Supporting Information for

Mobilizing Cu(I) for Carbon-Carbon Bond Forming Catalysis in the Presence of Thiolate. Chemical Mimicking of Metallothioneins

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General Methods

All reactions were performed under an atmosphere of dry argon in oven-dried glassware. THF, DMA, DMF, and toluene were dried over 4Å molecular sieves and titrated for water level prior to use with a Fisher Coulomatic K-F titrater. Hexanes, ethyl acetate (EtOAc), and ethyl ether (Et_2O) were obtained from Aldrich and used as purchased. 'Brine' refers to a saturated aqueous solution of NaCl. Purification by flash chromatography was performed using Whatman 60Å 230-400 mesh SiO_2 with compressed air as a source of positive pressure. Purification by plate chromatography was performed on EM Science Kieselgel 0.5 mm or 1 mm $60F_{254}$ plates. Analytical thin-layer chromatography (TLC) was carried out using Merck Kieselgel $60F_{254}$ plates with visualization by UV or phosphomolybdic acid. HPLC analyses were carried out using an Agilent 1100 system with a quaternary pump. Separations were achieved on a Zorbax Eclipse XDB C8 4.6 x 150 mm column or DAICEL chiral AD, AS, OD and OJ reversed phase column. Solvents used as reaction media were purchased in > 99% purity without further purification.

^{1}H NMR spectra were recorded on a Varian Inova 400 MHz NMR spectrometer at room temperature in $CDCl_3$ and were internally referenced to $CDCl_3$ (7.26 ppm); ^{13}C NMR spectra were recorded on a Varian Inova 100 MHz NMR spectrometer at room temperature in $CDCl_3$ and were internally referenced to $CDCl_3$ (77.23 ppm). ^{19}F NMR spectra were recorded on a Varian Inova 375 MHz NMR spectrometer at room temperature in $CDCl_3$ without a reference. Data are reported in the following order: chemical shifts are given (δ); multiplicities are indicated (br (broadened), s (singlet), d (doublet), t (triplet), q (quartet), hex (hextet), hept (heptext), m (multiplet), exch (exchangeable), app (apparent)); coupling constants, *J*, are reported (Hz); integration is provided. Infrared spectra were recorded ASI ReactIR 1000FT-IR spectrometer with a silicone probe. Peaks are reported (cm^{-1}) with the following relative intensities: s (strong, 67-100%), m (medium, 40-67%), w (weak, 20-40%) and br (broad). GC-MS spectra were recorded on a Shimadzu Gas Chromatograph GC-17A, Mass Spectrometer QP-5000. GC/MS analysis was carried out on a bonded 5% diphenylsiloxane capillary column (30 m, 0.25 mm id, 0.25 μm df). Uncalibrated melting points were taken on a Thomas-Hoover melting point apparatus in open capillary tubes

Microwave Irradiation Experiments

Microwave irradiation experiments were carried out using a Discover microwave reactor from CEM. All experiments were performed in sealed tubes (capacity 10 mL) under argon atmosphere utilizing microwave irradiation of 300 W. The temperature was ramped from room temperature to 150 °C in 1 minute. Once this temperature was reached, the reaction temperature was held at 150 °C for 60 minutes.

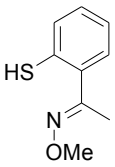
Starting materials

Thiosalicylic acid, *O*-methylhydroxylamine hydrochloride, *O*-phenylhydroxylamine hydrochloride, hydroxylamine hydrochloride, triethylborane, styrene, 9-BBN (0.5 M in THF), *p*-toluoyl chloride，thiophene-2-carbonyl chloride，butyryl chloride，cyclohexanecarbonyl chloride，but-2-enoyl chloride，acetic acid chlorocarbonylmethyl ester，*N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC), L-phenylalanine and D-phenylalanine were purchased from Aldrich and used without future purification. All boronic acids, organostannanes and Cu^I-3-methylsalicylate (CuMeSal) were obtained from Synthonix, Inc. *B*-2-phenylethyl-9-BBN was prepared following the known procedure.[1]

[1] Yu, Y.; Liebeskind, L. S. *J. Org. Chem.* **2004**, *69*, 3554–3557.

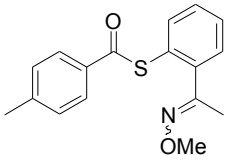
Scheme 3. Construction of the Metallothionein Mimic

1-(2-Mercapto-phenyl)ethanone *O*-methyloxime (2)



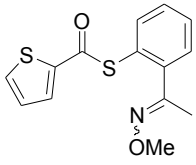
2'-Mercaptoacetophenone[2] (3.04 g, 20 mmol) and *O*-methylhydroxylamine hydrochloride (2.51 g, 30 mmol) were dissolved in 60 mL MeOH. Pyridine (2.77 g, 35 mmol) was slowly added *via* syringe and the reaction mixture was stirred at room temperature overnight. The solvent was evaporated and the residue was dissolved into diethyl ether (20 mL). The organic phase was washed with 1 M HCl (2×10 mL), water (10 mL) and brine (5 mL). After drying over $MgSO_4$ the solvent was evaporated. Purification by flash chromatography (silica gel, 20:1 hexanes:EtOAc) afforded the title compound as a yellow oil (6:1 mixture of *E/Z* isomers, 3.11 g, 86%). Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.27 (m, 2H), 7.16-7.14 (m, 2H), 4.01 (s, 3H), 3.97 (s, 1H), 2.22 (s, 3H); characteristic signals for minor isomer: ^{1}H NMR δ 2.16 (s, 3H), 3.84 (s, 3H); Major Isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 135.8, 131.2, 129.2, 128.9, 125.7, 62.2, 15.3; IR (neat, cm^{-1}): 3061 (m), 2937 (s), 2548 (m), 1613 (m); HRMS (FAB) Calcd for $C_9H_{12}ONS$ ($M+H^+$): 182.0634. Found: 182.0632.

