

Preparation and Determination of the Absolute Configuration of Optically Active 9-Hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-ones

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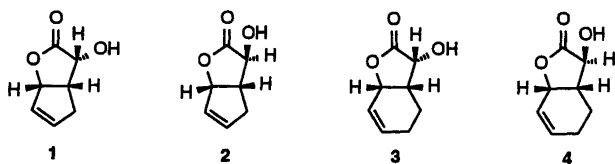
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Both enantiomers of *endo*-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one (+)-**3** and (–)-**3** as well as *exo*-(1*R*,6*R*,9*R*)-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one (+)-**4** have been obtained in states of high optical purity by kinetic resolutions involving enzyme-catalysed hydrolyses. Absolute configurations were assigned by chemical interconversions and by X-ray crystallography on Mosher's ester (+)-**7**.

The bicyclic lactones **1** and **2** are readily prepared,¹ easily resolved² and have been shown to be very useful synthons.^{3–5} The homologous compounds **3** and **4** are also available¹ (following the procedure originally described by Lubineau *et al.*¹), and recently we have investigated the resolution of these compounds prior to their use in synthetic schemes.⁶ Herein we report the results of these investigations.



Results and discussion

The *endo*-hydroxy lactone (±)-**3** was treated with *Pseudomonas fluorescens* lipase (Pfl) in vinyl acetate to afford the unchanged alcohol (+)-**3** and the ester (–)-**5** (Scheme 1). This ester was hydrolysed in aqueous phosphate buffer using Pfl as catalyst to yield the alcohol (–)-**3**.

Surprisingly the *exo*-hydroxy lactone (±)-**4** is unaffected by Pfl in vinyl acetate. This racemic hydroxy lactone is best resolved using *Candida cylindracea* lipase

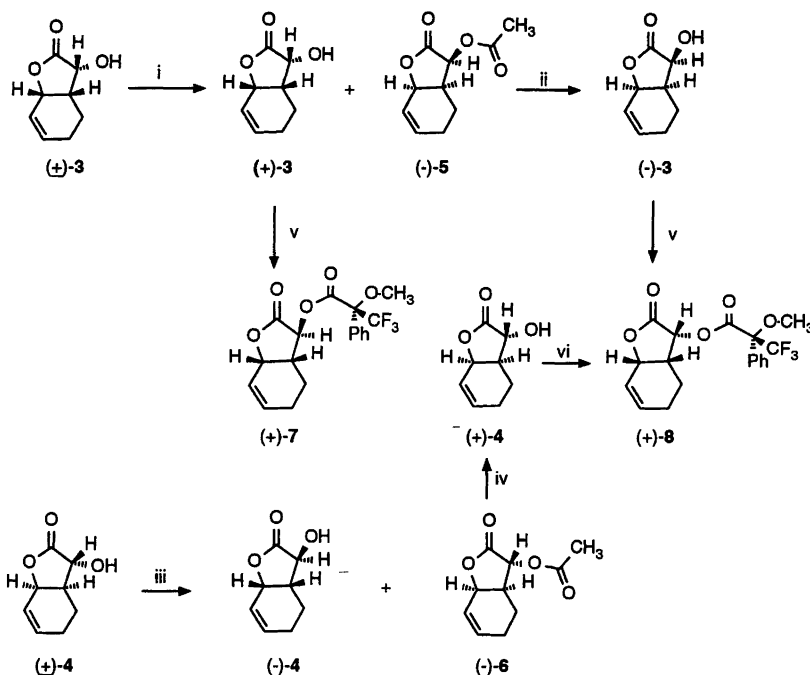
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(Ccl) in vinyl acetate to give unchanged alcohol (–)-**4** and ester (–)-**6**. However this biotransformation is extremely slow, taking 21 days to effect a 13% conversion.

