

SUPPLEMENTARY MATERIAL

Synthesis of (-)-Conocarpan by Two Routes Based on Radical Cyclization and Establishment of its Absolute Configuration†

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Toluene-4-sulfonic Acid 4-[(1*E*)-3-Hydroxy-1-propenyl]phenyl Ester (22).

(a) (2*E*)-3-[4-(Toluene-4-sulfonyloxy)phenyl]-2-propenoic Acid Ethyl Ester.

(EtO)₂P(O)CH₂CO₂Et (11.6 mL, 58.47 mmol), followed by Et₃N (8.2 mL, 8.2 mmol), were added to a suspension of LiBr (5.27 g, 61.11 mmol) in THF (136 mL) and the mixture was stirred for 15 min. Toluene-4-sulfonic acid 4-formylphenyl ester⁵⁴ (13.69 g, 49.55 mmol) was then added in one portion and stirring was continued for 4 h. Et₂O (250 mL) was added and the organic layer was washed with water, saturated aqueous Na₂CO₃ and brine, dried (MgSO₄) and evaporated. The residue was dissolved in EtOH (150 mL) and, after a few min, the product [(2*E*)-3-[4-(toluene-4-sulfonyloxy)phenyl]-2-propenoic acid ethyl ester] crystallized and was collected. A second crop was obtained when the filtrate was allowed to stand for several h. The total product, which was a white crystalline solid, weighed 13.88 g (81%): mp 75-78 °C; ¹H NMR (CDCl₃, 400 MHz) δ 1.35 (t, *J* = 7.1 Hz, 3 H), 2.47 (s, 3 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 6.38 (d, *J* = 16.1 Hz, 1 H), 7.02 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.33 (apparent d as part of AA'BB' system, *J* = 8.1 Hz, 2 H), 7.45 (apparent d as part of AA'BB' system, *J* = 8.8 Hz, 2 H), 7.62 (d, *J* = 16.1 Hz, 1 H), 7.73 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H); ¹³C NMR (CDCl₃, 100 MHz) (in this spectrum two signals are coincident) δ 14.3 (q), 21.7 (q), 60.6 (t), 119.3 (d), 122.9 (d), 128.5 (d), 129.2 (d), 129.8 (d), 132.3 (s), 133.4 (s), 142.8 (d), 145.6 (s), 150.7 (s), 166.6 (s); ν_{max} (CH₂Cl₂ cast; cm⁻¹) 3068, 2982, 1710, 1415, 1200, 1177; exact mass *m/z* calcd for C₁₈H₁₈O₅S 346.08749, found 346.08836. Anal. Calcd for C₁₈H₁₈O₅S: C 62.40; H 5.24; S 9.26. Found: C 62.38; H 5.10; S 9.10.

(b) Toluene-4-sulfonic Acid 4-[(1E)-3-Hydroxy-1-propenyl]phenyl Ester (22).

A three-necked flask was equipped with a stopper, a septum, a magnetic stirring bar and an addition funnel. The flask was charged with (2E)-3-[4-(toluene-4-sulfonyloxy)phenyl]-2-propenoic acid ethyl ester from the previous experiment (20.20 g, 58.32 mmol) and THF (200 mL) was added. The resulting solution was cooled to 0 °C in an ice bath, and the addition funnel was charged with DIBAL-H (1 M in hexane, 128 mL), which was then added dropwise over 1 h with stirring. After the addition, stirring at 0 °C was continued for 1 h, and the mixture was then quenched by addition of aqueous NaOH (1 M, 50 mL). The aqueous layer was extracted with Et₂O (3 x 50 mL) and the combined organic extracts were washed with aqueous NaOH (1 M, 2 x 50 mL) and brine (1x 50 mL). The ethereal solution was allowed to stand overnight, during which time a precipitate formed. MgSO₄ and Celite were added and the mixture was filtered. Evaporation of the filtrate and flash chromatography of the residue over silica gel (5 x 30 cm), using 30-50% EtOAc-hexane (gradient elution), gave **22** (16.84 g, 95%) as a crystalline solid: mp 64-67 °C; ¹H NMR (CDCl₃, 400 MHz) δ 1.80 (br s, 1 H), 2.45 (s, 3 H), 4.31 (d, *J* = 5.1 Hz, 2 H), 6.30 (dt, *J* = 15.9, 5.5 Hz, 1 H), 6.56, (d, *J* = 16.0 Hz, 1 H), 6.92 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.27 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.31 (apparent dd as part of AA'BB' system, *J* = 8.6, 0.6 Hz, 2 H), 7.70 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 21.7 (q), 63.4 (t), 122.5 (d), 127.5 (d), 128.5 (d), 129.4 (d), 129.7 (d), 132.3 (s), 135.8 (s), 145.4 (s), 148.8 (s); ν_{max} (CHCl₃ cast; cm⁻¹) 3363, 2868, 1597, 1501, 1371, 1197; exact mass *m/z* calcd for C₁₆H₁₆O₄S 304.07693, found 304.07651.

