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β-Hydroxy-α-tosyloxy esters as chiral building blocks for the enantioselective synthesis of benzo-annulated oxa-heterocycles: scope and limitations☆

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Abstract

The enantioselective synthesis of benzo-annulated oxa-heterocycles 2,3-dihydrobenzofuran and 1-benzopyran derivatives is described using β-hydroxy-α-tosyloxy esters as chiral building blocks, which are easily accessible through the regioselective α-tosylation of Sharpless asymmetric dihydroxylation-derived *syn*-2,3-dihydroxy esters.

1. Introduction

Over the past several years, organic synthesis of natural product-like molecules have received significant attention due to the growing use of small-molecule libraries for studies of protein function and discovery of novel drug leads.[1] Small-molecule libraries generated from the core scaffolds derived from natural products are proving to be a valuable source of biologically active compounds that provide new probes for molecular targets. In this context, new methodologies have to be designed for stereoselective synthesis of small-molecule libraries with distinct skeletal frame works via diversity-oriented synthesis (DOS).[2]

Following our interest in the field of diversity-oriented synthesis of benzo-annulated heterocycles as privileged structures, we recently employed naturally occurring α-amino acids as chiral pools that provided an access to a large array of benzofused heterocycles.[3–5] As part of our research program related to the diversity-oriented synthesis (DOS), we became interested in the enantioselective synthesis of natural product-like small molecules (Fig. 1)[6–11] containing 2,3-dihydrobenzofuran, 1-benzopyran, and 1-benzoxepin frame works.

Since the pioneering report of Sharpless on the regioselective arenesulfonylation of the α-hydroxy group of *syn*-2,3-dihydroxy esters,[12] the resulting trifunctional β-hydroxy-α-arenesulfonyloxy esters have been extensively used for their conversions into the corresponding α-azido-β-hydroxy esters[12,13] and glycidic esters.[12,14] The only other synthetic utility we are aware of is their use in the synthesis of a combinatorial library of tetrahydroquinoline based polycyclic molecules.[15] Thus, despite their easy accessibility and multifunctionalities, β-hydroxy-α-arenesulfonyloxy esters have not been largely utilized for benzo-annulated heterocycle synthesis. This paper describes our efforts toward generation of benzo-annulated oxa-heterocycles through phenoxide ion mediated intramolecular S_N2 reaction on the tosyloxy group of β-hydroxy-α-tosyloxy esters and ring opening of *syn*-glycidic esters, which were derived from β-hydroxy-α-tosyloxy esters.

2. Results and discussion

Initially, we focused our attention on a stereoselective synthesis of 2,3-dihydro-3-hydroxy-2-[1-hydroxy-1-(methyl)-ethyl]benzofuran ring system, which constitutes the core skeleton of a number of biologically important natural products (Fig. 1,

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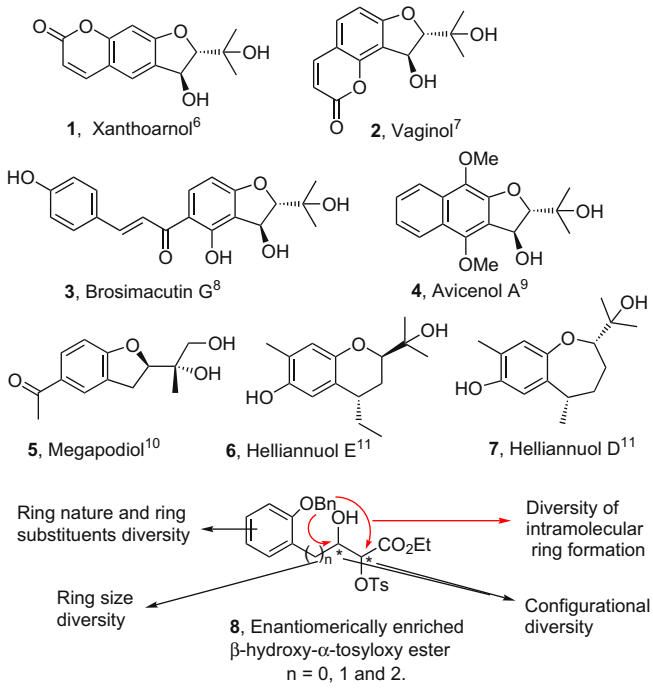
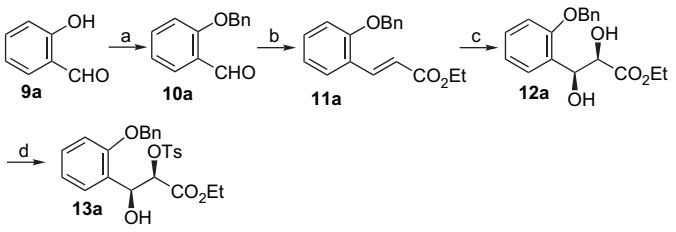


Figure 1. Bioactive natural products (**1**–**7**) containing benzo-annulated oxaheterocycles and the synthetic versatility of β-hydroxy-α-tosyloxy esters (**8**) in our synthetic strategy.

compounds **1**–**4**). Although these compounds were known for a long time, these compounds have not been the subjects of much organic synthesis. The only successful synthetic study of the natural products in this family, we are aware of are the recent reports by Snider et al.[16]

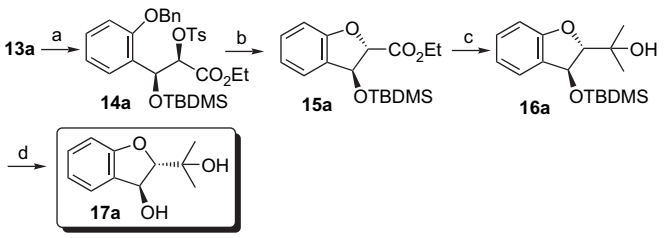
Our model synthesis to obtain enantiopure 2,3-dihydro-3-hydroxy-2-[1-hydroxy-1-(methyl)-ethyl]-benzofuran derivative is shown in Scheme 1. Benzylation of commercially available 2-hydroxybenzaldehyde **9a** with benzyl bromide and anhydrous K_2CO_3 in dry acetone under reflux condition followed by Wittig olefination of the resulting 2-benzyloxybenzaldehyde **10a** with (carbethoxymethylene)triphenylphosphorane in dry CH_2Cl_2 at room temperature furnished the corresponding *trans* cinnamate ester **11a**. The *trans* cinnamate ester **11a** was then subjected to Sharpless asymmetric dihydroxylation[17] with AD-mix-α in *t*-BuOH/H_2O (1:1) at 0 °C for 28 h furnishing enantiopure dihydroxyl derivatives **12a** in good yield and high enantiomeric excess (92%, ee>99%).



Scheme 1. Reagents and conditions: (a) BnBr, anhyd K_2CO_3, dry acetone, reflux, 4 h, 85%; (b) $Ph_3P{=}CHCO_2Et$, dry CH_2Cl_2, rt, 2 h, 78%; (c) AD-mix-α, *t*-BuOH/H_2O (1:1), 0 °C, 28 h, 92%; (d) TsCl, dry Et_3N, dry CH_2Cl_2, 0 °C, 72 h, 87%.

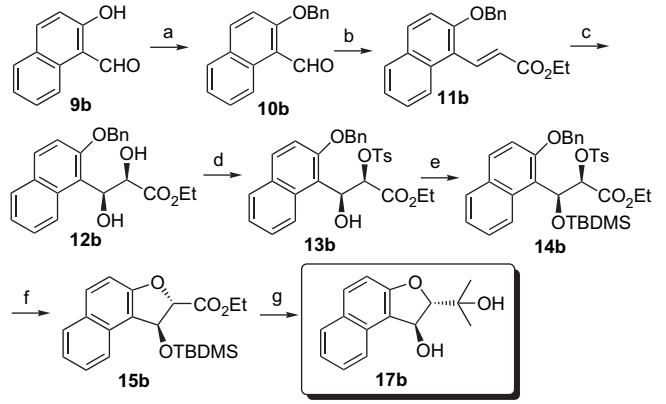
Conversion of diol **12a** into β-hydroxy-α-tosyloxy ester **13a** was achieved by the regioselective α-tosylation of diol **12a** with tosyl chloride (1.05 equiv) and triethyl amine in dry CH_2Cl_2 at 0 °C for 72 h.[12] All the products were well characterized by NMR and MS studies.

Next, hydroxyl group of **13a** was protected as its *tert*-butyl dimethylsilyl ether by using *tert*-butyl dimethylsilyl triflate in the presence of 2,6-lutidine affording **14a** with excellent yield (Scheme 2). Catalytic debenzylation of **14a** with hydrogen and 10% Pd/C in ethyl acetate followed by cyclization of the resulting debenzylated product in the presence of anhydrous K_2CO_3 in dry acetone afforded 2,3-dihydrobenzofuran derivative **15a** in good yield. Treatment of the ester **15a** with an excess of methylmagnesium iodide furnished the tertiary alcohol **16a**. Finally, removal of the TBDMS of **16a** with TBAF in dry THF afforded **17a** in 91% yield.



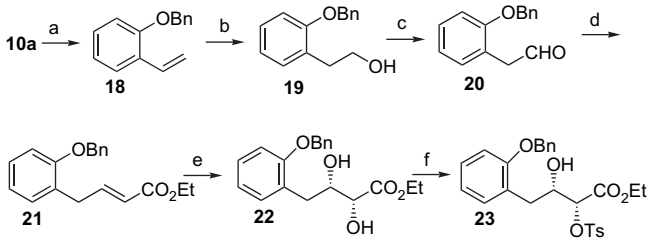
Scheme 2. Reagents and conditions: (a) TBDMS-OTf, 2,6-lutidine, 0 °C–rt, 6 h, 85%; (b) (i) H_2, 10% Pd/C, EtOAc, 4 h; (ii) anhyd K_2CO_3, dry acetone, 6 h, 69% (based on two steps); (c) MeMgI, dry ether, reflux, 4 h, 77%; (d) TBAF, dry THF, 0 °C, 5 h, 91%.

