Convergent, stereoselective syntheses of the glycosidase inhibitors broussonetines D and M

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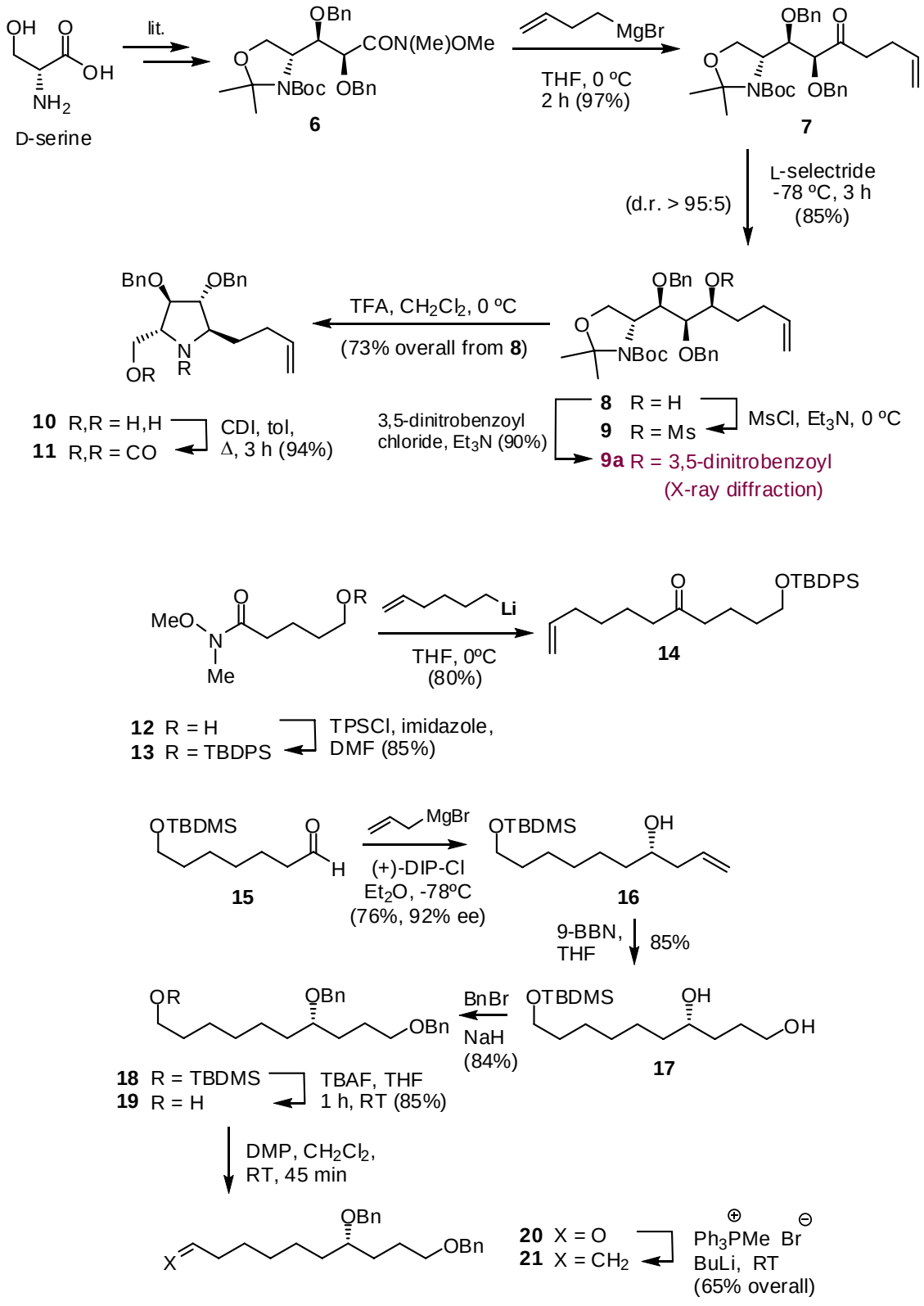
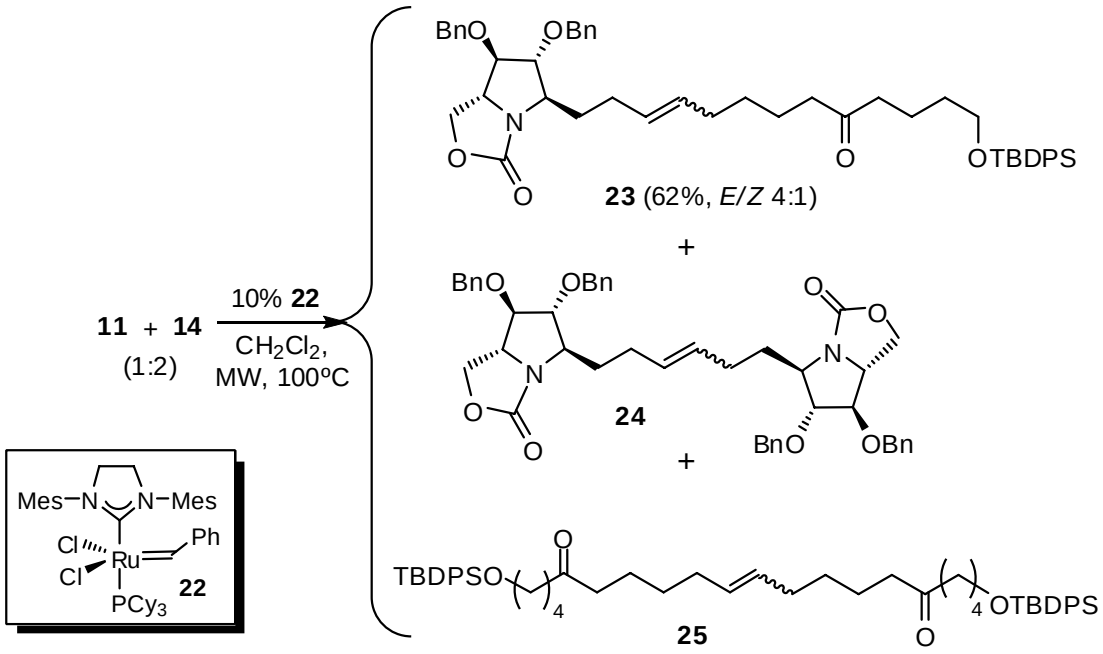
Supporting Information

