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Sodium dithionite initiated regio- and stereoselective radical addition of polyfluoroalkyl iodide with norbornene analogs

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Abstract—Sodium dithionite initiated free-radical addition of polyfluoroalkyl iodides (**2m–2s**) with norbornene **1a** and its derivatives, such as norbornene-2-carboxylates **1b** and **1c**, and norbornene-2-carboxylic acids **1d** and **1e** was investigated. In all the cases, the addition of R_F group was stereoselectively delivered at *exo*-position and the predominant configuration of products was trans. Under the similar condition, norbornene-2-carboxylic ethyl ester **1b** reacted with **2p** to give 6-*exo*-R_F-5-*endo*-iodo adduct **3bp** and 5-*exo*-R_F-6-*endo*-iodo adduct **5bp** in the ratio of 4:1. While **1c**, which has a heavy crowded group in the 2-*endo*-position, gave 6-*exo*-R_F-5-*endo*-iodo adduct **3cp** and polyfluoroalkylated product **4cp** retaining the trans-configuration and the *exo*-orientation of R_F group. The fluoroalkylation–lactonization reaction occurred in the reaction of norbornene-2-*endo*-carboxylic acids **1d** and **1e** with polyfluoroalkyl iodides to afford the corresponding fluoroalkylated γ-lactone products (**7dp–7ds**, and **7em–7er**). The configuration of the products was further confirmed by 2D NMR and X-ray diffraction analyses for the first time.

1. Introduction

The free-radical addition reaction of polyfluoroalkyl iodides with unsaturated compounds, such as olefins and alkynes, was an important method to prepare fluorinated compounds, which could usually be initiated by high temperature, UV, peroxide, metals, metal complexes, etc.[1] The reactions initiated by the sulfinatodehalogenated reagents, such as sodium dithionite, sodium disulfite, Rongalite, thiourea dioxide, and so on, have been extensively studied in our laboratory.[2] This reaction and its applications in industry have been described in many literatures,[3] however, the stereochemistry of this addition reaction, which played important roles in its theoretical chemistry and industrial utility, had seldom been mentioned. Accordingly, we had paid much attention to it and hoped to do some research in this aspect. Norbornene and its derivatives were usually chosen for the investigation of stereoselective addition of electrophiles at the double bond due to its special spatial structure,[4] however, the addition of norbornene analogs with polyfluoroalkyl iodides was examined in few cases in the literature. Brace investigated the reaction of norbornene and its symmetrical 2,3-dicarboxylic acid derivatives with polyfluoroalkyl iodides and pointed out that the configuration of the adducts was determined by the steric and electronic factor of the substrates and the reaction conditions,[5] therefore the high stereoselective addition might be reasonable by using the asymmetrical substrates under mild reaction conditions. Herein we investigated the regio- and stereoselectivity of the radical anion addition of polyfluoroalkyl iodides with norbornene and some asymmetrical derivatives initiated by sodium dithionite.

2. Results and discussion

2.1. The reaction of norbornene 1a with polyfluoroalkyl iodide

The reaction of norbornene **1a** with polyfluoroalkyl iodides was investigated at first. In the presence of sodium dithionite and sodium bicarbonate, the free-radical addition of R_FI (**2m–2q**) to norbornene **1a** occurred smoothly at room temperature in aqueous acetonitrile solution (CH_3CN–H_2O=3:1 (v/v)), after usual workup only trans-adduct with R_F at the *exo*-position (**3am–3aq**) was isolated in 63–91% yields by column chromatography (Scheme 1 and Table 1), which were consistent with the results reported by Brace.[5a,b] The heavy steric hindrance of R_F led to its attacking at the double bond from the *exo*-position of **1a** followed by the *endo*-oriented attack of iodine. By changing R_FI to uncrowded ethyl iododifluoroacetate (**2r**) the mixture of trans-adduct (**3ar**) and cis-adducts (**4ar**) was obtained in 87% overall yield in the ratio of 5:1 (Scheme 2). We had reported that the addition of **2r** with cyclopentene and cyclohexene gave only trans-adduct for the former and cis–trans mixture

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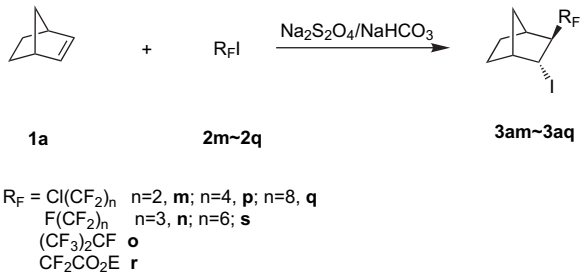
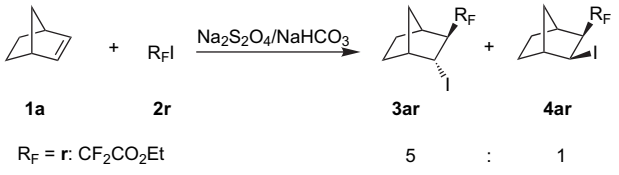


Scheme 1.

Table 1. Addition of norbornene with R_FI

Entry	Substrates	R_FI	Products	Configuration		Yields (%)
				R_F	R_F/I	
1	**1a**	**2m**	**3am**	*exo*	trans	78
2	**1a**	**2n**	**3an**	*exo*	trans	82
3	**1a**	**2o**	**3ao**	*exo*	trans	87
4	**1a**	**2p**	**3ap**	*exo*	trans	87
5	**1a**	**2q**	**3aq**	*exo*	trans	91
6	**1a**	**2r**	**3ar–4ar** (5:1)	*exo*	trans+cis	87

(1:1.6) for the latter under the similar condition.[6] It has been reported that different ratio of trans- and cis-adducts was obtained in the radical addition of ethyl bromoacetate with norbornene bearing various steric substituents.[5a,7] Therefore it can be speculated that the mode of addition depends heavily on the adding group and the structure of substrates in this reaction.



Scheme 2.

The IR and ^1H NMR spectra were usually utilized to determine the configuration of adducts in the literatures,[5a,b] herein the stereo configuration of adducts was determined via 2D NMR spectrum. Compound **3ap** (Fig. 1) was taken as a typical example for the configuration analyses of compounds **3**. The assignment of the chemical shift in ^1H NMR was accomplished by the analysis of ^1H NMR, ^{13}C NMR, DEPT, HMBC, HMQC, etc. The observation of strong correlativity of H1–H2 and no obvious correlativity of H3–H4 in ^1H–^1H COSY combined with interaction of H2–H7s and no or weak interaction of H3–H7s in NOESY

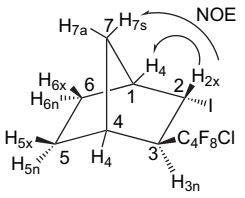


Figure 1.

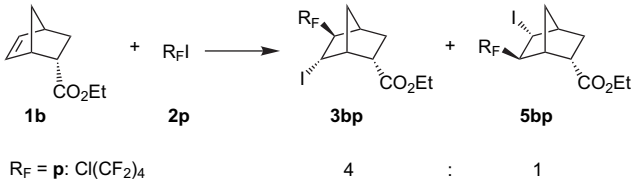
demonstrated its trans-configuration with R_F at *exo*-position and iodine atom at *endo*-position.

2.2. The reaction of 5-norbornene-2-*endo*-carboxylic acid ester 1b and 1c with R_FI

When **1b** reacted with **2p** under the same condition, two adducts **3bp** and **5bp** were obtained in the ratio of 4:1 (Table 2). Spectral data (1D and 2D NMR) showed that R_F was at the *exo*-position of C5 and iodine was at the *endo*-position of C6 of norbornene in **3bp** whereas R_F was at the *exo*-position of C5 and iodine was at the *endo*-position of C6 in **5bp** (Scheme 3).

