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Communications

An Efficient and General Synthesis of Perfluoroalkyl Dithioketals

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Major concern in organofluorine chemistry is to develop the new synthetic methods to fluoroorganics because of unique biological property of fluorinated compounds in medicinal and agrochemical agents.^{1,2} Recently, it was reported that the presence of a phenylthio group attached to carbon atom bearing a trifluoromethyl group facilitated the formation of carbocation³ destabilized by β -fluorine atoms as well as that of carbanion⁴ stabilized by β -fluorine atoms. The remarkable effect of phenylthio group in the formation of carbocation and carbanion bearing a trifluoromethyl group originates from the ability of sulfur atom to stabilize electron deficient carbon atom⁵ as well as electron rich carbon atom.⁶ With this point in mind, we are interested in the synthesis and utility of perfluoroalkyl dithioketals which have two phenylthio groups attached to carbon atom bearing a perfluoroalkyl group. Especially, one strong feature of these structures is to be able to utilize two phenylthio groups synthetically, which may provide versatile synthetic routes to new fluorinated compounds.

Although the synthesis of nonfluorinated dithioketals has been well established⁷, there has been only one report on the synthesis of perfluoroalkyl dithioketals.⁸ To make things worse, this previous method, which provided only one specific dithioketal, lacks efficiency and generality. The unfavorable formation of carbocation bearing a trifluoromethyl group, which is possible intermediate in the preparation of trifluoro-

methyl dithioketal, accounts for the lack of the report. In the present paper, we wish to describe an efficient and general preparation of perfluoroalkyl dithioketals.

The treatment of phenyltrifluoromethyl ketone **1a** with thiophenol (2 eq.) in the presence of AlCl_3 (1 eq.) at room temperature resulted in the formation of messy reaction mixture which allowed isolation of phenyltrifluoromethyl dithioketal **2a** in less than 10% yield. The use of $\text{BF}_3 \cdot \text{OEt}_2$, TiCl_4 , SnCl_4 , ZnCl_2 or FeCl_3 as a Lewis acid to control the reaction did not initiate the reaction at all even at reflux temperature of CH_2Cl_2 . When the reaction was carried out in the presence of AlCl_3 (1 eq.) at -78°C for 20 hours, however, **2a** was isolated in 92% yield. The attempt of this reaction at higher temperature (-40°C) or at -78°C followed by slowly warming to room temperature resulted in the decrease of isolated yield of **2a**, which may be due to the decomposition of **2a** in the reaction mixture at that condition. The use of less than 1 eq. of AlCl_3 did not make completion of this reaction and starting material **1a** was always recovered. This result indicates that only AlCl_3 can act as a Lewis acid to complex with oxygen for the formation of carbocation intermediate bearing a trifluoromethyl group. Reactions of several types of perfluoroalkylated ketones⁹ with thiophenol under same reaction condition also afforded the corresponding dithioketals in good to excellent yields (Table 1). In contrast to the synthesis of **2a**, the reaction of pentafluoroethyl substituted ketones, such as phenylpentafluoroethyl ketone **1h** and *n*-butylpentafluoroethyl ketone **1k**, with thiophenol under same reaction condition provided the corresponding dithioketals **2h** and **2k** in relatively low yields. Although difference in reactivity between two reactions is unclear, destabilization of intermediate (I) due to the increasing electronic effect of pentafluoroethyl group may account for the formation of **2h** and **2k** in low yields.

A plausible mechanism is that a strong complex is first formed between the carbonyl oxygen and AlCl_3 , thereby facilitating the formation of trivalent carbocation intermediate (I) bearing a perfluoroalkyl group. Although (I) is destabilized by a perfluoroalkyl group, the presence of a phenylthio group can diminish the influence caused by a perfluoroalkyl group.³ The reaction of (I) with a second mole of thiophenol afforded the desired dithioketal **2**.

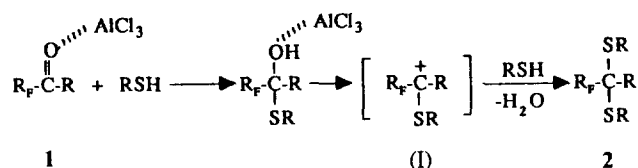
Table 1. Preparation of Perfluoroalkyl Dithioketals **2**

$$\text{R}_F\text{C}(=\text{O})\text{R} + \text{PhSH} \xrightarrow[\text{T}^\circ\text{C}, 20 \text{ hrs}]{\text{AlCl}_3 (1 \text{ eq.})/\text{CH}_2\text{Cl}_2} \text{R}_F\text{C}(\text{SPh})_2\text{R}$$

1 **2**

Compound No.	R _F	R	T (°C)	Yield (%) ^a
2a	CF ₃		-78→25 ^b	80
2a	CF ₃		-40→25 ^b	53
2a	CF ₃		-78	92
2b	CF ₃		-78	82
2c	CF ₃		-78	79
2d	CF ₃		-78	81
2e	CF ₃		-78	87
2f	CF ₃		-78	84
2g	CF ₃		-78	89
2h	CF ₃ CF ₂		-78	60 ^c
2i	CF ₃	CH ₃	-78	82
2j	CF ₃	n-C ₄ H ₉	-78	84
2k	CF ₃ CF ₂	n-C ₄ H ₉	-78	63 ^c

^a Isolated yield. ^b It took 7 hours. ^c When the reaction mixture was allowed to warm to room temperature, product was isolated in only 10 to 15% yield.



In a typical procedure, a 500 ml three-neck round bottom flask equipped with a septum, a solid addition tube filled with AlCl₃ (2.67 g, 0.02 mole), a magnetic stir bar and a nitrogen tee connected to a source of nitrogen was charged with 2, 2, 2-trifluoroacetophenone (3.48 g, 0.02 mole), thiophenol (4.40 g, 0.04 mole) and 200 ml dry CH₂Cl₂. The reaction mixture was cooled to -78°C by using dry-ice/isopropanol slush and AlCl₃ was added in several portions *via* a solid addition tube. After stirring at -78°C for 20 hours, the reaction mixture was quenched with water at -78°C. The mix-

ture was poured into 150 ml of H₂O, extracted with methylene chloride (300 ml×2). After washing with saturated NaCl water solution, methylene chloride layer was dried with anhydrous Na₂CO₃. Column chromatography (hexane) provided 6.9 g (92% yield) of bis(phenylthio)phenyltrifluoromethylmethane **2a**: mp. 72-73°C; ¹H NMR (CDCl₃) δ 7.80-7.15 (m, 15H); ¹⁹F NMR (standard vs. CF₃COOH) δ 15.8 (s); IR (KBr) 3063, 1249, 1173, 1142, 752, 687 cm⁻¹; MS, m/e (relative intensity) 376 (M⁺, parent ion), 267 (100), 234 (15), 197 (20), 165 (20), 109 (13), 77(20).

In conclusion, AlCl₃-promoted condensations of perfluoroalkylated ketones with thiophenol represent a mild, efficient and general approach to the synthesis of perfluoroalkyl dithioketals.

Further studies on the synthetic utility of perfluoroalkyl dithioketals are currently underway and results will be published in the future.

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