Available online at www.sciencedirect.com
ScienceDirect
Journal of Fluorine Chemistry 129 (2008) 280–285
JOURNAL OF FLUORINE CHEMISTRY
www.elsevier.com/locate/fluor

Synthesis of fluoroalkyl-δ-lactones from polyfluoroalkyl iodides and 5-hexenoic acids

Xiang Fang [a], Qi Ying [a], Yang Chen [a], Xueyan Yang [a], Xianjin Yang [a,b], Fanhong Wu [a,b,*]

[a] *Laboratory for Advanced Material and Institute of fine chemicals, School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China*
[b] *Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China*

Received 3 December 2007; received in revised form 27 December 2007; accepted 27 December 2007
Available online 4 January 2008

Abstract

The polyfluoroalkyl-lactonization of 5-hexenoic acids with the polyfluoroalkyl iodides initiated by sodium dithionite was carried out in aqueous acetonitrile, providing an efficient method for the synthesis of fluorine-containing δ-valerolactones. Formation of $R_fCH_2CH{=}CH(CH_2)_2COOH$ appeared to be unexpected minor product in sulfinatodehalogenation reagents.

Keywords: 5-Hexenoic acids; Polyfluoroalkyl iodide; δ-valerolactone; Sodium dithionite; Polyfluoroalkyl-lactonization

1. Introduction

Functionalized valerolactones are present in a large amount of natural products and biologically active compounds such as compactin, mevinclin and close relatives, collectively the mevinic acids [1] and artemisinin, which is used to treat multi-drug resistant strains of falciparum malaria [2]. Introduction of fluorine into lactones is of great interest to synthetic chemists due to two facts. First, fluorination of natural products and drugs has demonstrated significant improvements of activities and properties. Second, functionalized lactones have been found as substructures in a variety of biologically active natural products including flavor components, sex attractant pheromones of different insects, plant-growth regulators, alkaloids, macrocyclic antibiotics, and lignanlactones [3,4]. Brace described that thermally-induced reaction of $C_6F_{13}I$ to 5-hexenoic acid in ethyl acetate at 175–200 °C (bis-*tert*-butyl peroxide) afforded 6-(perfluorohexyl)-5-hydroxyhexanoic acid δ-lactone in 60% yield [5].

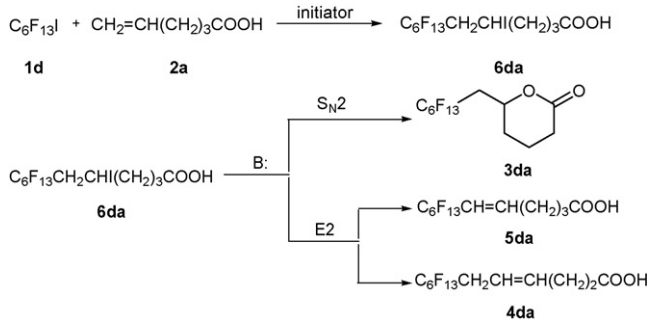
The addition reaction of polyfluoroalkyl iodides with unsaturated compounds, such as olefins and alkynes, initiated by sulfinatodehalogenation reagents (sodium dithionite) has been thoroughly studied in our laboratory [6]. Herein we extended our research to 5-hexenoic acids, the corresponding polyfluoroalkylated δ-valerolactones were obtained as the major products and the unexpected elimination products were obtained as minor products under the same reaction conditions. The detailed experimental results and analysis are described here.

2. Results and discussion

Free radical-induced reaction of R_fI (n-C_6F_{13}) to 5-hexenoic acid gave the primary adduct $R_fCH_2CHI(CH_2)_3COOH$ (**6da**) in excellent yield, using AIBN [7] copper powder [8] and sulfuroxy-acid salts [6b] as initiator. Base induced S_N2 internal reaction of β-iodo(perfluoroalkyl)-alkanoic acid (**6da**) would assume a conformation in which the carboxylate anion approaches the back side of the CHI in order to smoothly displace the iodide ion and form a δ-valerolactone (**3da**), also base induced a likely possible dehydrohalogenation of the adduct would give the α,β olefin (**5da**) by attack of the proton adjacent to the strong electron withdrawing perfluoroalkyl (R_f) group [9] or give the β,γ olefin (**4da**) by attack of the proton

* Corresponding author at: Laboratory for Advanced Material and Institute of fine chemicals, School of Chemistry and Molecular Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China. Tel.: +86 21 64253530.
E-mail address: wfh@ecust.edu.cn (F. Wu).

0022-1139/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jfluchem.2007.12.004



Scheme 1.

adjacent to the carboxyl group (Scheme 1). The reduction of polyfluoroalkyl adduct had been reported by Qiu and Burton [10]. A mixture of corresponding reduction product and β,γ olefin product was formed in a variety of solvents.

Base induced reaction of intermediate adduct **6da** was attempted under various conditions. With K_2CO_3 in stronger coordinating solvent DMF, a mixture of $C_6F_{13}CH{=}CH(CH_2)_3COOH$ **5da** and $C_6F_{13}CH_2CH{=}CH(CH_2)_2COOH$ **4da** was obtained, in poorly coordinating solvent acetonitrile solution, only **4da** was obtained. In sodium dithionite reagents, **3da** was obtained as major product and only **4da** was obtained as minor product.

