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Electronic Supplementary Information

Stable glycosylamines at the reducing ends of cellulose nanocrystals

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Abstract: The reaction of reducing end groups in cellulose nanocrystals with dodecylamine was examined. Using a direct solution-state NMR protocol, the regioselective formation of glucosylamines was shown. This provides an elegant approach to sustainably functionalize these bio-based nanomaterials, that may not require further reduction to the more stable secondary amine.

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Experimental Procedures

S1. Materials

D-(+)-glucose (>99.5 %, Sigma-Aldrich, USA)
dodecylamine (>98 %, Sigma-Aldrich)
methanol (MeOH, > 99.99 %, Fischer Chemicals, Finland)
diethyl ether (anhydrous, J.T Baker, Finland)
cellulose nanocrystals (CNCs, 10.4 wt.% water solution, The University of Maine, Process Development Center, produced by sulphuric acid digestion of softwood sulphite pulp)
5-ethyl-2-methylpyridine borane (PEMB, reductive reagent, Sigma-Aldrich, USA)
trifluoroacetic acid (TFA, 99 %, Fischer Chemical, Finland)
dimethyl sulfoxide (DMSO, 99.99%, Fischer Scientific Oy, Finland, stored over pre-dried 3 Å molecular sieves)
tetrabutylphosphonium acetate ($[P_{4444}][OAc]$) was purchased from IoLiTec GmbH (Germany) and vacuum-dried at 80 °C for 5 h

S2. Pre-Optimisation Study

An initial optimisation study was conducted to assess the conditions required to form glucosylamines, using glucose as model or by reaction of different amines directly on CNCs: aniline, *n*-butylamine and Jeffamine® M-1000 (high molecular weight secondary amine, Fig. S1) were tested with glucose and CNCs. A brief summary of our, mainly negative, trial and error experiments are given here. For butylamine, the glucosylamine was isolable but was found to undergo rapid hydrolysis upon aqueous workup. A CNC adduct with butylamine was not isolable, presumably due to rapid hydrolysis during the workup. Reactions of glucose with concentrated butylamine were also found to undergo rapid colouration. The aniline glucose or CNC adducts were not isolable, presumably due to rapid hydrolysis during workup. The CNC Jeffamine adduct was also not formed although this is a very high molecular weight reagent so kinetics of reaction are expected to be rather slow. In addition, it is a secondary amine so reactivity may be much lower, due to steric and/or electronic effects. Upon testing, the long-chain aliphatic primary amine dodecylamine (DDA) gave stable products for both the glucose and CNC models.

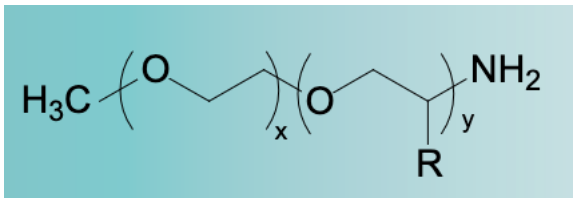

Fig. S1. Structure of Jeffamine® M-1000 used in the preliminary optimisation study – x = ~ 19 & y = ~ 3.

S3. Glycosylamine formation

Glucose and dodecylamine

1 g (5.55 mmol) of glucose and 1.23 g (6.63 mmol) of dodecylamine were mixed with 5 mL methanol. The mixture was heated at 50 °C for 40 minutes. The solution became clear and yellowish indicating that the reaction has finished. Then the solution was cooled down to room temperature and the crude product precipitated as white solid. The precipitate was washed with 10 mL of diethyl ether and the product was filtered out. Finally, the product was dissolved in 10 ml of ethanol at 60 °C, cooled down to room temperature and recrystallized.

CNC and dodecylamine

Two solvents we used in the glucosylamine formation reaction: a) water and b) dimethyl sulfoxide (DMSO).

a) CNC were first freeze-dried from the original 10.4 wt.% aqueous dispersion. 1 g (6.16 mmol anhydrous glucose unit (AGU)) of dried CNC were dispersed in 40 mL of DMSO at room temperature. Then 0.278 g (1.5 mmol) of dodecylamine were added into the CNC-DMSO dispersion;

b) The original 10.4 wt.% CNC aqueous dispersion was first diluted to 2.5 wt.% using distilled water upon stirring. Then 0.278 g (1.5 mmol) of dodecylamine were added into the CNC-water dispersion.

