5.1. INTRODUCTION

Di-tert-butyl dicarbonate (Boc$_2$O) is the most widely used reagent for the introduction of the tert-butoxycarbonyl (Boc) group for the protection of the amino group in the peptide synthesis (Greene and Wuts, 2007). However, the main drawback of Boc$_2$O is its low melting range of 22-24 °C, making it a liquid in most geographical regions and seasons. It tends to decompose on storage. Bottles of Boc$_2$O build internal pressure in sealed containers caused by its slow decomposition to tert-butanol and CO$_2$ in the presence of moisture. For this reason, it is usually sold and stored in plastic bottles rather than glass ones (Wakselman, 1995). The inhalational toxicity of Boc$_2$O is also high and is comparable to that of phosgene (Wakselman, 1995; Wikipedia the free encyclopedia, 2017). Thus there is a need for an alternative reagent which is solid and more stable for the introduction of Boc group.

This chapter describes tert-butyl (2, 4-dioxo-3-azaspiro [5,5] undecan-3-yl) carbonate (Boc-OASUD) as a new Boc reagent for preparing N-Boc-amino acids (Scheme 5.1). The Boc-OASUD is a crystalline solid exhibiting better stability and is a good alternative for Boc$_2$O.

![Scheme 5.1](image)

Scheme 5.1. Synthesis of N-Boc protected amino acids and esters using Boc-OASUD.

5.2. RESULTS AND DISCUSSION

The reagent Boc-OASUD is prepared by reacting HO-ASUD with Boc$_2$O in a suitable solvent such as acetonitrile in the presence of a base such as triethylamine (Scheme 5.2). The reaction results in a colorless crystalline Boc-OASUD in high yields (>85%) and purity (>99.5% HPLC). The reagent is soluble in most organic solvents such as methanol, ethanol, 2-propanol, tert-butanol, ethyl acetate, methyl tert-butyl ether, toluene,
chloroform, acetonitrile, acetone, 1,4-dioxane, THF, 2-MeTHF, DMF and DMSO. It is insoluble in petroleum ether, n-Hexane, cyclohexane and water.

Scheme 5.2. Synthesis of Boc-OASUD.

The reagent was found to be stable when stored at room temperature (25± 3 °C) protected from air and moisture. After nine months storage, slight degradation (<0.5%) was observed and the main degradation product was HO-ASUD. The reagent was also found to be stable when kept at 40 °C and 70 °C for 24 hours (99.9% and 99.7% HPLC respectively). However at 90 °C, it melted (mp: 85-88 °C) and decomposed completely to HO-ASUD (97.8% HPLC).

The reagent Boc-OASUD has high reactivity towards the aliphatic amino group under mild conditions. A number of N-Boc-amino acids were prepared by reacting amino acids with Boc-OASUD in the presence of a base at room temperature in high yields and purity (Table 5.1). The amino acid is dissolved in an aqueous solution containing a base such as sodium carbonate and reacted with a solution of Boc-OASUD dissolved in a suitable water miscible solvent such as acetone at room temperature. Depending on amino acid, the reaction is completed in 9 to 18 hours (TLC). After the reaction, the pH was adjusted to 6 with KHSO₄ and washed with an organic solvent such as ethyl acetate to remove the liberated HO-ASUD and unreacted Boc-OASUD. The HO-ASUD can be recovered again and converted back to Boc-OASUD by evaporating the organic layer and by reacting the crude obtained with fresh Boc₂O and triethylamine. The aqueous solution was further acidified using KHSO₄ to pH 2 to 4 and extracted with ethyl acetate. Evaporation of the solvent and recrystallization of the residue from ethyl acetate and hexane results in N-Boc-amino acid. In the case of Lysine and Valine, the corresponding Boc amino acids were isolated as their dicyclohexylamine salts. The H-Lys(Boc)-OH (N⁶-Boc-lysine, entry
12), was prepared using lysine copper complex to block the alpha amino group. The copper complex was reacted with the reagent Boc-OASUD. After the reaction the complex was cleaved using EDTA, which resulted in the H-Lys(Boc)-OH.

All the N-Boc-derivatives were obtained in good yields and purity. During the reaction, the chiral integrity is maintained. In addition to sodium carbonate, other bases such as sodium hydroxide, or organic bases such as triethyl amine can also be used.

Apart from room temperature, the reaction was also studied at 50 (±2) °C. In the case of L-Phenyl alanine, at both the temperatures, similar yields and purity were obtained. However in the case of L-Serine, racemization was observed at 50 (±2) °C (Chiral purity: 92.93 vs 99.8%).

For comparison, N-Boc-L-Phe-OH and N-Boc-L-Ala-OH was prepared using both the Boc-OASUD and Boc₂O. Reacting L-Phenyl alanine with Boc-OASUD in acetone using Na₂CO₃ for 9 hours at 25 (±2) °C resulted in N-Boc-L-Phe-OH in 95% yield (99.9% HPLC). Reacting with Boc₂O under same conditions resulted in 93% yield (99.9% HPLC). Similarly, reaction of L-Alanine with Boc-OASUD in acetonitrile using Na₂CO₃ for 10 hours at 25 (±2) °C resulted in N-Boc-L-Ala-OH in 92% yield (99.2% HPLC) and with Boc₂O the yield was 96% (98.6% HPLC). Thus both reagents gave similar yields and purity.

