

Supplementary Materials: Debenzylation of Benzyl-Protected Methylcellulose

Payam Hashemi ^{1,*}, Saskia Wenderoth ¹, Andreas Koschella ², Thomas Heinze ² and Petra Mischnick ^{1,*}

¹ Institute of Food Chemistry, Technische Universität Braunschweig, Schleinitzstraße 20, 38106 Braunschweig, Germany; saskia.wenderoth@t-online.de

² Institute of Organic Chemistry and Macromolecular Chemistry, Faculty of Chemistry and Earth Sciences, Friedrich Schiller University Jena, Humboldtstraße 10, 07743 Jena, Germany; andreas.koschella@uni-jena.de (A.K.); thomas.heinze@uni-jena.de (T.H.)

* Correspondence: payam.hashemi@tu-dresden.de (P.H.); p.mischnick@tu-braunschweig.de (P.M.)

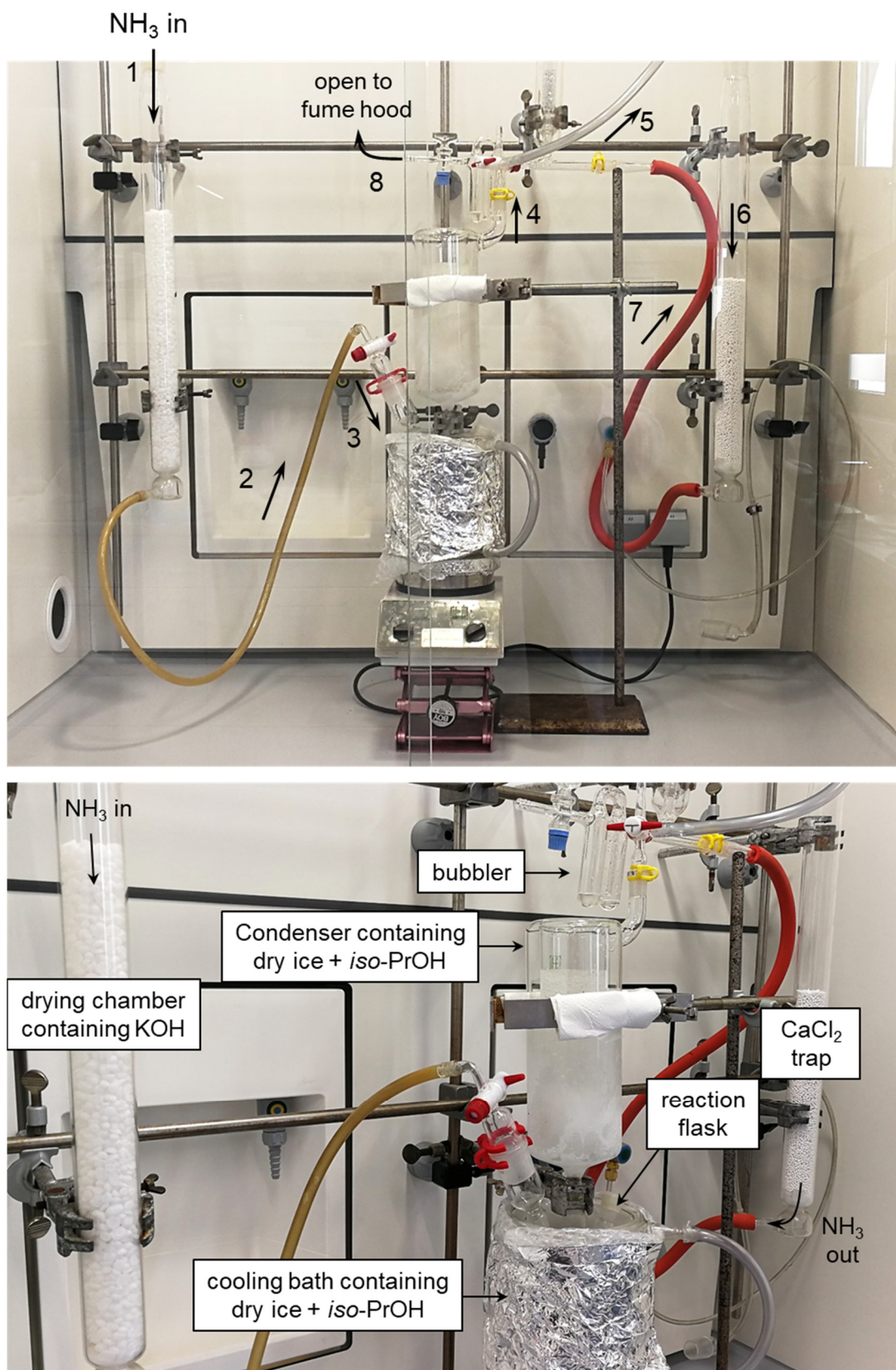
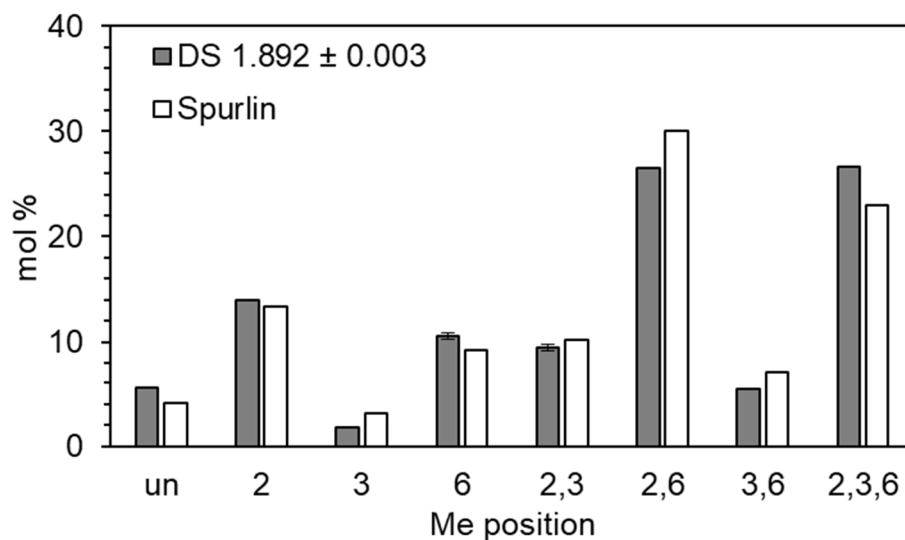


Figure S1. Reaction setup for debenzylation by Method-3 (Na/NH_3). Arrows with numbers in the upper image show the flow direction of ammonia/nitrogen in the system.

