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Trifluoromethylation and pentafluoroethylation of terpenoid carbonyl compounds used in perfumery

Shoji Watanabe [a*], Tsutomu Fujita [a], Masami Sakamoto [a], Yasuhiro Mino [a], Tomoya Kitazume [b]

[a] *Department of Applied Chemistry, Faculty of Engineering, Chiba University, Yayoicho, Inageku, Chiba 263, Japan*
[b] *Department of Bioengineering, Tokyo Institute of Technology, Nagatsuta, Midoriku, Yokohama 227, Japan*

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Abstract

The reaction of trifluoromethyltrimethylsilane with a variety of terpenoid carbonyl compounds and other carbonyl compounds used in perfumery gave the corresponding trifluoromethylated derivatives. Pentafluoroethylated compounds were similarly obtained from the reaction of pentafluoroethyltrimethylsilane with various substrates. (−)-2-Trifluoro-1-furyl ethanol has been obtained with high optical purity by enzymatic hydrolysis of 2-trifluoro-1-furyl ethyl acetate.

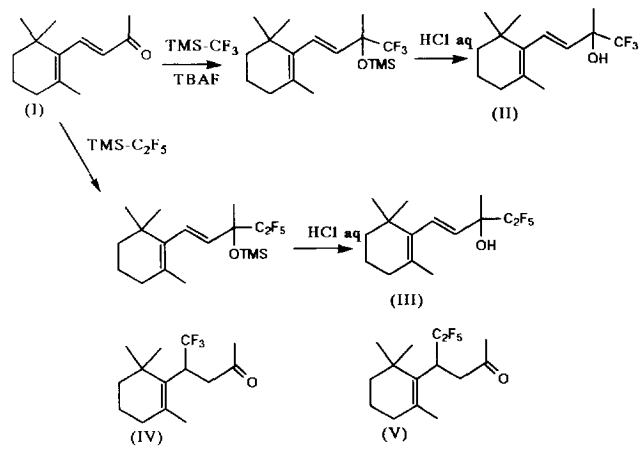
Keywords: Trifluoromethylation; Pentafluoroethylation; Terpenoid carbonyl compounds; NMR spectroscopy; Enzymatic hydrolysis

1. Introduction

Many preparative methods for introducing perfluoroalkyl groups into carbonyl compounds through organometallic reagents of zinc [1], calcium [2], manganese [3], magnesium [4], silver [3] and lithium [5] have been published. Recently, a very efficient trifluoromethylation reaction for carbonyl compounds using trifluoromethyltrimethylsilane (TMS−CF_3, Olah reagents) was reported [6]. In Ref. [6], the trifluoromethylation of standard compounds is reported, but that of terpenoid carbonyl compounds and other related compounds was not examined. In work described in this paper, we have prepared new trifluoromethylated compounds and pentafluoroethylated compounds from the reaction of Olah reagents with terpenoid and perfumery compounds. We have studied simple synthetic methods for the preparation of optically active alcoholic compounds bearing an α-trifluoromethyl group. Enzymatic hydrolysis of 2-trifluoro-1-furylethyl acetate (**VI**) with lipase MY gave the corresponding optically active alcohol **VII**.

2. Results and discussion

The reaction of β-ionone (**I**) with TMS−CF_3 produces 2-trifluoromethyl-4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-ol (**II**) in a yield of 72% (Scheme 1). Elementary analyses of the product agreed with the calculated data. Its ^{19}F NMR showed signals of CF_3. The presence of a hydroxy group was confirmed by an absorption at 3430 cm^{-1} in the IR spectrum. The ^1H NMR spectrum supported the structure of **II** as shown in the Experimental section. In this reaction, compound **IV** was not obtained. We believe that this result is due to the steric hindrance of compound **I**. It is suspected that the reaction proceeds according to the mechanism [6] shown in Scheme 2.



Scheme 1.

* Corresponding author.

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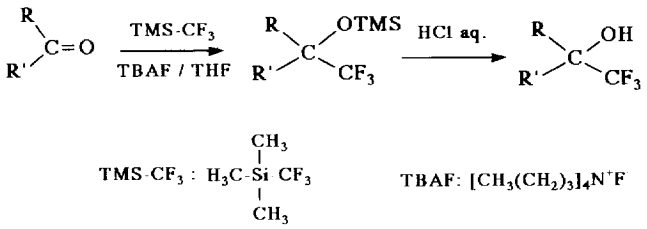


Scheme 2.

