Enantioselective Synthesis of the Apple Aroma Constituent 1,3,3-Trimethyl-2,7-dioxabicyclo[2.2.1]heptane via Asymmetric Dihydroxylation

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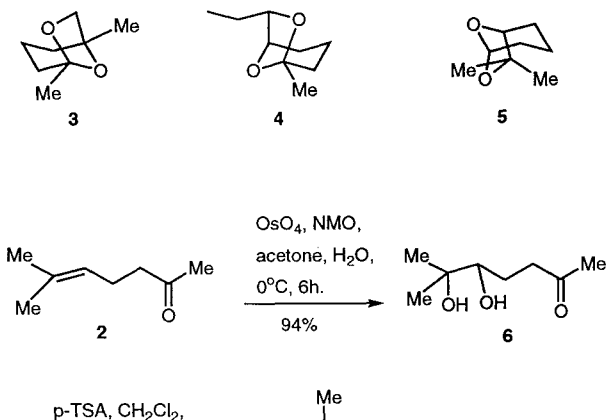
The enantiomers of 1,3,3-trimethyl-2,7-dioxabicyclo[2.2.1]heptane **(1)** were prepared in two steps from 6-methylhept-5-en-2-one using Sharpless asymmetric dihydroxylation.

1,3,3-Trimethyl-2,7-dioxabicyclo[2.2.1]heptane **(1)** has been identified as a constituent of the anal gland of the meat ant Iridomyrmex purpureus[1] and in the aroma of "Granny Smith" apples[2] where a likely source was the oxidation of α-farnesene. Klein and Rohjahn[3] in 1967, and subsequent workers[4-7] showed that 6-methylhept-5-en-2-one **(2)** is easily oxidized by peracids and may be subsequently cyclized to bicyclic acetal **1**. Although **2** is a major volatile autoxidation product of α-farnesene[5,8] and seems a likely intermediate in the *in vivo* production of bicyclic acetal **1** by apples, *in vitro* autoxidation experiments with α-farnesene and **2** suggest otherwise.[2] Oxidation of α-farnesene positively correlates with the occurrence of superficial scald, an economically important post-harvest storage disorder of apples. In order to examine the stereochemistry of the oxidation process occurring on the apples, an asymmetric synthesis of 1,3,3-trimethyl-2,7-dioxabicyclo[2.2.1]heptane **(1)** was carried out using the Sharpless asymmetric dihydroxylation procedure[9] to introduce the desired chirality.

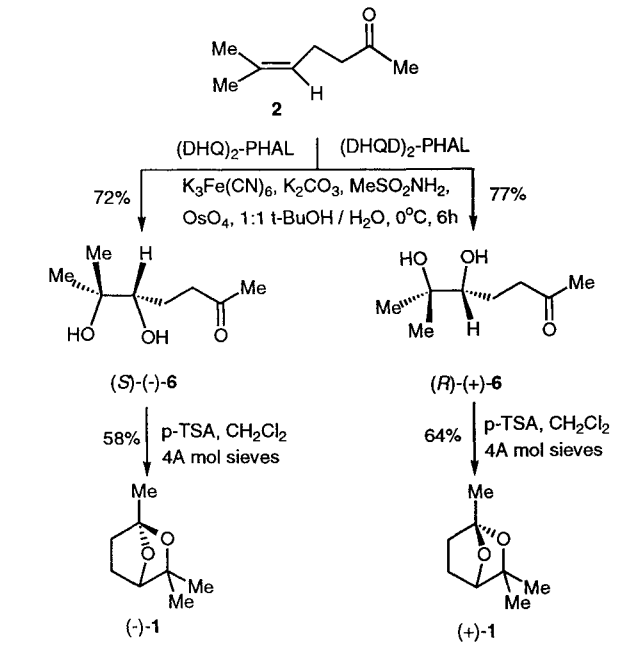
Several syntheses of bicyclic acetals related to **1** have recently been reported which employed the Sharpless asymmetric dihydroxylation methodology for the key chiral induction step.[10-13] The 6,8-dioxabicyclo-[3.2.1]octane skeleton present in the aggregation pheromones of pine beetles *Dendroctonus frontalis* and *Dendroctonus brevicomis*, frontalin **(3)** and exobrevicomin **(4)**, were prepared[10-12] enantioselectively via asymmetric dihydroxylation of disubstituted alkenes in modest (35%) and excellent (95%) enantiomeric excess, respectively. 7,7-Dimethyl-6,8-dioxabicyclo[3.2.1]octane **(5)** which contains the same carbon skeleton as frontalin **(3)** and brevicomin **(4)** is a volatile contributor to the aroma of beer and has been prepared enantioselectively by Sharpless and Crispino.[13] In this case, use of the asymmetric dihydroxylation procedure allowed the preparation of both enantiomers of **5** in high yield and enantiomeric excess.

