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Synthesis of 1-fluoroindan-1-carboxylic acid (FICA) and its properties as a chiral derivatizing agent

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Abstract

1-Fluoroindan-1-carboxylic acid (FICA) (**1**) was designed and synthesized as its methyl ester (FICA Me ester) (**4**) in order to develop an efficient chiral derivatizing agent (CDA) which excels α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) in capability. FICA Me ester (**4**) was prepared by fluorination of methyl 1-hydroxyindan-1-carboxylate (**3**) with (diethylamino)sulfur trifluoride (DAST) and derived to the esters of racemic secondary alcohols by ester exchange reaction. The resulting $\Delta\delta_F$ value was large in the case of 2-butyl ester of FICA (**5a**), whereas not detectable in the case of the corresponding MTPA ester (**6a**). The magnitude of the $\Delta\delta_H$ values was similar to that of MTPA esters. The diastereomers of (*R*)-(−)-8-phenylmenthyl ester of FICA (**5i**) was separated and their ^{1}H NMR analyses revealed that the concept of the modified Mosher's method was successfully applied to **5i**.

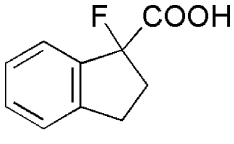
Keywords: 1-Fluoroindan-1-carboxylic acid; Chiral derivatizing agent; $\Delta\delta_F$; $\Delta\delta_H$

1. Introduction

The development of convenient methods for the determination of absolute configurations of chiral organic compounds has become more important with the progress of asymmetric synthesis. Among several instrumental methods, the approaches using NMR spectroscopy are very appealing because of the economy and simplicity of the methods and the wide availability of NMR equipments [1]. The modified Mosher's method with α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) is one of the most popular and reliable procedures on the basis of ^{1}H NMR anisotropy effects [2]. However, the results obtained from ^{1}H NMR are not always reliable because of relatively small $\Delta\delta_H$ values of the MTPA diastereomers. Riguera reported the causes as follows: MTPA esters are constituted by three main conformers in close populations due to restricted rotation around C–CO and Cα-Ph bonds. The small predominance of one conformer and the simultaneous operation of aromatic shielding and deshielding effects on the substrate part, due to the orientation of the phenyl ring, explain the small $\Delta\delta_H$ values observed [3]. In addition, Mosher's method using ^{19}F NMR is not generally applicable to the assignment of configuration because of inconsistencies in the signs of $\Delta\delta_F$ [2].

Several agents containing F atoms have been reported as chiral derivatizing agents (CDAs) for the determination of the absolute configurations of chiral molecules by ^{19}F NMR [1b,c]. For α-*cyano*-α-fluoro-*p*-tolylacetic acid (CFTA) ester, theoretical calculations on the geometry and conformational composition revealed that the signs of $\Delta\delta_F$ is based on an anisotropic deshielding effect of carbonyl group on the F atom in the *sp* rotamer and the difference of the biases of conformational equilibrium between *sp* and *ap* rotamers in the diastereomers [4,5].

In this setting, we set out to investigate the development of a new CDA, 1-fluoroindan-1-carboxylic acid (FICA) (**1**) (Chart 1).



1: FICA

Chart 1.

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2. Results and discussion

FICA (**1**) was designed as a new CDA for the assignment of the absolute configurations of chiral organic compounds by both ^{1}H and ^{19}F NMR. The feature of FICA (**1**) compared with MTPA is as follows: (1) Fixation of the orientation of aromatic ring by a fused structure is expected to give larger $\Delta\delta_H$ values; (2) F atom on the stereogenic carbon is more sensitive to diastereotopic magnetic difference, which is expected to bring larger $\Delta\delta_F$ values.

FICA (**1**) was synthesized as its methyl ester (FICA Me ester) (**4**) as shown in Scheme 1. Enolate of methyl indan-1-carboxylate (**2**) was oxidized by molybdenum pentoxide-pyridine-HMPA complex [6] to give the α-hydroxy ester (**3**). Replacing hydroxyl group of (**3**) with fluorine using (diethylamino)sulfur trifluoride (DAST) [7] gave the desired FICA Me ester (**4**).

FICA esters of secondary alcohols (**5**) were obtained by ester exchange reaction of FICA Me ester (**4**) using lithium alkoxides [8]. As a preliminary experiment, these esters (**5**) were subjected to ^{1}H and ^{19}F NMR analyses to elucidate the chemical shift differences. Table 1 shows a comparison of $\Delta\delta_H$ values of the selected signals in FICA and MTPA esters (**5**) and (**6**). Contrary to our expectations, $\Delta\delta_H$ values of the FICA esters (**5**) were similar to those of the corresponding MTPA esters (**6**).

In contrast with ^{1}H NMR, the fluorine shift data allow only a single point comparison. Table 2 shows a comparison of $\Delta\delta_F$ values of FICA and MTPA esters (**5**) and (**6**). The magnitude of $\Delta\delta_F$ values of the FICA esters (**5**) was 2–16 times larger than that of the MTPA esters (**6**). Especially, $\Delta\delta_F$ value was large in the case of 2-butyl ester of FICA (**5a**), whereas not detectable in the case of the corresponding MTPA ester (**6a**). In spite of triplet multiplicity, all signals of the diastereomeric mixture of FICA esters (**5**) showed base line separation.

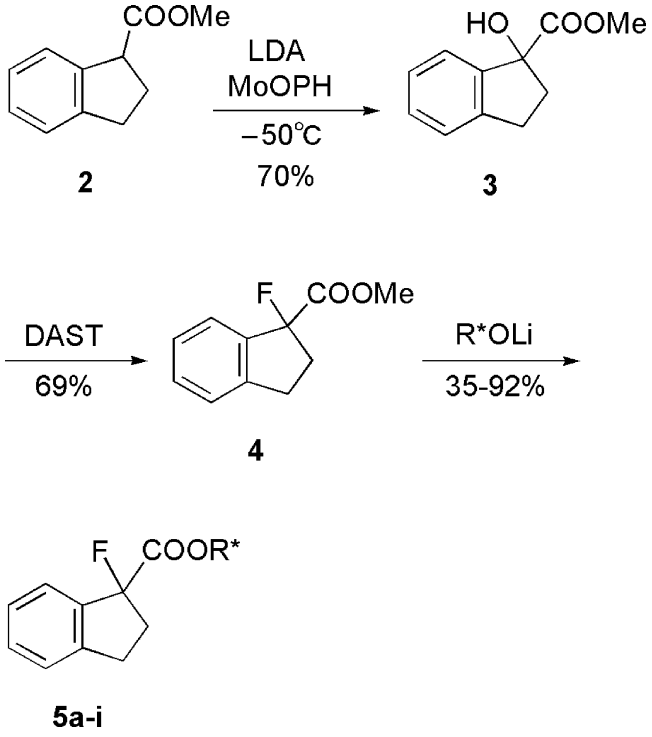
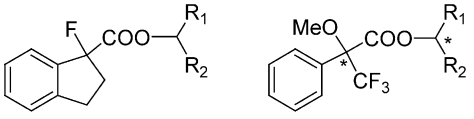


Table 1
^{1}H NMR properties of FICA esters (**5a–h**) and MTPA esters (**6a–h**)



FICA ester (**5a-h**) MTPA ester (**6a-h**)

	R_1	R_2	$\Delta\delta_H$ (ppm)		$\Delta\delta_H$ (ppm) = $\delta_{SR} - \delta_{RR}$ [a]	
			R_1	R_2	R_1	R_2
a	CH_3CH_2	CH_3	0.15	0.07	−0.11 [b]	+0.08 [b]
b	$CH_3(CH_2)_2$	CH_3	0.09	0.07	−0.07	+0.08
c	$CH_3(CH_2)_3$	CH_3	0.09	0.06	−0.06	+0.08
d	$CH_3(CH_2)_4$	CH_3	0.05	0.06	−0.04	+0.08
e	$CH_3(CH_2)_5$	CH_3	0.02	0.06	−0.02 [b]	+0.08 [b]
f	$CH_3(CH_2)_6$	CH_3	0.01	0.06	−0.01	+0.08
g	Ph	CH_3		0.05		+0.06 [b]
h	Menthyl					
	8-CH_3	10-CH_3	0.18	0.03	−0.12 [b]	+0.03 [b]
	9-CH_3		0.16		−0.10 [b]	

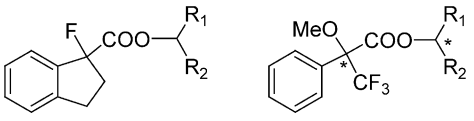
[a] Ref. [9].
[b] Ref. [4].

In order to apply FICA as a CDA, we attempted to resolve FICA (**1**). FICA Me ester (**4**) was converted to a diastereomeric mixture of (*R*)-(−)-8-phenylmenthyl ester (**5i**) which was separated by preparative TLC (PTLC) using hexane/AcOEt (29/1) as an eluent (Scheme 2).

Less polar fraction was (−)-FICA (*R*)-(−)-8-phenylmenthyl ester (**5ia**) {44%; oil; $[\alpha]_D^{27}$ −33.2 (c 2.69, $CHCl_3$)} and more polar fraction (+)-FICA (*R*)-(−)-8-phenylmenthyl ester (**5ib**) {48%; m.p. 88 °C; $[\alpha]_D^{27}$ + 1.0 (c 1.13, $CHCl_3$)}.