The reagent was found to be specific to the amino group without reacting with either phenolic or aliphatic hydroxyl group when one equivalent of Boc-OASUD was used. When L-Ser was reacted with 1.5 and two equivalents of 2, about 0.39% and 1.98% of N-Boc-Ser (OBoc)-OH was observed respectively. Similarly, about 0.52% and 1.92% of N-Boc-Tyr (OBoc)-OH was observed respectively.
TABLE 5.1. Synthesis of N-Boc protected amino acids with Boc-OASUD.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>N-Boc Amino acid</th>
<th>L/D</th>
<th>Base</th>
<th>Solvent</th>
<th>Time(h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Boc-Phe-OH</td>
<td>L</td>
<td>Na(_2)CO(_3)</td>
<td>acetone</td>
<td>9</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>Boc-Ala-OH</td>
<td>L</td>
<td>Na(_2)CO(_3)</td>
<td>acetonitrile</td>
<td>10</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>Boc-Gly-OH</td>
<td>-</td>
<td>NaOH</td>
<td>acetone</td>
<td>12</td>
<td>94</td>
</tr>
<tr>
<td>4</td>
<td>Boc-Leu-OH</td>
<td>L</td>
<td>Na(_2)CO(_3)</td>
<td>1, 4-dioxane</td>
<td>15</td>
<td>88</td>
</tr>
<tr>
<td>5</td>
<td>Boc-Trp-OH</td>
<td>L</td>
<td>Triethyl amine</td>
<td>acetonitrile</td>
<td>15</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td>Boc-Pro-OH</td>
<td>L</td>
<td>Triethyl amine</td>
<td>acetone</td>
<td>12</td>
<td>86</td>
</tr>
<tr>
<td>7</td>
<td>Boc-Tyr-OH</td>
<td>L</td>
<td>Na(_2)CO(_3)</td>
<td>acetonitrile</td>
<td>9</td>
<td>91</td>
</tr>
<tr>
<td>8</td>
<td>Boc-Lys (Boc)-OH (^b)</td>
<td>L</td>
<td>NaOH</td>
<td>1, 4-dioxane</td>
<td>18</td>
<td>81</td>
</tr>
<tr>
<td>9</td>
<td>Boc-Val-OH (^b)</td>
<td>L</td>
<td>Na(_2)CO(_3)</td>
<td>acetone</td>
<td>14</td>
<td>90</td>
</tr>
<tr>
<td>10</td>
<td>4-Cl-Boc-Phe-OH</td>
<td>D</td>
<td>Triethyl amine</td>
<td>acetone</td>
<td>14</td>
<td>90</td>
</tr>
<tr>
<td>11</td>
<td>3-F-Boc-Phe-OH</td>
<td>L</td>
<td>Na(_2)CO(_3)</td>
<td>acetonitrile</td>
<td>12</td>
<td>85</td>
</tr>
<tr>
<td>12</td>
<td>H-Lys (Boc)-OH (^c)</td>
<td>L</td>
<td>Na(_2)CO(_3)</td>
<td>acetone</td>
<td>18</td>
<td>78</td>
</tr>
<tr>
<td>13</td>
<td>Boc-Asp-OH</td>
<td>L</td>
<td>NaOH</td>
<td>acetonitrile</td>
<td>15</td>
<td>80</td>
</tr>
<tr>
<td>14</td>
<td>Boc-Phg-OH</td>
<td>D</td>
<td>Na(_2)CO(_3)</td>
<td>1, 4-dioxane</td>
<td>12</td>
<td>89</td>
</tr>
<tr>
<td>15</td>
<td>Boc-Ser-OH</td>
<td>D</td>
<td>Triethyl amine</td>
<td>acetone</td>
<td>11</td>
<td>89</td>
</tr>
<tr>
<td>16</td>
<td>Boc-Sar-OH</td>
<td>-</td>
<td>NaOH</td>
<td>acetone</td>
<td>10</td>
<td>93</td>
</tr>
</tbody>
</table>

\(^a\) Experimental conditions: The amino acid is dissolved in an aqueous solution containing a base and reacted with a solution of Boc-OASUD dissolved in a suitable solvent at room temperature. After the reaction, the base was neutralized, extracted with an organic solvent. Evaporation followed by crystallization from EtOAc/hexane gives the required N-Boc amino acids. All products were identified by comparison with their spectral data (FTIR, \(^1\)H & \(^13\)CNMR and Mass).

\(^b\) The Boc-Lys (Boc)-OH (entry.8) and Boc-Val-OH (entry. 9) were isolated as a DCHA salt.
The H-Lys (Boc)-OH (entry. 12) was prepared using copper complex method. DCHA: dicyclohexylamine.

It is always a challenge to prepare N-Boc amino acid ester from the corresponding ester because of the possibility of ester hydrolysis in an alkaline aqueous medium. However, by using triethylamine as a base and reacting the ester with reagent Boc-OASUD, in a non-aqueous organic solvent such as dichloromethane, a number of N-Boc-amino acid esters have been prepared (Table 5.2). Here also, in all the cases, good yields have been obtained without any racemization.

**TABLE 5.2. Synthesis of N-Boc amino acid esters with Boc-OASUD.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>R&lt;sub&gt;1&lt;/sub&gt;</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PhCH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Me</td>
<td>92</td>
</tr>
<tr>
<td>2</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Me</td>
<td>89</td>
</tr>
<tr>
<td>3</td>
<td>CH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Et</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>H</td>
<td>Me</td>
<td>93</td>
</tr>
<tr>
<td>5</td>
<td>H</td>
<td>Et</td>
<td>91</td>
</tr>
<tr>
<td>6</td>
<td>H</td>
<td>Bn</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;OH</td>
<td>Me</td>
<td>81</td>
</tr>
<tr>
<td>8</td>
<td>CH&lt;sub&gt;2&lt;/sub&gt;OH</td>
<td>Bn</td>
<td>86</td>
</tr>
<tr>
<td>9</td>
<td>(CH&lt;sub&gt;3&lt;/sub&gt;)&lt;sub&gt;2&lt;/sub&gt;CH</td>
<td>Me</td>
<td>87</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>Me</td>
<td>85</td>
</tr>
<tr>
<td>11</td>
<td>4-OH-PhCH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Me</td>
<td>82</td>
</tr>
<tr>
<td>12</td>
<td>4-OH-PhCH&lt;sub&gt;2&lt;/sub&gt;</td>
<td>Et</td>
<td>84</td>
</tr>
</tbody>
</table>
* L-amino acid ester hydrochloride (23.2 mmol), triethyl amine (24.4 mmol) and Boc-OASUD (24.4 mmol) were added to dichloromethane (50 mL). The resulting mixture was refluxed for 3 to 5h. The reaction mixture was filtered and concentrated under reduced pressure. The obtained residue was purified using column chromatography. All products were identified by comparison with their spectral data (FTIR, $^1$H & $^{13}$C NMR and Mass).

5.3. CONCLUSION

In conclusion, this chapter describes tert-butyl (2, 4-dioxo-3-azaspiro [5,5] undecan-3-yl) carbonate (Boc-OASUD) as a novel reagent for the preparation of N-Boc protected amino acids and their esters. The new reagent is a stable crystalline material and reacts with the amino group in a facile manner under mild conditions without causing racemization.

