Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Double Diastereoselection in *Anti* Aldol Reactions Mediated by Dicyclohexylchloroborane between An L-Erythrulose Derivative and Chiral Aldehydes

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Supporting Information

Contents:

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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. ^{13}C NMR signal multiplicities were determined with the DEPT pulse sequence. Mass spectra were run in the EI (70 eV), the FAB (*m*-nitrobenzyl alcohol matrix) or the electrospray (ESMS) 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.

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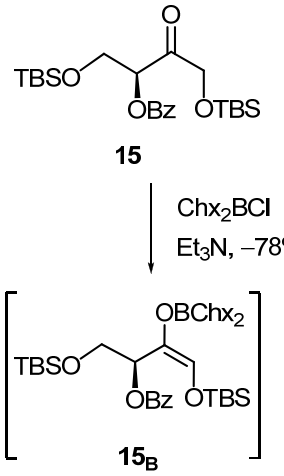
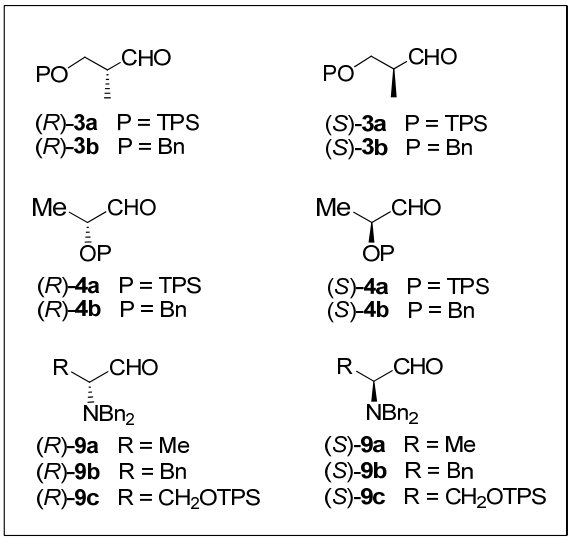
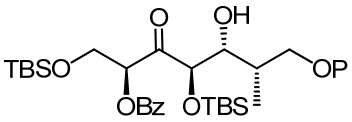
General reaction scheme

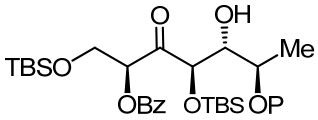




15_B —(*R*)-**3a,b**→ Complex mixtures (+ decomp.)

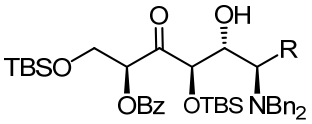
15_B —(*S*)-**3a,b**, d.r.> 95:5→ 

17a (P = TPS, 76 %)
17b (P = Bn, 81 %)

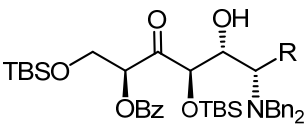
15_B —(*R*)-**4a,b**, d.r.> 95:5→ 

18a (P = TPS, 73 %)
18b (P = Bn, 79 %)

15_B —(*S*)-**4a,b**→ Complex mixtures (+ decomp.)

15_B —(*R*)-**9a,b,c**, d.r.> 95:5→ 

19a (R = Me, 84 %)*
19b (R = $PhCH_2$, 77 %)
19c (R = CH_2OTPS, 82 %)
(* d.r. = 88:12)

15_B —(*S*)-**9a,b,c**, d.r.> 95:5→ 

20a (R = Me, 63 %)
20b (R = $PhCH_2$, 88 %)
20c (R = CH_2OTPS, 76 %)

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General experimental procedures

Experimental procedure for the one-pot aldolization/reduction. Procedure as described in the main text up to aldehyde addition. After stirring for 5 h at −78°C, the solution was treated dropwise with a 2M solution of $LiBH_4$ in THF (1.5 mL, 3 mmol). The stirring was then continued at −78°C for 2 h. The reaction was quenched with pH 7 phosphate buffer (6 mL) and MeOH (6 mL), followed by a 30% aq H_2O_2 solution (3 mL). After stirring for 1 h at room temperature, the mixture was poured into satd. aq $NaHCO_3$ and worked up as above. Removal of volatiles under reduced pressure and column chromatography of the residue on silica gel (hexanes-EtOAc mixtures) afforded the desired 1,3-diols. Yields are indicated in each case (see below).

***O*-Methylation of alcohols with Meerwein salt.** The appropriate alcohol (1 mmol) was dissolved under N_2 in anhydrous CH_2Cl_2 and treated with trimethyloxonium tetrafluoroborate (5 mmol per hydroxyl group) and 1,8-bis(N,N-dimethylamino)naphthalene (5 mmol per hydroxyl group). The mixture was stirred at room temp. for 24 h. Work-up (extraction with CH_2Cl_2) and column chromatography on silica gel (hexanes-EtOAc mixtures) gave the desired *O*-methylated derivative. Yields are indicated in each case (see below).

Formation of acetonides from 1,3-diols. The 1,3-diol (1 mmol) and *p*-toluenesulfonic acid (19 mg, 0.1 mmol) were dissolved in a 4:1 acetone / 2,2-dimethoxypropane (2,2-DMP) mixture (5 mL). The mixture was then stirred at room temperature until consumption of the starting material (TLC monitoring). After adding Et_3N (0.1 mL), all volatiles were removed under reduced pressure and the residue was chromatographed on silica gel (hexanes-EtOAc mixtures).

Formation of cyclic diol carbonates. A solution of the diol (1 mmol) in anhydrous toluene (8 mL) was treated with CDI (carbonyl-1,1´-diimidazole, 325 mg, 2 mmol). The reaction mixture was stirred at reflux until consumption of the starting material (several hours, TLC monitoring). Removal of volatiles under reduced pressure was followed by column chromatography of the residue on silica gel (hexanes-EtOAc mixtures) to afford the cyclic carbonate. Yields are indicated in each case (see below).

Formation of TPS derivatives. A solution of the alcohol (1 mmol) and imidazole (170 mg, 2.5 mmol) in dry CH_2Cl_2 (4 mL) was treated dropwise under Ar with a solution of TPS chloride (1.5 mmol) in dry CH_2Cl_2 (2 mL). The reaction mixture was stirred overnight at room temp., then diluted with CH_2Cl_2 and worked up. Column chromatography on silica gel (hexanes-EtOAc mixtures) afforded the desired silyl derivative.

Desilylation of silyl derivatives. The silyl derivative (1 mmol) was dissolved under Ar in dry THF (3 mL). Tetra-*n*-butylammonium fluoride trihydrate (TBAF, 315 mg, 1.2 mmol) dissolved in dry THF (1 mL) was then added. The reaction mixture was stirred at room temp. until consumption of the starting material. After addition of an aqueous satd. NH_4Cl solution (0.1 mL), the mixture was stirred for 5 min.

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and evaporated under reduced pressure. The residue was then chromatographed on silica gel (hexanes-EtOAc mixtures).

Saponification of benzoates. A solution of the ester (1 mmol) en MeOH (50 mL) was treated with K_2CO_3 (10 mmol) and stirred for 24 h at room temperature. After removal of volatiles under reduced pressure, the residue was diluted with water (50 mL) and extracted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4 and the volatiles were eliminated under reduced pressure. Column chromatography of the residue on silica gel (hexanes-EtOAc mixtures) furnished the desired alcohol.

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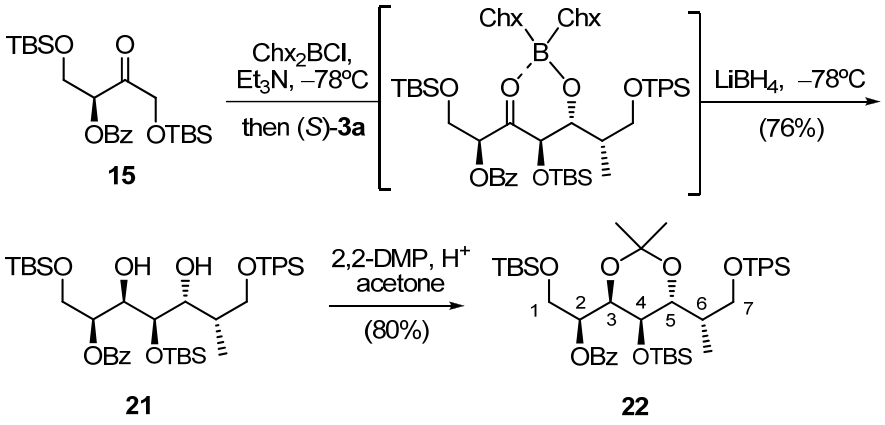
Chemical correlations

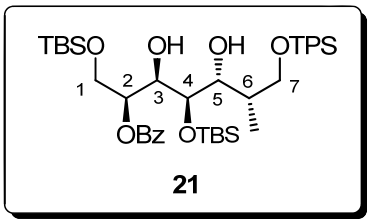
Aldols from α-methyl aldehydes (*S*)-3a and (*S*)-3b

The stereostructures of aldols **17a** and **17b**, obtained in the aldol reactions of **15** with aldehydes (*S*)-**3a** and (*S*)-**3b** (page S-3), were established indirectly by means of chemical correlations.

Aldol 17a

❖ In the case of the aldol reaction of **15** with (*S*)-**3a**, the intermediate boron aldolate was reduced in situ with $LiBH_4$ to yield diol **21**, which was then converted into acetonide **22** (for reaction conditions, see pages S-4/S-5). The relative configuration of stereocentres C3 and C5 was established as *anti*-1,3[1] on the basis of the ^{13}C NMR shifts of the methyl and acetal carbons in **22**.[2] The coupling constants involving H3, H4 and H5 (see below) further indicate the stereochemical relations within this carbon chain[3] (see references in page S-27).





Oil: $[\alpha]_D$ +44.5 (*c* 3.3; $CHCl_3$).

IR ν_{max} (cm^{-1}): 3470 (br, OH), 1722 (C=O).

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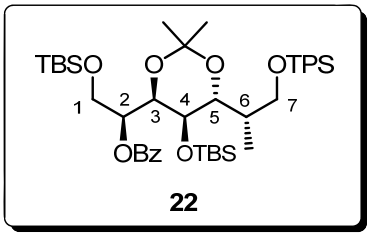
HR EIMS *m/z* (% rel. int.) 723.3597 (M^+–*t*Bu, 1), 269 (42), 105 (100). Calcd. for $C_{43}H_{68}O_7Si_3$–*t*Bu, 723.3568.

