Synthesis of Optically Pure Lactone Metabolites of Tea Catechins

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Abstract: Catechins and epicatechins are extremely useful compounds in the context of biological activities. These compounds afford many metabolites, including γ-valerolactone derivatives, through metabolic pathways in the human body. Several of these γ-valerolactone metabolites were synthesized as optically pure authentic standards.

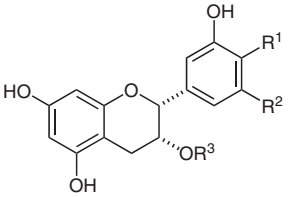
Key words: tea catechins, polyphenols, stereoselective synthesis, lactones, cyclizations

The tea catechins (–)-epicatechin (**1**), (–)-epigallocatechin (**2**), (–)-epicatechin gallate (**3**), and (–)-epigallocatechin gallate (**4**) are among a group of polyphenols that have a diverse range of biological activities including scavenging of free radicals,[1] antibacterial properties,[2] antiviral properties,[3] anticancer properties,[4] anti-inflammatory activities,[5] and inhibitory activities against DNA polymerases.[6] Orally administered tea catechins and procyanidins are metabolized to afford ring-fission metabolites, including 5-(3,4-dihydroxybenzyl)dihydrofuran-2(3*H*)-one [**5a**; 5-(3,4-dihydroxyphenyl)-γ-valerolactone], 5-(3-hydroxyphenyl)dihydrofuran-2(3*H*)-one (**5b**), 5-(3,5-dihydroxyphenyl)dihydrofuran-2(3*H*)-one (**5c**), and 5-(3,4,5-trihydroxyphenyl)dihydrofuran-2(3*H*)-one (**5d**) (Figure 1),[7–13] which show the same biological activities as the tea catechins.[14–17] These lactone derivatives each contain one stereogenic center at the C4 position that is derived from the C3 position of the corresponding catechin; however, there are no reports on the stereochemistry and optical purity of these lactones.

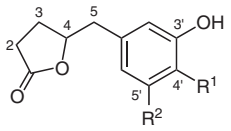
In 1959, Watanabe reported the synthesis of racemic **5a** and **5b**.[18] Recently, Lambert and co-workers have reported the synthesis and biological activities of the racemic tea catechin metabolites **5a** and **5d**.[19] We have also reported the first synthesis of optically pure (5*R*)-5-phenyldihydrofuran-2(3*H*)-one and (*S*)-**5a** from optically active (*R*)- and (*S*)-benzyl glycidyl ethers,[20] and we showed that the metabolite has an *R*-configuration because the specific rotation of the synthetic (*S*)-**5a** was opposite to that of the metabolite form of **5a** derived from (–)-epicatechin.

Here we report efficient syntheses of four optically pure (*R*)-type metabolite lactone derivatives **5a–d** to confirm their stereochemistry.

The problem in our previous synthesis of (*S*)-**5a** was the final lactonization step. We examined various continuous deprotection and lactonization conditions, but the isolated yield remained less than 20%. We therefore carefully reinvestigated the synthetic route. In the previous route (Scheme 1), (*S*)-benzyl glycidyl ether **7** was coupled with four aryl bromides **6a–d**, and subsequent acetylation with acetic anhydride, triethylamine, and 4-(*N*,*N*-dimethylamino)pyridine gave the corresponding acetates **8a–d** in 49–68% yields. The protecting benzyl group was removed by hydrogenolysis to give the corresponding alcohols **9a–d**, which were oxidized to aldehydes by Swern oxidation. Subsequent one-pot Wittig olefination gave the α,β-unsaturated esters **10a–d** in 79–96% yields. Hydrolysis of the acetyl groups with ethanolic potassium carbonate gave the allylic alcohols **11a–d** which were reduced to the saturated γ-hydroxy esters **12a–d** by hydrogenation. When esters **12a–c** were treated with an excess of *p*-toluenesulfonic acid monohydrate under conditions designed to remove ethanol, lactonization and desilylation occurred smoothly to give the desired lactones **5a–c** in 81–83% yields. The experimental ^{1}H and ^{13}C NMR spectra and mass spectra agreed with the reported values. However, the optical ro-



1 (–)-epicatechin: R^1 = OH, R^2 = R^3 = H
2 (–)-epigallocatechin: R^1 = R^2 = OH, R^3 = H
3 (–)-epicatechin gallate: R^1 = OH, R^2 = H, R^3 = galloyl
4 (–)-epigallocatechin gallate: R^1 = R^2 = OH, R^3 = galloyl



5a R^1 = OH, R^2 = H
5b R^1 = R^2 = H
5c R^1 = H, R^2 = OH
5d R^1 = R^2 = OH

Figure 1 The structures of tea catechins and their lactone metabolites

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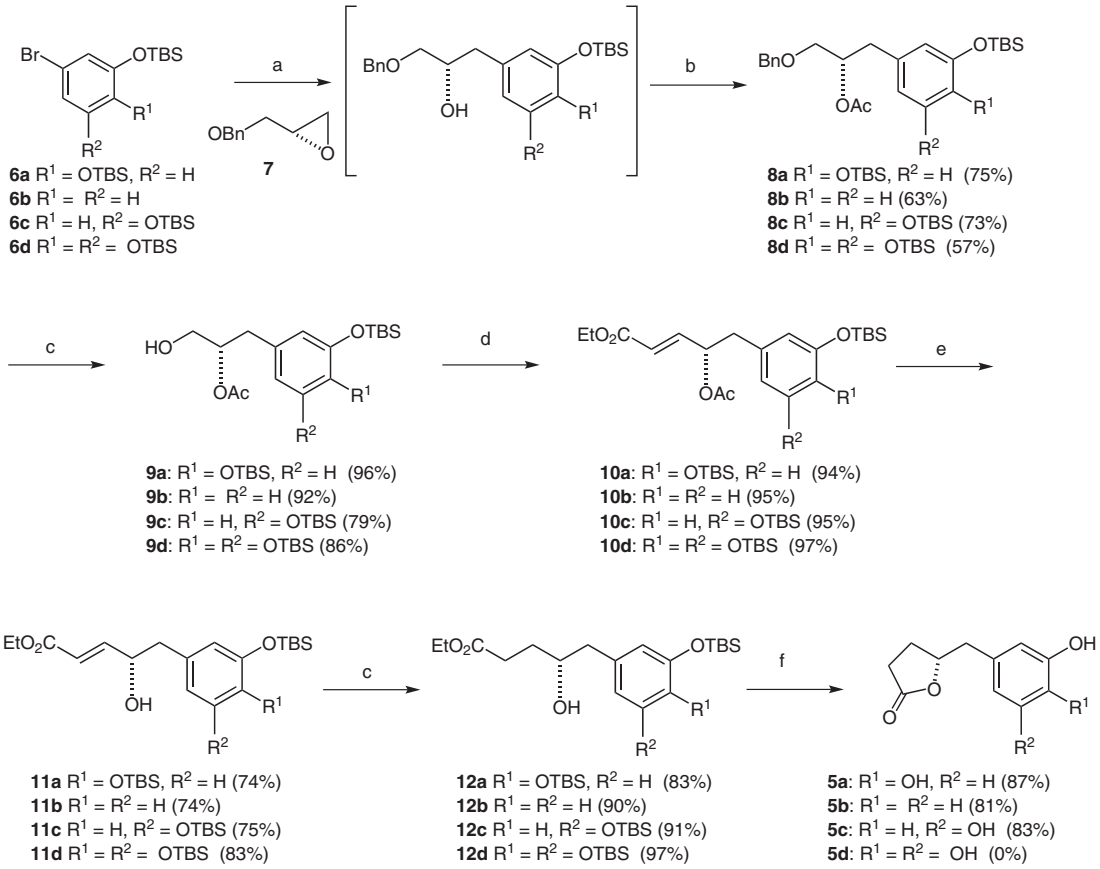


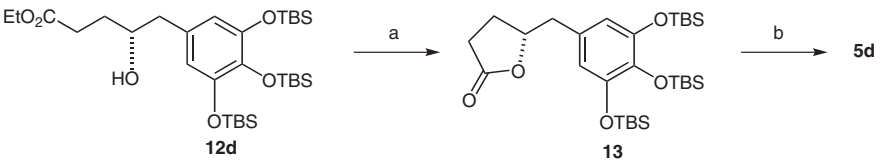
Scheme 1 *Reagents and conditions*: (a) BuLi, THF then **7**, $BF_3{\cdot}OEt_2$, THF, –78 °C to r.t.; (b) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (c) H_2, 10% Pd/C, EtOAc; (d) $(ClCO)_2$, DMSO, Et_3N, CH_2Cl_2 then $Ph_3P{=}CHCO_2Et$; (e) K_2CO_3, EtOH; (f) $TsOH{\cdot}H_2O$, 4 Å MS, benzene, reflux.

tations for **5a** {$[\alpha]_D^{28}$ –16.7 (*c* 0.70, MeOH)}, **5b** {$[\alpha]_D^{26}$ –29.2 (*c* 1.00, MeOH)}, and **5c** {$[\alpha]_D^{27}$ –20.6 (*c* 0.97, MeOH)} were greater than the literature values {**5a:** $[\alpha]_D^{28}$ –8.6 (*c* 0.5, MeOH),[8a] **5b**: $[\alpha]_D^{26}$ –11.6 (*c* 0.1, MeOH),[8a,11b] and **5c**: $[\alpha]_D^{27}$ –12.9 (*c* 0.4, MeOH)[11a]}.

