Supplementary Material (ESI) for Organic and Biomolecular Chemistry

Electronic Supplementary Information

Synthesis of Non-Symmetric Bis(oxazoline)-Containing Ligands and their Application in the Catalytic Enantioselective Nozaki-Hiyama-Kishi Allylation of Benzaldehyde

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Experimental

General Experimental

^{1}H NMR (300 and 400 MHz) and ^{13}C (75 and 100 MHz) spectra were recorded on Varian Oxford 300 or 400 spectrometers at room temperature in $CDCl_3$ using tetramethylsilane as an internal standard. Chemical shifts (δ) are given in parts per million and coupling constants are given as absolute values expressed in Hertz. HRMS was obtained using a Micromass/Waters LCT instrument. Infra-red spectra were recorded on a Perkin-Elmer Infra-red FT spectrometer. Optical rotation values were measured on a Perkin-Elmer 343 polarimeter at room temperature. Melting points were determined in open capillary tubes in a Gallenkamp melting point apparatus and are uncorrected. Thin layer chromatography (TLC) was carried out on plastic sheets pre-coated with silica gel 60 F254 (Merck). Column chromatography separations were performed using Merck Kieselgel 60 (0.040-0.063 mm). HPLC analysis was performed LC 2010A machine equipped with a UV-vis detector employing a Chiracel® OD column from Daicel

Chemical Industries. All reagents were purchased from Sigma-Aldrich and used as received. Solvents were dried before use by distillation from standard drying agents. Anhydrous chlorobenzene was purchased from Sigma-Aldrich and used without further purification. $ZnCl_2$ (Sigma-Aldrich) and $CrCl_3$ were flame-dried under vacuum immediately prior to use.

General Procedure for the Screening of Conditions for Palladium-Catalysed Aryl Aminations

To an oven-dried Radleys® tube was added 2-(*o*-aminophenyl)oxazoline **8a** (0.60 mmol), 3-(bromo-thiophene)oxazoline **10** (0.50 mmol), base (0.60 mmol), ligand (0.05 mmol) and palladium precursor (0.025 mmol Pd). Dry degassed solvent (1.5 mL) was added and the reaction stirred under an atmosphere of nitrogen at the required temperature for 7 days. The reaction mixture was cooled to room temperature, solvent was removed *in vacuo* and the resulting brown oil was passed through a short pad of silica using pentane/ethyl acetate as eluent. The solvent was removed *in vacuo* and a ^{1}H NMR obtained to determine if any aryl-amine product formed.

General Procedure for the Palladium-Catalysed Aryl Amination of 2-(2-aminophenyl)oxazoline 8a-d and 3-Bromo-thiophene-2-carbonitrile 9

An oven-dried Radleys® tube was charged with 3-bromo-thiophene-2-carbonitrile **9** (188 mg, 1.00 mmol), 2-(*o*-aminophenyl)oxazoline **8a-d** (1.20 mmol), 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) (62.3 mg 0.10 mmol), $Pd(OAc)_2$ (22.4mg, 0.10 mmol)and cesium carbonate (456 mg, 1.4 mmol). After the addition of dry, degassed toluene (10 mL) via syringe, the tube was capped under an atmosphere of nitrogen and the reaction mixture was heated at 120 ºC for 36-48 hours, with monitoring by TLC. On completion, the dark orange-brown reaction mixture was cooled to room temperature and concentrated *in vacuo* to give a brown oil which was purified by column chromatography on silica gel.

[2((4*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl)phenyl](thiophene-2-carbonitrile)amine (11a)

Yield: 96% (0.35 g), pale orange oil; TLC: R_f = 0.60 (CH_2Cl_2); $[\alpha]_D$ = +55.2 (c = 0.90 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.72 (dd, *J* = 13.8, 8.1 Hz, 1H, C*H*$_2$Ph), 3.14 (dd, *J* = 13.8, 5.6 Hz, 1H, C*H*$_2$Ph), 3.99 (m, 1H, C*H*$_2$O), 4.22 (m, 1H, C*H*$_2$O), 4.59 (m, 1H, C*H*N), 6.80 (m, 1H, Ar*H*C(2)), 7.09-7.36 (2 x m, 9H, Ar*H*C(3)), Ar*H*C(4), Ar*H*C(4'), Ar*H*C(5'), Ar*H*C(phenyl)), 7.70 (dd, *J* = 7.9, 1.5 Hz, 1H, ArHC(1)), 11.43 (br s, 1H, NH); ^{13}C NMR (300 MHz, $CDCl_3$): δ = 41.9 (*C*H$_2$Ph), 68.0 (*C*HN), 70.7 (*C*H$_2$O), 91.6 (Ar-*C*(2')), 112.0 (*C*≡N), 114.5 (Ar-*C*(5)), 114.8 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl), 119.6 (Ar-H*C*(2)), 121.0, 126.7, 128.8, 129.5 (Ar-H*C*(3), Ar-H*C*(4), Ar*H*C(4'), Ar*H*C(5'), Ar-H*C*(phenyl), 130.2 (Ar-H*C*(1)), 132.0, 132.4 (Ar-H*C*(3), Ar-H*C*(4), Ar*H*C(4'), Ar*H*C(5'), Ar-H*C*(phenyl), 138.0 (*ipso*-Ph), 143.6 (Ar-*C*(6)), 150.6 (Ar-*C*(3'), 163.9 (*C*=N); IR ($CHCl_3$ film): ν = 1420, 1466, 1554, 1633, 2105, 2204, 3027, 3115 cm^{-1}; HRMS (ES$^+$) calculated for $C_{21}H_{18}N_3OS$ $[M+H]^+$: 360.1171, found:360.1161.