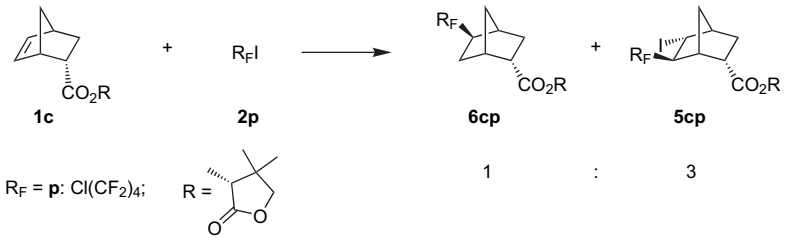
Table 2. Addition of norbornene-2-*endo*-carboxylic ester with R_FI

Entry	Substrates	R_FI	Products	Configuration		Overall yields (%)
				R_F	R_F/I	
1	**1b**	**2p**	**3bp–5bp** (4:1)	*exo*	trans	63
2	**1c**	**2p**	**6cp–5cp** (1:3)	*exo*	trans (**5cp**)	88



Scheme 3.

In order to examine steric hindrance effect, norbornene-2-*endo*-ester **1c**, bicyclo[2.2.1]hept-5-ene-2-carboxylic acid-4,4-dimethyl-2-oxo-tetrahydro-furan-3-yl ester, was allowed to react with **2p** (Scheme 4). Ester **1c** was synthesized via Diels–Alder addition of cyclopenta-1,3-diene with acrylic acid 4,4-dimethyl-2-oxotetrahydro-furan-3-yl ester, which was condensed from 3-hydroxy-4,4-dimethyl-dihydro-furan-2-one and acryl chloride.[10] The reaction of **1c** with **2p** proceeded at room temperature in the water and acetonitrile solution (v/v=1:1), two products (**5cp–6cp**=3:1) were isolated by column chromatography (eluent: PE–EA=30:1) in 88% overall yield (Table 2).



Scheme 4.

Similar analyses of the spectral data (1D and 2D NMR) showed that **5cp** was a trans-adduct with R_F at the *exo*-position of C5 and iodine at the *endo*-position of C6 of norbornene, and **6cp** was the fluoroalkylated–deiodined product with R_F at the *exo*-position of C6 of norbornene, which was formed via the addition of H atom (from the solvent) to the C5 after the addition of R_F to *exo*-position of norbornene. To ascertain our deduction, the structure was further confirmed by the X-ray crystallography of **5cp** and **6cp** (Figs. 2 and 3).

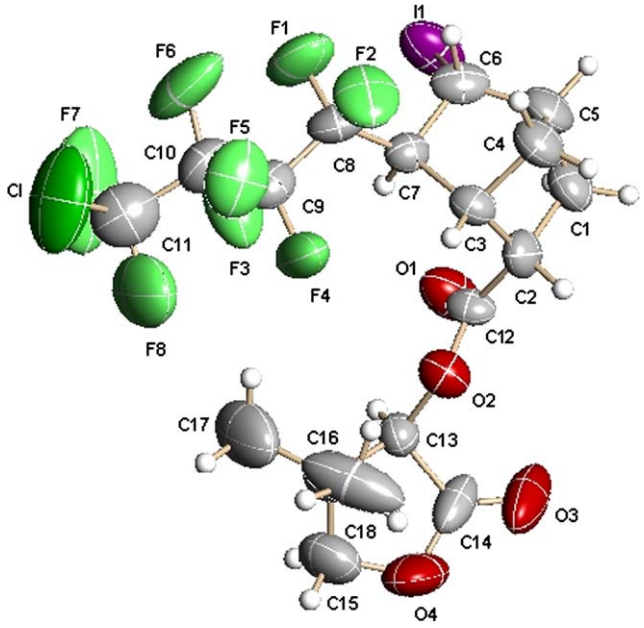


Figure 2. ORTEP of compound **5cp**.

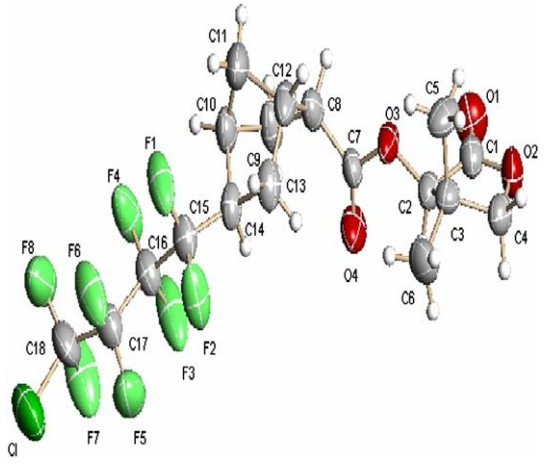


Figure 3. ORTEP of compound **6cp**.

It was observed from the crystallography of **6cp** that the 6-*endo*-position of norbornene had been filled with the crowded group (acrylic acid 4′,4′-dimethyl-2′-oxo-tetrahydro-furan-3′-yl ester) at 2-*endo*-position of norbornene, and the *exo*-position of the norbornene was crowded with great group C_4F_8Cl in the neighboring C3 and the 7-CH_2 group, which make it hard for the bulky iodine atom to approach the C6 from the *endo* or the *exo*-position of norbornene, however, the media H_2O molecule, which surrounded the free-radical intermediate could attack the C6 of norbornene to give compound **6cp**.

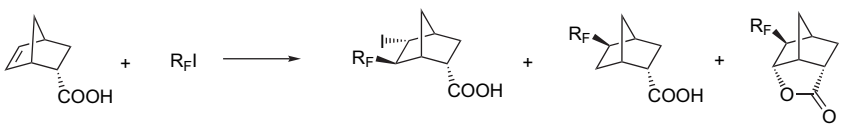
2.3. The reaction of norbornene-carboxylic acid 1d and 2-methyl-norbornene-carboxylic acid 1e with R_F

Besides the 6-*exo*-fluoroalkyl-5-*endo*-iodo adducts **5dp–5ds** and the fluoroalkylated compounds **6dp–6ds**, the addition of norbornene-2-*endo*-carboxylic acid **1d** with polyfluoroalkyl iodide gave the corresponding lactones **7dp–7ds** (Scheme 5 and Table 3). Similarly in all the cases R_F was added at *exo*-position of norbornene and iodine atom was added at *endo*-position. The lactone was produced via the iodolactonization of the intermediate adduct 5-*exo*-fluoroalkyl-6-*endo*-iodo-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid under the basic condition. The double peak at δ_H=4.95 ppm in ^{1}H NMR, the peak at δ_C=78.7 ppm in ^{13}C NMR, and ν=1780 cm^{-1} in IR revealed that there existed the latcone group in **7dp–7ds**. All the same configurations were confirmed by the analysis of COSY and NOESY spectra for **7dp–7ds**, **6dp–6ds**, and **5dp–5ds** and further by the crystallography of **5ds** (Fig. 4).

It is curious that there were no polyfluoroalkylated products formed except the 5-*exo*-R_F-latcone **7em–7ep** and the 6-*exo*-R_F-5-*endo*-adduct **5em–5ep** observed in the reaction of R_FI with **1e**, which have much similar structure with **1d** (Table 3 and Scheme 6). The ratio of **5em–5ep** and **7em–7ep** was from 2.1:1.0 to 0.9:1.0 with 50–72% overall yields. The crystallography of **5eo** (Fig. 5) and 2D NMR spectra were consistent with the trans-configuration of **5em–5ep** and **7em–7ep** with R_F at the *exo*-position of norbornene.

Table 3. Addition of norbornene-2-*endo*-carboxylic acid with R_FI

Entry	Substrate	R_FI	Product	Configuration		Yield (%)
				R_F	R_F/I	
1	**1d**	**2p**	**5dp–6dp–7dp** (1.0:1.1:0.8)	*exo*	trans (**5dp**)	70
2	**1d**	**2q**	**5dq–6dq–7dq** (1.0:1.5:0.3)	*exo*	trans (**5dq**)	52
3	**1d**	**2s**	**5ds–6ds–7ds** (1.0:1.1:0.8)	*exo*	trans (**5ds**)	58
4	**1e**	**2n**	**5en–7en** (1.0:1.0)	*exo*	trans (**5en**)	67
5	**1e**	**2o**	**5eo–7eo** (2.1:1.0)	*exo*	trans (**5eo**)	50
6	**1e**	**2p**	**5ep–7ep** (0.9:1.0)	*exo*	trans (**5ep**)	72



1d **2p, 2q, 2s** **5dp, 5dq, 5ds** **6dp, 6dq, 6ds** **7dp, 7dq, 7ds**

R_F = **p**: $Cl(CF_2)_4$; **q**: $Cl(CF_2)_8$; **s**: $F(CF_2)_6$

Scheme 5.

