Supporting Information (3 pages) to

Synthesis and Evaluation of Aminocyclopentitol Inhibitors of β-Glucosidases

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Data for **9a**: $[\alpha]_D^{22}$ = + 13.8° (c=0.92 $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): 7.35 (*m*, 25H); 6.0 (br. *s*, 1H); 4.60-4.40 (*m*, 10H); 3.98 (*m*, 2H); 3.80 (*m*, 1H); 3.61 (*m*, 3H); 2.53 (*m*, 1H).
^{13}C-NMR (75 MHz, $CDCl_3$): 138.8, 138.6, 138.4, 138.0, 128.6, 128.54, 128.5, 128.1, 128.0, 127.9, 127.7, 89.9, 84.2, 83.2, 76.5, 73.4, 72.2, 72.1, 71.7, 68.0, 63.9, 44.1.

HR-LSIMS: $C_{41}H_{44}NO_5$ (M^++1) calcd 630.321949, found 630.321410.

Data for **9b**: $[\alpha]_D^{22}$ = + 6.57° (c=0.35 $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$): 7.37 (*m*, 25H); 4.63-4.47 (*m*, 7H); 3.98 (*m*, 6H); 3.75 (*dd*, 1H, *J* = 9.2 Hz, 7 Hz); 3.66 (*dd*, 1H, *J* = 9.2 Hz, 6.6 Hz); 3.40 (*dd*, 1H, *J* = 6.2 Hz, 9.1 Hz); 2.50 (*quint*, 1H, *J* = 6 Hz).
^{13}C-NMR (75 MHz, $CDCl_3$): 138.3, 137.9, 128.3, 127.8, 127.7, 127.6, 127.5, 86.5, 84.9, 81.0, 76.6, 73.2, 71.9, 71.7, 68.6, 67.4, 42.6.

HR-LSIMS: $C_{41}H_{44}NO_5$ (M^++1) calcd 630.321949, found 630.321410.

Data for **12**: $[\alpha]_D^{22}$ = - 36° (c=0.38, MeOH).

^{1}H-NMR (D_2O, 300 MHz): 8.40 (*s*, 0.4 H, H-NAc); 4.15 (*m*, H-C(4)); 3.72 (*m*, 3H, H-C(1) + H-C(2) + H-C(3)); 3.62 (*dd*, 1H, *J* = 11.8 Hz, 5.9Hz, H-C(6)); 3.52 (*dd*, 1H, *J* = 11.6 Hz, 5.9Hz, H-C(6)); 2.20 (*quint*, 1H, *J* = 5.1 Hz); 1.99 (*s*, 3H).

NOE: H-C(5)→H-C(4) (18 %); H-C(5)→H-C(1) (5 %).

^{13}C-NMR: (D_2O, 75 MHz): 82.0, 79.5, 76.9 (H-C(1), H-C(2), H-C(3)), 61.6 (H_2-C(6)); 55.0 (H-C(4)); 47.2 (H-C(5)); 24.2 (CH_3).

EI-MS: 205 (M^+).

Data for **1**·HCl: $[\alpha]_D^{22}$ = - 92° (c=0.13, MeOH).

^{1}H-NMR (300 MHz, D_2O): 3.80-3.57 (*m*, 6H); 2.24 (*m*, 1H, H-C(5)).
^{13}C-NMR (75 MHz, D_2O): 81.5, 78.2, 75.8 (H-C(1), H-C(2), H-C(3)), 60.7 (H_2-C(6)), 56.3 (H-C(4)), 45.0 (H-C(5)).

ESI-MS: 164 (M^++1).

Data for **13**: $[\alpha]_D^{22}$ = - 13° (c=0.165, MeOH).

^{1}H-NMR (300 MHz, D_2O): 8.36 (*s*, 0.15 H, H-NAc); 3.99 (*dd*, 1H, *J* = 8.5 Hz, 5.2 Hz, H-C(1)); 3.85 (*t*, 1H, *J* = 9.4 Hz, H-C(4)); 3.67 (*m*, 3H, H-C(2) + H-C(3) + H-C(6)); 3.57 (*dd*, 1H, *J* = 11.4 Hz, 4.9 Hz, H-C(6)); 2.08 (*m*, 1H, H-C(5)); 1.92 (*s*, 3H).

NOE: H-C(5)→H-C(4) (3 %); H-C(5)→H-C(1) (16 %).

^{13}C-NMR (D_2O, 75 MHz): 176.8 (C=O); 83.6, 81.8 (H-C(2), H-C(3)), 75.8 (H-C(1)), 61.4 (H_2-C(6)); 56.7 (H-C(4)); 48.1 (H-C(5)); 24.5 (CH_3).

ESI-MS: 206 (M^++1).

Data for **14**·HCl: $[\alpha]_D^{22}$ = + 17° (c=0.195, MeOH).

