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MDPI

A Brønsted Acidic Deep Eutectic Solvent for *N*-Boc Deprotection

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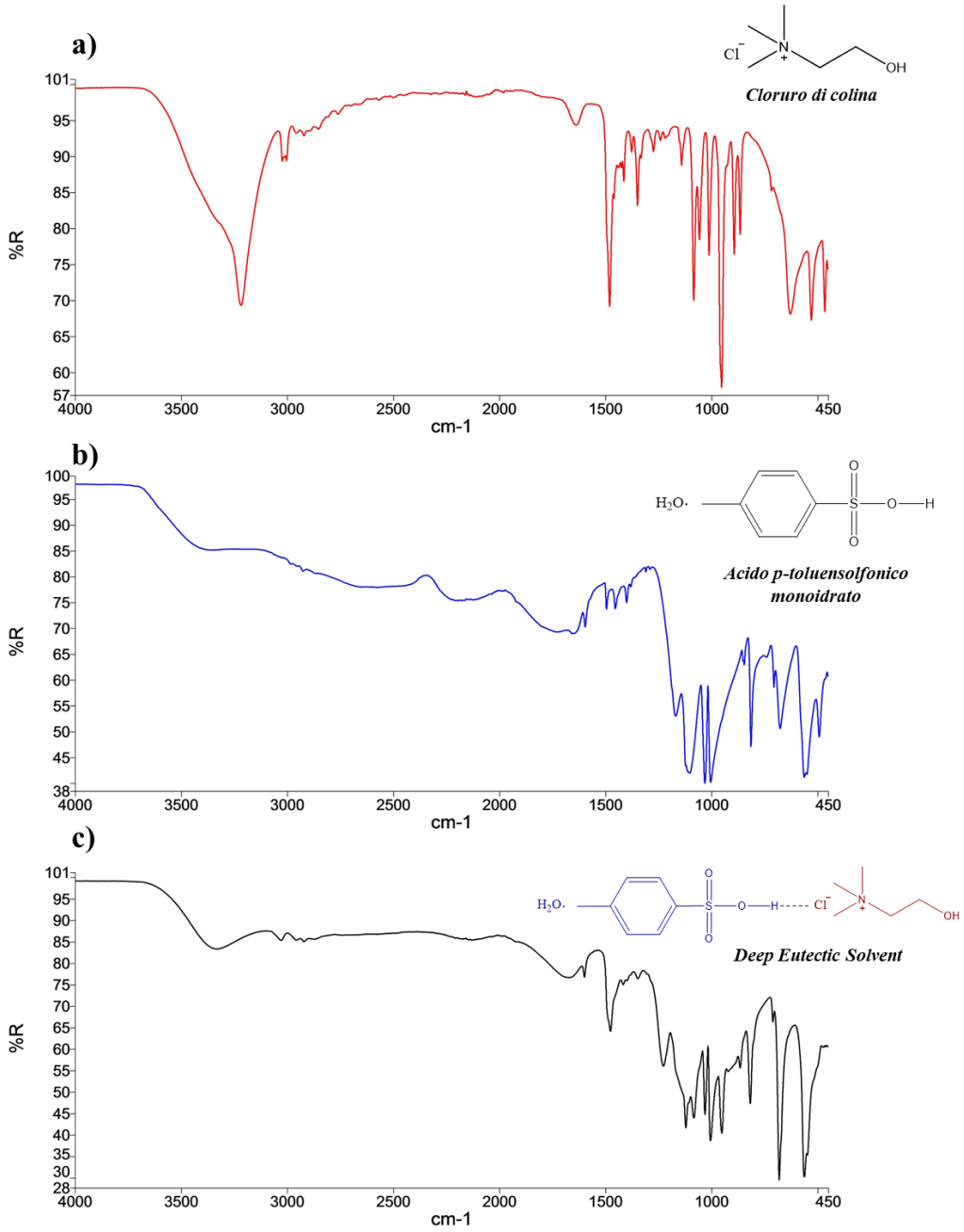
Supporting Information

Contents

1. General Information

Commercially available reagents were purchased from Sigma-Aldrich Chemical Co. (Milano, Italy) and used as supplied unless stated otherwise. All syntheses were carried out in atmospheric conditions. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 MHz. Spectral analysis was performed at 293 K on diluted solutions of each compound by using $CDCl_3$ as the solvent. Chemical shifts (δ) are reported in ppm and referenced to $CDCl_3$ (7.25 ppm for ^{1}H and 77.0 ppm for ^{13}C spectra). Coupling constants (J) are reported in hertz (Hz). Reaction mixtures were monitored by thin layer chromatography (TLC) using Merck Silica gel 60-F254 precoated glass plates or 0.2% ninhydrin in ethanol. GC-MS analyses were carried out using a 30-m HP-35MS capillary column with a 0.25 mm internal diameter and a 0.25 μm film thickness. The mass detector was operated in the electron impact ionization mode (EI-MS) at an electron energy of 70 eV. He was used as the carrier gas. The injection port was heated to 250 °C. The oven temperature program was initially set at 50 °C and held for 2 min, then ramped to 280 °C at 14 °C min/1 with a hold of 10 min. Infrared spectra (FTIR) were recorded using a Perkin-Elmer 1720 FTIR spectrophotometer in the range of 4,000–400 cm^{-1} at a rate of 0.5 cm/s. Fifty scans were recorded, the average for each spectrum was calculated and corrected with respect to ambient air as a background.

2. FTIR analysis : a) Choline chloride; b) pTSA; c) ChCl:pTSA DES (1:1)

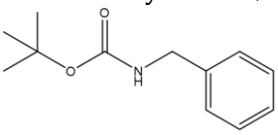


3. General procedure for the synthesis of N-Boc amines and amino acid derivatives

A 50 mL round-bottom flask containing 10 mL of dichloromethane (DCM) was charged with the starting amine or amino acid derivative (1 equiv) and triethylamine (TEA) (1.5 equiv). Di-tert-butyl dicarbonate ($(Boc)_2O$) (1 equiv) was then added to the former solution and the resulting mixture was stirred at r.t. The reaction was monitored by TLC and was complete in 3-4 h. The reaction mixture was acidified with an aqueous solution of HCl 1N and then extracted with DCM (3 x 10 mL). The combined organic layers were dried over Na_2SO_4. The filtrate was concentrated in vacuo under reduced pressure to obtain the pure N-Boc protected amines or amino acid derivatives without need of further purification. All N-Boc-protected starting materials were characterized by GC-MS, ^{1}H-NMR and ^{13}C-NMR before their use. Spectral data are consistent with those already reported in the literature [43].

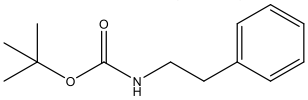
4. Characterization data for Boc-protected starting materials

_N_-Boc-Benzylamine (1a):



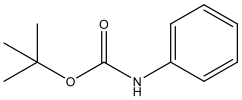
^{1}H NMR (300 MHz, $CDCl_3$,) δ = 7.39- 7.20 (m, 5H, ArH), 4.97 (br s, 1H, NH), 4.28 (s, 2H, CH_2), 1.43 (s, 9H, tbu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 155.9, 139.0, 128.7, 128.5, 127.4, 79.4, 44.7, 28.4. GC/MS (EI): m/z (%) 207 ($M^{\cdot+}$) (4), 151 (90), 150 (100), 133 (7), 106 (49), 91 (73), 77 (15), 65 (11), 57 (91), 51 (9), 41 (27).

_N_-Boc -2-Phenylethylamine (1b):



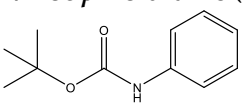
^{1}H NMR (300 MHz, $CDCl_3$,) δ = 7.30-7.15 (m, 5 H, ArH), 4.54 (br s, 1H, NH), 3.50-3.47 (m, 2H, CH_2), 2.77 (t, 2H, J= 7.0 Hz, CH_2), 1.48 (s, 9H, tbu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 155.9, 139.0, 128.8, 128.5, 126.5, 80.5, 41.8, 36.2, 28.4. GC/MS (EI): m/z (%) 221 ($M^{\cdot+}$) (3), 165 (48), 104 (29), 92, 24), 91 (30), 77 (8), 65 (10), 57 (100), 41 (20), 30 (27).

