Supporting Information (SI)

Intramolecular [4+2]-Cycloaddition of 5-Aza Substituted Oxazoles as an Approach Toward the Left-Hand Segment of Haplophytine

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Experimental Section

General
Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70eV. Unless otherwise noted, all reactions were performed in flame dried glassware under an atmosphere of dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate-hexane mixture as the eluent unless specified otherwise.

N-(2-Iodophenyl)-2,4-dimethyloxazol-5-amine (18). To a solution of 1.11 g of N-tert-butoxycarbonylalanine (12) (5.9 mmol) in 10 mL of dichloromethane was added 1.2 g of 1,3-dicyclohexyl carbodiimide (5.9 mmol) and a catalytic amount of 4-dimethyl-aminopyridine. After stirring for 10 min, a solution of 1.29 g of o-iodoaniline (5.9 mmol) in 5 mL of dichloromethane was slowly added via syringe and the reaction mixture was stirred at rt for 24 h. The mixture was filtered through Celite and the filtrate was washed with 1M HCl. The aqueous portion was further extracted with dichloromethane and the combined organic extracts were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford 1.62 g of tert-butyl 1-(2-iodophenylamino)-1-oxopropan-2-yl carbamate (14) in 73% yield; mp 116-118 ºC; IR (KBr) 3347, 3297, 1711, 1669, 1585, and 1522 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 8.36 (brs, 1H), 8.22 (d, 1H, $J = 7.9$ Hz), 7.76 (dd, 1H, $J = 7.8$ and 1.2 Hz), 7.33 (t, 1H, $J = 7.8$ Hz), 6.84 (td, 1H, $J = 7.8$ and 1.2 Hz), 5.17 (brs, 1H), 4.39 (brs, 1H), and 1.47 (s, 9H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 170.9, 155.3, 138.7, 137.8, 129.1, 125.9, 121.7, 89.8, 80.4, 51.1, 28.3, and 18.0.

To a solution containing 0.54 g of the above carbamate in 2 mL of dichloromethane was added an equal volume of trifluoroacetic acid. The mixture was stirred for 1 hr and then concentrated under reduced pressure. The residue taken up in 2 mL of tetrahydrofuran and was treated with 2 mL of acetic anhydride and 0.5 mL of pyridine. After stirring at rt for 18 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to afford 0.28 g of 2-acetamido-N-(2-iodophenyl)propanamide (16) in 64% yield over the two steps; mp 160-161 ºC; IR (KBr) 3278, 2360, 1653, 1584, 1519, and
1433 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 8.24 (brs, 1H), 8.06 (dd, 1H, J = 7.1 and 1.1 Hz), 7.77 (dd, 1H, J = 8.2 and 1.6 Hz), 7.32 (td, 1H, J = 7.8 and 1.6 Hz), 6.86 (td, 1H, J = 7.4 and 1.1 Hz), 6.45 (brd, 1H, J = 5.9 Hz), 4.74 (pent., 1H, J = 7.4 Hz), 2.07 (s, 3H), and 1.49 (d, 3H, J = 7.4 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 170.8, 170.6, 139.2, 138.1, 129.3, 126.7, 123.0, 90.9, 49.3, 23.4, and 18.1.

To a solution containing 0.17 g (0.5 mmol) of the above amide in 2 mL of dichloromethane was sequentially added 347 µL of trifluoroacetic anhydride and 193 µL of trifluoroacetic acid. The mixture was stirred at rt for 30 h and was then diluted with 5 mL of carbon tetrachloride and concentrated under reduced pressure. The residue was poured into a cold solution of aqueous sodium bicarbonate and then extracted with dichloromethane. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 0.15 g of N-(2-iodophenyl)-2,4-dimethyloxazol-5-amine (18) in 92% yield; IR (thin film) 3351, 1673, 1595, 1493, and 1284 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 7.70 (dd, 1H, J = 8.2 and 1.6 Hz), 7.17 (td, 1H, J = 8.2 and 1.2 Hz), 6.60 (td, 1H, J = 8.2 and 1.2 Hz), 6.47 (dd, 1H, J = 8.2 and 1.6 Hz), 5.70 (brs, 1H), 2.39 (s, 3H), and 2.05 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 158.6, 144.8, 141.0, 139.3, 129.6, 129.5, 121.8, 113.5, 84.6, 14.7, and 11.2; HRMS Calcd. for [C₁₁H₁₁N₂O]: 313.9916. Found: 313.9913.

