Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Enhanced site-selectivity in acylations with substrate-optimized catalysts on solid support

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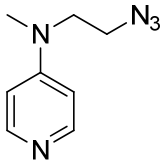
General experimental details

All commercially available reagents were used as received. For the peptide synthesis, all amino acids (only *L*-amino acids) were purchased from *Iris Biotech GmbH* and used without further purification. Thin-layer chromatography (TLC) was conducted with precoated glass-backed plates (silica gel 60 F254) containing a fluorescence indicator. The compounds were visualized by exposure to UV light (254 nm) or by staining with aqueous ceric ammonium molybdate (CAM) or aqueous basic potassium permanganate ($KMnO_4$) and subsequent heating. Flash column chromatography was performed on silica gel 60 (40 – 63 µm) and the used eluents are reported at the individual experiments. ^{1}H-NMR spectra were recorded at 600 MHz FT-NMR or 400 MHz FT-NMR spectrometers and ^{13}C-NMR spectra were recorded at 151 MHz or 101 MHz at room temperature. Chemical shifts are reported in ppm relative to solvent signal ($CDCl_3$: ^{1}H: δ = 7.26 (s); ^{13}C: δ = 77.16 (t), DMSO-d_6: 1H: δ = 2.50 (quint); 13C: δ = 39.52 (sept)). Coupling constants *J* are reported in Hz. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets). IR spectra were recorded from the neat substance using ATR technique in the range from 400–4000 cm^{-1}. Low resolution mass spectra were recorded using GC-MS (EI) or LC-MS (ESI). High resolution mass spectra were obtained using ESI on a MicroTOFMS. A fully automated synthesizer from *MultiSynTech GmbH* (*SYRO I*) was used for peptide synthesis. A Fmoc-*Rink*-Amid MBHA resin (100-200 mesh, loading: 0,68 mmol/g) from *Iris Biotech GmbH* was used for the synthesis of the cleaved peptides and a Boc-Gly-*Merrifield* resin (100-200 mesh, loading: 2,0 mmol/g) from *Iris Biotech GmbH* was used for the resin-supported peptides. The sequences of the peptides were produced in a random way and contain the DMAP-amino acid at one position.

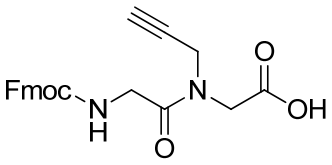
Synthesis of solid-supported peptides

Peptide library generation

The alkyne amino acid and DMAP azide were synthesized according to the published procedures[1].



DMAP-azide



Alkyne amino acid

The Boc-Gly-*Merrifield* resin (150 mg, 300 µmol, loading: 2,0 mmol/g) was used for the synthesis of one peptide sequence with the peptide synthesizer *Syro I*. Prior to the synthesis, the resin was swollen for 30 min in dichloromethane and the solvent was removed by vacuum filtration.

Boc deprotecion: For the deprotection of the Boc-protected resin, a 25% TFA solution in Dichloromethane (5 mL, 16.3 mmol, 54 eq.) was added and the mixture was reacted for a period of 12 min at room temperature with a vortexing time of 10 s followed by a break of 1 min. After removing the liquid in vacuo, the resin was washed with Dichloromethane (5 x 3 mL) and DMF (3 x 3 mL).

Afterwards, the solid-phase peptide synthesis was carried out according to the Fmoc strategy by repeating peptide coupling and Fmoc deprotection.

Peptide coupling: A 0.51 M solution of Fmoc-protected amino acid in DMF (1.20 mL, 612 µmol, 2.0 eq.), a 0.49 M solution of HBTU in DMF (1.26 mL, 617 µmol, 2.1 eq.) and a 2.04 M solution of DIPEA in NMP (600 µL, 1.22 mmol, 4.1 eq.) were successively added to the resin. The mixture was reacted for a period of 40 min at room temperature with a vortexing time of 15 s followed by a break of 2 min. Afterwards, the liquid was removed by vacuum filtration and the resin was washed with DMF (6 × 3.15 mL).

Fmoc deprotection: 1.80 mL (7.27 mmol, 24.2 eq.) of 40% piperidine solution in DMF were added to the resin. The reaction was reacted for a period of 3 min with a vortexing time of

10 s followed by a break of 1 min. The liquids were removed by vacuum filtration, a piperidine solution (900 µL, 3.64 mmol, 12.1 eq.) and 900 µL DMF were added to the reacion. The mixture was reacted for a period of 12 min with a vortexing time of 10 s followed by a break of 2 min. The resin was vacuum filtrated and washed with DMF (6 x 1.95 mL).

Acetylation of the final *N*-terminal amino acid: Acetic anhydride (1.5 mL, 16.2 mmol, 54.0 eq.) was added to the resin with the final peptide sequence attached. The mixture was reacted for 1 h with a vortexing time of 15 s followed by a break of 3 min. The liquids were removed by vacuum filtration and the resin was washed with DMF (3 × 3.0 mL).

1,3-Dipolar cycloaddition on the resin: DMAP-Azide (20.2 mg, 1.20 mmol, 4.0 eq.) and tris(benzyltriazolylmethyl)amine (TBTA) (23.5 mg, 44.3 µmol, 15 mol%) in 0.8 mL DMF were added to the resin-supported peptide. A solution of sodium ascorbate (48 mg, 0.24 mmol, 0.4 eq.) in 75 µL water and 200 µL DMF and a solution of copper sulfatepentahydrate (23 mg, 0.1 mmol, 0.4 eq.) in 75 µL water and 200 µL DMF were added. The mixture was then reacted for a period of 10 h at room temperature, with a vortexing time of 15 s followed by a break of 10 min. The liquids were removed by vacuum filtration and the resin was washed with a 1 M solution of sodium diethyldithiocarbamate trihydrate in DMF (6 x 2.0 mL, 2.0 mmol, 13 eq.). Afterwards the resin was washed with water, DMF, dichloromethane and methanol (each 6 x 2.5 mL). The resin was dried in vacuo.

Removal of the protecting groups of amino acid side chains: For cleaving the protecting groups of the side chains, a solution of 25% TFA in dichloromethane (6.6 mL) was added to the dry resin and reacted for a period of 4 hours at room temperature with a vortexing time of 15 s followed by a break of 5 min. The resin was washed with DCM (3 × 3.0 mL) and dried in vacuo.

Cleavage of the peptide from resin: To verify if the peptide synthesis was succesful, the peptide was cleaved from the resin according to the Boc strategy and analyzed with LCMS. 600 µL of a thioanisole /propan-1,3-dithiole (2:1) solution were added to the dry resin. TFA (5 mL) was added at 0 °C to the mixture and the reaction was stirred 10 min. TFMSA (400 µL) was added dropwise and after stirring for 4 h the resin was vacuum filtered and washed with TFA (3 × 3 mL).

The volume of the filtrates was reduced in vacuo, and 100 mL diethyl ether were added. The suspension was centrifuged for 5 min at 4°C (4200 rpm) and the supernatant liquid was removed. The remaining solid was dissolved in 10 mL water and lyophilized. The resulting solids were characterized via LCMS.

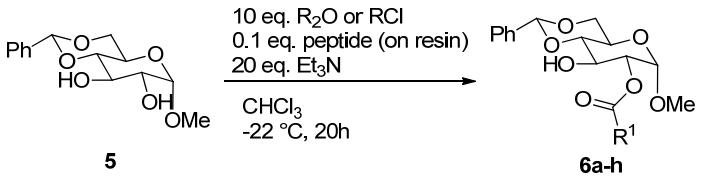
A calculated value (with 100% yield for the peptide synthesis) was used for the determination of the loading of the resin. Therefore the fragments at the resin prior to and after the peptide synthesis were used.

$$loading = \frac{M(Boc-Gly)}{M(peptide)} \bullet loading(Boc-Gly)$$

Catalyzed reactions with resin supported DMAP-peptides

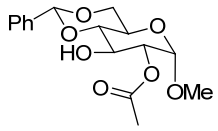
Acylation of compound 5 with DMAP-peptides on solid phase

General procedure for the acylation of acetal 5



The peptide resin (0.1 eq., VPF1LD) was swollen and washed several times with a mixture of methanol/CH_2Cl_2 (1/9 + 3 % NEt_3) and the resin was dryed in vacuum. Acetal **5** and 20 eq. triethylamine were dissolved in chloroform. The mixture was cooled to -22 °C or -40 °C and the resin was added. $R^1{}_2O$ or R^1Cl (10 eq.) in chloroform was added dropwise. After full conversion of the starting material, the reaction was stopped by the addition of methanol. The resin was filtrated and washed several times (3 × 5 mL) with a CH_2Cl_2/methanol solution (9/1 + 3 % NEt_3). The filtrate was reduced in vacuum purified with flash chromatography. The resin was dryed in vacuum and reused for the next reaction.

Methyl-2-acetyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (6d)



$C_{16}H_{20}O_7$
324,33 g/mol

Compound **5** (30.0 mg, 106 µmol, 1.0 eq.) was reacted with acetic anhydride following the general procedure. After column chromatography (PE/EA 8/2 + 3% NEt_3) **6d** (28.3 mg, 87.3 µmol, 82%) was obtained.

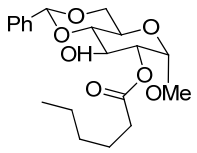
TLC: R_f = 0.07 (PE/EA = 8/2 + 3% NEt_3) [UV, Vanilin/H_2SO_4].

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 7.51 – 7.48 (m, 2H), 7.39 – 7.36 (m, 3H), 5.54 (s, 1H), 4.95 (d, *J* = 3.7 Hz, 1H), 4.80 (dd, *J* = 9.7, 3.7 Hz, 1H), 4.29 (dd, *J* = 9.9, 4.5 Hz, 1H), 4.17 (t, *J* = 9.5 Hz, 1H), 3.87 – 4.81 (m, 1H), 3.75 (t, *J* = 10.2 Hz, 1H), 3.55 (t, *J* = 9.3 Hz, 1H), 3.40 (s, 3H), 2.56 (s, 1H), 2.15 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$, 300 K) δ [ppm] = 170.8, 137.1, 129.4, 128.4, 126.4, 102.1, 97.6, 81.5, 73.7, 69.0, 68.7, 62.1, 55.5, 21.0.

