



# Continuous production of cellulose mixed esters via homogeneous reactive twin-screw extrusion catalyzed by ionic liquid

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**Abstract** Cellulose mixed esters (CMEs) substituted with two different types of acyl groups are promising polymeric materials with various tunable properties but are arduous to produce. This is because of the insolubility of cellulose in common solvents, and thus, the industrial production of CMEs with desired degrees of substitution (DSs) requires a costly multistep process. To accomplish their facile production, homogeneous reactions have been performed using ionic liquids (ILs) as solvents for cellulose. However, the high viscosity of the cellulose-IL solutions causes insufficient mixing in batch reactors; thereby, favoring low cellulose concentrations with long reaction times (typically hours). Herein, we demonstrate a rapid and scalable production of CMEs by exploiting the excellent shear mixing of a twin-screw extruder as a flow reactor. A co-solvent system

comprising an IL, 1-ethyl-3-methylimidazolium acetate, and dimethyl sulfoxide was applied to dissolve cellulose at a high concentration (15 wt.%) via twin-screw extrusion. During continuous extrusion at 80 °C, cellulose reacted with two acyl reagents, isopropenyl acetate (IPAc) and vinyl propionate (VPr) (2.5:0.5, mol/mol), to yield cellulose acetate propionate (CAP) within minutes. The CAP was stably produced during the operation time of 50 min with an average isolated yield of 71%. The DSs of the acetyl and propionyl groups of CAP were 1.77 and 0.50, respectively, corresponding to sufficiently high conversion rates of 70% for IPAc and 100% for VPr.

**Keywords** Reactive extrusion · Transesterification · Cellulose mixed esters · Ionic liquid · Catalyst

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## Introduction

Cellulose mixed esters (CMEs) are promising polymeric materials with customizable functions controlled by the substitution of at least two distinct types of acyl groups (Glasser 2004). Short acyl chains (carbon number,  $C < 6$ ) impart solubility (Maim et al. 1951), fatty esters improve thermal processability (Willberg-Keyriläinen et al. 2017), phosphate esters provide flame resistance (Aoki and Nishio 2010; Xiao et al. 2014), and aromatic esters provide UV barrier properties (Song et al. 2017). Some CMEs, such as cellulose acetate propionate (CAP), are commercially

available for use in coatings (Edgar 2007), films (Amim 2008), and membranes (Kujawa et al. 2019). However, because of the insolubility of cellulose in common solvents, the industrial production of CMEs with desired degrees of substitution (DSs) requires a costly multistep process, which involves a heterogeneous acylation step, a partial acid-hydrolysis step to adjust the DS, and further per-acylation with another substituent (Cao et al. 2011; Tosh 2014).

Homogeneous processes are more advantageous because of the superior control over the DSs of CMEs, compared to heterogeneous processes. Although several cellulose solvents, such as 4-methylmorpholine-*N*-oxide and *N,N'*-dimethylacetamide/LiCl, have been previously reported, there remain issues with toxicity, low thermal stability, and poor recyclability. Recently, ionic liquids (ILs) have been expected as green solvents to replace them, because cellulose is found to be highly soluble in ILs (> 20 wt.% cellulose) (Dorn et al. 2008; Pinkert et al. 2009) without thorough pretreatments (Wendler et al. 2012). Moreover, ILs are recyclable (Hinner et al. 2016; van Nguyen et al. 2017; Milotskyi et al. 2021) and safe to handle, owing to their non-volatility and non-flammability (Gericke et al. 2012). In general, the cellulose-dissolving capacity of ILs is governed by hydrogen-bond basicity of the anions (Fukaya et al. 2008; Kostag et al. 2019). Furthermore, ILs such as 1-ethyl-3-methylimidazolium acetate (EmimOAc) act as both the solvent and catalyst for cellulose acylation (Kakuchi et al. 2015, 2017). However, a typical homogeneous acylation using ILs in batch processes requires low cellulose concentrations: e.g., 1–5 wt.% cellulose, and the total process for completing the dissolution and reaction of cellulose requires approximately 36 h (Schenzel et al. 2014; Wen et al. 2017; Hirose et al. 2019). This is because the high viscosity of the IL-cellulose solution impedes the penetration of anions into hydrogen bond networks between the cellulose chains (Pinkert et al. 2009). The viscosity of the solution can be lowered by adding an aprotic cosolvent (Zhao et al. 2013; Xu et al. 2013; Minnick et al. 2016) and/or by selecting an IL with a lower viscosity (Zhang et al. 2005). Consequently, transesterification reactions with cellulose concentrations of 12 wt.% were achieved in relatively shorter times, but still required several hours (Cao et al. 2010).

Extruders are often used for handling high-viscosity fluids, owing to their excellent-shear mixing.

