Electronic Supplementary Material (ESI) for Green Chemistry.

First Evidence of Metal Transfer into Hydrophobic Deep Eutectic and Low-Transition-Temperature Mixtures: Indium Extraction from Hydrochloric and Oxalic Acids

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Materials, preparation, extraction method and analyses

Materials

Tetraheptylammonium chloride, indicated as $(C_7H_{15})_4NCl$ (95% purity); DL-menthol; decanoic, lauric, and oleic acids (> 98% purity); (RS)-2-(4-(2-methylpropyl)phenyl)propanoic acid (ibuprofen, 98% purity); oxalic acid; diethylene triamine pentaacetic acid; kerosene; hydrochloric acid; sodium hydroxide; and anhydrous indium chloride salt were purchased from VWR. Concentrated hydrochloric acid was of analytical grade. All chemical reagents were used as received without any further purification. Deionized water from a PURELAB flex purification system (ELGA) with a resistivity of 18.2 MΩ cm was used for solution preparation and dilutions.

Indium radionuclide

Carrier-free ^{111}In (half-life 2.8047 d, 245 keV gamma-ray, 94% intensity) medical radioisotope (~10 mCi) was purchased from Mallinckrodt (St. Louis, Missouri, USA). The production method was ^{112}Cd(p,2n)^{111}In. The material was received as indium chloride in 0.05 M HCl. The ^{111}In concentration per sample in our experiments after multistep dilution was below 1×10^{-11} M. This amount of ^{111}In provided an optimal level of the activity for gamma counting of each phase after extraction.

DES and LTTM preparation

The three deep eutectic solvents (DESs) and one low-transition-temperature mixture (LTTM) were all prepared following the same experimental method. The weighed amounts of hydrogen bond donor and acceptor were taken in a given molar ratio and placed together in a flask: $(C_7H_{15})_4NCl$ and decanoic acid (1:2 molar ratio); $(C_7H_{15})_4NCl$ and oleic acid (1:2 molar ratio); $(C_7H_{15})_4NCl$ and ibuprofen acid (7:3 molar ratio); DL-menthol and lauric acid (2:1 molar ratio). The flask was then heated for at least 30 min in a water bath at a temperature of 60 °C with a periodical mixing of the contents. After the mixture of two compounds became a completely clear and homogeneous liquid, it was cooled down to room temperature. The prepared mixtures were liquids at room temperature, immiscible with water and had densities below that of water.

Extraction sample preparation and technical procedure

The distribution of In was measured by a standard liquid-liquid extraction technique. Typically, equal volumes of organic and aqueous phases were used (0.5 mL each, 1:1 phase ratio). The aqueous phases were obtained by dilution of concentrated HCl. The pH of the solutions was adjusted with NaOH and measured by a SympHony pH-meter (VWR). After both phases were placed into a test tube, the aqueous phase was spiked with an aliquot of the radioactive In stock solution. The biphasic system was shaken mechanically (VWR Signature digital vortex mixer) at 3000 rpm for 5 min (unless stated otherwise) at room temperature and then separated by centrifuging at 4000 rpm for 1 min (Eppendorf model 5702). Then, an aliquot was taken from each phase to determine the indium concentration or activity. Stable In was used to determine effect of pH on the extraction of this metal and measured as described below. In all other experiments, radioactive ^{111}In was applied and the activity ratio was used to calculate distribution ratios. See Fig. S1 for extraction data using the components of the mixtures studied in the current work.

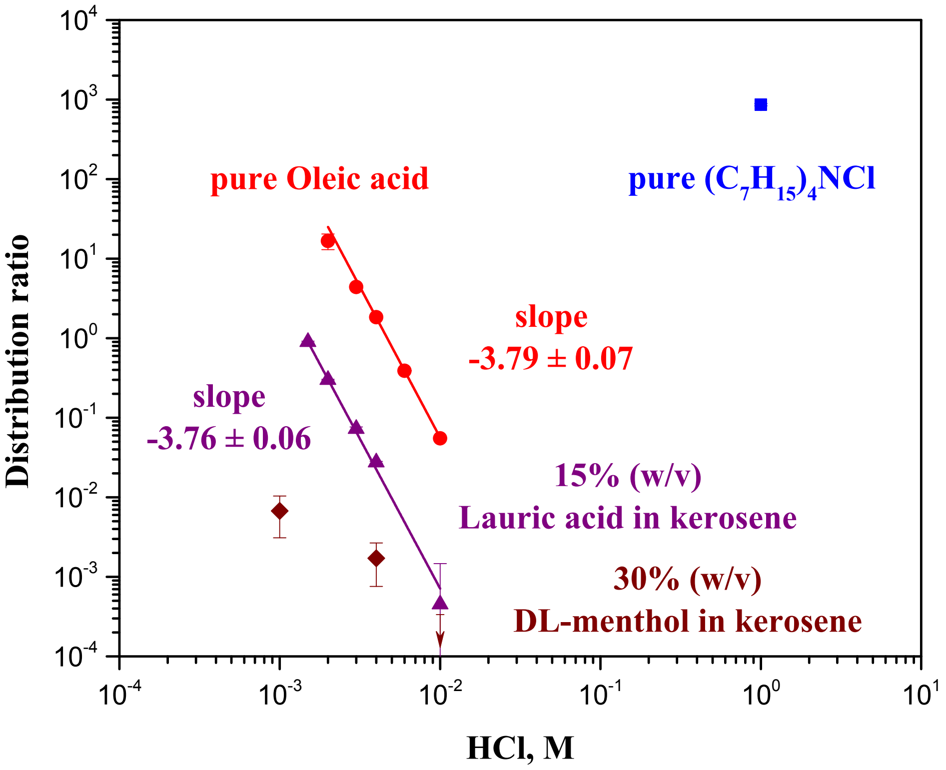

Figure S1: Distribution ratio of ^{111}In between HCl solution and individual compounds used for DES/LTTM preparation.

A PerkinElmer automatic gamma counter with an NaI detector was used to determine the ^{111}In activity level in the samples. An example spectrum is shown in Fig. S2. The stable In concentration in the stock and work solutions was determined by inductively coupled plasma mass-spectroscopy (ICP-MS, Agilent 7500i) after dilution with a 1% HCl solution to a concentration suitable for measurements.