4-Nitrobenzoic Acid 3-[(2R,3R)-4-(Toluene-4-sulfonyloxy)phenyl]oxiranylmethyl Ester (23a).

p-Nitrobenzoyl chloride (43.6 mg, 0.235 mmol) was added in one portion to a stirred solution of **23** (64.3 mg, 0.201 mmol) and Et₃N (0.04 mL, 0.3 mmol) in CH₂Cl₂ (3 mL). Stirring was continued for 2 h, and the mixture was then washed once with water, twice with saturated aqueous NaHCO₃, and dried (MgSO₄). Evaporation of the solvent and crystallization of the residue from MeOH gave **23a** (67.2 mg, 70%) as small white needles: mp 102-104 °C; [α]_D²² +20.42 (*c* 0.62, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 2.47 (s, 3 H), 3.37 (m, 1 H), 3.88 (d, *J* = 1.9 Hz, 1 H), 4.38 (dd, *J* = 12.4, 6.0 Hz, 1 H), 4.81 (dd, *J* = 12.3, 3.2 Hz, 1 H), 7.01 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.24 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.33 (apparent d as part of AA'BB' system, *J* = 8.1 Hz, 2 H), 7.72 (apparent d as part of

AA'BB' system, $J = 8.3$ Hz, 2 H), 8.27 (apparent d as part of AA'BB' system, $J = 8.9$ Hz, 2 H), 8.33 (apparent d as part of AA'BB' system, $J = 8.9$ Hz, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 21.7 (q), 55.8 (d), 59.2 (d), 65.3 (t), 122.7 (d), 123.6 (d), 126.9 (d), 128.5 (d), 129.8 (d), 130.9 (d), 132.3 (s), 134.8 (s), 134.9 (s), 145.5 (s), 149.7 (s), 150.8 (s), 164.4 (s); ν_{max} (CH_2Cl_2 cast; cm^{-1}) 3112, 3057, 2997, 2955, 2868, 1926, 1728, 1598, 1528, 1373; exact mass m/z calcd for $\text{C}_{23}\text{H}_{19}\text{NNaO}_8\text{S}$ 492.07236, found 492.07249. Anal. Calcd for $\text{C}_{23}\text{H}_{19}\text{NO}_8\text{S}$: C 58.84; H 4.08; S 6.83. Found: C 58.82; H 4.14; S 7.07.

A separate sample from a later and larger-scale experiment was crystallized from 7:3 EtOAc-hexane and gave large prisms which had $[\alpha]_{\text{D}}^{22} +20.22$ (c 0.70, CHCl_3). This nitrobenzoate was recrystallized again twice from EtOH, and the resulting material (total yield 62%) was used for the conocarpan synthesis by the second route.

Toluene-4-sulfonic acid 4-[(2*R*,3*R*)-(3-Hydroxymethyloxiranyl)]phenyl Ester (23b).

K_2CO_3 (1.90 g, 13.7 mmol) was added to a stirred solution of **23a** (crystallized several times, as described above, 5.46 g, 11.6 mmol) in 80% MeOH (100 mL). The mixture was stirred until a clear solution was obtained (ca 2.5 h). The MeOH was then evaporated, the residue was dissolved in EtOAc and the solution was washed three times with saturated aqueous NaHCO_3 and once with brine, and dried (MgSO_4). Evaporation of the solvent and flash chromatography of the residue over silica gel (2.5 x 40 cm), using first 50% EtOAc-hexane containing Et_3N (ca 3 drops/100 mL) and then 60% EtOAc-hexane containing Et_3N (ca 3 drops/100 mL), gave **23b** (3.618 g, 97%).

