Electronic Supplementary Material (ESI) for Green Chemistry.

Electronic Supplementary Information

Introduction to Zwitterionic Salts

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Materials and methods

N,N,N',N'-Tetramethylethylenediamine (Sigma-Aldrich, 99%), 1,3-propanesultone (Alfa Aesar, 99%), 2-bromoethanol (Alfa Aesar, 97%), 1-bromobutane (Sigma-Aldrich, 99%), 1-bromohexane (Aldrich 98%), acrylic acid (Acros Organics, 98%), were used without further purification.

Experimental

Instrumental procedures:

NMR spectroscopy. All NMR spectra were recorded on a Bruker Avance spectrometer DPX 300 at 27 °C, using deuterated water as solvent.

Mass spectrometry. ESMS measurements were carried out on a Waters LCT Premier instrument with an Advion TriVersa NanoMate injection system (cone voltage 50 V, source 120 °C). Both positive and negative ions were detected, with an m/z range of 50 to 1500. Samples were injected as dilute solutions in acetonitrile.

Differential scanning calorimetry (DSC). The melting points of the synthesised ZWSs were measured by DSC, using a TA Instruments Modulated DSC 2920. Cooling was accomplished by using a refrigerated cooling system capable of controlling the temperature down to 220 K. Dry nitrogen gas (flow rate of *ca*. 20 cm^3 min^{-1}) was purged through the DSC cell. For each sample, three scans were run with scan rates of 5 °C min^{-1}.

Thermogravimetric analysis (TGA). Decomposition temperature measurements were performed in a TA Instruments Q50 thermogravimetric analyser. The measurements were done in platinum pans, at a heating rate of 10 °C min^{-1}, in air. The onset of the weight loss in each thermogram was used as a measure of the decomposition temperature.

Solubilisation experiments were done by equilibrating ZWSs with organic solvents overnight at room temperature. The excess of solute was left to precipitate and then centrifuged, and the liquid solution was analysed by ^{1}H-NMR using an external standard.

Densitymeter. Density measurements were performed using a DM40 oscillating tube density meter (Mettler Toledo, accuracy: ± 1 x 10^{-4} g cm^{-3}) at 298.15 K (± 0.1 K). The instrument was cleaned using acetone and dried using dehumidified air prior to any measurements.

Solid-Liquid Equilibria. The solid-liquid equilibrium temperatures at atmospheric pressure were determined using following method: the mixtures of the ZWS and water were placed in a Pyrex glass cell. The exact composition of the mixture was determined gravimetrically (within an accuracy of 10^{-4} g). The cell was inserted in thermostatic water-bath or ethanol-bath cooled by adding liquid nitrogen or ice, respectively. After solidification, the samples were heated very slowly (5 °C·h^{-1} near the equilibrium temperature) with continuous stirring inside the cell during the melting process. The temperature at which the last crystal disappeared was taken as the temperature of the solid-liquid equilibrium. Temperature was measured by Omega Engineering thermocouple with 0.05% reading accuracy. Estimated error of the temperature measurement was ± 1 K.