After the enantioselective synthesis of 2,3-dihydrobenzofuran derivative **17a**, our next attention was to synthesize structurally related dihydronaphthofuran analog of **17a**. Thus, commercially available 2-hydroxy-1-naphthaldehyde **9b** was converted into **17b** using the same reaction sequence as that described for the synthesis of **17a** (Scheme 3).



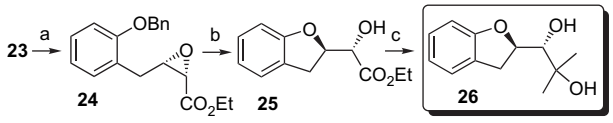
Scheme 3. Reagents and conditions: (a) BnBr, anhyd K_2CO_3, dry acetone, reflux, 4 h, 83%; (b) $Ph_3P{=}CHCO_2Et$, dry CH_2Cl_2, rt, 2 h, 80%. (c) AD-mix-α, *t*-BuOH/H_2O (1:1), 0 °C, 28 h, 93%; (d) TsCl, dry Et_3N, dry CH_2Cl_2, 0 °C, 72 h, 94%; (e) TBDMS-OTf, 2,6-lutidine, 0 °C–rt, 6 h, 88%; (f) (i) H_2, 10% Pd/C, EtOAc, 4 h; (ii) anhyd K_2CO_3, dry acetone, 6 h, 72% (based on two steps); (c) (i) MeMgI, dry ether, reflux, 4 h; (ii) TBAF, dry THF, 0 °C, 5 h, 74% for two steps.

The successful synthesis of enantiomerically pure **17a**,**17b** encouraged us to initiate further application of this strategy on homologated analog of **13a** for the synthesis of other 2,3-dihydrobenzofuran and 1-benzopyran derivatives. Toward that direction, aldehyde **10a** was converted into olefin **18** by Wittig reaction with methyltriphenylphosphonium iodide and potassium *tert*-butoxide in dry THF (Scheme 4). Olefin **18** was converted into primary alcohol **19** by hydroboration with 9-BBN and oxidation with hydrogen peroxide and NaOH. Compound **19** was oxidized to its corresponding aldehyde **20** by PCC in dry CH_2Cl_2. With aldehyde **20** in hand, next work was the conversion of it into β-hydroxy-α-tosyloxy ester **23** using a similar reaction sequence as that described for the synthesis of **13a**.



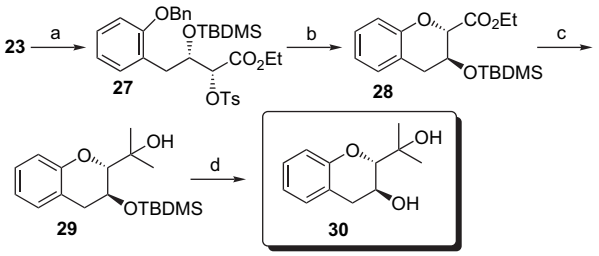
Scheme 4. Reagents and conditions: (a) methyltriphenylphosphonium iodide, *t*-BuOK, dry THF, 0 °C–rt, 2 h, 80%; (b) (i) 9-BBN, dry THF, 0 °C–rt, overnight; (ii) $NaOH/H_2O_2$, reflux, 2 h, 96%; (c) PCC, dry CH_2Cl_2, 2 h, 0 °C–rt, 76%; (d) $Ph_3P{=}CHCO_2Et$, dry CH_2Cl_2, rt, overnight, 75%; (e) AD-mix-α, *t*-BuOH/H_2O (1:1), 0 °C, 40 h, 89%; (f) TsCl, dry Et_3N, dry CH_2Cl_2, 0 °C, 72 h, 85%.

With the availability of **23**, its conversion into 2,3-dihydrobenzofuran derivative (Scheme 5) was first attempted. Accordingly, treatment of β-hydroxy-α-tosyloxy ester **23** with anhydrous K_2CO_3 in absolute ethanol furnished epoxy ester **24** in good yield. Next, debenzylation of **24** under hydrogen atmosphere using 10% Pd/C as catalyst followed by anhydrous K_2CO_3 induced phenoxide ion mediated intramolecular 5-*exo*-tet epoxide ring opening produced enantiomerically pure dihydrobenzofuran based α-hydroxy ester **25**, which on methylmagnesium iodide Grignard reaction furnished **26**. To the best of our knowledge, this is the first report of phenoxide ion mediated intramolecular ring opening of *syn*-glycidic ester.



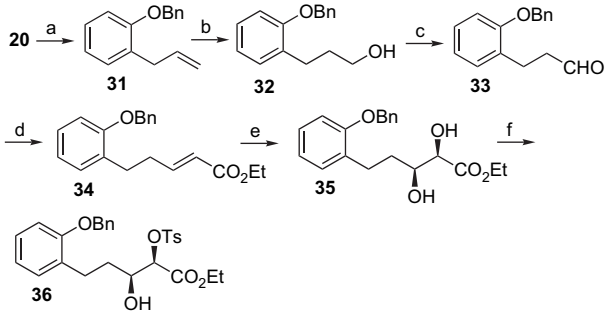
Scheme 5. Reagents and conditions: (a) anhyd K_2CO_3, ethanol, rt, 8 h, 75%; (b) (i) H_2, 10% Pd/C, ethyl acetate, 2 h; (ii) anhyd K_2CO_3, dry acetone, rt, 6 h, 81% (for two steps); (c) MeMgI, dry ether, reflux, 4 h, 88%.

After the effective utilization of **23** in the synthesis of enantiomerically pure **26**, we wanted to further utilize it for the synthesis of 1-benzopyran derivative involving phenoxide ion mediated intramolecular S_N2 reaction of tosyloxy group. Thus, **23** was converted into 1-benzopyran derivative **30** using a similar reaction sequence as that described for the synthesis of **17a** (Scheme 6).



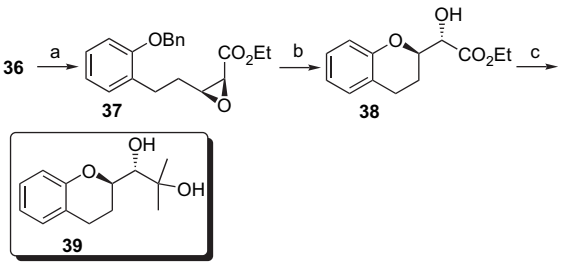
Scheme 6. Reagents and conditions: (a) TBDMS-OTf, 2,6-lutidine, 0 °C–rt, 6 h, 89%; (b) (i) H_2, 10% Pd/C, EtOAc, 4 h; (ii) anhyd K_2CO_3, dry acetone, 8 h (70%, based on two steps); (c) MeMgI, dry ether, reflux, 4 h, 91%; (d) TBAF, dry THF, 0 °C, 5 h, 87%.

The successful utilization of β-hydroxy-α-tosyloxy esters in the synthesis of novel 2,3-dihydrobenzofurans and 1-benzopyran derivative inspired us to initiate further application of this strategy for the synthesis of another structurally related 1-benzopyran and 1-benzoxepin derivatives by using a β-hydroxy-α-tosyloxy ester **36** homologated by one more carbon atom. The synthesis of **36** was achieved from aldehyde **20** by following the same reaction sequence as that described for **23** (Scheme 7).

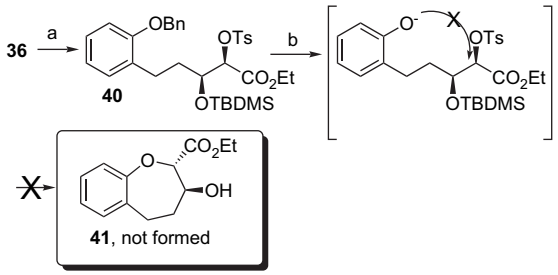


Scheme 7. Reagents and conditions: (a) methyltriphenylphosphonium iodide, *t*-BuOK, dry THF, 0 °C–rt, 2 h, 88%; (b) (i) 9-BBN, dry THF, 0 °C–rt, overnight; (ii) $NaOH/H_2O_2$, reflux, 2 h, 96%; (c) PCC, dry DCM, 2 h, 0 °C–rt, 72%; (d) $Ph_3P{=}CHCO_2Et$, dry DCM, rt, overnight, 77%; (e) AD-mix-α, *t*-BuOH/H_2O (1:1), 0 °C, 40 h, 87%; (f) TsCl, dry Et_3N, dry DCM, 0 °C, 72 h, 80%.

With the availability of **36**, attention was first turned to its elaboration into 1-benzopyran derivative (Scheme 8). Thus, β-hydroxy-α-tosyloxy ester **36** was converted into 1-benzopyran derivative **39** using a similar reaction sequence as that described for the synthesis of **26**.



Scheme 8. Reagents and conditions: (a) anhyd K_2CO_3, ethanol, 8 h, 78%; (b) (i) H_2, 10% Pd/C, ethyl acetate, 2 h; (ii) anhyd K_2CO_3, dry acetone, 6 h, (68%, for two steps); (c) MeMgI, dry ether, reflux, 4 h, 83%.



Scheme 9. Reagents and conditions: (a) TBDMS-OTf, 2,6-lutidine, 0 °C—rt, 8 h, 85%; (b) (i) H_2, 10% Pd/C, ethyl acetate; (ii) anhyd K_2CO_3, dry acetone, reflux, 15 h.

In an attempt to utilize β-hydroxy-α-tosyloxy ester **36** for the synthesis of 1-benzoxepin derivative, **36** was converted into **40**, which was first debenzylated and subsequently treated with anhydrous K_2CO_3 (as described for the synthesis of **15a**,**15b** and **28**). To our dismay, the reaction did not proceed at all to give **41** and the starting phenolic derivative remained unchanged. Varying the base, solvent, reaction time, and temperature did not give any fruitful result. This is perhaps for the easy formation of five- and six-membered rings over seven-membered ones (Scheme 9).