Given the excellent precedent set by these syntheses, the enantioselective synthesis of bicyclic acetal **1** was undertaken. Initial attention focused on the synthesis of racemic acetal **1** in order to optimize reaction conditions. Dihydroxylation of 6-methylhept-5-en-2-one **(2)** using osmium tetroxide and *N*-methylmorpholine *N*-oxide (Scheme 1) afforded diol **6** in 94% yield. Cyclization of **6** and purification of acetal **1** proved to be problematic due to the sensitivity of the cyclization reaction to the presence of water and the volatility of the product. Successful cyclization required the presence of activated, powdered molecular sieves, dry recrystallized *p*-toluenesulfonic acid and anhydrous dichloromethane. The reaction was then quenched with solid sodium hydrogen carbonate and the entire mixture filtered through a plug of flash silica using diethyl ether/pentane (1:1) as eluent. Isolation of acetal **1** in 58% yield was achieved after careful removal of this more volatile eluent under reduced pressure at 0 °C. Attempts to prepare **1** by epoxidation and thermal cyclization of **2**[4] were unsuccessful.



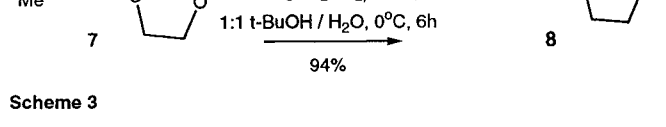
Scheme 1

Asymmetric dihydroxylation of **2** using commercial AD-mix-α or AD-mix-β was unsuccessful in that no reaction occurred and the addition of methanesulfonamide[14] led to incomplete reaction. Since the commercial AD-mixes contain only 0.6% ligand and osmium salt, the conditions earlier employed by Sharpless and Crispino[13] using 1 mol% of osmium tetroxide 5 mol% phthalazine ligand [$(DHQ)_2$-PHAL or $(DHQD)_2$-PHAL] and 1 equivalent of methanesulfonamide were used and this resulted in improved yields of diol **6**. A minimum quantity of 1 M aqueous potassium hydroxide was used to remove the methanesulfonamide and a more polar solvent (ethyl acetate) to extract the diol product. Use of these optimized conditions afforded (−)-keto-diol **6** in 72% yield using $(DHQ)_2$-PHAL and (+)-keto-diol **6** in 77% yield using $(DHQD)_2$-PHAL (Scheme 2). (−)-Diol **6** and (+)-diol **6** were then converted into (−)-acetal **1** and (+)-acetal **1** in 58% and 64% yield, respectively, using the conditions outlined above.



Scheme 2

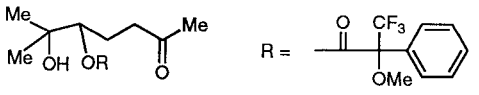
In view of the difficulties encountered in the isolation of the polar keto-diol **6**, the ketone functionality was protected as a 1,3-dioxolane **7** using ethylene glycol and *p*-toluenesulfonic acid (Scheme 3). Although 1,3-dioxolane **7** underwent smooth asymmetric dihydroxylation in 94% yield using $(DHQ)_2$-PHAL we were unable to effect cyclization of diol **8** to acetal **1**.



