Supplementary data

General

All experiments were carried out under air, using glassware. All starting materials were obtained from commercial suppliers and used without further purification unless otherwise noted. Melting points were determined on a Büchi B-540 apparatus and are uncorrected. Elemental analyses were performed by the Spectropole of the Université Paul Cézanne, France. ^{1}H and ^{13}C NMR spectra were determined on a Bruker ARX 200 spectrometer. The ^{1}H chemical shifts were referenced to the solvent peak: $CDCl_3$ (7.26 ppm), and the ^{13}C chemical shifts were referenced to the solvent peak: $CDCl_3$ (77.0 ppm). Solvents were dried by conventional methods. The following adsorbent was used for column chromatography: silica gel 60 (Merck, particle size 0.063-0.200 mm, 70-230 mesh ASTM). TLC was performed on 5 cm × 10 cm aluminium plates coated with silica gel 60F-254 (Merck) in an appropriate solvent.

Microwave instrumentation

The multimode reactor used was an ETHOS Synth Lab station (Ethos start, Milestone Inc.). The multimode microwave has a twin magnetron (2 × 800 W, 2.45 GHz) with a maximum delivered power of 1000 W in 10 W increments (pulsed irradiation). The multimode microwave features a built-in magnetic stirrer (Teflon-coated stirring bar), direct temperature control of the reaction mixture with the aid of IR-sensor on the reactor wall and software that enables on line temperature control by regulation of microwave power output.

Experimental procedure

5-bromo-4-(chloromethyl)-2-methylthiazole 3

To a mixture of **2** (400 mg, 2.71 mmol) diluted in acetonitrile (5 mL) was added *N*-bromosuccinimide (1 eq, 2.71 mmol, 482 mg) at room temperature under continuous stirring for 1 hour (monitored by TLC). After evaporation of solvent and dissolution in water, the mixture was neutralized with a saturated sodium carbonate solution and extracted with EtOAc. Purification was conducted by flash chromatography on a silica gel column eluting with EtOAc/cyclohexane (5/5) and gave 225 mg (75%) of a brown oil. δ_H(200 MHz; $CDCl_3$) 2.68 (3 H, s, CH_3), 4.64 (2 H, s, CH_2); δ_C(50 MHz; $CDCl_3$) 19.7, 38.5, 107.3, 149.8, 166.9; *m/z* (EI) 227.9067 ($[M+H]^+$. $C_5H_5NSBrCl$ requires 227.9064).

5-bromo-2-methyl-4-(tosylmethyl)-thiazole 4

To a mixture of **3** (100 mg, 0.44 mmol) in water (20 mL), was added *p*-toluenesulfinic acid sodium salt (3 eq, 1.32 mmol, 236 mg). The reaction mixture was irradiated in a microwave oven (300 W; 100 °C; 10 min). A precipitate appeared and was filtered after cooling, washed with water (3 × 20 mL) and dried in vacuum drying oven. Recrystallization from propan-2-ol gave brown needles of thiazole **4** (140 mg, 92%), mp 165 °C. δ_H(200 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 2.62 (3 H, s, CH_3), 4.48 (2 H, s, CH_2), 7.29 (2 H, d, *J* 8.3, H ar), 7.65 (2 H, d, *J* 8.3, H ar); δ_C(50 MHz; $CDCl_3$) 19.7, 21.7, 56.6, 109.9, 128.7, 129.7, 135.6, 142.4, 144.9, 166.5; *m/z* (EI) 347.9542 ($[M+H]^+$. $C_{12}H_{12}NO_2S_2Br$ requires 347.9544).

General procedure for the synthesis of compounds 5 - 20

In a 100 mL round-bottom flask were placed 5-bromo-2-methyl-4-(tosylmethyl)thiazole **4** (300 mg, 0.87 mmol), arylboronic or styrylboronic acid (3.5 eq, 3.05 mmol), palladium catalyst (0.05 eq, 4.35 µmol), tetrabutylammonium bromide (1 eq, 0.87 mmol), sodium carbonate (5 eq, 4.35 mmol) and water (20 mL). The vessel was then placed into the Ethos start cavity and carried out under microwave irradiation at 100 °C for appropriate time and power. The reaction mixture was stirred continuously during the reaction. The disappearance of starting materials was monitored by TLC. After being cooled down, the mixture was then extracted with EtOAc (8 × 15 mL). The organic layers were dried over anhydrous sodium sulfate and removed under vacuum. Purification by chromatographic column, eluting with EtOAc/cyclohexane (5/5), and recrystallization from propan-2-ol gave the corresponding required product.