Other trifluoromethylated products were prepared from various aldehydes and ketones with high yields in the same manner and the results are listed in Table 1. The reaction of β-ionone (**I**) with TMS−C_2F_5 produced 2-pentafluoroethyl-4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-ol (**III**) in 30.4% yield. The structure of **III** was confirmed by spectral data as listed in the Experimental section. In this case, compound **V** was not obtained, similar to TMS−CF_3 not yielding **IV**. Other pentafluoroethylated products were obtained in the same manner. However, their yields were low despite the use of a large amount of catalyst. The results obtained are listed in Table 1.

A simple preparation of optically active (−)-α-trifluoromethyl alcohol (**VII**) has been obtained by the enantioselective enzymatic hydrolysis of α-trifluoromethyl ester **VI** using lipase MY (30 000 unit g^{-1}; Meito Sangyo Co. Ltd.) as shown in Scheme 3. Since the present biochemical method leads to a kinetic resolution, not only the hydrolyzed product **VII** but also the unreacted ester **VI** are optically active. The *E* value of this reaction with lipase MY was 91 [7]. Interestingly, the hydrolysis of **VI** with lipase PS gave (+)-**VII** and (−)-**VI**.

These fluorinated products did not possess a sweet smell as did the original carbonyl compounds. They had odours like hydrocarbons. We had expected that trifluoromethylated and pentafluoroethylated compounds derived from terpenoid compounds would have biological activity [8]. However, our biological tests showed no antimicrobial activity against Gram positive and Gram negative bacteria, mycelial fungi and yeasts.

3. Experimental details

3.1. General procedure

Trifluoromethyltrimethylsilane (TMS−CF_3) and pentafluoroethyltrimethylsilane (TMS−C_2F_5) were provided by F Tech Co. Ltd. (formerly Nihon Halon Co. Ltd., Japan). The reaction products were analyzed by gas chromatographic methods using a 3 mm i.d.×3 m column containing 15% Silicone DC 200 on 60–80 mesh Celite 545. NMR spectra were recorded at 60 or 200 MHz for ^1H NMR and 56.4 MHz or 470 MHz for ^{19}F NMR in $CDCl_3$. ^{19}F NMR chemical shifts are reported in parts per millions (ppm) relative to trifluoroacetic acid (δ 0.00) as an external standard, low field positive.

3.2. Trifluoromethylation of β-ionone (I)

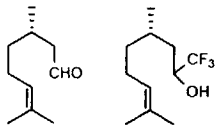
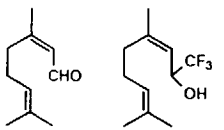
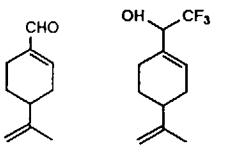
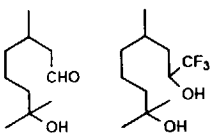
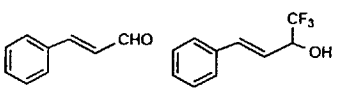
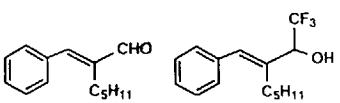
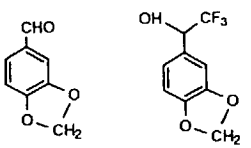
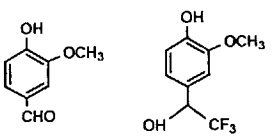
A mixture of β-ionone (**I**) (1.15 g, 0.006 mol) and TMS−CF_3 (1.53 g, 0.009 mol) in 30 ml of anhydrous tetrahydrofuran was treated with a catalytic amount (ca. 45 mg) of tetra-n-butylammonium fluoride trihydrate (TBAF). A yellow color developed with the initial evolution of fluorotrimethylsilane, and the reaction mixture was stirred for 24 h. The mixture was then hydrolyzed with 1 N aqueous HCl. The mixture was extracted with ether, the ether extracts washed with water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was chromatographed over silica gel column using a mixture of hexane and ethyl acetate (20:1 v/v) as a solvent to give 1.14 g (72% yield) of 2-trifluoromethyl-4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-ol (**II**) (an oily product). This product showed one spot (R_f=0.3) in thin layer chromatography with Kieselgel 60 (Merck Art 5735) using a mixture of hexane and ethyl acetate (5:1 v/v) as a solvent. The compound exhibited the following spectral data: IR (cm^{-1}): 3430 (OH). ^{19}F NMR δ: −3.62 (3F, s, CF_3) ppm. ^1H NMR δ: 0.98 [3H×2, s, $-C(CH_3)_2$]; 1.50 (3H, s, $-C=C-CH_3$); 1.65 (3H, s, CF_3-C-CH_3); 1.36–1.72 (4H, m, $-(CH_2)_2-$); 1.88–2.24 (2H, m, $-CH_2-C=C$); 5.55 [1H, d, J=16.1 Hz, $-CH=CH=C(CF_3)$]; 6.36 (1H, d, J=16.1 Hz, $-CH=CH-C-CF_3$) ppm.