1,3-Dimethyl-9H-pyrido[3,4-b]indole (21). To a solution containing 0.16 g (0.5 mmol) of the above anilino-oxazole 18 in 1 mL of degassed DMF was added a solution of 0.24 g of n-tributylvinylstannane (0.75 mmol) in 1 mL of degassed DMF. This was followed by the addition of 0.08 g (0.5 mmol) of cesium fluoride and 35 mg (0.05 mmol) of trans-dichlorobis(triphenylphosphine)palladium (II). The vessel was sealed and purged with argon and heated at 100 ºC for 14 h. After cooling to rt, the reaction mixture was quenched by the addition of water and extracted with ethyl acetate. The organic extracts were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.07 g of the titled compound in 70% yield as a clear oil; IR (thin film) 3129, 3062, 2956, 1626, 1573, and 1502 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 8.47 (brs, 1H), 8.08 (d, 1H, J = 7.6 Hz), 7.68 (s, 1H), 7.54-7.48 (m, 2H), 7.24 (td, 1H, J = 7.6 and 1.2 Hz), 2.80 (s, 3H), and 2.71 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 147.2, 140.9, 140.7, 133.1, 129.6, 128.3, 122.1, 122.0, 120.1, 111.8, 111.7, 24.4, and 20.5; HRMS Calcd. for [C₁₃H₁₂N₂]: 196.1000. Found: 196.1002.

3-Methyl-1-phenyl-9H-pyrido[3,4-b]indole (22). To a solution of 2.51 g of 2-(tert-butoxycarbonylamino)-2-phenylacetic acid (13) (10 mmol) in 10 mL of dichloromethane was added 2.2 g of 1,3-dicyclohexyl carbodiimide (10 mmol) and 0.12 g of 4-dimethylaminopyridine (0.1 mmol). After stirring for 10 min at rt, a solution of 2.06 g of o-idoaniline (10 mmol) in 10 mL of dichloromethane was slowly added via syringe and the solution was stirred
at rt for 24 h. The mixture was filtered through Celite and the filtrate was washed with 1M HCl. The aqueous portion was further extracted with dichloromethane and the combined organic extracts were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash silica gel chromatography to give 3.15 g of tert-butyl 2-(2-iodophenylamino)-2-oxo-1-phenyl-ethylcarbamate (15) in 70% yield as a white solid; mp 150-152 °C; IR (KBr) 3419, 3351, 1681, 1585, 1522, and 1433 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 8.21 (d, 1H, $J$ = 7.6 Hz), 7.95 (brs, 1H), 7.71 (dd, 1H, $J$ = 7.6 and 1.1 Hz), 7.47-7.29 (m, 6H), 6.82 (td, 1H, $J$ = 7.6 and 1.2 Hz), 5.82 (brs, 1H), 5.37 (brs, 1H), and 1.41 (s, 9H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 168.6, 155.4, 139.0, 137.8, 129.5, 129.4, 127.8, 126.4, 121.8, 89.8, 80.6, 60.1, and 28.5.

To a solution of 0.5 g (1.11 mmol) of the above carbamate in 2 mL of dichloromethane was added an equal volume of trifluoroacetic acid. The mixture was stirred for 1 h and was then concentrated under reduced pressure. The residue was taken up in 3 mL of THF and was treated with 3 mL of acetic anhydride and 1 mL of pyridine. After stirring at rt for 16 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.27 g of 2-acetamido-N-(2-iodo-phenyl)-2-phenylacetamide (17) in 62% yield over the two steps; mp 218-220 °C; IR (KBr) 3279, 1637, and 1529 cm$^{-1}$; $^1$H-NMR (400 MHz, CD$_3$OD) $\delta$ 7.74-7.71 (m, 1H), 7.46-7.43 (m, 3H), 7.31-7.22 (m, 4H), 6.87-6.83 (m, 1H), 5.53 (brs, 1H), and 1.95 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 169.9, 169.0, 139.1, 138.9, 138.1, 128.7, 128.4, 127.7, 127.6, 126.5, 95.3, 56.8, and 22.4.

