Green Chemistry

Enhancing the stability of ionic liquid media for cellulose processing: acetal protection or carbene suppression?

Matthew T. Clough,[a,b] Jeraime A. Griffith,[a] Olga Kuzmina[a] and Tom Welton*[a]

[a] *Department of Chemistry, Imperial College London, London, UK, SW7 2AZ, United Kingdom*
[b] *Max-Planck-Institut für Kohlenforschung, Kaiser-Wilhelm-Platz 1, 45470 Mülheim-an-der-Ruhr, Germany*

** Corresponding Author: t.welton@imperial.ac.uk*

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1. General laboratory procedures

All reactions requiring an inert atmosphere were performed under a blanket of nitrogen gas, which was dried through a column of phosphorus pentoxide. All commercially acquired chemicals were obtained from Sigma-Aldrich and were used without further purification, unless otherwise stated. 'Sigmacell' cellulose was employed, with a measured degree of polymerisation (DP) of 263. NMR spectra were recorded on Bruker Avance-400 (^{1}H NMR (400 MHz), ^{13}C {^{1}H} NMR (100 MHz)) NMR spectrometers. Chemical shifts (δ) are reported in ppm (relative to the DMSO-d6 solvent residual peak). Where 'high vacuum' is used, a pressure of 0.1-0.05 mbar was achieved. Electrospray ionisation mass spectra were performed using Waters 'LCT Premier' (ES-ToF)/Acquity 'i-Class' mass spectrometers, LSIMS spectra were obtained employing a 'Micromass AutoSpec Premier' spectrometer.

2. Synthesis of ionic liquids

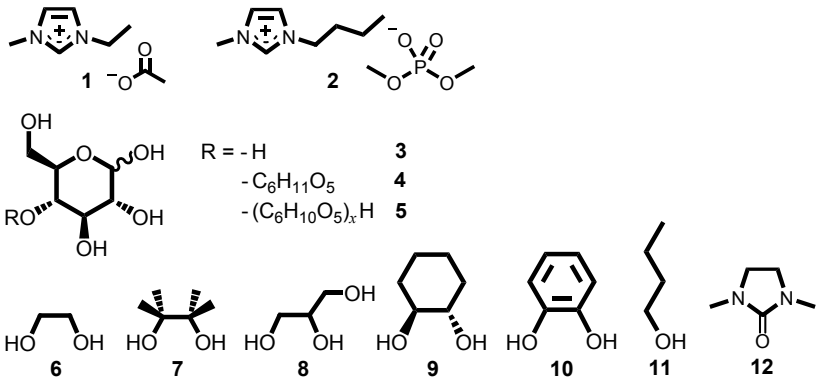


Fig. E1 Investigated ionic liquids (**1**, **2**), carbohydrates, (**3**-**5**), and co-solvents/additives (**6**-**12**).

1-Ethyl-3-methylimidazolium acetate, [C_2C_1im][OAc] (**1**). The ionic liquid was prepared from the metathesis of 1-ethyl-3-methylimidazolium bromide, [C_2C_1im]Br,[1] with silver(I) acetate, according to a previous literature protocol.[1] The product was obtained as a colourless, viscous liquid (55%). Found: ^{1}H NMR (400 MHz, DMSO-d6): δ 10.11 (1H, s), 7.89 (1H, t, J = 2 Hz), 7.80 (1H, t, J = 2 Hz), 4.22 (2H, q, J = 7 Hz), 3.88 (3H, s), 1.60 (3H, s), 1.40 (3H, t, J = 7 Hz). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d6): δ 173.4, 138.1, 123.9, 122.4, 44.4, 35.9, 26.8, 15.7. The spectral data is consistent with previous literature.[1]

1-Butyl-3-methylimidazolium dimethyl phosphate, [C_4C_1im][$(CH_3)_2PO_4$] (**2**). The employed sample of ionic liquid was prepared previously in our research laboratory, according to a protocol described in the chemical literature.[2]

3. Preparation & analysis of mixtures

Solvent-carbohydrate mixtures: preparation & analysis

A sample of carbohydrate (D-(+)-glucose **3**, D-(+)-cellobiose **4**, or cellulose **5**) (0.050±0.001 g) was carefully weighed into a 5 ml single-necked round-bottomed flask, fitted with an adapter for Schlenk apparatus and a magnetic stirrer bar. Where employed, a co-solvent/additive (ethane-1,2-diol, **6**, 2,3-dimethylbutane-2,3-diol (pinacol), **7**, glycerol, **8**, *trans*-cyclohexane-1,2-diol, **9**, benzene-1,2-diol, **10**, 1-butanol, **11**, or 1,3-dimethylimidazolidin-2-one, **12**) and acid (one drop, 11±3 mg) were added to the reaction flask. A sample of the IL ($[C_2C_1im][OAc]$ **1**, or $[C_4C_1im][(CH_3)_2PO_4]$, **2**) (0.50±0.01 g), was then measured into the flask (water content of each ionic liquid sample <3 wt% for **3**, **4**, <0.5 wt% for **5**). Subsequently, the flask was suspended in an oil bath, and the mixture was maintained at a temperature of 60 °C and at ~0.1 mbar pressure for a pre-determined period of time (the 'protection time'), with gentle stirring at a rate of 250 rpm. The flask was then raised from the oil bath and the temperature of the bath was rapidly increased to 120 °C. The vacuum in the flask was replaced by an ambient pressure of dry nitrogen gas. The flask was again suspended in the oil bath, and the mixture was maintained at 120 °C for a further minimum of four hours, with stirring at 250 rpm under a gentle flow of dry nitrogen.

