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Supporting Information

Mandelic Acid Derived Ionic Liquids: Synthesis, Toxicity and Biodegradability

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Strain[a]	Time (h)	IL MIC (mM)[b]	
		19–21	**22**
CA1	24h	>2.0	**2.0**
	48h	>2.0	**2.0**
CA2	24h	>2.0	>2.0
	48h	>2.0	>2.0
CP	24h	>2.0	>2.0
	48h	>2.0	>2.0
CK1	24h	>2.0	>2.0
	48h	>2.0	>2.0
CK2	24h	>2.0	>2.0
	48h	>2.0	>2.0
CT	24h	>2.0	**2.0**
	48h	>2.0	>2.0
CG	24h	>2.0	>2.0
	48h	>2.0	>2.0
CL	24h	>2.0	**2.0**
	48h	>2.0	>2.0
TA	24h	>2.0	>2.0
	48h	>2.0	>2.0
AF	24h	>2.0	>2.0
	48h	>2.0	>2.0
AC	24h	>2.0	>2.0
	48h	>2.0	>2.0
TM	72h	>2.0	>2.0
	120h	>2.0	>2.0

[a]**CA1:** *Candida albicans* ATCC 44859, **CA2:** *Candida albicans* ATCC 90028, **CP**: *Candida parapsilosis* ATCC 22019, **CK1**: *Candida krusei* ATCC 6258, **CK2**: *Candida krusei* E28, **CT**: *Candida tropicalis* 156, **CG**: *Candida glabrata* 20/I, **CL**: *Candida lusitaniae* 2446/I, **TA**: *Trichosporon asahii* 1188, **AF**: *Aspergillus fumigatus* 231, **AC**: *Absidia corymbifera* 272, **TM**: *Trichophyton mentagrophytes* 445. [b]IC_{50} values were assessed for AF, AC and TM and IC_{80} for all other strains.

Table S2 Antibacterial screening results for ILs **19**–**22** (MIC, IC_{95}).[1,2]

Strain[a]	Time (h)	IL MIC (mM)
		19–**22**
SA	24h	>2.0
	48h	>2.0
MRSA	24h	>2.0
	48h	>2.0
SE	24h	>2.0
	48h	>2.0
EF	24h	>2.0
	48h	>2.0
EC	24h	>2.0
	48h	>2.0
KP	24h	>2.0
	48h	>2.0
KP-E	24h	>2.0
	48h	>2.0
PA	24h	>2.0
	48h	>2.0

[a]**SA**: *Staphylococcus aureus* ATTC 6538, **EC:** *Escherichia coli* ATTC 8739, **PA**: *Pseudomonas aeruginosa* ATTC 9027, **MRSA**: *Staphylococcus aureus* MRSA HK5996/08, **SE**: *Staphylococcus epidermidis* HK6966/08, **EF**: *Enterococcus* sp. HK14365/08, **KP**: *Klebsiella pneumoniae* HK11750/08, **KP-E**: *Klebsiella pneumoniae* ESBL HK14368/08.

Materials and Methods

All chemicals were purchased at Sigma-Aldrich. Pyridine (99.8 %), bromoacetyl bromide (≥98 %), thionyl chloride (≥99 %), thionyl bromide (97 %) were used without further purification. 1-methylimidazole (99 %) was distilled before use and all organic solvents were also dried before use. All NMR spectra were recorded in deuterated chloroform (99.8 % D) on a Bruker 400 MHz spectrometer with chemical shifts reported in parts per million (ppm) relative to the internal standard (TMS) and coupling constants (J) are reported in Hertz (Hz). All IR analysis was carried out on a Perkin Elmer FT-IR spectrum GX spectrometer with a Thermo Scientific iD5 Diamond ATR attachment. All melting points (uncorrected) were obtained using a Stuart

SMP40 Melting Point Apparatus and the values are expressed in degrees Celsius (°C). High resolution mass spectrometry (HRMS) was obtained in the ABCRF Mass Spectrometry Laboratory in UCC, Cork using a Waters Micromass LCT Premier mass spectrometer (KD 160). The analysis was performed in ESI+ mode with an external reference standard of leucine enkephalin. A sulfadimethoxine concentration test was performed to ensure peak accuracy in the ion count range 1 x e^3 to 1 x e^6. Methyl 2-hydroxy-2-phenylacetate (**11**),[3] ethyl 2-hydroxy-2-phenylacetate (**12**),[4] n-butyl-2-hydroxy-2-phenylacetamide (**14**)[5] and methyl 2-bromo-2-phenylacetate (**15**)[6] were prepared according to modified versions of the literature methods described below. 1-(2-Ethoxy-2-oxo-1-phenylethyl)pyridin-1-ium bromide (**4**),[7] butyl 2-hydroxy-2-phenylacetate (**13**)[8] and ethyl 2-bromo-2-phenylacetate (**16**)[9] were prepared using new procedures described below.

Antifungal Activity Screening – Charles University

In vitro antifungal activities of the compounds were evaluated on a panel of four ATCC strains (*Candida albicans* ATCC 44859, *Candida albicans* ATCC 90028, *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 6258) and eight clinical isolates of fungi, five yeasts (*Candida krusei* E28, *Candida tropicalis* 156, *Candida glabrata* 20/I, *Candida lusitaniae* 2446/I, *Trichosporon asahii* 1188) and three filamentous fungi (*Aspergillus fumigatus* 231, *Absidia corymbifera* 272, *Trichophyton mentagrophytes* 445), from the collection of fungal strains deposited at the Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic. Three of the above ATCC strains (*Candida albicans* ATCC 90028, *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 6258) also served as the quality control strains. All the isolates were maintained on Sabouraud dextrose agar prior to being tested. Minimum inhibitory concentrations (MICs) were determined by modified CLSI standard of the microdilution format of the M27-A3[10] and M38-A2[11] documents for yeasts and filamentous fungi respectively.

Dimethyl sulfoxide (100 %) served as a diluent for all compounds; the final concentration did not exceed 2 %. RPMI 1640 (Sevapharma, Prague) medium supplemented with L-glutamine and buffered with 0.165 M morpholinepropanesulfonic acid (Serva) to pH 7.0 by 10 N NaOH was used as the test medium. The wells of the microdilution tray contained 200 μL of the RPMI 1640 medium with 2-fold serial dilutions of the compounds (2000 or 1000 to 0.24 μmol L^{-1}) and 10 μL of inoculum suspension. Fungal inoculum in RPMI 1640 was prepared to give a final concentration of $5 \times 10^3 \pm 0.2$ cfu mL^{-1}. The trays were incubated at 35 °C and MICs

were read visually for filamentous fungi and photometrically for yeasts at an absorbance at 540 nm after 24 h and 48 h. The MIC values for the dermatophytic strain (*T. mentagrophytes*) were determined after 72 h and 120 h. For all other strains MIC values were evaluated after 24 and 48 h. The MICs were defined as 50 % inhibition (IC_{50}) of the control growth for yeasts or 80 % inhibition (IC_{80}) of the growth of control for filamentous fungi. MICs were determined twice and in duplicate. The deviations from the usually obtained values were no higher than the nearest concentration value up and down the dilution scale.

Antibacterial Activity Screening – Charles University

In vitro antibacterial activities of the compounds were evaluated on a panel of three ATCC strains (*Staphylococcus aureus* ATTC 6538, *Escherichia coli* ATTC 8739, *Pseudomonas aeruginosa* ATTC 9027) and five clinical isolates (*Staphylococcus aureus* MRSA HK5996/08, *Staphylococcus epidermidis* HK6966/08, *Enterococcus sp.* HK14365/08, *Klebsiella pneumoniae* HK11750/08, *Klebsiella pneumoniae* ESBL HK14368/08) from the collection of bacterial strains deposited at the Department of Biological and Medical Sciences, Faculty of Pharmacy, Charles University, Hradec Králové, Czech Republic. The abovementioned ATCC strains also served as the quality control strains. All the isolates were maintained on Mueller-Hinton dextrose agar prior to being tested.

Dimethyl sulfoxide (100 %) served as a diluent for all compounds; the final concentration did not exceed 2 %. Mueller-Hinton agar (MH, HiMedia, Čadersky-Envitek, Czech Republic) buffered to pH 7.4 (±0.2) was used as the test medium. The wells of the microdilution tray contained 200 μL of the Mueller-Hinton medium with 2-fold serial dilutions of the compounds (2000 or 1000 to 0.24 μmol L^{-1}) and 10 μL of inoculum suspension. Inoculum in MH medium was prepared to give a final concentration of 0.5 McFarland scale (1.5×10^8 cfu mL^{-1}). The trays were incubated at 35 °C and MICs were read visually after 24 h and 48 h. The MICs were defined as 95 % inhibition (IC_{95}) of the control growth. MICs were determined twice and in duplicate. The deviations from the usually obtained values were no higher than the nearest concentration value up and down the dilution scale.

Antibacterial Activity Screening – DCU

Mueller-Hinton broth was purchased from Oxoid. Five bacterial strains that used in this study were the Gram-positive bacterium *Bacillus subtilis* DSMZ 10 (*B. subtilis*) and the Gram-negative bacteria *Escherichia coli* DSMZ 498 *(E. coli)*, *Pseudomonas fluorescens* DSMZ 270

50090 (*P. fluorescence)*, *Pseudomonas putida* CP1 (*P. putida* CP1) and *Pseudomonas putida* KT2440 (*P. putida* KT2440). All strains were purchased at DSMZ (German Collection of Microorganisms and Cell Cultures).

IC_{50} values for the compounds were determined using a modification of the broth microdilution method described by Amsterdam.[10] Strains were grown in nutrient broth overnight, washed with 0.01 M sodium phosphate buffer (pH 7) and the cell number adjusted to give an optical density reading of 0.07 at 660 nm. The antimicrobial activity of the ILs was tested in 96 well round bottom microplates. Stock solutions of the ILs were prepared in deionised water to a maximum concentration of 2000 mM. The concentration of each stock solution was determined by the maximum aqueous solubility of each IL (Table 3).

Table S3 Aqueous solubility of ILs **1–10** up to a maximum concentration of 2000 mM.

IL	Solubility (mM)
1	2000
2	890
3	2000
4	1000
5	2000
6	2000
7	890
8	2000
9	1000
10	2000

180 μL of Mueller-Hinton broth was pipetted into column 1 of the wells and 100 μL into the other wells. 20 μL of the chemical solution was transferred into column 1 giving a maximum concentration of 200 mM. 100 μL of the solution from column 1 was then transferred to the next column and mixed. The procedure was repeated to give a series of two-fold dilutions. Each well was inoculated with 5 μL of bacterial culture. Wells containing medium only were used as blanks and wells containing medium and culture only were used as positive controls. All the toxicity tests were carried out in triplicate. The microplates were incubated overnight

at 30 °C. The presence or absence of growth was determined by measuring the optical density of the wells at a wavelength of 405 nm using a plate reader. The IC_{50} values were determined as the concentration or range of concentrations that caused a 50 % reduction in growth.

Closed Bottle Biodegradation Test (CBT) Procedure

The CBT measures aerobic biodegradability and is one of six test methods described in the OECD Guidelines for Testing of Chemicals[11] used to evaluate readily biodegradability of organic compounds. The test was undertaken at 20 ± 1 °C in the dark in the laboratories of the Institute of Sustainable and Environmental Chemistry at Leuphana University Lüneburg as described in details elsewhere.[12] It consisted of four different test series all run in duplicate. The blank series contained only mineral medium and inoculum. The test series contained additionally the IL as the only organic carbon available for the microorganisms during the test. The quality control contained, in addition to the blank, the readily biodegradable compound sodium acetate, which was used to monitor the activity of the microorganisms. The toxicity control contained both the IL and the sodium acetate in addition to the mineral medium ad inoculum. The amount of IL and sodium acetate corresponded to a theoretical oxygen demand (ThOD) of 5 mg L^{-1}. The same mineral salt solution was used for all the test vessels with two drops of inoculum obtained from the effluent of the municipal sewage treatment plant in Lüneburg, Abwasser, Grünund Lüneburger Service GmbH, Germany.

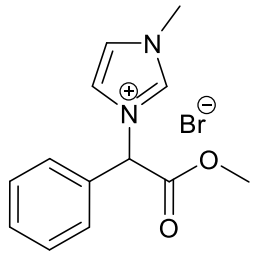
According to the guidelines, for the test to be valid the reference compound sodium acetate needs to degrade by at least 60 % within 14 days. Toxicity towards the test microorganisms was evaluated by comparing the oxygen consumption of the toxicity control to the predicted level of oxygen consumption, calculated from the oxygen consumption of the quality control and the test control. A compound is labelled toxic if the difference between the predicted oxygen consumption and the measured oxygen consumption exceeds 25 %.[11]

The biochemical oxygen demand (BOD) was measured in accordance with international standard methods[13] using sensor spots in the bottles and an oxygen electrode (Oxi 196 with EO 196-1.5 WTW Weilheim, Germany)[14] at a day 0, 0 (after 3 h), 1, 7, 14, 21 and 28.

