Rapid Procedure for N-Phthaloylation of α-Amino Carboxamides, α-Amino Alcohols, α-Amino Esters and Dipeptide Derivatives

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Abstract: A rapid, one-pot synthesis and mild procedure for the *N*-phthaloylation of α-amino carboxamides is described. In acetonitrile, these derivatives react with *mono*-methylphthalate in the presence of BOP and *i*-Pr_2NEt to afford the intermediate N^{α}-[(*o*-methoxycarbonyl)benzoyl]amino carboxamides, which undergo rapid cyclization in the presence of aqueous sodium carbonate to afford the corresponding N^{α}-phthaloylamino carboxamides in excellent yields. The reaction also works efficiently with α-amino esters, α-amino alcohols and dipeptide esters or amides.

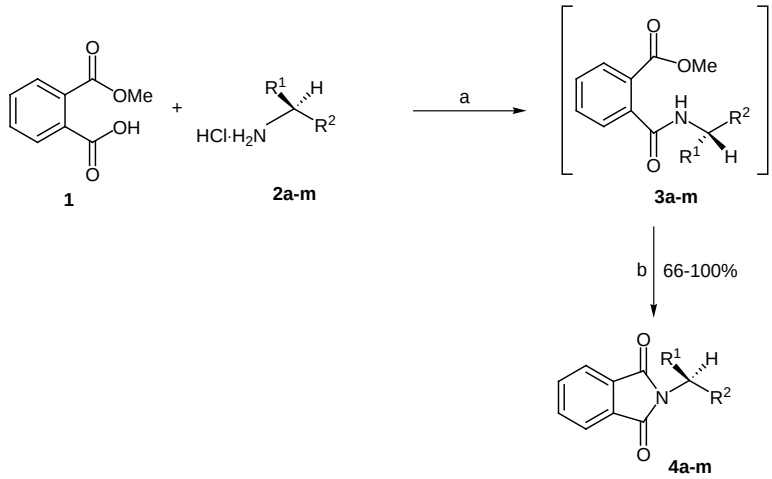
Key words: phthaloyl protection, α-amino carboxamides, *mono*-methylphthalate, α-amino alcohols, cyclization

N-Phthaloylation is a widely used methodology for protecting the primary amino groups in amino acids and peptides. In addition to the fact that *N*-phthaloylated compounds are stable and easily recrystallized, the phthaloyl protection can be easily removed under mild conditions using methylhydrazine, phenylhydrazine, or hydrazine.[1–3] However, although the phthaloylation of α-amino acids, carboxamides, esters, nitriles, and alcohols are well documented,[3–12] low yields and low optical purities have been experienced with the literature procedures.[13] In particular, the reaction of amino acids with phthalic anhydride requires heating and can cause racemization.[14-16] Although this latter problem was thought to be resolved by the introduction of the well-known *N*-(ethoxycarbonyl)phthalimide by Nefkens et al,[6] low yields have been experienced when this reagent was used with amino alcohols or sterically hindered amino acids.[7,17–19]

In our ongoing work on the synthesis of 4-amino-2-benzazepin-3-ones,[20,21] we required a mild and rapid method for the sythesis of N^{α}-phthaloylamino carboxamides. However, only 50-60% yields of the desired phthaloylated products were obtained when the Nefkens' procedure was repeated with α-amino carboxamides. For this reason, we decided to investigate new methods for the protection of these compounds.

In this paper, we report a rapid and mild procedure for the preparation of N^{α}-phthaloylamino carboxamides, which is also applicable to N-phthaloylation of α-amino alcohols, α-amino esters, and dipeptide derivatives.

The procedure is based on the activation of 2-(methoxycarbonyl)benzoic acid **1** with BOP [benzotriazole-1-yloxy-tris-(dimethylamino)-phosphoniumhexafluorophos-



a. MeCN, BOP, *i*-Pr_2NEt, r.t., 30 min. b. Na_2CO_3/H_2O, r.t., 30-240 min.

