Parallel Synthesis of a Library of Benzoxazoles and Benzothiazoles using Ligand Accelerated Copper Catalyzed Cyclizations of Ortho-halobenzanilides

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Experimental Procedures and Characterization Data

All reagents, unless otherwise stated, were used as received from commercial suppliers. THF was distilled from sodium metal/benzophenone ketyl under argon. CH₂Cl₂ was distilled from CaH₂ under argon. Thin layer chromatography (TLC) was performed on aluminum-backed plates of silica precoated with Alugram SIL/G/UV₂₅₄. Flash chromatography was performed using silica gel (60 Å, 230-400 mesh) with reagent grade solvents. NMR spectra were recorded at either 300 or 400 MHz (¹H NMR) and 75 or 100 MHz (¹³C NMR), referenced to an internal standard (TMS) or residual solvent protons and signals are reported in ppm (δ). Low resolution mass spectra (LRMS) were recorded on a Bell and Howell 21-490 spectrometer. High resolution mass spectra (HRMS) were recorded on a AEI MS3074 spectrometer. Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. FT-IR spectra were obtained on a Perkin-Elmer Spectrum 1000 with samples loaded as thin films on NaCl plates or as KBr discs.

Starting Material Preparation (6 or 8)

General Procedure for Preparation of Amides from *ortho*-Haloanilines and Acid Chlorides:

To a solution of *ortho*-haloaniline (9.16 mmol, 1.0 equiv) in dry THF (20 mL) at room temperature was added acyl chloride (10.01 mmol, 1.1 equiv). The reaction mixture was stirred for 24 hours then diluted with EtOAc (50 mL). The organic layer was washed with 5% NaHCO₃ (2 x 50 mL), sat. NaCl (1 x 25 mL), dried over MgSO₄ and the solvent was removed *in vacuo*. The product was carried on to next step without any further purification in most cases. However, if necessary a silica gel column chromatography was performed.

Synthesis of *N*-(2-bromophenyl)benzamide (6a): The product was obtained as a white solid in 99% yield (2.53 g). mp = 107-108 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.60 (dd, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 8.54 (br s, 1H), 7.94-8.02 (m, 2H), 7.52-7.67 (m, 4H), 7.42 (td, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.06 (td, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 165.3, 135.9, 134.6, 132.3, 132.2, 129.0, 128.6, 127.1, 125.3, 121.8, 113.8. (*Tetrahedron* **1984**, 40, 1919-1925)

Synthesis of *N*-(2-bromophenyl)-4-chlorobenzamide (6b): The product was obtained as a white solid in 99% yield (2.85 g). mp = 135-136 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.56 (dd, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 8.43 (br s, 1H), 7.88-7.95 (m, 2H), 7.63 (dd, 1H, *J* = 8.1 Hz, *J* = 1.4 Hz), 7.51-7.58 (m, 2H), 7.42 (td, 1H, *J* = 8.5 Hz, *J* = 1.4 Hz), 7.07 (td, 1H, *J* = 7.8 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 164.2, 138.6, 135.6, 133.0, 132.3, 129.3, 128.6, 128.6, 125.5, 121.8, 113.8. (*J. Chem. Soc., Perkin Trans I* **1972**, 11, 1296-1304)

Synthesis of 4-bromo-*N*-(2-bromophenyl)benzamide (6c): The product was obtained as a yellowish solid in 99% yield (3.25 g). mp = 138-139 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.55 (dd, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 8.43 (br s, 1H), 7.81-7.87 (m, 2H), 7.62-7.74 (m, 2H), 7.62 (dd, 1H, *J* = 8.1 Hz, *J* = 1.5 Hz), 7.40 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.07 (td, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 164.3, 135.6, 133.4, 132.3, 132.2, 128.7, 128.6, 127.1, 125.5, 121.8, 113.8.

Synthesis of *N*-(2-bromophenyl)-4-cyanobenzamide (6d): The product was obtained as a yellowish solid in 98% yield (2.68 g). mp = 175-176 °C; TLC (3:1 CH₂Cl₂:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 8.55 (dd, 1H, *J* = 8.2 Hz, *J* = 1.4 Hz), 8.47 (br s, 1H), 8.07 (d, 2H, *J* = 8.2 Hz), 7.87 (d, 2H, *J* = 8.2 Hz), 7.65 (dd, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.44 (td, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.11 (td, 1H, *J* = 7.8 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 163.4, 138.4, 135.2, 132.8, 132.4, 128.7, 127.8, 126.0, 121.9, 117.8, 115.8, 114.0.

Synthesis of *N*-(2-bromophenyl)-4-nitrobenzamide (6e): The product was obtained as a yellowish solid in 99% yield (2.90 g). mp = 116-117 °C; TLC (3:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.22-8.29 (m, 2H), 8.14 (d, 1H, *J* = 7.8 Hz), 7.57-7.64 (m, 2H), 7.55 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.33 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.29 (br s, 1H), 6.98 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 152.6, 147.8, 143.2, 135.4, 132.4, 128.5, 128.5, 124.8, 123.9, 123.9, 120.4. (*Botanical Gazette (Chicago)* **1946**, 107, 476-507)

Synthesis of *N*-(2-bromophenyl)-3-phenylacrylamide (6f): The product was obtained as a yellowish solid in 99% yield (2.80 g). mp = 148-149 °C; TLC (3:1 CH₂Cl₂:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 8.55 (br d, 1H, *J* = 7.8 Hz), 7.83 (br s, 1H), 7.82 (d, 1H, *J* = 15.5

Hz), 7.57-7.66 (m, 3H), 7.35-7.49 (m, 4H), 7.04 (td, 1H, $J = 7.5$ Hz, $J = 1.7$ Hz), 6.63 (d, 1H, $J = 15.5$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 163.9, 143.0, 135.9, 134.5, 132.3, 130.2, 128.9, 128.5, 128.1, 125.3, 122.1, 120.6, 113.6. (*J. Am. Chem. Soc.* **1979**, 101, 5281-5283)

Synthesis of *N*-(2-bromophenyl)propionamide (6g): The product was obtained as a yellowish solid in 98% yield (2.05 g). mp = 89-91 °C; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.4$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.41 (d, 1H, $J = 8.0$ Hz), 7.67 (br s, 1H), 7.56 (dd, 1H, $J = 8.0$ Hz, $J = 1.4$ Hz), 7.35 (td, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 7.00 (td, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 2.51 (q, 2H, $J = 7.5$ Hz), 1.32 (t, 3H, $J = 7.5$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 171.9, 135.7, 132.2, 128.4, 125.0, 121.9, 113.3, 31.0, 9.6. (*Nippon Kagaku Kaishi* **1985**, 438-441)

Synthesis of *N*-(2-bromophenyl)isobutyramide (6h): The product was obtained as a yellowish solid in 97% yield (2.15 g). mp = 99-101 °C; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.4$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.42 (d, 1H, $J = 7.5$ Hz), 7.74 (br s, 1H), 7.56 (dd, 1H, $J = 8.0$ Hz, $J = 1.4$ Hz), 7.35 (td, 1H, $J = 8.2$ Hz, $J = 1.5$ Hz), 7.00 (td, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 2.64 (heptuplet, 1H, $J = 7.0$ Hz), 1.34 (d, 6H, $J = 7.0$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 175.1, 135.8, 132.2, 128.4, 125.2, 121.9, 113.5, 37.0, 19.6.