^{1}H NMR (500 MHz) δ 8.16 (2H, br d, *J* ~ 7.5 Hz; aromatic), 7.60-7.30 (13H, br m; aromatic), 5.53 (1H, td, *J* = 6, 2.5 Hz; H-2), 4.10-4.05 (3H, m; H-3/H-5/OH), 3.98 (1H, dd, *J* = 10.2, 6 Hz; H-1), 3.94 (1H, dd, *J* = 8.6, 3.5 Hz; H-4), 3.87 (1H, dd, *J* = 10.2, 6 Hz; H-1´), 3.72 (2H, dd, *J* = 10, 3 Hz; H-7 overlapped by OH broad singlet), 3.60 (1H, dd, *J* = 10, 4 Hz; H-7´), 1.88 (1H, m; H-6), 1.02 (3H, d, *J* = 7 Hz; *Me*-C6), 0.96 (9H, s; *Me*$_3$CSi), 0.89 (9H, s; *Me*$_3$CSi), 0.88 (9H, s; *Me*$_3$CSi), 0.16 (3H, s; *Me*Si), 0.09 (3H, s; *Me*Si), 0.06 (3H, s; *Me*Si), 0.04 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 165.9, 132.8, 132.6, 129.6, 19.1, 18.3, 18.0 (quat C), 135.7 (x 2), 135.5 (x 2), 129.8 (x 4), 129.7, 128.3 (x 2), 127.7 (x 4), 77.1, 72.8, 72.5, 70.6, 35.0 (CH), 69.9, 62.4 (CH_2), 26.8 (x 3, *Me*$_3$CSi), 25.9 (x 6, 2 *Me*$_3$CSi), 9.2 (*Me*-C6), –3.9 (*Me*Si), –4.7 (*Me*Si), –5.5 (x 2) (*Me*Si).



22

Oil: $[\alpha]_D$ +1.8 (*c* 1.15; $CHCl_3$).

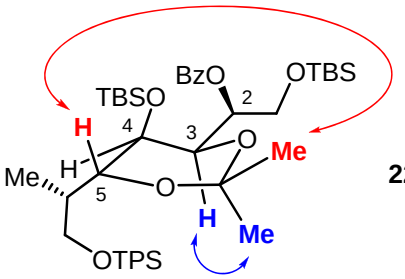
IR ν_{max} (cm^{-1}): 1720 (C=O).

HR EIMS *m/z* (% rel. int.) 763.3949 (M^+–*t*Bu, 2), 179 (100), 105 (63). Calcd. for $C_{46}H_{72}O_7Si_3$–*t*Bu, 763.3881.

^{1}H NMR (500 MHz) δ 8.08 (2H, br d, *J* ~ 7.5 Hz; aromatic), 7.70 (4H, m; aromatic), 7.54 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.45-7.35 (8H, br m; aromatic), 5.33 (1H, dt, *J* = 9, 2 Hz; H-2), 4.19 (1H, dd, *J* = 9, 2.2 Hz; H-3), 4.09 (1H, dd, *J* = 4.6, 2.2 Hz; H-4), 4.05 (1H, dd, *J* = 4.6, 1.8 Hz; H-5), 4.02 (1H, dd, *J* = 12, 2 Hz; H-1), 3.97 (1H, dd, *J* = 12, 2 Hz; H-1´), 3.66 (1H, t, *J* = 9.5 Hz; H-7), 3.50 (1H, dd, *J* = 9.5, 6 Hz; H-7´), 2.11 (1H, m; H-6), 1.37 (3H, s; acetonide Me), 1.29 (3H, s; acetonide Me), 1.07 (9H, s; *Me*$_3$CSi), 0.96 (9H, s; *Me*$_3$CSi), 0.89 (3H, d, *J* = 7 Hz; *Me*-C6), 0.88 (9H, s; *Me*$_3$CSi), 0.18 (3H, s; *Me*Si), 0.15 (3H, s; *Me*Si), 0.01 (6H, s; 2 *Me*Si).

^{13}C NMR (125 MHz) δ 166.2, 133.8, 133.7, 130.9, 100.4, 19.2, 18.3, 18.2 (quat C), 135.7 (x 4), 132.6, 129.5 (x 4), 128.2 (x 2), 127.6 (x 4), 74.4, 73.6, 71.8, 70.2, 38.3 (CH), 65.7, 61.7 (CH_2), 26.9 (x 3, *Me*$_3$CSi), 26.0 (x 3, *Me*$_3$CSi), 25.7 (x 3, *Me*$_3$CSi), 25.4 (acetonide Me), 23.7 (acetonide Me), 9.7 (*Me*-C6), –2.8 (*Me*Si), –4.5 (*Me*Si), –5.4 (*Me*Si), –5.5 (*Me*Si).

The chemical shift values of the methyl acetonide carbons (25.4, 23.7 ppm) and of the acetal carbon (100.4 ppm) indicate that compound **22** is the acetonide of an *anti*-1,3-diol.[2] NOE measurements, including the absence of NOE between H-3 and H-5, are consistent with this stereochemical assignment. The coupling constant values in the C3-C4-C5 segment support the configuration assignments at these stereocentres.[3]

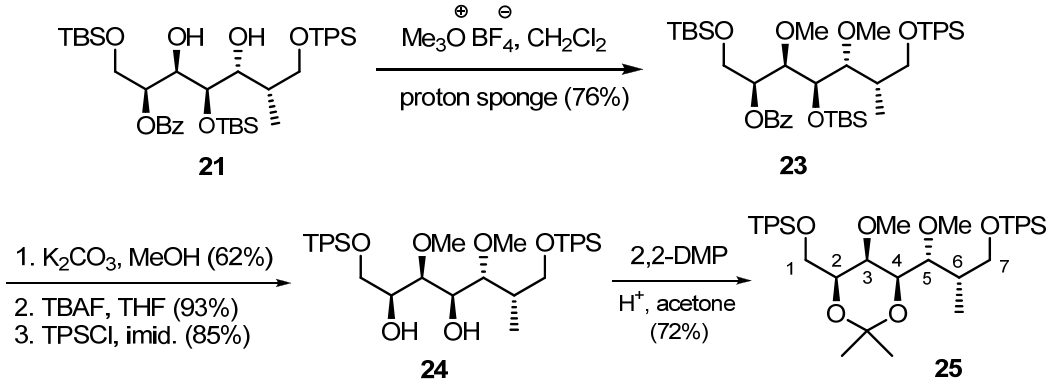


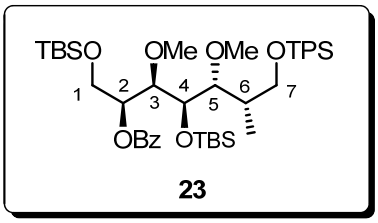
22

NOEs indicate that H-3 and H-5 are on opposite sides of the ring

H-3 δ **4.19 (dd, $J_{2,3}$ = 9, $J_{3,4}$ = 2.2 Hz)**
H-4 δ **4.09 (dd, $J_{3,4}$ = 2.2 Hz, $J_{4,5}$ = 4.6 Hz)**
H-5 δ **4.05 (dd, $J_{5,6}$ = 1.8 Hz, $J_{4,5}$ = 4.6 Hz)**

Compound **21**, obtained as described above (page S-6), was methylated with Meerwein salt to **23** and then debenzoylated by means of alkaline hydrolysis (for reaction conditions, see pages S-4/S-5). The intermediate alcohol was desilylated with TBAF and then selectively resilylated at the two primary alcohol functions to give diol **24**, which was subsequently converted into acetonide **25**. The relative configuration of stereocentres C2 and C4 in the latter compound was established as *syn*-1,3 on the basis of the ^{13}C NMR shifts of the methyl and acetal carbons.[2] The coupling constants involving H2, H3 and H4 further indicate the stereochemical relations within this carbon chain.





23

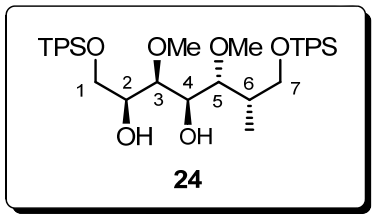
Oil: $[\alpha]_D$ +9.2 (*c* 1.68; $CHCl_3$).

IR ν_{max} (cm^{-1}): 1724 (C=O).

HR EIMS *m/z* (% rel. int.) 751.3941 (M^+–*t*Bu, 8), 179 (74), 105 (100). Calcd. for $C_{45}H_{72}O_7Si_3$–*t*Bu, 751.3881.

^{1}H NMR (500 MHz) δ 8.12 (2H, br d, *J* ~ 8 Hz; aromatic), 7.70 (4H, br t, *J* ~ 6 Hz; aromatic), 7.56 (1H, br t, *J* ~ 7.3 Hz; aromatic), 7.45-7.35 (8H, br m; aromatic), 5.40 (1H, apparent q, *J* ~ 5.3 Hz; H-2), 4.02 (1H, t, *J* = 5.5 Hz; H-4), 3.92 (1H, dd, *J* = 10.3, 6 Hz; H-1), 3.88 (1H, dd, *J* = 10.3, 5.6 Hz; H-1´), 3.65 (2H, m; H-3/H-7), 3.55-3.50 (2H, m; H-5/H-7), 3.54 (3H, s; OMe), 3.33 (3H, s; OMe), 2.19 (1H, m; H-6), 1.10 (9H, s; *Me*$_3$CSi), 0.96 (9H, s; *Me*$_3$CSi), 0.93 (3H, d, *J* = 7 Hz; *Me*-C6), 0.89 (9H, s; *Me*$_3$CSi), 0.16 (3H, s; *Me*Si), 0.09 (3H, s; *Me*Si), 0.06 (3H, s; *Me*Si), 0.05 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 165.8, 133.9 (x 2), 130.5, 19.3, 18.5, 18.1 (quat C), 135.7 (x 2), 135.6 (x 2), 132.8, 129.8 (x 2), 129.5 (x 2), 128.3 (x 2), 127.7 (x 4), 81.3, 79.8, 75.2, 72.5, 37.2 (CH), 66.7, 61.3 (CH_2), 61.2 (OMe), 59.5 (OMe), 26.9 (x 3, *Me*$_3$CSi), 26.2 (x 3, *Me*$_3$CSi), 25.8 (x 3, *Me*$_3$CSi), 11.4 (*Me*-C6), –3.8 (*Me*Si), –4.0 (*Me*Si), –5.5 (x 2) (*Me*Si).



24

Oil: $[\alpha]_D$ +4.1 (*c* 0.8; $CHCl_3$).

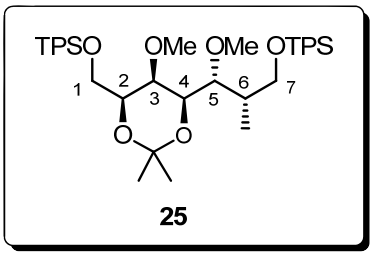
IR ν_{max} (cm^{-1}): 3460 (br, OH).

HR FABMS *m/z* 715.3877 ($M+H^+$). Calcd. for $C_{42}H_{59}O_6Si_2$, 715.3844.

^{1}H NMR (500 MHz) δ 7.75-7.70 (8H, br m; aromatic), 7.50-7.35 (12H, br m; aromatic), 3.97 (1H, apparent quint, *J* ~ 4.5 Hz; H-2), 3.85-3.80 (2H, m; H-1/H-1´), 3.75-3.65 (3H, br m; H-4/H-7/H-7´), 3.63 (5H, br s; OMe signal overlapping the signals of H-3 and H-5), 3.48 (3H, s; OMe), 2.80 (1H, br d, *J* = 4

Hz; OH), 2.70 (1H, br s; OH), 2.24 (1H, m; H-6), 1.11 (9H, s; *Me*$_3$CSi), 1.10 (9H, s; *Me*$_3$CSi), 0.88 (3H, d, *J* = 7 Hz; *Me*-C6).