3. Conclusion

In summary, an efficient enantioselective synthesis of 'natural product-like' benzo-annulated oxa-heterocycles 2,3-dihydrobenzofuran and 1-benzopyran is described using β-hydroxy-α-tosyloxy esters as chiral building blocks, which are easily accessible through regioselective α-tosylation of Sharpless asymmetric dihydroxylation-derived *syn*-2,3-dihydroxy esters. However, the methodology was not feasible to synthesize 1-benzoxepine derivatives. The ease of the reaction sequence, as well as the commercial availability of large array of starting 2-hydroxyaromatic aldehydes, makes this process a practical method for the preparation of 'natural product-like' 2,3-dihydrobenzofuran and 1-benzopyran derivatives. In addition, the scope of the reaction sequence is much broader, and the synthesis of various substituted aromatic and heteroaromatic nuclei can be envisioned from the starting hydroxy aldehydes.

4. Experimental

4.1. General methods

All dry reactions were carried out under argon or nitrogen in oven-dried glassware using standard gas-light syringes, cannulas, and septa. All reagents and solvents were dried prior to use according to the standard methods. Commercial reagents were used without further purification unless otherwise stated. Reactions were monitored on silica gel TLC plates (coated with TLC grade silica gel, obtained from Merck). Detecting agents used (for TLC) were iodine vapors and/or spraying with an aqueous solution of vanillin in 10% sulfuric acid followed by heating at 150 °C. Column chromatography was performed over silica gel (60–120 mesh) procured from Qualigens (India) using freshly distilled solvents. Mass spectra were recorded as electron spray ionization (ESI-MS) or fast atom bombardment spectra (FABMS) on a JEOL SX 102 spectrometer using argon/xenon as the FAB gas. Elemental analyses were done on Varian EL-III CHN analyzer. Melting points were determined on COMPLAB melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer FT-IR RXI spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on Brucker DPX-200 (operating at 200 MHz for ^{1}H and 50 MHz for ^{13}C) or DPX-300 (operating at 300 MHz for ^{1}H and 75 MHz for ^{13}C) spectrometer using $CDCl_3$ or acetone-d_6 as solvent. Tetramethylsilane (0.00 ppm) served as an internal standard in ^{1}H NMR and $CDCl_3$ (77.0 ppm) in ^{13}C NMR. All spectra were recorded at 25 °C. Coupling constants (*J* values) are given in hertz (Hz). Chemical shifts are expressed in parts per million. The enantiomeric excess was determined by LichroCART Chiradex column (250×4 mm, 5 μm) using water and methanol as eluent at 25 °C. Optical rotations were measured at the sodium D-line at ambient temperature, with a Perkin Elmer 141 polarimeter.

4.2. 2-Benzyloxy-benzaldehyde (*10a*)

To a solution of commercially available 2-hydroxybenzaldehyde (10 mL, 95.64 mmol) in dry acetone (200 mL) was added anhydrous K_2CO_3 (20.0 g, 144.70 mmol) and benzyl bromide (13.0 mL, 109.52 mmol) and refluxed for 4 h. The mixture was then filtered through Celite and the filter cake was well washed with acetone (200 mL). The filtrate was concentrated and the resulting residue was redissolved in ethyl acetate (300 mL), washed with water (2×100 mL) and brine (100 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated in vacuo. Purification of the crude product by silica gel column chromatography (4% ethyl acetate in hexane) afforded **10a** (17.25 g, 85%) as a colorless oil. R_f: 0.52 (20% ethyl acetate in hexane). IR (neat): 2874, 1680, 1597, 1237, 991, 755 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 10.55 (s, 1H), 7.85 (dd, 1H, J_1=2.0, J_2=7.9), 7.52–7.36 (m, 6H), 7.06–7.02 (m, 2H), 5.17 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.5, 160.9, 135.9, 135.8, 128.6, 128.2, 128.1, 127.1, 124.9, 120.8, 112.9, 70.2. MS (ESI): *m/z* 212 $[M]^+$, 91 $[C_6H_5CH_2]^+$. Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.37; H, 5.88. The above spectroscopic data are in full agreement with the literature data.[18]

4.3. 2-Benzyloxy-naphthalene-1-carbaldehyde (*10b*)

Using commercially available 2-hydroxy-1-naphthaldehyde (2.0 g, 11.61 mmol), the title compound was prepared in the same manner as that described for **10a**. Purification of the crude product by silica gel column chromatography (4% ethyl acetate in hexane) afforded **10b** (2.52 g, 83%) as a light-yellow solid. Mp: 118–119 °C. R_f: 0.49 (20% ethyl acetate in hexane). IR (KBr): 2886, 1660, 1589, 1510, 1347, 1269,

1220, 1147, 1055, 807, 750 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 10.96 (s, 1H), 9.28 (d, 1H, J=8.6), 8.01 (d, 1H, J=9.1), 7.75 (d, 1H, J=8.0), 7.65–7.57 (m, 1H), 7.43–7.28 (m, 7H), 5.31 (s, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 192.5, 163.6, 137.9, 136.4, 131.9, 130.3, 129.2, 129.1, 128.8, 128.6, 127.8, 125.4, 125.3, 117.6, 114.4, 71.9. MS (ESI): *m/z* 263 $[M+1]^+$, 91 $[C_6H_5CH_2]^+$. Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.51; H, 5.49. The above spectroscopic data are in full agreement with the literature data.[19]

4.4. (2E)-3-(2-Benzyloxy-phenyl)-acrylic acid ethyl ester (*11a*)

To a solution of **10a** (1.50 g, 7.06 mmol) in dichloromethane (20 mL) was added (carbethoxymethylene)triphenylphosphorane (3.0 g, 8.60 mmol) at room temperature. The reaction mixture was stirred at room temperature for 2 h. Solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (4% ethyl acetate in hexane) to afford **11a** (1.55 g, 78%) as a colorless gum. R_f: 0.58 (20% ethyl acetate in hexane). IR (KBr): 2937, 1715, 1502, 1277, 1179, 1066, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, 1H, J=16.1), 7.54 (dd, 1H, J_1=1.3, J_2=7.6), 7.44–7.25 (m, 6H), 6.99–6.93 (m, 1H), 6.53 (d, 1H, J=16.1), 5.17 (s, 2H), 4.24 (q, 2H, J=7.1), 1.32 (t, 3H, J=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 157.3, 139.8, 136.6, 131.3, 128.6, 128.6, 127.9, 127.1, 123.9, 121.0, 118.8, 112.8, 70.3, 60.2, 14.3. MS (FAB): *m/z* 283 $[M+1]^+$, 237 $[M-OEt]^+$. Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.46; H, 6.34.

4.5. (2E)-3-(2-Benzyloxy-naphthalen-1-yl)-acrylic acid ethyl ester (*11b*)

Using 1.5 g (5.71 mmol) of **10b**, the title compound was prepared in the same manner as that described for **11a**. Purification of the crude product by silica gel column chromatography (4% ethyl acetate in hexane) afforded **11b** (1.51 g, 80%) as a colorless semi-solid. R_f: 0.50 (20% ethyl acetate in hexane). IR (KBr): 2927, 2363, 1707, 1592, 1267, 1165, 1044, 745 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ ^1H NMR (200 MHz, $CDCl_3$): δ 8.38 (d, 1H, J=16.1), 8.19 (d, 1H, J=8.5), 7.79–7.75 (m, 2H), 7.55–7.24 (m, 8H), 6.78 (d, 1H, J=16.1), 5.29 (s, 2H), 4.30 (q, 2H, J=7.1), 1.35 (t, 3H, J=7.1). ^{13}C NMR (50 MHz, $CDCl_3$): δ 168.2, 155.9, 138.1, 137.1, 131.7, 130.0, 129.6, 129.0, 128.4, 127.8, 127.5, 127.0, 124.5, 124.2, 123.9, 118.1, 114.9, 71.6, 60.8, 14.8. MS (ESI): *m/z* 333 $[M]^+$, 287 $[M-OEt]^+$. Anal. Calcd for $C_{22}H_{20}O_3$: C, 79.50; H, 6.06. Found: C, 79.59; H, 6.18.

4.6. (2R,3S)-3-(2-Benzyloxy-phenyl)-2,3-dihydroxy-propionic acid ethyl ester (*12a*)

To a stirred solution of *tert*-butyl alcohol (18 mL) and water (18 mL) were added AD-mix-α (5.0 g) and methanesulfonamide (0.34 g, 3.54 mmol) at room temperature. The mixture was vigorously stirred at room temperature until both phases were clear and then cooled to 0 °C. A solution of cinnamate ester **11a** (1.0 g, 3.54 mmol) in *tert*-butyl alcohol (5 mL) was added 0 °C. The reaction mixture was stirred at the same temperature for 28 h. The reaction was quenched at 0 °C by the addition of sodium sulfite (5.1 g), warmed to room temperature, and further stirred for 1 h. The reaction mixture was then extracted with ethyl acetate (3×50 mL). The combined organic layer was washed with aqueous 2 N KOH solution (50 mL), water (50 mL), and brine (50 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and then concentrated in vacuo. Purification of the crude product by silica gel column chromatography (25% ethyl acetate in hexane) afforded **12a** (1.03 g, 92%) as a colorless solid. Mp: 96–97 °C. R_f: 0.35 (40% ethyl acetate in hexane). $[\alpha]_D^{25}$ +8.4 (*c* 0.9, $CHCl_3$). The enantiomeric excess was estimated to be >99% by chiral HPLC analysis (instrument: HP1100, column: LichroCART Chiradex column 250×4 mm, 5 μm), flow rate: 0.5 mL/min, detection: UV 254 nm (eluent: methanol/H_2O). IR (KBr): 3537, 3512, 2982, 1722, 1601, 1496, 1456, 1386, 1290, 1240, 1111, 1049, 760, 736 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.45–7.24 (m, 7H), 7.03–6.93 (m, 2H), 5.42 (s, 1H), 5.10 (d, 1H, J=11.8), 5.09 (d, 1H, J=11.8), 4.50 (s, 1H), 4.27–4.17 (m, 2H), 3.13 (br s, 1H), 3.01 (br s, 1H), 1.22 (t, 3H, J=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.0, 155.1, 136.7, 128.8, 128.5, 127.9, 127.2, 127.0, 121.0, 111.5, 73.2, 70.3, 70.0, 61.9, 14.0. MS (ESI): *m/z* 339 $[M+Na]^+$, 334 $[M+NH_4]^+$, 299 $[M-OH]^+$, 91 $[C_6H_5CH_2]^+$. Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.29; H, 6.51.