Synthesis of *N*-(2-bromophenyl)-3,4-dichlorobenzamide (6i): The product was obtained as a yellowish solid in 99% yield (3.25 g). mp = 127 °C; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.5$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.49 (dd, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 8.38 (br s, 1H), 8.06 (d, 1H, $J = 8.2$ Hz), 7.76 (dd, 1H, $J = 8.2$ Hz, $J = 1.5$ Hz), 7.58-7.66 (m, 2H), 7.41 (td, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 7.07 (td, 1H, $J = 8.2$ Hz, $J = 1.5$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 163.1, 136.8, 135.3, 134.3, 133.6, 132.4, 131.0, 129.5, 128.6, 126.0, 125.8, 122.0, 114.0.

Synthesis of *N*-(2-bromophenyl)-4-methoxybenzamide (6j): The product was isolated by silica gel column chromatography (CH_2Cl_2) as a white solid in 99% yield (2.80 g). mp = 147-148 °C; TLC (2:1 CH_2Cl_2 :Hexanes), $R_f = 0.5$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.59 (dd, 1H, $J = 8.2$ Hz, $J = 1.4$ Hz), 8.43 (br s, 1H), 7.91-7.98 (m, 2H), 7.61 (dd, 1H, $J = 8.2$ Hz, $J = 1.5$ Hz), 7.40 (td, 1H, $J = 8.0$ Hz, $J = 1.4$ Hz), 7.00-7.08 (m, 3H), ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.8, 162.8, 136.0, 132.2, 129.0, 128.5, 126.8, 125.0, 121.7, 114.2, 113.7, 55.5. (*J. Org. Chem.* **2002**, 67, 7424-7428)

Synthesis of *N*-(2-bromophenyl)-2-methoxybenzamide (6k): The product was obtained as a white solid in 99% yield (1.40 g). mp = 115-117 °C; TLC (CH₂Cl₂), R_f = 0.5; ¹H NMR (CDCl₃, 300 MHz) δ 10.55 (br s, 1H), 8.71 (dd, 1H, *J* = 8.4 Hz, *J* = 1.8 Hz), 8.35 (dd, 1H, *J* = 7.8 Hz, *J* = 1.9 Hz), 7.62 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.56 (td, 1H, *J* = 8.4 Hz, *J* = 1.8 Hz), 7.39 (td, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.18 (td, 1H, *J* = 8.2 Hz, *J* = 1.1 Hz), 7.10 (d, 1H, *J* = 8.2 Hz), 7.02 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 163.4, 157.4, 137.2, 133.6, 132.7, 132.4, 128.3, 124.8, 122.4, 121.5, 113.4, 111.5, 56.3.

Synthesis of thiophene-2-carboxylic acid (2-bromophenyl)amide (6l): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 96% yield (1.25 g). mp = 116-117 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 8.48 (dd, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 8.33 (br s, 1H), 7.65-7.70 (m, 1H), 7.53-7.60 (m, 2H), 7.35 (td, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 7.16 (dd, 1H, *J* = 4.8 Hz, *J* = 3.7 Hz), 7.00 (dd, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 159.6, 139.1, 135.6, 132.3, 131.3, 128.7, 128.6, 128.0, 125.3, 121.7, 113.5. (*Heterocycles* **1991**, 32, 975-984)

Synthesis of *N*-(2-bromophenyl)-nicotinamide (6m): The product was obtained as a white solid in 99% yield (1.28 g). mp = 93-95 °C; TLC (1:1 EtOAc:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 9.69 (br s, 1H), 8.85 (d, 1H, *J* = 4.1 Hz), 8.52 (dd, 2H, *J* = 8.4 Hz, *J* = 1.5 Hz), 8.31 (dt, 1H, *J* = 8.0 Hz, *J* = 1.8 Hz), 7.63 (dd, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.53 (dd, 1H, *J* = 8.0 Hz, *J* = 4.8 Hz), 7.42 (td, 1H, *J* = 8.2 Hz, *J* = 1.4 Hz), 7.09 (td, 1H, *J* = 7.6 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 163.3, 152.7, 147.9, 135.4, 135.3, 132.4, 130.4, 128.6, 125.9, 123.9, 122.1, 114.1. (*J. Org. Chem.* **1999**, 64, 8546-8556)

Synthesis of *N*-(2-bromophenyl)-2-chloronicotinamide (6n): The product was obtained as a white solid in 99% yield (1.45 g). mp = 124-126 °C; TLC (1:1 EtOAc:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 8.86 (br s, 1H), 8.59 (dd, 1H, *J* = 4.7 Hz, *J* = 1.9 Hz), 8.55 (d, 1H, *J* = 8.0 Hz), 8.29 (dd, 1H, *J* = 7.7 Hz, *J* = 1.8 Hz), 7.65 (dd, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 7.39-7.51 (m, 2H), 7.11 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 162.6, 151.6, 147.1, 140.2, 135.4, 132.6, 131.1, 128.5, 126.1, 123.0, 122.4, 114.0.

Synthesis of *N*-(2-bromo-4-methylphenyl)benzamide (6p): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 98% yield (1.18 g). mp = 149-150 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.44 (d, 1H, *J* = 8.4 Hz), 8.41 (br s, 1H), 7.94-8.00 (m, 2H), 7.51-7.65 (m, 3H), 7.44 (dd, 1H, *J* = 1.8 Hz, *J* = 1.1 Hz), 7.23 (dd, 1H, *J* = 8.0 Hz, *J* = 1.8 Hz), 2.37 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 165.2, 135.4, 134.7, 133.3, 132.5, 132.1, 129.2, 128.9, 127.1, 121.7, 113.7, 20.6. (*Tetrahedron* **2001**, 57, 9963-9972)

Synthesis of *N*-(2-bromo-4-chlorophenyl)benzamide (6q): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 97% yield (0.73 g). mp = 122-124 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.58 (d, 1H, *J* = 8.9 Hz), 8.45 (br s, 1H), 7.93-7.99 (m, 2H), 7.53-7.67 (m, 4H), 7.40 (dd, 1H, *J* = 8.9 Hz, *J* = 2.3 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 165.2, 134.6, 134.3, 132.4, 131.7, 129.5, 129.0, 128.7, 127.1, 122.3, 113.8. (*Tetrahedron* **1964**, 20, 2195-2199)

Synthesis of *N*-(2-bromo-4-fluorophenyl)benzamide (6r): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 98% yield (1.27 g). mp = 140-141 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 8.55 (dd, 1H, *J* = 9.2 Hz, *J* = 5.6 Hz), 8.36 (br s, 1H), 7.93-8.00 (m, 2H), 7.52-7.67 (m, 3H), 7.38 (dd, 1H, *J* = 7.8 Hz, *J* = 2.9 Hz), 7.11-7.20 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 165.3, 158.6 (d, *J* = 248.5 Hz), 134.4, 132.4, 132.3, 129.0, 127.1, 122.9 (d, *J* = 8.1 Hz), 119.4 (d, *J* = 25.6 Hz), 115.4 (d, *J* = 21.6 Hz), 113.8 (d, *J* = 9.8 Hz). (*Comptes Rendus des Seances de l'Academie des Sciences, Serie C: Sciences Chimiques* **1966**, 263, 145-148)

Synthesis of *N*-(2-bromo-5-fluorophenyl)benzamide (6s): The product was isolated by silica gel column chromatography (1:2 CH₂Cl₂:Hexanes) as a white solid in 96% yield (0.74 g). mp = 82-83 °C; TLC (1:2 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.54 (br s, 1H), 8.50 (dd, 1H, *J* = 11.0 Hz, *J* = 3.0 Hz), 7.94-8.00 (m, 2H), 7.52-7.67 (m, 4H), 6.76-6.85 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 165.2, 162.3 (d, *J* = 245.9 Hz), 137.0 (d, *J* = 12.1 Hz), 134.2, 132.7 (d, *J* = 9.2 Hz), 132.5, 129.1, 127.1, 112.2 (d, *J* = 23.3 Hz), 109.1 (d, *J* = 29.4 Hz), 107.4 (d, *J* = 3.5 Hz). (*J. Heterocycl. Chem.* **1965**, 2, 148-151)