^{13}C NMR (125 MHz) δ 133.7, 133.6, 133.2, 133.1, 19.2 (x 2) (quat C), 135.6 (x 4), 135.5 (x 4), 129.8 (x 2), 129.6 (x 2), 127.7 (x 4), 127.6 (x 4), 79.9, 78.6, 74.0, 72.1, 36.5 (CH), 66.3, 64.4 (CH_2), 60.8 (OMe), 59.9 (OMe), 26.9 (x 3, *Me*$_3$CSi), 26.8 (x 3, *Me*$_3$CSi), 10.1 (*Me*-C6).



25

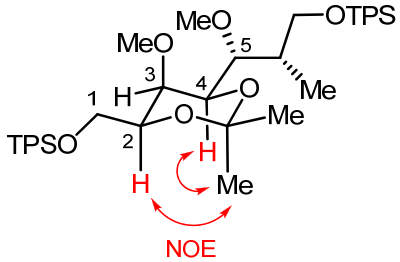
Oil: $[\alpha]_D$ +12.2 (*c* 0.9; $CHCl_3$).

HR EIMS *m/z* (% rel. int.) 739.3869 (M^+–*t*Bu, 2), 213 (100). Calcd. for $C_{45}H_{62}O_6Si_2$–*t*Bu, 739.3850.

^{1}H NMR (500 MHz) δ 7.75-7.65 (8H, br m; aromatic), 7.45-7.35 (12H, br m; aromatic), 3.93 (1H, br dd, *J* ~ 9, 8.3 Hz; H-1), 3.88 (1H, br dd, *J* ~ 8.3, 4.8 Hz; H-2), 3.80 (1H, br d, *J* ~ 8.5 Hz; H-5), 3.75-3.70 (2H, m; H-1´/H-7), 3.64 (1H, br d, *J* ~ 8.5 Hz; H-4), 3.60 (1H, m; H-7´), 3.58 (3H, s; OMe), 3.48 (3H, s; OMe), 3.45 (1H, br s; H-3), 2.21 (1H, m; H-6), 1.36 (3H, s; acetonide Me), 1.30 (3H, s; acetonide Me), 1.09 (9H, s; *Me*$_3$CSi), 1.08 (9H, s; *Me*$_3$CSi), 0.85 (3H, d, *J* = 7 Hz; *Me*-C6).

^{13}C NMR (125 MHz) δ 134.1, 133.9, 133.5, 133.4, 98.5, 19.3, 19.2 (quat C), 135.7 (x 4), 135.6 (x 4), 129.7 (x 2), 129.5 (x 2), 127.7 (x 4), 127.6 (x 4), 78.2, 73.5, 72.1, 71.3, 36.1 (CH), 66.5, 62.8 (CH_2), 60.6 (OMe), 60.0 (OMe), 29.5 (acetonide Me), 26.9 (x 6, 2 *Me*$_3$CSi), 18.7 (acetonide Me), 10.1 (*Me*-C6).

The chemical shift values of the methyl acetonide carbons (29.5, 18.7 ppm) and of the acetal carbon (98.5 ppm) indicate that compound **25** is the acetonide of an *syn*-1,3-diol.[2] The observed NOEs confirm this conclusion.



25

NOEs indicate that H-2 and H-4 are on the same side of the ring

H-2 δ 3.88 (br dd, $J_{1,2}$ ≈ 8.3 $J_{1',2}$ ≈ 4.8)
H-3 δ 3.45 (br s, $J_{2,3}$ ≈ $J_{3,4}$ < 1 Hz)
H-4 δ 3.64 (br d, $J_{4,5}$ ≈ 8.5 Hz)

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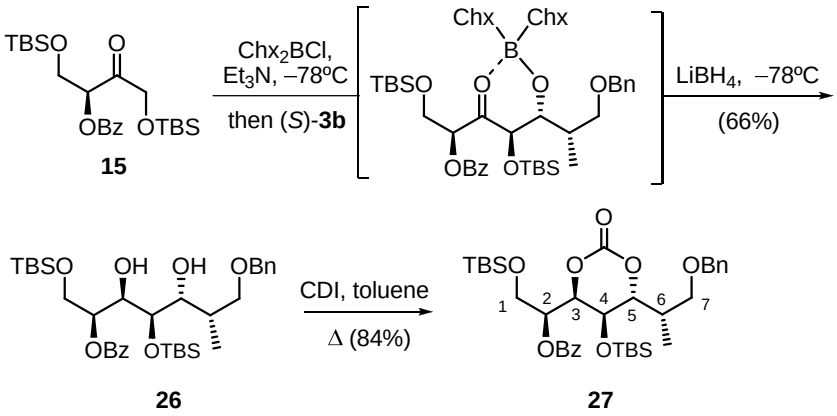
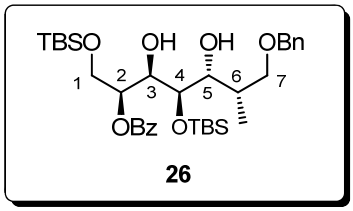
Aldol 17b

❖ In the case of the aldol reaction of **15** with (*S*)-**3b**, the intermediate boron aldolate was reduced in situ with $LiBH_4$ to yield diol **26**, which was then converted into cyclic carbonate **27** through reaction with CDI (for reaction conditions, see pages S-4/S-5). The relative configuration of stereocentres C3, C4 and C5 in **27** was established as depicted on the basis of the coupling constants involving H3/H4/H5.





Oil: $[\alpha]_D$ +32.5 (*c* 0.4; $CHCl_3$).

IR ν_{max} (cm^{-1}): 3470 (br, OH), 1723 (C=O).

HR FABMS *m/z* 633.3638 ($M+H^+$). Calcd. for $C_{34}H_{57}O_7Si_2$, 633.3642.

^{1}H NMR (500 MHz) δ 8.12 (2H, br d, *J* ~ 8 Hz; aromatic), 7.52 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.42 (2H, br t, *J* ~ 7.5 Hz; aromatic), 7.30-7.25 (3H, br m; aromatic), 7.12 (2H, m; aromatic), 5.46 (1H, br td, *J* ~ 5.5, 3.5 Hz; H-2), 4.28, 4.24 (2H, AB system, *J* = 11.7 Hz; benzyl C*H*$_2$), 4.07 (1H, br dt, *J* ~ 9.2, 3.5 Hz; H-3), 4.00-3.90 (5H, br m; H-1/H-4/H-5/2 OH), 3.85 (1H, dd, *J* = 10.2, 5.5 Hz; H-1´), 3.45 (2H, m; H-7/H-7´), 1.97 (1H, m; H-6), 1.02 (3H, d, *J* = 7 Hz; *Me*-C6), 0.90 (9H, s; *Me*$_3$CSi), 0.88 (9H, s; *Me*$_3$CSi), 0.14 (3H, s; *Me*Si), 0.09 (3H, s; *Me*Si), 0.06 (3H, s; *Me*Si), 0.04 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 166.1, 137.8, 130.6, 18.3, 18.0 (quat C), 132.9, 129.8 (x 2), 128.4 (x 2), 128.3 (x 2), 127.6, 127.4 (x 2), 77.0, 72.8, 72.6, 70.6, 34.0 (CH), 76.3, 73.4, 62.4 (CH_2), 25.9 (x 6, 2 *Me*$_3$CSi), 9.9 (*Me*-C6), –3.9 (*Me*Si), –4.7 (*Me*Si), –5.5 (x 2) (*Me*Si).

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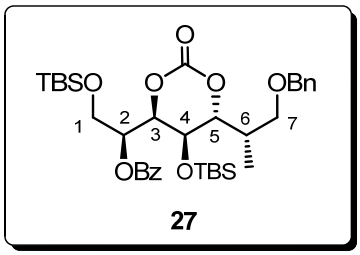


27

Oil: $[\alpha]_D$ +50 (*c* 1; $CHCl_3$).

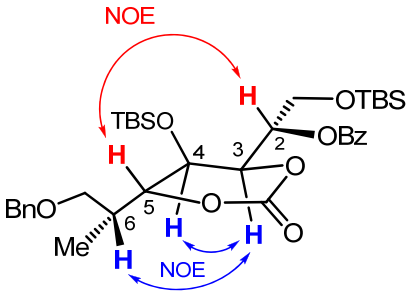
IR ν_{max} (cm^{-1}): 1765, 1728 (C=O).

HR FABMS *m/z* 659.3420 ($M+H^+$). Calcd. for $C_{35}H_{55}O_8Si_2$, 659.3435.

^{1}H NMR (500 MHz) δ 7.99 (2H, br d, *J* ~ 8 Hz; aromatic), 7.48 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.36 (2H, br t, *J* ~ 7.5 Hz; aromatic), 7.25-7.20 (3H, br m; aromatic), 7.07 (2H, m; aromatic), 5.48 (1H, dt, *J* = 6.5, 4.5 Hz; H-2), 4.83 (1H, br t, *J* ~ 4.5 Hz; H-3), 4.47 (1H, dd, *J* = 6.8, 4.4 Hz; H-5), 4.27 (1H, dd, *J* = 6.8, 4.5 Hz; H-4), 4.20, 4.14 (2H, AB system, *J* = 12 Hz; benzyl C*H*$_2$), 3.90 (1H, dd, *J* = 10.3, 6.5 Hz; H-1), 3.83 (1H, dd, *J* = 10.3, 4.5 Hz; H-1´), 3.35-3.25 (2H, m; H-7/H-7´), 2.04 (1H, m; H-6), 0.96 (3H, d, *J* = 7 Hz; *Me*-C6), 0.88 (9H, s; *Me*$_3$CSi), 0.87 (9H, s; *Me*$_3$CSi), 0.08 (3H, s; *Me*Si), 0.06 (3H, s; *Me*Si), 0.03 (6H, s; 2 *Me*Si).

^{13}C NMR (125 MHz) δ 165.1, 148.4, 137.8, 129.4, 18.3, 17.9 (quat C), 133.3, 129.8 (x 2), 128.4 (x 2), 128.3 (x 2), 127.5, 127.3 (x 2), 81.7, 75.8, 71.1, 62.5, 35.0 (CH), 73.0, 71.2, 60.2 (CH_2), 25.8 (x 3, *Me*$_3$CSi), 25.6 (x 3, *Me*$_3$CSi), 10.5 (*Me*-C6), –4.4 (*Me*Si), –4.6 (*Me*Si), –5.5 (x 2) (*Me*Si).

The absence of NOE between H-3 and H-5 suggests that compound **27** is the carbonate of an *anti*-1,3-diol. This conclusion is further supported by the NOEs between the hydrogen pairs H-2/H-5 and H-3/H-6. The coupling constant values in the C3-C4-C5 segment are consistent with this conclusion[3] and indicate the relative configurations at these three stereocentres.



