*2.2.1 Synthesis of 1-substituted phenoxypropan-2-one (**3a-3m**).*[10]

A mixture of phenol **2**, KI (0.1 mol equiv) and anhydrous K_2CO_3 (1.5 mol equiv) in dry acetone (30 mL) was heated to 60 °C for 1 h. α-Chloroacetone **1** (1 mol equiv) was added dropwise, and the mixture was heated to 60 °C for 3 h. The mixture was filtered and the solvent was removed under vacuum. The residue was purified by column chromatography over silica gel, to give the corresponding products **3a-m**.

1-phenoxypropan-2-one 3a: light yellow oil, yield: 87.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.18 (m, 2H, Ar-**H**), 7.09 – 6.95 (m, 1H, Ar-**H**), 6.91 (d, *J* = 8.1 Hz, 2H, Ar-**H**), 4.55 (s, 2H, C**H**$_2$), 2.30 (s, 3H, C**H**$_3$).

1-(4-fluorophenoxy)propan-2-one 3b: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05 – 6.88 (m, 2H, Ar-**H**), 6.88 – 6.73 (m, 2H, Ar-**H**), 4.51 (s, 2H, C**H**$_2$), 2.26 (s, 3H, C**H**$_3$).

1-(2-fluorophenoxy)propan-2-one 3c: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 – 6.75 (m, 4H, Ar-**H**), 4.61 (s, 2H, C**H**$_2$), 2.32 (s, 3H, C**H**$_3$).

1-(4-chlorophenoxy)propan-2-one 3d: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 9.0 Hz, 2H, Ar-**H**), 6.87 – 6.82 (m, 2H, Ar-**H**), 4.56 (s, 2H, C**H**$_2$), 2.31 (s, 3H, C**H**$_3$).

1-(4-bromophenoxy)propan-2-one 3e: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.36 (m, 2H, Ar-**H**), 6.85 – 6.76 (m, 2H, Ar-**H**), 4.54 (s, 2H, C**H**$_2$), 2.30 (d, *J* = 5.3 Hz, 3H, C**H**$_3$).

1-(p-tolyloxy)propan-2-one 3f: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.2 Hz, 2H, Ar-**H**), 6.80 (d, *J* = 8.6 Hz, 2H, Ar-**H**), 4.52 (s, 2H, C**H**$_2$), 2.30 (d, *J* = 4.3 Hz, 3H, Ar-C**H**$_3$), 2.29 (s, 3H, C**H**$_3$).

1-(m-tolyloxy)propan-2-one 3g: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.8 Hz, 1H, Ar-**H**), 6.85 (d, *J* = 7.5 Hz, 1H, Ar-**H**), 6.75 (s, 1H, Ar-**H**), 6.71 (d, *J* = 8.2 Hz, 1H, Ar-**H**), 4.54 (s, 2H, C**H**$_2$), 2.36 (s, 3H, Ar-C**H**$_3$), 2.30 (s, 3H, C**H**$_3$).

1-(4-(tert-butyl)phenoxy)propan-2-one 3h: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.23 (m, 2H, Ar-**H**), 6.91 – 6.72 (m, 2H, Ar-**H**), 4.55 (s, 2H, C**H**$_2$), 2.31 (s, 3H, C**H**$_3$), 1.31 (s, 9H, *t*-Bu).

1-(4-(trifluoromethyl)phenoxy)propan-2-one 3i: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.7 Hz, 2H, Ar-**H**), 6.87 (d, *J* = 8.7 Hz, 2H, Ar-**H**), 4.53 (s, 2H, C**H**$_2$), 2.22 (s, 3H, C**H**$_3$).

1-(4-methoxyphenoxy)propan-2-one 3j: light yellow oil, ^{1}H NMR (300 MHz,

$CDCl_3$) δ 6.85 (s, 4H, Ar-**H**), 4.51 (s, 2H, C**H**$_2$), 3.79 (s, 3H, OC**H**$_3$), 2.29 (s, 3H, C**H**$_3$).

1-(2-methoxyphenoxy)propan-2-one 3k: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.87 (qd, *J* = 9.3, 2.6 Hz, 4H, Ar-**H**), 4.54 (s, 2H, C**H**$_2$), 3.78 (d, *J* = 1.1 Hz, 3H, OC**H**$_3$), 2.01 (d, *J* = 5.5 Hz, 3H, C**H**$_3$).

1-(4-(trifluoromethoxy)phenoxy)propan-2-one 3l: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.9 Hz, 2H, Ar-**H**), 6.91 – 6.87 (m, 2H, Ar-**H**), 4.57 (s, 2H, C**H**$_2$), 2.30 (s, 3H, C**H**$_3$).

1-(4-(benzyloxy)phenoxy)propan-2-one 3m: white solid, m.p.: 81-82 ^{o}C, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 – 7.19 (m, 5H, Ar-**H**), 6.91 – 6.67 (m, 4H, Ar-**H**), 4.94 (s, 2H, Ph-C**H**$_2$), 4.41 (s, 2H, CH_3COC**H**$_2$), 2.20 (s, 3H, C**H**$_3$).

*2.2.2 General Synthetic Procedures for 1- substituted phenoxypropan-2-one oxime (**4a-4m**).*[11]

Sodium hydroxide (30 mmol) was added in a single portion to a solution of the corresponding ketone **3** (20 mmol) and hydroxylamine hydrochloride (2.07 g, 30 mmol) in anhydrous ethanol (50 mL), and the resulting mixture was stirred in room temperature for 3h. The solvents were evaporated under reduced pressure and the residue treated with water (40 mL). The aqueous phase was extracted with AcOEt (3×30 mL) and the combined organic phases were dried over anhydrous $MgSO_4$. The solvents were removed under vacuum and the residue was purified by flash column chromatography.

1-phenoxypropan-2-one oxime 4a: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 – 7.20 (m, 2H, Ar-**H**), 7.06 – 6.87 (m, 3H, Ar-**H**), 4.97 + 4.59 (s + s, 2H, C**H**$_2$), 2.05 (d, *J* = 5.1 Hz, 3H, C**H**$_3$).

1-(4-fluorophenoxy)propan-2-one oxime 4b: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94 – 6.64 (m, 4H, Ar-**H**), 4.77 + 4.42 (s + s, 2H, C**H**$_2$), 1.92 – 1.84 (m, 3H, C**H**$_3$).

1-(2-fluorophenoxy)propan-2-one oxime 4c: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 – 6.78 (m, 4H, Ar-**H**), 4.89 + 4.55 (s + s, 2H, C**H**$_2$), 1.97 (d, *J* = 7.1 Hz, 3H, C**H**$_3$).

1-(4-chlorophenoxy)propan-2-one oxime 4d: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 2H, Ar-**H**), 6.93 – 6.83 (m, 2H, Ar-**H**), 4.92 + 4.56 (s + s, 2H, C**H**$_2$), 2.03 (s, 3H, C**H**$_3$).

