

Novel Synthetic Reactions Using Bis(2,2,2-trifluoroethoxy)diorganosulfuranes

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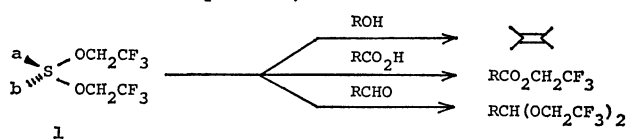
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Alkoxy- or acyloxysulfuranes prepared *in situ* by the ligand exchange of bis(2,2,2-trifluoroethoxy)diorganosulfuranes with alcohols or carboxylic acids were found to behave as a potential alkylating or acylating reagent for the preparation of unsymmetrical sulfides, ketones, and esters.

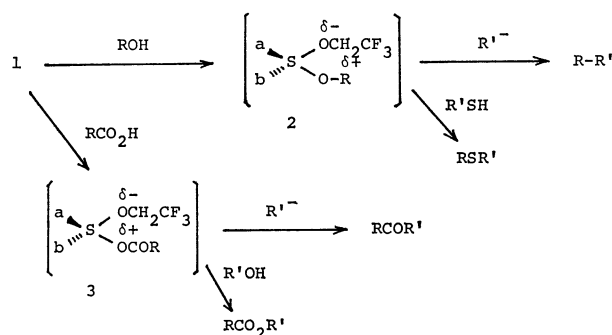
Many studies have been made on the use of sulfuranes^{1–18}) but only a very few report on their application to organic synthesis, *viz.*, sulfilimines,^{7,8,16}) epoxides,⁶) and olefins.^{6,18})

Recently we reported the preparation of bis(2,2,2-trifluoroethoxy)diorganosulfuranes (**1**) in CH₂Cl₂–Et₂O system, and its reactions with alcohols, aldehydes, and carboxylic acids, affording olefins, 2,2,2-trifluoroethylated acetals, respectively.¹)



1A (a=b=Ph), 1B (a=Me, b=Ph)

The rapid ligand exchange of one of 2,2,2-trifluoroethoxyl groups of **1** with alcohol or carboxylic acid, giving (2,2,2-trifluoroethoxy)(alkoxy)diorganosulfurane (**2**) or (2,2,2-trifluoroethoxy)(acyloxy)diorganosulfurane (**3**) which affords a positive alkyl or acyl group, has a marked effect on the use of sulfuranes in organic synthesis.



In a continuation of our research on the reactivity of **1**, we report on the formation of unsymmetrical sulfides, ketones, and esters.

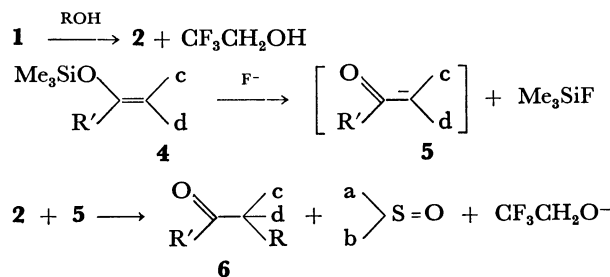
Results and Discussion

Extensive investigations have been carried out on carbon–carbon bond formation, but only a few reports have appeared on C-alkylation by alcohols.^{19–22})

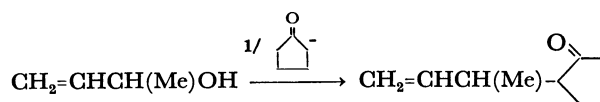
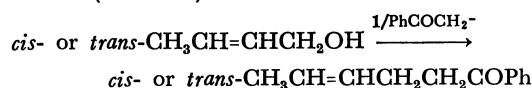
We postulated the presence of (2,2,2-trifluoroethoxy)-(alkoxy)diorganosulfurane (**2**) with a positive alkyl group,¹) and have attempted to establish the carbon chain lengthening using **2**.

The reaction between **2** and Grignard or organolithium reagents was carried out first. However, 2,2,2-trifluoroethyl alcohol released in these systems reacts readily with magnesium or organolithium reagents, and the yields of the expected products were poor.

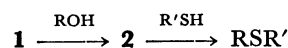
In contrast, an enolate anion, **5**, generated from trimethylsilyl ether–potassium fluoride system^{23–27}) readily attacked a positive carbon atom in alkoxy-sulfurane **2** to form a C–C bond compound (**6**).



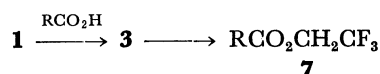
The results showing that no reaction occurs without an alcohol, olefins being obtained from alcohols in the absence of potassium fluoride, support the mechanism in which the ligand exchange of one of 2,2,2-trifluoroethoxyl groups for an alkoxy group takes place first, the resulting **2** affording a positive alkyl group. A fluoride ion from potassium fluoride would aid formation of the carbanion (**5**) from the silyl enol ether (**3**), and the carbanion would attack the positive carbon atom of **2** to give a product **6**. The procedure seems to be effective for regioselective C–C coupling together with retention of configuration. No allylic rearrangement was observed in the reaction with allyl alcohols (Table 1).