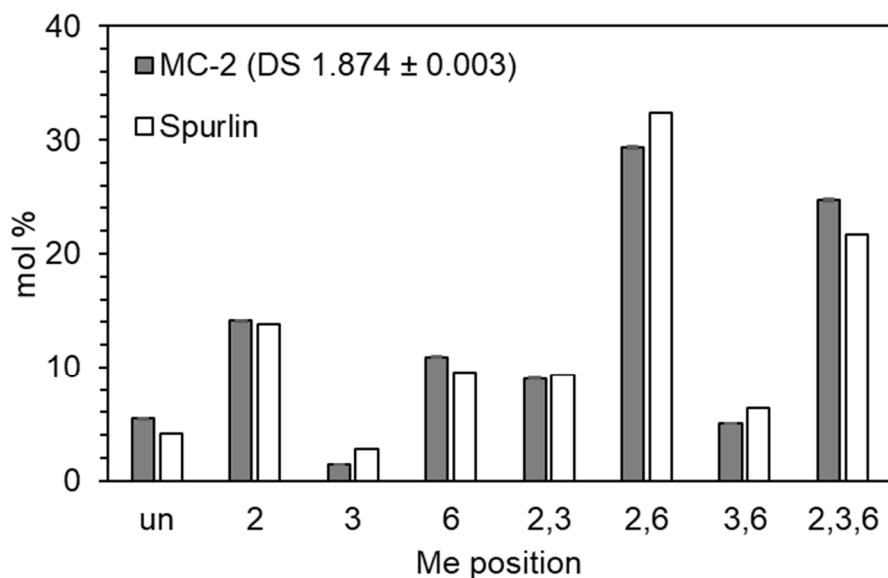


MC-1

GLC derived data

<i>S</i> 0	5.54
<i>S</i> 2	14.00
<i>S</i> 3	1.83
<i>S</i> 6	10.54
<i>S</i> 23	9.43
<i>S</i> 26	26.53
<i>S</i> 36	5.45
<i>S</i> 236	26.67
<i>C</i> 0	5.54
<i>C</i> 1	26.37
<i>C</i> 2	41.41
<i>C</i> 3	26.67
<i>X</i> 2	0.77
<i>X</i> 3	0.43
<i>X</i> 6	0.69
DS	1.892 ± 0.003

Figure S2. Methyl pattern of MC-1 before benzylation (For further information regarding the monomer analysis of methylcellulose derivatives by GLC-FID refer to [2]). Sample MC-1 was ethylated first; thereafter, from the ethylated MC-1, 3 separate samples were taken and prepared independently of each other (independent total hydrolysis, reduction, alkaline acetylation, as described in the Materials and Methods section). Each independently prepared sample was measured 3 times by GLC and the data were averaged as described in the Materials and Methods section 2.6.

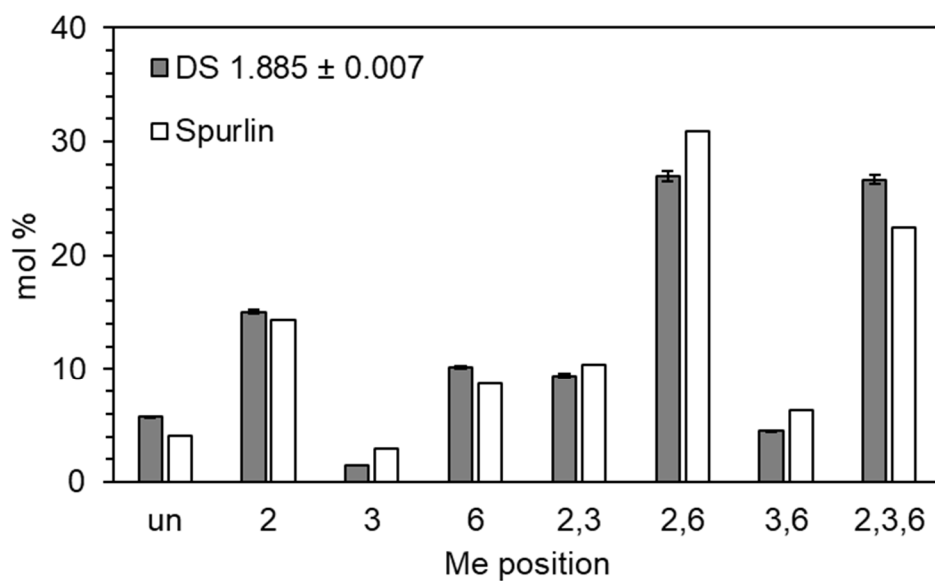


MC-2

GLC derived data

<i>S</i> ₀	5.43
<i>S</i> ₂	14.10
<i>S</i> ₃	1.42
<i>S</i> ₆	10.94
<i>S</i> ₂₃	9.00
<i>S</i> ₂₆	29.38
<i>S</i> ₃₆	5.03
<i>S</i> ₂₃₆	24.71
<i>C</i> ₀	5.43
<i>C</i> ₁	26.45
<i>C</i> ₂	43.41
<i>C</i> ₃	24.71
<i>X</i> ₂	0.77
<i>X</i> ₃	0.40
<i>X</i> ₆	0.70
DS	1.874 ± 0.003

Figure S3. Methyl pattern of MC-2 before benzylation (For further information regarding the monomer analysis of methylcellulose derivatives by GLC-FID refer to [2]). To produce the presented data, 4 separate samples from MC-2 were taken and prepared independently of each other (independent total hydrolysis, reduction, alkaline acetylation, as described in the Materials and Methods section). Each independently-prepared sample was measured 3 times. Evaluated results were averaged as described in the Materials and Methods section 2.6.



