Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

NHC-Mediated Cross-Coupling of Sugar-Derived Cyclic Nitrones with Enals: General and Efficient Synthesis of Polyhydroxylated Pyrrolizidines and Indolizidines

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Supporting information (Part I)

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The enzymes α-glucosidases (from rice, yeast, *Aspergillus niger* and rat intestinal maltase), β-glucosidases (from almond and bovine liver), α-galactosidase (from coffee beans), β-galactosidase (from bovine liver), α-mannosidase (from jack beans), β-mannosidase (from *Helix pomatia*), α-L-rhamnosidase (from *Penicillium decumbens*), α-L-fucosidase (from bovine kidney), β-glucronidase (from *E. coli*), α, α-trehalase (from porcine kidney), amyloglucosidase (from *Aspergillus niger*). Brush border membranes prepared from rat small intestine according to the method of Kessler et al.[1] (Kessler et al., 1978) were assayed at pH 5.8 for rat intestinal maltase using maltose. The released D-glucose was determined colorimetrically using the Glucose CII-test Wako (Wako Pure Chemical Ind.; Osaka, Japan). Other glycosidase activities were determined using an appropriate *p*-nitrophenyl glycoside as substrate. The reaction was stopped by adding 400 mM Na_2CO_3. The released *p*-nitrophenol was measured spectrometrically at 400 nm. The assay results are summarized in the following Table.

[1] M. Kessler, O. Acuto, C. Storelli, H. Murer, M. Muller and G. Semenza, A modified procedure for the rapid preparation of efficiently transporting vesicles from small intestinal brush border membranes. Their use in investigating some properties of D-glucose and choline transport systems. *Biochim. Biophys. Acta.*, 1978, **506**, 136.

Table 1 Concentrations of iminosugars giving 50% inhibition of various glycosidases (to be continued)

	IC_{50} (μM)						
enzyme	**10aa**	**10ab**	**10ad**	**10ad'**	**10ba**	**10bb**	**10bd**
α-glucosidase							
Yeast	NI[a] (22.0%)[b]	NI (29.6%)	NI (19.6%)	NI (9.5%)	NI (41.3%)	NI(19.2%)	NI(10.3%)
Aspergillus niger	NI (3.2%)	NI (13.3%)	NI (0%)	NI (0%)	NI (6.1%)	NI (0%)	NI(0 %)
Rice	NI (12.0%)	NI (8.7%)	NI (6.5%)	NI (12.0%)	NI (14.9%)	NI (11.5%)	246
Rat intestinal maltase	NI (13.3%)	NI (9.0%)	NI (11.8%)	NI (15.4%)	NI (49.8%)	NI (7.2%)	184
β-glucosidase							
Almond	NI (13.8%)	NI (6.8%)	NI(2.7%)	NI (8.6%)	NI (20.8%)	NI (10.4%)	NI (5.8%)
Bovine liver	NI (20.5%)	NI (33.0%)	NI(47.0%)	NI (32.0%)	NI (32.8%)	480	NI(46.4%)
α-galactosidase							
Coffee beans	NI (21.3%)	NI (10.0%)	NI(15.7%)	NI (2.7%)	NI (8.0%)	NI (6.4%)	NI (4.0%)
β-galactosidase							
Bovine liver	NI (22.7%)	NI (46.4%)	509	NI (45.2%)	NI (45.2%)	259	482
α-mannosidase							
Jack beans	NI (2.1%)	NI (8.5%)	NI(5.1%)	NI (5.5%)	NI (2.6%)	NI (0.4%)	NI (5.1%)
β-mannosidase							
Helix pomatia	NI (1.3%)	NI (0%)	NI(0%)	NI (0%)	NI (1.7%)	NI (0%)	NI (3.3%)
α-L-fucosidase							
Bovine kidney	NI (1.5%)	NI (46.4%)	NI(0.6%)	NI (4.0%)	NI (10.5%)	NI (15.2%)	NI (4.3%)
α-L-rhammosidase							
Penicillium decumbens	NI (7.8%)	NI (2.2%)	NI(0.3%)	NI (5.4%)	NI (0.6%)	NI (7.8%)	NI (4.1%)
β-glucronidase							
E. coli	NI (18.7%)	NI (41.0%)	NI(29.4%)	NI (24.2%)	NI (46.9%)	NI (19.0%)	NI(2.2%)
α,α-trehalase							
Porcine kidney	NI (1.2%)	NI (0%)	NI(3.9%)	NI (0%)	NI (0.5%)	NI (5.3%)	NI (5.0%)
Amyloglucosidase							
Aspergillus niger	NI (0%)	NI (10.0%)	NI(0%)	NI (0%)	NI (0%)	NI (0%)	NI (0%)

[a] NI: No inhibition (less than 50% inhibition at 1000 μM). [b] ( ): inhibition % at 1000 μM.