Experimental data

2-methyl-5-phenyl-4-(tosylmethyl)thiazole **5** (290 mg, 97%)
Yellow needles; mp 166 °C (from propan-2-ol); (Found: C, 62.9; H, 5.0; N, 4.05. $C_{18}H_{17}NO_2S_2$ requires C, 62.9; H, 5.0; N, 4.1%). δ_H(200 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 2.67 (3 H, s, CH_3), 4.51 (2 H, s, CH_2), 7.22-7.36 (7 H, m, H ar), 7.62 (2 H, d, *J* 8.2, H ar); δ_C(50 MHz, $CDCl_3$) 18.7, 21.7, 56.0, 128.6, 128.9, 129.1, 129.5, 129.6, 136.0, 136.6, 139.4, 144.8, 165.3.

5-(4-chlorophenyl)-2-methyl-4-(tosylmethyl)thiazole **6** (310 mg, 95%)
Grey needles; mp 176 °C (from propan-2-ol); (Found: C, 57.2; H, 4.3; N, 3.7. $C_{18}H_{16}ClNO_2S_2$ requires C, 57.2; H, 4.3; N, 3.7%). δ_H(200 MHz; $CDCl_3$) 2.44 (3 H, s, CH_3), 2.71 (3 H, s, CH_3), 4.49 (2 H, s, CH_2), 7.30-7.37 (6 H, m, H ar), 7.68 (2 H, d, *J* 8.2, H ar); δ_C(50 MHz, $CDCl_3$) 19.0, 21.7, 56.3, 128.4, 128.6, 129.1, 129.7, 130.8, 135.2, 136.0, 137.6, 137.9, 144.9, 165.2.

5-(4-fluorophenyl)-2-methyl-4-(tosylmethyl)thiazole **7** (280 mg, 89%)
Grey needles; mp 150 °C (from propan-2-ol); (Found: C, 59.85; H, 4.55; N, 3.9. $C_{18}H_{16}FNO_2S_2$ requires C, 59.8; H, 4.5; N, 3.9%). δ_H(200 MHz; $CDCl_3$) 2.44 (3 H, s, CH_3), 2.64 (3 H, s, CH_3), 4.44 (2 H, s, CH_2), 7.02-7.41 (6 H, m, H ar), 7.63 (2 H, d, *J* 8.3, H ar); δ_C(50 MHz, $CDCl_3$) 19.1, 21.7, 56.5, 115.9 (d, *J* 21.7), 126.1 (d, *J* 3.2), 128.6, 129.6, 131.4 (d, *J* 8.3), 136.2, 137.9, 138.0, 144.8, 163.0 (d, *J* 249.6), 164.6.

Crystal data for compound **7**

$C_{18}H_{16}FNO_2S_2$, colorless prism (0.2 × 0.16 × 0.12 mm^3), MW = 361.44, triclinic, space group *P*1 (T = 293 K), *a* = 8.1330 (2) Å, *b* = 10.9315 (3) Å, *c* = 11.3491 (4) Å, α = 111.001 (1)°, β = 103.328 (2)°, γ = 103.603 (3)°; *V* = 858.68 (4) $Å^3$, *Z* = 2, μ = 0.33 mm^{-1}, *F*(000) = 376, index ranges $0 \le h \le 10$, $-14 \le k \le 14$, $-15 \le l \le 14$; θ range = 2.05-28.16°, 219 variables and 0 restraints, were defined for 3045 independant reflections with $I \ge 2\sigma(I)$ to *R1* = 0.0772, *wR2* = 0.2084, *GooF* = 1.098. CCDC 727244 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.cdcc.cam.ac.uk/data_request/cif of from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: + 44 (1223) 336033; email: deposit@ccdc.cam.ac.uk.