The analytical data corresponds with the previously published data.[2]

Methyl-2-acetyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (6e)



$C_{20}H_{28}O_7$
380,43 g/mol

According to the general procedure, compound **5** (30.8 mg, 109 µmol, 1.0 eq.) was reacted with caproic anhydride. After flash chromatography on silica (PE/EA = 8/2 + 3% NEt_3) compound **6e** (27.5 mg, 72.3 µmol, 66%) was obtained as a white solid.

TLC: R_f = 0.53 (PE/EA = 8/2 + 3% NEt_3) [UV, Vanilin/H_2SO_4].

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 7.51 – 7.48 (m, 2H), 7.40 – 7.36 (m, 3H), 5.55 (s, 1H), 4.96 (d, *J* = 3.7 Hz, 1H), 4.80 (dd, *J* = 9.7, 3.8 Hz, 1H), 4.29 (dd, *J* = 9.9, 4.6 Hz, 1H), 4.18 (t, *J* = 9.7 Hz, 1H), 3.88 – 3.81 (m, 1H), 3.76 (t, *J* = 10.2 Hz, 1H), 3.55 (t, *J* = 9.3 Hz, 1H), 3.40 (s, 3H), 2.48 (s, 1H), 2.41 (t, *J* = 7.5 Hz, 2H), 1.70 – 1.62 (m, 2H), 1.34 – 1.30 (m, 4H), 0.92 – 0.88 (m, 3H).

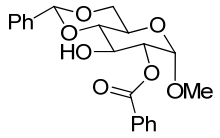
^{13}C-NMR (101 MHz, $CDCl_3$, 300 K) δ [ppm] = 173.7, 137.1, 129.4, 128.5, 126.4, 102.2, 97.8, 81.6, 73.6, 69.0, 68.8, 62.2, 55.5, 34.2, 31.3, 24.7, 22.4, 14.0.

IR (ATR) [cm^{-1}]: 3479 (bs), 2956, 2932, 2863, 1737, 1456, 1414, 1378, 1315, 1292, 1245, 1213, 1170, 1149, 1094, 1058, 1039, 993, 938, 917, 803, 750, 699, 675, 656, 522.

LRMS (ESI): m/z (%): 779 (9), 778 (21), 399 (6), 398 (31), 382 (18), 381 (100), [M + H^+], 350 (7), 349 (41), 275 (25), 243 (25).

HRMS (ESI) m/z: 403.1728 [403.1727 calc. for $C_{20}H_{28}NaO_7$ (M + Na^+)].

Methyl-2-benzoyl-4,6-*O*-benzylidene-*α*-D-glucopyranoside (6a)



$C_{21}H_{22}O_7$
386,40 g/mol

According to the general procedure, compound **5** (31.0 mg, 110 µmol, 1.0 eq.) was reacted with benzoyl chloride at -40°C. After flash chromatography on silica (PE/EA = 8/2 + 3% NEt_3) compound **6a** (40.8 mg, 106 µmol, 96%) was obtained as a white solid.

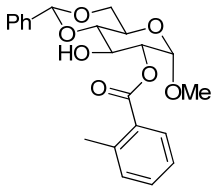
TLC: R_f = 0.77 (PE/EA = 1/1) [UV, CAM].

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 8.12 – 8.09 (m, 2H), 7.60 – 7.56 (m, 1H), 7.53 – 7.51 (m, 2H), 7.47 – 7.44 (m, 2H), 7.39 – 7.37 (m, 3H), 5.57 (s, 1H), 5.08 (d, $_J$ = 3.8 Hz, 1H), 5.04 (dd, $_J$ = 9.5, 3.8 Hz, 1H), 4.37 – 4.31 (m, 2H), 3.94 – 3.88 (m, 1H), 3.79 (t, $_J$ = 10.3 Hz, 1H), 3.62 (t, J = 9.4 Hz, 1H), 3.40 (s, 3H), 2.62 (s, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$, 300 K) δ [ppm] = 166.4, 137.2, 133.5, 130.1, 129.7, 129.4, 128.6, 128.5, 126.5, 102.2, 97.9, 81.6, 74.2, 69.0, 69.0, 62.2, 55.6.

The analytical data are in accordance with the literature.[3]

Methyl-2-(*o*-toluoyl)-4,6-*O*-benzyliden-α-D-glucopyranoside (6f)



$C_{22}H_{24}O_7$
400,42 g/mol

According to the general procedure, compound **5** (35.9 mg, 127 µmol, 1.0 eq.) was reacted with o-toluoyl chloride at -40°C. After flash chromatography on silica (PE/EA 8/2 + 3% NEt_3) (compound **6f** 43.7 mg, 109 µmol, 86%) was obtained as a white solid.

TLC: R_f = 0.25 (PE/EA = 8/2 + 3% NE_{t3}) [UV, Vanilin/H_2SO_4].

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 8.02 – 8.00 (m, 1H), 7.55 – 7.53 (m, 2H), 7.46 – 7.40 (m, 4H), 7.30 – 7.27 (m, 2H), 5.59 (s, 1H), 5.12 (d, *J* = 3.8 Hz, 1H), 5.05 (dd, *J* = 9.6, 3.8 Hz, 1H), 4.37 – 4.32 (m, 2H), 3.96 – 3.90 (m, 1H), 3.81 (t, *J* = 10.3 Hz, 1H), 3.63 (t, *J* = 9.5 Hz, 1H), 3.43 (s, 3H), 2.65 (s, 4H).

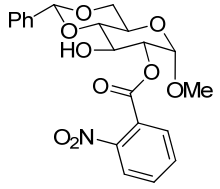
^{13}C-NMR (101 MHz, $CDCl_3$, 300 K) δ [ppm] = 167.4, 140.5, 137.2, 132.4, 131.8, 131.1, 129.4, 129.2, 128.5, 126.5, 125.9, 102.2, 97.9, 81.6, 74.1, 69.0, 69.0, 62.2, 55.6, 21.8.

IR (ATR) [cm^{-1}]: 3481, 2933, 2866, 1719, 1602, 1576, 1490, 1456, 1378, 1332, 1293, 1256, 1213, 1194, 1145, 1122, 1080, 1055, 1039, 991, 918,876, 856, 793, 738, 699, 675, 658, 576, 522, 473.

LRMS (EI): m/z (%): 818 (26), 418 (28), 401 (100) [M + H^+], 369 (56), 295 (27), 263 (16), 119 (15).

HRMS (ESI): m/z: 423.1415 [423.1414 calc. for $C_{22}H_{24}NaO_7$ (M + Na^+)].

Methyl-2-(*o*-nitrobenzoyl)-4,6-*O*-benzylidene-*α*-D-glucopyranoside (6h)



$C_{21}H_{21}NO_9$
431,39 g/mol

According to the general procedure, compound **5** (33.7 mg, 119 µmol, 1.0 eq.) was reacted with o-nitrobenzoyl chloride at -40°C. After flash chromatography on silica (PE/EA 6/4 + 3% NEt_3) compound **6h** (46.3 mg, 107 µmol, 90%) was obtained as a white solid.

TLC: R_f = 0.44 (PE/EA = 4/6 + 3% NEt_3) [UV, Vanilin/H_2SO_4].

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 7.93 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.80 – 7.76 (m, 1H), 7.71 – 7.59 (m, 2H), 7.51 – 7.49 (m, 2H), 7.38 – 7.35 (m, 3H), 5.56 (s, 1H), 5.10 – 5.06 (m, 2H), 4.31 (dd, *J* = 10.0, 4.7 Hz, 1H), 4.23 (t, *J* = 9.2 Hz, 1H), 3.92 – 3.86 (m, 1H), 3.78 (t, *J* = 10.2 Hz, 1H), 3.61 (t, *J* = 9.4 Hz, 1H), 3.45 (s, 3H), 2.64 (s, 1H).

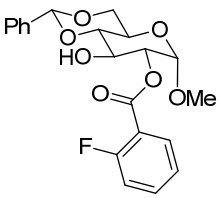
^{13}C-NMR (101 MHz, $CDCl_3$, 300 K) δ [ppm] = 165.2, 148.1, 137.1, 133.2, 132.0, 130.2, 129.4, 128.5, 127.4, 126.4, 124.1, 102.2, 97.5, 81.5, 75.1, 69.0, 68.7, 62.2, 55.7.

IR (ATR) [cm^{-1}]: 3446 (bs), 3297 (bs), 3092, 3068, 3040, 2936, 2868, 2844, 1736, 1532, 1376, 1350, 1292, 1256, 1148, 1116, 1094, 1074, 1041, 993, 763, 737, 700.

LRMS (ESI): m/z (%): 880 (66), 449 (38), 432 (100) [M + H^+], 400 (31), 294 (31), 150 (15).

HRMS (ESI): m/z: 454.1109[454.1109 calc. for $C_{21}H_{21}NNaO_9$ (M + Na^+)].

Methyl-2-(*o*-fluorobenzoyl)-4,6-*O*-benzylidene-*α*-D-glucopyranoside (6g)



$C_{21}H_{21}FO_7$
404,39 g/mol

According to the general procedure, compound **5** (30.9 mg, 109 µmol, 1.0 eq.) was reacted with o-fluorobenzoyl chloride at -40°C. After flash chromatography on silica (PE/EA 8/2 + 3% NEt_3) compound **6g** (37.4 mg, 92.5 µmol, 85%) was obtained as a white solid.

TLC: R_f = 0.25 (PE/EA = 7/3 + 3% NEt_3) [UV, Vanilin/H_2SO_4].

