ELECTRONIC SUPPLEMENTARY INFORMATION

3,4,5-Triarylisothiazoles *via* C-C Coupling Chemistry

Irene C. Christoforou and Panayiotis A. Koutentis*

Department of Chemistry, University of Cyprus, P.O. Box 20537, 1678 Nicosia, Cyprus, koutenti@ucy.ac.cy

Experimental

CCl_4 and MeOH were freshly distilled from CaH_2 under argon. DMF was azeotropically distilled with PhH then distilled under vacuum from anhydrous $MgSO_4$ and stored over 4Å molecular sieves. THF was freshly distilled from potassium under argon. Anhydrous K_2CO_3 was freshly powdered using an agate pestle and mortar before use. Reactions were protected by $CaCl_2$ drying tubes or performed under an argon atmosphere. Anhydrous Na_2SO_4 was used for drying organic extracts, and all volatiles were removed under reduced pressure. All reaction mixtures and column eluents were monitored by TLC using commercial glass backed thin layer chromatography (TLC) plates (Merck Kieselgel 60 F_{254}). The plates were observed under UV light at 254 and 365 nm. The technique of dry flash chromatography was used throughout for all non-TLC scale chromatographic separations using Merck Silica Gel 60 (less than 0.063 mm). A Hastelloy B-2 Parr pressure vessel with a teflon sleeve and a 600 mL capacity (3000psi limit) was used for the autoclave reactions. Melting points were determined using a PolyTherm-A, Wagner & Munz, Koefler - Hotstage Microscope apparatus. Solvents used for recrystallization are indicated after the melting point. UV spectra were obtained using a Perkin-Elmer Lambda-25 UV/vis spectrophotometer and inflections are identified by the abbreviation "inf". IR spectra were recorded on a Shimidazu FTIR-NIR Prestige-21 spectrometer with Pike *Miracle*

Ge ATR accessory and strong and medium peaks are represented by s and m respectively. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 machine (at 300 and 75 MHz respectively). *C*H assignments were supported by ^{13}C NMR DEPT 90 experiments. Deuterated solvents were used for homonuclear lock and the signals are referenced to the deuterated solvent peaks. Low resolution (EI) mass spectra were recorded on a Shimadzu Q2010 GCMS with direct inlet probe whilst high resolution spectra were recorded ona VG Autospec "Q" mass spectrometer. Petrol refers to light petroleum, bp 40–60 ^{o}C. 3-Chloro-5-phenylisothiazole-4-carbonitrile **1**[30], 3-iodo-5-phenylisothiazole-4-carbonitrile **18**[31] and 3,5-diphenylisothiazole-4-carbonitrile **26**[31] were prepared according to literature procedures.

3-Chloro-5-phenylisothiazole-4-carboxamide 2

A stirred solution of 3-chloro-5-phenylisothiazole-4-carbonitrile **1** (1.5 g, 6.82 mmol) in c. H_2SO_4 (25 ml) protected with $CaCl_2$ drying tube, was heated to *ca.* 100 ^{o}C until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^{o}C and then was poured into ice-water to afford a white precipitate. The white precipitate was filtered, washed (H_2O) and dried under vacuum to give the *title compound* **2** (1.57 g, 97%) as colourless needles, mp 168-171 ^{o}C (from PhH); (Found: C, 50.4; H, 3.0; N, 11.6. $C_{10}H_7ClN_2OS$ requires C, 50.3; H, 3.0; N, 11.7%); λ_{max}(DCM)/nm 269 (log ε 3.90); ν_{max}/cm^{-1} 3380w (NH), 3184w (Ar CH), 1642s (C=O), 1618m, 1529w, 1491m, 1446w, 1403w, 1321w, 1295m, 1275m, 1103w, 1039m, 1018w, 1000w, 917w, 846m, 793w, 762m; δ_H(300 MHz; DMSO-d_6) 8.08 (1H, br s, N*H*), 7.80 (1H, br s, N*H*), 7.60-7.56 (2H, m, Ph C*H*), 7.49-7.46 (3H, m, Ph C*H*); δ_C(75 MHz; DMSO-d_6) 165.6, 163.6, 146.3, 129.5 (Ph *C*H), 128.8, 128.3 (Ph *C*H), 128.1, 126.7 (Ph *C*H); δ_C(75

MHz; DEPT 90, DMSO-d_6) 129.5 (Ph *C*H), 128.3 (Ph *C*H), 126.7 (Ph *C*H); *m*/*z* (EI) 240 (M^++2, 25%), 239 (M^++1, 44), 238 (M^+, 68), 237 (M^+-H, 100), 224 (27), 223 (13), 222 (72), 221 (13), 219 (3), 203 (M^+-Cl, 4), 186 (3), 159 (12), 133 (18), 129 (11), 127 (15), 121 (4), 114 (4), 101 (4), 100 (3), 89 (18), 77 (13), 75 (5), 63 (6), 51 (10) (Found: M^+, 237.9959, $C_{10}H_7ClN_2OS$ requires *M*, 237.9968).

3-Chloro-5-phenylisothiazole-4-carboxylic acid 3

To a stirred solution of 3-chloro-5-phenylisothiazole-4-carboxamide **2** (1.5 g, 6.29 mmol) in c. H_2SO_4 (250 ml) cooled to *ca.* 0 ^oC and protected with $CaCl_2$ drying tube, was added in portions sodium nitrite (4.34 g, 62.9 mmol, 10 equiv.). The reaction mixture then was heated to *ca.* 100 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC and was poured into ice-water to afford a white precipitate. The white precipitate was filtered out, washed (H_2O) and dried under vacuum to give the *title compound* **3** (1.33 g, 88%) as colourless crystals, mp 162-164 ^oC (from cyclohexane); (Found: C, 50.0; H, 2.4; N, 5.7. $C_{10}H_6ClNO_2S$ requires C, 50.1; H, 2.5; N, 5.8%); λ_{max}(DCM)/nm 268 (log ε 3.98); ν_{max}/cm^{-1} 2847br (OH), 1695s (C=O), 1517m, 1479m, 1436m, 1391m, 1345m, 1290w, 1283w, 1246m, 1221m, 1077w, 1043m, 1023w, 926w, 847m, 791w, 757w; δ_H(300 MHz; CD_2Cl_2) 10.72 (1H, br s, CO_2H), 7.54-7.45 (5H, m, Ph C*H*); δ_C(75 MHz; CD_2Cl_2) 175.3 (*C*=O), 166.4, 150.3, 131.0 (Ph *C*H), 129.4 (Ph *C*), 129.2 (Ph *C*H), 129.0 (Ph *C*H), 123.1; δ_C(75 MHz; DEPT 90, CD_2Cl_2) 131.0 (Ph *C*H), 129.2 (Ph *C*H), 129.0 (Ph *C*H); *m*/*z* (EI) 241 (M^++2, 37%), 240 (M^++1, 39), 239 (M^+, 100), 238 (M^+-1, 79), 224 (23), 222 (63), 204 (M+-Cl, 2), 186 (6), 176 (5), 159 (10), 133 (19), 129 (8), 127 (17), 121

(6), 114 (8), 100 (6), 89 (22), 77 (19), 63 (12), 51 (20) (Found: M^+, 238.9803, $C_{10}H_6ClNO_2S$ requires *M*, 238.9808).

4-Bromo-3-chloro-5-phenylisothiazole 5

To a stirred mixture of 3-chloro-5-phenylisothiazole-4-carboxylic acid **3** (1.0 g, 4.18 mmol) in H_2O (30 ml) was added a solution of KOH (234 mg, 4.18 mmol, 1 equiv.) in H_2O (10 ml) and the mixture was allowed to stirred at *ca.* 20 °C until the starting material had completely dissolved. To the reaction mixture was added, in one portion, a solution of silver nitrate (710 mg, 4.18 mmol, 1 equiv.) in H_2O (5 ml) to afford a grey-white precipitate. The grey-white precipitate was filtered, washed first with H_2O and then with acetone and dried in a vacuum oven at *ca.* 80 °C for 12 h to give silver 3-chloro-5-phenylisothiazole-4-carboxylate **4** (1.45 g, 100%). To a stirred mixture of silver 3-chloro-5-phenylisothiazole-4-carboxylate **4**, (100 mg, 0.29 mmol) in tetrachloromethane (3 ml) protected with $CaCl_2$ drying tube was added in one portion Br_2 (18 μl, 0.35 mmol, 1.2 equiv.) and the reaction was kept at 20 °C for 1 h. The reaction mixture was filtred and the filtrate was absorbed on silica. Chromatography (hexane-DCM 8 : 2) gave the title compound **5** (63 mg, 80%) as colourless needles, mp 40-41 °C (lit.,[34] 44-46 °C) (from pentane); (Found: C, 39.3; H, 1.9; N, 5.0. $C_9H_5BrClNS$ requires C, 39.4; H, 1.8; N, 5.1%); λ_{max}(DCM)/nm 274 (log ε 3.91); ν_{max}/cm^{-1} 3049w (Ar CH), 1577w, 1559w, 1517w, 1507w, 1476m, 1457w, 1443m, 1388m, 1336w, 1313w, 1294s, 1278m, 1245w, 1217w, 1076w, 1032m, 996m, 920w, 901m, 819m; δ_H(300 MHz; $CDCl_3$) 7.67-7.60 (2H, m, Ph C*H*), 7.53-7.45 (3H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 163.4, 151.0, 130.4 (Ph *C*H), 129.3 (Ph *C*), 129.1 (Ph *C*H), 128.2 (Ph *C*H), 106.2; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.4 (Ph *C*H), 129.1 (Ph *C*H), 128.2 (Ph *C*H); *m*/*z* (EI) 277 (M^++4, 28%), 275 (M^++2, 100), 273 (M^+, 58), 240 (4),

238 (4), 229 (7), 227 (5), 196 (5), 194 (14), 193 (4), 159 (50), 150 (4), 148 (4), 137 (3), 133 (17), 127 (29), 121 (6), 113 (11), 100 (10), 89 (18), 77 (11), 74 (10), 63 (12), 51 (19) (Found: M^+, 272.9015, $C_9H_5BrClNS$ requires *M*, 272.9004).

4-Amino-3-chloro-5-phenylisothiazole 6

To a stirred solution of NaOH (42 mg, 1.05 mmol, 5 equiv.) in water (2 ml) cooled to *ca.* 0 °C was first added Br_2 (13 μl, 0.25 mmol, 1.2 equiv.) and then 3-chloro-5-phenylisothiazole-4-carboxamide **2** (50 mg, 0.21 mmol). The reaction mixture was allowed to warm to *ca.* 20 °C and was kept at this temperature until the starting material had completely dissolved. The reaction mixture was then heated to *ca.* 70 °C for 1 h. The mixture was allowed to cool to *ca.* 20 °C, diluted with water (5 ml) and washed with DCM (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane-DCM, 5 : 5) gave the *title compound* **6** (36.7 mg, 83%) as colourless plates, mp 58-59 °C (from cyclohexane); (Found: C, 51.2; H, 3.2; N, 13.3. $C_9H_7ClN_2S$ requires C, 51.3; H, 3.4; N, 13.3%); λ_{max}(DCM)/nm 315 (log ε 2.79), 262 (2.66); ν_{max}/cm^{-1} 3373w and 3309w (NH_2), 3212w, 3061w (Ph CH), 1623w, 1576w, 1492w, 1445w, 1420m, 1374m, 1316w, 1282w, 1136w, 1086w, 1061w, 1027w, 994w, 974w, 926w, 823m, 764s; δ_H(300 MHz; $CDCl_3$) 7.50-7.37 (5H, m, Ph C*H*), 3.76 (2H, br s, NH_2); δ_C(75 MHz; $CDCl_3$) 140.8, 139.8, 134.0, 130.6 (Ph *C*), 129.5 (Ph *C*H), 128.8 (Ph *C*H), 127.1 (Ph *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.5 (Ph *C*H), 128.8 (Ph *C*H), 127.1 (Ph *C*H); *m*/*z* (EI) 212 (M^++2, 31%), 210 (M^+, 82), 175 (11), 148 (29), 142 (62), 121 (100), 104 (16), 93 (9), 89 (14), 77 (63), 69 (14), 63 (15), 62 (15), 53 (14), 51 (37).

3-Chloro-4-iodo-5-phenylisothiazole 7

To a stirred mixture of I_2 (90.5 mg, 0.358 mmol, 2.5 equiv.) and isoamyl nitrite (77 μl, 0.573 mmol, 4 equiv.) in MeCN (2 ml) protected with $CaCl_2$ drying tube at *ca.* 80 ^oC was added dropwise an MeCN (1 ml) solution of 4-amino-3-chloro-5-phenyl-isothiazole **6** (30 mg, 0.143 mmol). The mixture was kept at *ca.* 80 ^oC until no starting material remained (TLC), allowed to cool to *ca.* 20 ^oC and absorbed on silica. Chromatography (hexane-DCM, 7 : 3) gave the *title compound* **7** (37.7 mg, 82%) as colourless needles, mp 67-68 ^oC (from pentane); (Found: C, 33.5; H, 1.5; N, 4.3. C_9H_5ClINS requires C, 33.6; H, 1.6; N, 4.4%); λ_{max}(DCM)/nm 275 (log ε 2.70); ν_{max}/cm^{-1} 3046w (Ph CH), 1471m, 1442m, 1381m, 1335w, 1325w, 1286m, 1270s, 1238w, 1207w, 1077w, 1033m, 990m, 966w, 921w, 893m, 841w, 822m, 783w, 750s; δ_H(300 MHz; $CDCl_3$) 7.60-7.57 (2H, m, Ph C*H*), 7.53-7.51 (3H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 168.0, 154.5, 130.7 (Ph *C*), 130.4 (Ph *C*H), 129.1 (Ph *C*H), 128.5 (Ph *C*H), 79.5; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.4 (Ph *C*H), 129.1 (Ph *C*H), 128.5 (Ph *C*H); *m*/*z* (EI) 323 (M^++2, 36%), 321 (M^+, 100), 194 (13), 159 (74), 148 (4), 133 (58), 127 (60), 121 (7), 113 (17), 100 (14), 89 (31), 77 (14), 75 (13), 74 (13), 73 (4), 69 (8), 63 (20), 51 (26).