Synthesis of *N*-(2-bromo-5-trifluoromethylphenyl)benzamide (6t): The product was isolated by silica gel column chromatography (1:2 CH₂Cl₂:Hexanes) as a white solid in 97% yield (1.16 g). mp = 146-147 °C; TLC (1:2 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.98 (d, 1H, *J* = 1.8 Hz), 8.60 (br s, 1H), 7.95-8.01 (m, 2H), 7.75 (d, 1H, *J* = 8.4 Hz), 7.52-7.67 (m, 3H), 7.31 (dd, 1H, *J* = 8.5 Hz, *J* = 1.7 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 165.4, 136.5, 134.0, 132.7, 132.6, 131.1 (q, *J* = 33.1 Hz), 129.1, 127.1, 123.6 (q, *J* = 272.7 Hz), 121.6 (q, *J* = 3.7 Hz), 118.4 (q, *J* = 4.0 Hz), 116.9.

Synthesis of *N*-(2-bromophenyl)malonamic acid methyl ester (6v): The product was obtained as a yellow solid in 99% yield (0.80 g). mp = 79-80 °C; TLC (1:2 EtOAc:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 9.57 (br s, 1H), 8.35 (dd, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 7.58 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.33 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.01 (td, 1H, *J* = 8.2 Hz, *J* = 1.5 Hz), 3.85 (s, 3H), 3.57 (s, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 169.8, 163.1, 135.7, 132.5, 128.2, 135.6, 122.3, 113.8, 52.8, 41.7.

Synthesis of *N*-(2-bromophenyl)malonamic acid ethyl ester (6w): The product was obtained as a yellowish solid in 99% yield (1.35 g). mp = 58-59 °C; TLC (1:2 EtOAc:Hexanes), R_f = 0.6; ¹H NMR (CDCl₃, 300 MHz) δ 9.63 (br s, 1H), 8.38 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.60 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.35 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.03 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 4.33 (q, 2H, *J* = 7.0 Hz), 3.57 (s, 2H), 1.38 (d, 6H, *J* = 7.0 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 169.4, 163.2, 135.7, 132.5, 128.2, 125.5, 122.3, 113.7, 62.0, 42.0, 14.1.

Synthesis of *N*-(2-bromophenyl)-3-(1,3-dioxo-1,3-dihydroisoindol-2-yl)-propionamide (6ab): The product was obtained as a white solid in 99% yield (0.48 g). mp = 189-192 °C; TLC (1:2 EtOAc:Hexanes), R_f = 0.2; ¹H NMR (CDCl₃, 300 MHz) δ 8.32 (br d, 1H, *J* = 7.5 Hz), 7.85-7.93 (m, 2H), 7.73-7.79 (m, 2H), 7.64 (br s, 1H), 7.54 (dd, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.33 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.01 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 4.16 (t, 2H, *J* = 7.0 Hz), 2.93 (t, 2H, *J* = 7.0 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 168.1, 168.0, 135.3, 134.1, 132.2, 132.0, 128.4, 125.4, 123.4, 122.3, 121.9, 35.1, 23.7.

Synthesis of but-2-enoic acid (2-bromophenyl)amide (6ac): The product was obtained as a white solid in 99% yield (2.20 g). mp = 80-82 °C; TLC (2:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR

(CDCl₃, 300 MHz, mixture isomers) δ 8.44 (d, 1H, J = 8.2 Hz), 7.67 (br s, 1H), 7.55 (dd, 1H, J = 8.0 Hz, J = 1.4 Hz), 7.28-7.37 (m, 1H), 6.94-7.08 (m, 2H), 5.98-6.08 (m, 1H), 1.95 (dd, 3H, J = 6.9 Hz, J = 1.6 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 163.8, 142.2, 135.9, 132.2, 128.4, 125.4, 125.1, 122.0, 113.5, 17.9. (*J. Chem. Soc., Chem. Comm.* **1986**, 2, 115-116)

Synthesis of *N*-(2-iodophenyl)benzamide (6a-I): The product was obtained as a yellowish solid in 99% yield (1.49 g). mp = 133-134 °C; TLC (1:4 EtOAc:Hexanes), R_f = 0.5; ¹H NMR (CDCl₃, 300 MHz) δ 8.46 (dd, 1H, J = 8.2 Hz, J = 1.5 Hz), 8.30 (br s, 1H), 7.98-8.01 (m, 2H), 7.82 (dd, 1H, J = 8.0 Hz, J = 1.5 Hz), 7.48-7.63 (m, 3H), 7.40 (td, 1H, J = 8.2 Hz, J = 1.5 Hz), 6.88 (td, 1H, J = 8.0 Hz, J = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 165.4, 138.9, 138.3, 134.5, 132.3, 129.5, 129.0, 127.2, 126.1, 121.8, 90.3. (*Chem. Commun.* **1967**, 13, 614-615)

Synthesis of 4-chloro-*N*-(2-iodophenyl)benzamide (6b-I): The product was obtained as a brownish solid in 99% yield (0.96 g). mp = 150-151 °C; TLC (1:4 EtOAc:Hexanes), R_f = 0.6; ¹H NMR (CDCl₃, 300 MHz) δ 8.44 (dd, 1H, J = 8.2 Hz, J = 1.4 Hz), 8.26 (br s, 1H), 7.93 (d, 2H, J = 8.4 Hz), 7.85 (dd, 1H, J = 8.0 Hz, J = 1.4 Hz), 7.53 (d, 2H, J = 8.4 Hz), 7.44 (td, 1H, J = 8.2 Hz, J = 1.5 Hz), 6.93 (td, 1H, J = 8.2 Hz, J = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 164.3, 138.9, 138.6, 138.0, 132.9, 131.0, 129.5, 129.3, 128.6, 121.9, 90.4.

Synthesis of 4-cyano-*N*-(2-iodophenyl)benzamide (6d-I): The product was obtained as a brownish solid in 99% yield (0.88 g). mp = 153-154 °C; TLC (1:4 EtOAc:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.43 (dd, 1H, J = 8.2 Hz, J = 1.4 Hz), 8.30 (br s, 1H), 8.06-8.13 (m, 2H), 7.82-7.90 (m, 3H), 7.46 (td, 1H, J = 8.0 Hz, J = 1.4 Hz), 6.97 (td, 1H, J = 7.8 Hz, J = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 163.5, 139.0, 138.4, 137.6, 132.9, 129.6, 127.9, 126.8, 122.0, 117.9, 115.8, 90.6.

Synthesis of 3,4-dichloro-*N*-(2-iodophenyl)benzamide (6i-I): The product was obtained as a brownish solid in 99% yield (1.10 g). mp = 158-159 °C; TLC (1:4 EtOAc:Hexanes), R_f = 0.6; ¹H NMR (CDCl₃, 300 MHz) δ 8.39 (dd, 1H, J = 8.2 Hz, J = 1.5 Hz), 8.22 (br s, 1H), 8.09 (d, 1H, J = 2.1 Hz), 7.85 (dd, 1H, J = 8.0 Hz, J = 1.5 Hz), 7.80 (dd, 1H, J = 8.0 Hz, J = 2.1 Hz), 7.63 (d, 1H, J = 8.2 Hz), 7.44 (td, 1H, J = 8.2 Hz, J = 1.5 Hz), 6.94 (td, 1H, J = 8.2 Hz, J = 1.5 Hz); ¹³C

NMR (CDCl₃, 75 MHz) δ 163.1, 138.9, 137.7, 136.8, 134.3, 133.6, 131.0, 129.6, 129.5, 126.6, 126.0, 122.0, 90.6.