To a solution of 0.11 g (0.27 mmol) of the above acetamide in 2 mL of dichloromethane was sequentially added 190 µL of trifluoroacetic anhydride (1.37 mmol) and 105 µL of trifluoroacetic acid (1.37 mmol). The reaction mixture was stirred at rt for 2 h and then diluted with 2 mL of carbon tetrachloride and concentrated under reduced pressure. The residue was poured into a cold solution of aqueous sodium bicarbonate and then extracted with dichloromethane. The combined organic extracts were washed with brine, dried over MgSO$_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 0.08 g (82%) of N-(2-iodophenyl)-2-methyl-4-phenyloxazol-5-amine (19) as a pale yellow oil; IR (thin film) 3340, 2360, 1735, 1585, 1488 1433 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.83-7.80 (m, 2H), 7.76 (dd, 1H, $J$ = 7.8 and 1.2 Hz), 7.39-7.35 (m, 2H), 7.29-7.26 (m, 1H), 7.16 (td, 1H, $J$ = 8.2 and 1.1 Hz), 6.66-6.62 (m, 2H), 6.04 (brs, 1H), and 2.39 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 158.7, 143.8, 140.4, 139.5, 132.1, 131.1, 130.9, 129.8, 128.9, 127.9, 126.1, 122.3, 114.1, 85.2, 14.7; HRMS Calcd. for [C$_{16}$H$_{13}$N$_2$OI]: 376.0073. Found: 376.0074.

To a solution of 0.04 g (0.16 mmol) of the above anilino-oxazole in 1 mL of degassed DMF was added a solution of 0.05 g of n-tributylvinylstannane (0.17 mmol) in 1 mL of degassed DMF. This was followed by the addition of 2 mg (0.01 mmol) of cesium fluoride
and 7 mg of *trans*-dichlorobis(triphenylphosphine)palladium (II) (0.01 mmol). The vessel was sealed and purged with argon and the mixture was heated at 100 °C for 16 h. After cooling to rt, the reaction mixture was quenched by the addition of water and extracted with ethyl acetate. The organic extracts were washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 15 mg of the titled compound 22 in 54% yield as a pale yellow oil; IR (KBr) 3334, 1718, and 1433 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 8.36 (brs, 1H), 8.11 (d, 1H, *J* = 7.8 Hz), 7.99-7.96 (m, 2H), 7.80 (s, 1H), 7.61-7.42 (m, 5H), 7.31-7.27 (m, 1H), and 2.82 (s, 3H); HRMS Calcd. for [C₁₈H₁₄N₂]: 258.1157. Found: 258.1161.