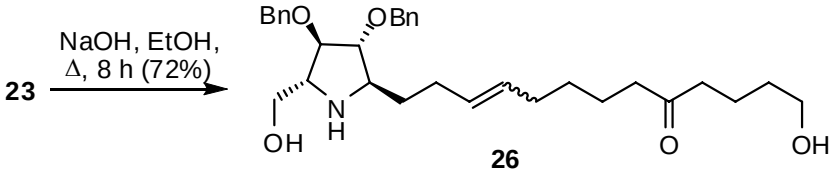
Contents:

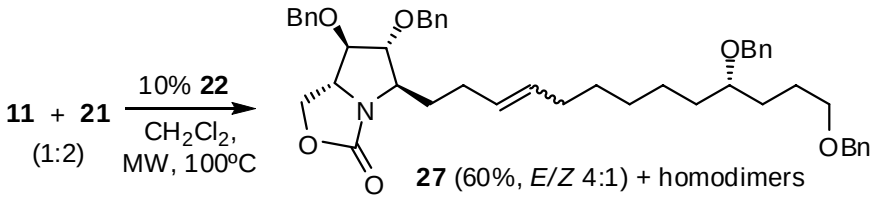
General Features. NMR spectra were recorded at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR) in $CDCl_3$ solution at 25 °C, if not otherwise indicated, with the solvent signals as internal reference. The spectra of compounds with N-Boc residues were measured at higher temperatures in order to have sharper signals. ^{13}C NMR signal multiplicities were determined with the DEPT pulse sequence. Mass spectra were run in the EI (70 eV) or the FAB (*m*-nitrobenzyl alcohol matrix) mode. IR data, which were measured as films on NaCl plates (oils) or as KBr pellets (solids), are given only when relevant functions (C=O, OH) are present. Optical rotations were measured at 25 °C. Reactions which required an inert atmosphere (all except those involving water in the reaction medium) were carried out under dry N_2 with flame-dried glassware. Commercial reagents were used as received. THF and Et_2O were freshly distilled from sodium-benzophenone ketyl. Dichloromethane was freshly distilled from CaH_2. Toluene was freshly distilled from sodium wire. Tertiary amines were freshly distilled from KOH. Unless detailed otherwise, "work-up" means pouring the reaction mixture into brine, *followed by extraction with the solvent indicated in parenthesis*. If the reaction medium was acidic, an additional washing of the organic layer with 5% aq $NaHCO_3$ was performed. If the reaction medium was basic, an additional washing with aq NH_4Cl was performed. Where solutions were filtered through a Celite pad, the pad was additionally washed with the same solvent used, and the washings incorporated to the main organic layer. The latter was dried over anhydrous Na_2SO_4 and the solvent was eliminated under reduced pressure. Column chromatography of the residue on a silica gel column (60-200 μm) was performed with elution with the indicated solvent mixture.

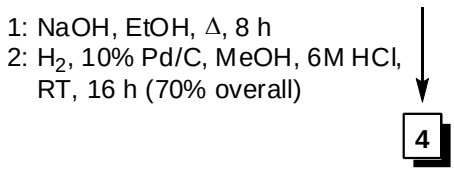
General reaction schemes



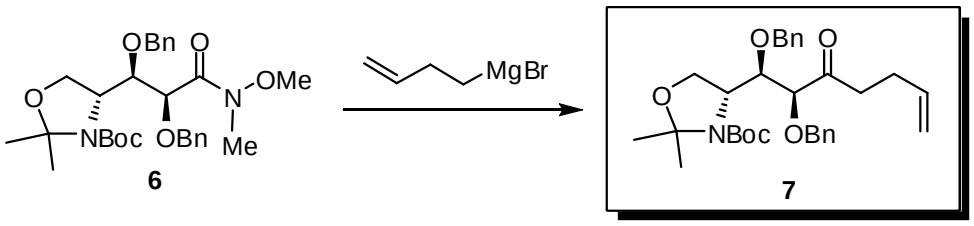








Experimental procedures



***Tert*-butyl (4*R*)-4-[(1*R*,2*S*)-1,2-bis(benzyloxy)-3-oxohept-6-enyl]-2,2-dimethyloxazolidine-3-carboxylate (7)**. An ice-cooled solution of Weinreb amide **6** (8.46 g, 16 mmol) in THF (50 mL) was treated dropwise (within 10 min) under N_2 with a 0.5 M solution of 3-butenylmagnesium bromide (96 mL, 48 mmol). The reaction mixture was then stirred for 2 h at 0 ºC. Work-up (extraction with Et_2O, 3 x 50 mL) and column chromatography on silica gel (hexanes-EtOAc, 8:2) afforded **7** (8.12 g, 97%).

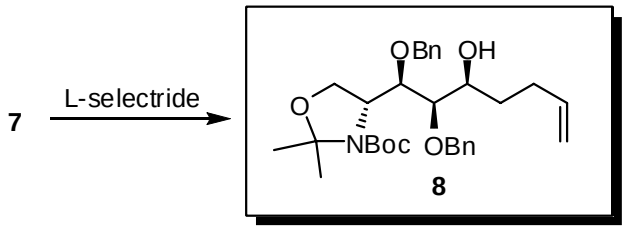
Colorless oil: $[\alpha]_D$ +6 (c 2.2; $CHCl_3$).