Synthesis of *N*-(2-iodophenyl)-4-methoxybenzamide (6j-I): The product was obtained as a brownish solid in 99% yield (0.97 g). mp = 151-152 °C; TLC (1:4 EtOAc:Hexanes), R_f = 0.5; ¹H NMR (CDCl₃, 300 MHz) δ 8.48 (dd, 1H, J = 8.2 Hz, J = 1.4 Hz), 8.26 (br s, 1H), 7.94-8.01 (m, 2H), 7.84 (dd, 1H, J = 8.0 Hz, J = 1.4 Hz), 7.42 (td, 1H, J = 8.2 Hz, J = 1.4 Hz), 7.01-7.08 (m, 2H), 6.90 (td, 1H, J = 8.0 Hz, J = 1.4 Hz), 3.91 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 164.9, 162.8, 138.8, 138.4, 132.4, 129.4, 129.1, 125.8, 121.7, 114.2, 90.2, 55.5.

Synthesis of *N*-(2-chlorophenyl)benzamide (6a-Cl): The product was obtained as a white solid in 99% yield (2.21 g). mp = 97-98 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.56 (dd, 1H, J = 8.2 Hz, J = 1.5 Hz), 8.45 (br s, 1H), 7.87-7.95 (m, 2H), 7.45-7.61 (m, 3H), 7.40 (dd, 1H, J = 8.0 Hz, J = 1.4 Hz), 7.32 (td, 1H, J = 8.0 Hz, J = 1.4 Hz), 7.07 (td, 1H, J = 8.2 Hz, J = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 165.3, 134.8, 134.6, 132.2, 129.1, 129.0, 127.9, 127.1, 124.8, 123.1, 121.6. (*J. Am. Chem. Soc.* **1954**, 76, 431-436)

General Procedure for Preparation of Amides from *ortho*-Haloanilines and Precursor Acids Using EDC/HOBt Coupling Agents: To a suspension of precursor acid (4.60 mmol, 1.0 equiv) in dry CH₂Cl₂ (20 mL) under nitrogen, at 0 °C, was added DIPEA (2.40 mL, 13.77 mmol, 3.0 equiv). To the reaction mixture was added HOBt (0.74 g, 5.51 mmol, 1.2 equiv) and EDC (1.05 g, 5.51 mmol, 1.2 equiv). The reaction was stirred for 10 minutes then 2-bromoaniline (4.60 mmol, 1.0 equiv) was added. The reaction was then stirred at 0 °C for 10 minutes and at room temperature for 24 hours. The mixture was diluted with EtOAc (50 mL) and washed with 10% NH₄Cl (2 x 50 mL), 5% NaHCO₃ (1 x 50 mL), and saturated NaCl (1 x 25 mL). The organic layer was then dried over MgSO₄ and the solvent was removed *in vacuo*. The product was isolated *via* silica gel column chromatography.

Synthesis of 1*H*-pyrrole-2-carboxylic acid (2-bromophenyl)amide (6o): The product was isolated by silica gel column chromatography (1:2 EtOAc:Hexanes) as a white solid in 44% yield (0.530 g). mp = 175-177 °C; TLC (1:2 EtOAc:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 9.40 (s, 1H), 8.14 (d, 1H, J = 8.4 Hz), 7.42-7.64 (m, 4H), 7.26-7.34 (m, 2H), 6.48-6.51 (m, 1H);

^1H NMR (DMSO- d_6 , 300 MHz) δ 12.79 (s, 1H), 8.18 (d, 1H, J = 8.4 Hz), 7.85 (d, 1H, J = 8.4 Hz), 7.67 (t, 1H, J = 7.8 Hz), 7.54 (t, 1H, J = 7.8 Hz), 7.44-7.48 (m, 1H), 7.39-7.44 (m, 1H), 6.43-6.48 (m, 1H); ^{13}C NMR (DMSO- d_6 , 75 MHz) δ 156.9, 143.2, 129.7, 129.4, 129.1, 125.7, 120.6, 120.3, 115.6, 112.0, 109.7.

Synthesis of *N*-(2-bromophenyl)-2-phenylacetamide (6u): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 55% yield (0.72 g). mp = 126-128 $^\circ\text{C}$; TLC (1:1 CH_2Cl_2 :Hexanes), R_f = 0.2; ^1H NMR (CDCl_3 , 300 MHz) δ 8.40 (d, 1H, J = 8.4 Hz), 7.68 (br s, 1H), 7.32-7.52 (m, 7H), 6.98 (td, 1H, J = 7.8 Hz, J = 1.5 Hz), 3.84 (s, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.4, 135.5, 133.9, 132.2, 129.9, 129.4, 128.4, 128.0, 125.3, 121.5, 113.3, 45.2. (*Chem. Pharm. Bull.* **1984**, 32, 5003-5009)

Synthesis of (2*S*)-[1-(2-bromophenylcarbamoyl)-2-phenylethyl]carbamic acid benzyl ester (6aa): The product was isolated by silica gel column chromatography (1:4 EtOAc:Hexanes) as a white solid in 12% yield (0.256 g).

General One-Pot Procedure for Preparation of Amides from *ortho*-Haloanilines and Precursor Acids Using Oxalyl Chloride: To a solution of precursor acid (8.0 mmol, 1.0 equiv) in dry THF or CH_2Cl_2 (40 mL) at room temperature, under a nitrogen atmosphere, was added oxalyl chloride (9.63 mmol, 1.2 equiv). To the reaction was added DMF (2-10 drops). Generally after 2 hours to the mixture was added the desired aniline then reaction was stirred for 24 hours. After diluting the mixture with EtOAc (100 mL), it was washed with 5% Na_2CO_3 (2 x 100 mL), and sat. NaCl (1 x 50 mL). The organic layer was then dried over MgSO_4 and the solvent was removed *in vacuo*.

Synthesis of *N*-(2-bromophenyl)-2-phenylacetamide (6u): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 91% yield (1.20 g).

Synthesis of (2*S*)-Pyrrolidine-2-carboxylic Acid (2-Bromophenyl)amide (6x): To a solution of Fmoc-Pro amide (1.50 g, 3.05 mmol, 1.0 equiv) in DMF (12 mL) at room temperature was added piperidine (3 mL). The reaction mixture was stirred for 2 hours, and then the solvents removed under reduced pressure. The product was isolated by silica gel column chromatography (EtOAc) as a colourless oil in 88% yield (0.72 g). TLC (EtOAc), R_f = 0.4; ^1H NMR (CDCl_3 , 300

MHz) δ 10.49 (s, 1H), 8.74 (br s, 1H), 8.49 (dd, 1H, $J = 8.2$ Hz, $J = 1.5$ Hz), 7.57 (dd, 1H, $J = 8.0$ Hz, $J = 1.4$ Hz), 7.35 (td, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 6.99 (td, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz), 3.95 (dd, 1H, $J = 9.2$ Hz, $J = 4.9$ Hz), 3.06-3.22 (m, 2H), 2.19-2.34 (m, 1H), 2.05-2.18 (m, 1H), 1.72-1.94 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 173.9, 136.0, 132.3, 128.3, 124.8, 121.1, 113.6, 61.4, 47.4, 31.0, 26.3. (PCT Int. Appl. 2002, 92 pp. WO 2002018335)