Identification of **3da** as δ-lactone was based on its infrared spectrum which showed the carbonyl frequency at 1740 cm^{-1} [11] and ^1H NMR spectrum, which showed the anticipated multi-pattern for H_5 at 4.77–4.71 ppm. ^{13}C NMR spectrum of **5da** showed the anticipated three line pattern for C_6 of **5da** at 118.7 ppm showing 23.2 Hz coupling with CF_2 group, ^{13}C NMR spectrum for C_6 of **4da** at 35.5 ppm with $J = 22.6$ Hz. Also ^1H NMR spectrum of **4da** showed proton resonances of the expected complexity and shifts. The doublet of triplet at 2.79 ppm could be interpreted as arising from a 18.1 Hz coupling of H_6 with F_7 and 7.0 Hz coupling of H_6 with the proton H_5 (Table 1).

In order to obtain the δ-valerolactone in one-pot, the polyfluoroalkylation-lactonization reaction in the presence of different bases and solvents was investigated. The results were summarized in Table 2. At room temperature the adduct **6da** could not be converted completely even in different bases (Table 2, entries 1–5). While with high temperature, the adduct **6da** disappeared (Table 2, entries 6–8). It was found that the mixture at reflux overnight after the addition reaction at 0 °C in aqueous acetonitrile solution ($CH_3CN/H_2O = 3:1$ (v/v)) gave the best results, with **3da** in 68% yield and **4da** in 30% yield (Table 2, entry 7).

When R_FI reacted with 5-hexenoic acid and analogues with a substituent at the C-2 position, separation of **3** and **4** proved troublesome, which result in the 50–88% of GC yields of **3** while the actual isolated yields were much low, only 16–27% (Scheme 2 and Table 3). The reason was the tailing effect of **4** and the mixture of most **3** and **4** was obtained when the crude product was purified by column chromatography. The elimination products without substituent were obtained in very small amount with 1.7:1–5.5:1 *E*:*Z*-isomers and the elimination products with a substituent at the C-2 position could not be separated sufficiently.

The results indicated that for 2-substituted 5-hexenoic acids **2b** or **2c**, a mixture of *trans*-/*cis*-isomers was obtained. Analysis of the crude product by ^1H NMR spectroscopy and integration of signals attributed to proton on C-3 indicated the *trans*/*cis* ratio of almost 1:1. The NMR signal of the proton on C-3 exhibited a multiplet in lower field for *trans*-isomer than for *cis*-isomer [6d].

Table 1
^1H NMR, ^{13}C NMR and IR spectra of δ-valerolactone **3da** and olefins **5da**, **4da**

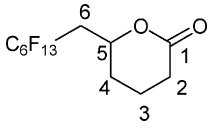
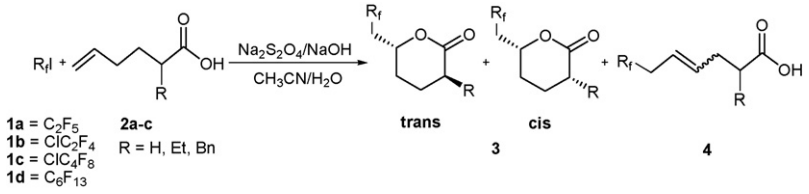
		δ (ppm)	J (Hz)	ν (cm^{-1})
 **3da**	H_5	4.77–4.71		1740
	C_6	37.8	21.1	
	C_5	74.0		
$C_6F_{13}CH{=}CHCH_2CH_2CH_2COOH$ **5da**	H_6	6.43–6.36		
	H_5	5.70–5.61		
	C_6	118.7	23.2	
	C_5	136.9		
$C_6F_{13}CH_2CH{=}CHCH_2CH_2COOH$ **4da**	H_6	2.79	$J_{H-F} = 18.1$, $J_{H-H} = 7.0$	1715
	H_5	5.78–5.72		
	H_4	5.53–5.46		
	C_6	35.5	22.6	
	C_5	118.9		

Table 2
The fluoroalkylation of 5-hexenoic acid initiated by sodium dithionite

Entry	Base	Solvent	Temperature (°C)	Yield[a]			
				6da	**3da**	**5da**	**4da**
1	–	CH_3CN/H_2O	R.T.	51	20		21
2	$NaHCO_3$	CH_3CN/H_2O	R.T.	42	31		24
3	K_2CO_3	CH_3CN/H_2O	R.T.	20	33		41
4	NaOH	CH_3CN/H_2O	0	59	20		19
5	NaOH	DMF/H_2O	R.T.	20	20	20	22
6	NaOH	DMF/H_2O	0–80	0	3	47	48
7	**NaOH**	**CH_3CN/H_2O**	**0–80**	**0**	**68**		**30**
8	NaOH	CH_3CN/H_2O	R.T.–80	0	55		41

[a] Determined by GC.



Scheme 2.