5.4. EXPERIMENTAL

5.4.1. Synthesis of tert-butyl (2,4-dioxo-3-azaspiro [5,5] undecan-3-yl) carbonate (Boc-OASUD)

N-Hydroxy-3-azaspiro [5,5] undecane-2,4-dione (5.0 g, 25.3 mmol), and triethyl amine (3.08 g, 30.4 mmol) were dissolved in acetonitrile (50 mL). To this solution, was added Boc$_2$O (6.63 g, 30.4 mmol) at 0-5 °C and stirred at 25-30 °C for 5h. The reaction mixture was concentrated under reduced pressure and the crude material was dissolved in ethyl acetate (50 mL), washed with water (25 mL) and brine solution (25mL). The ethyl acetate layer was dried over anhydrous Na$_2$SO$_4$ and concentrated under reduced pressure. The resulting material was precipitated with hexane (50 mL) to yield Boc-OASUD as a colorless solid (6.50 g, 86.3% yield). Melting range: 85-88 °C; Purity: 99.86% [Figure 5.1] (by HPLC analysis: XTerra RP 18 (250 x 4.6 mm) column, 5 µm; eluent: water/acetonitrile (30:70); flow rate 1.0 mL/min; Temp 27 °C, detection at 210 nm). FT-IR (KBr, cm$^{-1}$) [Figure 5.2]: $\nu_{max}$ 3445, 3008, 2980, 2927, 2848, 2860, 1790, 1754, 1713, 1454, 1428, 1412, 1397, 1349, 1339, 1273, 1244, 1196, 1158, 1142, 1115, 1080, 1052, 982, 963, 944, 924, 904, 894, 874, 805, 768, 718, 642, 608, 566, 542; $^1$H NMR (300 MHz, CDCl$_3$) [Figure 5.3]: $\delta$ (ppm) 2.75-2.66 (m, 4H), 1.57-1.49 (m, 19H);
$^{13}$C NMR (75 MHz, CDCl$_3$) [Figure 5.4]: δ (ppm) 166.01, 150.19, 86.63, 44.10, 36.78, 34.88, 32.53, 27.48, 25.55, 21.45; MS [Figure 5.5]: m/z 319.75 [M+Na]$^+$. 

5.4.2 Synthesis of N-Boc protected amino acids

5.4.2.1 Synthesis of N-(tert-Butoxycarbonyl)-L-Phenylalanine (Table 5.1, entry 1)

L-Phenylalanine (1.0 g, 6.05 mmol) and sodium carbonate (0.71 g, 6.70 mmol) in water (10 mL) was reacted with a solution of Boc-OASUD (1.89 g, 6.36 mmol) in acetone (10 mL). The reaction mixture was stirred at room temperature till the reaction completes, as monitored by TLC. The resulting solution was concentrated, to the residue was added water (10 mL) and ethyl acetate (10 mL), pH adjusted to 6.0 with 10% KHSO$_4$ and stirred for 5 minutes. The organic layer was removed and the aqueous layer was acidified to pH 2.0 with 10% KHSO$_4$ at 0-5 °C and extracted with ethyl acetate (2 x 10 mL). The combined organic layers were washed with 5% NaHCO$_3$ solution, water, brine and dried over anhydrous Na$_2$SO$_4$. The ethyl acetate layer was concentrated and the residue was crystallized from EtOAc/ hexane (2:8) mixture to give the product as a white solid (1.53g, 95% yield). Melting range: 85-87 °C (lit.86-88 °C, Keller et al., 1985); [α]$_D^{20}$ = +25.9° (c 1 in EtOH) {lit. [α]$_D^{20}$ = +25.5° (c 1 in EtOH), Keller et al., 1985}; 99.88% purity by HPLC [Figure 5.6] (Method: XTerra RP 18 (250 x 4.6 mm) column, 5 µm; eluent: water/acetonitrile/glacial AcOH (65:35:0.1%); flow rate 1.0 mL/min; Temp 27 °C, detection at 210 nm); % ee: 99.76% [Figure 5.8] (D-isomer Rt = 6.26 min; L-isomer Rt = 12.40 min) [Method: Chiralpak IA, 250 x 4.6 mm, 5 µm; eluent: n-Hexane: IPA: TFA (90:10:0.1%); flow rate 1.2 mL/min; Temp 27 °C, detection: 215 nm]; FT-IR (KBr, cm$^{-1}$) [Figure 5.9]: $\nu$$_{max}$ 3373, 3028, 2984, 2935, 1724, 1708, 1692, 1525, 1442, 1421, 1392, 1366, 1342, 1297, 1269, 1252, 1168, 1082, 1053, 1028, 1003, 966, 949, 888, 853, 789, 758, 748, 701; $^1$H NMR (300 MHz, DMSO-$_d_6$) [Figure 5.10]: δ (ppm) 12.59 (br, 1H), 7.30-7.16 (m, 5H), 7.11-7.09 (d, 1H), 4.12-4.04 (m, 1H), 3.04-2.98 (dd, 1H), 2.85-2.77 (m, 1H), 1.31 (s, 6H) and 1.25 (s, 3H); $^{13}$C NMR (75 MHz, DMSO-$_d_6$) [Figure 5.11]: δ (ppm) 173.55, 155.39, 137.97, 129.03, 128.06, 126.25, 77.98, 55.08, 36.45, 28.01,27.78; MS [Figure 5.12]: m/z 288.88 [M+Na]$^+$. 

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The other amino acids given in Table 5.1 were prepared and characterized in a similar manner.

5.4.2.2 Synthesis of N-(tert-butoxycarbonyl)-L-alanine (Table 5.1, entry 2)

Yield: 92%. Melting range: 81-82 °C (lit. 82-83 °C, Keller et al., 1985); [α]_D^{20} = -25.2° (c 1, AcOH), [lit. [α]_D^{20} = -25.5° (c 2, AcOH), Keller et al., 1985); FT-IR (KBr, cm⁻¹): v_max 3402, 2993, 2946, 1736, 1688, 1665, 1514, 1459, 1420, 1369, 1349, 1293, 1234, 1200, 1163, 1072, 1041, 1020, 901, 864, 831, 786, 764; ¹H NMR (300 MHz, DMSO-d₆): δ (ppm) 12.34 (br s, 1H), 7.11-7.09 (d, 1H), 3.94-3.86 (m, 1H), 1.37 (s, 9H), 1.22-1.20 (d, 3H); ¹³C NMR (75 MHz, DMSO-d₆): δ (ppm) 174.57, 155.16, 77.84, 48.74, 28.09, 16.97; MS: m/z 189.75 [M+H]^+.

5.4.2.3 Synthesis of N-(tert-butoxycarbonyl) glycine (Table 5.1, entry 3)

Yield: 94%. Melting range: 87-89 °C (lit. 87-88 °C, Keller et al., 1985); FT-IR (KBr, cm⁻¹): v_max 3406, 3343, 2978, 2940, 1749, 1682, 1670, 1536, 1452, 1423, 1410, 1368, 1336, 1300, 1281, 1256, 1215, 1198, 1165, 1056, 1032, 958, 883, 859, 790, 780, 767, 734, 674, 659; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 8.10 (br s, 1H), 6.76 (s, 0.34H) and 5.08 (s, 0.66H), 3.97-3.91 (m, 2H), 1.45 (s, 9H); ¹³C NMR (75 MHz, CDCl₃): δ (ppm) 174.46, 156.17, 80.37, 42.18, 28.23; MS: m/z 198.74 [M+Na]^+.