In a similar manner to the procedure of modified Mosher's method, we assigned the signals of protons in each of the (−)-

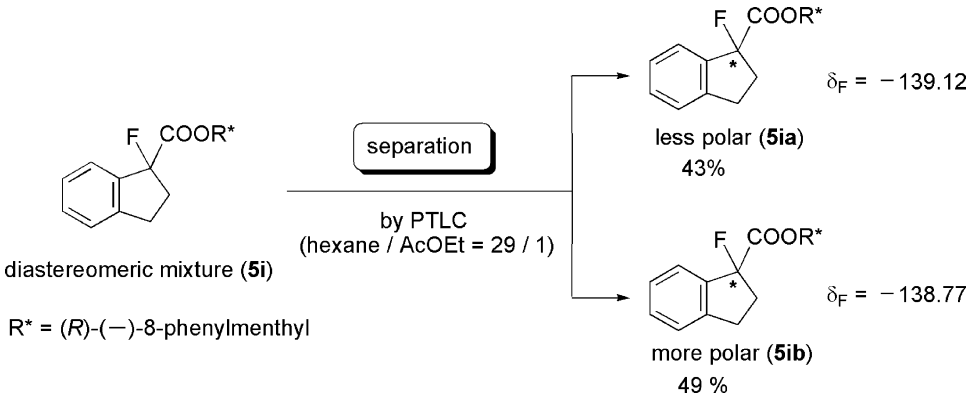
Table 2
^{19}F NMR properties of FICA esters (**5a–h**) and MTPA esters (**6a–h**)



FICA ester (**5a-h**) MTPA ester (**6a-h**)

	R_1	R_2	$\Delta\delta_F$ (ppm)	$\Delta\delta_F$ (ppm) = $\delta_{SR} - \delta_{RR}$ [a]
a	CH_3CH_2	CH_3	0.23	+0.00 [b]
b	$CH_3(CH_2)_2$	CH_3	0.32	−0.02
c	$CH_3(CH_2)_3$	CH_3	0.41	−0.06
d	$CH_3(CH_2)_4$	CH_3	0.33	−0.05
e	$CH_3(CH_2)_5$	CH_3	0.33	−0.05 [b]
f	$CH_3(CH_2)_6$	CH_3	0.33	−0.06
g	Ph	CH_3	0.51	−0.20 [b]
h	Menthyl		1.03	−0.11 [b]

[a] Ref. [9].
[b] Ref. [4].



Scheme 2.

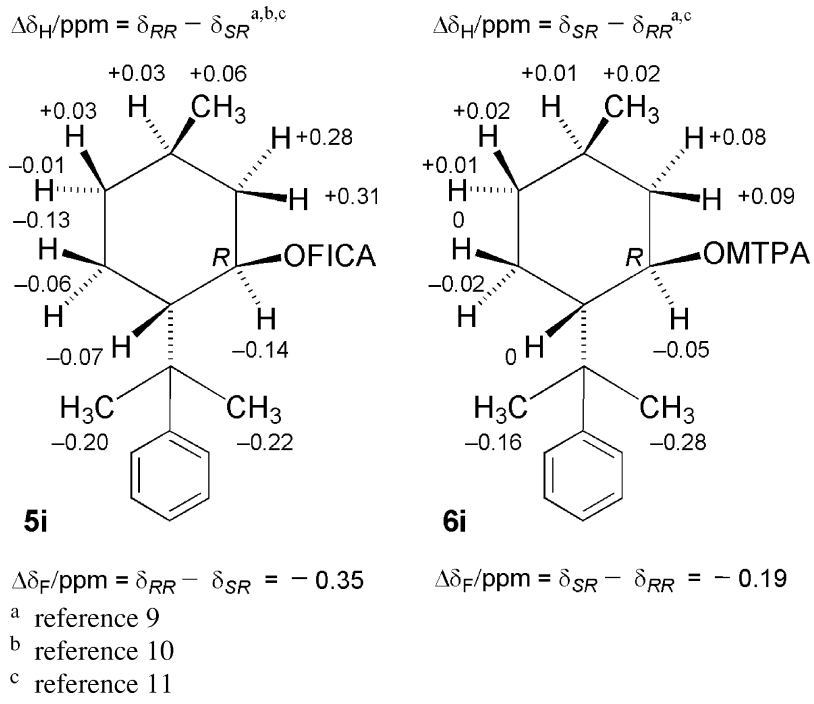


Chart 2.

and (+)-FICA esters (**5ia**) and (**5ib**) as many as possible by means of NMR techniques including H,H COSY. Then, $\Delta\delta_H$ values were obtained from the equation, $\delta_{RR} - \Delta\delta_{SR}$ for the FICA ester (**5i**) and $\delta_{SR} - \delta_{RR}$ for the MTPA ester (**6i**) [10,11]. The results are shown in Chart 2. A systematic trend for signs of $\Delta\delta_H$ were obtained also in the FICA ester (**5i**). When the plane including the carbinyl proton and the ester carbonyl is designated the FICA plane, $\Delta\delta_H$ values on the right side of the FICA plane were positive and those on the left side negative. Accordingly, the concept of modified Mosher's method can be successfully applied to the FICA ester (**5i**) to elucidate the absolute configuration.

3. Conclusion

FICA (**1**) was designed and synthesized as FICA Me ester (**4**) in two steps from methyl indan-1-carboxylate (**2**). FICA esters of secondary alcohols (**5**) were obtained by ester exchange reaction of FICA Me ester (**4**). In all cases examined, larger $\Delta\delta_F$ values were obtained in the FICA esters (**5**) than in the MTPA esters (**6**). In contrast to our expectations, the magnitude of the $\Delta\delta_H$ values of the FICA esters (**5**) was similar to that of MTPA esters (**6**). The diastereomers of (*R*)-(−)-8-phenylmenthyl ester of FICA (**5i**) was separated and their ^{1}H NMR analyses revealed that the concept of the modified Mosher's method was successfully applied to **5i**.

Further investigation is in progress in our group on resolution of FICA and both ^{1}H and ^{19}F NMR analyses.

4. Experimental

4.1. General

Melting points were measured with a Yanaco micro melting point apparatus and are uncorrected. Microanalyses were performed by Microanalysis Center of Toyama Medical &

Pharmaceutical University. Spectroscopic measurements were carried out with the following instruments: optical rotations, JASCO DIP-1000 digital polarimeter; IR, Perkin-Elmer 1600 Series FT-IR; mass (MS), JEOL JMS-GCmate; high resolution mass spectra (HRMS), JEOL JMS-AX505HAD; ^{1}H NMR, Varian Unity 500 (500 MHz) and Varian Gemini 300 (300 MHz) for solutions in $CDCl_3$ with Me_4Si as an internal standard; ^{13}C NMR, Varian Gemini 300 (75.46 MHz) for solutions in $CDCl_3$ with $CDCl_3$ as an internal standard (77.2 ppm); ^{19}F NMR, JEOL JNM-GX 270 (254 MHz) for solutions in $CDCl_3$ with $CFCl_3$ as an internal standard. Column chromatography, flash column chromatography, and preparative TLC (PLC) were performed on Kieselgel 60 (Merck Art. 7734, Art. 9385, and 7748, respectively). $\Delta\delta_H$ and $\Delta\delta_F$ values are shown in Tables 1 and 2. Methyl indan-1-carboxylate (**2**) was prepared from indene in four steps (Sections 4.2–4.4) by a modified method of the literatures [12,13].

4.2. 3-Indenecarboxylic acid

To a solution of indene (90%, 15 mL, 0.12 mol) in dry THF (100 mL) at −50 °C was added *n*-BuLi (1.58 mol/L in hexane, 81 mL, 0.13 mol) over a period of 20 min under nitrogen atmosphere. After being stirred at −50 °C for 20 min, CO_2 gas was introduced to the reaction mixture for 10 min. The reaction mixture was acidified with 10% HCl (40 mL) and the solvent was evaporated. To the residue was added 5% HCl (100 mL) and the aqueous layer was extracted with AcOEt (150 mL). The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue was treated with hexane to give a solid. The solid was filtered, washed with hexane, and dried under reduced pressure to give 3-indenecarboxylic acid (15 g, 94 mmol, 81%) as yellow crystalline mass; m.p. 163–165 °C (lit. m.p. 161–162 °C [12], lit. m.p. 158–161 °C [14]); IR (KBr) 3044–2600 cm^{-1} (OH), 1685 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 3.59 (d, 2H, J = 1.4 Hz, 1-H), 7.29 (ddd, 1H, J = 1.1, 7.4, 7.7 Hz, 6-H), 7.38 (dd, 1H, J = 7.4, 7.7 Hz, 5-H), 7.50 (dd, 1H, J = 0.6, 7.4 Hz, 7-H), 7.65 (t, 1H, J = 1.9 Hz, 2-H), 8.08 (dd, 1H, J = 0.6, 7.7 Hz, 4-H); ^{13}C NMR (75.46 MHz) δ 39.0 (CH_2, 1-C), 122.6 (CH, 5-C), 123.9 (CH, 6-C), 125.9 (CH, 7-C), 126.9 (CH, 2-C), 135.8 (C, 3a-C), 140.4 (C, 7a-C), 143.4 (C, 3-C), 147.2 (CH, 4-C), 169.3 (C, *C*OOH); MS *m/z*: 160 (M^+), 115 ([M − COOH]$^+$); Anal. calcd. for $C_{10}H_8O_2$: C, 74.99; H, 5.03. Found: C, 74.96; H, 5.04.