_N_-Boc-Aniline (1c):



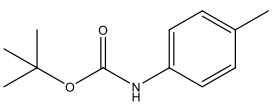
^{1}H NMR (300 MHz, $CDCl_3$,) δ = 7.39-7.20 (m, 4H, ArH), 6.99 (t, 1H, J=.7.2 Hz ArH), 6.42 (s, 1H, NH), 1.49 (s, 9H, tBu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 153.80, 138.3, 129.1, 123.0, 118.4, 80.5, 28.8. GC/MS (EI): m/z (%) 193 ($M^{\cdot+}$, 9), 137 (46), 119 (5), 93 (69), 77 (7), 65 (15), 57 (100), 51 (4), 41 (32).

_N_-Boc _p_-Toluidine (1d):



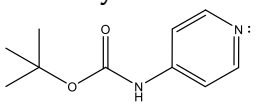
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.22 (d, J = 7.5 Hz, 2H, ArH), 7.06 (d, J = 7.5 Hz, 2H, ArH), 6.46 (br s, 1H, NH), 2.27 (s, 3H, CH_3), 1.51 (s, 9H, tBu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 152.9, 135.7, 132.5, 130.3, 129.4, 80,3, 28.4, 20.8. GC/MS (EI): m/z (%) 207 ($M^{\cdot+}$) (9), 151 (58), 133 (5), 107 (64), 106 (44), 91 (5), 77 (16), 57 (100), 51 (6), 41 (32).

_N_-Boc p-Anisidine (1e):



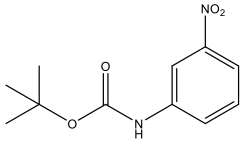
^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.23 (d, J = 8.7 Hz, 2H, ArH), 6.79 (d, J = 8.7 Hz, 2H, ArH), 6.48 (br s, 1H, NH), 3.73 (s, 3H, OCH_3), 1.51 (s, 9H, tBu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 155.6, 153.3, 131.5, 114.1, 80.2, 55.9, 28.4. GC/MS (EI): m/z (%) 223 ($M^{\cdot+}$) (14), 167 (100), 149 (9), 134 (5), 123 (34), 108 (65), 95 (7), 80 (9), 57 (74), 41 (28).

***N*-Boc Pyridin-4-amine (1f):**



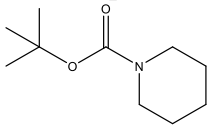
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (d, 2H, J= 4.5 Hz, ArH), 7.08 (2H, J= 4.5, ArH), 5.64 (br s, 1H, NH), 4.20 (m, 2H, CH_2), 1.43 (s, 9H, tbu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 156.1, 150.3, 149.8, 121.9, 79.7, 43.4, 28.3. GC/MS (EI): m/z (%) 208 ($M^{\cdot+}$) (4), 152 (56), 153 (54), 135 (30), 107 (14), 92 (30), 79 (17), 65 (9), 57 (100), 51 (9), 41 (24).

***N*-Boc 3-Nitroaniline (1g):**



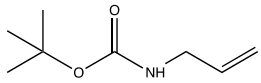
^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 8.32 (s, 1H, ArH), 7.89 (d, 1H, J = 8.1 Hz, ArH), 7.70 (d, 1H, J= 8.1 Hz, ArH), 7.46 (t, 1H, J = 8.1 Hz, ArH), 6.78 (br s, 1H, NH), 1.51 (s, 9H, tbu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 152.3, 148.1, 139.7, 123.5, 116.8, 113.3, 81.6, 28.3. GC/MS (EI): m/z (%) 238 ($M^{\cdot+}$) (5), 182 (7), 138 (15), 92 (6), 65 (7), 57 (100), 41 (22)

***N*-Boc Piperidine (1h**):



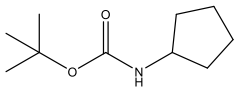
^{1}H-NMR: (300 MHz, $CDCl_3$, 25 °C) δ 3.40–3.30 (m, 2H, NCH_2), 3.19 3.09 (m, 2H, NCH_2), 1.52 (s, 9H, tbu), 1.47–1.40 [m, 6H, $NCH_2(CH_2)_3$] ppm. ^{13}C-NMR: (75 MHz, $CDCl_3$) 185 ($M^{\cdot+}$) (10), 129 (47), 112 (30), 84 (65), 69 (13), 57 (100), 41 (41)

***N*-Boc Allylamine (1i):**



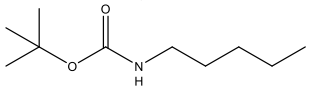
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.76 (m, 1H, CH), 5.14-5.02 (m, 2H CH_2CH), 4.66 (br, s, 1H, NH), 3.68 (s, 2H, CH_2NH), 1.43 (2, 9H, tbu) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 155.8, 134.9, 115.6, 79.3, 43.0, 28.4. GC/MS (EI): m/z (%) 157 ($M^{\cdot+}$) (3), 101 (72), 59 (47), 57 (100), 41 (49)

***N*-Boc Cyclopentylamine (1j**):



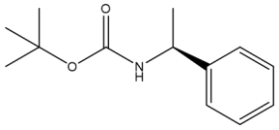
^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 4.49 (br s, 1H, NH), 3.93 (br s, 1H, CH), 2.01-1.84 (m, 2H, CH_2), 1.78-1.53 (m, 6H, $CH_2CH_2CH_2$), 1.42 (s, 9H, tbu) ppm. GC/MS (EI): m/z (%) 185 ($M^{\cdot+}$) (3), 170 (3), 130 (26), 129 (25), 100 (13), 85 (3), 69 (9), 62 (10), 59 (32), 57 (100) , 56 (42), 41 (34)

***N*-Boc Pentylamine (1k):**



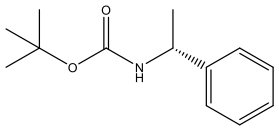
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (br s, 1H, NH), 3.019 (t, 2H, J= 6.8 Hz, $NHCH_2$), 1.39 (s, 9H, tBu), 1.41-1.44 (m, 2H, CH_2), 1.21-1.23 (m, 4H, CH_2CH_2), 0.82 (t, J = 6.7 Hz, 3H, CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 156.0, 78.9, 40.7, 29.7, 28.9, 28.4, 22.3, 13.9. GC/MS (EI): m/z (%)187 ($M^{\cdot+}$) (3), 132 (21), 131 (19), 87 (10), 74 (5), 57 (100), 41 (26), 30 (18)

***N*-Boc (R)-1-phenylethylamine (1l):**



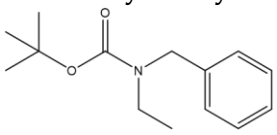
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H, ArH), 4.93 (br s 1H, NH), 4.78 (m, 1H, CH), 1.38 (s, 12H, tbu and CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 155.1, 141.6, 128.6, 127.1, 125.9, 79.3, 50.2, 28.4, 22.7. GC/MS (EI): m/z (%) 221 ($M^{\cdot+}$) (2), 165 (64), 150 (93), 132 (6), 120 (16), 106 (64), 105 (70), 91 (3), 77 (23), 57 (100), 51 (7), 41 (23)

***N*-Boc (S)-1-phenylethylamine (1m):**



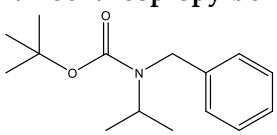
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.11 (m, 5H, ArH), 4.90-4.68 (m, 2H, NH, CH),1.35 (s, 12H, tbu and CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 155.6, 143.6, 128.7, 127.2, 126.0, 79.4, 55.1, 28.4, 22.7. GC/MS (EI): m/z (%) 221 ($M^{\cdot+}$) (2), 165 (64), 150 (100), 132 (6), 120 (16), 105 (70),106 (62), 91(3), 77 (23), 57 (87), 51 (7), 41 (23)

***N*-Boc Ethyl benzylamine (1n):**



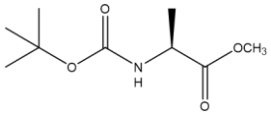
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.20 (m, 5H, ArH), 4.42 (s, 2H, CH_2Ph), 3.40-3.12 (m, 2H, CH_2CH_3), 1.52 (s, 9H, tbu), 1.06 (m, 3H, CH_2CH_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 154.2, 137.2, 128.5, 128.3, 127.1, 79.5, 50.6, 41.3, 28.5, 13.3. GC/MS (EI): m/z (%) 235($M^{\cdot+}$) (3), 220 (3), 179 (82), 164 (12), 150 (5), 134 (13), 120 (38), 106 (5), 92 (25), 91 (100), 77 (5), 65 (10), 57 (80), 41 (20)