Other carbonyl compounds were trifluoromethylated in a similar manner.

3.3. Pentafluoroethylation of β-ionone (I)

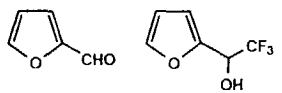
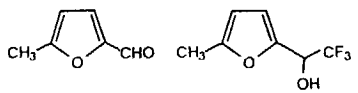
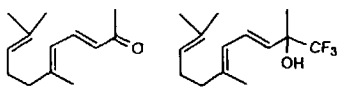
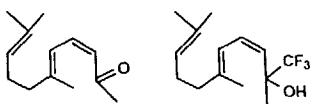
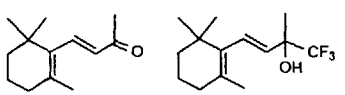
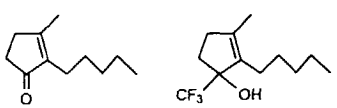
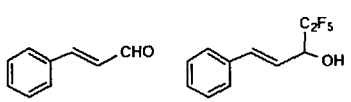
To a mixture of β-ionone (**I**) (0.96 g, 0.005 mol) and TMS−C_2F_5 (1.152 g, 0.006 mol) in 30 ml of anhydrous tetrahydrofuran, a solution of TBAF (1.307 g, 0.005 mol) in anhydrous tetrahydrofuran (10 ml) was added drop by drop under N_2 gas at 0 °C over 1 h, followed by stirring the reaction mixture for 12 h. The mixture was then hydrolyzed with 3 N aqueous HCl (50 ml) for 12 h at a room temperature. The mixture was extracted with ether, the ether extracts washed with water and brine, dried over anhydrous sodium sulfate and concentrated. The residue was chromatographed over silica gel column using a mixture of hexane and benzene (20:1 v/v) as a solvent to give 0.48 g (30.4% yield) of 2-pentafluoroethyl-4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-3-buten-2-ol (**III**) (an oily product). This product showed one spot (R_f=0.3) in thin layer chromatography with Kieselgel 60 (Merck Art 5735) using a mixture of benzene and ethyl acetate (5:1 v/v) as a solvent. The compound exhibited the following spectral

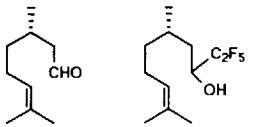
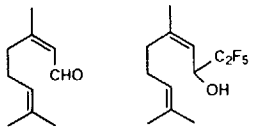
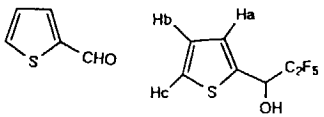
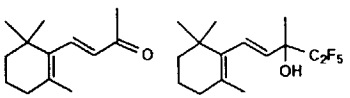
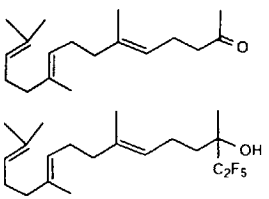
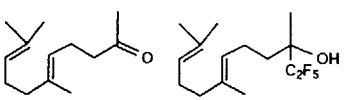
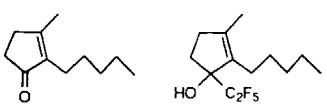
Table 1
Trifluoromethylation and pentafluoroethylation of terpenic and perfumery carbonyl compounds