NOEs indicate that H-3 and H-5 are on opposite sides of the ring whereas H-3 and H-4 are spatially proximal

27
- **H-3 δ 4.83 (br t, $J_{2,3} \approx J_{3,4} \approx 4.5$ Hz)**
- **H-4 δ 4.27 (dd, $J_{3,4} = 4.5$ Hz, $J_{4,5} = 6.8$ Hz)**
- **H-5 δ 4.47 (dd, $J_{5,6} = 4.4$ Hz, $J_{4,5} = 6.8$ Hz)**

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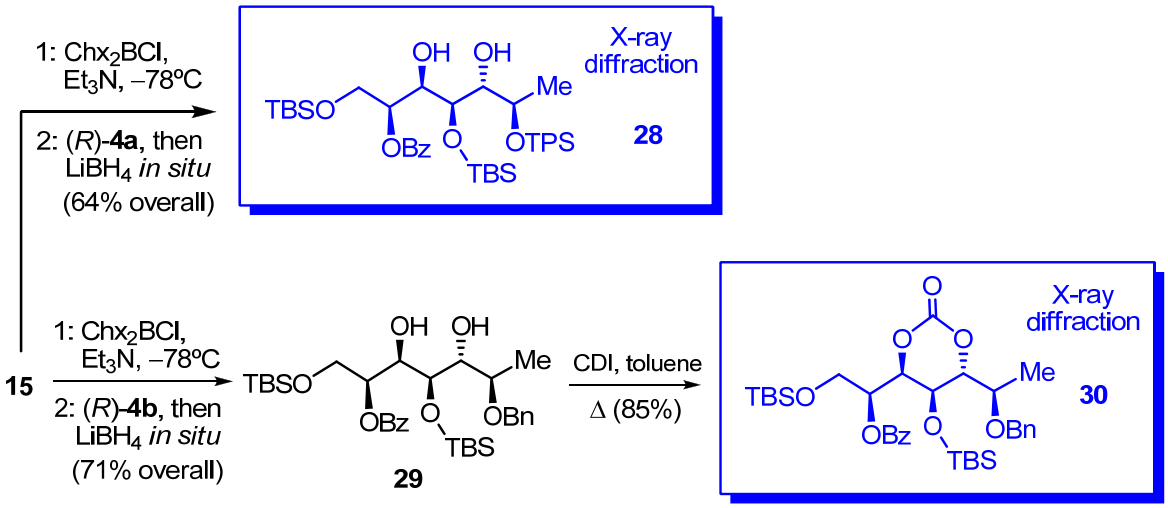
Aldols from α-oxygenated aldehydes

The stereostructures of the aldols **18a** and **18b**, generated in the reactions of **15** with α-oxygenated aldehydes (*R*)-**4a** and (*R*)-**4b** (page S-3), were determined by means of a combination of chemical correlations and X-ray diffraction analyses.

- Aldol reaction of **15** and (*R*)-**4a** followed by reduction *in situ*[1] with $LiBH_4$ (for reaction conditions, see pages S-4/S-5) gave diol **28**. The diol was crystalline and could be analyzed by means of X-ray diffraction. This established the absolute configuration of aldol **18a** in an unambiguous way.
- Aldol reaction of **15** and (*R*)-**4b** followed by reduction *in situ*[1] with $LiBH_4$ (page S-4) gave diol **28**. Treatment of the latter with CDI (for reaction conditions, see pages S-4/S-5) afforded the crystalline carbonate **30**, which was analyzed by means of X-ray diffraction. This established the absolute configuration of aldol **18b** in an unambiguous way.



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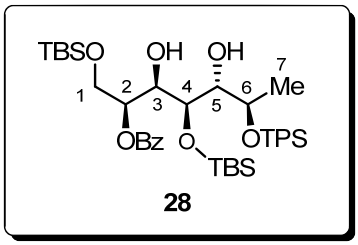


28

Solid: mp 83-84 ºC ($CHCl_3/CH_2Cl_2$); $[\alpha]_D$ +43.5 (*c* 1.05; $CHCl_3$).

IR ν_{max} (cm^{-1}): 3500 (br, OH), 1722 (C=O).

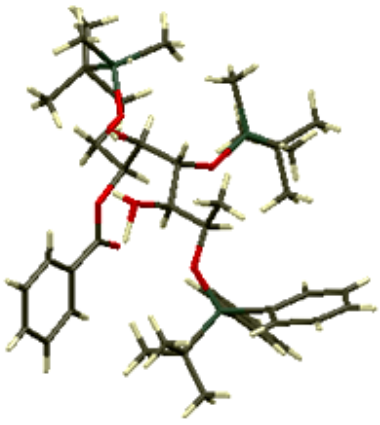
HR FABMS *m/z* 767.4191 ($M+H^+$). Calcd. for $C_{42}H_{67}O_7Si_3$, 767.4194.

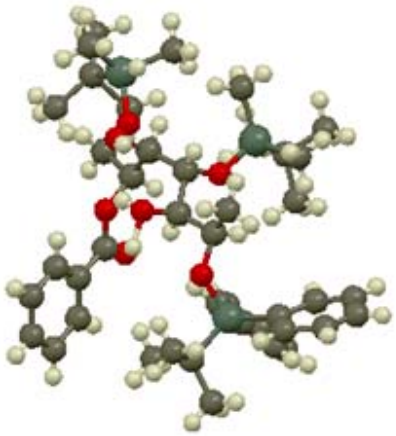
^{1}H NMR (500 MHz) δ 8.16 (2H, br d, *J* ~ 7.5 Hz; aromatic), 7.60-7.30 (13H, br m; aromatic), 5.46 (1H, dt, *J* = 6, 2.5 Hz; H-2), 4.05-3.95 (2H, m; H-6/OH), 3.93 (1H, dd, *J* = 10, 7 Hz; H-4), 3.90-3.80 (4H, br m; H-1/H-1´/H-3/H-5), 2.90 (1H, br s; OH), 0.97 (3H, d, *J* = 6.5 Hz; H-7), 0.88 (9H, s; *Me*$_3$CSi), 0.85 (9H, s; *Me*$_3$CSi), 0.74 (9H, s; *Me*$_3$CSi), 0.07 (6H, s; 2 *Me*Si), 0.05 (3H, s; *Me*Si), –0.12 (3H, s; *Me*Si).

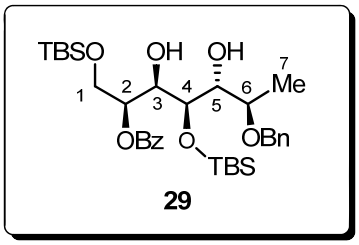
^{13}C NMR (125 MHz) δ 165.7, 134.8, 134.1, 130.4, 18.9, 18.4, 17.8 (quat C), 135.7 (x 4), 133.0, 129.8 (x 4), 128.3 (x 2), 127.7 (x 2), 127.5 (x 2), 77.3, 72.3 (x 2), 70.5, 69.8 (CH), 61.8 (CH_2), 26.8 (x 3, *Me*$_3$CSi), 25.9 (x 3, *Me*$_3$CSi), 25.7 (x 3, *Me*$_3$CSi), 15.3 (C7), –3.9 (*Me*Si), –4.9 (*Me*Si), –5.4 (*Me*Si), –5.5 (*Me*Si).

The definitive assignment came from an X-ray diffraction analysis (data deposited at the Cambridge Crystallographic Data Centre; deposition number: CCDC-880798).

Two views of the molecule of compound **28**







29

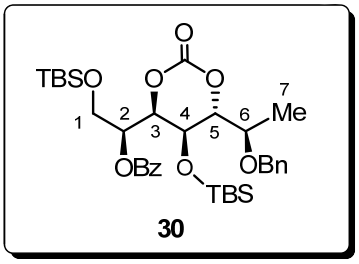
Oil: $[\alpha]_D$ +21.2 (*c* 1.5; $CHCl_3$).

IR ν_{max} (cm^{-1}): 3490 (br, OH), 1722 (C=O).

HR FABMS *m/z* 619.3492 ($M+H^+$). Calcd. for $C_{33}H_{55}O_7Si_2$, 619.3486.

^{1}H NMR (500 MHz) δ 8.12 (2H, br d, *J* ~ 7.5 Hz; aromatic), 7.57 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.43 (2H, br t, *J* ~ 7.5 Hz; aromatic), 7.30-7.25 (3H, br m; aromatic), 7.15 (2H, m; aromatic), 5.44 (1H, apparent q, *J* ~ 5 Hz; H-2), 4.43 (1H, d, *J* = 11.5 Hz; benzyl CH_2), 4.33 (1H, d, *J* = 11.5 Hz; benzyl CH_2), 4.12 (1H, dt, *J* = 9, 3.5 Hz; H-3), 3.98 (1H, dd, *J* = 6.5, 3.5 Hz; H-4), 3.95-3.90 (2H, m; H-1/H-5), 3.83 (1H, dd, *J* = 10.5, 5.5 Hz; H-1´), 3.67 (1H, apparent quint, *J* ~ 6 Hz; H-6), 3.60 (1H, d, *J* = 9 Hz; 3-OH), 2.90 (1H, d, *J* = 3 Hz; 5-OH), 1.22 (3H, d, *J* = 6 Hz; H-7), 0.90 (9H, s; *Me*$_3$CSi), 0.87 (9H, s; *Me*$_3$CSi), 0.13 (3H, s; *Me*Si), 0.08 (3H, s; *Me*Si), 0.04 (3H, s; *Me*Si), 0.02 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 166.2, 138.2, 130.4, 18.3, 18.1 (quat C), 133.0, 129.8 (x 2), 128.4 (x 4), 127.6 (x 3), 75.4, 75.0, 73.4, 72.0, 70.8 (CH), 70.4, 62.4 (CH_2), 25.9 (x 6, 2 *Me*$_3$CSi), 13.9 (C7), –4.1 (*Me*Si), –4.5 (*Me*Si), –5.4 (x 2) (*Me*Si).



30

Solid: mp 121-122 ºC (from Et_2O-pentane); $[\alpha]_D$ +33 (*c* 2; $CHCl_3$).

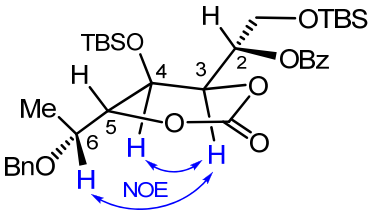
IR ν_{max} (cm^{-1}): 1768, 1723 (C=O).

HR FABMS *m/z* 645.3275 ($M+H^+$). Calcd. for $C_{34}H_{53}O_8Si_2$, 645.3279.

^{1}H NMR (500 MHz) δ 8.05 (2H, br d, *J* ~ 7.5 Hz; aromatic), 7.57 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.44 (2H, br t, *J* ~ 7.5 Hz; aromatic), 7.35-7.20 (5H, br m; aromatic), 5.42 (1H, dt, *J* ~ 6.5, 3 Hz; H-2), 5.10

(1H, dd, *J* ~ 6.5, 3 Hz; H-3), 4.60 (1H, d, *J* = 11.5 Hz; benzyl CH_2), 4.46 (1H, d, *J* = 11.5 Hz; benzyl CH_2), 4.46 (1H, H-4, signal overlapped by benzyl CH), 4.28 (1H, dd, *J* = 5, 3.3 Hz; H-5), 4.00 (1H, dd, *J* = 11.5, 4 Hz; H-1), 3.93 (1H, dd, *J* = 11.5, 3 Hz; H-1´), 3.67 (1H, apparent quint, *J* ~ 6 Hz; H-6), 1.30 (3H, d, *J* = 6.5 Hz; H-7), 0.92 (9H, s; *Me*$_3$CSi), 0.84 (9H, s; *Me*$_3$CSi), 0.14 (6H, s; 2 *Me*Si), –0.01 (3H, s; *Me*Si), –0.02 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 165.6, 147.9, 137.5, 129.8, 18.2, 18.0 (quat C), 133.2, 129.8 (x 2), 128.4 (x 4), 127.6 (x 3), 85.0, 77.3, 74.1, 73.1, 61.9 (CH), 71.6, 61.0 (CH$_2$), 25.6 (x 6, 2 *Me*$_3$CSi), 15.5 (C7), –4.1 (*Me*Si), –4.5 (*Me*Si), –5.4 (x 2) (*Me*Si).