^{1}H NMR (DMSO-d_6, 70 °C) δ 7.40-7.20 (10H, br m), 5.80-5.70 (1H, ddt, *J* = 17, 10.3, 6.5 Hz), 4.96 (1H, br dd, *J* = 17, 1.5 Hz), 4.91 (1H, br dd, *J* = 10.3, 1.5 Hz), 4.61 (1H, d, *J* = 11.3 Hz), 4.60 (1H, d, *J* = 11.3 Hz), 4.47 (1H, d, *J* = 11.3 Hz), 4.45 (1H, d, *J* = 11.3 Hz), 4.42 (1H, m), 4.18 (1H, m), 3.98 (1H, d, *J* = 4 Hz), 3.94-3.87 (2H, m), 2.70-2.60 (2H, br m), 2.25-2.15 (2H, br m), 1.47 (3H, s), 1.46 (9H, s), 1.40 (3H, s).

^{13}C NMR (DMSO-d_6, 70 °C) δ 208.5, 151.8*, 137.7, 137.2, 92.8, 79.4 (C), 137.1, 128.0 (x 2), 127.8 (x 2), 127.7, 127.4, 127.1 (x 4), 85.8, 78.6*, 58.6 (CH), 114.6, 74.0, 72.6, 62.6, 37.9, 26.2 (CH_2), 27.7 (x 3), 25.7, 23.5* (CH_3) (starred signals are low and/or broad).

IR ν_{max} 1700 (br, C=O) cm^{-1}.

HR FABMS *m/z* 524.3000 ($M+H^+$). Calcd. for $C_{31}H_{42}NO_6$, 524.3012.



***Tert*-butyl (4*R*)-[(1*R*,2*R*,3*S*)-1,2-bis(benzyloxy)-3-hydroxyhept-6-enyl]-2,2-dimethyloxazolidine-3-carboxylate (8)**. Ketone **7** (7.85 g, 15 mmol) was dissolved under N_2 in THF (45 mL), cooled to −78 °C and treated dropwise with a 1M solution of L-Selectride in THF (37.5 mL, 37.5 mmol). The reaction mixture was then stirred at the same temperature for 3 h. After this time, the reaction was quenched by addition of 10% aq NaOH (35 mL) and 30% H_2O_2 (25 mL), followed by stirring at 0 °C for 20 min.

Work-up (extraction with Et_2O, 3 x 40 mL) and column chromatography on silica gel (hexanes-EtOAc, 9:1) afforded alcohol **8** (6.70 g, 85%).

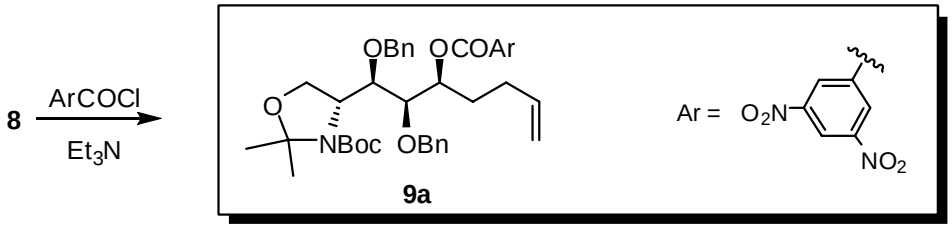
Colorless oil: $[\alpha]_D$ +48.8 (*c* 1.28; $CHCl_3$).

^{1}H NMR ($CDCl_3$, 58 °C) δ 7.40-7.25 (10H, br m), 5.80 (1H, m), 5.03 (1H, br dd, *J* = 17.2, 1.3 Hz), 4.98 (1H, br d, *J* = 10.3 Hz), 4.84 (1H, d, *J* = 11.2 Hz), 4.78 (1H, d, *J* = 11.3 Hz), 4.70 (1H, d, *J* = 11.3 Hz), 4.60 (1H, d, *J* = 11.2 Hz), 4.36* (1H, br m), 4.32 (1H, dd, *J* = 8.8, 3.5 Hz), 4.18* (1H, br m), 4.00 (1H, dd, *J* = 8.8, 7.3 Hz), 3.72* (1H, m), 3.32* (1H, m), 2.25-2.15 (1H, br m), 2.10-2.05 (1H, br m), 1.70-1.60 (2H, br m), 1.59 (3H, s), 1.54 (9H, s), 1.50 (3H, s) (starred signals are low and/or broad), hydroxyl proton not detected.

^{13}C NMR ($CDCl_3$, 58 °C) δ 153.0*, 138.6, 138.2, 94.0*, 80.4 (C), 138.3, 128.3 (x 4), 128.2 (x 2), 127.9 (x 2), 127.7, 127.5, 81.8*, 78.3*, 70.4, 58.8 (CH), 114.7, 75.0, 74.5*, 63.6, 34.0, 30.2 (CH_2), 28.6 (x 3), 26.5*, 24.5* (CH_3) (starred signals are low and/or broad).

IR ν_{max} 3480 (br, OH), 1692 (C=O) cm^{-1}.

HR FABMS *m/z* 526.3169 ($M+H^+$). Calcd. for $C_{31}H_{44}NO_6$, 526.3168.



***Tert*-butyl (4*R*)-[(1*R*,2*R*,3*S*)-1,2-bis(benzyloxy)-3-(3,5-dinitrobenzoyloxy)hept-6-enyl]-2,2-dimethyl-oxazolidine-3-carboxylate (9a)**. A solution of alcohol **8** (105 mg, 0.2 mmol) in dry CH_2Cl_2 (2 mL), was cooled to 0 °C and treated with 3,5-dinitrobenzoyl chloride (70 mg, 0.3 mmol), Et_3N (56 μL, 0.4 mmol) and DMAP (3 mg, ca. 0.02 mmol). The reaction mixture was then stirred at 0 ºC for 5 h. Work-up (extraction with CH_2Cl_2, 3 x 10 mL) and column chromatography on silica gel (hexanes-EtOAc, 8:2) provided ester **9a** (130 mg, 90%) as a yellowish oil. Slow crystallization from Et_2O at low temperature gave yellowish crystals (see ORTEP image below). The crystallographic data have been deposited at the Cambridge Crystallographic Data Centre. Deposition number: CCDC-711360.

Mp 105-106 °C; $[\alpha]_D$ +19.8 (*c* 0.8; $CHCl_3$).