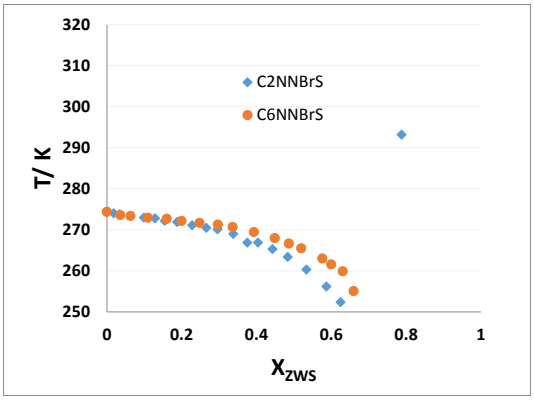


Figure S1. SLE of aqueous mixtures of •C_2NNBrS and ✸C_6NNBrS

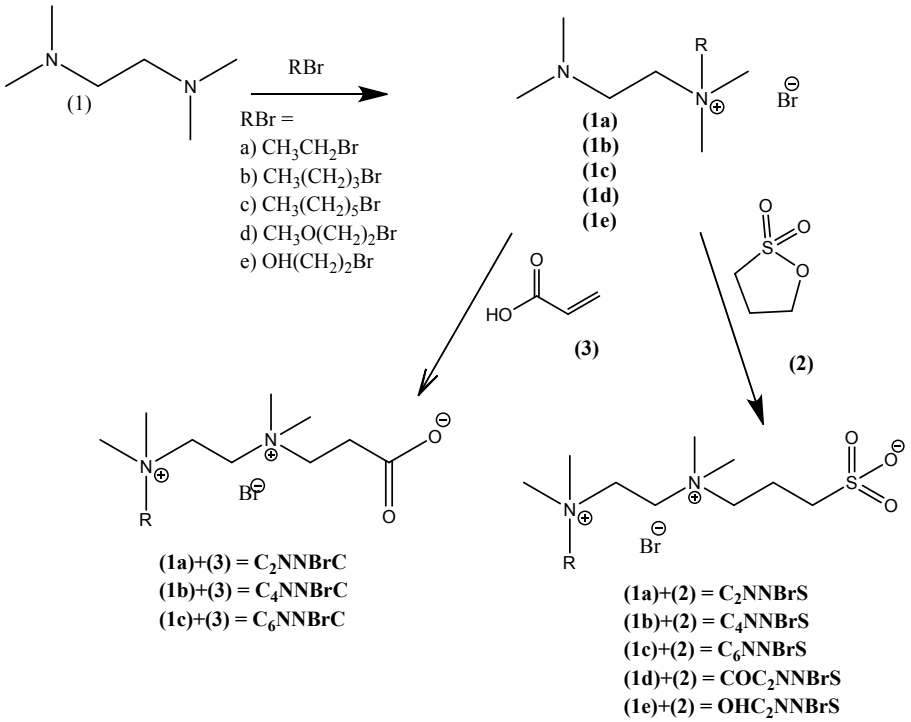
Vapour-Liquid Equilibria.

Before each measurement ZWS was dried under vacuum (pressure close to 1 Pa) for 24 h at 333 K.

A detailed description and a schematic presentation of the cell used for VLE was previously described[1]. Precisely known quantities of ZWS and water, previously degassed under vacuum and by successive melting and freezing cycles, are put in contact, under their own vapour pressure, inside a well-calibrated constant volume equilibrium cell. Herein, the exact composition of the liquid mixture is determined gravimetrically (within an accuracy of 10^{-4} g) when each component has been added into the equilibrium cell. To be able to record the vapour pressure of a given mixture, this cell is then connected to the measurement part of the whole equipment (which has been put previously under vacuum, *i.e.* pressure close to 1 Pa), which is based on an isochoric technique working under well-controlled conditions (*e.g.* constant volume and temperature)[1]. When the thermodynamic equilibrium is reached, the vapour pressure is recorded using a precise pressure transducer. To avoid any condensation issue, the whole equipment and the transducer are both housed inside an air thermostat whose temperature was controlled to within ±0.05 K. Pressure was measured using a pressure transducer from Omega Engineering (model PX409, operating pressure range from 0 to 1 bar within an uncertainty of 0.03% full scale).

General procedures for the synthesis of ZWs

All ZWSs were synthesised according to the synthetic scheme given below:



Scheme S1: Synthetic scheme for ZWSs

In a round bottom flask, N,N,N′,N′-tetramethylethylenediamine (1 eq.) and alkyl bromide (1 eq.) were added to dry acetone. The reaction mixture was stirred and heated at 25-40 °C. The progress of reaction was monitored by NMR spectroscopy. Once the reaction was finished (15-48 h, the time depends on setup temperature and synthesis scale), the product was filtered and washed with a small amount of THF and dried. Yields were in a range 94-98%. In the second step the product of the aforementioned reaction (1 eq.) was added to 1,3-propanesultone or acrylic acid in methanol and stirred at 30 °C. The progress of reaction was monitored by NMR spectroscopy. Once the reaction was finished, the methanol was removed and obtained solid product was purified by crystallisation from methanol/acetone mixture. The precipitate was finally dry under high vacuum and temperature of 60 °C.