***N*-Boc *N*-Isopropylbenzylamine (1o):**



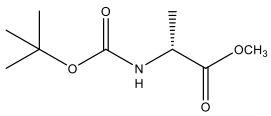
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29-7.15 (m, 5H, ArH), 4.32 -4.10 (m, 2H, NH, CH), 1.43 (s, 9H, tbu), 0.861 (d, 6H, J= 6Hz, $CH(CH_3)2$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ= 139.0, 128.1, 127.3, 126.6, 79.5, 57.3, 47.1, 28.4, 20.8. GC/MS (EI): m/z (%) 249 ($M^{\cdot+}$) (3), 234 (3), 193 (45), 178 (32), 150 (10), 134 (38), 106 (7), 92 (7), 91 (100), 77 (5), 65 (10), 57 (80), 41 (24)

N-Boc L-Alanine methyl ester (1p):



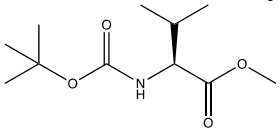
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.05 (br s, 1H NH), 4.32 (m, 1H, α-CH), 3.75 (s, 3H, OMe), 1.44 (s, 9H, tbu), 1.38 (d, J = 7.2 Hz, 3H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 173.8, 154.2, 79.8, 54.4, 49.1, 28.3, 18.6 .GC/MS (EI): m/z (%) 203 ($M^{\cdot+}$) (3), 188 (3), 144 (36), 130 (7), 116 (5), 102 (18), 88 (28), 70 (7), 59 (30), 57 (100).

N-Boc D-Alanine methyl ester (1q):



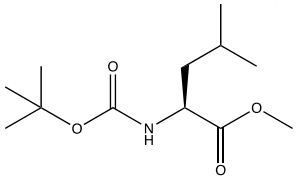
^{1}H NMR (300 MHz, CDCl3) δ 5.05 (br s, 1H NH), 4.32 (m, 1H, ⊚-CH), 3.75 (s, 3H, OMe), 1.44 (s, 9H, tbu), 1.38 (d, J = 7.2 Hz, 3H, CH3) ppm. ^{13}C NMR (150 MHz, CDCl3) δ 173.8, 154.2, 79.8, 54.4, 49.1, 28.3, 18.6. GC/MS (EI): m/z (%) 203 ($M^{\cdot+}$) (3), 144 (36), 130 (7), 116 (5), 102 (18), 88 (28), 70 (7), 57 (100)

N-Boc -L-Valine methyl ester (1r):



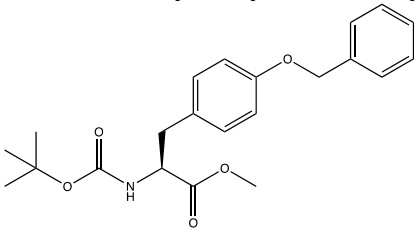
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.04 (d, 1H, J=6.9 Hz, NH), 4.17 (m, 1H, α-CH), 3.70 (s, 3H, OMe), 2.07 (m, 1H, $CH(CH_3)_3$), 1.42 (s, 9H, tbu), 0.92 (d, 3H, J= 6.6 Hz, CH_3), 0.86 (d, 3H, J= 6.9 Hz, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ172.8, 155.6, 79.6, 53,1, 51.5, 30.4, 28.3, 18.4. GC/MS (EI): m/z (%) 231 ($M^{\cdot+}$) (3), 172 (22), 158 (5), 130 (19), 116 (52), 98 (10), 88 (12), 72 (65), 57 (100).

N-Boc L-Leucine methyl ester (1s):



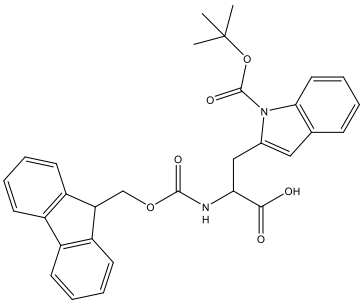
^{1}H NMR (300 MHz, $CDCl_3$) δ 5.10 (d, 1H, J= 8.1 Hz, NH), 4.18 (m, 1H, α-CH), 3.56 (s, 3H, OMe), 1.58 (m, 1H, CH_2), 1. 47 (m, 2H, CH_2, $CH(CH_3)_2$), 1.38 (s, 9H, tbu), 0.81 (d, 6H, J= 6.3 $(CH_3)_2$) ppm. ^{13}C NMR (150 MHz, CDCl3) δ 173.8, 155.9, 79.5, 53.6, 52.8, 41.6, 28.3, 24.5, 22.7. GC/MS (EI): m/z (%) 230 ($M^{\cdot+}$ - 15) (3), 186 (20), 172 (3), 144 (13), 130 (65), 86 (72), 57 (100).

N-Boc O-Benzyl-L-Tyrosine methyl ester (1t):



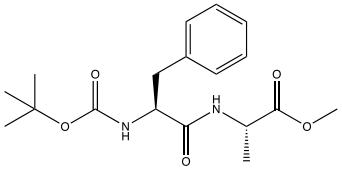
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.31 (m, 5H, ArH), 7.06 (d, 2H, J=7.2 Hz, ArH), 6.93 (d, 2H, J=7.2 Hz, ArH), 5.08 (s, 2H, OCH_2), 4.53 (m, 1H, α-CH), 3.71 (s, 3H, OMe), 3.13-2.99 (m, 2H, CH_2Ph), 1.42 (s,9H, tbu) ppm. ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.4, 155.1, 146.7, 137.1, 129.5, 128.7, 128.4, 127.3, 114.9, 79.8, 70.0, 54.6, 51.9, 37.5, 28.3.

Nα-Fmoc-N(in)-Boc-L-tryptophan (1u):



1H NMR (300 MHz, CDCl3) δ 8.08 (d, 1H, J = 7.5 Hz, NH), 7.73-7.71 (m, 3H, ArH), 7.56–7.16 (m, 10 H), 5.44 (d, 1H, J= 7.5 Hz, a-CH), 4.76 (m, 1H), 4.78 (m, 1H, CH-Fmoc), 4.35 (m, 2H, CH2-Fmoc), 3.31-3.14 (m, 2H, CH2-Trp), 3.49 (s, 1H), 1.62 (s, 9H, tBu) ppm. 13C NMR (150 MHz, CDCl3) δ 175.6, 143.7, 141.3, 135.3, 130.2, 127.6, 127.2, 125.2, 124.8, 120.5, 119.9, 118.8, 114.9, 110.9, 83.9, 67.3, 59.4, 47.0, 28.16.

N-Boc L-Phe-LAlaOMe (1v):



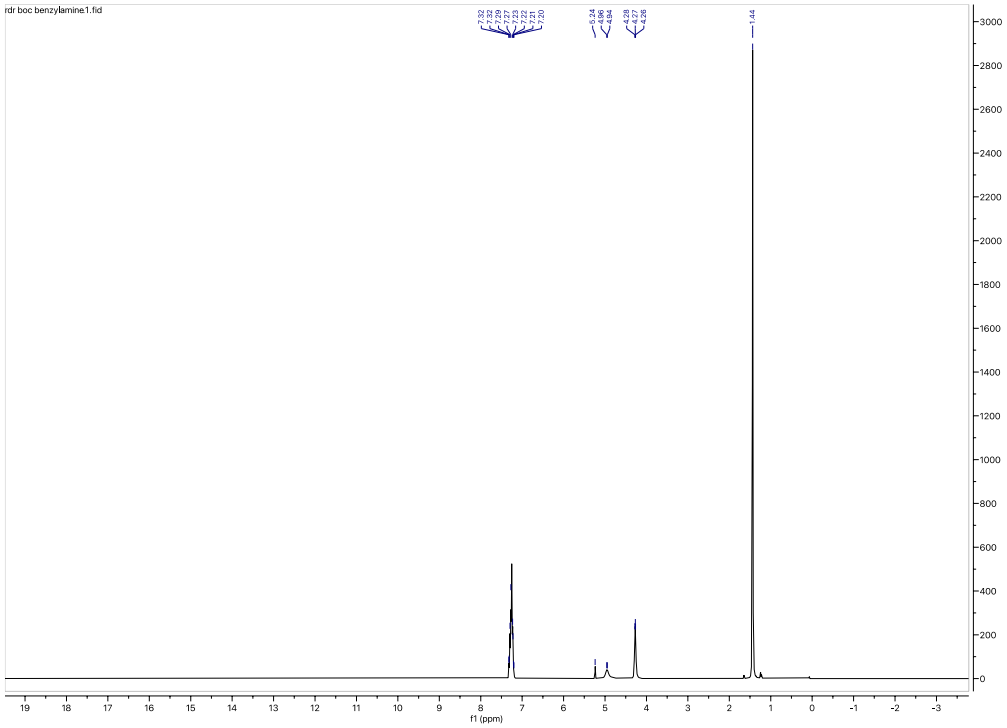
^{1}H NMR (300 MHz, $CDCl_3$) 7.23–7.15 (m, 5H, ArH), 6.70 (br s, 1H, OCONH), 5.14 (d, 1H, J = 8.2 Hz, $NHCHCH_3$), 4.47 (m, 1H, α-CHAla); 4.38 (m, 1H, α-CHPhe), 3.66 (s, 3H, OMe), 3.09–2.92 (m, 2H, CH_2Ph), 1.31 (s, 9H, tBu), 1.18-1.14 (d, 3H, $CHCH_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) 172.9, 171.0, 155.4, 136.6, 129.4, 128.5, 126.6, 80.1, 55.7, 52.1, 47.9, 38.3, 28.2, 17.8. GC/MS (EI): m/z (%) 350 (2), 294 (9), 277 (5), 263 (4), 233 (14), 174 (12), 164 (37), 159 (21), 120 (90), 91 (19), 77 (4), 57 (100).