4.3. Methyl 3-indenecarboxylate

A mixture of 3-indenecarboxylic acid (5.00 g, 31.2 mmol) and thionyl chloride (50 mL) was refluxed for 1 h and the excess reagent was evaporated. Methanol (100 mL) was added to the residue and the reaction mixture was stirred at room temperature for 2 h. After the solvent was evaporated, the residue was portioned between Et_2O (200 mL) and water (100 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution (100 mL) and brine (50 mL), and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography (hexane/Et_2O = 9:1) to give methyl 3-indenecarboxylate (5.06 g, 29.0 mmol, 93%) as a yellow oil; IR (neat) 2950 cm^{-1} (CH), 1720 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 3.58 (dd, 2H, J = 0.8, 1.4 Hz, 1-H), 3.89 (s, 3H, OCH_3), 7.25 (dt, 1H, J = 0.8, 7.4 Hz, 6-H), 7.35 (dddd, 1H, J = 0.6, 0.8, 7.4, 7.6 Hz, 5-H), 7.44–7.47 (m, 2H, 2, 7-H), 8.04 (dd, 1H, J = 0.8, 7.6 Hz, 4-H); ^{13}C NMR (75.46 MHz) δ 38.6 (CH_2, 1-C), 51.8 (CH_3, OCH_3), 122.5 (CH, 5-C), 123.8 (CH, 6-C), 125.6 (CH, 7-C), 126.7 (CH, 2-C), 136.1 (C, 3a-C), 140.8 (C, 7a-C), 143.4 (C, 3-C), 144.5 (CH, 4-C), 164.5 (C, *C*OO); MS *m/z*: 174 (M^+), 143 ([M − OCH_3]$^+$), 115 ([M − $COOCH_3$]$^+$); HRMS calcd. for $C_{11}H_{10}O_2$ (M^+): 174.0681, found: 174.0688.

4.4. Methyl indan-1-carboxylate (2)

A mixture of methyl 3-indenecarboxylate (7.25 g, 41.6 mmol), dry MeOH (100 mL) and 5% Pd/C (1.0 g) was hydrogenated at 4–6 kgf/cm^2 of H_2O at room temperature for 16 h. The reaction mixture was filtrated and the filtrate was evaporated. The residue was purified by column chromatography (hexane/Et_2O = 9:1) to give **2** (7.13 g, 40.5 mmol, 97%) as a colorless oil; IR (neat) 2950 cm^{-1} (CH), 1736 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 2.29–2.37 (m, 1H, 2-H), 2.40–2.68 (m, 1H, 2-H), 2.91 (ddd, 1H, J = 7.7, 8.5, 15.8 Hz, 3-H), 3.10 (ddd, 1H, J = 6.0, 8.5, 15.8 Hz, 3-H), 3.73 (s, 3H, OCH_3), 4.06 (t, 1H, J = 7.7 Hz, 1-H), 7.15–7.25 (m, 3H, 4–6-H), 7.37 (d, 1H, J = 6.8 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 29.0 (CH_2, 2-C), 32.0 (CH_2, 3-C), 50.3 (CH, 1-C), 52.2 (CH_3, OCH_3), 124.8 (CH, 7-C), 124.9 (CH, 4-C), 126.5 (CH, 6-C), 127.6 (CH, 5-C), 140.7 (C, 3a-C), 144.1 (C, 7a-C), 174.4 (C, *C*OO); MS *m/z*: 176 (M^+), 115 (indenyl cation); HRMS calcd. for $C_{11}H_{12}O_2$ (M^+): 176.0838, found: 176.0830.

4.5. Methyl 1-hydroxyindan-1-carboxylate 3

To a solution of the ester (**2**) (4.46 g, 25.3 mmol) in dry THF (80 mL) was added dropwise LDA (1.8 mol/L in heptane/THF/ethylbenzene, 14.8 mL, 26.6 mmol) at −50 °C under nitrogen atmosphere and the reaction temperature was raised slowly to −20 °C. After being stirred for 30 min, molybdenum pentoxide–pyridine–HMPA complex (12.1 g, 27.9 mmol) was added to the mixture at −50 °C and then the reaction temperature was allowed to reach room temperature. The reaction was quenched with saturated aqueous Na_2SO_3 solution (50 mL) and extracted with Et_2O (160 mL). The organic layer was washed with 2% HCl (80 mL), water (80 mL), saturated aqueous $NaHCO_3$ solution (80 mL) and brine (40 mL), and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography (hexane/AcOEt = 7:1) to give **3** (4.00 g, 20.8 mmol, 82%) as a pale yellow solid; m.p. 44 °C; b.p. 180–190 °C/0.2 mmHg (glass tube oven); IR (neat) 3487 cm^{-1} (OH), 2950 cm^{-1} (CH), 1728 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 2.27 (ddd, 1H, J = 7.4, 8.5, 13.5 Hz, 2-H), 2.68 (ddd, 1H, J = 4.7, 7.4, 13.5 Hz, 2-H), 3.05–3.12 (m, 2H, 3-H), 3.73 (s, 3H, OCH_3), 3.88 (s, 1H, OH), 7.20–7.30 (m, 4H, 4–7-H); ^{13}C NMR (75.46 MHz) δ 30.6 (CH_2, 3-C), 38.9 (CH_2, 2-C), 53.3 (CH_3, OCH_3), 83.9 (C, 1-C), 123.1 (CH, 7-C), 125.1

(CH, 4-C), 127.0 (CH, 6-C), 129.1 (CH, 5-C), 143.5(C, 3a-C), 144.0 (C, 7a-C), 176.3 (C, *C*OO); MS *m/z*: 192 (M^+), 174 ($[M - H_2O]^+$), 132 ($[M - COOMe]^+$), 115 (indenyl cation); Anal. calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.88; H, 6.24.

4.6. 1-Fluoroindan-1-carboxylic acid methyl ester (FICA Me ester) (**4**)

To a solution of the hydroxy ester (**3**) (1.25 g, 6.49 mmol) in dry CH_2Cl_2 (45 mL) was added slowly a solution of DAST (90%, 0.95 mL, 6.49 mmol) in dry CH_2Cl_2 (15 mL). The reaction mixture was diluted with CH_2Cl_2 (50 mL) and ice-water (100 mL). The organic layer was separated, washed with brine (50 mL) and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography (hexane/AcOEt = 19:1) to give **4** (1.09 g, 5.63 mmol, 87%) as an oil. The oil was distilled by a glass tube oven to give pure **4** (0.80 g, 4.14 mmol, 64%) as a colorless oil; b.p. 125 °C/0.2 mmHg (glass tube oven); IR (neat) 2954 cm^{-1} (CH), 1750 cm^{-1} (C=O); ^{1}H NMR (300 MHz) δ 2.49 (dddd, 1H, J = 5.0, 8.5, 14.3, 23.4 Hz, 2-H), 2.84 (dddd, 1H, J = 5.7, 8.5, 14.3, 20.0 Hz, 2-H), 3.03–3.12 (m, 1H, 3-H), 3.13–3.23 (m, 1H, 3-H), 3.81 (s, 3H, OCH_3), 7.24–7.42 (m, 4H, 4–7-H); ^{13}C NMR (75.46 MHz) δ 30.4 (s, CH_2, 3-C), 36.5 (d, J = 23.2 Hz, CH_2, 2-C), 53.0 (s, CH_3, OCH_3), 102.3 (d, J = 190.4 Hz, C, 1-C), 124.3 (s, CH, 7-C), 125.3 (s, CH, 4-C), 127.2 (d, J = 2.4 Hz, CH, 6-C), 130.6 (d, J = 2.4 Hz, CH, 5-C), 139.3 (d, J = 20.7 Hz, C, 7a-C), 145.0 (d, J = 4.8 Hz, C, 3a-C), 171.1 (d, J = 33.0 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.02 (t, J = 22.2 Hz); MS *m/z*: 194 (M^+), 174 ($[M - HF]^+$), 135 ($[M - COOMe]^+$), 115 (indenyl cation); HRMS calcd. for $C_{11}H_{11}O_2F$ (M^+): 194.0743, found: 194.0773.

4.7. General procedure for ester exchange reaction of FICA Me ester (**4**) with a secondary alcohol

To a solution of a secondary alcohol (0.177 mmol) in dry THF (0.5 mL) was added dropwise *n*-BuLi (1.59 mol/L in hexane, 0.1 mL, 0.159 mmol) at −5 °C under nitrogen atmosphere. After being stirred for 30 min, a solution of the ester (**4**) (34.3 mg, 0.177 mmol) was added slowly to the mixture. After 15 min, the reaction was quenched with saturated aqueous NH_4Cl solution (1 mL), and then water (5 mL) and Et_2O (10 mL) was added to the reaction mixture. The organic layer was separated, washed with 2% HCl (5 mL), water (5 mL), and saturated aqueous $NaHCO_3$ solution (5 mL), and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography (hexane/AcOEt = 19:1) to give 1-fluoroindan-1-carboxylic acid ester of a secondary alcohol (**5**).