**Methyl 3-(5-(2-Iodophenylamino)-2-methyloxazol-4-yl)propanoate (23).** To a solution of 5.22 g of *N*-tert-butoxycarbonyl-L-glutamic acid 5-methyl ester¹ (20 mmol) in 20 mL of dichloromethane was added 4.12 g of 1,3-dicyclohexyl carbodiimide (20 mmol) and a catalytic amount of 4-dimethylaminopyridine. After stirring at rt for 10 min, a solution of 4.38 g of o-iodoaniline (20 mmol) in 20 mL of dichloromethane was slowly added via syringe and the reaction mixture was stirred at rt for 24 h. The mixture was filtered through Celite and the filtrate was washed with 1M HCl. The aqueous portion was extracted with dichloromethane and the combined organic extracts were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude residue was purified by flash column chromatography to afford 6.84 g of methyl 4-(tert-butoxycarbonylamino)-5-(2-iodophenylamino)-5-oxopentanoate in 74% yield as a white solid; mp 74-76 °C; IR (KBr) 3316, 3276, 1726, 1687, 1665, and 1521 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 8.34 (brs, 1H), 8.20 (d, 1H, *J* = 7.9 Hz), 7.78 (dd, 1H, *J* = 7.9 and 1.3 Hz), 7.34 (t, 1H, *J* = 7.3 Hz), 6.86 (td, 1H, *J* = 7.9 and 1.3 Hz), 5.42 (d, 1H, *J* = 7.3 Hz), 4.37 (m, 1H), 3.71 (s, 3H), 2.62-2.45 (m, 2H), 2.36-2.28 (m, 1H), 2.11-2.08 (m, 1H), 1.47 (s, 9H); ¹³C-NMR (100 MHz, CDCl₃) δ 173.9, 170.2, 155.9, 139.1, 138.0, 129.3, 126.4, 122.3, 90.4, 80.7, 55.1, 52.1, 30.6, 28.5 and 27.5.

To a solution of 2.61 g (5.65 mmol) of the above carbamate in 5 mL of dichloromethane was added an equal volume of trifluoroacetic acid. After stirring for 2 h at rt, the reaction mixture was concentrated under reduced pressure. The residue was taken up in 5 mL of THF and was treated with 8 mL of acetic anhydride and 2 mL of pyridine. After stirring at rt for 4 h, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash silica gel chromatography to give 2.03 g of methyl 4-acetamido-5-(2-iodophenylamino)-5-oxopentanoate in 89% yield over the two steps; mp 141-143 °C; IR (KBr) 3274, 1736, 1648, 1576, 1531, and 1435 cm⁻¹; ¹H-NMR (400 MHz, CDCl₃) δ 8.37 (brs, 1H), 8.03 (dd, 1H, *J* = 7.8 and 1.1 Hz), 7.77 (dd, 1H, *J* = 8.2 and 1.6 Hz), 7.31 (td, 1H, *J* = 8.2 and 1.1 Hz), 6.92 (brd, 1H, *J* = 7.8 Hz), 6.86 (td, 1H, *J* = 7.8 and 1.6 Hz), 4.73-4.68 (m, 1H), 3.69 (s, 3H), 2.63-2.51 (m, 1H), 2.49-2.43 (m, 1H), 2.33-2.26 (m, 1H), 2.13-2.03 (m, 1H), and
2.07 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 174.3, 171.0, 169.8, 139.2, 138.0, 129.3, 126.8, 123.1, 91.1, 53.6, 52.2, 30.5, 27.1 and 23.4.

To a solution of 0.4 g (1.0 mmol) of the above ester in 5 mL of dichloromethane was sequentially added 700 µL of trifluoroacetic anhydride (5.0 mmol) and 385 µL of trifluoroacetic acid. The reaction mixture was stirred at rt for 36 h and was then diluted with 5 mL of carbon tetrachloride and concentrated under reduced pressure. The residue was poured into a cold solution of aqueous sodium bicarbonate and extracted with dichloromethane. The combined organic extracts were washed with brine, dried over MgSO$_4$, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to afford 0.38 mg of methyl 3-(5-(2-iodophenylamino)-2-methyloxazol-4-yl)propanoate (23) in 98% yield as a pale yellow oil; IR (thin film) 3340, 2360, 1735, 1585, and 1488 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 7.68 (dd, 1H, $J = 7.9$ and 1.6 Hz), 7.17 (td, 1H, $J = 7.3$ and 1.5 Hz), 6.58 (td, 1H, $J = 7.9$ and 1.6 Hz), 6.07 (brs, 1H), 3.61 (s, 3H), 2.73-2.60 (m, 4H) and 2.39 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 173.4, 158.4, 144.8, 141.7, 139.4, 130.3, 129.6, 121.9, 113.8, 84.7, 51.9, 32.4, 20.9 and 14.7; HRMS Calcd. for [C$_{14}$H$_{15}$N$_2$O$_3$]: 386.0127. Found: 386.0125.