The alcohols (+)-**3** and (–)-**3** were converted into the esters (+)-**7** and (+)-**8** by Mitsunobu reactions using (*R*)-(+)-Mosher acid. Acylation of the hydroxy lactone (+)-**4** [obtained by hydrolysis of the ester (–)-**6** using Ccl in pH 6.5 buffer at room temp. over 24 h] using (*S*)-Mosher acid chloride also gave the ester (+)-**8**.

Crystallographic study. The structure and absolute configuration of the ester (+)-**7** was elucidated by X-ray crystallography, the latter by reference to the known chirality at C(1). The structure of a single molecule of **7** together with the atom numbering is shown in Fig. 1. The crystal data, molecular geometry parameters and the atom coordinates are given in Tables 1, 2 and 3, respectively.

The molecular dimensions are mostly as expected. The carbonyl angles O(2) = C(10)–C(1)/O(3) are nearly equal at ca. 125° but the O(4) = C(12)–C(11)/O(5) angles are quite asymmetric with values 128.2(2) and 123.3(2)°. The widening of the O(4)–C(12)–C(11) angle may be attributed to the short intramolecular O(4)⋯O(3) contact of 2.848(3) Å. Intramolecular short contacts involving C(9) [with C(2) and C(3)] and O(2) [with H(11)] may appear to be responsible for widening of the tetrahedral angles at O(1) [118.4(2)°] and at O(3) [116.9(2)°]. There are no unusually short intermolecular contacts.



Scheme 1. Reagents and conditions: (i) Pfl, vinyl acetate, 70 h; (ii) Pfl, phosphate buffer, 20 h; (iii) Ccl, vinyl acetate, 21 days, 30 °C; (iv) Ccl, phosphate buffer, 24 h; (v) diethyl azodicarboxylate, Ph_3P , (*R*)-Mosher acid, tetrahydrofuran; (vi) (*S*)-Mosher acid chloride, CH_2Cl_2 , pyridine.

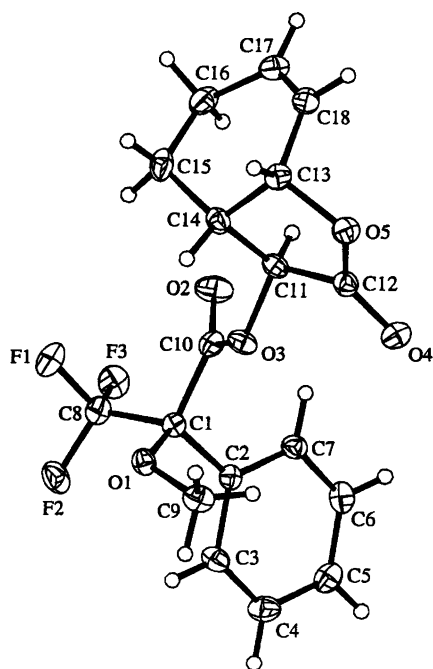


Fig. 1. Molecular structure and absolute configuration of (+)-7 showing the numbering scheme of the non-hydrogen atoms. The hydrogen atoms are represented by small circles.

Conclusions. Now that the optically pure compounds (+)-3 and (-)-3 are readily available, these bicyclic lactones can be considered as potential intermediates for the preparation of novel homochiral compounds.

Experimental

IR spectra were recorded on a Nicolet Magna-IR 550 spectrometer. Optical rotations were measured on an Optical Instrument A-1000 polarimeter. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-300 spectrometer. Chemical shifts are given in ppm and coupling constants in Hz. Mass spectra were recorded at the SERC Mass Spectrometry Centre, Swansea on a VG ZAB-F spectrometer (high resolution), or a VG 12-253 spectrometer (low resolution). Measurements of enantiomeric excesses were measured by NMR spectroscopy using tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphoro]-europium(III) as the chiral shift reagent (error $\pm 2\%$). Enzymes were obtained from Biocatalysts, Sketty, Swansea, UK.