In particular, twin-screws are more efficient than single-screws during mixing (Martínez-Bustos et al. 2012; Guiao et al. 2022). Extruders are also used as flow reactors. This so-called reactive extrusion (REX) has been attempted for the transesterification of concentrated cellulose (~20 wt.%) in 1-butyl-3-methylimidazolium chloride to achieve rapid modification. However, the resulting cellulose derivatives exhibited low DSs (<0.6) (Gibril et al. 2012; Gibril et al. 2013; Zhang et al. 2014). Recently, our group has succeeded in cellulose acylation via REX in EmimOAc/dimethyl sulfoxide (DMSO) using a twin-screw micro-compounder. Cellulose laurate was synthesized with vinyl laurate; high DS (2.7) and conversion (93%) were achieved within 10 min at 120 °C (Milotskyi et al. 2021). However, this micro-compounder is a circular batch reactor, and the REX was only applied to mono-acylation of cellulose. Hence, the continuous and scalable production of CMEs using a twin-screw extruder has never been achieved.

In this study, the continuous production of CMEs was first demonstrated using a twin-screw extruder as a flow reactor. For the rapid dissolution of highly concentrated cellulose, a mixed solvent of EmimOAc/DMSO at various ratios was applied. As a co-solvent, DMSO assists cellulose dissolution (Minnick et al. 2016) and facilitates the transesterification reaction catalyzed by EmimOAc (Kakuchi et al. 2017). A mixture of two acyl reagents, isopropenyl acetate (IPAc) and vinyl propionate (VPr), was subsequently introduced into the extruder. These reagents simultaneously reacted with the dissolved cellulose within minutes, resulting in the continuous production of CAP. Each DS was controlled by the molar ratio of IPAc/VPr, and the conversions of acyl reagents were evaluated. The average isolated yield and production rate of CAP (kg/day) were then examined.

## Materials and methods

### Materials

EmimOAc was purchased from Nippon Nyukazai Co. Ltd. (Tokyo, Japan) and vacuum-dried at room temperature (25 °C) for 3 d prior to use. DMSO, IPAc, VPr, deuterated DMSO-*d*<sub>6</sub> containing 0.05 (v/v) tetramethylsilane (TMS), and trifluoroacetic acid (TFA) were purchased from Tokyo Chemical Industry Co.

Ltd. (Tokyo, Japan). Microcrystalline cellulose, Avicel® PH-101, particle size < 50 µm, degree of polymerization ( $DP_n$ )=105 (van Nguyen et al. 2017), was purchased from Sigma-Aldrich Co. LLC. (St. Louis, MO, USA), and dried in a vacuum oven at 70 °C for more than 2 h prior to use.

#### Twin-screw extruder setup

Reactive extrusion (REX) was performed in an open system using a twin-screw extruder (ULTnano20TW-20MG-NH (600), Technovel Corp., Osaka, Japan) with a screw diameter of 20 mm and length to diameter ratio (L/D) of 20. This extrusion system had two individual inlet ports, C1 and C2, from the upstream side. The C1 port was connected to a Q-100-6 T-P-S Smoothflow pump (Tacmina Corp., Osaka, Japan) while the C2 port was connected to a PU-2086 plus dual syringe pump (JASCO Corp., Tokyo, Japan) (see Fig. S1). The extruder was preheated to 80 °C for each experiment, and the screw speed was set to 60 rpm. In such extruder systems, the screws convey, mix, and knead a substance along the length of the extruder before pushing it through the die. The resulting discharged paste-like material is called the extrudate. For continuous processes, “steady state” is the condition that describes when the mass flowing into the extruder is equal to the amount of mass dispelled from the die. All the experiments were performed under the steady state.

#### Solubility tests for cellulose in EmimOAc/DMSO

The cellulose-dissolving capacity of the EmimOAc/DMSO mixed solvent was investigated using a twin-screw extruder at 80 °C. For 10 wt.% cellulose solutions, dried cellulose was dispensed into the feeder at a feed rate of 0.6 g min<sup>-1</sup>, and a pre-mixed EmimOAc/DMSO solution was pumped into the C1 port at a flow rate of 5.4 g min<sup>-1</sup>. In order to collect a sample under the steady state, a small drop of the extrudate was collected 20 min after the first extrudate appeared. Then it was placed between two glass slides and observed using a cross-polarized optical microscope (POM, MT9430L polarizing microscope, Meiji Techno Co. Ltd., Saitama, Japan) at 50× magnification to confirm the dissolution of cellulose under continuous flow.

Next, the flow rate of the EmimOAc/DMSO mixed solvent was gradually decreased to 3.4 g min<sup>-1</sup> and then to 2.8 g min<sup>-1</sup>. Because the feed rate of cellulose was kept at 0.6 g min<sup>-1</sup>, the resultant cellulose concentrations increased to 15 and 20 wt.%. For each experiment after the flow rate was changed, the flow was uninterrupted for 20 min to reach the steady state; subsequently, the extrudate samples were analyzed using the POM.