1-(4-bromophenoxy)propan-2-one oxime 4e: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.0 Hz, 2H, Ar-**H**), 6.74 (d, *J* = 7.9 Hz, 2H, Ar-**H**), 4.63 (d, *J* = 142.3 Hz, 2H, C**H**$_2$), 1.90 (d, *J* = 8.0 Hz, 3H, C**H**$_3$).

1-(p-tolyloxy)propan-2-one oxime 4f: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.0 Hz, 2H, Ar-**H**), 6.88 (dd, *J* = 10.7, 4.6 Hz, 2H, Ar-**H**), 4.96 + 4.59 (s + s, 2H, C**H**$_2$), 2.33 (s, 3H, Ar-C**H**$_3$), 2.06 (d, *J* = 2.5 Hz, 3H, C**H**$_3$).

1-(m-tolyloxy)propan-2-one oxime 4g: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.13 (m, 1H, Ar-**H**), 6.79 (dt, *J* = 32.7, 13.9 Hz, 3H, Ar-**H**), 4.97 + 4.61 (s + s, 2H, C**H**$_2$), 2.38 (d, *J* = 3.1 Hz, 3H, Ar-C**H**$_3$), 2.07 (d, *J* = 6.1 Hz, 3H, C**H**$_3$).

1-(4-(tert-butyl)phenoxy)propan-2-one oxime 4h: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.24 (m, 2H, Ar-**H**), 7.00 – 6.79 (m, 2H, Ar-**H**), 4.99 + 4.61 (s + s, 2H, C**H**$_2$), 2.14 – 2.05 (m, 3H, C**H**$_3$), 1.40 – 1.32 (m, 9H, C(C**H**$_3$)$_3$).

1-(4-(trifluoromethyl)phenoxy)propan-2-one oxime 4i: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.6 Hz, 2H, Ar-**H**), 6.92 (d, *J* = 8.6 Hz, 2H, Ar-**H**), 4.70 (d, *J* = 140.0 Hz, 2H, C**H**$_2$), 1.93 (s, 3H, C**H**$_3$).

1-(4-methoxyphenoxy)propan-2-one oxime 4j: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.96 – 6.78 (m, 4H, Ar-**H**), 4.90 + 4.54 (s + s, 2H, C**H**$_2$), 3.78 (d, *J* = 1.1 Hz, 3H, OC**H**$_3$), 2.01 (d, *J* = 5.5 Hz, 3H, CH_2CNCH_3).

1-(2-methoxyphenoxy)propan-2-one oxime 4k: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 – 6.80 (m, 4H, Ar-**H**), 5.03 + 4.67 (s + s, 2H, C**H**$_2$), 3.91 – 3.82 (m, 3H, OC**H**$_3$), 2.12 – 1.99 (m, 3H, CH_2CNCH_3).

1-(4-(trifluoromethoxy)phenoxy)propan-2-one oxime 4l: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.12 (m, 2H, Ar-**H**), 6.99 – 6.86 (m, 2H, Ar-**H**), 4.91 + 4.59 (s + s, 2H, C**H**$_2$), 2.06 – 1.96 (m, 3H, C**H**$_3$).

1-(4-(benzyloxy)phenoxy)propan-2-one oxime 4m: white solid, m.p.: 92-94 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.23 (m, 5H, Ar-**H**), 6.88 – 6.72 (m, 4H, Ar-**H**), 4.93 (d, *J* = 2.6 Hz, 2H, Ph-C**H**$_2$), 4.43 (s, 2H, OC**H**$_2$C), 1.92 (s, 3H, C**H**$_3$).

*2.2.4 General procedure for the synthesis of the 1-substituted phenoxypropan-2-amine (**5a-5m**).*

Lithium aluminium hydride (45.3 mmol) was suspended in 50 mL of ether at 0 ^{o}C. The corresponding amines (18.1 mmol) was added slowly in small portions. The reaction mixture was heated to reflux for 3 h and then cooled to room temperature. NaOH solution was added slowly. Filtration and evaporation of the solvent gave

yellow solid. The residue was purified by flash column chromatography.

1-phenoxypropan-2-amine 5a: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 – 7.06 (m, 2H, Ar-**H**), 6.84 (dd, *J* = 15.7, 7.9 Hz, 3H, Ar-**H**), 3.77 (dd, *J* = 8.9, 4.0 Hz, 1H, C**H**$_2$), 3.58 (t, *J* = 8.3 Hz, 1H, C**H**$_2$), 3.24 (dq, *J* = 13.5, 6.6 Hz, 1H, C**H**), 1.73 (s, 2H, N**H**$_2$), 1.08 (d, *J* = 6.5 Hz, 3H, C**H**$_3$).

1-(4-fluorophenoxy)propan-2-amine 5b: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.96 – 6.84 (m, 2H, Ar-**H**), 6.74 (m, 2H, Ar-**H**), 3.85 – 3.69 (m, 1H, C**H**$_2$), 3.59 – 3.50 (m, 1H, C**H**$_2$), 3.33 – 3.19 (m, 1H, C**H**), 2.68 (s, 2H, N**H**$_2$), 1.09 (dd, *J* = 12.5, 7.5 Hz, 3H, CHC**H**$_3$).

1-(2-fluorophenoxy)propan-2-amine 5c: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 – 6.83 (m, 4H, Ar-**H**), 3.99 – 3.88 (m, 1H, C**H**$_2$), 3.81 – 3.65 (m, 1H, C**H**$_2$), 3.40 (dq, *J* = 13.4, 6.6 Hz, 1H, C**H**), 2.21 (s, 1H, N**H**$_2$), 1.20 (d, *J* = 6.0 Hz, 3H, C**H**$_3$).

1-(4-chlorophenoxy)propan-2-amine 5d: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.08 (m, 2H, Ar-**H**), 6.76 – 6.68 (m, 2H, Ar-**H**), 3.74 (dt, *J* = 9.4, 4.8 Hz, 1H, C**H**$_2$), 3.61 – 3.48 (m, 1H, C**H**$_2$), 3.32 – 3.16 (m, 1H, C**H**), 2.25 (s, 2H, N**H**$_2$), 1.11 – 1.02 (m, 3H, C**H**$_3$).

1-(4-bromophenoxy)propan-2-amine 5e: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 9.0 Hz, 2H, Ar-**H**), 6.69 (s, 2H, Ar-**H**), 3.73 (s, 1H, C**H**$_2$), 3.57 (dd, *J* = 8.7, 7.8 Hz, 1H, C**H**$_2$), 3.26 (d, *J* = 7.5 Hz, 2H, C**H**), 1.09 (d, *J* = 6.5 Hz, 3H, C**H**$_3$).

1-(p-tolyloxy)propan-2-amine 5f: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.3 Hz, 2H, Ar-**H**), 6.78 (t, *J* = 14.5 Hz, 2H, Ar-**H**), 3.82 (dt, *J* = 20.3, 10.2 Hz, 1H, C**H**$_2$), 3.64 (t, *J* = 8.3 Hz, 1H, C**H**$_2$), 3.32 (dq, *J* = 13.5, 6.6 Hz, 1H, C**H**), 2.29 (s, 3H, Ar-C**H**$_3$), 2.06 (s, 2H, N**H**$_2$),1.16 (d, *J* = 6.5 Hz, 3H, CHC**H**$_3$).

