

## Preparation of new mono- and bis-amide derivatives of L-isoleucine via amidation of carboxyl and amino groups

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**Abstract:** *N,N'*-Dicyclohexylcarbodiimide and hydroxybenzotriazole mediated amination of free COOH group of *N-tert*-butyloxycarbonyl-L-isoleucine **1** with three aromatic amines gave the corresponding amides **2a-c**. Deprotection of *N-tert*-butyloxycarbonyl groups of **2a-c** with AcOH yielded the related amine derivatives **3a-c**. The amidation of the free NH<sub>2</sub> groups of (**3a-c**) with phthaloyl dichloride yielded the bis-amide products **4a-c**. The synthesized compounds were purified by crystallization and their structures were elucidated by spectroscopic methods such as <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, FTIR, and micro analysis.

**Keywords:** Amides; tetraamides; N-boc-deprotection; coupling reaction; spectroscopy; heterocyclic. ©2021 ACG Publications. All right reserved.

### 1. Introduction

Due to the versatility of amides, they have gained a great importance in synthetic chemistry. Numerous methods have been developed to synthesize the amides for usage in the pharmaceutical and medicinal industries. The most common one is the treatment of carboxylic acid with amine. A large variety of natural products include the amide moiety, moreover, many drug formulations contain the amide groups<sup>1</sup>. Chiral amides consisting of vicinal stereo centres commonly exist in natural products and drug molecules.

The compounds having amide groups synthesised chemically were reported recently that revealed a large variety of biological activity such as anticancer<sup>2</sup>, antimicrobial<sup>3</sup>, antiviral<sup>4</sup>, antibacterial<sup>5</sup>, antituberculosis<sup>6</sup>, fungicidal and insecticidal<sup>7</sup>, pesticide<sup>8</sup>, anti-respiratory syncytial virus<sup>9</sup>. These compounds could be preferable ligands for synthesis of metal complex as well. Amide bonds play a major role in explanation and composition of biological system, representing main chemical bonds that link amino acid building blocks together to give proteins. Amide bonds are not limited to biological systems and indeed exist in a wide variety of molecules, including major marketed drugs. For instance, Atorvastatin, consists of amide bond, prevent the formation of cholesterol<sup>10</sup>, lisinopril, inhibitor of angiotensin converting enzyme<sup>11</sup>, valsartan, barricade the angiotensin II receptor<sup>12</sup>, diltiazem, calcium channel blocker, treatment of hypertension<sup>13</sup>. Amide bonds are typically formed by the treatment of carboxylic acids with amines. The removal of *tert*-butyl carbamate by TFA/DCM was also reported<sup>14,15</sup>

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## Preparation of carboxyl and amino groups

Herein, the diastereoselective syntheses of amides bearing two stereogenic centers in the 2,3 positions with respect to nitrogen atom were achieved with a good yield.

## 2. Experimental

### 2.1. General Procedure

NMR spectra were recorded on a Bruker spectrometer with  $^1\text{H}$  NMR at 400 MHz,  $^{13}\text{C}$  NMR at 100 MHz. The  $^1\text{H}$  NMR chemical shifts were measured relative to DMSO- $d_6$  as the internal reference ( $\text{CDCl}_3$ :  $\delta$  7.26, DMSO- $d_6$ :  $\delta$  2.5). TLC was carried out on alumina plates (60 F<sub>254</sub>). TLC spots were observed under UV light and sprayed with ceric sulfate reagent then heated. IR analysis was executed on Jasco FT/IR47700 spectrometer. Melting points were determined by a Buchi B-540 apparatus and were uncorrected. The solvents and chemicals were supplied from E. Merck (Darmstadt, Germany).

### 2.2. General Synthesis of Carbamate Derivatives (2a-c)

N-*tert*-butyloxycarbonyl-L-isoleucine **1** (12.0 mmol), hydroxybenzotriazole (HOBt) (14.4 mmol) were dissolved with  $\text{CH}_2\text{Cl}_2$  (300 mL) in an ice-bath reaction flask. Aromatic amines (**a-c**) (12.0 mmol) and *N,N'*-Dicyclohexylcarbodiimide (DCC) (13.2 mmol) were added to the reaction flask. The reaction mixture was stirred overnight at room temperature. After the completion of the reaction, hexyl cyclo urea formed was removed by filtration. The chloroform was added to the reaction flask, extracted with 1.0 M HCl, 5%  $\text{NaHCO}_3$  and distilled water successively then organic phase was separated by separatory funnel, dried with calcium chloride, filtered then solvent was removed by rotary evaporator to yield the product (**2a-c**).

