Supplementary Information

Efficient preparation of β–D-glucosyl and β–D-mannosyl ureas and other *N*-glucosides in carbohydrate melts

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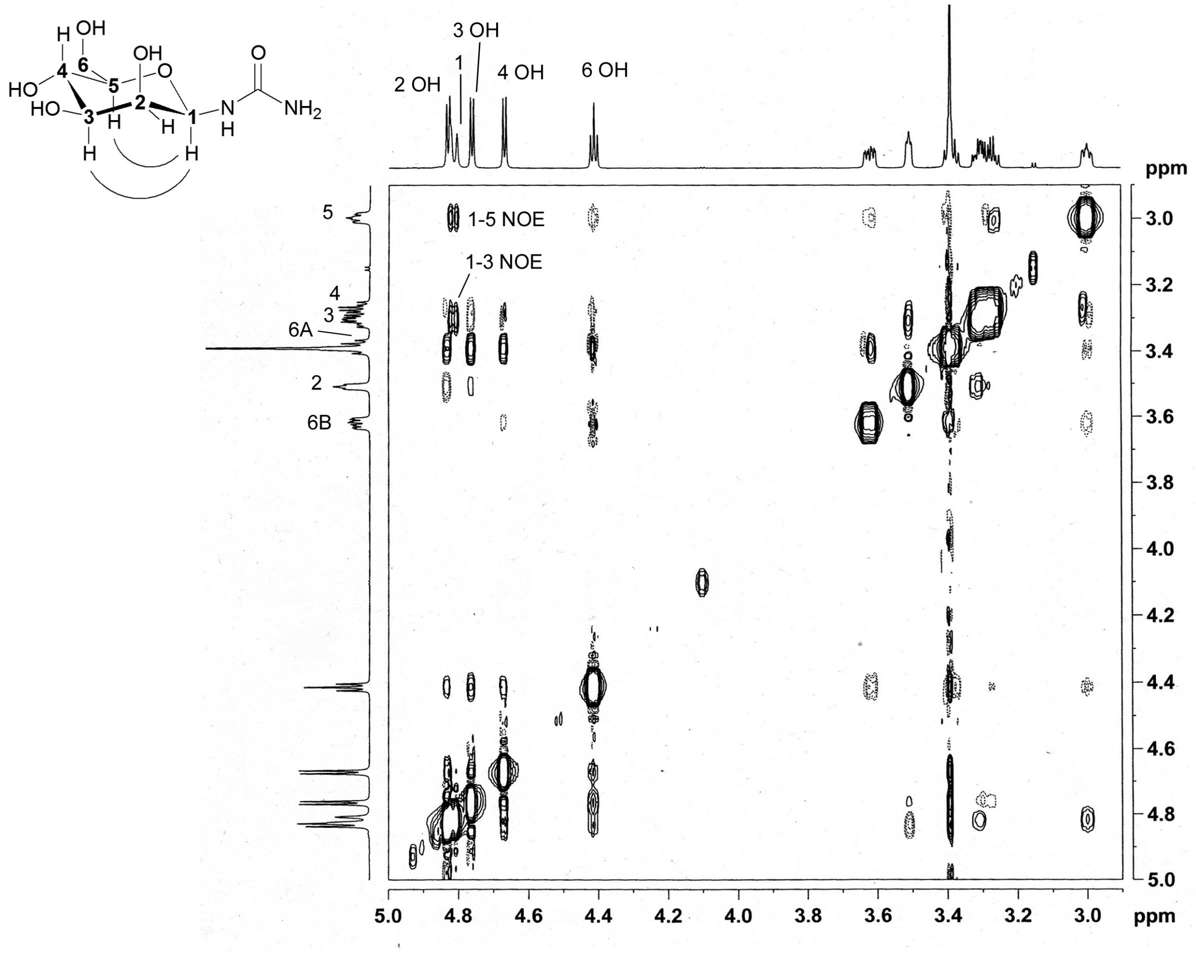
Experimental:

NOE spectrum for β-D-mannosyl urea 2b:

The C-1/C-5 and C-1/C-3 NOE contacts in the β-conformation are clearly observed.



Typical procedure for the preparation of β-D-glycosyl ureas 10-14

Monosaccharide **7-10** (0.6 g, 3.3 mmol), urea (1.4 g, 26.7 mmol) and NH_4Cl (0.2 g, 3.7 mmol) were molten in a 25 mL reaction flask at 80 °C until a clear melt was formed. Amberlyst (0.2 g) was added and the reaction was stirred for 2 h at that temperature. After the reaction was finished D_2O/H_2O was added to the still warm melt and reaction mixtures were directly used for further measurments.

D-Galactosyl urea 10

^{13}C-NMR (75 MHz, D_2O): δ [ppm] = 61.1, 68.8, 69.6, 73.5, 76.3, 81.4, 160.7. **ESI-MS:** mz (%) = 445.1 [2 MH^+] (100), 223.1 [MH^+] (46).