Scheme 3

The absolute configuration of the enantiomeric diols **6** was assigned using the mnemonic device described by Sharpless[9] and the enantiomeric excess was determined using several methods. Using the chiral solvating agent, *R*-(−)-2,2,2-trifluoro-1-(-anthryl)ethanol [*R*-(−)-TFAE], satisfactory resolution of the two enantiomers in the ^{1}H NMR spectrum was obtained upon the addition of seven equivalents of *R*-(−)-TFAE to racemic acetal **1** wherein the resonances for both of the 3-methyl groups separated into two peaks due to the different solute/solvent interactions for the individual enantiomers. Using this method the enantiomeric excesses were calculated to be 87% for (−)-**1** and 93% for (+)-**1**. The difference in ee for (−)-**1** is directly attributable to the nonenantiomeric relationship between the two phthalazine ligands used in the dihydroxylation reaction.[15]

Conversion of diols (−)-**6** and (+)-**6** to a Mosher ester derivative **9** allowed more accurate determination of the enantiomeric excesses due to better peak resolution and a cleaner ^{1}H NMR spectrum. Differences of up to 0.05 ppm were observed between diastereomers and ee calculations based on 1-H confirmed 95% ee for *R*-(+)-**6** and 86% for *S*-(−)-**6** in agreement with the values obtained using the chiral solvent. The ^{19}F NMR spectrum of racemic Mosher ester **9** exhibited two peaks at $\delta = -71.25$ and -71.08 relative to $CFCl_3$. Calculations using the peak integrations for the enantiomers revealed an ee of 98% for *R*-(+)-**6** and 89% for *S*-(−)-**6** which was in excellent agreement with the two methods discussed above.



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One possible disadvantage of using the unprotected ketone **2** as the AD substrate as opposed to the protected ketone **7** was that a remote carbonyl functionality may lower the observed enantiomeric excess.[10,12] In the related synthesis discussed above, Soderquist and Rane[12] overcame this problem via protection of the ketone as an acetal, whereas Sharpless and Crispino[13] carried out an AD on a diene followed by conversion of the less reactive monosubstituted alkene to an aldehyde via ozonolysis. The enantiomeric excesses in the current work were higher than those obtained by Soderquist and Rane[12] when they used an unprotected ketone and indicate no interference of the carbonyl group with the asymmetric induction.

In summary, the first enantioselective synthesis of 1,3,3-trimethyl-2,7-dioxabicyclo[2.2.1]heptane **(1)** has been carried out efficiently using the Sharpless asymmetric dihydroxylation to induce chirality. With the desired acetal **1** in hand, experiments to investigate the origin (biosynthetic or autoxidative) and the quantitiy of this compound on apples can be carried out.

All reagents were purchased from Aldrich Chemical Co. $(DHQ)_2$-PHAL and $(DHQD)_2$-PHAL were provided by Professor K.B. Sharpless. $[\alpha]_D$ Values are given in 10^{-1} deg cm^2 g^{-1} and concentrations are expressed in mol L^{-1}. IR spectra were recorded on a Bio-Rad FTS 40V spectrophotometer as Nujol mulls or thin films between NaCl discs. ^{1}H NMR spectra were recorded at 270 MHz in $CDCl_3$ using TMS as internal standard on a JEOL GX270 spectrometer. ^{19}F NMR spectra were recorded in $CDCl_3$ using $CFCl_3$ as internal standard on a Bruker AC 300 spectrometer. ^{13}C NMR spectra were recorded at 67.8 MHz on a JEOL GX270 spectrometer. All chemical shifts are given in parts per million (ppm) and *J* values are given in Hz. Mass spectra and accurate mass measurements were recorded by GCMS on a VG70-250S double focusing magnetic sector spectrometer with an ionization potential of 70 eV. Merck Kieselgel 60 (230–400) mesh was used for flash chromatography. TLC was carried out on precoated silica gel plates (Merck Kieselgel $60F_{254}$) and compounds were visualized by UV fluorescence or vanillin in methanolic H_2SO_4. All compounds were isolated as unstable oils for which purity and elemental composition were determined by high resolution GC/MS and/or high resolution mass spectrometry.