*tert*-Butyl [(2*R*,3*S*)-3-methyl-1-[[1-(naphthalen-1-yl)ethyl]amino]-1-oxopentan-2-yl]carbamate (**2a**): (4.20 g, 91%). Mp: 143-144 °C. Anal. Calcd (%) for  $\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}_3$ : C, 71.84; H, 8.39. Found: C, 71.79; H, 8.42. IR: ( $\nu/\text{cm}^{-1}$ ) 3317, 3253, 3060, 2967, 2931, 2878, 2850, 1683, 1639, 1521, 1449, 1390, 1365, 1314, 1292, 1244, 1166, 1124, 1085, 1043, 1015, 998, 917, 866, 797, 775 (Figure S1).  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$ : 8.46 (d,  $J = 7.7$  Hz, 1H), 8.11 (d,  $J = 7.9$  Hz, 1H), 7.94 (d,  $J = 7.4$  Hz, 1H), 7.83 (d,  $J = 8.0$  Hz, 1H), 7.53 (m, 2H), 7.47 (t,  $J = 7.6$  Hz, 1H), 6.58 (d,  $J = 9.0$  Hz, 1H), 5.75 – 5.72 (m, 1H), 3.91 (t,  $J = 8.0$  Hz, 1H), 1.60 – 1.75 (m, 2H), 1.50 (d,  $J = 6.7$  Hz, 3H), 1.38 (s, 9H), 1.02- 1.14 (m, 2H), 0.76 (m, 6H) (Figure S2).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ ) 170.9 (C=O amide), 155.8 (C=O carbamate), 140.6, 133.8, 130.8, 129.1, 127.8, 126.6, 126.0, 125.7, 123.6, 122.9, 78.4, 59.2, 44.4, 37.3, 28.6, 24.6, 22.0, 15.9, 11.4 (Figure S3).

*tert*-Butyl [(2*R*,3*S*)-1-[[4-(*tert*-butyl)benzyl]amino]-3-methyl-1-oxopentan-2-yl]carbamate (**2b**): (3.34 g, 74%). Mp: 118-122 °C. Anal. Calcd (%) for  $\text{C}_{22}\text{H}_{36}\text{N}_2\text{O}_3$ : C, 70.21; H, 9.57. Found: C, 70.19; H, 9.63. IR: ( $\nu/\text{cm}^{-1}$ ) 3345, 3315, 3266, 2962, 2931, 2872, 1686, 1642, 1515, 1459, 1390, 1365, 1317, 1292, 1244, 1172, 1043, 1018, 915 (Figure S4).  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$ : 8.29 (t,  $J = 5.3$  Hz, 1H), 7.31 (d,  $J = 8.1$  Hz, 2H), 7.18 (d,  $J = 8.0$  Hz, 2H), 6.70 (d,  $J = 8.9$  Hz, 1H), 4.24 (d,  $J = 5.7$  Hz, 2H), 3.83 (t,  $J = 8.3$  Hz, 1H), 1.70 (d,  $J = 5.9$  Hz, 1H), 1.39 (s, 9H), 1.26 (s, 9H), 1.18 (t,  $J = 7.1$  Hz, 1H), 1.10 (m, 1H), 0.83 – 0.79 (m, 6H) (Figure S5).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  171.9 (C=O amide), 155.8 (C=O carbamate), 149.6, 136.8, 127.5, 125.3, 78.4, 59.4, 42.2, 36.8, 34.6, 31.6, 28.6, 24.9, 16.0, 11.4 (Figure S6).

