Supporting Information for

tert-Butyloxycarbonyl-protected amino acid ionic liquids and their application to dipeptide synthesis

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Materials:

All of the commercial materials (except for the ionic liquids) were used without further purification. Phenylalanine-HMPB-ChemMatrix resin (0.58 mmol/g, 35–100 mesh) and the Boc-amino acids were purchased from Aldrich (Quebec, Canada) and Canex Industry (Xi'an, China), respectively. The 10% [emim][OH] solution was purchased from BASF SE (Ludwigshafen, Germany). [bmim][PF_6] was purchased from Lihua Pharma (Henan, China). EDC, HOBt, HATU, ByBOP, and the authentic peptide samples were purchased from GL Chem (Shanghai, China). DIEA was obtained from Alfa Aesar (Tianjin, China). CTAP was purchased from Kewei Chem (Shanghai, China). All of the organic solvents were obtained from Chemical Reagent Co. (Shanghai, China).

General methods:

Preparative HPLC was performed with an Agilent Prepstar SD-1 system equipped with an Agilent 325 ultraviolet (UV)/visible detector, Agilent G9302A/G9303A delivery modules equipped with 200 mL/min pump heads, and a ZORBAX 300SB-C18 column (21.2 mm × 150 mm, 5 μm particle size). The purities of the peptides were confirmed by analytical reversed-phase HPLC on an Agilent 1200 SL chromatograph with a Grace Vydac 208TP C8 column (4.6 mm × 250 mm, 5 μm particle size) and a mobile phase system consisting of 0.1% trifluoroacetic acid (TFA) in water (A) and 0.1% TFA in acetonitrile (B) with a flow rate of 1.0 mL/min. UV detection was performed at 220 nm. The peptide yield was calculated as the ratio between the obtained weight (mg) with the theoretical weight multiplied by the purity (%area) of the main peak.

High-resolution mass spectroscopy analysis was performed with a Shimadzu LCMS-8030 spectrometer. The sample (1 μL, 0.2 mM in 90% acetonitrile/water) was injected onto a Kinetex C18 column (2.1 mm × 100 mm, 1.7 μm particle size). Mass spectroscopy analysis was performed with a gradient of 5–95% acetonitrile in water with 0.1% formic acid in 40 min at a flow rate of 0.2 mL/min and a column temperature of 40 °C.

1 mg sample for proton NMR analysis/ 20 mg sample for ^{13}C NMR analysis was dissolved in 500 μL DMSO-*d6* and transferred to a 5 mm NMR tube. The ^{1}H and ^{13}C NMR spectra of samples were recorded with a Bruker ARX-400 spectrometer (^{1}H at 400 MHz and ^{13}C at 100 MHz). The chemical shifts (δ) are expressed in parts per million (ppm) and spin–spin coupling (J) is given in Hz. The following abbreviations are used for the peak multiplicities: singlet (s), doublet (d), doublet of doublets (dd), triplet (t), doublet of triplet (dt), and multiplet (m). The chemical shifts are relative to the residual DMSO-d_6 signal (at δ = 2.50 ppm for ^{1}H NMR) with DMSO-d_6 solvent.

Determination of the element (C/H/N) contents in the AAILs was performed with a 2400 CHN elemental analyzer (Perkin Elmer) with a thermal conductivity detector. Samples between 2 and 3 mg were weighed in tin capsules and loaded into an automatic sampler. High purity helium was used as carrier gas.

The specific rotations [α]D of corresponding AAILs were determined in DMF solution (1.0 g/100mL) at 20 °C using an automatic polarimeter Rudolph Autopol IV/IV-T.

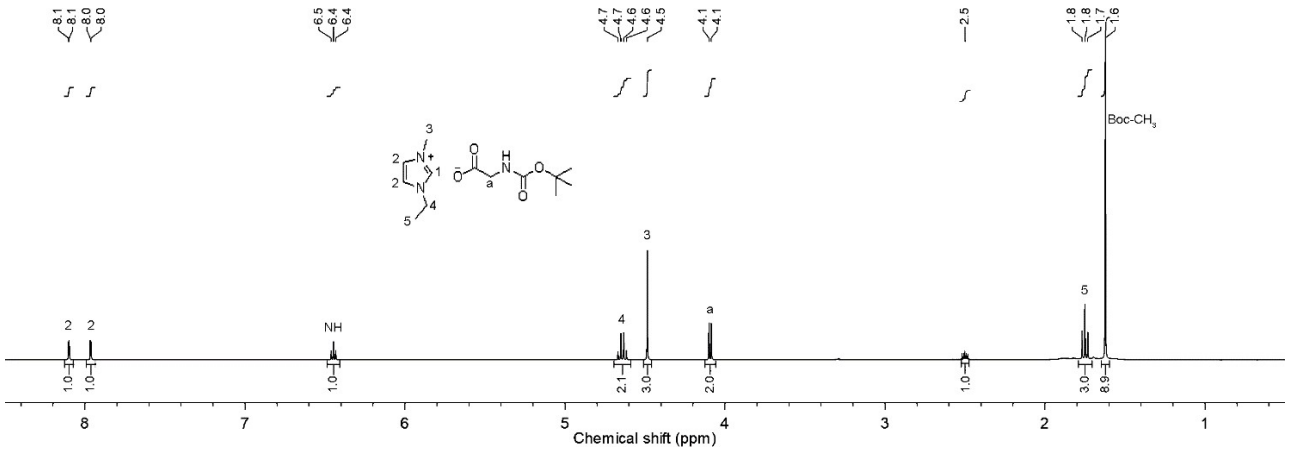
Infrared spectroscopy fourier transform infrared (FT-IR) spectra were recorded using the Thermo Fisher Nicolet 6700 FT-IR spectrometer. The dried samples were prepared by KBr film technique and the scan range was 4000–400 cm^{-1}.

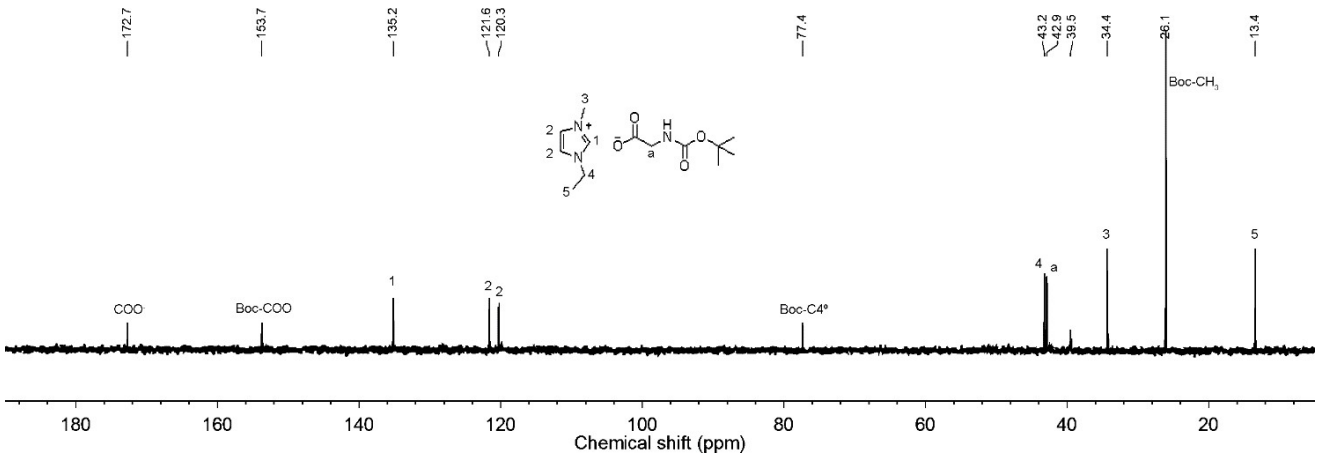
Thermogravimetric analysis was performed on a NETZSCH TG 209 F3 Tarsus® thermogravimetric analyzer under nitrogen. Samples between 5 and 10 mg were placed in open alumina pans and were heated from 30 °C to 500 °C with a heating rate of 20 °C/min. Decomposition temperatures (T_d) were reported from onset to 10 wt% mass loss.

Differential scanning calorimetry (DSC) measurements were performed using a NETZSCH DSC 200 F3 Maia® differential scanning calorimeter under nitrogen. The samples were sealed in aluminum crucibles and scanned from -60 ˚C to T_d with a scanning rate of 10 ˚C/min. The glass transition temperature (T_g) was determined from the midpoint of the heat capacity change.
Viscosity was measured using a Cannon-Fenske routine viscometer, constant 0.5 mm^2/s^2 (cSt/s). To obtain kinematic viscosity in mm^2/s (cSt) the efflux time in seconds was multiplied by the viscometer constant. To obtain viscosity in mPas (cP), the viscosity in mm^2/s (cSt) was multiplied by the density in grams per milliliter.

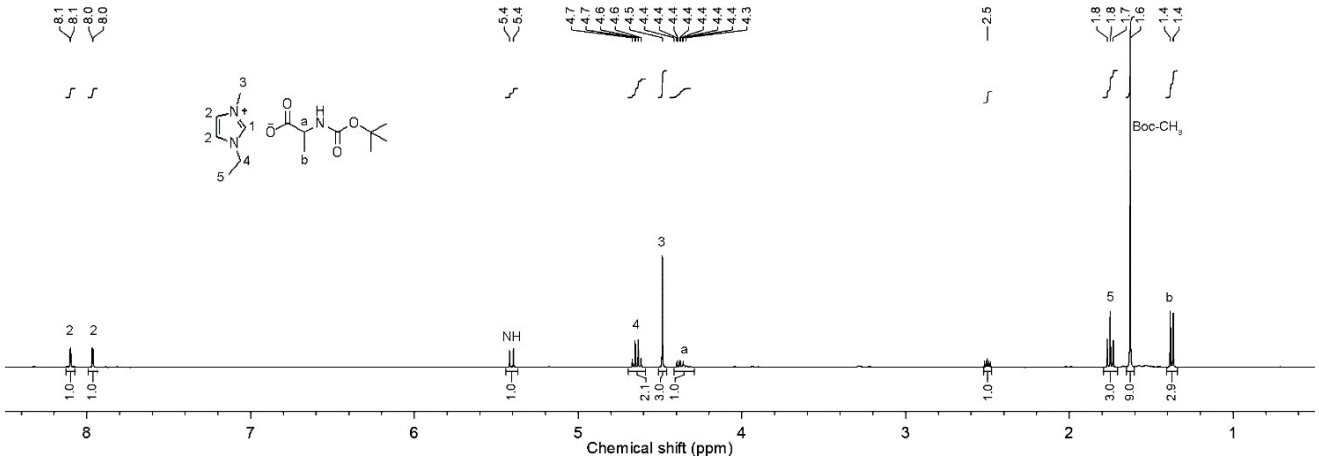
General procedures:
General procedure for amino acid ionic liquids. First, 10% [emim][OH] solution was added dropwise in slight excess of the equimolar Boc-protected amino acid (0.02 M in 3:1 THF/H_2O) under stirring for 6 h. After solvent removal by vacuum evaporation, a mixture containing the desired AAIL and unreacted amino acid was obtained. Ethanol was then added to recrystallize and remove the solvents. The mixture was centrifuged for 30 min to remove the insoluble amino acid. The remaining ethanol in the solution was then removed by evaporation. The product quantitatively formed in high purity, as determined by mass balance and NMR spectroscopy. The resulting AAILs were dried in vacuo at 50 °C for 24 h, except for [emim][Boc-Asn] which was lyophilized at 25 °C for 48 h. The water contents in the AAILs after drying were measured by Karl Fischer analysis using a Metrohm 870 KF Titrino titrator. Most of the AAILs contained less than 0.3 wt% water after the drying step. The water content of [emim][Boc-Asn] was 0.9 wt%.
General procedure for the manual SPPS. Peptide synthesis was performed using H-l-phenylalanine-HMPB-ChemMatrix resin (~100 mg, 0.58 mmol/g loading) according to the standard Boc strategy. The resin was swollen in DMF (2 mL) for 20 min and then drained. The resin was coupled with Boc-Ala (4 equiv), which was pre-activated with an appropriate coupling reagent, additive, and DIEA in DMF (2 mL). After the coupling step, the solid support was washed with DCM/methanol (1:1) (three times 4 mL) and dried under vacuum for 1 h prior to HF-mediated cleavage. The resin beads were removed by filtration through glass wool and the filtrate was then concentrated under vacuum. The crude peptide was obtained by precipitation with cold ether, and it was then washed and lyophilized. The peptide product was obtained after HPLC purification.

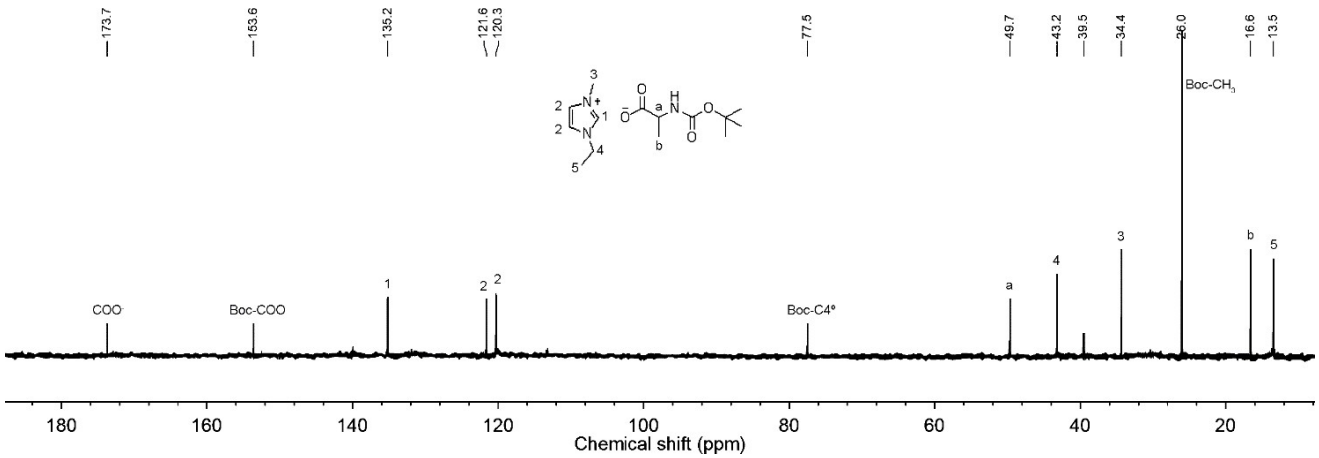
NMR analysis
[emim][Boc-Gly]: $[\alpha]_D^{20}$ 0.0 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 2.1 Hz, 1H), 7.96 (d, *J* = 2.2 Hz, 1H), 6.45 (t, *J* = 5.7 Hz, 1H), 4.64 (q, *J* = 7.1 Hz, 2H), 4.49 (s, 3H), 4.09 (d, *J* = 5.7 Hz, 2H), 2.50 (m, 1H, DMSO), 1.75 (t, *J* = 7.1 Hz, 3H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.70, 153.74, 135.17, 121.61, 120.28, 77.37, 43.20, 42.88, 39.52 (DMSO), 34.35, 26.05, 13.43. Elemental analysis calculated (%) for $C_{13}H_{23}N_3O_4$ 1.1H_2O: C 51.17; H 8.32; N 13.77; O 26.74; found: C 51.19; H 8.26; N 13.81.



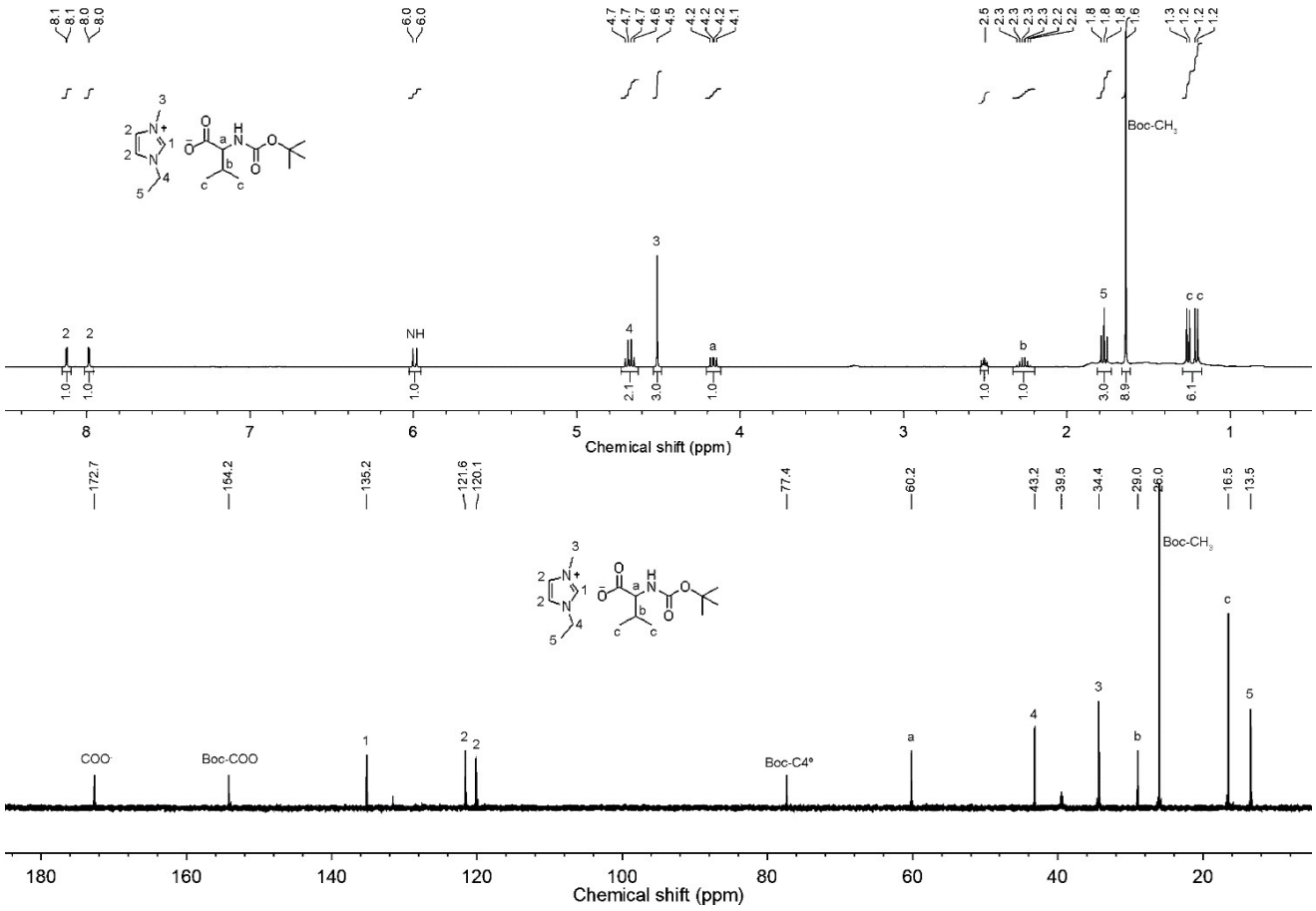


[emim][Boc-Ala]: $[\alpha]_D^{20}$ -15.2 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 2.1 Hz, 1H), 7.96 (d, *J* = 2.2 Hz, 1H), 5.41 (d, *J* = 9.2 Hz, 1H), 4.64 (q, *J* = 7.1 Hz, 2H), 4.49 (s, 3H), 4.38 (dq, *J* = 9.2, 6.8 Hz, 1H), 2.50 (m, 1H, DMSO), 1.75 (t, *J* = 7.1 Hz, 3H), 1.63 (s, 9H), 1.37 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.69, 153.61, 135.17, 121.61, 120.28, 77.49, 49.66, 43.20, 39.52 (DMSO), 34.35, 26.04, 16.61, 13.45. Elemental analysis calculated (%) for $C_{14}H_{25}N_3O_4$ H_2O: C 52.98; H 8.58; N 13.24; O 25.20; found: C 53.02; H 8.57; N 13.29.