Carbonyl compound	Structure	Yield (%)	Fluorinated products [a]	
			^{19}F NMR (δ, ppm)	^{1}H NMR (δ, ppm)
Trifluoromethylation				
1-Citronellal		54	31.71 (dd, J=14.45 Hz); 0.97 (3H, J=6.21Hz, CF_3)	0.97 (3H, d, J=6.2 Hz, CH_3-CH-); 1.30 (5H, m, $-CH_2-$, $-CH-$); 1.59 (3H, s, CH_3); 1.66 (3H, s, CH_3); 1.66 (3H, s, CH_3); 1.97 (2H, m, $-CH_2C=$); 2.73 (1H, broad s, $-OH$); 3.97 (1H, m, $-CH-CF_3$); 5.07 (1H, t, J=7.8 Hz, $-CH=$)
Citral		56	2.14 (d, J=5.53 Hz, CF_3)	1.58, 1.61 [3H and 3H, each s, $-C=(CH_3)_2$]; 1.75 [3H, s, $-C(CH_3)=C-$]; 2.01–2.20 (5H, m, $-CH_2-CH_2-$, $-OH$); 4.56–4.74 [1H, m, $-CH(CF_3)-$]; 5.02–5.12 [1H, m, $-C=CH-CH(CF_3)-$]; 5.29 [1H, t, J=10.68 Hz, $-CH_2-CH=C(CH_3)_2$]
Perillaldehyde		76	2.05 (dd, J=14.45 Hz, J=7.23 Hz, CF_3)	1.74 (3H, s, $-CH_3$); 1.97–2.47 (7H, m, $-CH_2-$, $-CH-$ and $OH-$); 2.57 (1H, m, $-CHCF_3$); 4.42 (2H, s, $CH_2=C$); 5.92–6.05 (1H, m, $-CH_2-CH-C-$)
Hydroxycitronellal		52	−1.34 (d, J=4.12 Hz, CF_3)	0.96 [3H, d, J=10.39 Hz, $-CH(CH_3)$]; 1.24–2.75 [11H, m, other $-CH_2-$ and $-CH-$]; 1.18, 1.20 [3H and 3H, each s, $-C(CH_3)_2-OH$]; 3.85–4.12 [1H, m, $-CH(CF_3)-$]
Cinnamic aldehyde		58	0.04 (d, J=6.89 Hz, CF_3)	2.35 (1H, s, $-OH$); 4.56–4.72 [1H, m, $-CH(CF_3)-$]; 6.21 (1H, dd, J=15.97 Hz, 6.51 Hz, $CH=CH-Ph$); 6.86 [1H, dd, J=15.97 Hz, 1.28 Hz, $-CH=CH-Ph$]; 7.21–7.53 (5H, m, Ph)
Osminal		66	2.14 (d. J=6.25 Hz, CF_3)	0.86 (3H, t, J=6.86 Hz, $-CH_2-CH_3$); 1.17–1.60 [5H, m, $-CH_2-(CH_2)_3-CH_3$]; 2.14–2.57 [3H, m, $-CH_2-(CH_2)_3-$, $-OH$]; 4.57 [1H, q, J=6.25 Hz, $-CH(CF_3)-OH$]; 7.21–7.43 (5H, m, Ph)
Heliotropine		63	2.94 (s, CF_3)	2.95 (1H, broad s, OH); 4.91 (1H, q, J=6.64 Hz, $-CH-CF_3$); 5.97 (2H, s, $-OCH_2-O$); 6.80–6.97 (3H, m, aromatic protons)
Vanillin		69	0.64 (d, J=6.15 Hz, CF_3)	2.75 [1H, s, $-CH(CF_3)-OH$]; 3.90 (3H, s, $-OCH_3$); 4.92 [1H, q, J=6.80 Hz, $-CH(CF_3)-$]; 5.77 (1H, s, Ph−OH); 6.93–7.00 (3H, m, Ph)

(continued)

Table 1 (*continued*)