Under the same conditions, we obtained the trihydroxyphenyl lactone **5d** as a complex mixture, because the pyrogallol part was unstable in the presence of *p*-toluenesulfonic acid monohydrate in refluxing benzene. The desired lactone **5d** was, however, obtained via the silyl-protected lactone **13**. Treatment of the γ-hydroxy ester **12d** with pyridinum *p*-toluenesulfonate in refluxing benzene gave **13** in 98% yield. This product was desilylated by treatment with concentrated hydrogen chloride in tetrahydrofuran–methanol (5:1) at 0 °C to afford **5d** in 81% yield (Scheme 2).

It is necessary to know the ee values for the synthesized lactones to compare them with the authentic standard tea catechin metabolites obtained by fermentation with enteric bacteria. We attempted to identify suitable conditions for separation by HPLC using several chiral columns, but complete separation could not be achieved. We therefore converted both (*R*)-**5b** and (*S*)-**5b**[21] into the corresponding (2*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate esters, (*S*,*S*)-**14** and (*R*,*S*)-**14**, in 96% and 98% yields, respectively (Scheme 3). In the ^{13}C NMR spectrum, the peaks of the two diastereomers at the C3, C4, and C5 positions could be differentiated,[22] and the ee values for both the (*R*)-**5b** and (*S*)-**5b** enantiomers were therefore >96%.

In conclusion, we synthesized optically pure forms of four tea catechin lactone metabolites in seven steps for **5a–c**, and in eight steps for **5d**, in 30–37% overall yields. The specific rotations of the synthetic products were larger than those previously reported for these metabolites. These results suggest that the epimerization step at the C3 position in epicatechin is vital to the metabolic pathway of enteric bacteria. It is therefore important to clarify this pathway in studying the medicinal chemistry of catechins.



Scheme 2 *Reagents and conditions*: (a) PPTS, benzene, reflux, 1 h, 98%; (b) concd HCl, THF–MeOH (5:1), 0 °C to r.t., 6 h, 81%.

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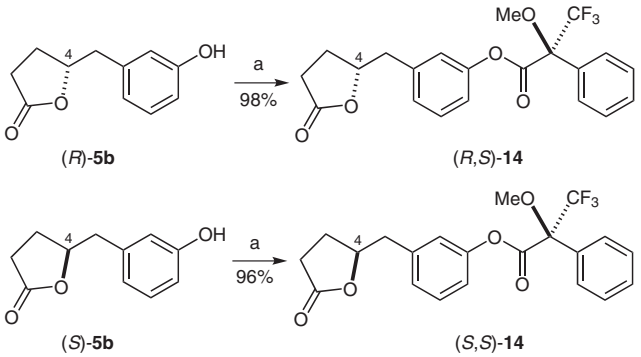

Scheme 3 *Reagents and conditions*: (a) (*R*)-PhC(OMe)(CF_3)COCl, Et_3N, DMAP, CH_2Cl_2.

Melting points were measured with an MPJ3 micro melting-point apparatus (Yanaco Co. Ltd., Kyoto, Japan) and are uncorrected. ATR-IR spectra were recorded by using a PerkinElmer Spectrum 100 spectrometer equipped with a Universal ATR accessory. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Biospin Avance II 400 spectrometer and a JEOL JNM LA-400 spectrometer with TMS or a solvent peak as the internal standard (chemical shifts are given in ppm). Low-resolution ESI MS spectra were recorded on an Agilent Technology 1100 LC-MSD spectrometer from solns in aq MeOH, aq MeCN, or 0.5% aq HCO_2H. We recorded the ESI HRMS spectra on a Bruker Daltonics micrOTOF spectrometer. Specific rotations were measured with a Horiba polarimeter. Analytical TLC was conducted on precoated TLC plates (silica gel 60F_{254}, Merck). Column chromatography was conducted by using silica gel 60N (70–230 mesh, Kanto Chemical). All reagents used were of commercial quality. Dehydrated-grade THF and CH_2Cl_2 (Kanto Chemical) were used without purification. All air- and moisture-sensitive reactions were performed under an inert gas (N_2 or argon).

(1*S*)-2-(Benzyloxy)-1-{3,4-bis[*tert*-butyl(dimethyl)siloxy]benzyl}ethyl Acetate [(*S*)-8a]; Typical Procedure

A 1.6 M soln of BuLi in hexane (1.78 mL, 2.83 mmol) was added to a soln of bromo compound **6a** (1.13 g, 2.70 mmol) in THF (15 mL) at –78 °C, and the mixture was stirred for 40 min at the same temperature. $BF_3{\cdot}OEt_2$ (402 mg, 2.83 mmol) and benzyl (*S*)-glycidyl ether [(*S*)-**7**, 422 mg, 2.57 mmol] were added at –78 °C. The mixture was stirred for 22 h at r.t. The reaction was quenched with sat. aq NH_4Cl (20 mL), and the mixed soln was extracted with EtOAc (60 mL). The organic layer was washed with H_2O and brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated in vacuo, and the residual oil was purified by column chromatography [silica gel, hexane–EtOAc (9:1)] to give the coupling product (936 mg) as a colorless oil containing a small amount of **7**. The coupling product was dissolved in CH_2Cl_2 (19 mL) and mixed with Et_3N (1.88 g, 18.6 mmol), DMAP (114 mg, 0.93 mmol), and Ac_2O (570 mg, 5.58 mmol) at 0 °C. The mixture was stirred for 8 h at r.t. The reaction was quenched with H_2O (20 mL), and the mixture was extracted with EtOAc (60 mL). The organic layer was washed with 1 M HCl, H_2O, and brine, then dried (Na_2SO_4) and filtered. The filtrate was concentrated in vacuo, and the residual oil was purified by column chromatography [silica gel, hexane–EtOAc (15:1)] to give (*S*)-**8a** as a colorless oil; yield: 995 mg (72% from **7**); R_f = 0.49 (hexane–EtOAc, 4:1); $[\alpha]_D^{27}$ +4.2 (*c* 0.40, $CHCl_3$).

ATR-IR (neat): 3032, 2886, 2955, 2930, 2858, 1738 (C=O), 1605, 1576, 1509, 1472, 1463, 1421, 1390, 1372, 1289, 1250, 1232, 1159, 1126, 1095, 1051, 1028, 982, 904, 836, 779, 734, 696, 667 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H, Ph-H), 6.71 (d, *J* = 8.1 Hz, 1 H, H-2′), 6.69 (d, *J* = 2.1 Hz, 1 H, H-5′), 6.62 (dd, *J* = 8.1 and 2.1 Hz, 1 H, H-6′), 5.16 (m, 1 H, H-2), 4.52 (ABq, $J_{1,2}$ = 23.5 Hz, $J_{A,B}$ = 12.1 Hz, 2 H, $C_6H_5CH_2$), 3.52–3.45 (m, 2 H, H-1), 2.86–2.77 (m, 2 H, H-3), 2.02 [s, 3 H, $C(O)CH_3$], 0.97 (s, 18 H, *t*-Bu), 0.18 [s, 6 H, $Si(CH_3)_2$], 0.17 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 146.6, 145.5, 138.1, 130.2, 128.4, 127.7, 127.6, 122.33, 122.30, 120.9, 73.6, 73.2, 70.1, 36.3, 25.9(6), 25.9(5), 21.2, 18.5, 18.4, –4.1.

MS (ESI): *m/z* (%) = 567 (20) $[M + Na]^+$, 562 (39) $[M + H_2O]^+$, 485 (100), 467 (20).

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{30}H_{48}NaO_5Si_2$: 567.2933; found: 567.2927.

(1*S*)-1-Benzyloxy-1-(3-[*tert*-butyl(dimethyl)siloxy]benzyl}ethyl Acetate [(*S*)-8b]

Colorless oil; yield: 62% (based on epoxide **7**); R_f = 0.32 (hexane–EtOAc, 4:1); $[\alpha]_D^{27}$ –2.8 (*c* 1.01, $CHCl_3$).

ATR-IR (neat): 3031, 2955, 2930, 2886, 2858, 1737 (C=O), 1602, 1585, 1485, 1472, 1463, 1443, 1371, 1271, 1233, 1158, 1126, 1096, 1050, 1028, 1003, 974, 939, 874, 836, 779, 734, 695, 665 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H, Ph-H), 7.12 (td, *J* = 7.6 and 0.6 Hz, 1 H, H-5′), 6.78, (d, *J* = 7.7 Hz, 1 H, H-4′), 6.70 (d, *J* = 0.5 Hz, 1 H, H-2′), 6.68 (dd, *J* = 2.2 and 0.8 Hz, 1 H, H-4′), 5.23–5.17 (m, 1 H, H-2), 4.52 (ABq, $J_{A,B}$ = 12.1 Hz, $J_{1,2}$ = 24.6 Hz, 2 H, benzylic), 3.53–3.46 (m, 2 H, H-1), 2.92–2.84 (m, 2 H, H-3), 2.03 [s, 3 H, $C(O)CH_3$], 0.97 (s, 9 H, *t*-Bu), 0.18 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5 (C=O), 155.6, 138.6, 138.0, 129.3, 128.4, 127.68, 127.65, 122.5, 121.3, 118.3, 73.4, 73.2, 70.1, 36.9, 25.7, 21.2, 18.2, –4.40, –4.42.