Enzymatic acetylation of endo-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one (\pm)-3. *Pseudomonas fluorescens* lipase (1.00 g) was added to a solution of (\pm)-endo-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one 3 (1.54 g, 10.0 mmol) in vinyl acetate (50 ml). The mixture was shaken for 70 h in an orbital incubator at 30 °C and then the enzyme was removed by filtration. The filtrate was concentrated under reduced pressure and the residue was chromatographed over silica gel (ethyl acetate–hexane 1:1). The first fractions gave (-)-endo-(1*R*,6*R*,9*S*)-9-acetoxy-7-oxabicyclo[4.3.0]non-4-en-8-one (-)-5 (0.911 g, 4.64 mmol, 46.3%) as white crystals. R_f 0.51 (ethyl acetate–hexane 1:1), m.p. 74.2 °C (ethyl acetate); $[\alpha]_D^{25} -22.3$ (c 1.0 in CHCl_3), 100% ee. (Found: 197.08177,

Table 1. Crystal data and details of data collection and structure refinement for $C_{18}H_{17}F_3O_5$ 7

Empirical formula	$C_{18}H_{17}F_3O_5$
Formula weight	370.32
Temperature	140(2) K
Radiation	Mo-K α
Wavelength	0.71069 Å
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	$a=6.8310(10)$ Å $b=11.481(2)$ Å $c=21.788(6)$ Å
Volume	$1708.8(6)$ Å ³
Z	4
Density (calculated)	1.439 Mg m ⁻³
Absorption coefficient (Mo K α)	0.125 mm ⁻¹
$F(000)$	768
Crystal size	$0.30 \times 0.15 \times 0.10$ mm
θ range for data collection	$1.87\text{--}24.93^\circ$
Index ranges	$-7 \leq h \leq 5$, $-12 \leq k \leq 12$, $-23 \leq l \leq 22$
Reflections collected	6543
Absorption correction factors	0.897–1.015
Independent reflections	2577 [$R_{int}=0.0539$]
Refinement method	Full-matrix least-squares on F^2
Data/parameters	2577/236
Goodness-of-fit on F^2	0.927
Final R^2 indices [$I > 2\sigma(I)$]	$R_1=0.0323$, $wR_2=0.0673$
R^* indices (all data)	$R_1=0.0384$, $wR_2=0.0695$
Largest diff. peak and hole	0.160 and -0.177 e Å ⁻³

$$^a R_1 = \Sigma(\Delta F) / \Sigma(F_o); \quad wR_2 = (\Sigma\{w[\Delta(F^2)]^2\} / \Sigma\{w(F_o^2)^2\})^{1/2}; \quad w = 1 / [\sigma^2(F_o^2) + (0.0268P)^2], \quad \text{where } P = [\text{Max}(F_o^2) + 2(F_o^2) + 2(F_c^2)] / 3.$$