The hydrolysis was repeated on a small scale, using the same batch of **23a**, and HPLC analysis of the product [Chiralpak AD-RH (150 x 4.6 mm), 1:1 MeCN-water, flow 0.5 mL/min, detection at 232 nm. Baseline separation of a racemic sample] showed the enantiomeric ratio to be 98.9:1.1. The material had: $[\alpha]_{\text{D}}^{25} 18.35$ (c 0.75, CHCl_3); all other data are identical to those reported in this work for **23**.

Toluene-4-sulfonic Acid 4-[(1*S*,2*S*)-1-(4-Allyloxyphenoxy)-3-(*tert*-butyldimethylsilyloxy)-2-iodopropyl]phenyl Ester (26).

(a) Toluene-4-sulfonic Acid 4-[(1*S*,2*R*)-1-(4-Allyloxyphenoxy)-3-(*tert*-butyldimethylsilyloxy)-2-hydroxypropyl]phenyl Ester.

$t\text{-BuMe}_2\text{SiCl}$ (1.2628 g, 8.3780 mmol) was added in one portion to a stirred solution of **25** (3.4748 g, 7.3850 mmol) and imidazole (634.8 mg, 9.324 mmol) in CH_2Cl_2 (18 mL), and

stirring was continued for 2 h. The mixture was washed with water, dried (MgSO₄) and evaporated. Flash chromatography of the residue over silica gel (2.5 x 30 cm), using 20% EtOAc-hexane containing Et₃N (ca 3 drops/100 mL), gave toluene-4-sulfonic acid 4-[(1*S*,2*R*)-1-(4-allyloxyphenoxy)-3-(*tert*-butyldimethylsilyloxy)-2-hydroxypropyl]phenyl ester (4.1301 g, 96%) as a colorless oil: $[\alpha]_D^{22} +26.49$ (*c* 4.05, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 0.00 (s, 3 H), 0.02 (s, 3 H), 0.86 (s, 9 H), 2.35 (s, 3 H), 2.56 (d, *J* = 5.5 Hz, 1 H), 3.69 (dd, *J* = 4.3, 10.1 Hz, 1 H), 3.81 (dd, *J* = 5.2, 10.1 Hz, 1 H), 3.89 (ddd, *J* = 5.3, 5.3, 10.6 Hz, 1 H), 4.38 (ddd, *J* = 1.4, 1.4, 5.2 Hz, 2 H), 4.99 (d, *J* = 6.5 Hz, 1 H), 5.18 (apparent dd, *J* = 1.4, 10.6 Hz, 1 H), 5.31 (dddd, *J* = 1.6, 1.6, 1.6, 17.3 Hz, 1 H), 5.95 (dddd, *J* = 5.3, 5.3, 10.5, 17.2 Hz, 1 H), 6.66-6.71 (m, 4 H), 6.92 (d, *J* = 8.6 Hz, 2 H), 7.19 (d, *J* = 8.1 Hz, 2 H), 7.30 (d, *J* = 8.6 Hz, 2 H), 7.60 (d, *J* = 8.3 Hz, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ -5.4 (q), -5.4 (q), 18.2 (s), 21.6 (q), 25.9 (q), 63.3 (t), 69.3 (t), 74.3 (d), 79.9 (d), 115.5 (d), 117.0 (d), 117.4 (s), 122.2 (d), 128.4 (d), 128.7 (d), 129.7 (d), 132.3 (s), 133.5 (d), 137.6 (s), 145.3 (s), 149.2 (s), 151.7 (s), 153.1 (s); ν_{\max} (CH₂Cl₂ cast; cm⁻¹) 3553, 2953, 2929, 2884, 2857, 1598, 1505, 1376, 1223; exact mass *m/z* calcd for C₃₁H₄₀NaO₇SSi 607.21563, found 607.21550. Anal. Calcd for C₃₁H₄₀O₇SSi: C 63.67; H 6.89; S 5.48. Found: C 63.54; H 6.89; S 5.46.

(b) Toluene-4-sulfonic Acid 4-[(1*S*,2*S*)-1-(4-Allyloxyphenoxy)-3-(*tert*-butyldimethylsilyloxy)-2-iodopropyl]phenyl Ester (26).

