# **Supporting information**

#### A low-viscous and flowable zwitterionic liquid

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# **Material and Methods**

# Materials

*tert*-Butyl 12-hydroxy-4,7,10-trioxiadodecanoate was purchased from Angene International Ltd. (Nanjing, China). *p*-Toluenesulfonyl chloride, sodium hydroxide, imidazole, benzenesulfonyl chloride, and diethylene glycol monomethyl ether were purchased from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan) and use as received. Toluene, dichloromethane, methanol, and diethyl ether were purchased from Kanto Chemical Co., Inc. (Tokyo, Japan) and use as received. Hydrochloric acid (36% solution) and *p*-nitroaniline were purchased from FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan) and use as received. Amberlite IRN-78 ion exchange resin (nuclear grade) was purchased from Alfa Aesar (Lancashire, United Kingdom). Avicel PH-101 and Reichardt's dye were purchased from Merck KGaA (Darmstadt, Germany) and use as received. *N*,*N*-Diethyl-4-nitroaniline was purchased from Nacalai Tesque Inc. (Kyoto, Japan) and use as received.

## Synthesis of OE2imOE3C

The synthetic scheme and intermediate structures are shown in Scheme S1 and S2 in supporting information. The intermediate **1** was synthesized referring literature.<sup>1</sup> *tert*-Butyl 12-hydroxy-4,7,10-trioxadodecanoate (3.0 g, 0.011 mol) was dissolved in dichloromethane (40 mL) and NaOH (1.4 g, 0.035 mol) was added. The solution was cooled on ice and *p*-toluenesulfonyl chloride (2.0 g, 0.010 mol) was added dropwise. The mixture was stirred at room temperature for 23 hours, and the solid impurities were removed by filtration. The solution was washed with ultrapure water until the pH of the aqueous layer became 6 (by using universal indicator paper pH 1–11, reel, MACHEREY-NAGEL GmbH & Co. KG) and the sodium concentration was 0 ppm (measured by sodium concentration meter, LAQUAtwin Na-11, HORIBA Advanced Techno, Co., Ltd.). The dichloromethane layer was dried under reduced pressure to give intermediate **1**.

An excess amount of 36% HCl aqueous solution (11.5 g) was added to intermediate **1** (3.9 g, 0.009 mol) and stirred at room temperature for 3 hours. Dichloromethane was added to the mixture to extract the intermediate **2**, and the resulting solution was washed with ultrapure water until the pH of the aqueous layer became 6. The dichloromethane layer was dried under reduced pressure to give liquid intermediate **2**.

1-(2-(2-Methoxy)ethyl)imidazole (OE<sub>2</sub>im) was synthesized with some modification referring literature.<sup>2</sup> Diethylene glycol monomethyl ether (7.2 g, 0.028 mol) was dissolved in toluene (40 mL)

and NaOH (5.9 g, 0.148 mol) was added. The solution with NaOH was cooled on ice and benzenesulfonyl chloride (10.5 g, 0.059 mol) was added dropwise. The mixture was stirred at room temperature for 72 hours, and the solid impurities were removed by filtration. The resulting solution was dried under reduced pressure to give diethylene glycol monomethyl benzenesulfonate. Diethylene glycol monomethyl benzenesulfonate was dissolved in toluene (30 mL) and NaOH (6.0 g, 0.150 mol) was added. The solution with NaOH was cooled on ice and imidazole (5.5 g, 0.081 mol) was added. The mixture was stirred at room temperature for 72 hours, and the solid impurities were removed by filtration. OE<sub>2</sub>im was purified by distillation.

The intermediate **2** (2.5 g, 0.007 mol) was dissolved in toluene (50 mL). The solution was cooled on ice and  $OE_2$ im (1.1 g, 0.006 mol) was added dropwise. The mixture was heated at 80 °C for 29 hours. The bottom layer containing the product was washed with diethyl ether and dried under reduced pressure to give intermediate **3**.

The intermediate **3** (3.2 g, 0.006 mol) was dissolved in a mixture of MeOH (150 mL) and ultrapure water (50 mL). Ion exchange was performed by anion exchange resin (Amberlite IRN-78) stirring at room temperature for 5-10 days to give intermediate **4**. The solution was dried under reduced pressure and washed with diethyl ether. The solution was dried under reduced pressure to give OE<sub>2</sub>imOE<sub>3</sub>C (**5**, product, yield: 32%).

The completion of synthesis was confirmed by the following analysis.