MC-3

GLC derived data

<i>S</i> ₀	5.71
<i>S</i> ₂	15.05
<i>S</i> ₃	1.51
<i>S</i> ₆	10.17
<i>S</i> ₂₃	9.42
<i>S</i> ₂₆	26.94
<i>S</i> ₃₆	4.52
<i>S</i> ₂₃₆	26.68
<i>C</i> ₀	5.71
<i>C</i> ₁	26.73
<i>C</i> ₂	40.88
<i>C</i> ₃	26.68
<i>X</i> ₂	0.78
<i>X</i> ₃	0.42
<i>X</i> ₆	0.68
DS	1.885 ± 0.007

Figure S4. Methyl pattern of MC-3 before benzylation (For further information regarding the monomer analysis of methylcellulose derivatives by GLC-FID refer to [2]). To produce the presented data, 5 separate samples from MC-3 were taken and prepared independently of each other (independent total hydrolysis, reduction, alkaline acetylation, as described in the Materials and Methods section). Each independently-prepared sample was measured 3 times. Evaluated results were averaged as described in the Materials and Methods section 2.6.

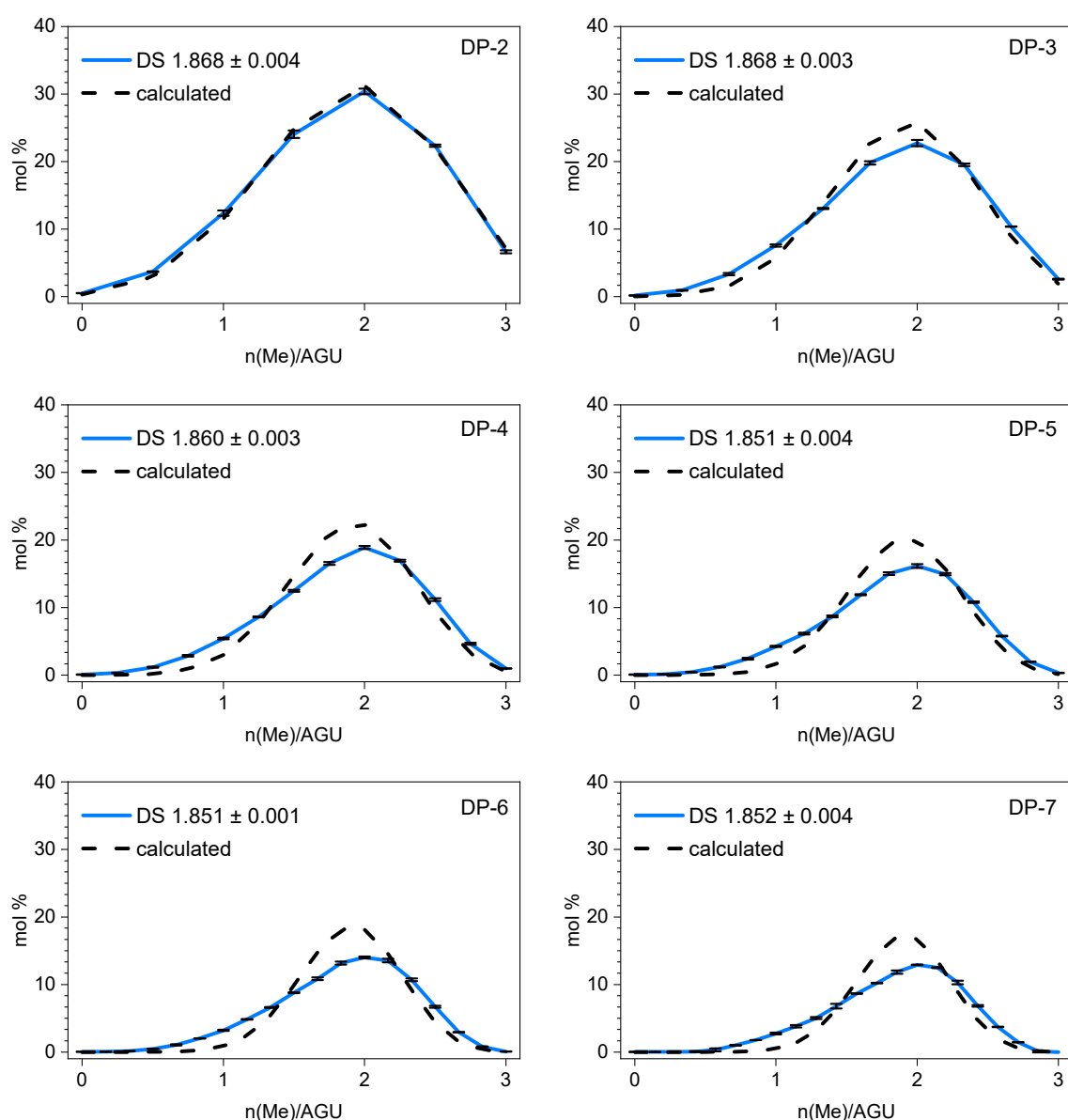


Figure S5. Me-profiles (blue solid lines) and DS values of MC-1 ($\text{DS}_{\text{GLC}} 1.892 \pm 0.003$, see Figure S4) based on the oligomer analysis by LC-MS. To produce the presented data, 3 separate samples were taken from the deuteromethylated MC-1 and prepared independent of each other (independent partial hydrolysis and labeling). Each independently-prepared sample was measured once by LC-MS. The obtained results were averaged and the standard deviations were calculated as a measure of the uncertainty of measurements. The black dashed lines show the calculated random distribution profiles based on the monomer composition analysis data shown in Figure S4.