The mixtures were heated at 70 °C for 3 days. After the glucosylamine formation reaction, the mixtures were cooled down to room temperature and dialyzed against water overnight. The mixtures were centrifuged with an Eppendorf 5810 R Centrifuge (3000 rpm for 20 min at room temperature), then the precipitates were freeze-dried (Heto Maxi Dry Lyo Freeze-dryer) to obtain the final product.

S4. Reductive amination

Glucose and dodecylamine

1 g (5.55 mmol) of glucose, 1.25 g (6.75 mmol) of dodecylamine and 2.5 g (18.37 mmol) of 5-ethyl-2-methylpyridine borane (PEMB) were mixed with 5 mL of methanol at room temperature then heated up to 70 °C for 18 h. 5 mL of trifluoroacetic acid (TFA) was added to the neutralized reductive reagent residue. Then the mixture was then azeotroped with methanol three times (3 * 10 mL) to remove boron impurities and to obtain the product as a yellow liquid. This liquid was rested at room temperature for 3 hours and the final product precipitated as white solid. Diethyl ether was used for washing, followed by filtration, yielding white powder.

CNC and dodecylamine

1 g (6.16 mmol AGU) of dry CNC powder was dispersed in 40 mL of DMSO. The CNC dispersion was heated and maintained at 70 °C. Since the reaction mixture is not homogeneous, we added dodecylamine and PEMB three times every 24 hours during the reaction to ensure continuation of the reaction: 0.278 g (1.5 mmol) of dodecylamine and 63 mmol of PEMB (reducing agent) in total were added to the CNC-DMSO dispersion in 3 portions (0.5 mmol of dodecylamine and 21 mmol of PEMB in each portion) over a period of 3 days. The reaction mixture was constantly stirred. After 3 days, the reaction mixture was cooled down to room temperature followed by addition of 10 mL of TFA and reacted for 2 hours to neutralize the excess of the reducing agent. The neutralized reaction mixture was dialyzed against water overnight. The dispersion of the product in water was centrifuged and then the precipitate was freeze-dried to obtain the final product. After NMR analysis, the success of the reductive amination was not apparent, based on the comparison with the glucose-derived models.

S5. NMR studies

The organic electrolyte solution (OES) for NMR measurements was prepared by mixing purified tetrabutylphosphonium acetate ([P_{4444}][OAc]) with DMSO-d_6 with the weight ratio of 1:4. The dissolution capacity of this OES is high enough to dissolve 5 wt.% cellulose [1] and the concentration of 5 wt.% was used in the NMR measurements, at a probe temperature of 65 °C. The products that were prepared from glucose via glucosylamine and reductive amination were analyzed with NMR spectrometers of 500 and 600 MHz (Bruker Instruments). A high-resolution NMR spectrometer at 850 MHz (Bruker Instruments) was used for analysis of the products obtained from CNC. Proton and carbon spectra were typically recorded. 2D HSQC, HSQC-TOCSY, ^{13}C-HMBC & ^{15}N-HMBC experiments were typically collected. Spectra were analyzed using Bruker Topspin 4 and Mestrenova 14 software. Typical NMR experimental conditions can be found from Koso *et al*.[2]

[spectra overpage]