5. General procedure for the N-Boc deprotection of amines and amino acid derivatives

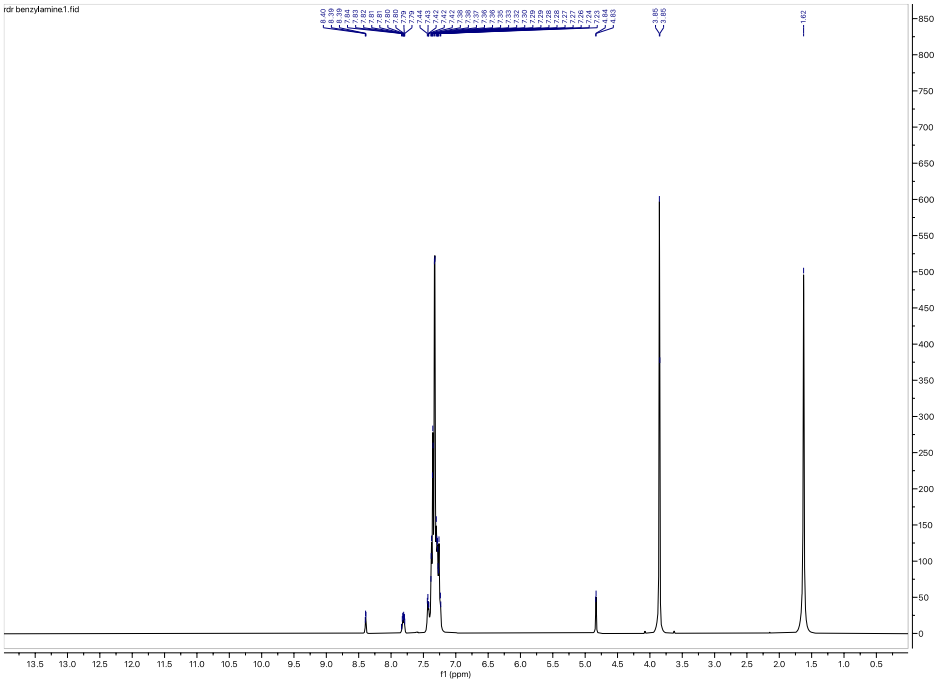
In a 10 ml round-bottomed flask 1 mL of DES (ChCl:pTSA) was maintained under stirring and N-Boc-protected amine or N-Boc-protected amino acid derivative (1 mmol) was added. The mixture was allowed to stir at room temperature. TLC and GC/MS were used to monitor the reaction. Upon completion of the reaction, an aqueous solution of sodium bicarbonate NaHCO3 (5%) was added. The crude material was then extracted with AcOEt (3x5mL). The organic layer was dried over anhydrous Na2SO4, filtered and finally concentrated under low vacuum using a rotary evaporator, to yield the pure deprotected amine. Spectroscopic data (GC-MS, 1H-NMR e 13C-NMR) were compared to those of the pure products. The obtained spectroscopic data agree with literature data.

6. Some representative 1H NMR spectra:

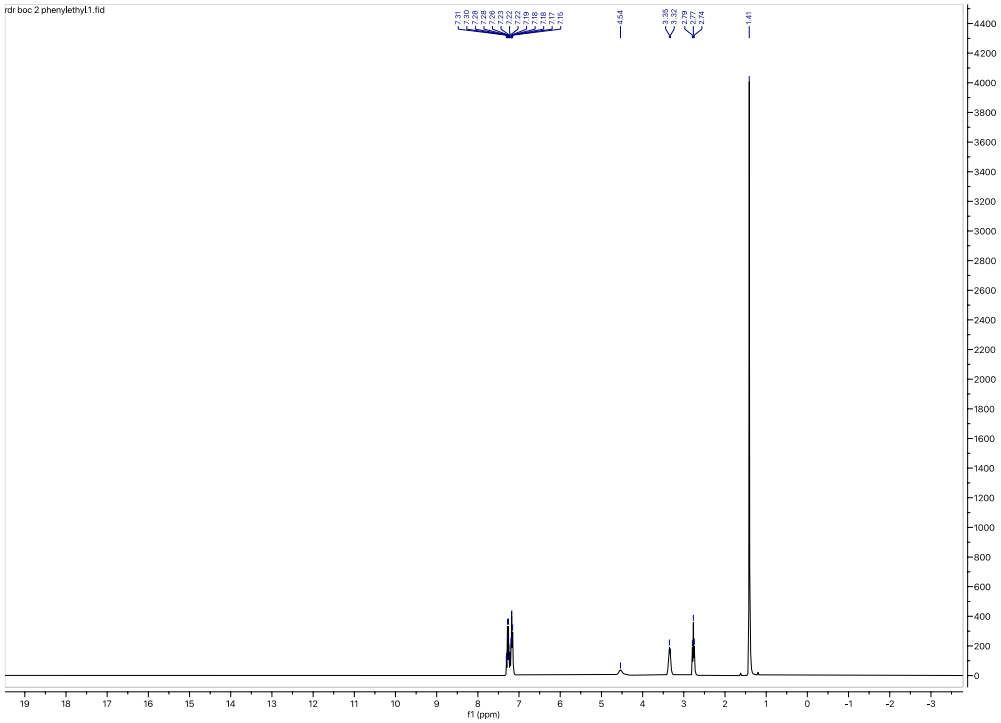
***N*-Boc-Benzylamine (1a):**



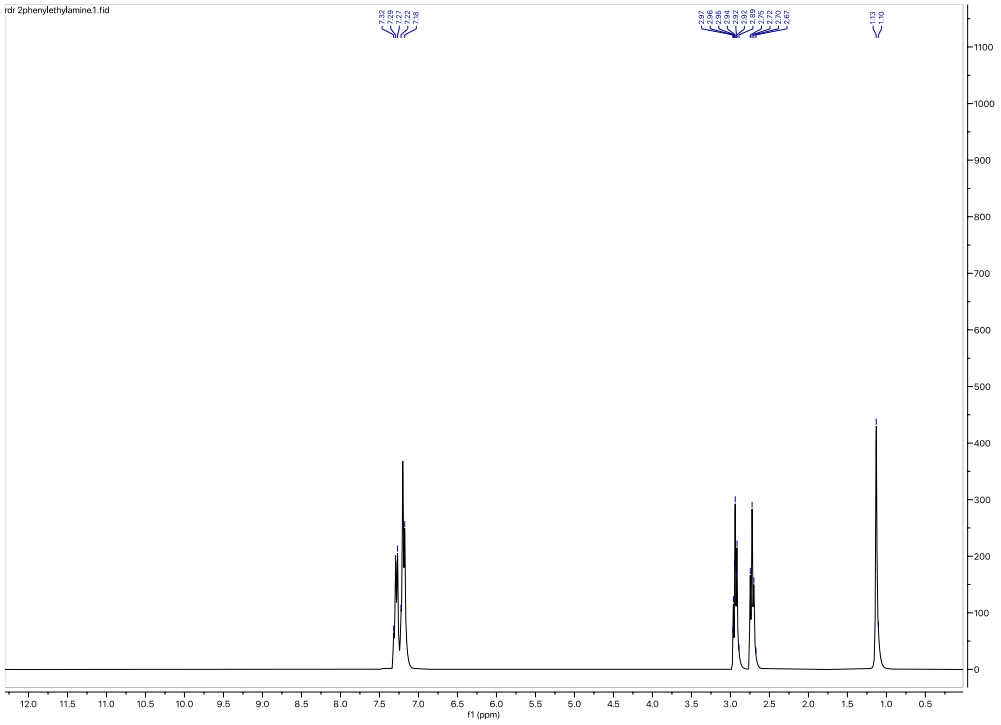
Benzylamine (2a):