1-(m-tolyloxy)propan-2-amine 5g: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (q, *J* = 7.7 Hz, 1H, Ar-**H**), 6.85 – 6.41 (m, 3H, Ar-**H**), 3.86 – 3.70 (m, 1H, C**H**$_2$), 3.58 – 3.52 (m, 1H, C**H**$_2$), 3.34 – 3.13 (m, 1H, C**H**), 2.23 (d, *J* = 4.8 Hz, 3H, Ar-C**H**$_3$), 1.97 (s, 2H, N**H**$_2$), 1.08 (d, *J* = 6.5 Hz, 3H, CHC**H**$_3$).

1-(4-(tert-butyl)phenoxy)propan-2-amine 5h: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, 2H, Ar-**H**), 6.77 (d, 2H, Ar-**H**), 3.85 – 3.73 (m, 1H, C**H**$_2$), 3.58 (dt, *J* = 19.9, 9.9 Hz, 1H, C**H**$_2$), 3.33 – 3.18 (m, 1H, C**H**), 2.50 (s, 2H, N**H**$_2$), 1.22 (s, 9H, C(C**H**$_3$)$_3$), 1.10 (d, *J* = 6.5 Hz, 3H, CHC**H**$_3$).

1-(4-(trifluoromethyl)phenoxy)propan-2-amine 5i: light yellow oil, ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.4 Hz, 2H, Ar-**H**), 6.95 (t, *J* = 18.3 Hz, 2H, Ar-**H**), 3.91 (d, *J* = 12.8 Hz, 1H, C**H**$_2$), 3.74 (t, *J* = 8.2 Hz, 1H, C**H**$_2$), 3.39 (s, 1H, C**H**$_2$), 1.82 (s, 2H, N**H**$_2$), 1.20 (d, *J* = 6.5 Hz, 3H, CHC**H**$_3$).

1-(4-methoxyphenoxy)propan-2-amine 5j: light yellow oil, ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 – 6.74 (m, 4H, Ar-**H**), 3.75 (dd, *J* = 8.9, 4.2 Hz, 1H, C**H**$_2$), 3.70 (s, 3H, OC**H**$_3$), 3.61 – 3.52 (m, 1H, C**H**$_2$), 3.34 – 3.19 (m, 1H, C**H**), 1.56 (s, 2H, N**H**$_2$), 1.10 (d, *J* = 6.5 Hz, 3H, CHC**H**$_3$).

1-(2-methoxyphenoxy)propan-2-amine 5k: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 – 6.72 (m, 4H, Ar-**H**), 3.83 (ddd, *J* = 12.2, 9.0, 7.2 Hz, 1H, C**H**$_2$**)**, 3.73 (s, 1H, OC**H**$_3$), 3.64 – 3.53 (m, 1H, C**H**$_2$), 3.36 – 3.18 (m, 1H, C**H**), 2.05 (s, 2H, N**H**$_2$), 1.05 (d, *J* = 6.4, 1.6 Hz, 3H,CHC**H**$_3$).

1-(4-(trifluoromethoxy)phenoxy)propan-2-amine 5l: light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 8.8 Hz, 2H,, Ar-**H**), 6.91 (t, *J* = 9.4 Hz, 2H, Ar-**H**), 3.87 (dd, *J* = 8.8, 4.0 Hz, 1H, C**H**$_2$), 3.69 (t, *J* = 8.2 Hz, 1H, C**H**$_2$), 3.43 – 3.30 (m, 1H, C**H**), 2.09 (d, *J* = 59.6 Hz, 2H, N**H**$_2$), 1.20 (t, *J* = 6.8 Hz, 3H, C**H**$_3$).

1-(4-(benzyloxy)phenoxy)propan-2-amine 5m: white solid, m.p.: 75-76 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.19 (m, 5H, Ar-**H**), 6.97 – 6.81 (m, 4H, Ar-**H**), 5.04 (s, 2H, ArC**H**$_2$), 3.94 – 3.81 (m, 1H, CHC**H**$_2$), 3.68 – 3.49 (m, 1H, CHC**H**$_2$), 3.35 (dq, *J* = 13.7, 6.7 Hz, 1H, NH_2C**H**), 2.03 (d, *J* = 30.0 Hz, 2H, N**H**$_2$), 1.29 – 1.12 (m, 3H, C**H**$_3$).

*2.2.5 Procedure for the synthesis of the 4-(2-aminopropoxy)phenol (**5n**).*

Amine **5m** (2.0 g, 7.78 mmol) was dissolved in 50 mL of ethanol, the solution was flushed with N_2 and the palladium on carbon (0.2 grams, 10 percent) were added. The mixture was treated with 15 atm of H_2 for 12 hours. The catalyst was filtered off, concentrated to afford a yellow solid. The solid was purified by flash column chromatography, yield: 73.1%, m.p.: 72 – 74 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.69 – 6.42 (m, 4H, Ar-**H**), 4.56 (s, 2H, N**H**$_2$), 3.68 (ddd, *J* = 28.8, 15.9, 10.9 Hz, 1H, C**H**$_2$), 3.47 (dd, *J* = 11.1, 5.8 Hz, 1H, C**H**$_2$), 3.22 (dd, *J* = 22.0, 10.8 Hz, 1H, C**H**), 1.11 (dt, *J* = 17.7, 8.8 Hz, 3H, C**H**$_3$).

*2.2.6 General procedure for the synthesis of isopropyl ((2S)-3-methyl-1-oxo-1-((1-substituted phenoxypropan-2-yl)amino)butan-2-yl)carbamate (7**a-n**).*

4-methylmorpholine (6 mmol) was added to a solution of (S)-2-

((isopropoxycarbonyl)amino)-3-methylbutanoic acid (5 mmol) in anhydrous tetrahydrofuran (20 mL) followed by ethyl chloroformate (5 mmol), and the resulting mixture was stirred at 0 °C for 1 h. A solution of the corresponding amines **5** (6 mmol) in anhydrous tetrahydrofuran (10 mL) was then added to the reaction in a drop-wise manner, and the resulting mixture was stirred at room temperature for 10 h. The reaction mixture was then filtered and the filtrate concentrated under vacuum to give a residue, which was extracted with ethyl acetate (3 × 20 mL). The combined organics were washed with brine (2 × 15 mL), dried over anhydrous sodium sulfate, and concentrated *in vacuo* to give compound **7**. The solid was purified by flash column chromatography.