(±)-5,6-Dihydroxy-6-methylheptan-2-one [(±)-6]:
N-Methylmorpholine *N*-oxide (321 mg, 2.74 mmol) was added to an ice-cooled solution of 6-methylhept-5-en-2-one (**2**; 288 mg, 2.28 mmol) in acetone/water (5 mL or enough water to solublize the *N*-methylmorpholine *N*-oxide) followed by OsO_4 (0.5 mL of a 2.5% w/w solution in *t*-BuOH). After 4 h, the reaction was quenched

with a 0.1 M aq $Na_2S_2O_4$ solution (1.89 mL, 0.19 mmol), then diluted further with acetone (5 mL) and water (0.5 mL). This mixture was stirred for 0.5 h, when sufficient anhydrous $MgSO_4$ was added to remove all water. The suspension was filtered through a plug of Celite and the solvent was removed under reduced pressure to yield a colourless oil. Purification by flash chromatography using hexane/EtOAc (1:1) as eluent afforded **6** as a colourless oil (337 mg, 94%).

HRMS: *m/z* Found: $M^+ - H_2O$ 142.0993, $C_8H_{16}O_3$ requires $M - H_2O$ 142.0993.

IR (neat): $\nu = 1708$ (C=O), 1110 cm^{-1} (C–O).

MS (CI, NH_3): *m/z* = 161 [$(M + H)^+$, 37%], 159 (48), 143 [100, $(M + H) - H_2O$], 118 (5), 100 (10), 60 (18), 43 (9).

Diol **6** was found by ^1H and ^{13}C NMR spectra to occur largely as an unstable mixture of hemiacetals and was characterized as the acetonide derivative. Conversion of diol **6** to the corresponding acetonide was carried out as follows: To a solution of **6** (25.8 mg, 0.161 mmol) in acetone (3 mL) was added a catalytic amount of camphorsulfonic acid (5 mg). After stirring overnight the solvent was removed under reduced pressure and the residue purified by flash chromatography using hexane/EtOAc (2:1) as eluent, to yield the acetonide derivative as a colourless oil (9.8 mg, 30%).

HRMS: *m/z* Found: M^+ 200.1412, $C_{11}H_{20}O_3$ requires M 200.1412.

IR (neat): $\nu = 2960$ (CH_2, CH_3), 1708 (C=O), 1110 cm^{-1} (C–O).

^1H NMR (270 MHz, $CDCl_3$) (acetonide derivative): $\delta = 1.11$, 1.26 [total 6H, 2s, $C(CH_3)_2$], 1.32, 1.41 (total 6H, 2s, acetonide CH_3), 1.63–1.76 (2H, m, 4-H), 2.18 (3H, s, 1-H), 2.49–2.79 (2H, m, 3-H), 3.62–3.67 (1H, m, 5-H).

^{13}C NMR (67.8 MHz, $CDCl_3$) (acetonide derivative): $\delta = 22.9$, 25.9, 26.9, 28.5 [$C(\underline{C}H_3)_2$ and acetonide CH_3], 23.2 (C-4), 30.0 (C-1), 40.9 (C-3), 80.2 (C-6), 82.5 (C-5), 106.7 [$\underline{C}(CH_3)_2$], 208.1 (C=O, C-2).

MS: *m/z* = 200 (M^+, 0.5%), 185 (40, $M - CH_3$), 143 (32), 125 (27), 107 (7), 84 (79), 71 (13), 59 (20), 43 (100).

(±)-1,3,3-Trimethyl-2,7-dioxabicyclo[2.2.1]heptane [(±)-1]:

To a suspension of powdered molecular sieves (4 Å, 10 mg) in CH_2Cl_2 (15 mL) was added a solution of (±)-**6** (160 mg, 1.0 mmol) in CH_2Cl_2 (2 mL) and a catalytic amount of TsOH (15 mg). When all of the diol **6** had reacted (as observed by TLC), solid $NaHCO_3$ (20 mg) was added to the mixture which was allowed to stir for an additional 5 min. The entire mixture was then filtered through a plug of flash silica using pentane/Et_2O (1:1) as eluent and the solvent removed under reduced pressure to give the title compound **1** as a colourless oil (93 mg, 64%).

HRMS: *m/z* Found: M^+, 142.0988. $C_8H_{14}O_2$ requires M, 142.0993.