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 7.98 (td, *J* = 7.5, 1.9 Hz, 1H), 7.56 – 7.48 (m, 3H), 7.41 – 7.35 (m, 3H), 7.22 (td, *J* = 7.6, 1.1 Hz, 1H), 7.15 (ddd, *J* = 10.8, 8.3, 1.1 Hz, 1H), 5.58 (s, 1H), 5.13 (d, *J* = 3.8 Hz, 1H), 5.00 (dd, J = 9.6, 3.8 Hz, 1H), 4.36 – 4.31 (m, 2H), 3.93 – 3.89 (m, 1H), 3.79 (t, *J* = 10.3 Hz, 1H), 3.63 (t, *J* = 9.4 Hz, 1H), 3.41 (s, 3H), 2.61 – 2.60 (m, 1H).

^{13}C-NMR (101 MHz, CDC_{l3}, 300 K) δ [ppm] = 164.0 (d, *J* = 3.6 Hz), 162.3 (d, *J* = 261 Hz), 137.2, 135.0 (d, *J* = 9.2 Hz), 132.4, 129.4, 128.5, 126.5, 124.2 (d, *J* = 3.9 Hz), 118.3 (d, *J* = 9.4 Hz), 117.2 (d, *J* = 22.3 Hz), 102.2, 97.7, 81.4, 74.8, 69.0, 68.9, 62.2, 55.7.

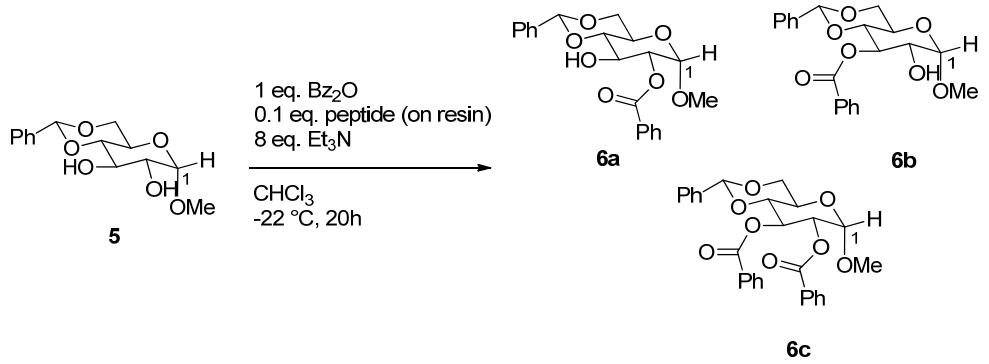
IR (ATR) [cm^{-1}]: 3487 (bs), 3068, 3039, 2936, 2915, 2866, 2844, 1729, 1613, 1490, 1456, 1378, 1334, 1298, 1276, 1256, 1146, 1118, 1084, 1038, 991, 758, 700.

LRMS (ESI): m/z (%): 831 (12), 826 (19), 422 (22), 405 (100)[M + H^+], 373 (65), 299 (32), 267 (38), 123 (27).

HRMS (ESI): m/z: 427,1159 [427,1164 calc. for $C_{21}H_{21}FNaO_7$ (M + Na^+)].

Resin-supported DMAP-peptide screening

Benzoylation of compound 5



General procedure for the solid phase catalyzed benzoylation: The resin (0.1 eq.) was swollen for 30 min and washed several times with a mixture of methanol/CH_2Cl_2 (1/9 + 3 % NEt_3). The liquids were removed by vacuum filtration. The acetal **5** (50.4 mg, 178 µmol, 1.0 eq.) and triethylamine (500 µL, 3.61 mmol, 20 eq.) were dissolved in 0.7 mL chloroform. The mixture was cooled to -22°C and the resin was added. Benzoic anhydride (40.3 mg, 178 mmol, 1 eq.) in 0.3 mL chloroform was added dropwise. After 20 h the reaction was stopped by the addition of methanol (1.4 mL, 35.7 mmol, 100 eq.). The mixture was filtered through silica and the filtrate was dried in vacuo. The residue was dissolved in $CDCl_3$ and analyzed with ^{1}H-NMR spectroscopy. The product ratios were determined with the published method[1] using following signals:

Compound **5**: 4.72 (d, *J* = 3.8 Hz, 1H, H-1); Compound **6a**: 5.05 (d, *J* = 3.8 Hz, 1H, H-1), Compound **6b**: 4.80 (d, *J* = 3.8 Hz, 1H, H-1); Compound **6c**: 5.15 (d, *J* = 3.7 Hz, 1H, H-1).

The analytical data for compounds **5**, **6a**, **6b**, **6c** were known from the literature.[1]

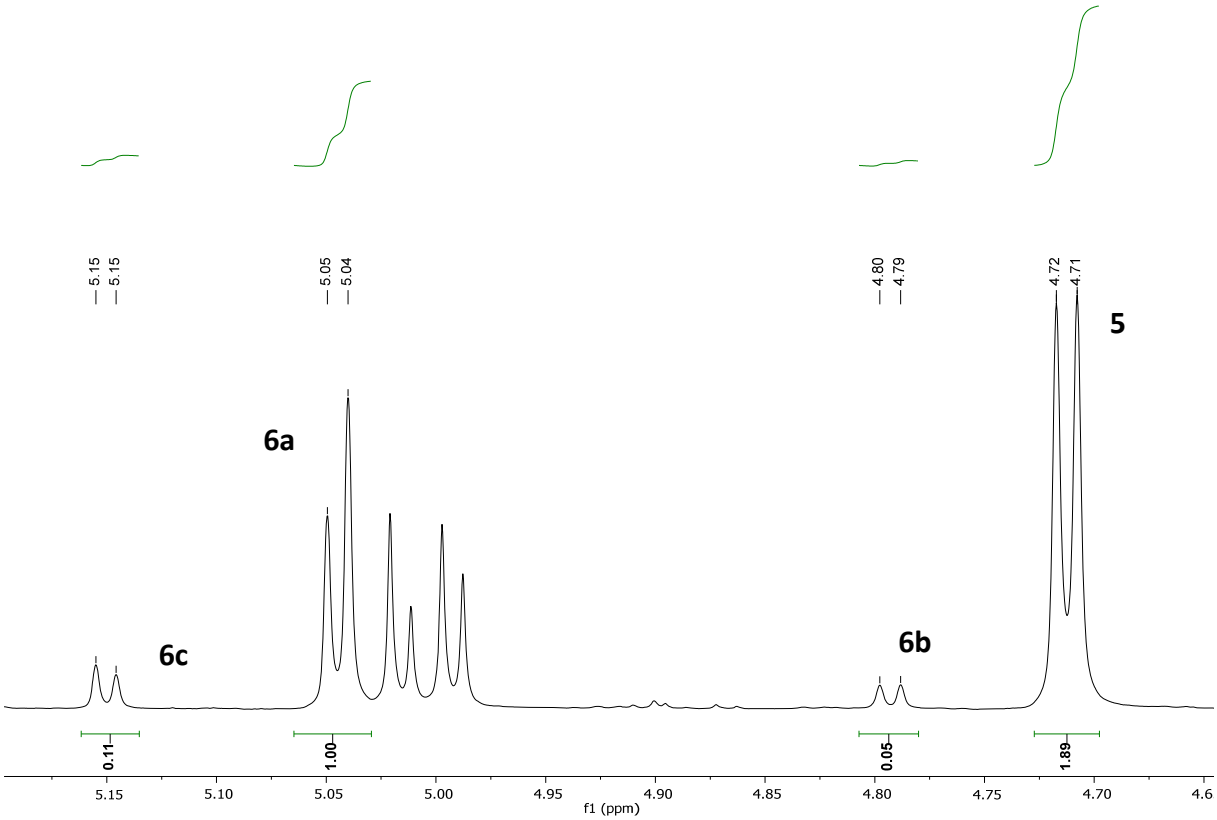


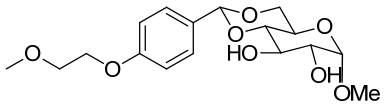
Figure 1: Excerpt from the ^{1}H-NMR spectrum of the benzoylation of **5** in the presence of FPD1QTV.

Table 1: Benzolyation of compound **5** (Catalyst Screening)

Entry	Peptide sequence N → C[a]	6a	6b	6c	Conversion [%]
1	DST1PV	1	0	0	24
2	1FDAQT	1	0	0	18
3	HPDSL1	1	0,01	0	22
4	PALVT1	1	0,04	0,05	25
5	H1QSFD	1	0,01	0	28
6	1PKTAS	1	0	0	26
7	V1PFLDP	1	0,04	0,20	45
8	TK1HLVA	1	0,02	0,04	48
9	FPD1QTV	1	0,05	0,11	38
10	QLTD1AH	1	0,02	0,07	29
11	DVKST1D	1	0,03	0,02	31
12	1QAFVLP	1	0,07	0,3	10
13	QAFPDST1	1	0	0	20
14	VL1TKPFH	1	0	0	19
15	TKH1FVAD	1	0	0	19
16	FDQTV1AH	1	0,03	0	21
17	1QAFVLKS	1	0,02	0	29
18	V1TFLDHA	1	0,01	0	23

a) *N*-Terminus acetyl-protected, *C*-Terminus bound on *Merrifield* resin b) calculated by H-NMR signal of the starting material

(2*R*,4a*R*,6*S*,7*R*,8*R*,8a*S*)-6-methoxy-2-(4-(2-methoxyethoxy)phenyl)hexahydropyrano[3,2-d][1,3]dioxine-7,8-diol (7)



$C_{17}H_{24}O_8$
356,37 g/mol

Methyl-α-D-glucopyranoside (2.96 g, 15.26 mmol, 1.1 eq.), *p*-toluenesulfonic acid (66 mg, 0.35 mmol, 0.03 eq.) and 4-(2-methoxyethoxy)benzaldehyde (2.50 g, 13.9 mmol, 1.0 eq.) were dissolved in 14 mL anhydrous DMF and the mixture was stirred for 5 min at room temperature. Triethyl orthoformate (2.8 mL, 16.6 mmol, 1.2 eq.) was added dropwise. After stirring for 15 min, the reaction was stirred for 3 h under reduced pressure (15-20 mbar) and then quenched with saturated $NaHCO_3$. Ethyl acetate was added and the solid was filtered and dried in vacuo. The mixture was filtrated and the solvent was removed in vacuo. Compound **7** (3.31 g, 9.29 mmol, 67%) was obtained as a white solid.