Scheme

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phate] in acetonitrile containing ethyl-diisopropylamine, followed by reaction with α-amino carboxamides **2a**–**f** (Table) to afford the intermediate phthalamic derivatives **3a**–**f** (scheme). As demonstrated by C_{18} RP-HPLC analysis of the reaction mixture after 30 min, compounds **2a**–**f**, were rapidly converted to the corresponding intermediates **3a**–**f**. However, in these conditions, the transformation of these intermediates into the desired phthaloylated derivatives **4a**–**f**, proceeded very slowly, showing that stronger bases were needed to accelerate the cyclization process. The miscibility of acetonitrile with water enabled us to take advantage of inorganic bases which could ultimately be removed from the reaction mixture by aqueous washings. Indeed, the intermediates **3a**–**f**, were rapidly converted to the *N*-phthaloyl derivatives **4a**–**f** when aqueous sodium carbonate was added to the mixture. In the case of α-amino carboxamides, the cyclization reaction was completed in less than 30 min and the desired products were isolated in very good yields (66–100%, Table) after dilution with ethylacetate, aqueous washings, and elimination of the solvents under reduced pressure. This implies phthalimides **4a**–**f** formed in this manner are stable to the aqueous sodium carbonate solution used and that only water-soluble by-products are formed during the reaction.

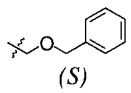
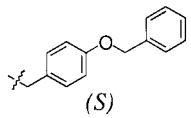
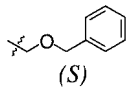
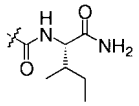
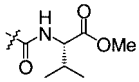
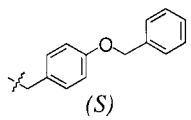
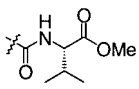
In order to evaluate the applicability of the procedure to the phthaloylation α-amino alcohols, α-amino esters and dipeptide esters, compounds **2g**–**m** were allowed to react with 2-(methoxycarbonyl)benzoic acid (**1**) under the conditions described above. As shown in the Table, the desired phthaloylated compounds **4g**–**m** were obtained in very good yields, although the cyclization proceeded less rapidly with benzyl and methyl valinates.

As demonstrated by GITC (1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate) analysis of compounds **4b** and **4d** after removal of the phthaloyl protection by hydrazinolysis,[4,22,23] only the *S*-isomers were obtained showing that no racemization takes place during the course of the reaction.

In conclusion, we report a rapid and racemization-free procedure for the preparation of phthaloyl derivatives of α-amino carboxamides, α-amino alcohols, α-amino esters, and dipeptides derivatives. We believe that this mild and simple procedure will be very useful for protecting the amino groups in a wide range of compounds.

Analytical grade CH_3CN was used without further purification for all experiments. Melting points were measured on a Büchi 530 instrument and were not corrected. Optical rotations were determined at 22 °C on a Perkin-Elmer 241 polarimeter. Mass spectra (positive mode) were recorded on a linear MALDI-TOF instrument (Bruker Bremen) using α-cyano-4-hydroxycinnamic acid as a matrix. Exact mass measurements (EMM) were recorded at low resolution using electrospray ionization and a quadrupole VG Quattro II mass spectrometer (EI^+, conevoltage 40) with poly(ethyleneglycol)monomethylether as standard.[24] 1D NMR spectra were recorded in DMSO-d_6 or $CDCl_3$ on a Bruker AC 200 MHz spectrometer. Analytical HPLC was recorded at 30 °C on a Nucleosil C_{18} column (8 μm, 3.9 × 150 mm) using a linear gradient of 0–100% of B (0.08% TFA in

Table BOP-Na_2CO_3 Promoted N-Phthaloylation of α-Amino Carboxamides, Esters, Alcohols and Dipeptide Derivatives

Product	R^1 (chirality)	R^2	Time (min)[a]	R_t (min)[b]	Yield (%)[c,d]
4a	 (*S*)	$CONH_2$	30	12.61	78
4b	 (*S,S*)	$CONH_2$	30	12.43	96
4c	 (*S*)	$CONH_2$	30	13.12	78
4d	 (*S*)	$CONH_2$	30	12.52	77
4e	 (*S*)	$CONH_2$	30	15.18	69
4f	 (*S*)	CO_2Bn	30	11.34	66
4g	 (*S*)	CO_2Me	210	17.29	100[e]
4h	 (*S*)	CO_2t-Bu	120	15.00	88[e]
4i	Me (*S*)	CO_2t-Bu	30	15.79	97
4j	 (*S*)	CH_2OH	30	13.63	76
4k	 (*S*)		30	14.56	66
4l	 (*S*)		30	15.66	100
4m	 (*S*)		30	17.29	67[f]

[a] Time taken for the cyclization of intermediates 2a–k into 4a–k.
[b] Determined by C_{18} RP-HPLC.
[c] Yields of isolated products.
[d] All products are white solids, except 4g and 4h.
[e] Colourless oil.
[f] Obtained after purification by flash chromatography in hexanes–ethyl acetate 70:30.