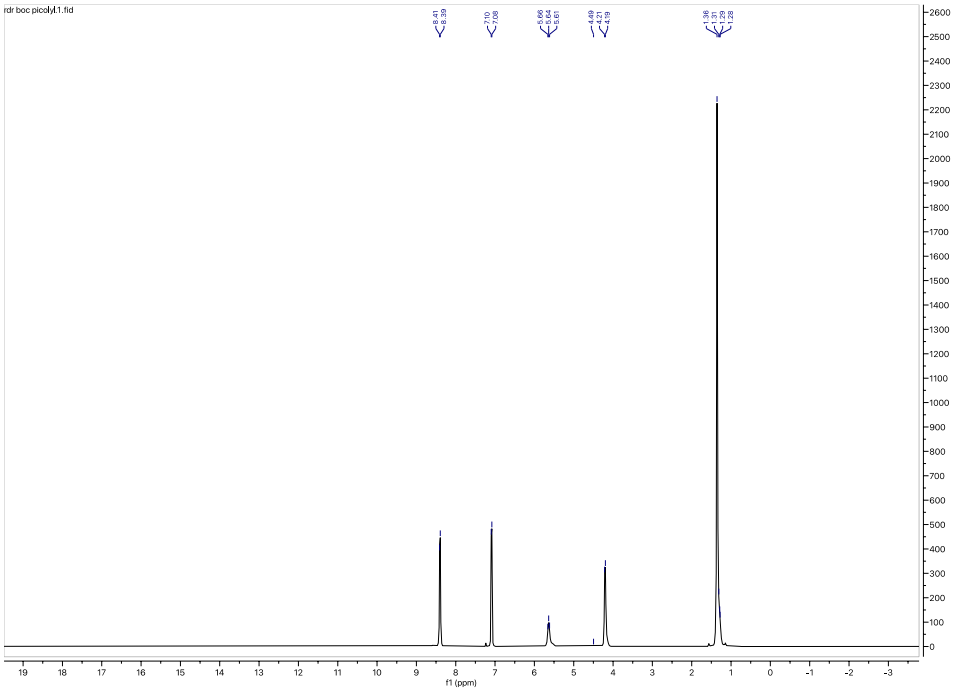
***N*-Boc -2-Phenylethylamine (1b):**



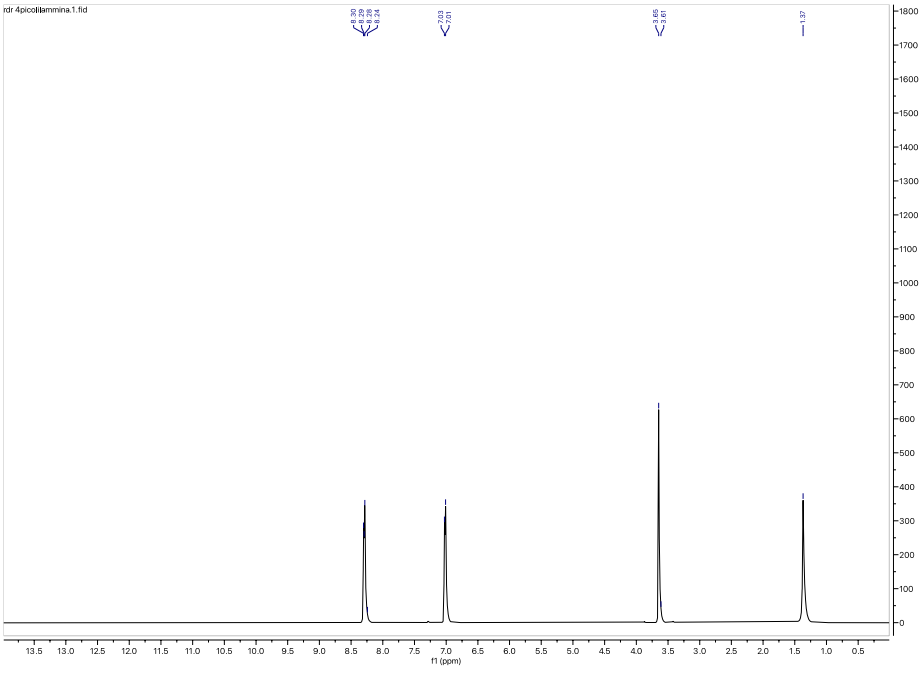
2-Phenylethylamine (2b):



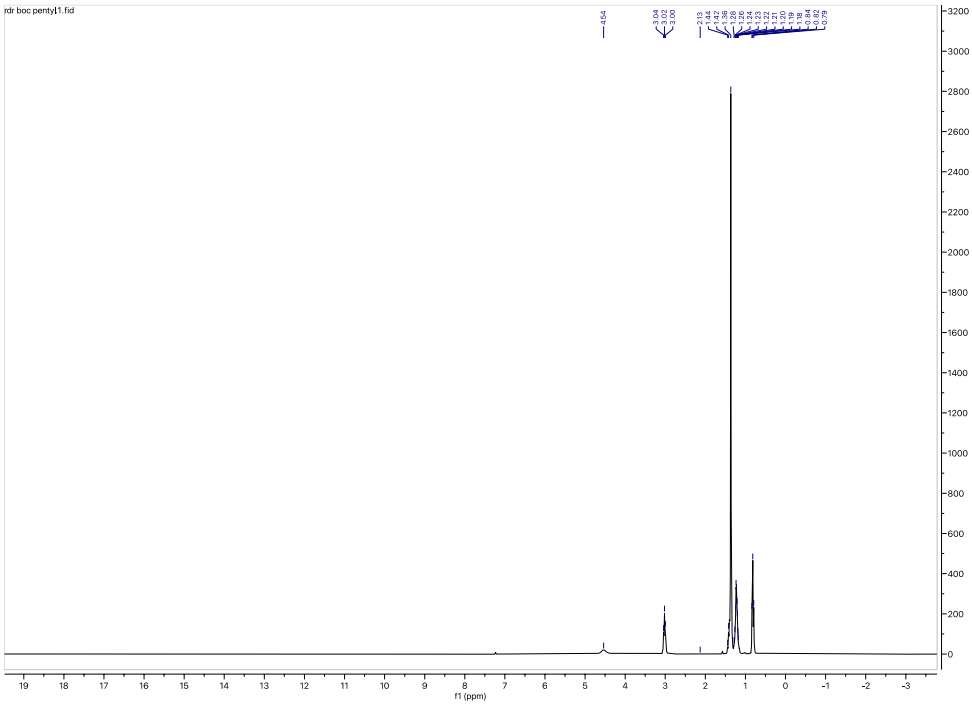
***N*-Boc Pyridin-4-amine (1f):**



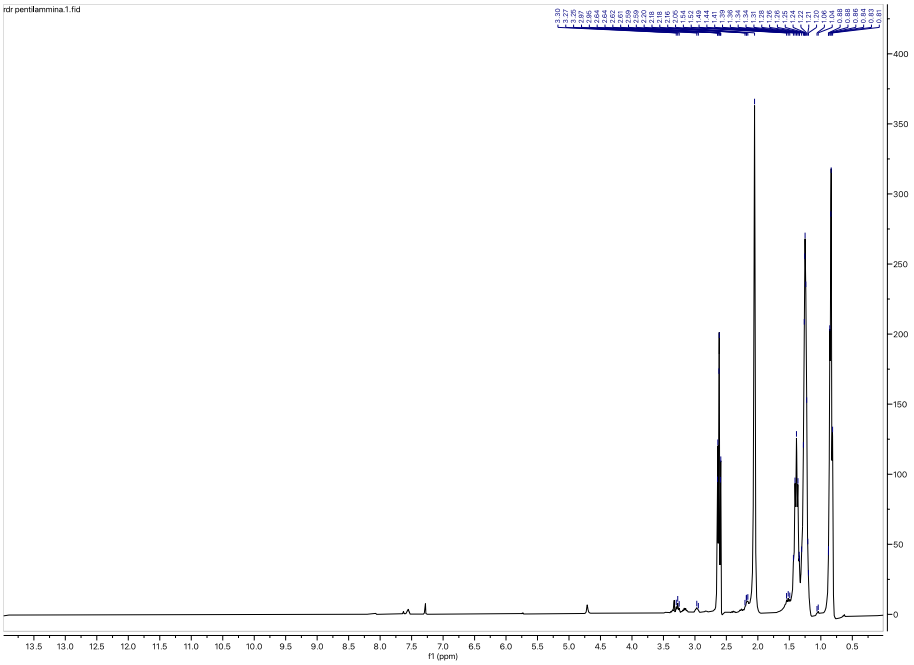
Pyridin-4-amine (2f):