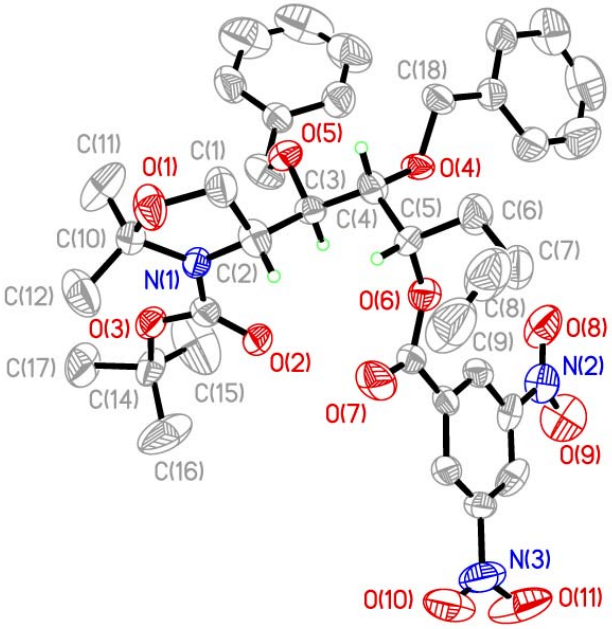
^{1}H NMR ($CDCl_3$, 58 °C) δ 9.15 (1H, br s), 9.01 (2H, br s), 7.40-7.25 (10H, br m), 5.80-5.70 (1H, m), 5.44* (1H, br m), 5.05-4.95 (2H, br m), 4.85-4.80* (1H, br m), 4.70* (1H, br m), 4.63 (1H, br d, *J* = 11.8 Hz), 4.61 (1H, d, *J* = 11.7 Hz), 4.40* (1H, br m), 4.35* (1H, br m), 4.05* (1H, br m), 3.95-3.90

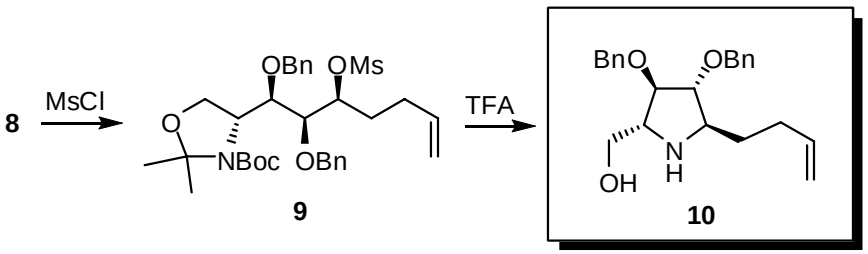
(1H, m), 3.70-3.65 (1H, m), 2.10-2.05 (2H, br m), 1.95-1.85* (2H, br m), 1.55* (3H, s), 1.46* (3H, s), 1.44* (9H, s) (starred signals are low and/or broad).

^{13}C NMR ($CDCl_3$, 58 °C) δ 162.4, 153.0*, 148.7 (x 2), 138.3*, 138.1*, 134.6*, 94.2*, 80.5 (C), 137.1, 129.4 (x 2), 128.3 (x 3), 128.0 (x 2), 127.7 (x 2), 127.5 (x 2), 121.8 (x 2), 81.5*, 78.0*, 76.4, 59.5 (CH), 115.6, 75.2, 75.0*, 63.3*, 30.2, 29.8 (CH_2), 28.4* (x 3), 26.5*, 24.7* (CH_3) (starred signals are low and/or broad).

IR ν_{max} 1733, 1684 (C=O) cm^{-1}.

HR FABMS *m/z* 719.3084 (M^+). Calcd. for $C_{38}H_{45}N_3O_{11}$, 719.3054.



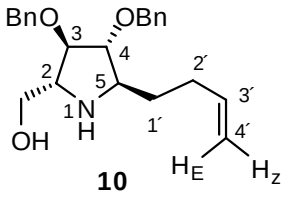


(2*R*,3*R*,4*R*,5*R*)-[3,4-Bis(benzyloxy)-5-(but-3-enyl)pyrrolidin-2-yl)]methanol (10). Alcohol **8** (5.25 g, 10 mmol) was dissolved in dry CH_2Cl_2 (40 mL), cooled to 0 °C and treated sequentially with Et_3N (4.2 mL, 30 mmol), mesyl chloride (1.55 mL, 20 mmol) and DMAP (12 mg, 0.1 mmol). The reaction mixture was stirred for 2 h at 0 °C, and then for 1 h at room temperature Work-up (extraction with

CH_2Cl_2, 3 x 30 mL) and solvent removal under reduced pressure gave crude mesylate **9**, which was used as such in the next reaction.

The crude mesylate from above was dissolved in dry CH_2Cl_2 (30 mL), cooled to 0 ºC ands treated with trifluoroacetic acid (30 mL). After stirring the reaction mixture at 0 °C for 2 h, all volatiles were removed under reduced pressure. The residue was dissolved in MeOH (20 mL) and added 30% aq ammonia until basic pH. Removal of all volatiles under reduced pressure and column chromatography on silica gel (CH_2Cl_2-MeOH, 95:5) furnished pyrrolidine **10** (2.68 g, 73% overall from **8**) as colorless crystals (from CH_2Cl_2).

Mp 54-55 °C; $[\alpha]_D$ +18.7 (*c* 0.9; $CHCl_3$).