Synthetic Procedures

General Procedure A: Preparation of Mandelate Bromide ILs (1-10)

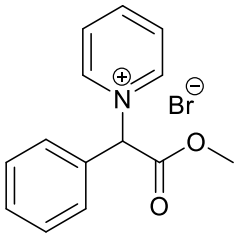
3-(2-Methoxy-2-oxo-1-phenylethyl)-1-methyl-1H-imidazol-3-ium bromide (1)



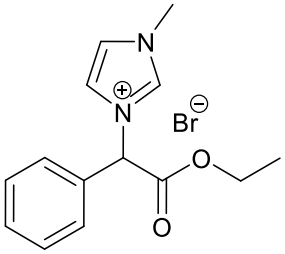
A flask was charged with methyl 2-bromo-2-phenylacetate (**15**) (5.04 g, 22.0 mmol) and diethyl ether (20 mL), under N_2. Whilst stirring 1-methylimidazole (1.72 mL, 21.6 mmol) was added and the reaction was stirred overnight at rt. TLC confirmed reaction completion. Diethyl ether was decanted and the product was washed with diethyl ether (5 × 25 mL). The volatiles were removed via rotary evaporation and the product was dried under reduced pressure to give the title compound (**1**) as a white solid (6.37 g, 20.5 mmol), 95 % yield. mp: 61−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.67 (bs, 1H), 7.62–7.55 (m, 2H), 7.48–7.41 (m, 4H), 7.41 (s, 1H), 7.34 (dd, *J* = 1.9, 1.9 Hz, 1H), 4.04 (s, 3H), 3.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 138.1, 132.1, 130.6, 130.0, 128.8, 122.6, 121.9, 64.0, 53.9, 37.0. IR (neat) 3042, 2954, 1744, 1552, 1437, 1278, 1216, 1160, 986, 733 cm^{-1}. HRMS (ESI$^+$, m/z) Calculated for $[M–Br^–]^+$ $C_{13}H_{15}N_2O_2^+$, requires 231.1128, found 231.1125.

1-(2-Methoxy-2-oxo-1-phenylethyl)pyridin-1-ium bromide (2)

The title compound (**2**) was synthesised from methyl 2-bromo-2-phenylacetate (**15**) (5.02 g, 21.9 mmol), diethyl ether (5 mL) and pyridine (1.73 mL, 21.5 mmol), according to the general procedure A to give a white solid (5.66 g, 18.4 mmol), 86 % yield. mp: 140−142 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63–9.56 (m, 2H), 8.56 (tt, *J* = 7.8, 1.4 Hz, 1H), 8.51 (s, 1H), 8.11–8.03 (m, 2H), 7.77–7.68 (m, 2H), 7.54–7.42 (m, 3H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 146.5, 145.3, 131.3, 131.1, 130.2, 129.9, 127.9, 73.3, 54.4. IR (neat) 3021, 2959, 1743, 1628, 1482, 1279, 1218, 1159, 993, 748 cm^{-1}. HRMS (ESI$^+$, m/z) Calculated for $[M–Br^–]^+$ $C_{14}H_{14}NO_2^+$, requires 228.1019 found 228.1022.

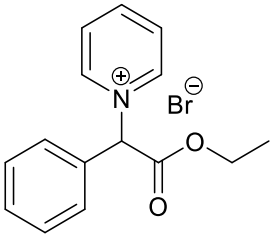


3-(2-Ethoxy-2-oxo-1-phenylethyl)-1-methyl-1H-imidazol-3-ium bromide (3)



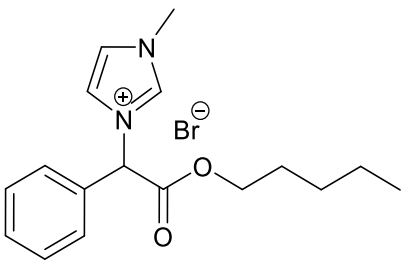
The title compound (**3**) was synthesised from ethyl 2-bromo-2-phenylacetate (**16**) (5.01 g, 20.6 mmol), diethyl ether (20 mL) and 1-methylimidazole (1.61 mL, 20.2 mmol), according to the general procedure A. The reaction was stirred for 2 days to give a white solid (6.15 g, 18.9 mmol), 94 % yield. mp: 101−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.87 (bs, 1H), 7.63–7.56 (m, 2H), 7.48–7.42 (m, 3H), 7.40 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.30 (s, 1H), 7.18 (dd, *J* = 1.8, 1.8 Hz, 1H), 4.308 (q, *J* = 7.1 Hz, 1H), 4.305 (q, *J* = 7.1 Hz, 1H), 4.03 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 137.9, 132.3, 130.5, 129.9, 128.7, 122.8, 121.9, 64.1, 63.4, 36.9, 14.0. IR (neat) 3070, 3016, 1746, 1576, 1280, 1209, 1170, 1010, 735 cm^{-1}. HRMS (ESI^+, m/z) Calculated for $[M–Br^–]^+$ $C_{14}H_{17}N_2O_2^+$, requires 245.1285, found 245.1277.

1-(2-Ethoxy-2-oxo-1-phenylethyl)pyridin-1-ium bromide (4)[7]



A flask was charged with ethyl 2-bromo-2-phenylacetate (**16**) (5.00 g, 20.6 mmol) under N_2. With no stirring, pyridine (1.62 mL, 20.1 mmol) was added and the reaction was left for 2 days at rt. TLC confirmed reaction completion. The product was washed with diethyl ether (5 × 25 mL). The volatiles were removed via rotary evaporation, and the product was dried under reduced pressure to give the title compound (**4**) as a white solid (6.35 g, 19.7 mmol), 98 % yield. mp: 161−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61–9.56 (m, 2H), 8.53 (tt, *J* = 7.8, 1.3 Hz, 1H), 8.41 (s, 1H), 8.08–8.01 (m, 2H), 7.79–7.70 (m, 2H), 7.53–7.44 (m, 3H), 4.43–4.35 (m, 1H), 4.35–4.28 (m, 1H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 146.3, 145.4, 131.2, 131.2, 130.2, 129.9, 127.8, 73.4, 64.1, 14.1. ^{1}H and ^{13}C NMR data are in agreement with the literature.[7]

3-(2-Butoxy-2-oxo-1-phenylethyl)-1-methyl-1H-imidazol-3-ium bromide (5)



The title compound (**5**) was synthesised from butyl 2-bromo-2-phenylacetate (**17**) (7.04 g, 26.0 mmol), diethyl ether (20 mL) and 1-methylimidazole (2.03 mL, 25.5 mmol), according to the general procedure A. The reaction was stirred for 5 days to give a white solid (7.55 g, 21.4 mmol), 84 % yield. mp: 99−101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.52 (bs, 1H), 7.59–7.51 (m, 2H), 7.49 (dd, *J* = 1.9, 1.9 Hz, 1H), 7.45 (dd, *J* = 1.9, 1.9 Hz,

1H), 7.43–7.35 (m, 3H), 7.23 (s, 1H), 4.23 (dt, *J* = 10.7, 6.8 Hz, 1H), 4.16 (dt, *J* = 10.7, 6.7 Hz, 1H), 4.03 (s, 3H), 1.64–1.48 (m, 2H), 1.21 (tq, *J* = 7.4, 7.4 Hz, 2H), 0.81 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 137.7, 132.3, 130.4, 129.8, 128.65, 123.0, 121.9, 67.1, 64.1, 36.9, 30.2, 18.9, 13.6. IR (neat) 3060, 2958, 1742, 1549, 1280, 1210, 1192, 1158, 794, 729 cm^{-1}. HRMS (ESI$^+$, m/z) Calculated for $[M–Br^-]^+$ $C_{16}H_{21}N_2O_2^+$, requires 273.1598, found 273.1601.

1-(2-Butoxy-2-oxo-1-phenylethyl)pyridin-1-ium bromide (6)

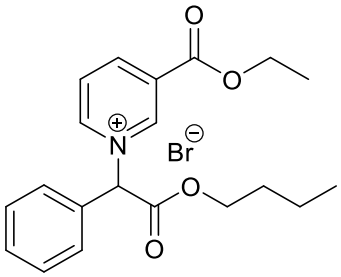
The title compound (**6**) was synthesised from butyl 2-bromo-2-phenylacetate (**17**) (7.03 g, 25.9 mmol), diethyl ether (7 mL) and pyridine (2.04 mL, 25.3 mmol), according to the general procedure A. The reaction was stirred for 5 days to give a brown solid (4.94 g, 14.1 mmol), 56 % yield. mp: 48−50 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59–9.53 (m, 2H), 8.54 (tt, *J* = 7.7, 1.4 Hz, 1H), 8.37 (s, 1H), 8.09–8.01 (m, 2H), 7.78–7.69 (m, 2H), 7.53–7.43 (m, 3H), 4.34 (dt, *J* = 10.7, 6.7 Hz, 1H), 4.23 (dt, *J* = 10.7, 6.7 Hz, 1H), 1.71–1.53 (m, 2H), 1.28 (tq, *J* = 7.5, 7.4 Hz, 2H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 146.6, 145.2, 131.2, 131.2, 130.1, 129.8, 127.9, 73.5, 67.8, 30.2, 18.9, 13.59. IR (neat) 3036, 2958, 2871, 1739, 1628, 1480, 1279, 1212, 1159, 748 cm^{-1}. HRMS (ESI$^+$, m/z) Calculated for $[M–Br^-]^+$ $C_{17}H_{20}NO_2^+$, requires 270.1489, found 270.1482.

1-(2-Butoxy-2-oxo-1-phenylethyl)-3-methoxypyridin-1-ium bromide (7)

The title compound (**7**) was synthesised from butyl 2-bromo-2-phenylacetate (**17**) (5.00 g, 18.4 mmol), diethyl ether (25 mL) and 3-methoxypyridine (1.77 mL, 17.6 mmol), according to the general procedure A. The reaction was stirred for 5 days to give a white solid (4.95 g, 13.0 mmol), 74 % yield. mp: 127−128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (dd, *J* = 2.6, 1.3 Hz, 1H), 8.63 (ddd, *J* = 6.0, 1.3, 1.1 Hz, 1H), 8.38 (s, 1H), 7.99 (ddd, *J* = 8.8, 2.6, 1.1 Hz, 1H), 7.87 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.74–7.68 (m, 2H), 7.50–7.41 (m, 3H), 4.32 (dt, *J* = 10.7, 6.8 Hz, 1H), 4.20 (dt, *J* = 10.7, 6.8 Hz, 1H), 4.16 (s, 3H), 1.61 (ddt, *J* = 13.8, 11.6, 6.8 Hz, 2H), 1.26 (tq, *J* = 7.5, 7.4 Hz, 2H), 0.83 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 158.5, 136.8, 132.6, 132.6, 131.4, 131.1, 130.0, 129.9, 127.7, 73.4, 67.7, 58.8, 30.2, 18.9, 13.60. IR (neat) 3034, 2956, 1741,

1624, 1519, 1294, 1284, 1209, 1153, 744 cm^{-1}. HRMS (ESI^+, m/z) Calculated for $[M–Br^–]^+$ $C_{18}H_{22}NO_3^+$, requires 300.1594, found 300.1592.

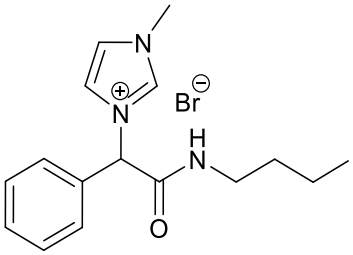
1-(2-Butoxy-2-oxo-1-phenylethyl)-3-(ethoxycarbonyl)pyridin-1-ium bromide (8)



The title compound (**8**) was synthesised from butyl 2-bromo-2-phenylacetate (**17**) (5.03 g, 18.2 mmol), diethyl ether (5 mL) and ethyl nicotinate (2.49 mL, 18.2 mmol), according to the general procedure A. The reaction was stirred for 5 days give a light pink solid (4.80 g, 11.4 mmol), 63 % yield. mp: 112−113 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (ddd, *J* = 6.3, 1.4, 1.4 Hz, 1H), 9.43 (bs, 1H), 8.96 (ddd, *J* = 8.0, 1.4, 1.4 Hz, 1H), 8.59 (s, 1H), 8.23 (dd, *J* = 8.0, 6.3 Hz, 1H), 7.85–7.76 (m, 2H), 7.56–7.48 (m, 3H), 4.47 (q, *J* = 7.1 Hz, 2H), 4.36 (dt, *J* = 10.7, 6.8 Hz, 1H), 4.25 (dt, *J* = 10.7, 6.8 Hz, 1H), 1.64 (ddt, *J* = 13.8, 12.0, 6.8 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H), 1.28 (tq, *J* = 7.4, 7.4 Hz, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.6, 160.8, 149.4, 146.1, 145.2, 131.5, 130.7, 130.5, 130.3, 130.1, 128.1, 73.9, 68.1, 63.8, 30.3, 19.0, 14.2, 13.6. IR (neat) 3045, 2961, 1737, 1721, 1635, 1456, 1297, 1280, 1177, 706 cm^{-1}. HRMS (ESI^+, m/z) Calculated for $[M–Br^–]^+$ $C_{20}H_{24}NO_4^+$, requires 342.1700, found 342.1692.