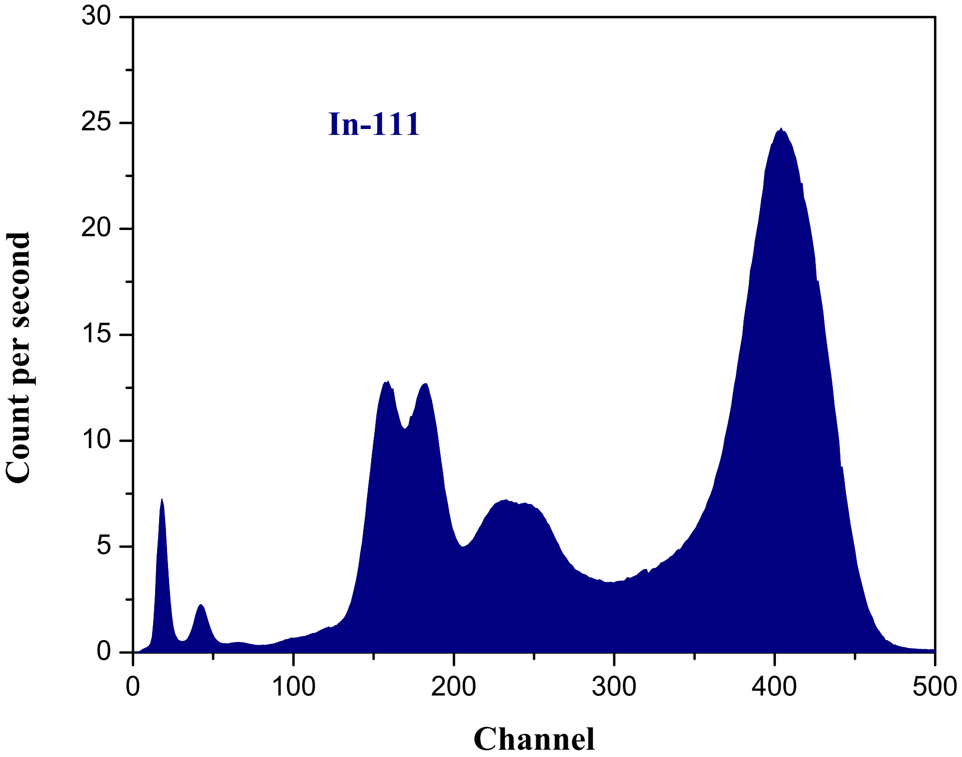

Figure S2: Gamma-spectrum of In-111 from NaI detector.

Only statistical errors in gamma-ray counts were plotted, and systematic experimental errors are estimated to be at a level of 10%; the ICP-MS errors are 4%. The experiments were generally repeated twice and some, especially with high *D* values, were carried out in triplicate.

In(III) loading

The method of determining the maximum concentration of In in the organic phase was as follows. Aliquots of stable In stock solution in 1 M HCl for tetraalkylammonium-based mixtures and in 4×10^{-3} M HCl for menthol-based DES were mixed with an organic phase to cover metal concentrations in the range from 1×10^{-6} to 5 M and spiked with radioactive ^{111}In. After extraction, the metal activity in each phase was measured as described above.

Back-extraction

After the ^{111}In forward extraction, an aliquot of the deep eutectic mixture was placed in a plastic tube, and an equal volume of either 0.2 M HCl or 0.1 M diethylene triamine pentaacetic acid (DTPA) was added (volume ratio 1:1). Then, the same procedure as in the case of forward extraction was applied.

Physicochemical properties

All kinematic viscosities were measured on a Cannon-Ubbelohde Size 400 viscometer. A 10 mL graduated cylinder suspended in a temperature-controlled water bath and a top loading scale to measure the weight of sample was used to determine densities. All viscosity and density measurements were performed in the range from 25 to 70 °C with 15 °C increments. The water content in the prepared mixtures was measured with the Karl Fischer titration method (907 Titrando Metrohm Karl Fischer). The results are given in Tables S1, S2 and S3.

Table S1: Physicochemical properties of studied mixtures measured at 25 °C

Mixture	**Kinematic viscosity, cS**	**Density, g/mL**	**Water content**		**Reference**
			Dry, wt %	**Water saturated, wt %**	
$(C_7H_{15})_4NCl$-Ibuprofen	1029.0 ± 1.0	0.892 ± 0.009	1.63 ± 0.05	9.99 ± 0.04	This work
$(C_7H_{15})_4NCl$-Oleic acid	244.7 ± 0.4	0.867 ± 0.009	0.88 ± 0.02	3.09 ± 0.15	This work
$(C_7H_{15})_4NCl$-Decanoic acid	194.08	0.8907	0.774	2.3387	Ref. 15
DL-menthol-Lauric acid	27.312	0.894	0.276	1.237	Ref. 16

Table S2: Kinematic viscosities (cS) of studied mixtures as a function of temperature

Mixture	**Temperature, °C**				**Reference**
	25	**40**	**55**	**70**	
$(C_7H_{15})_4NCl$-Ibuprofen	1029.0 ± 1.0	400.1 ± 0.4	181.7 ± 0.3	96.67 ± 0.11	This work
$(C_7H_{15})_4NCl$-Oleic acid	244.7 ± 0.4	121.01 ± 0.06	67.69 ± 0.02	41.64 ± 0.04	This work
$(C_7H_{15})_4NCl$-Decanoic acid	194.08	93.89	–	–	Ref. 15
DL-menthol-Lauric acid	27.312	12.971	7.242	4.485	Ref. 16

Table S3: Densities (g/mL) of studied mixtures as a function of temperature

Mixture	**Temperature, °C**				**Reference**
	25	**40**	**55**	**70**	
$(C_7H_{15})_4NCl$-Ibuprofen	0.892 ± 0.009	0.882 ± 0.009	0.873 ± 0.009	0.863 ± 0.009	This work
$(C_7H_{15})_4NCl$-Oleic acid	0.867 ± 0.009	0.852 ± 0.009	0.843 ± 0.008	0.834 ± 0.008	This work
$(C_7H_{15})_4NCl$-Decanoic acid	0.8907	0.8811	–	–	Ref. 15
DL-menthol-Lauric acid	0.894	0.883	0.872	0.861	Ref. 16

DSC

Differential scanning calorimetry (TA instruments, DSC Q20) was used to measure melting points and solid-solid transition temperatures of the prepared mixtures. The operating temperature range of the DSC is -180 to 725 °C. The measurements were conducted within a temperature range of -112 to 104 °F (-80 to 40 °C) at a heating rate of 5 °F/min (2.8 °C/min). The temperature measurement is accurate within ±0.1 °C. The calorimeter precision and sensitivity are ±0.1% and 1 µW, respectively. The resulting thermograms are shown in Figs. S3, S4 and S5.