All δ-valerolactones exhibited a typical AB pattern signal in the ^{19}F NMR spectra. For example, ^{19}F NMR of **3aa** exhibited two doublets of multiplets at −117.5 ppm and at −118.3 ppm. The lower field signal is a doublet of doublet of doublet with J = 267.9, 28.2, 9.4 Hz. The higher field signal is also a doublet of doublet of doublet with J = 267.9, 28.2, 9.4 Hz.

In conclusion, a convenient and efficient method of polyfluoroalkyl-lactonization by the reaction of 5-hexenoic acids with polyfluoroalkyl iodides initiated by sodium dithionite has been developed through sequential radical polyfluoroalkylation and nucleophilic cyclization, and unexpected $R_fCH_2CH{=}CH(CH_2)_2COOH$ were obtained as minor products.

3. Experimental

All melting points were uncorrected. IR spectra were measured on a Nicolet Magna IR-550 spectrometer using potassium bromide pellet. High-resolution mass spectra were carried out on a Finnigan GC-MS-4021 spectrometer. ^1H NMR (500 MHz) and ^{13}C (125.8 MHz) spectra were recorded on a Bruker AC-500 spectrometer with Me_4Si as internal standard. ^{19}F NMR spectra were obtained on Bruker AC-500 (470 MHz) spectrometer in $CDCl_3$ with $CFCl_3$ as external standard, downfield shifts being designated as negative. All chemical shifts (δ) are expressed in ppm, coupling constants (J) are given in Hz.

3.1. General procedure for the reaction of 5-hexenoic acids with polyfluoroalkyl iodides

5-Hexenoic acid (2 mmol) was dissolved in aqueous sodium hydroxide solution freshly prepared from 100 mg sodium hydroxide in 1 mL water and stirred while acetonitrile (3 mL) and R_fI (2.2 mmol) was added. To the solution was added

Table 3
Data of the reaction of R_fI **1** with 5-hexenoic acids **2**

Entry	Substance	R	R_f	Product	Yield of **3** (%)[a]	Yield of **3** (%)[b]	Yield of **4** (%)[a]	*E*:*Z* of **4**
1	**2a**	H	C_2F_5	**3aa**	88	24	10	3:1[c]
2	**2a**	H	ClC_2F_4	**3ba**	64	22	32	2.5:1[c]
3	**2a**	H	ClC_4F_8	**3ca**	51	20	39	1.7:1[c]
4	**2a**	H	C_6F_{13}	**3da**	60	22	35	5.5:1[c]
5	**2b**	Et	C_2F_5	**3ab**	56	19	39	
6	**2b**	Et	ClC_2F_4	**3bb**	59	18	37	
7	**2b**	Et	ClC_4F_8	**3cb**	67	20	28	
8	**2b**	Et	C_6F_{13}	**3db**	50	18	43	
9	**2c**	Bn	C_2F_5	**3ac**	71	20	22	
10	**2c**	Bn	ClC_2F_4	**3bc**	62	20	34	
11	**2c**	Bn	ClC_4F_8	**3cc**	80	16	17	
12	**2c**	Bn	C_6F_{13}	**3dc**	82	27	13	

[a] Determined by GC.
[b] Isolated yields.
[c] Based on ^{19}F and ^{13}C NMR.

sodium dithionite (440 mg) and sodium bicarbonate (210 mg). The mixture was stirred at 0 °C for 2–5 h to complete the reaction; after at reflux overnight the mixture was treated with about 10 mL of water and extracted with 3 × 5 mL of ether. The combined organic layer was washed with saturated brine solution and dried over anhydrous sodium sulfate. After evaporation of ether, the crude product was subjected to column chromatography to give the pure product.

*3.1.1. 5-(2,2,3,3,3-Pentafluoropropyl)-δ-valerolactone (**3aa**)*

Colorless oil; IR (cm^{-1}, KBr) 2932, 1743 (δ-lactone), 1197, 719. ^1H NMR ($CDCl_3$, 500 MHz) δ 4.75–4.68 (1H, m), 2.70–2.53 (1H, m), 2.55–2.45 (1H, m), 2.38–2.27 (1H, m), 2.14–2.08 (1H, m), 2.02–1.92 (2H, m), 1.73–1.64 (2H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 170.8, 126.5–113.3 (2C, m), 74.0, 37.6 (t, J = 21 Hz), 29.8, 29.1, 19.0. ^{19}F NMR ($CDCl_3$, 470 MHz) δ −86.8 (3F, s), −117.5 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −118.3 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz). EI-MS (*m/z*) 232 (M^+, 100), 188 (21). HRMS cacld for $C_8H_9O_2F_5$: 232.0523, found: 232.0523.