Table S1: ^{1}H- and ^{13}C-NMR spectroscopy, ESMS, and CNHS analysis.

ZWS	NMR data (400 MHz)	ESMS	CNHS
C_2NNBrS	^{1}H NMR (400 MHz, D_2O) δ 3.99 (s, 4H, -NC<u>H$_2$</u>C<u>H$_2$</u>N-), 3.66 (q, 2H, $CH_3C\underline{H_2}N$-), 3.56 (t, 2H, -$C\underline{H_2}CH_2CH_2SO_3^-$), 3.30 (s, 6H, $C_2H_5N\underline{(Me)_2}$), 3.23 (s, 6H, -$N\underline{(Me)_2}C_3H_6SO_3^-$), 3.03 (t, 2H, -$CH_2CH_2C\underline{H_2}SO_3$), 2.31 (m, 2H, -$CH_2C\underline{H_2}CH_2SO_3^-$), 1.45 (t, 3H, $C\underline{H_3}CH_2N$-). ^{13}C NMR (400 MHz, D_2O) δ 63.99, 62.05, 56.19, 55.53, 51.95, 51.16, 47.41, 18.80, 8.21.	Cation: calc. 267.17 Observed 267.18	C 37.85 (38.04) H 7.83 (7.84) N 7.51 (8.07) S 9.63 (9.32)