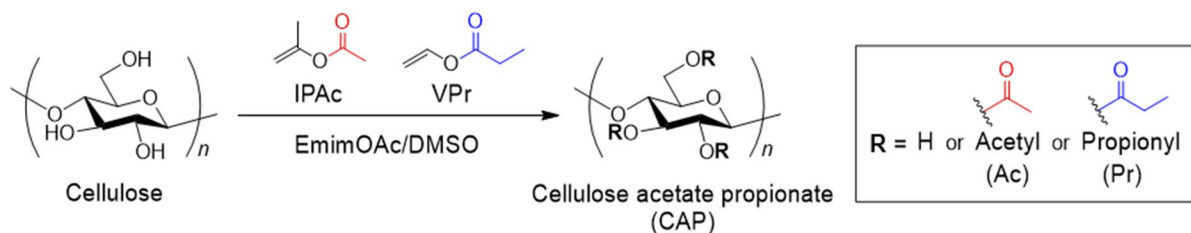
The above process was repeated for each EmimOAc/DMSO solution at different ratios (1:3, 1:2, and 1:1, g/g). In total, a series of experiments were performed under nine conditions, that is, three cellulose concentrations and three ratios of EmimOAc/DMSO (Table 1).

#### Continuous production of CAP via REX

The homogeneous acylation of cellulose with two substituents (Fig. 1) was performed in the EmimOAc/DMSO mixed solvent using a twin-screw extruder as a flow reactor. After preheating the extruder at 80 °C, cellulose was poured into the feeder at a feed rate of 0.6 g min<sup>-1</sup> (3.75 mmol min<sup>-1</sup>). The EmimOAc/DMSO mixed solvent (1:3, g/g) was introduced into the reactor from the C1 port to produce an extrudate with a cellulose concentration of 15 wt.%. The time gap between the introduction of cellulose/solvent media and the appearance of the first extrudate was recorded to be 10 min. After 20 min passed to afford the steady state, the pre-mixed acyl reagents of IPAc

**Table 1** Mixed ratio of EmimOAc/DMSO and cellulose concentrations in the extrudates for solubility tests

Entry	Cellulose		EmimOAc/DMSO	
	Feed rate/g min <sup>-1</sup>	Concentration/wt.%	g/g	Flow rate/g min <sup>-1</sup>
i	0.6	10	1:3	5.4
ii		15		3.4
iii		20		2.8
iv	0.6	10	1:2	5.4
v		15		3.4
vi		20		2.8
vii	0.6	10	1:1	5.4
viii		15		3.4
ix		20		2.8



**Fig. 1** Transesterification reaction of cellulose with IPAc and VPr in EmimOAc/DMSO

and VPr, 2.5:0.5 molar equiv./anhydroglucose unit (AGU) of cellulose, was introduced into the reactor from the C2 port at  $1.1 \text{ g min}^{-1}$ . The start of the flow of the mixed acyl reagents was arbitrarily labeled as the collection time ( $x=0 \text{ min}$ ). The flow of cellulose, mixed-solvent, and acyl reagents was continued for total 50 min to verify the steady production of CAP. The extruded reactant mixtures were collected in vials every five min ( $x=10, 15, 20, 25, 30, 35, 40, 45,$  and  $50 \text{ min}$ ) and weighed. A small amount ( $\sim 2.6 \text{ g}$ ) of the paste-like extrudate from each vial was poured into 100 mL of methanol. The generated precipitate was filtered, washed repeatedly with methanol, and vacuum-dried at  $70 \text{ }^\circ\text{C}$  for 24 h to obtain cellulose acetate propionate ( $\text{CAP}_{x \text{ min}}$ ).

#### Batch synthesis of CAP

The similar reaction as the above described was performed in a batch reactor to compare the performance with the twin-screw extruder. It was performed with a low cellulose concentration (5 wt.%). First, 57 g of EmimOAc/DMSO (1:3, g/g) mixed solvent was transferred into a 500 mL Schlenk flask with a stirrer bar, and 3 g of dried cellulose (18.5 mmol) was then added to the solution. The flask was purged with Ar gas and sealed with a rubber top. The mixture was heated at  $80 \text{ }^\circ\text{C}$  and stirred for 2 h to complete the dissolution of cellulose. Pre-mixed acyl reagents (IPAc and VPr, 2.5:0.5 molar equiv./AGU) were then injected into the flask, and the resulting solution was stirred at  $80 \text{ }^\circ\text{C}$  for 4 h to achieve the homogeneous acylation of cellulose. During this batch reaction, 2 mL samples were taken from the reaction mixture at different times ( $y=1, 10, 20, 30, 45, 60, 90, 120,$  and  $240 \text{ min}$ ) and then precipitated into 100 mL of methanol. The precipitate was filtered, washed repeatedly with methanol, and vacuum-dried

at  $70 \text{ }^\circ\text{C}$  for 24 h to yield batch-synthesized cellulose acetate propionate ( $\text{B-CAP}_{y \text{ min}}$ ).