[2((4*S*)-4-isopropyl-4,5-dihydrooxazol-2-yl)phenyl](thiophene-2-carbonitrile)amine (11b)

Yield: 89% (0.28 g), pale orange oil; TLC: R_f = 0.63 (pentane/ethyl acetate 10:1); $[\alpha]_D$ = +70.8 (c = 0.80 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)$_2$), 1.00 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)$_2$), 1.75 (m, 1H, C*H*(CH$_3$)$_2$), 3.96 (app t, *J* = 8.2 Hz, 1H, C*H*$_2$O), 4.08 (m, 1H, C*H*N), 4.29 (m, 1H, C*H*$_2$O), 6.81 (m, 1H, Ar-*H*C(2)), 7.14-7.37 (3 x m, 4H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5')), 7.79 (dd, *J* = 7.8, 1.4 Hz, 1H, Ar-*H*C(1)), 11.42 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.0 (CH(*C*H$_3$)$_2$), 19.2 (CH(*C*H$_3$)$_2$), 33.4 (*C*H(CH$_3$)$_2$), 69.5 (*C*H$_2$O), 73.0 (*C*HN), 91.0 (Ar-*C*(2'), 112.8 (*C*≡N), 114.4 (Ar-*C*(5)), 114.8 (Ar-H*C*(3), Ar-H*C*(4)), Ar-*H*C(4'), Ar-*H*C(5')), 119.6 (Ar-H*C*(2)), 120.6 (Ar-H*C*(3), Ar-H*C*(4), Ar-*H*C(4'), Ar-*H*C(5')), 130.1 (Ar-H*C*(1)), 132.0, 132.2 (Ar-H*C*(3), Ar-H*C*(4)), Ar-*H*C(4'), Ar-*H*C(5')), 143.5 (Ar-*C*(6)), 150.6 (Ar-*C*(3'), 163.4 (*C*=N); IR ($CHCl_3$ film): ν = 1553, 1636, 2096, 2204, 3433 cm^{-1}; HRMS (ES$^+$) calculated for $C_{17}H_{18}N_3OS$ $[M+H]^+$: 312.1171, found: 312.1169.

[2((4*S*)-4-Phenyl-4,5-dihydrooxazol-2-yl)phenyl](thiophene-2-carbonitrile)amine (11c)

Yield: 92% (0.32 g), orange oil; TLC: R_f = 0.39 (pentane/ethyl acetate 10:1); $[\alpha]_D$ = +248.0 (c = 0.63 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.20 (app t, *J* = 8.3 Hz, 1H, C*H*$_2$O), 4.74 (dd, *J* = 9.9, 8.5 Hz, 1H, C*H*$_2$O), 5.53 (dd, *J* = 9.8, 8.7 Hz, 1H, C*H*N), 6.91 (t, *J* = 7.5 Hz, 1H, Ar-*H*C(2)), 7.07-7.42 (m, 9H, Ar-*H*C(Ph), Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-HC(5'), 11.22 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.7 (*C*HN), 72.1 (*C*H$_2$O), 91.3 (Ar-*C*(2'), 110.3 (*C*≡N), 113.0 (Ar-*C*(5)), 113.3, (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-HC(5'), Ar-H*C*(Ph)), 118.2 (Ar-H*C*(2)), 120.2, 125.2, 126.5, 127.0, 127.7 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-HC(5'), Ar-H*C*(Ph)), 129.1 (Ar-H*C*(1)), 130.6, 131.4 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-HC(5'), Ar-H*C*(Ph)), 140.7 (*ipso*-Ph), 142.7 (Ar-*C*(6)), 148.9 (Ar-*C*(3')), 163.5 (*C*=N); IR ($CHCl_3$ film): ν = 1553, 1636, 2093, 2202, 2389, 3430cm^{-1}; HRMS (ES^+) calculated for $C_{20}H_{15}N_3OS$ $[M+H]^+$: 346.1016, found: 346.1017.

[2((4*S*)-4-*tert*-Butyl-4,5-dihydrooxazol-2-yl)phenyl](thiophene-2-carbonitrile)amine (11d)

Yield: 76% (0.29 g), orange oil; TLC: R_f = 0.45 (pentane/ethyl acetate 5:1); $[\alpha]_D$ = +70.2 (c = 0.57 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (s, 9H, C(C*H*$_3$)$_3$), 4.10 (m, 2H, C*H*$_2$O, C*H*N), 4.23 (m, 1H, C*H*$_2$O), 6.82 (t, *J* = 7.4 Hz, 1H, Ar-*H*C(2)), 7.18 (m, 2H, Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5')), 7.26-7.30 (m, 1H, Ar-*H*C(3)), 7.38 (d, *J* = 5.4 Hz, 1H, Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5')), 7.75 (dd, *J* = 7.9, 1.5 Hz, 1H, Ar-*H*C(1), 11.38 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.9 ((*C*H$_3$)$_3$), 32.8 ((*C*H$_3$)$_3$), 66.4 (*C*H$_2$O), 75.2 (*C*HN), 90.0 (Ar-*C*(2')), 110.0 (*C*≡N), 113.1 (Ar-*C*(5)), 113.3 (Ar-*H*C(4'), Ar-*H*C(5')), 118.3 (Ar-H*C*(2), 119.4 (Ar-*H*C(4'), Ar-*H*C(5')), 130.6 (Ar-H*C*(1)), 130.9 (Ar-H*C*(4)), 132.2 (Ar-H*C*(3), 142.3 (Ar-*C*(6)), 149.2 (Ar-*C*(3'), 162.1 (*C*=N); IR ($CHCl_3$ film): ν = 1553, 1636, 2105, 2204, 2960, 3433 cm^{-1}; HRMS (ES^+) calculated for $C_{18}H_{19}N_3OS$ $[M+H]^+$: 326.1309, found: 326.1329.

Supplementary Material (ESI) for Organic and Biomolecular Chemistry

General Procedure for the Synthesis of Ligands 5a-p

To a flame-dried Schlenk tube was added **11a-d** (0.40 mmol), the required amino alcohol (0.80 mmol, 2 equiv.) and flame-dried $ZnCl_2$ (163 mg, 1.20 mmol, 3 equiv.) under an atmosphere of nitrogen. Anhydrous chlorobenzene (5 mL) was added via syringe and the resulting mixture stirred at 145 °C for 12 hours. The reaction was cooled to room temperature and solvent was removed *in vacuo*. The crude product was purified by column chromatography on silica gel to yield pure product.