*tert*-Butyl [(2*R*,3*S*)-1-[[4-butylbenzyl]amino]-3-methyl-1-oxopentan-2-yl]carbamate (**2c**): (4.07 g, 90%). Mp: 113-118 °C. Anal. Calcd (%) for  $\text{C}_{21}\text{H}_{34}\text{N}_2\text{O}_3$ : C, 69.61.21; H, 9.39. Found: C, 69.50; H, 9.43. IR: ( $\nu/\text{cm}^{-1}$ ) 3343, 3312, 2959, 2952, 2872, 2853, 2372, 2352, 2321, 1686, 1661, 1596, 1516, 1462, 1412, 1365, 1312, 1284, 1244, 1166, 1115, 1046, 1018, 970, 925 (Figure S7).  $^1\text{H}$  NMR (400 MHz, DMSO- $d_6$ )  $\delta$  9.91 (s, 1H), 7.51 (d,  $J = 8.2$  Hz, 2H), 7.11 (d,  $J = 8.3$  Hz, 2H), 6.90 (d,  $J = 8.4$  Hz, 1H), 3.94 (t,  $J = 8.3$  Hz, 1H), 2.51 (t,  $J = 7.2$  Hz, 2H), 1.51 (m, 4H), 1.38 (s, 9H), 1.28 (m, 4H), 1.20 - 1.04 (m, 1H), 0.90 – 0.79 (m, 9H) (Figure S8).  $^{13}\text{C}$  NMR (100 MHz, DMSO- $d_6$ )  $\delta$  171.0 (C=O amide), 155.9

(C=O carbamate), 137.7, 137.0, 128.9, 119.7, 78.4, 59.9, 36.9, 34.7, 33.8, 33.7, 28.7, 25.1, 22.1, 15.8, 14.2, 11.3 (Figure S10).

### 2.3. General Synthesis of Pentanamide Derivatives (**3a-c**)

Carbamate derivatives (**2a-c**) (6.0 mmol) was added in a round bottom reaction flask. AcOH (60 mmol), CF<sub>3</sub>COOH (60 mmol) and CH<sub>2</sub>Cl<sub>2</sub> (5.0 mL) were added in a dropping funnel. The solution in dropping funnel was added slowly to the reaction flask for half an hour at 0 °C. After finishing the addition, the reaction mixture was stirred at room temperature overnight under the argon. The reaction mixture was completed after TLC application. 1 M KOH was added to the reaction mixture to adjust the pH at 9-10, then the H<sub>2</sub>O (30 mL) was added to the mixture, extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 20 mL), organic phase was separated by separatory funnel, dried (CaCl<sub>2</sub>), filtered and solvent was removed by rotary evaporator to yield the product (**3a-c**).

(2*R*,3*S*)-2-amino-3-methyl-*N*-[1-(naphthalen-1-yl)ethyl]pentanamide (**3a**): (1.62 g, %95). Mp: 95-96 °C. Anal. Calcd (%) for C<sub>18</sub>H<sub>24</sub>N<sub>2</sub>O: C, 76.02; H, 8.51. Found: C, 76.10 H, 8.55. IR: (ν/cm<sup>-1</sup>) 3368, 3303, 3048, 2967, 2925, 2872, 1614, 1533, 1452, 1378, 1337, 1218, 1258, 1239, 1219, 1172, 1118, 1082, 1037, 1024, 996, 973, 902, 869, 859, 833, 797, 775 (Figure S11). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 8.35 (d, *J* = 8.1 Hz, 1H), 8.13 (d, *J* = 8.8 Hz, 1H), 7.93 (dd, *J* = 8.1, 6.1 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.47 (m, 4H), 5.75 (m, 1H), 3.03 (d, *J* = 5.4 Hz, 1H), 1.55 – 1.66 (m, 3H), 1.52 (d, *J* = 6.9 Hz, 3H), 1.47 – 1.36 (m, 1H), 1.10 – 0.98 (m, 1H), 0.76-0.82 (m, 6H) (Figure S12). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ 174.2 (C=O amide), 140.6, 133.8, 130.9, 129.1, 127.6, 126.6, 126.1, 125.8, 123.7, 122.9, 59.7, 44.1, 39.06, 24.0, 22.0, 16.4, 11.9 (Figure S15).