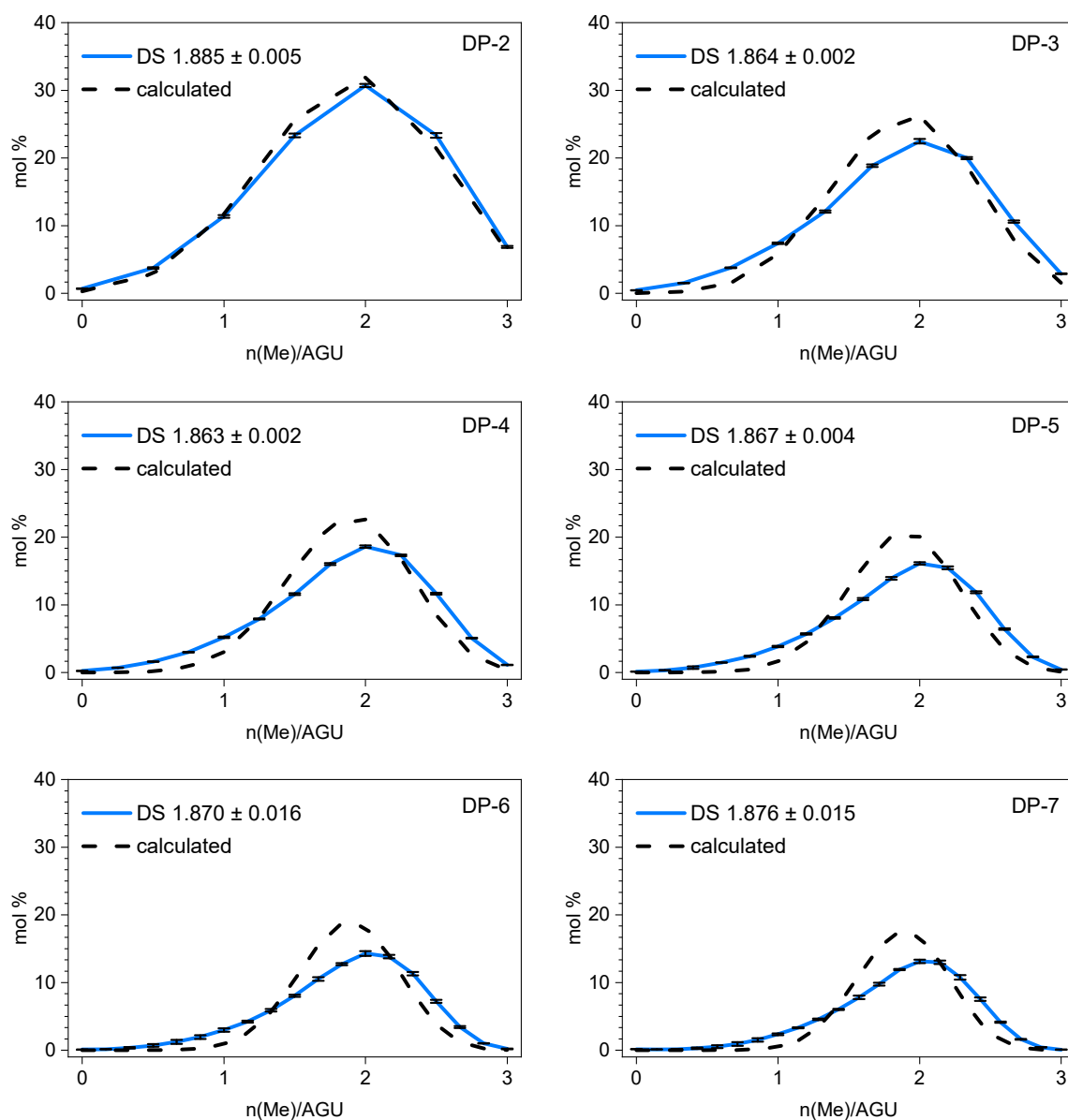


Figure S6. Me-profiles (blue solid lines) and DS values of MC-2 ($\text{DS}_{\text{GLC}} 1.874 \pm 0.003$, see Figure S5) based on the oligomer analysis by LC-MS. To produce the presented data, 4 separate samples were taken from the deuteromethylated MC-2 and prepared independent of each other (independent partial hydrolysis and labeling). Each independently-prepared sample was measured 3 times by LC-MS. The evaluated results were averaged as described in the Materials and Methods section. The black dashed lines show the calculated random distribution profiles based on the monomer composition analysis data shown in Figure S5.