Synthetic application of **1** has been examined as regards the conversion of alcohols into sulfides.^{28–30}) The high dehydrating ability of the sulfurane made possible the one-pot regioselective synthesis of unsymmetrical alkyl aryl and aryl aryl sulfides (Table 2).

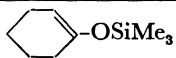

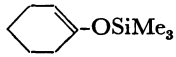

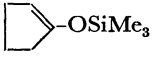

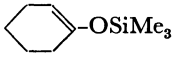



The formation of 2,2,2-trifluoroethyl esters (**7**) by the reaction of sulfurane **1** with carboxylic acids¹) leads to various applications of the intermediate sulfurane **3**.



In fact, the enolated anion **5** and other nucleophiles such as alcohols attacked the positive carbon atom of **3** at –78 °C.

TABLE 1. PREPARATION

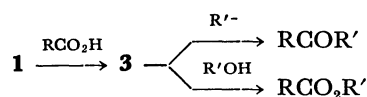
ROH or RCO ₂ H	Reagent	Product ^{a)}	Sulfurane	Bp °C/mmHg [Mp °C]	Yield %
<i>i</i> -PrOH		<i>i</i> -Pr- 	1 A	80—82/16 (83/17) ^{e)}	62
CH ₃ COCH ₂ CH(Me)OH		CH ₃ COCH ₂ CH(Me)- 	1 B	103—105/56 ^{d)}	53
<i>trans</i> -CH ₃ CH=CHCH ₂ OH	PhMgBr	<i>trans</i> -CH ₃ CH=CHCH ₂ Ph	1 A	101—102/15	28
<i>trans</i> -CH ₃ CH=CHCH ₂ OH	PhC(OSiMe ₃)=CH ₂	<i>trans</i> -CH ₃ CH=CHCH ₂ CH ₂ COPh	1 A	98—99/5 ^{b)}	51
<i>cis</i> -CH ₃ CH=CHCH ₂ OH	PhC(OSiMe ₃)=CH ₂	<i>cis</i> -CH ₃ CH=CHCH ₂ CH ₂ COPh	1 A	101—102/6 ^{b)}	62
CH ₂ =CHCH(Me)OH	PhMgBr	CH ₂ =CHCH(Me)Ph	1 A	132—135	36
CH ₂ =CHCH(Me)OH		CH ₂ =CHCH(Me)- 	1 A	96—97/31	81
<i>trans</i> -CH ₃ CH=CHCO ₂ H	PhC(OSiMe ₃)=CH ₂	<i>trans</i> -CH ₃ CH=CHCOCH ₂ COPh	1 A	153—154/1 ^{b)}	54
PhCO ₂ H	CH ₃ MgBr	PhCOCH ₃	1 A	80/11 (79/10) ^{e)}	20
CH ₃ CO ₂ H		CH ₃ CO- 	1 B	121—123/21 (111—112/18) ^{e)}	71
PhCO ₂ H	PhC(OSiMe ₃)=CH ₂	PhCOCH ₂ COPh	1 A	[80—81][81] ^{e)}	81
PhCO ₂ H	CH ₃ OH	PhCO ₂ CH ₃	1 A	94—96/25 (96—98/24) ^{e)}	81
PhCO ₂ H	C ₂ H ₅ OH	PhCO ₂ C ₂ H ₅	1 B	84—86/10	76
<i>trans</i> -CH ₃ CH=CHCO ₂ H	C ₂ H ₅ OH	<i>trans</i> -CH ₃ CH=CHCO ₂ C ₂ H ₅	1 A	97—98/18	79

a) Structures were confirmed by means of IR and NMR spectral data. b) New compound: The results of microanalysis agreed satisfactorily with the calculated value. c) "Dictionary of Organic Compounds," 4th ed, Eyre and Spottiswoode Pub. Ltd., (1965), Vol. 3. p. 1936. d) K. Narasaka, K. Soai, and T. Mukaiyama, *Chem. Lett.*, **1974**, 1223. e) "Spectral data and Physical Constants for Organic Compounds," ed by W. M. Ritchey, C. R. C. Press. Inc., (1975).

