Cobalt-catalyzed C-SMe bond activation of heteroaromatic thioethers

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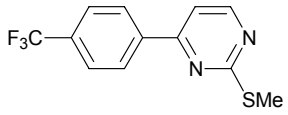
General Procedure 1: for the synthesis of 2-methylthio-4-arylpyrimidines 1a-e

Procedure 1 : from arylbromides: *Zinc insertion and cross-coupling*. To a solution of $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg) and Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL) were successively added at room temperature allylchloride (2.25 mmol, 190 µL) and trifluoroacetic acid (100 µL), causing an immediate rise in temperature and color change to dark grey. After stirring the resulting mixture for 3 minutes, aryl bromide (7.5 mmol) and 2-methylthio-4-chloropyrimidine (10 mmol, 1.16 mL) were added. The medium was then stirred at 50 °C until aryl bromide was consumed. *Work-up and purification*. The reaction mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with dichloromethane. The organic layer was washed with a saturated aqueous solution of NaCl and dried over $MgSO_4$. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether or petroleum ether/diethyl ether) afforded the coupling product characterized by NMR (^1H, ^{13}C) and mass spectrometry.

- 2-Methylsulfanyl-4-(4-trifluoromethyl-phenyl)-pyrimidine **1a**



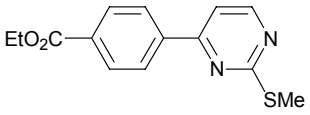
$C_{12}H_9F_3N_2S$
CAS: 637352-77-3
Exact mass: 270.0439
Molecular weight: 270.27
White solid

According to general procedure 1: from 4-bromobenzotrifluoride : ***Zinc insertion and cross-coupling:*** $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min; 4-bromobenzotrifluoride (7.5 mmol, 1.05 mL), 2-methylthio-4-chloropyrimidine (10 mmol, 1.16 mL), T= 50 °C, 4 h; ***work-up and purification*:** extracted with

dichloromethane (3 x 70 mL), purified by alumina (pentane : ether = 90:10) to give **1a** as a white solid (1.4 g, 70 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ/ppm: 2.68 (s, 3H) ; 7.42 (d, 5.2Hz, 1H) ; 7.78 (d, 8.2Hz, 2H) ; 8.23 (d, 8.2Hz, 2H) ; 8.63 (d, 5.2Hz, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ/ppm: 14.3 (CH_3), 112.1 (CH), 123.9 (q, $^{1}J_{C-F}$ = 271 Hz, C), 125.9 (q, $^{3}J_{C-F}$ = 3.8 Hz, 2CH), 127.5 (2 CH), 132.7 (q, $^{2}J_{C-F}$ = 32.4 Hz, C), 139.7 (q, $^{5}J_{C-F}$ = 1.4 Hz, C), 158.1 (CH), 162.3 (C), 173.3 (C).
HRMS ($C_{12}H_9F_3N_2S$): calc: 270.0439, found: 270.0435

- 4-(2-Methylsulfanyl-pyrimidin-4-yl)-benzoic acid ethyl ester **1b**

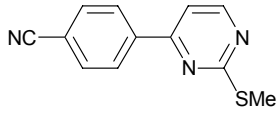


$C_{14}H_{14}N_2O_2S$
CAS: 259541-93-0
Exact mass: 274.0776
Molecular weight: 274.34
White Solid

According to general procedure 1: from ethyl 4-bromobenzoate: ***Zinc insertion and cross-coupling:*** $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min; ethyl 4-bromobenzoate (7.5 mmol, 1.22 mL), 2-methylthio-4-chloropyrimidine (10 mmol, 1.16 mL), T= 50 °C, 3 h 30; ***work-up and purification*****:** extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 70 : 30) to give **1b** as a white solid (1.54 g, 75%).

^{1}H-NMR (300MHz, $CDCl_3$) δ/ppm: 1.45 (t, 7.10Hz, 3H), 2.69 (s, 3H), 4.44 (q, 7.10Hz, 2H), 7.45 (d, 5.2 Hz, 1H), 8.19 (m, 4H), 8.63 (d, 5.1 Hz, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ/ppm: 12.3 (CH_3), 14.3 (CH_3), 59.3 (CH_2), 110.2 (CH), 125.2 (2CH), 128.1 (2CH), 130.8 (C), 138.1 (C), 155.4 (CH), 161.2 (C), 164.0 (C), 170.9 (C).
HRMS ($C_{14}H_{14}N_2O_2S$): calc: 274.0776, found: 274.0780

- 4-(2-Methylsulfanyl-pyrimidin-4-yl)-benzonitrile **1c**

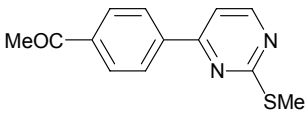


$C_{12}H_9N_3S$
CAS: 874778-91-3
Exact mass: 227.0517
Molecular weight: 227.29
White Solid

According to general procedure 1: from 4-bromobenzonitrile: ***Zinc insertion and cross-coupling:*** $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min; 4-bromobenzonitrile (7.5 mmol, 1.4 g), 2-methylthio-4-chloropyrimidine (7.5 mmol, 0.87 mL), T= 50 °C, 2 h; ***work-up and purification*****:** extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 30:70) to give **1c** as a white solid (1.2 g, 70 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ/ppm: 2.68 (s, 3H), 7.43 (d, 3.5Hz, 1H), 7.82 (d, 7.8Hz, 2H), 8.23 (d, 7.9Hz 2H), 8.67 (d, 2.8Hz, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ/ppm: 14.3 (CH_3), 112.2 (CH), 114.6 (C), 118.3 (C), 127.8 (2CH), 132.7 (2CH), 140.5 (C), 158.1 (CH), 161.9 (C), 173.5 (C).
HRMS ($C_{12}H_9N_3S$): calc: 227.0517, found: 227.0520