### Structural characterization

<sup>1</sup>H NMR (JNM-ECS 400, JEOL) (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si)  $\delta = 2.428$  (2H, t, J = 10.8 Hz, CH<sub>2</sub>COO), 3.354 (3H, CH<sub>3</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>N), s, 3.498-4.563 (22H, m, CH<sub>3</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>NCHNCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>COO), 7.242 and 7.395 (2H, m, NCHCHN), 10.659 (1H, s, NCHN). <sup>13</sup>C NMR (JNM-ECS 400, JEOL) (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si)  $\delta = 39.753, 49.745, 50.222, 59.346, 69.615, 69.834, 69.977, 70.216, 70.378, 70.645, 70.826, 71.226, 71.226, 70.826, 71.826,$ 72.008, 122.551, 122.656, 140.028, 177.518. Mass spectrometry with fast atom bombardment ionization (JMS-700, JEOL): in positive mode, m/z = 375.2129 (M + H<sup>+</sup>, found) and 375.2131 (calculated); and in negative mode, m/z = 373.1977 (M - H<sup>+</sup>, found) and 373.1975 (calculated). Elemental analysis: OE<sub>2</sub>imOE<sub>3</sub>C·1.1H<sub>2</sub>O (Found: C, 51.67; H, 8.31; N, 7.21. Calc. for C<sub>17</sub>H<sub>32.2</sub>N<sub>2</sub>O<sub>8.1</sub>: C, 51.79; H, 8.23; N, 7.11%).

#### NMR

<sup>1</sup>H PFG NMR was measured on JNM-ECS 400 (JEOL) and JNM-ECZ600R (JEOL) using D<sub>2</sub>O as deuterated solvent. Delta v5.3.1 (JEOL) was used for analysis. The diffusion coefficient was automatically calculated from the nuclear spin magnetic rotation ratio  $\gamma$  (= 2.67517 × 10<sup>8</sup> rad/sT), PFG height g (= 300 mT/m), the distance between two PFGs  $\Delta$  (= 100 ms) and PFG length  $\delta$  (= 2 ms for OE<sub>2</sub>imOE<sub>3</sub>C and 4 ms for OE<sub>2</sub>imC<sub>5</sub>C) using Delta v5.3.1 diffusion analysis mode.<sup>3</sup>

### **Cellulose dissolution**

The cellulose used was Avicel PH-101, a microcrystalline cellulose. The zwitterions (200 mg) were loaded into a 4 mL vial, to which 1 wt% of cellulose was added and stirred with heating for up to 1 h. If the cellulose dissolved within 1 h, another 1 wt% of cellulose was added and the same procedure was repeated until the cellulose no longer dissolved. The dissolution of cellulose was determined by visual observation.

#### Kamlet-Taft parameters

*N,N*-diethyl-4-nitroaniline / *p*-nitroaniline / Reichardt's dye were used. Since each dye can be degraded by light, the vials were covered by aluminum foil. The sample preparation and measurement procedures are described below.<sup>4</sup> The dye (10 mg for *N,N*-diethyl-4-nitroaniline / *p*-nitroaniline and 20 mg for Reichardt's dye) was added to a 4 mL vial and dissolved with 1 mL of methanol. The mixture (16  $\mu$ L for *N,N*-diethyl-4-nitroaniline / *p*-nitroaniline and 94  $\mu$ L for Reichardt's dye) was transferred to another 4 mL vial and dried under reduced pressure at room temperature to remove the methanol. To the vial containing the dried dye, 250 mg of the ionic liquid or zwitterion was added and the dye was dissolved. The absorbance was measured using an UV-vis spectrophotometer (V-630, Japan Spectroscopy) with a wavelength of 0.1 nm.

The estimated wavelength at maximum absorption was substituted into the formulas 1-5 to obtain

the Kamlet-Taft parameters.

$$\nu_{\rm dye} = 1/(\lambda_{\rm max} \times 10^{-4}) \tag{1}$$

$$\pi^* = \left(27.52 - \nu_{N,N-\text{diethyl-4-nitroaniline}}\right)/3.182 \tag{2}$$

$$\beta = (1.035\nu_{N,N-\text{diethyl-4-nitroaniline}} - \nu_{p-\text{nitroaniline}} + 2.64)/2.8$$
(3)

$$E_{\rm T}(30) = 2.8591 \nu_{\rm Reichardt's\,dye} \tag{4}$$

$$\alpha = 0.0649E_{\rm T}(30) - 0.72\pi^* - 2.03\tag{5}$$

# Toxicity of OE<sub>2</sub>imOE<sub>3</sub>C

The YPD medium was prepared with a composition of 10 g/L yeast extract, 20 g/L meat peptone, and 20 g/L D(+)-glucose. The *K. marxianus* (DMKU3-1042) was inoculated to YPD mediumand then incubated for 24 hours at 40 °C with a shaking speed of 200 rpm. The collected *K. marxianus* was inoculated into  $OE_2imOE_3C/YPD$  medium in 96-well plate (the initial  $OD_{600}$  was 0.2). The  $OD_{600}$  was measured by a multiplate reader (BioTek). The plates were incubated for 6 h under aerobic condition at 37°C in an incubator (TAITEK, DWMax M-BR-32P) with shaking at 700 rpm.