C_4NNBrS	^{1}H NMR (400 MHz, D_2O) δ 4.79 (D_2O), 3.97 (s, 4H, -NCH_2CH_2N-), 3.64 (t, 2H, $CH_3(CH_2)_2$CH_2N-), 3.45 (t, 2H, - C$H_2$$CH_2CH_2SO_3^-$), 3.29 (s, 6H, C_4H_9N(Me)$_2$), 3.27 (s, 6H, -N(Me)$_2C_3H_6SO_3^-$), 3.03 (t, 2H, -CH_2CH_2CH_2SO_3), 2.29 (m, 2H, -CH_2C$H_2CH_2SO_3^-$), 1.81 (m, 2H, CH_3CH_2CH_2CH_2N-), 1.40 (m, 2H, CH_3CH_2 $(CH_2)_2$N-), 0.97 (t, 3H, C$H_3(CH_2)_3$N-). ^{13}C NMR (400 MHz, D_2O) δ 66.09, 63.78, 56.03, 55.93, 51.81, 51.51, 47.23, 24.38, 19.33, 18.55, 13.17.	Cation: calc. 295.21 Observed 295.20	C 41.82 (41.60) H 8.63 (8.32) N 7.03 (7.46) S 8.91 (8.54)
C_6NNBrS	^{1}H NMR (400 MHz, D_2O) δ 4.79 (D_2O), 3.97 (s, 4H, -NCH_2CH_2N-), 3.64 (t, 2H, C_5H_{11}CH_2N-), 3.45 (t, 2H, - C$H_2$$CH_2CH_2SO_3^-$), 3.29 (s, 6H, C_6H_{13}N(Me)$_2$), 3.23 (s, 6H, -N(Me)$_2C_3H_6SO_3^-$), 3.02 (t, 2H, -CH_2CH_2CH_2SO_3), 2.31 (m, 2H, -CH_2C$H_2CH_2SO_3^-$), 1.81 (m, 2H, C_4H_9CH_2CH$_2$N-), 1.36 (m, 6H, CH_3(CH_2)$_3$ CH_2CH_2N-), 0.89 (t, 3H, C$H_3(CH_2)_5$N-). ^{13}C NMR (400 MHz, D_2O) δ 66.91, 63.74, 55.98, 55.88, 51.80, 51.44, 47.19, 30.79, 25.35, 22.34, 22.07, 18.62, 13.55.	Cation: calc. 323.24 Observed 323.23	C 44.31 (44.66) H 9.09 (8.74) N 6.11 (6.94) S 8.57 (7.95)
OHC_2NNBrS	^{1}H NMR (400 MHz, D_2O) δ 4.06 (m, 6H, -NCH_2CH_2N-, OHCH_2-), 3.66 (m, 4H, $OHCH_2$CH_2N-,-NC$H_2$$(CH_2)_2$), 3.34 (s, 6H, OHC_2H_5N(Me)$_2$), 3.28 (s, 6H, -N(Me)$_2C_3H_6SO_3^-$), 3.03 (t, 2H, -CH_2CH_2CH_2SO_3), 2.30 (m, 2H, -CH_2C$H_2CH_2SO_3^-$). ^{13}C NMR (400 MHz, D_2O) δ 66.37, 64.02, 56.93, 56.20, 55.78, 52.99, 51.89, 47.33, 18.65.	Cation: calc. 283.17 Observed 287.17	C 35.87 (36.36) H 7.40 (7.49) N 7.35 (7.71) S 9.35 (8.83)
COC_2NNBrS	^{1}H NMR (400 MHz, D_2O) δ 4.02 (m, 6H, -NCH_2CH_2N-, OC$H_2$$CH_2$N-), 3.72 (t, 2H, -$OCH_2CH_2$N-), 3.62 (t, 2H, C$H_2$$CH_2CH_2SO_3^-$), 3.42 (s, 3H, CH_3-), 3.32 (s, 6H,-OC_2H_4N(Me)$_2$), 3.27 (s, 6H, -N(Me)$_2C_3H_6SO_3^-$), 3.03 (t, 2H, -CH_2CH_2CH_2SO_3), 2.30 (m, 2H, -CH_2C$H_2CH_2SO_3^-$). ^{13}C NMR (400 MHz, D_2O) δ 65.86, 64.21, 64.01, 58.89, 56.87, 56.23, 53.12, 51.88, 47.33, 18.63.	Cation: calc. 297.18 Observed 297.18	C 38.36 (38.20) H 7.71 (7.75) N 7.42 (7.42) S 8.10 (8.5)
C_2NNBrC	^{1}H NMR (400 MHz, D_2O) δ 4.79 (D_2O), 3.97 (s, 4H, -NCH_2CH_2N-), 3.76 (t, 2H, C$H_2$$CH_2CO_2$), 3.53 (q, 2H, CH_3CH_2N-), 3.26 (s, 6H, C_2H_5N(Me)$_2$), 3.22 (s, 6H, -N(Me)$_2C_3H_4O_2^-$), 2.91 (t, 2H, -C$H_2$$CO_2$ 1.43 (t, 3H, CH_3CH_2N). ^{13}C NMR (400 MHz, D_2O) δ 176.69, 62.14, 61.93, 56.51, 55.44, 51.58, 51.01, 29.57, 8.04.	Cation: calc. 217.19 Observed 217.19	a
C_4NNBrC	^{1}H NMR (400 MHz, D_2O) δ 4.79 (D_2O), 3.99 (s, 4H, -NCH_2CH_2N-), 3.78 (t, 2H, C$H_2$$CH_2CO_2$), 3.45 (t, 2H, C_3H_7CH_2N-), 3.26 (s, 6H, C_4H_9N(Me)$_2$), 3.23 (s, 6H, -N(Me)$_2C_3H_4O_2^-$), 2.91 (t, 2H, -C$H_2$$CO_2$), 1.79 (m, 2H, CH_3CH_2CH_2-), 1.40 (m, 2H, CH_3CH_2-) 0.97 (t, 3H, C$H_3(CH_2)_3$). ^{13}C NMR (400 MHz, D_2O) δ 174.18, 66.25, 61.86, 56.80, 56.10, 51.72, 51.69, 29.10, 24.54, 19.48, 13.33.	Cation: calc. 245.22 Observed 245.22	a
C_6NNBrC	^{1}H NMR (400 MHz, D_2O) δ 3.99 (s, 4H, -NCH_2CH_2N-), 3.80 (t, 2H, C$H_2$$CH_2CO_2$), 3.45 (t, 2H, C_5H_{11}CH_2N-), 3.26 (s, 6H, C_6H_{13}N(Me)$_2$), 3.22 (s, 6H, -N(Me)$_2C_3H_4O_2^-$), 3.03 (t, 2H, -C$H_2$$CO_2$), 1.82 (m, 2H, C_4H_9CH_2-), 1.35 (m, 6H, CH_3(CH_2)$_3$-), 0.87 (t, 3H, C$H_3(CH_2)_5$). ^{13}C NMR (400 MHz, D_2O) δ 175.79, 68.83, 63.80, 59.30, 58.46, 54.12, 54.08, 33.34, 30.76, 27.90, 24.91, 24.62, 16.10.	Cation: calc. 273.25 Observed 273.25	a