(2*R*,3*S*)-2-amino-*N*-[4-(*tert*-butyl)benzyl]-3-methylpentanamide (**3b**): (1.56 g, %94). Mp: 70-71 °C. Anal. Calcd (%) for C<sub>17</sub>H<sub>28</sub>N<sub>2</sub>O: C, 73.91; H, 10.14. Found: C, 73.85 H, 10.19. IR: (ν/cm<sup>-1</sup>) 3396, 3331, 3263, 3063, 2953, 2928, 2903, 2869, 1667, 1633, 1540, 1510, 1462, 1443, 1409, 1375, 1362, 1300, 1267, 1244, 1228, 1183, 1155, 1135, 1115, 1107, 1049, 1021, 945, 928, 891, 825 (Figure S16). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>) δ 8.26 (t, *J* = 5.8 Hz, 1H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 4.26 (t, *J* = 6.2 Hz, 2H), 3.02 (d, *J* = 5.6 Hz, 1H), 1.66 – 1.59 (m, 3H), 1.49 – 1.43 (m, 1H), 1.27 (s, 9H), 1.12 – 1.05 (m, 1H), 0.84 (m, 6H) (Figure S17). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>) δ 175.1 (C=O amide), 149.5, 137.1, 127.6, 125.4, 59.9, 42.1, 38.96, 34.59, 31.6, 24.2, 16.4, 12.0 (Figure S18).

(2*R*,3*S*)-2-amino-*N*-(4-butylbenzyl)-3-methylpentanamide (**3c**): orange viscos (1.41 g, %85). Anal. Calcd (%) for C<sub>16</sub>H<sub>26</sub>N<sub>2</sub>O: C, 73.28; H, 9.92. Found: C, 73.35 H, 9.85. IR: (ν/cm<sup>-1</sup>) 3294, 2959, 2928, 2872, 2853, 1658, 1602, 1589, 1515, 1455, 1409, 1378, 1309, 1244, 1200, 1174, 1132, 1118, 828 (Figure S19). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.50 (s, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 2H), 3.34 (d, *J* = 3.8 Hz, 1H), 2.55 (m, 2H), 1.60 – 1.52 (m, 4H), 1.47-1.38 (m, 2H), 1.36 – 1.26 (m, 3H), 1.16 – 1.10 (m, 2H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.91 (m, 6H) (Figure S20). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.8 (C=O amide), 138.6, 135.5, 128.4, 119.6, 60.2, 38.1, 35.0, 33.7, 23.7, 22.2 (2C), 16.3, 13.9, 11.9 (Figure S21).

### 2.4. General Synthesis of Oxopentan-Phthalamide Derivative **4** (**a-c**)

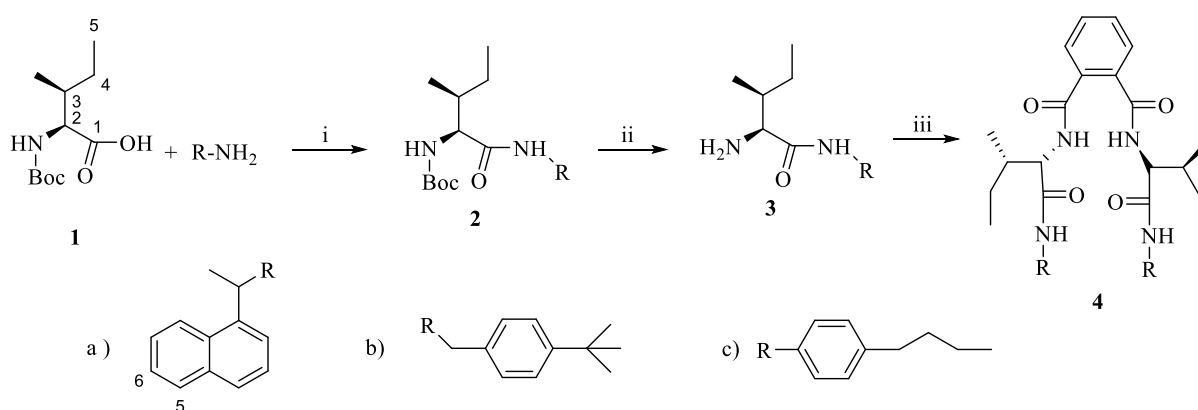
The compounds **3a-c** (5.0 mmol), THF (30 mL), pyridine (5.0 mmol) were added in two necked flask at 0 °C. A drying tube consisting of CaCl<sub>2</sub> was inserted to the one necked of the flask. A solution of phthaloyl dichloride (2.5 mmol) in THF (30 mL) was added to the reaction flask via dropping funnel for one hour. A white precipitate was formed while addition of phthaloyl dichloride. The reaction mixture was stirred overnight at room temperature. After the completion of reaction by TLC check, the precipitated solid was filtered. The solvent was removed under reduced pressure and chloroform (100 mL) was added to the reaction flask, extracted with 1 M HCl, 1 M KOH and distilled water sequentially, dried (MgSO<sub>4</sub>), filtered, and the solvent was removed under reduced pressure to yield the product.