N-Acetyl-D-glucosaminyl urea 11

^{13}C-NMR (75 MHz, D_2O): δ [ppm] = 22.1, 54.3, 60.71, 69.7, 74.3, 77.2, 80.2, 160.4, 174.9. **ESI-MS:** mz (%) = 264.1 [MH^+] (100), 527.2 [2 MH^+] (53).

L-rhamnosyl urea 12

^{13}C-NMR (75 MHz, D_2O): δ [ppm] = 16.8, 70.6, 71.8, 73.2, 73.3, 78.7, 160.0. **ESI-MS:** mz (%) = 413.1 [2 MH^+] (100), 207.1 [MH^+] (35).

2-Deoxy- D-glucosyl urea 13

^{13}C-NMR (75 MHz, D_2O): δ [ppm] =37.4, 61.0, 70.8, 71.1, 77.2, 77.6, 160.2. **ESI-MS:** mz (%) = 207.1 [MH^+] (100), 413.1 [2 MH^+] (66).

Preparation of N-D-Glucosyl-N'-ethylene urea-tetraacetate 18

A melt of D-glucose (0.5 g, 2.8 mmol) and *N,N'*-ethylene urea (0.5 g, 5.8 mmol) was stirred with 50 mg of Amberlyst 15 for 6 h at 75°C. After addition of water, filtering off the catalyst and freeze-drying, the white solid was heated to 90°C in a mixture of Ac_2O (2.2 ml, 23.3 mmol) and NaOAc (0.4 g, 4.9 mmol) for 1.5 h. Then, the solution was poured into saturated $NaHCO_3$ solution and the aqueous phase was three times extracted with CH_2Cl_2. The combined organic layers were washed twice with water. A colourless solid was obtained after recrystallisation from EtOAc/PE (4:1) (0.3 g, 27%).

^{1}H-NMR (300 MHz, D_2O): δ [ppm] = 2.00, 2.02, 2.03, 2.06 (4x s, 12 H), 3.33-3.47 (m, 2 H), 3.56-3.61 (m, 2 H), 3.77-3.83 (m, 1 H), 4.04-4.10 (m, 1 H), 4.21-4.26 (m, 1 H), 5.01-5.17 (m, 4 H), 5.26-5.32 (m, 1 H). **^{13}C-NMR (75 MHz, D_2O)**: δ [ppm] = 20.7, 20.7, 20.8, 20.9, 38.2, 39.7, 60.0, 68.3, 68.3, 73.5, 73.6, 80.6, 161.7, 169.7, 170.0, 170.8. **FT-IR (ATR)**: ν [cm^{-1}] = 2896, 1738, 1673, 1486, 1434, 1369, 1214, 1127, 1034, 900, 842, 765, 697, 599, 495, 461, 436. **MP:** 154 °C, **ESI-MS:** m/z (%) = 434.0 [MNH_4^+] (100), 417.0 [MH^+] (76).

Preparation of N-D-glucosyl-N'-allyl urea 19

A slurry of D-glucose (5.0 g, 0.03 mol) and *N,N'*-allyl urea (5.5 g, 0.05 mol) was stirred with 2 g of Amberlyst 15 for 6 h at 85 °C. After addition of water, the solid catalyst was filtered off and the aqueous solution decoulorized with charcoal and freeze-dried. The sample was subsequently subjected to Soxhlet extraction by EtOAc over three days, in which the solvent was exchanged after 24 h. Finally, a colourless powder precipitated from the EtOAc layer which was the product (54 mg, 0.7%).

^{1}H-NMR (300 MHz, D_2O): δ [ppm] = 3.32-3.91 (m, 8 H), 4.83 (d, J= 9.06 Hz, 1 H), 5.11-5.22 (m, 2 H), 5.94 (m, 1 H); **^{13}C-NMR (75 MHz, D_2O)**: δ [ppm] = 41.93, 60.74, 69.48, 72.01, 73.20, 76.62, 77.11, 81.15, 114.88, 135.00, 159.58; **FT-IR (ATR)**: ν [cm^{-1}] = 3300, 2920, 1639, 1557, 1420, 1363, 1272, 1073, 1012, 921, 559; **MP:** 136 °C (decomp.); **ESI-MS:** mz (%) = 525.2 [2 MH+] (100) 263.1 [MH^+] (32), **GC-MS ($SiMe_3$)**: m/z (%) = 479.0 [MH^+-$SiMe_3$] (100), 496.1 [MNH_4^+] (64).

Preparation of N-D-glucosyl-N'-allyl urea-tetraacetate 22

A slurry of D-glucose (1.0 g, 5.5 mmol) and *N,N'*-allyl urea (1.1 g, 11.1 mmol) was stirred with 0.4 g Amberlyst 15 for 2 h at 85 °C. After addition of 6 ml Ac_2O (63 mmol) and 0.9 g sodium acetate (11 mmol), the mixture was heated to 90 °C for 2 h. The reaction was stopped by pouring the cool solution into saturated $NaHCO_3$ solution. Then the aqueous phase was three times extracted with EE, the combined organic layers were washed with water, dried over $MgSO_4$ and evaporated. The crude product was purified by flash chromatography (EE:PE = 2:1) and afforded a colourless solid (1.4 g; 60 %).