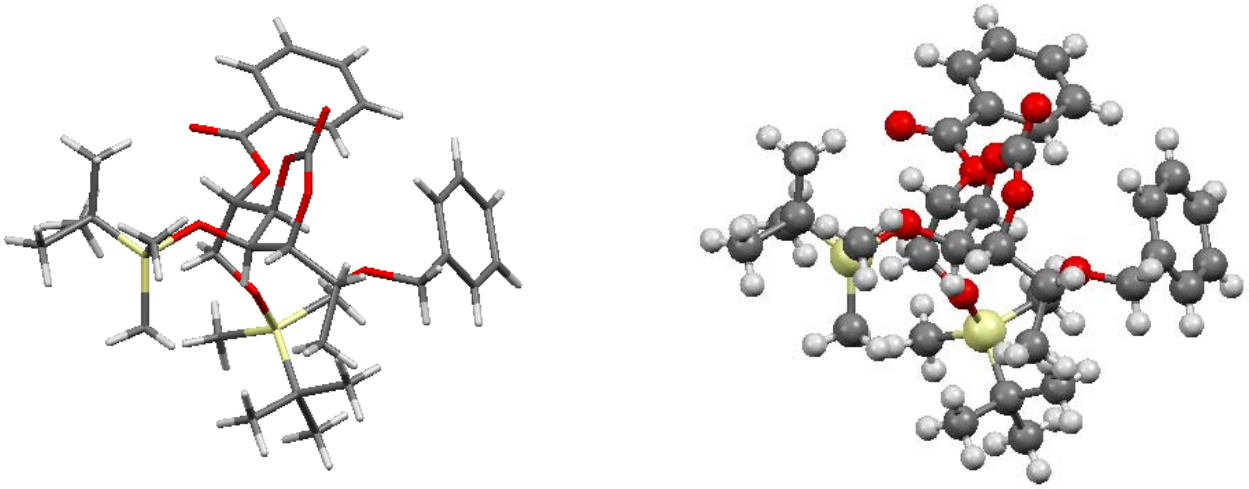
30

NOEs indicate that H-3 and H-5 are on opposite sides of the ring whereas H-3 and H-4 are spatially proximal

H-3 δ 5.10 (dd $J_{2,3}$ = 6.5, $J_{3,4}$ = 3 Hz)
H-4 δ 4.46 (overlapped signal)
H-5 δ 4.28 (dd, $J_{5,6}$ = 5 Hz, $J_{4,5}$ = 3.3 Hz)

The absence of NOE between H-3 and H-5 suggests that **30** is the carbonate of an *anti*-1,3-diol. This is confirmed by the NOEs between H-3 and H-6. The coupling constant values in the C3-C4-C5 segment support this conclusion and indicate the relative configurations at these stereocentres. The definitive assignment came from an X-ray diffraction analysis (data deposited at the Cambridge Crystallographic Data Centre; deposition number: CCDC-762867).

Two views of the molecule of compound **30**



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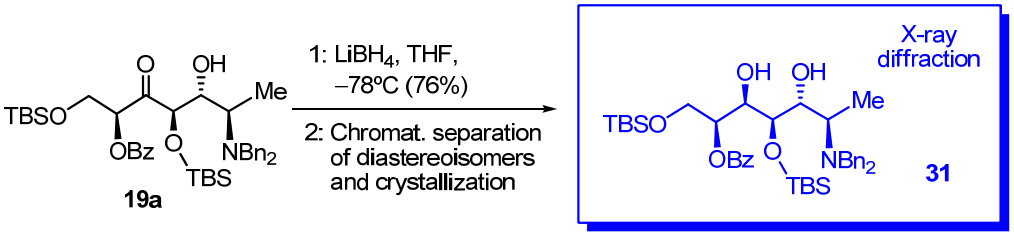
Aldols from α-amino aldehydes

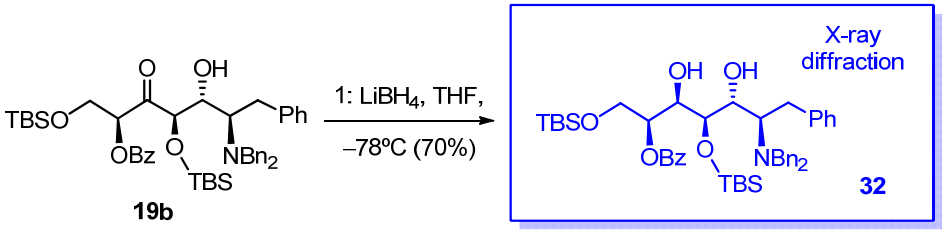
The stereostructures of the aldols **19a-c** and **20a-c**, generated in the reactions of **15** with α-amino aldehydes (*R*)- and (*S*)-**9a,b,c** (page S-3), respectively, were determined by means of a combination of chemical correlations and X-ray diffraction analyses.

Aldol reactions with aldehydes (*R*)-**9a,b,c**

➢ Reduction of aldol **19a** with $LiBH_4$ (page S-4) yielded a 1,3-diol as a mixture of diastereoisomers. The chromatographic separation of the mixture proved difficult but gave a fraction from which diol **31** could be crystallized and then analyzed by means of X-ray diffraction. This unambiguously establishes the absolute configuration of **19a**.



➢ Reduction of aldol **19b** with $LiBH_4$ (page S-4) yielded the crystalline 1,3-diol **32**, which was analyzed by means of X-ray diffraction. This unambiguously establishes the absolute configuration of **19b**.



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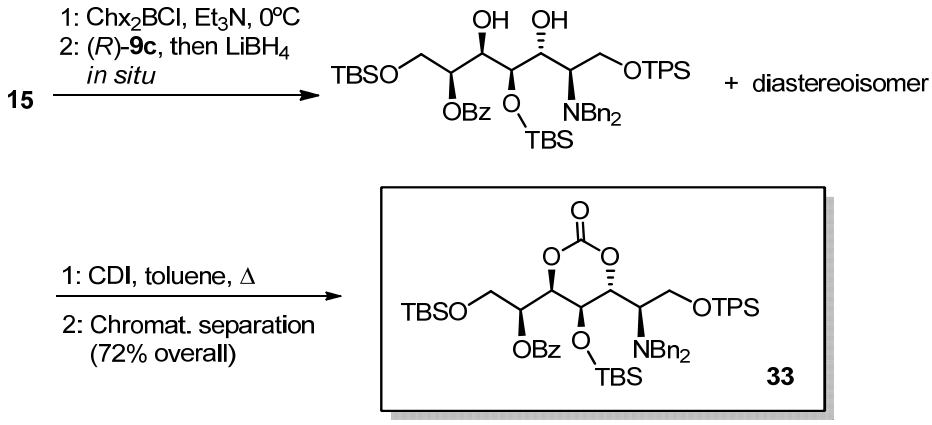
➢ Aldol reaction of **15** and (*R*)-**9c** followed by reduction *in situ*[1] with $LiBH_4$ (page S-4) gave a major 1,3-diol as an inseparable mixture with a minor diastereoisomer. Treatment of the mixture with CDI (page S-5) followed by chromatographic separation afforded carbonate **33**. No crystalline derivatives could be obtained in this case for X-ray diffraction analysis. However, NOE measurements in **33** (see below) indicate the same relative configuration within the C3-C4-C5 segment, which strongly suggests that the steric course of this aldol reaction is the same demonstrated for the other cases. This establishes the absolute configuration of aldol **19c**.



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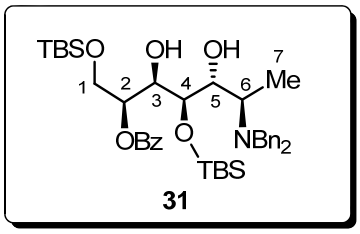


31

Solid: mp 102-103 ºC (from MeOH/Et_2O/CH_2Cl_2); $[\alpha]_D$ +28.1 (*c* 3; $CHCl_3$).

IR: 3470 (br, OH), 1721 (C=O) cm^{-1}

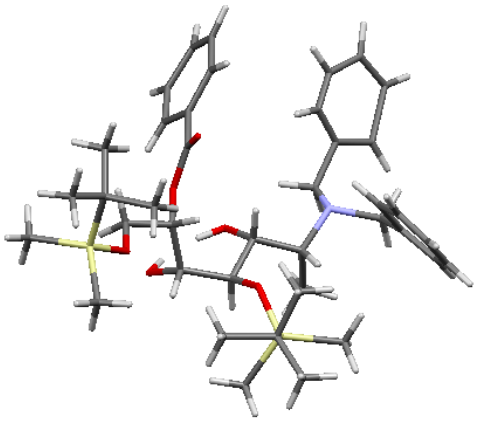
HR ESMS *m/z* 708.4117 ($M+H^+$). Calcd. for $C_{40}H_{62}NO_6Si_2$, 708.4115.

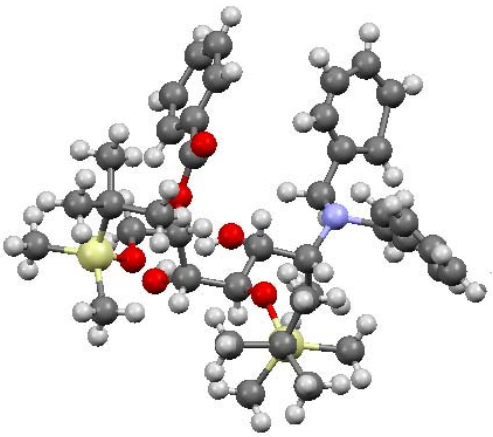
^{1}H NMR (500 MHz) δ 8.20 (2H, br d, *J* ~ 8 Hz; aromatic), 7.60 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.49 (2H, br t, *J* ~ 7.5 Hz; aromatic), 7.30-7.20 (10H, br m; aromatic), 5.44 (1H, m; H-2), 4.10-3.70 (6H, br m; H-1/H-1´/H-3/H-4/H-5/OH), 3.60, 3.55 (5H, AB system, *J* = 14 Hz; benzyl C*H*$_2$ signal overlapping an OH signal), 2.98 (1H, m; H-6), 1.20 (3H, d, *J* = 6.8 Hz; H-7), 0.90 (9H, s; *Me*$_3$CSi), 0.82 (9H, s; *Me*$_3$CSi), 0.09 (3H, s; *Me*Si), 0.07 (3H, s; *Me*Si), 0.05 (3H, s; *Me*Si), –0.08 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 166.3, 140.2 (x 2), 130.3, 18.1, 18.0 (quat C), 133.1, 129.8 (x 2), 128.5 (x 4), 128.3 (x 4), 128.2 (x 2), 126.6 (x 2), 75.6, 73.5, 73.3, 71.0, 53.9 (CH), 64.1, 54.3 (x 2) (CH_2), 25.7 (x 6, 2 *Me*$_3$CSi), 8.5 (C7), –4.5 (*Me*Si), –4.7 (*Me*Si), –5.5 (x 2) (*Me*Si).