3-Chloro-4,5-diphenylisothiazole 8 *via* Suzuki reaction at C-4

A stirred mixture of 4-bromo-3-chloro-5-phenylisothiazole **5** (30 mg, 0.11 mmol), phenylboronic acid (40 mg, 0.33 mmol, 3 equiv.), powdered K_2CO_3 (22.8 mg, 0.165 mmol, 1.5 equiv.) and $Pd(OAc)_2$ (1.2 mg, 5 mol%) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 100 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 6 : 4) gave the *title compound* **8**

(28.7 mg, 96%) as colourless needles, mp 106-107 °C (from pentane); (Found: C, 66.4; H, 3.6; N, 5.2. $C_{15}H_{10}ClNS$ requires C, 66.3; H, 3.7; N, 5.2%); λ_{max}(DCM)/nm 275 (log ε 2.74); ν_{max}/cm^{-1} 3055w (Ar CH), 1599w, 1574w, 1537w, 1499w, 1477w, 1377w, 1346m, 1312w, 1236m, 1182w, 1143w, 1076w, 1034w, 995w, 988w, 920w, 907w, 843w, 833m, 802m, 770m, 748s, 710w, 694s; δ_H(300 MHz; $CDCl_3$) 7.44-7.22 (10H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 164.4, 150.0, 132.6, 131.8, 130.3 (Ph *C*H), 130.1 (Ph *C*), 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.6 (Ph *C*H), 128.3 (Ph *C*H), 128.2 (Ph *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.3 (Ph *C*H), 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.6 (Ph *C*H), 128.3 (Ph *C*H), 128.2 (Ph *C*H); *m*/*z* (EI) 273 (M^++2, 34%), 271 (M^+, 100), 258 (7), 256 (19), 236 (27), 203 (30), 190 (20), 178 (12), 165 (13), 135 (3), 104 (15), 89 (4), 77 (15), 63 (4), 51 (10) (Found: M^+, 271.0207, $C_{15}H_{10}ClNS$ requires *M*, 271.0222).

3-Chloro-4,5-diphenylisothiazole 8 *via* Stille reaction at C-4 (typical Stille conditions for coupling at C-4: see Table 1)

A stirred mixture of 3-chloro-4-iodo-5-phenylisothiazole **7** (30 mg, 0.093 mmol), tributylphenylstannane (36.6 μl, 0.112 mmol, 1.2 equiv.) and $Pd(OAc)_2$ (1.0 mg, 5 mol%) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 100 °C, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 °C, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 6 : 4) gave the *title compound* **8** (25 mg, 99%) as colourless needles, mp 106-107 °C (from pentane) identical to that described above.

3-Chloro-5-phenyl-4-(thien-2-yl)isothiazole 9

Similar treatment of 3-chloro-4-iodo-5-phenylisothiazole **7** (30 mg, 0.093 mmol) with 2-(tributylstannyl)thiophene and $Pd(OAc)_2$ gave the *title compound* **9** (25.8 mg, 100%) as colourless needles, mp 90-91 ^oC (from pentane); (Found: C, 56.2; H, 2.7; N, 5.0. $C_{13}H_8ClNS_2$ requires C, 56.2; H, 2.9; N, 5.0%); λ_{max}(DCM)/nm 251 (log ε 3.10), 274 inf (3.00); ν_{max}/cm^{-1} 3087w (Ar CH), 1486w, 1447w, 1431w, 1381w, 1364w, 1353w, 1326w, 1316w, 1306w, 1284w, 1238w, 1216w, 1221w, 1109w, 1077w, 1043w, 1031w, 984w, 967w, 927w, 882w, 852m, 821m, 779w, 759s; δ_H(300 MHz; $CDCl_3$) 7.41-7.28 (6H, m, Ar C*H*), 7.09-7.06 (2H, m, Ar C*H*); δ_C(75 MHz; $CDCl_3$) 165.5, 150.4, 131.7, 129.9, 129.9 (Ar *C*H), 129.3 (Ar *C*H), 129.0 (Ar *C*H), 128.3 (Ar *C*H), 127.5 (Ar *C*H), 127.2 (Ar *C*H), 126.1; δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.9 (Ar *C*H), 129.3 (Ar *C*H), 129.0 (Ar *C*H), 128.3 (Ar *C*H), 127.5 (Ar *C*H), 127.2 (Ar *C*H); *m*/*z* (EI) 279 (M^++2, 41%), 277 (M^+, 100), 264 (3), 262 (6), 244 (16), 242 (21), 241 (23), 234 (7), 232 (18), 209 (31), 208 (9), 196 (14), 184 (9), 171 (14), 164 (5), 139 (14), 121 (18), 107 (10), 93 (8), 77 (28), 69 (13), 63 (7), 51 (19).

3-Chloro-5-phenyl-4-(fur-2-yl)isothiazole 10

Similar treatment of 3-chloro-4-iodo-5-phenylisothiazole **7** (30 mg, 0.093 mmol) with 2-(tributylstannyl)furan and $Pd(OAc)_2$ gave the *title compound* **10** (24.3 mg, 100%) as colourless needles, mp 71-72 ^oC (from pentane); (Found: C, 59.6; H, 3.2; N, 5.5. $C_{13}H_8ClNOS$ requires C, 59.7; H, 3.1; N, 5.4%); λ_{max}(DCM)/nm 238 (log ε 3.00), 272 inf (2.79), 303 inf (2.70); ν_{max}/cm^{-1} 3146w, 3125w and 3060w (Ar CH), 1577w, 1517w, 1498w, 1464w, 1442w, 1397w, 1379w, 1338m, 1316w, 1256w, 1222w, 1172w, 1140w, 1078w, 1033w, 1022w, 996m, 948w, 920w, 887w, 876w, 830w, 822m, 790w, 757s, 711m; δ_H(300 MHz; $CDCl_3$) 7.46-7.36 (4H, m, Ar C*H*), 7.33-7.29 (2H, m, Ar C*H*), 6.64, (1H, app d, *J* 3.6, furyl *H*-3), 6.48 (1H, dd, *J* 3.4, 2.0, furyl *H*-

4); δ_C(75 MHz; $CDCl_3$) 165.6, 149.2, 144.7, 143.0 (Ar *C*H), 130.1 (Ar *C*), 129.9 (Ar *C*H), 128.9 (Ar *C*H), 128.2 (Ar *C*H), 123.1 (Ar *C*), 111.3 (Ar *C*H), 111.2 (Ar *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 143.0 (Ar *C*H), 129.9 (Ar *C*H), 128.9 (Ar *C*H), 128.2 (Ar *C*H), 111.3 (Ar *C*H), 111.2 (Ar *C*H); *m*/*z* (EI) 263 (M^++2, 37%), 261 (M^+, 100), 236 (6), 234 (14), 226 (28), 208 (7), 198 (33), 196 (29), 193 (29), 171 (28), 153 (18), 139 (23), 127 (23), 121 (35), 104 (13), 99 (21), 95 (15), 93 (24), 85 (25), 77 (79), 69 (34), 63 (24), 51 (50).

3-Chloro-4,5-diphenylisothiazole 8 *via* Negishi reaction at C-4 position

A stirred mixture of 3-chloro-4-iodo-5-phenylisothiazole **7** (30 mg, 0.093 mmol), phenylzinc chloride (0.558 μl, 0.5 M in THF, 3 equiv.) and $(PPh_3)_2PdCl_2$ (3.3 mg, 5 mol%) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 100 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 6 : 4) gave 3-chloro-5-phenylisothiazole **11** (14.6 mg, 80%) as colourless needles, mp 50-51 ^oC (lit.,[34] 56 ^oC) (from pentane); ν_{max}/cm^{-1} 3092w (isothiazole CH), 3065w, 3052w and 3028w (Ph CH), 1616w, 1524m, 1483s, 1447m, 1395m, 1333m, 1312m, 1220w, 1137m, 1103w, 1074w, 1031w, 1001w, 980m, 916w, 876m, 834m, 814m, 754s, 719m; δ_H(300 MHz; $CDCl_3$) 7.58-7.53 (2H, m, Ph *H*), 7.50-7.43 (3H, m, Ph *H*), 7.23 (1H, s, isothiazole *H*-4); δ_C(75 MHz; $CDCl_3$) 169.4, 150.0, 130.3 (Ph *C*H), 129.8 (Ph *C*), 129.4 (Ph *C*H), 126.3 (Ph *C*H), 119.0 (isothiazole *H*-4); δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.3 (Ph *C*H), 129.4 (Ph *C*H), 126.3 (Ph *C*H), 119.0 (isothiazole *C*-4); *m*/*z* (EI) 197 (M^++2, 37%), 195 (M^+, 100), 160 (25), 149 (12), 133 (9), 128 (6), 127 (10), 116 (17), 102 (10), 93 (9), 89 (15), 77 (18), 63 (12), 51 (24). Further elution (hexane–

DCM, 6 : 4) gave the *title compound* **8** (5.0 mg, 20%) as colourless needles, mp 106-107 ^{o}C (from pentane) identical to that described above.

3-Chloro-5-phenylisothiazole 11

A stirred mixture of 3-chloro-4-iodo-5-phenylisothiazole **7** (30 mg, 0.093 mmol) and $Pd(OAc)_2$ (20.9 mg, 0.093 mmol, 1 equiv.) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 140 ^{o}C, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^{o}C, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 6 : 4) gave the *title compound* **11** (17.8 mg, 98%) as colourless needles, mp 50-51 ^{o}C (lit.,[34] 56 ^{o}C) (from pentane) identical to that described above.

3-Hydroxy-4,5-diphenylisothiazole 12

A mixture of 3-chloro-4,5-diphenylisothiazole **8** (1 g, 3.68 mmol) and KOH (825 mg, 14.7 mmol, 4 equiv.) in H_2O (150 ml) was placed in a bomb reactor with a teflon liner. The bomb reactor was sealed and heated to *ca.* 200 ^{o}C (250 psi) for 24 h. The bomb reactor was cooled to *ca.* 20 ^{o}C and opened. The reaction mixture was filtered and the filtrate was acidified to give a white precipitate. The white precipitate was filtered, washed (H_2O) and dried to give the title compound **12** (885 mg, 95%) as colourless needles, mp 233-235 ^{o}C (lit.,[35] 245-247 ^{o}C) (from cyclohexane); (Found: C, 71.0; H, 4.4; N, 5.6. $C_{15}H_{11}NOS$ requires C, 71.1; H, 4.4; N, 5.5%); λ_{max}(DCM)/nm 234 (log ε 3.94), 280 (3.90); ν_{max}/cm^{-1} 3059w (Ar CH), 1607w, 1583w, 1566w, 1500m, 1481m, 1444w, 1342w, 1265m, 1184w, 1081w, 1073w, 1057w, 1033w, 1024w, 943w, 880m, 851w, 844w, 770m, 754s; δ_H(300 MHz; DMSO-d_6) 11.97 (1H,

br s, O*H*), 7.34-7.29 (6H, m, Ph C*H*), 7.27-7.21 (4H, m, Ph C*H*); δ_C(75 MHz; DMSO-d_6) 166.8, 160.5, 132.3 (Ph *C*), 131.1 (Ph *C*), 129.8 (Ph *C*H), 129.2 (Ph *C*H), 129.0 (Ph *C*H), 128.3 (Ph *C*H), 127.9 (Ph *C*H), 127.4 (Ph *C*H), 122.1; δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.8 (Ph *C*H), 129.2 (Ph *C*H), 129.0 (Ph *C*H), 128.3 (Ph *C*H), 127.9 (Ph *C*H), 127.4 (Ph *C*H); *m*/*z* (EI) 254 (M^++1, 20%), 253 (M^+, 100), 252 (54), 238 (6), 219 (7), 209 (17), 205 (10), 190 (6), 178 (29), 165 (32), 152 (10), 139 (4), 126 (6), 121 (4), 104 (12), 89 (8), 77 (11), 63 (6), 51 (10) (Found: M^+, 253.0567, $C_{15}H_{11}NOS$ requires *M*, 253.0561).

3-Bromo-4,5-diphenylisothiazole 13

A stirred mixture of 3-hydroxy-4,5-diphenylisothiazole **12** (30 mg, 0.12 mmol) and $POBr_3$ (1.5 g), protected with $CaCl_2$ drying tube, was heated to *ca.* 100 °C for 24 h. The reaction mixture was cooled to *ca.* 20 °C, diluted with water and extracted with DCM (4 × 10 ml). The organic extracts were combined, dried and absorbed on silica. Chromatography (hexane–DCM, 7 : 3) gave the *title compound* **13** (32 mg, 85%) as colourless crystals, mp 112-113 °C (from pentane); (Found: C, 56.9; H, 3.3; N, 4.3. $C_{15}H_{10}BrNS$ requires C, 57.0; H, 3.2; N, 4.4%); λ_{max}(DCM)/nm 276 (log ε 3.01); ν_{max}/cm^{-1} 1533w, 1498w, 1474w, 1444w, 1372w, 1339m, 1227m, 1182w, 1138w, 1075w, 1034w, 988w, 920w, 898w, 849w, 843w, 825m, 785w, 769m, 747s; δ_H(300 MHz; $CDCl_3$) 7.43-7.40 (3H, m, Ph C*H*), 7.35-7.26 (5H, m, Ph C*H*), 7.22-7.17 (2H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 164.0, 140.0, 135.3, 132.5, 130.4 (Ph *C*H), 130.0, 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.6 (Ph *C*H), 128.3 (Ph *C*H), 128.3 (Ph *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.4 (Ph *C*H), 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.6 (Ph *C*H), 128.3 (Ph *C*H), 128.3 (Ph *C*H); *m*/*z* (EI) 317 (M^++2, 97%), 315 (M^+, 100), 302 (7), 300 (7), 236 (71), 235 (61), 221 (4), 208 (15), 203 (65), 190 (21), 178 (16), 165 (24), 152 (9), 139 (6), 121 (12), 118 (16), 104 (22), 89 (11), 77 (77), 63 (12), 51 (49).