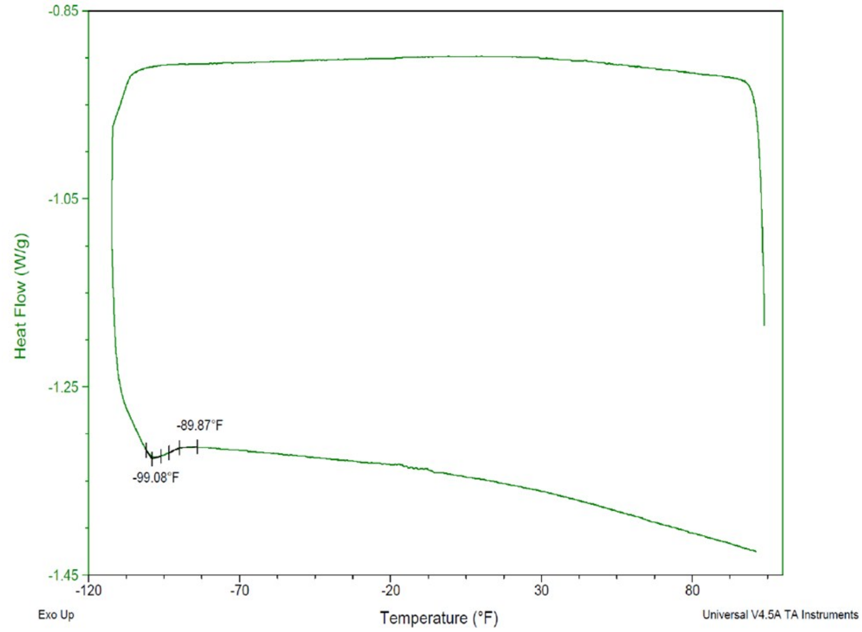

Figure S3: DSC thermogram of $(C_7H_{15})_4NCl$-Ibuprofen LTTM

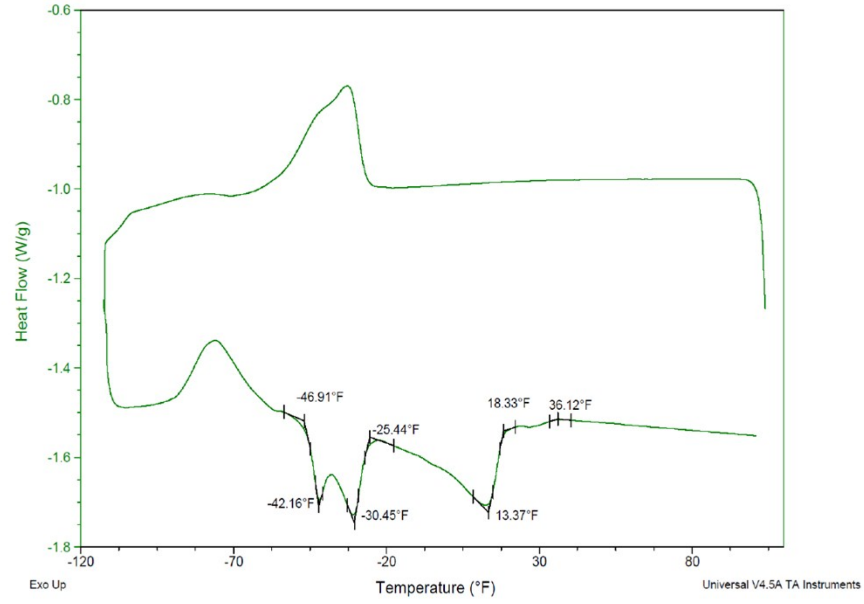

Figure S4: DSC thermogram of $(C_7H_{15})_4NCl$-Oleic acid DES

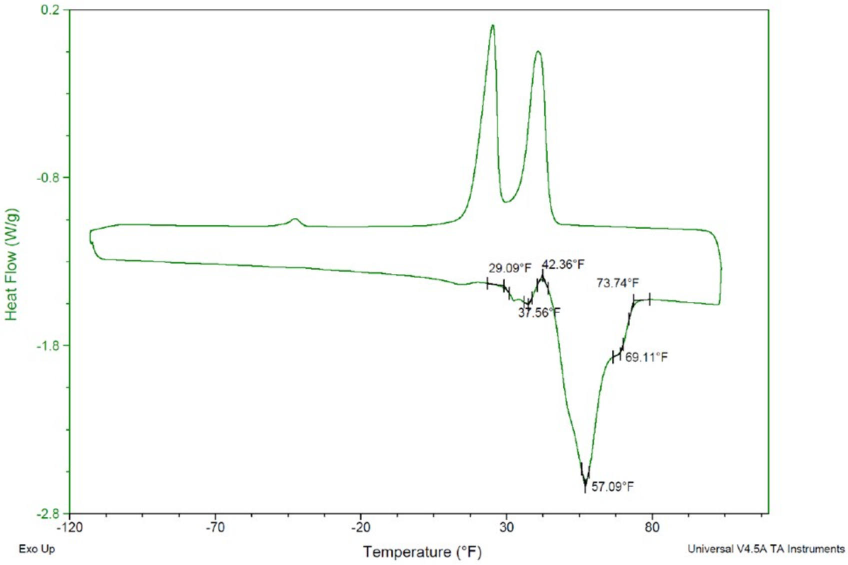

Figure S5: DSC thermogram of DL-menthol-Lauric acid DES

The DSC thermogram of the $(C_7H_{15})_4NCl$-Decanoic acid DES is given in Ref. 15 (see main text).

FTIR

All Fourier transformed infrared (FTIR) spectra were recorded on a Nicolet Impact 400D FT-IR spectrometer coupled with Omnic data collection software. All samples were scanned over a wavenumber range of 500 to 4000 cm^{-1}. The spectra of the mixtures were recorded in 16 scans. Samples of $(C_7H_{15})_4NCl$-Oleic acid and $(C_7H_{15})_4NCl$-Ibuprofen were placed in between NaCl plates for IR scans with the following parameters: resolution 8.000, sample gain 4.0, mirror velocity 0.6329, aperture 1.0, detector DTGS KBr, beamsplitter KBr.[1] The results are shown in Figs. S6 and S7. FTIR spectra of the $(C_7H_{15})_4NCl$-Decanoic acid and Menthol-Lauric acid DESs are given in Ref. 15 and Ref. 16, respectively (see main text).

The representative peak of carboxylic acid group of Oleic acid and Ibuprofen Acid (1715 cm^{-1} and 1710 cm^{-1} for the C=O group, respectively) can be also observed in the corresponding mixtures, where C=O group signals are slightly shifted by 20 cm^{-1} to the left. The peaks of hydroxyl group involved in the H-bonding are shifted and much broader in case of acids alone (2500-3500 cm^{-1} for the O-H groups of pure carboxylic acids).

