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FLUOROMETHYL PHENYL SULFOXIDE: HIGHLY CONVENIENT SYNTHESES OF VINYL FLUORIDES AND FLUOROMETHYLKETONES

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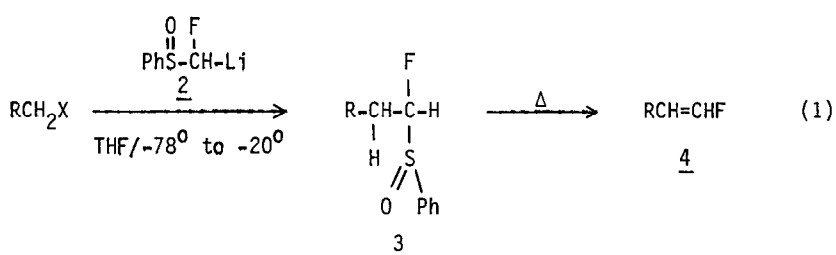
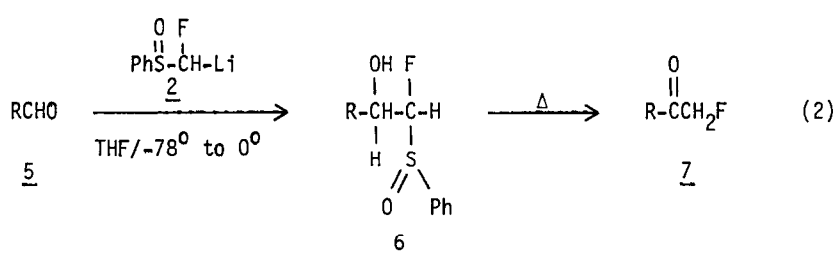
ABSTRACT: Alkylation of lithio fluoromethyl phenyl sulfoxide 2 gave the alkylated products in high yields. Pyrolysis of the products led to vinyl fluorides in excellent yields. The reaction of 2 with carbonyl compounds led to the corresponding β-hydroxy-α-fluoromethyl phenyl sulfoxides. Pyrolysis of some of the sulfoxides gave fluoromethylketones in moderate yields.

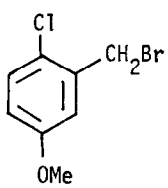
The introduction of fluorine into organic molecules has received wide interest in recent years. These fluorinated compounds have found useful applications in biological and pharmaceutical fields[1]. In this letter, we wish to report the utilization of fluoromethyl phenyl sulfoxide[2] as a reagent for the synthesis of fluorinated compounds. The lithio fluoromethyl phenyl sulfoxide 2 could be generated by the reaction of fluoromethyl phenyl sulfoxide with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at -78°C. The sulfinyl carbanion 2 seems to be stable at 0°C for at least one hour. The reaction of 2 with alkyl halides and aldehydes led to products 3 and 6 respectively. Pyrolysis of these products gave the corresponding vinyl fluorides[3] 4 and fluoromethylketones[4] 7 equation (1) and (2).





The following procedure is representative : lithio fluoromethyl phenyl sulfoxide was generated by the reaction of LDA in THF at -78°C. Alkyl halides or aldehydes were added at this temperature and the mixtures were stirred either at -20°C for 3 hr (for alkyl halides with the addition of 1 equiv. of HMPA) or at 0°C for 3 hr (for aldehydes). The reactions were quenched with saturated ammonium chloride. Products 3 or 6 were isolated with chloroform and the crude products were further purified by preparative layer chromatography (PLC). The results are summarized in Table I and II.

Table I

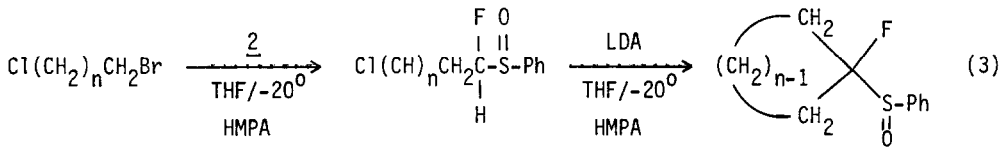
1, Halides	3, Products %	4, Products %
$CH_2(CH_2)_6CH_2I$	70[a]	86[b]
$CH_2(CH_2)_{10}CH_2I$	85[a]	93[b]
$CH_2(CH_2)_{14}CH_2I$	60[a]	95[b]
	67[a]	73[b]

[a] Products were purified by PLC - 4:1 chloroform-hexane.

[b] Products were purified by PLC - hexane.

The alkylated products 3 were pyrolyzed for 30 minutes in a sealed tube at 180°C. The reaction was very clean and only two products were isolated : the vinyl fluorides 4 and benzene sulphenic acid.

A stepwise cycloalkylation of 2 is also possible. Thus, the cycloalkanes 8 could be prepared as shown in equation (3).

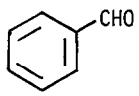


8

n = 2; 68% yield
n = 3; 65% yield

n = 2; 65% yield
n = 3; 59% yield

Table II

5, Aldehydes	6, Yields %	7, Yields %	Benzene sulphenic acid (Yields %)
n-C_2H_5CHO	58[a]	-	(81)
n-$C_5H_{11}CHO$	64[a]	-	(100)
n-$C_7H_{15}CHO$	68[a]	31[b]	(96)
	55[a]	29[b]	(62)

[a] Products were purified by PLC - chloroform.

[b] Products were purified by PLC - 1:4 chloroform-hexane.

Pyrolysis of 6 was carried out in a sealed tube at 180-182°C for 1 hr. We believed that some of the fluoromethylketones were decomposed at this temperature. Benzene sulphenic acid was always isolated in high yield.

Our results indicated that fluoromethyl phenyl sulfoxide is a synthetically useful reagent for the synthesis of fluorinated compounds. Further exploratory work is in progress.

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