4.7.1. 1-Fluoroindan-1-carboxylic acid 2-butyl ester (**5a**)

The product was isolated in 61% yield as a colorless oil. IR (neat) 2954 cm^{-1} (CH), 1750 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.77 (t, 1.5H, J = 7.3 Hz, 4′-H), 0.92 (t, 1.5H, J = 7.3 Hz, 4′-H), 1.20 (d, 1.5H, J = 6.4 Hz, 1′-H), 1.26 (d, 1.5H, J = 6.4 Hz, 1′-H), 1.48–1.70 (m, 2H, 3′-Hx2), 2.42–2.55 (m, 1H, 2-H), 2.77–2.88 (m, 1H, 2-H), 3.03–3.12 (m, 1H, 3-H), 3.16–3.24 (m, 1H, 3-H), 4.93–5.02 (m, 1H, 2′-H), 7.26 (t, 1H, J = 7.5 Hz, 6-H), 7.32 (d, 1H, J = 7.7 Hz, 4-H), 7.37 (t, 1H, J = 7.7 Hz, 5-H), 7.41 (d, 1H, J = 7.7 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 9.8 and 10.1 (each s, CH_3, 4′-C), 19.5 and 19.7 (each s, CH_3, 1′-C), 28.9 and 30.5 (each s, CH_2, 3-C), 36.4 and 36.5 (each d, J = 23.2 and 24.4 Hz, CH_2, 2-C), 74.2 and 74.3 (each s, CH, 2′-C), 102.1 and 102.2 (each d, J = 190.4 and 189.2 Hz, C, 1-C), 124.1 (s, CH, 7-C), 125.2 (s, CH, 4-C), 127.1 (d, J = 2.4 Hz, CH, 6-C), 130.4 (d, J = 3.7 Hz, CH, 5-C), 139.7 (d, J = 19.5 Hz, C, 7a-C), 145.0 (d, J = 4.9 Hz, C, 3a-C), 170.3 (d, J = 31.7 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.41 (t, J = 23.1 Hz), −139.18 (t, J = 23.1 Hz) ($\Delta\delta$ = 0.23); MS *m/z*: 236 (M^+), 216 ($[M - HF]^+$), 135 ($[M - COOR^*]^+$), 115 (indenyl cation); HRMS calcd. for $C_{14}H_{17}O_2F$ (M^+): 236.1212, found: 236.1210.

4.7.2. 1-Fluoroindan-1-carboxylic acid 2-pentyl ester (**5b**)

The product was isolated in 60% yield as a colorless oil. IR (neat) 2974 cm^{-1} (CH), 1746 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.82 (t, 1.5H, J = 7.3 Hz, 5′-H), 0.92 (t, 1.5H, J = 7.3 Hz, 5′-H), 1.10–1.68 (m, 4H, 4′-H x2, 3′-Hx2), 1.20 (d, 1.5H, J = 6.4 Hz, 1′-H), 1.26 (d, 1.5H, J = 6.4 Hz, 1′-H), 2.42–2.54 (m, 1H, 2-H), 2.76–2.88 (m, 1H, 2-H), 3.02–3.12 (m, 1H, 3-H), 3.16–3.24 (m, 1H, 3-H), 5.01–5.08 (m, 1H, 2′-H), 7.26 (t, 1H, J = 7.3 Hz, 6-H), 7.32 (dd, 1H, J = 1.1, 7.5 Hz, 4-H), 7.37 (tt, 1H, J = 1.3, 7.3 Hz, 5-H), 7.41 (d, 1H, J = 7.3 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 14.0 and 14.1 (each s, CH_3, 5′-C), 18.6 and 19.0 (each s, CH_2, 4′-C), 20.0 and 20.2 (each s, CH_3, 1′-C), 30.4 (s, CH_2, 3-C), 36.4 and 36.5 (each d, J = 23.2 and 24.4 Hz, CH_2, 2-C), 38.0 and 38.1 (each s, CH_2, 3′-C), 72.8 and 72.9 (each s, CH, 2′-C), 102.1 (d, J = 191.7 Hz, C, 1-C), 124.2 (s, CH, 7-C), 125.2 (s, CH, 4-C), 127.1 (d, J = 2.4 Hz, CH, 6-C), 130.4 (d, J = 2.4 Hz, CH, 5-C), 139.7 (d, J = 20.8 Hz, C, 7a-C), 144.9 and 145.0 (each d, J = 3.7 and 4.9 Hz, C, 3a-C), 170.3 (d, J = 33.0 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.44 (t, J = 21.3 Hz) and −139.12 (t, J = 22.2 Hz) ($\Delta\delta$ = 0.32); MS *m/z*: 250 (M^+), 230 ($[M - HF]^+$), 135 ($[M - COOR^*]^+$), 115 (indenyl cation); HRMS calcd. for $C_{15}H_{19}O_2F$ (M^+): 250.1369, found: 250.1384.

4.7.3. 1-Fluoroindan-1-carboxylic acid 2-hexyl ester (**5c**)

The product was isolated in 63% yield as a colorless oil. IR (neat) 2960 cm^{-1} (CH), 1746 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.80 and 0.89 (each t, 3H, J = 7.3 and 6.8 Hz, 6′-H), 1.05–1.14 (m, 1H, 4′-H), 1.14–1.26 (m, 1H, 5′-H), 1.20 and 1.26 (each d, 3H, J = 6.4 Hz, 1′-H), 1.24–1.36 (m, 2H, 4′-H and 5′-H), 1.42–1.68 (m, 2H, 3′-H), 2.40–2.54 (m, 1H, 2-H), 2.74–2.88 (m, 1H, 2-H), 3.00–3.12 (m, 1H, 3-H), 3.12–3.24 (m, 1H, 3-H), 4.96–5.07 (m, 1H, 2′-H), 7.26 (t, 1H, J = 7.5 Hz, 6-H), 7.32 (d, 1H, J = 7.7 Hz, 4-H) 7.37 (tt, 1H, J = 1.7, 7.3 Hz, 5-H), 7.41 (td, 1H, J = 1.7, 7.7 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 14.18 and 14.24 (each s, CH_3, 6′-C), 20.00 and 20.2 (each s, CH_3, 1′-C), 22.6 and 22.7 (each s, CH_2, 5′-C), 27.5 and 27.8 (each s, CH_2, 4′-C), 30.5 and 30.8 (each s, CH_2, 3-C), 35.6 and 35.7 (each s, CH_2, 3′-C), 36.4 and 36.5 (each d, J = 23.2 Hz, CH_2, 2-C), 73.0 and 73.1 (each s, CH, 2′-C), 102.1 (d, J = 190.4 Hz, C, 1-C), 124.2 (s, CH, 7-C), 125.2 (s, CH, 4-C),

127.1 (s, CH, 6-C), 130.4 (d, J = 3.7 Hz, CH, 5-C), 139.6 and 139.7 (each d, J = 20.8 Hz, C, 7a-C), 144.9 and 145.0 (each d, J = 4.9 Hz, C, 3a-C), 170.2 (d, J = 34.2 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.62 (t, J = 19.4 Hz) and −139.20 (t, J = 20.3 Hz) ($\Delta\delta$ = 0.41); MS *m/z*: 264 (M^+), 244 ([M − HF]$^+$), $^+$), 135 ([M − COOR*]$^+$), 115 (indenyl cation); HRMS calcd. for $C_{16}H_{21}O_2F$ (M^+): 264.1525, found: 264.1496.

*4.7.4. 1-Fluoroindan-1-carboxylic acid 2-heptyl ester (**5d**)*

The product was isolated in 66% yield as a colorless oil. IR (neat) 2954 cm^{-1} (CH), 1746 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.83 and 0.88 (each t, 3H, J = 7.1 Hz, 7′-H), 1.08–1.37 (m, 6H, 4′–6′-H), 1.20 and 1.26 (each d, 3H, J = 6.0 and 6.4 Hz, 1′-H), 1.41–1.67 (m, 2H, 3′-H), 2.42–2.54 (m, 1H, 2-H), 2.76–2.88 (m, 1H, 2-H), 3.03–3.12 (m, 1H, 3-H), 3.16–3.23 (m, 1H, 3-H), 4.87–5.07 (m, 1H, 2′-H), 7.26 (ddt, 1H, J = 0.9, 2.1, 7.6 Hz, 6-H), 7.32 (dd, 1H, J = 1.3, 7.7 Hz, 4-H), 7.37 (tt, 1H, J = 1.5, 9.0 Hz, 5-H), 7.40 (dd, 1H, J = 0.9, 7.3 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 14.2 and 14.3 (each s, CH_3, 7′-C), 20.0 and 20.2 (each s, CH_3, 1′-C), 22.7 and 22.8 (each s, CH_2, 6′-C), 25.0 and 25.3 (each s, CH_2, 4′-C), 30.5 and 30.8 (each s, CH_2, 3-C), 31.7 and 31.8 (each s, CH_2, 5′-C), 35.89 and 35.93 (each s, CH_2, 3′-C), 36.4 and 36.5 (each d, J = 23.2 Hz, CH_2, 2-C), 73.0 and 73.1 (each s, CH, 2′-C), 102.1 (d, J = 190.4 Hz, C, 1-C), 124.2 (s, CH, 7-C), 125.2 (s, CH, 4-C), 127.1 (s, CH, 6-C), 130.4 (d, J = 2.4 Hz, CH, 5-C), 139.6 (d, J = 20.8 Hz, C, 7a-C), 144.9 and 145.0 (each d, J = 4.9 Hz, C, 3a-C), 170.3 (d, J = 34.2 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.54 (t, J = 20.6 Hz) and −139.21 (t, J = 19.0 Hz) ($\Delta\delta$ = 0.33); MS *m/z*: 278 (M^+), 258 ([M − HF]$^+$), 135 ([M − COOR*]$^+$), 115 (indenyl cation); HRMS calcd. for $C_{17}H_{23}O_2F$ (M^+): 278.1682, found: 278.1635.