[2-((4*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-benzyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5a)

Yield: 61% (0.21 g), pale yellow solid; Mp: 50-54 °C; TLC: R_f = 0.50 (pentane/ethyl acetate 5:1); $[\alpha]_D$ = +87.7 (c = 0.80 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.60-2.73 (m, 2H, C*H*$_2$Ph), 3.08-3.19 (m, 2H, C*H*$_2$Ph), 3.88-3.98 (m, 2H, C*H*$_2$O), 4.16 (dd, *J* = 18.3, 9.2 Hz, 2H, C*H*$_2$O), 4.38 (t, *J* = 6.3 Hz, 1H, C*H*N), 4.47 (t, *J* = 7.1 Hz, 1H, C*H*N), 6.79 (t, *J* = 6.7 Hz, 1H, Ar-*H*C(2)), 7.14-7.32 (m, 14H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.72 (d, *J* = 7.6 Hz, 1H, Ar-*H*C(2)), 10.87 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 40.8 (*C*H$_2$Ph), 40.9 (*C*H$_2$Ph), 66.8 (*C*HN), 67.0 (*C*HN), 69.3 (*C*H$_2$O), 70.5 (*C*H$_2$O), 107.4 (Ar-*C*(2')), 112.0 (Ar-*C*(5)), 115.2 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-*H*C(4'), Ar-*H*C(5'), Ar-H*C*(phenyl)), 118.0 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-*H*C(4'), Ar-*H*C(5'), Ar-H*C*(phenyl)), 120.1 (Ar-H*C*(2)), 124.2, 125.3, 125.4, 127.0, 127.2, 127.4, 128.0, 128.2, 128.3, 129.0 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-*H*C(4'), Ar-*H*C(5'), 130.7 (Ar-H*C*(1)), 136.9 (*ipso*-Ph), 137.2 (*ipso*-Ph), 142.7 (Ar-*C*(6)), Ar-*C*(3')), 142.9 (Ar-*C*(6), Ar-*C*(3')), 158.7 (*C*=N), 162.0 (*C*=N); IR ($CHCl_3$ film): ν = 1412, 1557, 1584, 1633, 2360, 2924, 3026 cm^{-1}; HRMS (ES$^+$) calculated for $C_{30}H_{27}N_3O_2S$ $[M+H]^+$: 494.1884, found: 494.1878.

[2-((4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-*iso*propyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5b)

Yield: 78% (310 mg), off-white solid; Mp: 82-84 °C; TLC: R_f = 0.71 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = +29.8 (c = 0.57 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (q, *J* = 6.7 Hz, 6H, CH(C*H*$_3$)$_2$)), 0.95 (dd, *J* = 9.3, 6.7 Hz, 6H, CH(C*H*$_3$)$_2$)), 1.70-1.76 (m, 2H, C*H*(CH$_3$)$_2$)), 3.92-3.97 (m, 3H, C*H*$_2$O, C*H*N), 3.99-4.08 (m, 1H, C*H*N), 4.24-4.30 (m, 2H, C*H*$_2$O), 6.77 (m, 1H, Ar-*H*C(2)), 7.13-7.26 (m, 4H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5')), 7.72 (dd, *J* = 7.8, 1.3, 1H, Ar-*H*C(1)), 10.65 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.2 (CH(*C*H$_3$)$_2$), 17.4 (CH(*C*H$_3$)$_2$), 18.1 (CH(*C*H$_3$)$_2$), 18.2 (CH(*C*H$_3$)$_2$), 31.9 (*C*H(CH$_3$)$_2$), 32.0 (*C*H(CH$_3$)$_2$), 67.9 (*C*H$_2$O), 69.0 (*C*H$_2$O), 71.4 (*C*HN), 72.1 (*C*HN), 108.0 (Ar-*C*(2')), 112.3 (Ar-*C*(5)), 115.3 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5')), 117.8 (Ar-H*C*(2)), 120.5 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C* Ar-H*C*(4'), Ar-H*C*(5')), 126.6 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5')), 128.9 (Ar-H*C*(1)), 130.4 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5')), 142.5 (Ar-*C*(6)), 142.8 (Ar-*C*(3'), 158.0 (*C*=N), 161.5 (*C*=N); IR ($CHCl_3$ film): ν = 1410, 1464, 1637, 2093, 3424 cm^{-1}; HRMS (ES$^+$) calculated for $C_{22}H_{28}N_3O_2S$ $[M+H]^+$: 398.1902, found: 398.1907.

[2-((4*S*)-4-Phenyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-phenyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5c)

Yield: 65 % (225 mg), yellow solid; Mp: 48-50 °C; TLC: R_f = 0.65 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = +232.4 (c = 0.57 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (t, *J* = 7.9 Hz, 1H, C*H*$_2$O), 4.00 (t, *J* = 8.2 Hz, 1H, C*H*$_2$O), 4.25 (t, *J* = 9.0 Hz, 1H, C*H*$_2$O), 4.53 (t, *J* = 9.1 Hz, 1H, C*H*$_2$O), 5.02 (t, *J* = 8.7 Hz, 1H, C*H*N), 5.23 (t, *J* = 9.07 Hz, 1H, C*H*N), 6.82 (t, *J* = 7.3 Hz, 1H, Ar-*H*C(2)), 7.06-7.38 (m, 14H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.80 (d, *J* = 7.6 Hz, 1H, Ar-*H*C(1)), 11.07 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 68.4 (*C*HN), 69.0 (*C*HN), 72.4 (*C*H$_2$O), 73.5 (*C*H$_2$O), 106.8 (Ar-*C*(2')), 112.0 (Ar-*C*(5)), 115.3 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 118.1 (Ar-H*C*(2)), 119.8, 125.6, 125.7, 126.2, 127.4, 127.5 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 129.2 (Ar-H*C*(1)), 130.9 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 141.4 (*ipso*-Ph), 141.6 (*ipso*-Ph), 142.7 (Ar-*C*(6)), 143.1 (Ar-*C*(3')), 159.6 (*C*=N), 162.9 (*C*=N); IR ($CHCl_3$ film): ν = 1464,

1503, 1557, 1584, 1633, 2096, 2959 cm^{-1}; HRMS (ES^+) calculated for $C_{28}H_{24}N_3O_2S$ $[M+H]^+$: 466.1589, found: 466.1573.