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[1] FTIR spectra of oleic acid and ibuprofen were taken from http://sdbs.db.aist.go.jp/sdbs/cgi-bin/direct_frame_top.cgi
FTIR spectrum of tetraheptylammonium chloride was taken from http://www.sigmaaldrich.com/catalog/product/aldrich/419907?lang=en&region=US

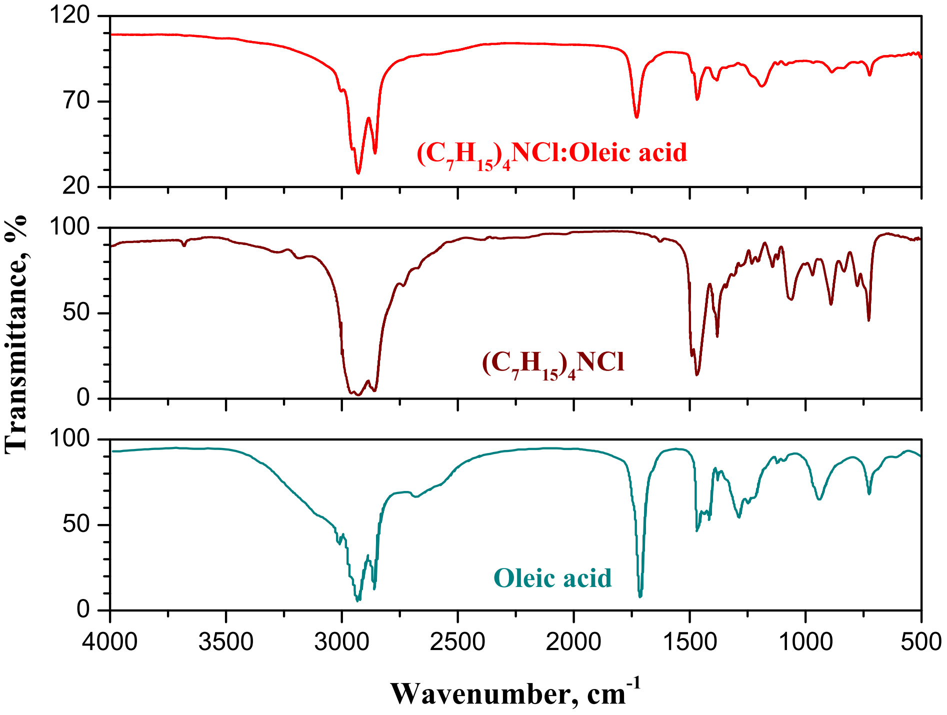

Figure S6: Stacked FTIR spectra of $(C_7H_{15})_4NCl$-Oleic acid DES and individual compounds.

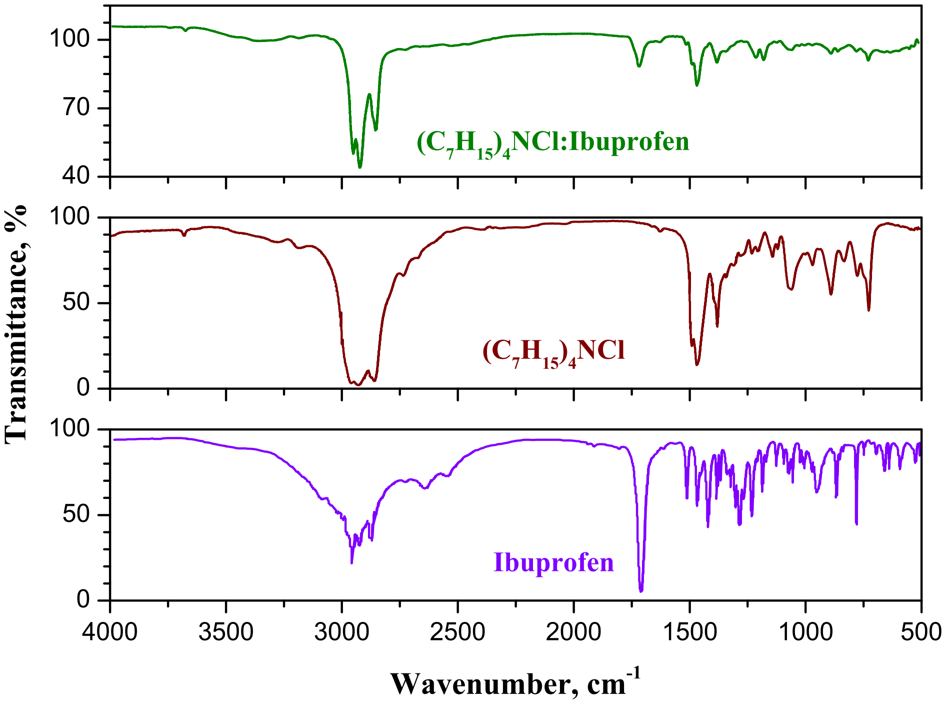

Figure S7: Stacked FTIR spectra of $(C_7H_{15})_4NCl$-Ibuprofen LTTM and individual compounds.

Ion Chromatography

The chloride concentration in the aqueous phase was measured with an IonPac AS11-HC Analytical Column (Dionex DX-600 IC/HPLC system) and Chromeleon software. Each mixture was in contact with pure water (no metal added) for at least several hours. The results are shown in Table S4.

Table S4: Results on DESs/LTTM solubility in water

Mixture	C_{anion}, mg/L	C_{anion}, mM	$m_{salt\ leached}/m_{salt\ mixture}$, mg/g	Reference
$(C_7H_{15})_4NCl$-Ibuprofen	324 ± 7	9.14 ± 0.20	4.89 ± 0.11	This work
$(C_7H_{15})_4NCl$-Oleic acid	1000 ± 4	28.21 ± 0.11	28.52 ± 0.11	This work
$(C_7H_{15})_4NCl$-Decanoic acid	1040	29.3	23.2	Ref. 15
DL-menthol-Lauric acid	328 ± 22*	2.10 ± 0.14*	0.54 ± 0.04*	This work

*This value was determined for DL-menthol by the qNMR technique described below

NMR spectra

Menthol-Lauric acid DES

The water solubility of DL-menthol and the DL-menthol-Lauric acid DES was determined using quantitative proton (^1H) nuclear magnetic resonance (qNMR) measurements. NMR spectra were recorded using a Bruker Avance 300 MHz spectrometer operated at room temperature. Aqueous phases were prepared by stirring of a small amount of DL-menthol and the DL-menthol-Lauric acid DES with heavy water (D_2O) for 1 h. The mixtures were then centrifuged for 5 min at 7000 rpm. Aliquots of the sample (590 µL) and an internal standard (20 µL, maleic acid solution in D_2O, 108.7 mM, δ_H = 6.3 ppm) solution were placed in a standard 5 mm NMR tube. The results of pure DL-menthol and menthol-based DES solubility in water are presented in Fig. S8/Table S5 and Fig. S9/Table S6, respectively. The menthol structure formula is drawn in the spectra. Each carbon atom is numbered and assigned to the appropriate peaks or peak groups, displayed in the tables. In this section, *f1* and δ (for figures and tables, respectively) are considered the chemical shift compared to the internal reference. The degree of leaching of DL-menthol to the water phase after mixing was determined from a decrease in the integral of the peaks.