#### Characterization of CAPs

Fourier transform infrared (FT-IR) spectra of the CAPs were recorded using a Thermo Fisher Scientific Nicolet iS10 (Thermo Fisher Scientific Inc., Tokyo, Japan) spectrophotometer equipped with an attenuated total reflection (ATR) unit. The FT-IR spectra were measured in the  $4000\text{--}400 \text{ cm}^{-1}$  range, and 64 scans were accumulated per spectrum. The resolution was kept as  $4 \text{ cm}^{-1}$ , and the signal-to-noise ratio (S/N) was 35 000:1.

$^1\text{H}$  and  $^{13}\text{C}$  nuclear magnetic resonance (NMR) spectra of the CAPs were recorded using a JNM-ECZ R 600 Hz spectrometer (JEOL Ltd., Tokyo, Japan) in  $\text{DMSO-}d_6$  at the Advanced Research Center of Kanazawa University. All NMR spectra were analyzed using delta NMR (JEOL Ltd., Tokyo, Japan), and the chemical shifts ( $\delta$ , ppm) were referenced to TMS ( $\delta=0 \text{ ppm}$ ) as an internal standard.

The DS of the propionyl (Pr) and acetyl (Ac) groups in CAP, denoted as  $\text{DS}_{\text{Pr}}$  and  $\text{DS}_{\text{Ac}}$ , were determined by  $^1\text{H}$  NMR analysis. A drop of TFA was added to the sample solution in  $\text{DMSO-}d_6$  to move the chemical shifts of the active hydrogen atoms downfield (Cao et al. 2010). According to the literatures (Aoki and Nishio 2010; Abe et al. 2016), each DS was determined using Eqs. (1) and (2):

$$\text{DS}_{\text{Pr}} = \frac{7 \times I - \text{Pr}(\text{CH}_3)}{3 \times I - \text{cellulose}} \quad (1)$$

$$\text{DS}_{\text{Ac}} = \frac{7 \times I - \text{Ac}(\text{CH}_3) - \text{Pr}(\text{CH}_2) - 2/3I - \text{Pr}(\text{CH}_3)}{3 \times I - \text{cellulose}} \quad (2)$$

where  $I\text{-Pr}(\text{CH}_3)$  is the integral ratio of chemical shifts assigned to the methyl protons of the Pr group;  $I\text{-Ac}(\text{CH}_3)\&\text{Pr}(\text{CH}_2)$  is the integral ratio of the region that includes the overlapping chemical shifts of the methyl protons of the Ac group and the methylene protons of the Pr group.  $I\text{-cellulose}$  denotes the integral ratio of the chemical shifts caused by the seven protons of the cellulose backbone.

The theoretical yields of the CAPs were calculated based on the resultant DSs, and the isolated yields were determined. The conversion of VPr and IPAc was defined and estimated as follows in Eq. (3):

$$\text{Conversion}(\%) = \text{DS}_R / \text{DS}_{\text{target}} \times 100 \quad (3)$$

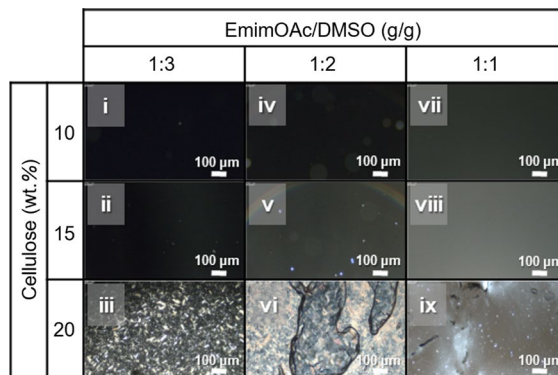
where  $\text{DS}_R$  is the resultant DS (i.e.,  $\text{DS}_{\text{Pr}}$  or  $\text{DS}_{\text{Ac}}$ );  $\text{DS}_{\text{target}}$  is the target DS of 0.5 for Pr group and 2.5 for Ac group, based on the molar ratio of the added acyl reagents per AGU.

The molar mass distribution of the CAPs was determined by size exclusion chromatography (SEC, Prominence UFLC system, Shimadzu Co., Tokyo, Japan) based on polystyrene standards. SEC was performed at 40 °C using a TSK gel  $\alpha\text{-M}$  (Tosoh Co., Tokyo, Japan). Moreover, 0.01 mol L<sup>-1</sup> of lithium bromide (LiBr) in dimethylformamide (DMF) was used as an eluent at a flow rate of 0.5 mL min<sup>-1</sup>.