Methyl 3-(3-Methyl-9H-pyrido[3,4-b]indol-1-yl)propanoate (26). To a solution of 0.1 g (0.25 mmol) of oxazole 23 in 1 mL of degassed DMF was added a solution of 0.12 g (0.38 mmol) of n-tributylvinylstannane in 1 mL of degassed DMF. This was followed by the addition of 0.04 g (0.25 mmol) of cesium fluoride and 0.02 g (0.03 mmol) of trans-dichloro-bis(triphenylphosphine) palladium (II) and then the vessel was sealed and purged with argon. The mixture was heated at 100 ºC for 14 h. After cooling to rt, the mixture was quenched by the addition of water and then extracted with ethyl acetate. The organic extracts were washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give the titled compound 26 as a yellow solid; mp 158-160 ºC; IR (KBr) 3334 and 1718 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 8.99 (brs, 1H), 8.06 (d, 1H, $J = 7.8$ Hz) 7.67 (s, 1H), 7.52-7.40 (m, 2H), 2.27-7.24 (m, 1H), 3.65 (s, 3H), 3.40 (t, 2H, $J = 6.6$ Hz), 2.96 (t, 2H, $J = 6.6$ Hz), and 2.69 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 175.4, 147.2, 143.1, 141.1, 133.1, 130.3, 128.3, 122.0, 121.8, 119.9, 112.2, 112.0, 52.2, 33.4, 29.1 and 24.5; Anal. Calcd. for C$_{16}$H$_{16}$N$_2$O$_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.53; H, 6.03; N, 10.57.

2-Methyl-4H-indolo[3,2,1-de][1,5]naphthyridin-6-(5H)-one (29). To a solution of 0.03 g (0.11 mmol) of the above carboline 26 in 1 mL of toluene was added 21 mg (0.11 mmol) of p-toluenesulfonic acid and the mixture was heated at reflux for 15 h. After concentrating the reaction mixture under reduced pressure, the crude residue was purified by flash silica gel chromatography to give 21 mg (75% yield) of the titled compound 29 as a pale yellow solid; mp 114-116 ºC; IR (KBr) 3392, 1699 and 1448 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) δ 8.47 (d, 1H, $J = 8.2$ Hz), 7.98 (d, 1H, $J = 7.8$ Hz), 7.63 (td, 1H, $J = 7.8$ and 1.1 Hz), 7.53 (s, 1H), 7.42
(td, 1H, $J = 7.8$ and 1.1 Hz), 3.43 (t, 2H, $J = 7.4$ Hz), 3.17 (t, 2H, $J = 7.4$ Hz) and 2.71 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 166.8, 152.9, 141.5, 138.1, 131.3, 130.5, 130.1, 124.6, 124.5, 124.5, 122.1, 116.8, 112.3, 33.4, 27.7 and 24.8; Anal. Calcd. for C$_{15}$H$_{12}$N$_2$O: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.18; H, 5.04; N, 11.75.

**Methyl 3-((2-Iodophenyl)(methyl)amino)-2-methyloxazol-4-yl)propanoate (24).** To a suspension of 0.07 g (1.86 mmol, 60% dispersion in mineral oil) of sodium hydride in 2 mL of THF was added a solution of 0.72 g (1.86 mmol) of oxazole 23 in 3 mL of THF at 0 ºC. After stirring for 20 min at 0 ºC, 177 $\mu$L (1.86 mmol) of methyl iodide was added and the reaction mixture was allowed to warm to rt and was stirred for an additional 6 h. The mixture was then quenched by the addition of an aqueous ammonium chloride solution and was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to furnish 0.33 g of the titled compound 24 in 44% yield as a pale yellow oil; IR (thin film) 2995, 2360 and 1737 cm$^{-1}$; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 7.82 (dd, 1H, $J = 7.9$ and 1.6 Hz), 7.31 (td, 1H, $J = 7.3$ and 1.5 Hz), 7.19 (dd, 1H, $J = 7.9$ and 1.6 Hz), 6.80 (td, 1H, $J = 7.9$ and 1.6 Hz), 3.60 (s, 3H), 3.21 (s, 3H), 2.50-2.39 (m, 4H), and 2.37 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 173.4, 156.0, 149.2, 148.4, 140.7, 129.5, 126.1, 124.8, 123.9, 94.8, 51.7, 41.7, 32.4, 21.0 and 14.6; HRMS Calcd. for [C$_{15}$H$_{17}$N$_2$O$_3$I]: 400.0284. Found: 400.0281.