- 1-[4-(2-Methylsulfanyl-pyrimidin-4-yl)-phenyl]-ethanone **1d**



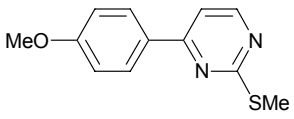
$C_{13}H_{12}N_2OS$
Exact mass: 244.0670
Molecular weight: 244.31
White solid, mp: 142°C

According to general procedure 1: from 4-bromoacetophenone: ***Zinc insertion and cross-coupling:*** $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min; 4-bromoacetophenone (7.5 mmol, 1.5 g), 2-methylthio-4-chloropyrimidine (7.5 mmol,

0.87 mL), T= 50 °C, 2 h; ***work-up and purification*****:** extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 40:60) to give **1d** as a white solid (732 mg, 40 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ/ppm: 2.68 (s, 6H), 7.44 (d, 5.2Hz, 1H), 8.10 (d, 8.2Hz, 2H), 8.21 (d, 8.2Hz, 2H), 8.63 (d, 5.2Hz, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ/ppm: 14.3 (CH_3), 26.8 (CH_3), 112.3 (CH), 127.4 (2CH), 128.8 (2CH), 138.8 (C), 140.5 (C), 158.0 (CH), 162.6 (C), 173.2 (C), 197.6 (C).
HRMS ($C_{13}H_{12}N_2OS$): calc: 244.0670, found: 244.0669
IR(neat,cm^{-1}): 2974, 1674 (C=O), 1555, 1418, 1396,1348, 1268, 1085

- 4-(4-Methoxy-phenyl)-2-methylsulfanyl-pyrimidine **1e**



$C_{12}H_{12}N_2OS$
CAS: 148990-17-4
Exact mass: 232.0670
Molecular weight: 232.30
White solid

According to general procedure 1: from 4-bromoanisole: ***Zinc insertion and cross-coupling:*** $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min; 4-bromoanisole (7.5 mmol, 0.94 mL), 2-methylthio-4-chloropyrimidine (7.5 mmol, 0.87 mL), T= 50 °C, 8 h; ***work-up and purification*****:** extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 40:60) to give **1e** as a white solid (470 mg, 27 %).

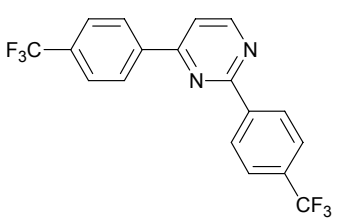
^{1}H-NMR (300MHz, $CDCl_3$) δ/ppm: 2.57 (s, 3H), 3.81 (s, 3H), 6.93 (d, 8.7Hz, 2H), 7.22 (d, 5.3Hz, 1H), 8.01 (d, 8.7Hz, 2H), 8.41 (d, 5.3Hz, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ/ppm: 15.3 (CH_3), 56.6 (CH_3), 112.1 (CH), 115.4 (2CH), 117.5 (C), 129.9 (2CH),158.5 (CH), 163.3 (C), 164.5 (C), 173.6 (C).
HRMS ($C_{12}H_{12}N_2OS$): calc: 232.0670, found: 232.0671

General Procedures 2.1 and 2.2 for the synthesis of 2,4-diaryl-pyrimidines 2a-c and 3a-e

Procedure 2.1. from arylbromides and 2-methylthio-4-chloropyrimidine: *Zinc insertion and cross-coupling*. To a solution of $CoBr_2$ (30 mol%, 2.25 mmol, 495 mg) and Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL) were successively added at room temperature allylchloride (6.8 mmol, 560 µL) and trifluoroacetic acid (100 µL), causing an immediate rise in temperature and color change to dark grey. After stirring the resulting mixture for 3 minutes, aryl bromide (7.5 mmol) and 2-methylthio-4-chloropyrimidine (3.7 mmol, 0.44 mL) were added. The medium was then stirred at 50 °C until aryl bromide was consumed. The amount of the corresponding coupling product was measured by GC (addition of iodine) using an internal reference (dodecane, 200 µL). *Work-up and purification*. The reaction mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with dichloromethane. The organic layer was washed with a saturated aqueous solution of NaCl and dried over $MgSO_4$. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether or petroleum ether/diethyl ether) afforded the coupling product characterized by NMR (^1H, ^{13}C) and mass spectrometry.

Procedure 2.2. from arylbromides and 2-methylthio-4-arylpyrimidines **1**: *Zinc insertion and cross-coupling*. To a solution of $CoBr_2$ (30 mol%, 1 mmol, 220 mg) and Zinc powder (7.5 mmol, 0.47 g) in acetonitrile (6 mL) were successively added at room temperature allylchloride (3 mmol, 250 µL) and trifluoroacetic acid (100 µL), causing an immediate rise in temperature and color change to dark grey. After stirring the resulting mixture for 3 minutes, aryl bromide (3 mmol) and 2-methylthio-4-arylpyrimidine (3 mmol) were added. The medium was then stirred at 50 °C until aryl bromide was consumed. *Work-up and purification*. The reaction mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with dichloromethane. The organic layer was washed with a saturated aqueous solution of NaCl and dried over $MgSO_4$. Evaporation of solvent and purification by column chromatography on silica gel (pentane/diethyl ether or petroleum ether/diethyl ether) afforded the coupling product characterized by NMR (^1H, ^{13}C) and mass spectrometry.