S6. NMR Spectra

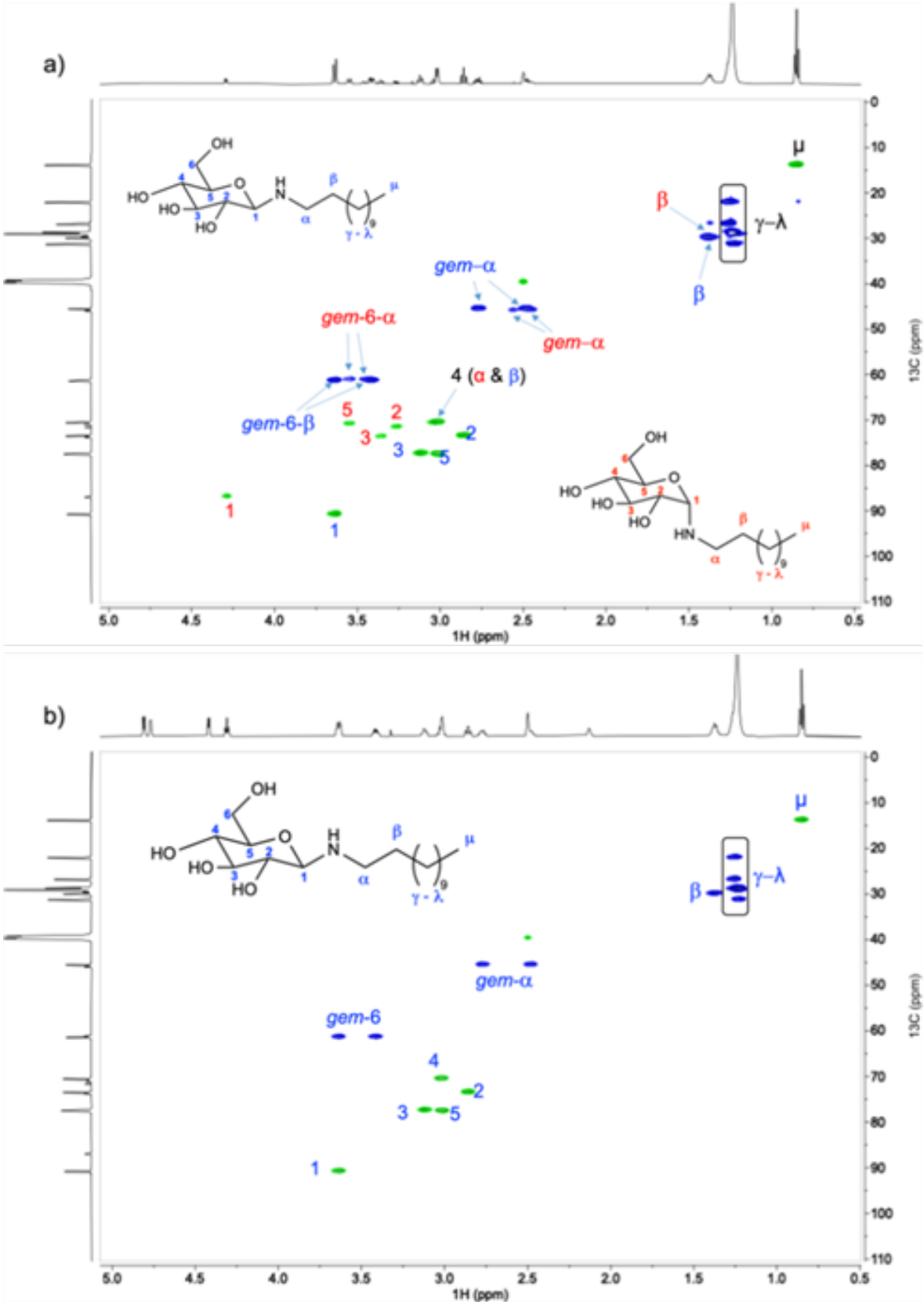

Fig. S2 Multiplicity edited ^{1}H-^{13}C HSQC spectra (DMSO-d_6, 600 MHz ^{1}H frequency) and peak assignments for the glucosylamine model compounds obtained from the reaction of glucose with DDA: (**a**) Mixture of both α (red) and β (blue) anomer. (**b**) Pure β anomer obtained after recrystallization of the reaction mixture. Spectra obtained at room temperature. CH and CH_3 groups are shown in green, CH_2 groups are shown in blue. ^{1}H trace shown on top and ^{13}C trace on the left.