$C_{10}H_{12}O_4 + H$ requires 197.08137). IR (KBr disc): 3046, 2980, 2955, 2930, 1772, 1751, 1652, 1382, 1234, 1100 cm⁻¹; ¹H NMR (300 MHz; CDCl₃): δ 6.25 (1 H, m, 4-H), 5.92 (1 H, m, 5-H), 5.65 (1 H, d, J 7.5, 9-H), 4.72 (1 H, t, J 4.5, 6-H), 2.84 (1 H, m, 1-H), 2.2 (4 H, m, 3-H and CH₃), 2.0 (1 H, m, 2-H), 1.64 (1 H, m, 3'-H) and 1.29 (1 H, m, 2'-H). ¹³C NMR (75.5 MHz; CDCl₃): δ 171.70 (CO), 169.83 (CO), 136.08 (CH, C-4), 121.62 (CH, C-5), 71.82 (CH, C-6), 71.35 (CH, C-9), 37.61 (CH, C-1), 22.96 (CH₂, C-3), 20.40 (CH₃) and 17.76 (CH₂, C-2); MS (CI): m/z 197 ($M+H$, 1.2%), 196 (M^+ , 0.1), 154 ($M - C_2H_3O$, 0.4), 137 ($M - C_2H_3O_2$, 7.0), 110 (46.8), 109 (10.2), 95 (24.2), 93 (31.6) and 92 (100.0). Later fractions contained (+)-endo-(1*S*,6*S*,9*R*)-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one (+)-3 (0.560 g, 3.63 mmol, 36.2%, $[\alpha]_D^{25} + 143.9$ (c 1.0 in CHCl₃), 100% ee). R_f 0.26 (ethyl acetate–hexane 1:1); m.p. 131.0°C (ether). (Found: M^+ 172.0974, $C_8H_{10}O_3 + NH_4$ requires M 172.0973). IR (KBr): 3448, 3044, 2965, 2942, 2916, 1761, 1201, 1110, 952 and 908 cm⁻¹; ¹H NMR (300 MHz): δ 6.24 (1 H, m, 4-H), 5.93 (1 H, m, 5-H), 4.69 (2 H, m, 6-H and 9-H), 3.12 (1 H, br s, OH), 2.7 (1 H, m, 1-H), 2.2 (1 H, m, 3-H), 2.07–1.98 (1 H, m, 2-H), 1.97–1.88 (1 H, m, 3'-H) and 1.28–1.12 (1 H, m, 2'-H); ¹³C NMR (75.5 MHz): δ 177.23 (CO), 136.55 (CH, C-4), 121.64 (CH, C-5), 71.80 (CH, C-6), 71.50 (CH, C-9), 39.11 (CH, C-1), 23.17 (CH₂, C-3), 17.29 (CH₂, C-2); MS (CI): m/z 172 ($M + NH_4$, 100%).

Enzymatic acetylation of *exo*-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one (\pm)-4. *Candida cylindracea* lipase (0.17 g) was added to a solution of (\pm)-*exo*-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one **4** (295 mg, 1.68 mmol) in vinyl acetate (25 ml). The mixture was shaken for 21 days in an orbital incubator at 30°C and then the enzyme was removed by filtration. The filtrate was concentrated under reduced pressure and the residue was chromatographed over silica gel (ethyl acetate–hexane 1:1). The first fractions gave (–)-*exo*-(1*R*,6*R*,9*R*)-9-acetoxy-7-oxabicyclo[4.3.0]non-4-en-8-one (–)-6 (43.3 mg, 0.22 mmol, 13.1%) as an oil. R_f 0.52 (ethyl acetate–hexane 1:1). $[\alpha]_D^{25} - 44.1$ (c 1.0 in CHCl₃), 100% ee. (Found: M^+ 197.08106, $C_{10}H_{13}O_4 + H$ requires M 197.08137). IR (neat): 3030, 2939, 1790, 1750, 1235, 1082, 993 and 965 cm⁻¹; ¹H NMR (300 MHz): δ 6.03 (1 H, dt, 4-H), 5.75 (1 H, m, 5-H), 5.41 (1 H, d, J 9, 9-H), 5.0 (1 H, m, 6-H), 2.75 (1 H, m, 1-H), 2.38–2.22 (1 H, m, 3-H), 2.14 (4 H, m, 3'-H and CH₃) and 1.80 (2 H, m, 2-H). ¹³C NMR (75.5 MHz): δ 172.33 (CO), 169.94 (CO), 133.12 (CH, C-4), 123.78 (CH, C-5), 73.75 (CH, C-6), 69.05 (CH, C-9), 39.27 (CH, C-1), 20.57 (CH₃), 20.36 (CH₂, C-3), 20.25 (CH₂, C-2); MS (CI): m/z 197 ($M+H$, 100%), 136 (18), 118 (29), 110 (30) and 92 (88). Later fractions contained *exo*-(1*S*,6*S*,9*S*)-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one (–)-4 (0.217 g, 1.40 mmol, 83.7%). R_f 0.33 (ethyl acetate–hexane 1:1); IR (neat): 3413, 3039, 2932, 1771, 1649, 1441, 1124, 1088 cm⁻¹; ¹H

Table 2. Bond lengths (Å) and angles (°) for C₁₈H₁₇F₃O₅ 7.