TABLE 2. PREPARATION OF UNSYMMETRICAL SULFIDES

ROH	R'SH	Product ^{a)}	Bp °C/mmHg	Yield %
C ₂ H ₅ OH	PhSH	C ₂ H ₅ SPh	72—74/6 (206) ^{b)}	62
C ₂ H ₅ OH	PhCH ₂ SH	C ₂ H ₅ SCH ₂ Ph	78—80/5 (229) ^{b)}	51
<i>i</i> -PrOH	PhSH	<i>i</i> -PrSPh	96—98/10 (102—104/14) ^{b)}	86
C ₈ H ₁₇ OH	PhSH	C ₈ H ₁₇ SPh	107—109/2 (147/18) ^{b)}	92
<i>trans</i> -CH ₃ CH=CHCH ₂ OH	PhSH	<i>trans</i> -CH ₃ CH=CHCH ₂ SPh	104—106/12 (70/1.3) ^{c)}	89
<i>trans</i> -CH ₃ CH=CHCH ₂ OH	PhCH ₂ SH	<i>trans</i> -CH ₃ CH=CHCH ₂ SCH ₂ Ph	102—104/5 (86/0.5) ^{d)}	78
<i>cis</i> -CH ₃ CH=CHCH ₂ OH	PhSH	<i>cis</i> -CH ₃ CH=CHCH ₂ SPh	102—105/12 ^{e)}	72
CH ₂ =CHCH(Me)OH	PhSH	CH ₂ =CHCH(Me)SPh	101—103/10 ^{e)}	76
CH ₂ =CHCH(Me)OH	PhCH ₂ SH	CH ₂ =CHCH(Me)SCH ₂ Ph	118—120/9 ^{e)}	72

a) Structures were confirmed by means of IR and NMR spectral data. b) H. H. Anderson, *J. Chem. Eng. Data*, **9**, 272 (1964). c) C. Cope, D. E. Morrison, and C. Field, *J. Am. Chem. Soc.*, **72**, 59 (1950). d) J. J. Bryan and D. W. Hysert, *Can. J. Chem.*, **49**, 325 (1971). e) T. Kubota, S. Miyashita, T. Kitazume, and N. Ishikawa, *Chem. Lett.*, **1979**, 845.



In each case, inhibition of the pseudorotation to produce 2,2,2-trifluoroethyl esters seems advantageous for producing ketones and esters.

In conclusion, the sulfurane **1** is a useful precursor through **2** or **3** for organic synthesis.

Experimental

General procedures are described.

2-Isopropylcyclohexanone. A mixture of bis(2,2,2-trifluoroethoxy)diphenylsulfurane (12 mmol) prepared from chlorodiphenylsulfonium chloride (14 mmol) and sodium 2,2,2-trifluoroethoxide (28 mmol) *in situ*,¹⁾ and isopropyl alcohol (10 mmol) in freshly dried tetrahydrofuran (10 ml) was stirred at room temperature for 5 min. Into the mixture, were added successively 2-cyclohexenyl trimethylsilyl ether (10 mmol) and calcined potassium fluoride (10 mmol). After being stirred for 24 h, the reaction mixture was poured into water and the resulting oily substance was extracted

with diethyl ether. On removing the solvent, the residue was subjected to distillation *in vacuo*. Final purification was performed by preparative gas chromatography through a column containing 25% Silicone DC 550 on Shimalite. The product, 2-isopropylcyclohexanone, was obtained in a 62% yield, bp 80–82 °C/16 mmHg.**

2-Acetylcyclohexanone. A mixture of bis(2,2,2-trifluoroethoxy)methylphenylsulfurane (12 mmol) prepared from chloromethylphenylsulfonium chloride (14 mmol) and sodium 2,2,2-trifluoroethoxide (28 mmol) *in situ*,¹⁾ acetic acid (10 mmol) and freshly dried tetrahydrofuran (10 ml) was stirred at –78 °C for 10 min. After successive addition of 2-cyclohexenyl trimethylsilyl ether (10 mmol) and calcined potassium fluoride (10 mmol), the mixture was stirred for 10 h. The resulting mixture was then poured into water, and subjected to the usual work-up. Distillation gave 2-acetylcyclohexanone in 71% yield, bp 121–123 °C/21 mmHg.

Ethyl Benzoate. A mixture of bis(2,2,2-trifluoroethoxy)methylphenylsulfurane (12 mmol),¹⁾ benzoic acid (10 mmol) and freshly dried tetrahydrofuran (10 ml) was stirred at –78 °C for 10 min. Ethyl alcohol (10 mmol) was added to the reaction mixture, which was then stirred at –78 °C for 10 h. The mixture was poured into water, and the oily substance extracted with diethyl ether. After removal of the solvent, distillation gave ethyl benzoate in 76% yield, bp 84–86 °C/10 mmHg.

Ethyl Phenyl Sulfide. A mixture of bis(2,2,2-trifluoroethoxy)diphenylsulfurane (12 mmol),¹⁾ ethyl alcohol (10 mmol), thiophenol (11 mmol) and freshly dried diethyl ether (10 ml) was stirred at room temperature for 24 h. The reaction mixture was poured into water and the oily layer extracted with diethyl ether. The ethereal extract was washed with 5% aq sodium hydroxide solution and dried over magnesium sulfate. After removal of the solvent, the residual oily material was distilled in a vacuum yielding ethyl phenyl sulfide in 62% yield, bp 72–74 °C/6 mmHg.

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** 1 mmHg = 133.3 Pa.