3-(2-(Butylamino)-2-oxo-1-phenylethyl)-1-methyl-1H-imidazol-3-ium bromide (9)

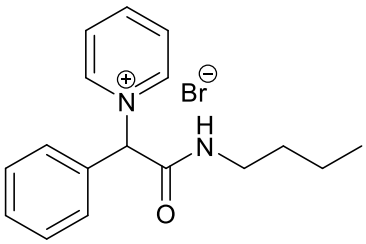
The title compound (**9**) was synthesised from 2-bromo-*N*-butyl-2-phenylacetamide (**18**)



(5.00 g, 18.5 mmol), diethyl ether (20 mL) and 1-methylimidazole (1.40 mL, 17.6 mmol), according to the general procedure A. The reaction was stirred for 2 days to give a white solid (6.12 g, 17.4 mmol), 99 % yield. mp: 143−145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (bs, 1H), 8.29 (t, *J* = 5.3 Hz, 1H), 7.79 (s, 1H), 7.75 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.67–7.60 (m, 2H), 7.42–7.34 (m, 3H), 7.19 (dd, *J* = 1.9, 1.9 Hz, 1H), 3.98 (s, 3H), 3.34–3.25 (m, 1H), 3.25–3.16 (m, 1H), 1.53 (dtd, *J* = 8.8, 7.4, 5.8 Hz, 2H), 1.38–1.23 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 136.3, 133.5, 130.0, 129.5, 128.4, 123.0, 122.3, 63.9, 39.9, 36.9, 31.1, 20.3, 13.79. IR (neat) 3158, 3022, 2929, 1675, 1554, 1227, 1164, 742 cm^{-1}. HRMS (ESI^+, m/z) Calculated for $[M–Br^–]^+$ $C_{16}H_{22}N_3O^+$, requires 272.1757, found 272.1757.

1-(2-(Butylamino)-2-oxo-1-phenylethyl)pyridin-1-ium bromide (10)

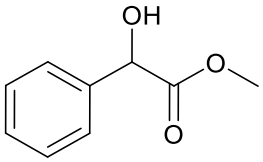
The title compound (**10**) was synthesised from 2-bromo-*N*-butyl-2-phenylacetamide (**18**) (5.00 g, 18.5 mmol), diethyl ether (5 mL) and pyridine (1.42 mL, 17.6 mmol), according to the general procedure A. The reaction was stirred for 2 days to give a white solid (5.26 g, 15.1 mmol), 86 % yield. mp: 167−169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60–9.53 (m, 2H), 8.72 (bs, 1H), 8.68 (s, 1H), 8.43 (tt, *J* = 7.8, 1.4 Hz, 1H), 8.01–7.92 (m, 2H), 7.69–7.62 (m, 2H), 7.51–7.41 (m, 3H), 3.43–3.31 (m, 1H), 3.31–3.21 (m, 1H), 1.65–1.52 (m, 2H), 1.35 (tq, *J* = 7.4, 7.3 Hz, 2H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 145.5, 144.9, 132.4, 130.8, 129.9, 129.4, 127.6, 72.6, 40.3, 31.1, 20.3, 13.8. IR (neat) 3126, 3014, 2958, 1674, 1626, 1553, 1481, 1226, 1157, 708 cm^{-1}. HRMS (ESI^+, m/z) Calculated for $[M–Br^–]^+$ $C_{17}H_{21}N_2O^+$, requires 269.1648, found 269.1644.



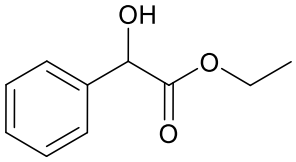
Procedure B: Preparation of Mandelate Esters (11-13)

Methyl 2-hydroxy-2-phenylacetate (11)[3,15]

A flask was charged with mandelic acid (10.10 g, 66.38 mmol) and methanol (50 mL), under N_2. Whilst stirring and cooling in an ice bath (0 °C), thionyl chloride (2.40 mL, 33.1 mmol) was added dropwise and the reaction was stirred at rt for 4 h. TLC confirmed reaction completion. N_2 was bubbled through the reaction for 1 h. The solvent was removed, deionised water (25 mL) was added and the product extracted with ethyl acetate (3 × 25 mL). The combined organic extracts were washed with saturated aqueous sodium bicarbonate (20 mL), dried over $MgSO_4$, filtered and the solvent removed. The organic phase was dried under reduced pressure to give the title compound (**11**) as a white waxy solid (10.20 g, 61.38 mmol), 92 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.30 (m, 5H), 5.18 (d, *J* = 5.1 Hz, 1H), 3.77 (s, 3H), 3.44 (d, *J* = 5.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 138.3, 128.8, 128.7, 126.7, 73.0, 53.2. ^{1}H and ^{13}C NMR data are in agreement with the literature.[15]



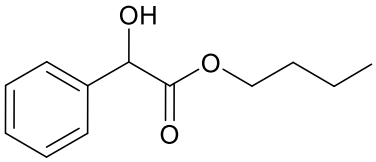
Ethyl 2-hydroxy-2-phenylacetate (12) [4,16]



The title compound (**12**) was synthesised from mandelic acid (10.03 g, 65.92 mmol), ethanol (50 mL) and thionyl chloride (2.40 mL, 33.1 mmol) according to the general procedure B to give a colourless liquid (10.90 g, 60.49 mmol), 92 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.29 (m, 5H), 5.16 (d, *J* = 5.8 Hz, 1H), 4.27 (dq, *J* = 10.8, 7.1 Hz, 1H), 4.17 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.51 (d, *J* = 5.8 Hz, 1H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.8, 138.5, 128.7, 128.5, 126.6, 73.0, 62.4, 14.1.

^{1}H and ^{13}C NMR data are in agreement with the literature.[16]

Butyl 2-hydroxy-2-phenylacetate (13)[8]

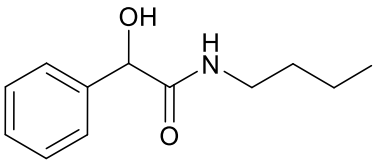


The title compound (**13**) was synthesised from mandelic acid (50.01 g, 328.7 mmol), *n*-butanol (250 mL) and thionyl chloride (12.0 mL, 165 mmol) according to the general procedure B to give a yellow liquid (66.68 g, 320.2 mmol), 97 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.39 (m, 2H), 7.39–7.28 (m, 3H), 5.16 (d, *J* = 5.8 Hz, 1H), 4.22–4.09 (m, 2H), 3.59 (bs, 1H), 1.61–1.50 (m, 2H), 1.30–1.19 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 138.6, 128.6, 128.5, 126.6, 72.9, 66.1, 30.5, 18.9, 13.7.

^{1}H and ^{13}C NMR data are in agreement with the literature.[8]

Preparation of Mandelate Amide (14)

N-Butyl-2-hydroxy-2-phenylacetamide (14)[5,17]



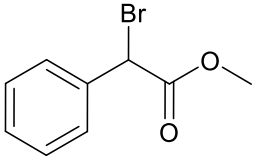
A flask was charged with mandelic acid (50.19 g, 329.9 mmol) and methanol (300 mL), under N_2. Whilst stirring and cooling in an ice bath (0 °C), acetyl chloride (24.0 mL, 336 mmol) was added dropwise and the reaction was stirred overnight at rt. TLC confirmed reaction completion. The solvent was removed and methanol (150 mL) was added. Whilst stirring and cooling in an ice bath (0 °C), *n*-butylamine (130 mL, 1.32 mol) was added dropwise and the reaction was left in the fridge (< 5 °C) overnight. TLC confirmed reaction completion. The solvent was removed, DCM (250 mL) was added, and the organic phase was washed with water (3 × 100 mL) and saturated aqueous ammonium chloride (100 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent removed. The

product was dried under reduced pressure to give the title compound (**14**) as a white crystalline solid (61.05 g, 294.5 mmol), 89 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.29 (m, 5H), 6.12 (bs, 1H), 4.98 (s, 1H), 3.77 (bs, 1H), 3.31–3.17 (m, 2H), 1.48–1.38 (m, 2H), 1.33–1.21 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.1, 139.7, 129.1, 128.8, 127.0, 74.3, 39.5, 31.6, 20.1, 13.8.

^{1}H and ^{13}C NMR data are in agreement with the literature.[17]

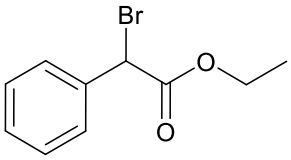
General Procedure C: Preparation of Mandelate Alkylating Reagents (15-18)

Methyl 2-bromo-2-phenylacetate (15)[6,18]



A flask was charged with methyl 2-hydroxy-2-phenylacetate (**11**) (18.08 g, 108.8 mmol) and dry DCM (100 mL), under N_2. Whilst stirring, triethylamine (22.8 mL, 163 mmol) was added. The reaction was cooled in an ice bath (0 °C), thionyl bromide (10.0 mL, 129 mmol) was added dropwise and the reaction was stirred overnight at rt. TLC confirmed reaction completion and N_2 was bubbled through the reaction for 1 h. The organic phase was washed with deionised water (3 × 50 mL) and the combined aqueous phase was subsequently washed with DCM (20 mL). The combined organic phase was dried over $MgSO_4$, filtered and the solvent removed. The crude product was purified by column chromatography (SiO_2, hexane to EtOAc:hexane, 20:80) and dried under reduced pressure to give the title compound (**15**) as a yellow liquid (16.68 g, 72.82 mmol), 67 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–7.50 (m, 2H), 7.41–7.31 (m, 3H), 5.37 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 135.9, 129.5, 129.0, 128.8, 53.6, 46.7. ^{1}H and ^{13}C NMR data are in agreement with the literature.[18]

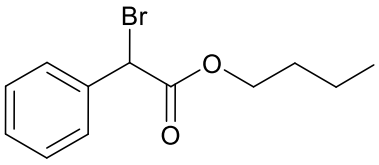
Ethyl 2-bromo-2-phenylacetate (16)[9]



The title compound (**16**) was synthesised from ethyl 2-hydroxy-2-phenylacetate (**12**) (15.00 g, 83.24 mmol), dry DCM (100 mL), triethylamine (17.5 mL, 125 mmol) and thionyl bromide (7.7 mL, 99 mmol), according to the general procedure C. The crude product was purified by column chromatography (SiO_2, EtOAc:hexane, 20:80) to give a yellow liquid (11.32 g, 46.57 mmol), 56 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.52 (m, 2H), 7.41–7.31 (m, 3H), 5.35 (s, 1H), 4.32–4.16 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 136.0, 129.38, 128.9, 128.8, 62.7, 47.0, 14.1.

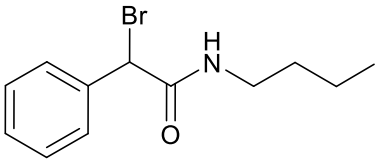
^{1}H and ^{13}C NMR data are in agreement with the literature.[9]

Butyl 2-bromo-2-phenylacetate (17)



The title compound (**17**) was synthesised from butyl 2-hydroxy-2-phenylacetate (**13**) (30.07 g, 144.4 mmol), dry DCM (250 mL), triethylamine (30.0 mL, 215 mmol) and thionyl bromide (13.5 mL, 174 mmol), according to the general procedure C. The organic phase was washed with deionised water (3 × 150 mL), and the crude product was purified by column chromatography (SiO_2, EtOAc:hexane, 40:60) to give a yellow liquid (19.85 g, 73.21 mmol), 51 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.51 (m, 2H), 7.41–7.31 (m, 3H), 5.35 (s, 1H), 4.25–4.12 (m, 2H), 1.68–1.58 (m, 2H), 1.44–1.27 (m, 2H), 0.91 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 136.0, 129.3, 128.9, 128.8, 66.4, 47.0, 30.5, 19.1, 13.7. IR (neat) 2960, 2874, 1744, 1455, 1251, 1138, 693 cm^{-1}. HRMS (ESI^+, m/z) Calculated for $[M+H]^+$ $C_{12}H_{16}{}^{79}BrO_2^+$, requires 271.0328 found 271.0329.