MS (ESI): *m/z* (%) = 453 (26) $[M + K]^+$, 437 (41) $[M + Na]^+$, 432 (17) $[M + H_2O]^+$, 415 (11) $[M + H]^+$, 355 (50), 337 (100), 247 (22).

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{24}H_{34}NaO_4Si$: 437.2119; found: 437.2131.

(1*S*)-2-(Benzyloxy)-1-{3,5-bis[*tert*-butyl(dimethyl)silyloxy]benzyl}ethyl Acetate [(S)-8c]

Colorless oil; yield: 73% (based on epoxide **7**); R_f = 0.5 (hexane–EtOAc, 4:1); $[\alpha]_D^{24}$ –3.9 (*c* 0.45, $CHCl_3$).

ATR-IR (neat): 3032, 2955, 2930, 2886, 2858, 1739 (C=O), 1588, 1496, 1471, 1451, 1390, 1371, 1362, 1336, 1251, 1234, 1160, 1096, 1040, 1006, 956, 939, 828, 814, 778, 736, 696, 669 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.26 (m, 5 H, Ph-H), 6.34 (d, *J* = 2.2 Hz, 2 H, H-2′ and 6′), 6.20 (t, *J* = 2.2 Hz, 1 H, H-4′), 5.21–5.15 (m, 1 H, H-2), 4.51 (ABq, $J_{1,2}$ = 21.1 Hz, $J_{A,B}$ = 12.1 Hz, 2 H, benzylic), 3.53–3.45 (m, 2 H, H-1), 2.82 (d, *J* = 6.8 Hz, 2 H, H-3), 2.03 [s, 3 H, $C(O)CH_3$], 0.96 (s, 18 H, *t*-Bu), 0.17 [s, 12 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 156.4, 139.0, 138.0, 128.4, 127.7, 127.6, 114.7, 110.5, 73.3, 73.2, 70.2, 36.9, 25.7, 21.2, 18.2, –4.38, –4.40.

MS (ESI): *m/z* (%) = 583 (29) $[M + Na]^+$, 545 (100) $[M + H]^+$, 81 (62).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{30}H_{49}O_5Si_2$: 545.3113; found: 545.3110.

(1*S*)-2-(Benzyloxy)-1-{3,4,5-tris[*tert*-butyl(dimethyl)siloxy]benzyl}ethyl Acetate [(*S*)-8d]

Colorless oil; yield: 57% (based on epoxide **7**); R_f = 0.56 (hexane–EtOAc, 4:1); $[\alpha]_D^{28}$ –1.7 (*c* 1.05, $CHCl_3$).

ATR-IR (neat): 2953, 2930, 2886, 2858, 1740 (C=O), 1574, 1494, 1472, 1463, 1430, 1390, 1361, 1344, 1230, 1081, 1029, 1005, 939, 894, 827, 779, 735, 696, 670 cm^{-1}.

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^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.26 (m, 5 H, Ph-H), 6.35 (s, 2 H, H-2′ and 6′), 5.18–5.12 (m, 1 H, H-2), 4.51 (ABq, $J_{A,B}$ = 12.1 Hz, $J_{1,2}$ = 17.2 Hz, 2 H, benzylic), 3.51–3.44 (m, 2 H, H-1), 2.77–2.71 (m, 2 H, H-3), 2.02 [s, 3 H, $C(O)CH_3$], 0.98 (s, 9 H, *t*-Bu), 0.92 (s, 18 H, *t*-Bu), 0.18 [s, 12 H, $Si(CH_3)_2$], 0.10 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 143.4, 138.1, 137.0, 128.9, 128.4, 127.6, 127.5, 115.4, 73.6, 73.1, 70.3, 36.7, 26.2(3), 26.1(8), 21.2, 18.8, 18.4, –3.6, –4.0.

MS (ESI): *m/z* (%) = 713 (18) $[M + K]^+$, 697 (33) $[M + Na]^+$, 675 (100) $[M + H]^+$, 615 (74).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{36}H_{63}O_6Si_3$: 675.3927; found: 675.3946.

(1*S*)-1-{3,4-Bis[*tert*-butyl(dimethyl)silyloxy]benzyl}-2-hydroxyethyl Acetate [(*S*)-9a)]; Typical Procedure

10% Pd/C (145 mg) was added to a soln of (*S*)-**8a** (1.62 g, 2.97 mmol) in EtOAc (30 mL) added at r.t. The mixture was stirred for 10 h at r.t. under H_2 (1 atm), and then filtered. The filtrate was concentrated in vacuo and the residual oil was purified by column chromatography [silica gel; hexane–EtOAc (4:1)] to give a colorless oil; yield: 1.28 g (95%); R_f = 0.15 (hexane–EtOAc, 4:1); $[\alpha]_D^{26}$ –6.5 (*c* 0.78, $CHCl_3$).

ATR-IR (neat): 3460 (OH), 2955, 2930, 2886, 2858, 1738 (C=O), 1605, 1576, 1509, 1472, 1463, 1421, 1390, 1373, 1362, 1288, 1251, 1232, 1159, 1126, 1033, 1006, 982, 938, 905, 836, 778, 695, 666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.74 (d, *J* = 8.1 Hz, 1 H, H-2′), 6.70 (d, *J* = 2.1 Hz, 1 H, H-5′), 6.65 (dd, *J* = 8.1 and 2.1 Hz, 1 H, H-6′), 5.03 (qd, *J* = 6.9 and 3.2 Hz, 1 H, H-2), 3.70 (one of ABqd, *J* = 2.6 Hz, $J_{A,B}$ = 11.9 Hz, 1 H, H-1), 3.59 (one of ABqd, *J* = 5.6 Hz, $J_{A,B}$ = 11.9 Hz, 1 H, H-1), 2.84–2.73 (m, 2 H, H-3), 2.05 [s, 3 H, $C(O)CH_3$], 0.99 (s, 9 H, *t*-Bu), 0.98 (s, 9 H, *t*-Bu), 0.19 [s, 6 H, $Si(CH_3)_2$], 0.18 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 146.7, 145.6, 129.8, 122.2, 121.0, 76.1, 63.6, 36.1, 25.9, 21.2, 18.4, –4.07, –4.11.

MS (ESI): *m/z* (%) = 493 (37) $[M + K]^+$, 477 (100) $[M + Na]^+$, 472 (18) $[M^+ + H_2O]$, 395 (40).

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{23}H_{42}NaO_5Si_2$: 477.2463; found: 477.2484.

(1*S*)-1-{3-[*tert*-Butyl(dimethyl)silyloxy]benzyl}-2-hydroxyethyl Acetate [(*S*)-9b]

Colorless oil; yield: 92%; R_f = 0.21 (hexane–EtOAc, 3:1); $[\alpha]_D^{28}$ –8.3 (*c* 1.10, $CHCl_3$).

ATR-IR (neat): 3452 (OH), 2956, 2930, 2886, 2858, 1737 (C=O), 1602, 1585, 1485, 1472, 1463, 1442, 1373, 1251, 1235, 1158, 1032, 1003, 974, 939, 871, 836, 779, 713, 695, 665 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.16–7.12 (m, 1 H, H-5′), 6.81 (br d, *J* = 7.6 Hz, 1 H, H-4′), 6.71–6.69 (m, 2 H, H-2′ and 4′), 5.08 (octet, *J* = 3.3 Hz, 1 H, H-2), 3.75–3.58 (m, 2 H, H-1), 2.92–2.81 (m, 2 H, H-3), 2.06 [s, 3 H, $C(O)CH_3$], 0.97 (s, 9 H, *t*-Bu), 0.19 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 155.7, 138.3, 129.4, 122.4, 121.2, 118.4, 75.9, 36.6, 25.7, 21.2, 18.2, –4.39, –4.41.

MS (ESI): *m/z* (%) = 363 (19) $[M + K]^+$, 347 (70) $[M + Na]^+$, 307 (11), 265 (63), 247 (100).

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{17}H_{28}NaO_4Si$: 347.1649; found: 347.1648.

(1*S*)-1-{3,5-Bis[*tert*-butyl(dimethyl)silyloxy]benzyl}-2-hydroxyethyl Acetate [(*S*)-9c]

Colorless oil; yield: 79%; R_f = 0.27 (hexane–EtOAc, 3:1); $[\alpha]_D^{26}$ –5.3 (*c* 1.05, $CHCl_3$).

ATR-IR (neat): 3494 (OH), 2955, 2930, 2886, 2859, 1739 (C=O), 1587, 1472, 1450, 1390, 1373, 1362, 1337, 1251, 1237, 1187, 1159, 1037, 1018, 1005, 939, 828, 814, 778, 743, 702, 669 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.34 (d, *J* = 2.1 Hz, 2 H, H-2′ and 6′), 6.21 (t, *J* = 2.1 Hz, 1 H, H-4′), 5.05 (qd, *J* = 6.8 and 3.2 Hz, 1 H, H-2), 3.74–3.68 (m, 1 H, H-1), 3.63–3.57 (m, 1 H, H-1), 2.79 (qd, *J* = 13.7 and 6.9 Hz, 2 H, H-3), 2.06 [s, 3 H, $C(O)CH_3$], 1.60 (br d, *J* = 2.1 Hz, 1 H, OH), 0.97 (s, 18 H, *t*-Bu), 0.18 [s, 12 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 156.5, 138.7, 114.6, 110.6, 75.8, 63.7, 36.6, 25.7, 21.2, 18.2, –4.38, –4.40.