4.7. 3-(2-Benzyloxy-naphthalen-1-yl)-2,3-dihydroxy-propionic acid ethyl ester (*12b*)

Starting from 1.25 g (3.76 mmol) of **11b**, the title compound was prepared in the same manner as that described for **12a**. Purification of the crude product by silica gel column chromatography (25% ethyl acetate in hexane) afforded **12b** (1.28 g, 93%) as a colorless gum. R_f: 0.37 (40% ethyl acetate in hexane). $[\alpha]_D^{25}$ −4.4 (*c* 1.13, $CHCl_3$). The enantiomeric excess was estimated to be >99% by chiral HPLC analysis as that described for **12a**. IR (KBr): 3509, 1720, 1250, 1125, 1048, 757, 742 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.04 (d, 1H, J=8.6), 7.78 (d, 2H, J=8.8), 7.52–7.29 (m, 8H), 5.82 (d, 1H, J=4.3), 5.25 (s, 2H), 4.88 (br s, 1H), 4.56 (d, 1H, J=4.7), 4.13–3.98 (m, 2H), 3.26 (br s, 1H), 1.01 (t, 3H, J=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.6, 155.0, 136.1, 131.7, 130.1, 129.5, 128.8, 128.7, 128.4, 127.5, 127.1, 123.9, 122.5, 119.8, 114.9, 74.4, 72.3, 72.1, 61.7, 13.7. MS (ESI): *m/z* 389 $[M+Na]^+$, 384 $[M+NH_4]^+$, 349 $[M-OH]^+$, 91 $[C_6H_5CH_2]^+$. Anal. Calcd for $C_{22}H_{22}O_5$: C, 72.12; H, 6.05. Found: C, 72.19; H, 6.18.

4.8. (2R,3S)-3-(2-Benzyloxy-phenyl)-3-hydroxy-2-(toluene-4-sulfonyloxy)-propionic acid ethyl ester (*13a*)

To a solution of diol **12a** (1.0 g, 3.16 mmol) in dry CH_2Cl_2 (20 mL) at 0 °C was added dry triethyl amine (0.75 mL,

5.37 mmol) followed by tosyl chloride (0.62 g, 3.25 mmol) and kept in the refrigerator for 3 days. The reaction mixture was diluted with H_2O (50 mL), and extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were washed with brine (50 mL) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and purification of the crude product by silica gel column chromatography (18% ethyl acetate in hexane) afforded **13a** (1.30 g, 87%) as a white solid. Mp: 105–106 °C. R_f: 0.41 (40% ethyl acetate in hexane). $[\alpha]_D^{25}$ +62.8 (*c* 1.5, $CHCl_3$). IR (KBr): 3436, 2989, 2364, 1749, 1618, 1509, 1445, 1284, 1204, 1039, 826, 730 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.18 (m, 9H), 7.08 (d, 2H, *J*=8.2), 6.91 (d, 1H, *J*=7.0), 6.77 (d, 1H, *J*=8.2), 5.39 (s, 1H), 5.23 (d, 1H, *J*=3.6), 5.00 (d, 1H, *J*=13.0), 4.99 (d, 1H, *J*=13.0), 4.13 (q, 2H, *J*=7.1), 2.82 (br s, 1H), 2.38 (s, 3H), 1.15 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 155.0, 144.4, 136.4, 132.7, 129.4, 129.1, 128.6, 128.0, 127.7, 127.1, 126.0, 121.1, 111.4, 79.3, 70.6, 70.0, 61.8, 21.5, 13.8. MS (ESI): *m/z* 493 $[M+Na]^+$, 488 $[M+NH_4]^+$, 453 $[M-OH]^+$. Anal. Calcd for $C_{25}H_{26}O_7S$: C, 63.81; H, 5.57. Found: C, 63.98; 5.50.

*4.9. (2R,3S)-3-(2-Benzyloxy-naphthalen-1-yl)-3-hydroxy-2-(toluene-4-sulfonyloxy)-propionic acid ethyl ester (**13b**)*

Starting from 1.0 g (2.72 mmol) of **12b**, the title compound was prepared in the same manner as that described for **13a**. Purification of the crude product by silica gel column chromatography (18% ethyl acetate in hexane) afforded **13b** (1.34 g, 94%) as a colorless solid. Mp: 109–110 °C. R_f: 0.44 (40% ethyl acetate in hexane). $[\alpha]_D^{25}$ +54.7 (*c* 2.3, $CHCl_3$). IR (KBr): 3502, 2923, 2363, 1767, 1597, 1367, 1169, 1040, 889, 856, 726 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, 1H, *J*=8.5), 7.70–7.66 (m, 2H), 7.50 (d, 1H, *J*=6.9), 7.44–7.27 (m, 7H), 7.18 (d, 1H, *J*=9.1), 6.87 (d, 1H, *J*=8.1), 5.91 (d, 1H, *J*=5.1), 5.22 (d, 1H, *J*=5.1), 5.18 (s, 2H), 4.34 (br s, 1H), 3.94 (q, 2H, *J*=7.1), 2.22 (s, 3H), 0.94 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 155.1, 144.3, 135.8, 132.1, 131.0, 130.5, 129.1, 128.7, 128.5, 128.3, 127.6, 127.3, 127.2, 123.8, 121.8, 117.2, 80.5, 71.6, 70.4, 61.6, 21.4, 13.5. MS (ESI): *m/z* 543 $[M+Na]^+$, 538 $[M+NH_4]^+$, 503 $[M-OH]^+$. Anal. Calcd for $C_{29}H_{28}O_7S$: C, 66.91; H, 5.42. Found: C, 67.11; H, 5.55.

*4.10. (2R,3S)-3-(2-Benzyloxy-phenyl)-3-(tert-butyl-dimethyl-silanyloxy)-2-(toluene-4-sulfonyloxy)-propionic acid ethyl ester (**14a**)*

To a stirring solution of **13a** (1.0 g, 2.12 mmol) in dry CH_2Cl_2 (30 mL) at 0 °C were added 2,6-lutidine (0.48 mL, 4.14 mmol) and TBDMS-OTf (0.73 mL, 3.18 mmol), successively. The reaction mixture was then stirred at room temperature for 6 h. The reaction was quenched with a saturated aqueous NH_4Cl solution (20 mL) and extracted with CH_2Cl_2 (3×25 mL). The combined organic layers were washed with water (50 mL), brine (50 mL), and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and purification of the crude product by silica gel column chromatography (6% ethyl acetate in hexane) afforded **14a** (1.05 g, 85%) as a colorless solid. Mp: 75–76 °C. R_f: 0.52 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ +45.4 (*c* 2.34, $CHCl_3$). IR (KBr): 2930, 2362, 1764, 1597, 1370, 1220, 1181, 1039, 901, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.41–7.31 (m, 8H), 7.18–7.12 (m, 1H), 7.04 (d, 2H, *J*=8.1), 6.89–6.84 (m, 1H), 6.69 (d, 1H, *J*=7.9), 5.62 (d, 1H, *J*=2.8), 5.04 (d, 1H, *J*=3.1), 5.01 (d, 1H, J_1=12.0), 4.98 (d, 1H, J_1=12.0), 4.19–4.05 (m, 2H), 2.16 (s, 3H), 1.17 (t, 3H, *J*=7.1), 0.84 (s, 9H), −0.04 (s, 3H), −0.19 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 154.2, 143.9, 136.7, 132.9, 129.2, 129.0, 128.7, 128.5, 127.8, 127.6, 127.0, 126.7, 120.6, 110.9, 79.8, 69.6, 69.1, 61.5, 25.5, 21.5, 18.0, 13.7, −4.9, −5.6. MS (ESI): *m/z* 608 $[M+Na]^+$, 602 $[M+NH_4]^+$. Anal. Calcd for $C_{31}H_{40}O_7SSi$: C, 63.67; H, 6.89. Found: C, 63.56; H, 7.07.

*4.11. (2R,3S)-3-(2-Benzyloxy-naphthalen-1-yl)-3-(tert-butyl-dimethyl-silanyloxy)-2-(toluene-4-sulfonyloxy)-propionic acid ethyl ester (**14b**)*

Starting from 1.0 g (1.92 mmol) of **13b**, the title compound was prepared in the same manner as that described for **14a**. Purification of the crude product by silica gel column chromatography (6% ethyl acetate in hexane) afforded **14b** (1.07 g, 88%) as a colorless semi-solid. R_f: 0.54 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ +60.0 (*c* 1.73, $CHCl_3$). IR (KBr): 2932, 2360, 1741, 1460, 1375, 1248, 1180, 1028, 885, 840, 737 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, 1H, *J*=8.5), 7.61 (d, 2H, *J*=8.6), 7.48–7.22 (m, 9H), 7.08 (d, 1H, *J*=9.1), 6.87 (d, 1H, *J*=8.1), 6.27 (d, 1H, *J*=5.2), 5.22 (d, 1H, *J*=5.2), 5.13 (s, 2H), 3.96 (q, 2H, *J*=7.1), 2.28 (s, 3H), 0.98 (t, 3H, *J*=7.1), 0.75 (s, 9H), −0.03 (s, 3H), −0.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.8, 152.6, 143.9, 136.8, 133.1, 132.5, 130.3, 129.5, 128.9, 128.6, 127.9, 127.7, 127.3, 127.2, 126.9, 125.8, 123.5, 119.4, 112.9, 81.3, 70.9, 69.3, 61.4, 25.5, 21.4, 17.9, 13.6, −5.4, −5.6. MS (ESI): *m/z* 658 $[M+Na]^+$, 652 $[M+NH_4]^+$. Anal. Calcd for $C_{35}H_{42}O_7SSi$: C, 66.22; H, 6.67. Found: C, 66.10; H, 6.43.

*4.12. (2S,3S)-3-(tert-Butyl-dimethyl-silanyloxy)-2,3-dihydro-benzofuran-2-carboxylic acid ethyl ester (**15a**)*

To a stirred solution of **14a** (1.0 g, 1.71 mmol) in ethyl acetate (20 mL) was added 10% Pd/C (100 mg). After stirring for 4 h at room temperature under pressure of a hydrogen balloon, the reaction mixture was filtered through a pad of Celite® and the filtrate was concentrated under reduced pressure to get the corresponding debenzylated product (0.733 g) as a colorless semi-solid, which was used for the next step without further purification.