The definitive stereochemical assignment of **31** came from an X-ray diffraction analysis (data deposited at the Cambridge Crystallographic Data Centre; deposition number: CCDC 766571).

Two views of the molecule of compound **31**





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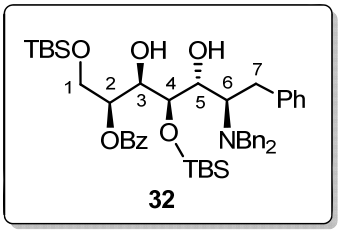


32

Solid: mp 50-51 ºC (from Et_2O/CH_2Cl_2); $[\alpha]_D$ +10.2 (*c* 0.4; $CHCl_3$).

IR: 3450 (br, OH), 1723 (C=O) cm^{-1}

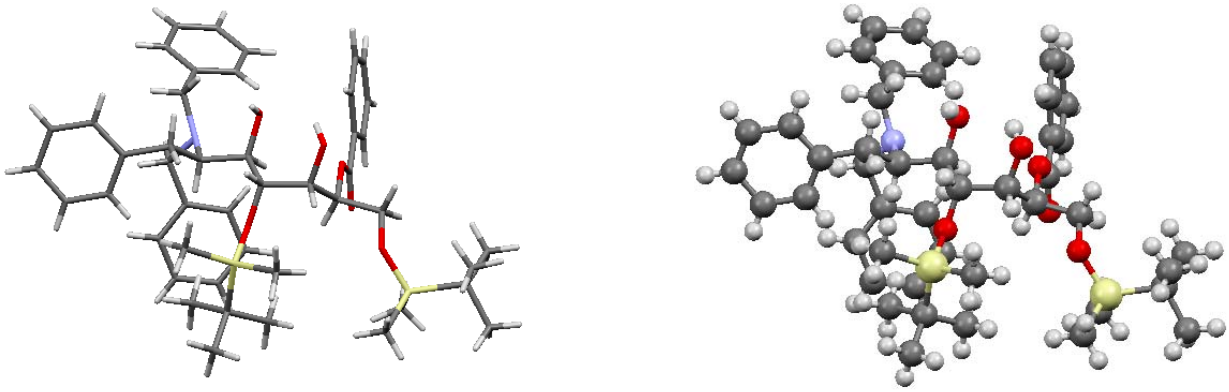
HR FABMS *m/z* 784.4427 ($M+H^+$). Calcd. for $C_{46}H_{66}NO_6Si_2$, 784.4428.

^{1}H NMR (500 MHz) δ 8.25 (2H, br d, *J* ~ 8 Hz; aromatic), 7.65 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.54 (2H, br t, *J* ~ 7.5 Hz; aromatic), 7.40-7.10 (11H, br m; aromatic), 6.90 (4H, m; aromatic), 5.50 (1H, m; H-2), 4.30 (1H, br d, *J* = 8 Hz; OH), 4.15 (1H, br s; OH), 4.13 (1H, dd, *J* = 11.4, 3 Hz; H-1), 4.10 (1H, m; H-3), 3.95 (1H, m; H-5), 3.91 (1H, dd, *J* = 11.4, 4 Hz; H-1´), 3.88 (1H, dd, *J* = 7.8, 4 Hz; H-4), 3.70 (2H, d, *J* = 14.5 Hz; benzyl CH_2), 3.25 (2H, d, *J* = 14.5 Hz; benzyl CH_2), 3.20-3.15 (2H, m; H-6/H-7), 2.95 (1H, br d, *J* = 11.3 Hz; H-7´), 0.91 (9H, s; *Me*$_3$CSi), 0.81 (9H, s; *Me*$_3$CSi), 0.08 (6H, s; 2 *Me*Si), 0.06 (3H, s; *Me*Si), –0.17 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 166.2, 140.6, 140.2 (x 2), 130.2, 18.2, 18.0 (quat C), 133.3, 130.1 (x 2), 130.0 (x 2), 128.5 (x 6), 127.9 (x 6), 126.4 (x 2), 125.7, 75.3, 72.0, 71.7, 71.2, 58.6 (CH), 65.5, 53.9 (x 2), 31.4 (CH_2), 25.9 (x 3, *Me*$_3$CSi), 25.7 (x 3, *Me*$_3$CSi), –4.4 (*Me*Si), –4.6 (*Me*Si), –5.6 (x 2) (*Me*Si).

The definitive stereochemical assignment of **32** came from an X-ray diffraction analysis (data deposited at the Cambridge Crystallographic Data Centre; deposition number: CCDC 764882).

Two views of the molecule of compound **32**



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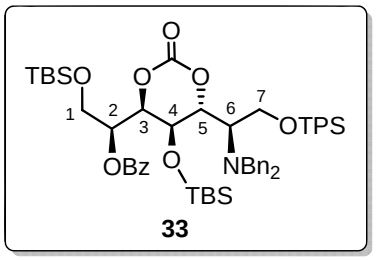


33

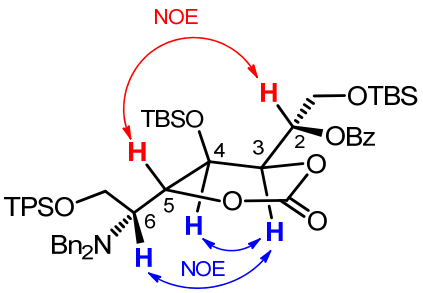
Oil: $[\alpha]_D$ +22 (*c* 1.35; $CHCl_3$).

IR: 1767, 1730 (C=O) cm^{-1}

HR ESMS *m/z* 988.5032 ($M+H^+$). Calcd. for $C_{57}H_{78}NO_8Si_3$, 988.5035.

^{1}H NMR (500 MHz) δ 8.16 (2H, br d, *J* ~ 7.5 Hz; aromatic), 7.76 (2H, br d, *J* ~ 7 Hz; aromatic), 7.67 (2H, br d, *J* ~ 7 Hz; aromatic), 7.60 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.50-7.40 (9H, m; aromatic), 7.20 (5H, m; aromatic), 7.10 (4H, br m; aromatic), 5.69 (1H, ddd, *J* = 7.8, 5.8, 2.5 Hz; H-2), 4.72 (1H, dd, *J* = 7.3, 3 Hz; H-5), 4.66 (1H, dd, *J* = 7.3, 4.8 Hz; H-4), 4.63 (1H, dd, *J* = 4.8, 2.5 Hz; H-3), 4.20 (1H, dd, *J* = 10.7, 7.3 Hz; H-7), 4.02 (1H, dd, *J* = 10.7, 5 Hz; H-7´), 3.95 (1H, dd, *J* = 9.8, 7.8 Hz; H-1), 3.86 (1H, dd, *J* = 9.8, 5.8 Hz; H-1´), 3.60 (2H, d, *J* = 14.3 Hz; benzyl CH_2), 3.39 (2H, d, *J* = 14.3 Hz; benzyl CH_2), 3.10 (1H, m; H-6), 1.11 (9H, s; *Me*$_3$CSi), 0.91 (9H, s; *Me*$_3$CSi), 0.87 (9H, s; *Me*$_3$CSi), 0.13 (3H, s; *Me*Si), 0.09 (3H, s; *Me*Si), –0.03 (3H, s; *Me*Si), –0.29 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 165.0, 147.5, 139.1 (x 2), 132.8, 132.4, 129.8, 19.1, 18.3, 17.8 (quat C), 135.6 (x 2), 135.5 (x 2), 133.5, 130.0 (x 3), 129.8, 128.7 (x 2), 128.3 (x 4), 128.1 (x 4), 128.0 (x 2), 127.8 (x 2), 126.9 (x 2), 80.3, 75.4, 70.7, 62.3, 58.5 (CH), 60.5, 60.1, 54.6 (x 2) (CH_2), 26.9 (x 3, *Me*$_3$CSi), 25.8 (x 6, 2 *Me*$_3$CSi), –4.7 (*Me*Si), –4.8 (*Me*Si), –5.4 (*Me*Si) , –5.5 (*Me*Si).



33

NOEs indicate that H-3 and H-5 are on opposite sides of the ring whereas H-3 and H-4 are spatially proximal

H-3 δ **4.63 (dd, $J_{2,3}$ = 2.5, $J_{3,4}$ = 4.8 Hz)**
H-4 δ **4.66 (dd, $J_{4,5}$ = 7.3, $J_{3,4}$ = 4.8 Hz)**
H-5 δ **4.72 (dd, $J_{5,6}$ = 3 Hz, $J_{4,5}$ = 7.3 Hz)**

The absence of NOE between H-3 and H-5 suggests that **33** is the carbonate of an *anti*-1,3-diol. This conclusion is further supported by the NOEs between the hydrogen pairs H-2/H-5 and H-3/H-6. The coupling constant values in the C3-C4-C5 segment are consistent with this conclusion[3] and indicate the relative configurations at these three stereocentres.

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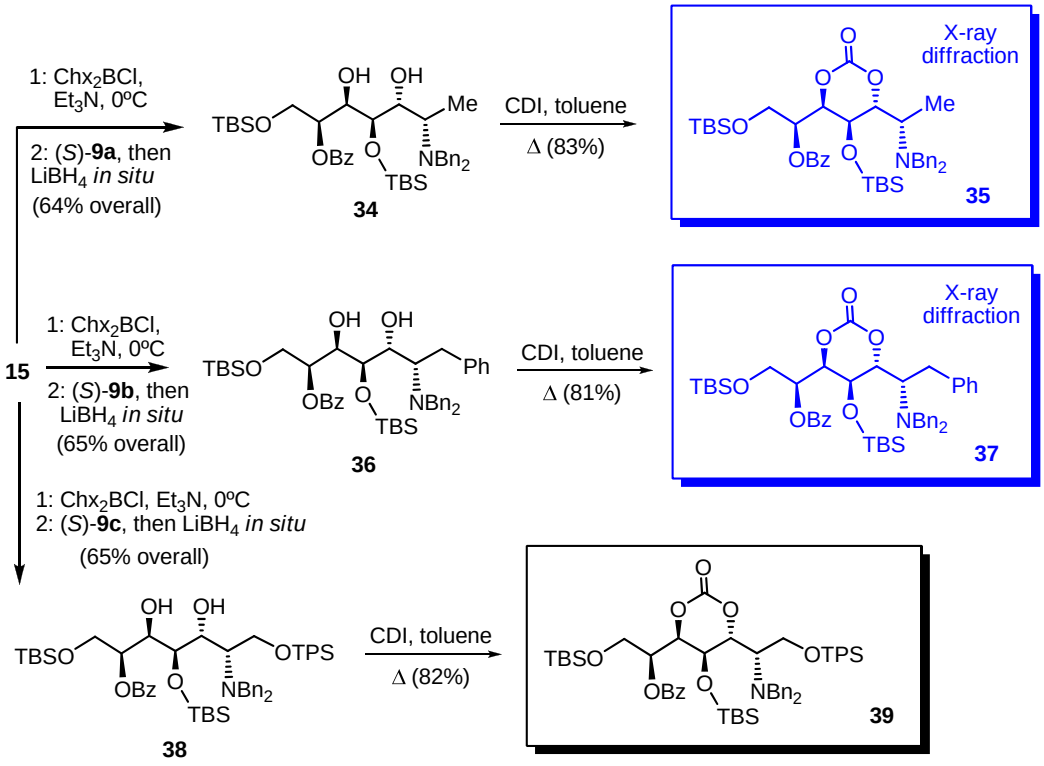
Aldol reactions with aldehydes (*S*)-**9a,b,c**

➢ Aldol reaction of **15** and (*S*)-**9a** followed by reduction *in situ*[1] with $LiBH_4$ (for reaction conditions, see pages S-4/S-5) gave diol **34**. Treatment of the latter with CDI (for reaction conditions, see pages S-4/S-5) afforded the crystalline carbonate **35**, which was analyzed by means of X-ray diffraction. This unambiguously establishes the absolute configuration of aldol **20a**.