MS (ESI): *m/z* (%) = 477 (9) $[M + Na]^+$, 455 (100) $[M + H]^+$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{23}H_{43}O_5Si_2$: 455.2644; found: 455.2647.

(1*S*)-2-Hydroxy-1-{3,4,5-tris[*tert*-butyl(dimethyl)silyloxy]benzyl}ethyl Acetate [(*S*)-9d]

White powder; yield: 86%; mp = 94–95 °C (hexane–EtOAc); R_f = 0.36 (hexane–EtOAc, 7:3); $[\alpha]_D^{26}$ –4.8 (*c* 1.02, $CHCl_3$).

ATR-IR (neat): 3488 (OH), 2950, 2929, 2896, 2857, 1740 (C=O), 1574, 1495, 1472, 1463, 1428, 1389, 1361, 1346, 1249, 1229, 1146, 1086, 1035, 1004, 939, 893, 827, 803, 779, 758, 736, 707, 673 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.36 (s, 2 H, H-2′ and 6′), 5.01 (octet, *J* = 3.2 Hz, 1 H, H-2), 3.71–3.54 (m, 2 H, H-1), 2.77–2.67 (m, 2 H, H-3), 2.05 [s, 3 H, $C(O)CH_3$], 1.75 (br t, *J* = 6.2 Hz, 1 H, OH), 0.98 (s, 9 H, *t*-Bu), 0.93 (s, 18 H, *t*-Bu), 0.20 [s, 12 H, $Si(CH_3)_2$], 0.11 (s, 6 H, *t*-Bu).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.0, 148.5, 137.1, 128.6, 115.3, 63.7, 36.3, 26.22, 26.17, 21.2, 18.8, 18.4, –3.60, –3.62, –4.0.

MS (ESI): *m/z* (%) = 607 (42) $[M + Na]^+$, 585 (100) $[M + H]^+$, 525 (6).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{29}H_{57}O_6Si_3$: 585.3458; found: 585.3463.

Ethyl (2*E*,4*S*)-4-(Acetoxy)-5-{3,4-bis[*tert*-butyl(dimethyl)silyloxy]phenyl}pent-2-enoate [(*S*)-10a]; Typical Procedure

$(ClCO)_2$ (715 mg, 5.63 mmol) was added to a soln of DMSO (880 mg, 11.3 mmol) in CH_2Cl_2 (28 mL) at –78 °C. The mixture was stirred at this temperature for 20 min and then mixed with a soln of alcohol (*S*)-**9a** (1.28 g, 2.81 mmol) in CH_2Cl_2 (28 mL). The mixture was stirred for 40 min at –78 °C and then added to Et_3N (2.85 g, 28.2 mmol). The resulting mixture was stirred at r.t. for 1 h. The soln was cooled to 0 °C and $Ph_3P{=}CHCO_2Et$ (1.96 g, 5.63 mmol) at 0 °C was added. The mixture was stirred at r.t. for 2 h. The reaction was quenched with sat. aq NH_4Cl (30 mL) and extracted with EtOAc (90 mL). The organic layer was washed with H_2O and brine, and then dried (Na_2SO_4) and filtered. The filtrate was concentrated in vacuo. The residual oil was purified by column chromatography [silica gel, hexane–EtOAc (12:1)] to give a colorless oil; yield: 1.38 g (94%); R_f = 0.67 (hexane–EtOAc, 7:3); $[\alpha]_D^{27}$ +6.9 (*c* 0.98, $CHCl_3$).

ATR-IR (neat): 2956, 2930, 2896, 2858, 1745, 1723, 1662, 1604, 1577, 1509, 1472, 1464, 1422, 1390, 1368, 1301, 1272, 1252, 1227, 1160, 1127, 1086, 1026, 980, 904, 836, 779, 755, 695, 666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.85 (dd, *J* = 15.8 and 5.3 Hz, 1 H, H-3), 6.74 (d, *J* = 8.1 Hz, 1 H, Ar-H), 6.65 (d, *J* = 2.1 Hz, 1 H, Ar-H), 6.62 (dd, *J* = 8.1 and 2.2 Hz, 1 H, Ar-H), 5.88 (dd, *J* = 15.8 and 1.5 Hz, 1 H, H-2), 5.54 (qd, *J* = 6.7 and 1.5 Hz, 1 H, H-4), 4.18 (qd, *J* = 7.1 and 1.0 Hz, 2 H, OCH_2CH_3), 2.87 (one of AB, dd, *J* = 13.9 and 7.2 Hz, 1 H, H-5), 2.81 (one of AB, dd, *J* = 13.9 and

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6.5 Hz, 1 H, H-5), 2.04 [s, 3 H, C(O)CH_3], 1.27 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 0.98 (s, 9 H, *t*-Bu), 0.97 (s, 9 H, *t*-Bu), 0.18 [s, 12 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 165.8, 146.7, 145.8, 144.6, 129.0, 122.4, 122.3, 121.9, 121.0, 73.2, 60.5, 39.7, 25.94, 25.93, 21.0, 18.5, 18.4, 14.2, –4.08, –4.11.

MS (ESI): *m/z* (%) = 545 (14) $[M + Na]^+$, 540 (100) $[M + H_2O]^+$, 523 (8) $[M + H]^+$, 463 (43).

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{27}H_{46}NaO_6Si_2$: 545.2725; found: 545.27388.

Ethyl (2*E*,4*S*)-4-(Acetoxy)-5-{3-[*tert*-butyl(dimethyl)silyloxy]phenyl}pent-2-enoate [(*S*)-10b]

Colorless oil; yield: 95%; R_f = 0.62 (hexane–EtOAc, 3:1); $[\alpha]_D^{27}$ +4.0 (*c* 1.07, $CHCl_3$).

ATR-IR (neat): 2956, 2931, 2898, 2859, 1744 (OAc), 1721 (ethyl ester), 1662, 1602, 1585, 1486, 1472, 1442, 1390, 1368, 1307, 1270, 1226, 1159, 1086, 1026, 1003, 974, 938, 920, 836, 779, 695, 665 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.14 (t, J = 7.8 Hz, 1 H, H-5′), 6.85 (dd, J = 15.7 and 5.3 Hz, 1 H, H-3), 6.78 (d, J = 7.6 Hz, 1 H, H-6′), 6.72–6.66 (m, 2 H, H-2′ and 4′), 5.90 (dd, J = 15.7 and 1.5 Hz, 1 H, H-2), 5.61–5.56 (m, 1 H, H-4), 4.18 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 2.94 (one of ABqd, J = 7.3 Hz, $J_{A,B}$ = 13.8 Hz, 1 H, H-5), 2.88 (one of ABqd, J = 6.4 Hz, $J_{A,B}$ = 13.8 Hz, 1 H, H-5), 2.05 [s, 3 H, C(O)CH_3], 1.28 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 0.98 (s, 9 H, *t*-Bu), 0.18 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 165.9, 155.7, 144.4, 137.4, 129.4, 122.5, 122.0, 121.3, 118.7, 73.0, 60.6, 40.2, 25.7, 20.1, 18.2, 14.2, –4.41, –4.43.

MS (ESI): *m/z* (%) = 431 (18) $[M + K]^+$, 415 (52) $[M + Na]^+$, 333 (100), 259 (13).

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{32}NaO_5Si$: 415.1911; found: 415.1916.

Ethyl (2*E*,4*S*)-4-(Acetoxy)-5-{3,5-bis[*tert*-butyl(dimethyl)silyloxy]phenyl}pent-2-enoate [(*S*)-10c]

Colorless oil; yield: 95%; R_f = 0.73 (hexane–EtOAc, 7:3); $[\alpha]_D^{26}$ +4.7 (*c* 1.01, $CHCl_3$).

ATR-IR (neat): 2956, 2931, 2897, 2859, 1744 (OAc), 1724 (ethyl ester), 1663, 1588, 1472, 1451, 1390, 1369, 1342, 1307, 1252, 1227, 1159, 1006, 978, 938, 917, 828, 814, 779, 743, 699, 676 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83 (dd, J = 15.7 and 5.3 Hz, 1 H, H-3), 6.30 (d, J = 2.1 Hz, 2 H, H-2′ and 6′), 6.22 (t, J = 2.1 Hz, 1 H, H-4′), 5.88 (dd, J = 15.8 and 1.5 Hz, 1 H, H-2), 5.58–5.53 (m, 1 H, H-4), 4.17 (qd, J = 7.1 and 1.1 Hz, 2 H, OCH_2CH_3), 2.87 (one of ABqd, J = 7.1 Hz, $J_{A,B}$ = 13.8 Hz, 1 H, H-5), 2.80 (one of ABqd, J = 6.5 Hz, $J_{A,B}$ = 13.8 Hz, 1 H, H-5), 2.05 [s, 3 H, C(O)CH_3], 1.27 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 0.97 (s, 18 H, *t*-Bu), 0.17 [s, 12 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 165.8, 156.5, 144.4, 137.8, 122.0, 114.7, 110.8, 60.6, 40.2, 25.7, 21.0, 18.2, 14.2, –4.40, –4.42.