*3.1.2. 7,7,8,8,8-Pentafluorooct-4-enoic acid (**4aa**)*

Colorless oil; IR (cm^{-1}, KBr) 2932, 1716, 1200, 1119, 715. ^1H NMR ($CDCl_3$, 500 MHz) δ 5.71–5.62 (1H, m), 5.48–5.35 (1H, m), 2.68 (2H, td, J = 17.4 Hz, J = 7.0 Hz), 2.46–2.27 (4H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ (*E*-isomer) 179.7, 136.7, 119.0, 124.6–113.2 (2C, m), 35.2 (t, J = 22.4 Hz), 34.0, 28.1; (*Z*-isomer) 181.1, 134.9, 118.2, 124.6–113.2 (2C, m), 34.4, 31.1 (t, J = 22.1 Hz), 29.1. ^{19}F NMR ($CDCl_3$, 470 MHz) δ (*E*-isomer) −85.8 (3F, s), −118.2 (2F, t, J = 16.5 Hz); (*Z*-isomer) −86.4 (3F, s), −119.3 (2F, t, J = 18.8 Hz). EI-MS (*m/z*) 232 (M^+, 8), 212 (22), 192 (29), 60 (100). HRMS cacld for $C_8H_9O_2F_5$: 232.0523, found: 232.0515.

*3.1.3. 5-(2,2,3,3-Tetrafluoro-3-chloropropyl)-δ-valerolactone (**3ba**)*

Colorless oil; IR (cm^{-1}, KBr) 2973, 1724 (δ-lactone), 1259, 1155, 1052, 939, 767. ^1H NMR ($CDCl_3$, 500 MHz) δ 4.76–4.70 (1H, m), 2.71–2.58 (2H, m), 2.54–2.47 (1H, m), 2.43–2.31 (1H, m), 2.15–2.08 (1H, m), 2.03–1.90 (2H, m), 1.73–1.63 (1H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 170.9, 123.9 (tt, J = 298.6 Hz, J = 37.0 Hz), 116.6 (tt, J = 256.3 Hz, J = 33.8 Hz), 74.3, 37.4 (t, J = 21.4 Hz), 29.7, 29.0, 18.9. ^{19}F NMR ($CDCl_3$, 470 MHz) δ −72.8 (2F, s), −112.8 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −114.2 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz). EI-MS (*m/z*) 250 (M + 2^+, 7), 248 (M^+, 21), 206 (30), 204 (100). HRMS cacld for $C_8H_9O_2F_4Cl$: 248.0227, found: 248.0228.

*3.1.4. 8-Chloro-7,7,8,8-tetrafluorooct-4-enoic acid (**4ba**)*

Colorless oil; IR (cm^{-1}, KBr) 2926, 1714, 1256, 1152. ^1H NMR ($CDCl_3$, 500 MHz) δ 5.77–5.69 (1H, m), 5.54–5.46 (1H, m), 2.80 (2H, td, J = 17.6Hz, J = 6.7 Hz), 2.51–2.38 (4H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) (*E*-isomer) δ 179.3, 136.5, 119.4, 126.8–115.5 (2C, m), 35.1 (t, J = 22.9 Hz), 34.0, 28.1; (*Z*-isomer) 181.0, 134.7, 118.8, 126.8–115.5 (2C, m), 34.3, 31.0 (t, J = 22.8 Hz), 29.1. ^{19}F NMR ($CDCl_3$, 470 MHz) (*E*-isomer) δ −71.5 (2F, s), −114.1 (2F, t, J = 16.5 Hz); (*Z*-isomer) δ −72.0 (2F, s), −115.3 (2F, t, J = 16.5 Hz). EI-MS (*m/z*) 251 (M + 2^+, 2), 249 (M^+, 6), 192 (39), 60 (100). HRMS cacld for $C_8H_9O_2F_4Cl$: 248.0227, found: 248.0225.

*3.1.5. 5-(2,2,3,3,4,4,5,5-Octafluoro-5-chloropentyl)-δ-valerolactone (**3ca**)*

Colorless oil; IR (cm^{-1}, KBr) 2959, 1741 (δ-lactone), 1186, 841, 697. ^1H NMR ($CDCl_3$, 500 MHz) δ 4.77–4.71 (1H, m), 2.70–2.56 (2H, m), 2.53–2.47 (1H, m), 2.45–2.30 (1H, m), 2.15–2.08 (1H, m), 2.03–1.89 (2H, m), 1.73–1.63 (1H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 170.9, 126.2–103.6 (4C, m), 74.1, 37.8 (t, J = 20.4 Hz), 30.0, 29.2, 18.9. ^{19}F NMR ($CDCl_3$, 470 MHz) δ −69.0 (2F, t, J = 13.4 Hz), −112.9 (1F, ddd, $J_{F–F}$ = 272.6 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 14.1 Hz), −114.2 (1F, ddd, $J_{F–F}$ = 272.6 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 14.1 Hz), −120.8 (2F, s), −123.9 (2F, s). EI-MS (*m/z*) 350 (M + 2^+, 2), 348 (M^+, 6), 306 (20), 304 (61), 99 (100). HRMS cacld for $C_{10}H_9O_2F_8Cl$: 348.0163, found: 348.0163.