^{1}H-NMR (300 MHz, D_2O): 3.95 (*dd*, 1H, *J* = 8.5 Hz, 5.9 Hz, H-C(1)); 3.72 - 3.63 (*m*, 4H, H-C(2) + H-C(3) + H_2-C(6)); 3.28 (*t*, 1H, *J* = 8.5 Hz, H-C(4)); 2.21 (*quint*, 1H, *J* = 8.0 Hz, H-C(5)).
^{13}C-NMR (D_2O, 75 MHz): 81.5, 77.6, 73.9 (H-C(1), H-C(2), H-C(3)), 60.2 (H_2-C(6)), 57.5 (H-C(4)), 44.1 (H-C(5)).

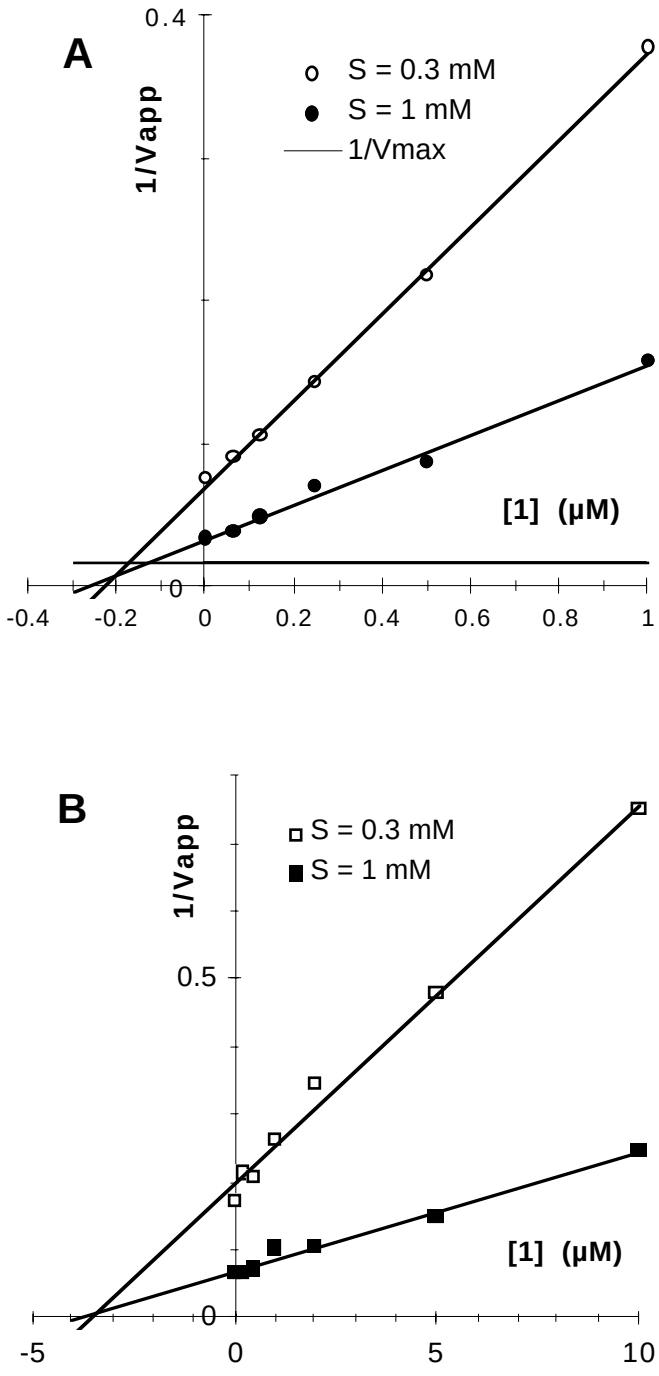
ESI-MS: 164 (M^++1).

Data for **15**·HCl: $[\alpha]_D^{22}$ = - 56° (c=0.125, MeOH).

^{1}H-NMR (300 MHz, D_2O): 3.82 - 3.68 (*m*, 6H); 3.12 (*q*, 2H, *J* = 7.4 Hz, N-CH_2-CH_3); 2.28 (*m*, 1H, H-C(5)); 1.20 (*t*, 3H, *J* = 7.4 Hz, N-CH_2-CH_3).
^{13}C-NMR (D_2O, 75 MHz): 81.6, 78.3, 75.9 (H-C(1), H-C(2), H-C(3)), 60.8 (H_2-C(6)), 56.4 (H-C(4)), 49.2 (N-CH_2), 45.1 (H-C(5)), 10.8 ((N-CH_2-CH_3).

ESI-MS: 192 (M^++1).

Figure 1. Dixon plot of inhibition by **1** for *Caldocellum Saccharolyticum* β-glucosidase (**A**) and for almonds β-glucosidase (**B**).[a]



[a] measured in 0.1 M HEPES-Buffer at pH 6.8, at 25 ˚C, with inhibitor **1** at the indicated concentrations, and (A) 0.1 U/mL *Caldocellum Saccharolyticum* β-glucosidase and 4-nitrophenyl-β-D-glucoside as substrate S (K_M = 970 µM), and almond β-glucosidase 4-nitrophenyl-β-D-glucoside as substrate S (K_M >> 10 mM). The x-coordinate of the intersection between the two lines and the horizontal line at $1/V_{max}$ gives $-K_i$(**1**). V_{app} is given in relative units derived from the absorbency change at 405 nm as given by the instrument. See also legend of Table 1 in the paper.