MS (ESI): *m/z* (%) = 545 (5) $[M + Na]^+$, 523 (100) $[M + H]^+$, 463 (14).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{27}H_{47}O_6Si_2$: 523.2906; found: 523.2910.

Ethyl (2*E*,4*S*)-4-(Acetoxy)-5-{3,4,5-tris[*tert*-butyl(dimethyl)silyloxy]phenyl}pent-2-enoate [(*S*)-10d]

Colorless oil; yield: 97%; R_f = 0.24 (hexane–EtOAc, 9:1); $[\alpha]_D^{28}$ +5.8 (*c* 1.05, $CHCl_3$).

ATR-IR (neat): 2954, 2930, 2896, 2858, 1746 (OAc), 1725 (ethyl ester), 1663, 1574, 1493, 1472, 1464, 1431, 1391, 1362, 1307, 1252, 1227, 1200, 1174, 1084, 1047, 1005, 977, 938, 893, 827, 779, 737, 705, 670 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (dd, J = 15.7 and 5.3 Hz, 1 H, H-3), 6.32 (s, 2 H, H-2′ and 6′), 5.85 (dd, J = 15.7 and 1.5 Hz, 1 H, H-2), 5.52 (qd, J = 6.6 and 1.3 Hz, 1 H, H-4), 4.20–4.11 (m, 2 H, OCH_2CH_3), 2.80 (one of ABqd, J = 6.9 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.75 (one of ABqd, J = 6.5 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.05 [s, 3 H, C(O)CH_3], 1.27 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 0.97 (s, 9 H, *t*-Bu), 0.92 (s, 18 H, *t*-Bu), 0.19 [s, 18 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 165.8, 148.5, 144.5, 137.3, 127.8, 122.0, 115.4, 73.3, 60.5, 39.9, 26.21, 26.16, 21.0, 18.8, 18.4, 14.2, –3.62, –3.64, –4.0.

MS (ESI): *m/z* (%) = 691 (24) $[M + K]^+$, 675 (55) $[M + Na]^+$, 670 (18) $[M + H_2O]^+$, 653 (100) $[M + H]^+$, 593 (53).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{33}H_{61}O_7Si_3$: 653.3720; found: 653.3742.

Ethyl (2*E*,4*S*)-5-{3,4-Bis[*tert*-butyl(dimethyl)silyloxy]phenyl}-4-hydroxypent-2-enoate [(*S*)-11a]; Typical Procedure

K_2CO_3 (1.28 g, 9.26 mmol) was added to a soln of (*S*)-**10a** (1.21 g, 2.31 mmol) in EtOH (46 mL), and the mixture was stirred for 4 h. The reaction was quenched with H_2O (50 mL), and the mixture was extracted with EtOAc (200 mL). The organic layer was washed with H_2O (90 mL) and brine (90 mL), dried (Na_2SO_4), and filtered. The filtrate was concentrated in vacuo, and the residual oil was purified by column chromatography [silica gel, hexane–EtOAc (4:1)] to give a colorless oil; yield: 795 mg (72%); R_f = 0.46 (hexane–EtOAc, 7:3); $[\alpha]_D^{28}$ –0.8 (*c* 1.11, $CHCl_3$).

ATR-IR (neat): 3456 (OH), 2955, 2930, 2896, 2858, 1721 (OC=O), 1657, 1605, 1576, 1509, 1472, 1463, 1421, 1390, 1364, 1295, 1271, 1252, 1229, 1159, 1125, 1097, 1040, 981, 905, 836, 778, 695, 666 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99 (dd, J = 15.7 and 4.5 Hz, 1 H, H-3), 6.78 (d, J = 8.0 Hz, 1 H, Ar-H), 6.68 (d, J = 2.1 Hz, 1 H, Ar-H), 6.65 (dd, J = 8.0 and 2.1 Hz, 1 H, Ar-H), 6.05 (dd, J = 15.7 and 1.7 Hz, 1 H, H-2), 4.45 (br q, J = 3.5 Hz, 1 H, H-4), 4.20 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 2.84 (one of AB, dd, J = 13.7 and 4.9 Hz, 1 H, H-5), 2.67 (one of AB, dd, J = 13.7 and 8.2 Hz, 1 H, H-5), 1.81 (br d, J = 4.1 Hz, 1 H, OH), 1.29 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 0.982 (s, 9 H, *t*-Bu), 0.981 (s, 9 H, *t*-Bu), 0.191 [s, 6 H, $Si(CH_3)_2$], 0.186 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4, 148.8, 146.9, 146.0, 129.5, 122.4, 122.3, 121.2, 120.6, 71.8, 60.4, 42.6, 25.9, 18.4, 14.2, –3.8, –4.1.

MS (ESI): *m/z* (%) = 503 (93) $[M + Na]^+$, 498 (62) $[M + H_2O]^+$, 81 (100).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{45}O_5Si_2$: 481.2800; found: 481.2802.

Ethyl (2*E*,4*S*)-5-{3-[*tert*-Butyl(dimethyl)silyloxy]phenyl}-4-hydroxypent-2-enoate [(*S*)-11b]

Colorless oil; yield: 74%; R_f = 0.44 (hexane–EtOAc, 3:1); $[\alpha]_D^{27}$ –1.5 (*c* 1.12, $CHCl_3$).

ATR-IR (neat): 3454 (OH), 2956, 2930, 2897, 2858, 1719 (C=O), 1702, 1657, 1602, 1584, 1486, 1472, 1464, 1442, 1390, 1367, 1304, 1271, 1253, 1157, 1098, 1039, 1003, 975, 939, 887, 836, 779, 707, 694, 665 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18 (t, J = 7.8 Hz, 1 H, H-5′), 7.00 (dd, J = 15.7 and 4.5 Hz, 1 H, H-3), 6.81 (d, J = 7.5 Hz, 1 H, H-6′), 6.76–6.70 (m, 2 H, H-2′ and 4′), 6.06 (dd, J = 15.7 and 1.8 Hz, 1 H, H-2), 4.53–4.49 (m, 1 H, H-4), 4.20 (q, J = 7.1 Hz, 2 H,

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OCH_2CH$_3$), 2.90 (one of ABqd, J = 4.8 Hz, $J_{A,B}$ = 13.6 Hz, 1 H, H-5), 2.73 (one of ABqd, J = 8.4 Hz, $J_{A,B}$ = 13.6 Hz, 1 H, H-5), 1.78 (br d, J = 3.4 Hz, 1 H, OH), 1.29 (t, J = 7.1 Hz, 3 H), 0.98 (s, 9 H, *t*-Bu), 0.19 [s, 6 H, Si(CH$_3$)$_2$].

^{13}C NMR (100 MHz, CDCl$_3$): δ = 166.4, 156.0, 148.7, 138.2, 129.7, 122.4, 121.2, 120.7, 118.7, 71.7, 60.4, 43.2, 25.7, 18.2, 14.3, –4.4.

MS (ESI): *m/z* (%) = 389 (10) [M + K]$^+$, 373 (23) [M + Na]$^+$, 368 (14) [M + H$_2$O]$^+$, 351 (3) [M + H]$^+$, 333 (55), 259 (13), 73 (100).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{30}NaO_4Si$: 373.1806; found: 373.1821.

Ethyl (2*E*,4*S*)-5-{3,5-bis[*tert*-butyl(dimethyl)silyloxy]phenyl}-4-hydroxypent-2-enoate [(*S*)-11c]

Colorless oil; yield: 75%; R_f = 0.35 (hexane–EtOAc, 4:1); [α]$_D^{28}$ –4.1 (*c* 1.00, CHCl$_3$).

ATR-IR (neat): 3465 (OH), 2956, 2930, 2887, 2858, 1721 (C=O), 1657, 1587, 1472, 1450, 1390, 1363, 1338, 1306, 1252, 1158, 1097, 1035, 1005, 936, 855, 828, 813, 778, 743, 717, 698, 676 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.97 (dd, J = 15.6 and 4.5 Hz, 1 H, H-3), 6.33, (d, J = 2.1 Hz, 2 H, H-2′ and 6′), 6.24 (t, J = 2.1 Hz, 1 H, H-4′), 6.05 (dd, J = 15.7 and 1.7 Hz, 1 H, H-2), 4.49–4.45 (m, 1 H, H-4), 4.19 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 2.83 (one of ABqd, J = 4.8 Hz, $J_{A,B}$ = 13.5 Hz, 1 H, H-5), 2.66 (one of ABqd, J = 8.3 Hz, $J_{A,B}$ = 13.5 Hz, 1 H, H-5), 1.80 (br d, J = 4.2 Hz, 1 H, OH), 1.29, (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3), 0.97 (s, 18 H, *t*-Bu), 0.18 [s, 12 H, Si(CH$_3$)$_2$].

^{13}C NMR (100 MHz, CDCl$_3$): δ = 166.4, 156.8, 148.6, 138.5, 120.7, 114.6, 110.8, 71.6, 60.4, 43.2, 25.7, 18.2, 14.2, –4.4.