- 2,4-Bis-(4-trifluoromethyl-phenyl)-pyrimidine **2a**



$C_{18}H_{10}F_6N_2$

Exact mass: 368.0748

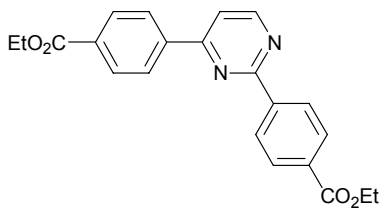
Molecular weight: 368.28

White solid, mp: 138°C

According to general procedure 2.1: from 4-bromobenzotrifluoride and 2-methylthio-4-chloropyrimidine: ***Zinc insertion and cross-coupling.*** $CoBr_2$ (30 mol%, 2.25 mmol, 495 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (6.8 mmol, 560 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 4-bromobenzotrifluoride (7.5 mmol, 1 mL) and 2-methylthio-4-chloropyrimidine (3.7 mmol, 0.44 mL), 50 °C, 5 h 30. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 80 : 20) to give **2a** as a white solid (831 mg, 61%).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 7.71 (m, 5H), 8.83 (m, 2H), 8.70 (m, 2H), 8.96 (m, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 115.5 (CH), 124.0 (q, $^1J_{C-F}$ = 254.1 Hz, C), 124.4 (q, $^1J_{C-F}$ = 254.4 Hz, C), 125.6 (q, $^3J_{C-F}$ = 3.8 Hz, 2CH), 126.0 (q, $^3J_{C-F}$ = 3.8 Hz, 2CH), 127.5 (2CH), 128.6 (2CH), 132.6 (q, $^2J_{C-F}$ = 31.9 Hz, C), 133.0 (q, $^2J_{C-F}$ = 31.9 Hz, C), 140.0 (C), 140.6 (C), 158.4 (CH), 162.6 (C), 163.4 (C).
HRMS ($C_{18}H_{10}F_6N_2$): calc: 368.0748, found: 368.0747
IR(neat,cm^{-1}): 2974**,** 1323, 1272, 1066, 1046

- 2,4-Bis-(4-carboethoxyphenyl)-pyrimidine **2b**



$C_{22}H_{20}N_2O_4$

Exact mass: 376.1423

Molecular weight: 376.41

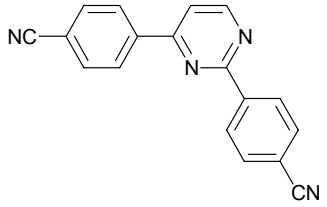
White solid, mp: 100°C

According to general procedure 2.1.: from ethyl 4-bromobenzoate and 2-methylthio-4-chloropyrimidine: ***Zinc insertion and cross-coupling.*** $CoBr_2$ (30 mol%, 2.25 mmol, 495 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (6.8 mmol, 560 µL), trifluoroacetic acid (100 µL), R.T., 3 min, ethyl 4-bromobenzoate (7.5 mmol, 1.22 mL) and 2-methylthio-4-chloropyrimidine (3.7 mmol, 0.44 mL), 50 °C, 4 h. ***work-up and purification***:

extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 30 : 70) to give **2b** as a white solid (835 mg, 60%).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 1.46 (t, 7.1Hz, 6H), 4.46 (q, 7.1Hz, 2H), 4.45 (q, 7.1Hz, 2H), 7.71 (d, 5.3Hz, 1H), 8.20-8.33 (m, 6H), 8.67 (d, 8.3Hz, 2H), 8.94 (d, 5.2Hz, 1H)
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 14.4 (CH_3), 14.4 (CH_3), 61.2 (CH_2), 61.4 (CH_2), 115.5 (CH), 127.2 (2CH), 128.2 (2CH), 129.8 (2CH), 130.2 (2CH), 132.3 (C), 132.6 (C), 140.6 (C), 141.5 (C), 158.3 (CH), 163.0 (C), 163.8 (C), 166.1 (C), 166.4 (C).
HRMS ($C_{22}H_{20}N_2O_4$): calc: 376.1423, found: 376.1419
IR(neat,cm^{-1}): 1722 (C=O), 1566, 1348, 1270, 1120, 1106, 1095

- 2,4-Bis-(4-cyanophenyl)-pyrimidine **2c**

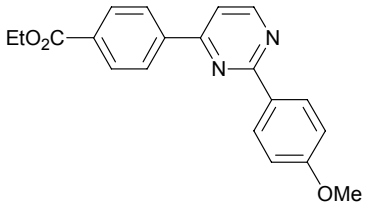


$C_{18}H_{10}N_4$
CAS: 160522-99-6
Exact mass: 282.0905
Molecular weight: 282.30
White solid,

According to general procedure 2.1.: from 4-bromobenzonitrile and 2-methylthio-4-chloropyrimidine: ***Zinc insertion and cross-coupling*.** $CoBr_2$ (30 mol%, 2.25 mmol, 495 mg), Zinc powder (19 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (6.8 mmol, 560 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 4-bromobenzonitrile (7.5 mmol, 1.4 g) and 2-methylthio-4-chloropyrimidine (3.7 mmol, 0.44 mL), 50 °C, 4 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 80 : 20 to 0 : 100) to give **2c** as a white solid (627 mg, 60%).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 7.74 (m, 1H), 7.83 – 7.90 (m, 4H), 8.34 (m, 2H) , 8.71 (m, 2H), 8.99 (m, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 114.2 (C), 114.6 (C), 115.8 (CH), 118.2 (C), 118.6 (C), 127.7 (2CH), 128.7 (2CH), 132.4 (2CH), 132.7 (2CH), 140.7 (C), 141.2 (C), 158.6 (CH), 162.0 (C), 163.0 (C)
HRMS ($C_{18}H_{10}N_4$): calc: 282.0905, found: 282.0911

- 4-[2-(4-Methoxy-phenyl)-pyrimidin-4-yl]-benzoic acid ethyl ester **3a**

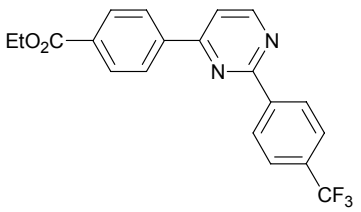


$C_{20}H_{18}N_2O_3$
Exact mass: 334.1317
Molecular weight: 334.37
White solid, mp: 128°C