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 7.46 – 7.40 (m, 2H), 6.97 – 6.91 (m, 2H), 5.51 (s, 1H), 4.82 (d, J = 3.9 Hz, 1H), 4.30 (dd, J = 9.8, 4.3 Hz, 1H), 4.17 – 4.12 (m, 2H), 3.95 (tt, J = 9.3, 2.1 Hz, 1H), 3.86 – 3.78 (m, 1H), 3.79 – 3.73 (m, 3H), 3.66 (td, J = 9.3, 4.0 Hz, 1H), 3.49 (s, 3H), 3.47 (s, 3H).

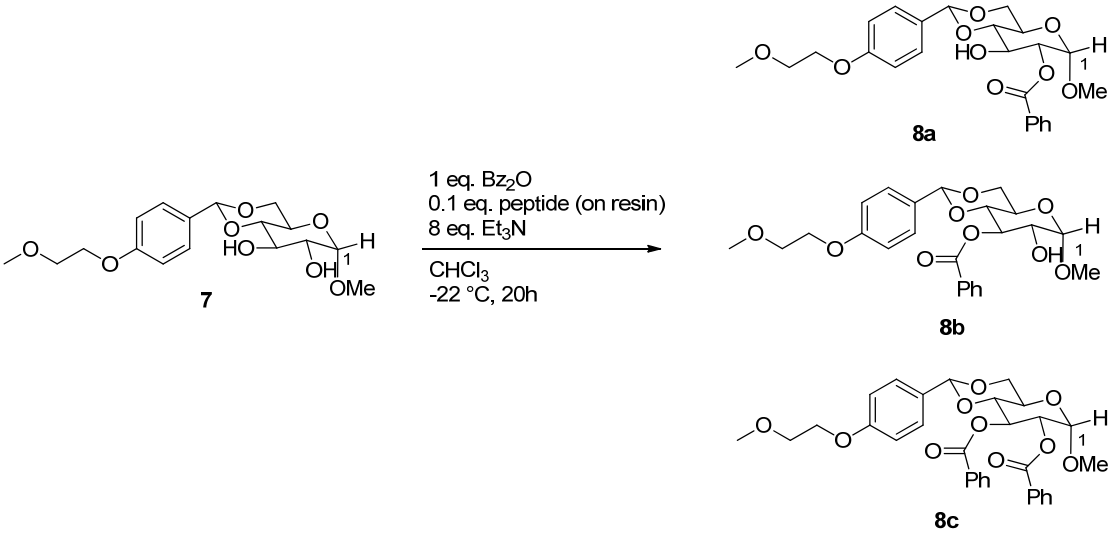
^{13}C-NMR (101 MHz, $CDCl_3$, 300K) δ [ppm] = 159.4, 129.8, 127.6, 114.4, 101.8, 99.8, 80.9, 72.9, 71.9, 71.0, 68.9, 67.3, 62.4, 59.2, 55.6.

IR (ATR) [cm^{-1}]: 3411, 3309, 2932, 2906, 2894, 2871, 2848, 1921, 1614, 1252, 1123, 1069, 1033, 994, 823.

LRMS (ESI): m/z (%): 735 (14), 357 (100) [M + H^+], 181 (9).

HRMS (ESI): m/z : 379.1362 [379.1363 calc.. for $C_{17}H_{24}NaO_8$ (M + Na^+)].

Benzoylation of compound 7



General procedure for the solid phase catalyzed benzolyation: The resin (0.1 eq.) was swollen for 30 min and washed several times with a mixture of methanol/CH_2Cl_2 (1/9 + 3 % NEt_3) and the liquids were removed by vacuum filtration. Acetal **7** (63.6 mg, 178 µmol, 1.0 eq.) and triethylamine (500 µL, 7.13 mmol, 20 eq.) were dissolved in 0.7 mL chloroform. The mixture was cooled to -22°C and the resin was added. Benzoic anhydride (40.3 mg, 178 mmol, 1 eq.) in 0.3 mL chloroform was added dropwise. After 20 h the reaction was stopped by the addition of methanol (1.4 mL, 35.7 mmol, 100 eq.). The mixture was filtered through silica and the filtrate was dried in vacuo. The residue was dissolved in $CDCl_3$ and analyzed with ^{1}H-NMR spectroscopy. The product ratios were determined with the published method[1] using following signals:

Compound **7**: 4.76 (d, *J* = 3.8 Hz, 1H, H-1); Compound **8a**: 5.07 (d, *J* = 3.8 Hz, 1H, H-1), Compound **8b**: 4.83 (d, *J* = 3.8 Hz, 1H, H-1); Compound **8c**: 5.17 (d, *J* = 3.7 Hz, 1H, H-1).

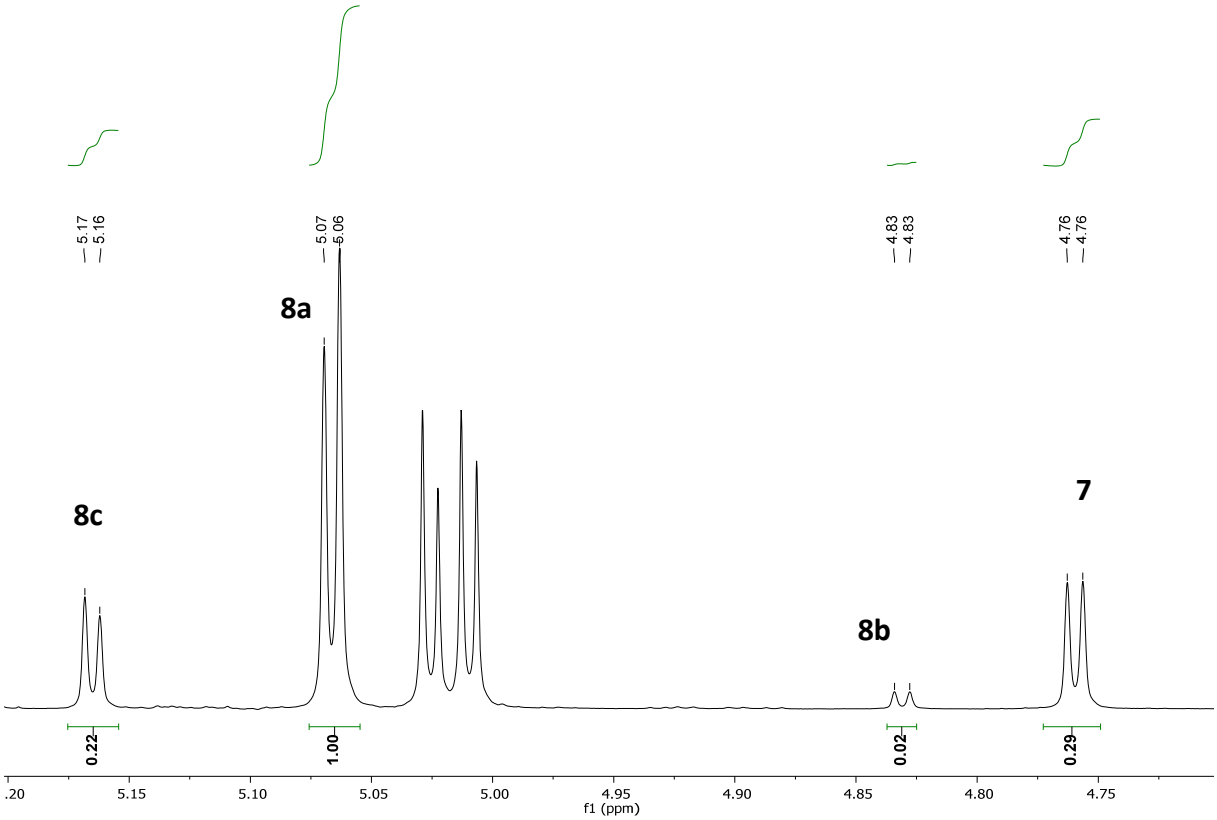


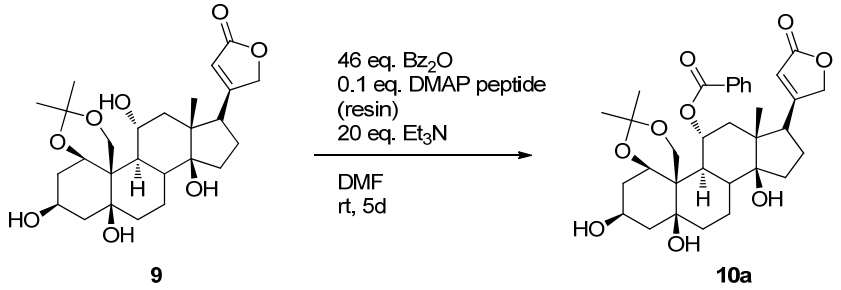
Figure 2: Excerpt from the ^{1}H-NMR spectrum of the benzoylation of **7** in the presence of PALVT1.