To a stirring solution of the above debenzylated product in dry acetone (20 mL), was added anhydrous K_2CO_3 (0.35 g, 2.53 mmol) and the mixture was stirred for 6 h at room temperature. After removing acetone from the reaction mixture under reduced pressure, water (10 mL) was added to the

resulting residue and extracted with ethyl acetate (3×20 mL) and washed with brine (1×20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (4% ethyl acetate in hexane) afforded **15a** (0.384 g, 69%, for two steps) as a colorless semi-solid. R_f: 0.42 (10% ethyl acetate in hexane). $[\alpha]_D^{25}$ +62.6 (*c* 1.31, $CHCl_3$). IR (KBr): 2932, 2361, 1752, 1471, 1217, 1082, 842, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.28–7.24 (m, 2H), 6.97–6.93 (m, 2H), 5.51 (d, 1H, *J*=3.1), 4.92 (d, 1H, *J*=3.1), 4.29–4.22 (m, 2H), 1.31 (t, 3H, *J*=7.1), 0.92 (s, 9H), 0.19 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 159.5, 130.4, 127.1, 125.3, 121.5, 110.7, 87.5, 76.8, 61.7, 25.7, 18.0, 14.1, −4.4, −4.5. MS (ESI): *m/z* 346 $[M+Na]^+$. Anal. Calcd for $C_{17}H_{26}O_4Si$: C, 63.32; H, 8.13. Found: C, 63.39; H, 8.25.

*4.13. (1S,2S)-1-(tert-Butyl-dimethyl-silanyloxy)-1,2-dihydro-naphtho[2,1-b]furan-2-carboxylic acid ethyl ester (**15b**)*

Starting from 0.85 g (1.34 mmol) of **14b**, the title compound was prepared in two steps in the same manner as that described for **15a**. Purification of the crude product by silica gel column chromatography (4% ethyl acetate in hexane) afforded **15b** (0.362 g, 72%) as a colorless solid. Mp: 92–93 °C. R_f: 0.44 (10% ethyl acetate in hexane). $[\alpha]_D^{25}$ +37.7 (*c* 1.43, $CHCl_3$). IR (KBr): 2932, 2855, 2362, 1750, 1460, 1366, 1259, 1195, 1072, 885, 840, 743 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.87–7.83 (m, 3H), 7.57–7.52 (m, 1H), 7.41–7.36 (m, 1H), 7.31 (d, 1H, *J*=8.8), 6.04 (d, 1H, *J*=2.1), 5.17 (d, 1H, *J*=2.1), 4.36–4.25 (m, 2H), 1.35 (t, 3H, *J*=7.1), 0.97 (s, 9H), 0.36 (s, 3H), 0.25 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 158.1, 132.1, 130.7, 130.0, 129.0, 127.2, 123.6, 122.6, 118.6, 112.7, 88.2, 77.6, 61.9, 25.8, 18.2, 14.2, −3.9, −4.7. MS (ESI): *m/z* 395 $[M+Na]^+$. Anal. Calcd for $C_{21}H_{28}O_4Si$: C, 67.71; H, 7.58. Found: C, 67.56; H, 7.66.

*4.14. 2-[(2S,3S)-3-(tert-Butyl-dimethyl-silanyloxy)-2,3-dihydro-benzofuran-2-yl]-propan-2-ol (**16a**)*

To a freshly prepared, magnetically stirred, ice-cold suspension of methylmagnesium iodide [prepared from methyl iodide (0.56 mL, 7.0 mmol) and magnesium (0.17 g, 7.0 mmol) in 10 mL of dry ether] was added a solution of ester **15a** (0.154 g, 0.46 mmol) in dry THF (10 mL). The reaction mixture was refluxed for 4 h, cooled, and quenched with aqueous NH_4Cl solution (10 mL). The mixture was extracted with ethyl acetate (2×25 mL), washed with water (25 mL) and brine (25 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (8% ethyl acetate in hexane) afforded **16a** (0.112 g, 77%) as a colorless semi-solid. R_f: 0.54 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ +93.1 (*c* 2.04, $CHCl_3$). IR (KBr): 3462, 3194, 2932, 2362, 1598, 1477, 1234, 1178, 1047, 750 cm^{-1}. ^1H NMR (300 MHz, acetone-d_6): δ 7.33 (d, 1H, *J*=7.3), 7.20 (t, 1H, *J*=7.7), 6.88 (t, 1H, *J*=7.3), 6.78 (d, 1H, *J*=8.0), 5.53 (d, 1H, *J*=2.4), 4.26 (d, 1H, *J*=2.8), 1.29 (s, 3H), 1.10 (s, 3H), 0.88 (s, 9H), 0.20 (s, 6H). ^{13}C NMR (75 MHz, acetone-d_6): δ 161.3, 130.4, 130.1, 126.2, 120.8, 110.3, 97.7, 74.6, 71.1, 27.1, 26.0, 24.6, 18.3, −3.8, −4.2. MS (ESI): *m/z* 332 $[M+Na]^+$. Anal. Calcd for $C_{17}H_{28}O_3Si$: C, 66.19; H, 9.15. Found: C, 66.26; H, 9.31.

*4.15. (2S,3S)-2-(1-Hydroxy-1-methyl-ethyl)-2,3-dihydro-benzofuran-3-ol (**17a**)*

To an ice-cooled solution of **16a** (80.5 mg, 0.26 mmol) in dry THF (5 mL) was added tetra-*n*-butylammonium fluoride (TBAF) (1 M in THF, 0.60 mL). After being stirred at 0 °C for 5 h, the reaction mixture was diluted with ethyl acetate (25 mL), washed with water (25 mL) and brine (25 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (30% ethyl acetate in hexane) afforded **17a** (46 mg, 91%) as a colorless solid. Mp: 95–96 °C. R_f: 0.55 (60% ethyl acetate in hexane). $[\alpha]_D^{25}$ +93.3 (*c* 0.9, $CHCl_3$). IR (KBr): 3462, 3194, 2932, 2362, 1598, 1477, 1234, 1178, 1047, 750 cm^{-1}. ^1H NMR (300 MHz, acetone-d_6): δ 7.33 (d, 1H, *J*=7.4), 7.19–7.13 (m, 1H), 6.87–6.82 (m, 1H), 6.74 (d, 1H, *J*=8.0), 5.39 (d, 1H, *J*=4.5), 4.74 (br s, 1H), 4.24 (d, 1H, *J*=4.6), 3.74 (br s, 1H), 1.25 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (75 MHz, acetone-d_6): δ 162.1, 132.1, 131.3, 127.3, 122.1, 111.4, 98.6, 74.4, 72.2, 26.9, 26.8. MS (ESI): *m/z* 217 $[M+Na]^+$. Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.16; H, 7.50.

*4.16. (2S,3S)-2-(1-Hydroxy-1-methyl-ethyl)-1,2-dihydro-naphtho[2,1-b]furan-1-ol (**17b**)*

Starting from 0.205 mg (0.55 mmol) of **15b**, the title compound was prepared in two steps. First step is the Grignard reaction as that described for **16a** and the second step deprotection of TBDMS group as that described for **16a**. The intermediate *tertiary* alcohol resulting from the Grignard reaction was not much stable and hence used for the next step (deprotection of TBDMS group) without purification by silica gel column chromatography. Purification of the crude product of the final step by silica gel column chromatography (30% ethyl acetate in hexane) afforded **17b** (113 mg, 74%, for two steps) as a colorless semi-solid. R_f: 0.58 (60% ethyl acetate in hexane). $[\alpha]_D^{25}$ +46.7 (*c* 1.97, $CHCl_3$). IR (KBr): 3355, 2925, 2360, 1595, 1488, 1457, 1257, 1050, 757 cm^{-1} ^1H NMR (300 MHz, acetone-d_6): δ 8.03 (d, 1H, *J*=8.3), 7.85–7.78 (m, 2H), 7.50–7.45 (m, 1H), 7.33–7.28 (m, 1H), 7.09 (d, 1H, *J*=8.0), 5.85 (d, 1H, *J*=3.6), 4.68 (br s, 1H), 4.43 (d, 1H, *J*=3.6), 3.71 (br s, 1H), 1.32 (s, 3H), 1.28 (s, 3H). ^{13}C NMR (75 MHz, acetone-d_6): δ 160.3, 133.3, 132.8, 131.4, 130.5, 128.6, 124.8, 124.7, 122.6, 114.2, 100.0, 74.6, 72.3, 27.1, 26.6. MS (ESI): *m/z* 267 $[M+Na]^+$. Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60. Found: C, 73.86; H, 6.73.

4.17. 2-Benzyloxystyrene (**18**)

To a suspension of methyltriphenylphosphonium iodide (17.15 g, 42.42 mmol) in dry THF (100 mL) under a nitrogen atmosphere at 0 °C was added *t*-BuOK (4.76 g, 42.42 mmol). The reaction mixture was stirred for 15 min at 0 °C and then warmed to room temperature while stirring was continued for 45 min. The solution was then recooled to 0 °C, and a solution of aldehyde **10a** (6.0 g, 28.27 mmol) in dry THF (50 mL) was added dropwise. The reaction mixture was then warmed to room temperature and stirred for an additional 2 h. The reaction was quenched with saturated aqueous NH_4Cl solution (50 mL) and extracted with Et_2O (3×100 mL). The combined organic extracts were washed with brine (200 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified by silica gel column chromatography (2% ethyl acetate in hexane) to give alkene **18** (4.75 g, 80%) as colorless oil. R_f: 0.46 (10% ethyl acetate in hexane). IR (neat): 3065, 3030, 2360, 1597, 1489, 1452, 1237, 1014, 751 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.51–7.30 (m, 6H), 7.22–7.08 (m, 2H), 6.96–6.90 (m, 2H), 5.75 (dd, 1H, J_1=17.7, J_2=1.4), 5.25 (dd, 1H, J_1=11.2, J_2=1.4), 5.08 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9, 137.1, 131.6, 128.8, 128.5, 127.8, 127.3, 126.5, 121.0, 114.4, 112.5, 70.3. MS (ESI): *m/z* 211 $[M+1]^+$. Anal. Calcd for $C_{15}H_{14}O$: C, 85.68; H, 6.71. Found: C, 85.56; H, 6.79.