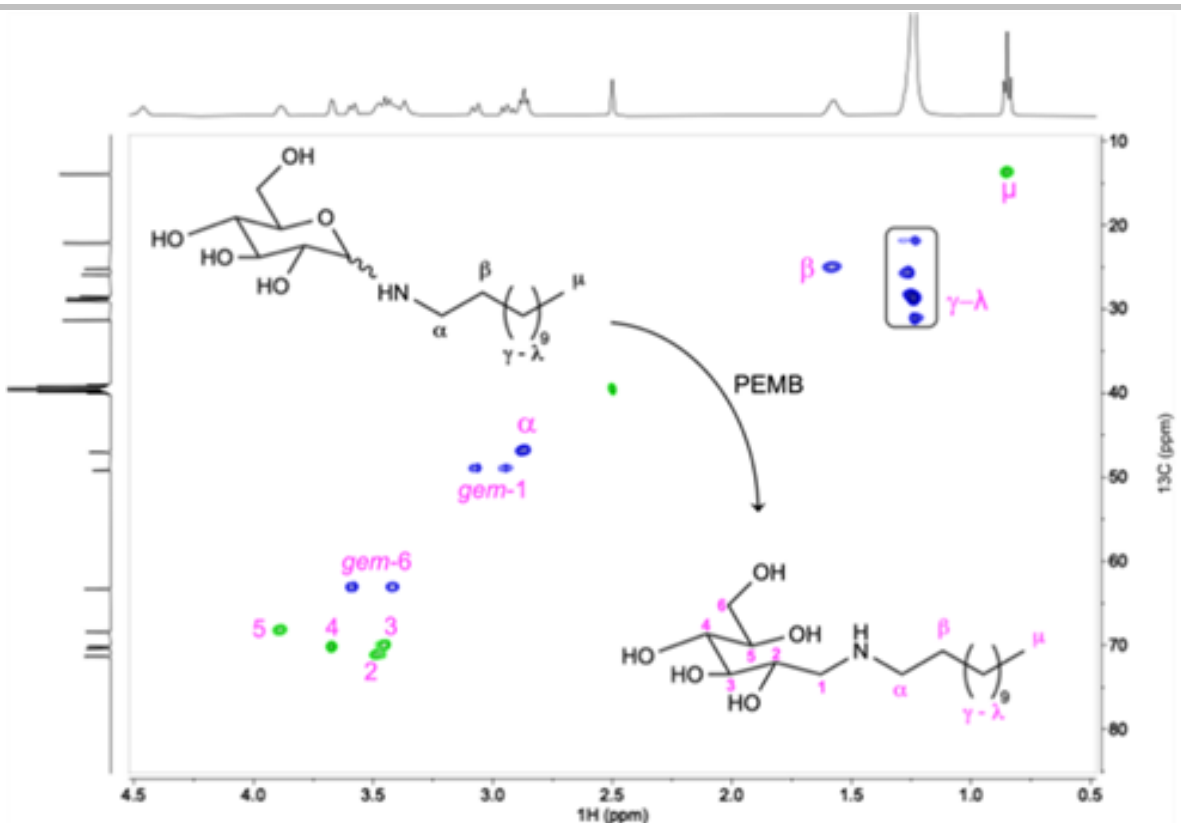

Fig. S3 Assignment of the dodecylglucamine product HSQC spectrum, in DMSO-d_6 at RT, after PEMB reduction of the glucose-DDA glucosylamine anomer mixture of α and β.