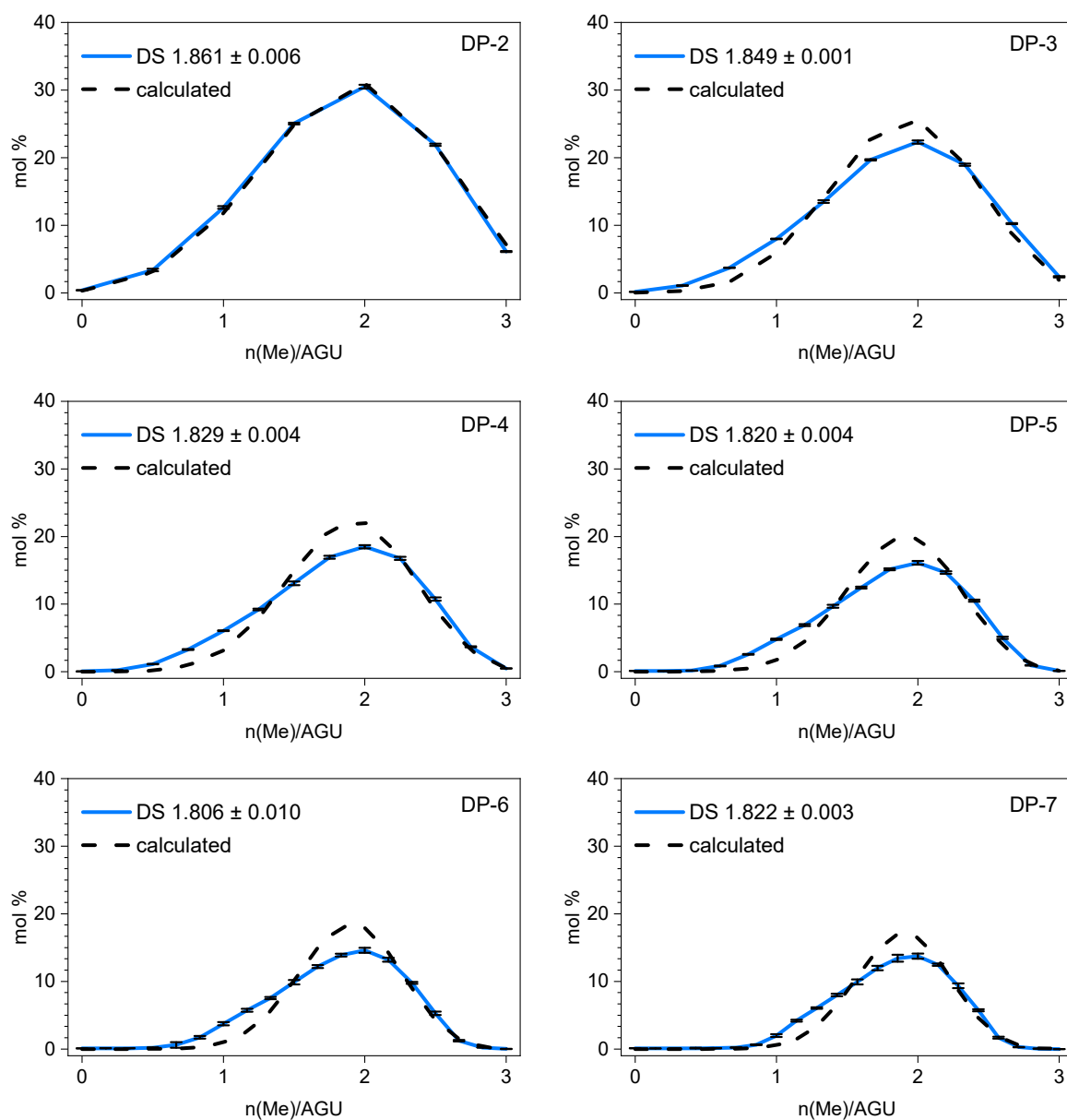


Figure S7. Me-profiles (blue solid lines) and DS values of MC-3 ($\text{DS}_{\text{GLC}} 1.885 \pm 0.007$, see Figure S6) based on the oligomer analysis by LC-MS. To produce the presented data, 3 separate samples were taken from the deuteromethylated MC-3 and prepared independent of each other (independent partial hydrolysis and labeling). Each independently-prepared sample was measured 3 times by LC-MS using a DP-dependent program. The evaluated results were averaged as described in the Materials and Methods section. The black dashed lines show the calculated random distribution profiles based on the monomer composition analysis data shown in Figure S6.

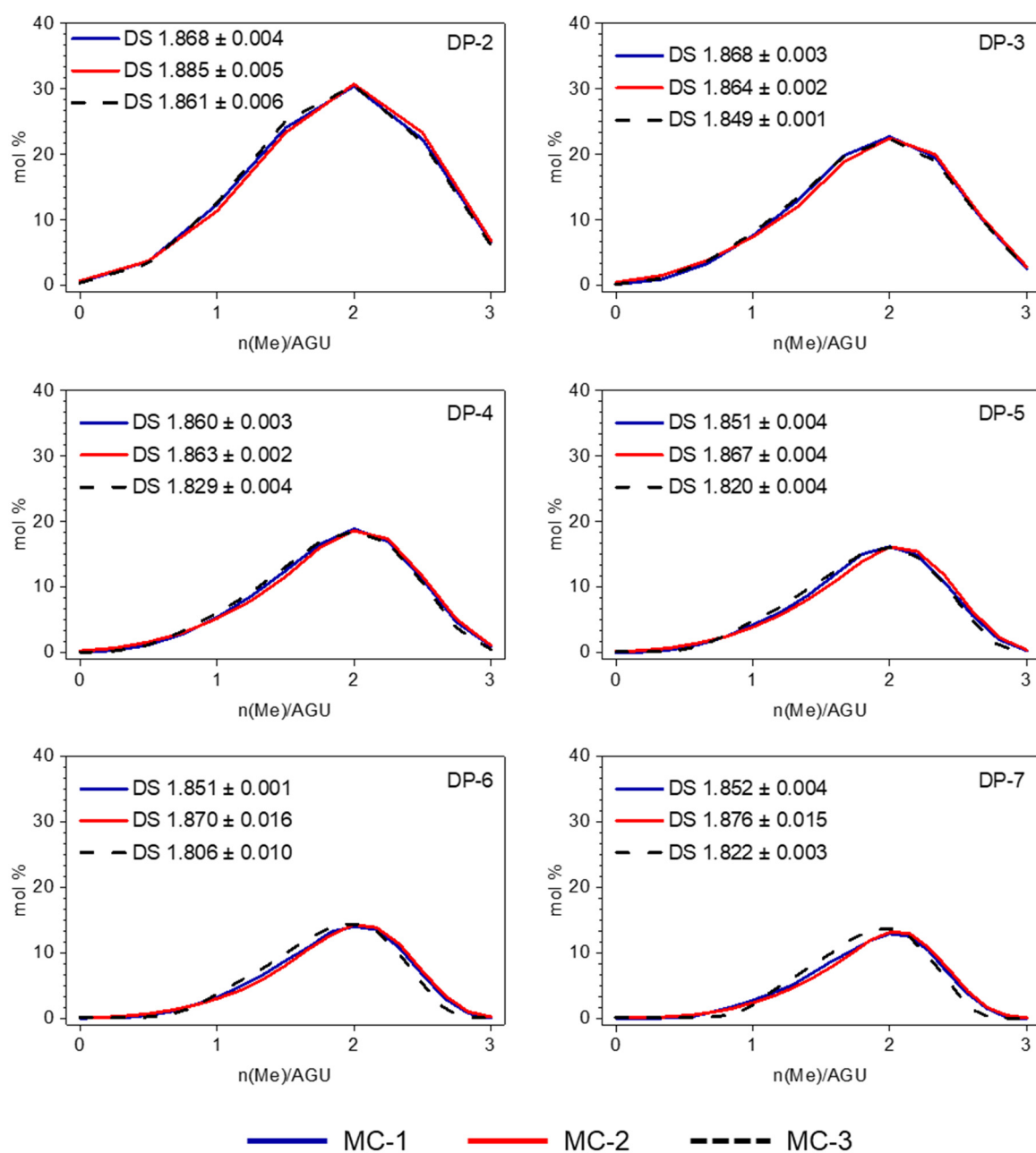


Figure S8. Overlay of the Me-profiles of MC 1–3 shown in Figure S7–9 and the corresponding DS values.

