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Trifluoromethylthiocopper-mediated oxirane ring opening

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Abstract

The reaction of styrene oxide with trifluoromethylthiocopper furnishes seven compounds; all arising from the free radical cleavage of the oxirane ring. The mechanism of the formation and mass spectral characterization of the various products are described in this communication. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: Free radical oxirane ring cleavage; Styrene oxide; Trifluoromethylthiocopper

1. Introduction

Because of their ready availability and exceptional reactivity, epoxides have attracted considerable attention and interest as an extremely versatile group in synthetic organic chemistry. The oxirane ring can be opened under almost all reaction conditions; electrophilic, nucleophilic, neutral, gas-phase, thermal and photochemical conditions (Fig. 1) [1a]. Intra- and intermolecular nucleophilic ring opening of epoxides, reduction to alcohols and deoxygenation to alkenes have all been discussed [1]. An excellent review on preparation and synthetic applications of oxiranes has also appeared [1h]. Chemoselective cleavage of the epoxides with metal halides has been the subject of a recent review [1i]. Of the oxiranes commonly used in the study of the regio- and stereoselective opening of the epoxide ring, styrene oxide (**1**) appears to be one of the most popular substrates. This, in part, may be due to its stereoelectronic effects. In continuation of our current interest in the synthesis of compounds containing the trifluoromethylthio function via the cleavage of the oxirane ring [2a], the reaction of trifluoromethylthiocopper (**2**) with styrene oxide (**1**) has been examined and found to furnish seven compounds. The mechanism of the formation of the seven compounds and their mass spectral characterization are presented in this paper.

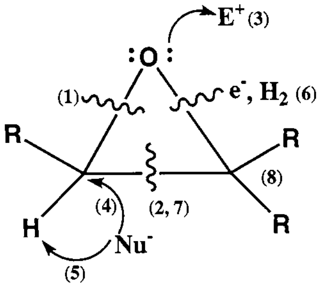

Fig. 1. Types of oxirane cleavages and reactions
(1, 2) Ring homolytic cleavage (thermal, photolysis, free radical).
(3) Electrophilic attack on ring oxygen.
(4) Nucleophilic attack on ring carbon.
(5) Nucleophilic attack on ring hydrogen.
(6) Reactions with electrons and surface reactions.
(7) Cycloadditions.
(8) Reactions of a substituent.

2. Results and discussion

Organometallic reagents are said to attack styrene oxide (**1**) either at the more electrophilic carbon of the epoxide or the more easily accessible site [3]. Sometimes, the epoxides undergo rearrangement to carbonyl intermediates, which become susceptible to further nucleophilic attack to form alcohols. In the presence of Lewis acids, the more highly substituted carbon is

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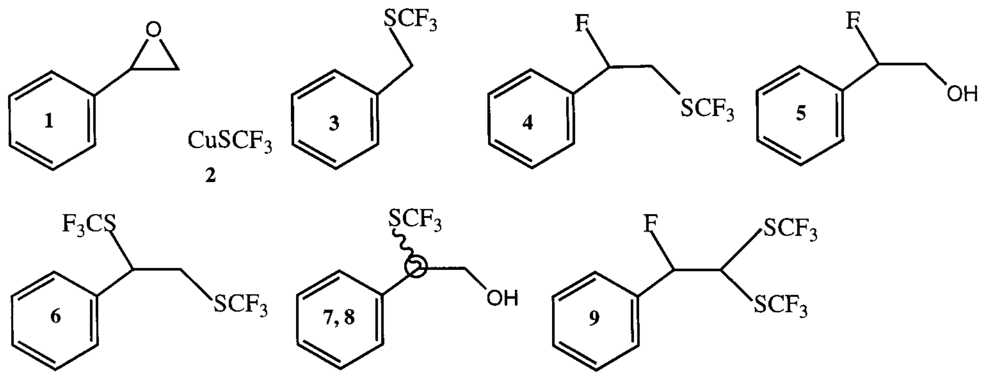


Fig. 2.