MS (ESI): *m/z* (%) = 519 (15) [M + K]$^+$, 503 (22) [M + Na]$^+$, 481 (100) [M + H]$^+$.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{25}H_{45}O_5Si_2$: 481.2800; found: 481.2809.

Ethyl (2*E*,4*S*)-4-Hydroxy-5-{3,4,5-tris[*tert*-butyl(dimethyl)silyloxy]phenyl}pent-2-enoate [(*S*)-11d]

White powder; yield: 83%; mp = 91–92 °C (hexane–EtOAc); R_f = 0.34 (hexane–EtOAc, 4:1); [α]$_D^{27}$ –0.3 (*c* 0.98, CHCl$_3$).

ATR-IR (neat): 2954, 2930, 2896, 2858, 1746 (OAc), 1725 (ethyl ester), 1663, 1574, 1493, 1472, 1464, 1431, 1391, 1362, 1307, 1252, 1227, 1200, 1174, 1084, 1047, 1005, 977, 938, 893, 827, 779, 737, 705, 670 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.95 (dd, J = 15.7 and 4.6 Hz, 1 H, H-3), 6.34 (s, 2 H, H-2′ and 6′), 6.02 (dd, J = 15.7 and 1.7 Hz, 1 H, H-2), 4.42–4.39 (m, 1 H, H-4), 4.19 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 2.76 (one of ABqd, J = 5.2 Hz, $J_{A,B}$ = 13.6 Hz, 1 H, H-5), 2.61 (one of ABqd, J = 7.9 Hz, $J_{A,B}$ = 13.6 Hz, 1 H, H-5), 1.78 (d, J = 4.2 Hz, 1 H, OH), 1.28 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3), 0.98 (s, 9 H, *t*-Bu), 0.93 (s, 18 H, *t*-Bu), 0.20 [s, 12 H, Si(CH$_3$)$_2$], 0.11 [s, 6 H, Si(CH$_3$)$_2$].

^{13}C NMR (100 MHz, CDCl$_3$): δ = 3482 (OH), 2953, 2930, 2859, 2858, 1698 (C=O), 1653, 1572, 1489, 1473, 1463, 1429, 1390, 1352, 1323, 1301, 1274, 1250, 1226, 1197, 1176, 1166, 1155, 1093, 1068, 1047, 1033, 999, 977, 956, 940, 887, 869, 854, 829, 778, 743, 706, 672.

MS (ESI): *m/z* (%) = 649 (14) [M + K]$^+$, 633 (41) [M + Na]$^+$, 611 (100) [M + H]$^+$.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{31}H_{59}O_6Si_3$: 611.3614; found: 611.3615.

Ethyl (4*R*)-5-{3,4-Bis[*tert*-butyl(dimethyl)silyloxy]phenyl}-4-hydroxypentanoate [(*R*)-12a]; Typical Procedure

A mixture of ester (*S*)-**11a** (795 mg, 1.65 mmol) and 10% Pd/C (65 mg) in EtOAc (16 mL) was stirred for 2 h at r.t. under H_2 (1 atm). The mixture was filtered and concentrated in vacuo to give a residual oil that was purified by column chromatography [silica gel, hexane–EtOAc, (4:1)] to give a colorless oil; yield: 662 mg (83%); R_f = 0.44 (hexane–EtOAc, 7:3); [α]$_D^{26}$ –0.3 (*c* 1.08, CHCl$_3$).

ATR-IR (neat): 3455 (OH), 2955, 2930, 2896, 2858, 1735 (C=O), 1605, 1575, 1509, 1472, 1463, 1420, 1390, 1362, 1295, 1252, 1221, 1158, 1125, 1070, 1031, 1007, 981, 906, 836, 778, 695, 666 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.76 (d, J = 8.1 Hz, 1 H, H-2′), 6.67 (d, J = 2.1 Hz, 1 H, H-5′), 6.64 (dd, J = 8.1 and 2.1 Hz, 1 H, H-6′), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.79–3.74 (m, 1 H, H-4), 2.69 (one of ABqd, J = 4.6 Hz, $J_{A,B}$ = 13.6 Hz, 1 H, H-5), 2.56 (one of ABqd, J = 8.2 Hz, $J_{A,B}$ = 13.6 Hz, 1 H, H-5), 2.52–2.42 (m, 2 H, H-2), 1.90–1.84 (m, 1 H, H-3), 1.81 (br d, J = 3.8 Hz, 1 H, OH), 1.78–1.71 (m, 1 H, H-3), 1.25 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3), 0.98 (s, 18 H, *t*-Bu), 0.19 [s, 12 H, Si(CH$_3$)$_2$].

^{13}C NMR (100 MHz, CDCl$_3$): δ = 174.0, 146.8, 145.6, 131.0, 122.3, 122.2, 121.1, 72.0, 60.4, 43.4, 31.4, 30.9, 25.9, 18.4, 14.2, –4.06, –4.09.

MS (ESI): *m/z* (%) = 521 (30) [M + K]$^+$, 505 (100) [M + Na]$^+$, 465 (60).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{25}H_{46}O_5Si_2Na$: 505.2776; found: 505.2767.

Ethyl (4*R*)-5-{3-[*tert*-Butyl(dimethyl)silyloxy]phenyl}-4-hydroxypentanoate [(*R*)-12b]

Colorless oil; yield: 90%; R_f = 0.72 (hexane–EtOAc, 1:1); [α]$_D^{26}$ –1.8 (*c* 1.10, CHCl$_3$).

ATR-IR (neat): 3455 (OH), 2955, 2930, 2858, 1733 (C=O), 1602, 1584, 1485, 1472, 1463, 1442, 1390, 1373, 1348, 1252, 1157, 1083, 1069, 1031, 1003, 973, 939, 882, 836, 779, 711, 695, 665 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.16 (t, J = 7.7 Hz, 1 H, H-5′), 6.80 (d, J = 7.6 Hz, 1 H, H-6′), 6.73–6.70 (m, 2 H, H-2′ and 4′), 4.14 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.83 (octet, J = 4.1 Hz, 1 H, H-4), 2.76 (one of ABqd, J = 4.6 Hz, $J_{A,B}$ = 13.5 Hz, 1 H, H-5), 2.65 (one of ABqd, J = 8.2 Hz, $J_{A,B}$ = 13.5 Hz, 1 H, H-5), 2.54–2.43 (m, 2 H, H-2), 1.94–1.86 (m, 1 H, H-3), 1.84 (br d, J = 4.0 Hz, 1 H, OH), 1.80–1.71 (m, 1 H, H-3), 1.25 (t, J = 7.1 Hz, 3 H, OCH$_2$CH_3), 0.98 (s, 9 H, *t*-Bu), 0.19 [s, 6 H, Si(CH$_3$)$_2$].

^{13}C NMR (100 MHz, CDCl$_3$): δ = 174.0, 155.9, 139.6, 129.6, 122.3, 121.2, 118.3, 72.0, 60.5, 44.1, 31.5, 30.9, 25.7, 18.2, 14.2, –4.4.

MS (ESI): *m/z* (%) = 391 (12) [M + K]$^+$, 375 (42) [M + Na]$^+$, 353 (32) [M + H]$^+$, 335 (18), 81 (71), 73 (100).

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{32}NaO_4Si$: 375.1962; found: 375.1954.

Ethyl (4*R*)-5-{3,5-Bis[*tert*-butyl(dimethyl)silyloxy]phenyl}-4-hydroxypentanoate [(*R*)-12c]

Colorless oil; yield: 91%; R_f = 0.38 (hexane–EtOAc, 3:1); [α]$_D^{28}$ –1.1 (*c* 1.02, CHCl$_3$).

ATR-IR (neat): 3465 (OH), 2955, 2930, 2897, 2858, 1736 (C=O), 1586, 1472, 1449, 1390, 1362, 1335, 1252, 1158, 1068, 1014, 1005, 939, 854, 828, 814, 778, 743, 699, 676 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ = 6.32 (d, J = 2.2 Hz, 2 H, H-2′ and 6′), 6.22 (t, J = 2.2 Hz, 1 H, H-4′), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2CH$_3$), 3.79 (octet, J = 4.0 Hz, 1 H, H-4), 2.69 (one of ABqd, J = 4.6 Hz, $J_{A,B}$ = 13.4 Hz, 1 H, H-5), 2.57 (one of ABqd, J = 8.2 Hz, $J_{A,B}$ = 13.4 Hz, 1 H, H-5), 2.52–2.41 (m, 2 H, H-2), 1.92–1.86 (m, 1 H, H-3), 1.84 (br d, J = 3.9 Hz, 1 H, OH), 1.79–1.70 (m, 1 H,

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H-3), 1.25 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 0.97 (s, 18 H, *t*-Bu), 0.18 [s, 12 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0, 156.7, 140.0, 114.5, 110.4, 71.9, 60.5, 44.1, 31.5, 30.9, 25.7, 18.2, 14.2, –4.4.

MS (ESI): *m/z* (%) = 521 (10) $[M + K]^+$, 505 (20) $[M + Na]^+$, 483 (100) $[M + H]^+$, 437 (6).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{25}H_{47}O_5Si_2$: 483.2957; found: 483.2963.