2-Bromo-*N*-butyl-2-phenylacetamide (18)



The title compound (**18**) was synthesised from *n*-butyl-2-hydroxy-2-phenylacetamide (**14**) (20.05 g, 96.73 mmol), dry DCM (110 mL), triethylamine (20.0 mL, 143 mmol) and thionyl bromide (9.0 mL, 0.12 mol), according to the general procedure B. The crude product was purified by column chromatography (SiO_2, EtOAc:hexane, 20:80) to give a light yellow crystalline solid (13.64 g, 50.49 mmol), 52 % yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.40 (m, 2H), 7.40–7.28 (m, 3H), 6.67 (bs, 1H), 5.43 (s, 1H), 3.32 (dt, *J* = 6.8, 6.8 Hz, 2H), 1.60–1.50 (m, 2H), 1.43–1.31 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 137.7, 129.2, 129.1, 128.4, 52.0, 40.4, 31.5, 20.2, 13.9. IR (neat) 3295, 2931, 1657, 1545, 1231, 1168, 692 cm^{-1}. HRMS (ESI^+, m/z) Calculated for $[M+H]^+$ $C_{12}H_{17}{}^{79}BrNO^+$, requires 270.0488 found 270.0485.

^{1}H and ^{13}C NMR Spectra

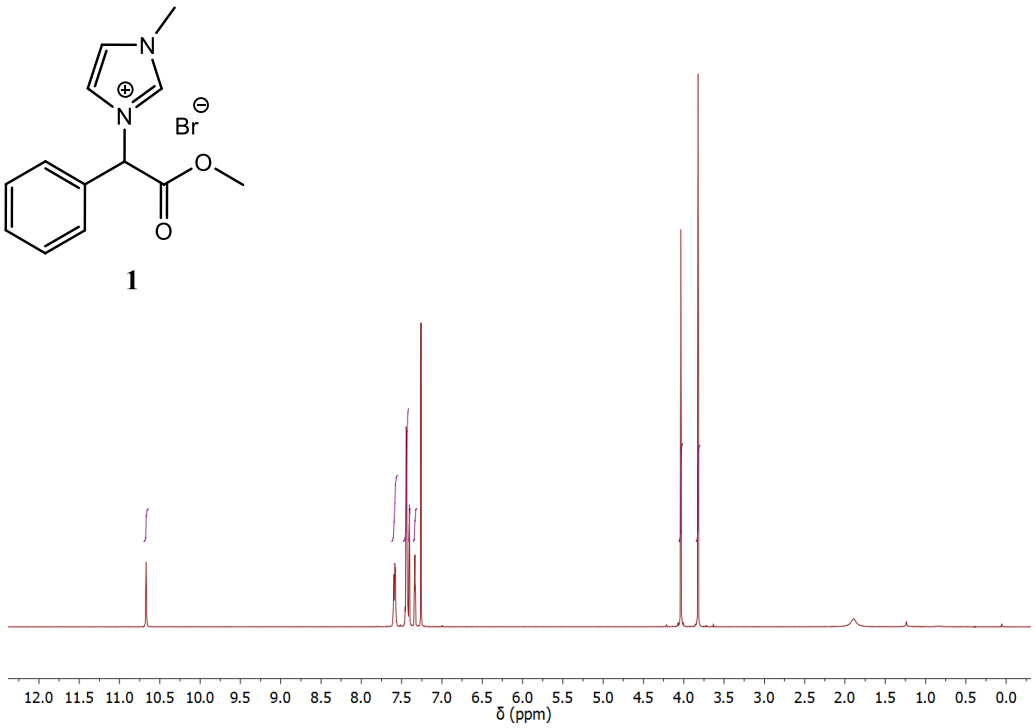


Figure S1 ^{1}H NMR spectra of IL **1** (400 MHz, $CDCl_3$).

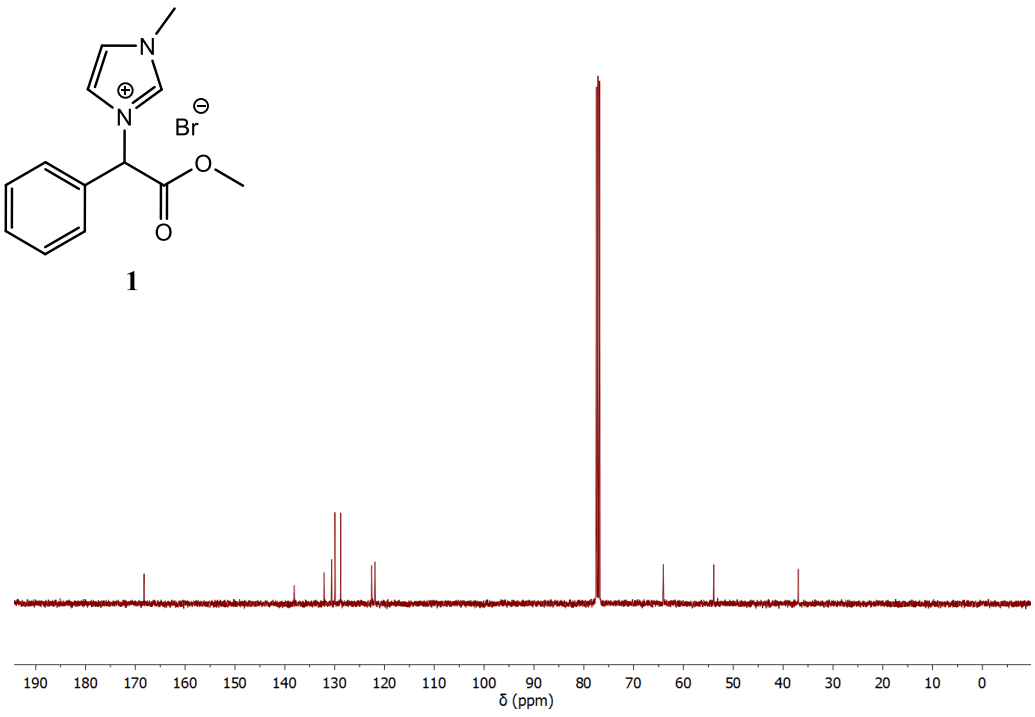


Figure S2 ^{13}C NMR spectra of IL **1** (101 MHz, $CDCl_3$).

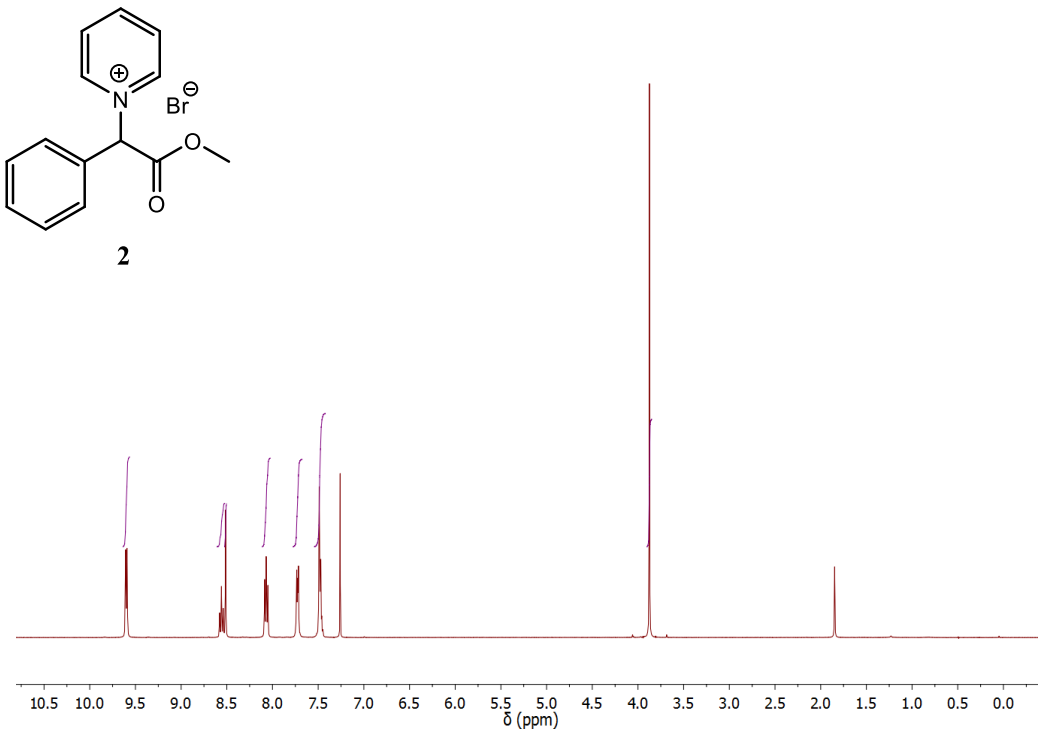


Figure S3 ^{1}H NMR spectra of IL **2** (400 MHz, $CDCl_3$).

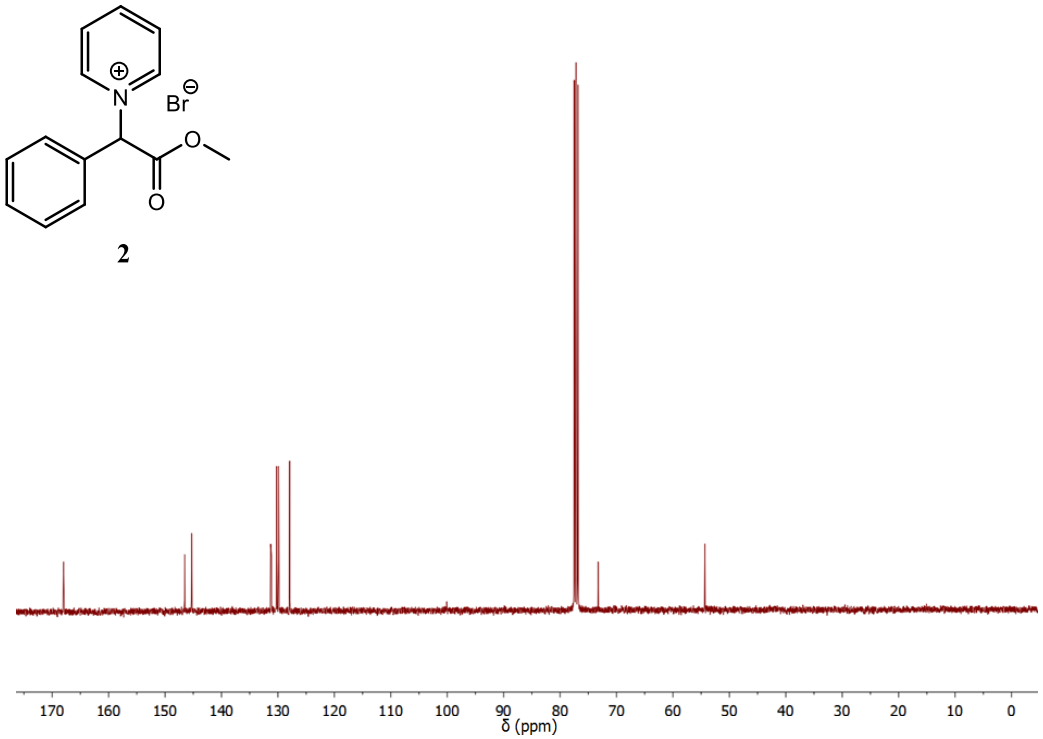


Figure S4 ^{13}C NMR spectra of IL **2** (101 MHz, $CDCl_3$).

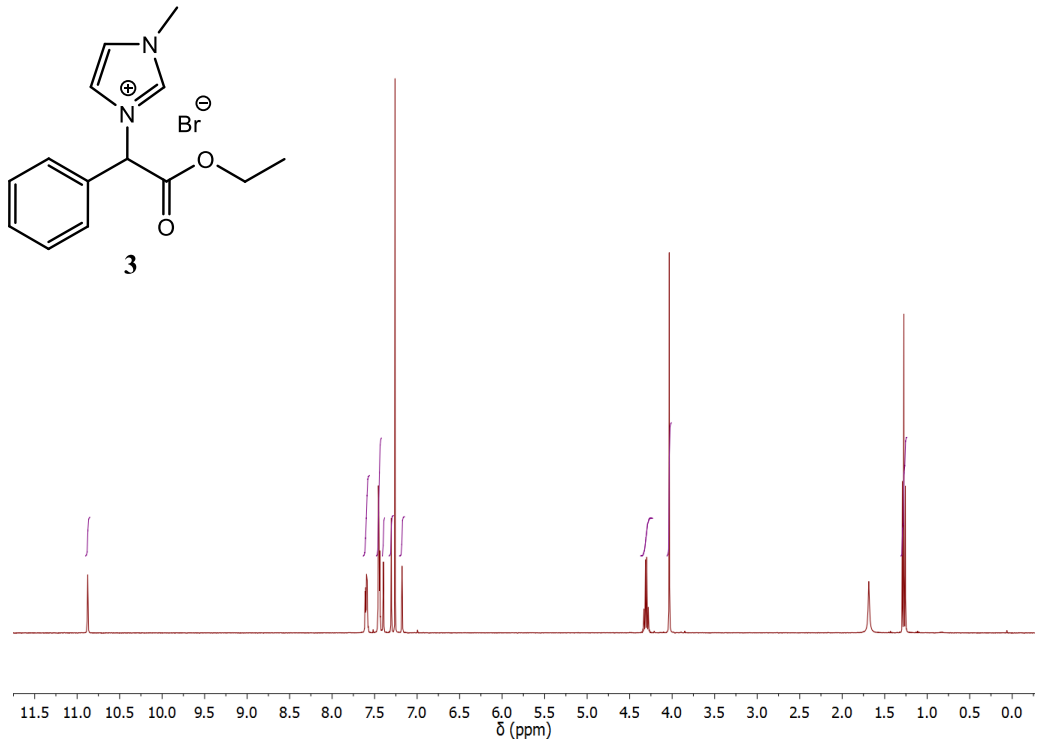


Figure S5 ^{1}H NMR spectra of IL **3** (400 MHz, $CDCl_3$).