5.4.2.4 Synthesis of N-(tert-butoxycarbonyl)-L-leucine (Table 5.1, entry 4)

Yield: 88%. Melting range: 83-85 °C (lit. 85-87 °C, Keller et al., 1985); [α]_D^{20} = -26.4° (c 1, AcOH), [lit. [α]_D^{20} = -24.7° (c 2, AcOH), Keller et al., 1985); FT-IR (KBr, cm⁻¹): v_max 3450, 3335, 2967, 2953, 2868, 1716, 1676, 1542, 1470, 1392, 1366, 1275, 1247, 1179, 1124, 1049, 1024, 921, 882, 857, 825, 790, 731; ¹H NMR (300 MHz, DMSO-d₆): δ (ppm) 7.06-7.04 (d, 1H), 3.93-3.85 (m, 1H), 1.65-1.58 (m, 1H), 1.55-1.40 (m, 2H), 1.37 (s, 9H), 0.88-0.83 (m, 6H); ¹³C NMR (75 MHz, DMSO-d₆): δ (ppm) 174.61,155.53, 77.82, 51.72, 39.93, 28.13, 24.27, 22.79, 21.14; MS: m/z 254.87 [M+Na]^+.
5.4.2.5 Synthesis of N-(tert-butoxycarbonyl)-L-tryptophan (Table 5.1, entry 5)

Yield: 91%. Melting range: 136-138 °C (lit. 137-138 °C, Keller et al., 1985); $\lbrack \alpha \rbrack_{D}^{20} = -18.9^\circ$ (c 1, DMF), {lit. $\lbrack \alpha \rbrack_{D}^{20} = -18.2^\circ$ (c 1, DMF), Keller et al., 1985}; FT-IR (KBr, cm$^{-1}$): v$_{\text{max}}$ 3440, 3264, 3109, 2975, 2926, 1716, 1605, 1518, 1453, 1393, 1367, 1352, 1308, 1276, 1250, 1224, 1153, 1124, 1094, 1020, 897, 869, 856, 837, 763, 755, 697; $^1$H NMR (300 MHz, DMSO-$d_6$ and D$_2$O-1:1 ratio): δ (ppm) 8.05-8.03 (d, 1H), 7.76-7.73 (d, 1H), 7.60 (s, 1H), 7.38-7.25 (m, 2H), 3.61-3.56 (m, 1H), 3.35-3.29 (m, 1H), 3.04-2.96 (m, 1H), 1.63 (s, 9H); $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ (ppm) 170.25, 149.11, 134.85, 130.28, 124.57, 124.16, 122.35, 119.37, 116.12, 114.59, 83.32, 53.76, 27.67, 26.55; MS: m/z 305.67 [M+H]$^+$.

5.4.2.6 Synthesis of N-(tert-butoxycarbonyl)-L-proline (Table 5.1, entry 6)

Yield: 86%. Melting range: 133-135 °C (lit.134-135 °C, Keller et al., 1985); $\lbrack \alpha \rbrack_{D}^{20} = -60.2^\circ$ (c 1, AcOH), {lit. $\lbrack \alpha \rbrack_{D}^{20} = -60.6^\circ$ (c 2, AcOH), Keller et al., 1985}; FT-IR (KBr, cm$^{-1}$): v$_{\text{max}}$ 3428, 2976, 2934, 2896, 2719, 1739, 1638, 1549, 1479, 1431, 1367, 1332, 1240, 1217, 1188, 1163, 1131, 1089, 1031, 978, 901, 852, 792, 775, 760, 728, 640, 587, 555; $^1$H NMR (300 MHz, CDCl$_3$): δ (ppm) 4.36-4.26 (m, 1H), 3.54-3.34 (m, 2H), 2.33-2.25 (m, 1H), 2.08-1.86 (m, 3H), 1.48-1.43 (d, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ (ppm) 178.18, 154.03, 80.35, 58.94, 46.29, 30.75, 28.20, 23.58; MS: m/z 237.93 [M+Na]$^+$.

5.4.2.7 Synthesis of N-(tert-butoxycarbonyl)-L-tyrosine (Table 5.1, entry 7)

Yield: 91%. Melting range: 134-136 °C (lit.137 °C, Keller et al., 1985); $\lbrack \alpha \rbrack_{D}^{20} = +2.7^\circ$ (c 1, AcOH), {lit. $\lbrack \alpha \rbrack_{D}^{20} = +2.6^\circ$ (c 1, AcOH), Keller et al., 1985}; FT-IR (KBr, cm$^{-1}$): v$_{\text{max}}$ 3382, 3176, 2990, 2819, 2710, 1726, 1672, 1613, 1601, 1515, 1480, 1458, 1405, 1371, 1330, 1301, 1244, 1221, 1202, 1164, 1136, 1110, 1056, 1032, 951, 915, 889, 847, 824, 784, 723, 660, 595, 534; $^1$H NMR (300 MHz, DMSO-$d_6$): δ (ppm) 12.5 (br, 1H), 9.20 (br s, 1H), 7.03-6.99 (d, 2H), 6.66-6.63 (d, 2H), 4.02-3.94 (m, 1H), 2.90-2.84 (dd, 1H), 2.73-2.65 (m, 1H), 1.32 (s, 9H); $^{13}$C NMR (75 MHz, DMSO-$d_6$): δ (ppm) 173.68, 155.78, 155.39, 129.94, 127.96, 114.87, 77.95, 55.46, 35.66, 28.13; MS: m/z 303.97 [M+Na]$^+$.
5.4.2.8 Synthesis of $\text{N}^2,\text{N}^6$-bis(tert-butoxycarbonyl)-L-lysine. DCHA (Table 5.1, entry 8)

Yield: 81%. Melting range: 138-140 °C (lit.138-139 °C, Keller et al., 1985); $[\alpha]_D^{20} = +5.9^\circ$ (c 1, DMF), [lit.$[\alpha]_D^{20} = +6.1^\circ$ (c 1.5, DMF), Keller et al., 1985); FT-IR (KBr, cm$^{-1}$): $v_{\text{max}}$ 3423, 3350, 2975, 2938, 2861, 1713, 1683, 1631, 1530, 1481, 1466, 1398, 1365, 1311, 1278, 1252, 1171, 1107, 1061, 1030, 975, 921, 897, 866, 812, 780, 760, 644; $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ (ppm) 5.49-5.46 (br d, 1H), 4.69 (br, 1H), 3.98-3.97 (m, 1H), 3.10-3.08 (m, 2H), 2.99-2.92 (m, 2H), 2.02-1.98 (d, 4H), 1.82-1.64 (2x d, 9H), 1.57-1.36 (m, 26H), 1.30-1.13 (m, 7H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ (ppm) 176.57, 155.94, 155.55, 78.78, 78.46, 55.24, 52.51, 40.57, 33.66, 29.57, 29.14, 29.07, 28.46, 28.39, 25.17, 24.74, 22.72; MS: m/z 345.05 [M-H$^+$].