According to general procedure 2.2.: from 4-bromoanisole and **1b**: ***Zinc insertion and cross-coupling.*** $CoBr_2$ (30 mol%, 1 mmol, 220 mg), Zinc powder (7.5 mmol, 0.47 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL). R.T., 3 min, 4-bromoanisole (3 mmol, 0.37 mL), 2-methylthio-4-arylpyrimidine **1b** (3 mmol, 823 mg), 50 °C, 7 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (pentane : ether = 40 : 60) to give **3a** as a white solid (652 mg, 65%).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 1.46 (t, 7.2 Hz, 3H) ; 3.92 (s, 3H) ; 4.45 (q, 7.2Hz, 2H) ; 7.05 (d, 8.8 Hz, 2H) ; 7.58 (d, 5.2Hz, 1H) ; 8.25 (dd, 8.3Hz and 23.3Hz, 4H) ; 8.56 (d, 8.8Hz, 2H) ; 8.84 (d, 5.2Hz, 1H)
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 14.3 (CH_3), 55.4 (CH_3), 61.3 (CH_2), 113.9 (2CH), 114.2 (CH), 127.1 (2CH), 130.0 (2CH), 130.1 (2CH), 130.3 (C), 132.4 (C), 141.1 (C), 158.1 (CH), 162.0 (C), 162.6 (C), 164.5 (C), 166.2 (C)
HRMS ($C_{20}H_{18}N_2O_3$): calc: 334.1317, found: 334.1312
IR(neat,cm^{-1}): 2973,1714 (C=O), 1269, 1090

- 4-[2-(4-Trifluoromethyl-phenyl)-pyrimidin-4-yl]-benzoic acid ethyl ester **3b**

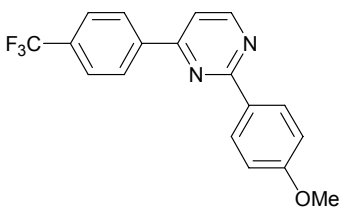


$C_{20}H_{15}F_3N_2O_2$
Exact mass: 372.1086
Molecular weight: 372.34
White solid

According to general procedure 2.2.: from 4-bromobenzotrifluoride and **1b**: ***Zinc insertion and cross-coupling.*** $CoBr_2$ (30 mol%, 1 mmol, 220 mg), Zinc powder (7.5 mmol, 0.47 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL). R.T., 3 min, 4-bromobenzotrifluoride (3 mmol, 0.4 mL), 2-methylthio-4-arylpyrimidine **1b** (3 mmol, 823 mg), 50 °C, 5 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 80 : 20) to give **3b** as a white solid (491 mg, 44 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 1.46 (t, 7.2 Hz, 3H), 4.46 (q, 7.2Hz, 2H), 7.73 (d, 5.3 Hz, 1H), 7.80 (d, 8.3 Hz, 2H), 8.28 (m, 4H), 8.72 (d, 7.90 Hz, 2H),8.94 (d, 5.3 Hz, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 14.3 (CH_3), 61.4 (CH_2), 115.7 (CH), 124.0 (q, $^1J_{C-F}$ = 254.1 Hz, C), 125.6 (q, $^3J_{C-F}$ = 3.8 Hz, 2CH), 127.2 (2CH), 128.6 (2CH), 130.2 (2CH), 132.3 (q, $^2J_{C-F}$ = 31.7 Hz , C), 132.7 (C), 140.5 (2C), 158.3 (CH), 163.1 (2C), 166.1 (C).
HRMS ($C_{20}H_{15}F_3N_2O_2$): calc: 372.1086, found: 372.1091

- 2-(4-Methoxy-phenyl)-4-(4-trifluoromethyl-phenyl)-pyrimidine **3c**



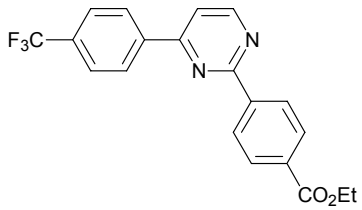
$C_{18}H_{13}F_3N_2O$
Exact mass: 330.0980
Molecular weight: 330.30
White solid, mp: 144°C

According to general procedure 2.2.: from 4-bromoanisole and **1a**: ***Zinc insertion and cross-coupling.*** $CoBr_2$ (30 mol%, 1 mmol, 220 mg), Zinc powder (7.5 mmol, 0.47 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL). R.T., 3 min, 4-bromoanisole (3 mmol, 0.37 mL), 2-methylthio-4-arylpyrimidine **1a** (3 mmol, 811 mg), 50 °C, 7 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **3c** as a white solid (525 mg, 53 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 3.92 (s, 3H) ; 7.05 (d, 8.8Hz, 2H) ; 7.57 (d, 5.22 Hz, 1H) ; 7.80 (d, 8.5Hz, 2H) ; 8.33 (d, 8.2Hz, 2H) ; 8.56 (d, 8.8Hz, 2H) ; 8.86 (d, 5.2Hz, 1H).

^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 55.4 (CH_3), 113.9 (2CH), 114.1 (CH), 125.9 (q, $^3J_{C-F}$ = 3.8 Hz, 2CH), 127.1 (q, $^1J_{C-F}$ = 250 Hz, C), 127.5 (2CH), 130.0 (2CH), 130.2 (C), 132.4 (q, $^2J_{C-F}$ = 30.2 Hz , C), 140.5 (q, $^5J_{C-F}$ = 1.4 Hz, C), 158.2 (CH), 162.1 (C), 162.2 (C), 164.6 (C).
HRMS ($C_{18}H_{13}F_3N_2O$): calc: 330.0980, found: 330.0980
IR(neat,cm^{-1}): 2974, 1088,

- 4-[4-(4-Trifluoromethyl-phenyl)-pyrimidin-2-yl]-benzoic acid ethyl ester **3d**