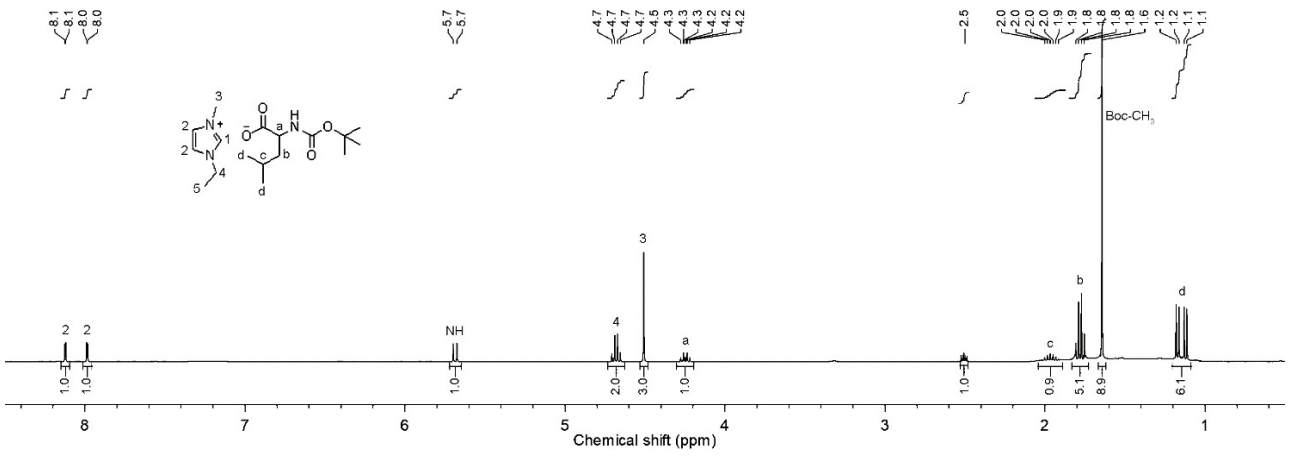


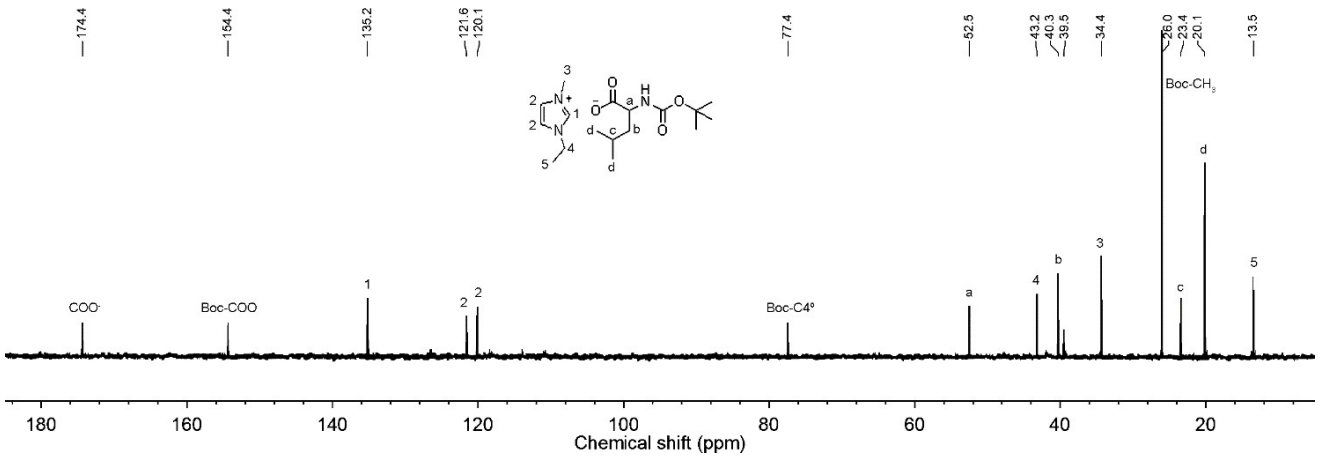


[emim][Boc-Val]: $[\alpha]_D^{20}$ 2.4 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 5.99 (d, *J* = 9.2 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (s, 3H), 4.16 (dd, *J* = 9.1, 6.6 Hz, 1H), 2.50 (m, 1H), 2.27 (h, *J* = 6.6 Hz, 1H), 1.77 (t, *J* = 7.1 Hz, 3H), 1.64 (s, 9H), 1.23 (dd, *J* = 20.0, 6.6 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.68, 154.19, 135.18, 121.59, 120.12, 77.36, 60.18, 43.20, 39.52 (DMSO), 34.35, 29.00, 26.04, 16.51, 13.45. Elemental analysis calculated (%) for $C_{16}H_{29}N_3O_4$ $0.5H_2O$: C 57.12; H 8.99; N 12.49; O 21.40; found: C 57.16; H 8.97; N 12.50.

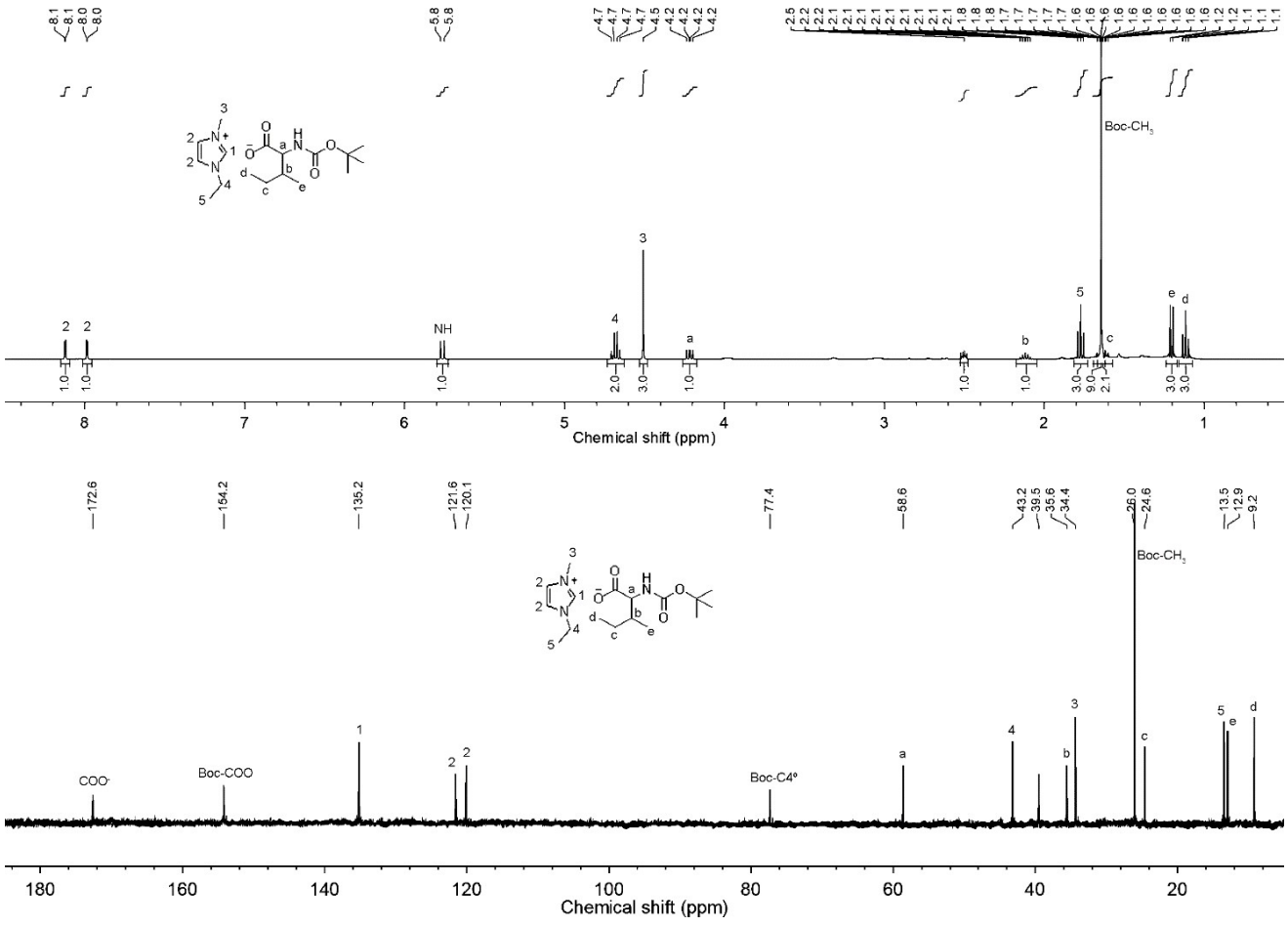


[emim][Boc-Leu]: $[\alpha]_D^{20}$ -27.5 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 5.69 (d, *J* = 9.3 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (s, 3H), 4.25 (dt, *J* = 9.3, 6.8 Hz, 1H), 2.50 (m, 1H, DMSO), 1.96 (dh, *J* = 13.9, 7.0 Hz, 1H), 1.78 (q, *J* = 7.0 Hz, 5H), 1.64 (s, 9H), 1.15 (dd, *J* = 20.0, 7.0 Hz, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.36, 154.37, 135.18, 121.58, 120.10, 77.43, 52.50, 43.20, 40.30, 39.52 (DMSO), 34.35, 26.04, 23.43, 20.15, 13.45. Elemental analysis calculated (%) for $C_{17}H_{31}N_3O_4$: C 59.80; H 9.15; N 12.31; O 18.74; found: C 59.75; H 9.18; N 12.29.

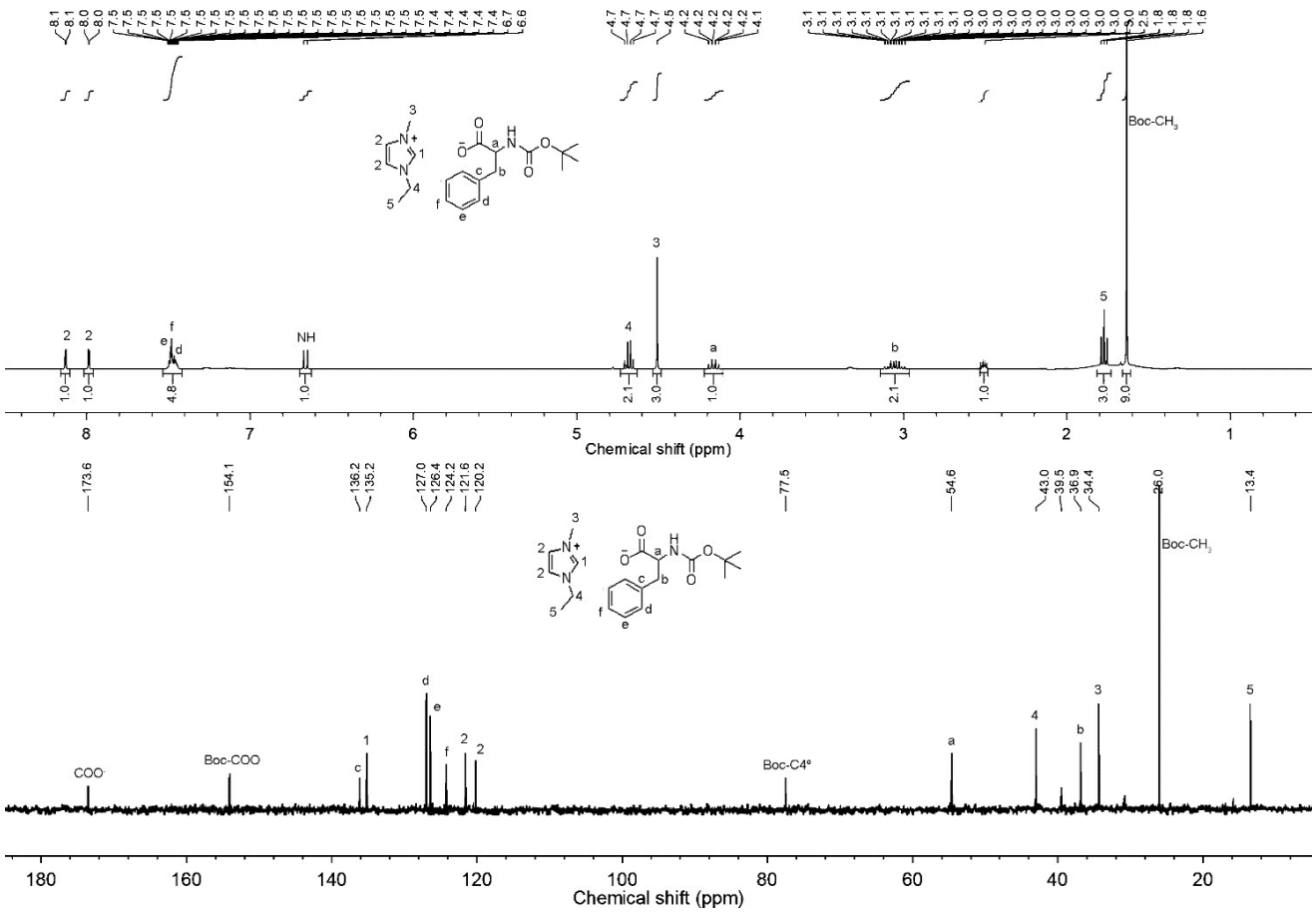




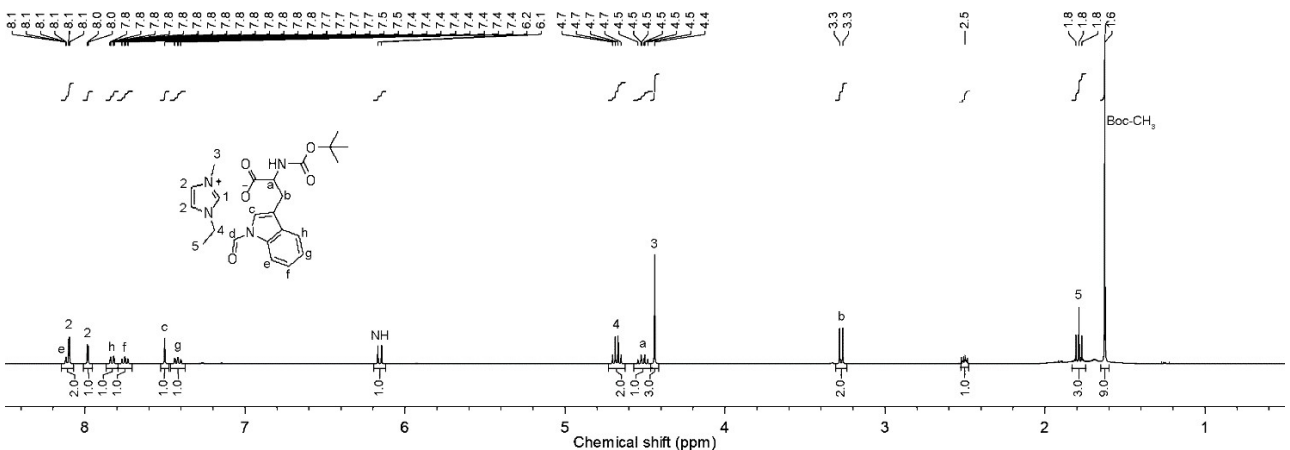
[emim][Boc-Ile]: $[\alpha]_D^{20}$ -15.9 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 5.76 (d, *J* = 9.0 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (s, 3H), 4.22 (dd, *J* = 9.0, 6.6 Hz, 1H), 2.50 (m, 1H, DMSO), 2.12 (tt, *J* = 6.8, 5.8 Hz, 1H), 1.77 (t, *J* = 7.1 Hz, 3H), 1.64 (s, 9H), 1.69 – 1.57 (m, 2H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.61, 154.18, 135.18, 121.58, 120.10, 77.36, 58.59, 43.20, 39.52 (DMSO), 35.58, 34.35, 26.04, 24.59, 13.45, 12.95, 9.20. Elemental analysis calculated (%) for $C_{17}H_{31}N_3O_4$ $2H_2O$: C 54.09; H 9.35; N 11.13; O 25.43; found: C 54.13; H 9.34; N 11.17.

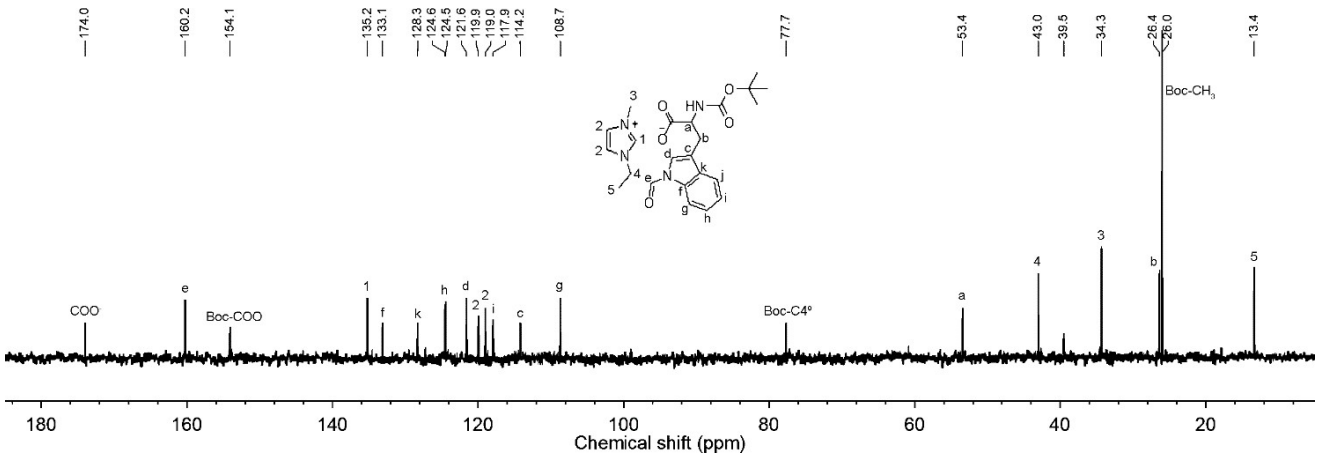


[emim][Boc-Phe]: $[\alpha]_D^{20}$ -59.5 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, *J* = 2.2 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.53 – 7.41 (m, 5H), 6.66 (d, *J* = 9.3 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (s, 3H), 4.16 (dt, *J* = 9.4, 7.8 Hz, 1H), 3.05 (qdt, *J* = 14.0, 7.7, 0.9 Hz, 2H), 2.50 (m, 1H, DMSO), 1.77 (t, *J* = 7.1 Hz, 3H), 1.63 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.56, 154.09, 136.17, 135.18, 126.97, 126.43, 124.23, 121.58, 120.17, 77.49, 54.62, 43.02, 39.52 (DMSO), 36.86, 34.35, 26.04, 13.44. Elemental analysis calculated (%) for $C_{20}H_{29}N_3O_4$ $0.5H_2O$: C 62.48; H 7.86; N 10.93; O 18.73; found: C 62.42; H 7.86; N 10.78.