Synthesis of (2S)-2-(2-bromophenylcarbamoyl)pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester (6y): The product was isolated by silica gel column chromatography (1:2 EtOAc:Hexanes) as a white solid in 63% yield (3.65 g). mp = 65-68 °C TLC (1:3 EtOAc:Hexanes), $R_f = 0.2$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.85 (br s, 1H), 8.37 (d, 2H, $J = 8.4$ Hz), 7.77 (br s, 2H), 7.65 (br s, 1H), 7.55 (dd, 2H, $J = 8.0$ Hz, $J = 1.2$ Hz), 7.20-7.48 (m, 3H), 7.14 (br s, 1H), 7.03 (br s, 1H), 4.54 (br s, 2H), 4.29 (br s, 2H), 3.67 (br s, 1H), 3.58 (br s, 1H), 2.47 (br s, 1H), 2.31 (br s, 1H), 2.04 (br s, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 170.0, 156.2, 143.8, 141.3, 135.7, 132.3, 128.3, 127.8, 127.1, 125.4, 124.9, 122.0, 120.0, 114.0, 68.0, 61.8, 47.2, 31.4, 28.8, 24.7. (PCT Int. Appl. 2002, 92 pp. WO 2002018335)

Synthesis of (2S)-2-(2-bromophenylcarbamoyl)pyrrolidine-1-carboxylic acid benzyl ester (6z): The product was isolated by silica gel column chromatography (1:3 EtOAc:Hexanes) as a yellowish solid in 88% yield (2.82 g). mp = 79-81 °C; TLC (1:3 EtOAc:Hexanes), $R_f = 0.3$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.87 (br s, 1H), 8.36 (dd, 1H, $J = 8.2$ Hz, $J = 1.4$ Hz), 7.55 (dd, 1H, $J = 8.0$ Hz, $J = 1.4$ Hz), 7.15-7.51 (m, 6H), 7.02 (t, 1H, $J = 7.8$ Hz), 5.24 (br s, 2H), 4.61 (br s, 1H), 3.68 (br s, 2H), 2.49 (br s, 1H), 2.06 (br s, 1H), 1.99-2.24 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz, rotamers) δ 170.1, 156.2, 136.2, 132.3, 128.5, 128.4, 128.3, 128.2, 128.0, 125.4, 122.1, 113.9, 67.6, 61.8, 41.3, 28.8, 24.6. (*Chem. Pharm. Bull.* **1984**, 32, 3840-3847)

Synthesis of (2S)-[1-(2-bromophenylcarbamoyl)-2-phenylethyl]carbamic acid benzyl ester (6aa): The product was isolated by silica gel column chromatography (1:4 EtOAc:Hexanes) as a white solid in 14% yield (0.412 g). mp = 158-159 °C; TLC (2:1 EtOAc:Hexanes), $R_f = 0.5$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.36 (d, 1H, $J = 8.4$ Hz), 8.13 (br s, 1H), 7.52 (dd, 1H, $J = 8.0$ Hz, $J = 1.4$ Hz), 7.23-7.43 (m, 8H), 7.02 (td, 1H, $J = 7.8$ Hz, $J = 1.5$ Hz), 5.33 (br s, 1H), 5.17 (q, 2H, $J = 9.3$ Hz), 4.65 (br s, 1H), 3.25 (d, 2H, $J = 6.7$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.2, 156.0,

135.9, 135.1, 132.3, 129.3, 129.0, 128.8, 128.6, 128.5, 128.3, 128.2, 125.6, 121.9, 113.8, 109.4, 85.1, 67.4, 38.2.

Synthesis of hexa-2,4-dienoic acid (2-bromophenyl)amide (6ad): The product was isolated by silica gel column chromatography (2:1 CH₂Cl₂:Hexanes) as a yellowish solid in 65% yield (0.796 g). mp = 146-147 °C; TLC (2:1 CH₂Cl₂:Hexanes), R_f = 0.2; ¹H NMR (CDCl₃, 300 MHz) δ 8.51 (br d, 1H, *J* = 8.2 Hz), 7.68 (br s, 1H), 7.58 (dd, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 7.32-7.44 (m, 2H), 7.02 (td, 1H, *J* = 7.8 Hz, *J* = 1.4 Hz), 6.16-6.36 (m, 2H), 5.98 (d, 1H, *J* = 14.9 Hz), 1.92 (d, 3H, *J* = 5.4 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 164.3, 143.2, 139.4, 136.0, 132.2, 130.0, 128.4, 125.0, 121.9, 121.5, 113.3, 18.7.

General Procedure for Preparation of Thioamides from their Corresponding Amides: To a solution of precursor amide (8.15 mmol, 1.0 equiv) in dry THF (40 mL) at room temperature was added Lawesson's reagent (9.78 mmol, 1.2 equiv). The reaction refluxed for a period of 6-48 hours, depending on the substrate, then the solvent was removed under reduced pressure. The product was isolated after silica gel column chromatography.

Synthesis of *N*-(2-bromophenyl)thiobenzamide (8a): The product was isolated by silica gel column chromatography (1:9 EtOAc:Hexanes) as a greenish white solid in 94% yield (2.23 g). mp = 83-85 °C; TLC (1:9 EtOAc:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 9.31 (br s, 1H), 8.70 (br s, 1H), 7.96 (br d, 1H, *J* = 6.6 Hz), 7.71 (dd, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.40-7.63 (m, 5H), 7.21 (td, 1H, *J* = 7.8 Hz, *J* = 1.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 198.5, 142.7, 137.0, 132.9, 131.6, 128.8, 128.2, 127.9, 127.0, 125.9, 118.1. (*J. Am. Chem. Soc.* **1961**, 83, 1691-1697)

Synthesis of *N*-(2-bromophenyl)-4-methoxythiobenzamide (8b): The product was isolated by silica gel column chromatography (1:6 EtOAc:Hexanes) as a white solid in 99% yield (2.80 g). mp = 124-126 °C; TLC (1:6 EtOAc:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 9.25 (br s, 1H), 8.64 (br s, 1H), 7.95-8.02 (m, 2H), 7.70 (dd, 1H, *J* = 8.0 Hz, *J* = 1.4 Hz), 7.44 (td, 1H, *J* = 8.2 Hz, *J* = 1.4 Hz), 7.20 (td, 1H, *J* = 8.0 Hz, *J* = 1.5 Hz), 6.96-7.04 (m, 2H), 3.92 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 197.3, 162.6, 137.2, 132.8, 129.0, 127.9, 127.8, 126.0, 118.0, 114.2, 113.9, 55.6.

Cyclization of 6 to Benzoxazoles 7

General Procedure for Preparation Benzoxazoles 7 or Benthizoles 9: The reactions were set up in a parallel synthesis fashion using reaction tubes with a water-cooled head at the top of the tubes (Radleys Discovery Technologies Carousel Reaction Stations), and were performed on a 1.00 mmol scale in groups of 12 reactions. To a mixture of the bromo- (or in some cases the chloro- or iodo-) amide precursor **6** or thioamide precursor **8** (1.0 mmol), CuI (9.5 mg, 0.05 mmol, 0.05 equiv), 1,10-phenanthroline (18.8 mg, 0.10 mmol, 0.10 equiv), and Cs₂CO₃ (0.49 g, 1.5 mmol, 1.5 equiv) was added DME (8 mL) at room temperature, under a nitrogen atmosphere. The reaction was refluxed for 24 hours and then allowed to cool to room temperature. To the reaction mixture was added H₂O (8 mL), and then CH₂Cl₂ (8 mL). After stirring for 10 minutes each solution was filtered through a hydrophobic membrane (Varian Bond Elute Reservoir) with the denser DME/CH₂Cl₂ layer passing through the hydrophobic membrane and the aqueous layer remaining in the reservoir. The reservoir was washed with CH₂Cl₂ (2 x 2 mL). The combined organic layers were then evaporated under reduced pressure. The final product **7** or **9** was passed through a short layer of silica gel to remove any traces of copper salts, ligand, or byproduct, as well as leftover starting material.