MeCN) in A (0.1% TFA in H_2O) for 20 min at a flow rate of 1.2 mL/min with UV detection at 214 nm, except for GITC experiments where a gradient of 20–50% of B in A was used with UV detection at 250 nm. TLC was performed on aluminium sheets coated with silica gel 60 F_{254} (Merck, Darmstadt) in hexanes–EtOAc–HOAc, 70:30:5.

N-Phthaloylation of α-Amino Carboxamides and Dipeptides; Typical Procedure

A solution of 2-(methoxycarbonyl)benzoic acid **1** (0.90 g, 5.0 mmol), α-amino carboxamide, α-amino ester or dipeptides **2** (5.0 mmol), BOP (2.26 g, 5.0 mmol), and *i*-Pr_2NEt (3.4 mL, 20.0 mmol) in CH_3CN (40 mL) were stirred at r.t. for 30 min. A solution of Na_2CO_3 (1.06 g, 10 mmol) in H_2O (20 mL) was then added and stirring was continued for 0.5–4 h (Table). After evaporation of the CH_3CN and dilution with EtOAc (100 mL), the organic phase was washed with saturated $NaHCO_3$ solution (3 × 50 mL), 1 N HCl (1 × 50 ml), H_2O (1 × 50 mL), dried with Na_2SO_4, and evaporated to afford the pure product in very good yield.

*N*α-Phthaloyl-(*S*)-leucinamide (4a)

White solid (1.02 g, 78%); mp 160–161 °C; R_f = 0.37; HPLC R_t = 12.61 min; $[\alpha]_D$ –13.2 (c = 1.1, MeOH).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 0.87 (d, 3 H, *J* = 6.6 Hz), 0.88 (d, 3 H, *J* = 6.5 Hz), 1.37 (m, 1 H), 1.90 (m, 1 H), 2.20 (m, 1 H), 4.67 (dd, 1 H, *J* =11.8, 4.3 Hz), 7.23 (s, 1 H), 7.62 (s, 1 H), 7.89 (m, 4 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 20.7 (CH_3), 23.1 (CH_3), 24.8 (CH), 36.5 (CH_2), 51.3 (CH), 123.1 (CH), 131.5 (C), 134.4 (CH), 167.7 (C), 170.4 (C).

MS: *m/z* = 261 (M^+ + H), 283 (M^+ + Na), 299 (M^+ + K).

*N*α-Phthaloyl-(*S*)-*iso*-leucinamide (4b)

White solid (1.25 g, 96%); mp 227–228 °C; R_f = 0.41; HPLC R_t = 12.43 min; $[\alpha]_D$ +4.4 (c = 0.9, HOAc).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 0.79 (t, 3 H, *J* = 7.1 Hz), 0.90 (m, 1 H), 0.99 (d, 3 H, *J* = 6.7 Hz), 1.38 (m, 1 H), 2.52 (m, 1 H), 4.36 (d, 1 H, *J* = 9.0 Hz), 7.14 (s, 1 H), 7.51 (s, 1 H), 7.89 (m, 4 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 10.6 (CH_3), 16.6 (CH_3), 25.2 (CH_2), 32.8 (CH), 57.9 (CH), 123.1 (CH), 131.2 (C), 134.5 (CH), 167.6 (C), 169.5 (C).

MS: *m/z* = 261 (M^+ + H), 283 (M^+ + Na), 299 (M^+ + K).