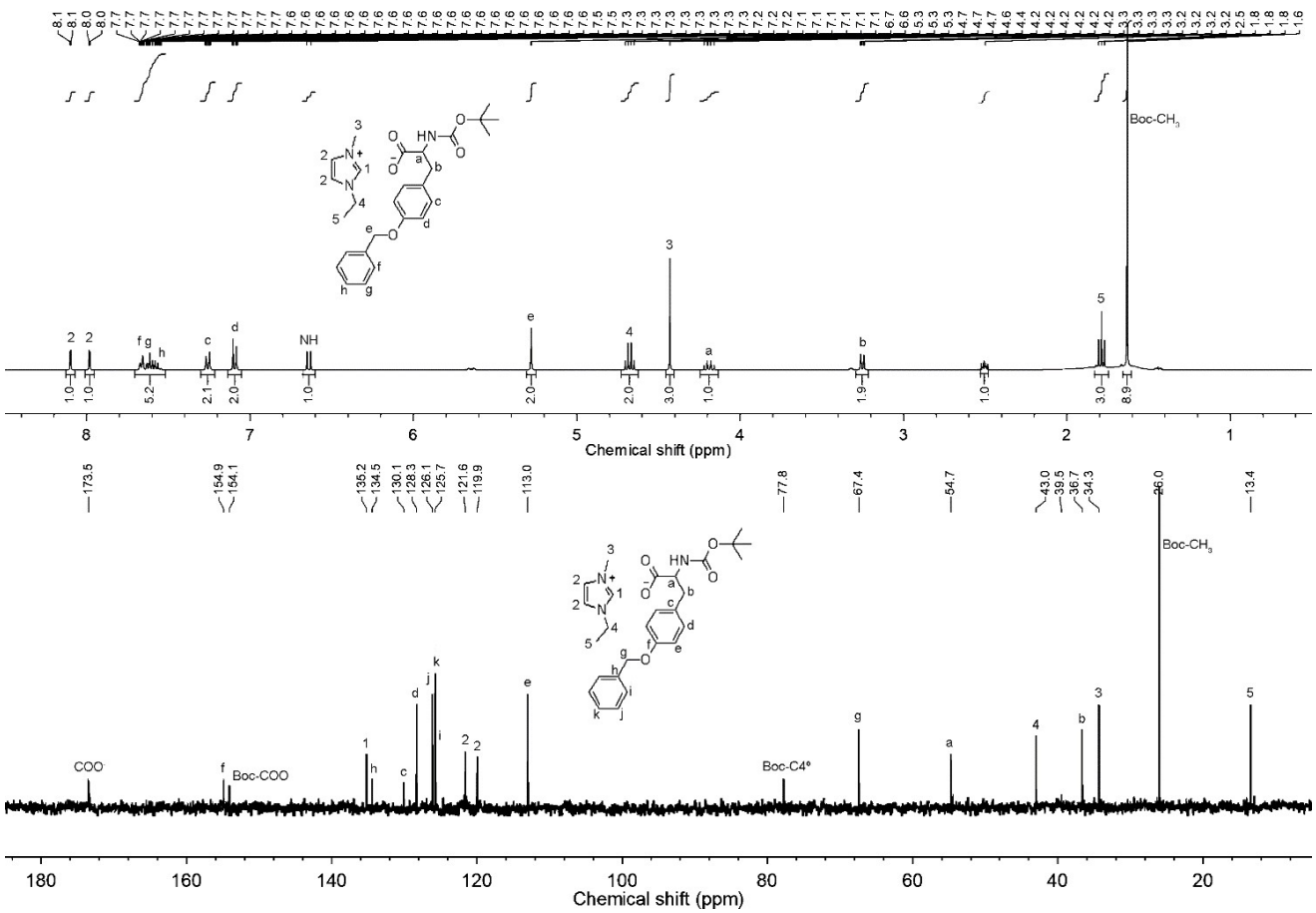


[emim][Boc-Trp(For)]: $[\alpha]_D^{20}$ -42.2 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.98 (d, *J* = 2.2 Hz, 1H), 7.83 (ddd, *J* = 7.8, 1.2, 0.6 Hz, 1H), 7.75 (ddd, *J* = 7.8, 7.2, 1.2 Hz, 1H), 7.50 (d, *J* = 0.5 Hz, 1H), 7.42 (ddd, *J* = 7.8, 7.2, 1.7 Hz, 1H), 6.16 (d, *J* = 9.4 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (dt, *J* = 9.3, 7.7 Hz, 1H), 4.44 (s, 3H), 3.27 (d, *J* = 7.8 Hz, 2H), 2.50 (m, 1H, DMSO), 1.79 (t, *J* = 7.1 Hz, 3H), 1.63 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.99, 160.25, 154.08, 135.20, 133.12, 128.31, 124.55, 124.46, 121.59, 119.94, 119.00, 117.94, 114.18, 108.70, 77.68, 53.42, 43.01, 39.52 (DMSO), 34.33, 26.38, 26.01, 13.35. Elemental analysis calculated (%) for $C_{23}H_{30}N_4O_5$ $1.3H_2O$: C 59.29; H 7.05; N 12.02; O 21.63; found: C 59.23; H 7.07; N12.00.

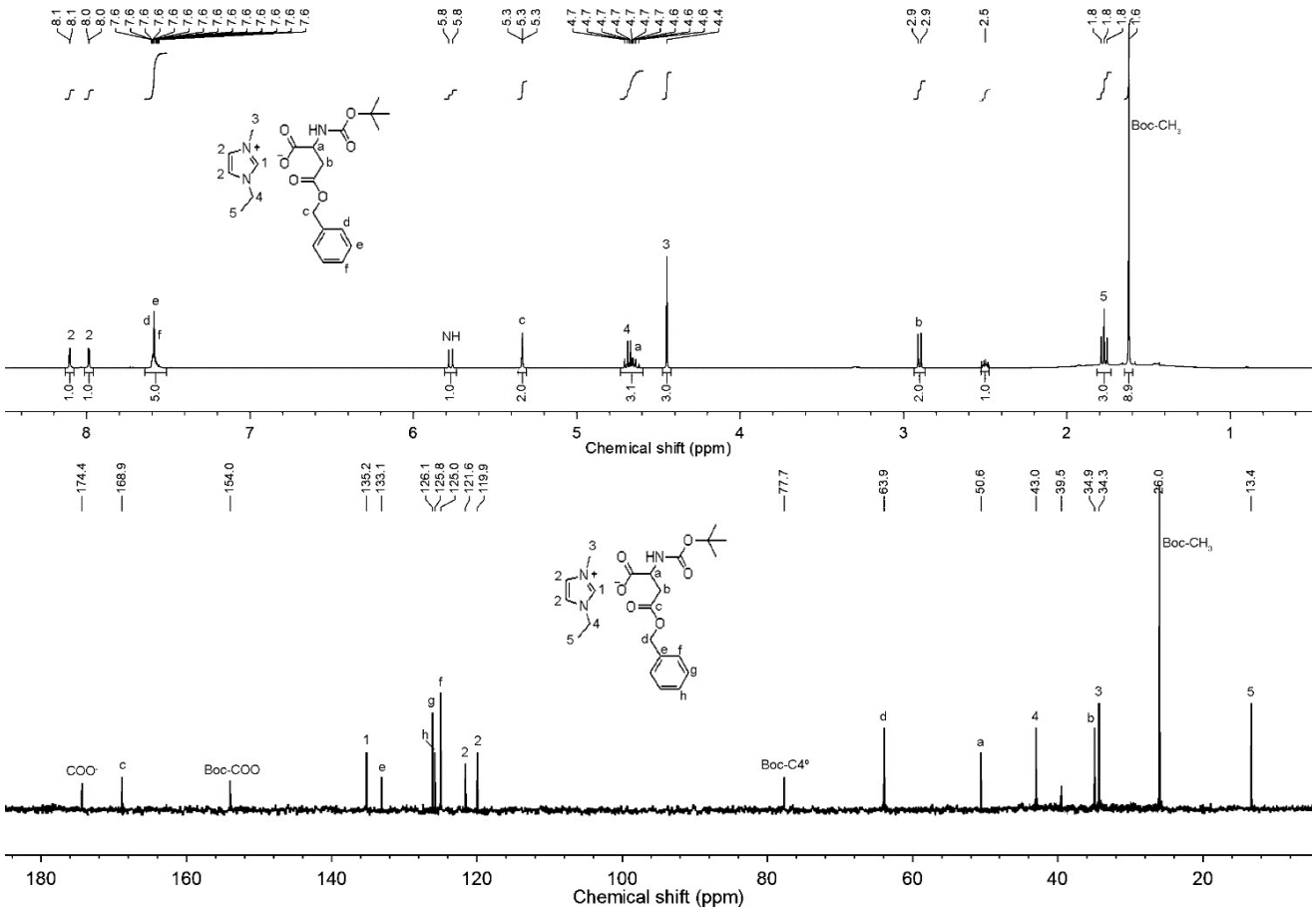




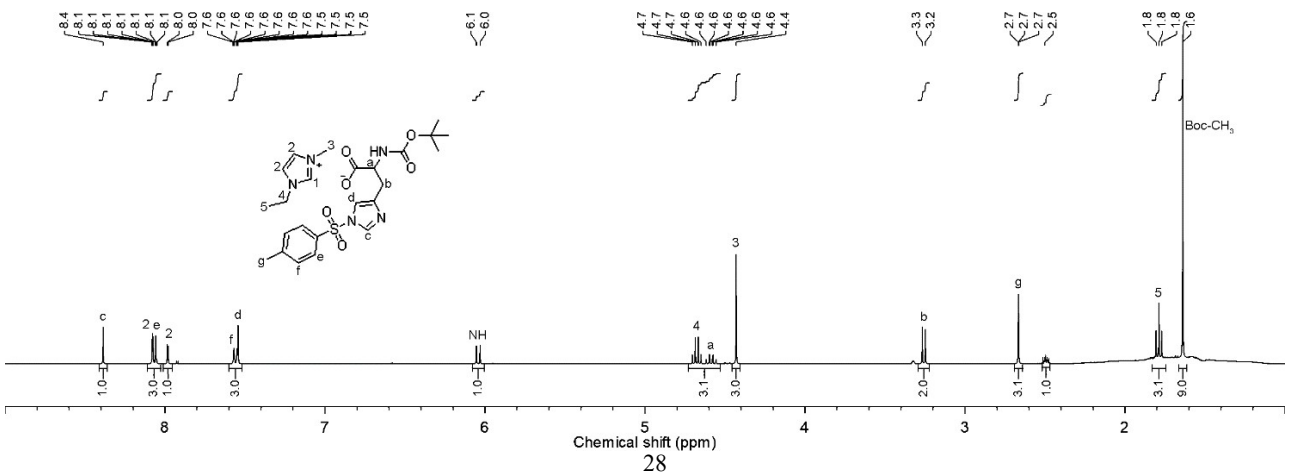
[emim][Boc-Tyr(Bn)]: $[\alpha]_D^{20}$ -22.1 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 2.1 Hz, 1H), 7.98 (d, *J* = 2.2 Hz, 1H), 7.71 – 7.52 (m, 5H), 7.30 – 7.21 (m, 2H), 7.13 – 7.05 (m, 2H), 6.64 (d, *J* = 9.4 Hz, 1H), 5.28 (t, *J* = 1.0 Hz, 2H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.43 (s, 3H), 4.19 (dt, *J* = 9.4, 7.7 Hz, 1H), 3.25 (dq, *J* = 7.6, 0.9 Hz, 2H), 2.50 (m, 1H, DMSO), 1.79 (t, *J* = 7.1 Hz, 3H), 1.63 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.48, 154.90, 154.09, 135.21, 134.46, 130.08, 128.31, 126.13, 125.75, 121.60, 119.95, 113.00, 77.77, 67.41, 54.72, 43.03, 39.52 (DMSO), 36.65, 34.34, 26.03, 13.44. Elemental analysis calculated (%) for $C_{27}H_{35}N_3O_5$ H_2O: C 64.91; H 7.47; N 8.41; O 19.21; found: C 64.87; H 7.50; N 8.36.

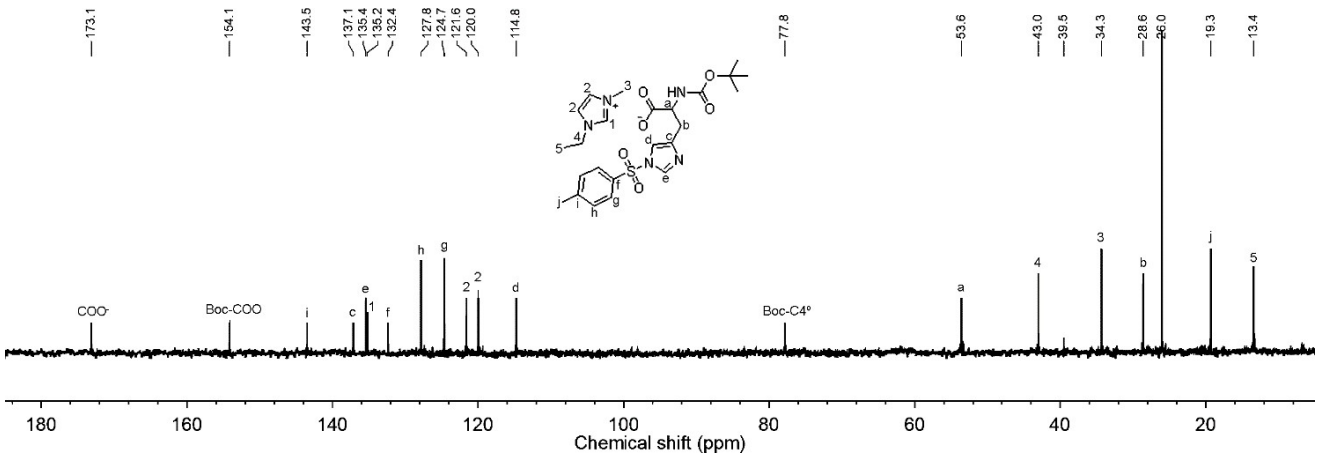


[emim][Boc-Asp(Bn)]: $[\alpha]_D^{20}$ 17.5 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.64 – 7.51 (m, 5H), 5.77 (d, *J* = 9.3 Hz, 1H), 5.33 (t, *J* = 0.6 Hz, 2H), 4.73 – 4.60 (m, 3H), 4.45 (s, 3H), 2.90 (d, *J* = 7.4 Hz, 2H), 2.50 (m, 1H, DMSO), 1.77 (t, *J* = 7.1 Hz, 3H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.39, 168.88, 153.97, 135.20, 133.14, 126.12, 125.79, 125.00, 121.59, 119.94, 77.68, 63.92, 50.60, 43.01, 39.52 (DMSO), 34.94, 34.33, 26.01, 13.35. Elemental analysis calculated (%) for $C_{22}H_{31}N_3O_6$ 0.4H_2O: C 59.96; H 7.27; N 9.53; O 23.24; found: C 59.93; H 7.28; N 9.52.

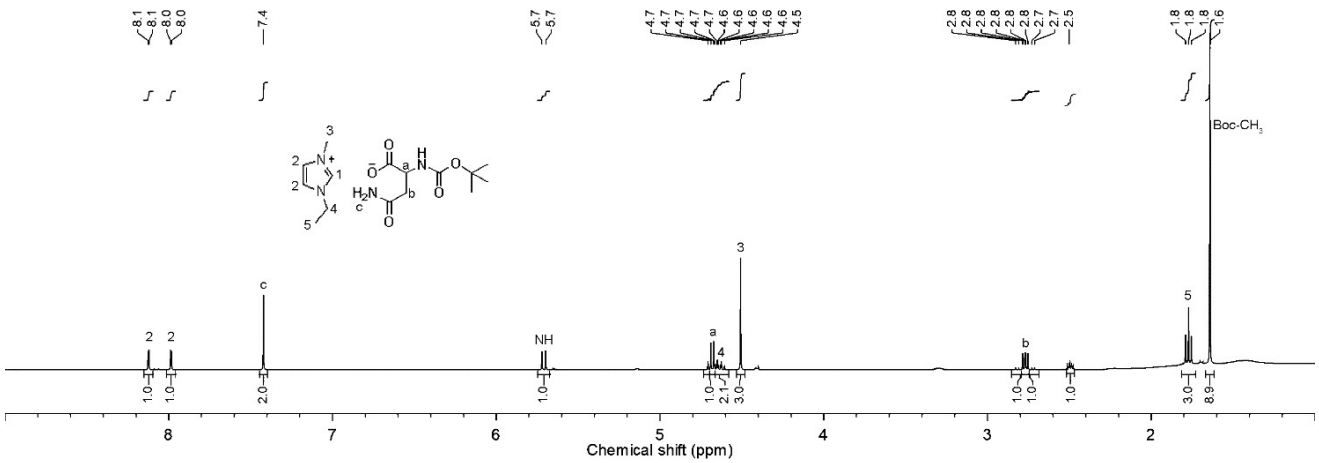


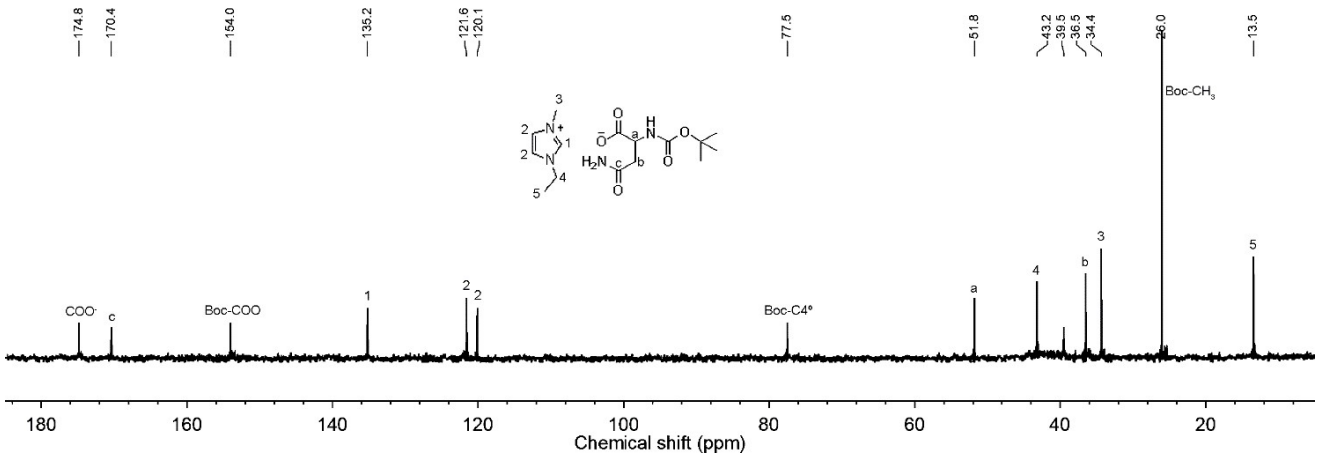
[emim][Boc-His(Ts)]: $[\alpha]_D^{20}$ -18.2 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 1H), 8.11 – 8.03 (m, 3H), 7.98 (d, *J* = 2.2Hz, 1H), 7.60 – 7.52 (m, 3H), 6.04 (d, *J* = 9.3 Hz, 1H), 4.73 – 4.53 (m, 3H), 4.43 (s, 3H), 3.26 (d, *J* = 7.7 Hz, 2H), 2.67 (d, *J* = 0.6 Hz, 3H), 2.50 (m, 1H), 1.79 (t, *J* = 7.1 Hz, 3H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.15, 154.14, 143.47, 137.13, 135.41, 135.21, 132.37, 127.84, 124.66, 121.60, 119.98, 114.75, 77.84, 53.58, 43.03, 39.52 (DMSO), 34.34, 28.60, 26.03, 19.30, 13.44. Elemental analysis calculated (%) for $C_{24}H_{33}N_5O_6S$ 2H_2O: C 51.88; H 6.71; N 12.60; O 23.04; S 5.77; found: C 51.82; H 6.68; N 12.58.