isopropyl ((2S)-3-methyl-1-oxo-1-((1-phenoxypropan-2-yl)amino)butan-2-yl)carbamate 7a: White solid; m.p.: 89 – 91 ^{o}C, yield:78.5%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.23 (m, 2H, Ar-**H**), 7.04 – 6.85 (m, 3H, Ar-**H**), 6.25 (t, *J* = 8.6 Hz, 1H, CHCON**H**), 5.24 (dd, *J* = 25.3, 8.1 Hz, 1H, OCON**H**), 4.89 (dt, *J* = 12.4, 6.1 Hz, 1H, OC**H**$(CH_3)_2$), 4.41 (d, *J* = 3.3 Hz, 1H, CH_2C**H**CH_3), 3.95 (qd, *J* = 9.4, 4.4 Hz, 3H, OCONHC**H** + OC**H**$_2$), 2.26 – 2.00 (m, 1H, CHC**H**$(CH_3)_2$), 1.33 (dd, *J* = 6.8, 3.4 Hz, 3H, CHC**H**$_3$), 1.23 (dd, *J* = 8.1, 6.4 Hz, 6H, OCH(C**H**$_3)_2$), 1.03 – 0.84 (m, 6H, CHCH(C**H**$_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.66, 158.50, 156.28, 129.46, 121.13, 114.73, 70.30, 68.60, 60.37, 44.71, 31.07, 22.07, 19.24, 17.59; HRMS (MALDI) m/z Calcd for $C_{18}H_{28}N_2O_4Na^+$ $[M + Na]^+$ 359.1941, found 359.1945.

isopropyl ((2S)-1-((1-(4-fluorophenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7b: White solid, m.p.: 97 – 99 ^{o}C, yield: 80.2%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (t, *J* = 8.6 Hz, 2H, Ar-**H**), 6.88 – 6.80 (m, 2H, Ar-**H**), 6.29 (s, 1H, CHCON**H**), 5.26 (dd, *J* = 18.0, 7.8 Hz, 1H, OCON**H**), 4.96 – 4.81 (m, 1H, OC**H**$(CH_3)_2$), 4.39 (s, 1H, CH_2C**H**CH_3), 3.98 – 3.92 (m, 1H, OCONHC**H**), 3.91 (t, *J* = 6.3 Hz, 2H, OC**H**$_2$), 2.18 – 2.03 (m, 1H, CHC**H**$(CH_3)_2$), 1.38 – 1.26 (m, 3H, CHC**H**$_3$), 1.26 – 1.18 (m, 6H, OCH(C**H**$_3)_2$), 1.04 – 0.88 (m, 6H, CHCH(C**H**$_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.94, 158.63, 156.28, 154.70, 116.00, 115.54, 71.04, 68.60, 60.30, 44.63, 31.07, 22.07, 19.25, 17.54; HRMS (MALDI) m/z Calcd for $C_{18}H_{27}FN_2O_4Na^+$ $[M + Na]^+$ 377.1847, found 377.1842.

isopropyl ((2S)-1-((1-(2-fluorophenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7c: White solid, m.p.: 115 – 117 ^{o}C, yield: 83.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (dd, *J* = 17.2, 9.0 Hz, 2H, Ar-**H**), 6.96 (dt, *J* = 13.1,

7.9 Hz, 2H, Ar-**H**), 6.31 (d, *J* = 6.7 Hz, 1H, CHCON**H**), 5.22 (d, *J* = 20.3 Hz, 1H, OCON**H**), 4.96 – 4.84 (m, 1H, OC**H**$(CH_3)_2$), 4.42 (d, *J* = 3.7 Hz, 1H, CH_2C**H**CH_3), 4.04 (d, *J* = 2.9 Hz, 2H, OC**H**$_2$), 3.99 (d, *J* = 7.0 Hz, 1H, OCONHC**H**), 2.14 (ddd, *J* = 25.5, 14.9, 8.4 Hz, 1H, CHC**H**$(CH_3)_2$), 1.37 (d, *J* = 6.8 Hz, 3H, CHC**H**$_3$), 1.23 (d, *J* = 7.0 Hz, 6H, OCH(C**H**$_3)_2$), 1.00 – 0.87 (m, 6H, CHCH(C**H**$_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.82, 156.28, 154.13, 151.60, 146.74, 124.41, 121.72, 116.30, 115.58, 72.00, 68.60, 60.22, 44.76, 31.03, 22.05, 19.13, 17.39; HRMS (MALDI) m/z Calcd for $C_{18}H_{27}FN_2O_4Na^+$ $[M + Na]^+$ 377.1847, found 377.1843.

isopropyl ((2S)-1-((1-(4-chlorophenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7d: White solid, m.p.: 108 – 110 °C, yield: 82.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.8 Hz, 2H, Ar-**H**), 6.82 (dd, *J* = 8.9, 2.0 Hz, 2H, Ar-**H**), 6.38 (s, 1H, CHCON**H**), 5.40 – 5.24 (m, 1H, OCON**H**), 4.88 (dd, *J* = 12.3, 6.2 Hz, 1H, OC**H**$(CH_3)_2$), 4.38 (s, 1H, CH_2C**H**CH_3), 3.98 – 3.85 (m, 3H, OCONHC**H** + OC**H**$_2$), 2.18 – 1.99 (m, 1H, CHC**H**$(CH_3)_2$), 1.30 (t, *J* = 6.7 Hz, 3H, CHC**H**$_3$), 1.27 – 1.14 (m, 6H, OCH(C**H**$_3)_2$), 1.00 – 0.87 (m, 6H, CHCH(C**H**$_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.09, 157.32, 156.32, 129.37, 125.99, 115.77, 70.66, 68.59, 60.38, 44.56, 31.10, 22.05, 19.16, 17.36; HRMS (MALDI) m/z Calcd for $C_{18}H_{27}ClN_2O_4Na^+$ $[M + Na]^+$ 393.1552, found 393.1548.

isopropyl ((2S)-1-((1-(4-bromophenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7e: White solid, m.p.: 142 – 144 °C; yield: 84.7%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 6.8 Hz, 2H, Ar-**H**), 6.75 (d, *J* = 8.8 Hz, 2H, Ar-**H**), 6.13 (s, 1H, CHCON**H**), 5.11 (s, 1H, OCON**H**), 4.85 (s, 1H, OC**H**$(CH_3)_2$), 4.36 (s, 1H, CH_2C**H**CH_3), 3.88 (s, 3H, OCONHC**H** + OC**H**$_2$), 2.10 (s, 1H, CHC**H**$(CH_3)_2$), 1.28 (d, *J* = 6.4 Hz, 3H, CHC**H**$_3$), 1.21 – 1.13 (m, 6H, OCH(C**H**$_3)_2$), 0.91 (dd, *J* = 16.0, 8.2 Hz, 6H, CHCH(C**H**$_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.06, 157.70, 156.32, 132.32, 116.30, 113.27, 70.60, 68.59, 60.34, 44.54, 31.14, 22.07, 19.25, 17.91, 17.49; HRMS (ESI) m/z Calcd for $C_{18}H_{28}BrN_2O_4^+$ $[M + H]^+$ 415.1227, found 415.1221.

isopropyl ((2S)-3-methyl-1-oxo-1-((1-(p-tolyloxy)propan-2-yl)amino)butan-2-yl)carbamate 7f: White solid; m.p.: 82 – 84 °C, yield: 83.8%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.2 Hz, 2H, Ar-**H**), 6.81 (dd, *J* = 8.5, 3.1 Hz, 2H, Ar-**H**), 6.15 (d, *J* = 23.9 Hz, 1H, CHCON**H**), 5.20 (d, *J* = 23.6 Hz, 1H, OCON**H**), 4.97 – 4.82 (m, 1H, OC**H**$(CH_3)_2$), 4.40 (d, *J* = 3.6 Hz, 1H, CH_2C**H**CH_3), 4.00 – 3.87 (m, 3H, OCONHC**H** + OC**H**$_2$), 2.30 (s, 3H, Ar-C**H**$_3$), 2.19 – 2.02 (m, 1H, CHC**H**$(CH_3)_2$), 1.33 (d, *J* = 6.8