*4.7.5. 1-Fluoroindan-1-carboxylic acid 2-octyl ester (**5e**)*

The product was isolated in 65% yield as a colorless oil. IR (neat) 2933 cm^{-1} (CH), 1747 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.86 and 0.88 (each t, 3H, J = 7.1 and 6.8 Hz, 8′-H), 1.06–1.36 (m, 8H, 4′–7′-H), 1.20 and 1.26 (each d, 3H, J = 6.4 Hz, 1′-H), 1.42–1.67 (m, 2H, 3′-H), 2.40–2.55 (m, 1H, 2-H), 2.75–2.90 (m, 1H, 2-H), 3.05–3.10 (m, 1H, 3-H), 3.15–3.25 (m, 1H, 3-H), 4.98–5.07 (m, 1H, 2′-H), 7.26 (t, 1H, J = 7.7 Hz, 6-H), 7.31 (d, 1H, J = 7.7 Hz, 4-H), 7.37 (tt, 1H, J = 1.3, 7.6 Hz, 5-H), 7.41 (d, 1H, J = 7.7 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 14.4 (s, CH_3, 8′-C), 20.0 and 20.2 (each s, CH_3, 1′-C), 22.7 and 22.8 (each s, CH_2, 7′-C), 25.3 and 25.6 (each s, CH_2, 4′-C), 29.1 and 29.3 (each s, CH_2, 5′-C), 30.5 (s, CH_2, 3-C), 31.9 and 32.0 (each s, CH_2, 6′-C), 35.9 (s, CH_2, 3′-C), 36.4 and 36.5 (each d, J = 23.2 Hz, CH_2, 2-C), 73.0 and 73.2 (each s, CH, 2′-C), 102.1 and 102.2 (each d, J = 190.4 Hz, C, 1-C), 124.2 (s, CH, 7-C), 125.2 (s, CH, 4-C), 127.1 (d, J = 2.4 Hz, CH, 6-C), 130.4 (d, J = 2.4 Hz, CH, 5-C), 139.7 (d, J = 20.8 Hz, C, 7a-C), 144.9 and 145.0 (each d, J = 4.9 Hz, C, 3a-C), 170.2 (d, J = 31.7 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.54 (t, J = 21.3 Hz) and −139.21 (t, J = 20.8 Hz) ($\Delta\delta$ = 0.33); MS *m/z*: 292 (M^+), 272 ([M − HF]$^+$), 135 ([M − COOR*]$^+$), 115 (indenyl cation); HRMS calcd. for $C_{18}H_{25}O_2F$ (M^+): 292.1839, found: 292.1847.

*4.7.6. 1-Fluoroindan-1-carboxylic acid 2-nonyl ester (**5f**)*

The product was isolated in 80% yield as a colorless oil. IR (neat) 2928 cm^{-1} (CH), 1747 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.87 and 0.88 (each t, 3H, J = 7.2 and 7.0 Hz, 9′-H), 1.06–1.37 (m, 10H, 4′–8′-H), 1.20 and 1.26 (each d, 3H, J = 6.0 Hz, 1′-H), 1.41–1.67 (m, 2H, 3′-H), 2.42–2.54 (m, 1H, 2-H), 2.76–2.88 (m, 1H, 2-H), 3.02–3.12 (m, 1H, 3-H), 3.16–3.24 (m, 1H, 3-H), 4.99–5.07 (m, 1H, 2′-H), 7.26 (dt, 1H, J = 2.8, 7.5 Hz, 6-H), 7.31 (dd, 1H, J = 0.9, 7.7 Hz, 4-H), 7.37 (tt, 1H, J = 1.5, 7.5 Hz, 5-H), 7.40 (d, 1H, J = 7.7 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 14.4 (s, CH_3, 9′-C), 20.0 and 20.2 (each s, CH_3, 1′-C), 22.9 (s, CH_2, 8′-C), 25.4 and 25.7 (each s, CH_2, 4′-C), 29.4 (s, CH_2, 6′-C), 29.4 (s, CH_2, 5′-C), 30.5 (s, CH_2, 3-C), 31.9 and 32.0 (each s, CH_2, 7′-C), 35.9 and 36.0 (each s, CH_2, 3′-C), 36.4 and 36.5 (each d, J = 23.2 Hz, CH_2, 2-C), 73.0 and 73.2 (each s, CH, 2′-C), 102.1 and 102.2 (each d, J = 184.3, 190.4 Hz, C, 1-C), 124.2 (s, CH, 7-C), 125.2 (s, CH, 4-C), 127.1 (s, CH, 6-C), 130.4 (d, J = 2.4 Hz, CH, 5-C), 139.7 (d, J = 20.8 Hz, C, 7a-C), 144.9 (d, J = 4.9 Hz, C, 3a-C), 170.3 (d, J = 31.7 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.54 (t, J = 20.8 Hz) and −139.21 (t, J = 20.8 Hz) ($\Delta\delta$ = 0.33); MS *m/z*: 306 (M^+), 286 ([M − HF]$^+$), 135 ([M − COOR*]$^+$), 115 (indenyl cation); HRMS calcd. for $C_{19}H_{27}O_2F$ (M^+): 306.1995, found: 306.1955.

*4.7.7. 1-Fluoroindan-1-carboxylic acid 1-phenylethyl ester (**5g**)*

The product was isolated in 35% yield as a colorless oil. IR (neat) 2981 cm^{-1} (CH), 1746 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 1.53 and 1.58 (each d, 3H, J = 6.8 and 6.4 Hz, 1′-H), 2.42–2.55 (m, 1H, 2-H), 2.76–2.90 (m, 1H, 2-H), 3.02–3.24 (m, 2H, 3-H), 5.99 and 6.01 (each q, 1H, J = 6.8 and 6.4 Hz, 2′-H), 7.17–7.40 (m, 9H, Ph-H, Ph′-H); ^{13}C NMR (75.46 MHz) δ 22.2 and 22.6 (each s, CH_3, 1′-C), 30.5 (s, CH_2, 3-C), 36.3 and 36.4 (each d, J = 23.2, 24.4 Hz, CH_2, 2-C), 73.9 and 74.2 (each s, CH, 2′-C), 102.1 (d, J = 190.4 Hz, C, 1-C), 124.2 and 124.4 (each s, CH, 7-C), 125.2 (s, CH, 4-C), 125.8 and 126.2 (each s, CH, 6′-C), 127.1 (d, J = 2.4 Hz, CH, 6-C), 128.2, 128.5 and 128.7 (each s, CH, 4′-, 5′-C), 130.5 (d, J = 2.4 Hz, CH, 5-C), 139.4 and 139.6 (each d, J = 20.8 Hz, C, 7a-C), 140.9 and 141.0 (each s, C, 3′-C) 145.0 (d, J = 4.9 Hz, C, 3a-C), 169.7 (d, J = 33.0 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.86 (t, J = 19.8 Hz) and –139.35 (t, J = 21.3 Hz) ($\Delta\delta$ = 0.51); MS *m/z*: 284 (M^+), 264 ([M − HF]$^+$), 135 ([M − COOR*]$^+$), 115 (indenyl cation); HRMS calcd. for $C_{18}H_{17}O_2F$ (M^+): 284.1213, found: 284.1178.

*4.7.8. 1-Fluoroindan-1-carboxylic acid l-menthyl ester (**5h**)*

The product was isolated in 85% yield as a colorless oil. IR (neat) 2954 cm^{-1} (CH), 1747 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.62 and 0.77 (each d, 3H, J = 6.8 Hz, 9′-H), 0.72 and 0.88 (each d, 3H, J = 6.8 Hz, 8′-H), 0.90 and 0.91 (each d, 3H, J = 6.4 Hz, 10′-H), 0.79–1.10 (m, 3H, 3′aq-H, 4′aq-H, 6′aq-H), 1.24–1.37 (m, 1H, 2′aq-H), 1.38–1.55 (m, 2H, 7′-H, 5′aq-H), 1.60–1.71 (m, 2H, 3′eq-H, 4′eq-H), 1.93–2.06 (m, 1H, 6′eq-H), 2.42–2.55 (m, 1H, 2-H), 2.73–2.86 (m, 1H, 2-

H), 3.02–3.11 (m, 1H, 3-H), 3.16–3.24 (m, 1H, 3-H), 4.76 and 4.81 (each ddd, 1H, J = 4.3, 11.1, 11.1 Hz, 1′aq-H), 7.18–7.42 (m, 4H, Ph-H); ^{13}C NMR (75.46 MHz) δ 16.3 and 16.4 (each s, CH_3, 9′-C), 20.8 and 21.1 (each s, CH_3, 8′-C), 22.2 and 22.3 (each s, CH_3, 10′-C), 23.4 and 23.6 (each s, CH_2, 3′-C), 26.2 and 26.5 (each s, CH, 7′-C), 30.5 (s, CH_2, 3-C), 31.6 and 31.7 (each s, CH, 5′-C), 34.3 and 34.4 (each s, CH_2, 4′-C), 36.4 and 36.6 (each d, J = 23.2 Hz, CH_2, 2-C), 40.5 and 40.9 (each s, CH_2, 6′-C), 47.0 and 47.2 (each s, CH, 2′-C), 76.1 and 76.2 (each s, CH, 1′-C), 102.0 and 102.1 (each d, J = 195.3, 200.2 Hz, C, 1-C), 124.1 (s, CH, 7-C), 125.1 (s, CH, 4-C), 127.1 (d, J = 12.2 Hz, CH, 6-C), 130.4 (d, J = 2.4 Hz, CH, 5-C), 139.6 (d, J = 20.8 Hz, C, 7a-C), 144.8 and 144.9 (each d, J = 4.9 Hz, C, 3a-C), 170.3 and 170.2 (each d, J = 33.0 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.83 (t, J = 19.0 Hz) and −138.80 (t, J = 21.7 Hz) ($\Delta\delta$ = 1.03); MS *m/z*: 318 (M^+), 298 ($[M - HF]^+$), 135 ($[M - COOR^*]^+$), 115 (indenyl cation); HRMS calcd. for $C_{20}H_{27}O_2F$ (M^+): 318.1995, found: 318.1976.