2-methyl-4-(tosylmethyl)-5-[4-(trifluoromethyl)phenyl] thiazole **8** (340 mg, 96%)
White solid; mp 145 °C (from propan-2-ol); (Found: C, 55.3; H, 3.9; N, 3.35. $C_{19}H_{16}F_3NO_2S_2$ requires C, 55.5; H, 3.9; N, 3.4%). δ_H(200 MHz; $CDCl_3$) 2.44 (3 H, s, CH_3), 2.68 (3 H, s, CH_3), 4.49 (2 H, s, CH_2), 7.23-7.27 (3 H, m, H ar), 7.51-7.66 (5 H, m, H ar); δ_C(50 MHz, $CDCl_3$) 19.1, 21.6, 56.4, 123.8 (q, *J* 272.6), 125.8 (q, *J* 3.7), 128.5, 129.6, 129.8, 130.8 (q, *J* 32.6), 133.9, 136.0, 137.3, 138.5, 144.9, 165.5.

2-methyl-4-(tosylmethyl)-5-[3-(trifluoromethyl)phenyl] thiazole **9** (290 mg, 81%)
White solid; mp 197 °C (from propan-2-ol); (Found: C, 55.4; H, 4.1; N, 3.4. $C_{19}H_{16}F_3NO_2S_2$ requires C, 55.5; H, 3.9; N, 3.4%). δ_H(200 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 2.69 (3 H, s, CH_3), 4.46 (2 H, s, CH_2), 7.24-7.28 (3 H, m, H ar), 7.48-7.64 (5 H, m, H ar); δ_C(50 MHz, $CDCl_3$) 19.2, 21.6, 56.4, 123.7 (q, *J* 272.8), 125.5 (q, *J* 3.7), 126.1 (q, *J* 3.7), 128.5, 129.5, 129.7, 131.2, 131.3 (q, *J* 32.1), 132.8, 136.0, 137.3, 138.6, 144.9, 165.4.

5-[3,5-bis(trifluoromethyl)phenyl]-2-methyl-4-(tosylmethyl) thiazole **10** (380 mg, 91%)
White solid; mp 142 °C (from propan-2-ol); (Found: C, 50.1; H, 3.1; N, 2.8. $C_{20}H_{15}F_6NO_2S_2$ requires C, 50.1; H, 3.15; N, 2.9%). δ_H(200 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 2.79 (3 H, s, CH_3), 4.46 (2 H, s, CH_2), 7.31 (2 H, d, *J* 8.1, H ar); 7.71 (2 H, d, *J* 8.1, H ar); 7.91-7.98 (3 H, m, H ar); δ_C(50 MHz; $CDCl_3$) 19.3, 21.6, 56.5, 122.5 (septuplet, *J* 23.7), 122.9 (q, *J* 272.9), 128.4, 129.6 (q, *J* 2.6), 129.9, 132.4 (q, *J* 33.7), 132.7, 135.7, 136.0, 139.4, 145.3, 166.4.

5-(4-methoxyphenyl)-2-methyl-4-(tosylmethyl)thiazole **11** (300 mg, 92%)
Yellow needles; mp 146 °C (from propan-2-ol); (Found: C, 60.9; H, 5.2; N, 3.7. $C_{19}H_{19}NO_3S_2$ requires C, 61.1; H, 5.1; N, 3.75%). δ_H(200 MHz; $CDCl_3$) 2.44 (3 H, s, CH_3), 2.68 (3 H, s, CH_3), 3.85 (3 H, s, CH_3); 4.50 (2 H, s, CH_2), 6.91 (2 H, d, *J* 8.6, H ar); 7.25-7.36 (4 H, m, H ar), 7.67 (2 H, d, *J* 8.6, H ar); δ_C(50 MHz, $CDCl_3$) 18.6, 21.7, 55.4, 55.9, 114.4, 121.5, 128.6, 129.7, 130.8, 135.8, 136.1, 139.5, 144.8, 160.4, 164.9.