Ethyl (4*R*)-4-Hydroxy-5-{3,4,5-tris[*tert*-butyl(dimethyl)silyloxy]phenyl}pentanoate [(*R*)-12d]

White powder; yield: 97%; mp = 45–46 °C (hexane–EtOAc); R_f = 0.44 (hexane–EtOAc, 3:1); $[\alpha]_D^{27}$ +0.8 (*c* 1.05, $CHCl_3$).

ATR-IR (neat): 3518 (OH), 2953, 2930, 2896, 2858, 1736, 1574, 1493, 1472, 1463, 1429, 1390, 1345, 1252, 1230, 1182, 1151, 1084, 1005, 939, 895, 857, 827, 778, 738, 707, 669 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.33 (s, 2 H, H-2′ and 6′), 4.13 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 3.73 (octet, J = 3.8 Hz, 1 H, H-4), 2.62 (one of ABqd, J = 4.8 Hz, $J_{A,B}$ = 13.5 Hz, 1 H, H-5), 2.52–2.39 (m, 3 H, H-2 and 5), 1.90–1.82 (m, 1 H, H-3), 1.81 (d, J = 3.8 Hz, 1 H, OH), 1.77–1.67 (m, 1 H, H-3), 1.25 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 0.98 (s, 9 H, *t*-Bu), 0.92 (s, 18 H, *t*-Bu), 0.20 [s, 12 H, $Si(CH_3)_2$], 0.11 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.0, 148.7, 137.0, 129.7, 115.3, 72.1, 60.4, 43.7, 31.3, 30.9, 26.2(2), 26.1(8), 18.8, 18.4, 14.2, –3.6, –4.0.

MS (ESI): *m/z* (%) = 651 (6) $[M + K]^+$, 635 (30) $[M + Na]^+$, 613 (100) $[M + H]^+$, 595 (8), 567 (6).

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{31}H_{61}O_6Si_3$: 613.3771; found: 613.3777.

(5*R*)-5-(3,4-Dihydroxybenzyl)dihydrofuran-2(3*H*)-one [(*R*)-5a]; Typical Procedure

A mixture of ester (*R*)-**12a** (661 mg, 1.37 mmol), $TsOH·H_2O$ (1.30 g, 6.84 mmol), and 4-Å MS (200 mg) in benzene (30 mL) was refluxed for 4 h then cooled to r.t. The mixture was then filtered and concentrated in vacuo to give a residue that was purified by column chromatography [silica gel, toluene–EtOAc (3:2)] to give a white powder; yield: 247 mg (87%); mp = 150–151 °C (toluene–EtOAc); R_f = 0.07 (toluene–EtOAc, 3:1); $[\alpha]_D^{28}$ –16.7 (*c* 0.70, MeOH).

ATR-IR (neat): 3318 (OH), 3041, 2945. 2910, 1709 (OC=O), 1620, 1599, 1519, 1470, 1418, 1341, 1287, 1231, 1194, 1150, 1110, 1088, 1014, 987, 926, 905, 870, 844, 815, 804, 788, 752, 729 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 6.69 (d, J = 8.0 Hz, 1 H, H-5′), 6.68 (d, J = 1.9 Hz, 1 H, H-2′), 6.55 (dd, J = 8.0 and 2.1 Hz, 1 H, H-6′), 4.71 (quint, J = 6.5 Hz, 1 H, H-4), 2.86 (one of ABqd, J = 6.1 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 2.78 (one of ABqd, J = 6.1 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 2.47 (ddd, J = 8.9, 9.7, 17.6 Hz, 1 H, H-2), 2.32 (ddd, J = 4.8, 9.5, 17.7 Hz, 1 H, H-2), 2.22 (dddd, J = 4.8, 6.8, 9.8, 12.6 Hz, 1 H, H-3), 1.95 (dddd, J = 7.3, 8.9, 9.4, 12.6 Hz, 1 H, H-3).

^{13}C NMR (100 MHz, CD_3OD): δ = 180.5 (C-1), 146.5 (C-3′), 145.4 (C-4′), 129.3 (C-1′), 122.1 (C-6′), 117.9 (C-5′), 116.6 (C-2′), 83.5 (C-4), 41.7 (C-5), 29.7 (C-2), 28.1 (C-3).

MS (ESI): *m/z* (%) = 439 (42) $[2M + Na]^+$, 417 (14) $[2M + H]^+$, 231 (95) $[M + Na]^+$, 209 (100) $[M + H]^+$. 439 (42) $[2M + Na]^+$, 417 (14) $[2M + H]^+$, 231 (95) $[M + Na]^+$, 209 (100) $[M + H]^+$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{11}H_{13}O_4$: 209.0808 found: 209.0826.

(5*R*)-5-(3-Hydroxybenzyl)dihydrofuran-2(3*H*)-one [(*R*)-5b]

White powder; yield: 81%; R_f = 0.41 (hexane–EtOAc, 1:1); $[\alpha]_D^{26}$ –29.2 (*c* 1.00, MeOH).

ATR-IR (neat): 3309 (OH), 3036, 2964, 2933, 1741, 1722, 1615, 1588, 1488, 1417, 1385, 1363, 1347, 1293, 1280, 1250, 1225, 1208, 1196, 1173, 1155, 1148, 1076, 1065, 1018, 992, 944, 926, 901, 877, 841, 804, 790, 750, 696 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 7.10 (t, J = 7.8 Hz, 1 H, H-5′), 6.72 (dd, J = 1.5, 7.6 Hz, 1 H, H-6′), 6.69 (dd, J = 1.5, 2.1 Hz, 1 H, H-2′), 6.66 (ddd, J = 0.8, 2.5, 8.1 Hz, 1 H, H-4′), 4.76 (quint, 6.8 Hz, 1 H, H-4), 2.95 (one of ABqd, J = 6.5 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.87 (one of ABqd, J = 6.0 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.51 (ddd, J = 9.1, 9.7, 17.7 Hz, 1 H, H-2), 2.32 (ddd J = 4.5, 9.5, 17.7 Hz, 1 H, H-2), 2.26 (dddd, J = 4.8, 6.8, 9.7, 12.7 Hz, 1 H, H-3), 1.95 (dtd, J = 7.5, 9.2, 12.7 Hz, 1 H, H-3).

^{13}C NMR (100 MHz, CD_3OD): δ = 180.1 (C-1), 158.6 (C-3′), 139.3 (C-1′), 130.5 (C-5′), 121.7 (C-6′), 117.4 (C-2′), 114.7 (C-4′), 83.0 (C-4), 42.1 (C-5), 29.5 (C-2), 28.1 (C-3).

MS (ESI): *m/z* (%) = 407 (18) $[2M + Na]^+$, 385 (15) $[2M + H]^+$, 215 (49) $[M + Na]^+$, 193 (100) $[M + H]^+$.

HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{11}H_{12}O_3Na$: 215.0679; found: 215.0671.

(5*R*)-5-(3,5-Dihydroxybenzyl)dihydrofuran-2(3*H*)-one [(*R*)-5c]

Amorphous powder; yield: 83%; R_f = 0.38 (toluene–EtOAc, 2:3); $[\alpha]_D^{27}$ –20.6 (*c* 0.97, MeOH).

ATR-IR (neat): 3322, 2950, 1744, 1597, 1506, 1480, 1454, 1416, 1337, 1304, 1287, 1224, 1186, 1143, 998, 927, 836, 802, 721, 695 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ = 6.20 (d, J = 2.2 Hz, 2 H, H-2′ and 6′), 6.16 (t, J = 2.2 Hz, 1 H, H-4′), 4.72 (quint, J = 6.5 Hz, 1 H, H-4), 2.86 (one of ABqd, J = 6.4 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.78 (one of ABqd, J = 6.0 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.49 (ddd, J = 9.2, 9.5, 17.8 Hz, 1 H, H-2), 2.38 (ddd, J = 4.7, 9.5, 17.8 Hz, 1 H, H-2), 2.24 (dddd, J = 4.7, 6.8, 9.7, 12.7 Hz, 1 H, H-3), 1.94 (dtd, J = 7.5, 9.2, 12.8 Hz, 1 H, H-3).

^{13}C NMR (100 MHz, CD_3OD): δ = 180.5 (C-1), 159.8 (C-3′,5′), 140.1 (C-1′), 109.18 (C-2′,6′), 102.2 (C-4′), 83.2 (C-4), 42.4 (C-5), 29.7 (C-2), 28.3 (C-3).

MS (ESI): *m/z* (%) = 231 (62) $[M + Na]^+$, 226 (100) $[M + H_2O]^+$, 209 (93) $[M + H]^+$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{11}H_{13}O_4$: 209.808; found: 209.0802.

(5*R*)-5-{3,4,5-Tris[*tert*-butyl(dimethyl)silyloxy]phenyl}dihydrofuran-2(3*H*)-one [(*R*)-13]

A mixture of ester (*R*)-**12d** (1.36 g, 2.22 mmol) and PPTS (669 mg, 2.66 mmol) in benzene (44 mL) was refluxed for 1 h with azeotropic removal of EtOH. The mixture was cooled to 0 °C and surplus PPTS was removed by filtration. The filtrate was concentrated in vacuo to give a residue that was purified by column chromatography [silica gel, hexane–EtOAc (4:1)] to give white crystals; yield: 1.24 g (98%); mp = 69.5–71.0 °C (hexane–EtOAc); R_f = 0.59 (toluene–EtOAc, 4:1); $[\alpha]_D^{28}$ +1.6 (*c* 1.04, $CHCl_3$).