Hz, 3H, CHC**H**$_3$), 1.27 – 1.16 (m, 6H, OCH(C**H**$_3$)$_2$), 1.03 – 0.88 (m, 6H, CHCH(C**H**$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.03, 156.49, 156.35, 130.28, 129.93, 114.37, 70.52, 68.50, 60.33, 44.70, 31.29, 22.08, 20.48, 19.24, 17.56; HRMS (MALDI) m/z Calcd for $C_{19}H_{30}N_2O_4Na^+$ $[M + Na]^+$ 373.2098, found 373.2095.

isopropyl ((2S)-3-methyl-1-oxo-1-((1-(m-tolyloxy)propan-2-yl)amino)butan-2-yl)carbamate 7g: White solid, m.p.: 82 – 84 °C, yield: 87.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (t, *J* = 7.7 Hz, 1H, Ar-**H**), 6.80 (d, *J* = 7.6 Hz, 1H, Ar-**H**), 6.72 (d, *J* = 9.9 Hz, 2H, Ar-**H**), 6.27 (s, 1H, CHCON**H**), 5.27 (d, *J* = 24.4 Hz, 1H, OCON**H**), 4.98 – 4.81 (m, 1H, OC**H**(CH$_3$)$_2$), 4.40 (s, 1H, CH$_2$C**H**CH$_3$), 3.94 (d, *J* = 11.3 Hz, 3H, OCONHC**H** + OC**H**$_2$), 2.35 (s, 3H, Ar-C**H**$_3$), 2.12 (d, *J* = 35.0 Hz, 1H, CHC**H**(CH$_3$)$_2$), 1.39 – 1.27 (m, 3H, CHC**H**$_3$), 1.24 (t, *J* = 6.7 Hz, 6H, OCH(C**H**$_3$)$_2$), 1.04 – 0.88 (m, 6H, CHCH(C**H**$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.82, 158.60, 156.29, 139.59, 129.26, 121.80, 115.36, 111.36, 70.41, 60.35, 56.02, 44.72, 31.07, 22.22, 21.51, 19.25, 17.54; HRMS (MALDI) m/z Calcd for $C_{19}H_{30}N_2O_4Na^+$ $[M + Na]^+$ 373.2098, found 373.2094.

isopropyl ((2S)-1-((1-(4-(tert-butyl)phenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7h: White solid, m.p.: 93 – 95 °C, yield: 83.6%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (t, *J* = 7.7 Hz, 2H, Ar-**H**), 6.87 (t, *J* = 13.3 Hz, 2H, Ar-**H**), 6.34 (s, 1H, CHCON**H**), 5.32 (s, 1H, OCON**H**), 5.03 – 4.81 (m, 1H, OC**H**(CH$_3$)$_2$), 4.41 (s, 1H, CH$_2$C**H**CH$_3$), 4.05 – 3.84 (m, 3H, OCONHC**H** + OC**H**$_2$), 2.08 (d, *J* = 6.3 Hz, 1H, CHC**H**(CH$_3$)$_2$), 1.32 (s, 12H, CHC**H**$_3$+C(C**H**$_3$)$_3$), 1.29 – 1.17 (m, 6H, OCH(C**H**$_3$)$_2$), 1.03 – 0.90 (m, 6H, CHCH(C**H**$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.87, 155.29, 142.78, 125.25, 112.93, 69.38, 67.49, 59.29, 43.66, 33.05, 30.48, 30.21, 21.04, 18.16, 16.49; HRMS (MALDI) m/z Calcd for $C_{22}H_{36}N_2O_4Na^+$ $[M + Na]^+$ 415.2567, found 415.2568.

isopropyl ((2S)-3-methyl-1-oxo-1-((1-(4-(trifluoromethyl)phenoxy)propan-2-yl)amino)butan-2-yl)carbamate 7i: White solid, m.p.: 134-135 °C, yield: 82.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.0 Hz, 2H, Ar-**H**), 6.90 (s, 2H, Ar-**H**), 6.05 (s, 1H, CHCON**H**), 5.09 (s, 1H, OCON**H**), 4.80 (s, 1H, OC**H**(CH$_3$)$_2$), 4.35 (s, 1H, CH$_2$C**H**CH$_3$), 3.92 (s, 1H, OCONHC**H**), 3.84 (s, 2H, OC**H**$_2$), 2.01 (s, 1H, CHC**H**(CH$_3$)$_2$), 1.25 (d, *J* = 6.2 Hz, 3H, CHC**H**$_3$), 1.14 (s, 6H, OCH(C**H**$_3$)$_2$), 0.85 (s, 6H, CHCH(C**H**$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.11, 159.97, 155.32, 125.96, 122.44, 122.11, 113.44, 69.49, 67.60, 59.36, 43.45, 30.05, 21.02, 18.13, 17.01, 16.33; HRMS (ESI) m/z Calcd for $C_{19}H_{28}F_3N_2O_4^+$ $[M + H]^+$ 405.1996, found 405.1994.

isopropyl ((2S)-1-((1-(4-methoxyphenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7j: White solid, m.p.: 133 - 135 °C, yield: 85.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (d, *J* = 4.3 Hz, 4H, Ar-**H**), 6.32 (d, *J* = 6.7 Hz, 1H, CHCON**H**), 5.28 (d, *J* = 21.7 Hz, 1H, OCON**H**), 4.90 (d, *J* = 5.3 Hz, 1H, OC**H**$(CH_3)_2$), 4.38 (s, 1H, CH_2C**H**CH_3), 3.98 (s, 1H, OCONHC**H**), 3.91 (s, 2H, OC**H**$_2$), 3.79 (d, *J* = 6.0 Hz, 3H, OC**H**$_3$), 2.12 (d, *J* = 26.6 Hz, 1H, CHC**H**$(CH_3)_2$), 1.32 (d, *J* = 4.4 Hz, 3H, CHC**H**$_3$), 1.23 (s, 6H, OCH(C**H**$_3)_2$), 1.03 – 0.89 (m, 6H, CHCH(C**H**$_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.91, 156.29, 154.08, 152.74, 115.57, 114.67, 70.95, 68.56, 60.15, 55.59, 44.64, 31.18, 22.09, 19.18, 17.77; HRMS (MALDI) m/z Calcd for $C_{19}H_{30}N_2O_5Na^+$ $[M + Na]^+$ 389.2047, found 389.2050.