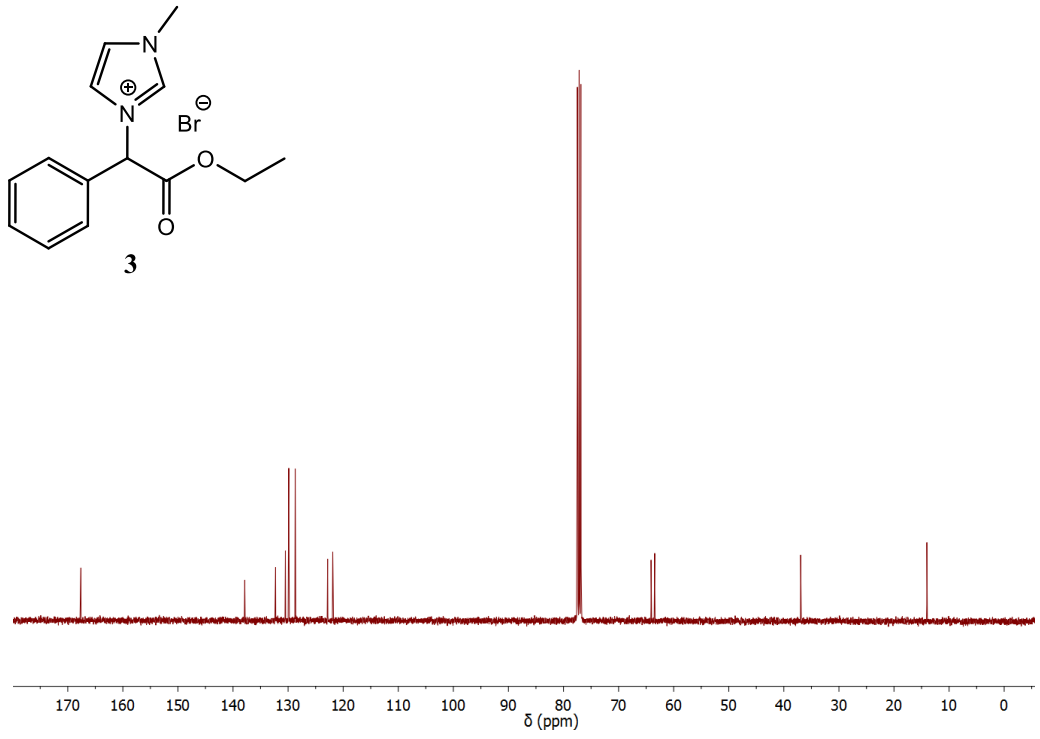


Figure S6 ^{13}C NMR spectra of IL **3** (101 MHz, $CDCl_3$).

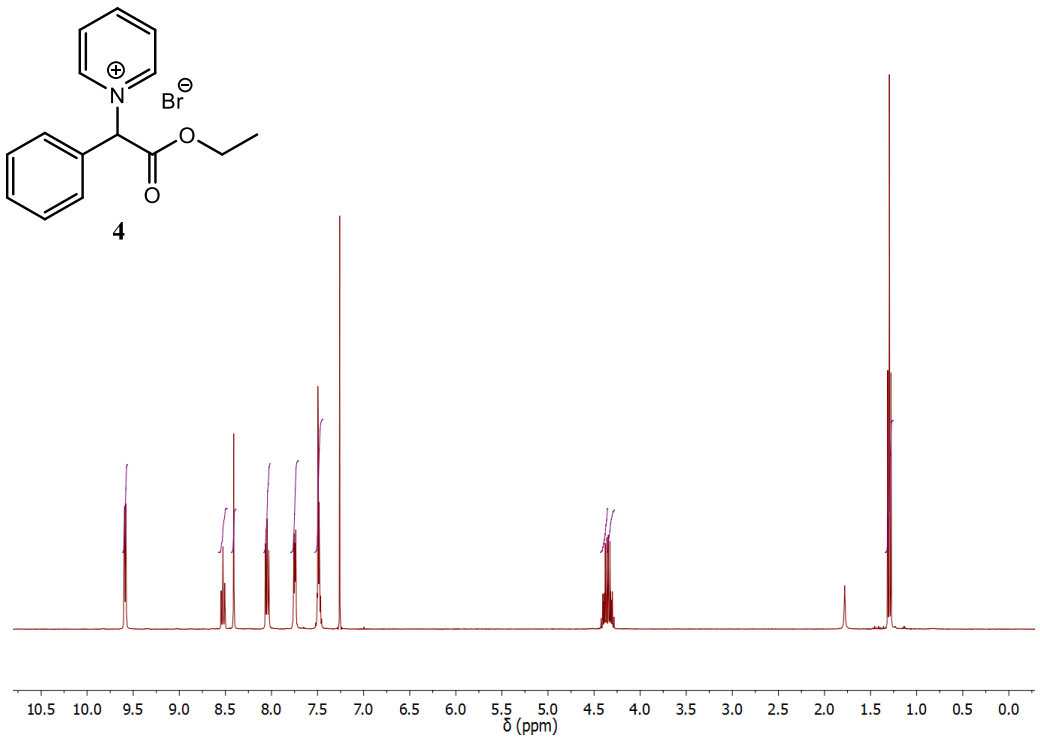


Figure S7 ^{1}H NMR spectra of IL **4** (400 MHz, $CDCl_3$). ^{1}H NMR data are in agreement with the literature.[7]

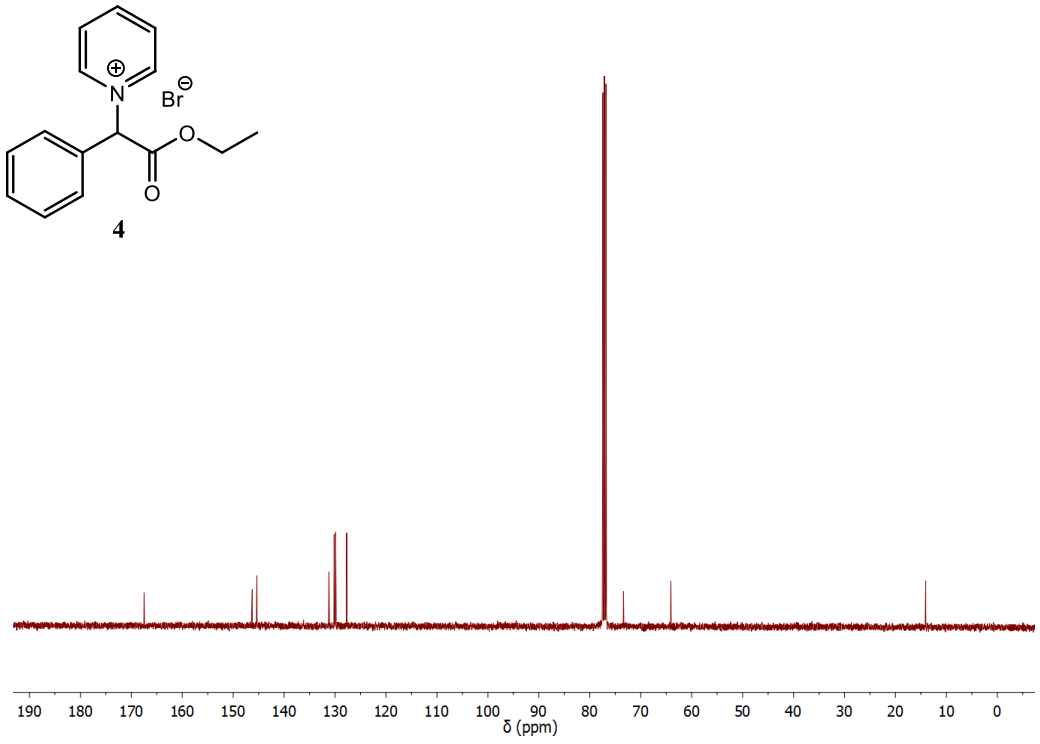


Figure S8 ^{13}C NMR spectra of IL **4** (101 MHz, $CDCl_3$). ^{13}C NMR data are in agreement with the literature.[7]

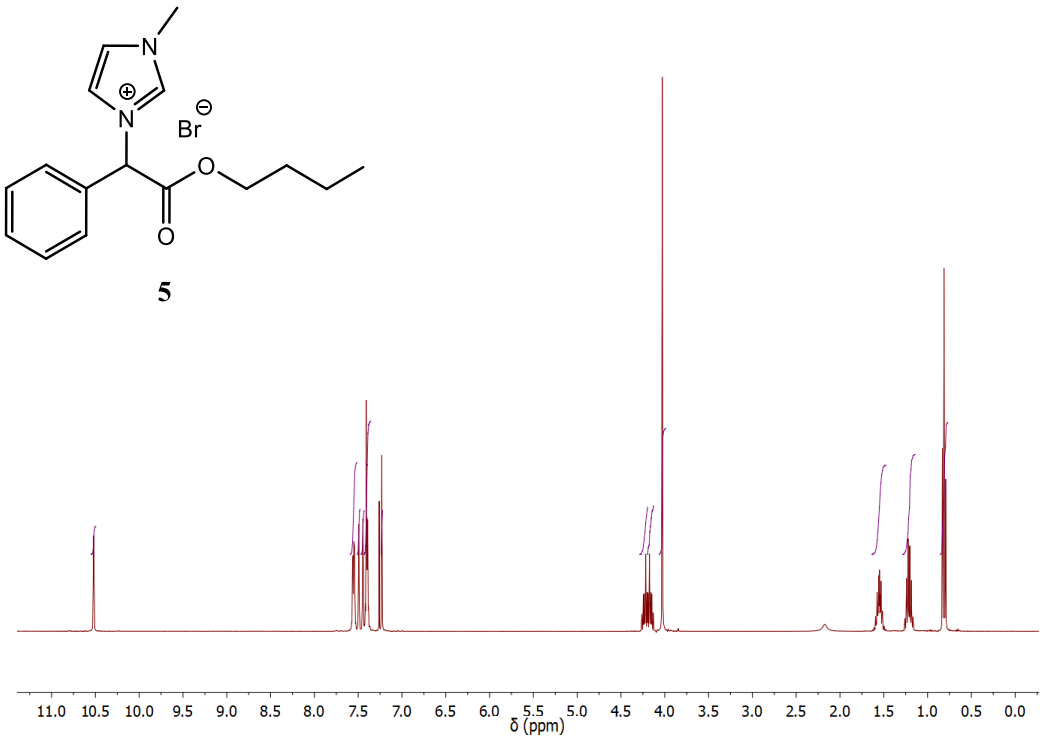


Figure S9 ^{1}H NMR spectra of IL **5** (400 MHz, $CDCl_3$).

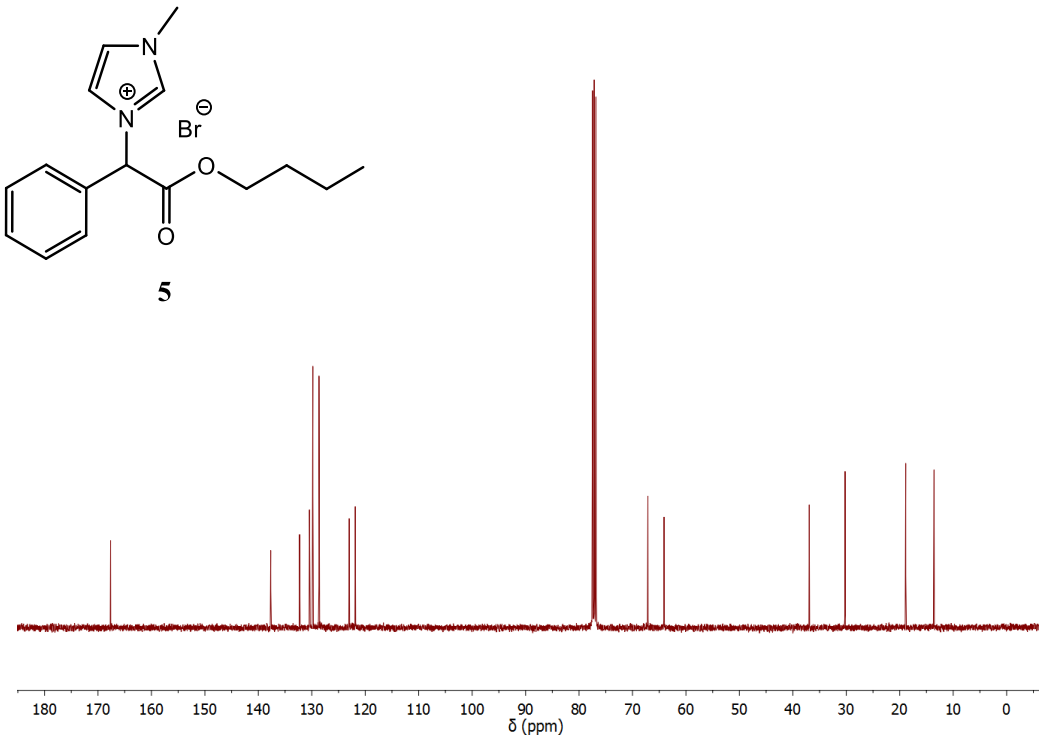


Figure S10 ^{13}C NMR spectra of IL **5** (101 MHz, $CDCl_3$).