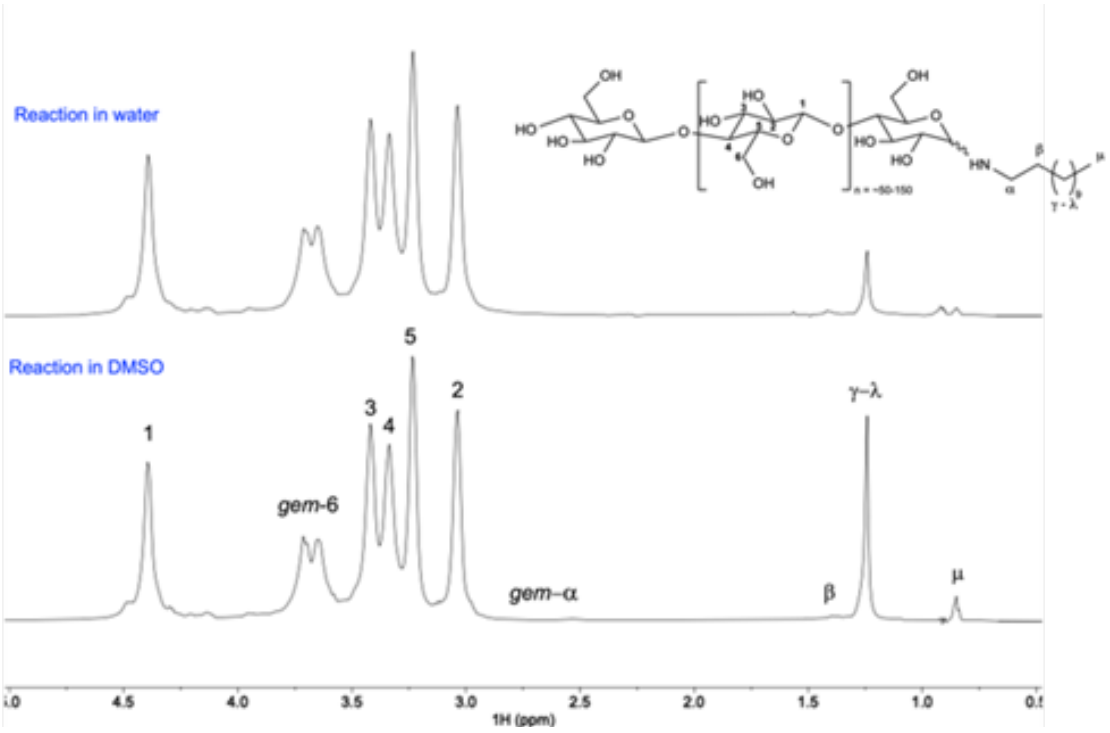

Fig. S4 Diffusion-edited ^{1}H NMR spectra ([P_{4444}][OAc]:DMSO-d_6 (1:4 wt%), 600 MHz, 65 °C, 5 wt% CNC) of the DDA modified CNCs obtained after reaction in water (**top**) compared to the ones isolated from DMSO (**bottom**). While both spectra show the incorporation of an aliphatic chain, the reaction in DMSO resulted in higher conversion.