4.7.9. (−)-1-Fluoroindan-1-carboxylic acid (−)-8-phenylmenthyl ester (**5ia**)

The product was isolated in 44% yield as a colorless oil. $[\alpha]_D^{27}$ −33.2 (c 2.69, $CHCl_3$); IR (neat) 2954 cm^{-1} (CH), 1732 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.78 (dddd, 1H, J = 3.4, 12.0, 12.8, 12.8 Hz, 4′aq-H), 0.86 (d, 3H, J = 6.4 Hz, 10′-H), 0.96 (dddd, 1H, J = 3.4, 12.8, 12.8, 13.2 Hz, 3′aq-H), 1.05 (s, 3H, 9′-H), 1.08 (ddd, 1H, J = 10.7, 12.0, 12.0 Hz, 6′aq-H), 1.16 (s, 3H, 8′-H), 1.37 (dddd, 1H, J = 3.4, 3.4, 3.8, 13.7 Hz, 3′eq-H), 1.45 (m, 1H, 5′aq-H), 1.53 (ddddd, 1H, J = 2.1, 3.4, 3.4, 3.8, 12.8 Hz, 4′eq-H), 1.92 (ddd, 1H, J = 3.4, 10.7, 12.4 Hz, 2′aq-H), 2.01 (dddddd, 1H, J = 1.7, 1.7, 1.7, 2.1, 2.6, 12.0 Hz, 6′eq-H), 2.39 (dddd, 1H, J = 5.6, 8.5, 14.1, 23.5 Hz, 2-H), 2.69 (dddd, 1H, J = 5.1, 8.5, 14.1, 17.9 Hz, 2-H), 3.04 (m, 1H, 3-H), 3.16 (m, 1H, 3-H), 4.87 (ddd, 1H, J = 4.3, 10.7, 10.7 Hz, 1′aq-H), 7.12 (tt, 1H, J = 1.3, 7.3 Hz, p'-H), 7.15–7.23 (m, 4H, Ph′-H), 7.26 (t, 1H, J = 7.7 Hz, 6-H), 7.29 (d, 1H, J = 6.8 Hz, 4-H), 7.35 (tt, 1H, J = 1.3, 7.7 Hz, 5-H), 7.43 (d, 1H, J = 7.7 Hz, 7-H); ^{13}C NMR (75.46 MHz) δ 22.0 (s, CH_3, 10′-C), 24.6(s, CH_3, 8′-C), 27.4 (s, CH_2, 3′-C), 29.3 (s, CH_3, 9′-C), 30.5 (s, CH_2, 3-C), 31.6 (s, CH, 5′-C), 34.7 (s, CH_2, 4′-C), 36.1 (d, J = 23.2 Hz, CH_2, 2-C), 40.3 (s, C, 7′-C), 41.7 (s, CH_2, 6′-C), 50.7 (s, CH, 2′-C), 77.1 (s, CH, 1′-C), 102.0 (d, J = 191.7 Hz, C, 1-C), 124.3 (s, CH, 7-C), 125.2 (s, CH, 4-C), 125.4 (s, CH, p'-C), 125.7 (s, CH, o'- or m'-C), 127.1 (s, CH, 6-C), 128.0 (s, CH, o'- or m'-C), 130.5 (d, J = 3.7 Hz, CH, 5-C), 139.3 (d, J = 22.0 Hz, C, 7a-C), 145.0 (d, J = 3.7 Hz, C, 3a-C), 150.2 (s, C, *ipso*′-C), 169.8 (d, J = 31.7 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −139.13 (t, J = 23.1 Hz); MS *m/z*: 394 (M^+), 374 ($[M - HF]^+$), 135 ($[M - COOR^*]^+$), 115 (indenyl cation); HRMS calcd. for $C_{26}H_{31}O_2F$ (M^+): 394.2308, found: 394.2266.

4.7.10. (+)-1-Fluoroindan-1-carboxylic acid (−)-8-phenylmenthyl ester (**5ib**)

The product was isolated in 48% yield as a colorless solid. m.p. 88 °C; $[\alpha]_D^{27}$ +1.0 (c 1.13, $CHCl_3$); IR (neat) 2957 cm^{-1} (CH), 1745 cm^{-1} (C=O); ^{1}H NMR (500 MHz) δ 0.75 (dddd, 1H, J = 3.0, 12.4, 12.4, 12.4 Hz, 4′aq-H), 0.77 (ddd, 1H, J = 12.4, 12.4, 12.4 Hz, 6′aq-H), 0.80 (d, 3H, J = 6.4 Hz, 10′-H), 1.03 (dddd, 1H, J = 3.4, 12.8, 12.8, 13.2 Hz, 3′aq-H), 1.25 (s, 3H, 9′-H), 1.38 (s, 3H, 8′-H), 1.41 (m, 1H, 5′aq-H), 1.50 (dddd, 1H, J = 3.4, 3.4, 3.4, 13.7 Hz, 3′eq-H), 1.54 (ddddd, 1H, J = 3.0, 3.4, 3.8, 3.8, 12.8 Hz, 4′eq-H), 1.73 (dddddd, 1H, J = 1.7, 2.1, 2.1, 2.1, 2.1, 12.0 Hz, 6′eq-H), 1.99 (ddd, 1H, J = 3.4, 10.7, 12.4 Hz, 2′aq-H), 2.14–2.21 (m, 2H, 2-H), 2.87 (m, 1H, 3-H), 3.07 (m, 1H, 3-H), 5.01 (ddd, 1H, J = 4.3, 10.7, 10.7 Hz, 1′aq-H), 7.14–7.17 (m, 1H, p'-H), 7.25 (t, 1H, J = 7.7 Hz, 6-H), 7.27–7.29 (m, 5H, 4, o'-, m'-H), 7.34–7.37 (m, 2H, 5, 7-H); ^{13}C NMR (75.46 MHz) δ 22.0 (s, CH_3, 10′-C), 26.6(s, CH_3, 9′-C), 27.2 (s, CH_2, 3′-C), 27.8 (s, CH_3, 8′-C), 30.4 (s, CH_2, 3-C), 31.5 (s, CH, 5′-C), 34.5 (s, CH_2, 4′-C), 35.5 (d, J = 23.2 Hz, CH_2, 2-C), 40.3 (s, C, 7′-C), 41.3 (s, CH_2, 6′-C), 50.0 (s, CH, 2′-C), 76.8 (s, CH, 1′-C), 102.0 (d, J = 189.2 Hz, C, 1-C), 124.2 (s, CH, 7-C), 125.1 (s, CH, 4-C), 125.4 (s, CH, p'-C), 125.6 (s, CH, o'- or m'-C), 127.0 (d, J = 2.4 Hz, CH, 6-C), 128.2 (s, CH, o'- or m'-C), 130.3 (d, J = 3.7 Hz, CH, 5-C), 139.5 (d, J = 20.8 Hz, C, 7a-C), 145.1 (d, J = 3.7 Hz, C, 3a-C), 150.9 (s, C, *ipso*′-C), 169.8 (d, J = 33.0 Hz, C, *C*OO); ^{19}F NMR (254 MHz) δ −138.77 (t, J = 22.2 Hz); MS *m/z*: 394 (M^+), 374 ($[M - HF]^+$); HRMS calcd. for $C_{26}H_{31}O_2F$ (M^+): 394.2308, found: 394.2269.

4.8. General procedure for condensation reaction of α-methoxy-α-(trifluoromethyl)phenylacetyl chloride with a secondary alcohol

(*R*)-or (*S*)-MTPA chloride (79.2 μmol, 15 μL) was added to a solution of pyridine (13 μL) and a secondary alcohol (95 μmol) in dry CH_2Cl_2 (1 mL) under nitrogen atmosphere and stirred for 1–2 days. The solvent was evaporated and the residue was purified by PLC (hexane/AcOEt = 6:1) to give α-methoxy-α-(trifluoromethyl)-phenylacetic acid ester of a secondary alcohol (**6**).

4.8.1. (S)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-pentyl ester (**6b**(SR))

The product was isolated in 41% yield as a colorless oil. $[\alpha]_D^{26}$ −62 (c 0.48, $CHCl_3$); IR (neat) 2962 cm^{-1} (CH), 1745 cm^{-1} (C=O), 1268 cm^{-1} (C–O), 1170 cm^{-1} (C–O); ^{1}H NMR (500 MHz) δ 0.86 (t, 3H, J = 7.3 Hz, 5′-H), 1.17–1.31 (m, 2H, 4′-H), 1.34 (d, 3H, J = 6.4 Hz, 1′-H), 1.48 (dddd, 1H, J = 5.1, 6.4, 9.8, 14.1 Hz, 3′-H), 1.63 (dddd, 1H, J = 5.1, 7.7, 9.8, 14.1 Hz, 3′-H), 3.57 (q, 3H, J = 1.3 Hz, OCH_3), 5.17 (qdd, 1H, J = 6.4, 5.1, 7.7 Hz, 2′-H), 7.39–7.41 (m, 3H, Ph-H), 7.53–7.55 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.0 (s, CH_3, 5′-C), 18.6 (s, CH_2, 4′-C), 20.1 (s, CH_3, 1′-C), 37.9 (s, CH_2, 3′-C), 55.6 (s, CH_3, OCH_3), 74.0 (s, CH, 2′-C), 84.6 (q, J = 28.1 Hz, C, 2-C), 123.5 (q, J = 286.9 Hz, C, CF_3), 127.4, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.7 (s, C, *ipso*-C), 166.1 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −72.01 (s); MS *m/z*: 303 ($[M - 1]^+$), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{15}H_{19}O_3F_3$ (M^+): 304.1286, found: 304.1261.