Small aliquots of the mixture (0.02±0.01 g) were extracted at pre-determined intervals, 't_x' (*e.g.* x = 0, 0.5, 1, 2, 4 hours, with additional points for cellulose, **5**) from which ^{1}H NMR spectra were obtained (in DMSO-d6 solvent). In addition, for the samples incorporating **5**, the cellulose 'degree of polymerisation' was determined at t_1 and t_4 time points by Gel Permeation Chromatography (GPC, see experimental description below). The oil bath temperature fluctuated by no more than ±2 °C from the desired value during the course of the experiment. Compositional and experimental data, for all investigated IL-carbohydrate-(co-solvent) mixtures, is tabulated in the ESI (Table E1). For each timepoint, t_x, the '% Conversion', representing the proportion of the parent IL cation ($[C_nC_1im]^+$) that had undergone degradation (conversion) with the carbohydrate to form the 'C1' adduct, $[C_nC_1(HO)C^2{}_1im]^+$, was evaluated according to the following equation:

$$\%\ Conversion = \left[\frac{\frac{1}{2}\int \delta_{C1}}{\left(\frac{1}{2}\int \delta_{C1} + \int \delta_{IL}\right)}\right] x\ 100$$

where:

'$\int\delta_{C1}$' is the integral of the hydroxymethyl methylene (CH_2OH) peak of the 'C1' adduct cation, $[C_2C_1(HO)C_2{}^1im]^+$ or $[C_4C_1(HO)C_2{}^1im]^+$, centred at δ = ~4.80 or ~4.73 ppm, respectively (^{1}H NMR, DMSO-d6 solvent);

'$\int\delta_{IL}$' is the integral of the aromatic imidazolium NC*H*CHN peak of $[C_2C_1im]^+$ or $[C_4C_1im]^+$, centred at δ = ~7.83 or ~7.81 ppm, respectively (^{1}H NMR, DMSO-d6 solvent).

These integral values are represented in graphical form in the ESI (Fig. E2).

It was observed that selecting different δ cut-off values, when integrating ^{1}H NMR peaks, yielded marginally different integral values ($\int\delta_{IL}$ and $\int\delta_{C1}$). For example, for a C1 adduct singlet peak centred at δ = 4.80 ppm, a different value of $\int\delta_{C1}$ is obtained by integrating across the range of 4.83-4.77 ppm instead of 4.82-4.78 ppm. Caution was therefore taken to integrate NMR peaks in a careful and consistent manner; nevertheless, error values arising from integration were observed to be smaller in magnitude than those of repeat experiments on the same mixture composition (*e.g.* experiments i-iii in Table E1, ESI).

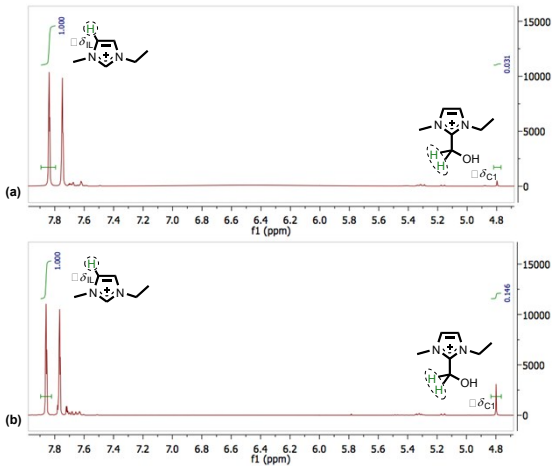
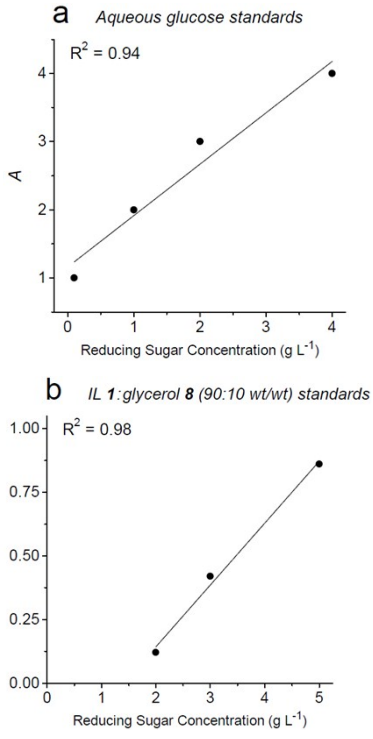


Fig. E2 Example annotated ^{1}H NMR spectra obtained following one hour heating at 120 °C (t_1, excluding the 'protection' time'), demonstrating the relative concentrations of the C1 adduct cation, $[C_2C_1(HO)C_1{}^2im]^+$, against the parent IL cation, $[C_2C_1im]^+$ for: (a) the 'protected' mixture of IL, **1** + 10 wt% D-(+)-glucose, **3** + glycerol, **8** (2:1 mol/mol **8**:**3**) and *cat*. AcOH, and; (b) the 'unprotected' mixture of IL, **1** + 10 wt% D-(+)-glucose, **3**. The two spectra are scaled so as to exhibit approximately equal-intensity aromatic $[C_2C_1im]^+$ C^4/C^5 peaks, and $\int\delta_{IL}$ is normalised to 1.000 in each case; integrals for the C1 adduct peak, $\int\delta_{C1}$, can therefore be compared between the two spectra.