5.4.2.9 Synthesis of N-(tert-butoxycarbonyl)-L-valine. DCHA (Table 5.1, entry 9)

Yield: 90%. Melting range: 140-142 °C (lit.138-140 °C, Anpeiji et al., 1983); $[\alpha]_D^{20} = -2.1^\circ$ (c 1, AcOH), [lit.$[\alpha]_D^{20} = -1^\circ$ (c 4, AcOH), Anpeiji et al., 1983); FT-IR (KBr, cm$^{-1}$): $v_{\text{max}}$ 3436, 2965, 2940, 2860, 1716, 1630, 1579, 1483, 1392, 1364, 1320, 1290, 1248, 1213, 1165, 1087, 1064, 1042, 1017, 897, 868, 761, 670; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 5.34-5.31 (d, 1H), 3.94-3.90 (m, 1H), 3.00-2.90 (m, 2H), 2.19-2.15 (m, 1H), 2.02-1.98 (br d, 4H), 1.81-1.77 (br d, 4H), 1.66-1.63 (br d, 2H), 1.48-1.37 (m, 13H), 1.299-1.13 (m, 6H), 0.97-0.95 (d, 3H), 0.89-0.87 (d, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ (ppm) 176.13, 155.85, 78.16, 60.63, 52.39, 31.90, 29.12, 28.85, 28.38, 25.13, 24.74, 19.65, 17.57; MS: m/z 215.88 [M-H$^+$].

5.4.2.10 Synthesis of 4-Chloro-N-(tert-butoxycarbonyl)-D-phenylalanine (Table 5.1, entry 10)

Yield: 90%. Melting range: 109-110 °C (lit. ~110 °C, Aldrich catalogue, 2009-10); $[\alpha]_D^{20} = -26.8^\circ$ (c 1, EtOAc), [lit. $[\alpha]_D^{20} = -26^\circ$ (c 1, EtOAc), Aldrich catalogue, 2009-10); FT-IR (KBr, cm$^{-1}$): $v_{\text{max}}$ 3346, 2988, 2931, 1713, 1686, 1520, 1491, 1463, 1427, 1392, 1367, 1339, 1307, 1284, 1267, 1254, 1229, 1166, 1090, 1052, 1028, 1016, 969, 942, 893, 854, 825, 776, 751, 736, 688, 657, 568, 525; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 7.29-7.26
5.4.2.11 Synthesis of 3-Fluoro-N-(tert-butoxycarbonyl)-L-phenylalanine (Table 5.1, entry 11)

Yield: 85%. Melting range: 75-78 °C (lit.75-80 °C, Aldrich catalogue, 2009-10); [α]D^20 = +7.3° (c 1, MeOH), [lit.[α]D^20 = +6.5° (c 1, MeOH), Aldrich catalogue, 2009-10]; FT-IR (KBr, cm⁻¹): v max 3350, 2984, 2933, 1716, 1686, 1619, 1586, 1522, 1487, 1445, 1427, 1392, 1368, 1345, 1323, 1293, 1250, 1164, 1078, 1053, 1029, 1013, 971, 932, 896, 848, 787, 750, 730, 699, 685, 605, 569, 520; ^1H NMR (300 MHz, CDCl₃): δ (ppm) 10.96 (br s, 1H), 7.29-7.21 (m, 1H), 6.97-6.78 (m, 3H), 5.09-5.06 (d, 1H), 4.62-4.40 (m, 1H), 3.22-2.87 (m, 2H), 1.41-1.29 (d, 9H); ^13C NMR (75 MHz, CDCl₃): δ (ppm) 176.08, 164.43, 155.36, 138.54, 130.04, 125.31, 116.53, 114.12, 80.47, 54.18, 37.61, 28.25; MS: m/z 282.17 [M-H]^+.

5.4.2.12 Synthesis of Preparation of H-Lys(Boc)-OH (Table 5.1, entry 12)

L-Lysine mono hydrochloride (3.0 g, 16.4 mmol), sodium carbonate (2.09g, 19.7 mmol) and Copper (II) carbonate hydroxide [Cu₃ (CO₃)₂(OH)₂] (1.81 g, 8.2 mmol) were added to water (30 mL) and stirred for 15 min. To this solution was added a solution of Boc-OASUD (5.37g, 18.1 mmol) in acetone (20 mL). The reaction mixture and stirred for 18h at room temperature. Methanol (5 mL) was added and further stirred for 6h. The solid obtained was filtered and washed with acetone (20 mL). Solid was suspended in water (30 mL), added disodium EDTA (3.60 g, 9.67 mmol) and heated to 80-90 °C for 1h. The reaction mixture was cooled to 5-10 °C and neutralized with dilute HCl carefully. The obtained solid was filtered and dried to give H-Lys (Boc)-OH (3.15g, 78% yield). Melting range: 247-250 °C (lit. 250 °C, Aldrich catalogue, 2009-10); [α]D^20 = +17.2° (c 1, AcOH) {lit.[α]D^20 = +18° (c 1, AcOH), Aldrich catalogue, 2009-10}; FT-IR (KBr, cm⁻¹) [Figure 5.13]: v max 3375, 2979, 2937, 2865, 1687, 1604, 1583, 1528, 1444, 1412, 1366, 1350, 1325, 1294, 1275, 1250, 1180, 1063, 1038, 1017, 994, 979, 925, 871, 810, 781,
5.4.2.13 Synthesis of N-(tert-butoxycarbonyl)-L-aspartic acid (Table 5.1, entry 13)

Yield: 80%. Melting range: 114-117 °C (lit. 116-118 °C, Aldrich catalogue, 2009-10); [α]D²⁰ = -6.4° (c 1, MeOH), [lit.[α]D²⁰ = -6.0° (c 1, MeOH), Aldrich catalogue, 2009-10); FT-IR (KBr, cm⁻¹): νmax 3357, 2979, 2931, 1706, 1692, 1536, 1517, 1417, 1393, 1368, 1300, 1253, 1175, 1061, 1002, 976, 935, 901, 860, 779, 747, 647, 598; ¹H NMR (300 MHz, DMSO-d₆ and D₂O-1:1): δ (ppm) 3.52 (t, 1H), 3.06-3.02 (t, 2H), 1.85-1.80 (m, 2H), 1.50-1.42 (m, 13H); ¹³C NMR (300 MHz, DMSO-d₆): δ (ppm) 174.49, 158.60, 79.91, 56.24, 41.02, 32.04, 30.65, 28.80, 23.59; MS [Figure 5.14]: m/z 246.93 [M+H]⁺.

5.4.2.14 Synthesis of N-(tert-butoxycarbonyl)-D-phenylglycine (Table 5.1, entry 14)

Yield: 89%. Melting range: 90-92 °C (lit. 88-91 °C, Aldrich catalogue, 2009-10); [α]D²⁰ = -144° (c 1, EtOH), [lit. [α]D²⁰ = -142° (c 1, EtOH), Aldrich catalogue, 2009-10); FT-IR (KBr, cm⁻¹): νmax 3363, 2982, 2935, 1718, 1701, 1512, 1478, 1456, 1394, 1368, 1342, 1282, 1248, 1164, 1061, 1030, 924, 910, 871, 850, 757; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 8.08-8.07 (d, 1H), 7.44-7.26 (m, 5H), 5.50-5.12 (m, 1H), 1.43 (s, 3H), 1.20 (s, 6H); ¹³C NMR (75 MHz, CDCl₃): δ (ppm) 173.40, 157.04, 138.39, 128.43, 127.96, 127.21, 81.67, 58.87, 27.99; MS: m/z 273.90 [M+Na]⁺.