Table 2: Benzoylation of compound **7** (Catalyst Screening)

Entry	Peptide sequence N → C[a]	8a	8b	8c	Conversion [%]
1	DST1PV	1	0	0	66
2	1FDAQT	1	0	0	55
3	HPDSL1	1	0	0	78
4	PALVT1	1	0.22	0.02	81
5	H1QSFD	1	0,03	0	83
6	1PKTAS	1	0	0	69
7	V1PFLDP	1	0	0	46
8	TK1HLVA	1	0	0	67
9	FPD1QTV	1	0	0.02	72
10	QLTD1AH	1	0	0	67
11	DVKST1D	-	-	-	-
12	1QAFVLP	-	-	-	-
13	QAFPDST1	1	0.02	0	74
14	VL1TKPFH	1	0	0.01	79
15	TKH1FVAD	1	0	0	50
16	FDQTV1AH	1	0	0	62
17	1QAFVLKS	1	0	0	62
18	V1TFLDHA	1	0	0	57

a) *N*-Terminus acetyl-protected, *C*-Terminus bound on *Merrifield* resin b) calculated by H-NMR signal of the starting material

Benzoylation of compound 9



9 **10a**

Procedure for the benzolyation of compound 9 reusing a resin-supported peptide catalyst: Compound **9** (250 mg, 0.52 mmol, 1.0 eq.) and DMAP peptide (on resin) (154 mg, 0.05 mmol, 0.1 eq.) (V1FPALK) were suspended in 4 mL DMF. To this mixture benzoic anhydride (1.17 g, 7.84 µmol, 15 eq.) was added, followed by the addition of triethylamine (1.45 mL, 10.5 mmol, 20 eq.). The reaction was stirred at room temperature for 5 days, then stopped through the addition of 2 mL methanol. After 10 min stirring, the peptide resin was filtered. The filtrate was washed with water, extracted with dichloromethane and dried with Na_2SO_4. The solvent was removed in vacuo and after flash chromatography on silica (0-10% MeOH in DCM) compound **10a** (318 mg, 0.55 mmol, quant.). The resin was dryed in vacuo and reused for the next reaction.

TLC: R_f = 0.38 (DCM/MeOH =9/1) [CAM].

^{1}H-NMR (400 MHz, $CDCl_3$, 300 K) δ [ppm] = 7.97 (dd, J = 1.3, 8.3 Hz, 2H), 7.64 - 7.55 (m, 1H), 7.53 - 7.41 (m, 2H), 5.85 (s, 1H), 5.59 (dt, J = 4.9, 9.4 Hz, 1H), 4.83 - 4.69 (m, 2H), 4.55 (t, J = 3.0 Hz, 1H), 4.47 (d, J = 12.4 Hz, 1H), 4.25 (br. s., 1H), 4.01 (d, J = 12.6 Hz, 1H), 2.83 (t, J = 7.6 Hz, 1H), 2.19 - 2.07 (m, 4H), 2.02 - 1.90 (m, 5H), 1.88 - 1.73 (m, 2H), 1.73 - 1.65 (m, 2H), 1.65 - 1.49 (m, 2H), 1.33 (s, 3H), 1.29 - 1.24 (m, 1H), 1.12 (s, 3H), 1.00 (s, 3H)

^{13}C-NMR (101 MHz, CDC_{l3}, 300 K) δ [ppm] = 174.4, 173.2, 165.3, 133.7, 129.8, 129.3, 128.8, 117.9, 100.2, 83.4, 75.1, 73.5, 70.5, 68.3, 66.7, 61.2, 49.9, 49.0, 44.1, 44.0, 43.9, 40.1, 37.5, 37.2, 33.3, 32.7, 26.6, 26.2, 23.7, 21.1, 17.0.

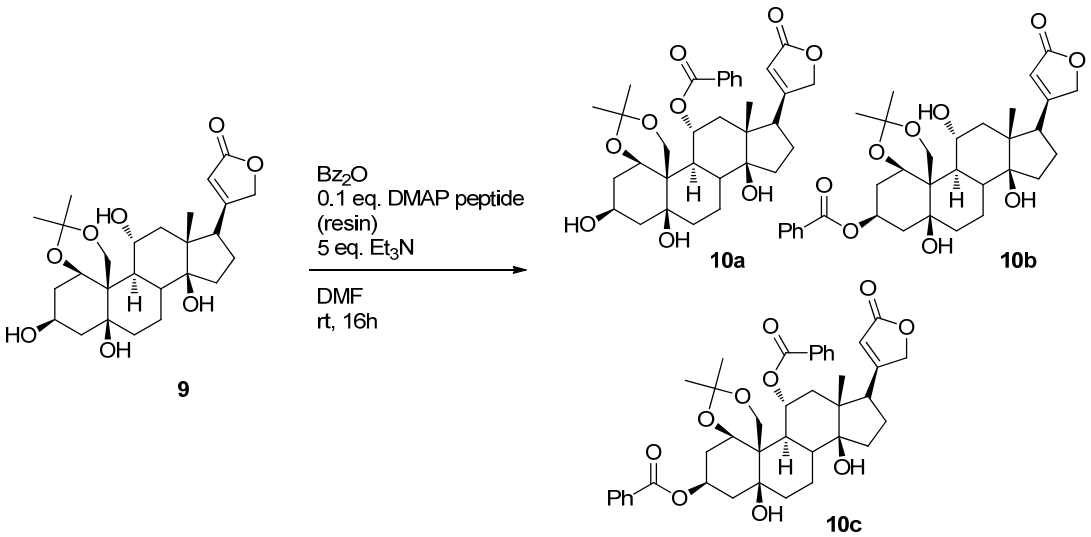
The analytical data corresponds with the previously published data.[1]

Table 3: Benzolyation of compound **9** (Reusing the same Catalyst)

Entry	Cycle[a]	Yield [%][b]
1	1	80
2	2	90
3	3	79
4	4	69
5	5	82
6	6	72
7	7	97
8	8	97
9	9	84
10	10	Quant.
11	11	Quant.

a) Times the resin-supported peptide catalyst was reused b) Isolated yield

Benzoylation of compound 9



Procedure for the solid phase catalyzed benzolyation of compound 9 (Catalyst Screening): 5.0 mg (10.5 µmol, 1.0 eq.) of compound **9**, 0.1 eq. of DMAP peptide and 7.2 µL (52.2 µmol, 5.0 eq.) triethylamine were dissolved in 200 µL DMF.To this mixture a solution of 108 mg (479 µmol, 46 eq.) benzoic anhydride in 100 µL DMF was added, and the reaction was stirred at room temperature for 16 h. The reaction was stopped through the addition of 85 µL (2.1

mmol, 200 eq.) methanol and the solvent was removed in vacuo. The residue was dissolved in DMSO-d6 and analyzed with ^{1}H-NMR spectroscopy. The product ratios were determined with the published method[1] using following signals:

Compound **a**: 6.07 (s, 1H), 5.45 – 5.49 (m, 1H); Compound **c**: 5.40 – 5.42 (m, 2H); Compound **b**: 5.35 – 5.37 (m, 1H).