Determination of cellulose degree of polymerisation

The degrees of polymerisation (DP) of cellulose samples were determined for the cellulose (**5**) solutions in solvents (neat IL **1**, 95:5 wt/wt **1**:**8**, and 90:10 wt/wt **1**:**8**) at timepoints t_1 and t_4 (Fig. 3). DP was measured using Gel Permeation Chromatography (GPC) in a lithium chloride/dimethylacetamide (LiCl/DMA) organic electrolyte mobile phase, as described by Potthast *et al*.[3]

Quantification of reducing sugars in recovered solvents



1 wt% 3,5-dinitrosalicylic acid (DNS) solution was prepared by carefully mixing 3,5-dinitrosalicylic acid (2.5 g), sodium sulfite (0.1 g) and sodium hydroxide (2.0 g) into a flask, and subsequently diluting the mixture with deionized water up to a volume of 0.25 L.

Following pretreatment at 60 °C under reduced pressure and consequent reaction for 4 hours at 120 °C, 0.5 ml samples of the neat IL-/organic electrolyte-cellulose solutions were treated with deionized water (20 ml) in order to precipitate cellulose, were filtered, and were dried under high vacuum to recover the solvents. Small samples (0.3 ml) of these recovered solvents were treated with an aliquot of the 1 wt% DNS solution (0.3 ml), and were heated to 90 °C for 15 minutes in order to develop the red-brown colouration. 40% Potassium sodium tartrate solution ('Rochelle salt', one drop) was added to the mixture, which was subsequently allowed to cool to room temperature. The UV-vis absorbance, *A*, for each sample was then measured at 537 nm. Finally, the reducing sugar concentration in each sample was determined by interpolation of an appropriate calibration curve (it was necessary to account for the possible influence of the IL and/or glycerol on the absorption behaviour of the DNS dye). Initially, one calibration curve was obtained from four *aqueous* glucose standard solutions (0.1, 1, 2 and 4 g L^{-1}, curve '**a**'). This calibration curve, based on aqueous glucose solutions, was validated to be suitable for determining reducing sugar concentration in the recovered neat IL, because analysis of a freshly-prepared 2 g L^{-1} glucose in IL (**1**) sample yielded a result of 2.16 g L^{-1} using the calibration curve. However, for determination of the reducing sugar concentration in the 90:10 wt/wt IL (**1**):glycerol (**8**) recovered solvent, it was observed to be necessary to create a second calibration curve ('**b**') based on three 90:10 wt/wt **1**:**8** standard solutions of known glucose concentration (2, 3 and 5 g L^{-1}).

Table E1 Table representing compositional and experimental details of the individual investigated mixtures, i-xviii.

Exp.	Ionic Liquid*	Carbohydrate	Diol / Triol	Acid Catalyst? †	Carbohydrate Added (wt%) #	Carbohydrate Added (mol%) #	Diol : Carbohydrate (mol/mol)	"Protection" Time ‡ (hours)	
i	**1**	**3**	/	✗	10	9.5	/	2	*Not protected*
ii	**1**	**3**	/	✗	10	9.5	/	2	
iii	**1**	**3**	/	✗	10	9.5	/	2	
iv	**1**	**3**	**6**	✓	10	9.5	2	1	*Modify Exp. Conditions*
v	**1**	**3**	**6**	✓	10	9.5	4	2	
vi	**1**	**3**	**6**	✗	10	9.5	2	2	
vii	**1**	**3**	**6**	✓ $^{n}C_7H_{15}CO_2H$	10	9.5	2	2	
viii	**1**	**3**	**6**	✓	10	9.5	2	2	*Modify Co-Solvent*
ix	**1**	**3**	**7**	✓	10	9.5	2	2	
x	**1**	**3**	**8**	✓	10	9.5	2	2	
xi	**1**	**3**	**9**	✓	10	9.5	2	2	
xii	**1**	**3**	**10**	✓	10	9.5	2	2	
xiii	**2**	**3**	/	✗	10	14.7	/	2	*Modify IL*
xiv	**2**	**3**	**6**	✓	10	14.7	2	2	
xv	**1**	**4**	/	✗	10	5.0	/	1	*Modify Carbohydrate*
xvi	**1**	**4**	**8**	✓	10	5.0	4	1	
xvii	**1**	**5**	/	✗	10	? §	/	1	
xviii	**1**	**5**	**8**	✓	10	? §	**1 + 8** (95 : 5 wt/wt)	1	
xix	**1**	**3**	**11**	✓	10	9.5	2	2	*Other Co-solvents*
xx	**1**	**3**	**12**	✓	10	9.5	2	2	

* 0.50 ± 0.01 g ionic liquid, of *water content* ≤ 3 wt% (**3**,**4**) or ≤ 0.5 wt% (**5**) prior to all experiments.

