Electronic Supplementary Information

A general method for the separation of amphiphilic surface-active poly(ethylene glycol) mono- and di-esters with long-chain ionic liquid-based biphasic systems

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Materials and Reagents

The ionic liquids (ILs) used in this study were purchased from Lanzhou Greenchem. ILS, LICP.CAS. (Lanzhou, China), including 1-alkyl-3-methylimidazolium chloride ([$C_n$mim]Cl, n = 2, 4, 6, 8, 12, 99%), N-alkyl-pyridine bromide ([C_nPy]Br, n = 2, 4, 6, 8, 12, 99%), 1-octyl-3-methylimidazolium bromide ([C_8mim]Br, 99%), 1-octyl-3-methylimidazolium dihydrogen phosphate ([C_8mim][H_2PO_4], 99%) and 1-octyl-3-methylimidazolium nitrate ([C_8mim][NO_3], 99%) with water content of these ILs below 0.5 wt%. Tocopherol succinate (≥95%) was obtained from Zhejiang Worldbest Pharmaceuticals Science Technic Development Co., Ltd. (Lanxi, China). Poly(ethylene glycol) (PEG) 400 mono- and di-laurates, PEG600 mono- and di-oleates, PEG1000 mono- and di-oleates, PEG400 mono- and di-stearates, PEG1000 mono- and di-stearates were purchased from Nantong Hantai Chemical Co., Ltd

(Nantong, China). PEG 1000 (Chemically Pure (CP)), *p*-toluene sulfonic acid (≥99%), n-Hexane (Analytical Reagent (AR)) and ethyl acetate (AR) were from Shanghai Reagent Company (Shanghai, China). Acetonitrile (AR) was obtained from Shanghai Lingfeng Chemical Reagent Co., Ltd (Shanghai, China). The purified water was obtained from Wahaha Group Co. Ltd. (Hangzhou, China). High performance liquid chromatography (HPLC) grade acetonitrile, isopropanol and methanol were from Tedia Company Inc (USA). The weakly basic anion exchange resin D315 was obtained from Shanghai Huazhen Science & Technology Co., Ltd. (Shanghai, China). Triton X-100 (polyethylene glycol octylphenol ether, Molecular Biology Reagent, mass fraction purity > 0.99) was bought from Sigma-Aldrich Co. LLC (MO, US). Sodium dodecyl sulfate (SDS, CP) was from Xilong Chemical Co., Ltd (Shantou, China).

The synthesis of PEG mono- and di-tocopherol succinate

PEG mono- and di-tocopherol succinate were prepared by esterification of tocopherol succinate and PEG 1000 with *p*-toluene sulfonic acid as a catalyst according to the literature.[1] 20.0 g PEG 1000 was accurately weighed to a three-necked bottle and melted at 393 K, acting as the reactant and reaction solvent simultaneously. 9.5 g tocopherol succinate and 0.5 g *p*-toluene sulfonic acid were added to the bottle to react for 4 h at 393 K. During the process bubbling with nitrogen was used to remove the water produced by the esterification. The reaction product was purified firstly by extraction with ethyl acetate and saturated saline aqueous solution biphasic system to remove unreacted PEG 1000, and *p*-toluene sulfonic acid. And the unreacted tocopherol succinate and possible by-product of tocopherol were removed by adsorption using the weakly basic anion exchange resin D315 and extraction with acetonitrile-hexane biphasic system, respectively.

Extraction equilibrium experiment

Before extraction, pre-phase equilibrium was carried out for the IL/water-ethyl acetate biphasic systems with equal volume of ethyl acetate and a certain

concentration of IL aqueous solution at a certain temperature, and the ethyl acetate-rich upper phase and IL-rich lower phase were separated. A known amount of PEG mono- and di-esters was dissolved in the ethyl acetate-rich solution and transferred into an Erlenmeyer flask. Then equal volume of IL-rich aqueous solution was added into the flask. The flask was shaken vigorously in a thermostatic rotary shaker under the speed of 200 rpm and a set temperature (± 0.1 K). Preliminary experiments showed that shaking for 2 h was enough to achieve distribution equilibrium. After shaking, the flaks were allowed to settle for at least 2 h at the same temperature. Then, samples were taken from both phases by syringes without disturbing the phase boundary and diluted with ethanol for the HPLC analysis.