*3.1.6. 7,7,8,8,9,9,10,10,10-Nonafluorodec-4-enoic acid (**4ca**)*

Colorless oil; IR (cm^{-1}, KBr) 2962, 1716, 1236, 1134, 798. ^1H NMR ($CDCl_3$, 500 MHz) δ 5.72–5.64 (1H, m), 5.49–5.37 (1H, m), 2.73 (2H, td, J = 17.5 Hz, J = 6.9 Hz), 2.42–2.38 (4H, m). ^{13}C NMR ($CDCl_3$, 125.8MHz) δ (*E*-isomer) 179.4, 137.0, 118.8, 122.1–109.0 (4C, m), 35.4 (t, J = 22.5 Hz), 34.0, 28.2; (*Z*-isomer) 180.1, 135.1, 118.2, 122.1–109.0 (4C, m), 34.3, 31.3 (t, J = 22.2 Hz), 29.1. ^{19}F NMR ($CDCl_3$, 470MHz) δ (*E*-isomer) −82.0 (2F, s), −114.5 (2F, t, J = 14.1 Hz), −125.0 (2F, s), −127.1 (2F, s); (*Z*-isomer) −82.0 (2F, s), −115.6 (2F, t, J = 14.1Hz), −125.5 (2F, s), −127.1 (2F, s). EI-MS (*m/z*) 350 (M + 2^+, 2), 348 (M^+, 6), 60 (100). HRMS cacld for $C_{10}H_9O_2F_8Cl$: 348.0163, found: 348.0163.

*3.1.7. 5-(2,2,3,3,4,4,5,5,6,6,7,7,7-Tridecafluoroheptyl)-δ-valerolactone (**3da**)*

White solid; m.p. 56–57 °C. IR (cm^{-1}, KBr) 2920, 1740 (δ-lactone), 1252, 1144, 699. ^1H NMR ($CDCl_3$, 500 MHz) δ 4.77–4.71 (1H, m), 2.70–2.58 (2H, m), 2.55–2.48 (1H, m), 2.46–2.31 (1H, m), 2.13–2.08 (1H, m), 2.03–1.93 (2H, m), 1.73–1.63 (1H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 170.8, 122.6–106.0 (6C, m), 74.0, 37.8 (t, J = 21.1 Hz), 29.8, 29.2, 19.0. ^{19}F NMR ($CDCl_3$, 470 MHz) δ −81.9 (3F, t, J = 11.8 Hz), −113.1 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −114.3 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −122.9 (2F, s), −124.0 (2F, s), −124.8 (2F, s), −127.3 (2F, s). EI-MS (*m/z*) 432 (M^+, 2), 388 (100). HRMS cacld for $C_{12}H_9O_2F_{13}$: 432.0395, found: 432.0394.

*3.1.8. 7,7,8,8,9,9,10,10,11,11,12,12,12-Tridecafluorododec-4-enoic acid (**4da**)*
*7,7,8,8,9,9,10,10,11,11,12,12,12-tridecafluorododec-5-enoic acid (**5da**)*

Colorless oil; IR (cm^{-1}, KBr) 2938, 1715, 1241, 1144, 709. ^1H NMR ($CDCl_3$, 500 MHz) δ 6.43–6.36 (1H, m), 5.78–5.72

(0.7H, m), 5.70–5.61 (1H, m), 5.53–5.46 (0.7H, m), 2.79 (1.4H, td, J = 18.1 Hz, J = 7.0 Hz), 2.49–2.46 (2H, m), 2.45–2.38 (3.4H, m), 2.32–2.26 (1.4H, m), 1.86–1.79 (2H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) **4da** δ 180.1, 136.9, 118.7 (t, J = 23.2 Hz), 121.4–106.9 (6C, m), 33.7, 31.8, 23.6; **5da** δ 179.8, 142.4 (t, J = 8.9 Hz), 118.9, 121.4–106.9 (6C, m), 35.5 (t, J = 22.6 Hz), 34.0, 28.2. ^{19}F NMR ($CDCl_3$, 470 MHz) **4da** δ −82.1 (3F, t, J = 9.9 Hz), −112.7 (2F, s), −122.9 (2F, s), −124.2 (2F, s), −124.8 (2F, s), −127.4 (2F, s); **5da** δ −82.1 (3F, t, J = 9.9 Hz), −114.6 (2F, s), −123.2 (2F, s), −124.4 (2F, s), −124.8 (2F, s), −127.4 (2F, s). EI-MS (*m/z*) 432 (M^+, 14), 412 (76), 392 (100). HRMS cacld for $C_{12}H_9O_2F_{13}$: 432.0395, found: 432.0396.

*3.1.9. 2-Ethyl-5-(2,2,3,3,3-pentafluoropropyl)-δ-valerolactone (**3ab**)*

Colorless oil; IR (cm^{-1}, KBr) 2970, 1742 (δ-lactone), 1196, 795, 719. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.74–4.66 (0.6H + 0.4H, m), 2.65–2.51 (0.6H + 0.4H, m), 2.48–2.34 (1.2H, m), 2.34–2.23 (0.8H, m), 2.21–2.06 (1.2H + 0.8H, m), 2.01–1.86 (1.2H, m), 1.80–1.53 (0.6H + 0.8H + 0.8H, m), 1.52–1.44 (0.6H, m), 1.01 (1.2H, t, J = 7.5 Hz), 0.98 (1.8H, t, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ *cis* 172.9, 123.9–119.8 (2C, m), 74.8, 42.6, 37.9 (t, J = 20.9 Hz), 30.3, 25.4, 24.4, 11.7; *trans* 174.7, 117.5–113.6 (2C, m), 71.4, 40.1, 37.1 (t, J = 21.1 Hz), 28.1, 25.4, 23.3, 12.2. ^{19}F NMR ($CDCl_3$, 470 MHz) δ *cis* −86.8 (3F, s), −116.7 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −118.4 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz); *trans* −86.8 (3F, s), −116.9 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −118.5 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz). EI-MS (*m/z*) 260 (M^+, 2), 232 (100). HRMS cacld for $C_{10}H_{13}O_2F_5$: 260.0836, found: 260.0836.