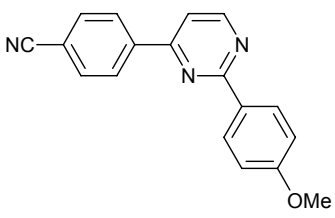


$C_{20}H_{15}F_3N_2O_2$
Exact mass: 372.1086
Molecular weight: 372.34
White solid, mp : 148°C

According to general procedure 2.2.: from ethyl 4-bromobenzoate and **1a**: ***Zinc insertion and cross-coupling.*** $CoBr_2$ (30 mol%, 1 mmol, 220 mg), Zinc powder (7.5 mmol, 0.47 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL). R.T., 3 min, ethyl 4-bromobenzoate (3 mmol, 0.5 mL), 2-methylthio-4-arylpyrimidine **1a** (3 mmol, 811 mg), 50 °C, 7 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 80 : 20) to give **3d** as a white solid (335 mg, 30 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 1.46 (t, 7.1 Hz, 3H) ; 4.45 (q, 7.1 Hz, 2H) ; 7.69 (m, 1H) ; 7.83 (m, 2H) ; 8.20 (m, 2H) ; 8.34 (m, 2H) ; 8.65 (m, 2H) ; 8.94 (m, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 14.3 (CH_3), 61.2 (CH_2), 115.4 (CH), 125.0 (q, $^1J_{C-F}$ = 254.1 Hz, C), 125.9 (q, $^3J_{C-F}$ = 3.8 Hz, 2CH), 127.6 (2CH), 128.2 (2CH), 129.8 (2CH), 132.1 (q, $^2J_{C-F}$ = 31.8 Hz , C), 132.4 (C), 140.0 (C), 141.4 (C), 158.4 (CH), 162.6 (C), 163.9 (C), 166.4 (C).
HRMS ($C_{20}H_{15}F_3N_2O_2$): calc: 372.1086, found: 372.1087
IR(neat,cm^{-1}): 1710 (C=O), 1562, 1323, 1272, 1066

- 4-[2-(4-Methoxy-phenyl)-pyrimidin-4-yl]-benzonitrile **3e**



$C_{18}H_{13}N_3O$
Exact mass: 287.1059

Molecular weight: 287.32
White solid

According to general procedure 2.2.: from 4-bromoanisole and **1c**: ***Zinc insertion and cross-coupling.*** $CoBr_2$ (30 mol%, 1 mmol, 220 mg), Zinc powder (7.5 mmol, 0.47 g) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL). R.T., 3 min, 4-bromoanisole (3 mmol, 0.43 mL), 2-methylthio-4-arylpyrimidine **1c** (3 mmol, 682 mg), 50 °C, 5 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (pentane : ether = 40 : 60) to give **3e** as a white solid (646 mg, 75 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 3.93 (s, 3H), 7.06 (d, 8.5Hz, 2H), 7.58 (d, 4.9Hz, 1H), 7.85 (d, 8.1Hz, 2H), 8.34 (d, 8.1Hz, 2H), 8.55 (d, 8.5Hz, 2H), 8.89 (d, 4.9Hz, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: : 55.4 (CH_3), 60.7 (C), 114.0 (2CH), 114.3 (CH), 118.5 (C), 127.8 (2CH), 129.9 (C), 130.1 (2CH), 132.7 (2CH), 141.3 (C), 158.3 (CH), 161.8 (C), 162.2 (C), 164.7 (C).
HRMS ($C_{18}H_{13}N_3O$): calc: 287.1059, found: 287.1060

General Procedures 3.1 and 3.2: for the synthesis of 2-benzylbenzo[b]thiazoles 4a-b and 2-arylbenzo[*b*]thiazoles 4c-g from benzyl- and arylzinc derivatives and 2-methylthiobenzo[*b*]thiazole

Procedure 3.1. from benzylchlorides: *Zinc insertion and cross-coupling*. To a solution of $CoBr_2$ (30 mol%), and Zinc powder (1.5 equivalents) in acetonitrile (4 mL) were successively added at room temperature allylchloride (90 mol%) and trifluoroacetic acid (100 µL), causing an immediate rise in temperature and color change to dark grey. After stirring the resulting mixture for 3 minutes, benzylchloride derivative and 2-methylthiobenzo[*b*]thiazole (1 equivalent) were added. The medium was then stirred at 50 °C until benzylchloride was consumed. *Work-up and purification*. The reaction mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with dichloromethane. The organic layer was washed with a saturated aqueous solution of NaCl and dried over $MgSO_4$. Evaporation of solvent and purification by column chromatography on silica gel (petroleum ether/diethyl ether) afforded the coupling product characterized by NMR (^{1}H, ^{13}C) and mass spectrometry.

Procedure 3.2. from arylbromides: *Synthesis of ArZnBr*. To a solution of $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg) and Zinc powder (12.5 mmol, 820 mg) in acetonitrile (6 mL) were successively added at room temperature allylchloride (2.25 mmol, 190 µL) and trifluoroacetic acid (100 µL), causing an immediate rise in temperature and color change to dark grey. After stirring the resulting mixture for 3 minutes, aryl bromide (7.5 mmol) was added. The medium was then stirred at room temperature until complete conversion of aryl bromide.

Cross-coupling reaction. 2-methylthio-benzo[*b*]thiazole (5 mmol, 906 mg) and $CoBr_2$ (20 mol%, 1 mmol, 220 mg) were added and the medium was stirred at 50 °C until ArZnBr was consumed. The amounts of the corresponding ArZnBr and coupling product were measured by GC (addition of iodine) using an internal reference (dodecane, 200 µL); *Work-up and purification*. The reaction mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with dichloromethane. The organic layer was washed with a saturated aqueous solution of NaCl and dried over $MgSO_4$. Evaporation of solvent and purification by column chromatography on silica gel (petroleum ether / diethyl ether) afforded the coupling product characterized by NMR (^1H, ^{13}C) and mass spectrometry.