Synthesis of 2-phenylbenzoxazole (7a): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 99% yield (0.195 g). mp = 101-102 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.5; ¹H NMR (CDCl₃, 300 MHz) δ 8.32 (dd, 2H, *J* = 5.6 Hz, *J* = 2.1 Hz), 7.79-7.86 (m, 1H), 7.53-7.67 (m, 4H), 7.36-7.44 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 163.1, 150.8, 142.2, 131.4, 128.9, 127.6, 127.2, 125.1, 124.6, 120.0, 110.6; MS (EI) *m/z* 196 (16), 195 (100, M⁺), 167 (21), 77 (12), 64 (18), 63 (22); HRMS (EI) calculated for (M⁺) C₁₃H₉NO 195.0684; observed 195.0683. (*Tetrahedron* **2002**, 58, 9605-9612)

Synthesis of 2-phenylbenzoxazole (7a) from 6a-I: The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 99% yield (0.197 g).

Synthesis of 2-phenylbenzoxazole (7a) from *N*-(2-chlorophenyl)benzamide 6a-Cl: The reaction was refluxed for 48 hours. The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 99% yield (0.196 g).

Synthesis of 2-(4-chlorophenyl)benzoxazole (7b): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 99% yield (0.232 g). mp = 148-150 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.22 (d, 2H, *J* = 7.8 Hz), 7.77-7.84 (m, 1H), 7.57-7.65 (m, 1H), 7.52 (d, 2H, *J* = 7.8 Hz), 7.36-7.44 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 162.1, 150.8, 142.0, 137.8, 129.3, 128.9, 125.7, 125.4, 124.8, 120.1, 110.6. (*Synth. Commun.* **2002**, 32, 2175-2179)

Synthesis of 2-(4-chlorophenyl)benzoxazole (7b) from 6b-I: The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 99% yield (0.230 g).

Synthesis of 2-(4-bromophenyl)benzoxazole (7c): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a white solid in 92% yield (0.253 g). mp = 157-158 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.5; ¹H NMR (CDCl₃, 300 MHz) δ 8.16 (m, 2H), 7.78-7.84 (m, 1H), 7.68-7.75 (m, 2H), 7.59-7.66 (m, 1H), 7.37-7.45 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 162.1, 150.8, 142.0, 132.3, 129.0, 126.3, 126.1, 125.4, 124.8, 120.1, 110.7. (*Tetrahedron Lett.* **2002**, 44, 175-178)

Synthesis of 4-benzoxazol-2-yl-benzonitrile (7d): The product was isolated by silica gel column chromatography (3:1 CH₂Cl₂:Hexanes) as a white solid in 93% yield (0.205 g). mp = 203-206 °C; TLC (3:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 300 MHz) δ 8.37 (d, 2H, *J* = 8.5 Hz), 7.80-7.87 (m, 3H), 7.60-7.68 (m, 1H), 7.39-7.49 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 160.6, 150.9, 141.9, 132.7, 131.1, 128.0, 126.2, 125.1, 120.6, 118.2, 114.7, 110.9. (*Macromolecules* **2003**, 36, 4699-4708)

Synthesis of 4-benzoxazol-2-yl-benzonitrile (7d) from 6d-I: The product was isolated by silica gel column chromatography (3:1 CH₂Cl₂:Hexanes) as a white solid in 98% yield (0.215 g).

Synthesis of 2-styrylbenzoxazole (7f): The product was isolated by silica gel column chromatography (3:1 CH₂Cl₂:Hexanes) as a yellow solid in 97% yield (0.215 g). mp = 79-80 °C; TLC (3:1 CH₂Cl₂:Hexanes), R_f = 0.4; ¹H NMR (CDCl₃, 400 MHz) δ 7.78 (d, 1H, *J* = 16.3 Hz), 7.68-7.74 (m, 1H), 7.58 (d, 1H, *J* = 7.7 Hz), 7.48-7.54 (m, 2H), 7.27-7.44 (m, 5H), 7.07 (dd, 1H,

$J = 16.3$ Hz, $J = 1.1$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 162.8, 150.5, 142.2, 139.5, 135.2, 129.8, 129.0, 127.6, 125.2, 124.5, 119.9, 114.0, 110.4. (*J. Org. Chem.* **1993**, 58, 7009-7015)

Synthesis of 2-ethylbenzoxazole (7g): The product was isolated by silica gel column chromatography (CH_2Cl_2) as a colourless oil in 99% yield (0.150 g). TLC (CH_2Cl_2), $R_f = 0.3$; IR (film) ν 3059, 2983, 2942, 2880, 1615, 1574, 1455, 1243, 1153, 926, 821, 745 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.67-7.74 (m, 1H), 7.48-7.55 (m, 1H), 7.30-7.37 (m, 2H), 3.00 (q, 2H, $J = 7.7$ Hz), 1.49 (t, 3H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 168.1, 150.8, 141.4, 124.4, 124.0, 119.5, 110.2, 22.2, 10.9. (*Heterocycles* **1999**, 51, 979-982)

Synthesis of 2-isopropylbenzoxazole (7h): The product was isolated by silica gel column chromatography (CH_2Cl_2) as a colourless oil in 99% yield (0.158 g). TLC (CH_2Cl_2), $R_f = 0.4$; IR (film) ν 3058, 2975, 2937, 2876, 1614, 1570, 1456, 1242, 1135, 1086, 934, 810, 764, 748 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.68-7.75 (m, 1H), 7.47-7.55 (m, 1H), 7.28-7.36 (m, 2H), 3.28 (heptuplet, 1H, $J = 7.0$ Hz), 1.49 (d, 6H, $J = 7.0$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 171.3, 150.7, 141.3, 124.4, 124.0, 119.6, 110.3, 28.9, 20.3. (*Tetrahedron* **1985**, 41, 3091-3094)

Synthesis of 2-(3,4-dichlorophenyl)benzoxazole (7i): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 93% yield (0.245 g). mp = 144-145 $^\circ\text{C}$; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.5$; ^1H NMR (CDCl_3 , 400 MHz) δ 8.37 (d, 1H, $J = 1.8$ Hz), 8.09 (dd, 1H, $J = 8.2$ Hz, $J = 1.8$ Hz), 7.77-7.83 (m, 1H), 7.58-7.65 (m, 2H), 7.38-7.45 (m, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 160.9, 150.8, 141.9, 135.9, 133.5, 131.1, 129.3, 127.1, 126.5, 125.7, 125.0, 120.3, 110.7. (*Current Sci. (India)* **1956**, 25, 86-87)

Synthesis of 2-(3,4-dichlorophenyl)benzoxazole (7i) from 6i-I: The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 97% yield (0.255 g).