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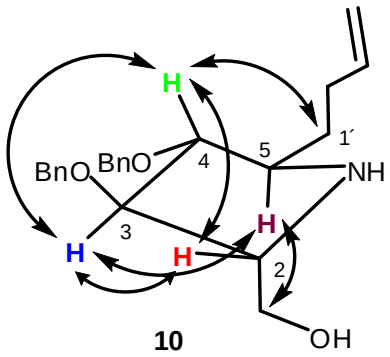
^{1}H NMR δ 7.40-7.25 (10H, br m, aromatic), 5.82 (1H, ddt, *J* = 17.2, 10.2, 6.5 Hz; H-3´), 5.05 (1H, br dd, *J* = 17.2, 1.5 Hz; H-4´$_E$), 5.00 (1H, br d, *J* = 10.2 Hz; H-4´$_Z$), 4.57 (1H, d, *J* = 11.8 Hz; benzyl), 4.56 (1H, d, *J* = 11.6 Hz; benzyl), 4.55 (1H, d, *J* = 11.6 Hz; benzyl), 4.53 (1H, d, *J* = 11.8 Hz; benzyl), 3.82 (1H, t, *J* = 3 Hz; H-3), 3.72 (1H, dd, *J* = 5.3, 3 Hz; H-4), 3.60-3.55 (2H, m; C*H*$_2$OH), 3.38 (1H, m; H-2), 3.15 (1H, dt, *J* = 8, 5.3 Hz; H-5), 2.65 (2H, br s; OH, NH), 2.25-2.05 (2H, br m; H-2´$_a$/2´$_b$), 1.80-1.70 (1H, m; H-1´$_a$), 1.65-1.55 (1H, m; H-1´$_b$).

NOE measurements

Irradiation at	**NOE enhancement at**
H-2	H-3,4, C*H*$_2$OH
H-3	Benzyl CH_2, H-2,4,5
H-4	Benzyl CH_2, H-2,3,1´
H-5	Benzyl CH_2, CH_2OH, H-3



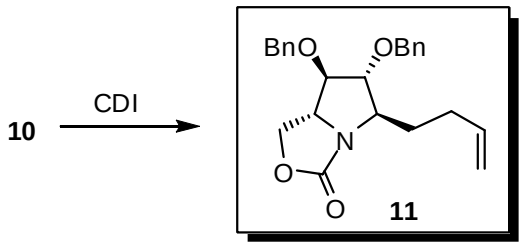
10

Note the absence of NOE between H-2 and H-5

^{13}C NMR δ 138.0 (x 2) (C), 137.9, 128.5 (x 2), 128.4 (x 2), 127.8, 127.7 (x 5), 89.4, 86.1, 63.6, 61.5 (CH), 115.0, 71.9, 71.8, 61.8, 33.1, 30.9 (CH_2).

IR ν_{max} 3400, 3320 (br, OH, NH) cm^{-1}.

HR EIMS *m/z* (% rel. int.) 367.2153 (M^+, 1), 336 (M^+–CH_2OH, 18), 276 (M^+–CH_2Ph, 10), 91 (100). Calcd. for $C_{23}H_{29}NO_3$, 367.2147. Anal. Calcd. for $C_{23}H_{29}NO_3$: C, 75.17; H, 7.95. Found: C, 75.01; H, 8.03.



(5*R*,6*R*,7*R*,7a*R*)-6,7-Bis(benzyloxy)-5-(but-3-enyl)tetrahydropyrrolo[1,2-c]oxazol-3(1H)-one (11). Pyrrolidine **10** (2.57 g, 7 mmol) was dissolved under N_2 in dry toluene (200 mL), treated with DMAP (9 mg, 0.07 mmol) and CDI (2.27 g, 14 mmol) and heated at reflux for 3 h. After cooling, work-up (extraction with EtOAc, 3 x 60 mL) and column chromatography on silica gel (hexanes-EtOAc, 8:2) yielded oxazolidinone **11** (2.59 g, 94%) as colorless crystals (from hexane-EtOAc):

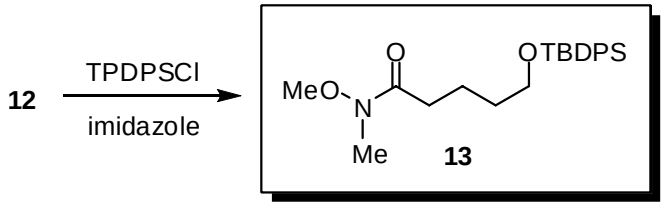
Mp 37-38 °C; $[\alpha]_D$ +2 (c 1.55; $CHCl_3$).

^{1}H NMR δ 7.40-7.25 (10H, br m, aromatic), 5.85 (1H, ddt, *J* = 17.1, 10.3, 6.5 Hz; H-3′), 5.08 (1H, br d, *J* = 17.1 Hz; H-4′$_E$), 5.02 (1H, br d, *J* = 10.3 Hz; H-4′$_Z$), 4.62 (1H, d, *J* = 11.6 Hz; benzyl), 4.61 (1H, d, *J* = 11.9 Hz; benzyl), 4.49 (1H, d, *J* = 11.9 Hz; benzyl), 4.46 (1H, d, *J* = 11.6 Hz; benzyl), 4.43 (1H, t, *J* = 9 Hz; C*H*OCON), 4.10 (1H, dd, *J* = 9, 4.2 Hz; C*H*OCON), 4.04 (1H, m; H-5), 3.95-3.90 (2H, m; H-2, H-4), 3.86 (1H, dd, *J* = 5.3, 3 Hz; H-3), 2.25-2.15 (2H, br m; H-2′$_a$/2′$_b$), 1.75-1.60 (2H, m; H-1′$_a$/1′$_b$) (see atom numbering above).

^{13}C NMR δ 161.3, 137.3, 137.2 (C), 137.4, 128.6 (x 2), 128.5 (x 2), 128.2, 127.9, 127.8 (x 2), 127.7 (x 2), 88.8, 87.8, 62.8, 62.3 (CH), 115.4, 72.7, 71.6, 67.2, 31.5, 30.4 (CH_2).

IR ν_{max} 1753 (C=O) cm^{-1}.

HR EIMS *m/z* (% rel. int.) 393.1945 (M^+, 1), 338 (M^+–C_4H_7, 8), 302 (M^+–CH_2Ph, 10), 91 (100). Calcd. for $C_{24}H_{27}NO_4$, 393.1940. Anal. Calcd. for $C_{24}H_{27}NO_4$: C, 73.26; H, 6.92. Found: C, 73.11; H, 7.05.



5-(*Tert*-butyldiphenylsilyloxy)-N-methoxy-N-methylpentanamide (13). A solution of Weinreb amide **12** (1.61 g, 10 mmol) in dry DMF (35 mL) was treated under N_2 with imidazole (1.36 g, 20 mmol) and TPSCl (2.86 mL, 11 mmol). The reaction mixture was stirred at room temperature for 16 h. Work-up (extraction with CH_2Cl_2, 3 x 30 mL) and column chromatography on silica gel (hexanes-EtOAc, from 8:2 to 1:1) yielded compound **13** (3.40 g, 85%).