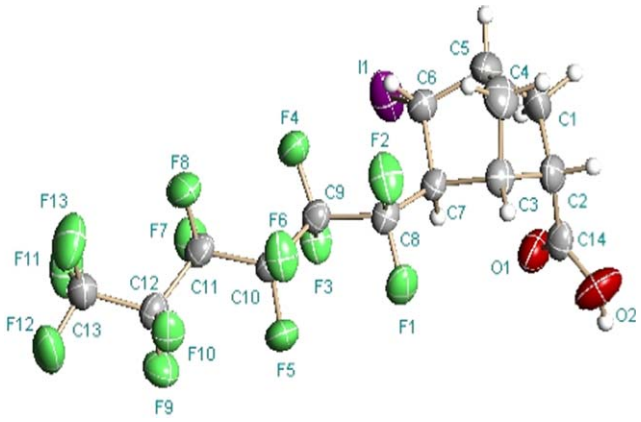
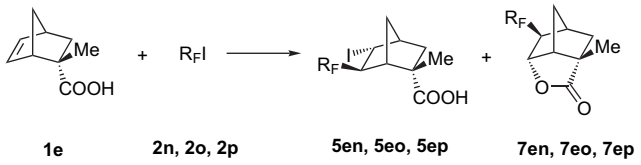


Figure 4. ORTEP of **5ds**.



1e **2n, 2o, 2p** **5en, 5eo, 5ep** **7en, 7eo, 7ep**

R_F = **n**: $F(CF_2)_3$; **o**: $(CF_3)_2CF$; **p**: $Cl(CF_2)_4$

Scheme 6.

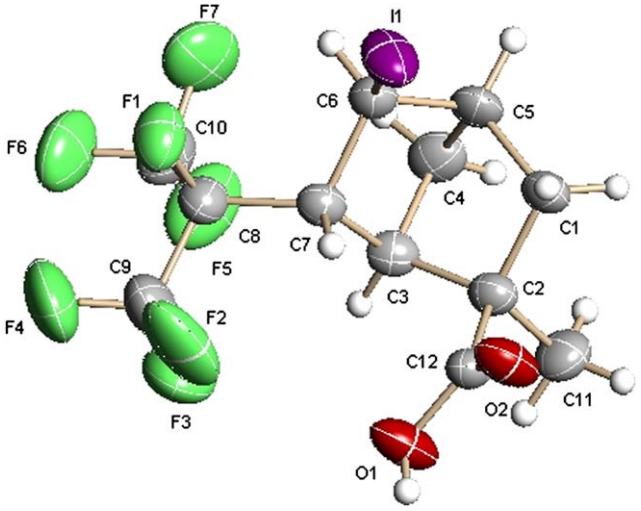
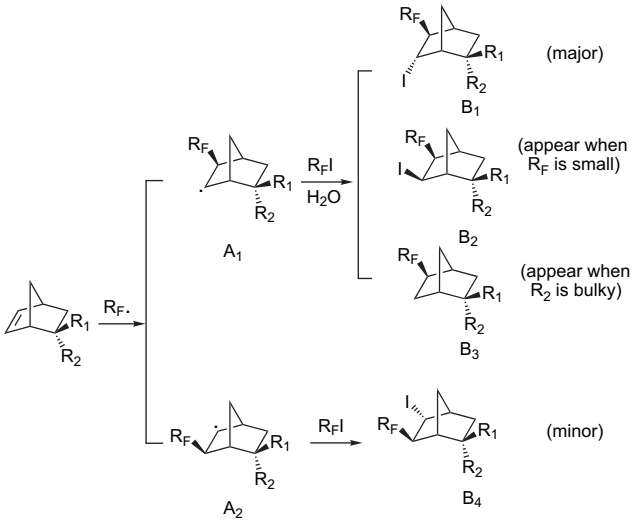


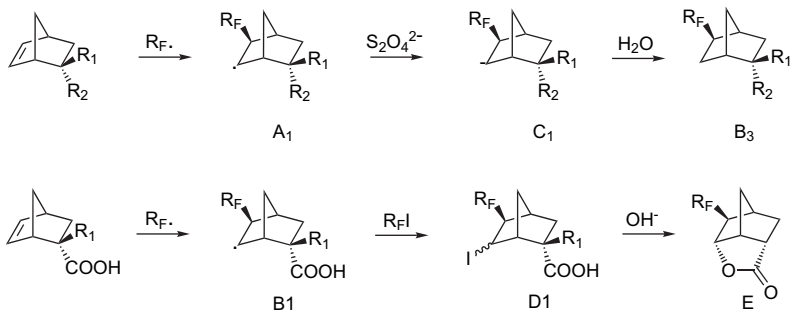
Figure 5. ORTEP of **5eo**.

2.4. Mechanism for the free-radical addition of norbornene and its 2-substituted derivatives with R_FI initiated by $Na_2S_2O_4$

According to the literatures,[3c,5] the supposed mechanism was described as following (Scheme 7): (1) R_F· was generated from R_FI under the initiation of $Na_2S_2O_4$, (2) 5-*exo*-R_F intermediates A_1 and 6-*exo*-R_F intermediate A_2 were produced by stereoselectively *exo*-oriented addition of R_F· to C=C of the norbornene and its derivatives, and (3) 5-*exo*-R_F-6-*endo*-iodo adduct B_1 was produced from the reaction of A_1 with R_FI and 6-*exo*-R_F-5-*endo*-iodo adduct B_2 was produced from the reaction of A_1 with R_FI. In this mechanism, the third step was the rate-determined step, which was influenced by steric and electronic effect of the substrate and adding group and played important roles in the configuration of the adducts. For the uncrowded R_FI (e.g., ICF_2COOEt), some cis-adducts were produced accompanying the trans-adducts and when the 2-*endo*-position was taken by bulky group, an anion C1 was obtained by transferring an electron to radical A1 from $S_2O_4^{2-}$, and then the hydrogenated product B_3 was obtained by the abstraction of proton from H_2O (Scheme 8). For norbornene-2-carboxylic acids **1d** and **1e**, the lactone E was obtained by base-catalyzed iodolactonization from the adduct D1 (Scheme 8).



Scheme 7. Mechanism proposed for this reaction.



Scheme 8. Mechanism proposed for the production of hydrogenated product and lactonizated product.

Generally we concluded that the free-radical addition reaction of norbornene and its 2-substituted derivatives with R_FI initiated by sodium dithionite was of high regio- and stereoselectivity with the addition of the R_F group to *exo*-position due to the narrow space of the *endo*-position of norbornene and its 2-*endo*-derivatives. The main products were of trans-configuration due to the heavily steric hindrance of the neighboring R_F group, which led to the predominant addition of iodine at the *endo*-position, and in some cases, the polyfluoroalkylated products were produced in concomitant with adducts. In the case of norbornene-2-*endo*-carboxylic acids, polyfluoroalkylated lactones were obtained from the polyfluoroalkylation–lactonization reaction of the adduct 5-*exo*-R_F-6-*endo*-iodobicyclo[2.2.1]heptane-2-*endo*-carboxylic acid under the basic condition.

3. Experimental

3.1. General

Melting points were measured in WRS-1B digital melting point instrument. IR spectra were taken on a Nicolet FTIR 20sx IR spectrophotometer. ^{1}H NMR spectra were measured on a Bruker AC500 (500 MHz) spectrometer using TMS as internal standard. ^{19}F NMR spectra were taken on a Bruker AC500 (500 MHz) spectrometer; chemical shifts are reported as $\delta_{CFCl_3}(\delta_{CFCl_3} = \delta_{TFA} - 76.8)$, negative for upfield shifts. Mass spectra were obtained on a Finnigan GC–MS 4021 spectrometer. X-ray data were measured at 293 K on a Bruker SMART CCD diffractometer with graphite monochromated Mok\α radiation. Column chromatography was performed using silica gel H, particle size was 10–40 μm.