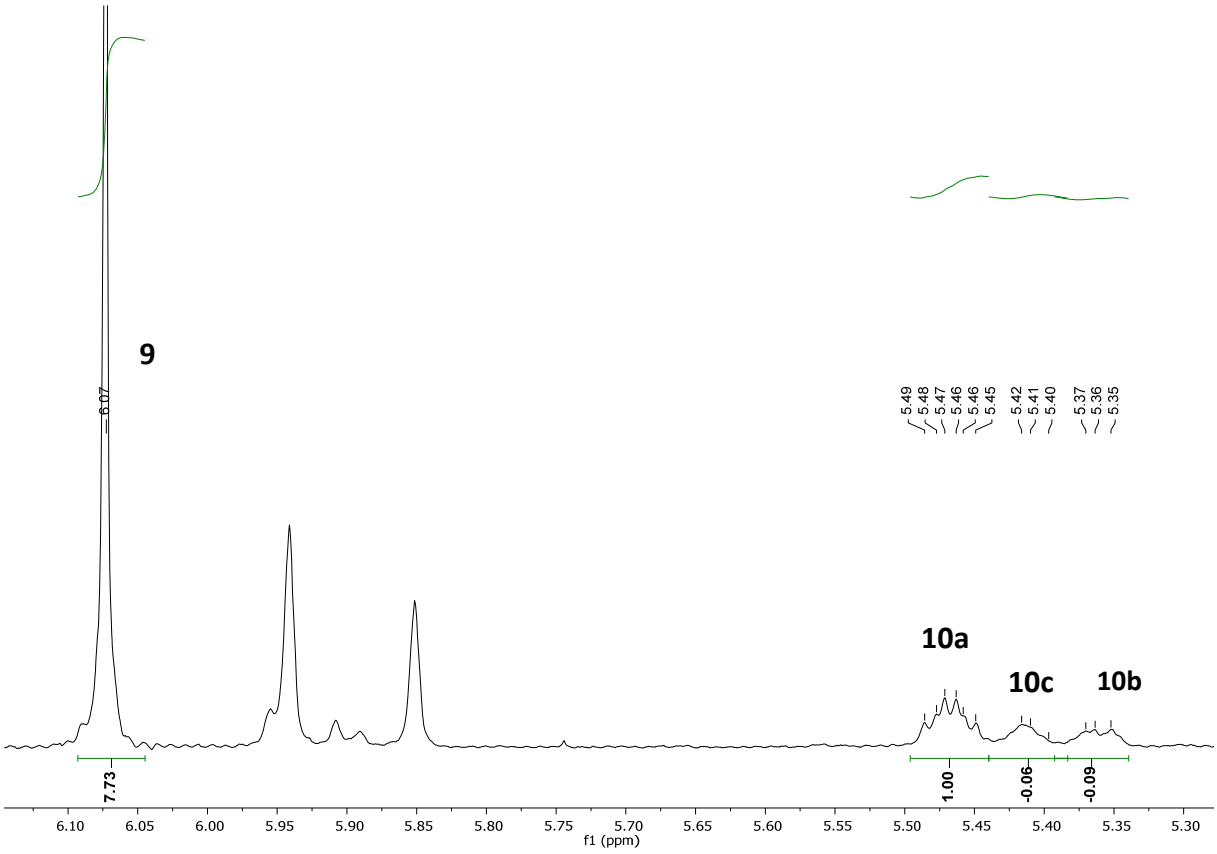


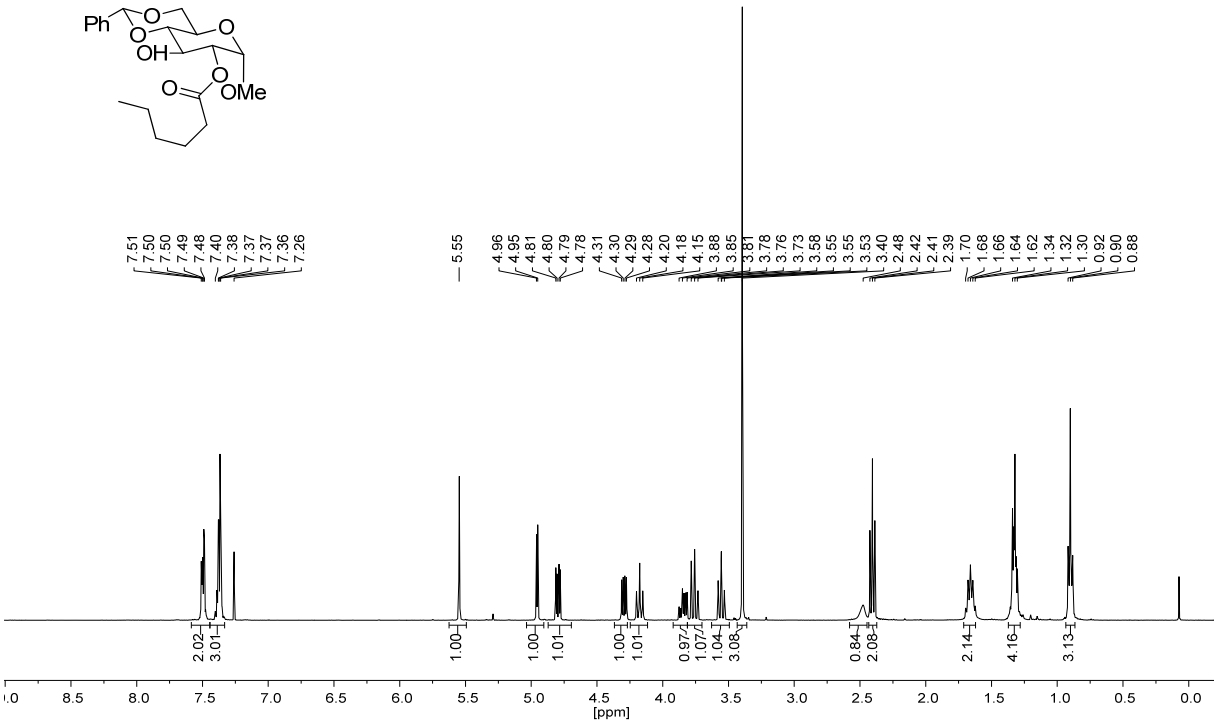
Figure 3: Excerpt from the ^{1}H-NMR spectrum of the benzoylation of **9**

Table 4: Benzolyation of compound **9** (Catalyst Screening)

Entry	Peptide sequence N → C[a]	Eq. Bz_2O	8a	8b	8c	Conversion [%][b]
1	V8FPALK	15	1	0	0	13
2	TK8HLVA	15	1	0,18	0	12
3	FPD8QTV	15	1	0,14	0	9
4	DST8PV	15	1	0,12	0	6
5	V8PFLDP	15	1	0	0	7
6	TKH8FVAD	15	1	0	0	9
7	FDQTV8AH	15	1	0	0	6
8	8QAFVLKS	15	1	0	0	5
9	V8TFLDHA	15	1	0	0	6
10	PALVT8	15	1	0	0	14

a) *N*-Terminus acetyl-protected, *C*-Terminus bound on *Merrifield* resin b) calculated by H-NMR signal of the starting material (6.07 (s, 1H) ppm)