The distribution coefficient (D_i) of solute i in biphasic system is calculated according to Eq. (1),

$$D_i = C_i^e / C_i^r \quad (1)$$

where C_i^e and C_i^r refer to the mass fractions of solute in the extract phase (IL-rich phase) and the raffinate phase (ethyl acetate-rich phase), respectively. The selectivity (α) of solute i to solute j is calculated according to Eq. (2),

$$\alpha = D_i / D_j \quad (2)$$

The extraction equilibrium experiments were repeated for at least three times and the relative uncertainties of distribution coefficients were less than 5%.

Extraction experiments with Triton X-100 aqueous solution and SDS aqueous solution as extractants were done similar to the IL/water-ethyl acetate system, except that the pre-phase equilibrium were done at volume ratios of ethyl acetate to the surfactant aqueous solution of 5:1 and 2:1 for Triton X-100 and SDS, respectively.

HPLC analysis

The concentrations of PEG mono- and di-esters in samples were analyzed by HPLC. The HPLC system included a Waters 1525 binary HPLC pump, a Waters 717 plus autosampler, a Waters thermostat, a Waters 2487 dual absorbance UV detector and a Waters 2414 Refractive Index (RI) detector. A Develosil® Rpaqueous C30

column (4.6×150 mm i.d., 5 μm) was used as the stationary phase. For the analysis of PEG mono- and di-TS, the mobile phase consisted of acetonitrile (A) and isopropanol (B), and were carried out with gradient conditions of 65/35 (A/B, v/v) for 10 min, 30/70 (A/B, v/v) for 10 min, 65/35 (A/B, v/v) for 10 min at a flow rate of 1 $mL \cdot min^{-1}$. The UV detector was set at 284 nm. The column temperature was 308.2 K.

The analysis of other PEG mono- and di-esters were conducted at twice by HPLC with the RI detector. The optical unit of the RI detector was set at 313.2 K, sensitivity of the detector was 64 and operations were done under positive mode. The Develosil® Rpaqueous C30 column (4.6×150 mm i.d., 5 μm) was also used as the stationary phase. For the analysis of PEG monoesters, the mobile phase consisted of acetonitrile: water (9: 1, v/v) was employed. While for the analysis of PEG diesters, the mobile phase consisted of acetonitrile: water: isopropanol (2.7: 0.3: 7, v/v/v). During the analysis, the flow rate and the column temperature were 1.0 $mL \cdot min^{-1}$ and 313.2 K, respectively.

The HPLC analysis for the concentrations of PEG mono- and di-esters were repeated at least two times, the deviation of the analysis were less than 3%.

POM Analysis

Polarizing optical microscopy measurements were carried out using ECLIPSE E600W microscope made by Nikon Corporation, Japan. Temperature was controlled by ED 600 hot stage (Linkam Scientific Instrument Ltd., UK) at 303 K. The images were captured by a CCD (charge-coupled device) camera.

DLS Analysis

The dynamic light scattering (DLS) measurements were carried out using a laser light scattering photometer (Zetasizer Nano ZS, Malvern Instruments, UK). Light of λ = 633 nm from a solid-state He-Ne laser (4.0mW) was used as the incident beam. All measurements were made at 303 K and at 90° scattering angle. At least three measurements were taken for each solution. DLS results of IL-rich aqueous phase of the IL/water-ethyl acetate systems with $[C_6Py]Br$ and $[C_8Py]Br$ are shown in Fig. S1.