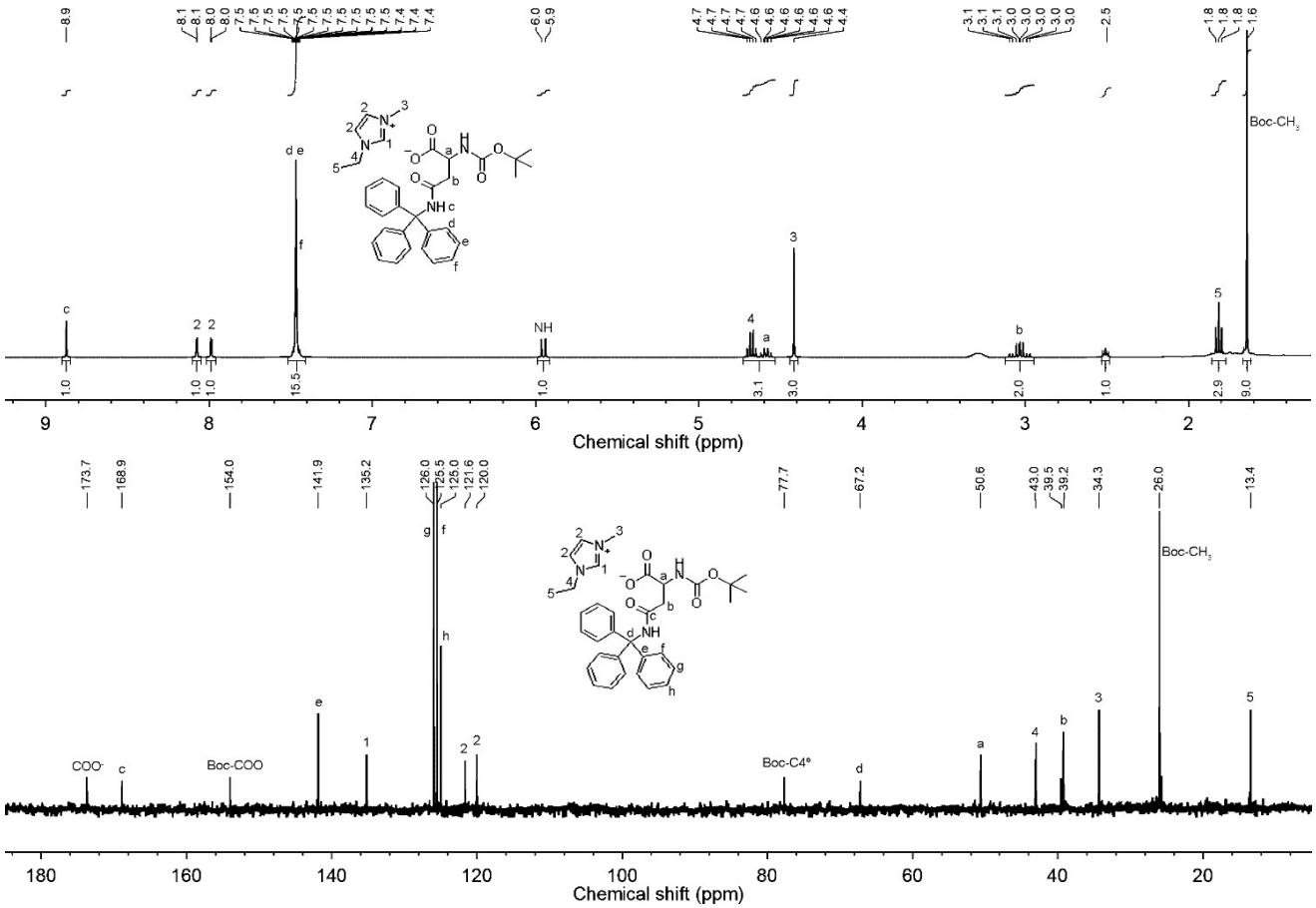


[emim][Boc-Asn]: $[\alpha]_D^{20}$ -11.7 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, J = 2.1 Hz, 1H), 7.99 (d, J = 2.2 Hz, 1H), 7.42 (s, 2H), 5.71 (d, J = 9.3 Hz, 1H), 4.70 (d, J = 7.1 Hz, 1H), 4.70 – 4.58 (m, 2H), 4.51 (s, 3H), 2.85 – 2.75 (m, 1H), 2.79 – 2.69 (m, 1H), 2.50 (m, 1H, DMSO), 1.77 (t, J = 7.1 Hz, 3H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.84, 170.38, 154.02, 135.18, 121.58, 120.10, 77.49, 51.79, 43.20, 39.52 (DMSO), 36.50, 34.35, 26.04, 13.45. Elemental analysis calculated (%) for $C_{15}H_{26}N_4O_3S$ 2.3H_2O: C 51.21; H 8.77; N 15.92; O 24.10; found: C 51.27; H 8.76; N 15.88.

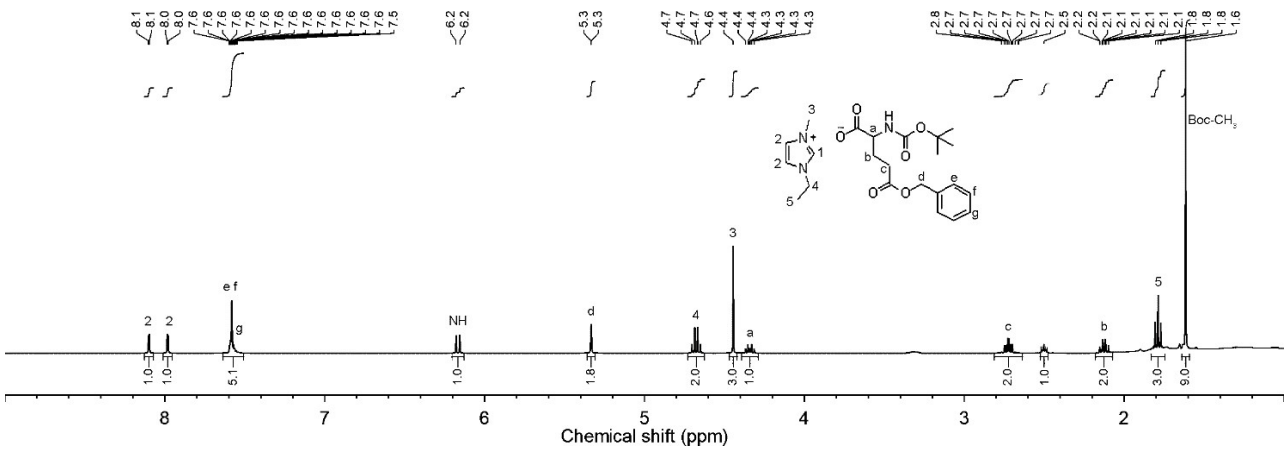


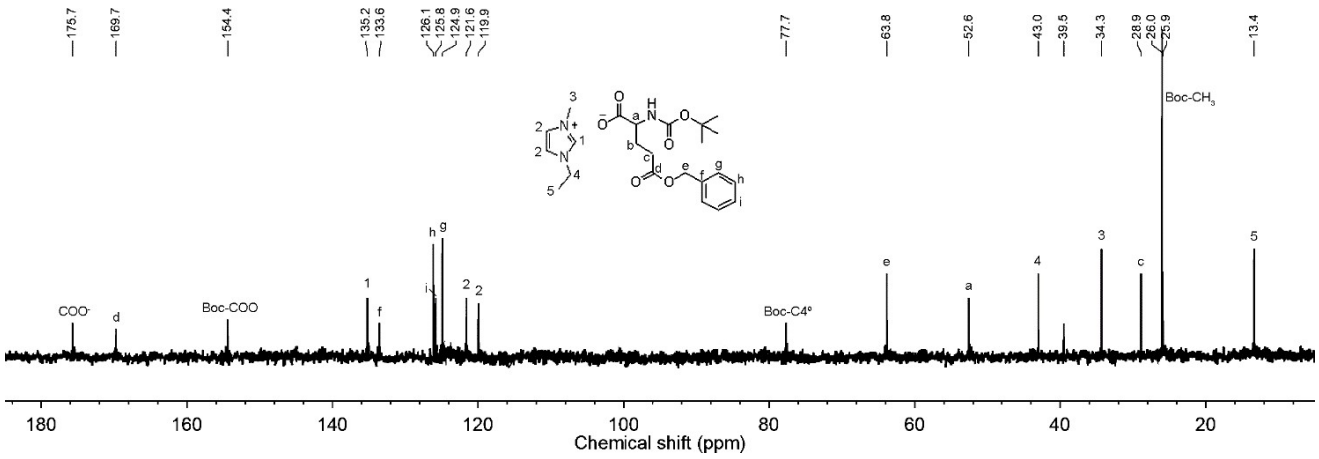


[emim][Boc-Asn(Trt)]: $[\alpha]_D^{20}$ -31.7 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.87 (s, 1H), 8.08 (d, J = 2.2 Hz, 1H), 7.99 (d, J = 2.2 Hz, 1H), 7.52 – 7.41 (m, 16H), 5.95 (d, J = 9.4 Hz, 1H), 4.73 – 4.53 (m, 3H), 4.42 (s, 3H), 3.12 – 2.95 (m, 2H), 2.50 (m, 1H, DMSO), 1.81 (t, J = 7.1 Hz, 3H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.71, 168.89, 153.99, 141.85, 135.21, 125.96, 125.50, 124.98, 121.64, 120.02, 77.69, 67.22, 50.63, 43.04, 39.52 (DMSO), 39.23, 34.34, 26.01, 13.44. Elemental analysis calculated (%) for $C_{34}H_{40}N_4O_5$ $0.2H_2O$: C 69.41; H 6.92; N 9.52; O 14.14; found: C 69.38; H 6.91; N 9.49.

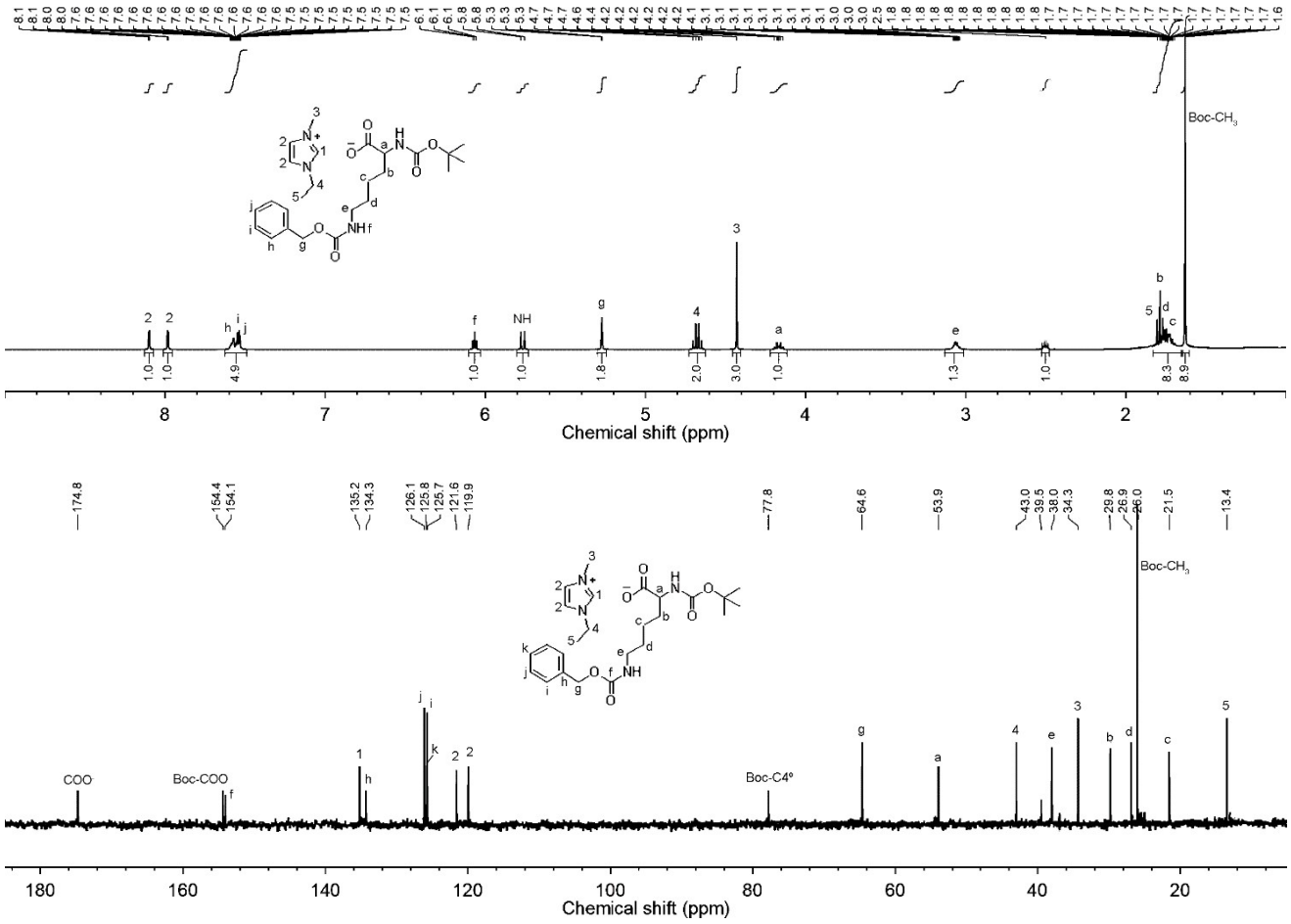


[emim][Boc-Glu(Bn)]: $[\alpha]_D^{20}$ -27.4 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, J = 2.1 Hz, 1H), 7.98 (d, J = 2.2 Hz, 1H), 7.64 – 7.51 (m, 5H), 6.17 (d, J = 9.4 Hz, 1H), 5.33 (d, J = 0.9 Hz, 2H), 4.68 (q, J = 7.1 Hz, 2H), 4.45 (s, 3H), 4.34 (dt, J = 9.4, 5.9 Hz, 1H), 2.72 (td, J = 7.9, 3.4 Hz, 2H), 2.50 (m, 1H, DMSO), 2.18 – 2.07 (m, 2H), 1.79 (t, J = 7.1 Hz, 3H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.71, 169.74, 154.39, 135.21, 133.56, 126.13, 125.82, 124.89, 121.60, 119.95, 77.69, 63.83, 52.57, 43.02, 39.52 (DMSO), 34.34, 28.90, 26.02, 25.91, 13.36. Elemental analysis calculated (%) for $C_{23}H_{33}N_3O_6$ $0.4H_2O$: C 60.75; H 7.49; N 9.24; O 22.52; found: C 60.49; H 7.42; N 9.22.

