Supplementary Information

Temperature-triggered microfluidic fabrication of monodisperse organic particles via LCST-mediated phase transition

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Materials

2-Propanol (IPA), 1-Hexanol, ethylene glycol monobutyl ether (C4E1) and polyvinyl alcohol (1500–1800, 98% hydrolyzed) were purchased from FUJIFILM Wako Pure Chemical Corporation. Diethylene glycol monohexyl ether (C6E2) and Sodium Alginate 100-200 were purchased from Tokyo Chemical Industry Co. Silpot 184 W/C was purchased from Dow Toray Co. Ltd. Clear Resin (V4) and Rigid 10K Resin (V1) were purchased from Formlabs.

Preparation of microfluidic devices

All the master molds prepared in this work were printed with an SLA 3D printer (Form 3, Formlabs) using Clear Resin (V4). The mold was printed at a 25 μm resolution on the build platform, followed by it was washed with IPA, dried and post-cured in a UV chamber (Form Cure, Formlabs). To prepare the PDMS channel, PDMS elastomer and curing agent were mixed in 10:1 w/w ratio and stirred in a cup for 5 min. The mixture was poured on the master mold, and subsequently degassed in a desiccator connected to a rotary pump for 60 min.

The PDMS sheet was pealed after curing at 50 °C for 120 min in an oven, and then 2.0 mm inserts were punch with a biopsy punch (BP-20F, Kai medical). The PDMS sheet with the imprinted channel was bonded to a smooth PDMS sheet after air plasma treatment in plasma chamber (SC-708, Sanyu Electron). Finaly, the prepared PDMS channel was enclosed in the housing printed with Form 3 using Rigid 10K Resin (V1).

Continuous generation of monodisperse droplets

A microfluidic device consisting of one channel (cross section: 100 × 100 μm^2) for the dispersed phase and two channels (cross section: 400 × 400 μm^2) for the continuous phase was heated 80 °C, above the critical temperature of the solvent mixture. Distilled water as the disperse phase was supplied to the microfluidic device at five sets of flow rates (Q_d = 1.0, 2.0, 3.0, 4.0 and 5.0 μL min^{-1}) using a syringe pump (BS4 70-2208, Harvard Apparatus). A mixed solvent of water and C6E2 with a volume ratio of 19:80 was prepared and used as the continuous phase. The continuous phase was supplied to the microfluidic device using a syringe pump (YSP-202, YMC Co., Ltd.), and the flow ratio of dispersed phase to continuous phase was fixed at 1:99 in all conditions. The generation of droplets was observed with a high-speed microscope camera system, which consists of a high-speed microscope (VW-9000, KEYENCE), a high-speed camera unit (VW-600C, KEYENCE) and a zoom lens (VH-Z20R, KEYENCE).

Fabrication and characterization of monodisperse PVA microparticles

3 wt% PVA aqueous solution as the dispersed phase and water-C6E2 binary mixture (80:19, v/v) as the continuous phase were supplied to the microfluidic devices at 3 μL min^{-1} and 297 μL min^{-1}, respectively. The generation of droplets in which PVA dissolved was observed with a high-speed camera system described above.

After collecting, the obtained PVA microparticles was characterized using a scanning electron microscope (TM4000PlusII, Hitachi).

Fabrication and characterization of PVA particles via droplet with a large variation in size