3-Chloro-4,5-diphenylisothiazole 8 from 3-hydroxy-4,5-diphenylisothiazole 12

A stirred mixture of 3-hydroxy-4,5-diphenylisothiazole **12** (20 mg, 0.079 mmol) and $POCl_3$ (1 ml) was placed in a sealed tube and heated to *ca.* 150 °C for 72 h. The reaction mixture was cooled to *ca.* 20 °C, diluted (H_2O) and extracted with DCM (4 × 10 ml). The organic extracts were combined, dried and absorbed on silica. Chromatography (hexane–DCM, 7 : 3) gave the *title compound* **8** (21 mg, 98%) as colourless needles, mp 106-107 °C (from pentane) identical to that described above.

4,5-Diphenylisothiazol-3-yl trifluoromethanesulfonate 14

To a stirred solution of 3-hydroxy-4,5-diphenylisothiazole **12** (30 mg, 0.118 mmol) and triethylamine (16.5 μl, 0.118 mmol, 1 equiv.) in DCM (2 ml) cooled to *ca*. 0 °C and protected with $CaCl_2$ drying tube was added dropwise trifluoromethanesulfonic anhydride (20 μl, 0.118 mmol, 1 equiv.). The reaction mixture was kept at *ca*. 0 °C until no starting material remained (TLC). Chromatography (hexane–DCM, 7 : 3) gave the *title compound* **14** (32.3 mg, 71%) as colourless crystals mp 66-67 °C (from pentane) (Found: C, 50.1; H, 2.7; N, 3.7. $C_{16}H_{10}F_3NO_3S_2$ requires C, 49.9; H, 2.6; N, 3.6%); λ_{max}(DCM)/nm 277 (log ε 2.94); ν_{max}/cm^{-1} 1449w, 1424m, 1409w, 1374m, 1274w, 1233s, 1220s, 1162w, 1132m, 1080w, 1042m, 1018w, 1000w, 941m, 922w, 877m, 856m, 802s, 773w, 763m, 751m, 736m; δ_H(300 MHz; $CDCl_3$) 7.42-7.31 (6H, m, Ph C*H*), 7.27-7.24 (4H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 166.2, 154.4, 130.1 (Ph *C*H), 129.8 (Ph *C*H), 129.8 (Ph *C*), 129.4 (Ph *C*), 129.1 (Ph *C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.2 (Ph *C*H), 125.4, 118.3 (1C, q, $^1J_{CF}$ 321.0, *C*F$_3$); δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.1 (Ph *C*H), 129.8 (Ph *C*H), 129.1 (Ph *C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.2 (Ph *C*H); *m*/*z* (EI) 386 (M^++1, 16%), 385 (M^+, 77), 252 (100), 234 (10), 219 (19), 210 (11), 190 (16), 178 (43), 176 (20), 152 (14), 139 (4), 126 (6),

121 (6), 89 (4) 77 (10), 69 (19). Further elution (hexane–Et_2O, 2 : 8) gave *4,5-diphenyl-2-(trifluoromethylsulfonyl)isothiazol-3(2*H*)-one* **15** (13.2 mg, 29%) as colourless crystals mp 96-97 ^oC (from pentane) (Found: C, 50.1; H, 2.7; N, 3.5. $C_{16}H_{10}F_3NO_3S_2$ requires C, 49.9; H, 2.6; N, 3.6%); λ_{max}(DCM)/nm 236 (log ε 3.05), 307 (2.83); ν_{max}/cm^{-1} 1715s (C=O), 1653w, 1599w, 1579w, 1564w, 1560w, 1506w, 1487w, 1451w, 1445w, 1415s, 1397w, 1337w, 1235s, 1200s, 1170w, 1138s, 1131s, 1081w, 1030w, 1001s, 976w, 971w, 933w, 925w, 855w, 840w, 796m, 768m, 754s, 729m; δ_H(300 MHz; $CDCl_3$) 7.52-7.47 (1H, m, Ph C*H*), 7.43-7.29 (9H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 163.9, 157.3, 131.8 (Ph *C*H), 129.8 (Ph *C*), 129.7 (Ph *C*H), 129.6 (Ph *C*H), 128.9 (Ph *C*H), 128.6 (Ph *C*H), 128.0 (Ph *C*H), 121.0, 119.2 (1C, q, $^1J_{CF}$ 324.3, CF_3); δ_C(75 MHz; DEPT 90, $CDCl_3$) 131.8 (Ph *C*H), 129.7 (Ph *C*H), 129.6 (Ph *C*H), 128.9 (Ph *C*H), 128.6 (Ph *C*H), 128.0 (Ph *C*H); *m*/*z* (EI) 386 (M^++1, 12%), 385 (M^+, 59), 252 (100), 234 (9), 219 (20), 210 (12), 190 (12), 178 (45), 176 (21), 165 (20), 152 (14), 139 (4), 126 (5), 121 (7), 89 (6) 77 (11), 69 (23), 63 (5), 51 (9).

3-Amino-4,5-diphenylisothiazole 16

A stirred mixture of 3-chloro-4,5-diphenylisothiazole **8** (50 mg, 0.184 mmol) and sodium amide (71.8 mg, 1.84 mmol, 10 equiv.) in dry THF (2 ml) was kept to *ca.* 20 ^oC, under argon, until no starting material remained (TLC). Chromatography (hexane–DCM, 3 : 7) gave the *title compound* **16** (45 mg, 97%) as colourless needles, mp 130-131 ^oC (from cyclohexane); (Found: C, 71.4; H, 4.8; N, 10.9. $C_{15}H_{12}N_2S$ requires C, 71.4; H, 4.8; N, 11.1%); λ_{max}(DCM)/nm 276 (log ε 3.71); ν_{max}/cm^{-1} 3458w and 3302w (NH), 3196 (Ar CH), 1622m, 1576w, 1558w, 1541w, 1506w, 1495m, 1458m, 1443w, 1402m, 1339w, 1161w, 1072w, 1053w, 1028w, 999w, 934w, 924w, 851w, 843m, 772m, 756s, 739w, 704s; δ_H(300 MHz; $CDCl_3$) 7.42-7.23 (10H, m, Ph

C*H*), 4.37 (2H, br s, NH_2); δ_C(75 MHz; $CDCl_3$) 162.9, 161.5, 133.0 (Ph *C*), 131.0 (Ph *C*), 129.9 (Ph *C*H), 129.2 (Ph *C*H), 128.9 (Ph *C*H), 128.7 (Ph *C*H), 128.2 (Ph *C*H), 128.1 (Ph *C*H), 122.7; δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.9 (Ph *C*H), 129.2 (Ph *C*H), 128.9 (Ph *C*H), 128.7 (Ph *C*H), 128.2 (Ph *C*H), 128.1 (Ph *C*H); *m*/*z* (EI) 253 (M^++1, 27%), 252 (M^+, 100), 251 (59), 234 (5), 218 (12), 209 (7), 190 (13), 178 (10), 176 (10), 165 (28), 152 (7), 139 (4), 126 (6), 121 (4), 104 (8), 89 (8), 77 (12), 74 (9), 69 (3), 63 (5), 51 (10) (Found: M^+, 252.0718, $C_{15}H_{12}N_2S$ requires *M*, 252.0721).

Sandmeyer iodination reaction of 3-amino-4,5-diphenylisothiazole 16

To a stirred mixture of benzyltriethylammonium iodide (113.9 mg, 0.357 mmol, 3 equiv.) and isoamyl nitrite (63.9 μl, 0.476 mmol, 4 equiv.) in MeCN (2 ml) protected with $CaCl_2$ drying tube at *ca.* 20 ^oC was added dropwise an MeCN (1 ml) solution of 3-amino-4,5-diphenyl-isothiazole **16** (30 mg, 0.119 mmol). The mixture was kept at *ca.* 20 ^oC for 30min and then was heated to *ca.* 80 ^oC for 1h. The mixture was allowed to cool to *ca.* 20 ^oC and absorbed on silica. Chromatography (hexane-DCM, 7 : 3) gave a colourless material which was a mixture of inseparable compounds: ν_{max}/cm^{-1} 2954w, 2923m, 2854w, 2208w (C≡N), 1594w, 1582w, 1576w, 1564w, 1485w, 1467w, 1457w, 1444m, 1378w, 1363w, 1331w, 1262w, 1222w, 1180w, 1157w, 1134w, 1078w, 1046w, 1031w, 998w, 985w, 969w, 919w, 900w, 873w, 854w, 822w, 793w, 768s, 746m, 738s; δ_H(300 MHz; $CDCl_3$) 7.63-7.60 (m, Ph C*H*), 7.54-7.40 (m, Ph C*H*), 7.26-7.12 (m, PhC*H*); δ_C(75 MHz; $CDCl_3$) 142.0, 141.1, 137.9, 133.8, 130.7 (Ph *C*H), 130.4 (Ph *C*H), 129.6 (Ph *C*H), 129.6, 129.1 (Ph *C*H), 129.1 (Ph *C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.7 (Ph *C*H), 128.6 (Ph *C*H), 128.5 (Ph *C*H), 128.4 (Ph *C*H), 128.3 (Ph *C*H), 125.1, 121.1, 121.0, 116.8, 115.8; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.7 (Ph *C*H), 130.4 (Ph *C*H), 129.6 (Ph *C*H), 129.1 (Ph *C*H), 129.1 (Ph

*C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.7 (Ph *C*H), 128.6 (Ph *C*H), 128.5 (Ph *C*H), 128.4 (Ph *C*H), 128.3 (Ph *C*H); *m*/*z* (EI) 364 (M^++1%), 363 (M^+, 19), 332 (6), 331 ($C_{15}H_{10}IN^+$, 33), 236 (8), 205 (17), 204 (100), 203 (37), 202 (7), 177 (22), 176 (17), 127 (8), 102 (10), 88 (13), 77 (33), 51 (29).

3,4,5-Triphenylisothiazole 17

A stirred mixture of 3-bromo-4,5-diphenylisothiazole **13** (30 mg, 0.095 mmol), phenylzinc chloride (570 μl, 0.5 M in THF, 3 equiv.) and $(PPh_3)_2PdCl_2$ (3.3 mg, 5 mol%) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 100 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 5 : 5) gave the title compound **17** (21.4 mg, 72%) as colourless crystals, mp 210-211 ^oC (lit.,[17] 211.5-212.5 ^oC) (from cyclohexane); (Found: C, 80.5; H, 4.8; N, 4.4. $C_{21}H_{15}NS$ requires C, 80.5; H, 4.8; N, 4.5%); λ_{max}(DCM)/nm 241 (log ε 4.06), 284 (3.85); ν_{max}/cm^{-1} 3063w (Ph CH), 1601w, 1576w, 1539w, 1533w, 1499w, 1479w, 1440w, 1398w, 1363w, 1291w, 1272w, 1188w, 1179w, 1159w, 1153w, 1073w, 1030w, 977w, 920w, 908w, 842w, 802w, 782w, 764m, 748s, 726m, 701m; δ_H(300 MHz; $CDCl_3$) 7.44-7.41 (2H, m, Ph C*H*), 7.37-7.23 (11H, m, Ph C*H*), 7.13-7.10 (2H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 167.6, 164.0, 135.7, 134.2, 134.1, 131.0, 130.6 (Ph *C*H), 128.9 (Ph *C*H), 128.7 (Ph *C*H), 128.7 (Ph *C*H), 128.7 (Ph *C*H), 128.5 (Ph *C*H), 128.4 (Ph *C*H), 128.0 (Ph *C*H), 127.5 (Ph *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.6 (Ph *C*H), 128.9 (Ph *C*H), 128.7 (Ph *C*H), 128.7 (Ph *C*H), 128.7 (Ph *C*H), 128.5 (Ph *C*H), 128.4 (Ph *C*H), 128.0 (Ph *C*H), 127.5 (Ph *C*H); *m*/*z* (EI) 314 (M^++1, 30%), 313 (M^+,

98), 312 (100), 297 (3), 280 (3), 278 (3), 236 (4), 210 (5), 208 (5), 178 (10), 165 (24), 155 (7), 149 (10), 139 (4), 126 (3), 121 (4), 103 (4), 89 (5), 77 (14), 63 (4), 51 (9).