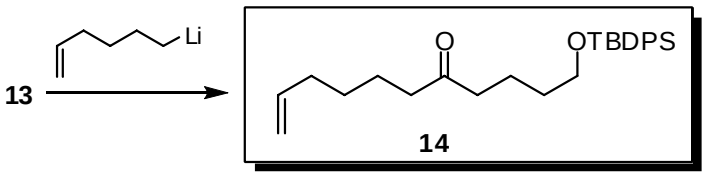
Colorless oil.

^{1}H NMR δ 7.70 (4H, br d, J ~ 7.5 Hz), 7.45-7.35 (6H, m), 3.72 (2H, t, J = 6.3 Hz), 3.66 (3H, s), 3.20 (3H, s), 2.45 (2H, br t, J = 7.5 Hz), 1.80-1.75 (2H, m), 1.75-1.65 (2H, m), 1.07 (9H, s).

^{13}C NMR δ 174.5*, 134.0 (x 2), 19.2 (C), 135.5 (x 4), 129.5 (x 2), 127.5 (x 4) (CH), 63.6, 32.2 (x 2), 21.1 (CH_2), 61.1, 31.6, 26.9 (x 3) (CH_3) (the starred signal is low and broad).

IR ν_{max} 1670 (C=O) cm^{-1}.

HR EIMS *m/z* (% rel. int.) 399.2239 (M^+, 1), 384 (M^+–Me, 3), 342 (M^+–*t*Bu, 100). Calcd. for $C_{23}H_{33}NO_3Si$, 399.2229.



1-(*Tert*-butyldiphenylsilyloxy)undec-10-en-5-one (14). A 1.7 M pentane solution of *tert*-butyllithium (11.8 mL, ca. 20 mmol) was added under N_2 to THF (10 mL) cooled to −78 ºC. Subsequently, a solution of 6-bromo-1-hexene (1.34 mL, 10 mmol) in dry THF (6 mL) was added dropwise. The mixture was stirred for 3 h at the same temperature Weinreb amide **13** (2 g, 5 mmol) was dissolved in dry THF (8 mL) and added dropwise during 10 min. The cooling bath was then removed and the solution was left to reach room temperature and stirred for further 30 min. Work-up (extraction with EtOAc, 3 x 25 mL) and column chromatography on silica gel (hexanes-EtOAc, from 95:5) gave ketone **14** (1.69 g, 80%).

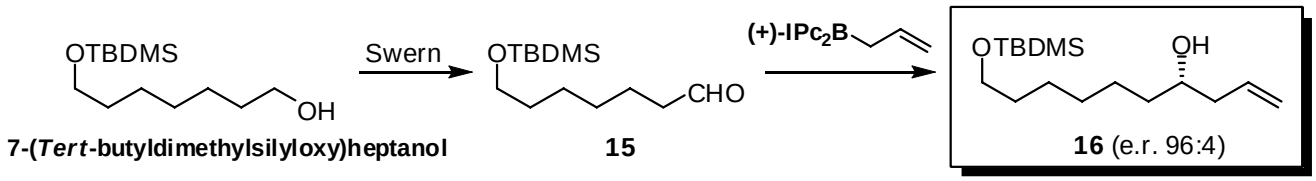
Colorless oil.

^{1}H NMR δ 7.70 (4H, br d, *J* ~ 7.5 Hz), 7.45-7.35 (6H, m), 5.80 (1H, ddt, *J* = 17.3, 10.2, 6.5 Hz), 5.02 (1H, br dd, *J* = 17.3, 1.5 Hz), 4.97 (1H, br d, *J* = 10.2 Hz), 3.67 (2H, t, *J* = 6.3 Hz), 2.40-2.35 (4H, m), 2.07 (2H, br q, *J* ~ 7 Hz), 1.70-1.65 (2H, m), 1.60-1.50 (4H, m), 1.38 (2H, br quint, *J* ~ 7.5 Hz), 1.06 (9H, s).

^{13}C NMR δ 211.1, 134.0 (x 2), 19.2 (C), 138.5, 135.5 (x 4), 129.5 (x 2), 127.6 (x 4) (CH), 114.6, 63.5, 42.5 (x 2), 33.5, 32.0, 28.5, 23.3, 20.3 (CH_2), 26.9 (x 3) (CH_3).

IR ν_{max} 1714 (C=O) cm^{-1}.

HR FABMS *m/z* 423.2730 ($M+H^+$). Calcd. for $C_{27}H_{39}O_2Si$, 423.2719.



7-(*Tert*-butyldimethylsilyloxy)heptanol **15** **16** (e.r. 96:4)

(4*S*)-10-(*Tert*-butyldimethylsilyloxy)dec-1-en-4-ol (16). DMSO (1.4 mL, 20 mmol) was dissolved under N_2 in dry CH_2Cl_2 (20 mL), cooled to −78 °C and treated with oxalyl chloride (875 μL, 10 mmol). After stirring at this temperature for 5 min., a solution of 7-(*tert*-butyldimethylsilyloxy)heptanol (2 g, ca. 8 mmol) in dry CH_2Cl_2 (6 mL) was added dropwise, followed by triethyl amine (5.6 mL, 40 mmol). The reaction mixture was stirred for 15 min. at −78 °C and then for further 40 min. at 0 °C. Work-up (extraction with CH_2Cl_2, 3 x 25 mL) and removal of all volatiles under reduced pressure provided crude aldehyde **15**, which was directly used in the next step.