Aqueous phase NMR spectrum after pure DL-menthol mixing with water

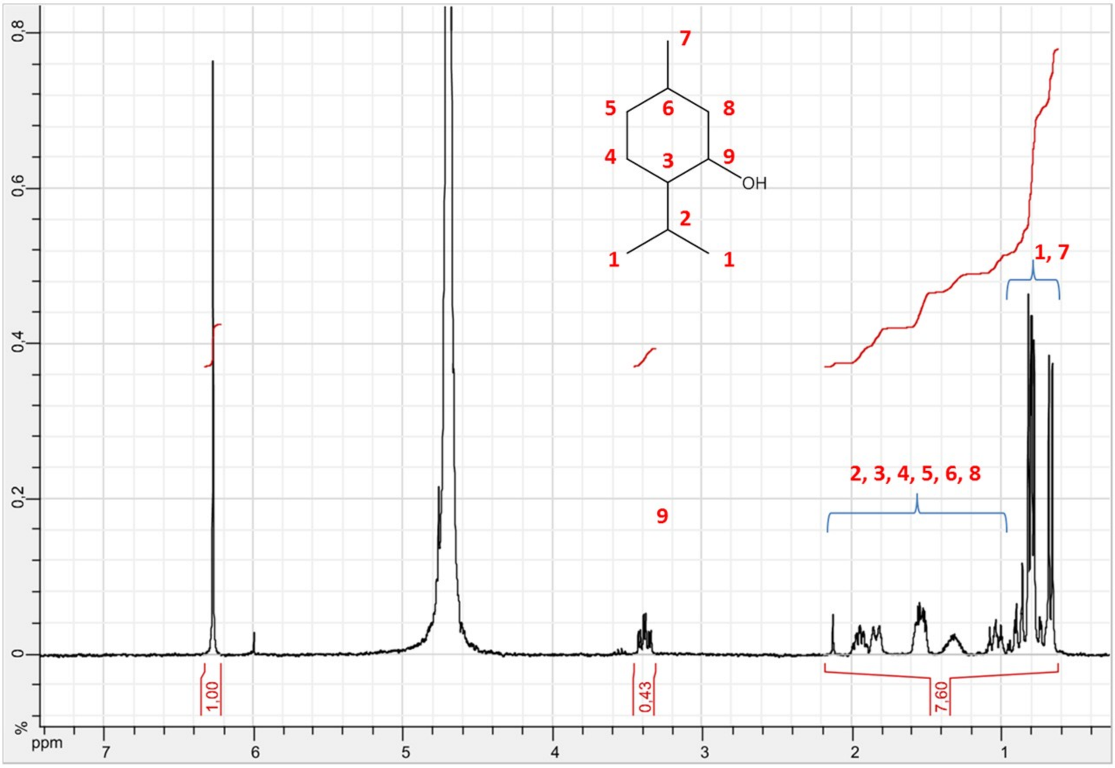

Figure S8: ^{1}H NMR spectra of DL-menthol and maleic acid in D_2O.

Table S5: Peak assignments and integrals of the ^{1}H-NMR spectrum of the DL-menthol solution in D_2O.

Maleic acid		DL-Menthol			Pure DL-menthol solubility, mM
	δ (ppm)	Group	δ (ppm)	I_X/I_{std}	
2 CH	6.3	C(9)H	3.35 – 3.43	0.43	3.1
		$2C(1)H_3$, C(2,3,6)H, $C(4,5,8)H_2$, $C(7)H_3$	0.66 – 2.13	0.76	3.1

The aqueous concentration of DL-menthol was calculated by the following equation:

$$C_X = (I_X/I_{std})(N_{std}/N_X)(V_{std}/V_X)C_{std}$$

where I, N, V and C are integral area, number of protons, aliquot volume and concentration of analyte (X) and standard (std), respectively.[2]

Literature data (see Ref. 16 in the main text) gives the water solubility of DL-menthol as 2.9 mM, in agreement with our result.

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[2] S. K. Bharti and R. Roy, *Trends Anal. Chem.*, 2012, **35**, 5-26.

Aqueous phase NMR spectrum after DL-menthol-Lauric acid DES mixing with water

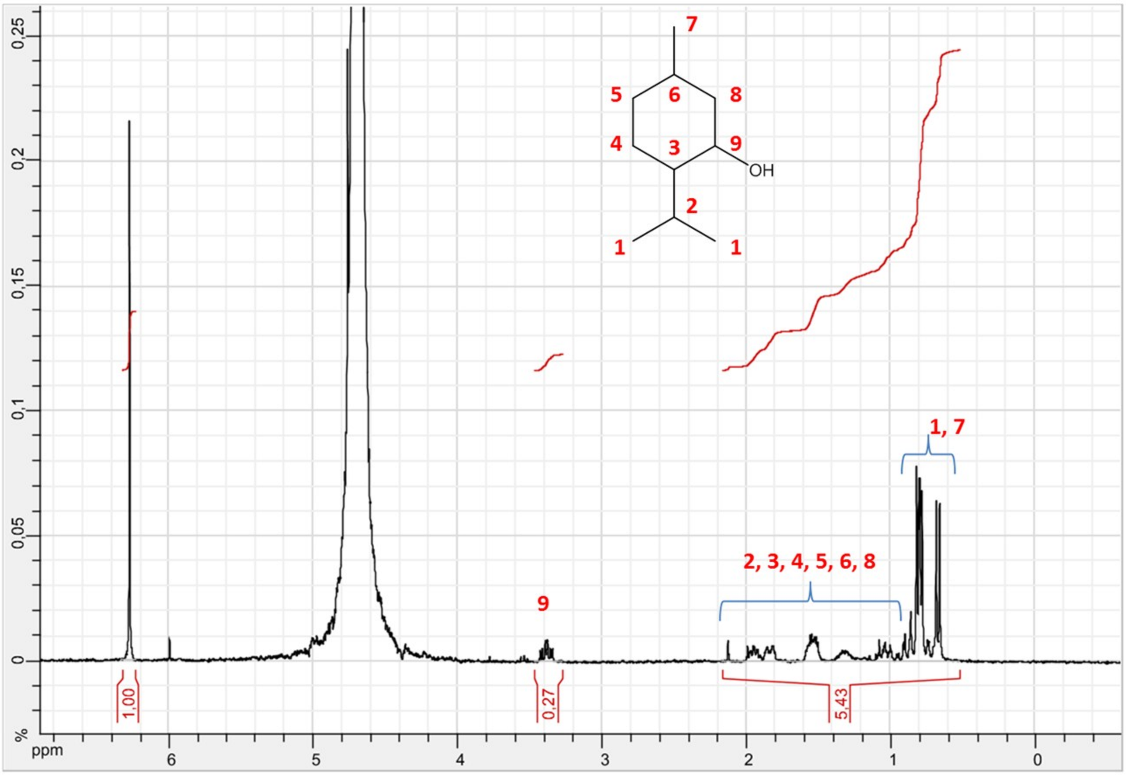

Figure S9: ^1H NMR spectra of the aqueous phase obtained by contact of DL-menthol-Lauric acid DES and D_2O.

Table S6: Peak assignments and integrals of the ^1H-NMR spectrum of aqueous phase obtained by contact of DL-menthol-Lauric acid DES and D_2O.