Ph₃P (93.5 mg, 0.356 mmol) was added to a stirred solution of the above toluene-4-sulfonic acid 4-[(1*S*,2*R*)-1-(4-allyloxyphenoxy)-3-(*tert*-butyldimethylsilyloxy)-2-hydroxypropyl]phenyl ester (91.2 mg, 0.156 mmol) and imidazole (33.8 mg, 0.496 mmol) in PhMe (1.3 mL). I₂ (64.8 mg, 0.255 mmol) was then added in one portion and the mixture was refluxed for 1.5 h, cooled and diluted with EtOAc (6 mL). The resulting mixture was washed with water and brine, and dried (MgSO₄). (When performed on a larger scale, the crude reaction mixture was first washed with saturated aqueous Na₂S₂O₃ until both layers were colorless.) Evaporation of the solvent and flash chromatography of the residue over silica gel (1.5 x 30 cm), using 3-5% EtOAc-hexane containing Et₃N (ca 3 drops/100 mL) (gradient elution), gave **26** (97.0 mg, 89%) as a yellowish oil [(containing ca 6.5% of the *anti* diastereoisomer (¹H NMR)]: $[\alpha]_D^{22} +10.81$ (*c* 3.27, CH₂Cl₂); ¹H NMR (CDCl₃, 400 MHz) δ 0.00 (s, 3 H), 0.05 (s, 3 H), 0.89 (s, 9 H), 2.45 (s, 3 H), 3.80 (dd, *J* = 4.4, 10.5 Hz, 1 H), 4.00 (dd, *J* = 8.3, 10.5 Hz, 1 H), 4.22 (ddd, *J* = 4.2, 4.2, 8.3 Hz, 1 H), 4.46 (ddd, *J* = 1.3, 1.3, 5.3 Hz, 2 H), 5.07 (d, *J* = 4.0 Hz, 1 H), 5.26 (apparent dd, *J* = 1.3, 10.5 Hz, 1 H), 5.38 (apparent dd, *J* = 1.5, 17.3 Hz, 1 H), 6.03 (dddd, *J* = 5.3, 5.3, 10.5, 17.2 Hz, 1 H), 6.74-6.80 (m, 4 H), 6.89 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.29

(d, $J = 8.3$ Hz, 2 H), 7.31 (d, $J = 8.9$ Hz, 2 H), 7.67 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ -5.5 (q), -5.4 (q), 18.2 (s), 21.7 (q), 25.8 (q), 40.9 (d), 65.7 (t), 69.4 (t), 77.7 (d), 115.5 (d), 117.3 (d), 117.5 (s), 122.4 (d), 127.8 (d), 128.5 (d), 129.7 (d), 132.2 (s), 133.4 (d), 138.7 (s), 145.3 (s), 149.2 (s), 151.9 (s), 153.4 (s); ν_{max} (CH_2Cl_2 cast; cm^{-1}) 2953, 2929, 2857, 1598, 1504, 1377, 1254, 1200, 1177; exact mass m/z calcd for $\text{C}_{31}\text{H}_{39}\text{IO}_6\text{SSi}$ 717.11736, found 717.11724. Anal. Calcd for $\text{C}_{31}\text{H}_{39}\text{IO}_6\text{SSi}$: C 53.60; H 5.66; S 4.62. Found: C 53.98; H 5.53; S 4.77.

Toluene-4-sulfonic Acid 4-[(2*R*,3*S*)-3-(*tert*-Butyldimethylsilanyloxymethyl)-2,3-dihydro-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl Ester (33).