Spectra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7.37
7.36
7.26
5.55
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4.95
4.81
4.80
4.79
4.78
4.31
4.30
4.29
4.28
4.20
4.18
4.15
3.88
3.85
3.81
3.78
3.76
3.73
3.58
3.55
3.55
3.53
3.40
2.48
2.42
2.41
2.39
1.70
1.68
1.66
1.64
1.62
1.34
1.32
1.30
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0.90
0.88
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3.01
1.00
1.00
1.01
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2.08
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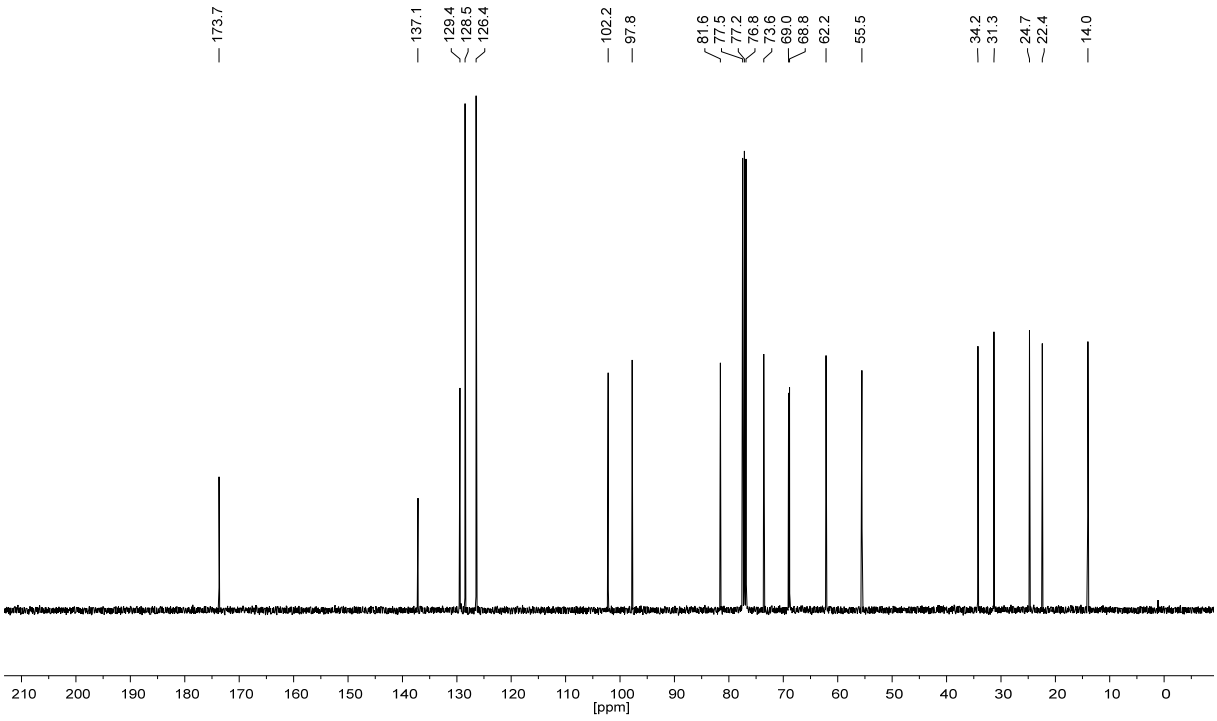
3.13
[ppm]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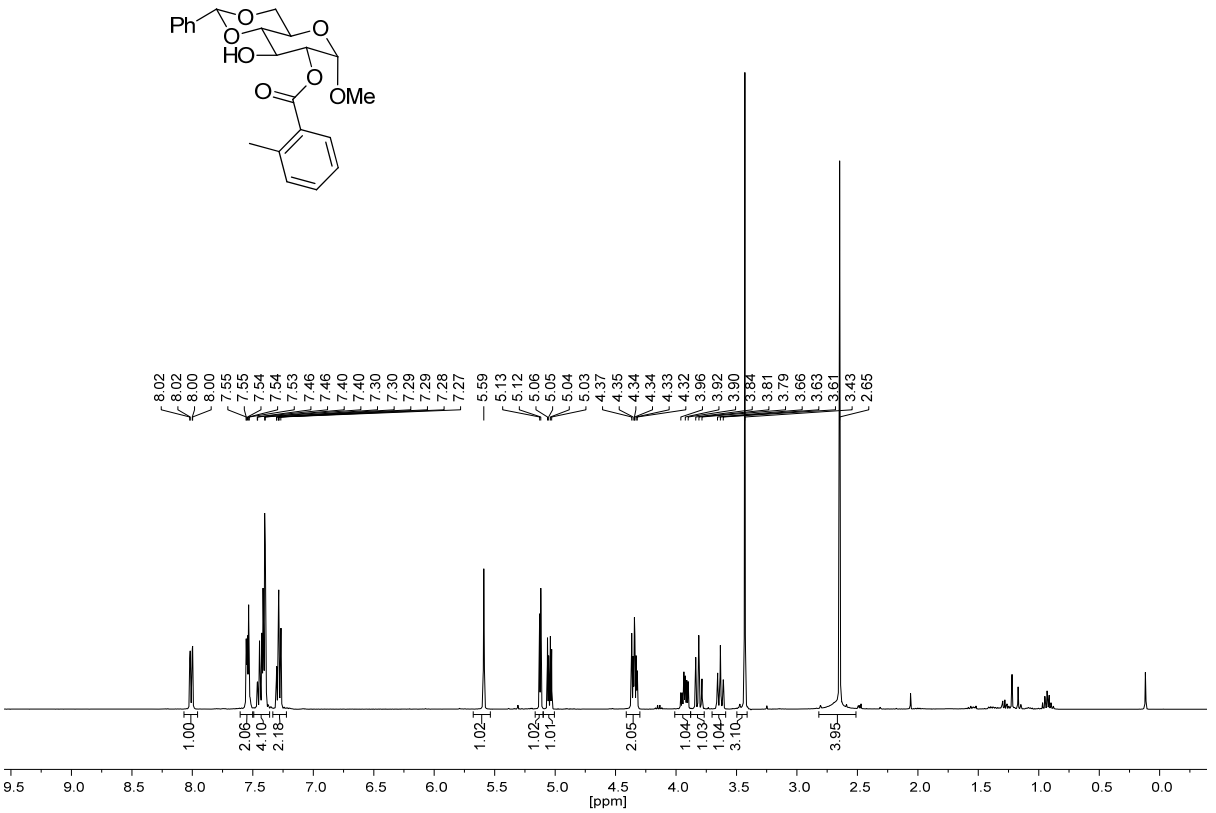
55.5
34.2
31.3
24.7
22.4
14.0
[ppm]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2.18
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1.02
1.01
2.05
1.04
1.03
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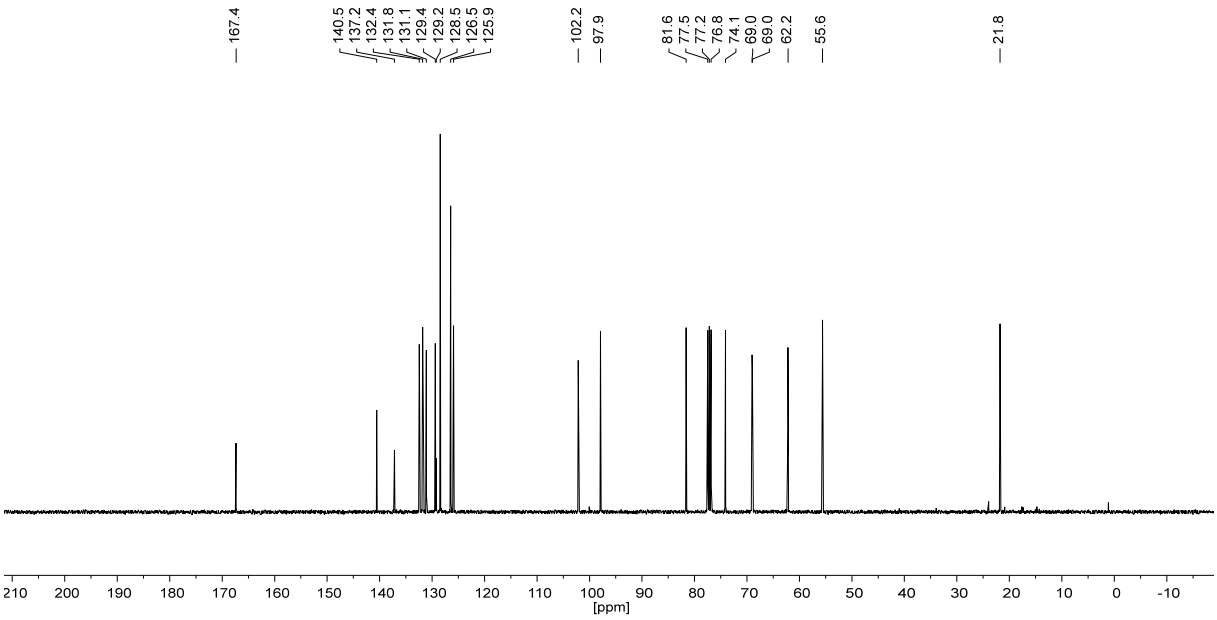
[ppm]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21.8
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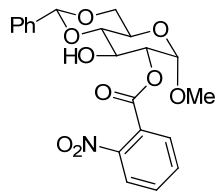
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4.23
4.21
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3.61
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1.95
1.01
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1.05
1.07
1.05
2.95
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6.5
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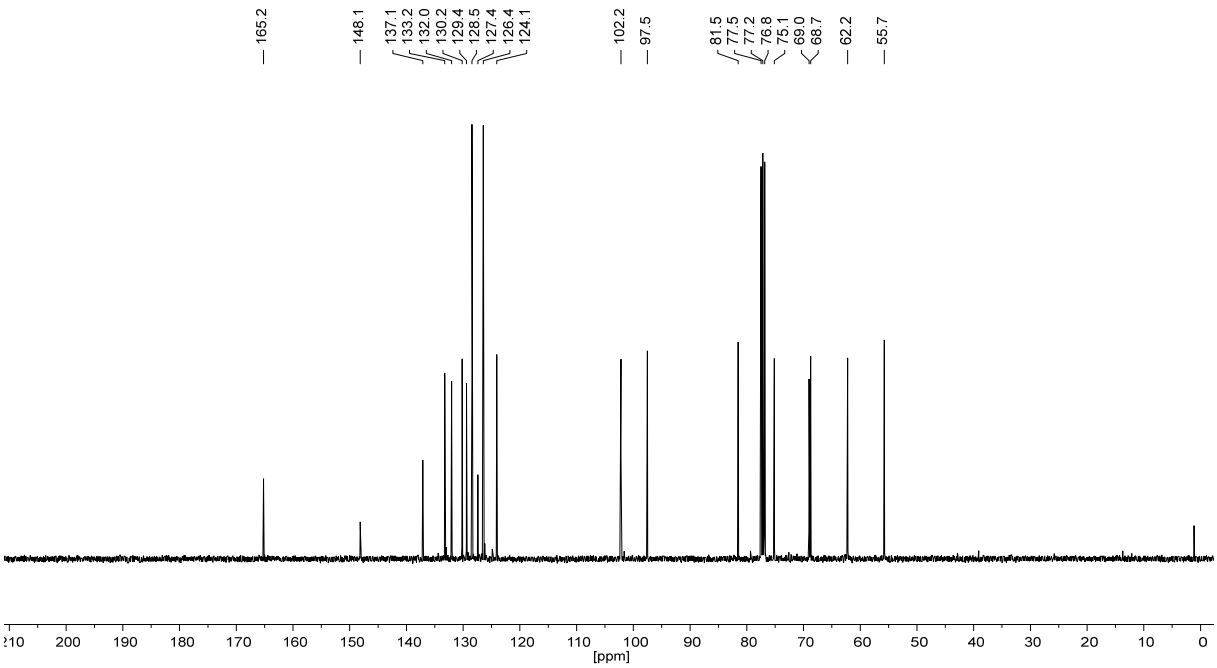
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77.2
76.8
75.1