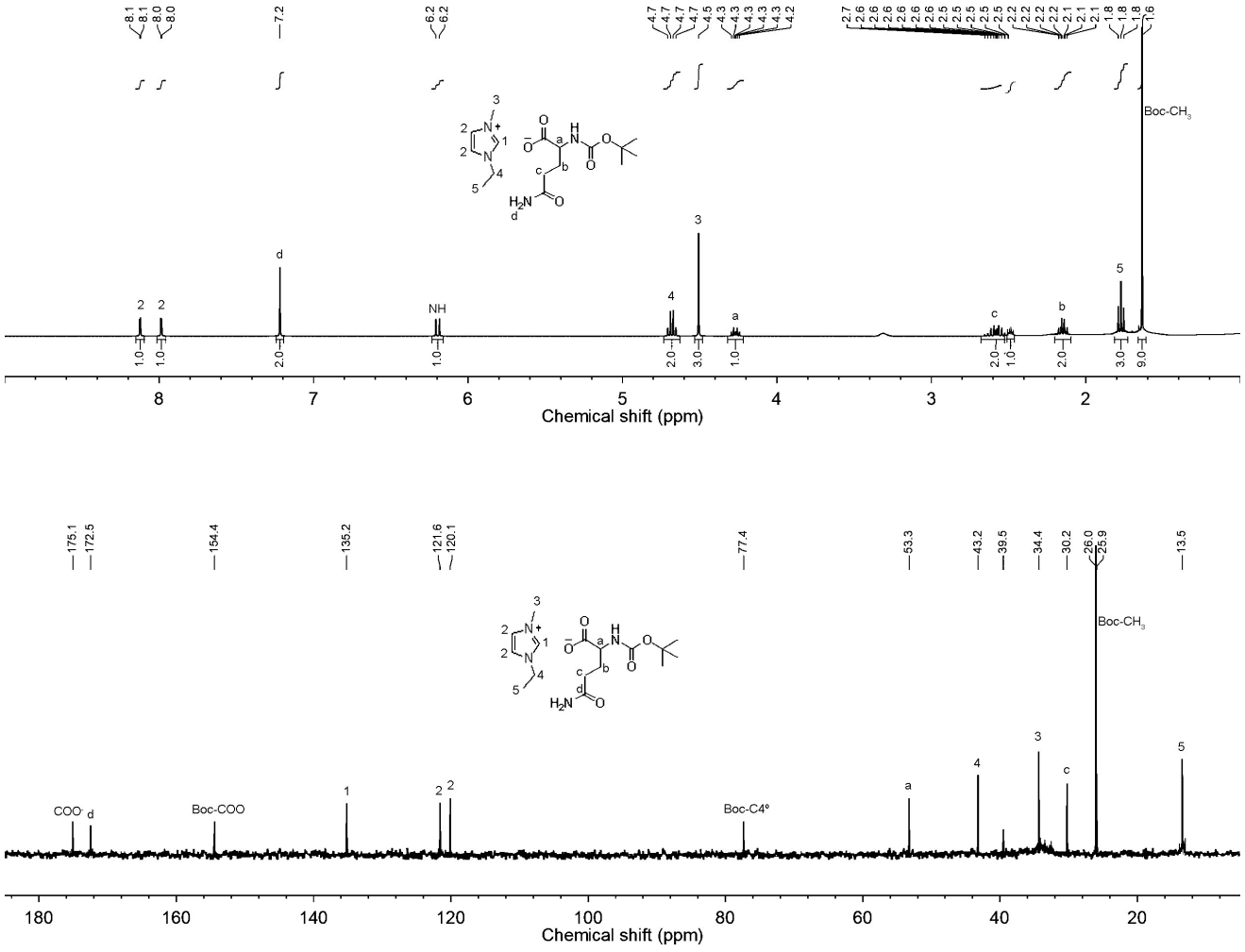




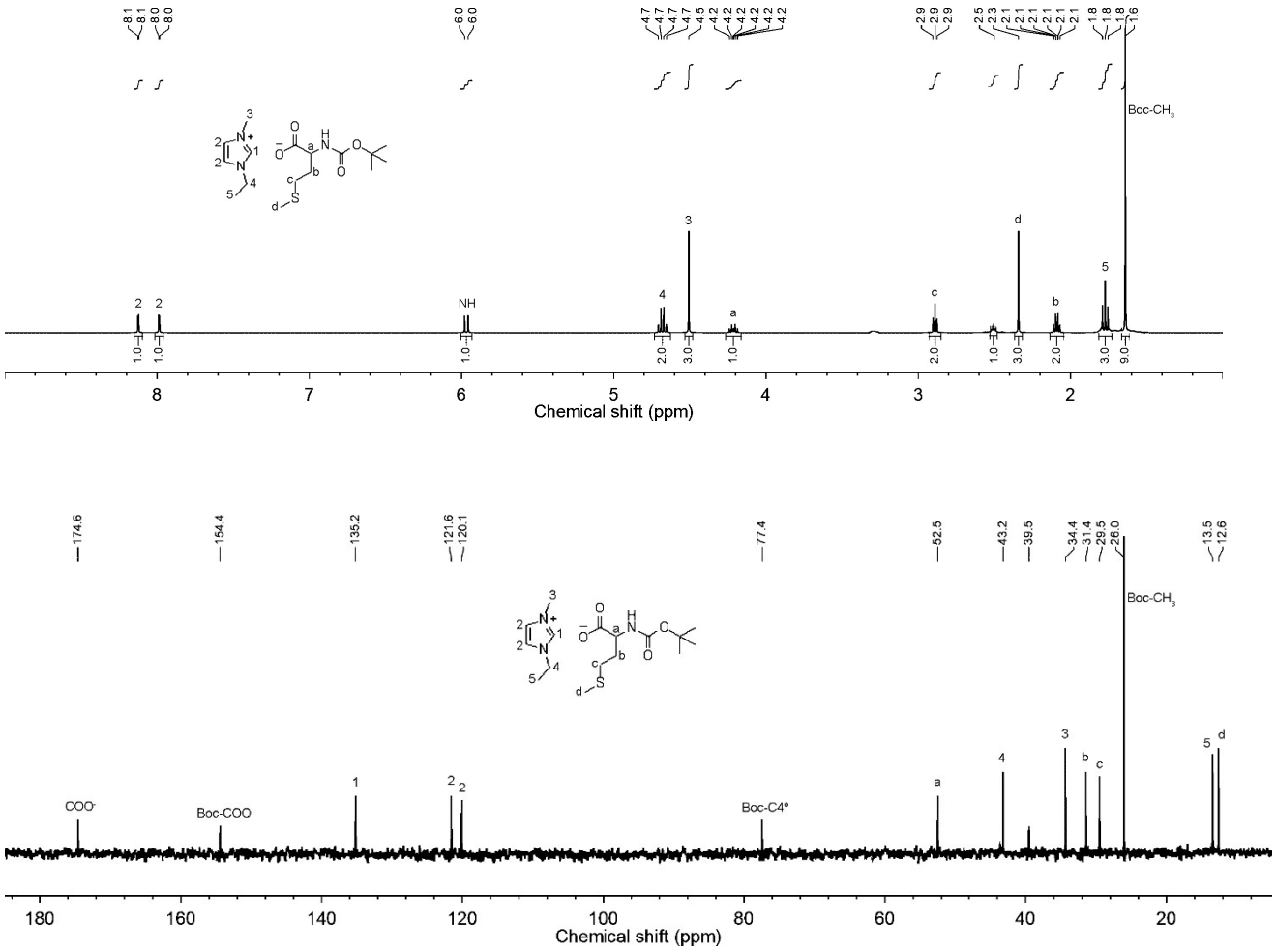
[emim][Boc-Lys(Z)]: $[\alpha]_D^{20}$ -15.2 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.10 (d, *J* = 2.1 Hz, 1H), 7.98 (d, *J* = 2.2 Hz, 1H), 7.62 – 7.49 (m, 5H), 6.07 (t, *J* = 4.3 Hz, 1H), 5.77 (d, *J* = 9.3 Hz, 1H), 5.27 (d, *J* = 1.3 Hz, 2H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.43 (s, 3H), 4.22 – 4.12 (m, 1H), 3.06 (tdd, *J* = 6.1, 4.3, 2.8 Hz, 1H), 2.50 (m, 1H, DMSO), 1.83 – 1.65 (m, 8H), 1.63 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.77, 154.39, 154.07, 135.21, 134.30, 126.12, 125.81, 125.72, 121.60, 119.95, 77.79, 64.65, 53.93, 43.03, 39.52 (DMSO), 38.03, 34.34, 29.81, 26.89, 26.03, 21.54, 13.44. Elemental analysis calculated (%) for $C_{25}H_{38}N_4O_6$ $0.7H_2O$: C 59.67; H 7.89; N 11.13; O 21.31; found: C 59.62; H 7.87; N 11.13.



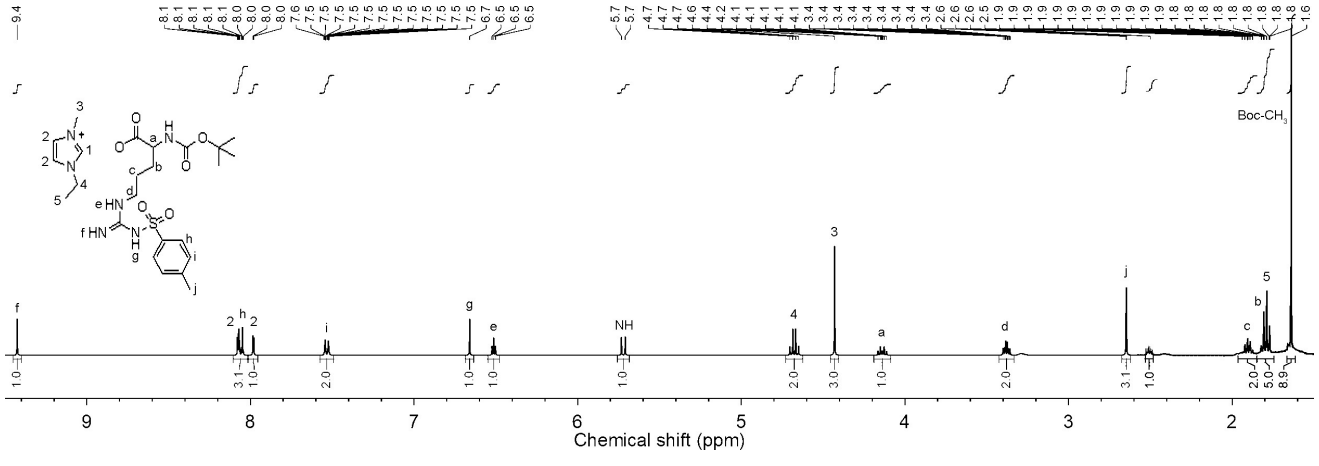
[emim][Boc-Gln]: $[\alpha]_D^{20}$ -19.8 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.22 (s, 2H), 6.20 (d, *J* = 9.4 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (s, 3H), 4.27 (dt, *J* = 9.3, 5.9 Hz, 1H), 2.68 – 2.48 (m, 2H), 2.50 (m, 1H, DMSO), 2.15 (td, *J* = 7.8, 5.8 Hz, 2H), 1.77 (t, *J* = 7.1 Hz, 3H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.08, 172.48, 154.43, 135.18, 121.58, 120.10, 77.36, 53.25, 43.20, 39.52 (DMSO), 34.35, 30.23, 26.04, 25.92, 13.45. Elemental analysis calculated (%) for $C_{16}H_{28}N_4O_5$ 1.4H_2O: C 50.35; H 8.13; N 14.68; O 26.83; found: C 50.33; H 8.14; N 14.65.

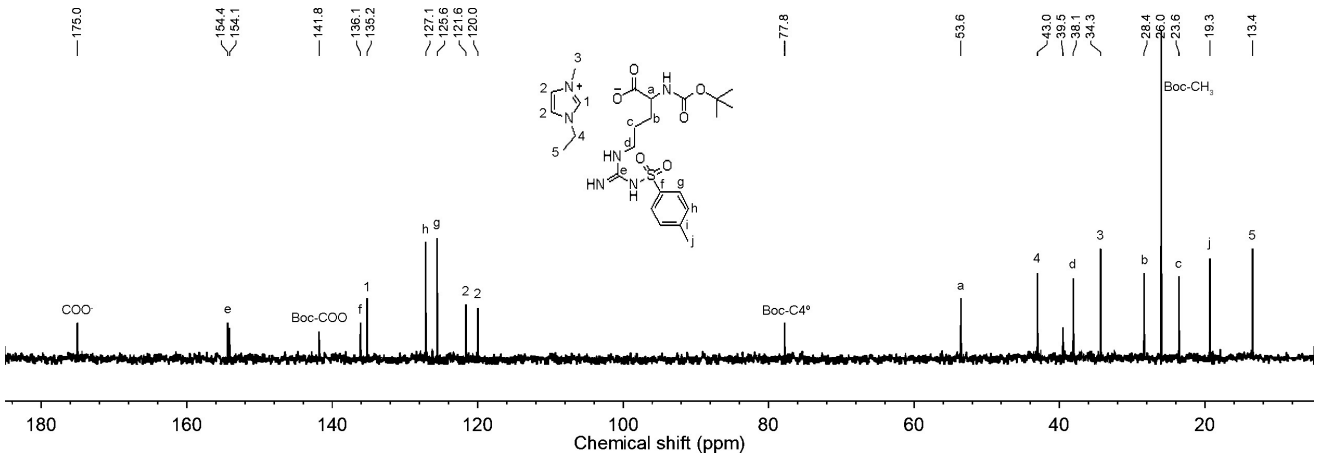


[emim][Boc-Met]: $[\alpha]_D^{20}$ -25.0 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 5.97 (d, *J* = 9.3 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (s, 3H), 4.21 (dt, *J* = 9.4, 5.9 Hz, 1H), 2.89 (t, *J* = 5.3 Hz, 2H), 2.50 (m, 1H, DMSO), 2.34 (s, 3H), 2.09 (dt, *J* = 5.9, 5.3 Hz, 2H), 1.77 (t, *J* = 7.1 Hz, 3H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.59, 154.43, 135.18, 121.58, 120.10, 77.43, 52.48, 43.20, 39.52 (DMSO), 34.35, 31.43, 29.51, 26.04, 13.45, 12.60. Elemental analysis calculated (%) for $C_{16}H_{29}N_3O_4S$ 0.6H_2O: C 51.90; H 8.22; N 11.35; O 19.88; S 8.66; found: C 51.80; H 8.18; N 11.37.

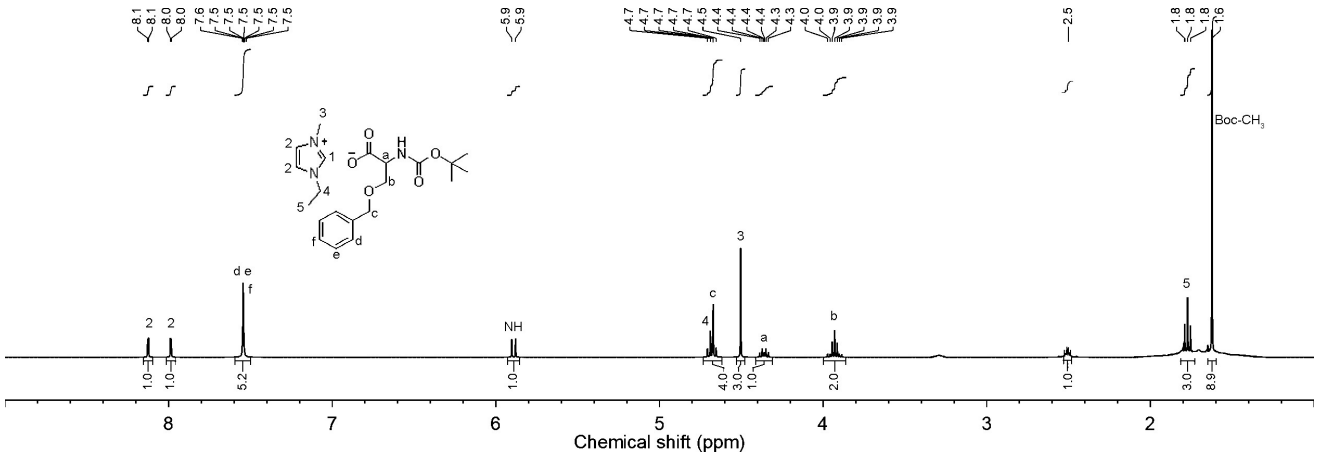


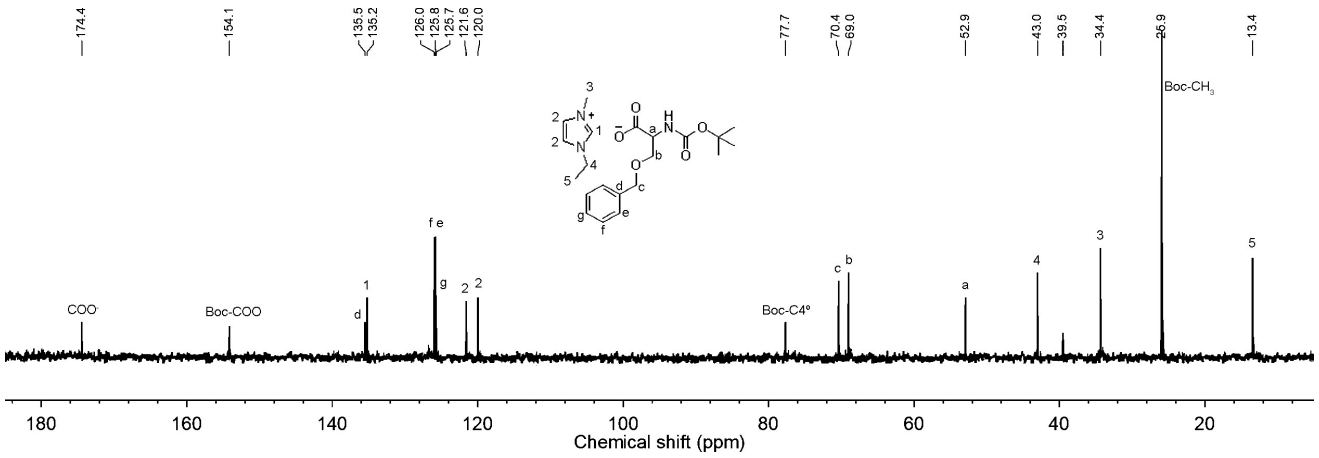
[emim][Boc-Arg(Ts)]: $[\alpha]_D^{20}$ 13.1 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.43 (s, 1H), 8.10 – 8.02 (m, 3H), 7.98 (d, *J* = 2.2 Hz, 1H), 7.53 (ddt, *J* = 7.3, 1.3, 0.7 Hz, 2H), 6.66 (s, 1H), 6.51 (t, *J* = 4.3 Hz, 1H), 5.72 (d, *J* = 9.3 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.43 (s, 3H), 4.14 (dt, *J* = 9.3, 5.9 Hz, 1H), 3.43 – 3.33 (m, 2H), 2.65 (t, *J* = 0.7 Hz, 3H), 2.50 (m, 1H, DMSO), 1.96 – 1.85 (m, 2H), 1.85 – 1.75 (m, 5H), 1.64 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.05, 154.38, 154.12, 141.80, 136.12, 135.21, 127.15, 125.56, 121.62, 119.97, 77.79, 53.55, 43.03, 39.52 (DMSO), 38.09, 34.34, 28.36, 26.01, 23.56, 19.30, 13.44. Elemental analysis calculated (%) for $C_{24}H_{38}N_6O_6S\ H_2O$: C 51.78; H 7.24; N 15.10; O 20.12; S 5.76; found: C 51.75; H 7.22; N 15.13.



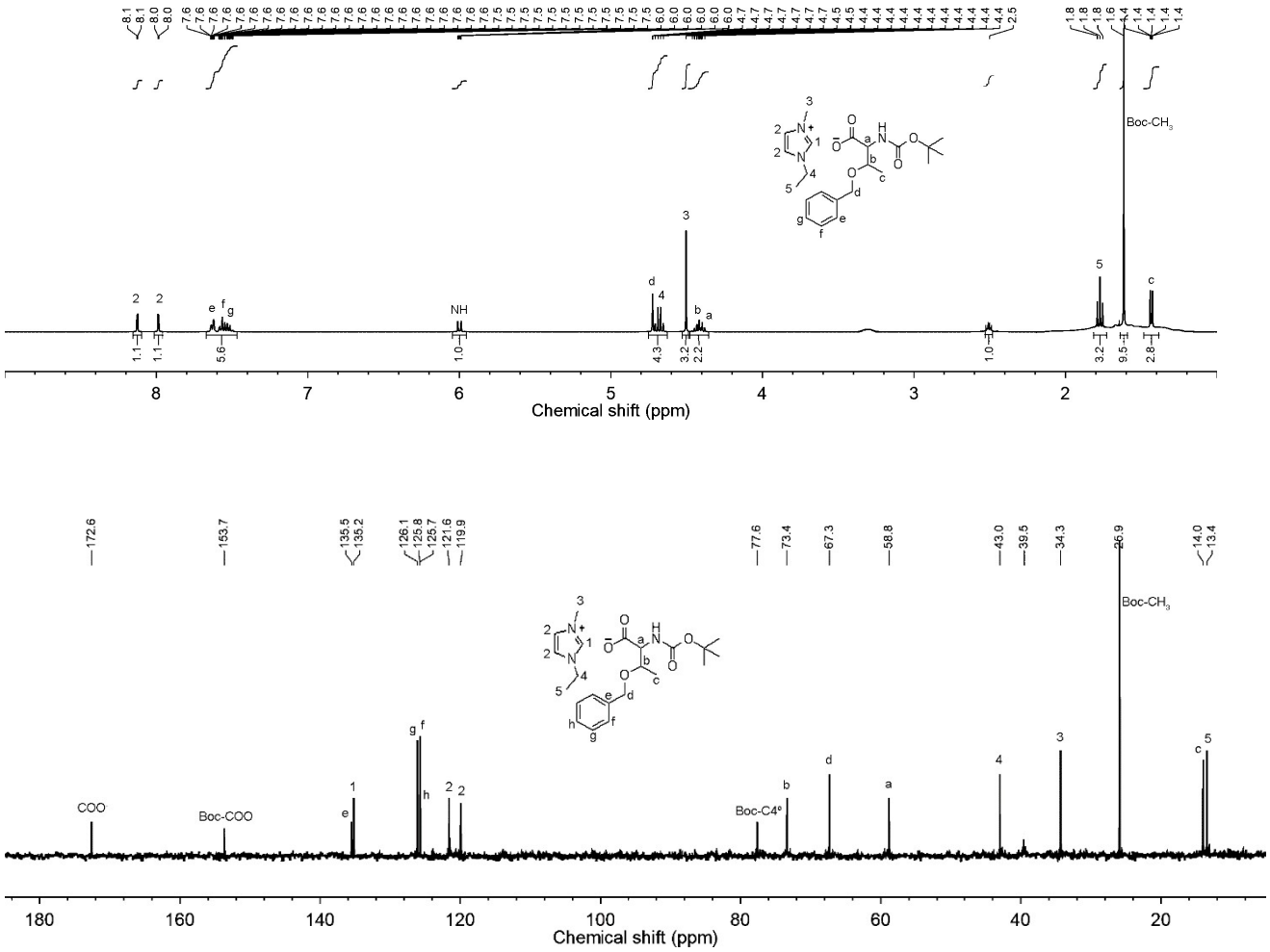


[emim][Boc-Ser(Bn)]: $[\alpha]_D^{20}$ -7.2 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.54 (d, *J* = 0.6 Hz, 5H), 5.89 (d, *J* = 9.3 Hz, 1H), 4.73 – 4.62 (m, 4H), 4.50 (s, 3H), 4.36 (dt, *J* = 9.3, 6.0 Hz, 1H), 4.00 – 3.86 (m, 2H), 2.50 (m, 1H, DMSO), 1.77 (t, *J* = 7.1 Hz, 3H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.44, 154.14, 135.49, 135.20, 125.95, 125.78, 125.72, 121.58, 119.97, 77.68, 70.37, 69.01, 52.92, 43.01, 39.52 (DMSO), 34.35, 25.93, 13.44. Elemental analysis calculated (%) for $C_{21}H_{31}N_3O_5$ 0.1H_2O: C 61.93; H 7.72; N 10.32; O 20.03; found: C 61.90; H 7.69; N 10.28.