2-methyl-4-(tosylmethyl)-5-(3,4,5-trimethoxyphenyl)thiazole **12** (370 mg, 98%)
Yellow needles; mp 165 °C (from propan-2-ol); (Found: C, 58.4; H, 5.4; N, 3.2. $C_{21}H_{23}NO_5S_2$ requires C, 58.2; H, 5.35; N, 3.2%). δ_H(200 MHz; $CDCl_3$) 2.45 (3 H, s, CH_3), 2.66 (3 H, s, CH_3), 3.90 (3 H, s, CH_3), 3.91 (6 H, s, 2 × CH_3), 4.52 (2 H, s, CH_2), 6.85 (2 H, s, H ar), 7.32 (2 H, d, *J* 8.2, H ar), 7.74 (2 H, d, *J* 8.2, H ar); δ_C(50 MHz, $CDCl_3$) 18.6, 21.7, 56.2, 56.4, 60.9, 107.0, 124.6, 128.6, 129.7, 136.0, 136.3, 138.9, 139.9, 145.0, 153.5, 165.1.

2-methyl-5-*p*-tolyl-4-(tosylmethyl)thiazole **13** (260 mg, 84%)
White solid; mp 160 °C (from propan-2-ol); (Found: C, 63.9; H, 5.3; N, 3.8. $C_{19}H_{19}NO_2S_2$ requires C, 63.8; H, 5.4; N, 3.9%). δ_H(200 MHz; $CDCl_3$) 2.39 (3 H, s, CH_3), 2.43 (3 H, s, CH_3), 2.72 (3 H, s, CH_3), 4.54 (2 H, s, CH_2), 7.17-7.31 (6 H, m, H ar), 7.69 (2 H, d, *J* 8.3, H ar); δ_C(50 MHz, $CDCl_3$) 18.6, 21.3, 21.6, 55.9, 126.5, 128.6, 129.3, 129.6, 136.0, 136.1, 139.3, 139.6, 144.8, 165.1.

2-methyl-5-*o*-tolyl-4-(tosylmethyl)thiazole **14** (230 mg, 74%)
White needles; mp 156 °C (from propan-2-ol); (Found: C, 63.9; H, 5.4; N, 3.9. $C_{19}H_{19}NO_2S_2$ requires C, 63.8; H, 5.4; N, 3.9%). δ_H(200 MHz; $CDCl_3$) 2.12 (3 H, s, CH_3), 2.44 (3 H, s, CH_3), 2.71 (3 H, s, CH_3), 4.33 (2 H, s, CH_2), 6.99-7.35 (6 H, m, H ar), 7.60 (2 H, d, *J* 8.3, H ar); δ_C(50 MHz, $CDCl_3$) 19.0, 20.3, 21.7, 56.0, 125.9, 128.6, 128.8, 129.5, 129.6, 130.4, 131.3, 136.3, 137.6, 137.9, 138.8, 144.7, 165.6.

2-methyl-5-(3-nitrophenyl)-4-(tosylmethyl)thiazole **15** (250 mg, 74%)
Yellow needles; mp 182 °C (from propan-2-ol); (Found: C, 55.7; H, 4.2; N, 7.1. $C_{18}H_{16}N_2O_4S_2$ requires C, 55.65; H, 4.15; N, 7.2%). δ_H(200 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 2.70 (3 H, s, CH_3), 4.48 (2 H, s, CH_2), 7.26-8.25 (8 H, m, H ar); δ_C(50 MHz, $CDCl_3$) 19.1, 21.6, 56.2, 123.5, 124.2, 128.5, 129.7, 130.0, 131.9, 135.2, 135.8, 136.2, 138.9, 145.1, 148.3, 165.9.

2-methyl-5-(naphthalen-1-yl)-4-(tosylmethyl)thiazole **16** (250 mg, 73%)
Yellow solid; mp 153 °C (from propan-2-ol); (Found: C, 67.3; H, 4.9; N, 3.5. $C_{22}H_{19}NO_2S_2$ requires C, 67.15; H, 4.9; N, 3.6%). δ_H(200 MHz; $CDCl_3$) 2.39 (3 H, s, CH_3), 2.80 (3 H, s, CH_3), 4.36 (2 H, s, CH_2), 7.14-7.91 (11 H, m, H ar); δ_C(50 MHz, $CDCl_3$) 19.2, 21.6, 56.4, 124.9, 125.0, 126.2, 126.6, 126.9, 128.3, 128.4, 129.4, 129.6, 132.0, 133.4, 135.9, 136.0, 140.2, 144.4, 165.9.