## Results and discussion

### Cellulose solubility in EmimOAc/DMSO within the twin-screw extruder

To optimize the ratio of EmimOAc/DMSO for cellulose dissolution using the twin-screw extruder, the solubility of cellulose under three different concentrations (10, 15, and 20 wt.% cellulose) was investigated by POM observation of the extrudates. At 20 wt.% cellulose concentration as shown in Fig. 2 (iii), (vi), and (ix), the POM images show bright particles appeared in the extrudates at all mixed ratios of EmimOAc/DMSO (1:1–1:3, g/g). The presence of these particles was attributed to the undissolved cellulose crystals (Ngo 2019), and the number of remaining particles decreased with increasing the EmimOAc content. In contrast, no particles were observed in either 10 or 15 wt.% cellulose solutions, indicating the complete dissolution of cellulose in all mixed



**Fig. 2** POM images of the extrudates containing (i) 10 wt.%, (ii) 15 wt.%, and (iii) 20 wt.% cellulose in EmimOAc/DMSO (1:3, g/g), (iv) 10 wt.%, (v) 15 wt.%, and (vi) 20 wt.% cellulose in EmimOAc/DMSO (1:2, g/g), and (vii) 10 wt.%, (viii) 15 wt.%, and (ix) 20 wt.% cellulose in EmimOAc/DMSO (1:1, g/g). The extrusion of cellulose and EmimOAc/DMSO was performed at 80 °C within minutes at the screw speed of 60 rpm

ratios of EmimOAc/DMSO. In the FT-IR spectra of the regenerated cellulose obtained after the solubility tests, there was no distinct band that newly appeared from that of pristine cellulose, which indicates that no chemical reaction occurred between the cellulose and EmimOAc during the dissolution process. Moreover, the OH bands in the range from 3000 to 3500 cm<sup>-1</sup> broadened (Fig. S2), suggesting that a part of crystalline cellulose became amorphous (Kondo 1997) through the dissolution in EmimOAc/DMSO and subsequent regeneration.

The optimal solvent should dissolve the largest amount of cellulose while containing the least amount of EmimOAc. While DMSO alone cannot dissolve cellulose, it coordinates to the IL cations, which dissociates the ion pairs of the IL and promote cellulose-anion bonding (Minnick et al. 2016). Consequently, the use of the proper amount of DMSO accelerates cellulose dissolution. Therefore, 1:3 (g/g) was considered to be the optimal ratio of EmimOAc/DMSO for the REX with 15 wt.% cellulose, as shown in Fig. 2 (ii), within the examined experimental conditions.

### REX for continuous production of CAP

REX was carried out with adding pre-mixed acyl reagents to the 15 wt.% cellulose solution in EmimOAc/DMSO (1:3, g/g) to produce CAPs. Figure 3a shows