[2-((4*S*)-4-*tert*-Butyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-*tert*-butyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5d)

Yield: 56 % (95 mg), pale yellow solid; Mp: 116-120 °C; TLC: R_f = 0.59 (4 pentane/1 ethyl acetate); $[\alpha]_D$ = +26.9 (c = 0.6 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 (s, 9H, (C(C*H*$_3$)$_3$), 0.87 (s, 9H, (C(C*H*$_3$)$_3$), 3.39-3.94 (m, 1H, C*H*N), 4.01-4.08 (m, 3H, C*H*N, C*H*$_2$O), 4.17-4.23 (m, 2H, C*H*$_2$O), 6.78 (m, 1H, Ar-*H*C(1)), 7.14-7.28 (m, 4H, Ar-*H*C(3)), Ar-*H*C(4)), Ar-*H*C(4'), Ar-*H*C(5')), 7.73 (dd, *J* = 7.7, 0.9 Hz, 1H, Ar-*H*C(2)), 10.69 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.8 (C(*C*H$_3$)$_3$), 24.9 (C(*C*H$_3$)$_3$), 32.8 (*C*(CH$_3$)$_3$), 33.0 (*C*(CH$_3$)$_3$), 66.2 (*C*H$_2$O), 67.5 (*C*H$_2$O), 74.8 (*C*HN), 75.6 (*C*HN), 108.3 (Ar-*C*(2')), 112.1 (Ar-*C*(5)), 115.1 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5')), 117.7 (Ar-H*C*(2)), 120.8 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5')), 126.3 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5')), 129.0 (Ar-H*C*(1)), 130.4 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5')), 142.0 (Ar-*C*(6)), 143.0 (Ar-*C*(3')), 157.7 (*C*=N), 161.3 (*C*=N); IR ($CHCl_3$ film): ν = 1463, 1558, 1604, 1639, 2958, 3218 cm^{-1}; HRMS (ES^+) calculated for $C_{24}H_{31}N_3O_2S$ $[M+H]^+$: 426.2197, found: 426.2202.

[2-((4*S*)-4-Phenyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-benzyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5e)

Yield: 71% (136 mg), pale yellow solid; Mp: 50-51 °C; TLC: R_f = 0.32 (5 pentane/1 ethyl acetate); $[\alpha]_D$ = +248.6 (c = 0.7 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 2.30 (dd, *J* = 13.6, 9.5 Hz, 1H, C*H*$_2$Ph), 2.80 (dd, *J* = 13.6, 4.4 Hz, 1H, C*H*$_2$Ph), 3.66 (dd, *J* = 8.3, 7.4 Hz, 1H, C*H*$_2$O'), 3.78 (app t, *J* = 8.7 Hz, 1H, C*H*$_2$O'), 4.07 (t, *J* = 8.1 Hz, 1H, C*H*$_2$O), 4.14-4.22 (m, 1H, C*H*N'), 4.62 (dd, *J* = 9.9, 8.2 Hz, 1H, C*H*$_2$O), 5.35 (dd, *J* = 9.8, 8.5 Hz, 1H, C*H*N), 6.83 (m, 1H, Ar-*H*C(2)), 6.92-7.36 (m, 14H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), 7.83 (dd, *J* = 7.8, 1.4 Hz, 1H, Ar-*H*C(1)), 11.13 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.6 (*C*H$_2$Ph), 67.7 (*C*HN'), 70.6 (*C*HN), 71.5 (*C*H$_2$O,

CH_2O'), 73.7 (*C*H_2O, *C*H_2O'), 109.0 (Ar-*C*(2')), 112.9 (Ar-*C*(5)), 116.5, 119.2 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 121.1 (Ar-H*C*(2)), 126.4, 127.0, 127.1, 127.7, 128.3, 128.5, 128.8, 128.9, 129.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 130.4 (Ar-H*C*(1)), 132.2 (*ipso*-Ph), 138.4 (*ipso*-Ph), 142.8 (Ar-*C*(6)), Ar-*C*(3')), 144.0 (Ar-*C*(6)), Ar-*C*(3')), 160.0 (*C*=N), 164.2 (*C*=N); IR ($CHCl_3$ film): ν = 1411, 1495, 1557, 1585, 1633, 2086, 3433 cm^{-1}; HRMS (ES^+) calculated for $C_{29}H_{25}N_3O_2S$ $[M+H]^+$: 480.1746, found: 480.1737.

[2-((4*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-phenyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5f)

Yield: 70% (134 mg), pale orange solid; Mp: 51-53 °C; TLC: R_f = 0.35 (5 pentane/1 ethyl acetate); $[\alpha]_D$ = +77.2 (c = 0.7 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30 (dd, *J* = 13.3, 9.5 Hz, 1H, C*H*$_2$Ph), 2.79 (dd, *J* = 13.7, 4.5 Hz, 1H, C*H*$_2$Ph), 3.67 (app t, *J* = 8.0 Hz, 1H, C*H*$_2$O), 3.78 (app t, *J* = 9.0 Hz, 1H, C*H*$_2$O), 4.07 (t, *J* = 8.3 Hz, 1H, C*H*$_2$O'), 4.14-4.22 (m, 1H, CHN), 4.62 (dd, *J* = 10.0, 8.4 Hz, 1H, C*H*$_2$O'), 5.35 (t, *J* = 9.1 Hz, 1H, CHN'), 6.83 (app t, *J* = 7.0 Hz, 1H, Ar-*H*C(2)), 6.93 (d, *J* = 6.9 Hz, 1H, Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.03-7.26 (m, 13H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.83 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar-*H*C(1)), 10.87 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.7 (*C*H_2Ph), 67.8 (*C*HN), 70.6 (*C*HN'), 71.5 (*C*H_2O, *C*H_2O'), 73.7 (*C*H_2O, *C*H_2O'), 108.5 (Ar-*C*(2')), 112.9 (Ar-*C*(5)), 116.6, 119.2 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 121.1 (Ar-H*C*(2)), 126.4, 127.0, 127.7, 128.2, 128.5, 128.8, 128.9, 129.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 130.4 (Ar-H*C*(1)), 132.1 (*ipso*-Ph), 138.5 (*ipso*-Ph), 142.8 (Ar-*C*(6)), Ar-*C*(3')), 144.1 (Ar-*C*(6)), Ar-*C*(3')), 160.0 (*C*=N), 164.2 (*C*=N); IR ($CHCl_3$ film): ν = 1412, 1464, 1557, 1583, 1633, 2092, 3433 cm^{-1}; HRMS (ES^+) calculated for $C_{29}H_{25}N_3O_2S$ $[M+H]^+$: 480.1746, found: 480.1798.