t-BuLi (1.7 M in pentane, 1.12 mL, 1.90 mmol) was added dropwise by syringe to a stirred and cooled (-5 °C) solution of (*E*)-1-bromo-1-propene (0.082 mL, 0.95 mmol) in dry hexane (2 mL). The mixture was stirred for 1 h 40 min, and then cooled to -78 °C. Stirring was continued for 15 min, and **28** (295.9 mg, 0.5296 mmol) in THF (4 mL plus 1 mL as a rinse) was added dropwise by syringe. Stirring was continued for 10 min, the cooling bath was removed, and stirring was continued for 15 min. The mixture was quenched by addition of saturated aqueous NaHCO_3 (2 mL), EtOAc (10 mL) was added and the aqueous phase was extracted once with EtOAc (6 mL). The combined organic extracts were washed with water and brine, dried (MgSO_4) and evaporated. The residue was dissolved in CH_2Cl_2 (8 mL), CSA (15 mg, 0.065 mmol) was added and the mixture was stirred for 30 min. Saturated aqueous NaHCO_3 (2 mL) was added, and the organic phase was washed with water and dried (MgSO_4). Evaporation of the solvent and flash chromatography of the residue over silica gel (1.5 x 30 cm), using 0-8% EtOAc-hexane (gradient elution), gave **33** (156.4 mg, 54%) as a colorless oil. The material was contaminated with ca 3% of the *Z* olefin (measured by integration of the allylic methyl peaks in the ^1H NMR spectrum) which was not separable from the desired *E* isomer. The material had: $[\alpha]_{\text{D}}^{22}$ -58.74 (c 2.45, CHCl_3); ^1H NMR (CDCl_3 , 400 MHz) δ 0.05 (s, 3 H), 0.07 (s, 3 H), 0.90 (s, 9 H), 1.85 (dd, $J = 1.6, 6.6$ Hz, 3 H), 2.45 (s, 3 H), 3.45 (ddd, $J = 5.1, 5.1, 9.5$ Hz, 1 H), 3.75 (dd, $J = 8.9, 9.8$ Hz, 1 H), 3.92 (dd, $J = 5.4, 9.9$ Hz, 1 H), 5.57 (d, $J = 4.9$ Hz, 1 H), 6.06 (dq, $J = 6.6, 15.6$ Hz, 1 H), 6.33 (dd, $J = 1.5, 15.6$ Hz, 1 H), 6.80 (d, $J = 8.9$ Hz, 1 H), 6.94 (apparent d as part of AA'BB' system, $J = 8.6$ Hz, 2 H), 7.14-7.15 (m, 2 H), 7.28-7.31 (m, 4 H), 7.70 (apparent d as part of AA'BB' system, $J = 8.4$ Hz, 2 H); ^{13}C NMR (CDCl_3 , 100 MHz) δ -5.5 (q), 18.2 (s), 18.4 (q), 21.7 (q), 25.8 (q), 53.9 (d), 65.8 (t), 86.5 (d), 109.3 (d), 122.0 (d), 122.4 (d), 123.3 (d), 126.7 (d), 127.0 (d), 128.5 (d), 129.2 (s), 129.7 (d), 130.5 (d), 131.3 (s), 132.4 (s), 141.3 (s), 145.3 (s), 149.0 (s), 158.8 (s); ν_{max} (CDCl_3 cast; cm^{-1}) 3021, 2953, 2928, 2856, 1502, 1490, 1377, 1294, 1253, 1198, 1154, 1176, 1095, 866, 836; exact mass m/z calcd for $\text{C}_{31}\text{H}_{38}\text{NaO}_5\text{SSi}$ 573.21051,

found 573.21001. Anal. Calcd for C₃₁H₃₈O₅SSi: C 67.60; H 6.95; S 5.82. Found: C 67.69; H 6.93; S 6.00.

Toluene-4-sulfonic Acid 4-[(2*R*,3*S*)-3-(*tert*-Butyldimethylsilanyloxymethyl)-2,3-dihydro-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl Ester and Toluene-4-sulfonic Acid 4-[(2*R*,3*S*)-3-(*tert*-Butyldimethylsilanyloxymethyl)-2,3-dihydro-5-(1*Z*)-1-propenylbenzofuran-2-yl]phenyl Ester (33).