2-methyl-5-(naphthalen-2-yl)-4-(tosylmethyl)thiazole **17** (300 mg, 88%)
Yellow solid; mp 133 °C (from propan-2-ol); (Found: C, 67.2; H, 5.0; N, 3.5. $C_{22}H_{19}NO_2S_2$ requires C, 67.15; H, 4.9; N, 3.6%). δ_H(200 MHz; $CDCl_3$) 2.37 (3 H, s, CH_3), 2.71 (3 H, s, CH_3), 4.58 (2 H, s, CH_2), 7.17 (2 H, d, *J* 8.2, H ar), 7.36-7.88 (9 H, m, H ar); δ_C(50 MHz, $CDCl_3$) 19.1, 21.6, 56.5, 126.7, 126.8, 126.9, 127.3, 127.7, 128.2, 128.5, 128.6, 128.8, 129.5, 133.0, 133.1, 136.1, 137.7, 139.2, 144.7, 165.0.

5-(biphenyl-4-yl)-2-methyl-4-(tosylmethyl)thiazole **18** (350 mg, 96%)

Yellow solid; mp 195 °C (from propan-2-ol); *m/z* (EI) 420.1082 ($[M+H]^+$. $C_{24}H_{21}NO_2S_2$ requires 420.1086). δ_H(200 MHz; $CDCl_3$) 2.43 (3 H, s, CH_3), 2.67 (3 H, s, CH_3), 4.55 (2 H, s, CH_2), 7.23-7.66 (13 H, m, H ar); δ_C(50 MHz, $CDCl_3$) 19.1, 21.7, 56.6, 127.1, 127.5, 127.8, 128.6, 129.0, 129.1, 129.6, 129.8, 136.2, 137.7, 138.9, 140.1, 141.6, 144.7, 164.6.

(*E*)-2-methyl-5-styryl-4-(tosylmethyl)thiazole **19** (280 mg, 87%)

White needles; mp 170 °C (from propan-2-ol); (Found: C, 65.1; H, 5.3; N, 3.8. $C_{20}H_{19}NO_2S_2$ requires C, 65.0; H, 5.2; N, 3.8%). δ_H(200 MHz; $CDCl_3$) 2.24 (3 H, s, CH_3), 2.62 (3 H, s, CH_3), 4.60 (2 H, s, CH_2), 6.65 (H, d, *J* 15.9, *CH*=CH), 6.77 (H, d, *J* 15.9, CH=*CH*), 7.16-7.43 (7 H, m, H ar), 7.64 (2 H, d, *J* 8.3, H ar); δ_C(50 MHz, $CDCl_3$) 19.3, 21.4, 57.0, 116.7, 126.6, 128.4, 128.6, 128.7, 129.7, 132.8, 135.2, 136.0, 137.5, 139.3, 145.1, 163.4.

(*E*)-2-methyl-5-(4-methylstyryl)-4-(tosylmethyl)thiazole **20** (310 mg, 93%)

Yellow needles; mp 208 m°C (from propan-2-ol); *m/z* (EI) 384.1088 ($[M+H]^+$. $C_{21}H_{21}NO_2S_2$ requires 384.1086). δ_H(200 MHz; $CDCl_3$) 2.24 (3 H, s, CH_3), 2.36 (3 H, s, CH_3), 2.59 (3 H, s, CH_3), 4.57 (2 H, s, CH_2), 6.60 (H, d, *J* 15.9, *CH*=CH), 6.70 (H, d, *J* 15.9, CH=*CH*), 7.07-7.31 (6 H, m, H ar), 7.62 (2 H, d, *J* 8.3, H ar); δ_C (50 MHz; $CDCl_3$) 19.3, 21.3, 21.5, 57.0, 115.7, 126.6, 128.7, 129.4, 129.7, 133.0, 133.3, 135.3, 137.9, 138.5, 138.8, 145.1, 163.2.