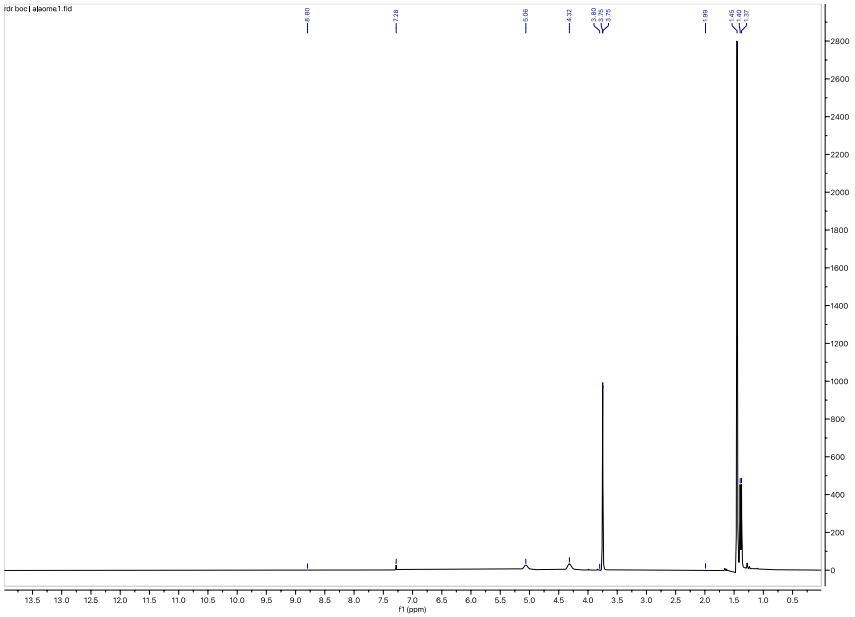
N-Boc Pentylamine (1k):



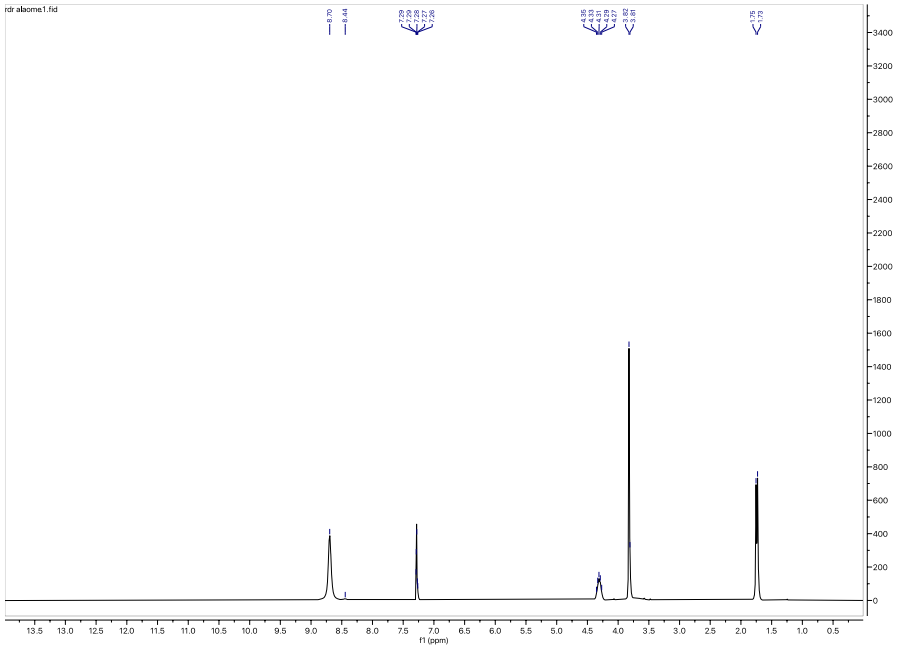
Pentylamine (2k):



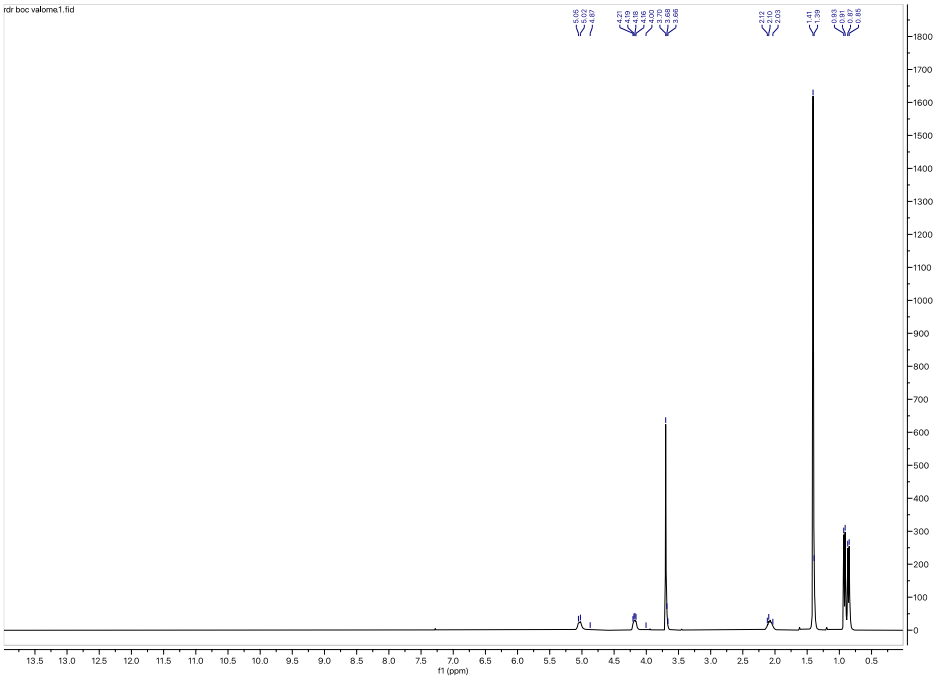
_N_-Boc L-Alanine methyl ester (1p):



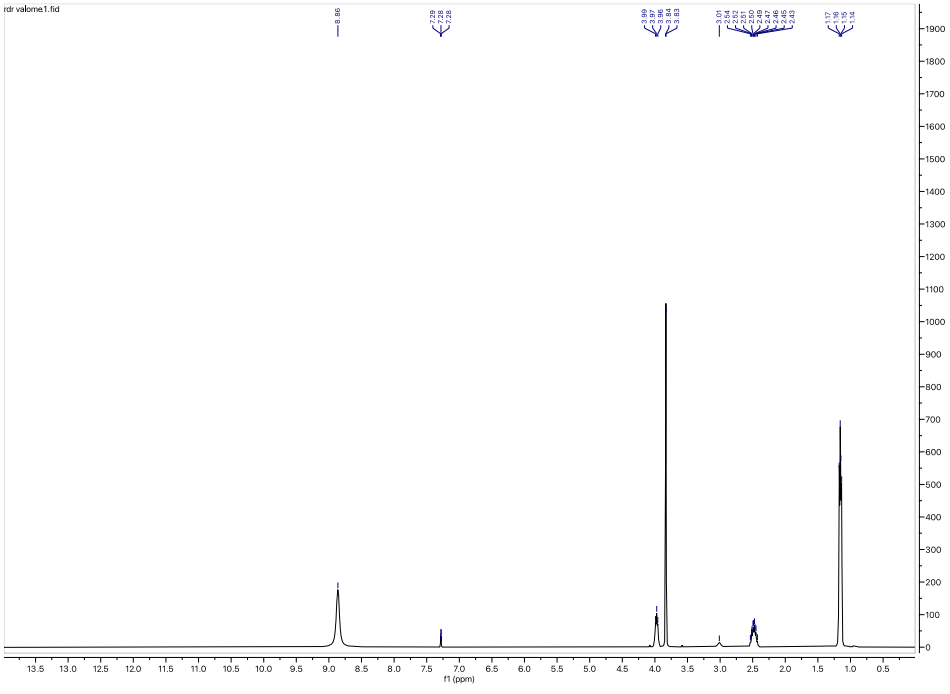
_N_-Boc L-Alanine methyl ester (2p):