3-Iodo-5-phenylisothiazole-4-carboxamide 19

A stirred solution of 3-iodo-5-phenylisothiazole-4-carbonitrile **18** (2 g, 6.41 mmol) in c. H_2SO_4 (50 ml) protected with $CaCl_2$ drying tube, was heated to *ca.* 100 ^oC until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC and then was poured into ice-water to form a white precipitate. The white precipitate was filtered out, washed (H_2O) and dried under vacuum to give the *title compound* **19** (2.12 g, 100%) as colourless crystals, mp 184-185 ^oC (from PhH); (Found: C, 36.4; H, 2.1; N, 8.5. $C_{10}H_7IN_2OS$ requires C, 36.4; H, 2.1; N, 8.5%); λ_{max}(DCM)/nm 274 (log ε 3.90); ν_{max}/cm^{-1} 3375w (NH), 3186w (Ph CH), 1643s (C=O), 1617w, 1522w, 1485w, 1415m, 1363w, 1289w, 1259m, 1228w, 1119w, 1080w, 1036w, 993w, 940w, 917w, 830w, 787w, 772m, 756w; δ_H(300 MHz; CD_2Cl_2) 7.58-7.55 (2H, m, Ph C*H*), 7.51-7.45 (3H, m, Ph C*H*), 5.91 (1H, br s, N*H*), 5.69 (1H, br s, N*H*); δ_C(75 MHz; CD_2Cl_2) 166.7, 165.1, 130.9 (Ph *C*H), 129.7 (Ph *C*H), 128.7, 128.6, 128.4 (Ph *C*H), 111.0; δ_C(75 MHz; DEPT 90, CD_2Cl_2) 130.9 (Ph *C*H), 129.7 (Ph *C*H), 128.4 (Ph *C*H); *m*/*z* (EI) 331 (M^++1, 15%), 330 (M^+, 100), 329 (80), 314 (46), 202 (10), 187 (10), 159 (24), 133 (16), 127 (18), 121 (13), 116 (11), 100 (6), 89 (27), 77 (29), 63 (9), 51 (22).

3-Iodo-5-phenylisothiazole-4-carboxylic acid 20

To a stirred solution of 3-iodo-5-phenylisothiazole-4-carboxamide **19** (49.5 mg, 0.15 mmol) in c. H_2SO_4 (1 ml) cooled to *ca.* 0 ^oC and protected with $CaCl_2$ drying tube, was added in portions sodium nitrite (259 mg, 3.75 mmol, 25 equiv.). The reaction mixture was heated to *ca.* 100 ^oC, until no starting material remained (TLC). The

mixture was allowed to cool to *ca.* 20 °C and then was poured into ice-water to form a white precipitate. The white precipitate was filtered out, washed (H_2O) and dried under vacuum to give the *title compound* **20** (38.7 mg, 78%) as colourless neadles, mp 156-157 °C (from cyclohexane); (Found: C, 36.3; H, 1.8; N, 4.3. $C_{10}H_6INO_2S$ requires C, 36.3; H, 1.8; N, 4.2%); λ_{max}(DCM)/nm 230 (log ε 2.78), 273 (2.86); ν_{max}/cm^{-1} 1689s (C=O), 1537w, 1507m, 1473s, 1445w, 1433m, 1371m, 1337m, 1282w, 1267w, 1220m, 1076w, 1034w, 1006w, 962w, 915w, 828s, 788w, 773w, 754w, 735s; δ_H(300 MHz; CD_2Cl_2) 8.83 (1H, br s, O*H*), 7.55-7.45 (5H, m, Ph C*H*); δ_C(75 MHz; CD_2Cl_2) 173.1, 166.6, 130.9 (Ph *C*H), 129.9, 129.1 (Ph *C*H), 129.0 (Ph *C*H), 128.9, 112.6; δ_C(75 MHz; DEPT 90, CD_2Cl_2) 130.9 (Ph *C*H), 129.1 (Ph *C*H), 129.0 (Ph *C*H); *m*/*z* (EI) 332 (M^++1, 13%), 331 (M^+, 100), 330 (24), 314 (35), 187 (4), 186 (5), 159 (13), 133 (13), 127 (14), 121 (7), 116 (12), 100 (5), 89 (22), 77 (28), 69 (5), 63 (7), 51 (23).

4-Amino-3-iodo-5-phenylisothiazole 21

To a stirred solution of sodium hydroxide (18.2 mg, 0.455 mmol, 5 equiv.) in water (2 ml) cooled to *ca.* 0 °C was first added Br_2 (5.6 μl, 0.109 mmol 1.2 equiv.) and then 3-iodo-5-phenylisothiazole-4-carboxamide **19** (30 mg, 0.091 mmol). The reaction mixture was allowed to warm to *ca.* 20 °C and was kept at this temperature until the starting material had completely dissolved. The reaction mixture was then heated to *ca.* 70 °C for 1 h. The mixture was allowed to cool to *ca.* 20 °C, diluted with water (2 ml) and extracted with DCM (4 × 10 ml). The organic extracts were combined, dried and absorbed on silica. Chromatography (hexane-DCM, 5 : 5) gave the *title compound* **21** (24.5 mg, 89%) as orange cubes, mp 74-76 °C (from cyclohexane); (Found: C, 35.9; H, 2.3; N, 9.3. $C_9H_7IN_2S$ requires C, 35.8; H, 2.3; N, 9.3%); λ_{max}(DCM)/nm 231 (log ε 2.76), 266 (2.68), 320 (2.86); ν_{max}/cm^{-1} 3368w and 3308

(NH), 1622w, 1597w, 1572w, 1538w, 1487w, 1442w, 1400m, 1347m, 1316w, 1275w, 1182w, 1157w, 1117w, 1078w, 1040m, 999w, 992w, 970w, 926w, 859w, 807m, 773m, 761s; δ_H(300 MHz; CD_2Cl_2) 7.52-7.37 (5H, m, Ph C*H*), 3.96 (2H, br s, N*H*); δ_C(75 MHz; CD_2Cl_2) 140.4, 138.1, 130.6 (Ph *C*), 129.8 (Ph *C*H), 129.1 (Ph *C*H), 127.7 (Ph *C*H), 108.5; δ_C(75 MHz; DEPT 90, CD_2Cl_2) 129.8 (Ph *C*H), 129.1 (Ph *C*H), 127.7 (Ph *C*H); *m*/*z* (EI) 303 (M^++1, 11%), 302 (M^+, 100), 175 (15), 148 (31), 142 (78), 127 (4), 121 (83), 89 (6), 77 (39), 69 (6), 63 (6), 51 (16).

3,4-Diiodo-5-phenylisothiazole 22

To a stirred mixture of I_2 (62.9 mg, 0.248 mmol, 2.5 equiv.) and isoamyl nitrite (53.2 μl, 0.396 mmol, 4 equiv.) in MeCN (2 ml) protected with $CaCl_2$ drying tube at *ca.* 80 ^oC was added dropwise an MeCN (1 ml) solution of 4-amino-3-iodo-5-phenylisothiazole **21** (30 mg, 0.099 mmol). The mixture was kept at *ca.* 80 ^oC until no starting material remained (TLC), allowed to cool to *ca.* 20 ^oC and absorbed on silica. Chromatography (hexane-DCM, 7 : 3) gave the *title compound* **22** (34.8 mg, 85%) as colourless plates, mp 84-85 ^oC (from pentane); (Found: C, 26.2; H, 1.2; N, 3.4. $C_9H_5I_2NS$ requires C, 26.2; H, 1.2; N, 3.4%); λ_{max}(DCM)/nm 281 (log ε 3.72); ν_{max}/cm^{-1} 3046w (Ph CH), 1459s, 1439m, 1356m, 1317w, 1290w, 1235s, 1217m, 1202w, 1076w, 1033m, 971m, 920w, 870s, 841w, 800m, 766s, 745s; δ_H(300 MHz; $CDCl_3$) 7.56-7.44 (5H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 166.9, 130.6, 130.3 (Ph *C*H), 128.9 128.9 (Ph *C*H), 128.7 (Ph *C*H), 125.5; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.3 (Ph *C*H), 128.9 (Ph *C*H), 128.7 (Ph *C*H); *m*/*z* (EI) 414 (M^++1, 12%), 413 (M^+, 100), 286 (M^+-I, 2), 254 (2), 206 (3), 159 (M^+-2I, 89), 133 (5), 127 (26), 115 (11), 100 (7), 89 (8), 77 (12), 69 (5), 63 (8), 51 (17).

4-Bromo-3-iodo-5-phenylisothiazole 24

To a stirred mixture of 3-iodo-5-phenylisothiazole-4-carboxylic acid **20** (1.0 g, 3.02 mmol) in H_2O (50 ml) was added aqueous solution of KOH (169.5 mg, 3.02 mmol, 1 equiv.) and the mixture was allowed to stirred at *ca.* 20 ^oC until the complete solution of the starting material. To the reaction mixture was added, in one portion, a solution of silver nitrate (513 mg, 3.02 mmol, 1 equiv.) in H_2O (5 ml) to form a white-grey precipitate. The white-grey precipitate was filtered out, washed first with H_2O and then with acetone and dried in a vacuum oven at *ca.* 80 ^oC for 12 h to give the *title compound* **23** (1.32 g, 100%). To a stirred mixture of silver 3-iodo-5-phenylisothiazole-4-carboxylate **23** (50 mg, 0.114 mmol) in tetrachloromethane (3 ml) protected with $CaCl_2$ drying tube was added in one portion Br_2 (7.02 μl, 0.137 mmol, 1.2 equiv.) and the reaction was kept at 20 ^oC for 1 h. The reaction mixture was filtered and the filtrate was absorbed on silica. Chromatography (hexane-DCM 8 : 2) gave the *title compound* **24** (31.3mg, 75%) as pale yellow oil; (Found: C, 29.5; H, 1.8; N, 3.8. C_9H_5BrINS requires C, 29.5; H, 1.4; N, 3.8%); λ_{max}(DCM)/nm 280 (log ε 2.82); ν_{max}/cm^{-1} 3062w (Ph CH), 2921w, 1575w, 1521w, 1467s, 1442m, 1361w, 1250s, 1224w, 1210w, 1075w, 1032w, 977w, 917w, 884s, 802m, 767m, 744s; δ_H(300 MHz; $CDCl_3$) 7.62-7.56 (2H, m, Ph C*H*), 7.54-7.47 (3H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 161.9, 130.3 (Ph *C*H), 129.1 (Ph *C*H), 129.0 (Ph *C*), 128.4 (Ph *C*H), 119.7, 115.4; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.3 (Ph *C*H), 129.0 (Ph *C*H), 128.4 (Ph *C*H); *m*/*z* (EI) 367 (M^++2, 83%), 365 (M^+, 81), 240 (3), 238 (M^+-I, 3), 159 (100), 127 (34), 121 (7), 115 (13), 114 (11), 100 (9), 89 (10), 77 (24), 69 (10), 63 (13), 51 (35).

Suzuki reaction on 4-bromo-3-iodo-5-phenylisothiazole 24

A stirred mixture of 4-bromo-3-iodo-5-diphenylisothiazole **24** (30 mg, 0.082 mmol), phenylboronic acid (30.0 mg, 0.246 mmol, 3 equiv.), powdered K_2CO_3 (17.0 mg, 0.123 mmol, 1.5 equiv.) and $Pd(OAc)_2$ (0.9 mg, 5 mol%) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 140 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 7 : 3) gave a colourless material which was (tentatively) an inseparable mixture of mainly 4-bromo-3,5-diphenylisothiazole **30** (see below for independent synthesis and characterisation) and a trace of 3-iodo-4,5-diphenylisothiazole; (Found: C, 55.8; H, 3.1; N, 4.0.); δ_H(300 MHz; $CDCl_3$) 7.86-7.83 (2H, m, Ph C*H*), 7.68-7.65 (2H, m, Ph C*H*), 7.54-7.42 (6H, m, PhC*H*); *m*/*z* (EI) 364 (M^++1, 3%), 363 (M^+, $C_{15}H_{10}INS$, 15), 318 (17), 317 (M^+, $C_{15}H_{10}Br^{81}NS$, 100), 316 (19), 315 (M^+, $C_{15}H_{10}Br^{79}NS$, 93), 237 (32), 236 (77), 235 (27), 204 (10), 203 (17), 189 (11), 135 (11), 134 (26), 133 (31), 118 (25), 104 (11), 89 (52), 77 (31), 63 (11), 57 (8), 51 (21).

3,3'-Bi(4-bromo-5-phenylisothiazole) 25

A stirred mixture of 4-bromo-3-iodo-5-phenylisothiazole **24** (30 mg, 0.082 mmol) and $Pd(OAc)_2$ (18.4 mg, 0.082 mmol, 1 equiv.) in DMF (2 ml) under an argon atmosphere, was heated to *ca.* 140 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 2 : 8) gave the *title compound* **25** (14.5 mg, 74%) as colourless needles, mp 208-209 ^oC (from cyclohexane); (Found: C, 45.4; H, 2.2; N, 6.0. $C_{18}H_{10}Br_2N_2S_2$ requires C, 45.2; H, 2.1; N, 5.9%); λ_{max}(DCM)/nm 285 (log ε

4.09); ν_{max}/cm^{-1} 3062w (Ph CH), 1684w, 1653w, 1576w, 1559w, 1539w, 1506w, 1473m, 1445m, 1357w, 1288w, 1243s, 1213w, 1181w, 1159w, 1077w, 1056w, 1035w, 1000w, 977w, 967w, 912w, 882s, 846w, 829m, 754m, 746s, 728w, 724w; δ_H(300 MHz; $CDCl_3$) 7.74-7.66 (4H, m, Ph C*H*), 7.59-7.48 (6H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 163.0, 161.3, 130.1 (Ph *C*H), 129.4 (Ph *C*), 129.1 (Ph *C*H), 128.7 (Ph *C*H), 107.3; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.1 (Ph *C*H), 129.1 (Ph *C*H), 128.7 (Ph *C*H); *m*/*z* (EI) 480 (M^++2, 54%), 478 (M^++2, 100), 476 (M^+, 50), 399 (3), 397 (3), 318 (15), 239 (8), 214 (4), 159 (18), 145 (8), 133 (42), 127 (10), 121 (13), 101 (4), 89 (40), 77 (10), 63 (6), 51 (8).