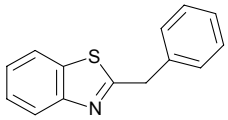
General Procedure 4: for the synthesis of 2-arylbenzo[*b*]thiazoles 4c-g and 2-arylthiazoles 5a-c from arylhalides and zinc species from 2-methylthiobenzo[*b*]thiazole and 2-methylthiothiazole.

Procedure 4. from 2-methylthiothiazole or 2-methylthiobenzo[*b*]thiazole: *Synthesis of HetArZnSMe*. To a solution of $CoBr_2$ (1.14 mmol, 250 mg) and Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL) were successively added at room temperature allylchloride (3.68 mmol, 300 µL) and trifluoroacetic acid (100 µL), causing an immediate rise in temperature and color change to dark grey. After stirring the resulting mixture for 3 minutes, 2-methylthiobenzo[b]thiazole (5 mmol, 906 mg) or 2-methylthiothiazole (5 mmol, 0.5 mL) was added. The medium was then stirred at 30 °C until complete conversion of the 2-methylthio derivative.

Cross-coupling reaction. DMF (2 mL) was added. Then, $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg) and the arylhalide (8.5 mmol) were added to the solution and the medium was stirred at 35 °C until HetArZnSMe was consumed. The amounts of the corresponding HetArZnSMe and coupling product were measured by GC (addition of iodine) using an internal reference

(dodecane, 200 µL); *Work-up and purification*. The reaction mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with ethyl acetate. The organic layer was washed with a saturated aqueous solution of NaCl and dried over $MgSO_4$. Evaporation of solvent and purification by column chromatography on silica gel (petroleum ether / diethyl ether or petroleum ether / ethyl acetate) afforded the coupling product characterized by NMR (^1H, ^{13}C) and mass spectrometry.

- 2-Benzyl-benzothiazole **4a**

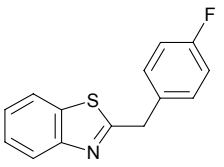


$C_{14}H_{11}NS$
CAS: 6265-94-7
Exact mass: 225.0612
Molecular weight: 225.31
Yellow oil

According to general procedure 3.1.: from benzyl chloride: ***Zinc insertion and Cross-coupling reaction***. $CoBr_2$ (30 mol%, 1.5 mmol, 330 mg), Zinc powder (12.5 mmol, 820 mg) in acetonitrile (4 mL), allylchloride (4.5 mmol, 375 µL), trifluoroacetic acid (100 µL), R.T., 3 min, benzylchloride (5 mmol, 0.57 mL), 2-methylthio-benzo[*b*]thiazole (5 mmol, 906 mg), 50 °C, 17 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether: ether = 90 : 10) to give **4a** as a yellow oil (709 mg, 63 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 4.47 (s, 2H), 7.33-7.40 (m, 6H), 7.48 (m, 1H), 7.81 (m, 1H), 8.02 (m, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 40.7 (CH_2), 121.5 (CH), 122.8 (CH), 124.8 (CH), 125.9 (CH), 127.4 (CH), 128.9 (2CH), 129.2 (2CH), 135.7 (C), 137.2 (C), 153.3 (C), 171.2 (C)

- 2-(4-Fluoro-benzyl)-benzothiazole **4b**



$C_{14}H_{10}FNS$
CAS: 37859-33-9
Exact mass: 243.0518

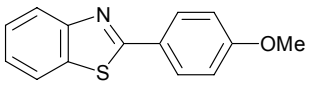
Molecular weight: 243.30

Pale yellow oil

According to general procedure 3.1.: from 4-fluorobenzyl chloride: ***Zinc insertion and Cross-coupling reaction***. $CoBr_2$ (30 mol%, 0.9 mmol, 198 mg), Zinc powder (7.5 mmol, 491 mg) in acetonitrile (3 mL), allylchloride (2.7 mmol, 225 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 4-fluorobenzyl chloride (3 mmol, 0.40 mL), 2-methylthio-benzo[*b*]thiazole (3 mmol, 544 mg), 50 °C, 17 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **4b** as a pale yellow oil (401 mg, 55 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 4.43 (s, 2H), 7.03-7.08 (m, 2H), 7.33-7.40 (m, 3H), 7.45-7.51 (m, 1H), 7.81-7.84 (m, 1H), 8.00-8.03 (m, 1H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 38.2 (CH_2), 114.1 (CH), 114.4 (CH), 120.0 (CH), 121.3 (CH), 123.4 (CH), 124.6 (CH), 129.2 (CH), 129.3 (CH), 131.4 (C), 131.4 (C), 151.8 (C), 159.0 (C), 169.3 (C).

- 2-(4-Methoxy-phenyl)-benzothiazole **4c**



$C_{14}H_{11}NOS$

CAS: 6265-92-5

Exact mass: 241.0561

Molecular weight: 241.31

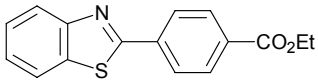
White solid

According to general procedure 3.2.: from 4-bromoanisole: ***Synthesis of ArZnBr***. $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (12.5 mmol, 820 mg) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 4-bromoanisole (7.5 mmol, 0.94 mL), R.T., 45 min. ***Cross-coupling reaction.*** 2-methylthio-benzo[*b*]thiazole (5 mmol, 906 mg), $CoBr_2$ (20 mol%, 1 mmol, 220 mg) 50 °C, 12 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **4c** as a white solid (724 mg, 60 %).