3.2. Typical experimental procedure for the reaction of the norbornene 1a with R_FI

Norbornene (10 mmol) and polyfluoroalkyl iodide (12 mmol) were dissolved in the solution of water (10 mL) and acetonitrile (10 mL). Sodium dithionite (3.7 g) and sodium bicarbonate (1.85 g) were added to the solution. The mixture was stirred at ambient temperature for 6 h. When the reaction was accomplished, the mixture was treated with water (ca. 50 mL). The mixture was extracted with ether of 3×20 mL. The combined organic layers were washed with saturated brine and dried over anhydrous sodium sulfate. After the evaporation of ether, the crude product was purified by column chromatography (PE–EA=200:1) to give products **3am–3ar** and **4ar**.

3.2.1. 3-e*xo*-(2-Chloro-1,1,2,2-tetrafluoroethyl)-2-*endo*-iodobicyclo[2.2.1]heptane (3am). Oil. IR (film): ν_{max} 2980 (C–H), 1230 (C–F), 1150, 1080, 930, 800, 750, 640 (C–I) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.24–1.26 (2H, m, H-7, H-5), 1.56–1.58 (2H, m, H-6, H-5), 1.62–1.67 (1H, m, H-7), 1.82–1.90 (1H, m, H-6), 2.20–2.32 (1H, m, H-3), 2.38 (1H, s, H-4), 2.42 (1H, s, H-1), 4.15–4.25 (1H, m, H-2); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −117.1 (2F, dd, *J*=385.8, 268.2 Hz, CF_2CF_2Cl), −69.3 (2F, dd, *J*=240.0, 174.1 Hz, CF_2Cl); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 27.3 (s, C-2), 28.2 (s, C-6), 30.4 (s, C-5), 35.6 (s, C-7), 38.8 (s, C-4), 45.4 (s, C-1), 56.0 (t, *J*=20 Hz, C-3), 115.5–118.0 (m, CF_2), 119.0–124.7 (m, CF_2Cl); HRMS calcd for $C_9H_{10}ClF_4I$: 355.9452, found: 355.9464.

3.2.2. 3-*exo*-(Heptfluoro-propyl)-2-*endo*-iodobicyclo-[2.2.1]heptane (3an). Oil. IR (film): ν_{max} 2980 (C–H), 1340, 1230 (C–F), 1180, 1110, 930, 740, 650 (C–I) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.24–1.26 (2H, m, H-7, H-5), 1.56–1.60 (1H, m, H-6), 1.61–1.75 (2H, m, H-5, H-7), 1.80–1.90 (1H, m, H-6), 2.20–2.28 (1H, m, H-3), 2.36 (1H, s, H-4), 2.42 (1H, s, H-1), 4.20–4.26 (1H, m, H-2); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −126.1 (2F, s, CF_2CF_3), −119.1 (2F, dd, *J*=1411.5, 277.8 Hz, $CHCF_2$), −81.5 (3F, t, *J*=10.4 Hz, CF_3); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 24.8 (s, C-2), 26.4 (s, C-6), 28.7 (s, C-5), 34.0 (s, C-7), 36.8 (s, C-4), 43.6 (s, C-1), 54.5 (t, *J*=20.1 Hz, C-3), 106.0–120.5 (m, $CF_2CF_2CF_3$); HRMS calcd for $C_{10}H_{10}F_7I$: 389.9716, found: 389.9720.

3.2.3. 3-*exo*-(Heptfluoroisopropyl)-2-*endo*-iodo-bicyclo-[2.2.1]heptane (3ao). Oil. IR (film): ν_{max} 2980 (C–H), 1300, 1220 (C–F), 1150, 1030, 970, 740, 650 (C–I) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.25–1.40 (2H, m, H-5, H-7), 1.62–1.75 (3H, m, H-5, H-6, H-7), 1.80–2.00 (1H, m, H-6), 2.25–2.31 (1H, m, H-3), 2.41 (1H, s, H-4), 2.43 (1H, s, H-1), 4.30–4.50 (1H, m, H-2), ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −75.8 (6F, d, *J*=682.2 Hz, $(CF_3)_2$), −76.4 (1F, m, CF); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 28.5 (s, C-2), 28.7 (s, C-6), 31.3 (s, C-5), 35.3 (s, C-7), 39.1 (s, C-4), 46.1 (s, C-1), 55.6 (d, *J*=18.9 HZ, C-3), 92.1 (dm, *J*=206.1, 30.8 Hz, CF), 121.7 (ddd, *J*=576.0, 288.0, 28.9 Hz, $(CF_3)_2$); HRMS calcd for $C_{10}H_{10}F_7I$: 389.9716, found: 389.9717.

3.2.4. 3-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-2-*endo*-iodo-bicyclo[2.2.1]heptane (3ap). Oil. IR (film): ν_{max} 2980 (C–H), 1230 (C–F), 1080, 760, 720, 640 (C–I) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.20–1.40 (2H, m, H-5, H-7), 1.50–1.68 (1H, m, H-6), 1.80–1.92 (2H, m, H-5, H-7), 2.35–2.40 (1H, m, H-3), 2.44 (1H, s, H-4), 2.49 (1H, s, H-1), 4.31–4.35 (1H, m, H-2); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −120.9 (4F, m, CF_2CF_2), −118.8 (2F, m $CHCF_2$), −68.8 (2F, m, CF_2Cl); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 26.7 (s, C-2), 28.2 (s, C-6), 30.4 (s, C-5), 35.7 (s, C-7), 38.6 (s, C-4), 45.3 (s, C-1), 56.4 (t, *J*=20.1 Hz, C-3), 110.0–125.2 (m, $(CF_2)_4$); HRMS calcd for $C_{11}H_{10}ClF_8I$: 455.9388, found: 455.9407.

3.2.5. 3-*exo*-(8-Chloro-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluorooctyl)-2-*endo*-iodo-bicyclo[2.2.1]heptane (3aq). White solid. Mp: 56–57 °C; IR (film): ν_{max} 2980 (C–H), 1220 (C–F), 1150, 840, 770, 670, 650 (C–I) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31–1.33 (2H, m, H-7, H-5), 1.60–1.65 (1H, m, H-6), 1.68–1.72 (2H, m, H-5, H-7), 1.80–1.90 (1H, m, H-6), 2.35–2.38 (1H, m, H-3), 2.44 (1H, s, H-4), 2.49 (1H, s, H-1), 4.30–4.33 (1H, m, H-2); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −122.7 (6F, m, 3×CF_2), −122.2 (2F, m, CF_2), −121.8 (2F, m, CF_2), −121.1 (2F, m, CF_2), −118.2 (2F, dd, *J*=1270.4, 282.3 Hz, $CHCF_2$), −69.0 (2F, m, CF_2Cl); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 26.0 (s, C-2), 27.5 (s, C-6), 29.7 (s, C-5), 35.0 (s, C-7), 37.9 (s, C-4), 44.6 (s, C-1), 57.7 (t, *J*=20.1 Hz, C-3), 108.7–124.2 (m, $(CF_2)_8$); HRMS calcd for $C_{15}H_{10}ClF_{16}$ (M−I): 529.0216, found: 529.0222.

3.2.6. 3-*exo*-Difluoro-(2-*endo*-iodo-bicyclo[2.2.1]hept-3-yl)-acetic acid ethyl ester (3ar). Oil. IR (film): ν_{max} 2980, 2900, 1770 (s, ester), 1450, 1310, 1080, 850, 780 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.25–1.31 (1H, m, H-7, H-5), 1.38 (3H, t, J=7.1 Hz, CH_3), 1.60–1.62 (1H, m, H-6), 1.63–1.65 (1H, m, H-5), 1.68–1.70 (1H, m, H-7), 1.75–1.85 (1H, m, H-5), 2.20–2.30 (1H, m, H-2), 2.35 (1H, s, H-1), 2.47 (1H, s, H-4), 4.20–4.40 (1H, m, H-3), 4.37 (2H, q, J=7.1 Hz, OCH_2); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −116.2 (dd, $J_{F,F}$=253.8 Hz, $J_{F,H}$=18.8 Hz, 1F), −110.1 (dd, $J_{F,F}$=253.8 Hz, $J_{F,H}$=14.1 Hz, 1F); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 14.6 (s, CH_3), 27.9 (s, C-6), 27.9 (s, C-2), 30.6 (s, C-5), 35.6 (s, C-7), 38.0 (s, C-4), 45.6 (s, C-1), 58.3 (t, C-3), 63.9 (s, OCH_2), 116.2 (t, CF_2), 164.3 (t, C=O); HRMS calcd for $C_{11}H_{15}F_2IO_2$: 344.0085, found: 344.0080.