*3.1.10. 2-Ethyl-5-(2,2,3,3-tetrafluoro-3-chloropropyl)-δ-valerolactone (**3bb**)*

White solid; m.p. 50–51 °C. IR (cm^{-1}, KBr) 2972, 1725 (δ-lactone), 1153, 1097, 939. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.74–4.66 (0.5H + 0.5H, m), 2.70–2.56 (0.5H + 0.5H, m), 2.44–2.30 (1H + 1H, m), 2.18–2.06 (1H + 1H, m), 2.0–1.91 (1H, m), 1.76–1.56 (0.5H + 1H + 1H, m), 1.50–1.45 (0.5H, m), 1.01 (1.5H, J = 7.5 Hz), 0.98 (1.5H, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ *cis* 172.3, 125.4–120.8 (2C, m), 74.5, 42.0, 37.2 (t, J = 21.3Hz), 29.6, 24.8, 22.6, 11.0; *trans* 174.2, 120.6–116.0 (2C, m), 71.1, 39.4, 36.3 (t, J = 21.4Hz), 27.5, 24.8, 23.8, 11.5. ^{19}F NMR ($CDCl_3$, 470 MHz) δ *cis* −72.7 (2F, s), −112.6 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 30.6 Hz, $J_{F–H}$ = 7.1 Hz), −114.3 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz); *trans* −72.7 (2F, s), −112.8 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 30.6 Hz, $J_{F–H}$ = 7.1 Hz), −114.3 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz). EI-MS (*m/z*) 276 (M^+, 2), 250 (29), 248 (100). HRMS cacld for $C_{10}H_{13}O_2F_4Cl$: 276.0540, found: 276.0540.

*3.1.11. 2-Ethyl-5-(2,2,3,3,4,4,5,5-octafluoro-5-chloropentyl)-δ-valerolactone (**3cb**)*

White solid; m.p. 59–60 °C. IR (cm^{-1}, KBr) 2953, 1731 (δ-lactone), 1186, 1128, 795, 695. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.76-4.68 (1H, m), 2.71–2.55 (1H, m), 2.46–2.36 (2H, m), 2.19–2.05 (2H, m), 2.01–1.91 (1H, m), 1.77–1.58 (3H, m), 0.98 (3H, t, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ 171.2, 121.1–114.1 (4C, m), 73.2, 40.9, 36.4 (t, J = 21.0 Hz), 28.7, 23.8, 21.6, 10.0. ^{19}F NMR ($CDCl_3$, 470 MHz) δ −69.0 (2F, t, J = 12.7 Hz), −112.5 to −114.7 (2F, m), −120.8 (2F, s), −123.9 (2F, s). EI-MS (*m/z*) 376 (M^+, 2), 350 (30), 348 (100). HRMS cacld for $C_{12}H_{13}O_2F_8Cl$: 376.0476, found: 376.0476.

*3.1.12. 2-Ethyl-5-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)-δ-valerolactone (**3db**)*

White solid; m.p. 60–61 °C. IR (cm^{-1}, KBr) 2981, 1728 (δ-lactone), 1206, 1146, 702, 659. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.76–4.68 (0.5H + 0.5H, m), 2.71–2.56 (0.5H + 0.5H, m), 2.47–2.25 (1H + 1H, m), 2.22–2.06 (1H + 1H, m), 2.01–1.87 (1H, m), 1.81–1.56 (0.5H + 1H + 1H, m), 1.54–1.45 (0.5H, m), 1.01 (1.5H, t, J = 7.4 Hz), 0.98 (1.5H, t, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ *cis* 174.7, 120–108 (6C, m), 71.4, 40.1, 37.3 (t, J = 21.0 Hz), 28.2, 24.4, 23.3, 12.1; *trans* 172.9, 120–108 (6C, m), 74.8, 42.6, 38.1 (t, J = 20.8 Hz), 30.4, 29.8, 25.5, 11.7. ^{19}F NMR ($CDCl_3$, 470 MHz) δ −81.7 (3F, t, J = 9.4 Hz), −112.4 to −114.6 (2F, m), −122.7 (2F, s), −123.8 (2F, s), −124.5 (2F, s), 127.1 (2F, q, J = 9.4 Hz). EI-MS (*m/z*) 460 (M^+, 3), 432 (100). HRMS cacld for $C_{14}H_{13}O_2F_{13}$: 460.0708, found: 460.0703.