Table 2 Concentrations of iminosugars giving 50% inhibition of various glycosidases (to be continued)

	IC_{50} (μM)							
enzyme	**10ca**	**10cb**	**10cd**	**10da**	**10db**	**10dd**	**10ea**	**10eb**
α-glucosidase								
Yeast	NI(6.7%)	NI(15.0%)	156	NI(47.2%)	NI (3.9%)	NI(25.0%)	NI(33.5%)	84
Aspergillus niger	NI (0%)	NI(17.3%)	NI(0%)	NI (1.1%)	NI (3.2%)	NI (5.0%)	NI (0%)	NI (0%)
Rice	NI(7.6%)	NI(10.3%)	NI(6.7%)	NI(13.4%)	NI (4.7%)	NI(21.5%)	NI(37.7%)	NI(48.8%)
Rat intestinal maltase	NI(11.5%)	NI(10.4%)	NI(6.1%)	NI (9.1%)	NI (6.0%)	NI(30.5%)	1000	NI(43.8%)
β-glucosidase								
Almond	NI (0.7%)	NI(10.0%)	NI(37.0%)	NI(12.4%)	NI(10.8%)	NI(12.4%)	NI(7.8%)	377
Bovine liver	NI(46.3%)	NI(36.8%)	255	NI(48.7%)	NI(40.7%)	875	NI(39.2%)	893
α-galactosidase								
Coffee beans	NI(3.0%)	NI (5.6%)	407	NI (1.0%)	NI (3.3%)	NI (0.4%)	NI(6.2%)	228
β-galactosidase								
Bovine liver	NI(47.1%)	NI(48.7%)	255	NI(48.4%)	NI(49.1%)	618	NI(48.8%)	254
α-mannosidase								
Jack beans	NI (0%)	NI (0.7%)	NI(20.8%)	NI (0%)	NI (0.8%)	NI (0%)	NI(1.9%)	410
β-mannosidase								
Helix pomatia	NI (0%)	NI (0.6%)	NI(19.8%)	NI (0%)	NI (0%)	NI (1.5%)	NI(7.7%)	653
α-L-fucosidase								
Bovine kidney	NI(2.6%)	NI (0.8%)	572	NI (0%)	NI (7.3%)	NI (2.5%)	NI(10.0%)	109
α-L-rhammosidase								
Penicillium decumbens	NI(8.8%)	NI (9.6%)	NI (8.4%)	NI (5.4%)	NI (7.0%)	NI(45.9%)	NI(4.3%)	NI(9.8%)
β-glucronidase								
E. coli	NI (1.2%)	NI (0.4%)	141	NI(33.7%)	NI (2.0%)	NI(16.0%)	NI(24.9%)	57
α,α-trehalase								
Porcine kidney	NI (0%)	NI (1.4%)	NI (1.4%)	NI (2.7%)	NI (4.0%)	NI (2.7%)	NI(5.4%)	NI(16.3%)
Amyloglucosidase								
Aspergillus niger	NI(4.9%)	NI (6.3%)	NI (4.7%)	NI (3.1%)	NI (0%)	NI (8.4%)	NI(5.3%)	NI(9.3%)

Table 3 Concentrations of iminosugars giving 50% inhibition of various glycosidases (to be continued)