C(1)–O(1)	1.419(3)	C(1)–C(2)	1.523(3)
C(1)–C(8)	1.540(3)	C(1)–C(10)	1.541(3)
C(2)–C(7)	1.386(3)	C(2)–C(3)	1.400(3)
C(3)–C(4)	1.376(3)	C(4)–C(5)	1.394(3)
C(5)–C(6)	1.368(3)	C(6)–C(7)	1.389(3)
C(8)–F(1)	1.339(3)	C(8)–F(2)	1.339(3)
C(8)–F(3)	1.344(3)	C(9)–O(1)	1.446(3)
C(10)–O(2)	1.200(3)	C(10)–O(3)	1.341(3)
C(11)–O(3)	1.450(2)	C(11)–C(14)	1.509(3)
C(11)–C(12)	1.525(3)	C(12)–O(4)	1.202(3)
C(12)–O(5)	1.346(3)	C(13)–O(5)	1.476(3)
C(13)–C(18)	1.484(3)	C(13)–C(14)	1.537(3)
C(14)–C(15)	1.522(3)	C(15)–C(16)	1.514(3)
C(16)–C(17)	1.499(3)	C(17)–C(18)	1.315(3)
O(1)–C(1)–C(2)	113.7(2)	O(1)–C(1)–C(8)	101.4(2)
C(2)–C(1)–C(8)	109.9(2)	O(1)–C(1)–C(10)	112.2(2)
C(2)–C(1)–C(10)	111.9(2)	C(8)–C(1)–C(10)	107.0(2)
C(7)–C(2)–C(3)	118.7(2)	C(7)–C(2)–C(1)	122.7(2)
C(3)–C(2)–C(1)	118.5(2)	C(4)–C(3)–C(2)	120.6(2)
C(3)–C(4)–C(5)	120.1(2)	C(6)–C(5)–C(4)	119.5(2)
C(5)–C(6)–C(7)	120.9(2)	C(2)–C(7)–C(6)	120.2(2)
F(1)–C(8)–F(2)	106.8(2)	F(1)–C(8)–F(3)	107.3(2)
F(2)–C(8)–F(3)	106.5(2)	F(1)–C(8)–C(1)	112.1(2)
F(2)–C(8)–C(1)	111.7(2)	F(3)–C(8)–C(1)	112.1(2)
O(2)–C(10)–O(3)	124.6(2)	O(2)–C(10)–C(11)	124.7(2)
O(3)–C(10)–C(1)	110.7(2)	O(3)–C(10)–C(14)	112.8(2)
O(3)–C(11)–C(12)	108.0(2)	C(14)–C(11)–C(12)	104.3(2)
O(4)–C(12)–O(5)	123.3(2)	O(4)–C(12)–C(11)	128.2(2)
O(5)–C(12)–C(11)	108.5(2)	O(5)–C(13)–C(18)	109.4(2)
O(5)–C(13)–C(14)	104.7(2)	C(18)–C(13)–C(14)	113.1(2)
C(11)–C(14)–C(15)	116.5(2)	C(11)–C(14)–C(13)	100.4(2)
C(15)–C(14)–C(13)	112.2(2)	C(16)–C(15)–C(14)	113.0(2)
C(17)–C(16)–C(15)	112.0(2)	C(18)–C(17)–C(16)	124.2(2)
C(17)–C(18)–C(13)	124.0(2)	C(1)–O(1)–C(9)	118.4(2)
C(10)–O(3)–C(11)	116.9(2)	C(12)–O(5)–C(13)	110.2(2)

NMR (300 MHz): δ 6.0 (1 H, m, 4-H), 5.77 (1 H, m, 5-H), 5.0 (1 H, m, 6-H), 4.3 (1 H, dd, J 10, 4, 9-H), 3.54 (1 H, m, OH), 2.7 (1 H, m, 1-H), 2.28–1.78 (4 H, m, 2-H and 3-H); ¹³C NMR (75.5 MHz) 177.76 (CO), 132.75 (CH, C-4), 124.28 (CH, C-5), 74.22 (CH, C-6), 68.50 (CH, C-9), 40.67 (CH, C-1), 20.16 (CH₂, C-3) and 20.13 (CH₂, C-2); MS (EI): m/z 154 (M , 0.9%), 153 (M – H, 3.8), 110 (M – CO₂, 45), 92 (41) and 79 (100).