5.4.2.15 Synthesis of N-(tert-butoxycarbonyl)-D-serine (Table 5.1, entry 15)

Yield: 89%, light yellow oil; [α]D²⁰ = +21.6° (c 1, MeOH), [lit. [α]D²⁰ = -10.0° (c 0.499, MeOH), Cortes-Clerget et al., 2016); FT-IR (NaCl, cm⁻¹): νmax 3367, 2980, 2935, 1718, 1701, 1512, 1478, 1456, 1394, 1368, 1342, 1282, 1248, 218, 1164, 1061, 1030, 924, 910, 871, 850, 757; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 6.04-5.91 (br, 1H), 5.74-5.71 (d, 1H), 4.37-4.21 (br d, 1H), 4.13-3.99 (m, 1H), 3.88-3.84 (m, 1H), 1.46 (s, 9H); ¹³C NMR
(75 MHz, CDCl₃): δ (ppm) 174.00, 156.25, 80.55, 62.89, 55.45, 28.27; MS: m/z 227.68 [M+Na]⁺.

5.4.2.16 Synthesis of N-( tert-butoxycarbonyl)-N-methylglycine (Table 5.1, entry 16)

Yield: 93%, white solid. Melting range: 89-91 °C (lit. 88-90 °C, Aldrich catalogue, 2009-10); FT-IR (KBr, cm⁻¹): v_max 3444, 2985, 1748, 1648, 1451, 1413, 1370, 1299, 1249, 1192, 1158, 975, 897, 865, 770, 685, 631, 577; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 8.59 (br s, 1H), 4.02-3.95 (d, 2H), 2.94 (s, 3H), 1.47-1.43 (d, 9H); ¹³C NMR (75 MHz, CDCl₃): δ (ppm) 174.85, 156.37, 80.64, 50.70, 35.56, 28.26; MS: m/z 190.47 [M+H]⁺.

5.4.3 Synthesis of N-Boc amino acid esters

5.4.3.1 Synthesis of Methyl ( tert-butoxycarbonyl)-L-phenylalaninate (Table 5.2, entry 1)

L-Phenylalanine methyl ester hydrochloride (5.0 g, 23.2 mmol), triethyl amine (2.47 g, 24.4 mmol) and Boc-OASUD (7.24 g, 24.4 mmol) were added to dichloromethane (50 mL) and stirred at reflux temp (38-40 °C) for 5h. After completion of the reaction, filtered to remove salts and the filtrate was washed with 5% KHSO₄ (20 mL), water (25 mL), brine (25 mL), and dried over sodium sulfate. The solvent was evaporated under reduced pressure to obtain a pale yellow oil. The oil was purified by column chromatography (silica gel, n-hexane/ethyl acetate, 8:2) to afford 5.96 g (92%) Methyl ( tert-butoxycarbonyl)-L-phenylalaninate as a colorless oil. R_f 0.5 (n-Hexane: EtOAc-4:1); [α]D²⁵ = -4.5° (c 1 in MeOH) {lit. [α]D²⁵ = -6.0° (c 2.5, MeOH), Ouchi et al., 2002}; FT-IR (neat, cm⁻¹) [Figure 5.17]: v_max 3437, 3020, 2980, 2954, 1735, 1719, 1604, 1507, 1492, 1454, 1444, 1437, 1391, 1364, 1250, 1177, 1154, 1079, 1053, 1015, 951, 932, 858, 817, 779, 739, 701, 668; ¹H NMR (300 MHz, CDCl₃) [Figure 5.18]: δ (ppm) 7.32-7.11 (m, 5H), 4.98-4.95 (d, 1H), 4.62-4.55 (q, 1H), 3.71 (s, 3H), 3.15-3.01 (m, 2H), 1.41 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) [Figure 5.19]: δ (ppm) 172.33, 155.08, 136.05, 129.28, 128.53, 127.00, 79.86, 54.44, 52.15, 38.34, 28.28; MS [Figure 5.20]: m/z 302.90 [M+Na]⁺.
The other N-Boc- amino acid esters given in Table 5.2 were prepared and characterized in a similar manner.

5.4.3.2 Synthesis of Methyl (tert-butoxycarbonyl)-L-alaninate (Table 5.2, entry 2)

Yield: 89%, colorless oil (lit. 31-33 °C, Surprenant and Lubell, 2006), $[\alpha]_D^{25} = -43.2^\circ$ (c 1, MeOH) (lit. $[\alpha]_D^{20} = -45.1^0$ (c 1.0, MeOH), Surprenant and Lubell, 2006); FT-IR (neat, cm$^{-1}$): $\nu_{\text{max}}$ 3364, 2980, 1808, 1744, 1716, 1516, 1455, 1392, 1367, 1349, 1307, 1250, 1214, 1167, 1119, 1069, 1027, 981, 952, 920, 869, 845, 781, 760; $^1$HNMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 5.03 (s, 1H), 4.34-4.29 (t, 1H), 3.74 (s, 3H), 1.44 (s, 9H), 1.39-1.37 (d, 3H); $^{13}$CNMR (75 MHz, CDCl$_3$): $\delta$ (ppm) 173.79, 155.05, 146.69, 85.07, 79.73, 52.20, 49.11, 28.25, 27.34, 18.52; MS: m/z 225.90 [M+Na]$^+$. Eluents for silica gel column chromatography- 3: 7 (EtOAc: hexane).

5.4.3.3 Synthesis of Ethyl (tert-butoxycarbonyl)-L-alaninate (Table 5.2, entry 3)

Yield: 85%, colorless oil, $[\alpha]_D^{25} = -40.5^0$ (c 1 in MeOH) (lit. $[\alpha]_D^{20} = -39.8^\circ$ (c 2.5, MeOH), Ouchi et al., 2002); FT-IR (neat, cm$^{-1}$) : $\nu_{\text{max}}$ 3366, 2981, 2937, 1809, 1739, 1717, 1512, 1455, 1392, 1367, 1343, 1303, 1250, 1230, 1166, 1118, 1068, 1028, 951, 894, 854, 780, 759; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 5.04 (br, 1H), 4.31-4.26 (m 1H), 4.23-4.16 (q, 2H), 1.44 (s, 9H), 1.39-1.36 (d, 3H), 1.30-1.25 (t, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ (ppm) 173.29, 155.05, 146.69, 85.07, 79.73, 52.20, 49.11, 28.25, 27.34, 18.52; MS: m/z 217.72 [M+H]$^+$. Eluents for silica gel column chromatography- 2: 8 (EtOAc: hexane).