*N*α-Phthaloyl-(*S*)-*O*-benzylserinamide (4c)

White hygroscopic solid (1.27 g, 78%); R_f = 0.28; HPLC R_t = 13.12 min; $[\alpha]_D$ –32.1 (c = 1.0, MeOH).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.88 (dd, 1 H, *J* = 6.0, 9.6 Hz), 4.39 (m, 1 H), 4.61 (d, 2 H, *J* = 4.0 Hz), 5.04 (dd, 1 H, *J* = 6.0, 8.7 Hz), 6.34 (s, 1 H), 6.89 (s, 1 H), 7.31 (s, 5 H), 7.67–7.85 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 52.0 (CH), 67.6 (CH_2), 73.4 (CH_2), 123.6 (CH), 127.9 (CH), 128.1 (CH), 128.6 (CH), 131.8 (C), 134.3 (CH), 137.0 (C), 167.8 (C), 169.8 (C).

MS: *m/z* = 347 (M^+ + Na), 363 (M^+ + K).

EMM (*m/z*): $[M + H]^+$ calcd for $C_{18}H_{16}N_2O_4$, 325.1188; found, 325.1192.

*N*α-Phthaloyl-(*S*)-phenylalaninamide (4d)

White solid (1.13 g, 77%); mp 226–228 °C; R_f = 0.27; HPLC R_t = 12.52 min; $[\alpha]_D$ –20.4 (c = 1.0, MeOH).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 3.34 (dd, 1 H, *J* = 14.0, 11.8 Hz), 3.53 (dd, 1 H, *J* = 14.0, 4.8 Hz), 4.93 (dd, 1 H, *J* =11.8, 4.8 Hz), 7.12 (m, 5 H), 7.32 (s, 1 H), 7.72 (s, 1 H), 7.80 (s, 4 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 33.7 (CH_2), 54.2 (CH), 122.9 (CH), 126.3 (CH), 128.2 (CH), 128.6 (CH), 131.2 (C), 134.4 (CH), 137.7 (C), 167.4 (C), 169.6 (C).

MS: *m/z* = 295 (M^+ + H), 317 (M^+ + Na), 333 (M^+ + K).

*N*α-Phthaloyl-(*S*)-*O*-benzyltyrosinamide (4e).

White solid (1.38 g, 69%); mp 158 °C; R_f = 0.26; HPLC R_t = 15.18 min; $[\alpha]_D$ –162.1 (c = 1.0, MeOH).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 3.41 (m, 2 H), 4.94 (dd, 1 H, *J* = 11.7, 4.7 Hz), 5.0 (s, 2 H), 6.84 (d, 2 H , *J* = 8.6 Hz), 7.08 (d, 2 H, *J* = 8.6 Hz), 7.33–7.43 (m, 6 H), 7.75 (s, 1 H), 7.85 (s, 4 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 32.8 (CH_2), 54.4 (CH), 68.9 (CH_2), 114.5 (CH), 122.9 (CH), 127.5 (CH), 128.2 (CH), 129.5 (CH), 129.8 (C), 131.2 (C), 134.3 (CH), 136.9 (C), 156.8 (C), 167.4 (C), 169.6 (C).

MS: *m/z* = 423 (M^+ + Na), 439 (M^+ + K).

EMM (*m/z*): $[M + H]^+$ calcd for $C_{24}H_{20}N_2O_4$, 401.1501; found, 401.1510.

*N*α-Phthaloyl-(*S*)-valinamide (4f)

White solid (0.81 g, 66%); mp 194–195 °C; R_f = 0.36; HPLC R_t = 11.34 min; $[\alpha]_D$ –21.0 (c = 0.7, MeOH).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 0.77 (d, 3 H, *J* = 6.8 Hz), 1.02 (d, 3 H, *J* = 6.7 Hz), 2.69 (m, 1 H), 4.29 (d, 1 H, *J* = 8.6 Hz), 7.11 (s, 1 H), 7.50 (s, 1 H), 7.88 (m, 4 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 19.2 (CH_3), 20.9 (CH_3), 27.1 (CH), 58.4 (CH), 123.1 (CH), 131.3 (C), 134.5 (CH), 167.6 (C), 169.4 (C).

MS: *m/z* = 247 (M^+ + H), 269 (M^+ + Na), 285 (M^+ + K).