Allylmagnesium bromide (commercial 1M solution in Et_2O, 10 mL, 10 mmol) was added dropwise under N_2 via syringe to a solution of (+)-DIP-Cl (3.85 g, 12 mmol) in dry Et_2O (50 mL) cooled to −78 °C. The mixture was then placed in an ice bath, stirred for 1 h and allowed to stand, which caused precipitation of magnesium chloride. The supernatant solution was then carefully transferred to another flask via cannula. After cooling this flask to −78 °C, a solution of aldehyde **15** from above in dry Et_2O (20 mL) was added dropwise via syringe. The resulting solution was further stirred at the same temperature for 1 h. The reaction mixture was then quenched through addition of phosphate pH 7 buffer solution (50 mL), MeOH (50 mL) and 30% H_2O_2 (25 mL). After stirring for 30 min. at room temperature, the mixture was poured onto satd. aq $NaHCO_3$ and worked up (extraction with EtOAc). Removal of all volatiles under reduced pressure and column chromatography of the residue on silica gel (hexanes-EtOAc, 95:5) afforded homoallylic alcohol **16** (1.74 g, 76% overall from the starting primary alcohol).

Colorless oil: $[\alpha]_D$ −4 (c 1.1; $CHCl_3$).

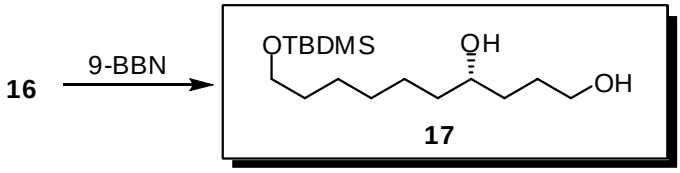
^{1}H NMR δ 5.84 (1H, ddt, *J* = 17, 10, 6.5 Hz), 5.15-5.10 (2H, m), 3.65 (1H, m), 3.60 (1H, t, *J* = 6.6 Hz), 2.30 (1H, br dt, *J* = 14, 5.5 Hz), 2.14 (1H, dt, *J* = 14, 8 Hz), 1.58 (1H, m), 1.55-1.45 (6H, br m), 1.40-1.30 (5H, m), 0.90 (9H, s), 0.04 (6H, s).

^{13}C NMR δ 18.4 (C), 134.9, 70.7 (CH), 118.0, 63.3, 42.0, 36.8, 32.8, 29.5, 25.8, 25.7 (CH_2), 26.0 (x 3), –5.3 (x 2) (CH_3).

IR ν_{max} 3360 (br, OH) cm^{-1}.

HR EIMS *m/z* (% rel. int.) 245.1939 (M^+–C_3H_5, 20), 229 (M^+–*t*Bu, 2), 95 (100), 75 (96). Calcd. for $C_{16}H_{34}O_2Si$–C_3H_5, 245.1937.

The enantiomeric purity of **16** was determined as 92% (e.r. 96:4) by means of HPLC on a chiral, analytical column (Chiralcel OD-H, 4.6 mm ∅ × 25 cm). Elution was made with hexane/*iso*propanol 99:1 at 0.25 mL/min. The retention times of the enantiomers were 11.38 min. for the major enantiomer and 12.37 min. for the minor one.



(4*S*)-10-(*Tert*-butyldimethylsilyloxy)decane-1,4-diol (17). An ice-cooled solution of olefin **16** (1.72 g, 6 mmol) in dry THF (30 mL) was treated under N_2 with a 0.5 M solution of 9-BBN in THF (30 mL, 15 mmol). The reaction mixture was then stirred at room temperature for 3 h in an ultrasound bath. After re-cooling to 0 ºC, the reaction was quenched through sequential addition of MeOH (10 mL), 6M aq NaOH (4 mL) and 30% H_2O_2 (1.5 mL). After stirring at 50 ºC for 1 h, work-up (extraction with EtOAc, 3 x 25 mL) and column chromatography on silica gel (hexanes-EtOAc, 7:3 to 1:1), diol **17** (1.55 g, 85%) was obtained.

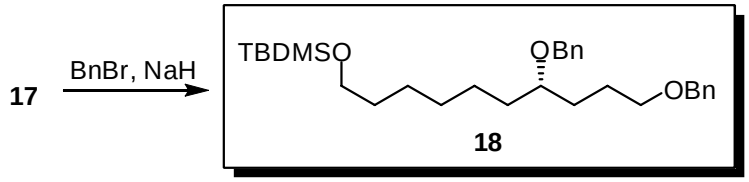
Colorless oil: $[\alpha]_D$ +0.8 (c 2; $CHCl_3$).

^{1}H NMR δ 3.70-3.55 (5H, br m), 3.30 (2H, br s, 2 OH), 1.70-1.55 (3H, m), 1.50-1.40 (6H, br m), 1.35-1.25 (5H, m), 0.88 (9H, s), 0.02 (6H, s).

^{13}C NMR δ 18.3 (C), 71.7 (CH), 63.2, 62.7, 37.5, 34.4, 32.8, 29.5, 29.1, 25.8, 25.7 (CH_2), 25.9 (x 3), –5.3 (x 2) (CH_3).

IR ν_{max} 3330 (br, OH) cm^{-1}.

HR FABMS *m/z* 305.2517 ($M+H^+$). Calcd. for $C_{16}H_{37}O_3Si$, 305.2512.



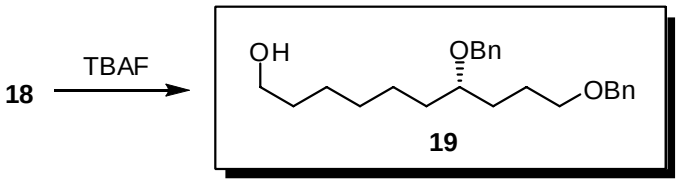
(4*S*)-1,4-Bis(benzyloxy)-10-(*tert*-butyldimethylsilyloxy)decane (18). Sodium hydride (600 mg of a 60% suspension in mineral oil, 15 mmol) was suspended under N_2 in dry THF (12 mL) and cooled to 0 ºC. A solution of diol **17** (1.52 g, 5 mmol) in THF (8 mL) was then added, after which the mixture was stirred for 1 h at room temperature, followed by addition of TBAI (20 mg, ca. 0.05 mmol) and benzyl bromide (1.9 mL, 16 mmol). The mixture was then heated at reflux for 6 h. Work-up (extraction with EtOAc, 3 x 20 mL) and column chromatography on silica gel (hexanes-EtOAc, 98:2 to 95:5) afforded **18** (2.04 g, 84%).