➢ Aldol reaction of **15** and (*S*)-**9b** followed by reduction *in situ*[1] with $LiBH_4$ gave diol **36**. Treatment of the latter with CDI afforded the crystalline carbonate **37**, which was analyzed by means of X-ray diffraction. This unambiguously establishes the absolute configuration of aldol **20b**.

➢ An analogous aldolization-reduction-carbonylation sequence was performed in the case of the reaction of **15** with (*S*)-**9c** to yield first diol **38** and then cyclic carbonate **39**. Unfortunately, no crystalline derivatives could be obtained in this case for X-ray diffraction analysis. However, NOE measurements (see below) indicate the same relative configuration within the C3-C4-C5 segment, which strongly suggests that the steric course of this aldol reaction is the same demonstrated for the other cases. This establishes the absolute configuration of aldol **20c**.



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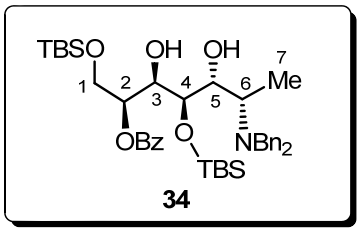


34

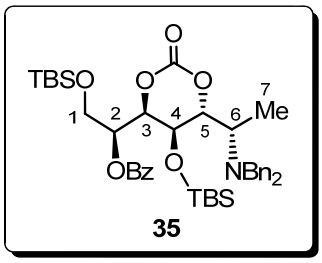
Oil: $[\alpha]_D$ +11.1 (*c* 1; $CHCl_3$).

IR: 3480 (br, OH), 1721 (C=O) cm^{-1}

HR FABMS *m/z* 708.4111 ($M+H^+$). Calcd. for $C_{40}H_{62}NO_6Si_2$, 708.4115.

^1H NMR (500 MHz) δ 8.21 (2H, br d, *J* ~ 8 Hz; aromatic), 7.57 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.45-7.30 (12H, br m; aromatic), 5.36 (1H, td, *J* ~ 6, 3 Hz; H-2), 5.20 (1H, br s; OH), 4.00-3.95 (3H, m; H-1/H-1´/H-3), 3.90 (1H, br s; OH), 3.80 (3H, H-4, signal overlapped by benzyl CH_2), 3.40 (2H, d, *J* = 13.7 Hz; benzyl CH_2), 3.65 (1H, dd, *J* = 9.2, 4 Hz; H-5), 2.88 (1H, dq, *J* = 9.2, 6.8 Hz; H-6), 1.20 (3H, d, *J* = 6.8 Hz; H-7), 0.96 (9H, s; *Me*$_3$CSi), 0.95 (9H, s; *Me*$_3$CSi), 0.14 (3H, s; *Me*Si), 0.12 (3H, s; *Me*Si), 0.10 (3H, s; *Me*Si), –0.09 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 166.1, 138.4 (x 2), 130.5, 18.3, 18.0 (quat C), 132.7, 129.8 (x 2), 129.1 (x 4), 128.5 (x 4), 128.1 (x 2), 127.4 (x 2), 74.2, 73.8, 73.3, 70.3, 55.9 (CH), 61.6, 53.3 (x 2) (CH_2), 25.9 (x 3, *Me*$_3$CSi), 25.8 (x 3, *Me*$_3$CSi), 9.9 (C7), –4.5 (*Me*Si), –4.7 (*Me*Si), –5.5 (x 2) (*Me*Si).



35

Solid: mp 125-126 ºC (from Et_2O-pentane); $[\alpha]_D$ +18.1 (*c* 1; $CHCl_3$).

IR: 1763, 1723 (C=O) cm^{-1}

HR FABMS *m/z* 734.3918 ($M+H^+$). Calcd. for $C_{41}H_{60}NO_7Si_2$, 734.3908.

^1H NMR (500 MHz) δ 8.06 (2H, br d, *J* ~ 8 Hz; aromatic), 7.59 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.50-7.25 (12H, br m; aromatic), 5.35 (1H, dt, *J* ~ 7.5, 3 Hz; H-2), 4.51 (1H, br d, *J* = 7.7 Hz; H-3), 4.39 (1H, br d, *J* = 9.2 Hz; H-5), 4.14 (1H, br s; H-4), 3.98 (1H, dd, *J* = 12, 2.5 Hz; H-1), 3.90 (1H, dd, *J* = 12, 2.5

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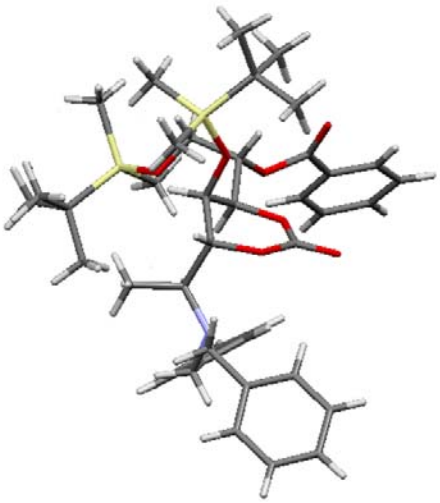
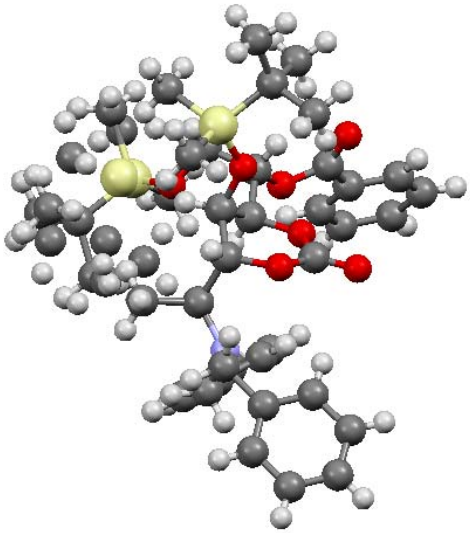
Hz; H-1´), 3.89 (2H, d, *J* = 13.5 Hz; benzyl C*H*$_2$), 3.61 (2H, d, *J* = 13.5 Hz; benzyl C*H*$_2$), 3.03 (1H, dq, *J* = 9.2, 6.8 Hz; H-6), 1.14 (3H, d, *J* = 6.8 Hz; H-7), 0.93 (9H, s; *Me*$_3$CSi), 0.80 (9H, s; *Me*$_3$CSi), 0.13 (6H, s; 2 *Me*Si), –0.03 (3H, s; *Me*Si), –0.07 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 165.6, 147.5, 139.3 (x 2), 129.9, 18.0, 17.9 (quat C), 133.2, 129.8 (x 2), 128.8 (x 4), 128.5 (x 4), 128.3 (x 2), 127.1 (x 2), 85.2, 76.9, 73.6, 63.6, 54.1 (CH), 61.4, 54.0 (x 2) (CH$_2$), 25.7 (x 6, 2 *Me*$_3$CSi), 12.2 (C7), –4.0 (*Me*Si), –4.6 (*Me*Si), –5.5 (*Me*Si), –5.6 (*Me*Si).

The definitive stereochemical assignment of **35** came from an X-ray diffraction analysis (data deposited at the Cambridge Crystallographic Data Centre; deposition number: CCDC-762868).

Two views of the molecule of compound **35**





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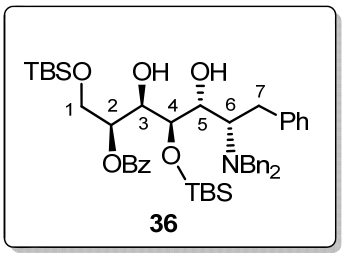


36

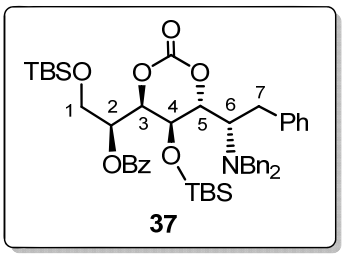
Oil: $[\alpha]_D$ +0.5 (*c* 1.2; $CHCl_3$).

IR: 3420 (br, OH), 1722 (C=O) cm^{-1}

HR FABMS *m/z* 784.4438 ($M+H^+$). Calcd. for $C_{46}H_{66}NO_6Si_2$, 784.4428.

^{1}H NMR (500 MHz) δ 8.11 (2H, br d, *J* ~ 8 Hz; aromatic), 7.52 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.40-7.10 (17H, br m; aromatic), 5.29 (1H, m; H-2), 5.10 (1H, br s; OH), 3.85-3.75 (6H, br m; H-1/H-1´/H-3/H-5/benzyl CH_2), 3.64 (1H, br dd, *J* ~ 8, 4 Hz; H-4), 3.30 (2H, d, *J* = 13 Hz; benzyl CH_2), 3.15 (1H, m; H-6), 3.05 (1H, dd, *J* = 14.3, 4 Hz; H-7), 2.90 (1H, dd, *J* = 14.3, 9.8 Hz; H-7´), 1.60 (1H, br s; OH), 0.84 (9H, s; *Me*$_3$CSi), 0.83 (9H, s; *Me*$_3$CSi), 0.04 (3H, s; *Me*Si), 0.00 (6H, s; 2 *Me*Si), –0.12 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 166.2, 139.5, 138.6 (x 2), 130.6, 18.2, 18.1 (quat C), 132.8, 129.8 (x 2), 129.5 (x 2), 129.2 (x 4), 128.6 (x 2), 128.5 (x 4), 128.2 (x 2), 127.3 (x 2), 126.5, 74.9, 73.6 (x 2), 70.5, 61.1 (CH), 61.9, 54.1 (x 2), 34.8 (CH_2), 26.0 (x 3, *Me*$_3$CSi), 25.8 (x 3, *Me*$_3$CSi), –4.1 (*Me*Si), –4.4 (*Me*Si), –5.4 (x 2) (*Me*Si).



37

Solid: mp 68-69 ºC; $[\alpha]_D$ +43.4 (*c* 1.05; $CHCl_3$).

IR: 1764, 1730 (C=O) cm^{-1}

HR FABMS *m/z* 810.4231 ($M+H^+$). Calcd. for $C_{47}H_{64}NO_7Si_2$, 810.4221.