*4.8.2. (R)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-pentyl ester (**6b**(RR))*

The product was isolated in 52% yield as a colorless oil. $[\alpha]_D^{26}$ +24.0 (c 0.827, $CHCl_3$); IR (neat) 2962 cm^{-1} (CH), 1744 cm^{-1} (C=O), 1267 cm^{-1} (C–O), 1172 cm^{-1} (C–O); ^1H NMR (500 MHz) δ 0.92 (t, 3H, *J* = 7.3 Hz, 5′-H), 1.25 (d, 3H, *J* = 6.4 Hz, 1′-H), 1.38 (m, 2H, 4′-H), 1.53 (dddd, 1H, *J* = 5.6, 6.0, 9.8, 13.7 Hz, 3′-H), 1.69 (dddd, 1H, *J* = 5.1, 7.7, 9.8, 13.7 Hz, 3′-H), 3.56 (s, 3H, OCH_3), 5.16 (qdd, 1H, *J* = 6.0, 6.4, 7.3 Hz, 2′-H), 7.38–7.41 (m, 3H, Ph-H), 7.52–7.54 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.1 (s, CH_3, 5′-C), 18.9 (s, CH_2, 4′-C), 19.8 (s, CH_3, 1′-C), 38.0 (s, CH_2, 3′-C), 55.6 (s, CH_3, OCH_3), 74.2 (s, CH, 2′-C), 84.8 (q, *J* = 28.1 Hz, C, 2-H), 123.5 (q, *J* = 288.1 Hz, C, CF_3), 127.4, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.5 (s, C, *ipso*-C), 166.2 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −72.00 (s); MS *m*/*z*: 304 (M^+), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{15}H_{19}O_3F_3$ (M^+): 304.1286, found: 304.1243.

*4.8.3. (S)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-hexyl ester (**6c**(SR))*

The product was isolated in 44% yield as a colorless oil. $[\alpha]_D^{27}$ −58 (c 0.59, $CHCl_3$); IR (neat) 2956 cm^{-1} (CH), 1745 cm^{-1} (C=O), 1269 cm^{-1} (C–O), 1171 cm^{-1} (C–O); ^1H NMR (500 MHz) δ 0.83 (t, 3H, *J* = 7.3 Hz, 6′-H), 1.12–1.21 (m, 2H, 4′-H), 1.21–1.31 (m, 2H, 5′-H), 1.34 (d, 3H, *J* = 6.4 Hz, 1′-H), 1.51 (dddd, 1H, *J* = 5.1, 6.4, 9.0, 14.1 Hz, 3′-H), 1.62 (dddd, 1H, *J* = 5.1, 7.7, 9.0, 13.7 Hz, 3′-H), 3.57 (q, 3H, *J* = 1.3 Hz, OCH_3), 5.16 (qdd, 1H, *J* = 6.4, 5.1, 6.4 Hz, 2′-H), 7.38–7.41 (m, 3H, Ph-H), 7.53–7.55 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.2 (s, CH_3, 6′-C), 20.2 (s, CH_3, 1′-C), 22.6 (s, CH_2, 5′-C), 27.4 (s, CH_2, 4′-C), 35.5 (s, CH_2, 3′-C), 55.6 (d, *J* = 2.4 Hz, CH_3, OCH_3), 74.2 (s, CH, 2′-C), 84.6 (q, *J* = 28.1 Hz, C, 2-H), 123.5 (q, *J* = 286.9 Hz, C, CF_3), 127.3, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.7 (s, C, *ipso*-C), 166.1 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −72.01 (s); MS *m*/*z*: 317 ($[M - 1]^+$), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{16}H_{21}O_3F_3$ (M^+): 318.1443, found: 318.1411.

*4.8.4. (R)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-hexyl ester (**6c**(RR))*

The product was isolated in 60% yield as a colorless oil. $[\alpha]_D^{26}$ +24.4 (c 1.01, $CHCl_3$); IR (neat) 2954 cm^{-1} (CH), 1744 cm^{-1} (C=O), 1269 cm^{-1} (C–O), 1171 cm^{-1} (C–O); ^1H NMR (500 MHz) δ 0.89 (t, 3H, *J* = 6.8 Hz, 6′-H), 1.25 (d, 3H, *J* = 6.4 Hz, 1′-H), 1.27–1.39 (m, 4H, 4′-, 5′-H), 1.51–1.60 (m, 1H, 3′-H), 1.65–1.73 (m, 1H, 3′-H), 3.55 (s, 3H, OCH_3), 5.14 (qdd, 1H, *J* = 6.0, 6.4, 7.3 Hz, 2′-H), 7.38–7.42 (m, 3H, Ph-H), 7.51–7.54 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.2 (s, CH_3, 6′-C), 19.8 (s, CH_3, 1′-C), 22.7 (s, CH_2, 5′-C), 27.8 (s, CH_2, 4′-C), 35.6 (s, CH_2, 3′-C), 55.6 (s, CH_3, OCH_3), 74.4 (s, CH, 2′-C), 84.8 (q, *J* = 28.1 Hz, C, 2-H), 123.5 (q, *J* = 288.1 Hz, C, CF_3), 127.5, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.5 (s, C, *ipso*-C), 166.2 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −71.95 (s); MS *m*/*z*: 318 (M^+), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{16}H_{22}O_3F_3$ ($[M + H]^+$): 319.1521, found: 319.1472.

*4.8.5. (S)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-heptyl ester (**6d**(SR))*

The product was isolated in 35% yield as a colorless oil. $[\alpha]_D^{28}$ −23 (c 0.56, $CHCl_3$); IR (neat) 2935 cm^{-1} (CH), 1745 cm^{-1} (C=O), 1266 cm^{-1} (C–O), 1172 cm^{-1} (C–O); ^1H NMR (500 MHz) δ 0.88 (t, 3H, *J* = 6.8 Hz, 7′-H), 1.26 (d, 3H, *J* = 6.4 Hz, 1′-H), 1.25–1.39 (m, 6H, 4′–6′-H), 1.55 (m, 1H, 3′-H), 1.69 (dddd, 1H, *J* = 5.1, 7.7, 9.8, 14.1 Hz, 3′-H), 3.55 (q, 3H, *J* = 1.3 Hz, OCH_3), 5.14 (qdd, 1H, *J* = 6.0, 6.4, 7.7 Hz, 2′-H), 7.38–7.42 (m, 3H, Ph-H), 7.52–7.54 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.3 (s, CH_3, 7′-C), 19.8 (s, CH_3, 1′-C), 22.8 (s, CH_3, 6′-C), 25.3 (s, CH_2, 4′-C), 31.7 (s, CH_2, 5′-C), 35.8 (s, CH_2, 3′-C), 55.6 (s, CH_3, OCH_3), 74.4 (s, CH, 2′-C), 84.8 (q, *J* = 28.1 Hz, C, 2-H), 123.5 (q, *J* = 288.1 Hz, C, CF_3), 127.5, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.5 (s, C, *ipso*-C), 166.2 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −71.95 (s); MS *m*/*z*: 331 ($[M - 1]^+$), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{17}H_{23}O_3F_3$ (M^+): 332.1599, found: 332.1637.

*4.8.6. (R)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-heptyl ester (**6d**(RR))*

The product was isolated in 57% yield as a colorless oil. $[\alpha]_D^{26}$ +57.2 (c 0.993, $CHCl_3$); IR (neat) 2936 cm^{-1} (CH), 1745 cm^{-1} (C=O), 1266 cm^{-1} (C–O), 1172 cm^{-1} (C–O); ^1H NMR (500 MHz) δ 0.84 (t, 3H, *J* = 7.3 Hz, 7′-H), 1.17–1.29 (m, 6H, 4′–6′-H), 1.33 (d, 3H, *J* = 6.4 Hz, 1′-H), 1.46–1.53 (m, 1H, 3′-H), 1.59–1.65 (m, 1H, 3′-H), 3.57 (s, 3H, OCH_3), 5.16 (qdd, 1H, *J* = 6.4, 6.0, 7.7 Hz, 2′-H), 7.37 7.41 (m, 3H, Ph-H), 7.52–7.56 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.2 (s, CH_3, 7′-C), 20.2 (s, CH_3, 1′-C), 22.7 (s, CH_3, 6′-C), 25.0 (s, CH_2, 4′-C), 31.7 (s, CH_2, 5′-C), 35.8 (s, CH_2, 3′-C), 55.6 (s, CH_3, OCH_3), 74.2 (s, CH, 2′-C), 84.6 (q, *J* = 28.1 Hz, C, 2-H), 123.5 (q, *J* = 288.1 Hz, C, CF_3), 127.3, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.7 (s, C, *ipso*-C), 166.1 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −71.99 (s); MS *m*/*z*: 333 ($[M + 1]^+$), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{17}H_{23}O_3F_3$ (M^+): 332.1599, found: 332.1573.