Synthesis of 2-(4-methoxyphenyl)benzoxazole (7j): The product was isolated by silica gel column chromatography (2:1 CH_2Cl_2 :Hexanes) as a white solid in 99% yield (0.230 g). mp = 98 $^\circ\text{C}$; TLC (2:1 CH_2Cl_2 :Hexanes), $R_f = 0.4$; ^1H NMR (CDCl_3 , 400 MHz) δ 8.13 (d, 2H, $J = 8.2$ Hz), 7.75-7.80 (m, 1H), 7.56-7.61 (m, 1H), 7.31-7.40 (m, 2H), 7.06 (d, 2H, $J = 8.2$ Hz), 3.91 (d, 3H, J

= 0.9 Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 163.2, 162.3, 150.7, 142.3, 129.4, 124.6, 124.4, 119.7, 119.6, 114.4, 110.4, 55.5. (*Synth. Commun.* **2002**, 32, 2175-2179)

Synthesis of 2-(4-methoxyphenyl)benzoxazole (7j) from 6j-I: The product was isolated by silica gel column chromatography (2:1 CH_2Cl_2 :Hexanes) as a white solid in 99% yield (0.228 g).

Synthesis of 2-(2-methoxyphenyl)benzoxazole (7k): The product was isolated by silica gel column chromatography (CH_2Cl_2) as a white solid in 99% yield (0.222 g). mp = 53-55 °C; TLC (CH_2Cl_2), R_f = 0.3; ^1H NMR (CDCl_3 , 400 MHz) δ 8.18 (dd, 1H, J = 7.7 Hz, J = 1.8 Hz), 7.83-7.90 (m, 1H), 7.60-7.66 (m, 1H), 7.52-7.58 (m, 1H), 7.35-7.42 (m, 2H), 7.11-7.17 (m, 2H), 4.06 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 161.6, 158.5, 150.4, 142.2, 132.8, 131.3, 124.9, 124.3, 120.7, 120.3, 116.2, 112.1, 110.5, 56.2. (*J. Antibiot.* **1993**, 46, 1095-1100)

Synthesis of 2-thiophen-2-yl-benzoxazole (7l): The product was isolated by silica gel column chromatography (2:1 CH_2Cl_2 :Hexanes) as a white solid in 99% yield (0.204 g). mp = 81-82 °C; TLC (2:1 CH_2Cl_2 :Hexanes), R_f = 0.3; ^1H NMR (CDCl_3 , 300 MHz) δ 7.93 (dd, 1H, J = 3.7 Hz, J = 1.2 Hz), 7.73-7.81 (m, 1H), 7.53-7.61 (m, 2H), 7.32-7.41 (m, 2H), 7.21 (dd, 1H, J = 5.1 Hz, J = 3.7 Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 159.1, 150.5, 142.0, 130.3, 130.0, 129.7, 128.3, 125.1, 124.7, 119.8, 110.4. (*Tetrahedron Lett.* **2002**, 44, 175-178)

Synthesis of 2-pyridin-3-yl-benzoxazole (7m): The product was isolated by silica gel column chromatography (1:1 EtOAc:Hexanes) as a white solid in 96% yield (0.188 g). mp = 114-115 °C; TLC (1:1 EtOAc:Hexanes), R_f = 0.5; ^1H NMR (CDCl_3 , 300 MHz) δ 9.47 (br s, 1H), 8.75 (br d, 1H, J = 3.8 Hz), 8.47 (dt, 1H, J = 8.0 Hz, J = 1.8 Hz), 7.74-7.83 (m, 1H), 7.55-7.64 (m, 1H), 7.44 (dd, 1H, J = 8.0 Hz, J = 4.9 Hz), 7.32-7.41 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 160.6, 152.0, 150.7, 148.8, 141.8, 134.7, 125.7, 124.9, 123.6, 123.5, 120.3, 110.8. (*J. Heterocycl. Chem.* **2002**, 39, 1279-1281)

Synthesis of 6-methyl-2-phenylbenzoxazole (7p): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 99% yield (0.210 g). mp = 93 °C; TLC (1:1 CH_2Cl_2 :Hexanes), R_f = 0.5; ^1H NMR (CDCl_3 , 300 MHz) δ 8.24-8.31 (m, 2H), 7.68

(d, 1H, $J = 8.2$ Hz), 7.51-7.58 (m, 3H), 7.40 (t, 1H, $J = 0.6$ Hz), 7.19 (ddd, 1H, $J = 8.0$ Hz, $J = 1.5$ Hz, $J = 0.6$ Hz), 2.53 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 162.6, 151.1, 140.0, 135.6, 131.3, 128.9, 127.5, 127.4, 125.8, 119.4, 110.8, 21.8. (*J. Org. Chem.* **1992**, 57, 2883-2887)

Synthesis of 6-chloro-2-phenylbenzoxazole (7q): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 95% yield (0.218 g). mp = 107-108 °C; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.4$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.16-8.23 (m, 2H), 7.64 (d, 1H, $J = 8.5$ Hz), 7.55 (d, 1H, $J = 1.9$ Hz), 7.45-7.57 (m, 3H), 7.30 (dd, 1H, $J = 8.5$ Hz, $J = 1.9$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 163.7, 151.0, 140.9, 131.8, 130.7, 129.0, 127.7, 126.8, 125.3, 120.5, 111.2. (*Z. Chem.* **1970**, 10, 144-145)

Synthesis of 6-fluoro-2-phenylbenzoxazole (7r): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 99% yield (0.218 g). mp = 109-110 °C; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.3$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.20-8.28 (m, 2H), 7.72 (dd, 1H, $J = 8.8$ Hz, $J = 4.9$ Hz), 7.50-7.59 (m, 3H), 7.33 (dd, 1H, $J = 8.0$ Hz, $J = 2.3$ Hz), 7.13 (td, 1H, $J = 8.8$ Hz, $J = 2.3$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 163.7 (d, $J = 4.0$ Hz), 160.7 (d, $J = 244.1$ Hz), 150.7 (d, $J = 14.9$ Hz), 138.4, 131.6, 128.9, 127.5, 126.9, 120.3 (d, $J = 10.0$ Hz), 112.5 (d, $J = 25.0$ Hz), 98.7 (d, $J = 28.7$ Hz). (*J. Org. Chem.* **2001**, 66, 991-996)

Synthesis of 5-fluoro-2-phenylbenzoxazole (7s): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 98% yield (0.208 g). mp = 114 °C; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.3$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.25 (dd, 2H, $J = 6.9$ Hz, $J = 1.8$ Hz), 7.44-7.60 (m, 5H), 7.10 (td, 1H, $J = 9.2$ Hz, $J = 2.6$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.8, 160.2 (d, $J = 240.7$ Hz), 147.1, 143.0 (d, $J = 13.8$ Hz), 131.8, 129.0, 127.7, 126.9, 112.7 (d, $J = 26.1$ Hz), 110.8 (d, $J = 10.0$ Hz), 106.4 (d, $J = 25.8$ Hz). (*J. Org. Chem.* **1992**, 57, 6351-6354)

Synthesis of 2-phenyl-5-trifluoromethylbenzoxazole (7t): The product was isolated by silica gel column chromatography (1:1 CH_2Cl_2 :Hexanes) as a white solid in 75% yield (0.198 g). mp = 86-87 °C; TLC (1:1 CH_2Cl_2 :Hexanes), $R_f = 0.5$; ^1H NMR (CDCl_3 , 300 MHz) δ 8.29 (dd, 2H, $J = 7.5$ Hz, $J = 1.4$ Hz), 8.08 (s, 1H), 7.53-7.73 (m, 5H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.7, 152.5,

142.3, 132.2, 129.0, 127.9, 127.4 (q, $J = 32.7$ Hz), 126.5, 124.2 (q, $J = 272.2$ Hz), 122.3 (q, $J = 3.7$ Hz), 117.7 (q, $J = 4.0$ Hz), 111.0. (*J. Org. Chem.* **1992**, 57, 6351-6354)