a- CNHS analysis for carboxylate based ZWSs gave results which were 2-3 % off the expected values and highly dependent on time and temperature of drying. We believed that the compounds had strongly bound water and/or methanol molecules left in the structures, and could not be properly prepared for CHNS analysis. Similar higher deviation from calculated values was reported in literature for carboxylate betaine zwitterions.[2]

Modelling of the solvated $C_2NNSO_3^+$

An exhaustive search for the lowest energy conformer has been initially done using OpenBabel (release 2.4.0)[3] The geometry of the lowest energy conformer has been subsequently refined by means of an all-electron DFT/B3LYP[4] optimisation using the Def2-TZVP basis for H, N, and O while using a less expensive Def2-SVP[5] for S an C (hereafter, the "small basis set"). All the electronic structure calculations have been done using NWCHEM (version 6.6)[5]. The route mean square deviation (RMSD) between this optimised geometry and the result of a DFT/B3LYP using the Def2-TZVP basis for all the atoms (hereafter, the "small basis set") is very small (only 0.0216 Å).

To quantify the effect of an aqueous environment on the cation geometry, we have also refined the geometry of the lowest energy conformer using an implicit model of the solvent. In particular, we have employed the 'COnductor-like Screening MOdel' (COSMO)[6] as implemented in NWCHEM (default value of the dielectric constant of water: 78.4). Also in this case, the RMSD between the "small basis set" and "larger basis set" optimised geometries is very small (only 0.021 Å). The implicitly solvated geometry from the "small basis set" optimisation is shown in Fig. S2.