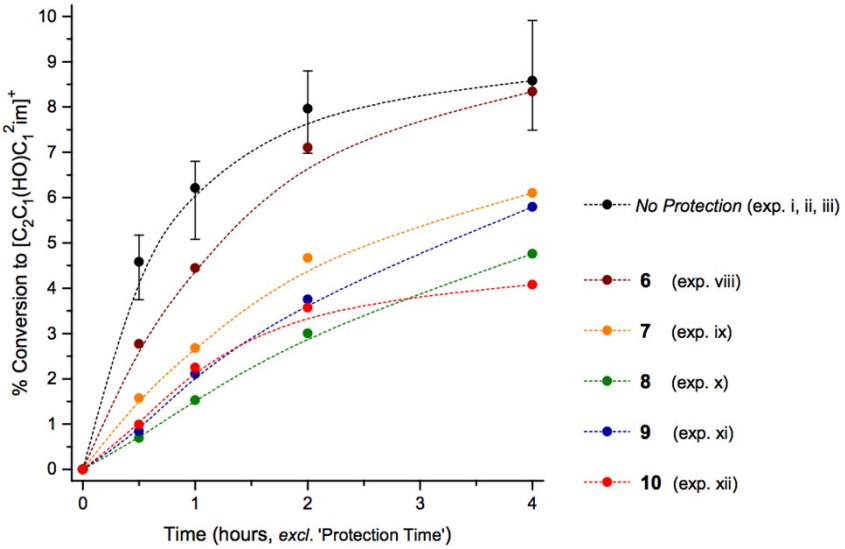
† 11±3 mg glacial acetic acid (CH_3CO_2H) catalyst employed, unless otherwise stated.

\# Relative to the quantity of *ionic liquid*.

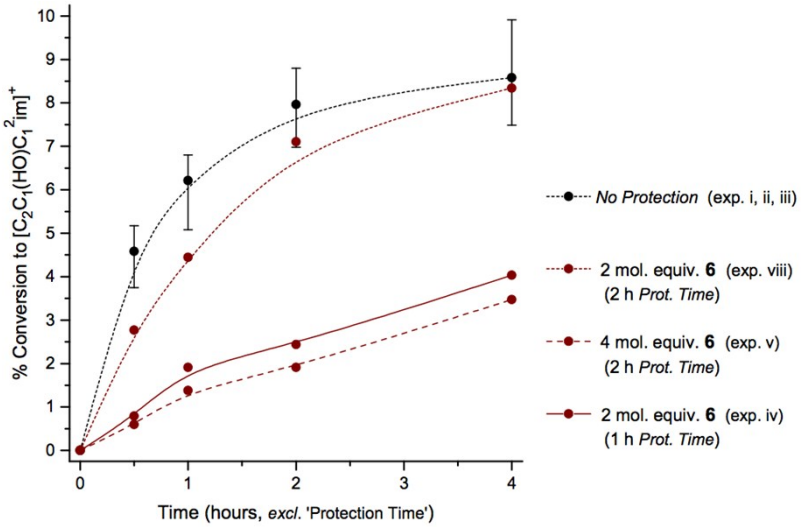
‡ 60 °C, ~0.1 mbar. A 'protection time' is quoted even in the absence of added diol/triol.

§ Precise molar quantities are difficult to assign.

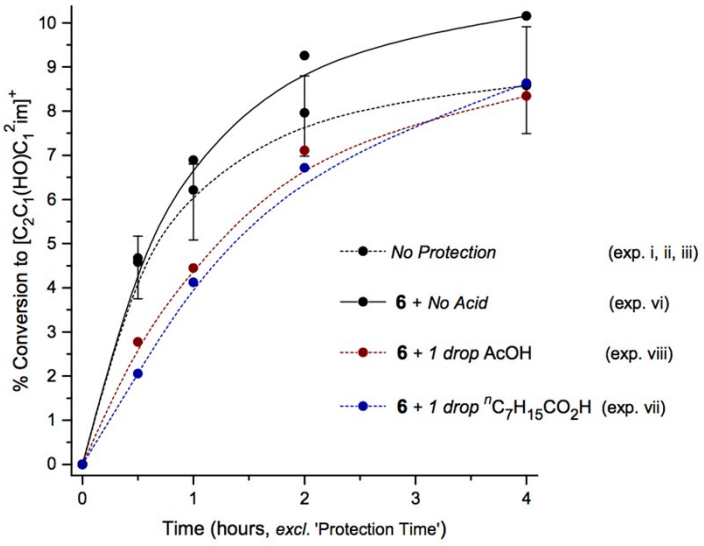
4. Graphs representing evolution of the C1 adduct for organic electrolyte (OE)-carbohydrate mixtures



(a)

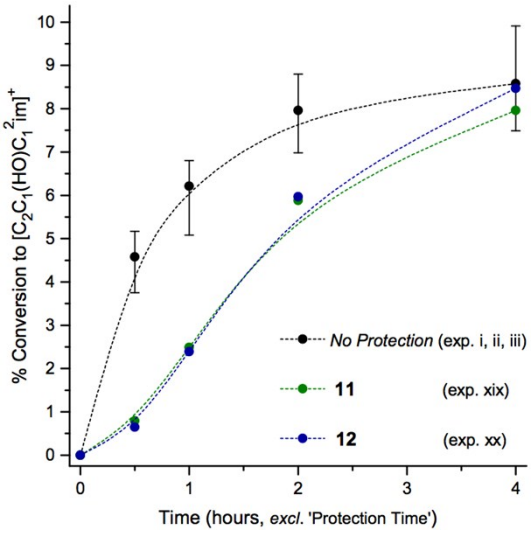


(b)



(c)

Fig. E3 Graphs representing formation of the C1 adduct cation, $[C_2C_1(HO)C_1{}^2im]^+$, for 'unprotected' and 'protected' mixtures; a comparison of: (a) different diol/(triol) protecting group precursors; (b) different diol concentration and 'protection time', and; (c) different acid catalysts. Full compositional data for mixtures i-xii is described in Table E1.