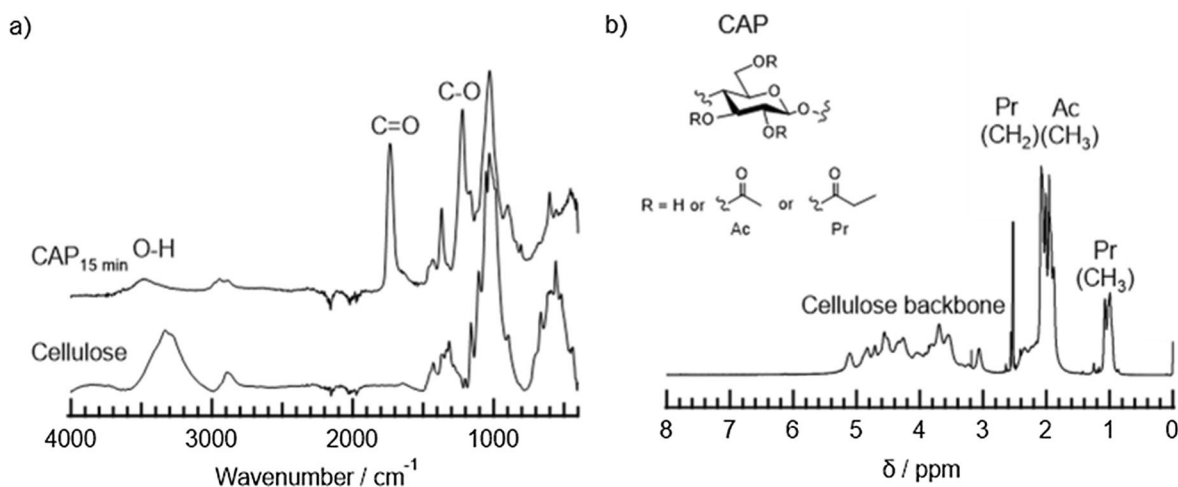


the FT-IR spectra of pristine cellulose as a reference and CAP<sub>15 min</sub> as a representative spectrum of all CAPs. The spectrum of cellulose showed characteristic bands at 1029 cm<sup>-1</sup> and 898 cm<sup>-1</sup>, which can be attributed to the C–O–C stretching of the sugar backbone and β-glycosidic linkages, respectively. In addition, a strong broad band was observed at 3330 cm<sup>-1</sup>, which corresponds to the O–H stretching vibrations of the hydroxy (OH) groups (Yue et al. 2012). In the spectrum of CAP<sub>15 min</sub>, similar bands derived from the pyranose ring were observed but these bands were sharpened and slightly shifted to 1030 and 900 cm<sup>-1</sup>, respectively. This might be attributed to the overlap with other bands due to the C–O–C asymmetric stretching vibrations of the introduced ester groups into cellulose. Moreover, there was a significant decrease in the intensity of the OH band at 3477 cm<sup>-1</sup>. In addition, new bands appeared at 1211 and 1736 cm<sup>-1</sup>, due to the C–O and C=O stretching of the ester groups, respectively (Fei et al. 2017). The spectra of all the CAPs shared similar traits (Fig. S3). These results suggest that the hydrogen network of pristine cellulose was disturbed due to dissolution in EmimOAc/DMSO, and the exposed OH groups were subsequently acylated via REX 10 min after the start of adding the pre-mixed acyl reagents into the reactor.

The structures of the CAPs were further elucidated using <sup>1</sup>H and <sup>13</sup>C NMR (Figs. S4 and S5). Figure 3b shows the <sup>1</sup>H NMR spectrum of CAP<sub>15 min</sub>. The chemical shifts of the protons of the cellulose backbone

range from 2.8 to 5.4 ppm. The methyl protons of the Ac and Pr groups were observed between 1.9–2.1 and at 1.0 ppm, respectively. The methylene protons of the Pr groups were observed at 2.2 ppm (Huang et al. 2011; Fei et al. 2017; Kujawa et al. 2019). All the other CAPs exhibited similar <sup>1</sup>H NMR spectra (Fig. S4), and the carbonyl carbons and the carbons of the cellulose backbone were also identified by <sup>13</sup>C NMR (Fig. S5). Hence, it was confirmed that cellulose was successfully modified with both the Ac and Pr groups via REX.

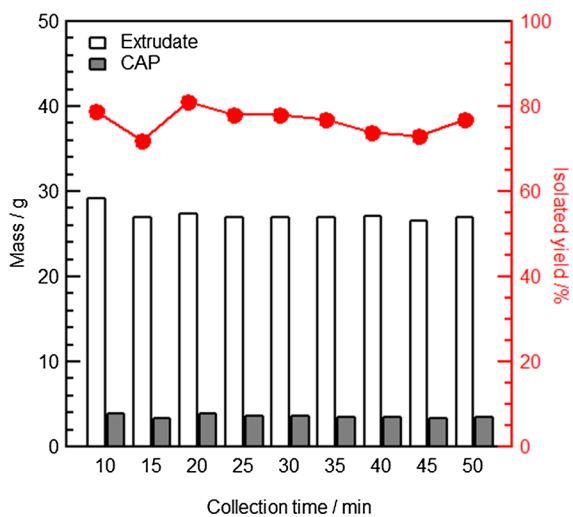
The DS<sub>Ac</sub> and DS<sub>Pr</sub> of CAPs were determined and summarized in Table S1. The CAPs showed the average DS<sub>Ac</sub> of 1.77 ± 0.04 and DS<sub>Pr</sub> of 0.50 ± 0.04 (n=9), and both the Ac and Pr groups on CAP<sub>15 min</sub> were distributed in the order of 6, 3, and 2 positions of cellulose-OH groups (Fig. S6 and Table S2). These DSs correspond to the sufficiently high conversion rates of 71 ± 2% and 100 ± 6% for IPAc and VPr, respectively. Owing to these high conversion rates, the DS<sub>Ac</sub> and DS<sub>Pr</sub> of CAP can be controlled by adjusting the molar ratio of IPAc to VPr in the mixed reagent solution. Notably, the average total DS (DS<sub>Total</sub>) of CAPs reached 2.27 ± 0.07 under mild conditions at 80 °C with the equimolar concentrations of acyl reagents. In contrast, previously reported continuous REXs for the heterogeneous mono-acylation of cellulose yielded extremely low DSs < 0.6 (Gibril et al. 2012, 2013; Zhang et al. 2014). These results suggest that the EmimOAc/DMSO mixed system



**Fig. 3** **a** ATR-mode FT-IR spectra of CAP<sub>15 min</sub> and pristine cellulose; **b** <sup>1</sup>H NMR spectrum of CAP<sub>15 min</sub>, measured in DMSO-*d*<sub>6</sub> containing a drop of TFA

applied in this study afforded the complete dissolution of cellulose, successfully allowing the excellent catalytic activity of EmimOAc for the subsequent cellulose acylation using the twin-screw extruder.