Carbonyl compound	Structure	Yield (%)	Fluorinated products [a]	
			^{19}F NMR (δ, ppm)	^{1}H NMR (δ, ppm)
Furfural		94	0.62 (d, J=6.15 Hz, CF_3)	3.64 (1H, s, −OH); 5.05 [1H, q, J=6.15 Hz, −CH(CF_3)−]; 6.43 (1H, dd, J=1.88 Hz, 3.48 Hz, −O−CH=C*H*−CH=); 6.53 (1H, d, J=3.48 Hz, −O−CH=CH−C*H*=); 7.47 (1H, d, J=1.88 Hz, −O−C*H*=)
5-Methylfurfural		92	−2.46 (d, J=6.10 Hz, CF_3)	2.31 (3H, d, J=1.14 Hz, $-CH_3$); 2.87 (1H, s, −OH); 4.97 (1H, q, J=6.10 Hz, −CH(CF_3)−); 5.99 (1H, dq, J=1.14 Hz, 3.19 Hz, CH_3−C=C*H*−); 6.39 (d, J=3.19 Hz, CH_3−C=CH−C*H*=)
trans-ϕ-Ionone		83	−3.38 (s, CF_3)	1.49 [3H, s, CF_3C(OH)−CH_3]; 1.61, 1.69 [3H and 3H, each s, −CH=C(CH_3)$_2$]; 1.80 [3H, s, −CH=CH−CH=C(*CH*$_3$)−]; 5.05–5.13 [1H, m, −CH=C(CH_3)$_2$]; 5.68 [1H, d, J=15.39 Hz, −CH=CH−C*H*=C(CH_3)−]; 5.87 [1H, d, J=10.99 Hz, −C*H*=CH−CH=C(CH_3)−]; 6.72 [1H, dd, J=10.99 Hz, 15.39 Hz, −CH=C*H*−CH=C(CH_3)−]
cis-ϕ-Ionone		58	−3.46 (s, CF_3)	1.48 [3H, s, −CH_2C(OH)−CH_3]; 1.61, 1.68 [3H and 3H, each s, −CH=C(CH_3)$_2$]; 1.81 [3H, s, −CH=CH−CH=C(CH_3)−]; 5.04–5.16 [1H, m, −C*H*=C(CH_3)$_2$]; 5.65 [1H, d, J=15.38 Hz, −CH=CH−C*H*=C(CH_3)−]; 5.87 [1H, d, J=11.07 Hz, −C*H*=CH−CH=C(CH_3)−]; 6.70 [1H, dd, J=15.38 Hz, 11.07 Hz, −CH=C*H*−CH=C(CH_3)−]
β-Ionone		72	−3.62 (s, CF_3)	See Experimental section
Dihydrojasmone		56	−4.25 (s, CF_3)	0.90 [3H, t, J=13.2 Hz, −CH_2−C*H*$_3$]; 1.21–1.52 [8H, m, −(*CH*$_2$)$_4$−CH_3]; 1.73 [3H, s, −C=C−CH]; 1.81–1.97 (1H, m, −OH); 2.04–2.16 (2H, m, −CH_2−C=C); 2.23–2.45 [2H, m, −*CH*$_2$C(OH)−CF_3]
Pentafluoroethylation Cinnamic aldehyde		18.3	−53.4655 (dd, J_{FaFb}=275.42 Hz, J_{FaH}=15.26 Hz, CF_2); −48.189 (dd, J_{FaFb}=275.42 Hz, J_{FbH}=9.15 Hz, CF_2); −5.914 (s, CF_3)	1.60 (1H, s, −OH); 6.70–6.75 (2H, m, −CH=CH−); 7.30–7.60 (5H, m, −Ph); 9.72 (1H, d, J=17.74 Hz, −C*H*(OH)C_2F_5)