The slower eluting isomer **29** (2.2485 g, 4.0240 mmol) in THF (14 mL plus 4 mL as a rinse) was added dropwise by syringe to a stirred and cooled (-78°C) solution of 1-propenylmagnesium bromide (0.5 M in THF, *E* and *Z* mixture, 16 mL, 8.0 mmol) in THF (32 mL). Stirring was continued for 25 min, the cooling bath was removed, and the reaction was quenched by addition of aqueous phosphate buffer (pH 7, 10 mL). The mixture was then poured into water (20 mL) and the aqueous layer was extracted with Et₂O (3 x 25 mL). The combined organic extracts were washed with brine (20 mL), dried (MgSO₄) and evaporated. The residue was dissolved in CH₂Cl₂ (50 mL), CSA (108.6 mg, 0.47 mmol) was added and the mixture was stirred for 2 h. Saturated aqueous NaHCO₃ (20 mL) was added, and the organic phase was washed with water and dried (MgSO₄). Evaporation of the solvent and flash chromatography of the residue over silica gel (2.5 x 40 cm), using 8% EtOAc-hexane, gave **33** (1.5846 g, 71%) as a colorless oil. Integration of the allylic methyl peaks in the ¹H NMR spectrum showed the *E/Z* ratio to be 1.8:1. The material had: ¹H NMR (CDCl₃, 400 MHz) δ 0.06 (s, 3 H), 0.08 (s, 3 H), 0.90-0.92 (m, 9 H), 1.86 (dd of *E* isomer, *J* = 1.6, 6.6 Hz, 1.9 H), 1.89 (dd of *Z* isomer, *J* = 1.8, 7.2 Hz, 1.1 H), 2.45 (s, 3 H), 3.44-3.51 (m, 1 H), 3.73-3.80 (m, 1 H), 3.91-3.95 (m, 1 H), 5.58-5.60 (m, 1 H), 5.69 (dq of *Z* isomer, *J* = 7.2, 11.6 Hz, 0.33 H), 6.07 (dq of *E* isomer, *J* = 6.6, 15.7 Hz, 0.67 H), 6.32-6.38 (m, 1 H), 6.79-6.87 (m, 1 H), 6.93-6.97 (m, 2 H), 7.11 (s, 1 H), 7.14-7.17 (m, 1 H), 7.27-7.33 (m, 4 H), 7.69-7.72 (m, 2 H); ¹³C NMR (the signals for the *Z* isomer were too small to identify unambiguously; the main signals correspond to the *E* isomer, for which the data are given above); ν_{max} (CH₂Cl₂ cast; cm⁻¹) 3019, 2954, 2928, 2856, 1597, 1502, 1490, 1471, 1377, 1254, 1198, 1154, 1177, 1095, 867, 837; exact mass *m/z* calcd for C₃₁H₃₈NaO₅SSi 573.21051, found 573. 21015.

Toluene-4-sulfonic Acid 4-[(2*R*,3*S*)-2,3-Dihydro-3-hydroxymethyl-5-(1*E*)-1-propenylbenzofuran-2-yl]phenyl Ester (35).

Bu₄NF (1 M in THF, 0.49 mL, 0.49 mmol) was added dropwise by syringe to a stirred solution of **34** (151.3 mg, 0.2747 mmol) in THF (2 mL), and stirring was continued for 15 min. The solvent was evaporated and the residue was partitioned between Et₂O and water. The organic extract was washed five times with water, and once with brine and dried (MgSO₄). Evaporation of the solvent and flash chromatography of the residue over silica gel (1.5 x 30 cm), using 1:1 EtOAc-hexane, gave **35** (122.0 mg, 100%) as a colorless oil, which contained 3% of the *Z* isomer (¹H NMR): [α]_D²² -71.10 (*c* 6.00, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 1.76 (br s, 1 H), 1.87 (dd, *J* = 1.6, 6.6 Hz, 3 H), 2.46 (s, 3 H), 3.47 (ddd, *J* = 5.8, 5.8, 5.8 Hz, 1 H), 3.92 (d, *J* = 5.5 Hz, 2 H), 5.61 (d, *J* = 5.8 Hz, 1 H), 6.09 (dq, *J* = 6.6, 15.8 Hz, 1 H), 6.36 (dd, *J* = 1.6, 15.7 Hz, 1 H), 6.82 (d, *J* = 8.8 Hz, 1 H), 6.97 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.19 (m, 2 H), 7.30-7.33 (m, 4 H), 7.72 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 18.6 (q), 22.0 (q), 53.8 (d), 64.8 (t), 86.4 (d), 109.8 (d), 122.0 (d), 122.8 (d), 123.8 (d), 126.6 (s), 127.1 (d), 127.5 (d), 128.7 (d), 130.1 (d), 130.7 (d), 131.9 (s), 132.6 (s), 141.2 (s), 145.7 (s), 149.4 (s), 159.2 (s); ν_{\max} (CHCl₃ cast; cm⁻¹) 3558, 3022, 2916, 2878, 1597, 1502, 1490, 1373, 1247, 1198, 1177, 1154, 1093, 869; exact mass *m/z* calcd for C₂₅H₂₄NaO₅S 459.12367, found 459.12439.

Toluene-4-sulfonic Acid 4-[(1*S*,2*R*)-1-(4-formyl-2-iodophenoxy)-2,3-bismethanesulfonyloxypropyl]phenyl Ester (42).