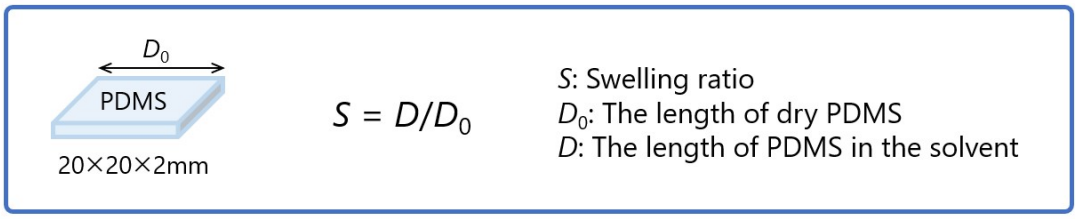
A 3 wt% PVA aqueous solution (0.1 mL) was poured into a mixture of water (1.9 mL) and C6E2 (8.0 mL) at 80 °C. The above two-phase solutions did not dissolve each other above the critical temperature and remained in a phase-separated state. Droplets of PVA aqueous solution were generated by simple stirring at 1500 rpm using a magnetic stirrer. After cooling, the obtained PVA precipitate was characterized using a scanning electron microscope.

Fabrication and characterization of monodispersed particles using ternary mixed solvent system

The used solvents were predicted using the COSMOtherm, and their composition was experimentally determined to be 1-hexanol:water:C4E1 = 25:15:60 (Fig. S4).

To fabricate monodisperse PVA particles, 1.5 wt% PVA aqueous solution as the dispersed phase and 1-hexanol-water-C4E1 ternary mixture (25:11:60, v/v/v) as the continuous phase were supplied to the microfluidic devices at 8 μL min^{-1} and 96 μL min^{-1}, respectively. The generation of droplets in which PVA dissolved was observed with a high-speed camera system described above. After collecting, the obtained PVA microparticles was characterized using a scanning electron microscope (TM4000Plus, Hitachi).

To fabricate monodisperse SA particles, 1.0 wt% SA aqueous solution as the disperse phase and 1-hexanol-water-C4E1 ternary mixture (25:13:60, v/v/v) as the continuous phase were supplied to the microfluidic devices at 2 μL min^{-1} and 440 μL min^{-1}, respectively. The generation of droplets in which SA dissolved was observed with a high-speed camera system described above. After collecting, the obtained PVA microparticles was characterized using a scanning electron microscope (TM4000Plus, Hitachi).



Compounds	S [-]	S_{ref} [-]
PDMS	—	∞
2-Butoxyethanol(C4E1)	1.03	—
Diethylene glycol diethyl ether (C6E2)	1.00	—
1-Hexanol	1.04	—
Ethanol	1.04	1.04
DMSO	1.00	1.00
Water	1.00	1.00

Fig. S1 Swelling ratios of various solvent against PDMS.

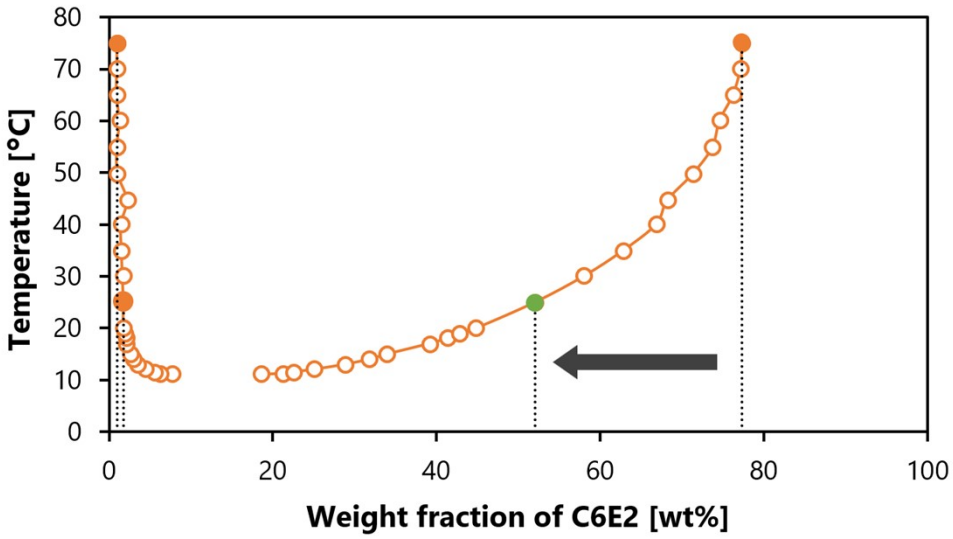


Fig. S2 Binary phase diagram of water-C6E2, redrawn based on the data reported by K. H. Lim et al (Ref. 26).

