

A Novel Method for the Preparation of Perfluoroalkylmethyl Substituted Electrophilic Cyclopropane Derivatives

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Abstract: Perfluoroalkylmethyl-substituted electrophilic cyclopropane derivatives are readily synthesized in excellent yields by a CrCl_3/Fe promoted reaction of perfluoroalkyl iodides with allylmalonate and its analogues in one-pot reaction. Functional groups like ester, cyano and carbonyl are tolerated under such reaction condition.

Cyclopropane derivatives are outstanding by virtue of their unusual structural, spectroscopic, chemical and biological properties.¹ These compounds offer potentially therapeutic and notably pesticidal activities.² In addition, they also can be considered as precursors to specifically ring-opened derivatives. Thus, works concerning the synthesis and investigation of the chemical properties of such cyclopropane derivatives have been expanding rapidly in recent years.³⁻⁵ The appearance of fluorine-containing pyrethroids stimulates scientists to search new ways in synthesizing cyclopropane derivatives bearing a fluorine-containing group.⁶ Till present, certain compounds were synthesized usually in 2 steps, introducing an F-group into molecules followed by cyclopropanation or introducing an F-group into pre-formed cyclopropane ring.⁷ Here, we report a novel, facile cyclopropanation reaction promoted by a new redox system CrCl_3/Fe to give perfluoroalkylmethyl substituted electrophilic cyclopropane derivatives in one-pot reaction.

In the presence of a catalytic amount of $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ (20 mol%) and 1.5 equiv. amount of iron powder, perfluoroalkyl iodides **1** reacted readily with alkenes **2** to offer excellent yields of perfluoroalkylmethyl substituted electrophilic cyclopropanes **3-5**. The results are summarized in Table.

General Procedure: A mixture of **1** (15 mmol), **2** (10 mmol), $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ (2.0 mmol), Fe (15 mmol) in 50 ml of absolute ethanol was stirred at 60-70 °C until the completion of the reaction which was monitored by GC and ^{19}F NMR. Usual workup gave pure products **3**, **4** or **5**.⁸

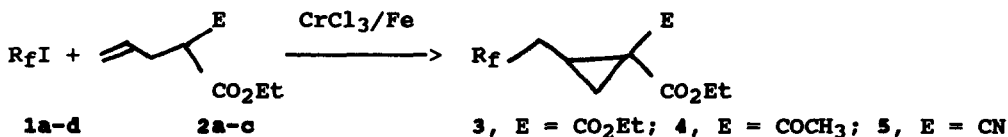


Table Cyclopropanation of R_FI 1 with 2.^a

Run	R _F I	1	E in Alkene 2	Time(h)	Product	Yield(%) ^b
1	C ₂ F ₅ I	1a	CO ₂ Et 2a	15	3a	89 ^c
2	C ₄ F ₉ I	1b	CO ₂ Et 2a	12	3b	82
3	C ₆ F ₁₃ I	1c	CO ₂ Et 2a	10	3c	92
4	C ₈ F ₁₇ I	1d	CO ₂ Et 2a	10	3d	85
5	C ₂ F ₅ I	1a	COCH ₃ 2b	15	4a	82 ^c
6	C ₄ F ₉ I	1b	COCH ₃ 2b	12	4b	87
7	C ₆ F ₁₃ I	1c	COCH ₃ 2b	10	4c	92
8	C ₈ F ₁₇ I	1d	COCH ₃ 2b	9	4d	85
9	C ₂ F ₅ I	1a	CN 2c	15	5a	64 ^c
10	C ₄ F ₉ I	1b	CN 2c	8	5b	76
11	C ₆ F ₁₃ I	1c	CN 2c	9	5c	69
12	C ₈ F ₁₇ I	1d	CN 2c	7	5d	70

a. All reactions were carried out in ethanol at 60-70 °C with a molar ratio of 1:2:CrCl₃.6H₂O:Fe=1.5:1:0.2:1.5 unless otherwise indicated; All products gave satisfactory elemental analyses, ¹⁹F, ¹H NMR, IR and MS data.

b. Isolated yield based on 2. c. 3-5 equiv. of C₂F₅I was used.

¹H, ¹⁹F and ¹³C NMR, IR spectra and GC revealed that cyclopropanes 3, 4, or 5 were the mere product. Neither straight chain adduct nor four-membered or five-membered ring product could be found. The cyclopropanation reaction proceeded well with various perfluoroalkyl iodides and gave products 3, 4 or 5 in excellent yields. In the case of C₂F₅I 1a, an excess of 1a was used to ensure a complete consumption of alkene 2a, 2b or 2c.

In conclusion, a novel one-pot cyclopropanation reaction was found. The ready availability of the catalyst, the simplicity of the procedure and the good yields made this approach a useful route to the synthesis of perfluoroalkylmethyl-containing cyclopropane derivatives.

References

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8. 3a: Bp. 113-115 °C/10 mmHg; Colourless oil; ¹⁹FNMR(CDCl₃/TFA): 8(s, 3F, CF₃), 41(s, 2F, CF₂)ppm; ¹HNMR(CDCl₃/TMS): 4.22(q, J=7Hz, 4H, 2XOEt), 2.5-2.1(m, 2H, CH₂CF₂), 2.0(m, 1H, cyc-CH), 1.5(d, J=8Hz, 2H, cyc-CH₂), 1.36(t, J=7Hz, 6H, 2 x OEt)ppm; ¹³CNMR(CDCl₃): 169, 168(C=O), 134-115(m, C₂F₅), 62(OCH₂), 33(s, cyc-C), 30(t, J=22Hz, CH₂), 20.1(s, cyc-CH₂), 19.4(t, J=5Hz, cyc-CH), 14.1(CH₃)ppm; m/z(±): 318(M⁺, 63.2), 273(M⁺ - OEt, 100).