Et₃N (0.022 mL, 0.16 mmol) and then MeSO₂Cl (0.012 mL, 0.16 mmol) were added to a stirred and cooled (0 °C) solution of **41** (37.4 mg, 0.0659 mmol) in CH₂Cl₂ (2 mL). After the addition stirring was continued for 10 min, the cooling bath was removed and stirring was continued overnight. The mixture was washed twice with water and dried (MgSO₄). Evaporation of the solvent gave an oil which was kept under oil pump vacuum for 12 h to give **42** (48.8 mg, 100%) as a white, crystalline solid: mp 60-64 °C; [α]_D²² -31.92 (*c* 4.10, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 2.50 (s, 3 H), 2.89 (s, 3 H), 3.11 (s, 3 H), 4.68 (dd, *J* = 2.5, 11.9 Hz, 1 H), 4.92 (dd, *J* = 5.9, 11.9 Hz, 1 H), 5.12 (ddd, *J* = 2.5, 5.8, 5.8 Hz, 1 H), 5.69 (d, *J* = 5.8 Hz, 1 H), 6.70 (d, *J* = 8.6 Hz, 1 H), 7.13 (apparent d as part of AA'BB' system, *J* = 8.7 Hz, 2 H), 7.36 (apparent dd as part of AA'BB' system, *J* = 0.6, 8.6 Hz, 2 H), 7.44 (apparent d as part of AA'BB' system, *J* = 8.6 Hz, 2 H), 7.73 (apparent d as part of AA'BB' system, *J* = 8.4 Hz, 2 H), 7.73 (dd, *J* = 2.0, 8.5 Hz, 1 H), 8.35 (d, *J* = 2.0 Hz, 1 H), 9.84 (s, 1 H); ¹³C NMR (CDCl₃, 100 MHz) δ 22.0 (q), 38.0 (q), 38.7 (q), 67.0 (t), 78.9 (d), 80.4 (d), 87.4 (s), 113.4 (d), 123.8 (d), 128.4 (d), 128.7 (d), 130.2 (d), 132.0 (d), 132.3 (s), 132.6 (s), 133.3 (s), 141.3 (d), 146.0 (s), 150.6 (s), 159.5 (s), 189.3 (d); ν_{\max} (CHCl₃ cast; cm⁻¹) 3031, 2939, 2849, 1694, 1588, 1503, 1480, 1412, 1365, 1251,

1199, 1178, 1156, 1041, 1017, 866; exact mass m/z calcd for $C_{25}H_{25}INaO_{11}S_3$ 746.94960, found 746.94935.

Toluene-4-sulfonic Acid 4-[(2*R*,3*R*)-3-(methanesulfonyloxymethyl)oxiranyl]phenyl Ester (44).

MeSO₂Cl (0.14 mL, 1.8 mmol) was added dropwise by syringe to a stirred and cooled (0 °C) solution of **23b** (514.6 mg, 1.606 mmol) and Et₃N (0.30 mL, 2.2 mmol) in CH₂Cl₂ (Ar atmosphere). The mixture was stirred for 1 h, diluted with CH₂Cl₂ (10 mL), washed once with water (6 mL) and dried (MgSO₄). Evaporation of the solvent gave **44** as a colorless oil that was used without further purification: $[\alpha]_D^{22} +16.33$ (c 1.56, CHCl₃); ¹H NMR (CDCl₃, 400 MHz) δ 2.48 (s, 3 H), 3.12 (s, 3 H), 3.30 (ddd, $J = 2.0, 3.2, 5.5$ Hz, 1 H), 3.87 (d, $J = 2.0$ Hz, 1 H), 4.31 (dd, $J = 5.6, 12.1$ Hz, 1 H), 4.58 (dd, $J = 3.2, 12.1$ Hz, 1 H), 7.01 (apparent d as part of AA'BB' system, $J = 8.6$ Hz, 2 H), 7.22 (apparent d as part of AA'BB' system, $J = 8.6$ Hz, 2 H), 7.34 (apparent d as part of AA'BB' system, $J = 8.3$ Hz, 2 H), 7.72 (apparent d as part of AA'BB' system, $J = 8.3$ Hz, 2 H); ¹³C NMR (CDCl₃, 100 MHz) δ 22.0 (q), 38.2 (q), 56.0 (d), 59.1 (d), 68.8 (t), 123.0 (d), 127.2 (d), 128.8 (d), 130.1 (d), 132.5 (s), 134.7 (s), 145.8 (s), 150.1 (s); ν_{\max} (CHCl₃ cast; cm⁻¹) 3032, 1598, 1506, 1359, 1199, 1177, 1155, 1093, 868; exact mass m/z calcd for C₁₇H₁₈NaO₇S₂ 421.03862, found 421.03835.