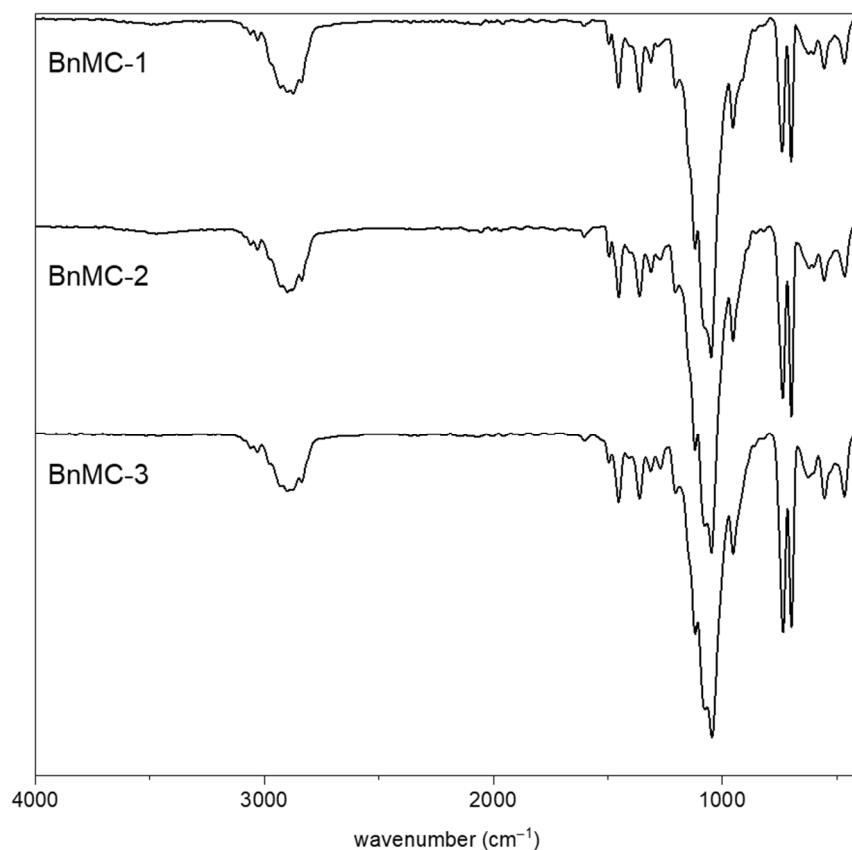


Figure S9. ATR-IR spectra of BnMC 1–3.

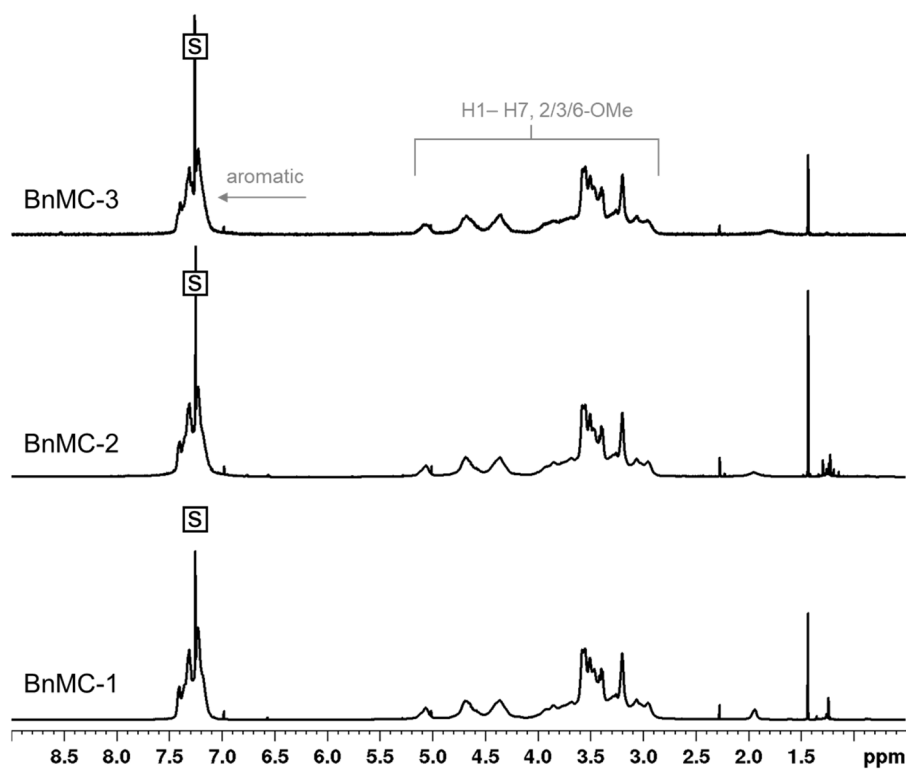


Figure S10. ^1H NMR spectra of BnMC-1 (600 MHz, CDCl_3), BnMC-2 (600 MHz, CDCl_3), BnMC-3 (300 MHz, CDCl_3). S-labeled squares indicate the residual solvent peak.

Further investigation of *O*-hydroxybutyl side-products:

GLC-FID analysis of alditol acetates (Figure 1, manuscript) allowed the estimation of *O*-hydroxybutyl side-products. Since these compounds are mixed Me/HBu/Ac derivatives with up to 27 possible patterns (besides the stereoisomers of HBu), not all individual peaks detected in the range of 14.5 – 17.5 min (Figure 1a) could be identified and corrected for their effective carbon response. The relative mole fraction of these side-products was estimated to be in total around 8 mol%.

For a glycosyl monomer, the probability of hydroxybutylation increases as methyl-DS (DS_{Me}) decreases. Thus, the DS_{Me} in these 8 mol% side-products should be lower than the average DS_{Me} ; thus, the DS_{Me} of MC should slightly increase. However, the DS_{Me} of MC-1 and deBnMC-1, only by considering the HBu-free constituents, did not differ significantly at this low degree of hydroxybutylation.