Enzymatic hydrolysis of (–)-endo-(1S,6R,9S)-9-acetoxy-7-oxabicyclo[4.3.0]non-4-en-8-one (–)-5 and (–)-exo-9-acetoxy-7-oxabicyclo[4.3.0]non-4-en-8-one (–)-6. *Pseudomonas fluorescens* lipase (33 mg) was added to a solution of ester (–)-endo-(1R,6R,9S)-9-acetoxy-7-oxabicyclo[4.3.0]non-4-en-8-one (–)-5 (0.200 g, 1.01 mmol, 100% ee) in a mixture of THF (2.5 ml) and aqueous phosphate buffer (0.1 mol l^{–1}, 5.0 ml, pH 7.0). The mixture was stirred for 20 h at room temperature. During the reaction aqueous sodium hydroxide (1 mol l^{–1}, 0.6 ml) was added to the mixture at 30-minute intervals to maintain the pH between 6.5 and 7.0. The lipase was removed by filtration and the filtrate was saturated with sodium chloride and extracted with ethyl acetate (10 × 10 ml). The extract was

concentrated under reduced pressure and the residue was chromatographed over silica gel (ethyl acetate–hexane 3:2) to give alcohol (–)-endo-(1R,6R,9S)-9-hydroxy-7-oxabicyclo[4.3.0]non-4-en-8-one (–)-3 {115 mg, 0.746 mmol, 73.2%, [α]_D²⁷ – 143.4 (c 1.0 in CHCl₃); 100% ee}. Treatment of the acetate (–)-6 (30 mg) with *Candida cylindracea* lipase in pH 6.5 buffer at room temperature for 24 h with work-up as above gave the hydroxy lactone (+)-4 [α]_D²³ + 5.7 (c 0.5 in CHCl₃) in 48% yield and 100% ee.

Preparation of Mosher ester (+)-8 by acylation. Hydroxy lactone (+)-4 (6.6 mg) in dichloromethane (2 ml) was reacted with (+)-(S)- α -methoxy- α -trifluoromethylphenylacetyl chloride (67.2 mg, 0.28 mmol) and dry pyridine (175 mg, 2.2 mmol) at room temperature for 12 h under nitrogen. The reaction mixture was diluted with dichloromethane (10 ml) and washed with an aqueous copper sulfate solution (2 × 3 ml), sodium hydrogen carbonate (2 × 3 ml) and brine (2 × 3 ml). The combined organic layers were dried over anhydrous sodium sulfate and the solvent evaporated off under reduced pressure to provide (+)-(1R,6R,9R)-9-[(R)- α -methoxy- α -trifluoromethyl-

Table 3. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for $\text{C}_{18}\text{H}_{17}\text{F}_3\text{O}_5$ **7**.