3,5-Diphenylisothiazole-4-carboxamide 27

A stirred solution of 3,5-diphenylisothiazole-4-carbonitrile **26** (1 g, 3.81 mmol) in c. H_2SO_4 (10 ml) protected with $CaCl_2$ drying tube, was heated to *ca.* 100 ^oC until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC and then was poured into ice-water to afford a white precipitate. The white precipitate was filtered, washed (H_2O) and dried under vacuum to give the *title compound* **27** (1.07 g, 100%) as colourless needles, mp 210-211 ^oC (from PhH); (Found: C, 68.6; H, 4.4; N, 9.9. $C_{16}H_{12}N_2OS$ requires C, 68.6; H, 4.3; N, 10.0%); λ_{max}(DCM)/nm 249 (log ε 4.19), 271 (4.11); ν_{max}/cm^{-1} 3398w (NH), 3198w, 1641s (C=O), 1616w, 1560w, 1533w, 1488w, 1446w, 1430w, 1385w, 1348w, 1099w, 1079w, 1029w, 1005w, 992w, 923w, 857w, 790w, 777w, 763w; δ_H(300 MHz; CD_2Cl_2) 7.83-7.77 (2H, m, Ph C*H*), 7.65-7.59 (2H, m, Ph C*H*), 7.53-7.43 (6H, m, Ph C*H*), 5.89 (1H, br s, N*H*), 5.68 (1H, br s, N*H*); δ_C(75 MHz; CD_2Cl_2) 167.4, 167.3, 166.5, 135.1, 130.4 (Ph *C*H), 130.1, 130.1, 129.7 (Ph *C*H), 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.5 (Ph *C*H), 128.4 (Ph *C*H); δ_C(75 MHz; DEPT 90, CD_2Cl_2) 130.4 (Ph *C*H), 129.7(Ph *C*H), 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.5 (Ph *C*H), 128.4 (Ph *C*H); *m*/*z* (EI) 280 (M^+, 91%), 279 (M^+-H, 100), 264

(50), 236 (4), 203 (5), 189 (4), 163 (3), 140 (10), 133 (29), 129 (19), 121 (9), 103 (8), 89 (37), 77 (38), 69 (6), 63 (10), 51 (23).

3,5-Diphenylisothiazole-4-carboxylic acid 28

To a stirred solution of 3,5-diphenylisothiazole-4-carboxamide **27** (1 g, 3.57 mmol) in c. H_2SO_4 (10 ml) cooled to *ca.* 0 ^oC and protected with $CaCl_2$ drying tube, was added in portions sodium nitrite (2.46 g, 35.7 mmol, 10 equiv.). The reaction mixture was heated to *ca.* 100 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC and then was poured into ice-water to afford a white precipitate. The white precipitate was filtered, washed (H_2O) and dried under vacuum to give the title compound **28** (0.87 g, 87%) as colourless needles, mp 202-203 ^oC (lit.,[36] 204-206 ^oC) (from cyclohexane); (Found: C, 68.5; H, 3.9; N, 5.0. $C_{16}H_{11}NO_2S$ requires C, 68.3; H, 3.9; N, 5.0%); λ_{max}(DCM)/nm 251 (log ε 4.00); ν_{max}/cm^{-1} 3055w (Ph CH), 1679s (C=O), 1559w, 1539w, 1533w, 1510m, 1476s, 1442m, 1356m, 1296m, 1208w, 1151w, 1077w, 1025w, 1005w, 990w, 953w, 917w, 856m, 821w, 801w, 769w, 755s; δ_H(300 MHz; CD_2Cl_2) 7.65-7.62 (2H, m, Ph C*H*), 7.56-7.53 (2H, m, Ph C*H*), 7.52-7.39 (6H, m, Ph C*H*) OH peak missing; δ_C(75 MHz; CD_2Cl_2) 171.8, 168.4, 167.5, 135.6, 130.4 (Ph *C*H), 130.0, 129.7 (Ph *C*H), 129.2 (Ph *C*H), 129.0 (Ph *C*H), 128.7 (Ph *C*H), 128.7 (Ph *C*H), 125.8; δ_C(75 MHz; DEPT 90, CD_2Cl_2) 130.4 (Ph *C*H), 129.7 (Ph *C*H), 129.2 (Ph *C*H), 129.0 (Ph *C*H), 128.7 (Ph *C*H), 128.7 (Ph *C*H); *m*/*z* (EI) 282 (M^++1, 24%), 281 (M^+, 100), 280 (57), 264 (21), 252 (5), 248 (7), 237 (57), 220 (3), 204 (7), 190 (4), 178 (3), 176 (3), 165 (7), 141 (7), 134 (19), 133 (20), 129 (14), 121 (16), 103 (15), 89 (32), 77 (44), 69 (8), 63 (13), 51 (28).

4-Bromo-3,5-diphenylisothiazole 30

To a stirred mixture of 3,5-diphenylisothiazole-4-carboxylic acid **28** (0.5 g, 1.78 mmol) in H_2O (50 ml) was added an aqueous solution of KOH (99.9 mg, 1.78 mmol, 1 equiv.) in H_2O (10 ml) and the mixture was allowed to stirred at *ca.* 20 ^oC until the starting material had completely dissolved. To the reaction mixture was added, in one portion, a solution of silver nitrate (302 mg, 1.78 mmol, 1 equiv.) in water (5 ml) to afford a white-grey precipitate. The white-grey precipitate was filtered, washed first with water and then with acetone and dried in a vacuum oven at *ca.* 80 ^oC for 12 h to give the *title compound* **29** (0.69 g, 100%). To a stirred mixture of silver 3,5-diphenylisothiazole-4-carboxylate **29** (100 mg, 0.258 mmol) in tetrachloromethane (3 ml) protected with $CaCl_2$ drying tube was added in one portion Br_2 (15.9 μl, 0.31 mmol, 1.2 equiv.) and the reaction was kept at 20 ^oC for 1 h. The reaction mixture was filtred and the filtrate was absorbed on silica. Chromatography (hexane-DCM 8 : 2) gave the *title compound* **30** (65.3 mg, 80%) as colourless needles, mp 114-115 ^oC (from pentane); (Found: C, 57.2; H, 3.2; N, 4.6. $C_{15}H_{10}BrNS$ requires C, 57.0; H, 3.2; N, 4.4%); λ_{max}(DCM)/nm 238 (log ε 4.03), 282 (3.96); ν_{max}/cm^{-1} 3054w (Ph CH), 1684w, 1653w, 1559w, 1539w, 1521w, 1506w, 1474s, 1444s, 1399w, 1343m, 1312w, 1208w, 1143w, 1075w, 1024m, 973w, 923w, 902s, 834m, 789w, 764s, 756s; δ_H(300 MHz; $CDCl_3$) 7.88-7.83 (2H, m, Ph C*H*), 7.69-7.66 (2H, m, Ph C*H*), 7.56-7.45 (6H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 167.0, 162.9, 134.7 (Ph *C*), 130.1 (Ph *C*), 129.8 (Ph *C*H), 129.3 (Ph *C*H), 129.0 (Ph *C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.2 (Ph *C*H), 106.0; δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.8 (Ph *C*H), 129.3 (Ph *C*H), 129.0 (Ph *C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.2 (Ph *C*H); *m*/*z* (EI) 317 (M^++2, 98%), 315 (M^+, 100), 236 (78), 203 (13), 189 (12), 134 (35), 133 (47), 118 (27), 109 (16), 89 (100), 77 (45), 63 (19), 51 (32).

3,5-Diphenylisothiazole 31

A stirred mixture of 3,5-diphenylisothiazole-4-carboxylic acid **28** (50 mg, 0.178 mmol), *p*-toluenesulfonic acid (3.4 mg, 10 mol%) and biphenyl (1 g) protected with $CaCl_2$ drying tube, was heated to *ca.* 250 ^oC until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC and absorbed on silica. Chromatography (hexane-DCM 8 : 2) gave the title compound **31** (39.7 mg, 94%)as colourless needles, mp 80-81 ^oC (lit.,[37] 81 ^oC) (from pentane); (Found: C, 75.9; H, 4.6; N, 5.8. $C_{15}H_{11}NS$ requires C, 75.9; H, 4.7; N, 5.9%); λ_{max}(DCM)/nm 256 (log ε 4.13), 280 (4.06); ν_{max}/cm^{-1} 3055w (Ph CH), 1530w, 1448m, 1453w, 1447w, 1391w, 1370w, 1337w, 1306w, 1206w, 1188w, 1157w, 1153w, 1087w, 1075w, 1027w, 1000w, 970w, 965w, 920w, 909w, 878m, 851w, 830m, 770w, 759m, 752s; δ_H(300 MHz; $CDCl_3$) 8.03-7.99 (2H, m, Ph C*H*), 7.76 (1H, s, isothiazole C*H*), 7.68-7.64 (2H, m, Ph C*H*), 7.53-7.39 (6H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 168.2, 168.2, 134.8, 130.9 (Ph C*H*), 129.5 (Ph C*H*), 129.2 (Ph C*H*), 128.8 (Ph C*H*), 126.8 (Ph C*H*), 126.5 (Ph C*H*), 117.5 (isothiazole *H*-4) one peak missing; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.9 (Ph C*H*), 129.5 (Ph C*H*), 129.2 (Ph C*H*), 128.8 (Ph C*H*), 126.8 (Ph C*H*), 126.5 (Ph C*H*), 117.5 (isothiazole *H*-4); *m*/*z* (EI) 238 (M^++1, 19%), 237 (M^+, 100), 204 (6), 159 (3), 134 (23), 121 (5), 118 (3), 108 (5), 103 (9), 89 (10), 77 (21), 76 (8), 69 (4), 63 (6), 51 (15).

Methyl 3,5-diphenylisothiazole-4-carbamate 32

To a stirred solution of 3,5-diphenylisothiazole-4-carboxamide **27** (0.2 g, 0.713 mmol) in methanol (3 ml) at *ca.* 20 ^oC, protected with $CaCl_2$ drying tube, was added sodium (65.6 mg, 2.85 mmol, 4 equiv.) and then Br_2 (43.9 μl, 0.856 mmol, 1.2 equiv.). The reaction mixture was heated to *ca.* 70 ^oC for 1 h. The mixture was

allowed to cool to *ca.* 20 °C and absorbed on silica. Chromatography (hexane-DCM 5 : 5) gave the *title compound* **32** (0.20 g, 95%) as colourless needles, mp 163-164 °C (from cyclohexane); (Found: C, 65.9; H, 4.7; N, 9.2. $C_{17}H_{14}N_2O_2S$ requires C, 65.8; H, 4.6; N, 9.0%); λ_{max}(DCM)/nm 243 (log ε 4.00), 276 inf (3.90); ν_{max}/cm^{-1} 3286w (NH), 1712s (C=O), 1582w, 1555w, 1522m, 1506m, 1484w, 1451w, 1424w, 1370w, 1251s, 1190w, 1181w, 1157w, 1097m, 1076w, 1037w, 1030w, 1017w, 1000w, 915w, 852w, 840w, 777w, 761s, 746s, 722w; δ_H(300 MHz; $CDCl_3$) 7.72-7.69 (2H, m, Ph C*H*), 7.51-7.42 (8H, m, Ph C*H*), 6.44 (1H, br s, N*H*), 3.62 (3H, br s, CH_3); δ_C[75 MHz; CD_2Cl_2 with Cr(acac)$_3$] 165.3, 162.0, 155.6, 135.2, 130.3, 130.0, 129.9 (Ph *C*H), 129.5 (Ph *C*H), 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.2 (Ph *C*H), 127.9 (Ph *C*H), 114.8, 1 peak missing; δ_C[75 MHz; DEPT 90, CD_2Cl_2 with Cr(acac)$_3$] 129.9 (Ph *C*H), 129.5 (Ph *C*H), 129.5 (Ph *C*H), 128.9 (Ph *C*H), 128.2 (Ph *C*H), 127.9 (Ph *C*H) 1 peak missing; *m*/*z* (EI) 311 (M^++1, 20%), 310 (M^+, 98), 279 (17), 278 (18), 265 (6), 251 (16), 233 (4), 218 (10), 173 (5), 162 (5), 148 (29), 130 (5), 121 (100), 120 (7), 104 (13), 89 (8), 77 (62), 59 (18), 51 (22). Further elution gave 3,5-diphenylisothiazole-4-carboxamide **27** (6 mg, 3%) as colourless needles, mp 210-211 °C (from PhH) identical to that described above.

4-Amino-3,5-diphenylisothiazole 33

A stirred solution of methyl 3,5-diphenylisothiazole-4-carbamate **32** (0.5 g, 1.61 mmol) in 48% aq. HBr (20 ml) was heated to *ca.* 100 °C until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 °C, diluted with water (10 ml) and extracted with DCM (4 × 10 ml). The organic extracts were combined, dried and absorbed on silica. Chromatography (hexane-DCM, 5 : 5) gave the *title compound* **33** (394 mg, 97%) as colourless needles, mp 113-114 °C (from

cyclohexane); (Found: C, 71.4; H, 4.9; N, 11.0. $C_{15}H_{12}N_2S$ requires C, 71.4; H, 4.8; N, 11.1%); λ_{max}(DCM)/nm 238 (log ε 3.11), 327 (4.01); ν_{max}/cm^{-1} 3430w and 3349 (NH), 3055w (Ph CH), 1734w, 1718w, 1700w, 1684w, 1653w, 1613m, 1559w, 1506w, 1487w, 1449m, 1417s, 1387w, 1340w, 1316w, 1291w, 1278w, 1232w, 1182w, 1116w, 1103w, 1079w, 1042w, 1029m, 1018m, 997w, 974w, 919w, 836m, 774w, 762w, 719w; δ_H(300 MHz; $CDCl_3$) 7.81 (2H, m, Ph C*H*), 7.59-7.37 (8H, m, Ph C*H*), 3.61 (2H, br s, N*H*); δ_C(75 MHz; $CDCl_3$) 159.4, 140.7, 136.2, 135.1, 131.3, 129.4 (Ph *C*H), 129.0 (Ph *C*H), 128.9 (Ph *C*H), 128.3 (Ph *C*H), 127.7 (Ph *C*H), 127.7 (Ph *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.4 (Ph *C*H), 129.0 (Ph *C*H), 128.9 (Ph *C*H), 128.3 (Ph *C*H), 127.7 (Ph *C*H), 127.7 (Ph *C*H); *m*/*z* (EI) 253 (M^++1, 19%), 252 (M^+, 100), 180 (2), 149 (22), 121 (68), 104 (51), 89 (8), 77 (31), 51 (10).