Benzyl *N*α-Phthaloyl-(*S*)-valinate (4g)

Colourless oil (1.69 g, 100%); R_f = 0.70; HPLC R_t = 17.29 min; $[\alpha]_D$ –47.4 (c = 1.0, MeOH).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 0.80 (d, 3 H, *J* = 6.8 Hz), 1.02 (d, 3 H, *J* = 6.7 Hz), 2.60 (m, 1 H), 4.62 (d, 1 H, *J* = 7.9 Hz), 5.09 (s, 2 H), 7.22 (s, 5 H), 7.86 (m, 4 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 18.9 (CH_3), 20.4 (CH_3), 28.0 (CH), 56.9 (CH), 66.3 (CH_2), 123.4 (CH), 127.6 (CH), 127.9 (CH), 128.2 (CH), 130.8 (C), 134.9 (CH), 135.4 (C), 167.3 (C), 168.1 (C).

MS: *m/z* = 360 (M^+ + Na), 376 (M^+ + K).

EMM (*m/z*): $[M + H]^+$ calcd for $C_{20}H_{19}NO_4$, 338.1392; found, 338.1489.

Methyl *N*α-Phthaloyl-(*S*)-valinate (4h)

Colourless oil (1.15 g, 88%); R_f = 0.68; HPLC R_t = 15.00 min; $[\alpha]_D$ –69.7 (c = 1.0, MeOH).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, 3 H, *J* = 6.8 Hz), 1.12 (d, 3 H, *J* = 6.7 Hz), 2.71 (m, 1 H), 3.68 (s, 3 H), 5.54 (d, 1 H, *J* = 8.3 Hz), 7.70–7.76 (m, 2 H), 7.77–7.87 (m, 2 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 19.4 (CH_3), 20.9 (CH_3), 28.6 (CH), 52.4 (CH), 57.6 (CH_3), 123.4 (CH), 131.7 (C), 134.2 (CH), 167.7 (C), 169.3 (C).

MS: *m/z* = 262 (M^+ + H), 284 (M^+ + Na).

t-Butyl *N*α-Phthaloyl-(*S*)-alaninate (4i)

White solid (1.34 g, 97%); mp 67–69 °C; R_f = 0.72; HPLC R_t = 15.79 min; $[\alpha]_D$ –10.3(c = 1.1, MeOH).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.43 (s, 9 H), 1.64 (d, 3 H, *J* = 7.3 Hz), 4.87 (q, 1 H, *J* = 7.3 Hz), 7.70–7.88 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 15.3 (CH_3), 27.9 (CH_3), 48.4 (CH), 82.3 (C), 123.4 (CH), 132.0 (C), 134.1 (CH), 167.6 (C), 168.7 (C).

MS: *m/z* = 298 (M^+ + Na), 314 (M^+ + K).

EMM (*m/z*): [M + Na]$^+$ calcd for $C_{15}H_{17}NO_4$, 298.1055; found, 298.1094.

N*α*-Phthaloyl-(*S*)-phenylalaninol (4j)
White solid (1.07 g, 76%); mp 104–106 °C; R_f = 0.41; HPLC R_t = 13.63 min; $[\alpha]_D$ –134.1(c = 1.1, MeOH).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.16 (m, 2 H), 3.29 (bs, 1 H), 3.88 (dd, 1 H, *J* =11.6, 4.0 Hz), 4.07 (m, 1 H), 4.61 (m, 1 H), 7.15 (m, 5 H), 7.56–7.74 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 34.8 (CH_2), 55.3 (CH), 62.6 (CH_2), 123.3 (CH), 126.7 (CH), 128.5 (CH), 129.0 (CH), 131.6 (C), 134.0 (CH), 137.5 (C), 169.0 (C).

MS: *m/z* = 282 (M^+ + H), 288 (M^+ + Li), 304 (M^+ + Na).

EMM (*m/z*): [M + H]$^+$ calcd for $C_{17}H_{15}NO_3$, 282.1130; found, 282.1157.