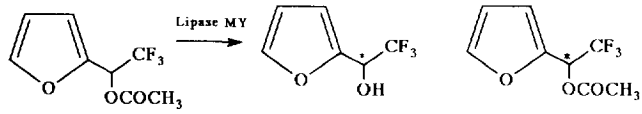
1-Citronellal		65.4	−48.555 (dd, J_{FaFb} = 149.53 Hz, J_{FaH} = 7.63 Hz, F_a); −49.142 (dd, J_{FaFb} = 149.53 Hz; J_{FbH} = 7.63 Hz, F_b); −5.969 (s, CF_3) [c] −55.2215 (dd, J_{FaFb} = 39.67 Hz, J_{FaH} = 16.78 Hz, F_a); −55.8085 (dd, J_{FaFb} = 39.67 Hz, J_{FbH} = 16.78 Hz, F_b); −6.015 (s, CF_3) [c]	0.97 [3H, d, J = 32.74 Hz, $-CH(CH_3)-$]; 1.10–2.08 [7H, m, $-(CH_2)-\times 3$, $-CH(CH_3)-$]; 1.61, 1.69 [3H and 3H, each s, $-C=C(CH_3)-CH_3$]; 4.07–4.16 (1H, m, $-CH-C_2F_5$); 5.09 (1H, t, J = 7.8 Hz, $-CH=C$)
Citral		64.3	−53.359 (dd, J_{FaFb} = 273.14 Hz, J_{FaH} = 13.74 Hz, F_a); −50.139 (dd, J_{FaFb} = 273.14 Hz, J_{FbH} = 7.63 Hz, F_b); −6.22 (s, CF_3) [d] −54.394 (dd, J_{FaFb} = 274.66 Hz, J_{FaH} = 15.26 Hz, F_a); −49.185 (dd, J_{FaFb} = 274.66 Hz, J_{FbH} = 9.15 Hz, F_b); −6.307 (s, CF_3) [d]	1.58 (3H, s, CH_3); 1.67 (3H, s, CH_3); 1.75 (3H, s, CH); 2.10 (4H, m, $-CH_2-$); 2.95 (1H, broad s, −OH); 4.59 (1H, m, $-CHC_2F_5$); 5.05 (1H, m, $=CH-$); 5.27 (1H, t, J = 10.2 Hz, $-CH_2-CH=$)
Thiophene aldehyde		63.3	−54.648 (dd, J_{FaFb} = 274.66 Hz, J_{FaH} = 16.79 Hz, F_a); −46.25 (dd, J_{FaFb} = 274.66 Hz, J_{FbH} = 6.11 Hz, F_b); −5.985 (s, CF_3)	2.68 (1H, s, −OH); 5.40 [1H, dd, J_{FaH} = 16.79 Hz, J_{FbH} = 6.11 Hz, $-CH(OH)-$]; 7.07 (1H, dd, J_{HbHa} = 3.78 Hz, J_{HbHc} = 5.13 Hz, $-CH_b=C$); 7.22 (1H, d, J_{HaHb} = 3.78 Hz, $-CH_a=C-$); 7.43 (1H, d, J_{HcHb} = 5.13 Hz, $-CH_c-S-$)
β-Ionone		30.4	−49.557 [d, J_{FaFb} = 276.19 Hz, $F_a(CF_2)$]; −48.192 [d, J_{FaFb} = 276.19 Hz, $F_b(CF_2)$]; −2.942 (s, CF_3)	See Experimental section
Farnesyl acetone		30.8	−49.197 [d, J_{FaFb} = 278.2 Hz, $F_a(CF_2)$]; −49.86 [d, J_{FaFb} = 278.2 Hz, $F_b(CF_2)$] (AB pattern); −2.996 (s, CF_3)	1.40 [3H, s, $-C(OH)-CH_3$]; 1.54 (3H, s, $-CH_3$); 1.56–1.67 [2H, m, $-C(OH)-CH_2-$]; 1.59 (3H, s, CH_3-); 1.63 (3H, s, CH_3-); 1.68 (3H, s, CH_3-); 1.94–2.24 [11H, m, $-(CH_2)-\times 5$, OH]; 5.07–5.16 (3H, m, $-C=CH-\times 3$)
Geranyl acetone		42.1	−48.876 (s, CF_2); −2.468 (s, CF_3) [b]	1.36 (3H, $-CH_3$); 1.59–1.70 (10H, m, $C=C-CH_3\times 3$, $-CH_2-C-OH$); 1.88–2.20 [7H, m, $-(CH_2)_3-$, −OH]; 5.05–5.15 (2H, m, $-C=CH\times 2$)
Methylundecyl ketone	$CH_3(CH_2)_{11}COCH_3$ $CH_3(CH_2)_{11}C(OH)(C_2F_5)CH_3$	33.8	−49.81 [d, J_{FaFb} = 277.71 Hz, $F_a(CF_2)$]; −49.28 [d, J_{FaFb} = 277.71 Hz, $F_b(CF_2)$] (AB pattern); −3.010 (s, CF_3)	0.88 (3H, t, J = 6.90 Hz, $-CH_2-CH_3$); 1.24–1.29 [20H, m, $-(CH_2)_{10}-$]; 1.29–1.35 [3H, m, $-C(OH)-CH_3$]; 1.38 (1H, s, −OH); 1.65–1.71 [2H, m, $-CH_2-C(OH)-CH_3$]
Dihydrojasmone		64.7	−46.34 [d, J_{FaFb} = 276.44 Hz, $F_a(CF_2)$]; −49.33 [d, J_{FaFb} = 276.44 Hz, $F_b(CF_2)$] (AB pattern); −4.15 (s, CF_3)	0.90 [3H, t, J = 13.2 Hz, $-CH_2-CH_3$]; 1.21–1.52 [8H, m, $-(CH_2)_4-CH_3$]; 1.73 [3H, s, $-C=C-CH_3$]; 1.81–1.97 (1H, m, −OH); 2.04–2.16 (2H, m, $-CH_2-C=C$); 2.23–2.45 [2H, m, $-CH_2C(OH)-CF_3$]