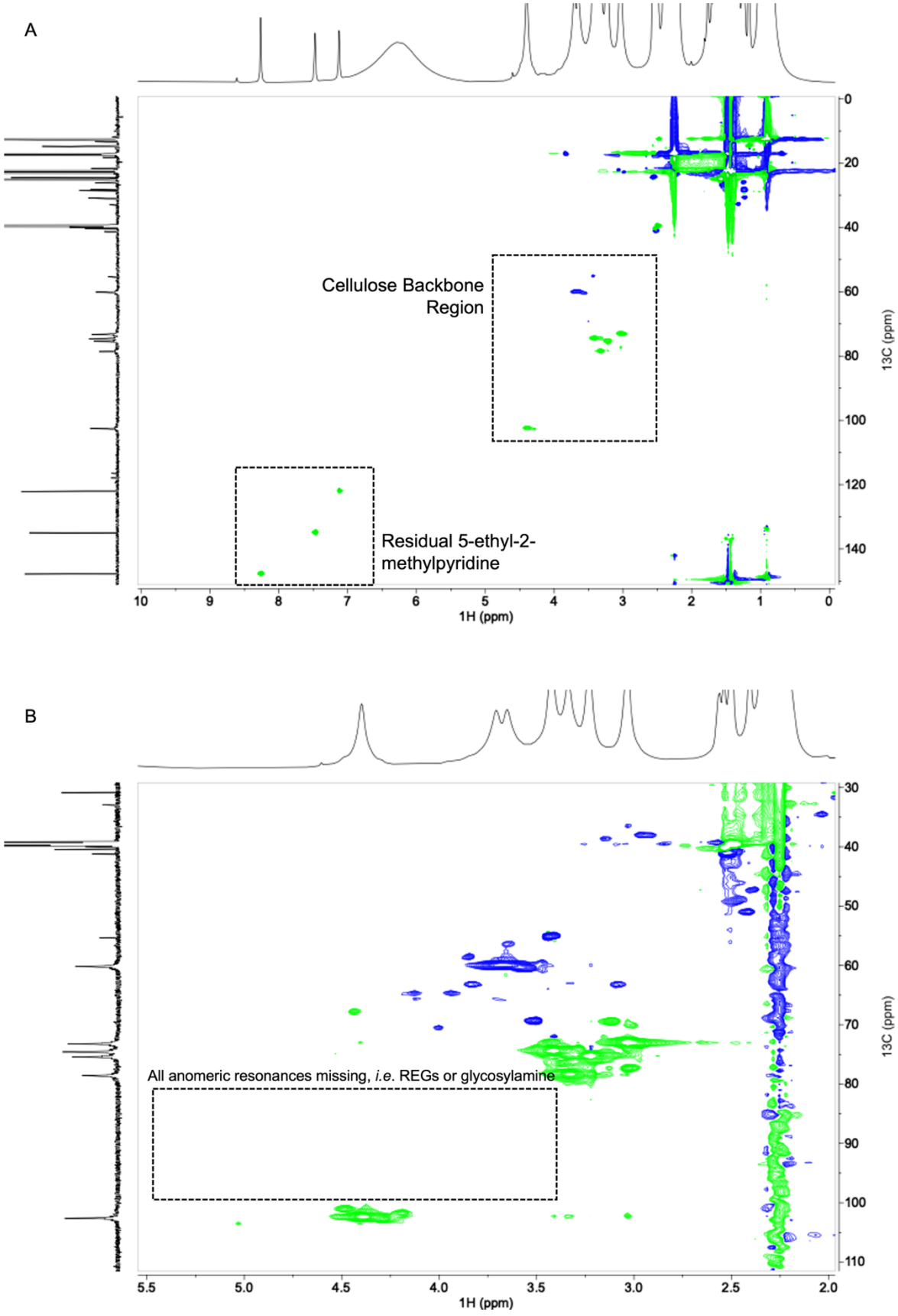

Fig. S5 Multiplicity edited ^{1}H-^{13}C HSQC spectra of the CNCs after reductive amination with PEMB and DDA.