^{1}H-NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.99, 2.00, 2.03, 2.05 (s, 12 H), 3.84 (m, 2 H), 4.06 (dd, J_1=1.92 Hz, J_2=12.35 Hz, 1H), 4.30 (dd, J_1=4.39 Hz, J_2=12.35 Hz, 1H), 4.86-5.31 (m, 6H), 5.70 (d, J= 9.39 Hz), 5.75-5.90 (m, 1H); **^{13}C-NMR (75 Hz, $CDCl_3$)**: δ [ppm] = 20.69, 20.85, 42.86, 68.46, 70.66, 73.08, 73.24, 80.24, 116.10, 134.87, 156.58, 169.79, 170.03, 170.81, 171.08; **FT-IR**:

v [cm^{-1}] = 3319, 2948, 1739, 1637, 1580, 1434, 1373, 1210, 1096, 1030, 907, 674, 599, 490, 464; **MP:** 131 °C **ESI-MS**: m/z (%) = 448 [MNH_4^+] (100), 431 [MH^+] (78).

Preparation of N-D-glucosyl-O-ethyl carbamate 21

A slurry of D-glucose (0.4 g, 2.2 mmol) and *N*-ethyl carbamate (0.4 g, 4.5 mmol) was stirred with 20 mol% $FeCl_3$*$6H_2O$ for 2.5 h at 80 °C and the excess of carbamate was removed by ultrasonic extraction with three times 10 ml of EtOAc and an extraction time of one hour. The residual solid was solved in the smallest amount of MeOH and dropped into ice-cooled Et_2O. Finally, the Et_2O phase was evaporated and a colourless solid was obtained (18 mg, 3 %).

^{1}H-NMR (300MHz, DMSO-d6): δ [ppm] = 1.16 (t, J=7.14 Hz, 3 H), 9.97-3.63 (m, 8 H), 3.99 (q, J=7.04 Hz, 2 H), 4.43-5.18 (m, 3 H), 7.73 (d, J=9.33 Hz, 1 H); **^{13}C-NMR (75 MHz, DMSO-d6)**: δ [ppm] = 14.53, 59.68, 60.80, 69.77, 71.83, 77.39, 78.18, 82.22, 155.94; **^{1}H-NMR (300 MHz, D_2O)**: δ [ppm] = 1.14 (t, J=7.14 Hz, 3 H), 3.22-3.79 (m, 6 H), 4.05 (q, J=6.95 Hz, 2 H), 5.32 (d, J=5.49 Hz, 1 H); **^{13}C-NMR (75 MHz, D_2O)**: δ [ppm] = 13.73, 60.58, 62.41, 69.26, 71.76, 76.48, 77.27, 81.75, 158.48; **FT-IR**: v [cm^{-1}] = 3122, 3037, 2817, 2674, 2361, 2323, 1607, 1558, 1402, 1253, 1180, 1120, 421; **MP:** 182 °C (decomp.); **ESI-MS**: m/z (%) = 269.1 [MNH_4^+] (100), 252.1 [MH^+].

Preparation of N-D-glucosyl-O-ethyl carbamate-tetraacetate 24

A slurry of D-glucose (0.4 g, 2.2 mmol) and *N*-ethyl carbamate (0.4 g, 4.5 mmol) was stirred with 10 mol% $FeCl_3$*$6H_2O$ for 4.5 h at 70 °C in a 10 ml reaction tube. After addition of water, $FeCl_3$ was precipitated with aqueous NH_3, filtered off and the remaining solution freeze-dried. Then, NaOAc (0.5 g 2.2 mmol) and 3 ml Ac_2O were added the mixture was stirred at 90°C for 1.5 h in a round bottom flask. The content of the flask was poured into 20 ml of ice water which was three times extracted with CH_2Cl_2.The combined organic phases were washed with saturated $NaHCO_3$ and water, dried over $MgSO_4$ and the solvent was evaporated. After recrystallizaton from Et_2O/PE a colourless solid was obtained. (yield: 73 %).

^{1}H-NMR (300MHz, DMSO-d6): δ [ppm] = 1.18-1.26 (m, 3 H), 1.97, 1.99, 2.02, 2.04 (4x s, 12 H), 3.77 (m, 1 H), 4.03-4.15 (m, 3 H), 4.25-4.29 (m, 1 H), 4.85-5.28 (m, 3 H), 6.02 (d, J=9.62 Hz, 1 H); **^{13}C-NMR (75 MHz, DMSO-d6)**: δ [ppm] = 14.4, 20.6, 20.7, 20.8, 22.1, 61.8, 68.2, 70.3, 72.9, 73.3, 80.8, 155.7, 169.6, 170.0, 170.7; **FT-IR**: v [cm^{-1}] =2961, 1736, 1531, 1434, 1367, 1211, 1094, 1029, 908, 782, 599, 554, 484; **MP:** 105 °C (lit.: 104 °C)[1] **ESI-MS**: m/z (%) = 437.0 [MNH_4^+] (100), 420.0 [MH^+] (70).

1. B. Helferich and W. Portz, *Chem. Ber.*, 1953, **86**, 604-612.