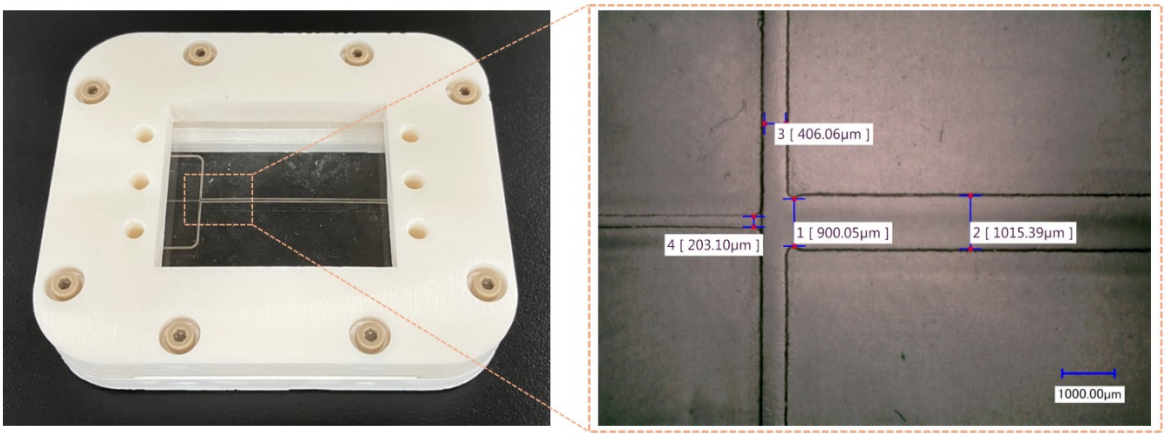


Fig. S3 A photograph of microfluidic device and enlarged view of microflow pathway.
(The height of the inlet channel (h_d) = 100 μm, The height of the collection channel (h_c) = 400 μm)

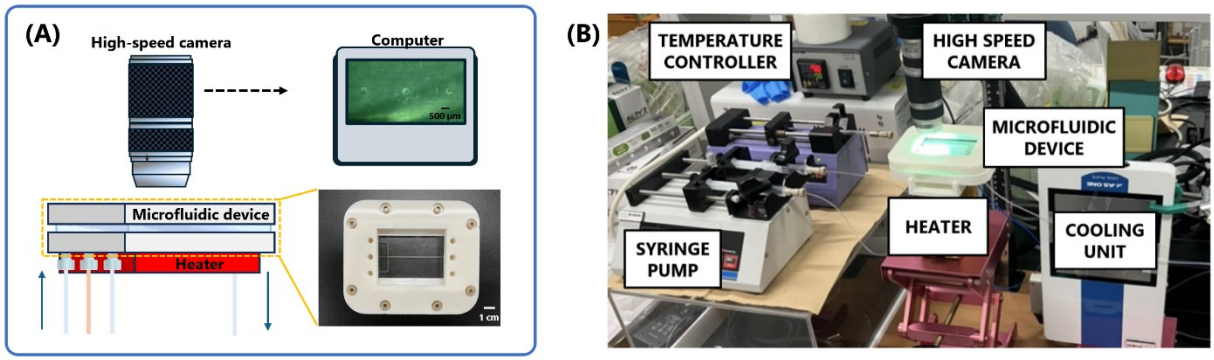


Fig. S4 (A) Schematic illustration of an experiment to observe continuous monodisperse droplet formation. (B) Overall view of the experimental apparatus.