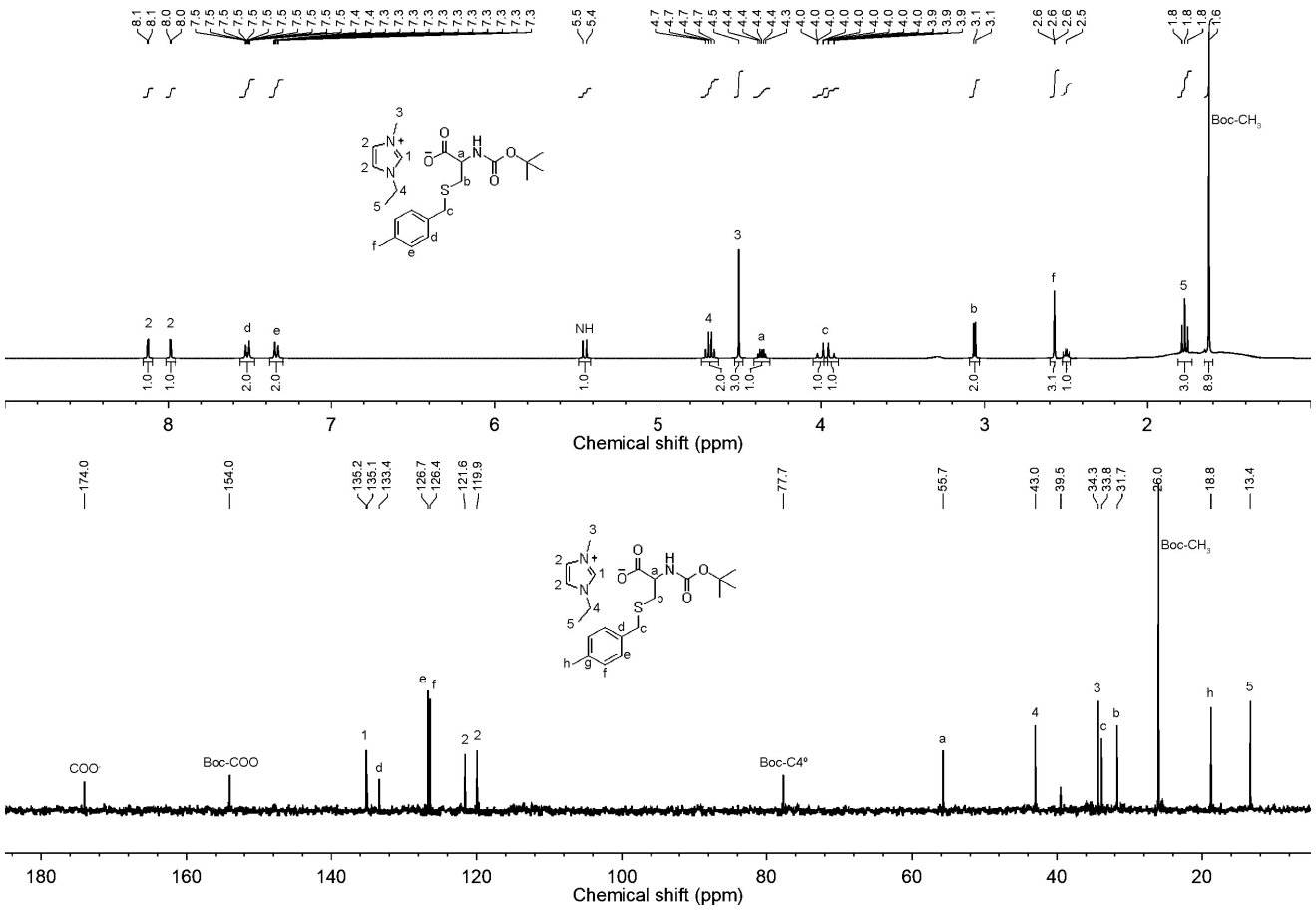




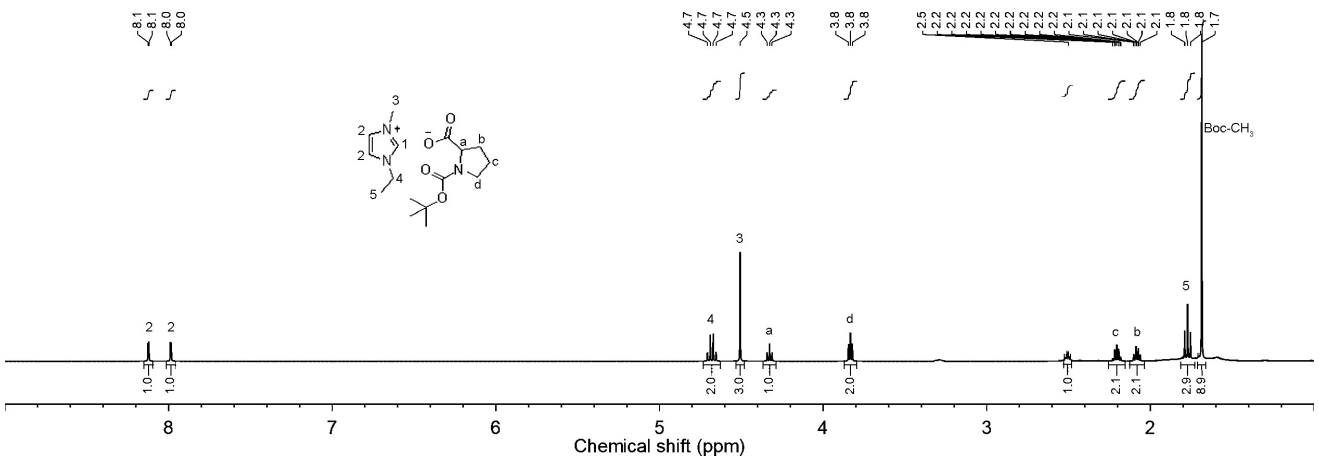
[emim][Boc-Thr(Bn)]: $[\alpha]_D^{20}$ 11.9 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.67 – 7.47 (m, 6H), 6.05 – 5.95 (m, 1H), 4.75 – 4.63 (m, 4H), 4.50 (s, 3H), 4.49 – 4.36 (m, 2H), 2.50 (m, 1H, DMSO), 1.77 (t, *J* = 7.1 Hz, 3H), 1.62 (s, 10H), 1.48 – 1.38 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.62, 153.68, 135.52, 135.20, 126.12, 125.76, 125.73, 121.59, 119.94, 77.63, 73.38, 67.31, 58.82, 43.01, 39.52 (DMSO), 34.33, 25.92, 14.00, 13.44. Elemental analysis calculated (%) for $C_{22}H_{33}N_3O_5$ 0.3H_2O: C 62.19; H 7.97; N 9.89; O 19.96; found: C 62.23; H 7.97; N 9.84.

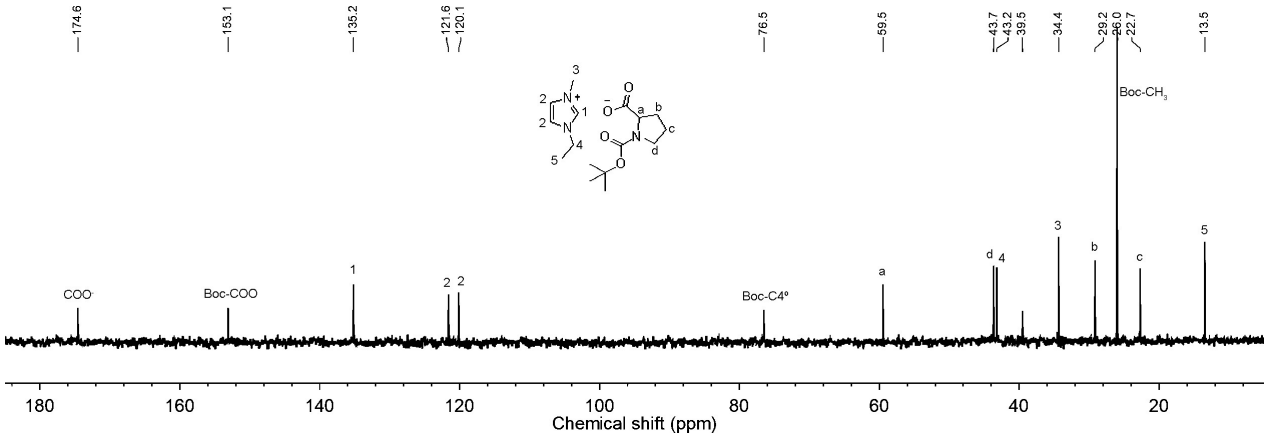


[emim][Boc-Cys(Meb)]: $[\alpha]_D^{20}$ -52.9 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.34 (ddt, *J* = 7.6, 1.3, 0.7 Hz, 2H), 5.45 (d, *J* = 9.3 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.50 (s, 3H), 4.36 (dt, *J* = 9.3, 4.6 Hz, 1H), 4.00 (dt, *J* = 13.9, 1.0 Hz, 1H), 3.94 (dt, *J* = 13.9, 1.1 Hz, 1H), 3.06 (d, *J* = 4.7 Hz, 2H), 2.57 (t, *J* = 0.7 Hz, 3H), 2.50 (m, 1H, DMSO), 1.77 (t, *J* = 7.1 Hz, 3H), 1.63 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.05, 154.02, 135.20, 135.09, 133.43, 126.69, 126.40, 121.59, 119.94, 77.70, 55.72, 43.01, 39.52 (DMSO), 34.33, 33.85, 31.70, 26.01, 18.77, 13.35. Elemental analysis calculated (%) for $C_{22}H_{33}N_3O_4S$ H_2O: C 58.25; H 7.78; N 9.26; O 17.64; S 7.07; found: C 58.33; H 7.72; N 9.25.



[emim][Boc-Pro]: $[\alpha]_D^{20}$ -37.2 (*c* 2.0, DMF); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.12 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 2.2 Hz, 1H), 4.68 (q, *J* = 7.1 Hz, 2H), 4.51 (s, 3H), 4.33 (t, *J* = 6.0 Hz, 1H), 3.83 (t, *J* = 4.8 Hz, 2H), 2.50 (m, 1H, DMSO), 2.26 – 2.16 (m, 2H), 2.13 – 2.04 (m, 2H), 1.77 (t, *J* = 7.1 Hz, 3H), 1.69 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.58, 153.10, 135.18, 121.59, 120.12, 76.49, 59.46, 43.67, 43.20, 39.52 (DMSO), 34.35, 29.15, 26.00, 22.70, 13.45. Elemental analysis calculated (%) for $C_{16}H_{27}N_3O_4$ $0.8H_2O$: C 56.55; H 8.48; N 12.37; O 22.60; found: C 56.59; H 8.45; N 12.34.





FT-IR analysis

From these curves (shown in Fig. S1-S3.) we can get the preliminary conclusion that what we synthesize were the aimed products of ionic liquids. For AAILs the signals between 3000 and 3200 cm^{-1} are assigned to C-H stretching modes predominantly originating from the aromatic imidazolium ring.[1] At wave number 1579 cm^{-1} and 1486 cm^{-1} there are the imidazole ring skeletons vibration absorption peaks. The signals between 2800 and 3000 cm^{-1} result from aliphatic CH groups in the ethyl and methyl moieties.[2-4] In the case of the protected amino acid anion, the peaks at 1528-1498 cm^{-1} and 1698-1691 cm^{-1} were attributed to the vibration absorption of CO-NH and CO of secondary amide (except for [emim][Boc-Pro]), respectively, indicating the Boc-protection of amine group.[5,6] The peaks at 1360 cm^{-1} and 1390 cm^{-1} belonged to the Boc group were also characteristic of the formation of *tert*-butyl-*N*-(3-hydroxypropyl) carbamate. At 1390-1370 cm^{-1} there is the typical symmetrical stretching vibration peak of COO^- group and its asymmetrical stretching vibration peak is found at 1610-1560 cm^{-1}.

References

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Supplementary figures

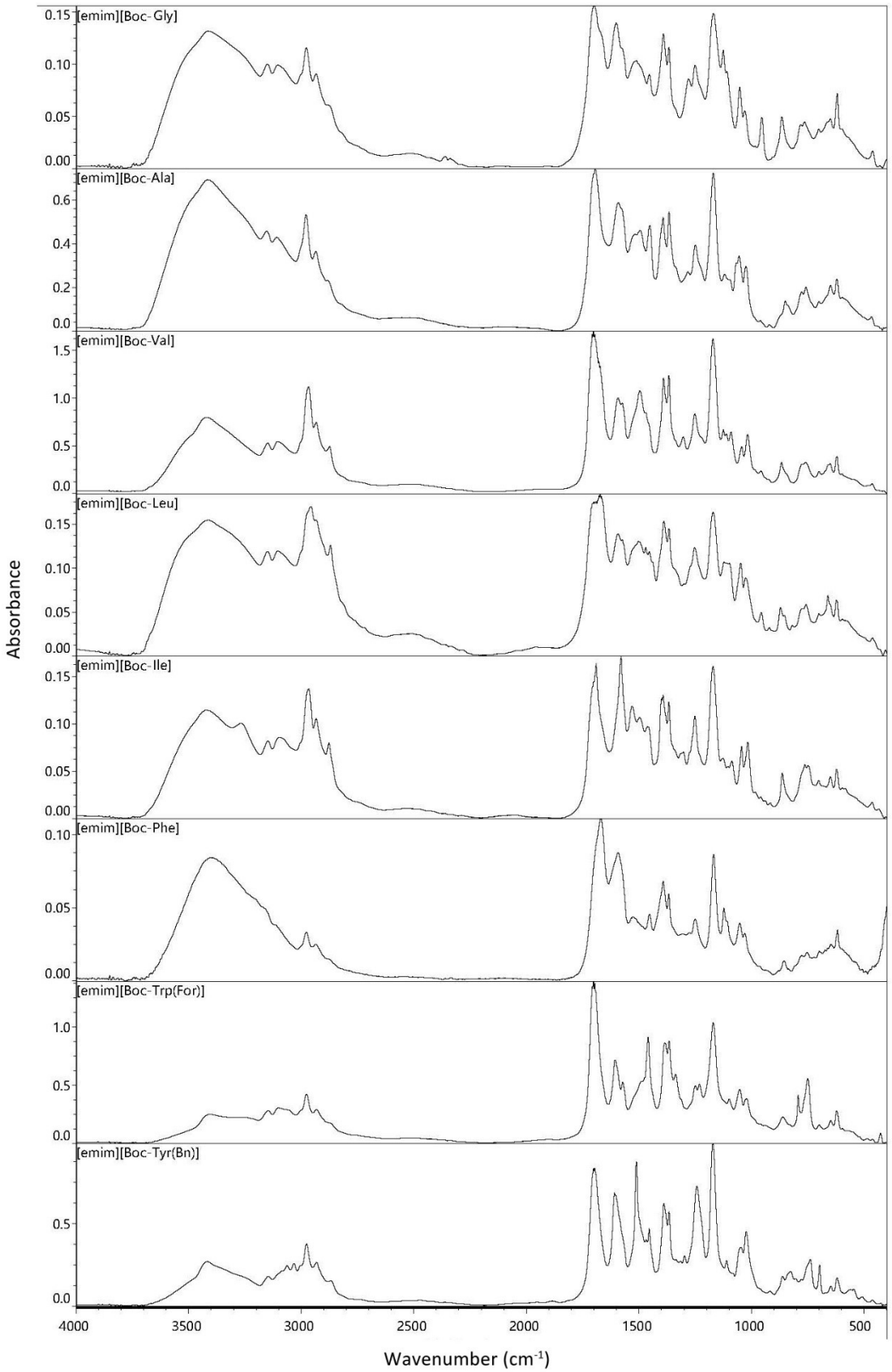

Figure S1. Infrared spectra of different ionic liquids: [emim][Boc-Gly], [emim][Boc-Ala], [emim][Boc-Val], [emim][Boc-Leu], [emim][Boc-Ile], [emim][Boc-Phe], [emim][Boc-Trp(For)] and [emim][Boc-Tyr(Bn)].

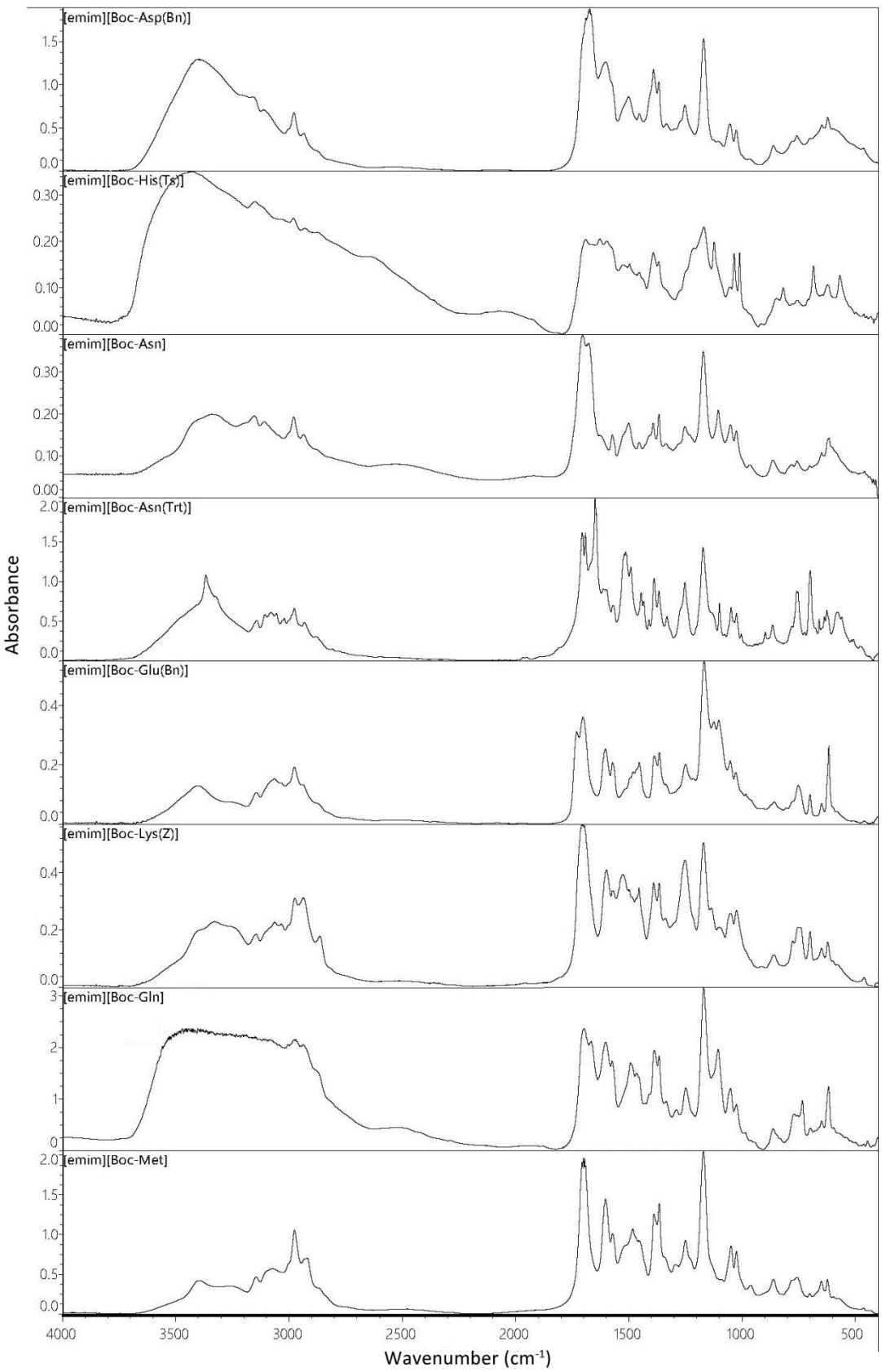

Figure S2. Infrared spectra of different ionic liquids: [emim][Boc-Asp(Bn)], [emim][Boc-His(Ts)], [emim][Boc-Asn], [emim][Boc-Asn(Trt)], [emim][Boc-Glu(Bn)], [emim][Boc-Lys(Z)], [emim][Boc-Gln] and [emim][Boc-Met].