4.18. 2-(2-Benzyloxy-phenyl)-ethanol (**19**)

To a stirring solution of **18** (4.0 g, 19.02 mmol) in anhydrous THF (30 mL) was added a 0.5 M THF solution of 9-BBN (60 mL) dropwise under a nitrogen atmosphere at 0 °C and the mixture was stirred at room temperature overnight. H_2O (5 mL) was added followed by 3 N NaOH solution (40 mL) and 30% aqueous hydrogen peroxide solution (30 mL). The reaction mixture was stirred for 2 h at 50 °C. The mixture was extracted with ethyl acetate (2×50 mL), washed with water (150 mL) and brine (150 mL). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification of the crude product by silica gel column chromatography (8% ethyl acetate in hexane) afforded alcohol **19** (4.15 g, 96%) as a colorless gum. R_f: 0.32 (20% ethyl acetate in hexane). IR (neat): 3429, 1601, 1462, 1247, 1046, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.54–7.41 (m, 5H), 7.32–7.27 (m, 2H), 7.05–7.00 (m, 2H), 5.14 (s, 2H), 3.92 (t, 3H, J=6.6), 3.05 (t, 3H, J=6.6), 2.48 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5, 136.9, 130.8, 128.4, 127.7, 127.5, 127.2, 127.0, 120.7, 111.6, 69.7, 62.3, 33.9. MS (FAB): *m/z* 228 $[M]^+$, 211 $[M-OH]^+$. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 79.08; H, 7.14.

4.19. (2-Benzyloxy-phenyl)-acetaldehyde (**20**)

To a stirring solution of **19** (3.0 g, 13.14 mmol) in anhydrous dichloromethane (50 mL) was added 4 Å molecular sieve (3.85 g) and PCC (3.85 g, 17.86 mmol) at 0 °C and the mixture was stirred at room temperature for 2 h. After evaporating dichloromethane, the reaction mixture was diluted with ether (50 mL) and filtered through a small pad of silica gel. Concentration of the filtrate and purification of the residue by silica gel column chromatography (4% ethyl acetate in hexane) afforded **20** (2.25 g, 76%) as a colorless gum. R_f: 0.55 (20% ethyl acetate in hexane). IR (neat): 3035, 2950, 2360, 1720, 1597, 1500, 1230, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 9.81 (t, 1H, J=1.9), 7.50–7.35 (m, 6H), 7.25–7.27 (m, 1H), 7.09–7.05 (m, 2H), 5.14 (s, 2H), 3.79 (d, 2H, J=1.9). ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.5, 156.4, 136.5, 131.1, 128.6, 128.3, 127.6, 126.9, 121.3, 120.8, 111.5, 69.6, 45.2. MS (FAB): *m/z* 226 $[M]^{+\cdot}$. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.73; H, 6.33.

4.20. (2E)-4-(2-Benzyloxy-phenyl)-but-2-enoic acid ethyl ester (**21**)

Starting from 2.0 g (8.83 mmol) of **20**, the title compound was prepared in the same manner as that described for **11a**. Purification of the crude product by silica gel column chromatography (6% ethyl acetate in hexane) afforded **21** (1.96 g, 75%) as a colorless gum. R_f: 0.58 (20% ethyl acetate in hexane). IR (neat): 2368, 1720, 1502, 1253, 1045, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.40–7.26 (m, 6H), 7.20–7.07 (m, 2H), 6.92–6.87 (m, 2H), 5.77 (d, 1H, J=15.5), 5.03 (s, 2H), 4.14 (q, 2H, J=7.1), 3.55–3.53 (m, 2H), 1.24 (t, 3H, J=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.51, 156.32, 147.10, 136.98, 130.20, 128.42, 127.91, 127.75, 127.14, 126.54, 121.88, 120.83, 111.72, 69.86, 59.98, 32.97, 14.16. MS (ESI): *m/z* 319 $[M+Na]^+$. Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.09; H, 6.65.

4.21. (2R,3S)-4-(2-Benzyloxy-phenyl)-2,3-dihydroxy-butyric acid ethyl ester (**22**)

Starting from 1.85 g (6.24 mmol) of **21**, the title compound was prepared in the same manner as that described for **12a**. Purification of the crude product by silica gel column chromatography (25% ethyl acetate in hexane) afforded **22** (1.83 g, 89%) as a colorless semi-solid. R_f: 0.41 (40% ethyl acetate in hexane). The enantiomeric excess was estimated to be >99% by chiral HPLC analysis as that described for **12a**. $[\alpha]_D^{25}$ −15.3 (*c* 2.4, $CHCl_3$). IR (KBr): 3346, 2927, 2362, 1759, 1497, 1453, 1240, 122, 749 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.43–7.27 (m, 5H), 7.24–7.15 (m, 2H), 6.93–6.88 (m, 2H), 5.08 (s, 2H), 4.31–4.25 (m, 1H), 4.19 (q, 2H, J=7.1), 4.05 (d, 1H, J=1.65), 3.10–2.91 (m, 2H), 2.56 (br s, 2H), 1.22 (t, 3H, J=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.4, 156.6, 136.9, 131.4, 128.5, 127.9, 127.8, 127.1, 126.4, 121.0, 111.8, 72.6, 72.3, 70.0, 61.7, 35.1, 14.0. MS (ESI): *m/z* 353 $[M+Na]^+$, 348, 331, 313, 295. Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.17; H, 6.56.

*4.22. (2R,3S)-4-(2-Benzyloxy-phenyl)-3-hydroxy-2-(toluene-4-sulfonyloxy)-butyric acid ethyl ester (**23**)*

Starting from 1.5 g (4.54 mmol) of **22**, the title compound was prepared in the same manner as that described for **13a**. Purification of the crude product by silica gel column chromatography (18% ethyl acetate in hexane) afforded **23** (1.87 g, 85%) as a colorless semi-solid. R_f: 0.46 (40% ethyl acetate in hexane). $[\alpha]_D^{25}$ −10.1 (*c* 2.1, $CHCl_3$). IR (KBr): 3464, 3022, 2401, 1756, 1599, 1494, 1373, 1217, 1028, 762 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, 2H, *J*=8.3), 7.37–7.28 (m, 7H), 7.20–7.09 (m, 2H), 6.89–6.85 (m, 2H), 5.06 (s, 2H), 4.87 (d, 1H, *J*=2.7), 4.36–4.35 (m, 1H), 4.10–4.02 (m, 2H), 2.92–2.83 (m, 2H), 2.40 (s, 3H), 2.39 (br s, 1H), 1.12 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.18, 156.56, 145.09, 136.73, 133.15, 131.41, 129.68, 128.62, 128.29, 128.14, 127.90, 127.06, 125.46, 121.05, 111.77, 79.49, 71.56, 69.97, 61.88, 34.74, 21.63, 13.86. MS (ESI): *m/z* 507 $[M+Na]^+$, 502 $[M+NH_4]^+$, 485 $[M]^+$. Anal. Calcd for $C_{26}H_{28}O_7S$: C, 64.45; H, 5.82. Found: C, 64.61; H, 5.90.

*4.23. (2S,3S)-3-(2-Benzyloxybenzyl)-oxirane-2-carboxylic acid ethyl ester (**24**)*

A solution of tosylate 23 (0.5 g, 1.03 mmol) in dry methanol (25 mL) was treated with anhydrous K_2CO_3 (0.21 g, 1.52 mmol) and the resulting suspension stirred vigorously at room temperature for 8 h. After removing acetone from the reaction mixture under reduced pressure, water (20 mL) was added to the resulting residue and extracted with ethyl acetate (3×20 m) and washed with brine (1×30 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give light-yellow oil. Purification of the crude product by silica gel column chromatography (10% ethyl acetate in hexane) afforded **24** (0.24 g, 75%) as a colorless gum. R_f: 0.54 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ +38.4 (*c* 1.9, $CHCl_3$). IR (KBr): 3020, 2363, 1742, 1495, 1216, 758 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.43–7.29 (m, 5H), 7.23–7.12 (m, 2H), 6.92–6.87 (m, 2H), 5.09 (s, 2H), 4.29–4.17 (m, 2H), 3.55–3.50 (m, 2H), 3.22–3.15 (m, 1H), 3.01–2.93 (m, 1H), 1.27 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.3, 156.5, 136.9, 130.6, 128.5, 128.1, 127.8, 127.1, 125.3, 120.9, 111.6, 69.8, 61.4, 56.8, 52.9, 28.7, 14.1. MS (ESI): *m/z* 345 $[M+Na]^+$. Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 72.89; H, 6.31.

*4.24. (S)-[(2R)-2,3-Dihydro-benzofuran-2-yl]-hydroxy-acetic acid ethyl ester (**25**)*

Starting from 0.225 g (0.72 mmol) of **24**, the title compound was prepared in the same manner as that described for **15a**. Purification of the crude product by silica gel column chromatography (10% ethyl acetate in hexane) afforded **25** (0.13 g, 81%, for two steps) as a white solid. Mp: 80–81 °C. R_f: 0.35 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ −76.9 (*c* 1.13, $CHCl_3$). IR (KBr): 3437, 2929, 2364, 1728, 1483, 1233, 1136, 1014, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.15 (d, 1H, *J*=7.1), 7.08 (t, 1H, *J*=7.6), 6.85–6.80 (m, 1H), 6.75 (d, 1H, *J*=7.9), 5.11–5.05 (m, 1H), 4.33–4.25 (m, 3H), 3.42–3.24 (m, 2H), 2.96 (d, 1H, *J*=6.9), 1.30 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.0, 159.5, 127.9, 126.4, 124.7, 120.7, 109.1, 82.4, 72.4, 62.1, 31.3, 14.1. MS (ESI): *m/z* 245 $[M+Na]^+$, 241. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.76; H, 6.48.