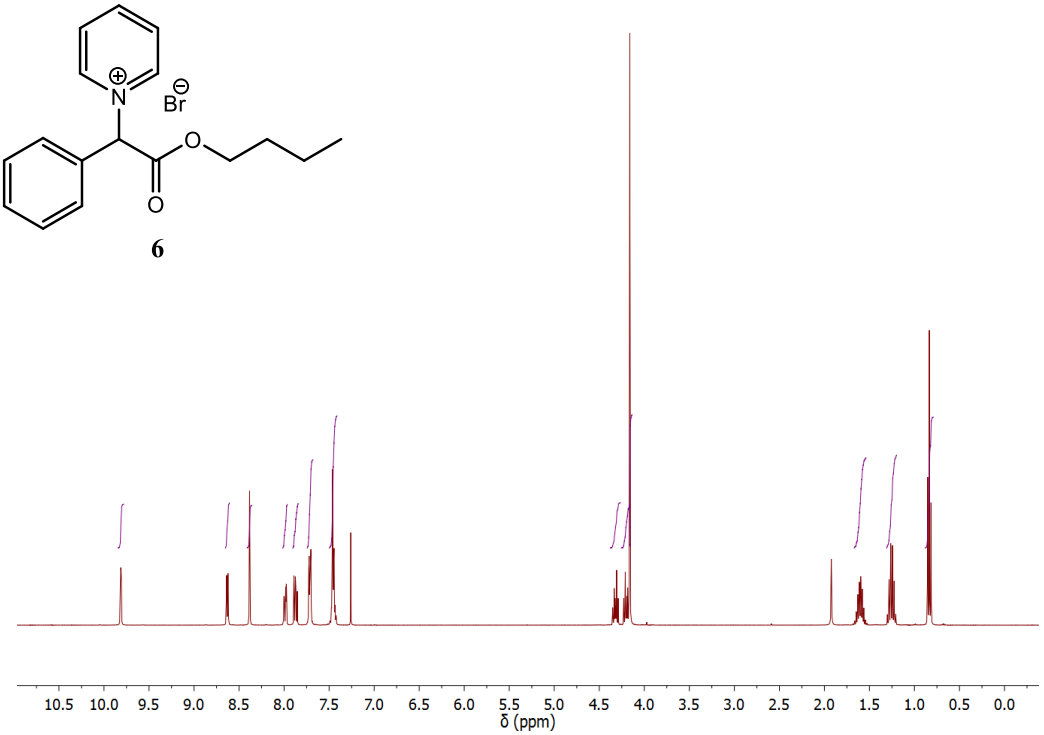


Figure S11 ^{1}H NMR spectra of IL **6** (400 MHz, $CDCl_3$).

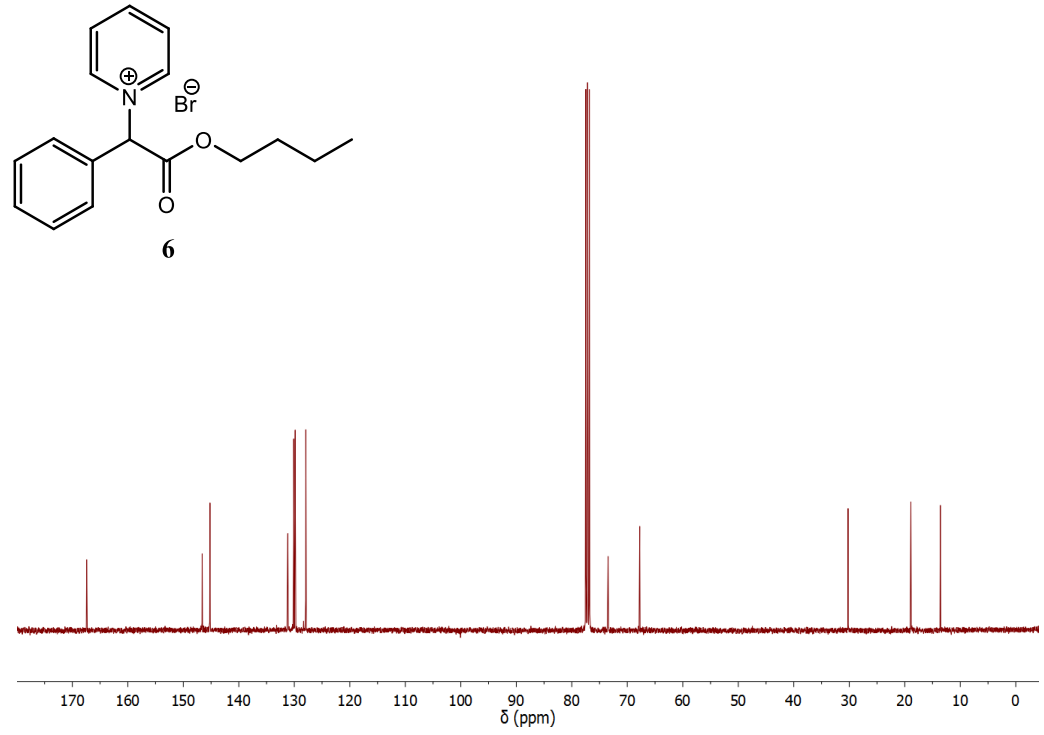


Figure S12 ^{13}C NMR spectra of IL **6** (101 MHz, $CDCl_3$).

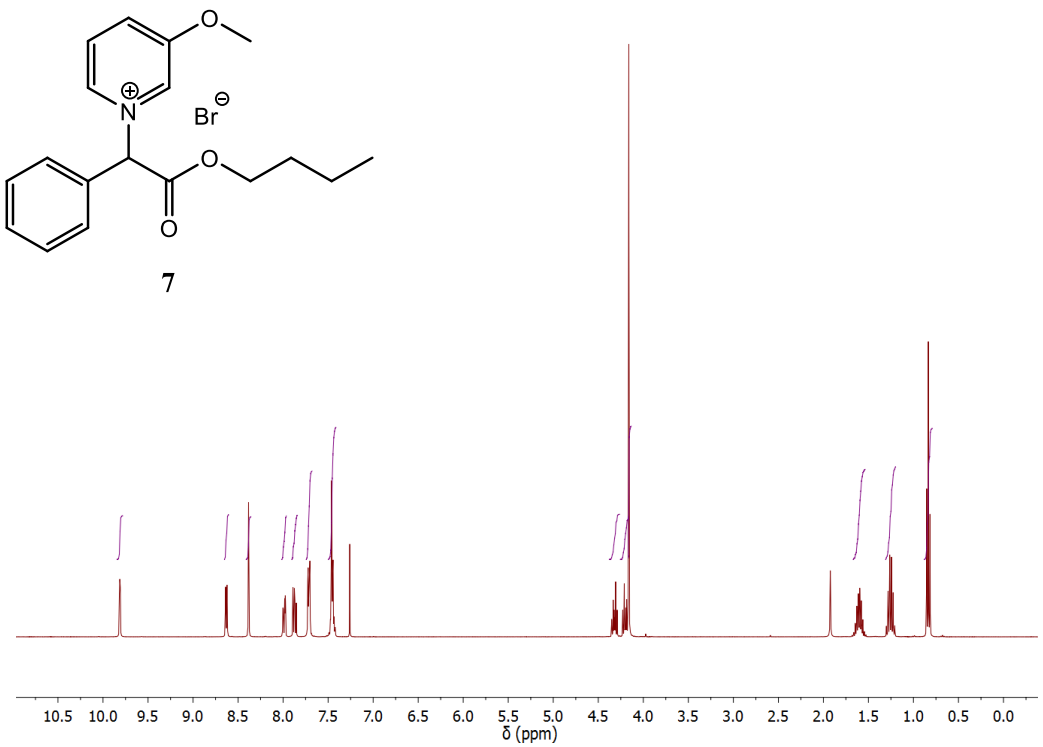


Figure S13 ^{1}H NMR spectra of IL **7** (400 MHz, $CDCl_3$).

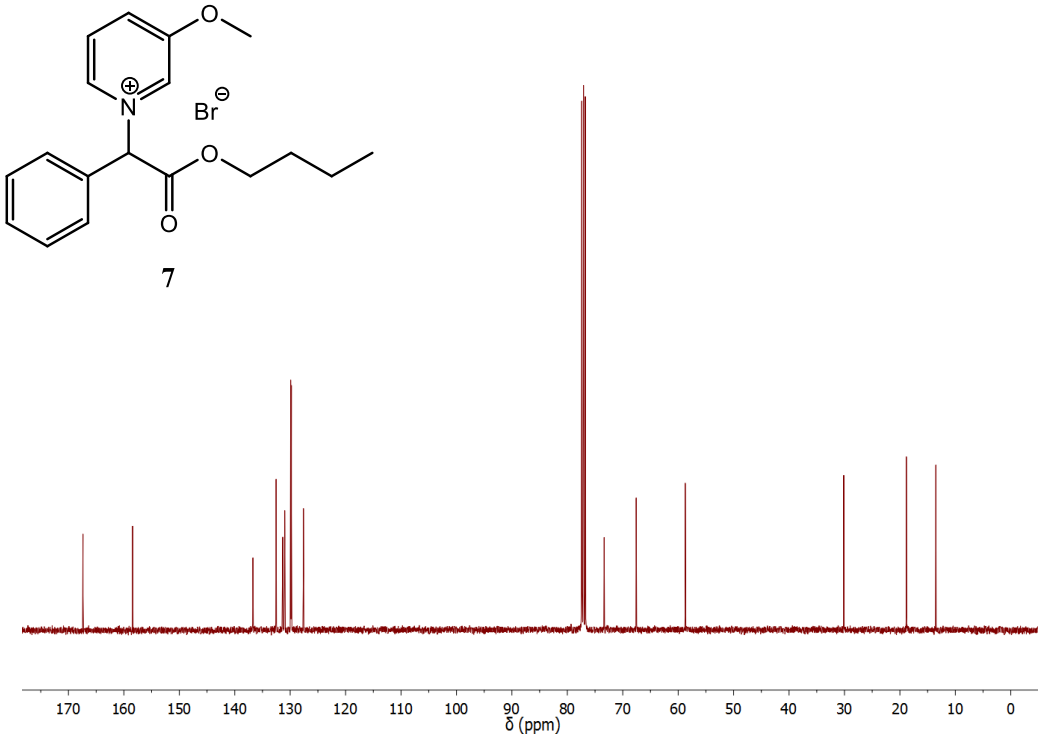


Figure S14 ^{13}C NMR spectra of IL **7** (101 MHz, $CDCl_3$).

