# Self-assembly and crystal structure of Boc-protected dipeptides containing L-phenylalanine and L-tyrosine

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**Supplementary Information (SI)**

**SI Section S1.1** *Structural Characterization by NMR Spectroscopy*

All the intermediates were characterized by NMR spectroscopy on a Bruker Avance III 400 at an operating frequency of 400 MHz for $^{1}H$ and $^{13}C$, respectively. The solvent used to prepare the samples was DMSO-$d_6$ (dimethylsulfoxide >99.80 atom% D). Chemical shifts were reported in parts per million and tetramethylsilane (TMS) was used as an external reference. $^{1}H$ NMR (400 MHz, DMSO-$d_6$, ppm) δ 1.10 (3 × $CH_3$-Boc, s, 9H), 2.59 ($CH_2$-β, m, 1H), 2.71 ($CH_2$-β, m, 2H), 3.09 ($CH_2$-β, m, 1H), 4.02 (CH-$\alpha$, m, 1H), 4.25 (CH-$\alpha$, m, 1H), 5.92 (NH, d, 1H), 6.36 (2 × CH-Tyr, d, 2H), 6.64 (2 × CH-Tyr, d, 2H), 7.23 (2 × CH-pNPhe, d, 2H), 7.71 (2 × CH-pNPhe, d, 2H), 8.08 (OH, broad s, 1H), 8.35 (NH, d, 1H); $^{13}C$ NMR (100.6 MHz, DMSO-$d_6$, ppm): δ 27.39, 32.56, 37.33, 53.53, 54.39, 77.19, 115.00, 122.27, 122.59, 130.32, 141.87, 144.94, 145.67, 146.27, 155.34, 156.63, 169.86, 171.79. The NMR spectroscopic data presented in this section correspond specifically to the newly synthesized compound Boc-pNPhe-Tyr, as this dipeptide has not been previously reported, unlike Boc-Phe-Tyr, whose synthesis and characterization are available in the literature [18].

**SI Section S1.2.** Crystal Data

**Table S1.** Crystallographic data and refinement parameters for the amino acid Boc-pNPhe and the dipeptides Boc-Phe-Tyr and Boc-pNPhe-Tyr.

| | **Boc-pNPhe** | **Boc-Phe-Tyr** | **Boc-pNPhe-Tyr** |
|---|---|---|---|
| CCDC number | 2529055 | 2529054 | 2530636 |
| Empirical formula | $C_{14}H_{18}N_2O_6$ | $C_{23}H_{27}N_2O_6$ | $C_{23}H_{29}N_3O_9$ |
| Formula weight | 310.30 | 427.46 | 490.48 |
| Temperature [K] | 100.00 | 300.00 | 293(2) |
| Crystal system | monoclinic | tetragonal | Monoclinic |
| Space group (number) | $P2_1$ (4) | $P4_3$ (78) | $P2_1$ (4) |
| $a$ [Å] | 10.7575(6) | 21.2134(13) | 11.050(2) |
| $b$ [Å] | 5.1460(3) | 21.2134(13) | 5.0136(9) |
| $c$ [Å] | 13.4066(8) | 5.1784(5) | 22.712(4) |
| $\alpha$ [°] | 90 | 90 | 90 |
| $\beta$ [°] | 91.739(4) | 90 | 102.348(6) |
| $\gamma$ [°] | 90 | 90 | 90 |
| Volume [Å$^3$] | 741.82(7) | 2330.3(4) | 1229.1(4) |
| $Z$ | 2 | 4 | 2 |
| $\rho_{calc}$ [gcm$^{-3}$] | 1.389 | 1.218 | 1.325 |
| $\mu$ [mm$^{-1}$] | 0.928 | 0.088 | 0.103 |
| $F$(000) | 328 | 908 | 518 |
| Crystal size [mm$^3$] | 0.213×0.034×0.026 | 0.12×0.05×0.04 | 0.02x0.08x0.50 |
| Crystal colour | clear light colourless | clear light colourless | Clear light colourless |
| Crystal shape | block | prism | Needle |
| Radiation | Cu$K_\alpha$ ($\lambda$=1.54178 Å) | Mo$K_\alpha$ ($\lambda$=0.71073 Å) | Mo$K_\alpha$ ($\lambda$=0.71073 Å) |
| 2θ range [°] | 8.22 to 144.70 (0.81 Å) | 5.43 to 50.86 (0.83 Å) | 5.51 to 51.36 (0.8/ Å |
| Index ranges | -13 ≤ h ≤ 13<br>-5 ≤ k ≤ 6<br>-16 ≤ l ≤ 16 | -25 ≤ h ≤ 25<br>-25 ≤ k ≤ 25<br>-6 ≤ l ≤ 6 | -13 ≤ h ≤ 13<br>-6 ≤ k ≤ 6<br>-27 ≤ l ≤ 27 |
| Reflections collected | 20560 | 60843 | 45623 |
| Independent reflections | 2864<br>$R_{int}$ = 0.0930<br>$R_{sigma}$ = 0.0427 | 4313<br>$R_{int}$ = 0.1084<br>$R_{sigma}$ = 0.0457 | 4630<br>$R_{int}$ = 0.5276<br>$R_{sigma}$ = 0.2883 |
| Completeness | 99.4 % | 99.8 % | 99.8% |
| Data / Restraints / Parameters | 2864/1/205 | 4313/322/271 | 4630/2/323 |
| Goodness-of-fit on $F^2$ | 1.085 | 1.247 | 0.938 |