**Methyl 3-(3,9-Dimethyl-9H-pyrido[3,4-b]indol-1-yl)propanoate (27).** To a solution of 0.14 g (0.35 mmol) of the above oxazole in 1 mL of degassed DMF was added a solution of 0.17 g (0.53 mmol) of $n$-tributylvinylstannane in 1 mL of degassed DMF. This was followed by the addition of 53 mg (0.35 mmol) of cesium fluoride and 28 mg (0.04 mmol) of $trans$-dichloro-bis(triphenylphosphine)palladium (II) and then the vessel was sealed and purged with argon. The mixture was heated at 100 ºC for 14 h, cooled to rt, and quenched by the addition of water. The solution was extracted with ethyl acetate and the organic extracts were washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 0.06 g (60% yield) of the titled compound 27 as a pale yellow oil; $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$ 8.04 (d, 1H, $J = 7.8$ Hz), 7.64 (s, 1H), 7.53 (td, 1H, $J = 7.3$ and 1.2 Hz), 7.39 (d, 1H, $J = 8.6$ Hz), 7.23 (td, 1H, $J = 7.8$ and 0.8 Hz), 4.14 (s, 3H), 3.72 (s, 3H), 3.67 (t, 2H, $J = 7.4$ Hz), 2.97 (t, 2H, $J = 7.8$ Hz) and 2.66 (s, 3H); $^{13}$C-NMR (100 MHz, CDCl$_3$) $\delta$ 174.1, 146.3, 142.7, 142.2, 133.8, 129.5, 126.1, 124.8, 123.9, 94.8, 51.7, 41.7, 32.4, 21.0 and 14.6; HRMS Calcd. for [C$_{17}$H$_{18}$N$_2$O$_2$]: 282.1368. Found: 282.1372.

**Methyl 3-(5-(Benzy1-(2-iodophenyl)amino)-2-methyloxazol-4-yl)propanoate (25).** To a suspension of 17 mg (0.41 mmol, 60% dispersion in mineral oil) of sodium hydride in 0.3 mL of DMF was added a solution of 0.11 g (0.23 mmol) of oxazole 23 in 0.3 mL of DMF at 0 ºC. After stirring for 15 min at 0 ºC, 49 $\mu$L (0.41 mmol) of benzyl bromide was added and the
reaction mixture was allowed to warm to rt and was stirred for an additional 3 h. The mixture was quenched by the addition of an aqueous ammonium chloride solution and was then extracted with ethyl acetate. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to give 0.1 g (74% yield) of the titled compound 25 as a pale yellow oil; IR (thin film) 2927, 2360, and 1737 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.84 (dd, 1H, \(J = 7.6\) and 1.3 Hz), 7.42-7.30 (m, 2H), 7.30-7.20 (m, 5H), 6.85-6.81 (m, 1H), 4.60 (s, 2H), 3.59 (s, 3H), 2.50-2.46 (m, 2H), 2.33 (s, 3H) and 2.32-2.28 (m, 2H); \(^13\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.5, 156.9, 148.4, 147.4, 140.7, 137.0, 129.4, 129.1, 129.0, 128.5, 127.8, 127.0, 126.3, 97.0, 58.6, 51.7, 32.5, 28.0, 21.1 and 14.7; HRMS Calcd. for \(\text{[C}_{21}\text{H}_{21}\text{N}_{2}\text{O}_{3}]\): 476.0597. Found: 476.0594.