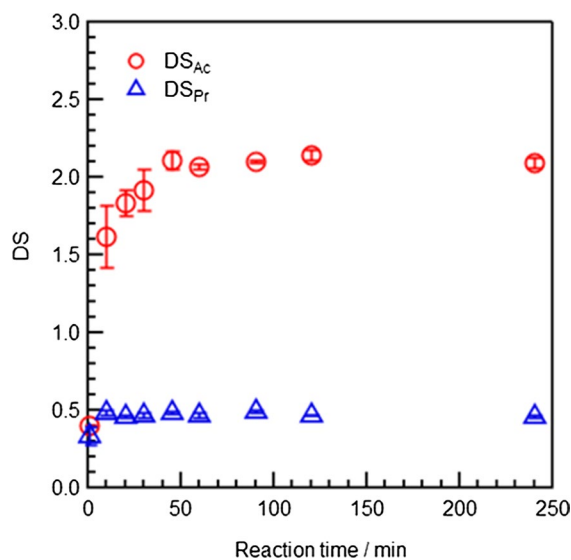
To evaluate the consistency of this continuous REX process, the mass of the extrudates and their respective CAP yields were measured and plotted against the collection time, as shown in Fig. 4. The yield of each CAP is also summarized in Table S1. The average mass of the extrudates collected ( $n=9$ ) was approximately  $27.3 \pm 0.09$  g. Assuming that the cellulose feed rate was constant at  $0.6 \text{ g min}^{-1}$ , 3.0 g of cellulose was fed into the extruder over 5 min. After purifying the extrudate, it was estimated that approximately 3.7 g of CAP was produced every 5 min during the flow reaction. Thus, the increased weight of the product ( $\sim 0.7$  g) could be attributed to the substitution of cellulose-OH groups with the ester groups. Furthermore, the average isolated yield of CAPs was  $77 \pm 2\%$  ( $n=9$ ). Notably, the respective fluctuations of the  $DS_{Ac}$ ,  $DS_{Pr}$ , and isolated yield of CAPs were quite small, indicating that CAP production via continuous REX proceeded stably for at least 50 min of flow. Although this first trial was stopped at 50 min because of the subsequent laborious purification, the operation time of this REX process can be further expanded for straightforward scalability.



**Fig. 4** Mass of the extrudates and CAPs ( $n=9$ ) and the corresponding isolated yields of CAPs at different collection times (10–50 min) during the continuous REX

### Comparison of REX and batch processes for CAP production

The performance of REX for cellulose acylation was compared with that of a batch process. Because of technical limitations, the batch process could only handle a narrow range of solution viscosities. Thus, 5 wt.% cellulose was applied to the homogeneous batch reaction with IPAc and VPr at  $80^\circ\text{C}$  with varying reaction times. Each reaction was performed in triplicate. The batch-synthesized CAPs (B-CAPs) were identified by FT-IR and  $^1\text{H}$  NMR (Figs. S7 and S8, respectively). The DSs and isolated yields of the B-CAPs are summarized in Table S3. The average  $DS_{Ac}$  and  $DS_{Pr}$  ( $n=3$ ) were plotted against the reaction time (1–240 min), as shown in Fig. 5. The  $DS_{Pr}$  of B-CAPs quickly increased to 0.33 after 1 min and achieved 0.48 after 10 min, demonstrating the rapid completion of propionylation. Meanwhile, acetylation gradually proceeded, and approximately 1 h was required for  $DS_{Ac}$  to attain an equilibrium at 2.1. This acetylation tendency is consistent with our previous result in which cellulose was acetylated using a batch reactor with an equimolar amount of IPAc ( $[\text{IPAc}]/[\text{OH}]=1$ ) to afford a DS of 2.3 after 1 h (Kakuchi et al. 2015). However, even after 4 h, B-CAP<sub>240 min</sub> showed a  $DS_{Pr}$  of  $0.46 \pm 0.01$  and  $DS_{Ac}$  of  $2.09 \pm 0.03$ .



**Fig. 5** Average  $DS_{Ac}$  (○) and  $DS_{Pr}$  (△) of B-CAPs ( $n=3$ ) plotted against the reaction time (0–240 min) at  $80^\circ\text{C}$  in batch synthesis; the error bar indicates the standard deviation

The corresponding conversion rates for VPr and IPAc were  $92 \pm 2\%$  and  $84 \pm 1\%$ , respectively.

In addition to the inherently lower reactivity of IPAc than that of VPr, the low cellulose concentration in the batch process may be responsible for the slow acetylation rate. However, despite the increased reaction time, the IPAc conversion did not drastically improve. The maximum conversion rate of IPAc in batch was comparable to that in REX ( $71 \pm 2\%$ ). This suggests that the incomplete conversion of IPAc in REX was not caused by the reaction system with the short residence time.