isopropyl ((2S)-1-((1-(2-methoxyphenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7k: White solid, m.p.: 113 - 115 °C, yield: 83.2%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 – 6.87 (m, 4H, Ar-**H**), 6.49 (dd, *J* = 48.9, 7.3 Hz, 1H, CHCON**H**), 5.29 (d, *J* = 8.9 Hz, 1H, OCON**H**), 4.91 (dd, *J* = 12.1, 6.0 Hz, 1H, OC**H**$(CH_3)_2$), 4.38 (d, *J* = 3.6 Hz, 1H, CH_2C**H**CH_3), 4.11 – 4.00 (m, 1H, OCONHC**H**), 3.97 (dd, *J* = 9.4, 4.6 Hz, 2H, OC**H**$_2$), 3.88 (s, 3H, OC**H**$_3$), 2.24 – 2.00 (m, 1H, CHC**H**$(CH_3)_2$), 1.36 (d, *J* = 6.7 Hz, 3H, CHC**H**$_3$), 1.25 (t, *J* = 7.1 Hz, 6H, OCH(C**H**$_3)_2$), 1.04 – 0.87 (m, 6H, CHCH(C**H**$_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.85, 156.24, 149.92, 148.26, 122.20, 121.04, 115.33, 112.15, 72.57, 68.50, 60.26, 55.85, 45.12, 31.41, 22.09, 19.19, 17.60; HRMS (MALDI) m/z Calcd for $C_{19}H_{30}N_2O_5Na^+$ $[M + Na]^+$ 389.2047, found 389.2041.

isopropyl ((2S)-3-methyl-1-oxo-1-((1-(4-(trifluoromethoxy)phenoxy)propan-2-yl)amino)butan-2-yl)carbamate 7l: White solid, m.p.: 133 - 135°C, yield: 82.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.7 Hz, 2H, Ar-**H**), 6.91 (dd, *J* = 9.2, 2.5 Hz, 2H, Ar-**H**), 6.23 (s, 1H, CHCON**H**), 5.23 (s, 1H, OCON**H**), 4.89 (dt, *J* = 12.3, 6.2 Hz, 1H, OC**H**$(CH_3)_2$), 4.42 (s, 1H, CH_2C**H**CH_3), 4.05 – 3.88 (m, 3H, OCONHC**H** + OC**H**$_2$), 2.23 – 2.01 (m, 1H, CHC**H**$(CH_3)_2$), 1.39 – 1.26 (m, 3H, CHC**H**$_3$), 1.24 (dd, *J* = 9.0, 6.4 Hz, 6H, OCH(C**H**$_3)_2$), 0.96 (dd, *J* = 15.7, 7.9 Hz, 6H, CHCH(C**H**$_3)_2$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.20, 157.01, 156.37, 142.95, 122.48, 121.81, 119.27, 115.33, 115.25, 70.78, 68.56, 60.37, 44.52, 31.14, 21.92, 19.15, 18.08, 17.33; HRMS (MALDI) m/z Calcd for $C_{19}H_{27}F_3N_2O_5Na^+$ $[M + Na]^+$ 443.1764, found 443.2155.

isopropyl ((2S)-1-((1-(4-(benzyloxy)phenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7m: White solid, m.p.: 140 - 142°C, yield: 84.5%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.31 (m, 5H, Ar-**H**), 6.93 (d, *J* = 8.9 Hz, 2H, Ar-**H**),

6.85 (dd, *J* = 9.2, 3.3 Hz, 2H, Ar-**H**), 6.14 (d, *J* = 22.1 Hz, 1H, CHCON**H**), 5.22 (s, 1H, OCON**H**), 5.05 (s, 2H, ArC$\mathbf{H}_2$), 4.98 – 4.84 (m, 1H, OC**H**$(CH_3)_2$), 4.40 (s, 1H, CH_2C**H**CH_3), 4.03 – 3.81 (m, 3H, OCONHC**H** + OC$\mathbf{H}_2$), 2.14 (d, *J* = 35.1 Hz, 1H, CHC**H**$(CH_3)_2$), 1.33 (d, *J* = 6.8 Hz, 3H, CHC$\mathbf{H}_3$), 1.30 – 1.20 (m, 6H, OCH(C$\mathbf{H}_3)_2$), 1.03 – 0.90 (m, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.85, 156.28, 153.27, 152.93, 137.21, 128.57, 127.92, 127.47, 115.87, 115.54, 71.09, 70.66, 68.59, 60.36, 44.76, 31.11, 22.08, 19.25, 17.52; HRMS (MALDI) m/z Calcd for $C_{25}H_{34}N_2O_5Na^+$ $[M + Na]^+$ 465.2360, found 465.2361.

isopropyl ((2S)-1-((1-(4-hydroxyphenoxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 7n: White solid, m.p.: 106 - 108^{o}C, yield: 83.3%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (d, *J* = 8.8 Hz, 2H, Ar-**H**), 6.81 (d, *J* = 8.8 Hz, 2H, Ar-**H**), 6.11 (s, 1H, CHCON**H**), 5.10 (d, *J* = 8.4 Hz, 1H, OCON**H**), 4.92 – 4.75 (m, 1H, OC**H**$(CH_3)_2$), 4.31 (s, 1H, CH_2C**H**CH_3), 3.84 (t, *J* = 7.3 Hz, 3H, OCONHC**H** + OC$\mathbf{H}_2$), 2.27 (d, *J* = 5.4 Hz, 1H, CHC**H**$(CH_3)_2$), 1.26 – 1.09 (m, 9H, CHC$\mathbf{H}_3$ + OCH(C$\mathbf{H}_3)_2$), 0.98 – 0.78 (m, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.95, 156.44, 156.20, 144.19, 122.24, 115.23, 70.79, 68.75, 58.80, 44.65, 31.47, 22.06, 19.09, 17.53; HRMS (MALDI) m/z Calcd for $C_{18}H_{28}N_2O_5Na^+$ $[M + Na]^+$ 375.1890, found 375.1896.

*2.2.7 Procedure for the synthesis of isopropyl ((2S)-3-methyl-1-oxo-1-((1-(4-(prop-2-yn-1-yloxy)phenoxy)propan-2-yl)amino)butan-2-yl)carbamate (**7o**).*

To a solution of compound **7n** (2.83 mmol) in dry acetone (30 mL), excess anhydrous K_2CO_3 (4.26 mmol) was added and the mixture was stirred for 1 h. To the mixture, propargyl bromide (4.3 mmol) was added over a period of 30 min. The resulting mixture was refluxed over a period of 10 h. The reaction mixture was then cooled, filtered and filtrate was evaporated. The brown oily residue was dissolved in methylene chloride and then solution was washed twice with water (50 mL). Organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under vacuo. The crude product was purified by flash column chromatography.

white solid, m.p.: 81 - 83^{o}C, yield: 80.9%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 – 6.69 (m, 4H, Ar-**H**), 6.03 (s, 1H, CHCON**H**), 5.08 (s, 1H, OCON**H**), 4.90 – 4.73 (m, 1H, OC**H**$(CH_3)_2$), 4.57 (d, *J* = 1.9 Hz, 2H, HCCC$\mathbf{H}_2$), 4.29 (s, 1H, CH_2C**H**CH_3), 3.82 (dd,

J = 13.8, 6.6 Hz, 3H, OCONHC**H** + OC**H**$_2$), 2.44 (s, 1H, OCH$_2$CC**H**), 2.06 (s, 1H, CHC**H**(CH$_3$)$_2$), 1.24 (d, *J* = 6.8 Hz, 3H, CHC**H**$_3$), 1.15 (t, *J* = 6.2 Hz, 6H, OCH(C**H**$_3$)$_2$), 0.92 – 0.77 (m, 6H, CHCH(C**H**$_3$)$_2$); ^{13}C NMR (101 MHz, CDCl$_3$) δ 170.95, 156.30, 153.37, 152.06, 116.13, 115.39, 78.82, 75.41, 71.02, 68.58, 60.26, 56.54, 44.68, 31.37, 21.96, 19.18, 17.56; HRMS (MALDI) m/z Calcd for $C_{21}H_{30}N_2O_5Na^+$ [M + Na]$^+$ 413.2047, found 413.2049.