attacked [4a–b]. With mixed lithiocopper halides, **1** yields 2-halo-2-phenylethanol as the primary product [4c–d]. A complete reversal of the regioselectivity was observed when **1** was treated with dilithiotetra-bromonickelate in THF [4e]. With NaI it reacted regioselectively to give 1-phenylethanol and 2-phenylethanol in a 6:1 ratio in the presence of Bu_3SnH [5]. However, with lithium halides and AcOH in THF 2-halo-2-phenylethanol and 2-halo-1-phenylethanol were identified as major and minor products [6]. A similar regioselectivity was reported with KHF_2–Bu_4NF–HF at 120° [6b]. When Amberlyst was substituted for AcOH in the above reaction, a slightly enhanced regioselectivity was noticed [6c]. Silica-supported lithium halides react with **1** to give various amounts of isomeric alcohols depending on the nature of the halides [6d]. Complete regio- and stereoselectivity was observed in the reaction of **1** with trimethylsilyl chloride and NaBr and/or Me_2BBr in Et_3N [7]. Styrene oxide (**1**) reacts with alkyl- and arylthiotrialkylsilanes, which represent 'a powerful combination of oxygenophiles and strong nucleophiles', under mild conditions in aprotic solvents and in the presence of mild Lewis acid catalysts to yield 2-phenyl-2-phentylthioethanol and 1-phenyl-2-phenylthioethanol [7c]. Although silicon is stated to initially form a bond with oxygen of the oxirane ring, nothing is said of the role of the Lewis acid in the overall reaction. However, this regioselectivity is reversed in the presence of a base.

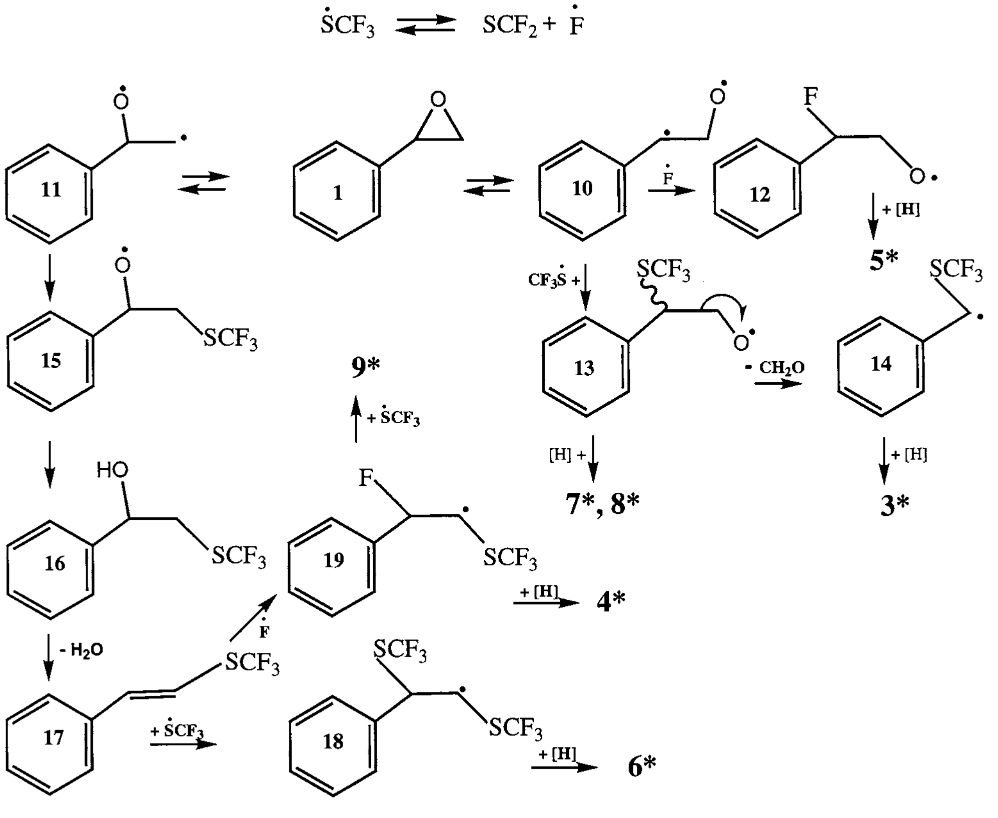
The reaction of SiF_4 with **1** in the presence of $(i\text{-}Pr)_2NH$ is said to be highly regio-, stereo- and chemoselective and primarily yields, via the attack at the more substituted carbon, 2-fluoro-2-phenylethanol (**5**, Fig. 2 [8a]), which was also obtained when **1** was treated with KH_2F_3 [8b]. It is interesting to note that the reaction of **1** with $(Et)_2NSF_3$ gives 2-phenyl-1,1-difluoroethane, *cis*-β-fluorostyrene plus two more fluorine containing compounds [8c].