*3.1.13. 2-Benzyl-5-(2,2,3,3,3-pentafluoropropyl)-δ-valerolactone (**3ac**)*

Colorless oil; IR (cm^{-1}, KBr) 2932, 1741 (δ-lactone), 1198, 1096, 746, 702. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33–7.29 (2.5H, m), 7.25–7.18 (2.5H, m), 4.72–4.65 (0.5H, m), 4.64–4.57 (0.5H, m), 3.40 (0.5H, dd, J = 13.7 Hz, J = 4.0 Hz), 3.34 (0.5H, dd, J = 13.9 Hz, J = 4.4 Hz), 2.88–2.74 (1H, m), 2.71–2.63 (1H, m), 2.62–2.48 (1H, m), 2.36–2.17 (1H, m), 2.11–1.95 (1H + 0.5H, m), 1.92–1.85 (0.5H, m), 1.78–1.68 (0.5H, m), 1.68–1.53 (0.5H + 1H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ *cis* 171.7, 138.4, 129.2, 128.6, 126.7, 120.1–118.3 (2C, m), 74.4, 42.5, 37.5, 37.2 (t, J = 21.0 Hz), 29.5, 24.8; *trans* 173.6, 138.6, 129.1, 128.6, 126.7, 118.0–116.2 (2C, m), 70.8, 39.9, 36.7, 36.3 (t, J = 21.2 Hz), 27.2, 22.3. ^{19}F NMR ($CDCl_3$, 470 MHz) δ *cis* −86.8 (3F, s), −116.7 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −118.3 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz); *trans* −86.7 (3F, s), −116.9 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −118.4 (1F, ddd, $J_{F–F}$ = 267.9 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz). EI-MS (*m/z*) 322 (M^+, 59), 91 (100). HRMS cacld for $C_{15}H_{15}O_2F_5$: 322.0992, found: 322.0992.

*3.1.14. 2-Benzyl-5-(2,2,3,3-tetrafluoro-3-chloropropyl)-δ-valerolactone (**3bc**)*

White solid; m.p. 50–53 °C. IR (cm^{-1}, KBr) 2958, 1720 (δ-lactone), 1094, 937, 741, 700. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.34–7.28 (2.5H, m), 7.25–7.18 (2.5H, m), 4.73–4.66 (0.5H, m), 4.65–4.57 (0.5H, m), 3.40 (0.5H, dd, J = 13.7 Hz, J = 4.1 Hz), 3.33 (0.5H, dd, J = 13.9 Hz, J = 4.4 Hz), 2.86–2.76 (1H, m), 2.72–2.55 (1H + 1H, m), 2.40–2.22 (1H, m), 2.10–1.95 (1H + 0.5H, m), 1.92–1.85 (0.5H, m), 1.78–1.68

(0.5H, m), 1.68–1.52 (0.5H + 1H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) δ *cis* 171.7, 138.4, 129.2, 128.6, 126.7, 116.1–111.6 (2C, m), 74.7, 42.5, 37.6, 37.1 (t, J = 21.4 Hz), 29.6, 24.8; *trans* 173.7, 138.6, 129.1, 128.6, 126.7, 123.5–120 (2C, m), 71.2, 39.9, 36.7, 36.3 (t, J = 21.5 Hz), 27.2, 22.4. ^{19}F NMR ($CDCl_3$, 470 MHz) *δ cis* −72.7 (2F, s), −112.6 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 4.7 Hz), −114.2 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz); *trans* −72.7 (2F, s), −112.9 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz), −114.3 (1F, ddd, $J_{F–F}$ = 258.5 Hz, $J_{F–H}$ = 28.2 Hz, $J_{F–H}$ = 9.4 Hz). EI-MS (*m*/*z*) 340 (M + 2$^+$, 31), 338 (M$^+$, 100), 91 (78). HRMS cacld for $C_{15}H_{15}O_2F_4Cl$: 338.0697, found: 338.0697.

*3.1.15. 2-Benzyl-5-(2,2,3,3,4,4,5,5-octafluoro-5-chloropentyl)-δ-valerolactone (**3cc**)*

White solid; m.p. 61–64 °C. IR (cm^{-1}, KBr) 2945, 1725 (δ-lactone), 1130, 742, 698. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.33–7.29 (2.5H, m), 7.25–7.18 (2.5H, m), 4.75–4.68 (0.5H, m), 4.67–4.61 (0.5H, m), 3.40 (0.5H, dd, J = 13.7 Hz, J = 4.1 Hz), 3.34 (0.5H, dd, J = 13.9 Hz, J = 4.4 Hz), 2.86–2.76 (1H, m), 2.72–2.53 (1H + 1H, m), 2.40–2.20 (1H, m), 2.10–1.95 (1H + 0.5H, m), 1.92–1.84 (0.5H, m), 1.79–1.53 (0.5H + 0.5H + 1H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) *δ cis* 172.4, 139.1, 129.9, 129.3, 127.4, 114.9–109.8 (4C, m), 75.1, 43.2, 38.2, 38.1 (t, J = 20.9 Hz), 30.3, 25.5; *trans* 174.3, 139.3, 129.8, 129.3, 127.4, 125.1–120.0 (4C, m), 71.6, 40.6, 37.4, 37.2 (t, J = 21.1 Hz), 27.9, 23.0. ^{19}F NMR ($CDCl_3$, 470 MHz) *δ* −69.0 (2F, t, J = 12.7 Hz), −112.5 to −114.7 (2F, m), −120.7 (2F, s), −123.9 (2F, s). EI-MS (*m*/*z*) 440 (M + 2$^+$, 12), 438 (M$^+$, 38), 91 (100). HRMS cacld for $C_{17}H_{15}O_2F_8Cl$: 438.0633, found: 438.0633.