[2-((4*S*)-4-*tert*-Butyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-benzyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5g)

Yield: 69% (126 mg), colourless oil; TLC: R_f = 0.85 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = + 62.1 (c = 0.60 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (s, 9H, C(C*H*$_3$)$_3$), 2.56 (dd, *J* = 13.6, 8.9 Hz, 2H, C*H*$_2$Ph), 3.12 (dd, *J* = 13.6, 5.0 Hz, 2H, C*H*$_2$Ph), 3.89-4.02 (m, 3H, C*H*$_2$O, C*H*$_2$O', C*H*N), 4.12-4.19 (m, 2H, C*H*$_2$O, C*H*$_2$O'), 4.36-4.43 (m, 1H, C*H*N'), 6.71-6.75 (m, 1H, Ar-*H*C(2)), 7.06-7.20 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl), 7.68 (dd, *J* = 8.2, 1.3 Hz, 1H, Ar-*H*C(1)), 10.59 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.2 (C(*C*H$_3$)$_3$), 34.0 (*C*(CH$_3$)$_3$), 42.2 (C*H*$_2$Ph), 67.3 (*C*HN', *C*H$_2$O, *C*H$_2$O'), 67.9 (*C*HN', *C*H$_2$O, *C*H$_2$O'), 72.1 (*C*H$_2$O, *C*H$_2$O'), 76.8 (*C*HN), 109.0 (Ar-*C*(2'), 113.3 (Ar-*C*(5)), 116.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5')), Ar-H*C*(phenyl)), 119.1 (Ar-H*C*(2)), 122.1, 126.6, 128.2, 128.7 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 129.5 (Ar-H*C*(1)), 130.2, 131.7 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5') , Ar-H*C*(phenyl)), 138.5 (*ipso*-Ph), 143.8, 144.2 (Ar-*C*(6), (Ar-*C*(3')), 160.0 (*C*=N), 162.7 (*C*=N); IR ($CHCl_3$ film): ν = 1464, 1637, 2096, 1639, 3424 cm^{-1}; HRMS (ES^+) calculated for $C_{27}H_{29}N_3O_2S$ $[M+H]^+$: 460.2059, found: 460.2048.

[2-((4*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-*tert*-butyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5h)

Yield: 75% (138 mg), colourless oil; TLC: R_f = 0.85 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = + 69.5 (c = 0.7 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.87 (s, 9H, C(C*H*$_3$)$_3$), 2.67 (dd, *J* = 13.7, 8.7 Hz, 2H, C*H*$_2$Ph), 3.15 (dd, *J* = 13.7, 5.0 Hz, 2H, C*H*$_2$Ph), 3.88 (dd, *J* = 9.7, 8.1 Hz, 1H, C*H*N'), 3.97-4.05 (m, 2H, C*H*$_2$O, C*H*$_2$O'), 4.14-4.25 (m, 2H, C*H*$_2$O, C*H*$_2$O'), 4.52-4.59 (m, 1H, C*H*N), 6.79 (app t, *J* = 6.8 Hz, 1H, Ar-*H*C(2)), 7.11-7.44 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl), 7.70 (dd, *J* = 7.9, 1.3 Hz, 1H, Ar-*H*C(1)), 10.63 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 26.1 (C(*C*H$_3$)$_3$), 34.2 (*C*(CH$_3$)$_3$), 42.0 (C*H*$_2$Ph), 68.3 (*C*HN, *C*H$_2$O, *C*H$_2$O'), 68.4 (*C*HN, *C*H$_2$O, *C*H$_2$O'), 70.6 (*C*H$_2$O, *C*H$_2$O'), 76.6 (*C*HN'), 108.4 (Ar-*C*(2'), 114.0 (Ar-*C*(5)), 117.1 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5')), Ar-H*C*(phenyl)), 119.4 (Ar-H*C*(2)), 121.3, 126.6, 127.5, 128.6 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-

H*C*(phenyl)), 129.5 (Ar-H*C*(1)), 131.8 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5') , Ar-H*C*(phenyl)), 138.2 (*ipso*-Ph), 143.9, 144.2 (Ar-*C*(6), (Ar-*C*(3')), 159.0 (*C*=N), 163.2 (*C*=N); IR ($CHCl_3$ film): ν = 1411, 1499, 1558, 1639, 2956, 3026 cm^{-1}; HRMS (ES^+) calculated for $C_{27}H_{29}N_3O_2S$ $[M+H]^+$: 460.2059, found: 460.2062.

[2-((4*S*)-4-*tert*-Butyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-isopropyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5i)

Yield: 68 % (112 mg), off-white solid; Mp: 85-87 °C; TLC: R_f = 0.78 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = + 45.1 (c = 0.2 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.81 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)$_3$), 0.87 (s, 9H, C(C*H*$_3$)$_3$), 0.93 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)$_3$), 1.63-1.80 (m, 1H, C*H*(CH$_3$)$_3$), 3.89-4.07 (m, 4H, C*H*$_2$O, C*H*N, C*H*$_2$O', C*H*N'), 4.15-4.31 (m, 2H, C*H*$_2$O, C*H*$_2$O'), 6.76 (dd, *J* = 6.4, 1.8 Hz, 1H, Ar-*H*C(2)), 7.12-7.25 (m, 4H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5')), 7.72 (dd, *J* = 8.2, 1.2 Hz, 1H, Ar-*H*C(1)), 10.64 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4 (CH(*C*H$_3$)$_2$), 19.4 (CH(*C*H$_3$)$_2$), 26.1 (C(*C*H$_3$)$_3$), 33.2 (*C*H(CH$_3$)$_2$), 34.1 (*C*(CH$_3$)$_3$), 67.4 (CH$_2$O, CH$_2$O'), 70.4 (CH$_2$O, CH$_2$O'), 72.6 (*C*HN, *C*HN'), 76.8 (*C*HN, *C*HN'), 109.8 (Ar-*C*(2'), 113.3 (Ar-*C*(5)), 116.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5')), 118.9 (Ar-H*C*(2)), 122.1, 127.8 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), 130.2 (Ar-H*C*(1)), 131.7 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), 143.5, 144.3 (Ar-*C*(6), (Ar-*C*(3')), 159.2 (*C*=N), 162.6 (*C*=N); IR ($CHCl_3$ film): ν = 1410, 1463, 1585, 1637, 2092, 3429 cm^{-1}; HRMS (ES^+) calculated for $C_{23}H_{30}N_3O_2S$ $[M+H]^+$: 412.2059, found: 412.2063.