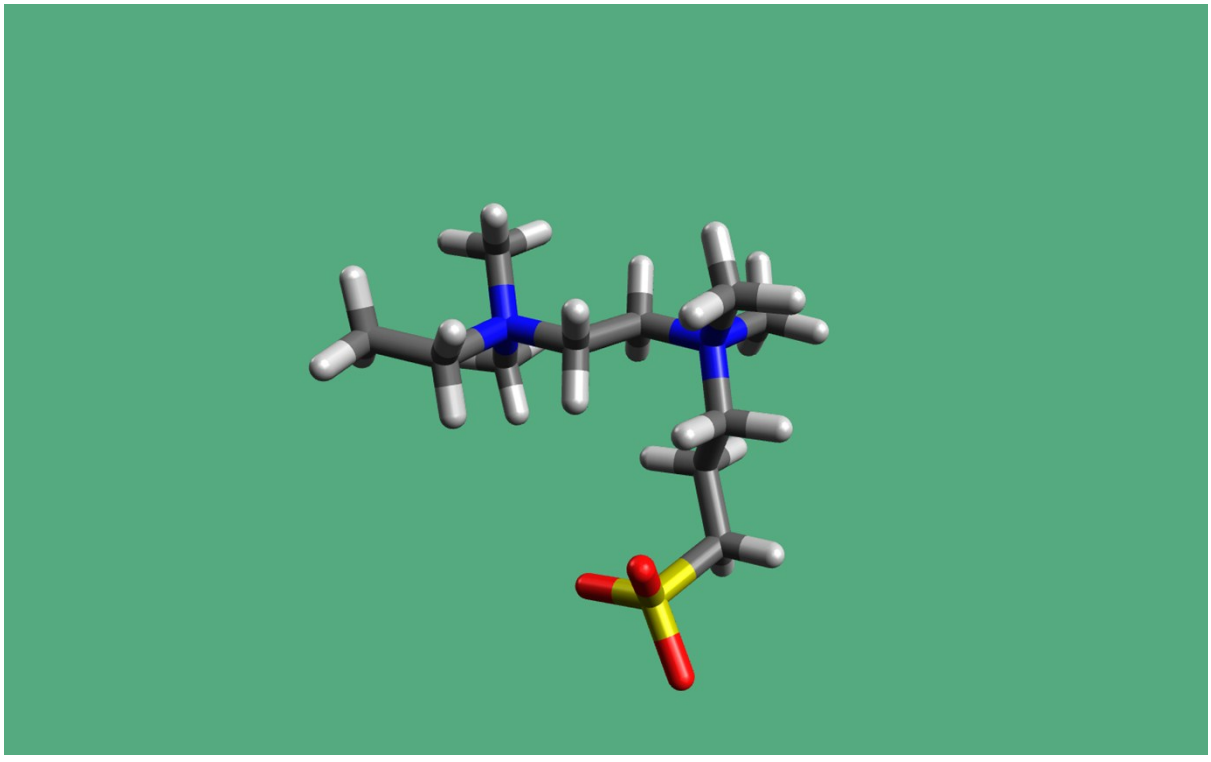


Figure S2: Optimal solvated geometry ("small basis set", see file C2NNSO3_COSMO_SB.xyz)

The solvated geometry is much less compact than the gas phase geometry (see Fig. 3 of the main article) and the intramolecular hydrogen bonds are completely disrupted. This result suggests that the cation in solution preferentially forms hydrogen bonds with the water molecules. As a qualitative test, we included the COSMO geometry in an explicit micro-solvation sphere containing 120 water molecules and re-optimise the geometry using the MMFF94 force field[7] as implemented in OpenBabel.

Despite the qualitative nature of this micro-solvation model, one can verify that the hydrogen bonds are preferentially formed with the water molecules (inter-molecular hydrogen bonds). The COSMO calculations also return an estimate of the (electrostatic) solvation energy: 123.80 kcal/mol (smaller basis); 121.94 kcal/mol (larger basis).

Finally, the infrared (IR) absorption spectra have been obtained from the vibrational analysis of the gas phase and solvated cation geometries ("small basis set", only). The results are compared in Fig.S3.