According to general procedure 4.: from 2-methylthiobenzo[*b*]thiazole: ***Synthesis of HetArZnSMe.*** $CoBr_2$ (1.14 mmol, 250 mg), Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (3.68 mmol, 300 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 2-methylthiobenzo[*b*]thiazole (5 mmol, 906 mg) , 35 °C. ***Cross-coupling reaction with 4-iodoanisole.*** DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), 4-iodoanisole (8.5 mmol, 1.99 g), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **4c** as a white solid (844 mg, 70 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 3.90 (s, 3H), 7.02 (m, 2H), 7.38 (m, 1H), 7.49 (m, 1H), 7.90 (m, 1H), 7.91 (m, 3H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 55.5 (CH_3), 114.4 (2CH), 121.5 (CH), 122.8 (CH), 124.8 (CH), 126.2 (CH), 126.4 (C), 129.1 (2 CH), 134.9 (C), 154.2 (C), 161.9 (C), 167.9 (C)
HRMS ($C_{14}H_{11}NOS$): calc: 241.0561, found: 241.0558

- 4-Benzothiazol-2-yl-benzoic acid ethyl ester **4e**



$C_{16}H_{13}NO_2S$
CAS: 1030513-24-6
Exact mass: 283.0667
Molecular weight: 283.35
White solid

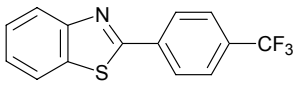
According to general procedure 3.2.: from ethyl 4-bromobenzoate: ***Synthesis of ArZnBr***. $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (12.5 mmol, 820 mg) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min, ethyl 4-bromobenzoate (7.5 mmol, 1.22 mL), R.T., 1 h. ***Cross-coupling reaction.*** 2-methylthio-benzo[*b*]thiazole (5 mmol, 906 mg), $CoBr_2$ (20 mol%, 1 mmol, 220 mg) 50 °C, 6 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **4e** as a white solid (807 mg, 57 %).

According to general procedure 4.: from 2-methylthiobenzo[*b*]thiazole: ***Synthesis of HetArZnSMe.*** $CoBr_2$ (1.14 mmol, 250 mg), Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (3.68 mmol, 300 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 2-methylthiobenzo[*b*]thiazole (5 mmol, 906 mg) , 35 °C. ***Cross-coupling reaction with ethyl 4-***

iodobenzoate. DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), ethyl 4-iodobenzoate (8.5 mmol, 1.41 mL), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **4e** as a white solid (920 mg, 65 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 1.45 (t, 7.1 Hz, 3H), 4.44 (q, 7.1 Hz, 2H), 7.45 (m, 2H), 7.69 (m, 1H), 7.96 (m, 1H), 8.17 (m, 4H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 14.3 (CH_3), 61.1 (CH_2), 121.7 (CH), 123.6 (CH), 125.7 (CH), 126.6 (CH), 127.2 (2CH), 127.3 (2CH), 132.4 (C), 135.3 (C), 144.3 (C), 154.1 (C), 166.0 (C), 166.7 (C).
HRMS ($C_{16}H_{13}NO_2S$): calc: 283.0667, found: 283.0667

- 2-(4-Trifluoromethyl-phenyl)-benzothiazole **4f**



$C_{14}H_8F_3NS$
CAS: 134384-31-9
Exact mass: 279.0330
Molecular weight: 279.28
White solid

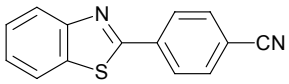
According to general procedure 3.2.: from 4-bromobenzotrifluoride: ***Synthesis of ArZnBr***. $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (12.5 mmol, 820 mg) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 4-bromobenzotrifluoride (7.5 mmol, 1.0 mL), R.T., 1 h. ***Cross-coupling reaction.*** 2-methylthio-benzo[*b*]thiazole (5 mmol, 906 mg), $CoBr_2$ (20 mol%, 1 mmol, 220 mg) 50 °C, 4 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **4f** as a white solid (698 mg, 50 %).

According to general procedure 4.: from 2-methylthiobenzo[*b*]thiazole: ***Synthesis of HetArZnSMe.*** $CoBr_2$ (1.14 mmol, 250 mg), Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (3.68 mmol, 300 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 2-methylthiobenzo[*b*]thiazole (5 mmol, 906 mg) , 35 °C. ***Cross-coupling reaction with 4-iodobenzotrifluoride.*** DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), 4-iodobenzotrifluoride (8.5 mmol, 1.95 g), 35 °C. ***work-up and purification***: extracted with

ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ether = 90 : 10) to give **4f** as a white solid (768 mg, 55 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 7.51 (m, 2H), 7.78 (m, 2H), 7.95 (m, 1H), 8.13 (m, 1H), 8.23 (m, 2H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 121.8 (CH), 122.0 (CH), 123.8 (q, $^1J_{C-F}$ = 272.4 Hz, C), 125.8 (CH), 126.0 (q, $^3J_{C-F}$ = 3.8 Hz, 2CH), 126.7 (CH), 127.8 (2CH), 132.4 (q, $^2J_{C-F}$ = 32.5 Hz, C), 135.2 (C), 136.7 (q, $^5J_{C-F}$ = 1.2 Hz, C), 154.0 (C), 166.0 (C).
HRMS ($C_{14}H_8F_3NS$): calc: 279.0330, found: 279.0332

- 4-Benzothiazol-2-yl-benzonitrile **4g**



$C_{14}H_8N_2S$
CAS: 17930-02-8
Exact mass: 236.0408
Molecular weight: 236.29
White solid

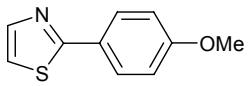
According to general procedure 3.2.: from 4-bromobenzonitrile: ***Synthesis of ArZnBr***. $CoBr_2$ (10 mol%, 0.75 mmol, 165 mg), Zinc powder (12.5 mmol, 820 mg) in acetonitrile (6 mL), allylchloride (2.25 mmol, 190 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 4-bromobenzonitrile (7.5 mmol, 1.4 g), R.T., 1 h. ***Cross-coupling reaction.*** 2-methylthio-benzo[*b*]thiazole (5 mmol, 906 mg), $CoBr_2$ (20 mol%, 1 mmol, 220 mg) 50 °C, 6 h. ***work-up and purification***: extracted with dichloromethane (3 x 70 mL), purified by silica gel (petroleum ether: ether = 80 : 20) to give **4g** as a white solid (530 mg, 45 %).