	x	y	z	U_{eq}^a
C(1)	1485(3)	4373(2)	6647(1)	23(1)
C(2)	313(3)	3609(2)	6209(1)	23(1)
C(3)	256(3)	2408(2)	6316(1)	30(1)
C(4)	-808(3)	1685(2)	5939(1)	35(1)
C(5)	-1861(3)	2147(2)	5448(1)	34(1)
C(6)	-1839(3)	3323(2)	5348(1)	32(1)
C(7)	-750(3)	4059(2)	5722(1)	26(1)
C(8)	309(3)	4581(2)	7240(1)	32(1)
C(9)	4533(3)	3293(2)	6450(1)	32(1)
C(10)	1926(3)	5579(2)	6368(1)	26(1)
C(11)	4410(3)	6715(2)	5891(1)	24(1)
C(12)	5732(3)	6467(2)	5343(1)	26(1)
C(13)	7036(3)	8023(2)	5882(1)	28(1)
C(14)	5705(3)	7369(2)	6334(1)	28(1)
C(15)	4681(4)	8189(2)	6779(1)	36(1)
C(16)	3549(4)	9147(2)	6459(1)	36(1)
C(17)	4657(3)	9644(2)	5927(1)	33(1)
C(18)	6202(3)	9152(2)	5677(1)	31(1)
O(1)	3193(2)	3826(1)	6880(1)	27(1)
O(2)	793(2)	6378(1)	6355(1)	39(1)
O(3)	3741(2)	5609(1)	6134(1)	28(1)
O(4)	5555(2)	5723(1)	4959(1)	34(1)
O(5)	7220(2)	7235(1)	5350(1)	30(1)
F(1)	1201(2)	5336(1)	7615(1)	45(1)
F(2)	59(2)	3595(1)	7558(1)	41(1)
F(3)	-1490(2)	5002(1)	7125(1)	39(1)

^a U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

phenylacetoxy]-7-oxabicyclo[4.3.0]non-4-en-8-one (+)-**8**. R_f 0.34 (ethyl acetate–hexane 1:4); m.p. 90–91 °C (toluene–light petroleum); $[\alpha]_D^{27} + 47.1$ (c 1.0 in CHCl_3). (Found: 370.10221, $\text{C}_{18}\text{H}_{17}\text{F}_3\text{O}_5$ requires 370.10280); IR (neat): 2946, 1797, 1766, 1459, 1336, 1257 and 1174 cm^{-1} ; ^{19}F NMR: δ 90.0831; ^1H NMR (CDCl_3): δ 7.60 (2 H, m, Ph), 7.42 (3 H, m, Ph), 6.08 (1 H, m, J 2.6, 4.6, 4-H), 5.80 (1 H, m, J 10.3, 2.7, 2.4, 1.6, 0.6, 5-H), 5.72 (1 H, J 9.9, 9-H), 5.01 (1 H, m, J 7.5, 2.4, 2.2, 6-H), 3.63 (3 H, OCH_3), 2.80 (1 H, m, J 9.9, 7.5, 4.6, 4.0, 0.6, 1-H), 2.42–2.28 (1 H, m, 3-H), 2.23–2.11 (1 H, m, 3'-H) and 1.91–1.70 (2 H, m, 2-H); ^{13}C NMR (75.5 MHz): δ 171.07 (CO, C-8), 166.16 (CO), 132.98 (CH, C-4), 131.71 (C, Ph), 129.88 (CH, Ph), 128.56 (CH, Ph), 127.31 (CH, Ph), 122.91 (CH, C-5), 123.12 (C, q, J_{CF} 289, CF_3), 84.86 (C, J_{CCF} 28, CCF_3), 73.90 (CH, C-6), 69.98 (CH, C-9), 55.71 (CH, OCH_3), 38.81 (CH, C-1), 20.08 (CH_2 , C-3) and 20.05 (CH_2 , C-2); MS (EI): m/z 370 (M^+ , 0.2%), 301 ($M - \text{CF}_3$, 0.5), 190 (9.8), 189 [$\text{C}_6\text{H}_5\text{C}(\text{CF}_3)(\text{OCH}_3)$, 100.0], 152 (4.7), 137 (1.5), 127 (2.2) and 105 (12.2).