4-Iodo-3,5-diphenylisothiazole 34

To a stirred mixture of I_2 (151 mg, 0.594 mmol, 3 equiv.) and isoamyl nitrite (106 μl, 0.794 mmol, 4 equiv.) in $MeNO_2$ (2 ml) protected with $CaCl_2$ drying tube at *ca.* 110 ^oC was added dropwise an $MeNO_2$ (1 ml) solution of 4-amino-3,5-diphenylisothiazole **33** (50 mg, 0.198 mmol). The mixture was kept at *ca.* 110 ^oC until no starting material remained (TLC), allowed to cool to *ca.* 20 ^oC and absorbed on silica. Chromatography (hexane-DCM, 7 : 3) gave the *title compound* **34** (57.5 mg, 80%) as colourless plates, mp 138-139 ^oC (from cyclohexane); (Found: C, 49.7; H, 3.0; N, 3.8. $C_{15}H_{10}INS$ requires C, 49.6; H, 2.8; N, 3.9%); λ_{max}(DCM)/nm 234 (log ε 3.13), 282 (2.96); ν_{max}/cm^{-1} 3054w (Ph CH), 1468m, 1442m, 1396w, 1339w, 1331w, 1308w, 1203w, 1180w, 1140w, 1076w, 1032w, 1024w, 973w, 922w, 893s, 836w, 784w, 762s, 752m; δ_H(300 MHz; $CDCl_3$) 7.80-7.77 (2H, m, Ph C*H*), 7.62-7.60 (2H, m, Ph C*H*), 7.52-7.48 (4H, m, Ph C*H*); δ_C(75 MHz; $CDCl_3$) 170.0, 167.1, 135.8,

131.6, 129.8 (Ph *C*H), 129.4 (Ph *C*H), 129.3 (Ph *C*H), 129.1 (Ph *C*H), 128.9 (Ph *C*H), 128.1 (Ph *C*H), 78.8; δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.8 (Ph *C*H), 129.4 (Ph *C*H), 129.3 (Ph *C*H), 129.1 (Ph *C*H), 128.9 (Ph *C*H), 128.1 (Ph *C*H); *m*/*z* (EI) 364 (M^++1, 18%), 363 (M^+, 100), 236 (40), 203 (8), 189 (6), 165 (3), 163 (3), 133 (15), 118 (14), 109 (9), 89 (23), 77 (10), 63 (5), 51 (8).

3,4,5-Triphenylisothiazole 17 (typical Suzuki conditions for coupling at C-4: see Table 2)

A stirred mixture of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol), phenylboronic acid (57.8 mg, 0.474 mmol, 3 equiv.), powdered K_2CO_3 (32.8 mg, 0.237 mmol, 1.5 equiv.) and $Pd(OAc)_2$ (1.8 mg, 5 mol%) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 110 °C, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 °C, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 7 : 3) gave the title compound **17** (49.5 mg, 98%) as colourless crystals, mp 210-211 °C (from cyclohexane) identical to that described above.

3,5-Diphenyl-4-(3-nitrobenzene)isothiazole 35

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 3-nitrobenzeneboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **35** (56 mg, 99%) as colourless needles, mp 203-204 °C (from cyclohexane); (Found: C, 70.3; H, 3.8; N, 7.9. $C_{21}H_{14}N_2O_2S$ requires C, 70.4; H, 3.9;

N, 7.8%); λ_{max}(DCM)/nm 245 (log ε 3.19), 274 inf (3.09); ν_{max}/cm^{-1} 3076w and 3067w (Ar CH), 1537m, 1518s, 1491w, 1470w, 1443w, 1398w, 1350s, 1275w, 1267w, 1179w, 1163w, 1123w, 1070w, 1028w, 988w, 972w, 939w, 918w, 908w, 864w, 843w, 818w, 800w, 781m, 760m, 743s, 731s, 710m; δ_H(300 MHz; $CDCl_3$) 8.14 (1H, ddd, *J* 7.7, 2.0, 2.0, Ar C*H*), 7.93 (1H, app t, *J* 1.9, Ar C*H*), 7.46-7.26 (10H, m, Ar C*H*), 7.20-7.17 (2H, m, Ar C*H*); δ_C(75 MHz; $CDCl_3$) 167.3, 165.6, 148.2, 136.8 (Ph *C*H), 136.0, 134.9, 131.7, 130.1, 129.5 (Ph *C*H), 129.3 (Ph *C*H), 129.0 (Ph *C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.7 (Ph *C*H), 128.3 (Ph *C*H), 125.4 (Ph *C*H), 122.5 (Ph *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 136.8 (Ph *C*H), 129.5 (Ph *C*H), 129.3 (Ph *C*H), 129.0 (Ph *C*H), 128.9 (Ph *C*H), 128.8 (Ph *C*H), 128.7 (Ph *C*H), 128.3 (Ph *C*H), 125.4 (Ph *C*H), 122.5 (Ph *C*H); *m*/*z* (EI) 359 (M^++1, 25%), 358 (M^+, 100), 357 (31), 328 (4), 311 (36), 296 (3), 278 (3), 237 (3), 208 (5), 190 (2), 176 (3), 165 (8), 155 (12), 135 (5), 121 (3), 103 (3), 89 (9), 77 (8), 73 (7), 51 (4) (Found: M^+, 358.0779, $C_{21}H_{14}N_2O_2S$ requires *M*, 358.0776).

3,5-Diphenyl-4-(4-methoxybenzene)isothiazole 36

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 4-methoxybenzeneboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **36** (53 mg, 98%) as colourless needles, mp 174-175 ^oC (from cyclohexane); (Found: C, 77.0; H, 4.9; N, 4.1. $C_{22}H_{17}NOS$ requires C, 76.9; H, 5.0; N, 4.1%); λ_{max}(DCM)/nm 241 (log ε 3.45), 282 inf (3.08); ν_{max}/cm^{-1} 3063w (Ar CH) and 2930w, 1611w, 1574w, 1539w, 1508w, 1483w, 1470w, 1456w, 1441w, 1400w, 1364w, 1287m, 1273w, 1248s, 1173m, 1157w, 1103w, 1072w, 1030m, 982w, 966w, 907w, 851w, 822m, 777m, 760m, 733s, 719m; δ_H(300 MHz; $CDCl_3$) 7.41 (2H, app d, *J* 6.9, Ar C*H*), 7.32-7.21 (8H, m, Ar C*H*), 6.99 (2H, d, *J* 8.6, Ar C*H*), 7.80 (2H, d, *J*

8.50, Ar C*H*), 3.80 (3H, s, OCH_3; δ_C(75 MHz; $CDCl_3$) 167.7, 163.6, 158.9, 135.8, 133.8, 131.7 (Ph *C*H), 131.1, 128.9 (Ph *C*H), 128.7 (Ph *C*H), 128.4 (Ph *C*H), 128.0 (Ph *C*H), 126.1, 114.0 (Ph *C*H), 55.1, 1 peak missing; δ_C(75 MHz; DEPT 90, $CDCl_3$) 131.7 (Ph *C*H), 128.9 (Ph *C*H), 128.7 (Ph *C*H), 128.7, (Ph *C*H), 128.4 (Ph *C*H), 128.0 (Ph *C*H), 114.0 (Ph *C*H), 1 peak missing; *m*/*z* (EI) 344 (M^++1, 25%), 343 (M^+, 100), 328 (3), 312 (3), 256 (2), 225 (7), 208 (7), 193 (3), 165 (7), 152 (3), 81 (3), 77 (3), 69 (8), 60 (3), 57 (4), 55 (5), (Found: M^+, 343.1031, $C_{22}H_{17}NOS$ requires *M*, 343.1031).

3,5-Diphenyl-4-(3-methoxybenzene)isothiazole 37

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 3-methoxybenzeneboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **37** (53 mg, 98%) as colourless crystals, mp 132-133 ^oC (from cyclohexane); (Found: C, 76.8; H, 4.8; N, 4.0. $C_{22}H_{17}NOS$ requires C, 76.9; H, 5.0; N, 4.1%); λ_{max}(DCM)/nm 232 (log ε 4.06), 245 inf (3.98), 282 (3.82); ν_{max}/cm^{-1} 3054w (Ar CH), 2962w, 2943w, 2919w, 2840w, 1700w, 1684w, 1608w, 1576m, 1491w, 1478w, 1455w, 1442w, 1430w, 1395w, 1362w, 1316w, 1285m, 1224s, 1171w, 1109w, 1102w, 1090w, 1075w, 1051m, 1030w, 985w, 971w, 940w, 923w, 915w, 883w, 846m, 832w, 791m, 780m, 773m, 757s, 727s; δ_H(300 MHz; $CDCl_3$) 7.41 (2H, dd, *J* 7.5, 2.0, Ph C*H*), 7.35-7.22 (8H, m, Ph C*H*), 7.17 (1H, dd, *J* 8.0, 8.0, Ar C*H*), 6.83 (1H, dd, *J* 8.4, 2.6, Ar C*H*), 6.68 (1H, app d, *J* 7.5, Ar C*H*), 6.60 (1H, dd, *J* 2.0, 2.0, Ar C*H*), 3.60 (3H, s, OCH_3); δ_C(75 MHz; $CDCl_3$) 167.6, 164.1, 159.5, 135.6, 135.3, 134.0, 131.0, 129.6 (Ar *C*H), 128.8 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.4 (Ar *C*H), 128.0 (Ar *C*H), 123.1 (Ar *C*H), 115.8 (Ar *C*H), 113.5 (Ar *C*H), 55.1 (O*C*H_3), 1 peak missing; δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.6 (Ar *C*H), 128.8 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.4 (Ar *C*H), 128.0 (Ar *C*H), 123.1 (Ar *C*H),

115.8 (Ar *C*H), 113.5 (Ar *C*H), 1 peak missing; *m*/*z* (EI) 344 (M^++1, 26%), 343 (M^+, 100), 342 (35), 328 (3), 326 (3), 312 (8), 298 (3), 272 (2), 240 (3), 208 (3), 197 (3), 178 (2), 165 (6), 155 (7), 121 (3), 77 (4), 62 (2), 51 (2) (Found: M^+, 343.1045, $C_{22}H_{17}NOS$ requires *M*, 253.1031).

3,5-Diphenyl-4-(2-methoxybenzene)isothiazole 38

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 2-methoxybenzeneboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **38** (53.7 mg, 99%) as colourless crystals, mp 114-115 ^oC (from pentane); (Found: C, 77.0; H, 4.9; N, 4.0. $C_{22}H_{17}NOS$ requires C, 76.9; H, 5.0; N, 4.1%); λ_{max}(DCM)/nm 235 (log ε 3.19), 279 (3.00); ν_{max}/cm^{-1} 3059w and 3025w (Ar CH), 2835w, 1601w, 1580w, 1559w, 1539w, 1496w, 1479w, 1464w, 1443w, 1433w, 1400w, 1362w, 1265w, 1242m, 1188w, 1161w, 1132w, 1123w, 1105w, 1097w, 1073w, 1046w, 1028m, 973w, 936w, 916w, 906w, 856w, 843w, 809w, 778m, 755s, 746m, 742m, 721w; δ_H(300 MHz; $CDCl_3$) 7.43-7.39 (2H, m, Ar C*H*), 7.33-7.23 (9H, m, Ar C*H*), 7.00 (1H, ddd, *J* 7.5, 1.8, 1.8, Ar C*H*), 6.87 (1H, dd, *J* 8.4, 8.4, Ar C*H*), 6.84 (1H, dd, *J* 7.8, 7.8, Ar C*H*), 3.33 (3H, s, OCH_3); δ_C(75 MHz; $CDCl_3$) 168.1, 164.1, 157.3, 136.3, 132.0 (Ar *C*H), 131.5, 130.7, 129.5 (Ar *C*H), 128.6 (Ar *C*H), 128.5 (Ar *C*H), 128.2 (Ar *C*H), 128.2 (Ar *C*H), 127.9 (Ar *C*H), 127.8 (Ar *C*H), 123.3, 120.9 (Ar *C*H), 111.4 (Ar *C*H), 55.0 (O*C*H_3); δ_C(75 MHz; DEPT 90, $CDCl_3$) 132.0 (Ar *C*H), 129.5 (Ar *C*H), 128.6 (Ar *C*H), 128.5 (Ar *C*H), 128.2 (Ar *C*H), 128.2 (Ar *C*H), 127.9 (Ar *C*H), 127.8 (Ar *C*H), 120.9 (Ar *C*H), 111.4 (Ar *C*H); *m*/*z* (EI) 344 (M^++1, 23%), 343 (M^+, 100), 342 (24), 328 (5), 312 (20), 207 (7), 197 (5), 165 (9), 155 (8), 121 (4), 77 (6) (Found: M^+, 343.1031, $C_{22}H_{17}NOS$ requires *M*, 343.1031).