*3.1.16. 2-Benzyl-5-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)-δ-valerolactone (**3dc**)*

White solid; m.p. 75–77 °C. IR (cm^{-1}, KBr) 1720 (δ-lactone), 1192, 1144, 701. ^{1}H NMR ($CDCl_3$, 500 MHz) *δ* 7.34–7.29 (2.5H, m), 7.25–7.18 (2.5H, m), 4.75–4.68 (0.5H, m), 4.67–4.60 (0.5H, m), 3.40 (0.5H, dd, J = 13.7 Hz, J = 4.1 Hz), 3.34 (0.5H, dd, J = 13.9 Hz, J = 4.4 Hz), 2.87–2.77 (1H, m), 2.72–2.53 (1H + 1H, m), 2.40–2.22 (1H, m), 2.10–1.96 (1H + 0.5H, m), 1.92–1.85 (0.5H, m), 1.80–1.54 (0.5H + 0.5H + 1H, m). ^{13}C NMR ($CDCl_3$, 125.8 MHz) *δ cis* 171.7, 138.4, 129.2, 128.6, 126.7, 102.3–97.9 (6C, m), 74.4, 42.5, 37.6, 37.4 (t, J = 21.2 Hz), 29.6, 24.9; *trans* 173.6, 138.6, 129.1, 128.6, 126.7, 117.6–113.2 (6C, m), 70.8, 39.9, 36.7, 36.6 (t, J = 21.3 Hz), 27.3, 22.3. ^{19}F NMR ($CDCl_3$, 470 MHz) *δ* −81.7 (3F, t, J = 9.6 Hz), −112.5 to −114.6 (2F, m), −122.7 (2F, s), −123.8 (2F, s), −124.5 (2F, s), 127.1 (2F, q, J = 9.4 Hz). EI-MS (*m*/*z*) 522 (M$^+$, 69), 91 (100). HRMS cacld for $C_{19}H_{15}O_2F_{13}$: 522.0864, found: 522.0864.

Acknowledgement

This research work was supported by the National Natural Science Foundation of China (Grant no. 20672034).

References

[1] F. Bennett, D.W. Knight, G. Fenton, J. Chem. Soc. Perkin Trans. 1 (1991) 133–140.
[2] N. Acton, R.J. Roth, J. Org. Chem. 57 (1992) 3610–3614.
[3] C. Wang, G.A. Russell, J. Org. Chem. 64 (1999) 2066–2069.
[4] (a) I. Ojima, J.R. McCarthy, J.T. Welch, ACS Symposium Series 639 American Chemical Society, Washington, DC, 1996;
(b) T. Itoh, K. Kudo, K. Yokota, N. Tanaka, S. Hayase, M. Renou, Eur. J. Org. Chem. (2004) 406–412.
[5] N.O. Brace, J. Org. Chem. 29 (1964) 1247–1249.
[6] (a) X.W. Zou, F.H. Wu, Y.J. Shen, S. Xu, W.Y. Huang, Tetrahedron 59 (2003) 2555–2560;
(b) F.H. Wu, X.Y. Yang, Z.H. Wang, W.Y. Huang, J. Fluorine Chem. 128 (2007) 84–86;
(c) S.J. Mao, X. Fang, L. Ba, F.H. Wu, J. Fluorine Chem. 128 (2007) 5–11;
(d) X.Y. Yang, Y.P. Zhu, X. Fang, X.J. Yang, F.H. Wu, Y.J. Shen, J. Fluorine Chem. 128 (2007) 174–178;
(e) X.Y. Yang, Z.H. Wang, X. Fang, X.J. Yang, F.H. Wu, Y.J. Shen, Synthesis 12 (2007) 1768–1778.
[7] (a) N.O. Brace, J. Fluorine Chem. 108 (2001) 147–175;
(b) N.O. Brace, Paper 0.20 Presented at the Fourth International Symposium Organic Free Radicals Sponsored by the Royal Society of Chemistry, July 10, University of St. Andrews, Scotland, 1984.
[8] (a) Q.Y. Chen, Z.Y. Yang, J. Fluorine Chem. 28 (1985) 399–411;
(c) Z.Y. Yang, D.J. Burton, J. Fluorine Chem. 45 (1989) 435–439.
[9] (a) N.O. Brace, J. Org. Chem. 27 (1962) 4491–4498;
(b) N.O. Brace, J. Org. Chem. 36 (1971) 1904–1909.
[10] W.M. Qiu, D.J. Burton, J. Org. Chem. 58 (1993) 419–423.
[11] R.T. Conley, Infrared Spectroscopy, Second ed., Allyn and Bacon, Inc., Boston, 1966, pp. 143–150/167–173.