*2.2.8 Procedure for the synthesis of (S)-2-aminopropan-1-ol (**9**).* [12]

Lithium aluminium hydride (11 g, 0.289 mol) was suspended in 300 mL of THF at 0 ^{o}C. L-Alanine (11.8 g, 0.132 mol) was added slowly in small portions. The reaction mixture was heated to reflux overnight and then cooled to room temperature. Saturated K_2CO_3 solution was added slowly. Filtration and evaporation of the solvent gave light yellow oil (0.66 g), yield: 78.3%。^{1}H NMR (400 MHz, CDCl$_3$) δ 3.48 (d, *J* = 3.9 Hz, 1H, C**H**$_2$), 3.29 – 3.15 (m, 1H, C**H**$_2$), 2.96 (s, 1H, C**H**), 2.74 (s, 2H, N**H**$_2$), 2.65 (s, 1H, O**H**), 1.00 (d, *J* = 6.9 Hz, 3H, C**H**$_3$).

*2.2.9 Procedure for the synthesis of isopropyl ((S)-1-(((S)-1-hydroxypropan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (**10**).*

The intermediate **10** was prepared according to the reported methods of chapter 2.2.6.

White solid, yield: 82.1%, m.p.： 179-181 ^{o}C; ^{1}H NMR (400 MHz, CDCl$_3$) δ 6.37 (d, *J* = 6.8 Hz, 1H, CHCON**H**), 5.31 (d, *J* = 7.4 Hz, 1H, OCON**H**), 5.02 – 4.77 (m, 1H, OC**H**(CH$_3$)$_2$), 4.09 (dt, *J* = 10.9, 6.8 Hz, 1H, CH$_2$C**H**CH$_3$), 3.93 (dt, *J* = 9.8, 5.0 Hz, 1H, OCONHC**H**), 3.69 (dd, *J* = 11.1, 3.6 Hz, 1H, OC**H**$_2$CH), 3.56 (dd, *J* = 11.1, 5.8 Hz, 1H, OC**H**$_2$CH), 2.59 (s, 1H, O**H**), 2.12 (d, *J* = 6.6 Hz, 1H, CHC**H**(CH$_3$)$_2$), 1.26 (dd, *J* = 6.2, 3.6 Hz, 6H, OCH(C**H**$_3$)$_2$), 1.21 (d, *J* = 6.9 Hz, 3H, CHC**H**$_3$), 1.04 – 0.93 (m, 6H, CHCH(C**H**$_3$)$_2$); ^{13}C NMR (101 MHz, CDCl$_3$) δ 171.97, 156.51, 68.84, 66.65, 60.61, 47.83, 30.88, 22.06, 19.26, 17.95, 16.86; HRMS (ESI) m/z Calcd for $C_{12}H_{25}N_2O_4^+$ [M + H]$^+$ 261.1809, found 261.1810.

*2.2.10 Procedure for the synthesis of isopropyl ((S)-1-(((S)-1-(substituted benzyloxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate (**11**).*

To a suspension of NaH (0.23 g, 0.57 mmol, 60%) in DMF (10 mL), was added the intermediate **10** (1.0 g, 3.8 mmol) in portions at -10 ^{o}C . The mixture was stirred for

20 mins, a solution of corresponding benzyl bromide (5.7 mmol) in DMF (10 mL) was added dropwisely to the mixture in 30 mins. After stirred for another 6 h at -10 °C, the mixture was poured into 200 mL ice water and white solid was precipitated. The solid was purified by recrystallization from ethanol to give compound **11**.

isopropyl ((S)-1-(((S)-1-(benzyloxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 11a: white solid, m.p.: 145-147 °C, yield: 68.9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.19 (m, 5H, Ar-**H**), 6.12 (s, 1H, CHCON**H**), 5.23 (s, 1H, OCON**H**), 4.90 (s, 1H, OC**H**$(CH_3)_2$), 4.53 (s, 2H, Ar-C$\mathbf{H}_2$), 4.22 (s, 1H, CH_2C**H**CH_3), 3.91 (s, 1H, OCONHC**H**), 3.43 (s, 2H, OC$\mathbf{H}_2$CH), 2.08 (s, 1H, CHC**H**$(CH_3)_2$), 1.23 (t, *J* = 7.2 Hz, 9H, CHC$\mathbf{H}_3$ + OCH(C$\mathbf{H}_3)_2$), 1.01 – 0.87 (m, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, CDCl3) δ 170.65, 156.27, 137.99, 128.43, 127.75, 127.66, 73.17, 72.84, 68.50, 60.30, 44.96, 31.24, 22.09, 19.18, 17.70; HRMS (ESI) m/z Calcd for $C_{19}H_{31}N_2O_4^+$ [M + H]$^+$ 351.2278, found 351.2277.

isopropyl ((S)-1-(((S)-1-((4-fluorobenzyl)oxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 11b: white solid, m.p.: 139-141 °C, yield: 65.5%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 6.9 Hz, 2H, Ar-**H**), 7.05 (t, *J* = 8.6 Hz, 2H, Ar-**H**), 6.01 (s, 1H, CHCON**H**), 5.16 (s, 1H, OCON**H**), 4.89 (s, 1H, OC**H**$(CH_3)_2$), 4.49 (s, 2H, Ar-C$\mathbf{H}_2$), 4.23 (s, 1H, CH_2C**H**CH_3), 3.88 (s, 1H, OCONHC**H**), 3.45 (d, *J* = 11.6 Hz, 2H, OC$\mathbf{H}_2$CH), 2.09 (s, 1H, CHC**H**$(CH_3)_2$), 1.24 (d, *J* = 13.4 Hz, 9H, CHC$\mathbf{H}_3$ + OCH(C$\mathbf{H}_3)_2$), 1.00 – 0.82 (m, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.61, 163.61, 161.16, 156.26, 133.71, 129.37, 115.41, 72.83, 72.46, 68.55, 60.35, 44.90, 31.14, 22.08, 19.18, 17.70; HRMS (ESI) m/z Calcd for $C_{19}H_{30}FN_2O_4^+$ [M + H]$^+$ 369.2184, found 369.2186.