3.3. Typical experimental procedure for the reaction of the norbornene (1b and 1c) with R_FI

Norbornene derivative **1b** or **1c** (10 mmol) and polyfluoroalkyl iodide **2p** (12 mmol) were dissolved in the solution of water (10 mL) and acetonitrile (10 mL). Sodium dithionite (3.7 g) and sodium bicarbonate (1.85 g) were added to the solution. The mixture was stirred at ambient temperature for 6 h. When the reaction was accomplished, the mixture was treated with water (ca. 50 mL). The mixture was extracted with ether of 3×20 mL. The combined organic layer was washed with saturated brine and dried over anhydrous sodium sulfate. After the evaporation of ether, the crude product was purified by column chromatography (PE–EA=40:1 for **1b** and 30:1 for **1c**) to give products **3bp** and **5bp** for **1b** or **5cp** and **6cp** for **1c**.

3.3.1. Bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid ethyl ester (1b).[8,9] ^1H NMR (500 MHz, $CDCl_3$): δ 1.23 (3H, t, J=7.1 Hz, CH_3), 1.20–1.26 (1H, m, H-7), 1.40–1.45 (2H, m, H-7, H-2), 1.88–1.92 (1H, m, H-3), 2.90 (1H, s, H-4), 2.90–2.95 (1H, m, H-2), 3.21 (1H, s, H-1), 4.09 (2H, q, J=7.1 Hz, CH_3CH_2), 5.93 (1H, q, J=3 Hz, H-5), 6.19 (1H, q, J=3.0 Hz, H-6).

3.3.2. Bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylic acid-4,4-dimethyl-2-oxotetrahydrofuran-3-yl ester (1c).[10] White solid. Mp: 116.5–117 °C. ^1H NMR (500 MHz, $CDCl_3$): δ 1.15 (3H, s, CH_3-a), 1.18 (3H, s, CH_3-b), 1.33 (1H, d, J=8.2 Hz, H-7), 1.47 (1H, s, H-7), 1.49 (1H, m, H-3), 1.95 (1H, m, H-3), 2.96 (1H, s, H-4), 3.16 (1H, m, H-2), 3.27 (1H, m, H-1), 4.04 (2H, dd, J=20.7, 9.0 Hz, H-5′), 5.33 (1H, s, H-3′), 5.91 (1H, dd, J=5.6, 2.8 Hz, H-5), 6.26 (1H, dd, J=5.6, 3.1 Hz, H-6).

3.3.3. 5-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-6-*endo*-iodo-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid ethyl ester (3bp). White solid. Mp: 39–41 °C; IR (film): ν_{max} 2980, 1720, 1200, 1140, 720, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.33 (3H, t, J=7.2 Hz, CH_3), 1.39 (1H, d, J=10.8 Hz, H-7a), 1.75 (1H, d, J=10.8 Hz, H-7s), 1.90–1.95 (1H, m, H-3x), 2.01 (1H, ddd, J=13.2, 5.6, 2.6 Hz, H-3n), 2.60 (1H, br s, H-4), 2.63–2.65 (1H, m, H-5), 2.97–3.00 (1H, m, H-2), 3.04 (1H, br s H-1), 4.10–4.20 (1H, m, CH_2O), 4.10–4.20 (1H, m, H-6), 4.25–4.28 (1H, m, CH_2O); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −121.9 (4F, m, 2×CF_2), −119.1 (2F, dd, J=2583, 282.3 Hz, CF_2), −68.8 (2F, m, CF_2); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 14.6 (s, CH_3), 16.3 (s, C-6), 32.2 (s, C-3), 39.5 (s, C-7), 39.6 (s, C-4), 46.0 (s, C-2), 47.7 (s, C-1), 55.2 (t, C-5), 61.7 (s, C–O), 109.6–125.1 (m, $(CF_2)_4$), 173.2 (s, C=O); HRMS calcd for $C_{14}H_{14}F_8ClO_2I$: 527.9599, found: 527.9594.

3.3.4. 6-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-5-*endo*-iodo-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid ethyl ester (5bp). Oil. IR (film): ν_{max} 2980, 1730, 1200, 1100, 740, 680 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.26 (3H, t, J=7.1 Hz, CH_3), 1.45 (1H, d, J=10.9 Hz, H-7a), 1.82 (1H, d, J=10.9 Hz, H-7s), 1.90–1.95 (1H, m, H-3x), 2.29 (1H, ddd, J=13.6, 5.8, 2.6 Hz, H-3n), 2.54 (1H, br s H-4), 2.65–2.68 (1H, m, H-6), 2.74 (1H, br s H-1), 2.80–2.84 (1H, m, H-2), 4.15–4.20 (2H, m, CH_2O), 4.32–4.34 (1H, m, H-5); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −120.9 (2F, m, CF_2), −120.8 (2F, dd, J=376.4, 282.3 Hz, CF_2), −118.1 (2F, dd, J=1882, 282.3 Hz, CF_2), −68.8 (2F, m, CF_2); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 14.7 (s, CH_3), 25.2 (s, C-5), 30.5 (s, C-3), 37.8 (s, C-7), 42.2 (s, C-1), 45.8 (s, C-4), 46.5 (s, C-2), 51.4 (t, C-6), 61.6 (s, C–O), 109.9–125.4 (m, $(CF_2)_4$), 173.3 (s, C=O); HRMS calcd for $C_{14}H_{14}F_8ClO_2I$: 527.9599, found: 527.9605.

3.3.5. 6-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-5-*endo*-iodo-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid-4′,4′-dimethyl-2′-oxo-tetrahydrofuran-3′-yl ester (5cp). White solid. Mp: 98.1–98.4 °C; IR (KBr): ν_{max} 2990, 1800 (γ-lactone), 1750, 1380, 1240 (C–F), 1180, 1120, 1080, 840, 740, 650, 560 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.11 (3H, s, CH_3, H-6′s), 1.15 (3H, s, CH_3, H-6a), 1.51 (1H, d, J=10.9 Hz, H-7a), 1.89 (1H, d, J=11.0 Hz, H-7s), 2.00–2.12 (1H, m, H-3x), 2.35–2.40 (1H, m, H-3n), 2.58 (1H, s, H-4), 2.70–2.77 (1H, m, H-6), 2.80 (2H, s, H-1), 3.00–3.10 (1H, m, H-2), 4.03 (1H, d, J=9.0 Hz, H-5′s), 4.06 (1H, d, J=9.0 Hz, H-5′a), 4.32–4.35 (1H, m, H-5), 5.42 (1H, s, H-3′); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −120.8 (2F, m, CF_2), −120.3 (2F, m, CF_2), −117.5 (2F, m, CF_2), −68.9 (2F, m, $ClCF_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.4 (s, C-6′s), 23.2 (s, C-6′a), 24.9 (s, C-5), 30.8 (s, C-3), 38.1 (s, C-7), 40.7 (s, C-4′), 42.4 (s, C-1), 45.9 (s, C-4), 46.3 (s, C-2), 50.1 (t, C-6), 76.3 (s, C-3′), 76.9 (s, C-5′), 108.3–123.0 (m, $(CF_2)_4$), 172.4 (s, C-8), 172.6 (s, C-2′), HRMS calcd for $C_{18}H_{18}ClF_8O_4$ (M−I): 485.0766, found: 485.0765.

