

Methyl Fluorosulphonyldifluoroacetate; a New Trifluoromethylating Agent

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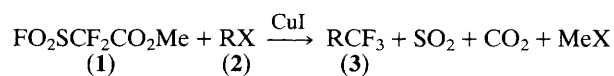
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Methyl fluorosulphonyldifluoroacetate, in the presence of copper(I) iodide, is used as the source of trifluoromethyl group which replaces the halogen in aryl, alkenyl, and alkyl halides.

Recently, considerable attention has been devoted to finding novel methods for introducing the trifluoromethyl group into organic compounds because of increasing demands in medicine and biochemistry.¹ During the course of our investigation into difluorocarbene chemistry² it was found that methyl fluorosulphonyldifluoroacetate (**1**) is a good carbene precursor, which after decarbomethoxylation by nucleophiles (*e.g.* KI, KBr, KCNS, amine) gives fluoroform as the major by-product. Compound (**1**) is an easy to handle liquid and can be obtained readily from the corresponding acid fluoride, which is a starting material for producing the commercial ion-exchange resins, Nafion H®.³ We envisaged that compound (**1**) could be used as a trifluoromethylating agent without the accompaniment of fluoroform. We report here, the preliminary results of the reaction of (**1**) with halogen compounds.

Treatment of (**1**) with aryl, alkenyl, and alkyl halide (**2**) in dimethylformamide (DMF) in the presence of catalytic amounts of copper(I) iodide (12 mol%) at 60–80 °C, 2–6 h gave the corresponding trifluoromethyl derivatives (**3**) in good

yields with simultaneous elimination of SO₂, CO₂, and methyl halide.



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| a; R = Ph, X = I | i; R = CH ₂ =CHCH ₂ , X = I |
| b; R = Ph, X = Br | j; R = PhCH=CH, X = Br |
| c; R = <i>p</i> -NO ₂ C ₆ H ₄ , X = I | k; R = C ₆ H ₄ (CF ₂) ₄ Cl, X = <i>p</i> -I |
| d; R = <i>p</i> -ClC ₆ H ₄ , X = I | l; R = naphthyl, X = α-Br |
| e; R = PhCH ₂ , X = Cl | m; R = naphthyl, X = α-I |
| f; R = PhCH ₂ , X = Br | n; R = CH ₂ CON(Et) ₂ , X = Br |
| g; R = PhCH ₂ , X = I | o; R = CH ₂ CONC ₅ H ₁₀ , X = Br |
| h; R = CH ₂ =CHCH ₂ , X = Br | |

The results in Table 1 show the order of reactivity to be RI > RBr > RCl, although the use of the bromo derivative is also quite efficient. However, the chlorine in (**2d**) was not displaced after substituting iodine by the trifluoromethyl group, even in a higher ratio (**1**) : (**2**) (see entry 7, in Table 1).

Table 1. Reaction of (1) with (2) in the presence of CuI (12 mol%)^a.

Entry	RX	(1):(2)	T/°C	t/h	Conversion % ^b	(3) % ^c	B.p./mmHg
1	2a	1:2	70	2.5	100	84	
2	2a ^d	1:2	60	2.5	100	84	
3	2b	1:2.5	80	3	100	61	
4	2c	1:2	65	3	95	80	
5	2c ^e	1:2	65	3	95	80	
6	2d	1:2	70	4	100	78	
7		3.5:1	70	4.5	95	90	
8	2e	1:2	80	4	95	53	
9	2f	1:2.5	80	3.5	100	72.4	
10	2g	1:2	70	2	100	81	
11	2h	1:3	60	4	100	70	
12	2i	1:3	60	4	100	74	
13	2j	1:2	70	3	95	62	
14	2j ^d	1:2	70	3	100	68	
15	2k	1:2	80	4	100	92	64 °C/1.5
16	2l	1:2	80	4	94	70	
17	2m	1:1.5	80	6	100	74	
18	2n	1:2	75	3	100	90	113 °C/28
19	2o	1:2	80	3	100	88	100 °C/2.5

^a In DMF unless noted otherwise. ^b Determined by ¹⁹F n.m.r. spectroscopy. ^c Isolated yield based on (1) except Entry 7. All the trifluoromethylated compounds obtained except (3k), (3n), and (3o) are known and their physical constants are consistent with those of authentic samples. The new compounds were identified by elemental analyses, ¹H n.m.r., ¹⁹F n.m.r., and i.r. spectroscopy. ^d In DMSO. ^e In the presence of *p*-dinitrobenzene (20% mol).

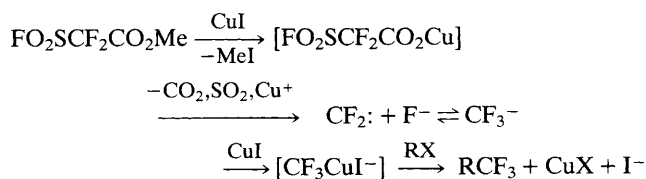
The presence of copper(I) iodide is essential to the reaction. For example, in the absence of copper(I) iodide, (2a) did not react with (1) in DMF at 70 °C for 2.5 h. When KI was used instead of CuI, (2a) was recovered completely under similar conditions with fluoroform (93%) as the product.

DMF is a suitable solvent for the reaction, although dimethyl sulphoxide (DMSO) can also be used with comparable yields.

Addition of 2,3-dimethylbut-2-ene, a trapping agent for difluorocarbene, to the reaction mixture of (1) and (2c) in the presence of CuI gave no cyclopropane derivative, only (3c) was obtained.

The results can be rationalised in terms of first the formation of the copper salt of (1) (or complex)⁴ with

elimination of methyl halide.¹ The salt readily decarboxylates to yield difluorocarbene and fluoride ion which are in equilibrium with CF₃⁻. The equilibrium readily shifts to form CF₃⁻ in the presence of CuI and to give [CF₃CuI]⁻.⁵ Therefore, the difluorocarbene generated could not be trapped by the alkene. The nucleophilic trifluoromethylation of [CF₃CuI]⁻ on aryl or alkyl halide leads to the obtained results. The fact that the reaction is not suppressed by *p*-dinitrobenzene (single electron transfer scavenger) (see entry 5 in Table 1) seems to show that the intermediate [CF₃CuI]⁻ rather than [CF₃CuI] is involved.^{1g} The possible mechanism of the reaction is shown below:



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