Maleic acid		DL-Menthol			DL-menthol solubility from DES, mM
	δ (ppm)	Group	δ (ppm)	I_X/I_{std}	
2 CH	6.3	C(9)H	3.35 – 3.43	0.27	2.0
		$2C(1)H_3$, C(2,3,6)H, $C(4,5,8)H_2$, $C(7)H_3$	0.66 – 2.13	5.43	2.2

Thus, concentration of DL-menthol leached from a corresponding DES into water was estimated to be 2.10 ± 0.14 mM. Lauric acid was not detected with ^1H NMR spectroscopy in the aqueous solution obtained by contact of DL-menthol-Lauric acid DES and D_2O because of its very low water solubility, 2.4×10^{-5} M.[3]

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[3] http://www.sigmaaldrich.com/catalog/product/aldrich/w261408?lang=en&region=US

Tetraalkylammonium-based mixtures

In the case of ammonium-based mixtures ^{1}H-NMR spectra were recorded at 300 K on a 500 MHz Bruker Avance 500. All samples were prepared in plastic tubes with 700 μL of deuterated dimethyl sulfoxide (DMSO-d_6) to which 5 μL of mixtures and 5 μL of toluene were added. In order to study the mixture solubilities, each mixture was in contact with an equal volume of deuterated water for 17 h and shaken mechanically at 3000 rpm. Afterwards, 5 μL of the mixtures was added to a system of DMSO with toluene. The system was shaken mechanically at 3000 rpm for 10 min at room temperature and then centrifuged at 4000 rpm for 1 min. All samples were placed without further pretreatment inside 8" (20 cm) Wilmad precision tubes with an outer diameter of 5 mm. A relaxation time of 1 s was applied and the spectra were recorded in 16 scans. The software NMRnotebook, version 2.70 (NMRTEC) was used to perform Fourier transformation of signals and further adjustments. Phase corrections, baseline correction and integrals were done manually.

In this section, *f1* and δ are considered the chemical shift compared to the internal reference toluene. The structure formulas of each mixture are drawn in the spectra. Each carbon atom is numbered and assigned to the appropriate peaks or peak groups, displayed in the tables.

The degree of leaching of salt from the mixture to the water phase after mixing was determined from a decrease in the integral of the groups that can be assigned to the protons of the quaternary ammonium salt and toluene. However, it should be noted that the accuracy of the integrals for specific peaks is not high enough to determine the loss quantitatively. This is mainly caused by overlap of the peaks of oleic acid and ibuprofen and the ammonium chloride salt in the region of chemical shifts between 0 and 2 ppm, and the overlap of water and the quaternary ammonium salts in the 3-4 ppm region. The presence of water in the NMR samples can be attributed to the usage of DMSO-d_6 that absorbed some water from the ambient air.

The results before and after mixing with water are presented in Figs. S10-S13 and Tables S7-S10.

$(C_7H_{15})_4NCl$-Oleic acid (1:2), before mixing with water

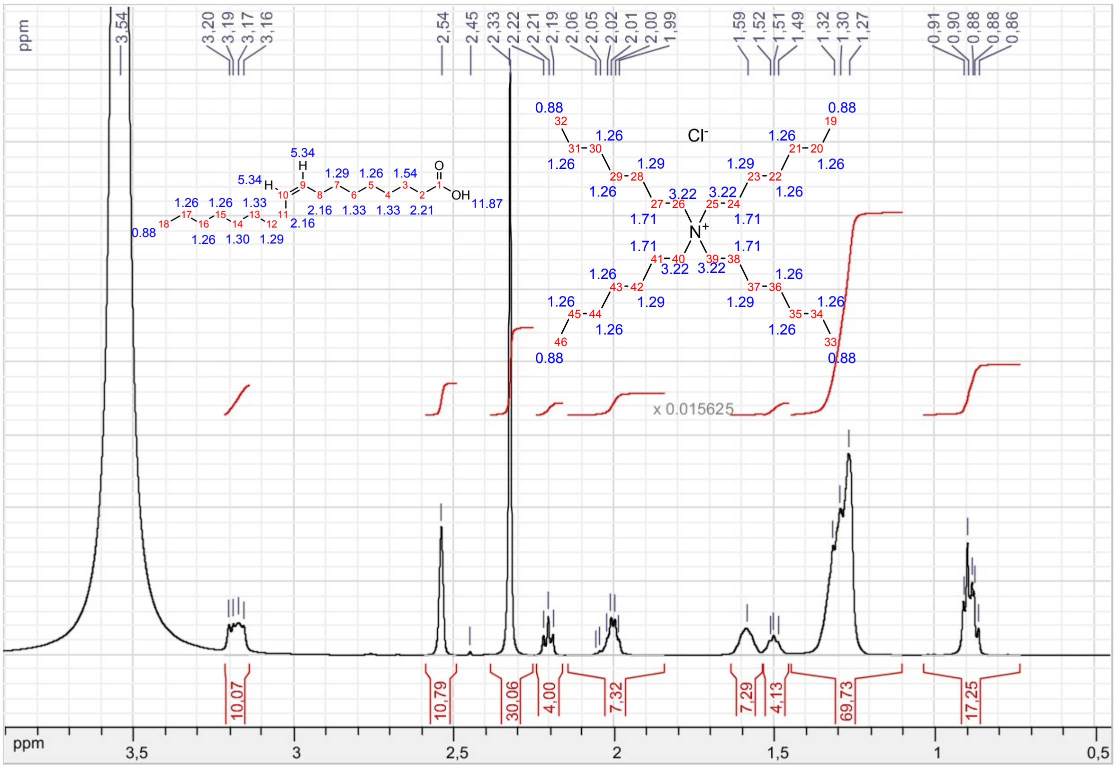

Figure S10: ^{1}H-NMR spectrum of $(C_7H_{15})_4NCl$-Oleic acid (1:2) before mixing with water.

Table S7: Peak assignments and integrals of the^{1}H-NMR spectrum of $(C_7H_{15})_4NCl$-Oleic acid (1:2) before mixing with water

Groups		**Before mixing with water**		
Oleic acid	**$(C_7H_{15})_4NCl$**	**Expected integral**	**δ (ppm)**	**Integral**
2 $C(18)H_3$	$C(19,32,33,46)H_3$	18	0.86 – 0.91	17.25
2 $C(4, 5, 6, 7, 12, 13, 14, 15, 16, 17)H_2$	$C(20–23, 28–31, 34–37, 42–45)H_2$	72	1.27 – 1.32	69.73
2 $C(3)H_2$	–	4	1.49 – 1.52	4.13
–	$C(24, 27, 38, 41)H_2$	8	1.59	7.29
2 $C(8, 11)H_2$	–	8	1.99 – 2.06	7.32
2 $C(2)H_2$	–	–	2.19 – 2.22	4
Toluene	–	–	2.33	30.06
DMSO	–	–	2.54	–
–	$C(25, 26, 39, 40)H_2$	8	3.16 – 3.20	10.07
Water	–	–	3.54	–