3.3.6. 5-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid-4,4-dimethyl-2-oxo-tetrahydrofuran-3-yl ester (6cp). White solid. Mp: 143.6–144.6 °C; IR (KBr): ν_{max} 2980, 1780 (γ-lactone), 1760, 1460, 1380, 1200 (C–F), 1150, 1100, 990, 720, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.12 (3H, s, CH_3), 1.22 (3H, s, CH_3), 1.44 (1H, d, J=10.3 Hz, H-7a), 1.60–1.65 (1H, m, H-6), 1.69 (1H, d, J=10.3 Hz, H-7s), 1.75–1.79 (2H, m, H-6, H-3n), 1.81 (1H, td, J=11.4, 4.2 Hz, H-3x), 2.35–2.38 (1H, m, H-5), 2.70 (2H, s, H-1, H-4), 3.04–3.10 (1H, m, H-2), 4.05 (1H, d, J=9.1 Hz, H-5′), 4.08 (1H, d, J=9.1 Hz, H-5′), 5.42 (1H, s, H-3′); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −121.5 (4F, m, 2×CF_2), −117.1 (2F, dd, J=1091.8, 272.9 Hz, CF_2), −68.8 (2F, m, $ClCF_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.7 (s, CH3, C-6′s), 23.8 (S, CH3, C-6′a), 27.9 (s, C-6), 33.6 (s, C-3),

38.2 (s, C-4), 39.4 (s, C-7), 40.6 (s, C-1), 40.9 (s, C-4′), 43.4 (t, C-5), 45.2 (s, C-2), 75.7 (s, C-3′), 76.8 (s, C-5′), 109.7–125.2 (m, $(CF_2)_4$), 172.9 (s, C-8), 173.9 (s, C-2′).

3.4. The addition of norbornene-2-*endo*-carboxylic acid (1d and 1e) with R_FI

Compound **1d** or **1e** (5 mmol) was dissolved in 2 N NaOH aqueous solution (5 mL). Acetonitrile (15 mL), R_FI (6 mmol), sodium dithionite (2.2 g), and sodium bicarbonate (1.70 g) were then added to the solution. After stirring for 5–8 h the mixture was treated with water (ca. 50 mL). The mixture was extracted with ether of 3×20 mL. The combined organic layer was washed with saturated brine and dried over anhydrous sodium sulfate. After the evaporation of ether, the crude product was purified by column chromatography (PE–EA=20:1) to give products **7dp–7ds**, **5dp–5ds**, and **6dp–6ds** for **1d** or **5em–5ep** and **7em–7ep** for **1e**.

3.4.1. 6-*exo*-Tridecafluorohexyl-5-*endo*-iodo-bicyclo-[2.2.1]heptane-2-*endo*-carboxylic acid (5ds). White solid. Mp: 83.4–84.0 °C; IR (KBr): ν_{max} 2500–3500, 3000, 1720, 1420, 1240, 1210, 1180, 1150, 1060, 700, 670 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.48 (1H, d, J=10.9 Hz, H-7a), 1.84 (1H, d, J=11.0 Hz, H-7s), 1.98 (1H, tm, J=12.4, H-3x), 2.27 (1H, dm, J=13.7 Hz, H-3n), 2.56 (1H, s, H-4), 2.76 (1H, dt, J=24.5, 7.4 Hz, H-6), 2.77 (1H, s, H-1), 2.80–2.92 (1H, m, H-2), 4.30–4.35 (1H, m, H-5); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −127.2 (2F, m, CF_2), −123.8 (2F, m, CF_2), −122.8 (2F, m, CF_2), −121.7 (2F, m, CF_2), −119.9 (1F, d, J=277.3 Hz, CF), −116.3 (1F, d, J=282.0 Hz, CF), −81.8 (3F, m, CF_3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 24.8 (s, C-5), 30.4 (s, C-7), 37.7 (s, C-3), 42.0 (s, C-4), 45.8 (s, C-1), 46.1 (s, C-2), 50.5 (t, J=20 Hz, C-6), 109.1–125.4 (m, $(CF_2)_6CF_3$), 178.6 (s, C=O, C-8); HRMS calcd for $C_{14}H_{10}F_{13}IO_2$: 583.9518, found: 583.9512.

3.4.2. 6-*exo*-Heptafluoropropyl-5-*endo*-iodo-2-*exo*-methyl-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (5en). White solid. Mp: 165–166 °C; IR (KBr): ν_{max} 2500–3500, 1700, 1220, 1100, 740, 680 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (3H, s, H-9), 1.50–1.55 (1H, m, H-3n), 1.74 (2H, s, H-7), 2.47 (1H, s, H-1), 2.51 (1H, s, H-4), 2.55 (1H, dt, H-6), 2.60–2.72 (1H, m, H-3x), 4.20–4.35 (1H, m, H-5); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −125.9 (2F, dd, J=442.3, 291.7 Hz, CF_2), −118.6 (2F, dd, J=1757.3, 284.7 Hz, CF_2), −81.4 (3F, t, J=11.3 Hz, CF_3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 23.6 (s, C-5), 26.9 (s, C-8), 34.3 (s, C-7), 38.8 (s, C-3), 45.8 (s, C-4), 47.3 (s, C-1), 51.4 (s, C-2), 52.5 (t, J=20 Hz, C-6), 107.9–120.7 (m, $CF_2CF_2CF_3$), 182.2 (s, C=O); HRMS calcd for $C_{12}H_{12}F_7IO_2$: 447.9770, found: 447.9775.

3.4.3. 6-*exo*-Heptafluoroisopropyl-5-*endo*-iodo-2-*exo*-methyl-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (5eo). White solid. Mp: 114.9–115.3 °C; IR (KBr): ν_{max} 2500–3500, 1700, 1280, 1220, 1160, 1100, 740, 680 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (3H, s, H-9), 1.53 (1H, ddd, J=13.7 Hz, J=4.4, 1.8 Hz, H-3n), 1.74 (2H, dd, H-7), 2.51 (2H, s, H-4, H-1), 2.57 (1H, dd, J_{HF}=8.2 Hz, J=6.0 Hz, H-6), 2.76 (1H, dd, J=13.9, 2.2 Hz, H-3x), 4.45–4.50 (1H, m, H-5); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −73.7 (3F, m, CF_3), −72.4 (3F, m, CF_3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 25.8 (s, C-5), 27.2 (s, C-9), 34.0 (s, C-7), 39.4 (s, C-3), 46.7 (s, C-4), 47.9 (s, C-1), 51.7 (d, J=19 Hz, C-6), 51.8 (s, C-2), 91.7–94.2 (m, CF), 120.3–122.9 (m, 2×CF_3), 181.3 (s, C=O); HRMS calcd for $C_{12}H_{12}F_7IO_2$: 447.9770, found: 447.9815.

3.4.4. 6-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-5-*endo*-iodo-2-*exo*-methyl-bicyclo[2.2.1]-heptane-2-*endo*-carboxylic acid (5ep). White solid. Mp: 173.7–174.1 °C; IR (KBr): ν_{max} 2500–3500 (OH), 1700, 1300, 1180, 1130, 720, 680 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.41 (3H, s, H-8), 1.53 (1H, dq, J=14, 2 Hz, H-3), 1.74 (2H, s, H-7), 2.47 (1H, s, H-1), 2.51 (1H, s, H-4), 2.55–2.60 (1H, m, H-6), 2.68 (1H, dd, J=14, 2 Hz, H-1), 4.30–4.34 (1H, m, H-5); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −120.8 (4F, m, 2×CF_2), −117.7 (2F, dd, J=1552.7, 282.3 Hz, CF_2), −68.9 (2F, m, $ClCF_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 23.2 (s, C-5), 26.2 (s, C-8), 36.6 (s, C-7), 38.2 (s, C-3), 45.2 (s, C-4), 46.6 (s, C-1), 50.6 (s, C-2), 52.1 (t, C-6), 107.4–124.5 (m, 4×CF_2), 180.8 (s, C=O); HRMS calcd for $C_{13}H_{12}ClF_8IO_2$: 513.9443, found: 513.9445.