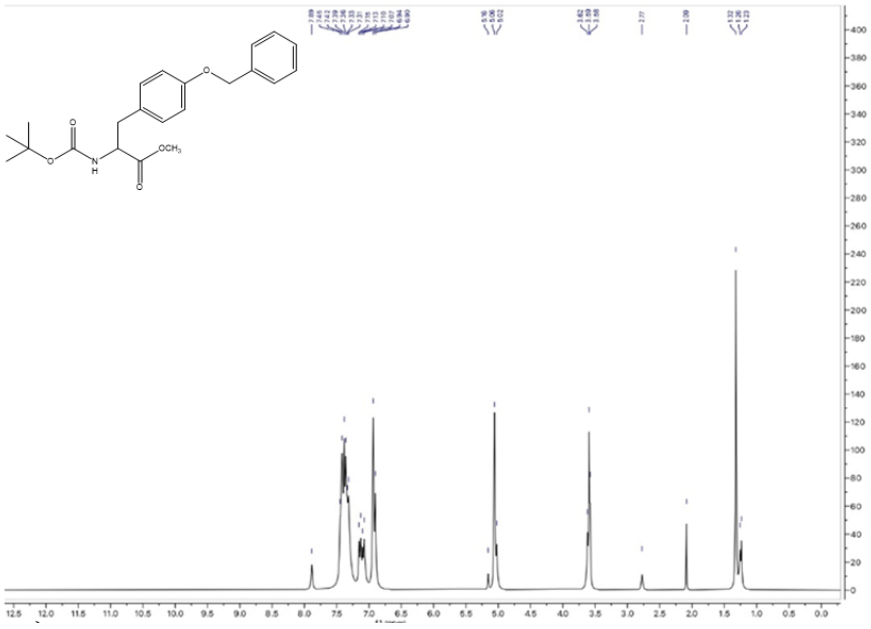
N-Boc -L-Valine methyl ester (1r):



L-Valine methyl ester (2r):

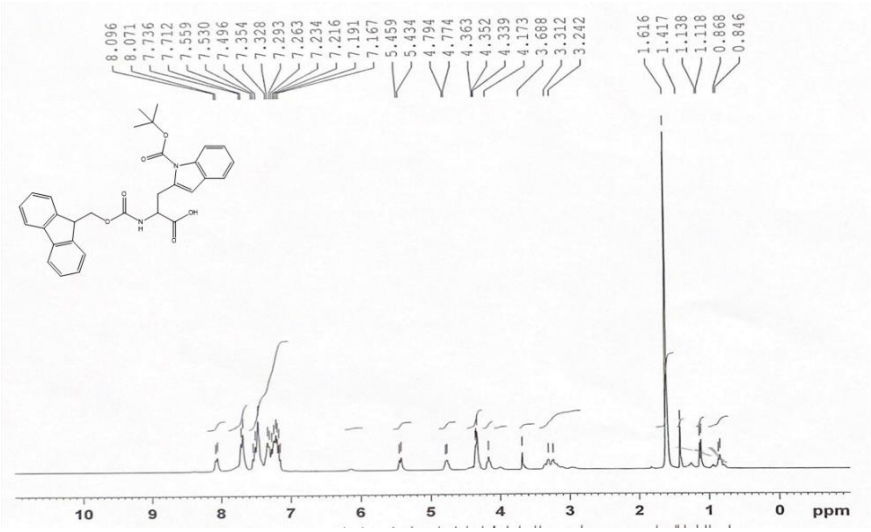


N-Boc O-Benzyl-L-Tyrosine methyl ester (1t):

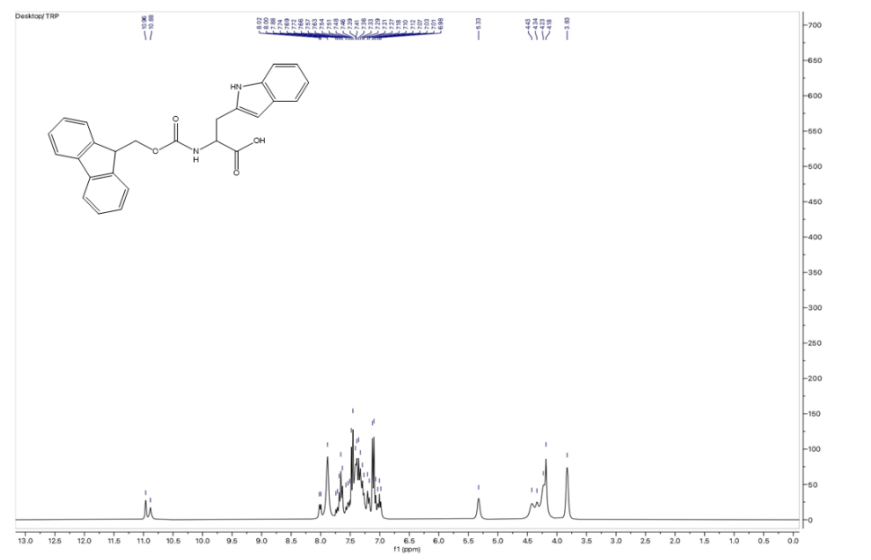


O-Benzyl-L-Tyrosine methyl ester (2t):

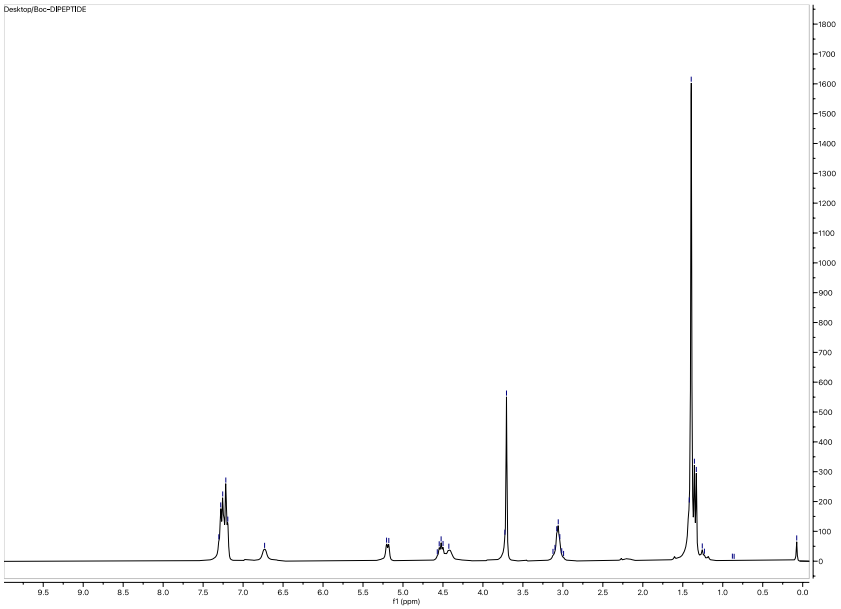
Nα-Fmoc-N(in)-Boc-L-tryptophan (1u):



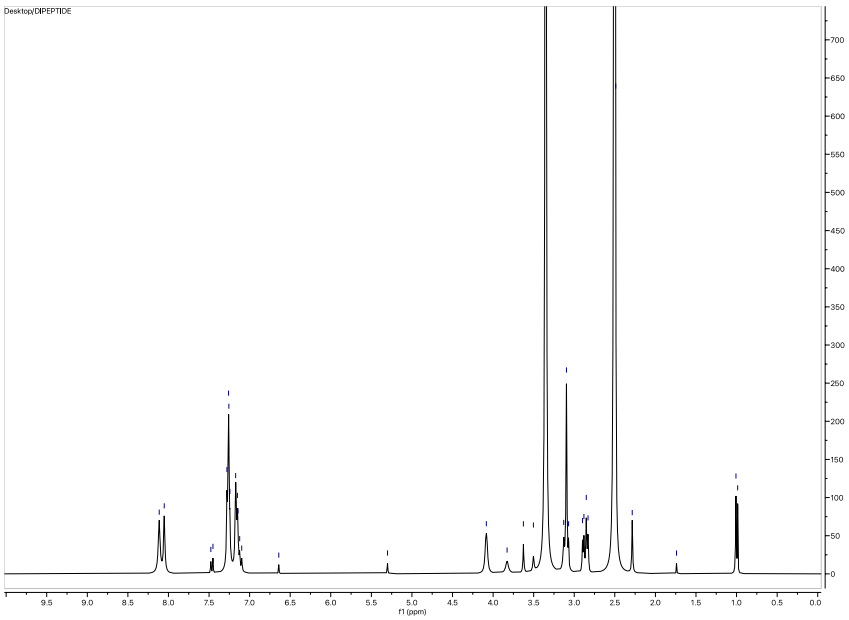
Nα-Fmoc-L-tryptophan (1u):



N-Boc L-Phe-LAlaOMe (1v):



L-Phe-LAlaOMe (2v):



E Factor and PMI calculation for our procedure and for some of the reported classical procedures:

Process Mass Efficiency (PMI) and **Efficiency Factor** (E-factor) are material ratios.