*4.25. (1S)-1-[(2R)-2,3-Dihydro-benzofuran-2-yl]-2-methyl-propane-1,2-diol (**26**)*

Starting from 0.125 g (0.562 mmol) of **26**, the title compound was prepared in the same manner as that described for **16a**. Purification of the crude product by silica gel column chromatography (30% ethyl acetate in hexane) afforded **26** (0.103 g, 88%) as a white solid. Mp: 89–90 °C. R_f: 0.57 (60% ethyl acetate in hexane). $[\alpha]_D^{25}$ −55.9 (*c* 1.42, $CHCl_3$). IR (KBr): 3431, 2925, 2363, 1729, 1634, 1332, 1224, 1163, 755, 678 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.18 (d, 1H, *J*=7.2), 7.10 (t, 1H, *J*=7.6), 6.86 (dd, 1H, J_1=7.0, J_2=7.5), 6.76 (d, 1H, *J*=7.9), 5.04 (m, 1H), 3.45–3.37 (m, 2H), 3.25–3.16 (m, 1H), 2.66 (br s, 2H), 1.39 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.9, 127.8, 126.8, 124.9, 121.0, 109.2, 82.7, 77.2, 72.8, 32.6, 26.6. MS (ESI): *m/z* 231 $[M+Na]^+$, 226. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.42; H, 7.79.

*4.26. (2R,3S)-4-(2-Benzyloxy-phenyl)-3-(tert-butyl-dimethyl-silanyloxy)-2-(toluene-4-sulfonyloxy)-butyric acid ethyl ester (**27**)*

Starting from 0.75 g (1.54 mmol) of **23**, the title compound was prepared in the same manner as that described for **14a**. Purification of the crude product by silica gel column chromatography (8% ethyl acetate in hexane) afforded **27** (0.82 g, 89%) as a colorless semi-solid. R_f: 0.55 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ −7.2 (*c* 0.92, $CHCl_3$). IR (KBr): 2931, 2360, 1745, 1495, 1370, 1216, 1031, 758, 671 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, 2H, *J*=8.3), 7.45–7.27 (m, 7H), 7.19–7.09 (m, 2H), 6.88–6.82 (m, 2H), 5.07 (s, 2H), 4.74 (d, 1H, *J*=3.4), 4.51–4.48 (m, 1H), 4.02–3.95 (m, 2H), 3.02–2.96 (m, 1H), 2.83–2.77 (m, 1H), 2.41 (s, 3H), 1.12 (t, 3H, *J*=7.1), 0.74 (s, 9H), −0.21 (s, 3H), −0.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.5, 156.9, 144.6, 137.0, 133.9, 132.6, 129.5, 128.6, 128.0, 127.9, 127.5, 125.4, 120.7, 111.3, 79.4, 71.2, 69.9, 61.5, 35.2, 25.6, 21.6, 17.8, 13.8, −5.3. MS (ESI): *m/z* 621 $[M+Na]^+$, 617, 599. Anal. Calcd for $C_{32}H_{42}O_7SSi$: C, 64.18; H, 7.07. Found: C, 64.06; H, 7.20.

*4.27. (2S,3S)-3-(tert-Butyl-dimethyl-silanyloxy)-chroman-2-carboxylic acid ethyl ester (**28**)*

Starting from 0.5 g (0.83 mmol) of **27**, the title compound was prepared in the same manner as that described for **15a**. Purification of the crude product by silica gel column chromatography (4% ethyl acetate in hexane) afforded **28** (0.195 g,

70%; based on two steps) as a colorless viscous liquid. R_f: 0.48 (10% ethyl acetate in hexane). $[\alpha]_D^{25}$ +51.2 (*c* 2.5, $CHCl_3$). IR (neat): 2932, 1751, 1250, 1197, 1119, 838, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.16–7.11 (m, 1H), 7.05–7.03 (m, 1H), 6.93–6.88 (m, 2H), 4.43–4.38 (m, 2H), 4.34–4.21 (m, 2H), 3.03–2.84 (m, 2H), 1.33 (t, 3H, *J*=7.1), 0.91 (s, 9H), 0.15 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.6, 152.8, 129.6, 127.5, 121.1, 119.3, 116.3, 78.76, 65.62, 61.32, 33.73, 25.51, 17.79, 13.96, −4.50, −5.10. MS (ESI): *m/z* 360 $[M+Na]^+$, 337 $[M]^+$. Anal. Calcd for $C_{18}H_{28}O_4Si$: C, 64.25; H, 8.39. Found: C, 64.36; H, 8.43.

*4.28. 2-[(2S,3S)-3-(tert-Butyl-dimethyl-silanyloxy)-chroman-2-yl]-propan-2-ol (**29**)*

Starting from 0.15 g (0.44 mmol) of **28**, the title compound was prepared in the same manner as that described for **16a**. Purification of the crude product by silica gel column chromatography (5% ethyl acetate in hexane) afforded **29** (0.132 g, 91%) as a colorless semi-solid. R_f: 0.36 (10% ethyl acetate in hexane). $[\alpha]_D^{25}$ +94.4 (*c* 1.56, $CHCl_3$). IR (KBr): 3512, 2933, 2362, 1586, 1489, 1363, 1248, 1089, 1049, 840, 755 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.16–7.06 (m, 2H), 6.93–6.84 (m, 2H), 4.32–4.24 (m, 1H), 4.17 (s, 1H), 3.67 (d, 1H, *J*=9.0), 3.10–2.91 (m, 2H), 1.41 (s, 3H), 1.39 (s, 3H), 0.98 (s, 9H), 0.26 (s, 3H), 0.25 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.9, 129.4, 127.5, 120.78, 120.1, 116.2, 82.8, 72.2, 68.5, 36.4, 27.0, 25.7, 23.7, 17.7, −3.2, −4.8. MS (ESI): *m/z* 346 $[M+Na]^+$, 323 $[M]^+$. Anal. Calcd for $C_{18}H_{30}O_3Si$: C, 67.03; H, 9.38. Found: C, 67.13; H, 9.11.

*4.29. (2S,3S)-2-(1-Hydroxy-1-methyl-ethyl)-chroman-3-ol (**30**)*

Starting from 0.102 g (0.31 mmol) of **29**, the title compound was prepared in the same manner as that described for **17a**. Purification of the crude product by silica gel column chromatography (30% ethyl acetate in hexane) afforded **30** (56 mg, 87%) as a colorless solid. Mp: 115–116 °C. R_f: 0.65 (60% ethyl acetate in hexane). $[\alpha]_D^{25}$ +85.2 (*c* 0.95, $CHCl_3$). IR (KBr): 3343, 2925, 2361, 1587, 1486, 1457, 1242, 1043, 755 cm^{-1}. ^1H NMR (300 MHz, acetone-d_6): δ 7.07–7.04 (m, 2H), 6.86–6.75 (m, 2H), 5.10 (s, 1H), 4.62 (s, 1H), 4.16–4.08 (m, 1H), 3.57 (d, 1H, *J*=9.0), 3.06–2.99 (m, 1H), 2.83–2.75 (m, 1H), 1.38 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, acetone-d_6): δ 156.0, 131.4, 129.2, 122.9, 122.5, 117.8, 84.9, 74.6, 67.5, 36.8, 29.4, 25.0. MS (ESI): *m/z* 231 $[M+Na]^+$, 226 $[M+NH_4]^+$. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.29; H, 7.98.

*4.30. 2-Benzyloxy allylbenzene (**31**)*

Starting from 4.0 g (17.67 mmol) of **20**, the title compound was prepared in the same manner as that described for **18**. Purification of the crude product by silica gel column chromatography (2% ethyl acetate in hexane) afforded **31** (3.50 g, 88%) as a colorless oil. R_f: 0.46 (10% ethyl acetate in hexane). IR (neat): 3069, 2908, 2370, 1597, 1494, 1453, 1241, 1022, 749 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–7.28 (m, 5H), 7.20–7.14 (m, 2H), 6.93–6.89 (m, 2H), 6.08–5.95 (m, 1H), 5.08 (s, 2H), 5.05–5.02 (m, 2H), 3.45 (d, 2H, *J*=6.6). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.4, 137.4, 137.0, 129.9, 129.0, 128.5, 127.7, 127.3, 127.1, 120.8, 115.4, 111.7, 69.9, 34.4. MS (ESI): *m/z* 225 $[M+1]^+$, 91 $[C_6H_5CH_2]^+$. Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.76; H, 7.30.

*4.31. 3-(2-Benzyloxy-phenyl)-propan-1-ol (**32**)*

Starting from 3.0 g (13.37 mmol) of **31**, the title compound was prepared in the same manner as that described for **19**. Purification of the crude product by silica gel column chromatography (8% ethyl acetate in hexane) afforded **32** (3.12 g, 96%) as a colorless gum. R_f: 0.32 (20% ethyl acetate in hexane). IR (neat): 3421, 1594, 1452, 1351, 1239, 1040, 750 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.41–7.25 (m, 5H), 7.16–7.10 (m, 2H), 6.91–6.86 (m, 2H), 5.03 (s, 2H), 3.54 (t, 2H, *J*=6.3), 2.74 (t, 2H, *J*=7.3), 2.01 (s, 1H), 1.87–1.78 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5, 137.1, 130.4, 130.1, 128.5, 127.8, 127.1, 127.0, 120.9, 111.7, 70.0, 61.8, 32.8, 26.1. MS (FAB): *m/z* 242 $[M]^+$. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.39; H, 7.61.

*4.32. 3-(2-Benzyloxy-phenyl)-propionaldehyde (**33**)*

Starting from 3.0 g (12.38 mmol) of **32**, the title compound was prepared in the same manner as that described for **20**. Purification of the crude product by silica gel column chromatography (5% ethyl acetate in hexane) afforded **33** (2.14 g, 72%) as a colorless oil. R_f: 0.55 (20% ethyl acetate in hexane). IR (neat): 3032, 2930, 2360, 1710, 1600, 1501, 1240, 751 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 9.77 (t, 1H, *J*=1.9), 7.41–7.32 (m, 5H), 7.23–7.15 (m, 2H), 6.93–6.87 (m, 2H), 5.08 (s, 2H), 3.00 (t, 2H, *J*=7.3), 2.75 (t, 2H, *J*=7.3), 2.01 (s, 1H), 1.87–1.78 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 202.9, 157.0, 137.6, 130.6, 129.4, 129.1, 128.4, 128.1, 127.6, 121.3, 112.1, 70.3, 44.3, 24.0. MS (FAB): *m/z* 240 $[M]^+$. Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.93; H, 6.79.