Synthesis of 2-benzylbenzoxazole (7u): The reaction was stirred at reflux for 3 days. The product was isolated by silica gel column chromatography (1:4 EtOAc:Hexanes) as a yellow oil in 89% yield (0.185 g). TLC (4:1 EtOAc:Hexanes), $R_f = 0.5$; ^1H NMR (CDCl_3 , 300 MHz) δ 7.70-7.77 (m, 1H), 7.46-7.53 (m, 1H), 7.28-7.46 (m, 7H), 4.32 (s, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 165.2, 151.1, 141.4, 134.8, 129.0, 128.9, 127.3, 124.7, 124.2, 119.9, 110.5, 35.3. (*J. Am. Chem. Soc.* **2003**, 125, 6646-6647)

Synthesis of (2S)-2-benzoxazol-2-yl-pyrrolidine-1-carboxylic acid benzyl ester (7z): The product was isolated by silica gel column chromatography (1:2 EtOAc:Hexanes) as a colourless oil in 90% yield (0.290 g). TLC (1:2 EtOAc:Hexanes), $R_f = 0.3$; IR (film) ν 3063, 3033, 2955, 2881, 1710, 1570, 1455, 1413, 1356, 1241, 1153, 1116, 1086, 766, 749, 698 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.68-7.78 (m, 1H), 7.28-7.58 (m, 5H), 7.68-7.22 (m, 3H), 4.94-5.31 (m, 3H), 3.77-3.90 (m, 1H), 3.57-3.75 (m, 1H), 2.32-2.51 (m, 1H), 2.11-2.32 (m, 2H), 1.95-2.11 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz, rotamers) δ 166.7, 166.5, 154.9, 154.4, 150.8, 150.6, 141.2, 141.1, 136.7, 136.3, 128.5, 128.2, 128.0, 127.7, 127.5, 127.5, 127.0, 124.9, 124.9, 124.4, 124.3, 120.1, 120.0, 110.7, 67.2, 67.0, 55.5, 55.1, 47.1, 46.6, 32.5, 31.4, 24.3, 23.6; MS (EI) m/z 323 (11), 322 (37, M^+), 209 (11), 187 (18), 160 (22), 146 (23), 92 (13), 91 (100), 84 (11), 65 (11); HRMS (EI) calculated for (M^+) $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3$ 322.1317; observed 322.1311.

Synthesis of 2-(2-benzoxazol-2-yl-ethyl)isoindole-1,3-dione (7ab): The product was isolated by silica gel column chromatography (1:3 EtOAc:Hexanes) as a colourless oil in 62% yield (0.180 g). mp = 179-180 $^\circ\text{C}$; TLC (1:2 EtOAc:Hexanes), $R_f = 0.4$; IR (film) ν 2946, 1774, 1709, 1614, 1572, 1456, 1433, 1395, 1362, 1231, 1167, 10306, 930, 768, 754, 714 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.81-7.89 (m, 2H), 7.69-7.78 (m, 2H), 7.62-7.69 (m, 1H), 7.44-7.52 (m, 1H), 7.27-7.36 (m, 2H), 4.26 (t, 2H, $J = 7.1$ Hz), 3.36 (t, 2H, $J = 7.1$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 167.9, 163.4, 150.9, 141.2, 134.2, 134.1, 132.0, 124.9, 124.3, 123.5, 123.4, 119.8, 110.4, 48.2, 35.1, 27.8; MS (EI) m/z 293 (26), 292 (100, M^+), 160 (65), 146 (18), 145 (71), 104 (16), 77 (22), 76 (16); HRMS (EI) calculated for (M^+) $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_3$ 292.0848; observed 292.0851.

Synthesis of 2-propenylbenzoxazole (7ac): The product was isolated by silica gel column chromatography (2:1 CH₂Cl₂:Hexanes) as a yellowish oil in 99% yield (0.162 g). TLC (2:1 CH₂Cl₂:Hexanes), R_f = 0.5; ¹H NMR (CDCl₃, 300 MHz) δ 7.67-7.75 (m, 1H), 7.47-7.55 (m, 1H), 7.30-7.38 (m, 2H), 7.01-7.15 (m, 1H), 6.46-6.54 (m, 1H), 2.03-2.10 (m, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 162.4, 150.3, 141.9, 139.1, 124.8, 124.3, 119.8, 118.2, 110.2, 18.8. (*Tetrahedron* **1986**, 42, 3905-3911)

Synthesis of 2-penta-1,3-dienylbenzoxazole (7ad): The product was isolated by silica gel column chromatography (2:1 CH₂Cl₂:Hexanes) as a yellowish oil in 84% yield (0.155 g). TLC (2:1 CH₂Cl₂:Hexanes), R_f = 0.5; IR (film) ν 3060, 2970, 2932, 1715, 1642, 1538, 1455, 1352, 1243, 1108, 1003, 762, 745 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.65-7.73 (m, 1H), 7.26-7.52 (m, 4H), 6.42 (dd, 1H, *J* = 15.6 Hz, *J* = 0.6 Hz), 6.26-6.38 (m, 1H), 6.08-6.21 (m, 1H), 1.90 (dd, 3H, *J* = 7.5 Hz, *J* = 0.7 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 163.1, 150.4, 142.3, 140.1, 137.4, 130.7, 124.9, 124.3, 119.7, 114.8, 110.2, 18.7; MS (EI) *m/z* 185 (33, M⁺), 175 (19), 174 (11), 171 (13), 170 (100), 146 (30), 145 (11); HRMS (EI) calculated for (M⁺) C₁₂H₁₁NO 185.0841; observed 185.0840.

Synthesis of 2-phenylbenzothiazole (9a): The product was isolated by silica gel column chromatography (1:1 CH₂Cl₂:Hexanes) as a yellow solid in 99% yield (0.210 g). mp = 110-111 °C; TLC (1:1 CH₂Cl₂:Hexanes), R_f = 0.3; ¹H NMR (CDCl₃, 300 MHz) δ 8.11-8.20 (m, 3H), 7.93 (dd, 1H, *J* = 8.0 Hz, *J* = 0.6 Hz), 7.49-7.59 (m, 4H), 7.42 (td, 1H, *J* = 8.0 Hz, *J* = 1.1 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 168.1, 154.2, 135.1, 133.7, 131.0, 129.1, 127.6, 126.4, 125.2, 123.3, 121.7. (*Tetrahedron Lett.* **2003**, 44, 6073-6077)

Synthesis of 2-(4-methoxyphenyl)benzothiazole (9b): The product was isolated by silica gel column chromatography (2:1 CH₂Cl₂:Hexanes) as a yellow solid in 93% yield (0.210 g). mp = 120-121 °C; TLC (2:1 CH₂Cl₂:Hexanes), R_f = 0.2; ¹H NMR (CDCl₃, 300 MHz) δ 8.04-8.11 (m, 3H), 7.91 (dd, 1H, *J* = 7.4 Hz, *J* = 0.6 Hz), 7.51 (td, 1H, *J* = 7.3 Hz, *J* = 0.4 Hz), 7.39 (td, 1H, *J* = 7.3 Hz, *J* = 1.1 Hz), 7.00-7.07 (m, 2H), 3.90 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 167.9, 162.0, 154.3, 134.9, 129.2, 126.5, 126.2, 124.8, 122.9, 121.5, 114.4, 55.5. (*Synth. Commun.* **2002**, 32, 3541-3547)

NMR Spectra of Benzoxazoles and Benzothiazole Products

7b

7c

7d

7f

7g

7h

7i

7j

7m

7s

7t

7ab

7ac

7ad

9b