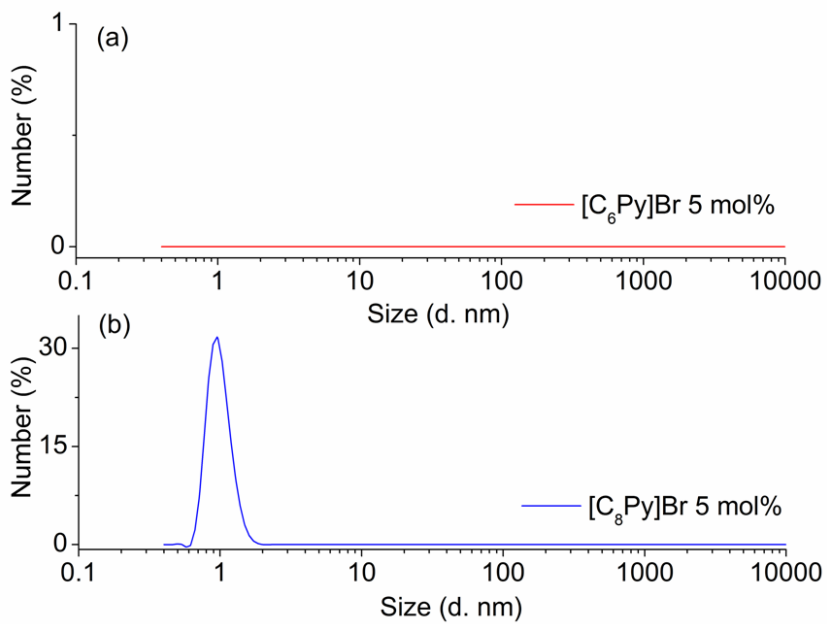

Fig. S1 DLS images of IL-rich aqueous phase of the IL/water-ethyl acetate systems with [C_6Py]Br (a) and [C_8Py]Br (b). The initial concentrations of ILs in water were 5 mol%, and the detection were done at 303 K.

Crosscurrent and countercurrent extraction

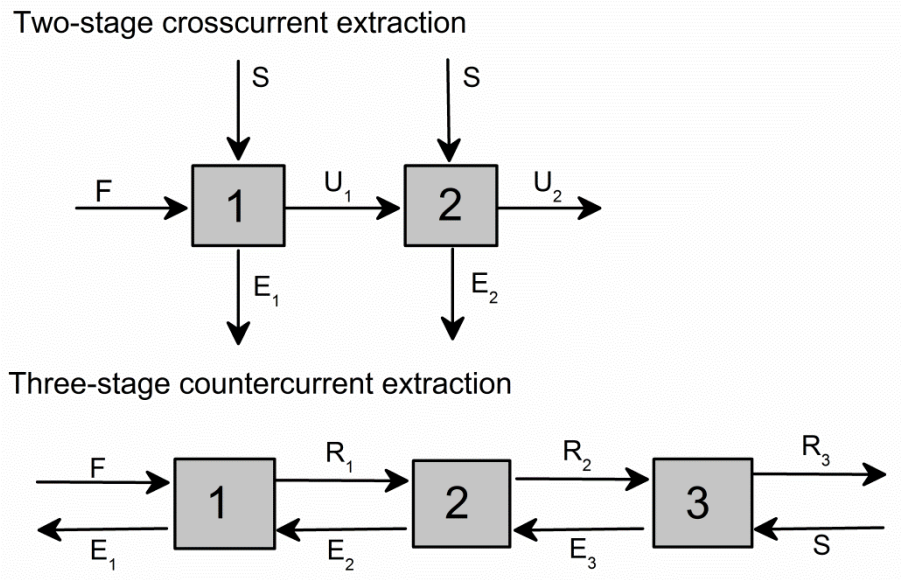

Fig. S2 General scheme of two-stage crosscurrent extraction of PEG mono- and di-TS (F = feed of PEG mono- and di-TS; S = fresh extractant; U = residue phase; E = extract phase) and three-stage countercurrent extraction (F = feed of PEG mono- and di-TS; S = fresh extractant; R = residue phase; E = extract phase).

Three-stage continuous countercurrent extraction

High purity as well as good recovery yield of PEG mono-TS could also be achieved

through a three-stage countercurrent extraction. The countercurrent extraction was carried out using an HL-20 centrifugal extractor made by the research institution of Beijng extraction applied technology (Beijing, China). A solution of PEG mono- and di-TS (80.0 wt% of PEG mono-TS in it) dissolved in ethyl acetate at a concentration of 16.0 mg/mL was used as the feed solution (F in Fig. S2), and 4 mol% $[C_8Py]Br$ aqueous solution was used as the extractant (S in Fig. S2). The ratio of the flow rate of the extractant to the flow rate of the feed was kept as 0.4 during the extract process. The speed of the centrifugation was set as 2900 rpm to reach complete separation of the extract phase and the residue phase at each stage. Concentrations of PEG mono- and di-TS in the extract and residue phases from each stage were analyzed by HPLC. The standard of the steady state (extraction equilibrium) was that the concentrations of PEG mono- and di-TS kept almost constant in samples collected from the same position in different periods.

Reference

1. B. L. Bernard and S. H.-W. Wu, *US. Pat.* 2005, 20050163828A1.