	IC_{50} (μM)							
enzyme	**10fa**	**12aa**	**12ab**	**12ad**	**12ba**	**12bb**	**12bd**	**12ca**
α-glucosidase								
Yeast	89	NI (7.9%)	NI (9.7%)	NI (0%)	NI(18.5%)	NI (8.7%)	NI(17.1%)	NI(8.9%)
Aspergillus niger	NI (0%)	NI (9.0%)	NI (0.1%)	NI (0%)	NI (0%)	NI (0%)	NI(0%)	NI (0%)
Rice	NI(13.7%)	NI (6.3%)	NI (6.8%)	NI (6.5%)	NI(13.3%)	NI(10.7%)	NI(40.7%)	NI(9.8%)
Rat intestinal maltase	NI(18.7%)	NI (4.3%)	NI(13.5%)	746	NI(34.7%)	NI(32.4%)	710	NI(12.1%)
β-glucosidase								
Almond	417	NI(20.1%)	NI (2.3%)	NI(20.7%)	NI(14.0%)	NI (3.4%)	NI (9.0%)	NI(10.8%)
Bovine liver	335	806	549	NI(41.7%)	NI(47.6%)	NI(44.1%)	NI(49.8%)	874
α-galactosidase								
Coffee beans	160	NI(11.3%)	NI(10.2%)	NI(14.8%)	NI (3.9%)	NI (5.1%)	NI (7.1%)	NI (5.1%)
β-galactosidase								
Bovine liver	244	287	135	NI(49.6%)	889	599	423	698
α-mannosidase								
Jack beans	NI(44.8%)	NI (3.4%)	NI (7.7%)	NI(6.0%)	NI(35.7%)	NI(37.9%)	NI(13.9%)	NI (8.5%)
β-mannosidase								
Helix pomatia	NI(35.6%)	NI (0%)	NI (0%)	NI(0%)	NI (0%)	NI (0%)	NI (0%)	NI (0%)
α-L-fucosidase								
Bovine kidney	197	NI (3.7%)	NI (2.9%)	NI(0%)	NI (0%)	NI (0%)	NI (0%)	NI (9.6%)
α-L-rhammosidase								
Penicillium decumbens	NI(9.8%)	NI (4.6%)	NI (7.4%)	NI(3.4%)	NI(46.9%)	1000	NI(45.8%)	NI(35.2%)
β-glucronidase								
E. coli	58	NI (7.6%)	NI(14.9%)	NI(7.5%)	NI (5.6%)	NI (5.4%)	NI (7.1%)	NI (9.3%)
α,α-trehalase								
Porcine kidney	NI(12.7%)	NI (3.1%)	NI (5.9%)	NI(4.3%)	NI (1.5%)	NI (0%)	NI (2.2%)	NI (1.4%)
Amyloglucosidase								
Aspergillus niger	NI(0.4%)	NI (0.5%)	NI (0%)	NI(0%)	NI (0%)	NI (0%)	NI (0%)	NI (0%)

Table 4 Concentrations of iminosugars giving 50% inhibition of various glycosidases (to be continued)

	IC_{50} (μM)						
enzyme	**12cb**	**12cd**	**12cd'**	**12da**	**12db**	**12dd**	**12dd'**
α-glucosidase							
Yeast	NI(3.1%)	NI(14.5%)	NI(4.2%)	NI (16.9%	NI(11.5%)	NI(46.8%)	NI (6.0%)
Aspergillus niger	NI(10.7%)	NI(0.9%)	NI (7.4%)	NI (7.6%)	NI (0%)	NI (0%)	NI (1.6%)
Rice	NI (7.4%)	NI(10.3%)	NI (3.1%)	NI (7.7%)	NI (7.7%)	NI(34.6%)	NI (8.8%)
Rat intestinal maltase	NI(14.1%)	NI(16.2%)	NI(15.8%)	NI (2.6%)	NI (3.4%)	287	NI (7.1%)
β-glucosidase							
Almond	NI (7.1%)	NI(16.2%)	NI(15.5%)	NI (2.7%)	NI(13.1%)	NI(21.0%)	NI(11.1%)
Bovine liver	NI(47.2%)	545	712	787	NI(20.5%)	NI(44.5%)	NI(41.1%)
α-galactosidase							
Coffee beans	NI (8.9%)	NI(11.3%)	NI (3.8%)	NI (4.4%)	NI (3.7%)	NI(23.8%)	NI(38.3%)
β-galactosidase							
Bovine liver	803	563	513	915	324	755	NI(46.4%)
α-mannosidase							
Jack beans	NI (0%)	NI (9.7%)	NI (0%)	NI (0%)	NI (0%)	NI (6.4%)	NI (5.9%)
β-mannosidase							
Helix pomatia	NI (0%)	NI (2.7%)	NI (0.8%)	NI (0%)	NI (0%)	NI (0.7%)	NI (0%)
α-L-fucosidase							
Bovine kidney	NI(17.4%)	685	583	NI (0%)	NI (0%)	NI(25.0%)	NI (1.5%)
α-L-rhammosidase							
Penicillium decumbens	NI(34.0%)	NI(13.5%)	NI(26.7%)	NI (0%)	NI (0%)	NI (0.8%)	NI (1.7%)
β-glucronidase							
E. coli	NI(12.5%)	NI(26.3%)	NI(25.1%)	NI(39.2%)	NI(38.9%)	532	NI(11.0%)
α,α-trehalase							
Porcine kidney	NI (0%)	NI (0%)	NI (2.8%)	NI (2.3%)	NI (4.3%)	NI (4.0%)	NI (0.3%)
Amyloglucosidase							
Aspergillus niger	NI (6.0%)	NI (0%)	NI (0.9%)	NI (0.8%)	NI (0%)	NI (3.7%)	NI(12.8%)