*4.8.7. (S)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-nonyl ester (**6f**(SR))*

The product was isolated in 43% yield as a colorless oil. $[\alpha]_D^{28}$ −46.9 (c 0.813, $CHCl_3$); IR (neat) 2930 cm^{-1} (CH), 1745 cm^{-1} (C=O), 1266 cm^{-1} (C–O), 1172 cm^{-1} (C–O); ^1H NMR (500 MHz) δ 0.87 (t, 3H, *J* = 7.3 Hz, 9′-H), 1.13–1.31 (m, 10H, 4′–8′-H), 1.33 (d, 3H, *J* = 6.4 Hz, 1′-H), 1.45–1.54 (m, 1H, 3′-H), 1.56–1.66 (m, 1H, 3′-H), 3.57 (q, 3H, *J* = 1.3 Hz, OCH_3), 5.15 (qdd, 1H, *J* = 6.4, 5.1, 7.7 Hz, 2′-H), 7.38–7.41 (m, 3H, Ph-H), 7.53–7.56 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.4 (s, CH_3, 9′-C), 20.2 (s, CH_3, 1′-C), 22.9 (s, CH_2, 8′-C), 25.3 (s, CH_2, 4′-C), 29.4 (s, CH_2, 6′-H), 29.5 (s, CH_2, 5′-H), 32.0 (s, CH_2, 7′-C), 35.8 (s, CH_2, 3′-C), 55.6 (s, CH_3, OCH_3), 74.2 (s, CH, 2′-C), 84.6 (q, *J* = 26.9 Hz, C, 2-H), 123.5 (q, *J* = 288.1 Hz, C, CF_3), 127.3, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.7 (s, C, *ipso*-C), 166.1 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −72.00 (s); MS *m*/*z*: 359 ($[M - 1]^+$), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{19}H_{27}O_3F_3$ (M^+): 360.1912, found: 360.1885.

*4.8.8. (R)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (R)-2-nonyl ester (**6f**(RR))*

The product was isolated in 58% yield as a colorless oil. $[\alpha]_D^{27}$ −20.6 (c 1.10, $CHCl_3$); IR (neat) 2931 cm^{-1} (CH), 1745 cm^{-1} (C=O), 1268 cm^{-1} (C–O), 1173 cm^{-1} (C–O); ^1H NMR (500 MHz) δ 0.88 (t, 3H, J = 6.8 Hz, 9′-H), 1.25 (d, 3H, J = 6.0 Hz, 1′-H), 1.25–1.40 (m, 10H, 4′–8′-H), 1.51–1.58 (m, 1H, 3′-H), 1.64–1.72 (m, 1H, 3′-H), 3.55 (s, 3H, OCH_3), 5.14 (qdd, 1H, J = 6.4, 6.0, 6.4 Hz, 2′-H), 7.38–7.42 (m, 3H, Ph-H), 7.51–7.55 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 14.4 (s, CH_3, 9′-C), 19.7 (s, CH_3, 1′-C), 22.9 (s, CH_2, 8′-C), 25.6 (s, CH_2, 4′-C), 29.4 (s, CH_2, 6′-H), 29.5 (s, CH_2, 5′-H), 32.0 (s, CH_2, 7′-C), 35.9 (s, CH_2, 3′-C), 55.6 (s, CH_3, OCH_3), 74.4 (s, CH, 2′-C), 84.8 (q, J = 28.1 Hz, C, 2-H), 123.5 (q, J = 288.1 Hz, C, CF_3), 127.5, 128.4 (s, CH, *o*-, *m*-C), 129.6 (s, CH, *p*-C), 132.5 (s, C, *ipso*-C), 166.2 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −71.94 (s); MS *m/z*: 361 ($[M+1]^+$), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{19}H_{27}O_3F_3$ ($[M+H]^+$): 361.1991, Found: 361.2022.

*4.8.9. (S)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (−)-8-phenylmenthyl ester (**6i**(SR))*

The product was isolated in 5% yield as a colorless oil. $[\alpha]_D^{26}$ −76 (c 0.11, $CHCl_3$); IR (neat) 2923 (CH), 1738 (C=O), 1263 (C–O), 1168 (C–O) cm^{-1}; ^1H NMR (500 MHz) δ 0.74 (dddd, 1H, J = 3.0, 12.8, 12.8, 12.8 Hz, 4′aq-H), 0.87 (s, 3H, 9′-H), 0.87 (dddd, 1H, J = 3.0, 12.8, 12.8, 12.8 Hz, 3′aq-H), 0.87 (d, 3H, 5.13 Hz, 10′-H), 1.06 (s, 3H, 8′-H), 1.10 (ddd, 1H, J = 11.1, 12.0, 12.0 Hz, 6′aq-H), 1.20 (dddd, 1H, J = 3.0, 3.4, 3.4, 13.7 Hz, 3′eq-H), 1.46 (m, 1H, 5′aq-H), 1.49 (m, 1H, 4′eq-H), 1.88 (ddd, 1H, J = 3.4, 10.7, 12.0 Hz, 2′aq-H), 2.15 (dddd, 1H, J = 3.4, 3.4, 3.4, 12.0 Hz, 6′eq-H), 3.59 (q, 3H, J = 1.3 Hz, OCH_3), 4.96 (ddd, 1H, J = 4.3, 10.7, 10.7 Hz, 1′aq-H), 7.10 (t, 1H, J = 7.7 Hz, *p*′-H), 7.11 (d, 2H, J = 7.7 Hz, *o*′-H), 7.19 (t, 2H, J = 8.5 Hz, *m*′-H), 7.34–7.41 (m, 3H, Ph-H), 7.61 (brd, 2H, J = 7.3 Hz, Ph-H); ^{13}C NMR (75.46 MHz) δ 22.0 (s, 10′-C), 23.0 (s, 8′-C), 27.8 (s, 3′-C), 30.3 (s, 9′-C), 31.7 (s, 5′-C), 34.6 (s, 4′-H), 40.4 (s, 7′-H), 41.8 (s, 6′-C), 50.8 (s, 2′-C), 55.9 (s, OCH_3), 78.8 (s, 1′-C), 123.5 (q, J = 288.1 Hz, CF_3), 125.4 (s, *p*′-C), 125.7, 128.0 (s, *o*′-, *m*′-C), 127.3, 128.3 (s, *o*-, *m*-C), 129.5 (s, *p*-C), 132.1 (s, *ipso*-C), 150.1 (s, *ipso*′-C), 166.0 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −71.52 (s); MS *m/z*: 448 (M^+), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{26}H_{31}O_3F_3$ (M^+): 448.2225, found: 448.2247.

*4.8.10. (R)-α-Methoxy-α-(trifluoromethyl)phenylacetic acid (−)-8-phenylmenthyl ester (**6i**(RR))*

The product was isolated in 18% yield as a colorless oil. $[\alpha]_D^{26}$ −16 (c 0.41, $CHCl_3$); IR (neat) 2925 (CH), 1738 (C=O), 1258 (C–O), 1171 (C–O) cm^{-1}; ^1H NMR (500 MHz) δ 0.71 (dddd, 1H, J = 3.0, 12.8, 12.8, 12.8 Hz, 4′aq-H), 0.85 (d, 3H, J = 6.4, 10′-H), 0.89 (dddd, 1H, J = 2.6, 12.8, 12.8, 12.8 Hz, 3′aq-H), 1.01 (ddd, 1H, J = 11.1, 12.0, 12.0 Hz, 6′aq-H), 1.15 (s, 3H, 9′-H), 1.20 (m, 1H, 3′eq-H), 1.22 (s, 3H, 8′-H), 1.45 (m, 1H, 5′aq-H), 1.47 (m, 1H, 4′eq-H), 1.88 (ddd, 1H, J = 3.4, 10.7, 12.4 Hz, 2′aq-H), 2.07 (dddd, 1H, J = 3.8, 3.8, 3.8, 12.0 Hz, 6′eq-H), 3.41 (s, 3H, OCH_3), 5.01 (ddd, 1H, J = 4.3, 10.7, 10.7 Hz, 1′aq-H), 7.15 (t, 1H, J = 7.3 Hz, *p*′-H), 7.21 (d, 2H, J = 7.3 Hz, *o*′-H), 7.26 (t, 2H, J = 7.5 Hz, *m*′-H), 7.37–7.46 (m, 3H, Ph-H), 7.53–7.58 (m, 2H, Ph-H); ^{13}C NMR (75.46 MHz) δ 22.0 (s, 10′-C), 22.9 (s, 8′-C), 27.8 (s, 3′-C), 30.8 (s, 9′-C), 31.6 (s, 5′-C), 34.5 (s, 4′-H), 40.5 (s, 7′-H), 41.4 (s, 6′-C), 50.8 (s, 2′-C), 55.3 (s, OCH_3), 78.8 (s, 1′-C), 85.0 (q, J = 28.1 Hz, 2-C), 123.6 (q, J = 285.7 Hz, CF_3), 125.5 (s, *p*′-C), 125.8, 128.1 (s, *o*′-, *m*′-C), 128.1, 128.6 (s, *o*-, *m*-C), 129.7 (s, *p*-C), 131.2 (s, *ipso*-C), 150.1 (s, *ipso*′-C), 166.1 (s, C, *C*OO); ^{19}F NMR (254 MHz) δ −71.33 (s); MS *m/z*: 448 (M^+), 189 ($[M - COOR^*]^+$); HRMS calcd. for $C_{26}H_{31}O_3F_3$ (M^+): 448.2225, found: 448.2239.

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