IR (neat): $\nu = 2981$ (CH_3, CH_2), 1172 cm^{-1} (C–O).

^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.20$, 1.26 [total 6H, 2s, $C(CH_3)_2$], 1.58 (3H, s, 1-CH_3), 1.60–2.09 (4H, m, 5-H and 6-H), 4.22 (1H, d, $J = 4.4$ Hz, 4-H).

^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 19.3$ (1-CH_3), 23.5, 27.9 [$C(\underline{C}H_3)_2$], 24.7 (C-5), 35.3 (C-6), 80.3 [$\underline{C}(CH_3)_2$], 83.5 (C-4), 109.2 ($\underline{C}CH_3$).

MS: *m/z* = 142 (M^+, 2%), 127 (7), 84 (41), 82 (30), 72 (61), 43 (100). The mass spectral, IR and ^1H NMR data obtained were in agreement with the literature.[2,4,7]

2-Methyl-2-(4-methylpent-3-en-1-yl)-1,3-dioxolane (7):

To a solution of **2** (4.00 g, 32.0 mmol) in benzene (200 mL) was added ethylene glycol (3.94 g, 64.0 mmol) and a catalytic amount of TsOH (300 mg, 1.58 mmol). The mixture was refluxed for 5 h using a Dean-Stark apparatus. The solvent was removed under reduced pressure followed by purification of the crude oil by flash chromatography using hexane/EtOH (9:1) as eluent to afford **7** (3.95 g, 73%).

HRMS: *m/z* Found: M^+ 170.1312, $C_{10}H_{18}O_2$ requires M 170.1307.

IR (neat) $\nu = 1667$ (C=C), 1135 cm^{-1} (C–O).

^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 17.5$ (2-CH_3), 22.7 (C-2'), 23.7, 25.5 [$C(\underline{C}H_3)_2$], 39.0 (CH_2, (C-1'), 64.5 (OCH_2CH_2O), 109.8 (C-2), 124.0 (=CH), 131.4 (C=$\underline{C}Me_2$). ^1H NMR and mass spectral data were in agreement with the literature.[16,17]

(–)-2-(3,4-Dihydroxy-4-methylpent-1-yl)-2-methyl-1,3-dioxolane [(–)-8]:

A suspension of $K_3Fe(CN)_6$ (1.51 g, 4.59 mmol), K_2CO_3 (633 mg, 4.59 mmol), methanesulfonamide (145 mg, 1.53 mmol) and 1,4-bis(9-*O*-dihydroquininyl)phthalazine [$(DHQ)_2$-PHAL] (59.5 mg, 0.0765 mmol) was prepared in water/*t*-BuOH (12 mL, 1:1) and cooled to 0 °C. To this mixture was added OsO_4 (0.19 mL of a 2.5% w/w solution in *t*-BuOH, 0.0153 mmol) followed by **7** (260 mg, 1.53 mmol) in a single portion. The reaction was maintained at 0 °C and stirred for 6 h, then quenched by the addition of solid $Na_2S_2O_4$ (500 mg, 2.87 mmol). After stirring for 0.5 h, the mixture was extracted with EtOAc (3 × 20 mL). The EtOAc extract was washed with 1 M aq KOH (2 × 5 mL) and dried ($MgSO_4$) followed by removal of the solvent under reduced pressure. A clear oil was obtained which was purified by flash chromatography using hexane/EtOAc (1:1) as eluent to give (–)-**8** (280 mg, 94%).

HRMS: *m/z* Found (acetonide derivative): $(M - CH_3)^+$ 229.1443, $C_{13}H_{24}O_4$ requires $(M - CH_3)^+$ 229.1440.

IR (neat): $\nu = 3410$ (OH), 1065 cm^{-1} (C–O).

^1H NMR (270 MHz, $CDCl_3$): $\delta = 1.15$, 1.20 [total 6H, 2 s, $C(CH_3)_2$], 1.34 (3H, s, 2-CH_3), 1.38–1.98 (4H, m, CH_2CH_2), 2.71–2.80 (1H, s, br, OH), 3.29–3.36 (2H, CHOH and OH), 3.96–3.99 (4H, m, OCH_2CH_2O).