## Preparation of carboxyl and amino groups

*Synthesis of N1-[(2S,3S)-3-methyl-1-[(R)-1-(naphthalen-1-yl)ethyl]amino]-1-oxopentan-2-yl]-N2-[(2R,3S)-3-methyl-1-[(S)-1-(naphthalen-1-yl)ethyl]amino]-1-oxopentan-2-yl]phthalamide (**4a**):* (3.32 g, 95%). Mp: 304–305 °C. Anal. Calcd (%) for C<sub>44</sub>H<sub>50</sub>N<sub>4</sub>O<sub>4</sub>: C, 75.62; H, 7.21. Found: C, 75.58 H, 7.16. IR: ( $\nu/\text{cm}^{-1}$ ) 3272, 3054, 2965, 2931, 2875, 1630, 1524, 1484, 1455, 1381, 1370, 1350, 1317, 1286, 1250, 1216, 1172, 1146, 1107, 1087, 1001, 919, 775 (Figure S22). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.86 (m, 4H), 8.55 (d, *J* = 8.8 Hz, 2H), 8.41 – 8.37 (m, 2H), 8.16 (d, *J* = 7.6 Hz, 2H), 8.04 (dd, *J* = 7.7, 1.5 Hz, 2H), 7.90 (m, 2H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.60 (d, *J* = 7.0 Hz, 2H), 7.57 – 7.48 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 5.77 (t, *J* = 8.8 Hz, 2H), 4.47 (t, *J* = 8.8 Hz, 2H), 1.94 (m, 2H), 1.52 (d, *J* = 6.9 Hz, 6H), 1.49 (m, 2H), 1.20 – 1.13 (m, 2H), 0.83 – 0.78 (m, 12H) (Figure S23). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>)  $\delta$  170.7 (C=O pentanamide), 166.4 (C=O phthalimide), 144.5, 140.9, 134.9, 133.8, 130.7, 129.1, 127.2, 126.8, 126.5, 126.0, 125.8, 123.6, 123.1, 58.5, 44.6, 36.7, 25.2, 22.4, 15.9, 11.1 (Figure S24).

*Synthesis of N1-[(2R,3S)-1-[[4-(tert-butyl)benzyl]amino]-3-methyl-1-oxopentan-2-yl]-N2-[(2S,3S)-1-[[4-(tert-butyl)benzyl]amino]-3-methyl-1-oxopentan-2-yl]phthalamide (**4b**):* (3.11 g, 91%). Mp: 247–249 °C. Anal. Calcd (%) for C<sub>42</sub>H<sub>58</sub>N<sub>4</sub>O<sub>4</sub>: C, 73.87; H, 8.56. Found: C, 73.91 H, 8.61. IR: ( $\nu/\text{cm}^{-1}$ ) 3275, 3060, 2959, 2875, 1636, 1524, 1459, 1381, 1362, 1342, 1289, 1269, 1250, 1219, 1172, 1152, 1107, 1057, 1021, 928, 808 (Figure S26). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  8.53 (t, *J* = 5.8 Hz, 2H), 8.48 (d, *J* = 8.7 Hz, 2H), 8.32 (brs, 2H), 8.02 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.32 (d, *J* = 8.3 Hz, 4H), 7.19 (d, *J* = 8.2 Hz, 4H), 4.41 (t, *J* = 8.6 Hz, 2H), 4.27 (dd, *J* = 5.2, 3.1 Hz, 4H), 1.96 (d, *J* = 6.6 Hz, 2H), 1.50 – 1.56 (m, 2H), 1.25 (s, 18H), 1.19 (m, 2H), 0.9 (d, *J* = 6.8 Hz, 6H), 0.85 (t, *J* = 7.4 Hz, 6H) (Figure S27). <sup>13</sup>C NMR (100 MHz, DMSO-d<sub>6</sub>)  $\delta$  171.5, 166.5, 149.6, 136.7, 134.9, 130.7, 127.5 (2C overlapped), 125.4, 58.5, 42.3, 36.4, 34.6, 31.6, 25.3, 16.0, 11.2 (Figure S30).