**Methyl 3-(9-Benzyl-3-methyl-9H-pyrido[3,4-b]indol-1-yl)propanoate (28).** To a solution of 35 mg (0.07 mmol) of the above oxazole in 1 mL of degassed DMF was added a solution of 35 mg (0.11 mmol) of \(n\)-tributylvinylstannane in 1 mL of degassed DMF. This was followed by addition of 11 mg (0.07 mmol) of cesium fluoride and 5 mg (0.01 mmol) of \(\text{trans-dichloro} \cdot \text{bis(triphenylphosphine)}\)palladium (II) and then the vessel was sealed and purged with argon. The mixture was heated at 100 ºC for 14 h. After cooling to rt, the reaction mixture was quenched by the addition of water and then extracted with ethyl acetate. The organic extracts were washed with brine, dried over Na\(_2\)SO\(_4\), filtered and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 14 mg (56% yield) of the titled compound 28 as a pale yellow oil; IR (thin film) 1734 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.12 (d, 1H, \(J = 7.8\) Hz), 7.73 (s, 1H), 7.53 (td, 1H, \(J = 7.0\) and 1.1 Hz), 7.37 (d, 1H, \(J = 8.2\) Hz), 7.30-7.23 (m, 4H), 7.02-6.98 (m, 2H), 5.82 (s, 2H), 3.67 (s, 3H), 3.42 (t, 2H, \(J = 7.5\) Hz), 2.76 (t, 2H, \(J = 7.5\) Hz) and 2.66 (s, 3H); \(^13\)C-NMR (100 MHz, CDCl\(_3\)) \(\delta\) 147.1, 142.6, 138.4, 131.2, 129.5, 128.9, 128.0, 126.1, 121.1, 120.3, 112.3, 82.1, 52.1, 48.9, 33.4, 30.2 and 24.6; HRMS Calcd. for \(\text{[C}_{23}\text{H}_{22}\text{N}_{2}O_{2}]\): 358.1681. Found: 358.1679.

**Ethyl 3-(2-Methyl-5-(2,2,2-trifluoroacetamido)oxazol-4-yl)propanoate (32).** A sample of the known ethyl 4,5-diamino-5-oxopentanolate hydrochloride\(^2\) was prepared from 5-oxopyrroolidine-2-carboxamide (30) using acetyl chloride and ethanol.\(^3\) To a solution of 3.0 g of the above hydrochloride in 3 mL of pyridine was added 12 mL of acetic anhydride. After stirring at room temperature for 12 h, the solution was concentrated under reduced pressure. The crude residue was purified by flash silica gel chromatography to give 2.72 g (88% yield) of ethyl 4-acetamido-5-amino-5-oxopentanolate (31) as a white solid; mp 136-138 ºC; IR (KBr) 3350, 3225, 1725, 1675, 1625, and 1550 cm\(^{-1}\); \(^1\)H-NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.62 (d, 1H, \(J = 7.2\) Hz), 6.58 (brs, 1H), 5.59 (brs, 1H), 4.51 (dd, 1H, \(J = 13.2\) and 7.6 Hz), 4.15 (q, 2H, \(J = 6.8\) Hz), 2.56 (dt, 1H, \(J = 8.8\) and 7.2 Hz), 2.41 (dt, 1H, \(J = 8.8\) and 7.2 Hz), 2.18-2.02 (m, 1H),
2.00-1.94 (m, 1H), 1.27 (t, 3H, J = 6.8 Hz); 13C-NMR (100 MHz, CDCl3) δ 174.0, 173.6, 170.7, 61.1, 52.3, 30.8, 27.9, 23.4 and 14.4.