In continuation of our interest in the chemistry of the F_3CS group [2b–g], the oxirane ring cleavage of styrene oxide (**1**) with F_3CSCu (**2**) was investigated and found to furnish seven compounds arising from C–C and C–O bond cleavages. All but one does not carry the F_3CS group, while two possess fluorine (Fig. 2). Various mechanisms such as a four-centered transition state [9a], non-involvement of carbonium ions [7c], the exclusion of the radical mechanism [9b], ion pair-like and carbonium ion intermediates [9c], have been proposed to rationalize products formed from the oxirane ring opening reactions. In the reaction of **1** with $Ce(IV)Cl_4$, the presence of the alkoxy radical intermediates has been said to cause polymerization of polyacrylamide gel [9c]. In another case, the use of free radical precursors, namely Bu_3SnH and AIBN, dictated the nature of the reaction and nothing unusual about the products of their reaction [5]. Although gas-phase and photochemical reactions of oxiranes have been reported [10a–b], to the best of our knowledge only a few non-photochemically induced free radical reactions of oxiranes have been cited in the literature. Photolysis of ethylene oxide gives 'a plethora of products' and the primary process produces both 'reactive' and normal ethylene, methyl radicals, formaldehyde, ethane, propane, butane, etc. [10c]. Although the initial photochemical process appears to be the formation of biradical intermediates, **10** and **11** (cf. Scheme 1) arising from the cleavage of the C–O bond, the authors also report the C–C bond fission [10d–e].

To begin with, the C–O bond of styrene oxide (**1**) cleaves to form biradicals **10** and **11** (Scheme 1); intermediate **10** reacts with the F radical formed from the dissociation of F_3CS radical to give intermediate **12**, which in turn abstracts hydrogen and yields 2-fluoro-2-phenylethanol (**5**). The proposed dissociation of $F_3CS^\bullet$ has precedents [11]. The intermediate **10** leads to a racemic mixture of alcohols, **7** and **8** via intermediate **13**, followed by hydrogen abstraction. Compounds **7** and **8**, can undergo β-fragmentation to give the benzylic radical **14**, which on hydrogen abstraction yields benzyl trifluoromethyl sulfide (**3**). The driving force for such a secondary homolysis to split off formaldehyde comes from the loss of a neutral entity. The preferential cleavage of the relatively stronger C–C bond as opposed to the weaker C–S bond has been attributed to the 'polar effects of sulfur' [12]. Such a fragmentation of CH_2O during the photolysis of oxirane has been documented [10c]. Similarly, the formation of compounds **4**, **6** and **9** can be attributed to the presence of the biradical intermediate **11** and to proceed via intermediates **15**, **16**, **17**, **18** and **19**. The suggested loss of H_2O from compounds similar to **16** has been reported [12]. The synthesis of compound **5** has been described [8]. Thus, the proposed free radical mechanism for the reaction of styrene oxide (**1**) with F_3CSCu (**2**) nicely accommodates the formation of compounds **3**–**9**, which have been characterized by their mass spectral fragmentation behavior (Table 1). The mass spectrum of **1** has been described [14a]. The mass spectral behavior of compounds **7**, **8** and **9** is briefly discussed below. Compound **7** shows M^+ while the ion due to $M - H_2O$ is relatively small. The most abundant ion in its spectrum arises from the loss of the CH_2OH fragment from the side-chain. The second most intense peak is due to the loss of F_3CS from the M^+. Two additional peaks at $m/e = 91$ and 77 are of diagnostic value. Compound **8** exhibits a similar mass spectral breakdown behavior. Their mass spectra have ions corresponding to $m/e =$ 79, 78 and 77 representing C_6H_7, C_6H_6 and C_6H_5. Such patterns are typical of alkylbenzenes [14b–c]. The mass spectral fragmentation of compound **9** is somewhat interesting. Though the M^+ was not seen, its structure was deduced from the presence of three peaks, namely (a) $m/e = 135$ ($C_6H_5C_2H_2S$); (b) $m/e = 115$ (CH_2SCF_3) and (c) $m/e = 107$ (C_2FS_2). These ions suggest that the two F_3CS groups are on the terminal carbon while F is on the β-carbon. The structures proposed for the various compounds derive additional support from the fragmentation behavior of various benzylic derivatives [14b–d].

3. Experimental

Trifluoromethylthiocopper (**2**) was prepared as described elsewhere [13]. All solvents were dry and freshly distilled prior to use. 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) or a Finnigan 5100 GC–MS equipped with a 15 m × 0.25 mm i.d. Rtx-5 capillary column (Restek, Bellefonte, PA). The conditions on 5100 were: oven temperature 60–270°C at 10°C min^{-1}, injection temperature was 210°C, interface temperature 230°C, electron energy 70 eV, emission current 500 μA



*** Compounds characterized**

Scheme 1.