$(C_7H_{15})_4$NCl-Oleic acid (1:2), after mixing with water

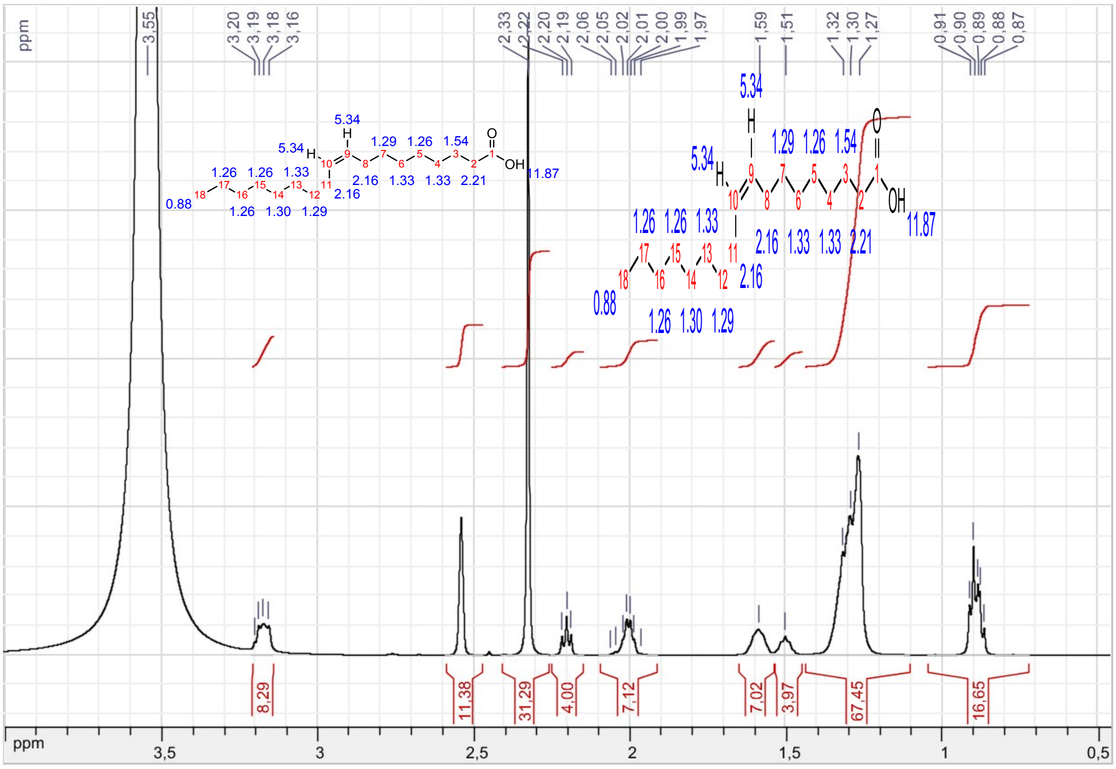

Figure S11: ^{1}H-NMR spectrum of $(C_7H_{15})_4$NCl-Oleic acid (1:2) after mixing with water.

Table S8: Peak assignments and integrals of the^{1}H-NMR spectrum of $(C_7H_{15})_4$NCl-Oleic acid (1:2) after mixing with water

Groups		After mixing with water		
Oleic acid	**$(C_7H_{15})_4$NCl**	**Expected integral**	**δ (ppm)**	**Integral**
2 C(18)H_3	C(19,32,33,46)H_3	18	0.86 – 0.91	16.65
2 C(4, 5, 6, 7, 12, 13, 14, 15, 16, 17)H_2	C(20–23, 28–31, 34–37, 42–45)H_2	72	1.27 – 1.32	67.45
2 C(3)H_2	–	4	1.49 – 1.52	3.97
–	C(24, 27, 38, 41)H_2	8	1.59	7.02
2 C(8, 11)H_2	–	8	1.99 – 2.06	7.12
2 C(2)H_2	–	–	2.19 – 2.22	4
Toluene	–	–	2.33	31.29
DMSO	–	–	2.54	–
–	C(25, 26, 39, 40)H_2	8	3.16 – 3.20	8.29
Water	–	–	3.54	–

$(C_7H_{15})_4NCl$-Ibuprofen (7:3), before mixing with water

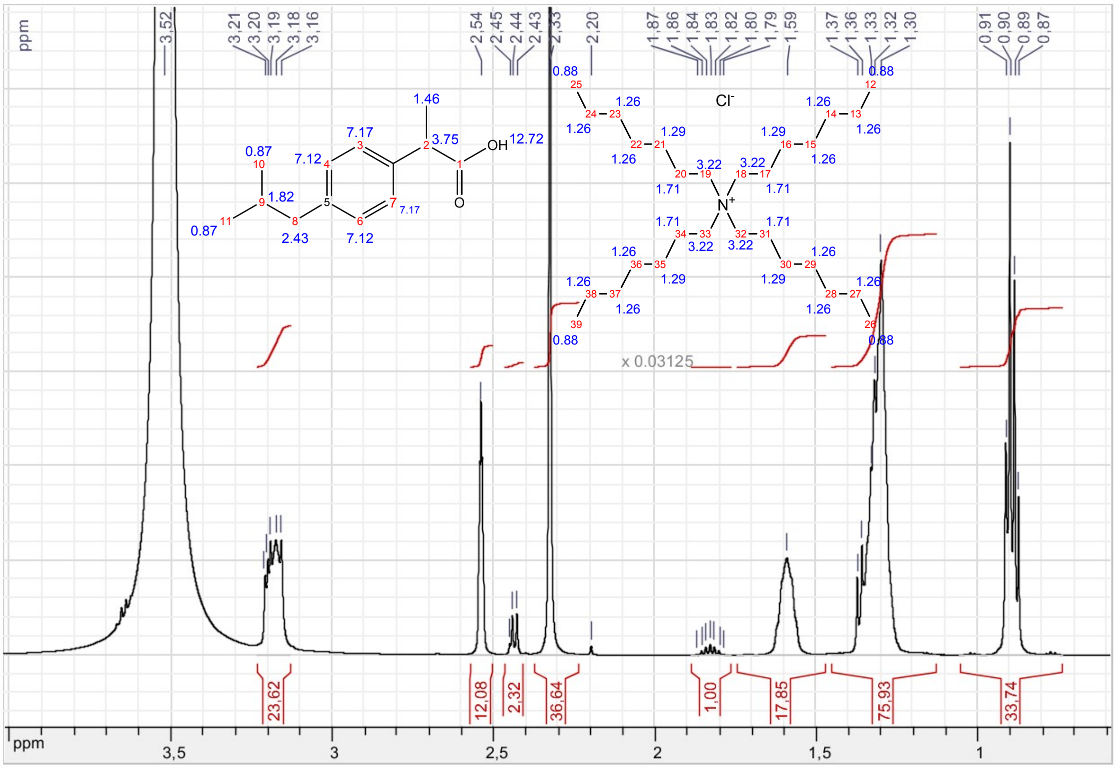

Figure S12: ^1H-NMR spectrum of $(C_7H_{15})_4NCl$-Ibuprofen (7:3) before mixing with water.