(d)

Fig. E3 continued Graph representing formation of the C1 adduct cation for 'unprotected' and 'protected' mixtures with 1-butanol, **11**, and 1,3-dimethylimidazolidin-2-one, **12**. Full compositional data for mixtures xix and xx is listed in Table E1.

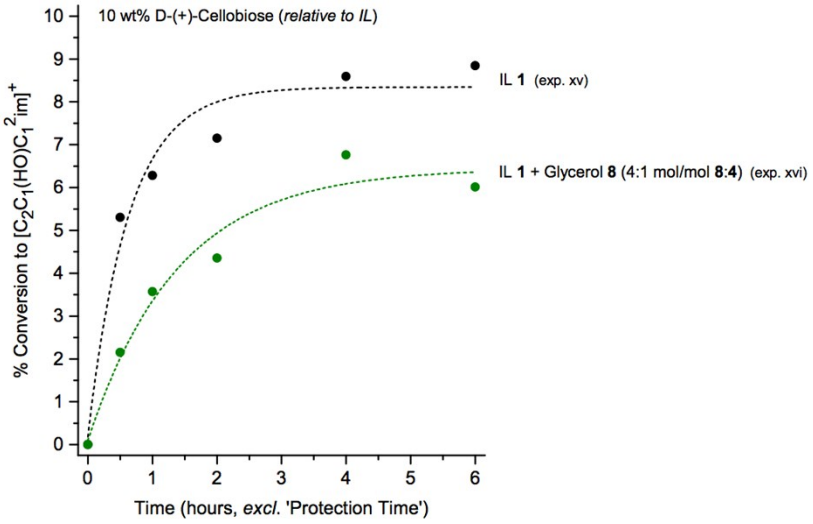


Fig. E4 Graphs representing formation of the C1 adduct cation, $[C_2C_1(HO)C_1{}^2im]^+$, for 'unprotected' and 'protected' mixtures of IL $[C_2C_1im][OAc]$ (**1**) + 10 wt% D-(+)-cellobiose (**4**). Full compositional data for mixtures xv and xvi is described in Table E1.

5. GPC traces for cellulose samples recovered at t_0 timepoint

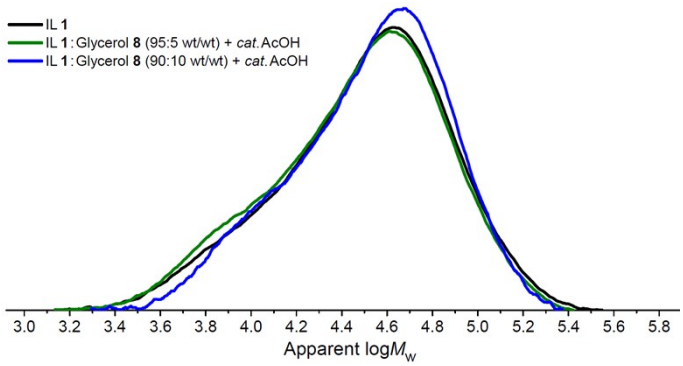
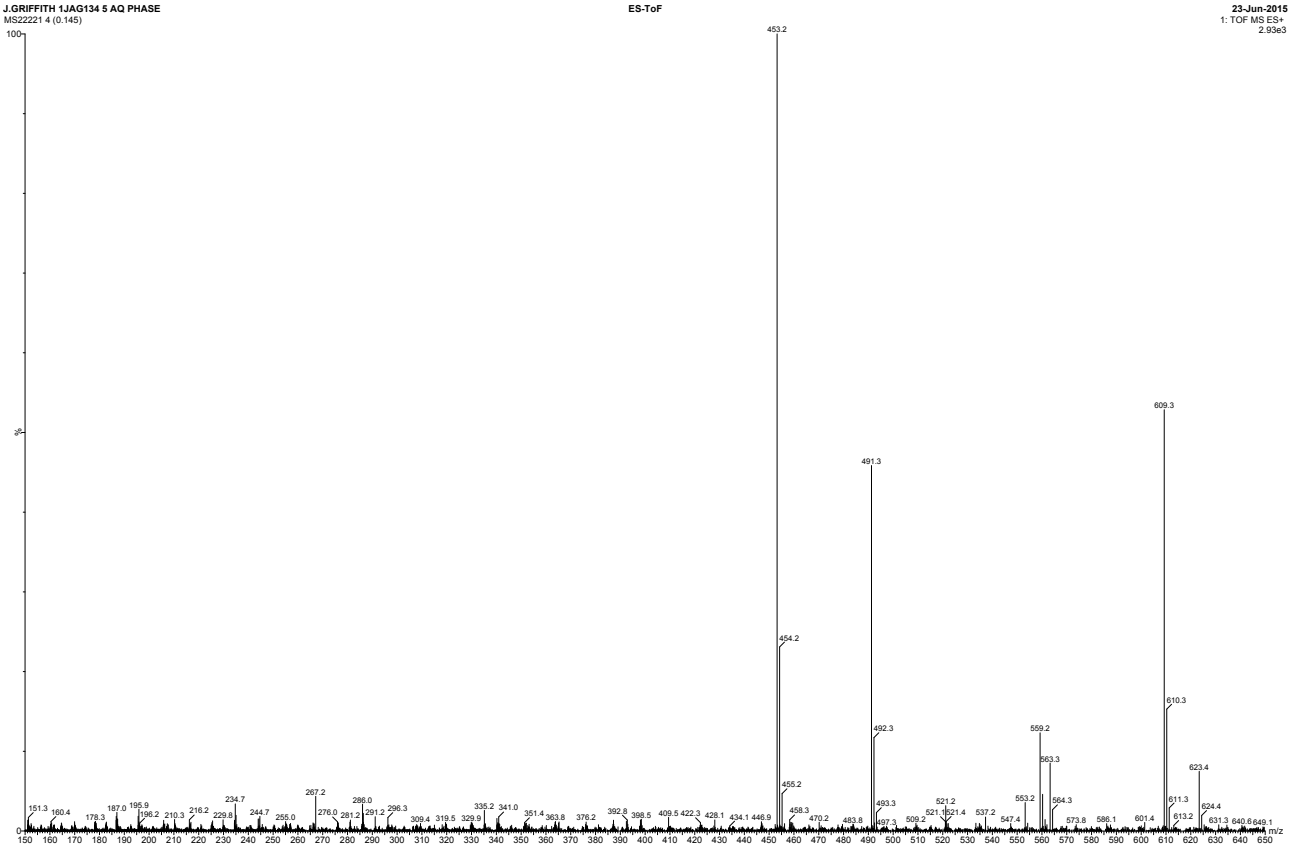