3,5-Diphenyl-4-(4-tolyl)isothiazole 39

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 4-tolylboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **39** (50.7 mg, 98%) as colourless needles, mp 203-205 ^oC (from cyclohexane); (Found: C, 80.8; H, 5.3; N, 4.2. $C_{22}H_{17}NS$ requires C, 80.7; H, 5.2; N, 4.3%); λ_{max}(DCM)/nm 231 (log ε 3.24), 284 (2.94); ν_{max}/cm^{-1} 3069w and 3028w (Ar CH), 2922w, 1537w, 1483m, 1443m, 1395m, 1360m, 1273w, 1180w, 1163w, 1109w, 1074w, 1028w, 918w, 907w, 851w, 843w, 818m, 802w, 783m, 775m, 758m, 729s, 716m; δ_H(300 MHz; $CDCl_3$) 7.43-7.40 (2H, m, Ar C*H*), 7.34-7.22 (8H, m, Ar C*H*), 7.08, (2H, d, *J* 7.9, Ar C*H*), 6.97 (2H, d, *J* 6.3, Ar C*H*), 2.35 (3H, s, C*H*$_3$); δ_C(75 MHz; $CDCl_3$) 167.7, 163.7, 137.2, 135.8, 134.2, 131.1, 130.9, 130.4 (Ar *C*H), 129.3 (Ar *C*H), 128.9 (Ar *C*H), 128.7 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.3 (Ar *C*H), 128.0 (Ar *C*H), 21.3 (C*H*$_3$); δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.4 (Ar *C*H), 129.3 (Ar *C*H), 128.9 (Ar *C*H), 128.7 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.3 (Ar *C*H), 128.0 (Ar *C*H); *m*/*z* (EI) 328 (M^++1, 25%), 327 (M^+, 100), 326 (49), 312 (22), 250 (7), 223 (4), 208 (3), 191 (6), 179 (37), 165 (11), 156 (8), 155 (8), 149 (5), 121 (3), 103 (3), 77 (6) (Found: M^+, 327.1072, $C_{22}H_{17}NS$ requires *M*, 327.1082).

3,5-Diphenyl-4-(3-tolyl)isothiazole 40

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 3-tolylboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **40** (51.2 mg, 99%) as colourless needles, mp 162-163 ^oC (from pentane); (Found: C, 80.8; H, 5.2; N, 4.3. $C_{22}H_{17}NS$ requires C, 80.7; H, 5.2; N, 4.3%); λ_{max}(DCM)/nm 237 (log ε 3.89), 283 (3.72); ν_{max}/cm^{-1} 3050w (Ar CH), 2955w, 2922w, 2850w, 1605w, 1586w, 1534w, 1490w, 1476w, 1447w, 1442m, 1394w, 1362m, 1291w, 1275w,

1182w, 1172w, 1154w, 1074w, 1030w, 1004w, 986w, 968w, 941w, 921w, 914w, 892w, 849m, 801m, 780m, 772m, 756s, 705s; δ_H(300 MHz; $CDCl_3$) 7.40 (2H, dd, *J* 7.8, 1.7, Ar C*H*), 7.31-7.21 (8H, m, Ar C*H*), 7.18-7.08 (2H, m, Ar C*H*), 6.89-6.87 (2H, m, Ar C*H*), 2.22 (3H, s, C*H*$_3$); δ_C(75 MHz; $CDCl_3$) 167.6, 163.9, 138.1, 135.7, 134.3, 134.0, 131.1 (Ar *C*H), 131.1, 128.8 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.6 (Ar *C*H), 128.4 (Ar *C*H), 128.4 (Ar *C*H), 128.3 (Ar *C*H), 128.0 (Ar *C*H), 127.7 (Ar *C*H), 21.3 (C*H*$_3$); δ_C(75 MHz; DEPT 90, $CDCl_3$) 131.1 (Ar *C*H), 128.8 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.6 (Ar *C*H), 128.4 (Ar *C*H), 128.4 (Ar *C*H), 128.3 (Ar *C*H), 128.0 (Ar *C*H), 127.7 (Ar *C*H); *m*/*z* (EI) 328 (M^++1, 27%), 327 (M^+, 100), 326 (56), 312 (17), 224 (4), 208 (4), 192 (5), 179 (4), 165 (7), 155 (8), 148 (4), 121 (3), 103 (2), 77 (5), 51 (3) (Found: M^+, 327.1073, $C_{22}H_{17}NS$ requires *M*, 327.1082).

3,5-Diphenyl-4-(2-tolyl)isothiazole 41

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 2-tolylboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **41** (25.4 mg, 49%) as colourless needles, mp 145-146 ^oC (from cyclohexane); (Found: C, 80.6; H, 5.2; N, 4.3. $C_{22}H_{17}NS$ requires C, 80.7; H, 5.2; N, 4.3%); λ_{max}(DCM)/nm 242 (log ε 3.31), 281 (3.12); ν_{max}/cm^{-1} 3058w and 3028w (Ar CH), 2919w, 1602w, 1576w, 1559w, 1533w, 1491w, 1476w, 1448m, 1443w, 1396m, 1379w, 1363m, 1269mw, 1205w, 1188w, 1178w, 1158w, 1095w, 1075w, 1072w, 1029m, 1003w, 983w, 969w, 950w, 921w, 909m, 846m, 788m, 779m, 765s, 750s, 733m, 723m; δ_H(300 MHz; $CDCl_3$) 7.43-7.40 (2H, m, Ar C*H*), 7.32-7.09 (12H, m, Ar C*H*), 1.87 (3H, s, C*H*$_3$); δ_C(75 MHz; $CDCl_3$) 167.4, 163.9, 137.2, 135.7, 133.9, 133.5, 131.2 (Ar *C*H), 131.1 (Ar *C*H), 130.5, 128.9 (Ar *C*H), 128.8 (Ar *C*H), 128.5 (Ar *C*H), 128.2 (Ar *C*H), 128.1 (Ar *C*H), 128.0 (Ar *C*H), 126.3 (Ar *C*H), 19.9 (C*H*$_3$) 1 peak missing;

δ_C(75 MHz; DEPT 90, $CDCl_3$) 131.2 (Ar *C*H), 131.1 (Ar *C*H), 128.9 (Ar *C*H), 128.8 (Ar *C*H), 128.5 (Ar *C*H), 128.2 (Ar *C*H), 128.1 (Ar *C*H), 128.0 (Ar *C*H), 126.3 (Ar *C*H), 1 peak missing; *m*/*z* (EI) 328 (M^++1, 31%), 327 (M^+, 100), 326 (51), 312 (32), 294 (2), 250 (18), 223 (8), 191 (15), 178 (3), 165 (8), 156 (8), 155 (9), 148 (6), 121 (3), 115 (3), 103 (3), 77 (6), 51(3) (Found: M^+, 327.1077, $C_{22}H_{17}NS$ requires *M*, 327.1082). Further elution (hexane-DCM, 7 : 3) gave 3,5-diphenylisothiazole **31** (19.1 mg, 51 %) as colourless needles, mp 80-81 °C (from pentane) identical to that described above.

3,5-Diphenyl-4-(4-chlorobenzene)isothiazole 42

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 4-chlorobenzeneboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **42** (48.9 mg, 89%) as colourless needles, mp 205-206 °C (from cyclohexane); (Found: C, 72.5; H, 3.9; N, 4.0. $C_{21}H_{14}ClNS$ requires C, 72.5; H, 4.1; N, 4.0%); λ_{max}(DCM)/nm 237 (log ε 3.25), 280 (2.98); ν_{max}/cm^{-1} 3067w (Ar CH), 2929w, 1598w, 1533w, 1494w, 1479w, 1442w, 1402w, 1394w, 1362w, 1290w, 1273w, 1180w, 1164w, 1113w, 1099w, 1090m, 1074w, 1029w, 1017m, 906w, 825s, 799w, 777m, 760m, 756m, 734m, 721s; δ_H(300 MHz; $CDCl_3$) 7.40-7.20 (12H, m, Ar C*H*), 7.02 (2H, ddd, *J* 9.6, 2.0, 1.9, Ar C*H*); δ_C(75 MHz; $CDCl_3$) 167.5, 164.4, 135.4, 133.6, 132.8, 132.5, 131.9 (Ar *C*H), 130.7, 129.0 (Ar *C*H), 128.9 (Ar *C*H), 128.9 (Ar *C*H), 128.8 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.2 (Ar *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 131.9 (Ar *C*H), 129.0 (Ar *C*H), 128.9 (Ar *C*H), 128.9 (Ar *C*H), 128.8 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.2 (Ar *C*H); *m*/*z* (EI) 349 (M^++2, 36%), 348 (M^++1, 40), 347 (M^+, 100), 327 (3), 312 (13), 244 (5), 212 (8), 208 (5), 199 (3), 176 (4), 165 (12), 156 (13), 155 (13), 135 (5), 121 (3), 103 (2), 77 (6), 51 (3)

(Found: M^+, 347.1531, $C_{21}H_{14}ClNS$ requires *M*, 347.0535). Further elution (hexane-DCM, 7 : 3) gave *4-(4'-chlorobiphenyl-4-yl)-3,5-diphenylisothiazole* **47** (7.4 mg, 11%) as colourless crystals, mp 224-225 ^oC (from cyclohexane); (Found: C, 72.4; H, 3.9; N, 4.0. $C_{27}H_{18}ClNS$ requires C, 76.5; H, 4.3; N, 3.3%); λ_{max}(DCM)/nm 269 (log ε 3.54); ν_{max}/cm^{-1} 3058w (Ar CH), 2926w, 2851w, 1488w, 1479w, 1448w, 1442w, 1395w, 1363w, 1272w, 1183w, 1093m, 1077w, 1030w, 1006w, 922w, 910w, 860w, 841w, 821s, 802w, 780m, 767m, 760m, 742w, 722m; δ_H(300 MHz; CD_2Cl_2) 7.57 (4H, ddd, *J* 8.7, 2.3, 2.3, Ar C*H*), 7.50 (2H, ddd, *J* 8.5, 1.8, 1.8, Ar C*H*), 7.41 (4H, ddd, *J* 8.7, 2.3, 2.3, Ar C*H*), 7.34-7.23 (8H, m, Ar C*H*), 7.16 (2H, ddd, *J* 8.5, 1.9, 1.9, Ar C*H*); δ_C(75 MHz; CD_2Cl_2) 167.9, 164.6, 139.1, 139.1, 136.2, 134.1, 134.0, 133.7, 131.5 (Ar C*H*), 131.4, 129.2 (Ar C*H*), 129.2 (Ar C*H*), 129.1 (Ar C*H*), 129.1 (Ar C*H*), 128.8 (Ar C*H*), 128.5 (Ar C*H*), 128.4 (Ar C*H*), 127.2 (Ar C*H*), 1 peak missing; δ_C(75 MHz; DEPT 90, CD_2Cl_2) 131.5 (Ar C*H*), 129.2 (Ar C*H*), 129.2 (Ar C*H*), 129.1 (Ar C*H*), 129.1 (Ar C*H*), 128.8 (Ar C*H*), 128.5 (Ar C*H*), 128.4 (Ar C*H*), 127.2 (Ar C*H*), 1 peak missing; *m*/*z* (EI) 426 (M^++3, 12%), 425 (M^++2, 36), 424 (M^++1, 41), 423 (M^+, 100), 422 (40), 347 (10), 329 (4), 312 (4), 298 (8), 290 (3), 288 (10), 275 (4), 252 (9), 249 (8), 239 (3), 193 (7), 120 (4), 77 (3) (Found: M^+, 423.0866, $C_{21}H_{14}ClNS$ requires *M*, 423.0848).

3,5-Diphenyl-4-(3-chlorobenzene)isothiazole 43

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 3-chlorobenzeneboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **43** (45.6 mg, 83%) as colourless cotton like needles, mp 175-176 ^oC (from cyclohexane); (Found: C, 72.4; H, 3.9; N, 4.0. $C_{21}H_{14}ClNS$ requires C, 72.5; H, 4.1; N, 4.0%); λ_{max}(DCM)/nm 234 (log ε 3.47), 280 (3.27); ν_{max}/cm^{-1} 3054w (Ar CH),