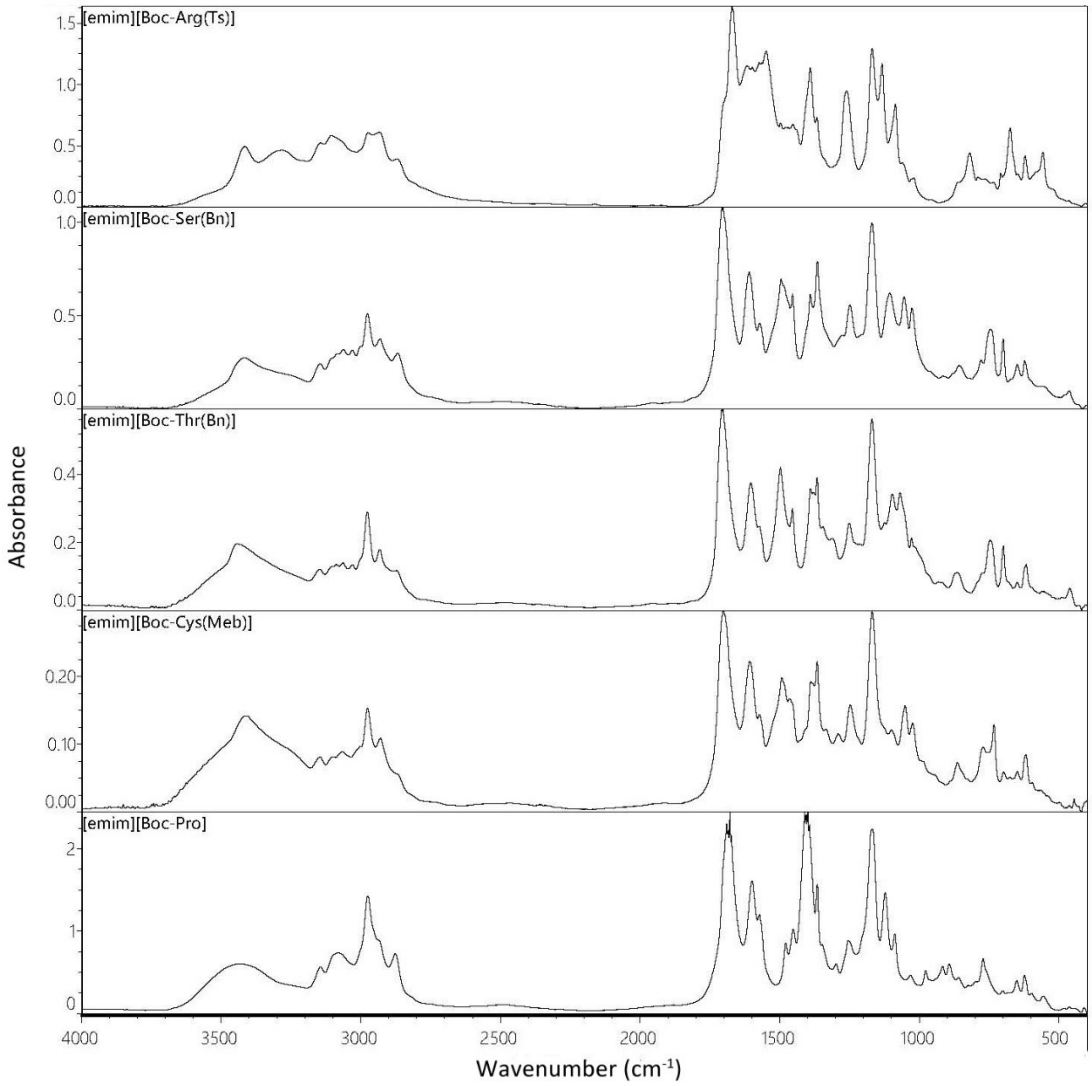

Figure S3. Infrared spectra of different ionic liquids: [emim][Boc-Arg(Ts)], [emim][Boc-Ser(Bn)], [emim][Boc-Thr(Bn)], [emim][Boc-Cys(Meb)] and [emim][Boc-Pro].

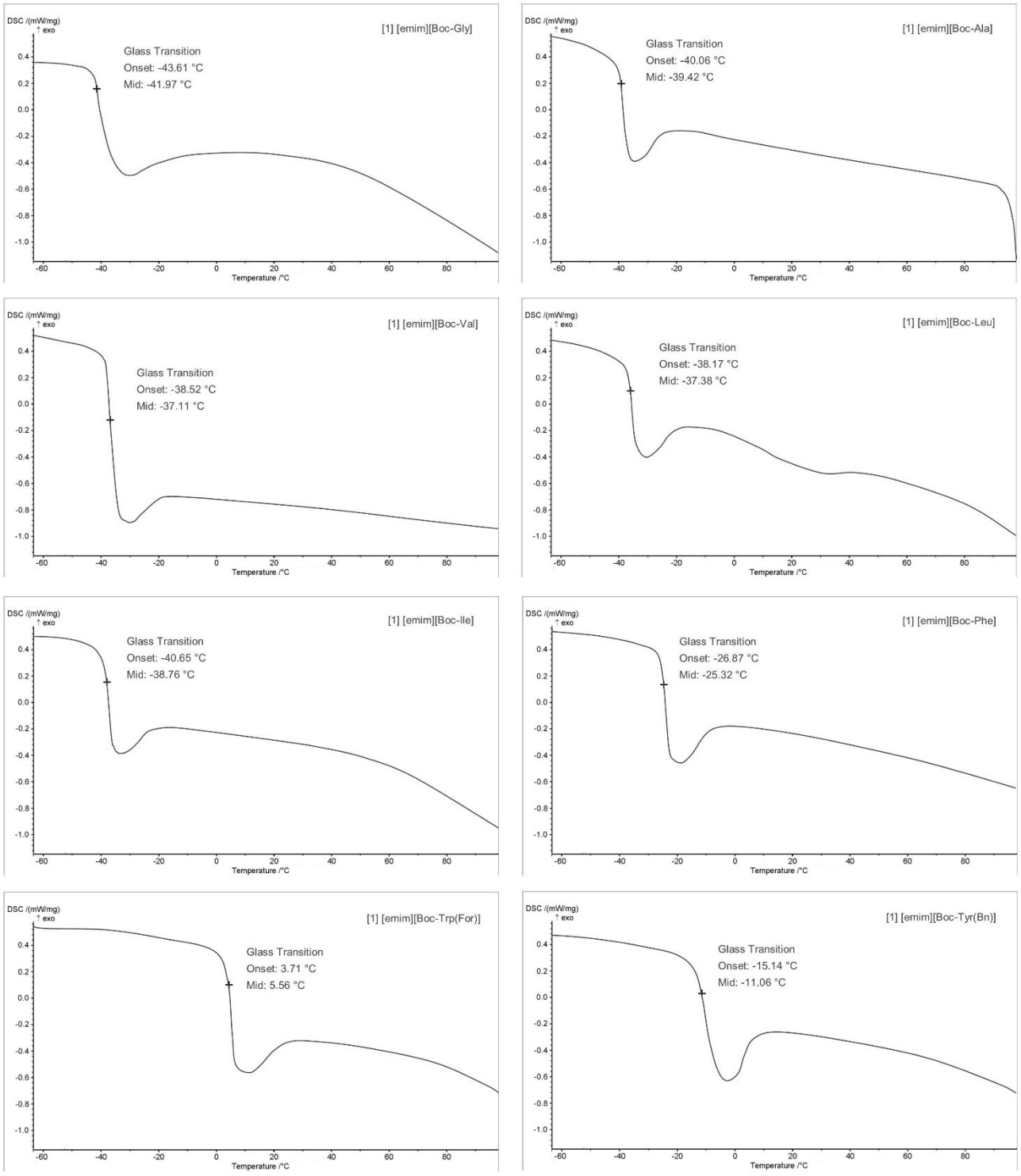

Figure S4. DSC determination of glass transition temperature (T_g) for [emim][Boc-Gly], [emim][Boc-Ala], [emim][Boc-Val], [emim][Boc-Leu], [emim][Boc-Ile], [emim][Boc-Phe], [emim][Boc-Trp(For)] and [emim][Boc-Tyr(Bn)].

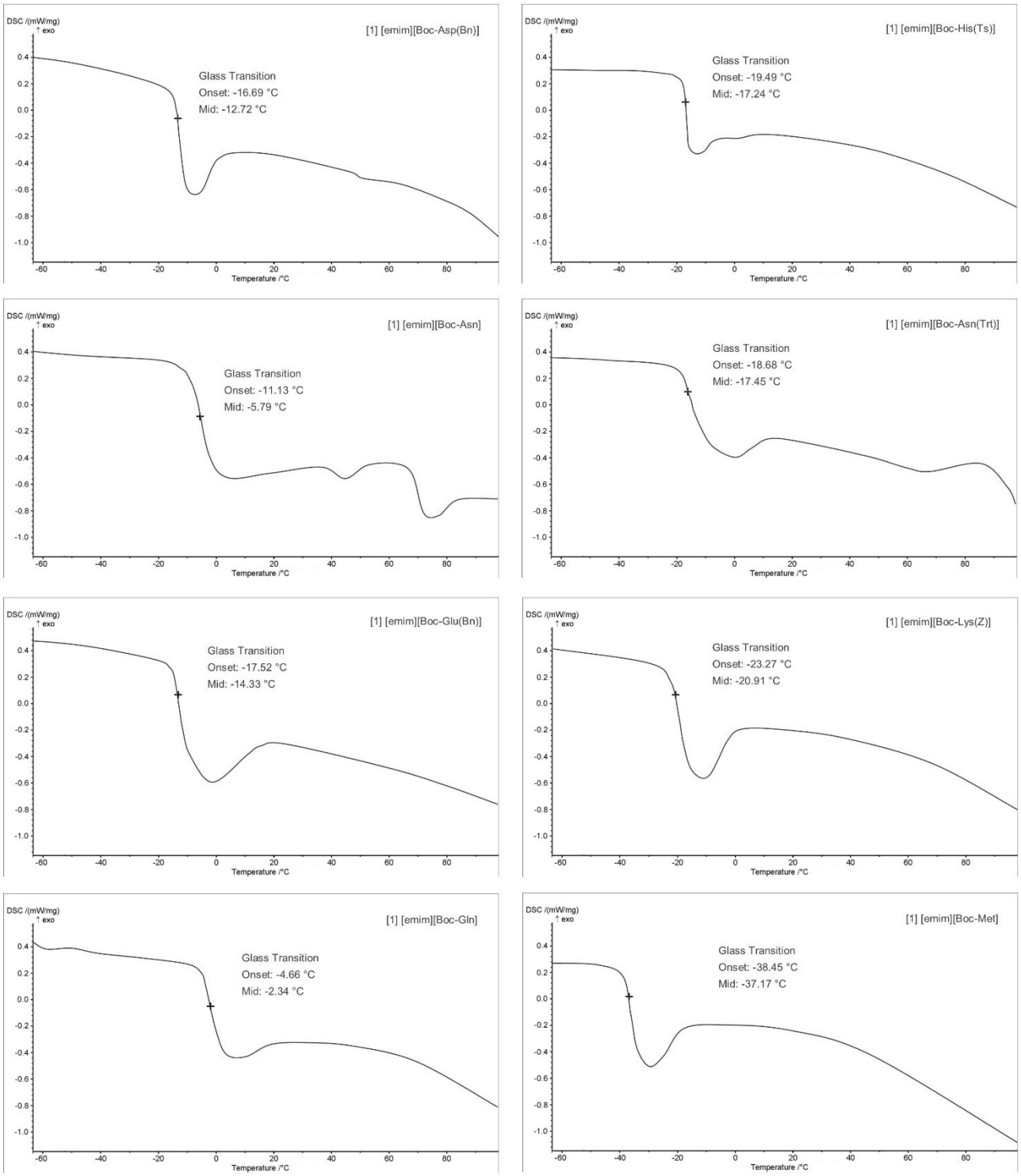

Figure S5. DSC determination of glass transition temperature (T_g) for [emim][Boc-Asp(Bn)], [emim][Boc-His(Ts)], [emim][Boc-Asn], [emim][Boc-Asn(Trt)], [emim][Boc-Glu(Bn)], [emim][Boc-Lys(Z)], [emim][Boc-Gln] and [emim][Boc-Met].

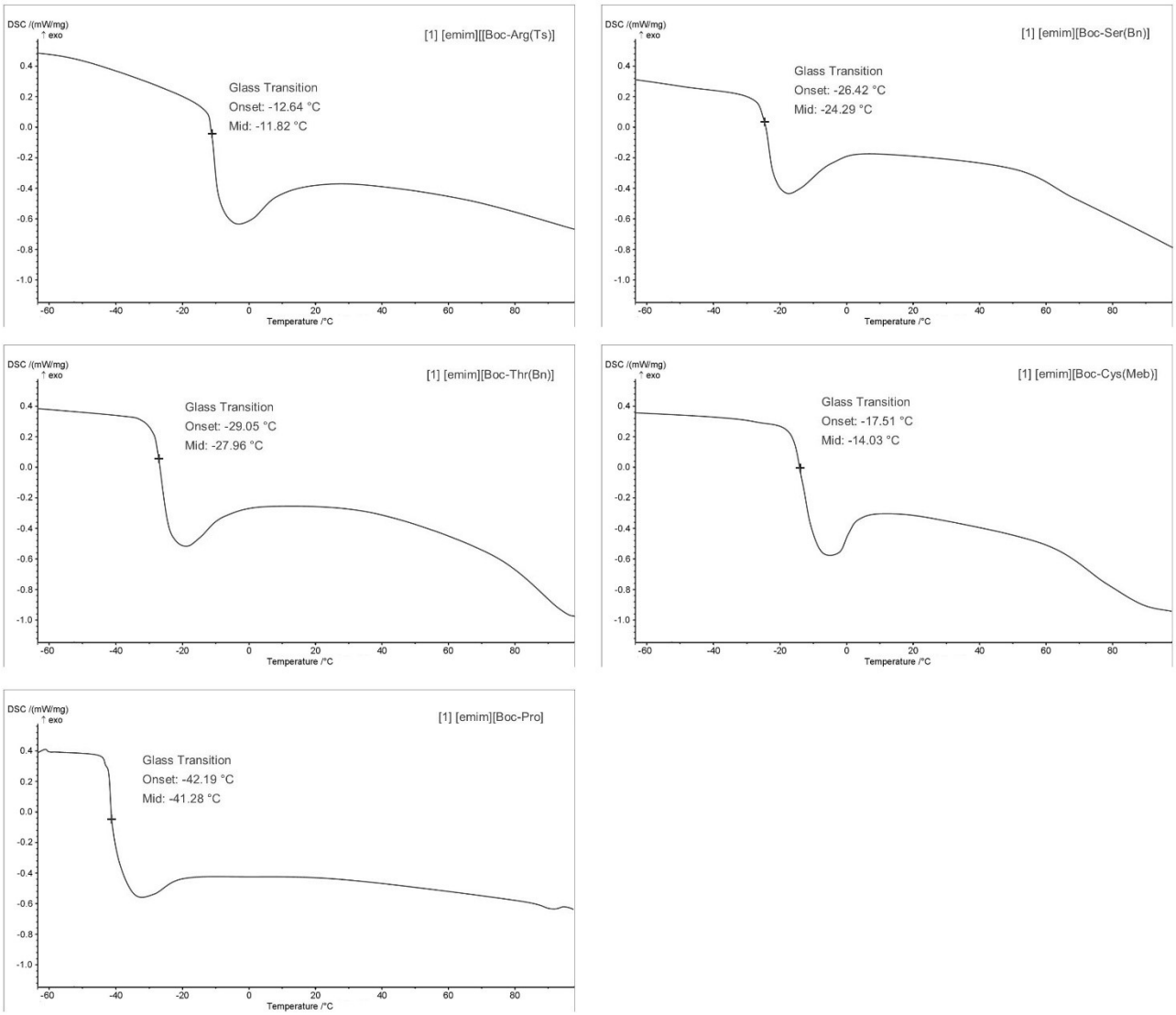

Figure S6. DSC determination of glass transition temperature (T_g) for [emim][Boc-Arg(Ts)], [emim][Boc-Ser(Bn)], [emim][Boc-Thr(Bn)], [emim][Boc-Cys(Meb)] and [emim][Boc-Pro].

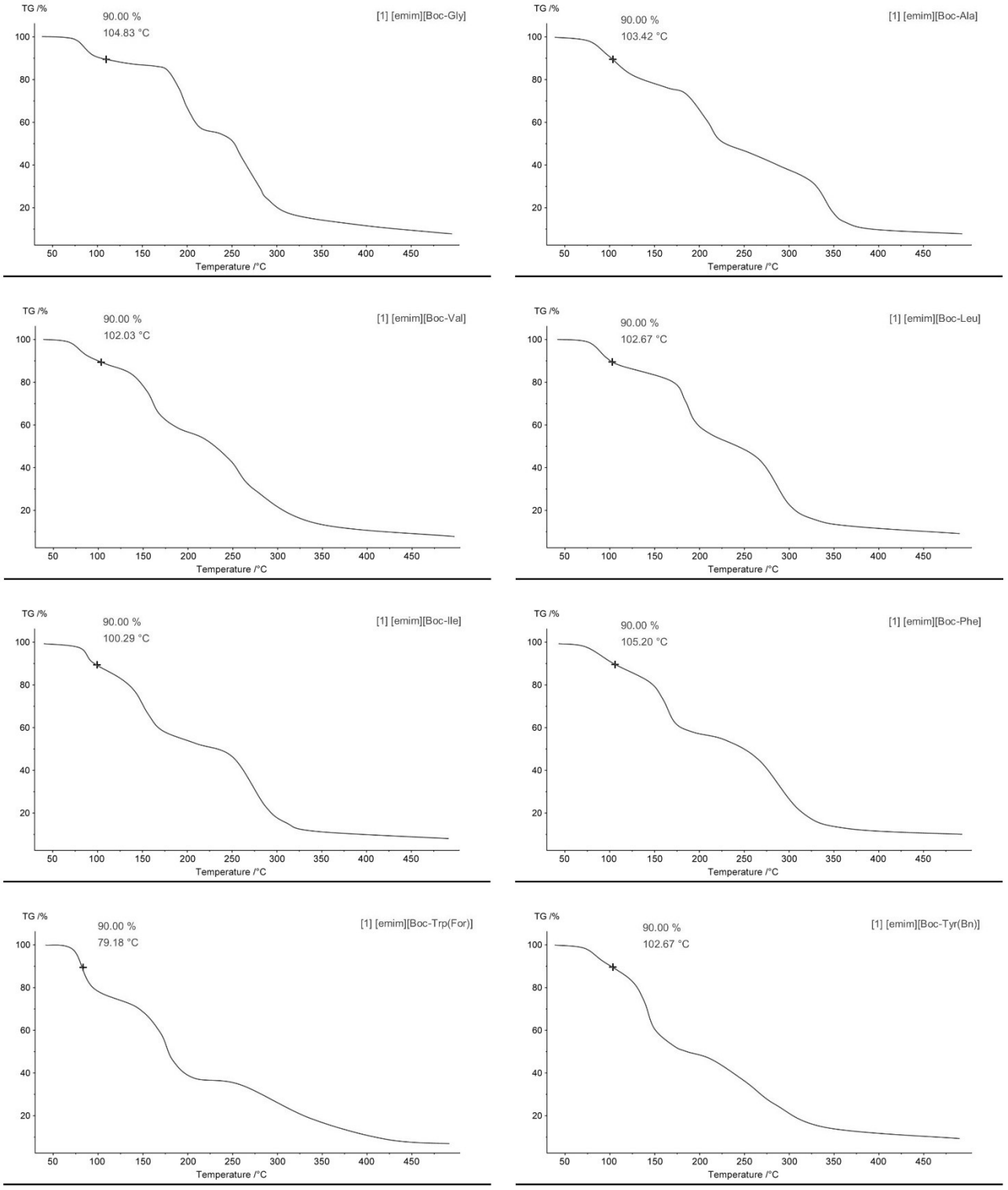

Figure S7. TGA thermogram for determination of decomposition temperature (T_d) for [emim][Boc-Gly], [emim][Boc-Ala], [emim][Boc-Val], [emim][Boc-Leu], [emim][Boc-Ile], [emim][Boc-Phe], [emim][Boc-Trp(For)] and [emim][Boc-Tyr(Bn)].