Table 1
Mass spectral fragmentation of compounds

Benzyl trifluoromethyl sulfide (**3**)	$M^+ = 192$, 121 (C_7H_5S); 91 ($M-SCF_3$, 100%); 77 (C_6H_5); 69 (CF_3) and 45 (CSH)
1-Fluoro-1-phenyl-2-(trifluoromethylthio)ethane (**4**)	$M^+ = 224$, 204 ($M-HF$); 165 ($204-HF-F$); 135 ($204-CF_3$); 123 ($M-SCF_3$); 115 (CH_2SCF_3); 109 ($M-CH_2SCF_3$, 100%); 103 ($135-S$); 91 (C_7H_7); 77 (C_6H_5); 69 (CF_3); and 45 (CSH)
2-Fluoro-2-phenylethanol (**5**, 0.5%)	$M^+ = 140$, 122 ($M-H_2O$); 120 ($M-HF$); 109 ($M-CH_2OH$, 100%); 102 ($120-H_2O$); 91 (C_7H_7) and 63 (C_2H_4FO)
1, 2-Bis-(trifluoromethylthio)-1-phenylethane (**6**)	$M^+ = 306$, 205 ($M-SCF_3$); 191 ($M-CH_2SCF_3$, 100%); 185 ($205-HF$); 165 ($185-HF$); 135 (C_8H_7S); 122 (C_7H_6S); 104 ($205-SCF_3$); 91 (C_7H_7); 77 (C_6H_5) and 69 (CF_3)
2-Phenyl-2-(trifluoromethylthio)ethanol (**7**)	$M^+ = 222$, 204 ($M-H_2O$); 191 ($M-CH_2OH$, 100%); 153 ($M-CF_3$); 135 ($153-H_2O$); 121 ($M-SCF_3$); 109 (C_6H_5S); 103 ($121-H_2O$); 91 (C_7H_7); 77 (C_6H_5) and 45 (CSH)
2-Phenyl-2-(trifluoromethylthio)ethanol (**8**)	$M^+ = 222$ (not seen), 205 ($M-OH$); 204 ($M-H_2O$, 97%); 191 ($M-CH_2OH$, 100%); 135 ($204-CF_3$); 121 ($M-SCF_{3,}$ 95%); 103 ($121-H_2O$); 91 (C_7H_7); 77 (C_6H_5); 69 (CF_3) and 45 (CSH)
1-Fluoro-1-phenyl-bis-(2,2-trifluoromethylthio)-ethane (**9**)	$M^+ = 324$ (not seen), 323 ($M-H$); 285 ($M-F$); 253 ($323-CF_3H$); 223 ($M-SCF_3$); 204 ($223-F$); 135 (C_8H_7S); 115 (CH_2SCF_3); 107 (C_2FS_2, 100%); 69 (CF_3) and 45 (CSH)

and scan time 1 s. The conditions on the TSQ-7000 were: oven temperature 60–270°C at 15°C min^{-1}, injection temperature 220°, interface temperature 250°C, source temperature 150°C, electron energy 70 (EI) or 200 eV (CI) and emission current 400 (EI) or 300 μA (CI) and scan time 0.7 s. Data were 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 (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).

Reaction of styrene oxide (**1**) with trifluoromethylthiocopper (**2**): a suspension of styrene oxide (**1**, 0.62 g) and trifluoromethylthiocopper (**2**, 1.8 g) in 10 ml of dry toluene was heated overnight at 100–110°C under an argon atmosphere. The reaction mixture was cooled to room temperature (r.t.), treated with water, extracted with chloroform, the organic layer separated, washed successively with water and a saturated solution of sodium chloride, dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure to give an oily residue. The GC analysis of the residue showed it to be a complex mixture. Careful analysis of the residue by GC–MS showed it to contain seven compounds: (a) benzyl trifluoromethyl sulfide (**3**, $M^+ = 192$, 0.2%, r.t. = 4.5 min); (b) 1-fluoro-1-phenyl-2-(trifluoromethylthio)ethane (**4**, $M^+ = 224$, 5.6%, r.t. = 6.0 min); (c) 2-fluoro-2-phenylethanol (**5**, $M^+ = 140$, 0.5%, r.t. = 6.92 min); (d) 1,2-bis-(trifluoromethylthio)-1-phenylethane (**6**, $M^+ = 306$, 1.7%, r.t. = 7.18 min); (e) 2-phenyl-2-(trifluoromethylthio)ethanol (**7**, $M^+ = 222$, 5.0%, r.t. = 8.83 min); (f) 2-phenyl-2-(trifluoromethylthio)ethanol (**8**, $M^+ = 222$, 0.5%, r.t. = 8.99 min) and (g) 1-fluoro-1-phenyl-bis-(2,2-trifluoromethylthio)ethane (**9**, $M^+ = 324$, 0.7%, 9.23 min).

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