Table S1 Physical properties used to predict droplet size (Q_c:Q_d = 1:99)

Entry	Q_c [µl min^{-1}]	Q_c [m^3 sec^{-1}]	$\bar{Q}_c$ [a] [-]	$\bar{D}$ [b] [-]	D [µm]	D_{exp} [c] [µm]
1	99.0	1.65×10^{-9}	0.3568	3.19	638.2	686.3 ± 2.7
2	198.0	3.30×10^{-9}	0.7136	2.59	517.1	564.3 ± 2.9
3	297.0	4.95×10^{-9}	1.0704	2.22	444.2	463.5 ± 4.2
4	396.0	6.60×10^{-9}	1.4272	1.99	397.0	402.7 ± 6.3
5	495.0	8.25×10^{-9}	1.7840	1.82	364.5	298.8 ± 47.3

[a] $\bar{Q}_c = 3\eta_c Q_c / (\text{Area}_d \gamma)$, where η_c = 2.038 ± 0.001 [mPa·s] and γ = 1.414 ± 0.011 [mN m^{-1}].

[b] $\bar{D} = \dfrac{-\bar{Q}_c + \sqrt{\bar{Q}_c^{\,2} + 4\text{Ca}_{cri}\left(\text{Ca}_{cri}\bar{w}_{or}^{\,2} + \bar{Q}_c\right)}}{2\text{Ca}_{cri}}$, where Ca_{cri} = 0.1 [-] and $\bar{w}_{or} = \sqrt{\text{Area}_c / \text{Area}_d}$ = 4.24 [-].

[c] $D_{exp} = \bar{D} \times w_d$

η_c is the continuous phase-viscosity at 80 °C measured using ubbelohde viscometer (n = 5), and γ is the interfacial tension measured by pendant drop method (n = 5). Area_c and Area_d were defined as a cross-sectional area of a collection microchannel and a cross-sectional area of dispersion phase, respectively.

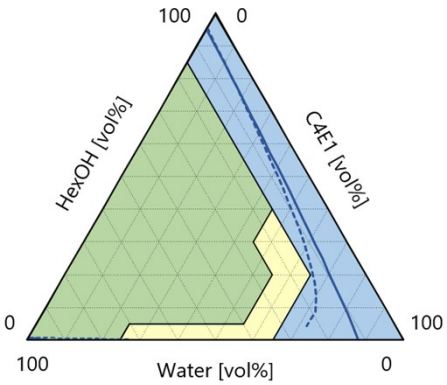


Fig. S5 Ternary phase diagram of 1-hexanol-water-C4E1. The blue solid line showed a COSMOtherm-predicted liquid-liquid equilibrium curve at 70°C. The blue dashed line showed a COSMOtherm-predicted liquid-liquid equilibrium curve at 25°C. The blue area indicated compositions that showed two-phase separation in the range from 25 °C to 70 °C; the pale-yellow area indicated compositions that exhibit a two-phase to one-phase phase transition as the temperature decrease from 70 °C to 25 °C; the green area indicated compositions that showed one-phase in the range from 25 °C to 70 °C.