PMI = total mass of inputs / mass of product. An ideal value is **1** (100% conversion of raw materials to product).

E-factor = mass of waste / mass of product. An ideal value is **close to 0** (i.e. no waste).

This calculation tool was brought to you by GreenChemWeb (www.greenchem.org)

We wish to acknowledge the ACS-GCI Pharmaceutical Roundtable for the concept of Process Mass Intensity and for producing the first calculation tool upon which this is based. Prof. Roger Sheldon of the Delft University of Technology is acknowledged for the concept of E-factor.

1. Our work

Mass Efficiency: PMI and E-factor

1 Fill out a form for each step in your reaction / process.

Reaction Steps

Step 01	
Substrate	mass (g)
Boc-benzylamine	0,1
Reagents	mass (g)
DES	0,360
Organic Solvents	mass (g)
AcOEt	5,4
Water or Aqueous Solutions	mass (g)
water	3,0
Desired Product	mass (g)
Benzylamine . TsOH	0,131

Material Inputs	mass (g)
Substrate	0,1
Reagents	0,4
Solvents	5,4
Aqueous	3,0
Total	8,9
Material Outputs	mass (g)
Product	0,1
Waste	8,7

PMI	**68**
E-factor	**67**

Ref 8 : Li, B.; Bemish, R.; Buzon, R. A.; Chiu, C. K.-F.; Colgan, S. T.; Kissel, W.; Le, T.; Leeman, K. R.; Newell, L.; Roth, J. Tetrahedron Lett. 2003, 44, 8113-8115;

Mass Efficiency: PMI and E-factor

1 Fill out a form for each step in your reaction / process.

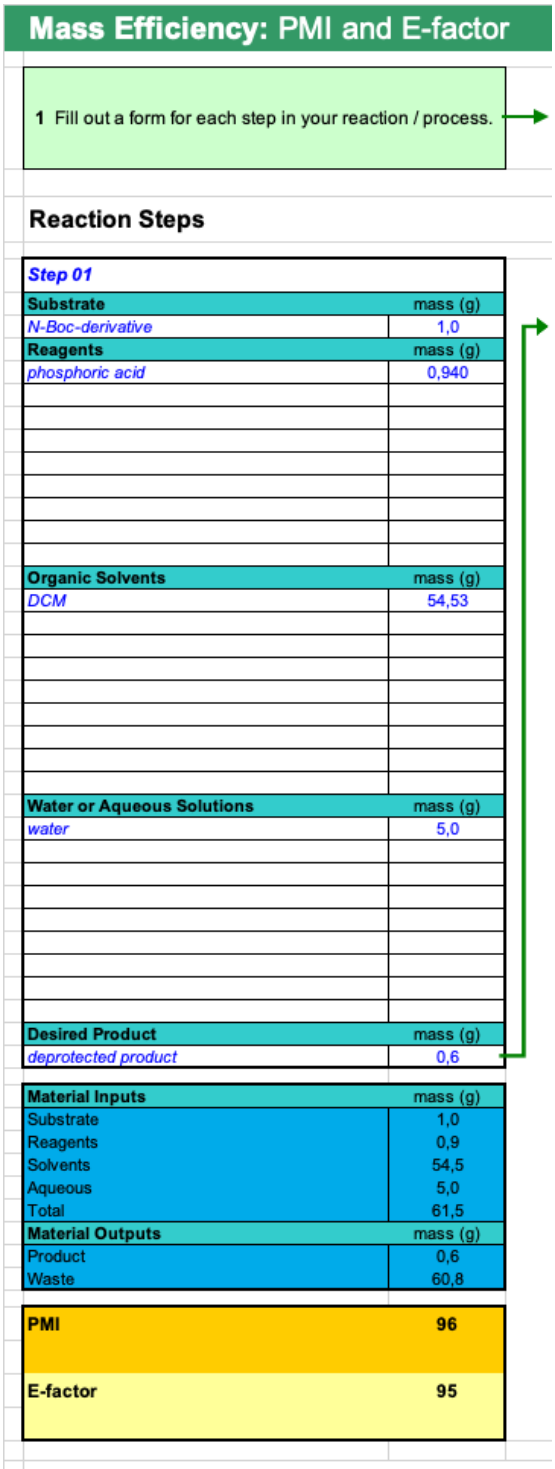
Reaction Steps

Step 01	
Substrate	mass (g)
N-Boc protected amine	1,0
Reagents	mass (g)
phosphoric acid	9,4
Organic Solvents	mass (g)
THF	0,9
AcOEt	35,6
Water or Aqueous Solutions	mass (g)
water	5,0
Desired Product	mass (g)
deprotected product	0,6

Material Inputs	mass (g)
Substrate	1,0
Reagents	9,4
Solvents	36,5
Aqueous	5,0
Total	51,9
Material Outputs	mass (g)
Product	0,6
Waste	51,3

PMI	**91**
E-factor	**90**

Ref. 9 . Li, B.; Berliner, M.; Buzon, R.; Chiu, C. K.-F.; Colgan, S. T.; Kaneko, T.; Keene, N.; Kissel, W.; Le, T.; Leeman, K. R.; Marquez, B.; Morris, R.; Newell, L.; Wunderwald, S.; Witt, M.; Weaver, J.; Zhang, Z.; Zhang, Z. J. Org. Chem. 2006, 71, 24, 9045–9050;



Mass Efficiency: PMI and E-factor

1 Fill out a form for each step in your reaction / process.

Reaction Steps

Step 01	
Substrate	mass (g)
N-Boc-derivative	1,0
Reagents	mass (g)
phosphoric acid	0,940
Organic Solvents	mass (g)
DCM	54,53
Water or Aqueous Solutions	mass (g)
water	5,0
Desired Product	mass (g)
deprotected product	0,6

Material Inputs	mass (g)
Substrate	1,0
Reagents	0,9
Solvents	54,5
Aqueous	5,0
Total	61,5
Material Outputs	mass (g)
Product	0,6
Waste	60,8

PMI	**96**
E-factor	**95**

Ref 12. P. Strazzolini, N. Misuri, P. Polese, *Tetrahedron Lett.* **2005**, *46*, 2075–2078;

Mass Efficiency: PMI and E-factor

1 Fill out a form for each step in your reaction / process.

Reaction Steps

Step 01	
Substrate	mass (g)
N-Boc protected amine	0,830
Reagents	mass (g)
H2SO4	0,590
Organic Solvents	mass (g)
DCM	79,80
Water or Aqueous Solutions	mass (g)
H20	20,00
NaOH	9,6
Na2SO4	53,2
Desired Product	mass (g)
deprotected product	0,428

Material Inputs	mass (g)
Substrate	0,8
Reagents	0,6
Solvents	79,8
Aqueous	82,8
Total	164,0
Material Outputs	mass (g)
Product	0,4
Waste	163,6

PMI	**383**
E-factor	**382**

Patent Reference: WO2016014463, page 66,

Mass Efficiency: PMI and E-factor

1 Fill out a form for each step in your reaction / process.

Reaction Steps

Step 01

Substrate	mass (g)
N-Boc protected amine	1,400
Reagents	mass (g)
TFA	6,600
Organic Solvents	mass (g)
DCM	60,00
Water or Aqueous Solutions	mass (g)
NaHCO3	10,00
Desired Product	mass (g)
deprotected product	0,850

Material Inputs	mass (g)
Substrate	1,4
Reagents	6,6
Solvents	60,0
Aqueous	10,0
Total	78,0
Material Outputs	mass (g)
Product	0,9
Waste	77,2

PMI	**92**
E-factor	**91**