| | | | |
|---|---|---|---|
| Final *R* indexes [$I \geq 2\sigma(I)$] | $R_1$ = 0.0893 | $R_1$ = 0.1193 | $R_1$ = 0.0876 |
| | w$R_2$ = 0.2141 | w$R_2$ = 0.1805 | w$R_2$ = 0.1864 |
| Final *R* indexes [all data] | $R_1$ = 0.1078 | $R_1$ = 0.1859 | $R_1$ = 0.1948 |
| | w$R_2$ = 0.2285 | w$R_2$ = 0.2075 | w$R_2$ = 0.2155 |
| Largest peak/hole [eÅ$^{-3}$] | 0.34/-0.33 | 0.24/-0.24 | 0.26/-0.24 |

**Table S2.** Intermolecular hydrogen bond geometry for Boc-pNPhe (Å, °)

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) | Symmetry Code |
|---|---|---|---|---|---|
| O4-H4...O1 | 0.84 | 1.97 | 2.807(9) | 176 | (i) |
| N1-H1...O5 | 0.88 | 2.36 | 3.063(9) | 138 | (ii) |
| C5-H5...O3 | 0.95 | 2.54 | 3.460(10) | 164 | (iii) |

Symmetry codes: (i) x-1, y-1, z; (ii) x, y-1, z; (iii) -x, y+1/2, -z+2.

**Table S3.** Intermolecular hydrogen bond geometry for Boc-Phe-Tyr (Å, °)

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) | Symmetry Code |
|---|---|---|---|---|---|
| O1-H1A...O4 | 0.82 | 1.91 | 2.729(10) | 174 | (iv) |
| N2-H2...O5 | 0.86 | 2.18 | 2.950(10) | 149 | (v) |
| C11-H11...O4 | 0.93 | 2.59 | 3.252(12) | 129 | (iv) |

Symmetry codes: (iv) 1-y, x, z+3/4; (v) x, y, z-1.

**Table S4.** Intermolecular hydrogen bond geometry for Boc-pNPhe-Tyr (Å, °)

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) | Symmetry Code |
|---|---|---|---|---|---|
| C1-H1C...O2 | 0.96 | 2.41 | 3.007(11) | 119.7 | |
| C4-H4B...O2 | 0.96 | 2.30 | 2.912(10) | 121.2 | |
| O6-H6...O7 | 0.82 | 1.97 | 2.671(7) | 143.7 | (vi) |
| N1-H100...O2 | 0.90(3) | 2.15(4) | 3.013(9) | 161(9) | (vii) |
| N2-H200...O5 | 0.91(3) | 2.14(5) | 2.968(9) | 151(8) | (viii) |
| O9-H1O9...O8 | 0.8443 | 1.947 | 2.722(9) | 152.27 | |
| O9-H2O9...O8 | 0.8587 | 2.223 | 3.081(9) | 177.0(2) | (vii) |

Symmetry codes: (vi) -x+1,y-1/2,-z+1; (vii) x,y+1,z; (viii) x,y-1,z