^{13}C NMR (67.8 MHz, $CDCl_3$): $\delta = 23.3$, 26.3 [$\underline{C}(CH_3)_2$], 25.7 (C-2'), 26.3 (2-CH_3), 36.1 (C-1'), 64.4, 64.5 (OCH_2CH_2O), 72.8 [$\underline{C}(CH_3)_2$], 78.3 (CHOH), 110.0 (C-2).

MS: *m/z* (acetonide derivative) = 229 [$(M - CH_3)^+$, 12%], 185 (65), 143 (97), 125 (76), 108 (18), 82 (30), 84 (34) and 43 (100).

(–)-5,6-Dihydroxy-6-methylheptan-2-one [(–)-6]:

A suspension of $K_3Fe(CN)_6$ (1.69 g, 5.13 mmol), K_2CO_3 (708 mg, 5.13 mmol), methanesulfonamide (162 mg, 1.71 mmol) and $(DHQ)_2$-PHAL (66.5 mg, 0.0855 mmol) was prepared in water/*t*-BuOH (12 mL, 1:1) and cooled to 0 °C. To this mixture was added OsO_4 (0.25 mL of a 2.5% w/w solution in *t*-BuOH, 0.0197 mmol) followed by **2** (215 mg, 1.71 mmol) in a single portion. The mixture was stirred at 0 °C and stirred for 6 h, then quenched by the addition of solid $Na_2S_2O_4$ (500 mg, 2.87 mmol). The mixture was stirred for a further 0.5 h and extracted with EtOAc (3 × 20 mL). The EtOAc extract was washed with KOH (2 × 5 mL 1 M solution in water) and dried ($MgSO_4$) followed by removal of the solvent under reduced pressure. A clear oil was obtained which was purified by flash chromatography using hexane/EtOAc (4:1) as eluent to give (–)-**6** (198 mg, 72%) for which the IR, ^1H, ^{13}C and MS data were in agreement with that listed for racemic diol **6**; $[\alpha]_D - 10.6$ ($c = 0.62$, in $CHCl_3$). Conversion to the Mosher ester derivative **9** (*vide infra*) established the enantiomeric excess to be 89%.

(+)-5,6-Dihydroxy-6-methylheptan-2-one [(+)-6]:

The (+)-enantiomer of **6** was prepared from **2** (203 mg, 1.61 mmol) as above using $K_3Fe(CN)_6$ (1.59 g, 4.83 mmol), K_2CO_3 (667 mg, 4.83 mmol), methanesulfonamide (153 mg, 1.61 mmol), 1,4-bis(9-*O*-dihydroquinidinyl)phthalazine [$(DHQD)_2$-PHAL] (62.6 mg, 0.0805 mmol) and OsO_4 (0.25 mL of a 2.5% w/w solution in *t*-BuOH, 0.0197 mmol). After workup, a clear oil was obtained which was purified by flash chromatography using hexane/EtOAc (4:1) as eluent to give (+)-**6** (197 mg, 77%) for which the IR, ^1H, ^{13}C and MS data were in agreement with that listed above; $[\alpha]_D + 10.2$ ($c = 0.62$, $CHCl_3$). Conversion to the Mosher ester derivative **9** (*vide infra*) established the enantiomeric excess to be 98%.

6-Hydroxy-6-methyl-2-oxohept-5-yl α-Methoxy-α-(trifluoromethyl)-phenylacetate (9):

To a solution of (–)-**6** (26.6 mg, 0.166 mmol) in pyridine (2 mL) was added Et_3N (0.1 mL, 0.665 mmol) and *R*-(–)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride [(–)-MTPA-Cl] (0.03 mL, 0.166 mmol) followed by a catalytic amount of *N,N*-dimethylaminopyridine (DMAP) (1–2 mg). After 7 h, the pyridine was removed under reduced pressure, and the residue purified by flash

chromatography using hexane/EtOAc (2:1) as eluent to give the Mosher ester derivative **9** as a colourless oil (50.6 mg, 81%).