ATR-IR (neat): 2955, 2930, 2896, 2858, 1767, 1570, 1494, 1473, 1463, 1430, 1381, 1360, 1341, 1316, 1255, 1235, 1199, 1170, 1143, 1093, 1044, 1004, 940, 920, 893, 835, 826, 780, 759, 735, 692, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.34 (s, 2 H, H-2′ and 6′), 4.62 (quint, J = 6.7 Hz, 1 H, H-4), 2.93 (one of ABqd, J = 5.5 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.69 (one of ABqd, J = 7.0 Hz, $J_{A,B}$ = 13.9 Hz, 1 H, H-5), 2.47 (td, J = 9.3, 17.7 Hz, 1 H, H-2), 2.40 (ddd, J = 4.8, 9.3, 17.7 Hz, 1 H, H-2), 2.17 (dddd, J = 4.8, 6.7, 9.3,

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12.8 Hz, 1 H, H-3), 1.90 (dtd, *J* = 7.8, 9.4, 12.8 Hz, 1 H, H-3), 0.98 (s, 9 H, *t*-Bu), 0.93 (s, 18 H, *t*-Bu), 0.20 [s, 12 H, $Si(CH_3)_2$], 0.11 [s, 6 H, $Si(CH_3)_2$].

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.9 (C-1), 148.6 (C-3′,5′), 137.3 (C-4′), 127.5 (C-1′), 115.4 (C-2′,6′), 80.9 (C-4), 40.7 (C-5), 28.7 (C-2), 27.0 (C-3), 26.21, 26.16, 18.8, 18.4, –3.9, –4.0.

MS (ESI): *m/z* (%) = 605 (25) $[M + K]^+$, 589 (48) $[M + Na]^+$, 584 (68) $[M + H_2O]^+$, 567 (100) $[M + H]^+$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{29}H_{55}O_5Si_3$: 567.3352; found: 567.3381.

(5*R*)-5-(3,4,5-Trihydroxyphenyl)dihydrofuran-2(3*H*)-one [(*R*)-5d]

A soln of (*R*)-**13** (199 mg, 0.35 mmol) and concd HCl (7 mL) in THF (10 mL) and MeOH (2 mL) was stirred at 0 °C for 2 h and then at r.t. for 4 h. The mixture was concentrated in vacuo and the residue was diluted with H_2O (5 mL) and extracted with EtOAc (30 mL). The organic layer was washed with brine, dried (Na_2SO_4), and filtered. The filtrate was concentrated in vacuo and the residue was purified by column chromatography [silica gel, toluene–EtOAc (1:1)]; to give a powder; yield: 68 mg (87%); mp = 142–143 °C (toluene–EtOAc); R_f = 0.33 (toluene–EtOAc, 3:7); $[\alpha]_D^{27}$ –12.6 (*c* 0.99, MeOH).

ATR-IR (neat): 3422 (OH), 2955, 2926, 2867, 1724 (C=O), 1614, 1536, 1523, 1504, 1455, 1412, 1355, 1304, 1277, 1224, 1191, 1152, 1099, 1078, 1013, 989, 940, 898, 857, 827, 802, 773, 757, 729, 720, 673, 660 cm^{-1}.

^{1}H NMR (400 MHz, CD_3OD): δ = 6.24 (s, 2 H, H-2′ and 6′), 4.70 (quint, *J* = 6.6 Hz, 1 H, H-4), 2.81 (one of ABqd, *J* = 6.0 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 2.71 (one of ABqd, *J* = 6.2 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 2.48 (ddd, *J* = 8.9, 9.7, 17.7 Hz, 1 H, H-2), 2.33 (ddd, *J* = 4.8, 9.5, 17.7 Hz, 1 H, H-2), 2.23 (dddd, *J* = 4.8, 6.8, 9.7, 12.8 Hz, 1 H, H-3), 1.95 (dtd, *J* = 7.3, 9.1, 12.8 Hz, 1 H, H-3).

^{13}C NMR (100 MHz, CD_3OD): δ = 180.6 (C-1), 147.2 (C-3′,5′), 133.2 (C-4′), 128.6 (C-1′), 109.7 (C-2′,6′), 83.5 (C-4), 41.9 (C-5), 29.7 (C-2), 28.1 (C-3).

MS (ESI): *m/z* (%) = 471 (42) $[2M + Na]^+$, 449 (14) $[2M + H]^+$, 247 (95) $[M + Na]^+$, 225 (100) $[M + H]^+$.

HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{11}H_{13}O_5$: 225.0758; found: 225.0771.

3-[(2*R*)-(5-Oxotetrahydrofuran-2-yl)methyl]phenyl (2*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoate [(*R*,*S*)-14]; Typical Procedure

(*S*)-PhC(OMe)(CF_3)COCl (29.7 mg, 0.122 mmol) was added to a soln of lactone **5b** (11.7 mg, 0.061 mmol), Et_3N (33.4 mg, 0.366 mmol), and DMAP (0.6 mg, 0.005 mmol) in CH_2Cl_2 (1 mL) at 0 °C, and the mixture was stirred for 1 h at r.t. The reaction was quenched with H_2O (2 mL) and extracted with EtOAc (20 mL). The combined organic layer was washed with H_2O and brine, dried (Na_2SO_4), filtered, and concentrated in vacuo. The residual oil was purified by preparative TLC (hexane–EtOAc, 1:1) to give a colorless oil; yield: 23.8 mg (98%); R_f = 0.45 (hexane–EtOAc, 1:1).

^{1}H NMR (400 MHz, C_6D_6): δ = 7.78 (d, *J* = 7.8 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 2 H), 7.07 (t, *J* = 7.2 Hz, 1 H, H-5′), 6.93 (t, *J* = 7.5 Hz, 1 H), 6.85 (s, 1 H, H-2′), 6.84 (d, *J* = 7.3 Hz, 1 H, H-6′), 6.74 (d, *J* = 7.4 Hz, 1 H, H-4′), 3.79 (quint, 7.6 Hz, 1 H, H-4), 3.49 (s, 3 H), 2.39 (one of ABqd, *J* = 6.5 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 2.18 (one of ABqd, *J* = 5.8 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 1.73 (ddd, *J* = 4.7, 9.6, 17.4 Hz, 1 H, H-2), 1.65 (td, *J* = 9.3, 17.4 Hz, 1 H, H-2), 1.12 (dddd, *J* = 4.8, 6.6, 9.1, 12.7 Hz, 1 H, H-3), 0.93 (dtd, *J* = 7.9, 9.5, 12.7 Hz, 1 H, H-3).

^{13}C NMR (100 MHz, C_6D_6): δ = 175.7 (C-1), 165.8, 150.9, 139.2, 132.9, 130.4, 130.2, 129.3, 129.0, 127.7, 124.6 (q, *J* = 286 Hz), 122.6, 120.1, 85.8 (q, *J* = 28.0 Hz), 79.5 (C-4), 55.9, 41.2 (C-5), 28.7 (C-2), 27.2 (C-3).

3-[(2*S*)-(5-Oxotetrahydrofuran-2-yl)methyl]phenyl (2*R*)-3,3,3-Trifluoro-2-methoxy-2-phenylpropanoate [(*S*,*S*)-14]

^{1}H NMR (400 MHz, C_6D_6): δ = 7.78 (d, *J* = 7.8 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 2 H), 7.07 (t, *J* = 7.2 Hz, 1 H, H-5′), 6.94 (t, *J* = 7.5 Hz, 1 H), 6.86 (s, 1 H, H-2′), 6.85 (d, *J* = 7.3 Hz, 1 H, H-6′), 6.76 (d, *J* = 7.5 Hz, 1 H, H-4′), 3.79 (quint, 6.4 Hz, 1 H, H-4), 3.49 (s, 3 H), 2.41 (one of ABqd, *J* = 6.7 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 2.12 (one of ABqd, *J* = 5.8 Hz, $J_{A,B}$ = 14.0 Hz, 1 H, H-5), 1.75 (ddd, *J* = 4.5, 9.4, 17.6 Hz, 1 H, H-2), 1.67 (td, *J* = 9.3, 17.4 Hz, 1 H, H-2), 1.14 (dddd, *J* = 4.6, 6.5, 9.3, 12.6 Hz, 1 H, H-3), 0.94 (dtd, *J* = 7.8, 9.4, 12.6 Hz, 1 H, H-3).

^{13}C NMR (100 MHz, C_6D_6): δ = 175.7 (C-1), 165.8, 150.9, 139.3, 132.9, 130.4, 130.2, 129.3, 129.0, 127.7, 124.6 (q, *J* = 286 Hz), 122.6, 120.1, 85.8 (q, *J* = 28.0 Hz), 79.7 (C-4), 55.9, 41.3 (C-5), 28.7 (C-2), 27.4 (C-3).

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(21) (*S*)-**5b** was prepared from (*R*)-**7** by a similar procedure to that used to prepare (*R*)-**5b**.
(22) The ^{13}C NMR chemical shifts for the C3, C4 and C5 atoms are observed at δ = 27.23, δ = 79.52, and δ = 41.21, respectively, for (*R*,*S*)-**14** and at δ = 27.36, δ = 79.66, and δ = 41.31, respectively, for (*S*,*S*)-**14**.

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