3.4.5. 5-*exo*-(8-Chloro-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluorooctyl)-bicyclo-[2.2.1]heptane-2-*endo*-carboxylic acid (6dq). White solid. Mp: 96.6–96.8 °C; IR (KBr): ν_{max} 3000–3600 (OH), 2980, 1720, 1450, 1400, 1220, 1160, 1110, 740, 560 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (1H, d, J=10.0 Hz, H-7a), 1.68 (1H, d, J=10.8 Hz, H-7s), 1.73 (3H, m, H-6, H-3n), 1.80 (1H, td, J=11.6, 4.2 Hz, H-3x), 2.30–2.34 (1H, m, H-5), 2.68 (1H, d, J=3.2 Hz, H-4), 2.72 (1H, s, H-1), 2.90 (1H, dt, J=10.8, 4.4 Hz, H-2), 11.10 (1H, br s OH); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −122.8 (6F, s, 3×CF_2), −122.2 (4F, m, 2×CF_2), −121.1 (2F, s, CF_2), −118.2 (1F, d, J=277.3 Hz, CF), −115.7 (1F, d, J=277.3 Hz, CF),−69.0 (2F, t, J=13.6 Hz, $ClCF_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 27.9 (s, C-6), 33.5 (s, C-3), 38.3 (s, C-4), 39.5 (s, C-7), 40.5 (s, C-1), 43.4 (t, J=20 Hz, C-5), 45.1 (s, C-2), 109.7–122.4 (m, 8×CF_2), 180.5 (s, C=O); HRMS calcd for $C_{16}H_{11}ClF_{16}IO_2$: 574.0192, found: 574.0187.

3.4.6. 5-*exo*-Tridecafluorohexyl-bicyclo[2.2.1]heptane-2-*endo*-carboxylic acid (6ds). Oil. IR (KBr): ν_{max} 2500–3500 (OH), 2980, 1710, 1420, 1300, 1240, 1200, 1160, 1060, 740, 700, 560 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.42 (1H, d, J=10.0 Hz, H-7a), 1.68 (1H, d, J=10.4 Hz, H-7s), 1.70–1.75 (1H, m, H-6, H-3n), 1.80 (1H, td, J=11.6, 4.2 Hz, H-3x), 2.30–2.36 (1H, m, H-5), 2.68 (1H, d, J=3.2 Hz, H-4), 2.72 (1H, s, H-1), 2.90 (1H, dt, J=11.2, 4.2 Hz, H-2), 11.10 (1H, br s OH); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −127.3 (2F, s, CF_2), −123.9 (2F, s, CF_2), −123.2 (2F, s, CF_2), −122.4 (2F, s, CF_2), −118.3 (1F, dd, J=277.3, 14.1 Hz, CF), −115.9 (1F, s, J=282.0, 14.1 Hz, CF),−81.9 (3F, t, J=9.4 Hz, CF_3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 27.9 (s, C-6), 33.5 (s, C-3), 38.3 (s, C-4), 39.5 (s, C-7), 40.5 (s, C-1), 43.5 (t, J=20 Hz, C-5), 45.2 (s, C-2), 106.7–121.7 (m, C_6F_{13}), 180.5 (s, C=O); HRMS calcd for $C_{14}H_{11}F_{13}IO_2$: 458.0551, found: 458.0559.

3.4.7. 2-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-4-oxa-tricyclo[4.2.1.0^{3,7}]nonan-5-one (7dp). White solid.

Mp: 39.3–40.8 °C; IR (KBr): ν_{max} 2990, 1780 (γ-lactone), 1350, 1220 (C–F), 1180, 1140, 1010, 840, 760, 620 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.66 (1H, d, *J*=11.8 Hz, H-8a), 1.81 (1H, d, *J*=13.4 Hz, H-9n), 2.07 (1H, d, *J*=13.4 Hz, H-8s), 2.10–2.20 (1H, m, H-9x), 2.37 (1H, t, *J*=18.2 Hz, H-2), 2.65 (1H, dd, *J*=11.3, 4.6 Hz, H-6), 2.86 (1H, s, H-1), 3.29 (1H, t, *J*=4.6 Hz, H-7), 5.00 (1H, d, *J*=4.8 Hz, H-3); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −122.0 (2F, m, CF_2), −121.0 (2F, dd, *J*=818.8, 282.4 Hz, CF_2), −114.4 (2F, dd, *J*=889.4, 282.4 Hz, CF_2), −69.0 (2F, dd, *J*=282.4, 188.2 Hz, $ClCF_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 36.0 (s, C-8), 36.2 (s, C-9), 38.0 (s, C-1), 39.0 (s, C-6), 46.6 (s, C-7), 52.0 (t, *J*=20 Hz, C-2), 80.6 (s, C-3), 110.0–125.0 (m, $(CF_2)_4$), 180.2 (s, C-5); HRMS calcd for $C_{12}H_9ClF_8O_2$: 372.0320, found: 372.0201.

3.4.8. 2-*exo*-(8-Chloro-1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-hexadecafluorooctyl)-4-oxa-tricyclo[4.2.1.0^{3,7}]nonan-5-one (7dq). White solid. Mp: 113.5–114.3 °C; IR (KBr): ν_{max} 3000, 1780 (γ-lactone), 1350, 1220 (C–F), 1150, 1020, 840, 650, 550 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.66 (1H, d, *J*=11.7 Hz, H-8a), 1.81 (1H, d, *J*=13.5 Hz, H-9n), 2.09–2.20 (2H, m, H-8s, H-9x), 2.37 (1H, t, *J*=18.0 Hz, H-2), 2.66 (1H, dd, *J*=11.2, 4.6 Hz, H-6), 2.86 (1H, s, H-1), 3.29 (1H, t, *J*=4.5 Hz, H-7), 5.00 (1H, d, *J*=4.8 Hz, H-3); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −122.65 (6F, m, 3×CF_2), −122.40 (4F, m, 2×CF_2), −121.12 (2F, dd, *J*=818.8, 282.4 Hz, CF_2), −114.30 (2F, dd, *J*=889.4, 282.4 Hz, CF_2), −69.06 (2F, m, $ClCF_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 35.3 (s, C-8), 35.6 (s, C-9), 37.3 (s, C-1), 38.3 (s, C-6), 46.0 (s, C-7), 51.4 (t, *J*=20 Hz, C-2), 80.1 (s, C-3), 106.8–124.1 (m, $(CF_2)_8$), 179.5 (s, C-5); HRMS calcd for $C_{16}H_9ClF_{16}O_2$: 572.0036, found: 572.0036.

3.4.9. 2-*exo*-Tridecafluorohexyl-4-oxa-tricyclo[4.2.1.0^{3,7}]-nonan-5-one (7ds). White solid. Mp: 84.6–85.2 °C; IR (KBr): ν_{max} 3000, 1780 (γ-lactone), 1350, 1240, 1210 (C–F), 1150, 1050, 1020, 980, 700, 650 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.66 (1H, d, *J*=11.7 Hz, H-8a), 1.81 (1H, d, *J*=13.4 Hz, H-9n), 2.08 (1H, d, *J*=12.4 Hz, H-8s), 2.12 (1H, dd, *J*=13.7 Hz, H-9x), 2.37 (1H, t, *J*=18.1 Hz, H-2), 2.66 (1H, dd, *J*=11.3, 4.6 Hz, H-6), 2.86 (1H, s, H-6), 3.29 (1H, t, *J*=4.5 Hz, H-7), 5.00 (1H, d, *J*=4.8 Hz, H-3); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −127.2 (2F, dd, *J*=413.6, 282.0 Hz, CF_2), −123.8 (2F, dd, *J*=310.2, 188.0 Hz, CF_2), −122.8 (4F, m, 2×CF_2), −114.3 (2F, dd, *J*=813.1, 282.0 Hz, CF_2), −81.8 (3F, m, CF_3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 34.8 (s, C-8), 35.1 (s, C-9), 36.8 (s, C-1), 37.8 (s, C-6), 45.5 (s, C-7), 50.9 (t, *J*=20 Hz, C-2), 79.6 (s, C-3), 108.4–125.0 (m, $(CF_2)_5CF_3$), 179.0 (s, C-5); HRMS calcd for $C_{14}H_9F_{13}O_2$: 456.0395, found: 456.0397.