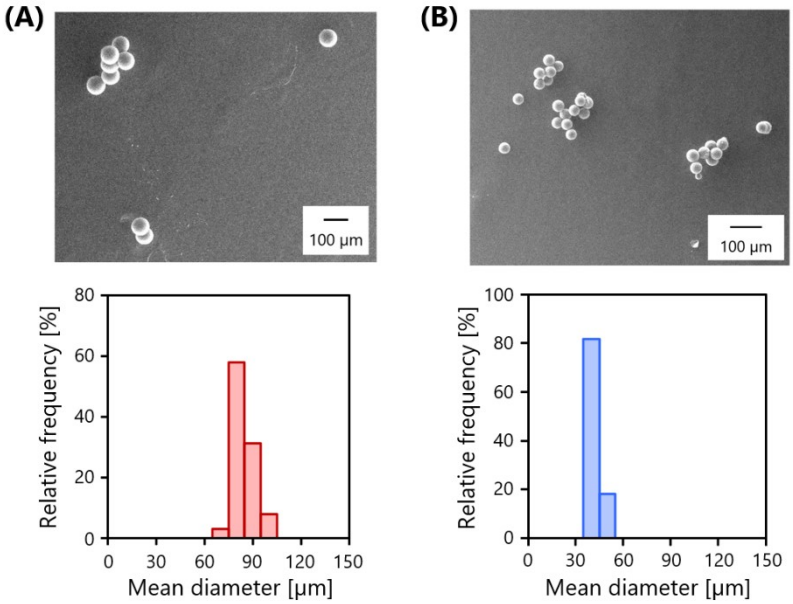


Fig. S6 SEM images of monodisperse particles fabricated by 1-hexanol-water-C4E1 ternary mixture and their size distribution histograms. (A) PVA particles (79.6 µm, CV = 6.9 %). (B) SA particles (38.4 µm, CV = 7.6 %).

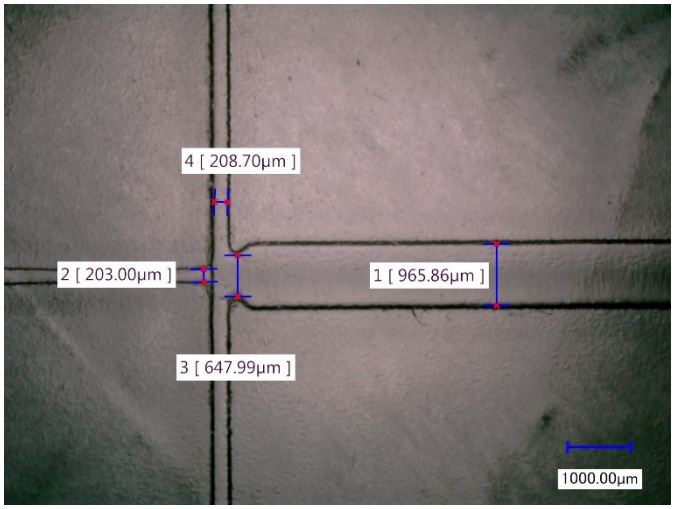


Fig. S7 Enlarged view of microflow pathway with narrow continuous phase route.
(The height of the inlet channel (h_d) = 100 µm, The height of the collection channel (h_c) = 200 µm)

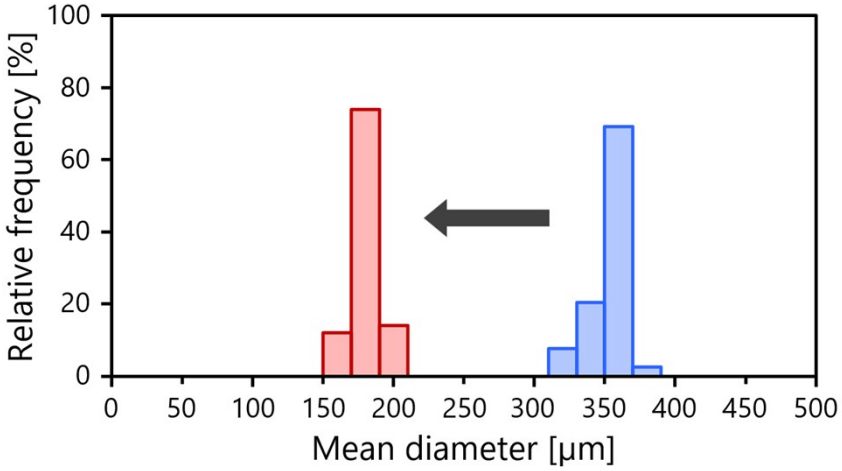


Fig. S8 Size distribution histogram of droplets. Generated large droplets using microfluidic device with wide pathway (blue). Generated small droplets using microfluidic device with narrow pathway (red).