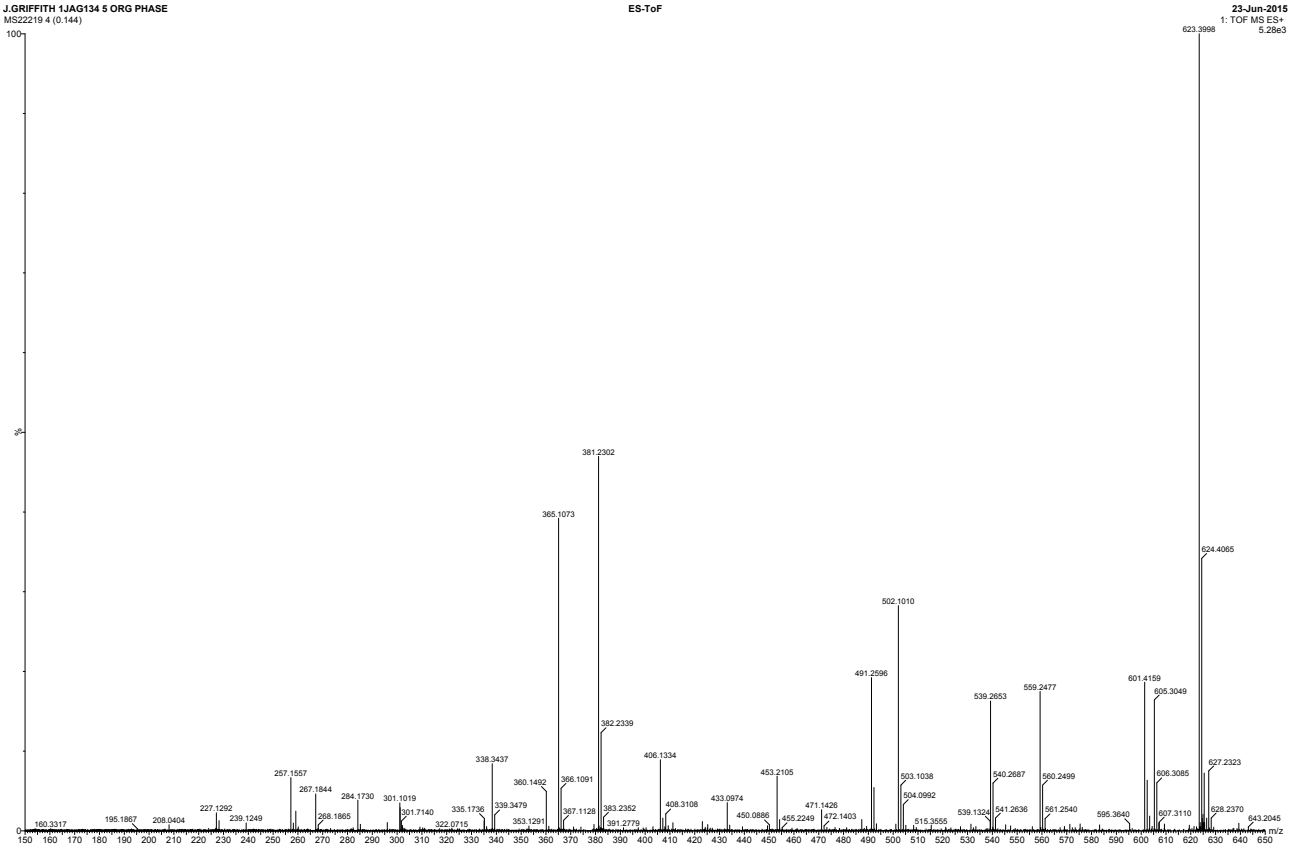
Fig. E5 Gel Permeation Chromatography (GPC) traces for the cellulose samples recovered from IL and organic electrolyte solvents at the 't_0' time point (1 h 'protection time' at 60 °C, 0 h at 120 °C).