3.4.10. 2-*exo*-Heptafluoroisopropyl-6-*exo*-methyl-4-oxa-tricyclo[4.2.1.0^{3,7}]nonan-5-one (7en). White solid. Mp: 65.0–65.4 °C; IR (KBr): ν_{max} 2980, 1780 (γ-lactone), 1350, 1230 (C–F), 1120, 1020, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.25 (3H, s, H-10), 1.63 (1H, dd, *J*=13.5, 4.0 Hz, H-9x), 1.72 (1H, d, *J*=11.8 Hz, H-8s), 1.90 (1H, dd, *J*=13.5, 2.2 Hz, H-9n), 2.07 (1H, dd, *J*=11.8, 1.6 Hz, H-8x), 2.31 (1H, dd, *J*=19.3, 17.1 Hz, H-2), 2.82 (1H, s, H-1), 2.89 (1H, d, *J*=5.0 Hz, H-7), 4.95 (1H, d, *J*=5.0 Hz, H-3); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −127.0 (2F, dd, *J*=705.8, 282.3 Hz, CF_2), −115.2 (2F, dd, *J*=1176.3, 282.3 Hz, CF_2), −81.5 (3F, t, *J*=10.4 Hz, CF_3); ^{13}C NMR (125.8 HMz, $CDCl_3$): δ 20.6 (s, C-10), 35.2 (s, C-9), 38.8 (s, C-1), 43.6 (s, C-6), 44.2 (s, C-8), 51.3 (t, C-2), 51.9 (s, C-7), 78.8 (s, C-3), 111.9–133.8 (m, $CF_2CF_2CF_3$), 182.0 (s, C-5); HRMS calcd for $C_{12}H_{11}F_7O_2$: 320.0647, found: 320.0699.

3.4.11. 2-*exo*-Heptafluoroisopropyl-6-*exo*-methyl-4-oxa-tricyclo[4.2.1.0^{3,7}]nonan-5-one (7eo). White solid. Mp: 96.6–96.7 °C; IR (KBr): ν_{max} 2980, 1800 (γ-lactone), 1300, 1220 (C–F), 1120, 1020, 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.30 (3H, s, H-10), 1.64 (1H, dd, *J*=13.6, 4.2 Hz, H-9x), 1.74 (1H, d, *J*=11.8 Hz, H-8s), 1.90 (1H, dd, *J*=13.6, 2.2 Hz, H-9n), 1.98 (1H, d, *J*=11.7, 1.6 Hz, H-8x), 2.18 (1H, d, *J*=33.3 Hz, H-2), 2.78 (1H, s, H-1), 2.88 (1H, d, *J*=4.8 Hz, H-7), 5.00–5.10 (1H, m, H-3); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −77.0 (3F, m, CF_3), −73.9 (3F, m, CF_3); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 19.8 (s, C-10), 34.6 (s, C-9), 39.8 (s, C-1), 42.8 (s, C-6), 43.8 (s, C-8), 49.1 (d, C-2), 51.1 (s, C-7), 78.9 (s, C-3), 111.9–133.8 (m, $CF(CF_3)_2$), 181.4 (s, C-5); HRMS calcd for $C_{12}H_{11}F_7O_2$: 320.0647, found: 320.0666.

3.4.12. 2-*exo*-(4-Chloro-1,1,2,2,3,3,4,4-octafluorobutyl)-6-*exo*-methyl-4-oxa-tricyclo-[4.2.1.0^{3,7}]nonan-5-one (7ep). White solid. Mp: 58.3–58.4 °C; IR (KBr): ν_{max} 2990, 1780 (γ-lactone), 1350, 1200 (C–F), 1120, 1080, 840, 700, 640 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 1.25 (3H, s, H-10), 1.63 (1H, dd, *J*=13.4, 4.0 Hz, H-8a), 1.72 (1H, d, *J*=11.8 Hz, H-9), 1.89 (1H, dd, *J*=13.4, 2.2 Hz, H-8), 2.07 (1H, dd, *J*=11.8, 1.7 Hz, H-9), 2.32 (1H, dd, *J*=20.3, 16.1 Hz, H-2), 2.82 (1H, s, H-1), 2.89 (1H, d, *J*=5.0 Hz, H-7), 4.95 (1H, d, *J*=5.0 Hz, H-3); ^{19}F NMR (470.5 MHz, $CDCl_3$): δ −122.1 (2F, m, CF_2), −120.9 (2F, dd, *J*=846.9, 291.7 Hz, CF_2), −114.3 (2F, dd, *J*=964.5, 272.9 Hz, CF_2), −69.0 (2F, dd, *J*=296.4, 178.8 Hz, $ClCF_2$); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 20.0 (s, C-10), 34.5 (s, C-9), 38.2 (s, C-1), 42.9 (s, C-6), 43.5 (s, C-8), 51.1 (t, C-2), 51.6 (s, C-7), 78.3 (s, C-3), 107.4–124.4 (m, $(CF_2)_4$), 181.4 (s, C-5); HRMS calcd for $C_{13}H_{11}ClF_8O_2$: 386.0320, found: 386.0336.

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Supplementary data

^1H NMR, ^{19}F NMR, ^{13}C NMR, and 2D NMR spectra for some new compounds; crystallographic information files are in CIF format for **5eo**, **5cp**, **6cp**, and **5ds**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.08.042.

References and notes

1. (a) Tiers, G. D. V. *J. Am. Chem. Soc.* **1960**, *82*, 5513; (b) Masutani, T.; Yamamoto, A. JP 278874, 2001; (c) Chen, Q. Y.; Yang, Z. Y. *J. Fluorine Chem.* **1988**, *39*, 217–226;

(d) Davis, C. R.; Barton, D. J.; Yang, Z. Y. *J. Fluorine Chem.* **1995**, *70*, 135–140; (e) Maria, L.; Marcial, M. M.; Adelina, V. *Tetrahedron* **2002**, *58*, 4061–4065; (f) Andrew, E. F. *J. Org. Chem.* **1985**, *50*, 3269–3274.

2. (a) Huang, W. Y.; Huang, B. N.; Hu, C. M. *J. Fluorine Chem.* **1983**, *23*, 193–204; (b) Huang, W. Y.; Huang, B. N. *Acta Chim. Sin.* **1984**, *42*, 1106–1108; (c) Huang, W. Y.; Wang, W.; Huang, B. N. *Acta Chim. Sin.* **1986**, *44*, 178–184.
3. (a) Huang, W. Y.; Wu, F. H. *Isr. J. Chem.* **1999**, *39*, 167–170; (b) Huang, W. Y.; Wu, F. H. *J. Fluorine Chem.* **1988**, *92*, 85–87; (c) Wu, F. H.; Huang, W. Y. *Youji Huaxue* **1997**, *17*, 106–125; (d) Zur, C.; Miethchen, R. *Eur. J. Org. Chem.* **1998**, *3*, 531–539; (e) Liu, J. T.; Sui, G. D.; Chen, G.; Huang, W. Y. *J. Fluorine Chem.* **1999**, *93*, 49–51.
4. (a) Bondar, N. F.; Golubeva, M. B.; Isaenya, L. P.; Konopiya, N. A.; Kuzmitsky, B. B.; Lyukin, G. S. *Eur. J. Med. Chim. Ther.* **2004**, *39*, 389–396; (b) Varela, J. A.; Pena, D.; Goldfuss, B.; Polborn, K.; Knochel, P. *Org. Lett.* **2001**, *15*, 2395–2398; (c) Renaud, P.; Ollivier, C.; Panchaud, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 3460–3462.
5. (a) Brace, N. O. *J. Org. Chem.* **1962**, *27*, 3027–3033; (b) Brace, N. O. *J. Org. Chem.* **1979**, *44*, 1964–1971; (c) Brace, N. O. *J. Fluorine Chem.* **2003**, *123*, 237–248.
6. Xiao, F. H.; Wu, F. H.; Shen, Y. J.; Zhou, L. F. *J. Fluorine Chem.* **2003**, *126*, 63–67.
7. Davies, D. I. *J. Chem. Soc. C* **1969**, 1585–1590.
8. (a) Farmer, R. F.; Hamer, J. *J. Org. Chem.* **1966**, *33*, 2418–2419; (b) Wu, Y. L.; Zhang, J. L. *Acta Chim. Sin.* **1982**, *40*, 157–163.
9. Poll, T.; Sobczak, A.; Hartmann, H.; Helmchen, G. *Tetrahedron Lett.* **1985**, *26*, 3095–3098.
10. (a) Nooy, C. D. V.; Rondestvedt, C. S., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 3583–3586; (b) Whitesides, G. M.; Kendall, P. E. *J. Org. Chem.* **1972**, *37*, 3718–3725.