isopropyl ((S)-1-(((S)-1-((3-fluorobenzyl)oxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 11c: white solid, m.p.: 135-137 °C, yield: 67.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.29 (m, 1H, Ar-**H**), 7.14 – 6.94 (m, 3H, Ar-**H**), 6.02 (s, 1H, CHCON**H**), 5.17 (s, 1H, OCON**H**), 4.91 (s, 1H, OC**H**$(CH_3)_2$), 4.53 (s, 2H, Ar-C$\mathbf{H}_2$), 4.24 (s, 1H, CH_2C**H**CH_3), 3.92 (s, 1H, OCONHC**H**), 3.47 (d, *J* = 4.0 Hz, 2H, OC$\mathbf{H}_2$CH), 2.11 (s, 1H, CHC**H**$(CH_3)_2$), 1.63 (s, 1H), 1.25 (s, 9H, CHC$\mathbf{H}_3$ + OCH(C$\mathbf{H}_3)_2$), 0.96 (d, *J* = 14.8 Hz, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.62, 164.18, 161.73, 156.26, 140.68, 129.91, 122.93, 114.48, 73.07, 72.42, 68.57, 60.34, 44.92, 31.12, 22.08, 19.18, 17.70; HRMS (ESI) m/z Calcd for $C_{19}H_{30}FN_2O_4^+$ [M + H]$^+$ 369.2184, found 369.2180.

isopropyl ((S)-1-(((S)-1-((2-fluorobenzyl)oxy)propan-2-yl)amino)-3-methyl-1-

oxobutan-2-yl)carbamate 11d: white solid, m.p.: 152-154 °C, yield: 74.3%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H, Ar-**H**), 7.29 (s, 1H, Ar-**H**), 7.16 (s, 1H, Ar-**H**), 7.08 (d, *J* = 9.1 Hz, 1H, Ar-**H**), 6.07 (s, 1H, CHCON**H**), 5.21 (s, 1H, OCON**H**), 4.90 (s, 1H, OC**H**$(CH_3)_2$), 4.60 (s, 2H, Ar-C$\mathbf{H}_2$), 4.24 (s, 1H, CH_2C**H**CH_3), 3.92 (s, 1H, OCONHC**H**), 3.49 (s, 2H, OC$\mathbf{H}_2$CH), 2.08 (s, 1H, CHC**H**$(CH_3)_2$), 1.24 (s, 9H, CHC$\mathbf{H}_3$ + OCH(C$\mathbf{H}_3)_2$), 0.94 (dd, *J* = 14.3, 6.5 Hz, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.62, 162.03, 159.58, 156.24, 130.04, 129.54, 124.11, 115.20, 73.10, 68.50, 66.83, 60.27, 44.85, 31.26, 22.08, 19.13, 17.66; HRMS (ESI) m/z Calcd for $C_{19}H_{30}FN_2O_4^+$ $[M + H]^+$ 369.2184, found 369.2180.

isopropyl ((S)-1-(((S)-1-((4-chlorobenzyl)oxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 11e: white solid, m.p.: 149-151 °C, yield: 65.4%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.13 (m, 4H, Ar-**H**), 6.12 (s, 1H, CHCON**H**), 5.22 (s, 1H, OCON**H**), 4.89 (s, 1H, OC**H**$(CH_3)_2$), 4.49 (s, 2H, Ar-C$\mathbf{H}_2$), 4.23 (s, 1H, CH_2C**H**CH_3), 3.91 (s, 1H, OCONHC**H**), 3.44 (s, 2H, OC$\mathbf{H}_2$CH), 2.08 (s, 1H, CHC**H**$(CH_3)_2$), 1.22 (d, *J* = 9.9 Hz, 9H, CHC$\mathbf{H}_3$ + OCH(C$\mathbf{H}_3)_2$), 0.99 – 0.88 (m, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, CDCl3) δ 170.71, 156.25, 136.50, 133.48, 128.92, 128.57, 72.97, 72.34, 68.53, 60.32, 44.86, 31.12, 22.06, 19.17, 17.64; HRMS (ESI) m/z Calcd for $C_{19}H_{30}ClN_2O_4^+$ $[M + H]^+$ 385.1894, found 384.1891.

isopropyl ((S)-1-(((S)-1-((4-methylbenzyl)oxy)propan-2-yl)amino)-3-methyl-1-oxobutan-2-yl)carbamate 11f: white solid, m.p.: 139-141 °C, yield: 72.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, *J* = 7.9 Hz, 4H, Ar-**H**), 6.13 (s, 1H, CHCON**H**), 5.25 (s, 1H, OCON**H**), 4.90 (s, 1H, OC**H**$(CH_3)_2$), 4.49 (s, 2H, Ar-C$\mathbf{H}_2$), 4.20 (s, 1H, CH_2C**H**CH_3), 3.91 (s, 1H, OCONHC**H**), 3.48 – 3.38 (m, 2H, OC$\mathbf{H}_2$CH), 2.37 (s, 3H, Ar-C$\mathbf{H}_3$), 2.07 (s, 1H, CHC**H**$(CH_3)_2$), 1.23 (t, *J* = 10.3 Hz, 9H, CHC$\mathbf{H}_3$ + OCH(C$\mathbf{H}_3)_2$), 0.94 (dd, *J* = 14.5, 6.8 Hz, 6H, CHCH(C$\mathbf{H}_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.61, 156.26, 137.49, 134.92, 129.12, 127.82, 73.05, 72.63, 68.47, 60.26, 44.96, 31.29, 22.09, 21.15, 19.18, 17.71; HRMS (ESI) m/z Calcd for $C_{20}H_{33}N_2O_4^+$ $[M + H]^+$ 365.2435, found 365.2434.

isopropyl ((S)-3-methyl-1-oxo-1-(((S)-1-((4-(trifluoromethyl)benzyl)oxy)propan-2-yl)amino)butan-2-yl)carbamate 11g: white solid, m.p.: 141-143 °C, yield: 67.1%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.3 Hz, 2H, Ar-**H**), 7.21 (d, *J* = 8.1 Hz, 2H, Ar-**H**), 6.03 (s, 1H, CHCON**H**), 5.16 (s, 1H, OCON**H**), 4.90 (s, 1H, OC**H**$(CH_3)_2$), 4.52 (s, 2H, Ar-C$\mathbf{H}_2$), 4.24 (s, 1H, CH_2C**H**CH_3), 3.91 (s, 1H, OCONHC**H**), 3.47 (d, *J* = 2.6 Hz, 2H, OC$\mathbf{H}_2$CH), 2.11 (s, 1H, CHC**H**$(CH_3)_2$), 1.23 (d, *J* = 10.5 Hz, 9H,

CHC**H**$_3$ + OCH(C**H**$_3$)$_2$), 0.94 (dd, *J* = 13.4, 6.8 Hz, 6H, CHCH(C**H**$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.66, 156.24, 148.70, 136.75, 128.90, 121.74, 120.96, 119.19, 73.09, 72.27, 68.57, 60.36, 44.87, 31.06, 22.05, 19.16, 17.67; HRMS (ESI) m/z Calcd for $C_{20}H_{30}F_3N_2O_5^+$ $[M + H]^+$ 435.2101, found 435.2097.