[2-((4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-*tert*-butyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5j)

Yield: 69 % (113 mg), pale yellow solid; Mp: 88-90 °C; TLC: R_f = 0.77 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = +48.0 (c = 0.15 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.85, 0.87 (2 x s, 12H, C(C*H*$_3$)$_3$, CH(C*H*$_3$)$_3$), 0.96 (d, *J* = 6.5 Hz, 3H, CH(C*H*$_3$)$_3$), 1.60-1.79 (m, 1H, C*H*(CH$_3$)$_3$), 3.94 (t, *J* = 7.8 Hz, 2H, C*H*$_2$O, C*H*N, C*H*$_2$O', C*H*N'), 4.01-4.10 (m, 2H, C*H*$_2$O, C*H*N, C*H*$_2$O', C*H*N'), 4.17-4.30 (m, 2H, C*H*$_2$O, C*H*$_2$O'), 6.81 (app t, *J* = 6.58 Hz, 1H, Ar-*H*C(2)), 7.03-7.28 (m, 4H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5')), 7.73 (d,

J = 7.7 Hz, 1H, Ar-*H*C(1)), 10.65 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.4 ($CH(CH_3)_2$), 18.1 ($CH(CH_3)_2$), 24.8 ($C(CH_3)_3$), 32.0 ($CH(CH_3)_2$), 33.0 ($C(CH_3)_3$), 67.4 (CH_2O, CH_2O'), 68.0 (CH_2O, CH_2O'), 72.1 (*C*HN, *C*HN'), 74.9 (*C*HN, *C*HN'), 109.0 (Ar-*C*(2'), 112.4 (Ar-*C*(5)), 115.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5')), 117.9 (Ar-H*C*(2)), 120.5, 126.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), 129.0 (Ar-H*C*(1)), 130.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), 142.6, 142.8 (Ar-*C*(6), (Ar-*C*(3')), 157.8 (*C*=N), 161.4 (*C*=N); IR ($CHCl_3$ film): ν = 1410, 1463, 1637, 2096, 3416 cm^{-1}; HRMS (ES^+) calculated for $C_{23}H_{30}N_3O_2S$ $[M+H]^+$: 412.2059, found: 412.2051.

[2-((4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-phenyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5k)

Yield: 72% (124 mg), pale yellow oil; TLC: R_f = 0.62 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = + 72.5 (c = 0.60 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.70 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)_3$), 0.78 (d, *J* = 6.7 Hz, 3H, $CH(CH_3)_3$), 1.54 (m, 1H, $CH(CH_3)_3$), 3.83-3.94 (m, 2H, CH_2O, C*H*N), 4.08-4.14 (m, 2H, C*H*N, CH_2O'), 4.64 (dd, *J* = 9.8, 8.1 Hz, 1H, CH_2O'), 5.27 (m, 1H, C*H*N'), 6.78 (m, 1H, Ar-*H*C(2)), 7.16-7.30 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.71 (dd, *J* = 7.8, 1.4 Hz, 1H, Ar-*H*C(1)), 10.78 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.7 ($CH(CH_3)_2$), 17.9 ($CH(CH_3)_2$), 31.4 ($CH(CH_3)_2$), 67.5 (CH_2O, CH_2O'), 69.0 (*C*HN'), 71.7 (*C*HN), 73.6 (CH_2O, CH_2O'), 107.2 (Ar-*C*(2'), 112.5 (Ar-*C*(5)), 115.3 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5')), Ar-H*C*(phenyl)), 118.1 (Ar-H*C*(2)), 120.4, 125.8, 126.4, 127.1, 127.5 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 128.9 (Ar-H*C*(1)), 130.4 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5') , Ar-H*C*(phenyl)), 141.8 (*ipso*-Ph), 142.6, 143.2 (Ar-*C*(6), (Ar-*C*(3')), 159.6 (*C*=N), 161.4 (*C*=N); IR ($CHCl_3$ film): ν = 1412, 1464, 1557, 1584, 2087, 2962, 3433 cm^{-1}; HRMS (ES^+) calculated for $C_{25}H_{26}N_3O_2S$ $[M+H]^+$: 432.1746, found: 432.1752.

[2-((4*S*)-4-Phenyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5l)

Yield: 71% (123 mg), yellow solid; Mp: 40-44 °C; TLC: R_f = 0.59 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = +246.8 (c = 0.69 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.73 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)$_3$), 0.83 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)$_3$), 1.56 (m, 1H, C*H*(CH$_3$)$_3$), 3.74 (app t, *J* = 7.6 Hz, 1H, C*H*$_2$O'), 3.82 (m, 1H, C*H*N'), 3.96 (t, *J* = 8.7 Hz, 1H, C*H*$_2$O'), 4.16 (t, *J* = 8.3 Hz, 1H, C*H*$_2$O), 4.72 (app t, *J* = 9.1 Hz, 1H, C*H*$_2$O), 5.47 (app t, *J* = 9.2 Hz, 1H, C*H*N), 6.90 (t, *J* = 7.2 Hz, 1H, Ar-*H*C(2)), 7.26-7.42 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.90 (d, *J* = 6.9 Hz, 1H, Ar-*H*C(1)), 10.94 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16.9 (CH(*C*H$_3$)$_2$), 18.0 (CH(*C*H$_3$)$_2$), 31.4 (*C*H(CH$_3$)$_2$), 68.4 (CH$_2$O'), 69.4 (*C*HN), 71.1 (*C*HN'), 72.4 (*C*H$_2$O), 107.5 (Ar-*C*(2'), 111.9 (Ar-*C*(5)), 115.5 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5')), Ar-H*C*(phenyl)), 117.9 (Ar-H*C*(2)), 119.9, 125.8, 126.4, 126.5, 127.2, 127.5 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 129.2 (Ar-H*C*(1)), 130.8 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5') , Ar-H*C*(phenyl)), 141.6 (*ipso*-Ph), 142.5, 142.9 (Ar-*C*(6), (Ar-*C*(3')), 158.0 (*C*=N), 163.0 (*C*=N); IR ($CHCl_3$ film): ν = 1410, 1464, 1637, 2096, 3433 cm^{-1}; HRMS (ES^+) calculated for $C_{25}H_{26}N_3O_2S$ $[M+H]^+$: 432.1746, found: 432.1726.