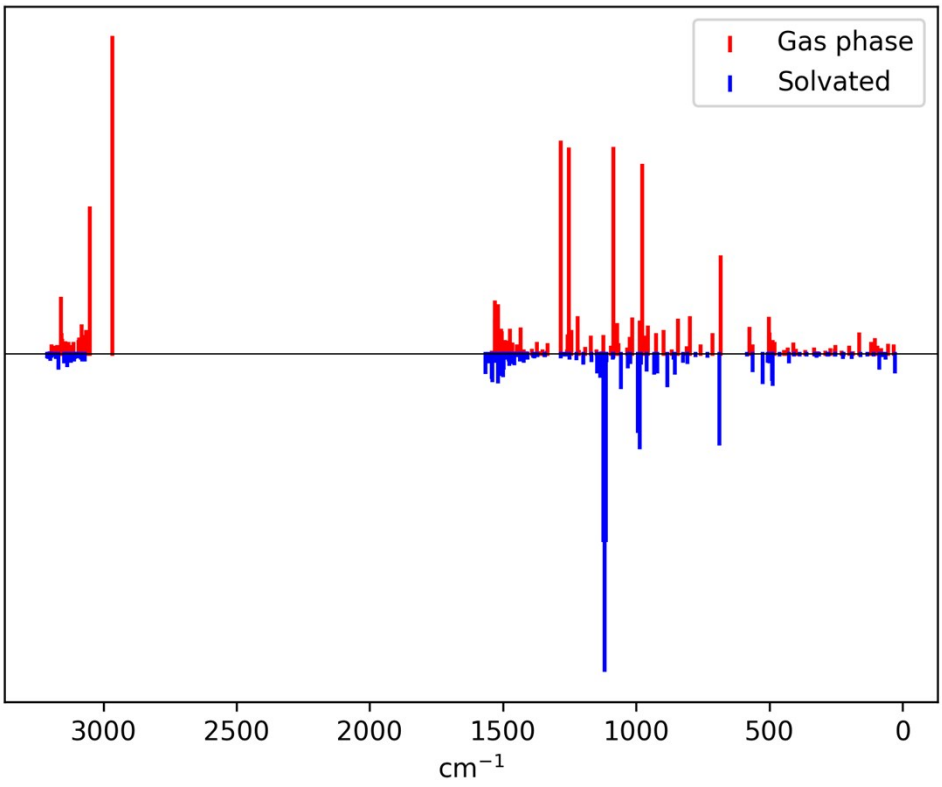


Figure S3: Comparison of the infrared spectra of the gas phase and solvated cation geometries. The negative spectral lines of the solvated case have been plotted to facilitate the comparison.

The strong feature at about 3,000 cm^{-1} in the IR spectrum of the gas phase can be associated to an intramolecular hydrogen bond, which is indeed no longer present in the solvated phase.

Crystallography data:

Experimental

Single crystals of the compounds C_2NNBrS and C_2NNBrC were crystallised methanol/acetone solution of the compound by evaporation. A suitable crystal was selected and measured on a SuperNova, Dual, Cu, EosS2 diffractometer. The crystal was kept at 100(2) K during data collection. Using Olex2 [8], the structure was solved with the ShelXT [9] structure solution program using Intrinsic Phasing and refined with the ShelXL[9] refinement package using Least Squares minimisation.