Toluene-4-sulfonic Acid 4-[(*S*)-1-(*tert*-Butyldimethylsilyloxy)allyl]phenyl Ester (46).

t-BuMe₂SiOSO₂CF₃ (0.25 mL, 1.1 mmol) was added dropwise by syringe to a stirred and cooled (-78 °C) solution of **45** (269.8 mg, 0.8865 mmol) and *sym*-collidine (0.26 mL, 2.0 mmol) in CH₂Cl₂ (3 mL) (Ar atmosphere). Stirring at -78 °C was continued for 15 min and then saturated aqueous NaHCO₃ (0.5 mL) was added and the cooling bath was removed. After ca 15 min, CH₂Cl₂ (10 mL) was added and the mixture was washed with water (8 mL), dried (MgSO₄) and evaporated. Flash chromatography of the residue over silica gel (1.5 x 25 cm), using 13% EtOAc-hexanes containing a trace (0.5-1%v/v) of Et₃N, gave **46** (370.6 mg, 100%) as a colorless oil: $[\alpha]_D^{22} -6.46$ (c 1.21, CHCl₃); ¹H NMR (C₆D₆, 400 MHz) δ 0.00 (s, 3 H), 0.11 (s, 3 H), 1.02 (s, 9 H), 1.84 (s, 3 H), 4.98 (dt, $J = 1.5, 10.3$ Hz, 1 H), 5.02 (d, $J = 6.0$ Hz, 1 H), 5.23 (dt, $J = 1.5, 17.0$ Hz, 1 H), 5.80 (ddd, $J = 5.9, 10.2, 17.0$ Hz, 1 H), 6.67 (apparent dd as part of AA'BB' system, $J = 0.7, 8.6$ Hz, 2 H), 7.06 (apparent d as part of AA'BB' system, $J = 8.8$ Hz, 2 H), 7.17 (apparent dd as part of AA'BB' system, $J = 0.6, 8.9$ Hz, 2 H), 7.71 (apparent d as part of AA'BB'

system, $J = 8.4$ Hz, 2 H); ^{13}C NMR (C_6D_6 , 100 MHz) δ -4.8 (q), 18.4 (s), 21.1 (q), 26.0 (q), 75.6 (d), 113.8 (t), 122.6 (d), 127.4 (d), 128.8 (d), 129.6 (d), 133.6 (s), 141.4 (d), 142.7 (s), 144.7 (s), 149.5 (s); ν_{max} (CHCl_3 cast; cm^{-1}) 2954, 2928, 2885, 2856, 1598, 1499, 1472, 1376, 1294, 1197, 1175, 1154, 1093, 865; exact mass m/z calcd for $\text{C}_{22}\text{H}_{30}\text{NaO}_4\text{SSi}$ 441.15263, found 441.15262.

(S)-1-Phenylpropan-1-ol (51).

Bu_4NF (1M in THF, 0.3 mL, 0.3 mmol) was added to a stirred solution of **50** (56.0 mg, 0.224 mmol) in THF (3.6 mL) (Ar atmosphere). The mixture was stirred for 12 h, diluted with Et_2O (8 mL) and washed with water (2 x 4 mL) and once with brine (4 mL), dried (MgSO_4) and evaporated. Flash chromatography of the residue over silica gel (0.5 x 30 cm), using 20% Et_2O -pentane containing a trace (0.5-1% v/v) of Et_3N , gave an impure product. Further purification by Kugelrohr distillation and flash chromatography over silica gel (0.5 x 30 cm), using 20% EtOAc-hexanes containing a trace (0.5-1% v/v) of Et_3N , gave **51** (21.5 mg, 71%) as a colorless liquid whose ^1H NMR spectrum was identical to that reported.⁴⁸ The material had: $[\alpha]_{\text{D}}^{22} -29.26$ (c 1.23, CHCl_3) [Lit.^{48,49} $[\alpha]_{\text{D}}^{22} -45.6$ (c 1.3, CHCl_3)] indicating an er = 88:12.

Reference

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