69.0
68.7
62.2
55.7
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200
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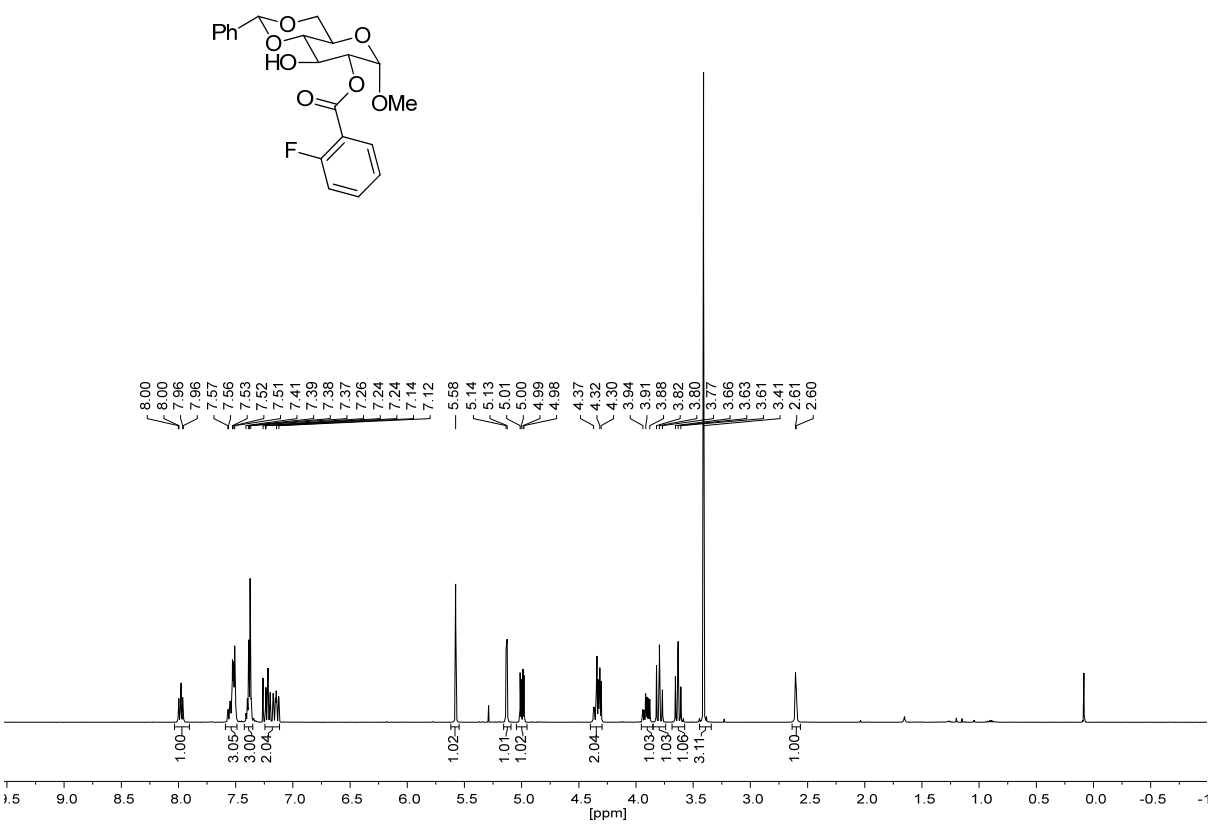
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4.99
4.98
4.37
4.32
4.30
3.94
3.91
3.88
3.82
3.80
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3.63
3.61
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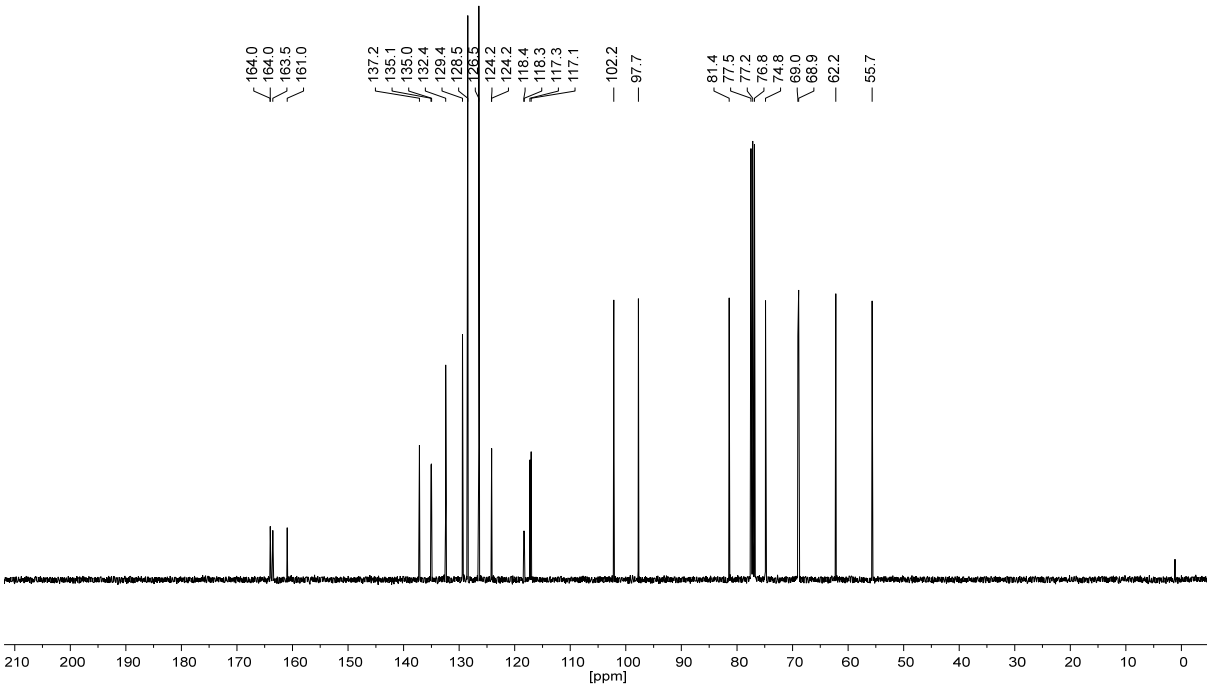
[ppm]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161.0
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135.0
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124.2
124.2
118.4
118.3
117.3
117.1
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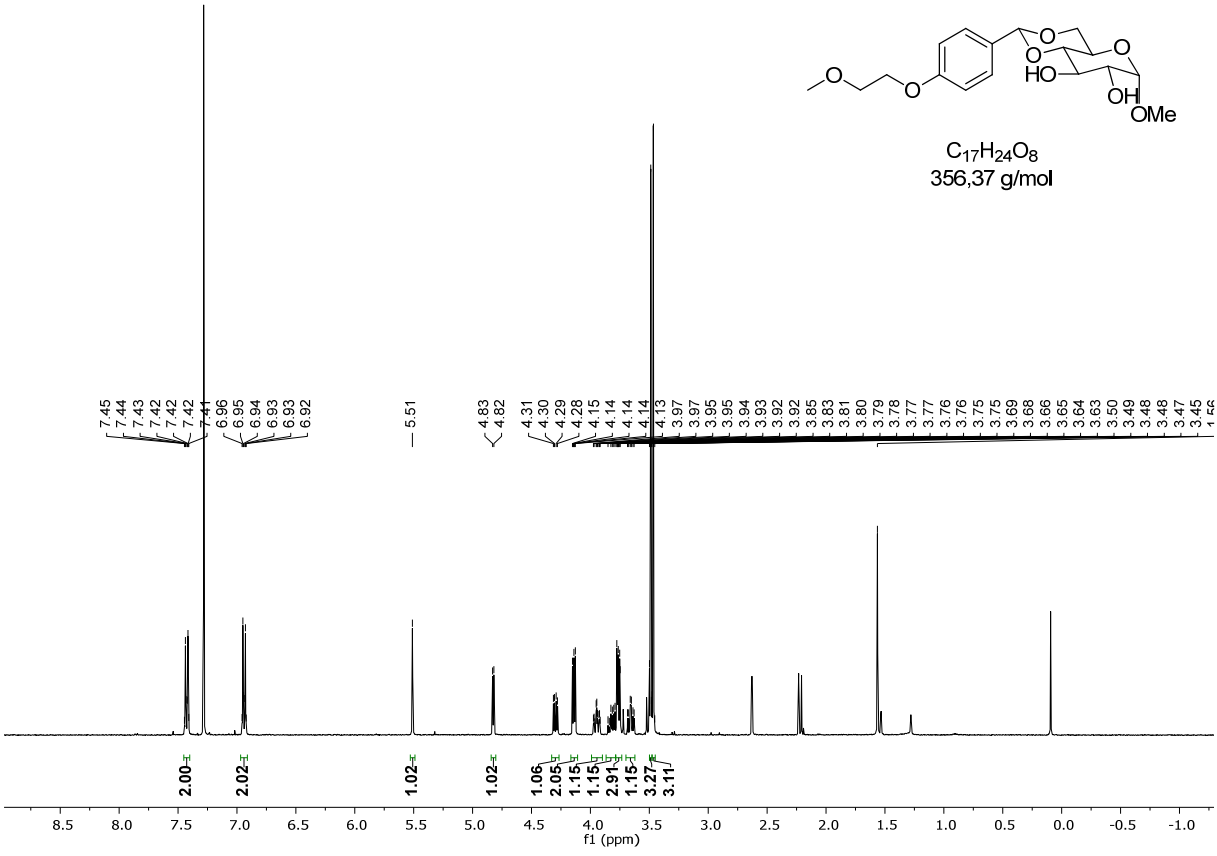
55.7
[ppm]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2.00 2.02 1.02 1.02 1.06 2.05 1.15 1.15 2.91 1.15 3.27 3.11
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
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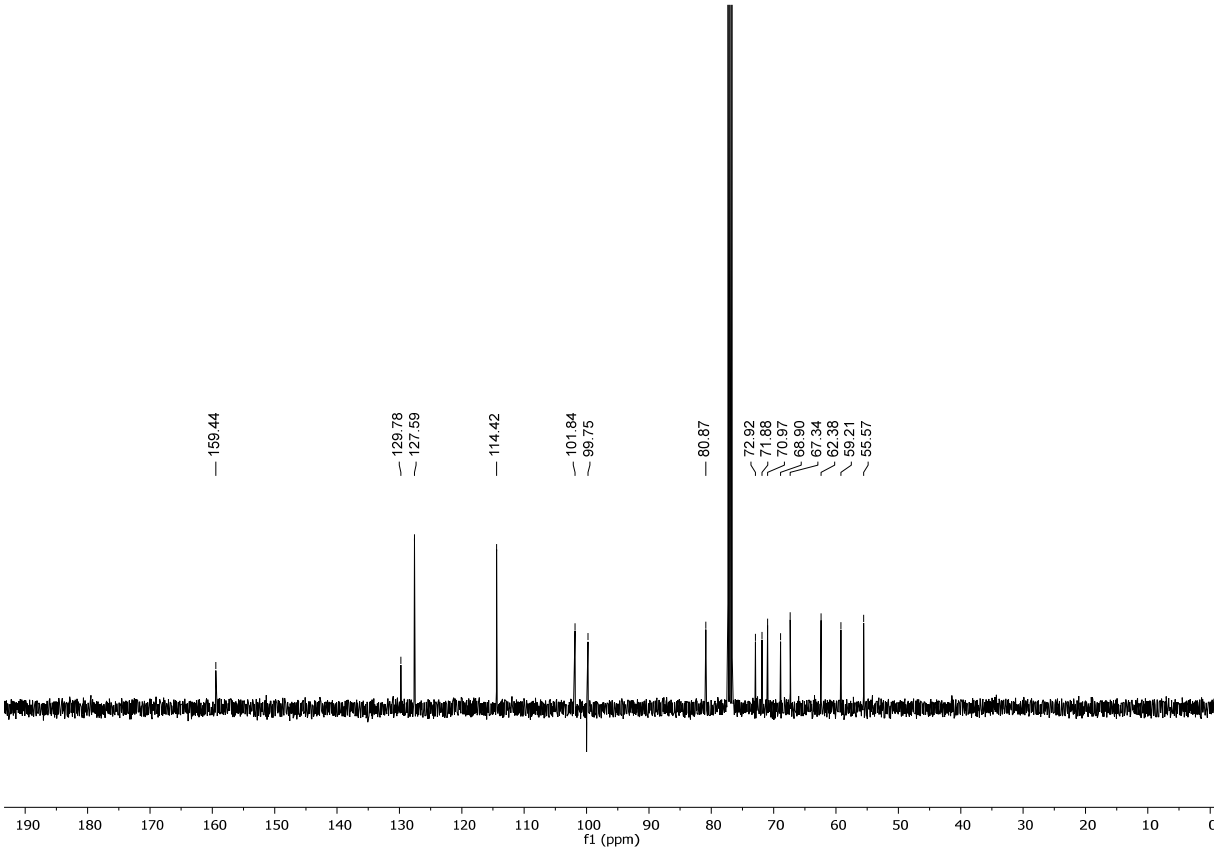
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59.21
55.57
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

Literature

[1] F. Huber, S. F. Kirsch, *Chem. Eur. J*. **2016**, *22*, 5914–5918.

[2] C.-C. Wang, J.-C. Lee, S.-Y. Luo, S. S. Kulkarni, Y.-W. Huang, C.-C. Lee, K.-L. Chang, S.-C. Hung, Nature **2007**, 446, 896–899.

[3] (a) J. M. Manthorpe, A. M. Szpilman, E. M. Carreira, *Synthesis* **2005**, 3380–3388. (b) H. Wang, J. She, L.-H. Zhang, X.-S. Ye, *J. Org. Chem.* **2004**, 69, 5774–5777. (c) S. Cheuk, E. D. Stevens, G. Wang, *Carbohyd. Res.* **2009**, 344, 417–425.