A straightforward comparison between the two processes is difficult because the reaction conditions, such as the cellulose concentration and reaction time, differ. Thus, one batch product, B-CAP<sub>20 min</sub>, was selected and compared with one REX product, CAP<sub>15 min</sub>, because their DSs and conversion rates were the most similar among all the REX and batch products. The results for these CAPs are summarized in Table 2. In addition, the weight-average molar mass ( $M_w$ ) and polydispersity indices ( $\mathcal{D}$ ) of B-CAP<sub>20 min</sub> ( $M_w = 2.1 \times 10^5 \text{ g mol}^{-1}$  and  $\mathcal{D} = 2.3$ ) and CAP<sub>15 min</sub> ( $M_w = 2.0 \times 10^5 \text{ g mol}^{-1}$  and  $\mathcal{D} = 2.2$ ) were similar (Fig. S9). This similarity in the molar mass distributions of the REX and batch products suggests that no significant depolymerization occurred despite strong shearing via the twin-screw extruder.

As shown in Table 2, the average isolated yields of CAPs in the REX and batch processes were comparably high at 77 and 73%, respectively, however, indicating some loss of the products in both processes. Considering its similarity to the batch process, the loss of products was not attributed to the REX process. Thus, it can be considered that a portion of CAPs (e.g., with low molecular mass and/or excess Pr

groups) synthesized in both processes was remained in the methanol filtrate during the precipitation step.

Totally, the CAP production via REX can outpace the batch production due to the continuous flow and higher cellulose concentration applied in the REX, which successfully contributed to the excellent production rate of 1 kg/day. In contrast, the batch reaction can produce CAP only at a gram scale each day. The reaction time could be shortened to some extent, as suggested from Fig. 5, but the batch process still required several hours because of the time-consuming dissolution step of cellulose. On the other hand, REX enabled a much shorter processing time, including both dissolution and subsequent reactions. Although it required an initial stabilization time, CAP was continuously produced within minutes while exhibiting high reaction efficiency, based on its high conversions of acyl reagents. Hence, this REX process can be applied as a facile, rapid, and scalable process for CME production.

## Conclusions

A facile, rapid, and scalable production of CME was first demonstrated in this study using a twin-screw extruder as a flow reactor. This process enabled the continuous production of highly substituted CAPs ( $DS_{\text{total}} = 2.27 \pm 0.07$ ) from concentrated cellulose (15 wt.%) solutions in EmimOAc and DMSO (1:3, g/g). The complete dissolution and successive transesterification of cellulose with pre-mixed IPAc and VPr (2.5:0.5, molar equiv./AGU) were carried out within minutes at 80 °C in an open-air system. During the 50-min flow, CAPs ( $n=9$ ) with consistently high  $DS_{\text{Ac}}$  ( $1.77 \pm 0.04$ ) and  $DS_{\text{Pr}}$  ( $0.50 \pm 0.04$ ) were obtained in sufficient isolated yields of  $77 \pm 2\%$ . This

**Table 2** Comparisons of CAPs synthesized via REX and batch processes

Process	Product	Cellulose <sup>a</sup> / wt. %	$DS_{\text{Pr}}$	$DS_{\text{Ac}}$	Conversion <sup>b</sup> /%		Yield <sup>c</sup> /%
					VPr	IPAc	
REX	CAP	15	$0.50 \pm 0.03^{\text{d}}$	$1.77 \pm 0.04^{\text{d}}$	$100 \pm 6^{\text{d}}$	$71 \pm 2^{\text{d}}$	$77 \pm 2^{\text{d}}$
Batch	B-CAP <sub>20 min</sub>	5	$0.46 \pm 0.01^{\text{e}}$	$1.83 \pm 0.08^{\text{e}}$	$92 \pm 2^{\text{e}}$	$73 \pm 4^{\text{e}}$	$73 \pm 5^{\text{e}}$

<sup>a</sup>Initial cellulose concentration during dissolution process. <sup>b</sup>Conversion rates of acyl reagents: the measured  $DS/DS_{\text{target}}$  of CAPs  $\times 100$ . The  $DS_{\text{target}}$  for the Pr and Ac groups were 0.5 and 2.5, respectively, based on the dosages of VPr and IPAc. <sup>c</sup>Isolated yield: the actual yield/theoretical yield of CAPs  $\times 100$ . The theoretical yield is based on the measured DSs. <sup>d</sup> $n=9$ . <sup>e</sup> $n=3$



REX process succeeded in shortening the total processing time for homogeneous acylation of highly concentrated cellulose with achieving high conversion rates for IPAc and VPr ( $71 \pm 2\%$  and  $100 \pm 6\%$ , respectively). Although this study focused on the synthesis of CAP in a lab-scale twin-screw extruder, our strategy can be applied to the large-scale production of various CMEs with further precise and technical conditioning.

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**Data availability statement** Not applicable.

**Declarations**

**Conflict of interest** The authors declare no conflicts of interest.

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