5.4.3.4 Synthesis of Methyl (tert-butoxycarbonyl) glycinate (Table 5.2, entry 4)

Yield: 93%, colorless oil; FT-IR (neat, cm$^{-1}$) : $\nu_{\text{max}}$ 3369,2979, 1752, 1718, 1523, 1439, 1410, 1392, 1368, 1286, 1251, 1210, 1167, 1057, 1032, 995, 946, 921, 895, 864, 784, 766, 742, 701; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ (ppm) 5.00 (br, 1H), 3.93-3.91 (d, 2H), 3.75 (s, 3H), 1.45 (s, 9H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ (ppm) 170.82, 155.05, 79.64, 61.17, 49.21, 28.25, 27.34, 18.57, 14.07, MS: m/z 211.97 [M+Na]$^+$. Eluents for silica gel column chromatography- 4: 6 (EtOAc: hexane).
5.4.3.5 Synthesis of Ethyl (tert-butoxycarbonyl) glycinate (Table 5.2, entry 5)

Yield: 91%, pale yellow oil, FT-IR (neat, cm⁻¹): ν_max 3371, 2980, 2936, 1755, 1716, 1517, 1453, 1392, 1368, 1285, 1252, 1202, 1167, 1097, 1056, 1028, 952, 864, 784, 766; 1H NMR (300 MHz, CDCl₃): δ (ppm) 5.01 (br, 1H), 4.24-4.17 (q, 2H), 3.91-3.89 (d, 2H), 1.45 (s, 9H), 1.30-1.26 (t, 3H); 13C NMR (75 MHz, CDCl₃): δ (ppm) 170.34, 155.71, 79.84, 61.23, 42.42, 28.25, 14.09; MS: m/z 226.83 [M+Na]⁺. Eluents for silica gel column chromatography- 3: 7 (EtOAc: hexane).

5.4.3.6 Synthesis of Benzyl (tert-butoxycarbonyl) glycinate (Table 5.2, entry 6)

Yield: 90%, white solid. Melting range: 72-74 °C (lit.73.4-74.6 °C, Sugawara et al., 1995); FT-IR (KBr, cm⁻¹): ν_max 3327, 3066, 3033, 2980, 2938, 1755, 1683, 1545, 1497, 1455, 1407, 1393, 1380, 1369, 1355, 1297, 1251, 1217, 1184, 1083, 1051, 1034, 963, 938, 915, 865, 828, 784, 772, 754, 702, 632, 603, 548; 1H NMR (300 MHz, CDCl₃): δ (ppm) 7.39-7.33 (m, 5H), 5.18 (s, 2H), 5.01 (br, 1H), 3.96-3.94 (d, 2H), 1.44 (s, 9H); 13C NMR (75 MHz, CDCl₃): δ (ppm) 170.27, 155.75, 135.32, 128.60, 128.46, 128.35, 79.95, 67.00, 42.50, 28.30; MS: m/z 265.71 [M]^⁺. Eluents for silica gel column chromatography- 2: 8 (EtOAc: hexane).

5.4.3.7 Synthesis of Methyl (tert-butoxycarbonyl)-L-serinate (Table 5.2, entry 7)

Yield: 81%, colorless oil, [α]D²⁵ = +8.2° (c 1, MeOH) {lit. [α]D²⁵ = +7.2° (c 2.5, MeOH), Ouchi et al., 2002}; FT-IR (neat, cm⁻¹): ν_max 3435, 3019, 2981, 2956, 1746, 1704, 1698, 1505, 1455, 1438, 1393, 1368, 1351, 1285, 1216, 1164, 1062, 1031, 978, 926, 873, 850, 768, 667; 1H NMR (300 MHz, CDCl₃): δ (ppm) 5.44 (br, 1H), 4.39-4.38 (br, 1H), 3.92-3.88 (m, 2H), 3.79 (s, 3H), 2.32-2.29 (t, 1H), 1.46 (s, 9H); 13C NMR (75 MHz, CDCl₃): δ (ppm) 171.46, 155.80, 80.24, 63.20, 55.71, 52.52, 28.25; MS: m/z 242.86 [M+Na]⁺. Eluents for silica gel column chromatography- 3: 7 (EtOAc: hexane).

5.4.3.8 Synthesis of Benzyl (tert-butoxycarbonyl)-L-serinate (Table 5.2, entry 8)

Yield: 86%, white solid. Melting range: 68-70 °C (lit. 66.6-68 °C, Itaya et al., 1993); [α]D²⁵ = -19.3° (c 1 in MeOH) {lit. [α]D²⁶ = -18.4° (c 2.01, MeOH), Itaya et al., 1993}; FT-IR
(KBr, cm\(^{-1}\)) : \(v_{\text{max}}\) 3436, 3018, 2980, 2935, 1739, 1708, 1500, 1456, 1393, 1368, 1346, 1283, 1216, 1163, 1061, 1029, 958, 913, 853, 755, 698, 668; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) 7.38-7.32 (m, 5H), 5.46 (br, 1H), 5.21 (s, 2H), 4.42 (br, 1H), 4.01-3.88 (m, 2H), 2.04 (br, 1H), 1.44 (s, 9H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) (ppm) 170.83, 155.81, 135.28, 128.59, 128.41, 128.16, 80.29, 67.32, 63.31, 55.90, 28.28; MS: m/z 318.96 [M+Na]\(^+\). Eluents for silica gel column chromatography- 3: 7 (EtOAc: hexane).

5.4.3.9 Synthesis of Methyl \((\text{tert-butoxycarbonyl})\)-L-valinate (Table 5.2, entry 9)

Yield: 87%, colorless oil, \([\alpha]_D^{25} = -22.5^\circ\) (c 1, MeOH) {lit. \([\alpha]_D^{25} = -21.9^\circ\) (c 2.2, MeOH), Ouchi et al., 2002}; FT-IR (neat, cm\(^{-1}\)) : \(v_{\text{max}}\) 3444, 3368, 2968, 2877, 1747, 1719, 1501, 1468, 1437, 1391, 1367, 1311, 1247, 1209, 1160, 1119, 1091, 1043, 1016, 925, 907, 867, 850, 779; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) 5.03-5.00 (br d, 1H), 4.24-4.20 (dd, 1H), 3.73 (s, 3H), 2.13-2.09 (m, 1H), 1.44 (s, 9H), 0.96-0.94 (d, 3H), 0.90-0.87 (d, 3H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) (ppm) 172.75, 155.56, 79.52, 58.48, 51.82, 31.19, 28.18, 27.28, 18.85, 17.53; MS: m/z 231.73 [M+H]\(^+\). Eluents for silica gel column chromatography- 4: 6 (EtOAc: hexane).