*4.33. (2E)-5-(2-Benzyloxy-phenyl)-pent-2-enoic acid ethyl ester (**34**)*

Starting from 2.0 g (8.32 mmol) of **33**, the title compound was prepared in the same manner as that described for **11a**. Purification of the crude product by silica gel column chromatography (5% ethyl acetate in hexane) afforded **34** (2.0 g, 77%) as a colorless oil. R_f: 0.58 (20% ethyl acetate in hexane). IR (neat): 2361, 1717, 1495, 1453, 1240, 1039, 749 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.41–7.21 (m, 5H), 7.16–6.98 (m, 2H), 6.92–6.88 (m, 3H), 5.81 (d, 1H, *J*=15.6), 5.07 (s, 2H), 4.16 (m, 2H), 2.82 (t, 2H, *J*=7.9), 2.57–2.46 (m, 2H), 1.26 (t, 3H, *J*=7.1). ^{13}C NMR (50 MHz, $CDCl_3$): δ 167.2, 157.0, 149.3, 137.7, 130.4, 130.0, 129.0, 128.2, 127.9,

127.5, 121.9, 121.2, 112.0, 70.2, 60.6, 32.9, 29.6, 14.7. MS (ESI): *m/z* 311 $[M+1]^+$. Anal. Calcd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.14. Found: C, 77.51; H, 7.09.

*4.34. (2R,3S)-5-(2-Benzyloxy-phenyl)-2,3-dihydroxy-pentanoic acid ethyl ester (**35**)*

Starting from 1.85 g (5.96 mmol) of **34**, the title compound was prepared in the same manner as that described for **12a**. Purification of the crude product by silica gel column chromatography (25% ethyl acetate in hexane) afforded **35** (1.78 g, 87%) as a colorless semi-solid. R_f: 0.38 (40% ethyl acetate in hexane). $[\alpha]_D^{25}$ −18.75 (*c* 1.71, $CHCl_3$). The enantiomeric excess was estimated to be >99% by chiral HPLC analysis as that described for **12a**. IR (KBr): 3431, 2933, 1731, 1595, 1492, 1449, 1238, 1023, 754 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.44−7.31 (m, 5H), 7.19−7.14 (m, 2H), 6.93−6.88 (m, 2H), 5.08 (s, 2H), 4.27−4.20 (m, 2H), 4.06 (dd, 1H, J_1=2.0, J_2=5.6), 3.04 (d, 1H, *J*=5.7), 2.88−2.79 (m, 2H), 2.14 (d, 1H, *J*=8.4), 1.95−1.90 (m, 2H), 1.27 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 173.5, 156.5, 137.2, 130.2, 130.2, 128.6, 127.9, 127.2, 127.2, 120.9, 111.8, 73.3, 71.9, 70.0, 61.9, 34.0, 26.4, 14.1. MS (ESI): *m/z* 367 $[M+Na]^+$, 362, 345. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.65; H, 7.12.

*4.35. (2R,3S)-5-(2-Benzyloxy-phenyl)-3-hydroxy-2-(toluene-4-sulfonyloxy)-pentanoic acid ethyl ester (**36**)*

Starting from 1.55 g (4.50 mmol) of **35**, the title compound was prepared in the same manner as that described for **13a**. Purification of the crude product by silica gel column chromatography (15% ethyl acetate in hexane) afforded **36** (1.79 g, 80%) as a colorless gum. R_f: 0.41 (40% ethyl acetate in hexane). $[\alpha]_D^{25}$ −1.5 (*c* 1.15, $CHCl_3$). IR (KBr): 3407, 2924, 2143, 1754, 1593, 1444, 1366, 1231, 1178, 1022, 755 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, 2H, *J*=8.3), 7.42−7.24 (m, 7H), 7.18−7.08 (m, 2H), 6.91−6.86 (m, 2H), 5.05 (s, 2H), 4.81 (d, 1H, *J*=3.3), 4.08−4.04 (m, 2H), 3.96−3.93 (m, 1H), 2.80−2.70 (m, 2H), 2.39 (s, 3H), 1.82−1.74 (m, 2H), 1.13 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.2, 156.5, 145.1, 137.0, 133.1, 130.2, 129.7, 129.5, 128.6, 128.1, 127.9, 127.4, 127.2, 120.9, 111.7, 80.0, 70.9, 70.0, 61.8, 33.1, 25.9, 21.6, 13.8. MS (ESI): *m/z* 521 $[M+Na]^+$, 516, 499. Anal. Calcd for $C_{27}H_{30}O_7S$: C, 65.04; H, 6.06. Found: C, 65.22; H, 6.14.

*4.36. (2S,3S)-3-[2-(2-Benzyloxy-phenyl)-ethyl]-oxirane-2-carboxylic acid ethyl ester (**37**)*

Starting from 1.15 g (2.30 mmol) of **36**, the title compound was prepared in the same manner as that described for **24**. Purification of the crude product by silica gel column chromatography (10% ethyl acetate in hexane) afforded **37** (0.585 g, 78%) as a colorless semi-solid. R_f: 0.58 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ +21.87 (*c* 1.6, $CHCl_3$). IR (KBr): 3021, 2366, 1744, 1218, 1028, 767 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.44−7.31 (m, 5H), 7.16−7.14 (m, 2H), 6.91−6.87 (m, 2H), 5.08 (s, 2H), 4.17−4.04 (m, 2H), 3.39 (d, 1H, *J*=4.5), 3.19−3.17 (m, 1H), 2.89−2.80 (m, 2H), 2.07−1.92 (m, 2H), 1.23 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.2, 156.5, 137.2, 130.1, 129.3, 128.5, 127.8, 127.4, 127.1, 120.8, 111.6, 69.8, 61.3, 57.3, 52.9, 27.5, 26.9, 14.1. MS (FAB): *m/z* 327 $[M+1]^+$. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.75; H, 6.53.

*4.37. (S)-[(2R)-Chroman-2-yl]-hydroxy-acetic acid ethyl ester (**38**)*

Starting from 0.45 g (1.38 mmol) of **37**, the title compound was prepared in the same manner as that described for **15a**. Purification of the crude product by silica gel column chromatography (15% ethyl acetate in hexane) afforded **38** (0.221 g, 68%; based on two steps) as a colorless semi-solid. R_f: 0.39 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ −80.86 (*c* 1.77, $CHCl_3$). IR (KBr): 3446, 2928, 1739, 1487, 1234, 1131, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.09−7.03 (m, 2H), 6.87−6.75 (m, 2H), 4.38−4.24 (m, 4H), 3.04−2.99 (m, 1H), 2.95−2.78 (m, 2H), 2.24−2.09 (m, 1H), 2.04−1.96 (m, 1H), 1.32 (t, 3H, *J*=7.1). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.4, 154.4, 129.3, 127.2, 121.5, 120.4, 116.7, 76.4, 72.9, 61.9, 24.7, 23.5, 14.1. MS (FAB): *m/z* 237 $[M+1]^+$. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.17; H, 6.99.

*4.38. (1S)-1-[(2R)-Chroman-2-yl]-2-methyl-propane-1,2-diol (**39**)*

Starting from 0.195 g (0.825 mmol) of **38**, the title compound was prepared in the same manner as that described for **17a**. Purification of the crude product by silica gel column chromatography (30% ethyl acetate in hexane) afforded **39** (0.152 g, 83%) as a colorless oil. R_f: 0.52 (60% ethyl acetate in hexane). $[\alpha]_D^{25}$ −93.75 (*c* 2.04, $CHCl_3$). IR (neat): 3555, 3015, 2933, 2362, 1583, 1489, 1388, 1231, 1090, 756 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.10−7.04 (m, 2H), 6.89−6.75 (m, 2H), 4.32−4.27 (m, 1H), 3.33 (d, 1H, *J*=6.5), 2.91−2.78 (m, 4H), 2.24−2.23 (m, 1H), 1.93−1.86 (m, 1H), 1.38 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 153.9, 129.7, 127.2, 122.1, 120.9, 116.6, 77.5, 76.4, 73.1, 26.6, 26.5, 24.8, 24.7. MS (ESI): *m/z* 246 $[M+Na]^+$. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.11; H, 8.40.

*4.39. (2R,3S)-5-(2-Benzyloxy-phenyl)-3-(tert-butyl-dimethyl-silanyloxy)-2-(toluene-4-sulfonyloxy)-pentanoic acid ethyl ester (**40**)*

Starting from 1.15 g (2.30 mmol) of **36**, the title compound was prepared in the same manner as that described for **14a**. Purification of the crude product by silica gel column chromatography (6% ethyl acetate in hexane) afforded **40** (1.21 g, 85%) as a colorless semi-solid. R_f: 0.58 (20% ethyl acetate in hexane). $[\alpha]_D^{25}$ +1.2 (*c* 2.10, $CHCl_3$). IR (KBr): 3022,

2932, 2362, 1741, 1599, 1372, 1216, 758, 699 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.77 (d, 2H, J=8.2), 7.44–7.24 (m, 7H), 7.17–7.07 (m, 2H), 6.90–6.86 (m, 2H), 5.06 (s, 2H), 4.88 (d, 1H, J=3.9), 4.07–3.94 (m, 3H), 2.70–2.65 (m, 1H), 2.54–2.50 (m, 1H), 2.40 (s, 3H), 1.93–1.90 (m, 1H), 1.80–1.68 (m, 1H), 1.13 (t, 3H, J=7.1), 0.79 (s, 9H), −0.07 (s, 3H), 0.076 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 156.4, 144.8, 137.3, 133.5, 129.9, 129.8, 129.6, 128.5, 128.1, 127.7, 127.2, 120.7, 111.5, 79.4, 72.1, 69.8, 61.5, 33.0, 25.8, 25.6, 21.6, 17.9, 13.8, −4.6, −4.9. MS (ESI): *m/z* 636 $[M+Na]^+$, 631, 613. Anal. Calcd for $C_{33}H_{44}O_7SSi$: C, 64.67; H, 7.24. Found: C, 64.81; H, 7.19.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.03.001.

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