[a] Satisfactory microanalyses (C, ±0.04%; H±0.4%) were obtained for each of the mentioned products. These compounds are all oily products. IR spectra of these compounds showed absorptions for OH groups at ca. 3400 cm^{-1}.

[b] The ^{19}F NMR spectrum of this compound was recorded using a 60 MHz apparatus.

[c] Diastereomers (50:50).

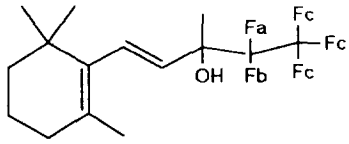
[d] *trans* and *cis* Isomers.



(VI) (VII) (VI)

Scheme 3.

data: IR (cm^{-1}): 3430 (OH). ^{19}F NMR δ: $F_a = -48.192$, $F_b = -49.557$ (AB quartet, $J_{F_aF_b} = 276.19$ Hz, 2F), $F_c = -2.942$ (s, 3F) ppm. Interestingly, spin–spin coupling of F_a and F_b with F_c was not detected. ^1H NMR δ: 0.98 [3H×2, s, $-C(CH_3)_2$]; 1.54 (3H, s, $-C{=}C{=}CH_3$); 1.64 (3H, s, $C_2F_5C-CH_3$); 1.46 [4H, m, $-(CH_2)_2-$]; 1.983 (2H, t, $J = 6.35$ Hz, $-CH_2-C{=}C$); 5.566 [1H, d, $J = 16.1$ Hz, $-CH{=}CH-$); 6.353 [1H, d, $J = 16.1$ Hz, $-CH{=}CH-$) ppm.



Other carbonyl compounds were pentafluoroethylated in a similar manner.

3.4. (−)-2-Trifluoro-1-furyl ethanol (VII)

A suspension of 2-trifluoro-1-furylethyl acetate (**VI**) (2.10 g, 10 mmol) and lipase MY (0.700 g, 30 000 unit g^{-1}; Meito Sangyo Co. Ltd.) in distilled water (20 ml) was stirred at 40 °C. The mixture was maintained at pH 7 by adding 0.1 N NaOH aqueous solution and the hydrolysis was carried out to less than 40% conversion. The reaction mixture was extracted with diisopropyl ether. The extract was washed with saturated aqueous NaCl and dried over Na_2SO_4. After removal of the solvent, the product was carefully chromatographed on silica gel using a mixture of n-hexane/ethyl acetate (30:1) as an eluent to give 0.425 g of (−)-**VII** ($[\alpha]_D^{20} = -12.7$, 64% yield, 94% *ee*) and 0.774 g of (+)-**VI** ($[\alpha]_D^{20} = +79.3$, 43% yield, 62% *ee*). The optical purity of **VII** was determined by GLC of its diastereomeric ester with optically active MTPA. The optical purity of **VI** was determined by GLC after conversion of **VI** to its carbinol with LAH and then to its diastereomeric ester with optically active MTPA. However, the absolute configurations of these compounds have not been determined at the present time.

Similar hydrolysis of **VI** with lipase PS gave a mixture of (+)-**VII** ($[\alpha]_D^{20} = +6.3$, 38% yield, 47% *ee*) and (−)-**VI** $[\alpha]]_D^{20} = -41.9$, 32% yield, 32% *ee*). The *E* value was 3.5.

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