5.4.3.10 Synthesis of Methyl \((\text{tert-butoxycarbonyl})\)-L-prolinate (Table 5.2, entry 10)

Yield: 85%, yellow oil, \([\alpha]_D^{25} = -58.8^\circ\) (c 1, MeOH) {lit. \([\alpha]_D^{18} = -63.3^\circ\) (c 2.1, MeOH), Ouchi et al., 2002}; FT-IR (neat, cm\(^{-1}\)) : \(v_{\text{max}}\) 3610, 3519, 3386, 3093, 2968, 2877, 1747, 1702, 1543, 1478, 1437, 1400, 1365, 1279, 1248, 1160, 1122, 1088, 1034, 1000, 974, 922, 888, 858, 791, 772, 685, 593; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) 4.34-4.20 (m, 1H), 3.72 (s, 3H), 3.57-3.36 (m, 2H), 2.26-2.15 (m, 1H), 2.00-1.84 (m, 3H), 1.46 and 1.41 (2 x s, 9H); \(^13\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) (ppm) 173.60, 154.29, 79.64, 58.99, 51.76, 46.20, 30.76, 28.30, 28.17, 23.56; MS: m/z 230.69 [M+H]\(^+\). Eluents for silica gel column chromatography- 3: 7 (EtOAc: hexane).

5.4.3.11 Synthesis of Methyl \((\text{tert-butoxycarbonyl})\)-L-tyrosinate (Table 5.2, entry 11)

Yield: 82%. Melting range: 101-103 °C {lit. 102-104 °C, Ouchi et al., 2002}; \([\alpha]_D^{25} = +9.1^\circ\) (c 1, MeOH) {lit. \([\alpha]_D^{21} = +8.8^\circ\) (c 1.7, MeOH), Ouchi et al., 2002}; FT-IR (KBr, cm\(^{-1}\)) : \(v_{\text{max}}\) 3390, 3026, 2980, 1715, 1689, 1617, 1597, 1519, 1478, 1454, 1444, 1396,
1374, 1367, 1344, 1313, 1292, 1276, 1258, 1227, 1201, 1158, 1110, 1063, 1026, 995, 881, 848, 829, 808, 784, 758, 727, 669, 646, 638; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) 6.98-6.95 (d, 2H), 6.74-6.72 (d, 2H), 5.51 (s, 1H), 5.01-4.98 (d, 1H), 4.55-4.50 (q, 1H), 3.70 (s, 3H), 3.05-2.95 (m, 2H), 1.42 (s, 9H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) (ppm) 172.78, 155.50, 155.44, 130.29, 127.11, 115.58, 80.40, 54.68, 52.32, 37.49, 28.29; MS: m/z 294.13 [M-H]\(^+\). Eluents for silica gel column chromatography- 3: 7 (EtOAc: hexane).

5.4.3.12 Synthesis of Ethyl (tert-butoxycarbonyl)-L-tyrosinate (Table 5.2, entry 12)

Yield: 84%. Melting range: 87-89 °C (lit. 87-88 °C, Takayuki et al., 2006); \([\alpha]_D^{25} = +2.1^\circ\) (c 1, MeOH) [lit. \([\alpha]_D^{20} = + 1.05^\circ\) (c 0.5, MeOH), Sarkar et al., 2011]; FT-IR (KBr, cm\(^{-1}\)) : \(v_{\text{max}}\) 3389, 3342, 2975, 2934, 1728, 1693, 1615, 1595, 1537, 1519, 1450, 1392, 1368, 1293, 1246, 1225, 1191, 1160, 1061, 1022, 973, 890, 830, 813, 784, 636, 538; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) (ppm) 6.99-6.96 (d, 2H), 6.74-6.71 (d, 2H), 5.02-4.99 (d, 1H), 4.54-4.47 (q, 1H), 4.20-4.13 (q, 2H), 3.06-2.93 (m, 2H), 1.42 (s, 9H), 1.26-1.22 (t, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) (ppm) 172.31, 155.48, 155.43, 130.35, 127.18, 115.52, 80.30, 61.50, 54.72, 37.52, 28.30, 14.08; MS: m/z 308.05 [M-H]\(^+\). Eluents for silica gel column chromatography- 2: 8 (EtOAc: hexane).
5.5. REFERENCES

Aldrich catalogue, India, 2009-2010.


Figure 5.1: HPLC chromatogram of Boc-OASUD.

**Column**: Xterra RP-18 250 X4.6mm, 5 µm(HP/WAT/527)
**Flow**: 1.0 ml/min
**Temp**: 27°C
**Mobile Phase**: A) H2O, B) ACN

![HPLC Chromatogram](image)

**Peak Results**

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<td>237</td>
<td>1652</td>
</tr>
</tbody>
</table>
Figure 5.2: FT-IR spectrum of Boc-OASUD.

Figure 5.3: $^1$H NMR spectrum of Boc-OASUD.
Figure 5.4: $^{13}$C NMR spectrum of Boc-OASUD.

Figure 5.5: Mass spectrum of Boc-OASUD.
Figure 5.6: HPLC chromatogram of N-Boc-L-Phe-OH.
**Figure 5.7:** Chiral HPLC chromatogram of racemic N-Boc-Phe-OH.

**Figure 5.8:** Chiral HPLC chromatogram of N-Boc-L-Phe-OH (L-isomer).
Figure 5.9: FT-IR spectrum of N-Boc-L-Phe-OH.

Figure 5.10: $^1$H NMR spectrum of N-Boc-L-Phe-OH.
Figure 5.11: $^{13}$C NMR spectrum of N-Boc-L-Phe-OH.

Figure 5.12: Mass spectrum of N-Boc-L-Phe-OH.
Figure 5.13: FT-IR spectrum of H-Lys(Boc)-OH.

![FT-IR spectrum of H-Lys(Boc)-OH](image)

Figure 5.14: $^1$H NMR spectrum of H-Lys(Boc)-OH.

![$^1$H NMR spectrum of H-Lys(Boc)-OH](image)
Figure 5.15: $^{13}$C NMR spectrum of H-Lys(Boc)-OH.

Figure 5.16: MASS spectrum of H-Lys(Boc)-OH.
**Figure 5.17**: FT-IR spectrum of Methyl (tert-butoxycarbonyl)-L-phenyl alaninate.

![FT-IR spectrum](image)

**Figure 5.18**: $^1$H NMR spectrum of Methyl (tert-butoxycarbonyl)-L-phenyl alaninate.

![NMR spectrum](image)
Figure 5.19: $^{13}$C NMR spectrum of Methyl (tert-butoxycarbonyl)-L-phenyl alaninate.

![NMR Spectrum](image1)

Figure 5.20: Mass spectrum of Methyl (tert-butoxycarbonyl)-L-phenyl alaninate.

![Mass Spectrum](image2)