According to general procedure 4.: from 2-methylthiobenzo[*b*]thiazole: ***Synthesis of HetArZnSMe.*** $CoBr_2$ (1.14 mmol, 250 mg), Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (3.68 mmol, 300 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 2-methylthiobenzo[*b*]thiazole (5 mmol, 906 mg) , 35 °C. ***Cross-coupling reaction with 4-iodobenzonitrile.*** DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), 4-iodobenzonitrile (8.5 mmol, 1.24 mL), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ether = 80 : 20) to give **4g** as a white solid (589 mg, 50 %). ***Cross-coupling reaction with 4-bromobenzonitrile.*** DMF (2 mL), $PdCl_2(PPh_3)_2$

(0.128 mmol, 90 mg), 4-bromobenzonitrile (8.5 mmol, 1.6 g), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ether = 80 : 20) to give **4g** as a white solid (648 mg, 55 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 7.50 (m, 2H), 7.79 (m, 2H), 7.96 (m, 1H), 8.13 (m, 1H), 8.23 (m, 2H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 114.1 (C), 118.3 (C), 121.8 (CH), 123.8 (CH), 126.1 (CH), 126.8 (CH), 127.9 (2CH), 132.8 (2 CH), 135.3 (C), 137.5 (C), 154.0 (C), 165.4 (C)
HRMS ($C_{14}H_8N_2S$): calc: 236.0408, found: 236.0401

- 2-(4-methoxyphenyl)thiazole **5a**

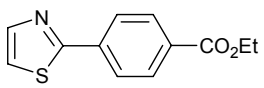


$C_{10}H_9NOS$
CAS: 27088-84-2
Exact mass: 191.0405
Molecular weight: 191.25
White solid

According to general procedure 4.: from 2-methylthiothiazole: ***Synthesis of HetArZnSMe.*** $CoBr_2$ (1.14 mmol, 250 mg), Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (3.68 mmol, 300 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 2-methylthiothiazole (5 mmol, 0.5 mL), 35 °C. ***Cross-coupling reaction with 4-iodoanisole.*** DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), 4-iodoanisole (8.5 mmol, 1.99 g), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ethyl acetate) to give **5a** as a white solid (526 mg, 55 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 7.93 (d, 8.64 Hz, 2H), 7.83 (d, 2.9Hz, 1H), 7.28 (d, 2.9 Hz, 1H), 6.98 (d, 8.67Hz, 2H), 3.88 (s, 3H).
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 168.7 (C), 161.5 (C), 143.7 (CH), 128.4 (2CH), 126.9 (C), 118.2 (CH), 114.7 (2CH), 55.8 (CH_3)

- ethyl 4-(thiazol-2-yl)benzoate **5b**



$C_{12}H_{11}NO_2S$

CAS: 257876-04-3

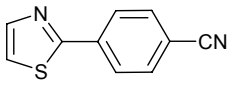
Exact mass: 233.051
Molecular weight: 233.29
White solid

According to general procedure 4.: from 2-methylthiothiazole: ***Synthesis of HetArZnSMe.*** $CoBr_2$ (1.14 mmol, 250 mg), Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (3.68 mmol, 300 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 2-methylthiothiazole (5 mmol, 0.5 mL), 35 °C. ***Cross-coupling reaction with ethyl 4-iodobenzoate.*** DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), ethyl 4-iodobenzoate (8.5 mmol, 1.41 mL), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ethyl acetate) to give **5b** as a white solid (338 mg, 29 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 8.26 (d, 8.1 Hz, 2H), 8.18 (d, 8.1Hz, 2H), 8.06 (d, 3 Hz,1H), 7.54 (d, 3Hz, 1H), 4.53 (q, 2H), 1.56 (t, 3H)

^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 167.5 (C), 166.4 (C), 144.5 (CH), 137.6 (C), 131.9 (C), 130.6 (2CH), 126.8 (2CH), 120.3 (CH), 61.6 (CH_2), 14.7 (CH_3)

- 4-(thiazol-2-yl)benzonitrile **5c**



$C_{10}H_6N_2S$
CAS: 672324-84-4
Exact mass: 186.0252
Molecular weight: 186.23
White solid

According to general procedure 4.: from 2-methylthiothiazole: ***Synthesis of HetArZnSMe.*** $CoBr_2$ (1.14 mmol, 250 mg), Zinc powder (18 mmol, 1.2 g) in acetonitrile (6 mL), allylchloride (3.68 mmol, 300 µL), trifluoroacetic acid (100 µL), R.T., 3 min, 2-methylthiothiazole (5 mmol, 0.5 mL), 35 °C. ***Cross-coupling reaction with 4-iodobenzonitrile.*** DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), 4-iodobenzonitrile (8.5 mmol, 1.95 g), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ethyl acetate) to give **5c** as a white solid (317 mg, 34

%). ***Cross-coupling reaction with 4-bromobenzonitrile.*** DMF (2 mL), $PdCl_2(PPh_3)_2$ (0.128 mmol, 90 mg), 4-bromobenzonitrile (8.5 mmol, 1.6 g), 35 °C. ***work-up and purification***: extracted with ethylacetate (3 x 70 mL), purified by silica gel (petroleum ether : ethyl acetate) to give **5c** as a white solid (2.45 g, 49 %).

^{1}H-NMR (300MHz, $CDCl_3$) δ /ppm: 8.06 (d, 8.2 Hz, 2H), 7.93 (d, 3 Hz, 1H), 7.72 (d, 8.2 Hz, 2H), 7.44 (d, 3Hz, 1H)
^{13}C-NMR (75MHz, $CDCl_3$) δ /ppm: 166.3 (C), 144.9 (CH), 137.8 (C), 133.2 (2CH), 127.4 (2CH), 121.0 (CH), 118.8 (C), 113.6 (C)