Colorless oil: $[\alpha]_D$ –2.7 (c 1.58; $CHCl_3$).

^{1}H NMR δ 7.40-7.30 (10H, br m), 4.55-4.50 (4H, two overlapped AB systems, J ~ 11.5 Hz), 3.64 (2H, t, J = 6.5 Hz), 3.50 (2H, m), 3.43 (1H, quint, J = 5.8 Hz), 1.85-1.50 (8H, br m), 1.45-1.30 (6H, m), 0.94 (9H, s), 0.09 (6H, s).

^{13}C NMR δ 139.1, 138.7, 18.3 (C), 128.3 (x 2), 128.2 (x 2), 127.7 (x 2), 127.6 (x 2), 127.5, 127.4, 78.7 (CH), 72.8, 70.7, 70.5, 63.3, 33.8, 32.8, 30.4, 29.6, 25.8, 25.6, 25.3 (CH_2), 26.0 (x 3), –5.3 (x 2) (CH_3).

HR FABMS *m/z* 485.3469 ($M+H^+$). Calcd. for $C_{30}H_{49}O_3Si$, 485.3451.



(7*S*)-7,10-Bis(benzyloxy)decan-1-ol (19). A solution of compound **18** (1.94 g, 4 mmol) in dry THF (15 mL) was treated with solid TBAF trihydrate (1.57 g, 5 mmol). The reaction mixture was stirred at room temperature for 2 h and quenched by addition of water (0.5 mL). Removal of all volatiles under reduced pressure and column chromatography of the residue on silica gel (hexanes-EtOAc, 1:1) furnished alcohol **19** (1.26 g, 85%).

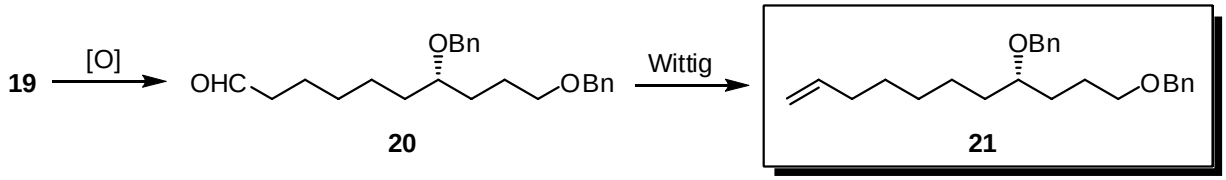
Colorless oil: $[\alpha]_D$ +1.2 (c 1.54; $CHCl_3$).

^{1}H NMR δ 7.40-7.25 (10H, br m), 4.53 (4H, br s), 3.63 (2H, t, J = 6.5 Hz), 3.48 (2H, m), 3.41 (1H, quint, J = 5.8 Hz), 1.80-1.50 (8H, br m), 1.45-1.30 (6H, m) (hydroxyl signal not detected).

^{13}C NMR δ 139.0, 138.6 (C), 128.3 (x 2), 128.2 (x 2), 127.7 (x 2), 127.6 (x 2), 127.5, 127.4, 78.7 (CH), 72.8, 70.7, 70.5, 62.9, 33.7, 32.7, 30.3, 29.6, 25.7, 25.6, 25.3 (CH_2).

IR ν_{max} 3400 (br, OH) cm^{-1}.

HR FABMS *m/z* 371.2573 ($M+H^+$). Calcd. for $C_{24}H_{34}O_3$, 371.2580.



(4*S*)-1,4-Bis(benzyloxy)undec-10-ene (21). A solution of alcohol **19** (1.11 g, 3 mmol) in dry CH_2Cl_2 (20 mL) was treated under N_2 with Dess-Martin periodinane (2.55 g, 6 mmol). The reaction mixture was stirred for 45 min. at room temperature, quenched by addition of 10% aq $Na_2S_2O_8$ (70 mL) and stirred for further 15 min. Work-up (extraction with CH_2Cl_2, 3 x 25 mL) and removal of all volatiles under reduced pressure provided crude aldehyde **20**, which was directly used in the next step.
Methyl triphenylphosphonium bromide (1.61 g, 4.5 mmol) was suspended under N_2 in dry THF (7 mL) and treated with *n*BuLi (1.6 M solution in hexanes, 2.25 mL, 3.6 mmol). The mixture was stirred for 1 h at room temperature and then cooled to −78 °C. A solution of the crude aldehyde **20** from above in dry THF (1.5 mL) was then added via syringe. The reaction mixture was stirred for 5 min. at −78 °C and then for further 90 min. at room temperature Work-up (extraction with EtOAc, 3 x 20 mL) and column chromatography on silica gel (hexanes-EtOAc, 9:1) yielded olefin **21** (715 mg, 65% overall from **19**).

Colorless oil: $[\alpha]_D$ +2.2 (c 1.1; $CHCl_3$).

^{1}H NMR δ 7.40-7.30 (10H, br m), 5.84 (1H, ddt, *J* = 17.2, 10.2, 6.6 Hz), 5.03 (1H, br d, *J* = 17.2 Hz), 4.97 (1H, br d, *J* = 10.2 Hz), 4.53 (4H, br s), 3.50 (2H, m), 3.43 (1H, quint, *J* = 5.8 Hz), 2.08 (2H, br q, J ~ 7 Hz), 1.80-1.50 (6H, br m), 1.45-1.30 (6H, m).

^{13}C NMR δ 139.0, 138.6 (C), 139.1, 128.3 (x 2), 128.2 (x 2), 127.7 (x 2), 127.6 (x 2), 127.4, 127.3, 78.7 (CH), 114.2, 72.8, 70.7, 70.5, 33.7, 33.6, 30.3, 29.3, 28.8, 25.6, 25.1 (CH_2).

HR EIMS *m/z* (% rel. int.) 366.2548 (M^+, 1), 91 (100). Calcd. for $C_{25}H_{34}O_2$, 366.2558.