HRMS: *m/z* Found: $(M+H)^+$ 377.1573, $C_{18}H_{24}O_5F_3$ requires (M + H) 377.1576.

IR (neat): ν = 3448 (OH), 1740 (C=O, ester), 1712 (C=O, ketone), 2847 cm^{-1} (CH of $COCH_3$).

^{19}F NMR (282 MHz, $CDCl_3$): $\delta = -71.25$ (s, CF_3).

^1H NMR (270 MHz, $CDCl_3$): δ = 1.16, 1.19 [$C(CH_3)_2$], 1.74–1.78 (2H, m, 4-H), 2.09 (3H, s, CH_3CO), 2.40–2.45 (2H, m, 3-H), 3.55 (3H, s, OCH_3), 4.95 (1H, d, J = 7.3 Hz, 5H), 7.41–7.61 (5H, m, ArH).

^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 23.7 (C-4), 24.7, 26.0 [$C(\underline{C}H_3)_2$], 30.0 (C-1), 39.5 (C-3), 55.4 (OCH_3), 72.2 (C-6), 82.1 (C-5), 127.4, 128.5, 129.8 (ArCH), 131.8 (ArC), 166.6 (CO_2), 207.4 ($CH_3\underline{C}O$).

MS: *m/z* = 377 [$(M+H)^+$, 1%], 359 (20), 189 (100), 143 (50), 125 (52), 105 (32), 85 (24), 77 (18), 71 (36), 59 (36), 43 (66).

Using the same procedure as above Mosher ester derivative **9** was prepared from (+)-**6** (52.2 mg, 0.326 mmol) using pyridine (1 mL), Et_3N (0.3 mL), (−)-MTPA-Cl (0.06 mL, 0.35 mmol) and a catalytic amount of DMAP (5 mg). Purification was carried out by flash chromatography using hexane/EtOAc (2:1) as eluent, to afford the Mosher ester derivative **9** as a colourless oil (47.4 mg, 39%).

^{19}F NMR (282 MHz, $CDCl_3$): $\delta = -71.08$ (s, CF_3).

^1H NMR (270 MHz, $CDCl_3$): δ = 1.16, 1.24 (total 6H, 2s, $C(CH_3)_2$], 1.58–1.68 (2H, m, 4-H), 2.05 (3H, s, CH_3CO), 2.27–2.32 (2H, m, 3-H), 3.57 (3H, s, OCH_3), 4.95 (1H, d, J = 8.1 Hz, 5-H), 7.42–7.63 (5H, m, ArH).

^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 23.6 (C-4), 24.8, 25.9 [$C(\underline{C}H_3)_2$], 29.9 (C-1), 39.4 (C-3), 55.4 (OCH_3), 72.1 (C-6), 82.0 (C-5), 127.4, 128.5, 129.7 (ArCH), 131.8 (ArC), 166.5 (CO_2), 207.4 ($CH_3\underline{C}$=O). IR and MS data was in agreement with that listed above.

Optical rotations for Mosher esters were not obtained due to the relatively large amount of material required to obtain accurate measurements.

(−)-1,3,3-Trimethyl-2,7-dioxabicyclo[2.2.1]heptane [(−)-1]:
The title compound (−)-**1** was prepared from (−)-**6** (47.6 mg, 0.298 mmol) as described for the racemic material above as a colourless oil (24.5 mg, 58%) for which the IR, ^1H, ^{13}C and MS data were in agreement with that listed above; $[\alpha]_D$ −29.0 (c = 0.18, $CHCl_3$). Addition of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol (7 equiv), followed by ^1H NMR measurement established the enantiomeric excess to be 87%.

(+)-1,3,3-Trimethyl-2,7-dioxabicyclo[2.2.1]heptane [(+)-1]:
The title compound (+)-**1** was prepared from (+)-**6** (159 mg, 0.994 mmol) as above as a colourless oil (90.4 mg, 64%) for which the IR, ^1H, ^{13}C and MS data were in agreement with that listed above; $[\alpha]_D$ +27.7 (c = 0.13, $CHCl_3$). Addition of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol (7 equiv), followed by ^1H NMR measurement, established the enantiomeric excess to be 95%.

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