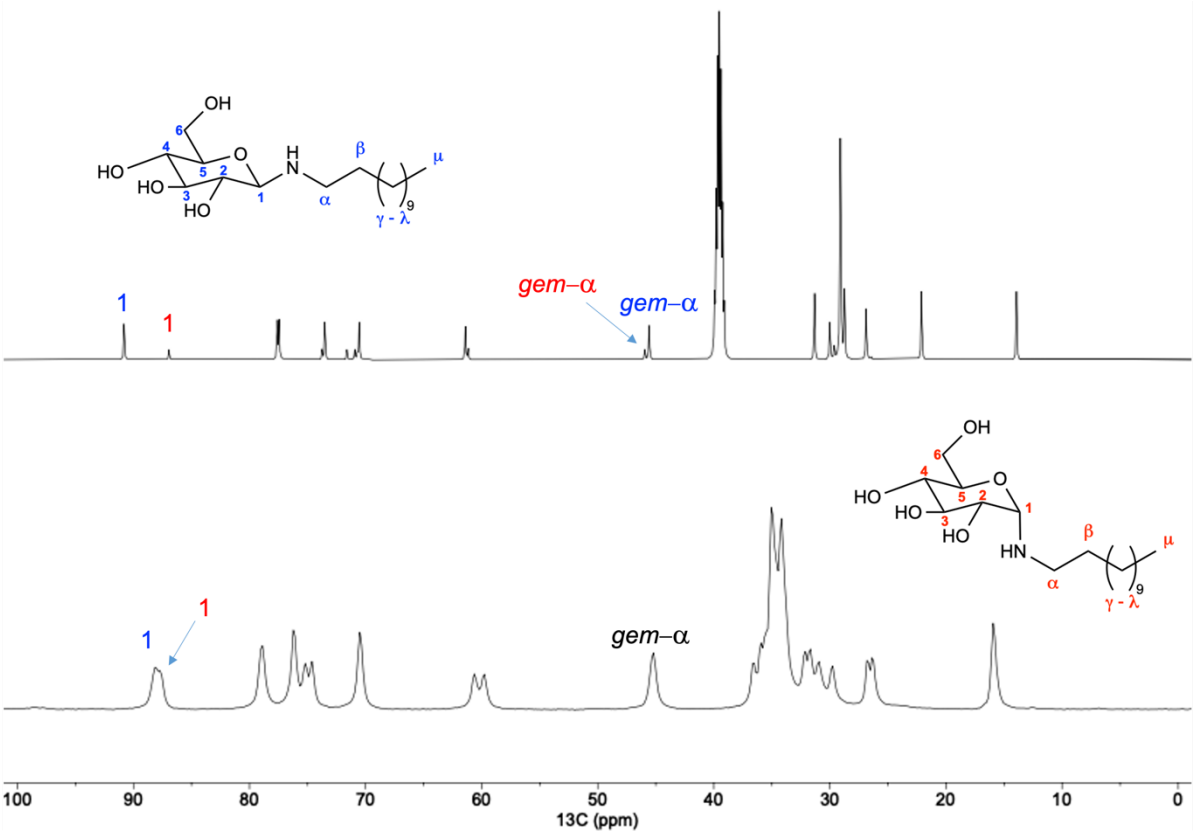

Fig. S6 Spectra for glucose-DDA glucosylamine anomer mixture of α and β using: a) solution-state ^{13}C NMR (power-gated decoupling) in DMSO-d_6 at RT, b) solid-state ^{13}C CP MAS NMR, with the most comparable assignments highlighted.