# Molecular dynamics simulation

Two systems ( $OE_2imOE_3C$  and  $OE_2imC_5C$ ) consisting of a single zwitterion (500 molecules) were constructed and MD calculations were performed at constant temperature (197 °C) and pressure (1 bar) for 1 µs. Prior to the production run, the systems were subjected to structural optimization calculations and equilibrated MD calculations with stepwise temperature heating.  $OE_2imOE_3C$  and  $OE_2imC_5C$  were described by the general AMBER force field (GAFF).<sup>5</sup> The MD simulations were performed using the Amber 20 package with a NVIDIA Pascal GPU system.<sup>6</sup>



Scheme S1 Synthetic scheme of  $OE_2 im OE_3 C$ .



Scheme S2 Synthetic scheme of  $OE_2$ im.



Fig. S1 <sup>1</sup>H NMR spectrum of OE<sub>2</sub>imOE<sub>3</sub>C



Fig. S2 <sup>13</sup>C NMR spectrum of OE<sub>2</sub>imOE<sub>3</sub>C



OE2imOE3C

	Position	Chemical shift	Diffusion [m <sup>2</sup> /s]
Cation side chain	1	3.323	$2.10 \times 10^{-9}$
	2,4	3.564-3.783	$2.04 \times 10^{-9}$
	3	3.894	$2.21 \times 10^{-9}$
	5	4.391	$2.18\times10^{-9}$
	Average (1-5)	_	$2.11 \times 10^{-9}$
Spacer	6	4.391	$2.18  imes 10^{-9}$
	7	3.894	$2.21  imes 10^{-9}$
	8-12	3.564-3.783	$2.04  imes 10^{-9}$
	13	2.425-2.434	$2.17 imes10^{-9}$
	Average (6-13)	_	$2.10 \times 10^{-9}$



OE2imC5C

	Position	Chemical shift	Diffusion [m <sup>2</sup> /s]
Cation side chain	1'	3.329	$4.57\times10^{-10}$
	2'	3.651-3.664	$4.57\times10^{-10}$
	3'	3.876-3.892	$4.93 \times 10^{-10}$
	4'	3.560-3.574	$4.84\times10^{-10}$
	5'	4.190-4.213	$4.88\times10^{-10}$
	Average (1'-5')	_	$4.76\times10^{-10}$
Spacer	6'	4.368-4.384	$4.09\times10^{-10}$
	7'	1.857-1.906	$3.06 \times 10^{-10}$
	8'	1.263-1.314	$4.49\times10^{-10}$
	9'	1.554-1.594	$3.74\times10^{-10}$
	10'	2.141-2.165	$4.47 \times 10^{-10}$
	Average (6'-10')	_	$3.97 \times 10^{-10}$

Fig. S3 Diffusion coefficients of OE<sub>2</sub>imOE<sub>3</sub>C and OE<sub>2</sub>imC<sub>5</sub>C measured by <sup>1</sup>H NMR with 0.1 M

zwitterion/D<sub>2</sub>O at room temperature.



Fig. S4 Distribution profiles of distance between the gravity center of cation and terminal edge of

anion for OE<sub>2</sub>imOE<sub>3</sub>C and OE<sub>2</sub>imC<sub>5</sub>C.

Zwitterionic liquid	Temperature [°C]	Viscosity [mPa·s]
	30	26,927 (calculated)
	40	12,480
	50	5,645
OE21mOE3C	60	2,748
	70	1,432
	80	810
	30	156,981 (calculated)
	66.1	26,389 <sup>a</sup>
OE <sub>2</sub> imC <sub>5</sub> C	71.4	22,160 <sup><i>a</i></sup>
	75.7	18,237 <sup><i>a</i></sup>
	80.6	14,436 <sup><i>a</i></sup>

Table S1 Viscosities of zwitterionic liquids at several temperatures.

<sup>*a*</sup>The values were cited from literature<sup>7</sup>.

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