To a solution containing 0.43 g (2.0 mmol) of the above compound in 5 mL of dichloromethane was sequentially added 1.38 mL (10.0 mmol) of trifluoroacetic anhydride and 742 µL (10.0 mmol) of trifluoroacetic acid. The reaction mixture was stirred at rt for 16 h and then diluted with 10 mL of carbon tetrachloride and concentrated under reduced pressure. The residue was poured into a cold solution of aqueous sodium bicarbonate and extracted with dichloromethane. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to afford 0.55 g (94% yield) of the titled compound 32 as a pale yellow oil; IR (thin film) 3400, 1720, 1645, and 1620 cm⁻¹; 1H-NMR (400 MHz, CD6D6) δ 8.92 (brs, 1H), 3.63 (q, 2H, J = 6.8 Hz), 2.33-2.25 (m, 4H), 1.77 (s, 3H), and 0.72 (t, 3H, J = 6.8 Hz); 13C-NMR (100 MHz, CDCl3) δ 188.0, 174.8, 159.0, 136.1, 129.4, 94.6, 61.4, 32.4, 20.3, 14.4 and 14.3; HRMS Calcd. for [C11H13F3N2O4]: 294.0827. Found: 294.0824.

Ethyl 3-(5-But-3-enamido-2-methyloxazol-4-yl)propanoate (33). To a solution of 51 µL of butenoic acid (0.6 mmol) in THF at 0 ºC was slowly added 78 µL (0.6 mmol) of isobutyl chloroformate and 66 µL (0.6 mmol) of N-methyl morpholine and the solution was stirred for 30 min. The white precipitate that formed was removed by filtration and washed with THF to give the mixed anhydride. In a separate vessel, a solution of 0.15 g (0.5 mmol) of the above ester 32 in THF was treated with 0.5 mL of a 1.0 M LHMDS solution (0.5 mmol) at 0 ºC. After stirring for 20 min, the mixed anhydride was introduced via syringe addition and the resulting solution was allowed to reach rt and was stirred for 1 h. The solution was quenched by the addition of an aqueous ammonium chloride solution and was extracted with ethyl acetate. The combined organic extracts were washed with brine, dried over Na2SO4, filtered and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography to afford 0.08 g (57% yield) of the titled compound 33 as a pale yellow oil; IR (thin film) 3256, 1733, 1698, and 1665 cm⁻¹; 1H-NMR (400 MHz, CDCl3) δ 8.03 (brs, 1H), 6.05-5.95 (m, 1H), 5.30 (d, 1H, J = 6.7 Hz), 5.27 (s, 1H), 4.07 (d, 2H, J = 7.0 Hz), 3.17 (2H, d, J = 7.0 Hz), 2.61 (s, 4H), 2.35 (s, 3H), 1.20 (t, 3H, J = 7.0 Hz); 13C-NMR (100 MHz, CDCl3) δ 174.0, 170.7, 158.5, 138.0, 130.5, 129.6, 120.7, 60.9, 41.5, 32.4, 20.6, 14.5 and 14.3; HRMS Calcd. for [C15H17F3N2O5]: 362.1090. Found: 362.1088.

Ethyl 3-(5-Methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-c]pyridin-7-yl)propanoate (34). A solution of 0.04 g of the above compound 33 in 5 mL of toluene was heated at reflux for 12 h. The mixture was then concentrated under reduced pressure and the residue was purified by flash silica gel chromatography to afford 20 mg (61% yield) of the titled compound 34 as a pale yellow oil; IR (thin film) 3073, 2981, 2385, 1718, and 1565 cm⁻¹; 1H-NMR (400 MHz, CDCl3) δ 8.42 (brs, 1H), 6.93 (s, 1H), 4.13 (q, 2H, J = 7.3 Hz), 3.51 (s, 2H), 2.99 (t, 2H, J =
6.0 Hz), 2.81 (t, 2H, $J = 6.0$ Hz), 2.49 (s, 3H), and 1.24 (t, 3H, $J = 7.3$ Hz); $^{13}$C-NMR (100 MHz, CDCl$_3$) δ 175.7, 174.1, 152.4, 140.1, 136.0, 135.4, 117.9, 61.2, 36.4, 33.2, 28.5, 24.4 and 14.4; HRMS Calcd. for [C$_{15}$H$_{15}$F$_3$N$_2$O$_4$]: 344.0984. Found: 344.0986.

References: