific, Folsom, CA, USA) or a Finnigan 5100 GC/MS equipped with a 15 m × 0.25 mm i.d. Rtx-5 capillary column (Restek, Bellefonte, PA, USA). The conditions on 5100 were: oven temperature 60–270°C at 10°C/min, injection temperature was 210°C, interface temperature 230°C, electron energy 70 eV, emission current 500 μA, and scan time 1 s. The conditions on the TSQ-7000 were: oven temperature 60–270°C at 15°C/min, injection temperature 220°C, interface temperature 250°C, source temperature 150°C, electron energy 70 eV (EI) or 200 eV (CI), emission current 400 μA (EI) or 300 μA (CI), and scan time 0.7 s. Data was obtained in both the electron ionization mode (range 45–450 da) and chemical ionization mode (mass range 60–450 da). Ultrahigh purity methane was used as the CI agent gas with a source pressure of 0.5 Torr (5100) or 4 Torr (TSQ-7100). Routine GC analyses were accomplished with a Hewlett-Packard 5890A gas chromatograph equipped

with a J and W Scientific 30 m × 0.53 mm i.d. DB-5 column (J and W Scientific, Folsom, CA, USA). Stoichiometric amounts of the respective reagents were mixed in glass vials, vigorously shaken on a vibro-mixer and heated in the microwave oven for a specified period. The reaction mixture was allowed to come to ambient temperature. The cooled product was first analyzed by gas chromatography and then subjected to GC-MS analysis. The $CuSCF_3$ used in this work was prepared as described by us elsewhere.[22]

General Procedure

Stoichiometric amounts of the respective epoxide and $CuSCF_3$ (**2**) were mixed in a freshly distilled solvent (preferably acetonitrile or toluene), and the mixture was gently refluxed overnight. The reaction mixture was cooled to ambient temperature, filtered over celite, and solvent was evaporated under reduced pressure. The residue was first analyzed using GC and then with GC-MS, as described above. The mass spectral breakdown patterns of the various compounds cited in the text are given in Table I.

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