General procedure for the Mitsunobu reaction using (+)-(*R*)-Mosher acid. Diethyl azodicarboxylate (3.45 mmol) in dry tetrahydrofuran (THF) (10 ml) was added dropwise to a mixture of hydroxy lactone (2.0 mmol), triphenylphosphine (3.44 mmol) and (+)-(*R*)-Mosher acid

(6.09 mmol) in dry THF (20 ml). The mixture was stirred overnight at room temperature. Solvents were evaporated off under reduced pressure and the residue was purified by column chromatography (ethyl acetate–light petroleum 1:4). Reaction of hydroxy lactone (+)-**3** under these conditions provided the ester (+)-**7**. M.p. 95–96 °C (toluene–light petroleum), R_f 0.28 (1:4 ethyl acetate–hexane); $[\alpha]_D^{27} + 5.1$ (c 1.0 in CHCl_3); IR (neat): 2946, 1793, 1758, 1459, 1331, 1255 and 1174 cm^{-1} ; ^{19}F NMR: δ 89.4861; ^1H NMR (300 MHz; CDCl_3): δ 7.61 (2 H, m, Ph), 7.43 (3 H, m, Ph), 6.08 (1 H, m, 4-H), 5.81 (1 H, m, 5-H), 5.60 (1 H, d, 9-H), 5.06 (1 H, m, 6-H), 3.54 (3 H, OCH_3), 2.95 (1 H, m, 1-H), 2.41–2.27 (1 H, m, 3-H), 2.23–2.11 (1 H, m, 3'-H) and 1.97–1.77 (2 H, m, 2-H); ^{13}C NMR: δ 170.67 (CO, C-8), 165.98 (CO), 132.95 (CH, C-4), 131.20 (C, Ph), 129.89 (CH, Ph), 128.52 (CH, Ph), 127.69 (CH, Ph), 124.03 (C, q, J_{CF} 289, CF_3), 123.93 (CH, C-2), 85.01 (C, J_{CCF} 28, CCF_3), 73.79 (CH, C-6), 70.63 (CH, C-9), 55.49 (CH, OCH_3), 38.62 (CH, C-1), 20.20 (CH_2 , C-2) and 20.17 (CH_2 , C-3); MS: m/z 370 (M^+ , 0.2%), 301 ($M - \text{CF}_3$, 0.6), 233 (0.2), 190 (9.8), 189 [$\text{C}_6\text{H}_5\text{C}(\text{CF}_3)(\text{OCH}_3)$, 100.0], 158 (1.4), 137 (1.4) and 105 (9.5). (Found: M^+ , 370.10180). $\text{C}_{18}\text{H}_{17}\text{F}_3\text{O}_5$ requires M , 370.10280. The hydroxy lactone (–)-**3** provided the ester (+)-**8** with spectral characteristics as described previously.

X-Ray structure determination. The crystal data and the details of data collection and structure refinement are given in Table 1. The intensity data were collected at 140 K using a Delft Instruments FAST TV area detector diffractometer positioned at the window of rotating anode generator with Mo-K α radiation ($\lambda = 0.71069$ Å), by following previously described procedures.⁷ 250 reflections within $\theta = 1.87$ – 24.93° were used for the refinement of the unit cell parameters. The data were corrected for Lorentz and polarization factors, and also for adsorption using the program DIFFABS.⁸

The structure was solved by direct methods (SHELX-S)⁹ and refined on F^2 by full-matrix least-squares (SHELXL-93)¹⁰ using all unique intensities above background. The non-hydrogen atoms were all anisotropic; the hydrogen were included in idealised positions with U_{iso} set at $n U_{\text{eq}}$ of the parent carbons ($n = 1.2$ for tertiary and 1.5 for methyl hydrogens). The weighting scheme given in Table 1 was chosen to obtain satisfactory agreement analyses. Final wR_2 (on F^2) and R_1 (on F) values were 0.0695 and 0.0384, respectively, for 236 parameters and all 2577 data. The corresponding R -indices for 2214 data with $I > 2\sigma(I)$ were 0.0673 and 0.0323, respectively. All calculations were done on a 486DX2/66 personal computer. Sources of scattering factor data are given in Ref. 10.

The anisotropic displacement parameters of the non-hydrogen atoms and hydrogen atom parameters have been deposited at the Cambridge Crystallographic Data Centre.

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