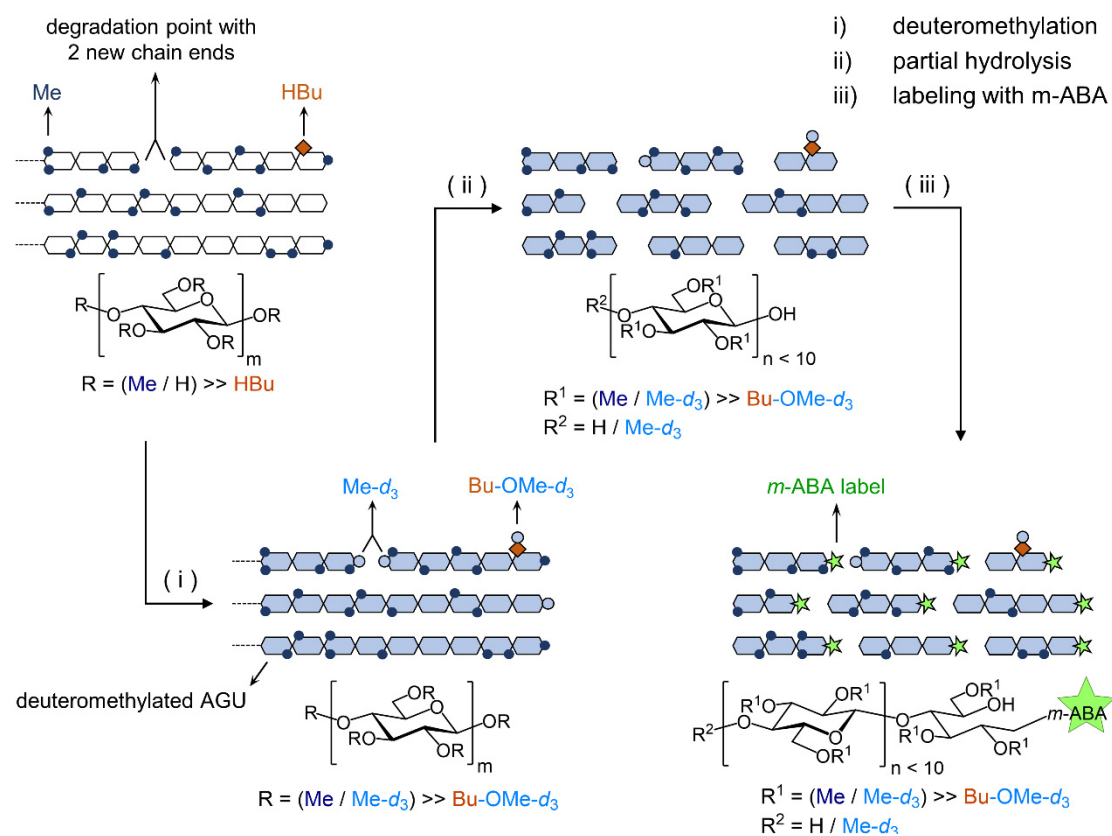


Figure S11. Sample preparation procedure for quantitative LC-MS analysis of MC and deBnMC, respectively.

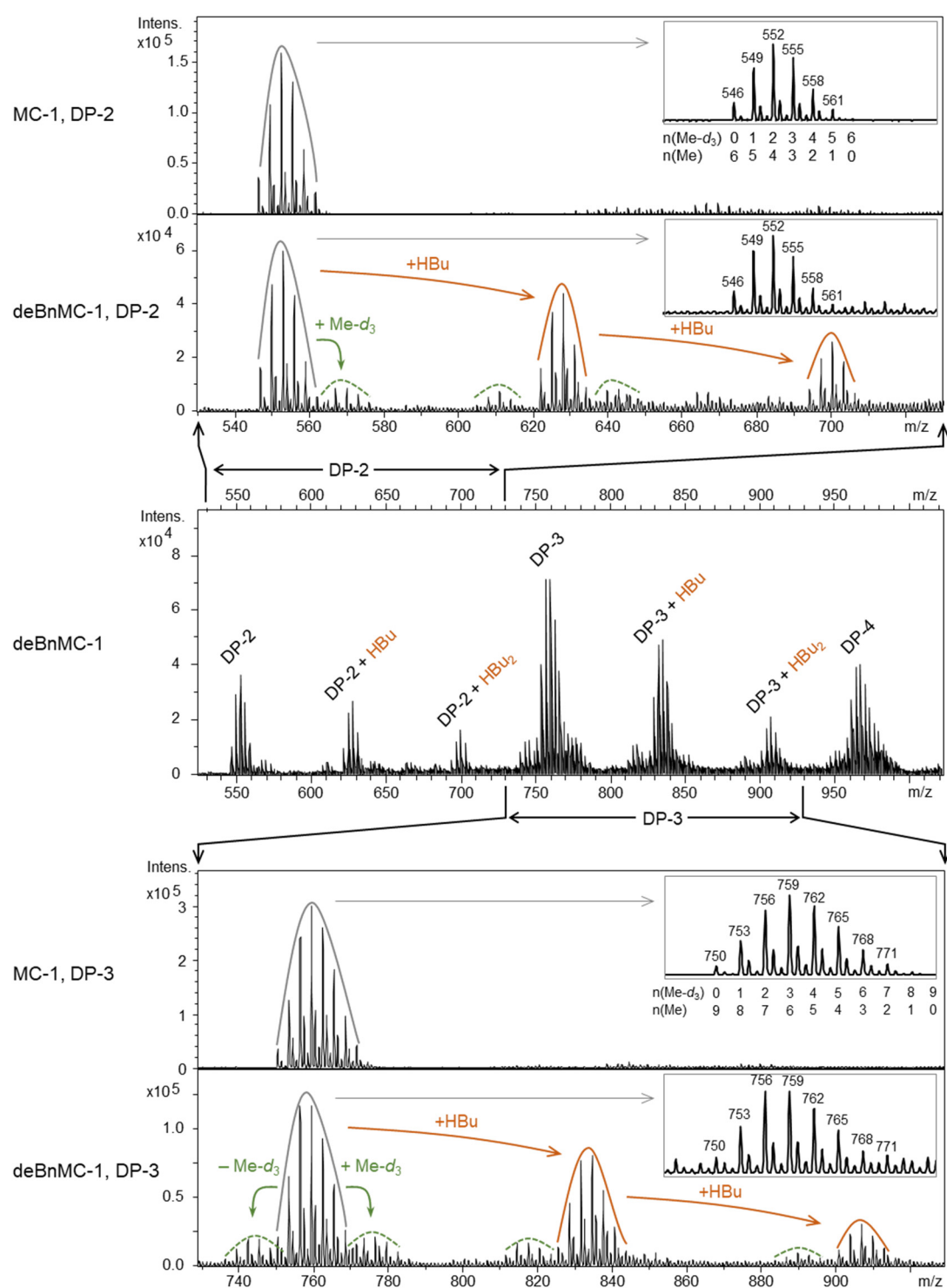


Figure S12. LC-ESI-MS spectrum (negative ion mode) of deBnMC-1 (middle), and comparison of corresponding mass spectra of DP-2 (up) and DP-3 (down) of MC-1 and deBnMC-1. Peaks of “DP-2 + 3 HBU” and “DP-3 + 3 HBU” overlap with the main peaks of their following DP and are, thus, not assigned on the graph. Samples are deuteromethylated, partially hydrolyzed, and labeled with *m*-ABA as described in the Materials and Methods section 2.7. Insets illustrate the zoomed-in views of the main methyl substitution profile of each spectrum.