N*α*-Phthaloyl-(*S*)-O-benzylserinyl-(*S*)-*iso*-leucinamide (4k)
White solid (1.44 g, 66%); mp 164–165 °C; R_f = 0.27; HPLC R_t = 14.56 min; $[\alpha]_D$ –43.9(c = 0.9, MeOH).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 0.69 (t, 3 H, *J* = 7.3 Hz), 0.74 (d, 3 H, *J* = 7.0 Hz), 0.97 (m, 2 H), 1.65 (m, 1 H), 3.92–4.15 (m, 3 H), 4.36 (d, 1 H, *J* = 12.1 Hz), 4.48 (d, 1 H, *J* = 12.1 Hz), 5.00 (dd, 1 H, *J* = 9.4, 5.9 Hz), 6.98 (s, 1 H), 7.14 (m, 5 H), 7.38 (s, 1 H), 7.83 (m, 4 H), 8.16 (d, 1 H, *J* = 8.8 Hz).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 10.7 (CH_3), 15.4 (CH_3), 24.1 (CH_2), 35.8 (CH), 51.8 (CH), 56.8 (CH), 66.4 (CH_2), 71.7 (CH_2), 123.0 (CH), 127.3 (CH), 128.1 (CH), 131.7 (C), 134.4 (CH), 137.9 (C), 166.2 (C), 167.5 (C), 172.7 (C).

MS: *m/z* = 460 (M^+ + Na).

EMM (*m/z*): [M + H]$^+$ calcd for $C_{24}H_{27}N_3O_5$, 438.2029; found, 438.2106.

Methyl N*α*-Phthaloyl-(*S*)-phenylalanyl-(*S*)-valinate (4l)
White solid (2.04 g, 100%); mp 88-89°C; R_f = 0.49; HPLC R_t = 15.66 min; $[\alpha]_D$ –27.4 (c = 0.7, MeOH).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.83 (d, 3 H, *J* = 6.9 Hz), 0.92 (d, 3 H, *J* = 6.9 Hz), 2.14 (m, 1 H), 3.42–3.60 (m, 2 H), 3.67 (s, 3 H), 4.58 (dd, 1 H, *J* = 4.7, 8.6 Hz), 5.18 (dd, 1 H, *J* = 6.8, 9.9 Hz), 6.69 (d, 1 H, *J* = 8.6 Hz), 7.06–7.19 (m, 5 H), 7.66–7.80 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.7 (CH_3), 18.9 (CH_3), 31.4 (CH), 35.1 (CH_2), 52.2 (CH), 56.0 (CH), 57.4 (CH_3), 123.6 (CH), 127.0 (CH), 128.7 (CH), 128.9 (CH), 131.5 (C), 134.3 (CH), 136.6 (C), 168.0 (C), 168.4 (C), 172.1 (C).

MS: *m/z* = 409 (M^+ + H), 431 (M^+ + Na), 447 (M^+ + K).

EMM (*m/z*): [M + H]$^+$ calcd for $C_{23}H_{24}N_2O_5$, 409.1763; found, 409.1769.

Methyl N*α*-Phthaloyl-(*S*)-*O*-benzyltyrosinyl-(S)-valinate (4m)
White solid (1.77 g, 67%); mp 113–115 °C; R_f = 0.42; HPLC R_t = 17.29 min; $[\alpha]_D$ –114.9 (c = 1.1, MeOH).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.88 (d, 3 H, *J* = 6.9 Hz), 0.97 (d, 3 H, *J* = 6.9 Hz), 2.20 (m, 1 H), 3.53–3.58 (m, 2 H), 3.70 (s, 3 H), 4.63 (dd, 1 H, *J* = 8.62, 4.75 Hz), 4.98 (s, 2 H), 5.18 (dd, 1 H, *J* = 9.71, 6.96 Hz), 6.77 (m, 1 H), 6.83 (d, 2 H, *J* = 8.6 Hz), 7.15 (d, 2 H, *J* = 8.6 Hz), 7.38 (m, 5 H), 7.70–7.85 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 17.7 (CH_3), 18.9 (CH_3), 31.3 (CH), 34.3 (CH_2), 52.2 (CH_3), 56.1 (CH), 57.4 (CH), 70.0 (CH_2), 115.1 CH), 123.6 (CH), 127.4 (CH), 127.9 (CH), 128.5 (CH), 128.9 (C), 13.0 (CH), 131.5 (C), 134.3 (CH), 136.9 (C), 157.8 (C), 168.0 (C), 168.5 (C), 172.1 (C).

MS: *m/z* = 515 (M^+ + H), 537 (M^+ + Na), 553 (M^+ + K).

EMM (*m/z*): [M + H]$^+$ calcd for $C_{30}H_{30}N_2O_6$, 515.2182; found, 515.2189.

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