6. Mass spectrometry investigation of D-(+)-cellobiose with 2,3-naphthalenediol

D-(+)-cellobiose **4** (90 mg, 0.26 mmol) and 2,3-naphthalenediol (100 mg, 0.62 mmol, 2.4 equivalents relative to **4**) were carefully weighed into a round-bottomed flask. IL [C_2C_1im][OAc], **1** (0.9 g), and glacial acetic acid (11±3 mg) were subsequently added to the flask. The flask was suspended in an oil bath and the mixture was maintained at a temperature of 60 °C and ~0.1 mbar pressure for one hour, with gentle stirring. The mixture was allowed to cool to room temperature and was diluted with deionized water (5 ml). The resultant aqueous solution was washed with EtOAc (3 × 10 ml) in order to remove excess 2,3-naphthalenediol and the combined EtOAc (organic) fraction was retained. TLC experiments confirmed that all unreacted 2,3-naphthalenediol had been extracted from the aqueous phase. The aqueous solution was concentrated by rotary evaporation and subsequently under high vacuum at 50 °C. Compositions of the aqueous and organic phases were analyzed by ESI mass spectrometry. Aqueous and organic-phase mass spectra are shown below (Figs. E6a and E6b, respectively).



(a)



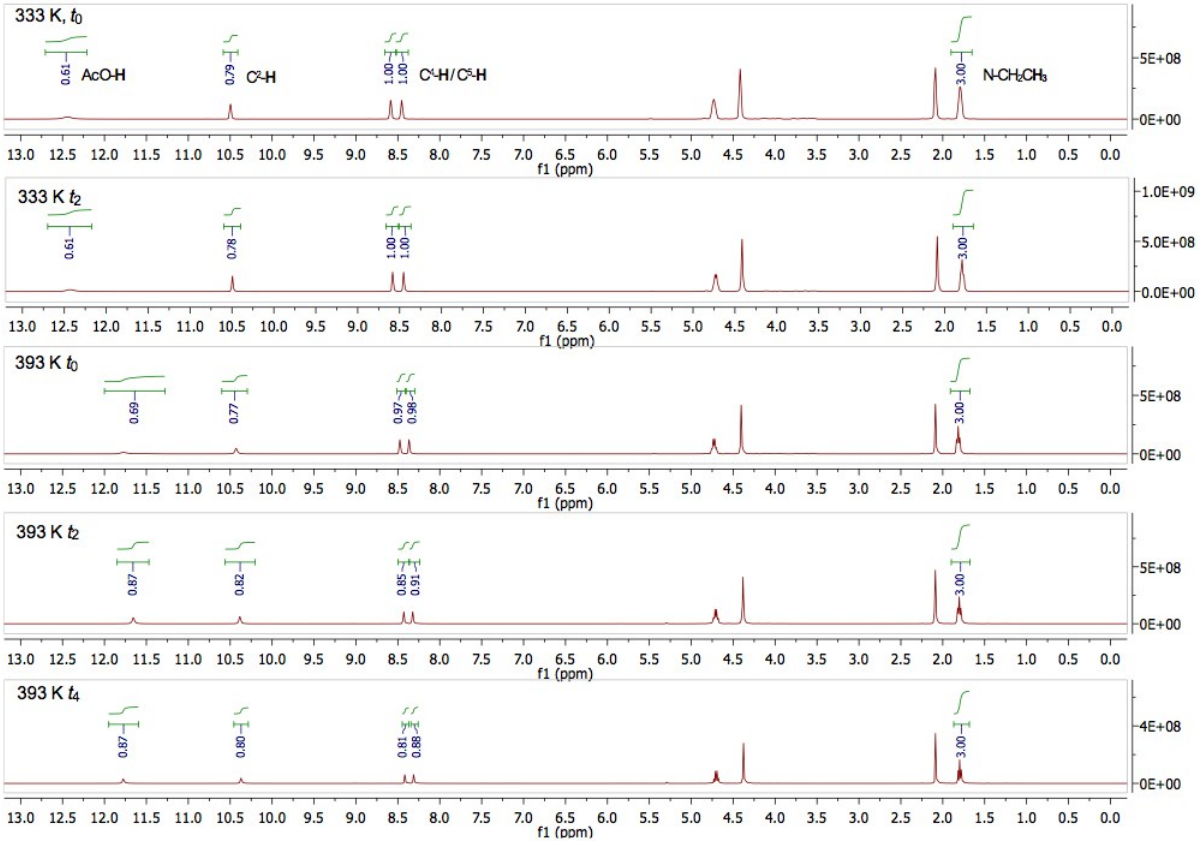
(b)

Fig. E6 Electrospray ionisation mass spectra (ESI-MS) obtained for the aqueous phase (a) and organic (EtOAc) phase (b) of experiments performed with the mixture IL **1** (0.9 g), D-(+)-cellobiose, **4** (90 mg), 2,3-naphthalenediol (100 mg) and glacial acetic (1 drop), as described in the paragraph above.