1597w, 1565w, 1489w, 1468w, 1442w, 1395w, 1361w, 1272w, 1188w, 1119w, 1088w, 1079w, 1072w, 1029w, 999w, 915w, 889w, 843w, 812w, 791m, 778s, 760m, 738s; δ_H(300 MHz; $CDCl_3$) 7.37-7.15 (12H, m, Ar C*H*), 7.06 (1H, dd, *J* 1.7, 1.7, Ar C*H*), 6.95 (1H, ddd, *J* 7.5, 1.3, 1.3, Ar C*H*); δ_C(75 MHz; $CDCl_3$) 167.4, 164.8, 136.0, 135.3, 134.3, 132.6, 130.5, 130.5 (Ar *C*H), 129.8 (Ar C*H*), 129.1 (Ar C*H*), 128.9 (Ar C*H*), 128.8 (Ar C*H*), 128.7 (Ar C*H*), 128.1 (Ar C*H*), 127.8 (Ar C*H*) 2 peak missing; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.5 (Ar *C*H), 129.8 (Ar C*H*), 129.1 (Ar C*H*), 128.9 (Ar C*H*), 128.8 (Ar C*H*), 128.7 (Ar C*H*), 128.1 (Ar C*H*), 127.8 (Ar C*H*) 2 peak missing; *m*/*z* (EI) 349 (M^++2, 39%), 348 (M^++1, 46), 347 (M^+, 100) 346 (64), 312 (18), 310 (11), 244 (3), 212 (5), 208 (7), 199 (4), 176 (4), 165 (12), 156 (13), 155 (14), 135 (4), 121 (3), 77 (7), 51 (4) (Found: M^+, 347.0535, $C_{21}H_{14}ClNS$ requires *M*, 347.0535). Further elution (hexane-DCM, 7 : 3) gave 4-(3'-chlorobiphenyl-3-yl)-3,5-diphenylisothiazole **48** (7.4 mg, 11%) as colourless crystals, mp 143-144 ^oC (from pentane); (Found: C, 72.5; H, 4.0; N, 4.0. $C_{21}H_{14}ClNS$ requires C, 72.5; H, 4.1; N, 4.0%); λ_{max}(DCM)/nm 233 (log ε 2.79), 325 (3.18); ν_{max}/cm^{-1} 3068w and 3025w (Ar CH), 1594w, 1565w, 1506w, 1485w, 1473w, 1441w, 1398w, 1388w, 1361w, 1293w, 1250w, 1182w, 1156w, 1100w, 1075w, 1047w, 1029w, 999w, 985w, 968w, 936w, 924w, 914w, 880w, 852w, 828w, 810w, 788m, 777s, 756m, 729s, 708m; δ_H(300 MHz; $CDCl_3$) 7.47-7.07 (14H, m, Ar C*H*); δ_C(75 MHz; $CDCl_3$) 167.7, 164.3, 142.4, 139.9, 135.7, 134.6, 134.5, 133.8, 131.0, 130.0 (Ar *C*H), 129.9 (Ar *C*H), 129.6 (Ar *C*H), 129.1 (Ar *C*H), 129.0 (Ar *C*H), 129.0 (Ar *C*H), 128.9 (Ar *C*H), 128.8, (Ar *C*H), 128.6 (Ar *C*H), 128.2 (Ar *C*H), 127.3 (Ar *C*H), 127.2 (Ar *C*H), 126.2 (Ar *C*H), 125.1 (Ar *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.0 (Ar *C*H), 129.9 (Ar *C*H), 129.6 (Ar *C*H), 129.1 (Ar *C*H), 129.0 (Ar *C*H), 129.0 (Ar *C*H), 128.9 (Ar *C*H), 128.8, (Ar *C*H), 128.6 (Ar *C*H), 128.2 (Ar *C*H), 127.3 (Ar *C*H), 127.2 (Ar *C*H), 126.2 (Ar *C*H), 125.1

(Ar *C*H); *m*/*z* (EI) 425 (M^++2, 42%), 424 (M^++1, 45), 423 (M^+, 100), 422 (39), 387 (3), 347 (5), 310 (5), 309 (3), 298 (7), 288 (9), 284 (4), 275 (4), 252 (10), 239 (4), 192 (6), 186 (7), 165 (3), 155 (3), 120 (5), 103 (3), 77 (9), 51 (4) (Found: M^+, 423.0864, $C_{27}H_{18}ClNS$ requires *M*, 423.0848).

3,5-Diphenyl-4-(2-chlorobenzene)isothiazole 44

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 2-chlorobenzeneboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **44** (44.5 mg, 81%) as colourless crystals, mp 176-177 ^oC (from cyclohexane); (Found: C, 72.5; H, 4.0; N, 4.0. $C_{21}H_{14}ClNS$ requires C, 72.5; H, 4.1; N, 4.0%); λ_{max}(DCM)/nm 233 (log ε 3.23), 281 (3.01); ν_{max}/cm^{-1} 3061 (Ar CH), 1597w, 1565w, 1489w, 1468w, 1442w, 1419w, 1410w, 1395w, 1361w, 1272w, 1188w, 1119w, 1089w, 1079w, 1073w, 1029w, 888w, 843w, 815w, 792w, 779s, 761m, 744m, 738s, 729m; δ_H(300 MHz; $CDCl_3$) 7.39-7.17 (12H, m, Ar C*H*), 7.08-7.07 (1H, m, Ar C*H*), 6.97 (1H, ddd, *J* 7.5, 1.4, 1.4, Ar C*H*); δ_C(75 MHz; $CDCl_3$) 167.4, 164.8, 136.0, 135.3, 134.3, 132.6, 130.6, 130.5 (Ar *C*H), 129.8 (Ar *C*H), 129.1 (Ar *C*H), 128.9 (Ar *C*H), 128.8 (Ar *C*H), 128.7, (Ar *C*H), 128.7 (Ar *C*H), 128.2 (Ar *C*H), 127.8 (Ar *C*H), 1 peak missing; δ_C(75 MHz; DEPT 90, $CDCl_3$) 130.5 (Ar *C*H), 129.8 (Ar *C*H), 129.1 (Ar *C*H), 128.9 (Ar *C*H), 128.8 (Ar *C*H), 128.7, (Ar *C*H), 128.7 (Ar *C*H), 128.2 (Ar *C*H), 127.8 (Ar *C*H), 1 peak missing; *m*/*z* (EI) 349 (M^++2, 38%), 348 (M^++1, 41), 347 (M^+, 100), 346 (58), 312 (21), 244 (4), 208 (8), 176 (14), 165 (6), 156 (18), 155 (18), 135 (5), 121 (4), 103 (4), 89 (6), 77 (16), 62 (24), 51 (8) (Found: M^+, 347.0544, $C_{21}H_{14}ClNS$ requires *M*, 347.0535). Further elution (hexane-

DCM, 7 : 3) gave 3,5-diphenylisothiazole **31** (7.1 mg, 19%) as colourless needles, mp 80-81 ^{o}C (from pentane) identical to that described above.

3,5-Diphenyl-4-(thien-3-yl)isothiazole 45

Similar treatment of 4-bromo-3,5-diphenylisothiazole **30** (50 mg, 0.158 mmol) with 3-thienylboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **45** (50.4 mg, 100%) as colourless needles, mp 186-187 ^{o}C (from cyclohexane); (Found: C, 71.3; H, 4.1; N, 4.3. $C_{19}H_{13}NS_2$ requires C, 71.4; H, 4.1; N, 4.4%); λ_{max}(DCM)/nm 245 (log ε 4.09), 284 (3.80); ν_{max}/cm^{-1} 3092w and 3057w (Ar CH), 1481w, 1441w, 1418w, 1350w, 1188w, 1072w, 1032w, 856m, 849m, 789s, 775m, 764m, 750s, 722s; δ_H(300 MHz; $CDCl_3$) 7.47-7.43 (2H, m, Ar C*H*), 7.37-7.26 (9H, m, Ar C*H*), 6.95 (1H, dd, *J* 3.0, 1.2, thienyl *H-2*) 6.78 (1H, dd, *J* 5.0, 1.2, thienyl *H-4*); δ_C(75 MHz; $CDCl_3$) 167.7, 164.1, 135.7, 133.6, 131.0, 129.1, 129.1 (Ar *C*H), 128.9 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.6 (Ar *C*H), 128.5 (Ar *C*H), 128.1 (Ar *C*H), 125.7 (Ar *C*H), 125.0 (Ar *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.1 (Ar *C*H), 128.9 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.6 (Ar *C*H), 128.5 (Ar *C*H), 128.1 (Ar *C*H), 125.7 (Ar *C*H), 125.0 (Ar *C*H); *m*/*z* (EI) 320 (M^++1, 25%), 319 (M^+, 100), 318 (63), 286 (10), 285 (4), 272 (4), 242 (3), 216 (3), 184 (16), 171 (15), 159 (3), 143 (5), 139 (5), 121 (3), 103 (2), 84 (3), 77 (7), 62 (3) (Found: M^+, 319.0488, $C_{19}H_{13}NS_2$ requires *M*, 319.0489).

3,5-Diphenyl-4-(thien-2-yl)isothiazole 46

Similar treatment of 4-iodo-3,5-diphenylisothiazole **34** (50 mg, 0.138 mmol) with 2-thienylboronic acid (3 equiv.), powdered K_2CO_3 and $Pd(OAc)_2$ gave the *title compound* **46** (43.6 mg, 99%) as colourless needles, mp 189-190 ^{o}C (from

cyclohexane); (Found: C, 71.4; H, 4.0; N, 4.3. $C_{19}H_{13}NS_2$ requires C, 71.4; H, 4.1; N, 4.4%); λ_{max}(DCM)/nm 245 (log ε 3.34), 285 (2.96); ν_{max}/cm^{-1} 3065w (Ar CH), 1601w, 1481w, 1447w, 1441w, 1434w, 1389w, 1360w, 1336w, 1309w, 1283w, 1262w, 1220w, 1186w, 1178w, 1155w, 1092w, 1076w, 1062w, 1033w, 970w, 922w, 916w, 906w, 882w, 848w, 831m, 775m, 752m, 745w, 726m, 720m, 707s; δ_H(300 MHz; $CDCl_3$) 7.51-7.47 (2H, m, Ar C*H*), 7.37-7.28 (9H, m, Ar C*H*), 6.97 (1H, dd, *J* 5.1, 3.6, thienyl *H-4*) 6.79 (1H, dd, *J* 3.6, 1.2, thienyl *H-5*); δ_C(75 MHz; $CDCl_3$) 167.9, 165.6, 135.4, 134.4, 130.7, 129.1 (Ar *C*H), 128.9 (Ar *C*H), 128.7 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.6 (Ar *C*H), 128.1 (Ar *C*H), 127.3 (Ar *C*H), 127.0 (Ar *C*H), 126.9; δ_C(75 MHz; DEPT 90, $CDCl_3$) 129.1 (Ar *C*H), 128.9 (Ar *C*H), 128.7 (Ar *C*H), 128.7 (Ar *C*H), 128.6 (Ar *C*H), 128.6 (Ar *C*H), 128.1 (Ar *C*H), 127.3 (Ar *C*H), 127.0 (Ar *C*H); *m*/*z* (EI) 320 (M^++1, 27%), 319 (M^+, 100), 318 (57), 286 (19), 274 (8), 242 (3), 216 (10) 184 (21), 171 (23), 159 (6), 158 (5), 143 (8), 139 (12), 121 (7), 89 (3), 77 (13), 69 (5), 51 (8).

3,4,5-Triphenylisothiazole 17 (typical Stille conditions for coupling at C-4: see Table 3)

A stirred mixture of 3,5-diphenyl-4-iodoisothiazole **34** (30 mg, 0.083 mmol), tributylphenylstannane (40.5 μl, 0.124 mmol, 1.5 equiv.) and $Pd(OAc)_2$ (0.9 mg, 5 mol%) in dry and degassed DMF (2 ml) under an argon atmosphere, was heated to *ca.* 100 ^oC, until no starting material remained (TLC). The mixture was allowed to cool to *ca.* 20 ^oC, diluted with DCM (15 ml) and washed with H_2O (4 × 10 ml). The organic layer was separated, dried and absorbed on silica. Chromatography (hexane–DCM, 6 : 4) gave the title compound **17** (25.5 mg, 98%) as colourless needles, mp 210-211 ^oC (from cyclohexane) identical to that described above.

3,5-Diphenyl-4-(thien-2-yl)isothiazole 46 *via* Stille coupling at C-4

Similar treatment of 4-iodo-3,5-diphenylisothiazole **34** (30 mg, 0.083 mmol) with tributyl(2-thienyl)stannane (1.5 equiv.) and $Pd(OAc)_2$ gave the *title compound* **46** (26.2 mg, 99%) as colourless needles, mp 189-190 ^oC (from cyclohexane) identical to that described above.

3,5-Diphenyl-4-(fur-2-yl)isothiazole 49

Similar treatment of 4-iodo-3,5-diphenylisothiazole **34** (30 mg, 0.083 mmol) with tributyl(2-furyl)stannane (1.5 equiv.) and $Pd(OAc)_2$ gave the *title compound* **49** (24.6 mg, 98%) as colourless needles, mp 114-115 ^oC (from cyclohexane); (Found: C, 75.2; H, 4.2; N, 4.6. $C_{19}H_{13}NOS$ requires C, 75.2; H, 4.3; N, 4.6%); λ_{max}(DCM)/nm 247 (log ε 3.18), 280 (2.86); ν_{max}/cm^{-1} 3125w and 3109w (Ar CH), 1598w, 1525w, 1502w, 1478w, 1447w, 1441w, 1389w, 1352w, 1271w, 1226w, 1181w, 1160w, 1072w, 1031w, 1022w, 1001w, 985w, 940w, 926w, 916w, 885w, 872w, 853w, 842w, 830w, 780m, 767m, 757m, 725s; δ_H(300 MHz; $CDCl_3$) 7.50-7.46 (2H, m, Ar C*H*), 7.44 (1H, dd, *J* 2.0, 0.6, furyl *H*-5), 7.42-7.30 (8H, m, Ar CH), 6.38 (1H, dd, *J* 3.3, 1.8, furyl *H*-4) 6.11 (1H, dd, *J* 3.3, 0.6, furyl *H*-3); δ_C(75 MHz; $CDCl_3$) 168.0, 167.0, 146.2, 142.5 (Ar *C*H), 135.5, 130.6, 129.3 (Ar *C*H), 128.8 (Ar *C*H), 128.8 (Ar *C*H), 128.3 (Ar *C*H), 128.2 (Ar *C*H), 128.2 (Ar *C*H), 124.1, 111.3 (Ar *C*H), 111.0 (Ar *C*H); δ_C(75 MHz; DEPT 90, $CDCl_3$) 142.5 (Ar *C*H), 129.3 (Ar *C*H), 128.8 (Ar *C*H), 128.8 (Ar *C*H), 128.3 (Ar *C*H), 128.2 (Ar *C*H), 128.2 (Ar *C*H), 111.3 (Ar *C*H), 111.0 (Ar *C*H); *m*/*z* (EI) 304 (M^++1, 23%), 303 (M^+, 100), 286 (4), 274 (32), 259 (3), 249 (12), 241 (5), 240 (4), 200 (6), 171 (15), 139 (11), 121 (9), 102 (3), 89 (3), 77 (12), 69 (4), 51 (7).