*N1-[(2R,3S)-1-[[4-butylbenzyl]amino]-3-methyl-1-oxopentan-2-yl]-N2-[(2S,3S)-1-[[4-butylbenzyl]amino]-3-methyl-1-oxopentan-2-yl]phthalamide (**4c**):* (3.24 g, 95%). Mp: 140–142 °C. Anal. Calcd (%) for C<sub>42</sub>H<sub>58</sub>N<sub>4</sub>O<sub>4</sub>: C, 73.87; H, 8.56. Found: C, 73.91 H, 8.61. IR: ( $\nu/\text{cm}^{-1}$ ) 3264, 2959, 2931, 2875, 2856, 2601, 2495, 1639, 1611, 1524, 1474, 1415, 1398, 1373, 1317, 1281, 1250, 1174, 1074, 1037 (Figure S31). <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  10.12 (s, 2H), 8.65 (d, *J* = 7.9 Hz, 2H), 8.04 (dd, *J* = 7.7, 1.5 Hz, 2H), 7.54 (d, *J* = 8.4 Hz, 4H), 7.12 (d, *J* = 8.4 Hz, 4H), 4.49 (t, *J* = 8.7 Hz, 2H), 2.51 (m, 10 H), 2.03 (d, *J* = 6.5 Hz, 2H), 1.63 – 1.48 (m, 6H), 1.33 – 1.23 (m, 6H), 0.94 (d, *J* = 6.7 Hz, 6H), 0.89 (t, *J* = 7.3 Hz, 12H) (Figure S32). <sup>13</sup>C NMR (101 MHz, DMSO-d<sub>6</sub>)  $\delta$  170.7, 166.7, 137.8, 137.0, 134.8, 130.8, 128.9, 128.6, 119.9, 59.2, 36.4, 34.7, 33.7, 25.5, 22.1 (2 peaks overlapped), 15.8, 14.2, 11.1 (Figure S33).



**Scheme 1.** Reagent and conditions: i) R-NH<sub>2</sub>, OH, HOBt, DCC, CH<sub>2</sub>Cl<sub>2</sub>, rt, overnight, **2a** 91%, **2b** 74%, **2c** 90%; ii) AcOH, TFA, CH<sub>2</sub>Cl<sub>2</sub>, rt, overnight, **3a** 95%, **3b** 94%, **3c** 85%; iii) phthaloyl dichloride, THF, rt, overnight, **4a** 95%, **4b** 91%, **4c** 95%.

### 3. Results and Discussion

The synthetic pathways for the synthesised compounds were given in Scheme 1. Firstly, the reaction of *tert*-butoxycarbonyl-L-isoleucine **1** with aromatic amine (**a-c**) in the presence of HOBt and DCC in CH<sub>2</sub>Cl<sub>2</sub> at room temperature yielded the formation of compound **2 (a-c)**. 1-hydroxy-1H-benzotriazole (HOBt) was used as a coupling reagent to reduce the epimerisation level and to increase the reaction yield<sup>16</sup>.

Removal of Boc protection group of **2 (a-c)** with TFA gave the compound **3 (a-c)**. The coupling reaction was executed for the last stage. In this stage, the compound **3 (a-c)** was treated with phthaloyl dichloride in THF yielded the formation of compound **4 (a-c)**.

As a conclusion, starting from N-Boc protected isoleucine, three N-Boc protected amide derivatives (**2a-c**), monoamide derivatives (**3a-c**) and bisamide derivatives (**4a-c**) were synthesized with good yields. The desired products (**4a-c**) and intermediate products could be valuable compounds for pharmaceutical materials. Since similar scaffold compounds have been used in drug production.

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### Supporting Information

Supporting information accompanies this paper on <http://www.acgpubs.org/journal/organic-communications>

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## Preparation of carboxyl and amino groups

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