Table S9: Peak assignments and integrals of the^1H-NMR spectrum of $(C_7H_{15})_4NCl$-Ibuprofen (7:3) before mixing with water

Groups		**Before mixing with water**		
Ibuprofen	**$(C_7H_{15})_4NCl$**	**Expected integral**	**δ (ppm)**	**Integral**
$C(10,11)H_3$	2.33 $C(12,25,26,39)H_3$	33.96	0.87 – 0.91	33.74
–	2.33 $C(13–16, 21–24, 27–30, 35–38)H_2$	74.56	1.30 – 1.37	75.93
–	2.33 $C(17, 20, 31, 34)H_2$	18.64	1.59	17.85
$C(9)H$	–	–	1.79 – 1.87	1
$C(8)H_2$	–	2	2.43 – 2.45	2.32
Toluene	–	–	2.33	36.64
DMSO	–	–	2.54	–
–	2.33 $C(25, 26, 39, 40)H_2$	18.64	3.16 – 3.21	23.62
Water	–	–	3.54	–

$(C_7H_{15})_4NCl$-Ibuprofen (7:3), after mixing with water

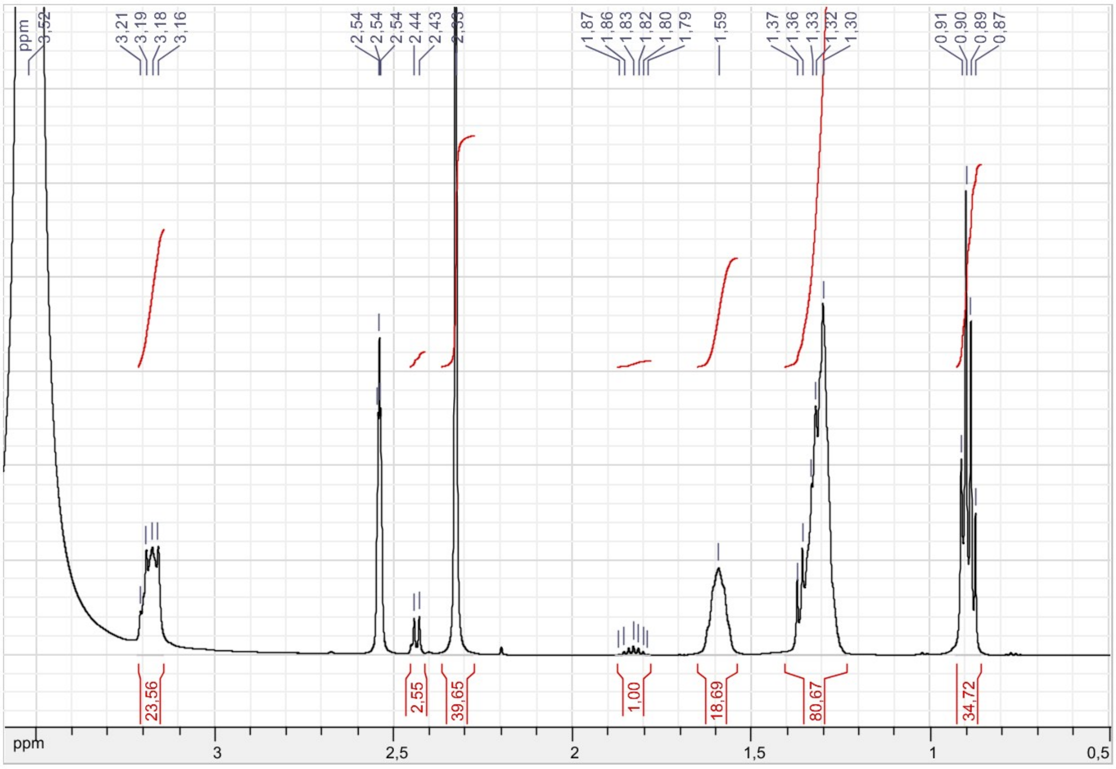

Figure S13: ^{1}H-NMR spectrum of $(C_7H_{15})_4NCl$-Ibuprofen (7:3) after mixing with water.

Table S10: Peak assignments and integrals of the^{1}H-NMR spectrum of $(C_7H_{15})_4NCl$-Ibuprofen (7:3) after mixing with water

Groups		**After mixing with water**		
Ibuprofen	**$(C_7H_{15})_4NCl$**	**Expected integral**	**δ (ppm)**	**Integral**
$C(10,11)H_3$	2.33 $C(12,25,26,39)H_3$	33.96	0.87 – 0.91	34.72
–	2.33 $C(13–16, 21–24, 27–30, 35–38)H_2$	74.56	1.30 – 1.37	80.67
–	2.33 $C(17, 20, 31, 34)H_2$	18.64	1.59	18.69
C(9)H	–	–	1.79 – 1.87	1
$C(8)H_2$	–	2	2.43 – 2.45	2.55
Toluene	–	–	2.33	–
DMSO	–	–	2.54	–
–	2.33 $C(25, 26, 39, 40)H_2$	18.64	3.16 – 3.21	23.56
Water	–	–	3.54	–

The loss of mixtures was estimated based on equation

$$Loss = \left(1 - \frac{I_a/I_{toluene,\,a}}{I_b/I_{toluene,\,b}}\right) \cdot 100\%\ ,$$

where *I* is an integral of corresponding peak and subscripts *a* and *b* represent conditions after or before mixing with water, respectively. The results for the two mixtures are presented in Tables S9 and S10.

Table S11: Peak assignments and integrals of the^{1}H-NMR spectrum of $(C_7H_{15})_4NCl$-Oleic acid (1:2) before and after mixing with water

Groups		Before mixing with water		After mixing with water		Loss, %
Oleic acid	**$(C_7H_{15})_4NCl$**	**δ (ppm)**	**Integral**	**δ (ppm)**	**Integral**	
2 $C(3)H_2$	–	1.49 – 1.52	4.13	1.49 – 1.52	3.97	8
–	$C(24, 27, 38, 41)H_2$	1.59	7.29	1.59	7.02	7
2 $C(8, 11)H_2$	–	1.99 – 2.06	7.32	1.99 – 2.06	7.12	7
2 $C(2)H_2$	–	2.19 – 2.22	4	2.19 – 2.22	4	4
Toluene		2.33	30.06	2.33	31.29	–

Table S12: Peak assignments and integrals of the^{1}H-NMR spectrum of $(C_7H_{15})_4NCl$-Ibuprofen (7:3) before and after mixing with water

Groups		Before mixing with water		After mixing with water		Loss, %
Ibuprofen	**$(C_7H_{15})_4NCl$**	**δ (ppm)**	**Integral**	**δ (ppm)**	**Integral**	
–	2.33 $C(13–16, 21–24, 27–30, 35–38)H_2$	1.30 – 1.37	75.93	1.30 – 1.37	80.67	2
–	2.33 $C(17, 20, 31, 34)H_2$	1.59	17.85	1.59	18.69	3
$C(9)H$	–	1.79 – 1.87	1	1.79 – 1.87	1	8
Toluene		2.33	36.64	2.33	39.65	–