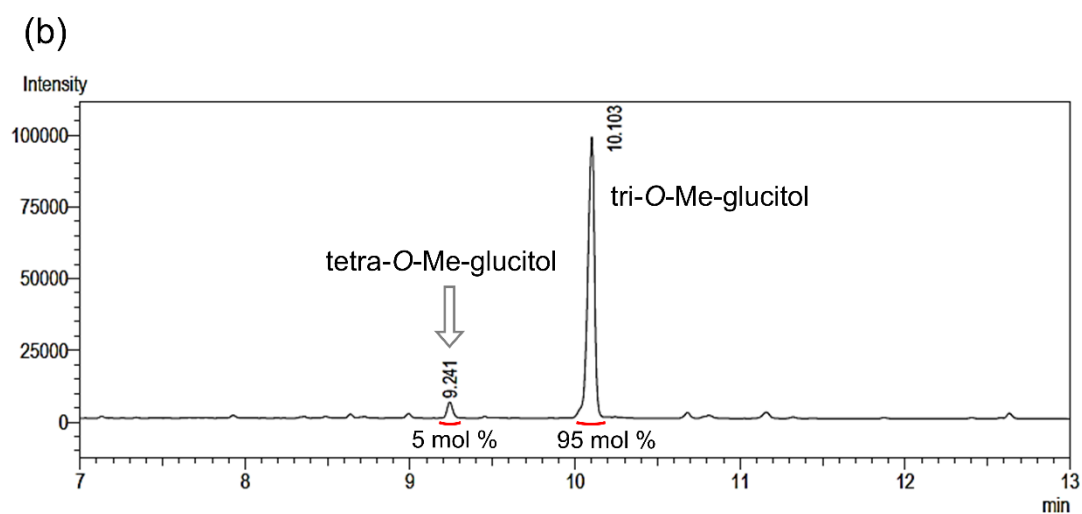
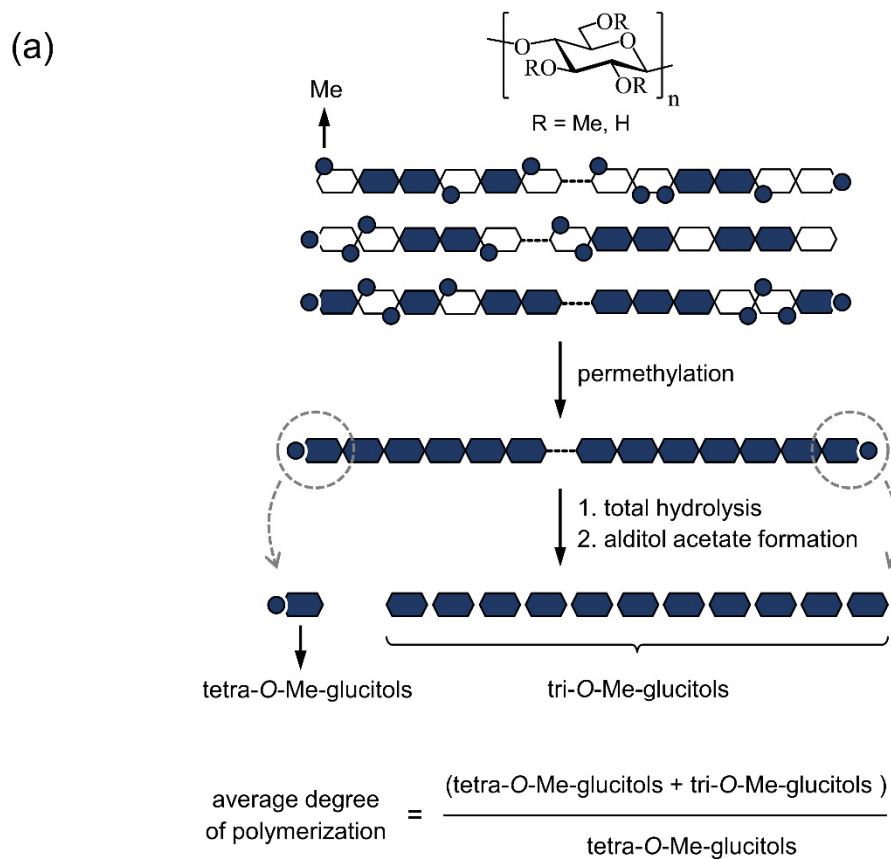


Figure S13. (a) Sample preparation procedure for estimation of the average degree of polymerization by end-group analysis using GLC; **(b)** GLC-FID chromatogram of deBnMC-2* (Method-2a, Table 1) obtained by following the procedure shown in Figure S19a.

References

- [1] Mayhoub, A. S.; Talukdar, A.; Cushman, M. An oxidation of benzyl methyl ethers with NBS that selectively affords either aromatic aldehydes or aromatic methyl esters. *J Org Chem* **2010**, *75*, 3507–3510. DOI: 10.1021/jo1004313.
- [2] Voiges, K.; Adden, R.; Rinken, M.; Mischnick, P. Critical re-investigation of the alditol acetate method for analysis of substituent distribution in methyl cellulose. *Cellulose* **2012**, *19*, 993–1004. DOI: 10.1007/s10570-012-9663-y.
- [3] Lu, P.; Hou, T.; Gu, X.; Li, P. Visible-light-promoted conversion of alkyl benzyl ether to alkyl ester or alcohol via O- α -sp³ C-H cleavage. *Org Lett* **2015**, *17*, 1954–1957. DOI: 10.1021/acs.orglett.5b00663.