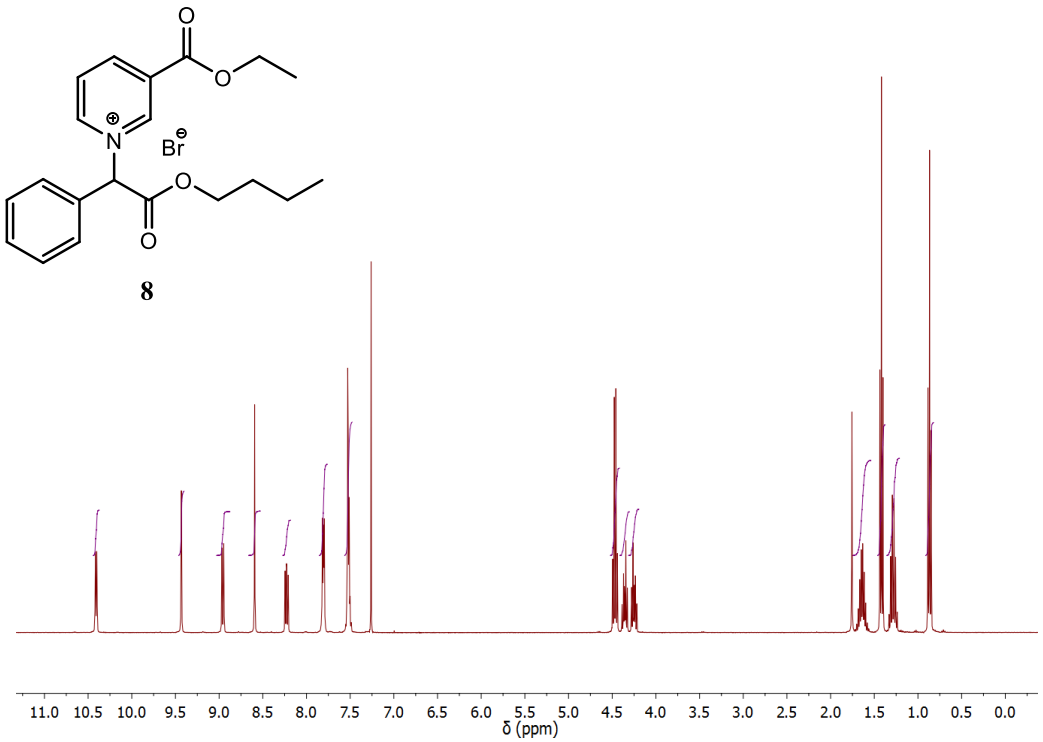


Figure S15 ^{1}H NMR spectra of IL **8** (400 MHz, $CDCl_3$).

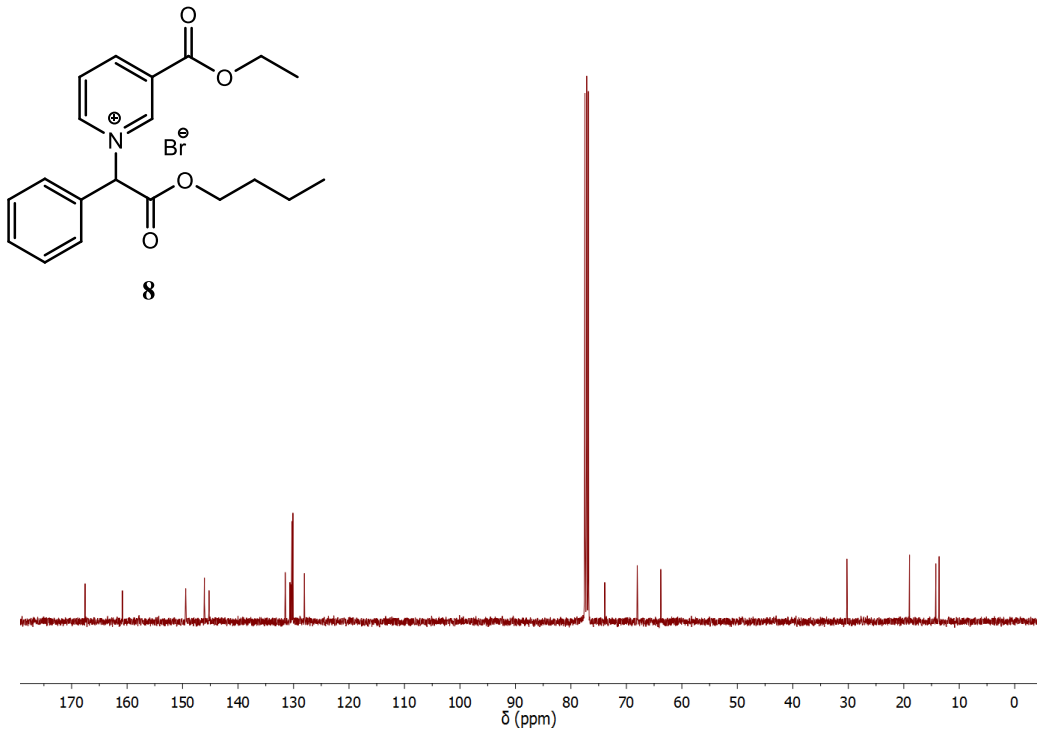


Figure S16 ^{13}C NMR spectra of IL **8** (101 MHz, $CDCl_3$).

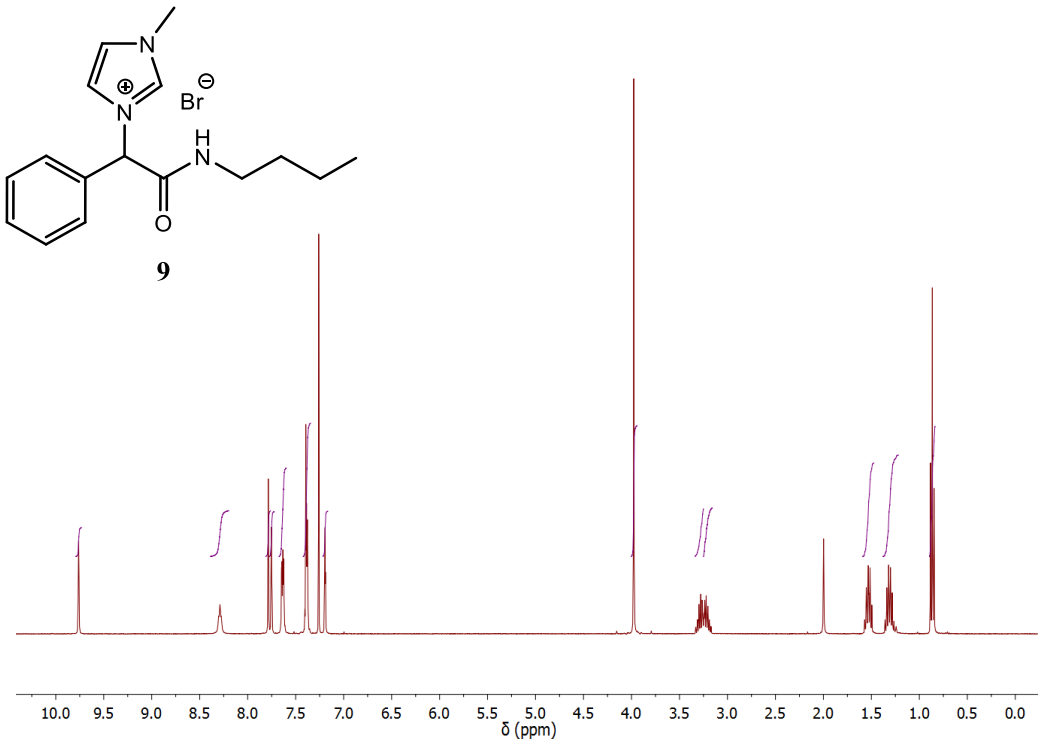


Figure S17 ^{1}H NMR spectra of IL **9** (400 MHz, $CDCl_3$).

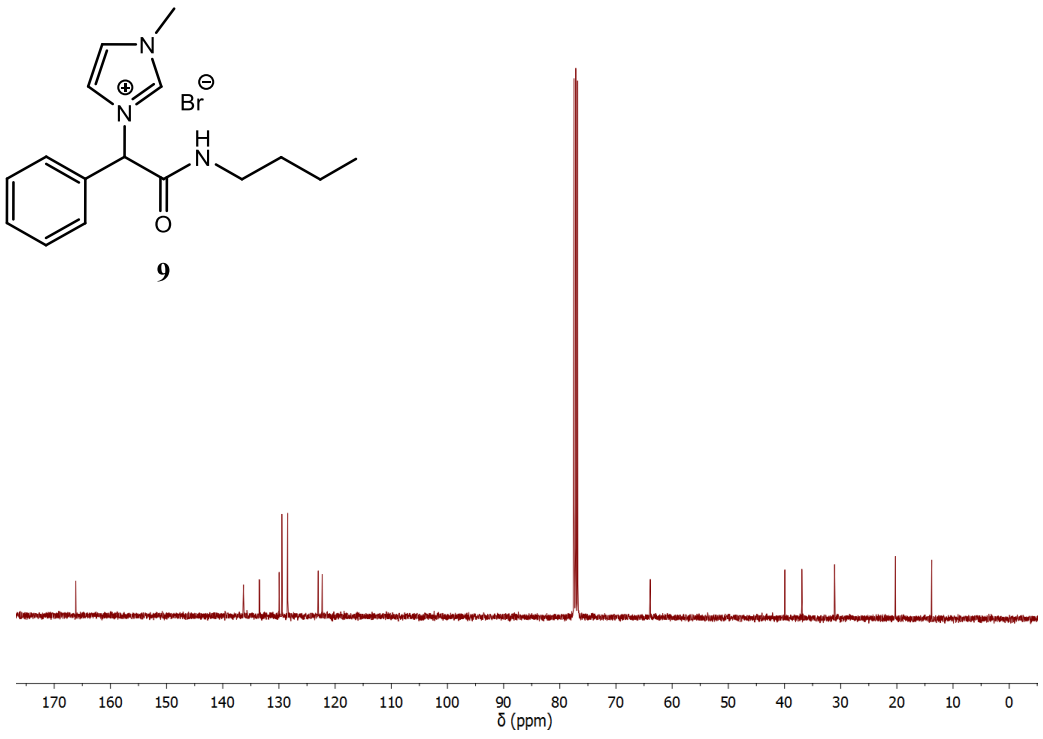


Figure S18 ^{13}C NMR spectra of IL **9** (101 MHz, $CDCl_3$).

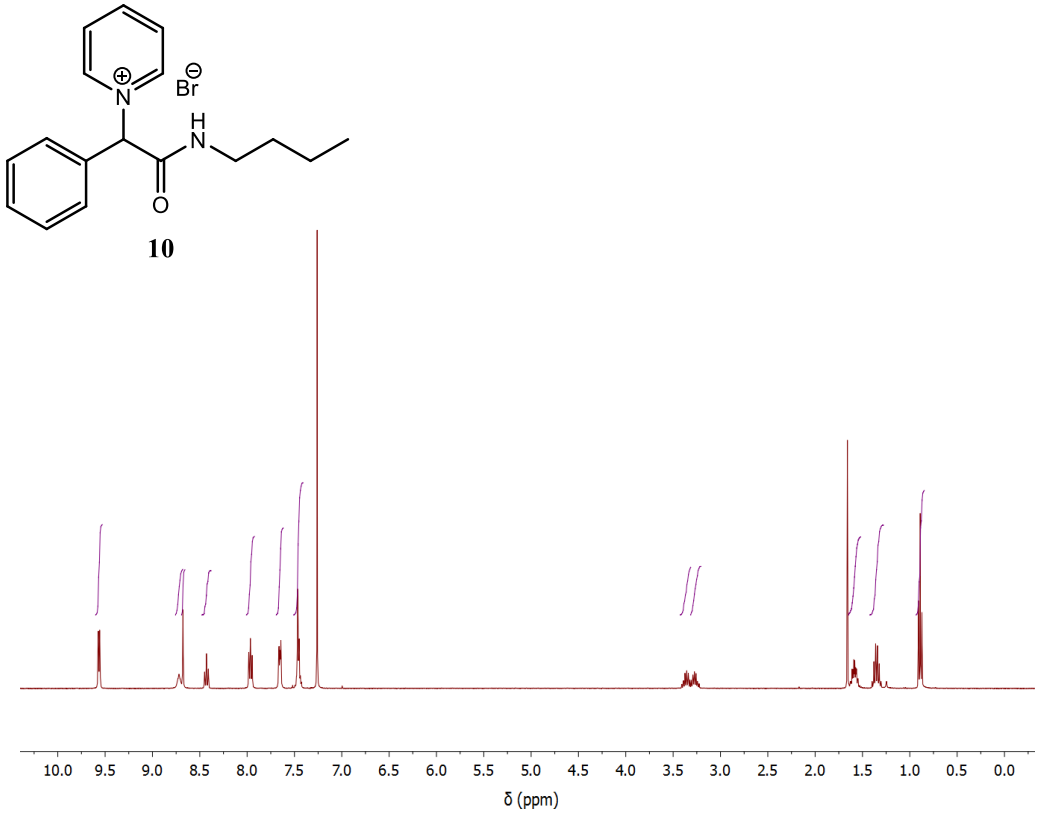


Figure S19 ^{1}H NMR spectra of IL **10** (400 MHz, $CDCl_3$).

