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A Convenient Method of Polyfluoroalkyl-lactonization

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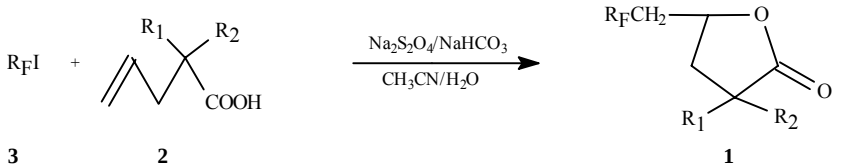
Abstract: A novel synthesis of polyfluoroalkyl substituted γ-butyrolactones from the reaction of polyfluoroalkyl iodides with 4-pentenoic acid initiated with sodium dithionite was realized in good yields.

Keywords: Polyfluoroalkyl iodide, γ-butyrolactones, sodium dithionite.

Lactones are presented in a large amount of natural products and biologically active compounds and also used as chiral building blocks for the organic synthesis[1]. The formation of halolactones from olefinic carboxylic acids, so-called "halolactonization" has been well recognized as one of the most useful construction process[2]. In connection with our recent studies on the sulfinatohalogenation[3], we describe herein a novel convenient method of polyfluoroalkylation-lactonization of 4-pentenoic acids **2** to the corresponding γ-butyrolactones **1.**

Pentenoic acid **2a**, **2b** was neutralized by sodium hydroxide solution and reacted with polyfluoroalkyliodides **3a**~**3f** initiated by sodium dithionite in aqueous acetonitrile solution to give polyfluoroalkylated γ-butyrolactones **1a**~**1m** in excellent yields. While **2c** was reacted with **3e**, **3a** to form **1l**, **1m** respectively, the yields of products were moderate (**Table 1**) .

This reaction resembles to the halolactionization, so the name of this reaction was proposed "polyfluoroalkyl-lactonization". However, the reaction mechanism is different. The key feature of the mechanism may involve the radical reaction of polyfluoroalkyl iodide with pentenoic acid and then the neuclophilic attack of the carboxylic group to the iodide atom to form the lactone.



3 **2** **1**

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Typical experimental procedure for **1c**[4]: **2a** (1.28 g, 10 mmol) was dissolved in 5mL 8% aqueous sodium hydroxide solution and stirred with acetonitrile (15 mL) then **3c** (5.08 g, 11 mmol) was added. To the mixture was added sodium dithionite (2.2 g, 12.1 mmol) and sodium bicarbonate (1.70 g, 20.2 mmol). The reaction mixture was stirred for 6 hours and treated with about 50 mL of water. The product was purified with chromatography (PE/EA=10:1) to give **1c** (4.3 g, 92%).

The yields of the products were summarized in **Table 1.**

Table1 The yields of compounds **1a~1m**

Entry	Acid	R_FI	Product	Isolated yield(%)
1	**2a** (R_1=R_2=CH_3)	**3a** (R_F=$Cl(CF_2)_2$)	**1a**	86
2	**2a**	**3b** (R_F=$Cl(CF_2)_4$)	**1b**	88
3	**2a**	**3c** (R_F=$Cl(CF_2)_6$)	**1c**	92
4	**2a**	**3d** (R_F=$Cl(CF_2)_8$)	**1d**	92
5	**2a**	**3e** (R_F=$F(CF_2)_6$)	**1e**	90
6	**2b** (R_1=R_2=H)	**3a**	**1f**	81
7	**2b**	**3b**	**1g**	84
8	**2b**	**3c**	**1h**	86
9	**2b**	**3d**	**1i**	88
10	**2b**	**3e**	**1j**	87
11	**2b**	**3f** (R_F=$F(CF_2)_8$)	**1k**	90
12	**2c** (R_1=H, R_2=n-Bu)	**3e**	**1l**	62
13	**2c**	**3a**	**1m**	70

All the products were characterized by IR, ^{19}F, $^{1}HNMR$, MS and elemental analysis.

In conclusion, a convenient method of polyfluoroalkyl-lactonization of 4-pentenoic acids with polyfluoroalkyl iodides initiated by sodium dithionite was realized.

Acknowledgments

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References and Notes

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4. **1c**: mp 80-82°C; $^{1}HNMR$(500Hz, $CDCl_3$, δ_{ppm}): 4.78 (m, 1H, CH), 1.90-2.68 (m, 4H, 2×CH_2), 1.29 (d, 6H, J=4.96Hz, 2×CH_3); $^{19}FNMR$(500Hz, $CDCl_3$, δ_{ppm}): 66.5 (s, 2F, $ClCF_2$), 111.1 (m, 2F, CF_2CH_2), 118.8 (d, 2F, CF_2), 120.1(s, 4F, 2×CF_2), 123.1 (d, 2F, CF_2). IR(KBr, cm^{-1}) 2900, 1780 (γ -lactone), 1220, 1140, 680; Anal. Calcd for $C_{13}H_{11}ClF_{12}O_2$: C 33.7; H, 2.39; F 49.35; Found: C 33.82; H 2.35; F 49.10; MS (*m/z*): 463 (M^++1, 4.51), 418 (M^+-CO_2, 12.97), 85 (32.33), 69 (100.00), 57 (25.93), 55 (31.94), 41(40.07).

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