^{1}H NMR (500 MHz) δ 8.08 (2H, br d, *J* ~ 7.5 Hz; aromatic), 7.63 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.50 (2H, br t, *J* ~ 7.5 Hz; aromatic), 7.40-7.25 (10H, br m; aromatic), 7.15 (3H, m; aromatic), 7.04 (2H, m; aromatic), 5.48 (1H, m; H-2), 4.97 (1H, dt, *J* = 6.2, 3 Hz; H-3), 4.17 (1H, m; H-5), 4.10 (2H, br d, *J* =

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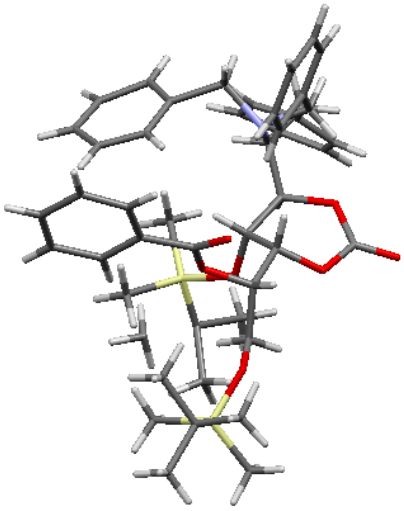
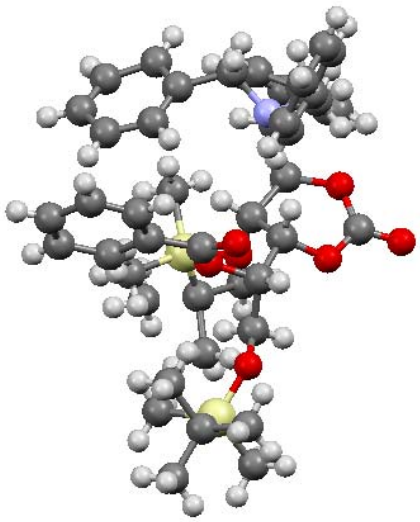
13.6 Hz; benzyl CH_2), 3.99 (1H, m; H-4), 3.92 (1H, br dd, *J* = 11.2, 4.2 Hz; H-1), 3.82 (1H, br dd, *J* = 11.2, 5.2 Hz; H-1´), 3.68 (2H, br d, *J* = 13.6 Hz; benzyl CH_2), 3.04 (1H, m; H-6), 3.00-2.95 (2H, m; H-7/H-7´), 0.84 (9H, s; *Me*$_3$CSi), 0.71 (9H, s; *Me*$_3$CSi), 0.04 (3H, s; *Me*Si), 0.03 (3H, s; *Me*Si), –0.15 (3H, s; *Me*Si) , –0.47 (3H, s; *Me*Si).

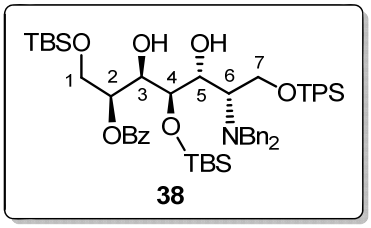
^{13}C NMR (125 MHz) δ 165.3, 148.4, 138.6 (x 2), 138.4, 129.3, 18.3, 17.7 (quat C), 133.2, 130.0 (x 2), 129.3 (x 2), 129.1 (x 4), 128.6 (x 2), 128.5 (x 4), 128.3 (x 2), 127.4 (x 2), 126.5, 84.6, 77.2, 72.4, 65.0, 61.6 (CH), 61.0, 55.7 (x 2), 31.5 (CH_2), 25.8 (x 3, *Me*$_3$CSi), 25.5 (x 3, *Me*$_3$CSi), –4.6 (*Me*Si), –4.8 (*Me*Si), –5.3 (x 2) (*Me*Si).

The definitive stereochemical assignment of **37** came from an X-ray diffraction analysis (data deposited at the Cambridge Crystallographic Data Centre; deposition number: CCDC-764883).

Two views of the molecule of compound **37**







38

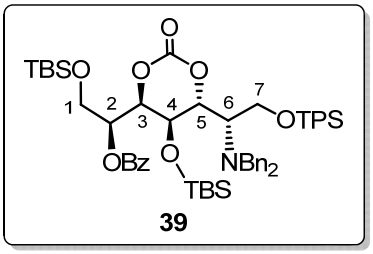
Oil: $[\alpha]_D$ +0.4 (*c* 1; $CHCl_3$).

IR: 3450 (br, OH), 1722 (C=O) cm^{-1}

HR FABMS *m/z* 962.5234 ($M+H^+$). Calcd. for $C_{56}H_{80}NO_7Si_3$, 962.5242.

^{1}H NMR (500 MHz) δ 8.09 (2H, br d, *J* ~ 8 Hz; aromatic), 7.72 (4H, m; aromatic), 7.50-7.20 (19H, br m; aromatic), 5.30 (1H, br s; OH), 5.25 (1H, td, *J* = 6.2, 3 Hz; H-2), 3.96 (1H, dd, *J* = 11.3, 3.5 Hz; H-7), 3.85-3.75 (6H, m; H-1/H-1´/H-7´/benzyl C*H*$_2$/OH), 3.66 (3H, d, *J* = 13.3 Hz; benzyl C*H*$_2$ overlapping signal from H-3), 3.51 (1H, br t, *J* ~ 5 Hz; H-4), 3.42 (1H, br dd, *J* ~ 8.2, 5 Hz; H-5), 3.00 (1H, td, *J* = 8.2, 3.5 Hz; H-6), 1.16 (9H, s; *Me*$_3$CSi), 0.82 (9H, s; *Me*$_3$CSi), 0.74 (9H, s; *Me*$_3$CSi), 0.01 (3H, s; *Me*Si), –0.01 (3H, s; *Me*Si), –0.10 (3H, s; *Me*Si), –0.28 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 166.0, 138.9 (x 2), 133.1, 132.9, 130.6, 19.2, 18.3, 18.0 (quat C), 136.0 (x 2), 135.9 (x 2), 132.7, 130.0, 129.9 (x 2), 129.8 (x 3), 129.2 (x 4), 128.6 (x 4), 128.2 (x 2), 127.8 (x 3), 127.3, 74.4, 74.0, 70.8, 68.6, 61.2 (CH), 63.2, 61.7, 54.6 (x 2) (CH_2), 27.2 (x 3, *Me*$_3$CSi), 26.0 (x 3, *Me*$_3$CSi), 25.8 (x 3, *Me*$_3$CSi), –4.4 (*Me*Si), –4.8 (*Me*Si), –5.4 (x 2) (*Me*Si).



39

Oil: $[\alpha]_D$ +16.2 (*c* 1; $CHCl_3$).

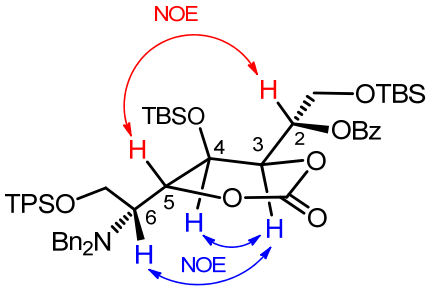
IR: 1769, 1729 (C=O) cm^{-1}

HR FABMS *m/z* 988.5076 ($M+H^+$). Calcd. for $C_{57}H_{78}NO_8Si_3$, 988.5035.

^{1}H NMR (500 MHz) δ 8.04 (2H, br d, *J* ~ 8 Hz; aromatic), 7.60 (4H, m; aromatic), 7.55 (1H, br t, *J* ~ 7.5 Hz; aromatic), 7.50-7.40 (8H, br m; aromatic), 7.30-7.20 (10H, br m; aromatic), 5.60 (1H, apparent q, *J* ~ 5 Hz; H-2), 4.80 (1H, dd, *J* = 6, 3.3 Hz; H-3), 4.71 (1H, dd, *J* = 4.5, 3.3 Hz; H-5), 4.14 (1H, br t, *J* ~ 3.3

Hz; H-4), 4.06 (3H, d, *J* = 13.7 Hz; benzyl CH_2 overlapping the signal from H-1 or H-7), 3.90-3.85 (2H, br m; H-1 or H-1´/H-7 or H-7´), 3.81 (1H, dd, *J* = 11, 5 Hz; H-1 or H-7´), 3.52 (2H, d, *J* = 13.7 Hz; benzyl CH_2), 3.02 (1H, dt, *J* = 5, 4.5 Hz; H-6), 1.01 (9H, s; *Me*$_3$CSi), 0.86 (9H, s; *Me*$_3$CSi), 0.80 (9H, s; *Me*$_3$CSi), 0.00 (3H, s; *Me*Si), –0.01 (3H, s; *Me*Si), –0.03 (3H, s; *Me*Si), –0.08 (3H, s; *Me*Si).

^{13}C NMR (125 MHz) δ 165.4, 148.3, 138.9 (x 2), 132.9, 132.7, 129.6, 19.1, 18.2, 17.9 (quat C), 135.6 (x 2), 135.5 (x 2), 133.2, 130.0, 129.9, 129.6 (x 3), 129.0 (x 4), 128.5 (x 4), 128.4 (x 2), 127.8 (x 3), 127.3 (x 2), 83.1, 76.9, 72.4, 64.6, 60.7 (CH), 60.9, 60.1, 55.7 (x 2) (CH_2), 26.9 (x 3, *Me*$_3$CSi), 25.8 (x 3, *Me*$_3$CSi), 25.6 (x 3, *Me*$_3$CSi), –4.2 (*Me*Si), –4.5 (*Me*Si), –5.4 (x 2) (*Me*Si).



39

NOEs indicate that H-3 and H-5 are on opposite sides of the ring whereas H-3 and H-4 are spatially proximal

H-3 δ 4.80 (dd, $J_{2,3}$ = 6, $J_{3,4}$ = 3.3 Hz)
H-4 δ 4.14 (br t, J ≈ 3.3 Hz)
H-5 δ 4.71 (dd, $J_{5,6}$ = 4.5 Hz, $J_{4,5}$ = 3.3 Hz)

The absence of NOE between H-3 and H-5 suggests that **39** is the carbonate of an *anti*-1,3-diol. This conclusion is further supported by the NOEs between the hydrogen pairs H-2/H-5 and H-3/H-6. The coupling constant values in the C3-C4-C5 segment are consistent with this conclusion and indicate the relative configurations at these three stereocentres.

References

[1] For an explanation of this unexpected stereochemical outcome during the reduction step, see: J. Murga, P. Ruiz, E. Falomir, M. Carda, G. Peris and J. A. Marco, *J. Org. Chem.*, 2004, **69**, 1987-1992.

[2] S. D. Rychnovsky, B. N. Rogers and T. I. Richardson, *Acc. Chem. Res.*, 1998, **31**, 9-17.

[3] J. Pawlak, K. Nakanishi, T. Iwashita and E. Borowski, *J. Org. Chem.*, 1987, **52**, 2896-2901. Compare with the coupling constants values in *syn*-1,3-diol derivatives: J.A. Marco, M. Carda, S. Díaz-Oltra, J. Murga, E. Falomir and H. Roeper, *J. Org. Chem.*, 2003, **68**, 8577-8582.