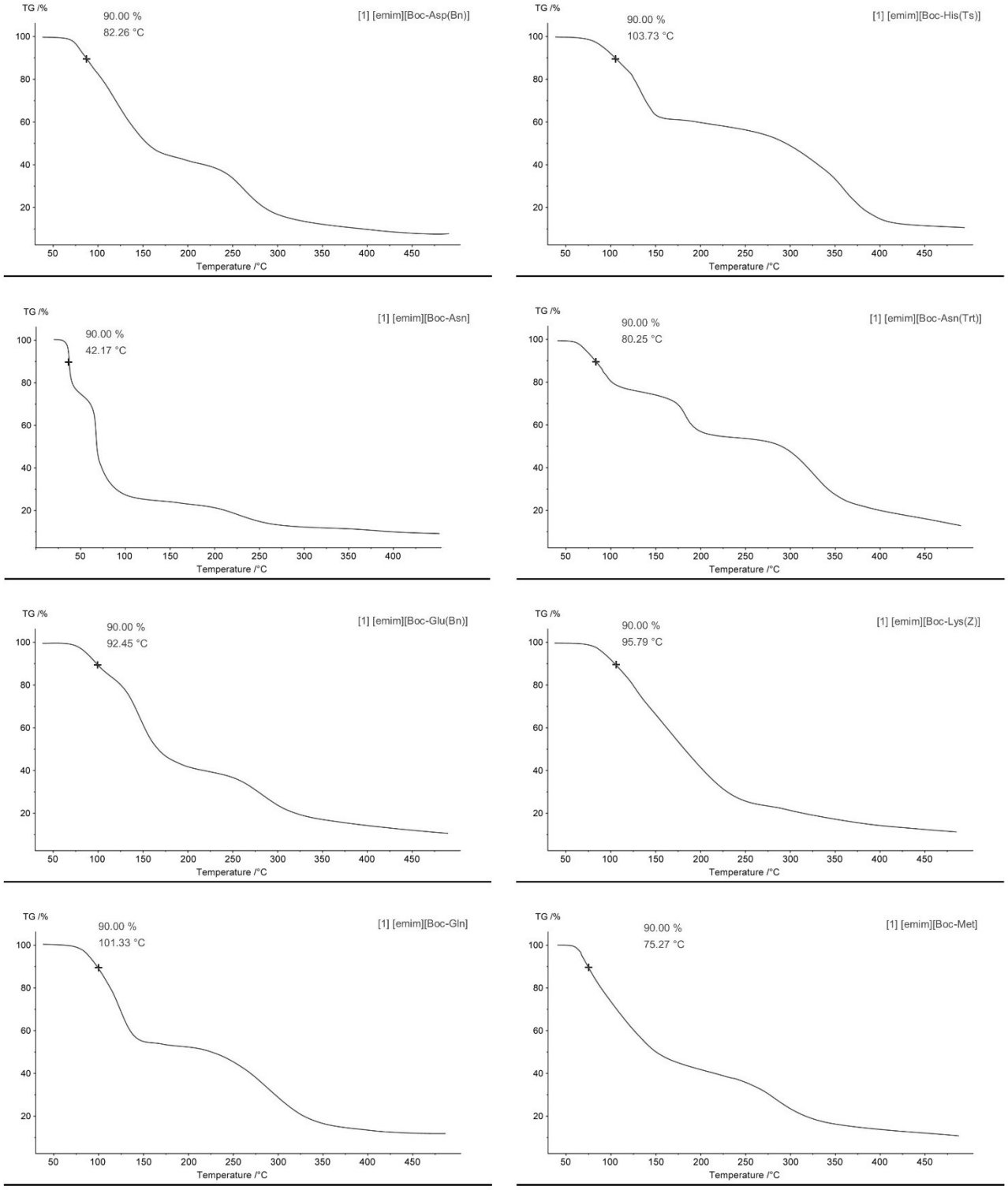

Figure S8. TGA thermogram for determination of decomposition temperature (T_d) for [emim][Boc-Asp(Bn)], [emim][Boc-His(Ts)], [emim][Boc-Asn], [emim][Boc-Asn(Trt)], [emim][Boc-Glu(Bn)], [emim][Boc-Lys(Z)], [emim][Boc-Gln] and [emim][Boc-Met].

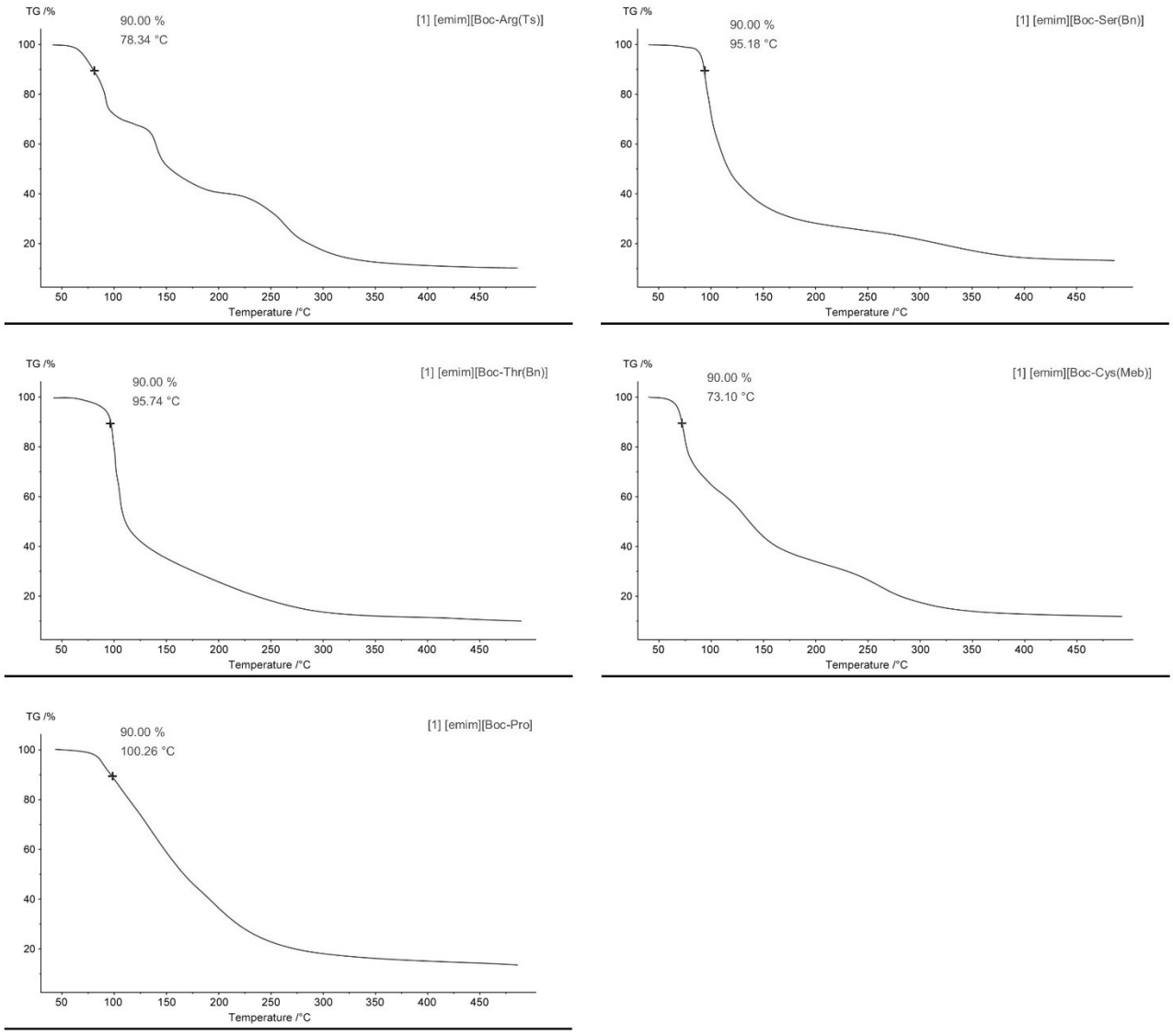

Figure S9. TGA thermogram for determination of decomposition temperature (T_d) for [emim][Boc-Arg(Ts)], [emim][Boc-Ser(Bn)], [emim][Boc-Thr(Bn)], [emim][Boc-Cys(Meb)] and [emim][Boc-Pro].

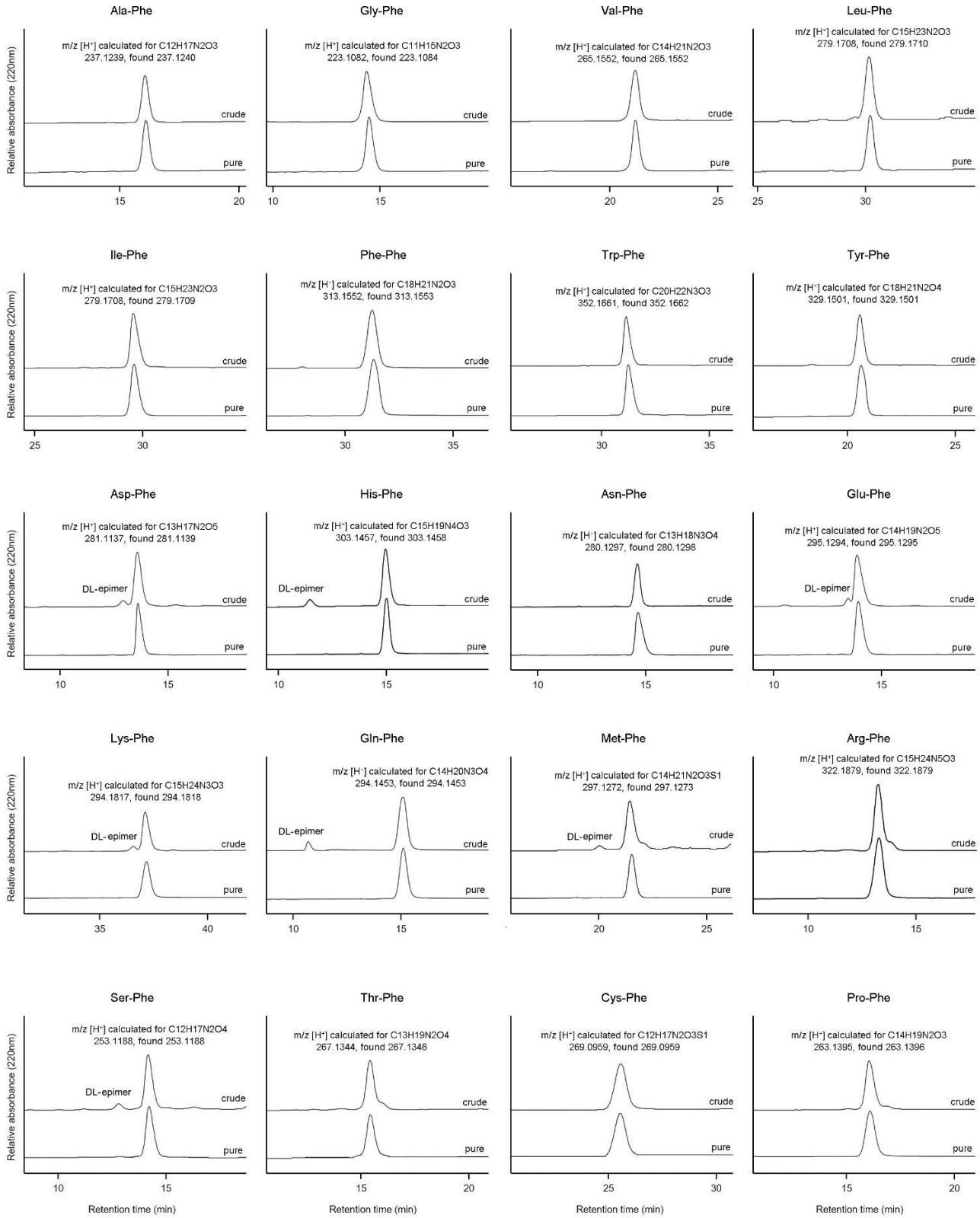

Figure S10. RP-HPLC chromatogram of dipeptide products synthesized from AAILs [emim][Boc-Gly], [emim][Boc-Ala], [emim][Boc-Val], [emim][Boc-Leu], [emim][Boc-Ile], [emim][Boc-Phe], [emim][Boc-Trp(For)], [emim][Boc-Tyr(Bn)], [emim][Boc-Asp(Bn)], [emim][Boc-His(Ts)], [emim][Boc-Asn(Trt)], [emim][Boc-Glu(Bn)], [emim][Boc-Lys(Z)], [emim][Boc-Gln], [emim][Boc-Met], [emim][Boc-Arg(Ts)], [emim][Boc-Ser(Bn)], [emim][Boc-Thr(Bn)], [emim][Boc-Cys(Meb)] and [emim][Boc-Pro].

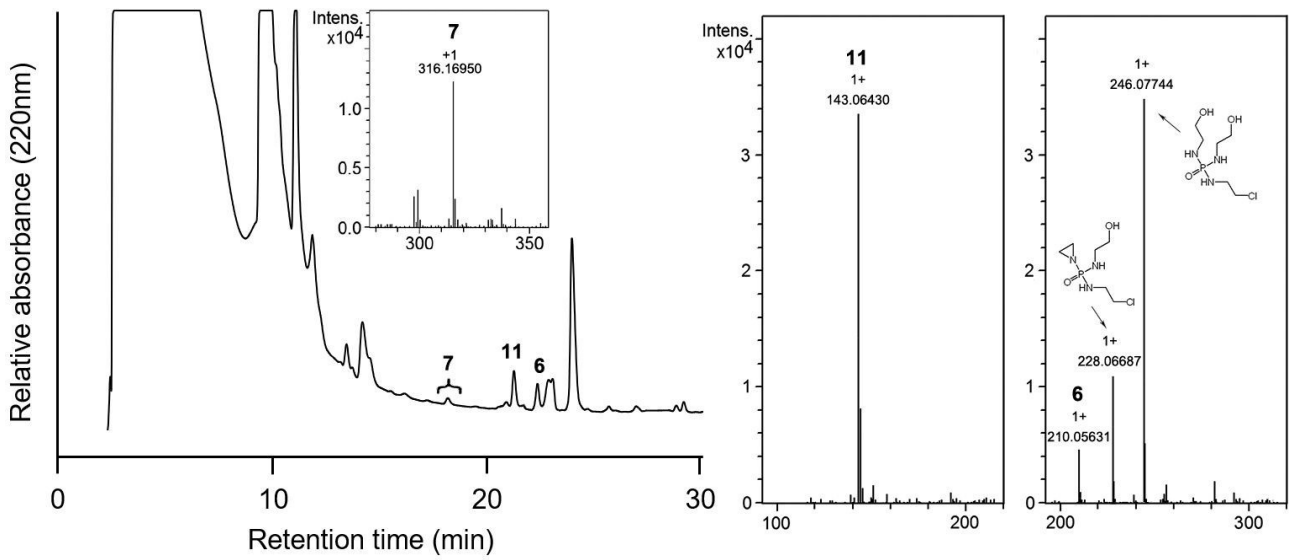

Figure S11. Mass spectrometric analysis of the separated liquid mixture of the coupling reaction of [emim][Boc-Ala] on resin with CTPA, which was quenched with 2% TFA solution after 5 min, demonstrating the possible formation of the intermediate **7** (R= -H) and by-products **6** and **11**.

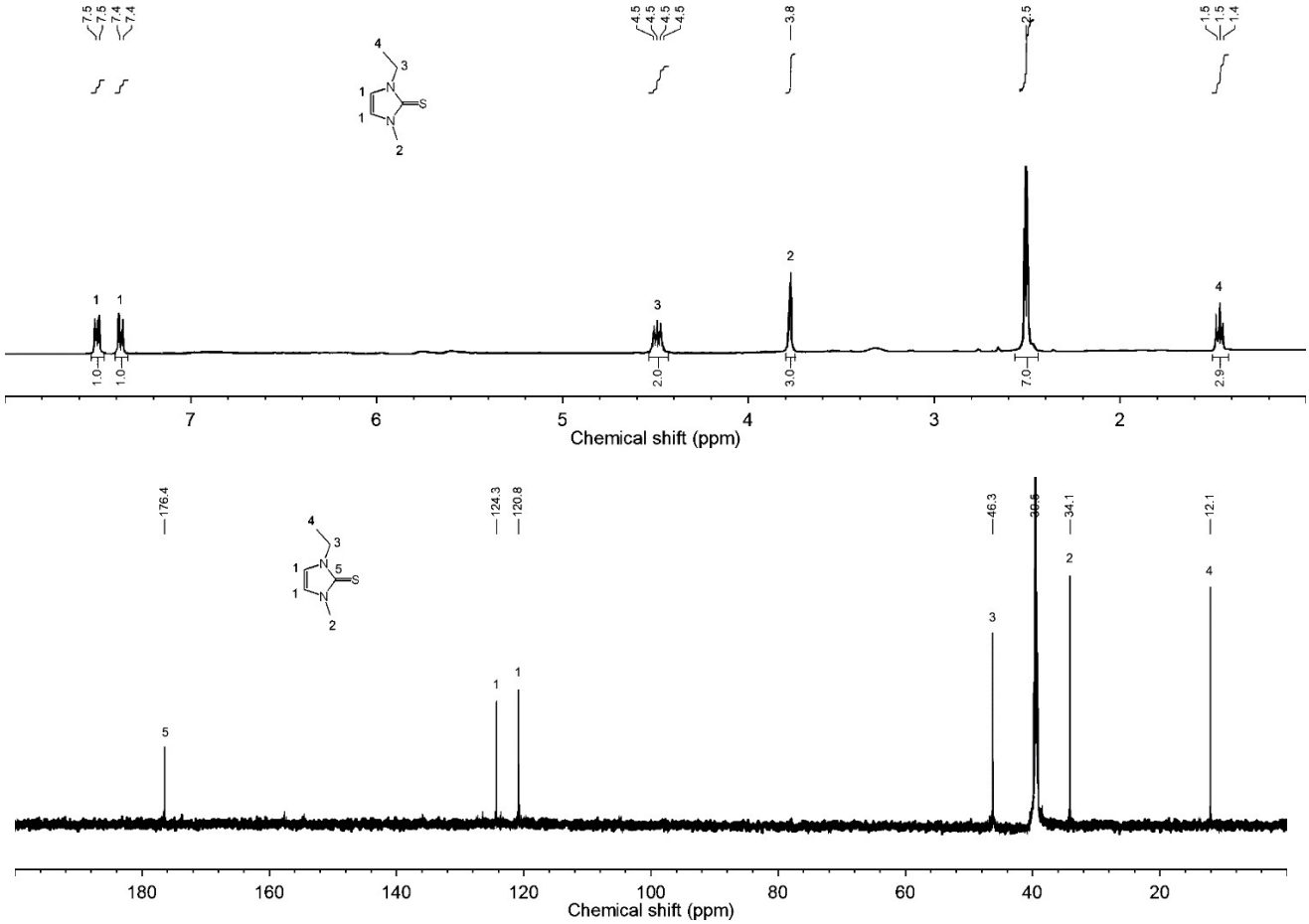

Figure S12. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of by-product **11**. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.50 (d, J = 7.1 Hz, 1H), 7.37 (d, J = 7.1 Hz, 1H), 4.48 (q, J = 7.2 Hz, 2H), 3.77 (s, 3H), 2.50 (s, 7H, DMSO), 1.46 (t, J = 7.2 Hz, 3H). ^{13}C NMR spectrum (100 MHz, DMSO-d_6) of by-product **11**. ^{13}C NMR (100 MHz, DMSO-d_6) δ 176.45, 124.28, 120.83, 46.27, 39.52 (DMSO), 34.14, 12.05.