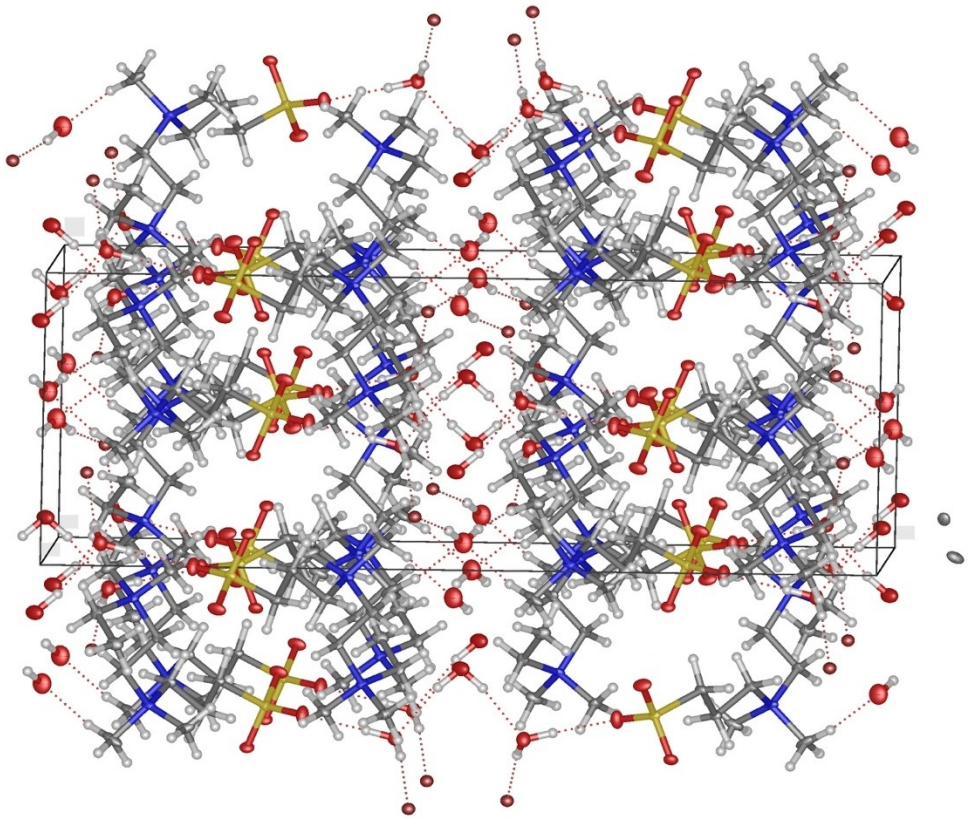


Figure S4: Packing in the crystal structure of ZWS C_2NNBrS.

Crystal data and structure refinement for C_2NNBrS.

Identification code	exp_327
Empirical formula	$CHNOBrS_{0.02}Cl_{0.02}$
Formula weight	44.12
Temperature/K	293(2)
Crystal system	monoclinic

Space group	C2/c
a/Å	24.0379(3)
b/Å	8.61570(10)
c/Å	16.3926(2)
α/°	90.00
β/°	99.7000(10)
γ/°	90.00
Volume/Å^3	3346.43(7)
Z	62
ρ_{calc}g/cm^3	1.357
μ/mm^{-1}	1.387
F(000)	1397.0
Crystal size/mm^3	0.3 × 0.2 × 0.2
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	10.92 to 146.78
Index ranges	-29 ≤ h ≤ 29, -10 ≤ k ≤ 10, -20 ≤ l ≤ 20
Reflections collected	30205
Independent reflections	3322 [R_{int} = 0.0432, R_{sigma} = 0.0167]
Data/restraints/parameters	3322/0/198
Goodness-of-fit on F^2	1.182
Final R indexes [I>=2σ (I)]	R_1 = 0.0326, wR_2 = 0.0809
Final R indexes [all data]	R_1 = 0.0326, wR_2 = 0.0809
Largest diff. peak/hole / e Å^{-3}	0.64/-0.61

Crystal data and structure refinement for C_2NNBrC.

Identification code	exp_442 MB2
Empirical formula	$C_{15}H_{37}N_2O_3Br_2$
Formula weight	172.20
Temperature/K	105(8)
Crystal system	triclinic
Space group	P-1
a/Å	7.1520(7)
b/Å	8.1484(6)
c/Å	20.7756(9)
α/°	90.232(5)
β/°	98.462(6)
γ/°	113.488(9)
Volume/Å^3	1095.71(16)
Z	5
ρ_{calc}g/cm^3	1.305
μ/mm^{-1}	0.672
F(000)	455.0
Crystal size/mm^3	0.2 × 0.2 × 0.2
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.626 to 142.482
Index ranges	-7 ≤ h ≤ 8, -9 ≤ k ≤ 9, -25 ≤ l ≤ 25
Reflections collected	5665
Independent reflections	3160 [R_{int} = 0.0398, R_{sigma} = 0.0394]
Data/restraints/parameters	3160/0/207
Goodness-of-fit on F^2	1.440
Final R indexes [I>=2σ (I)]	R_1 = 0.0907, wR_2 = 0.3108
Final R indexes [all data]	R_1 = 0.0955, wR_2 = 0.3187

Largest diff. peak/hole / e $Å^{-3}$	2.24/-1.20

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