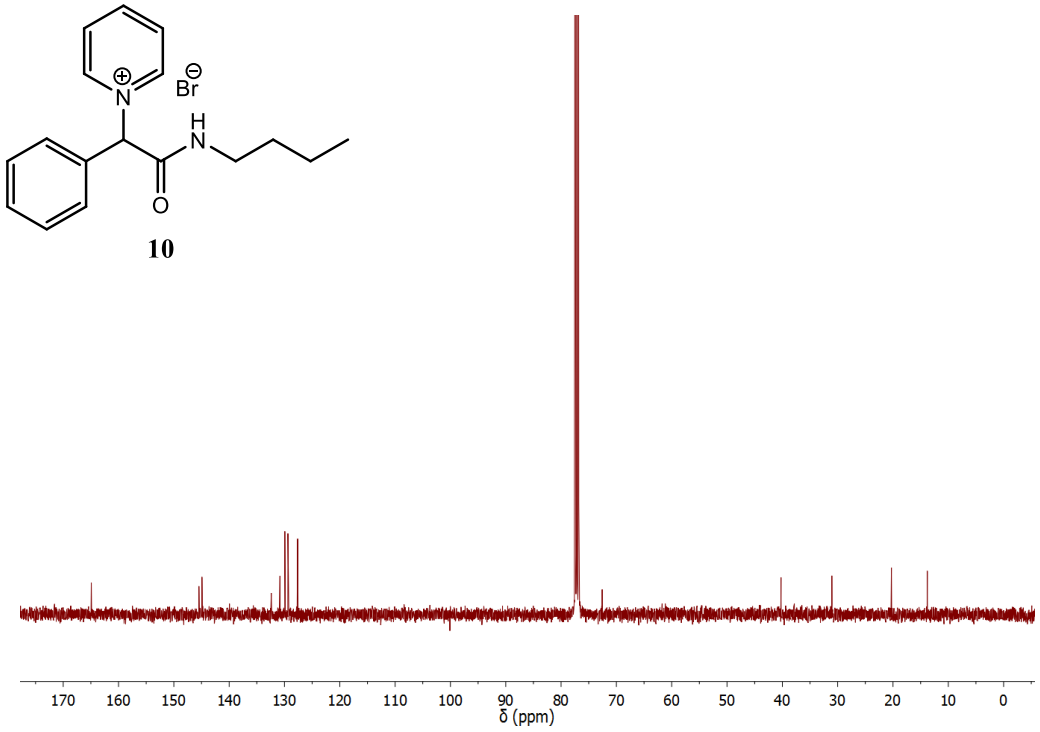


Figure S20 ^{13}C NMR spectra of IL **10** (101 MHz, $CDCl_3$).

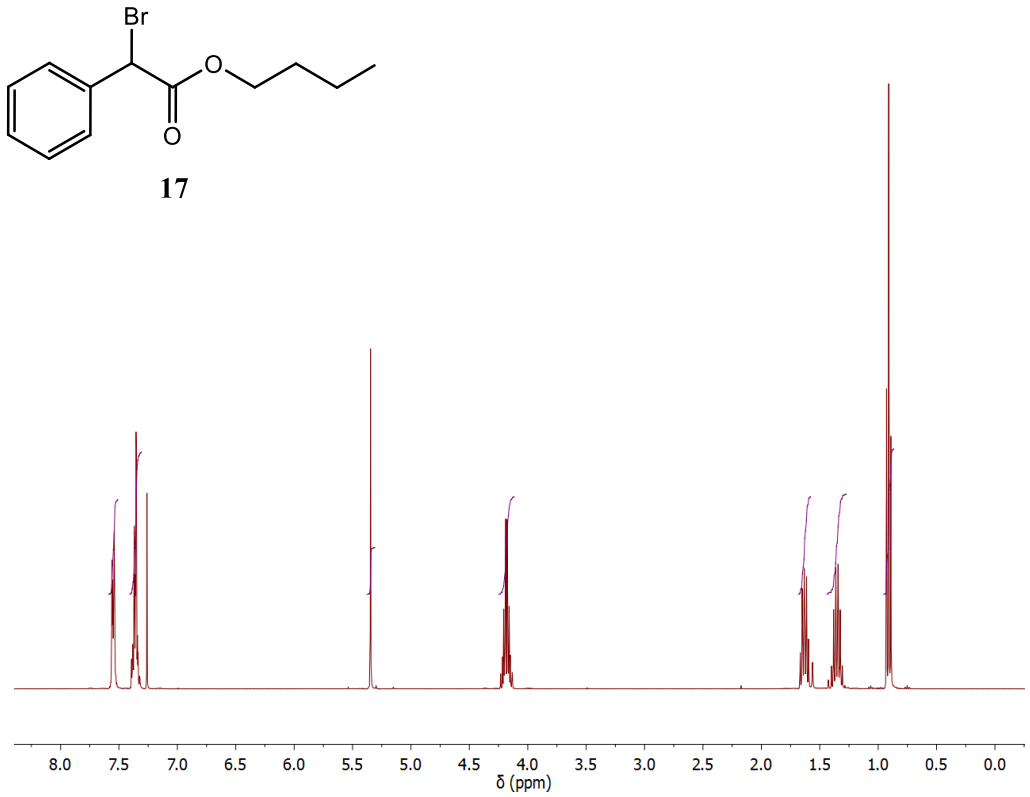


Figure S21 ^{1}H NMR spectra of compound **17** (400 MHz, $CDCl_3$).

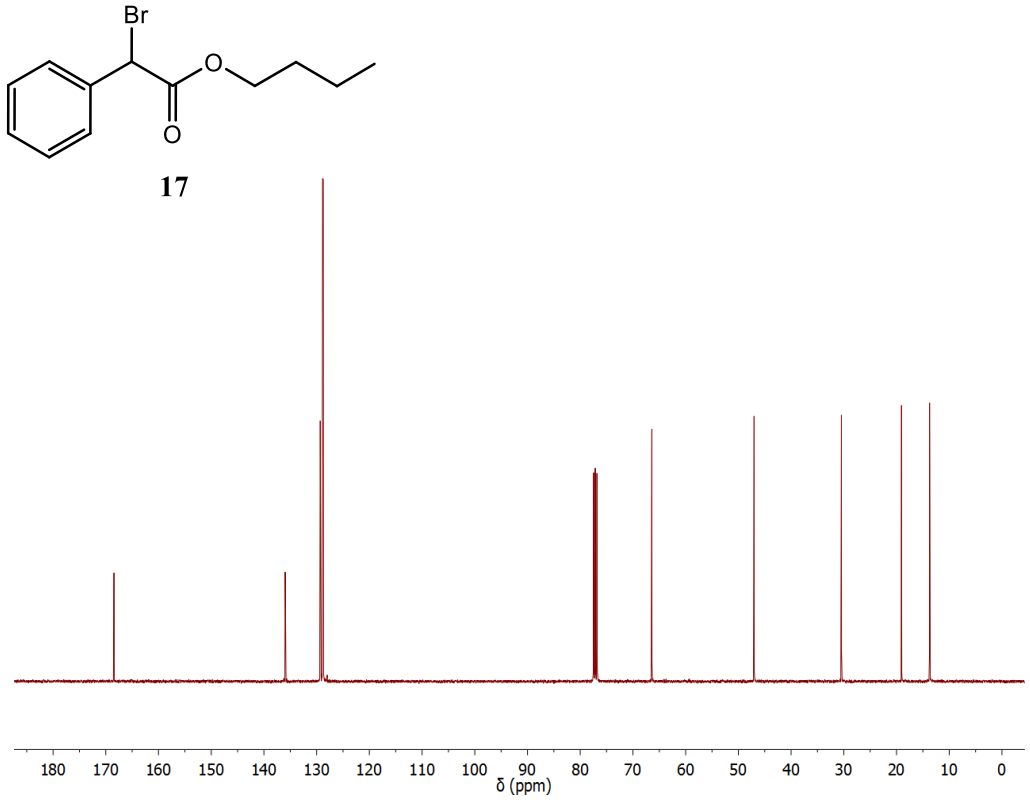


Figure S22 ^{13}C NMR spectra of compound **17** (101 MHz, $CDCl_3$).

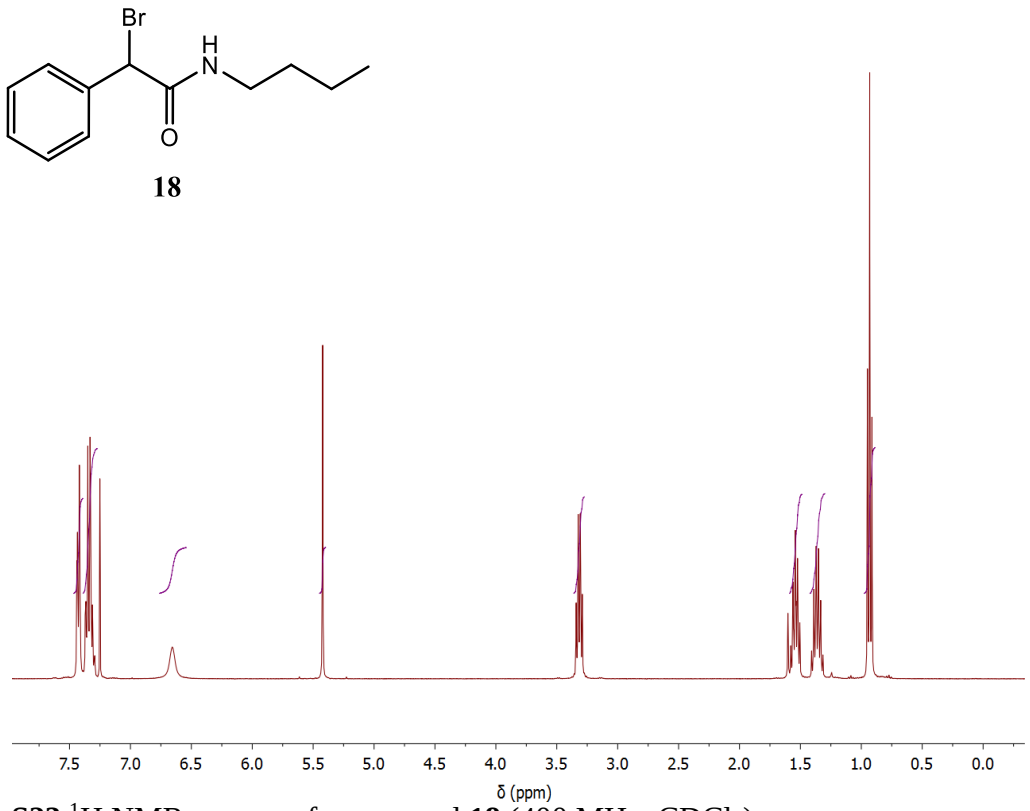


Figure S23 ^{1}H NMR spectra of compound **18** (400 MHz, $CDCl_3$).

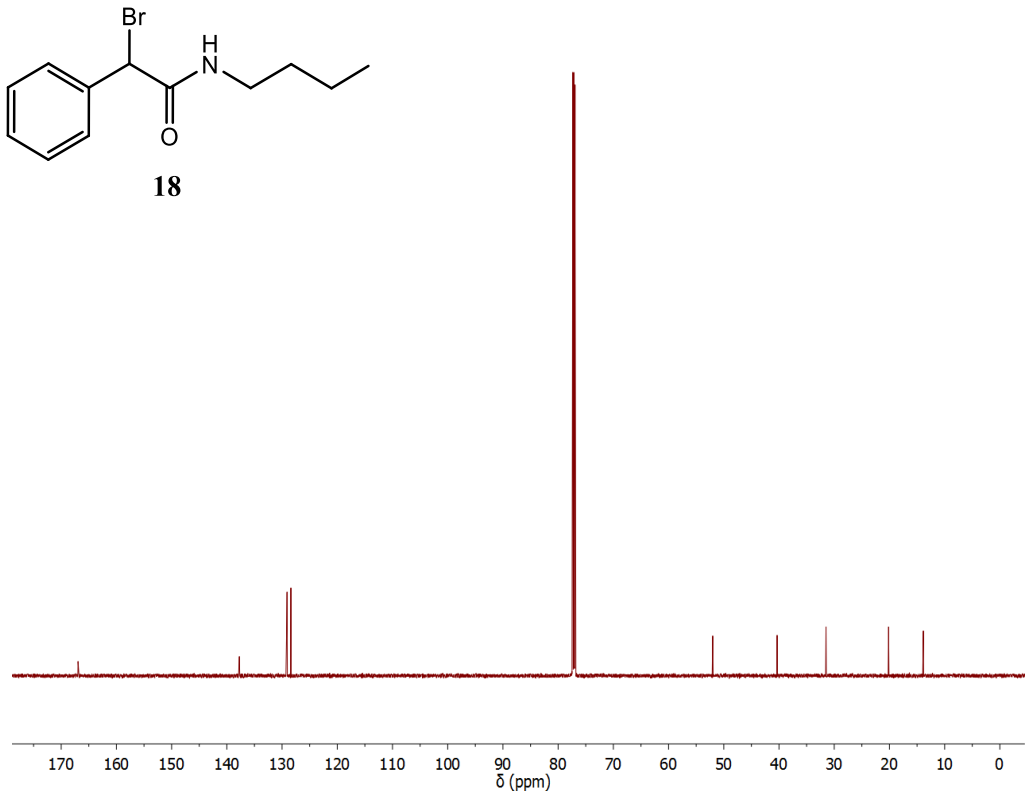


Figure S24 ^{13}C NMR spectra of compound **18** (101 MHz, $CDCl_3$).

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