[2-((4*S*)-4-*tert*-Butyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-phenyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5m)

Yield : 65 % (115 mg), colourless oil; TLC : R_f = 0.84 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = +85.2 (c = 0.7 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (s, 9H, C(C*H*$_3$)$_3$), 3.97-4.06 (m, 2H, C*H*N, C*H*$_2$O), 4.13-4.21 (m, 2H, C*H*$_2$O, C*H*$_2$O'), 4.73 (app t, *J* = 8.1 Hz, 1H, C*H*$_2$O'), 5.33 (app t, *J* = 8.0 Hz, 1H, C*H*N'), 6.86 (m, 1H, Ar-HC(2)), 7.24-7.36 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.79 (dd, *J* = 7.8, 1.4 Hz, Ar-*H*C(1)), 10.75 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$) : δ = 26.0 (C(*C*H$_3$)$_3$), 34.0 (*C*(CH$_3$)$_3$), 67.4 (*C*HN), 69.9 (*C*H$_2$O), 75.1 (*C*HN), 76.7 (*C*H$_2$O), 107.6 (Ar-*C*(2')), 113.6 (Ar-*C*(5)), 116.5 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 119.2 (Ar-H*C*(2)), 122.2, 127.1, 127.6, 128.5, 128.8 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 130.2 (Ar-H*C*(1)), 131.7 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 143.0 (*ipso*-Ph), 144.0, 144.2 (Ar-*C*(6)), (Ar-*C*(3')), 160.9

(*C*=N), 162.7 (*C*=N); IR ($CHCl_3$ film): ν = 1411, 1463, 1556, 1631, 2095, 2867, 2956 cm^{-1}; HRMS calculated for $C_{26}H_{27}N_3O_2S$ $[M+H]^+$: 446.1902, found: 446.1894.

[2-((4*S*)-4-Phenyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-*tert*-butyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5n)

Yield : 67 % (119 mg), white solid; Mp: 46-49 ºC; TLC : R_f = 0.90 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = +251.6 (c = 0.50 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.713, 0.708 (2 x s, 9H, C(C*H*$_3$)$_3$), 3.68 (m, 3H, C*H*N', C*H*$_2$O'), 4.09 (ddd, *J* = 10.2, 8.3, 1.9 Hz, 1H, C*H*$_2$O), 4.65 (m, 1H, CH_2O), 5.39 (m, 1H, C*H*N), 6.82 (t, *J* = 7.1 Hz, 1H, Ar-HC(2)), 7.18-7.70 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.82 (d, *J* = 7.9 Hz, Ar-*H*C(1)), 10.78 (br s, 1H, N*H*) ; ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.7 (C(*C*H$_3$)$_3$), 32.7 (*C*(CH$_3$)$_3$), 67.2 (*C*HN), 69.3 (*C*H$_2$O), 72.5 (*C*HN), 74.8 (*C*H$_2$O), 107.5 (Ar-*C*(2')), 112.2 (Ar-*C*(5)), 115.7 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 118.0 (Ar-H*C*(2)), 120.0, 125.8, 125.7, 126.4, 126.5, 127.5 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 129.2 (Ar-H*C*(1)), 130.8 (Ar-H*C*(3)), Ar-H*C*(4)), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 141.6 (*ipso*-Ph), 142.5, 142.9 (Ar-*C*(6)), (Ar-*C*(3')), 157.9 (*C*=N), 162.9 (*C*=N); IR ($CHCl_3$ film): ν = 1410, 1464, 1586, 1635, 2096, 2959, 3436 cm^{-1}; HRMS calculated for $C_{26}H_{27}N_3O_2S$ $[M+H]^+$: 446.1902, found: 446.1906.

[2-((4*S*)-4-Benzyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5o)

Yield : 73 % (130 mg), pale yellow oil; TLC: R_f = 0.42 (pentane/ethyl acetate 10:1); $[\alpha]_D$ = +47.4 (c = 0.70 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (d, *J* = 7.1 Hz, 3H, CH(C*H*$_3$)$_2$)), 0.91 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)$_2$)), 1.79 (m, 1H, C*H*(CH$_3$)$_2$)), 2.76 (dd, *J* = 13.7, 8.6 Hz, 2H, C*H*$_2$Ph), 3.22 (dd, *J* = 13.6, 4.9 Hz, 2H, C*H*$_2$Ph), 3.93-4.10 (m, 3H, C*H*N', C*H*$_2$O), 4.23-4.65 (m, 2H, C*H*$_2$O), 4.58-4.65 (m, 1H, C*H*N), 6.85 (t, *J* = 7.3 Hz, 1H, Ar-*H*C(2)), 7.18-7.37 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5')Ar-*H*C(phenyl)), 7.77 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar-*H*C(1)), 10.78 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.2 (CH(*C*H$_3$)$_2$), 18.3 (CH(*C*H$_3$)$_2$), 31.9 (*C*H(CH$_3$)$_2$), 40.7

(*C*H_2Ph), 67.1 (*C*HN), 68.8, 69.4 (*C*H_2O, *C*H_2O'), 71.8 (*C*HN'), 107.3 (Ar-*C*(2'), 112.5 (Ar-*C*(5)), 115.3, 118.0 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5'),), 120.0 (Ar-H*C*(2)), 125.4, 126.5, 127.4, 128.2 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 129.0 (Ar-H*C*(1)), 130.6 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 137.0 (*ipso*-Ph), 142.7 (Ar-*C*(6), Ar-*C*(3')), 142.8 (Ar-*C*(6), Ar-*C*(3')), 158.0 (*C*=N), 162.0 (*C*=N); IR ($CHCl_3$ film): ν = 1464, 1635, 2091, 2341, 2360, 3414 cm^{-1}; HRMS calculated for $C_{26}H_{27}N_3O_2S$ $[M+H]^+$: 446.1904, found: 446.1890.