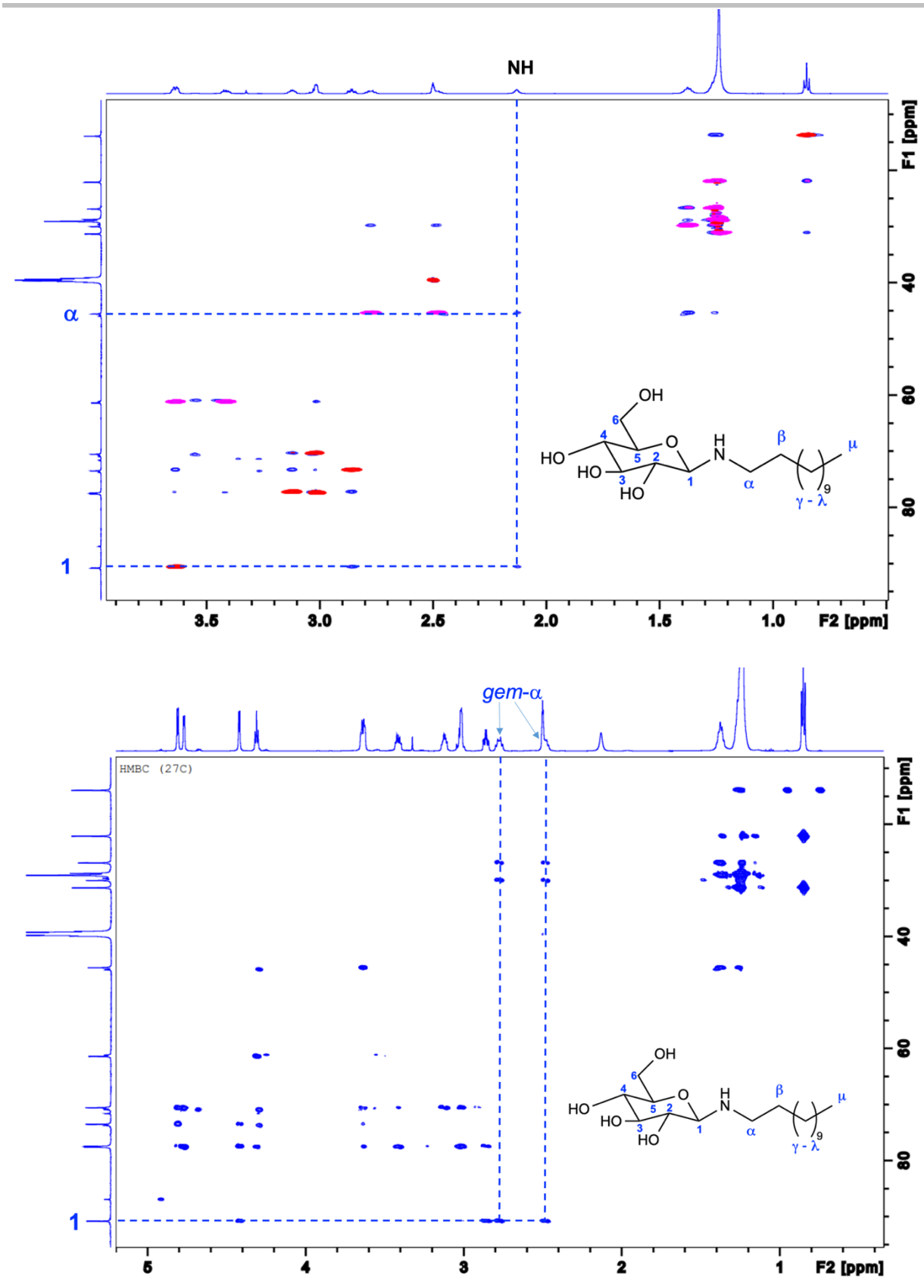

Fig. S7 ^{1}H-^{13}C HMBC showing the linkage between the DDA and glucose moiety for the α-DDA glucosylamine anomer.

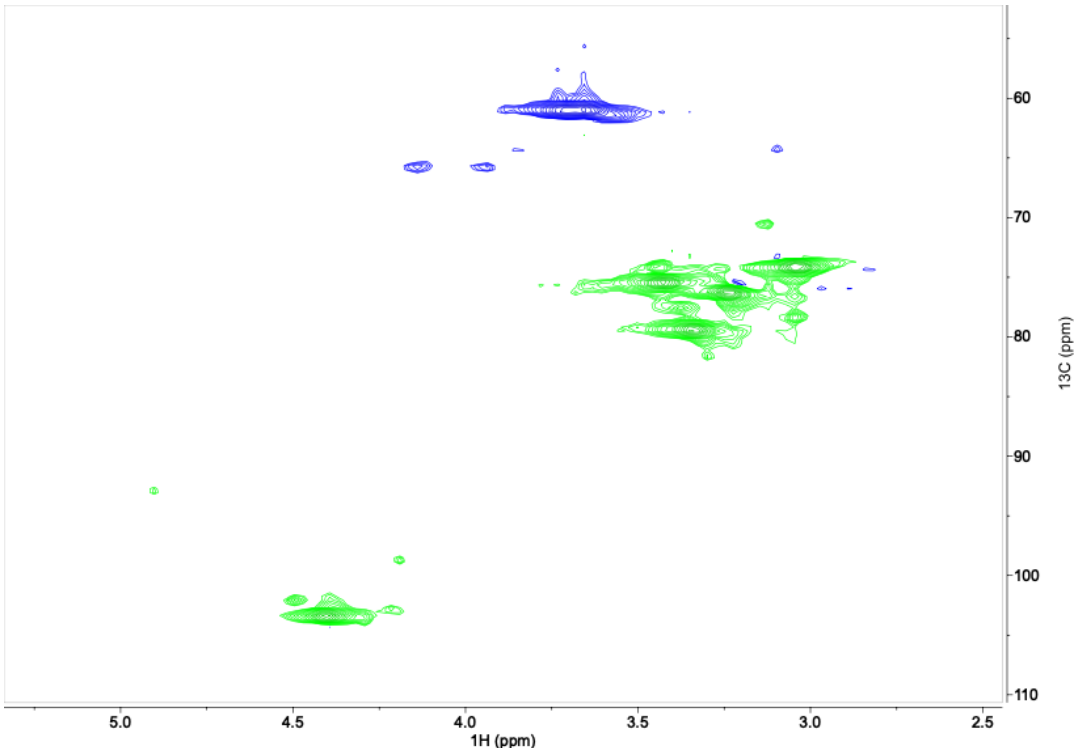

Fig. S8 ^{1}H-^{13}C HSQC for the commercial CNCs.

References

1. J. Xia, A. W. T. King, I. Kilpeläinen, V. Aseyev, *Cellulose,* 2021. **28**(17): p. 10921-10938.
2. T. Koso, D. Rico del Cerro, S. Heikkinen, T. Nypelö, J. Buffiere, J. E. Perea-Buceta, A. Potthast, T. Rosenau, H. Heikkinen, H. Maaheimo, A. Isogai, I. Kilpeläinen, A. W. T. King, *Cellulose,* 2020, **27**, 7929