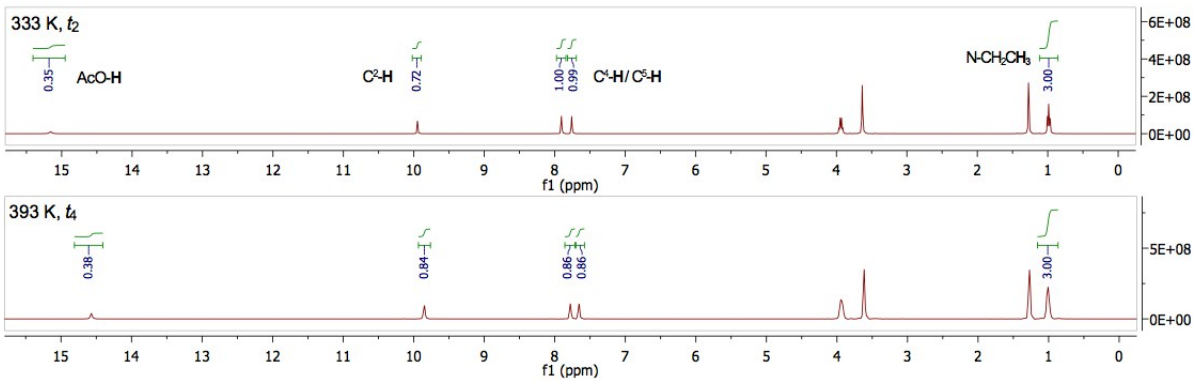
7. ^{1}H NMR investigation employing acetic acid-d$_4$ and glycer(ol-d$_3$)

Mixtures of an IL, [C_2C_1im][OAc] (**1**) or [C_4C_1im][NTf_2]), with D-(+)-glucose (**3**)/cellulose (**5**) (where applicable) and a deuterated co-solvent (AcOH-d$_4$ or glycer(ol-d$_3$), four molar equivalents relative to the carbohydrate), were carefully prepared in sealed high-pressure NMR tubes. The mixtures were heated initially at 60 °C for two hours, and subsequently at 120 °C for four hours, with ^{1}H NMR spectra recorded at 30-minute intervals. The integrals of C^2, C^4 and C^5 imidazolium ring protons were monitored, analysed relative to the NCH_2CH_3 peak at 3.00 that is assumed not to undergo exchange with deuterium.

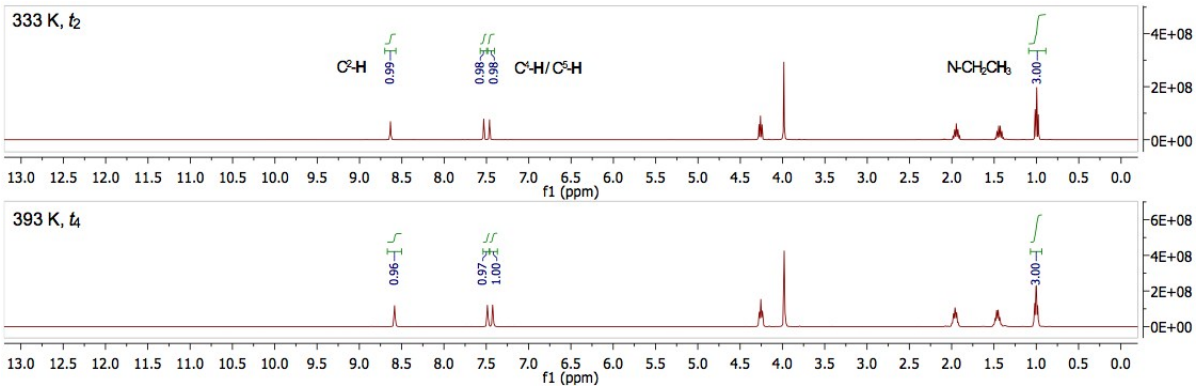
Selected ^{1}H NMR spectra are displayed below, Figure E7. The heating times 't_x' refer to the time of the same sample maintained *at that specified temperature* (not total heating time). Mixture compositions are described below each graph.



(a) [C_2C_1im][OAc] (**1**) + 10 wt% cellulose (**5**) + AcOH-d$_4$ (four molar equivalents relative to **5**).



(b) [C_2C_1im][OAc] (**1**) + AcOH-d$_4$ (as for Fig. E6a) *without addition of carbohydrate*.



(c) $[C_4C_1im][NTf_2]$ + 10 wt% cellulose (**5**) + AcOH-d_4 (four molar equivalents relative to **5**).

Fig. E7 *In situ* ^{1}H NMR spectra for H/D exchange reaction of ILs with deuterated co-solvent, AcOH-d_4.

References

1. M. T. Clough, K. Geyer, P. A. Hunt, J. Mertes and T. Welton, *Phys. Chem. Chem. Phys*., 2013, **15**, 20480-20495.

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