[2-((4*S*)-4-Isopropyl-4,5-dihydrooxazol-2-yl)-phenyl]-[2-((4*S*)-4-benzyl-4,5-dihydrooxazol-2-yl)-thiophene-3-yl]amine (5p)

Yield: 76 % (135 mg), pale yellow oil; TLC: R_f = 0.46 (pentane/ethyl acetate 3:1); $[\alpha]_D$ = +42.1 (c = 0.65 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)$_2$)), 0.95 (d, *J* = 6.5 Hz, 3H, CH(C*H*$_3$)$_2$)), 1.73 (m, 1H, C*H*(CH$_3$)$_2$)), 2.60 (dd, *J* = 13.5, 9.0 Hz, 2H, C*H*$_2$Ph), 3.16 (dd, *J* = 13.7, 4.9 Hz, 2H, C*H*$_2$Ph), 3.90-4.01 (m, 3H, C*H*N, C*H*$_2$O), 4.17-4.26 (m, 2H, C*H*$_2$O), 4.41-4.48 (m, 1H, C*H*N'), 6.78 (ddd, *J* = 14.5, 6.8, 1.4 Hz, 1H, Ar-*H*C(2)), 7.05-7.27 (m, 9H, Ar-*H*C(3), Ar-*H*C(4), Ar-*H*C(4'), Ar-*H*C(5'), Ar-*H*C(phenyl)), 7.73 (dd, *J* = 8.0, 1.3 Hz, 1H, Ar-*H*C(1)), 10.70 (br s, 1H, N*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5 (CH(*C*H$_3$)$_2$), 18.1 (CH(*C*H$_3$)$_2$), 32.0 (*C*H(CH$_3$)$_2$), 40.9 (*C*H_2Ph), 66.7 (*C*HN), 67.9, 70.7 (*C*H_2O, *C*H_2O'), 72.1 (*C*HN'), 108.0 (Ar-*C*(2'), 112.1 (Ar-*C*(5)), 115.2, 117.9 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5'),), 120.6 (Ar-H*C*(2)), 125.3, 126.9, 127.4, 128.2 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 128.9 (Ar-H*C*(1)), 130.5 (Ar-H*C*(3), Ar-H*C*(4), Ar-H*C*(4'), Ar-H*C*(5'), Ar-H*C*(phenyl)), 137.2 (*ipso*-Ph), 142.7 (Ar-*C*(6), Ar-*C*(3')), 142.8 (Ar-*C*(6), Ar-*C*(3')), 158.8 (*C*=N), 161.5 (*C*=N); IR ($CHCl_3$ film): ν = 1412, 1464, 1502, 1585, 2092, 3423 cm^{-1}; HRMS (ES^+) calculated for $C_{26}H_{27}N_3O_2S$ $[M+H]^+$: 446.1902, found: 446.1891.

General Procedure for the Nozaki-Hiyama-Kishi allylation of benzaldehyde

A flame-dried Schlenk tube was charged with dry THF (1 mL) and dry acetonitrile (150 µL). Anhydrous chromium(III) chloride (4.0 mg, 25.3 µmol) and manganese (41.7 mg,

0.76 mmol) were added simultaneously to the solvent mixture. The resulting suspension was allowed to stand at room temperature for approximately 30 minutes until the characteristic purple colour of the chromium(III) salt disappeared. The mixture was stirred vigorously under an atmosphere of nitrogen for 1 h resulting in a green reaction mixture. DIPEA (13 μL, 75.9 μmol) was added followed by the ligand 5 (30.4 μmol) resulting in an immediate green catalyst mixture. This was stirred at room temperature for 1 hour prior to the addition of the allyl bromide (0.51 mmol) with the resulting chromium(III) allyl solution being stirred for a further 1 h. The reaction was initiated by the addition of aldehyde (0.25 mmol) and chlorotrimethylsilane (64 μL, 0.51 mmol) and stirred under an atmosphere of nitrogen at room temperature for 16 h. The resulting green/brown suspension was quenched with saturated aqueous $NaHCO_3$ (1 mL) and extracted with Et_2O (3 x 1 mL). The combined organic layers were concentrated in vacuo to give a green residue. This was flushed through a small silica gel column (1.5 x 5 cm, pentane/AcOEt 9:1) to remove the catalyst and after evaporation of the solvent, the reaction products were isolated as a yellow oil. The % conversion of the reaction was determined at this stage from the ^1H NMR spectrum of the crude product (generally a mixture of silylated and free alcohol) by measuring the ratio of aldehyde to product and assuming that all aldehyde consumed went to product. Peaks consistent with the product of pinacol coupling were not observed in any of the catalytic studies employing ligands **5**. The yellow oil was dissolved in THF (1 mL), a few drops of aqueous 1 M HCl were added, and the resulting solution was stirred for 10 min when TLC (pentane/AcOEt 9:1)) showed complete desilylation. The solvent was removed *in vacuo* and the resulting aqueous phase was extracted with Et_2O (3 x 2 mL). The organic layers were combined, dried over anhydrous Na_2SO_4 and concentrated in vacuo to give a yellow oil. This was purified by flash column chromatography on silica gel (1 x 15 cm) using cyclohexane/AcOEt 5:1 as the eluent to give the required product as a pale yellow oil. Enantioselectivity was determined by HPLC: Chiralcel OD, Hexane/isopropanol 98:2, flow rate 0.3 mL/min: (*R*) 35.1 min, (*S*) 41.7 min.