***S*-2-(1-(Methoxyimino)ethyl)phenyl 4-methylbenzothioate (3a)**



1-(2-Mercaptophenyl)ethanone *O*-methyloxime (181 mg, 1.0 mmol) and *p*-toluoyl chloride (162 mg, 1.05 mmol) were dissolved in 20 mL THF. Pyridine (87 mg, 1.1 mmol) was added slowly *via* syringe and after stirring at room temperature for 4 h a white precipitate was removed by filtration. The filtrate was washed with water (10 mL) and brine (5 mL) and then dried over $MgSO_4$. The solvent was evaporated to give a yellow oil. Purification by flash chromatography (silica gel 10:1 hexanes:EtOAc) afforded the title compound as a clear oil (6:1 mixture of *E/Z* isomers, 293 mg, 98%). Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.0 Hz, 2H), 7.57-7.54 (m, 1H), 7.46-7.40 (m, 3H), 7.28 (d, J = 8.0 Hz, 2H), 3.92 (s, 3H), 2.42 (s, 3H), 2.12 (s, 3H); characteristic signals for minor isomer: ^{1}H NMR δ 3.76 (s, 3H), 2.42 (s, 3H), 2.10 (s, 3H); Major Isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.5, 156.6, 144.9, 142.6, 137.7, 134.1, 130.1, 129.6, 129.4, 127.8, 126.3, 62.1, 21.9, 16.6; IR (neat, cm^{-1}): 3065 (m), 1695 (s), 1671 (s); HRMS (FAB) Calcd for $C_{17}H_{18}O_2NS$ ($M+H^+$): 300.1052. Found: 300.1051.

***S*-2-(1-(Methoxyimino)ethyl)phenyl thiophene-2-carbothioate (3b)**

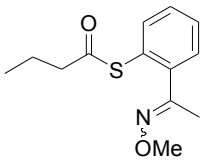


1-(2-Mercaptophenyl)ethanone *O*-methyloxime (181 mg, 1.0 mmol) and thiophene-2-carbonyl chloride (153 mg, 1.05 mmol) were dissolved in 20 mL THF. Pyridine (87 mg, 1.1 mmol) was added slowly *via* syringe and after stirring at room temperature for 4 h a white precipitate was removed by filtration. The filtrate was washed with

[2] 2'-mercaptoacetophenone was prepared following the known procedure: Topolski , M. *J. Org. Chem.* **1995**, *60*, 5588–5594.

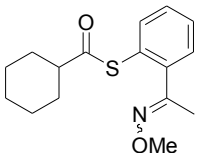
water (10 mL) and brine (5 mL) and then dried over $MgSO_4$. The solvent was evaporated to give a yellow oil. Purification by flash chromatography (silica gel 10:1 hexanes:EtOAc) afforded the title compound as a yellow oil (5:1 mixture of *E/Z* isomers, 276 mg, 95%). Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.63 (dd, *J* = 5.2, 1.2 Hz, 1H), 7.58 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.46-7.39 (m, 3H), 7.14-7.12 (m, 1H), 3.93 (s, 3H), 2.14 (s, 3H); characteristic signals for minor isomer: ^{1}H NMR δ 3.77 (s, 3H), 2.12 (s, 3H); Major Isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.9, 156.4, 142.4, 141.4, 137.6, 133.6, 132.0, 130.2, 129.6, 129.4, 128.3, 125.7, 62.1, 16.7; IR (neat, cm^{-1}): 3069 (m), 1660 (s), 1617 (s); HRMS (FAB) Calcd for $C_{14}H_{14}O_2NS$ ($M+H^+$): 292.0460. Found: 292.0463.

***S*-2-(1-(Methoxyimino)ethyl)phenyl butanethioate (3c)**



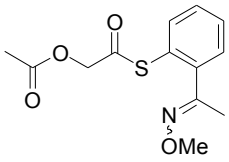
1-(2-Mercaptophenyl)ethanone *O*-methyloxime (181 mg, 1.0 mmol) and butyryl chloride (111 mg, 1.05 mmol) were dissolved in 20 mL THF. Pyridine (87 mg, 1.1 mmol) was added slowly *via* syringe and after stirring at room temperature for 4 h a white precipitate was removed by filtration. The filtrate was washed with water (10 mL) and brine (5 mL) and then dried over $MgSO_4$. The solvent was evaporated to give a yellow oil. Purification by flash chromatography (silica gel 10:1 hexanes:EtOAc) afforded the title compound as a clear oil (4:1 mixture of *E/Z* isomers, 241 mg, 96%). Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.36 (m, 4H), 3.94 (s, 3H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.10 (s, 3H), 1.72 (q, 2 H), 0.98 (t, *J* = 7.6, 3H); characteristic signals for minor isomer: ^{1}H NMR δ 3.76 (s, 3H), 2.08 (s, 3H); Major Isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.2, 156.4, 142.0, 137.0, 129.9, 129.5, 129.3, 126.7, 62.1, 45.7, 19.4, 16.7, 13.6; IR (neat, cm^{-1}): 3061 (m), 2964 (s), 1702 (s); HRMS (FAB) Calcd for $C_{13}H_{18}O_2NS$ ($M+H^+$): 252.1052. Found: 252.1054.

***S*-2-(1-(Methoxyimino)ethyl)phenyl cyclohexanecarbothioate (3d)**



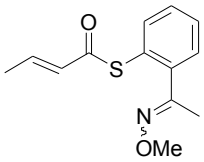
1-(2-Mercaptophenyl)ethanone *O*-methyloxime (181 mg, 1.0 mmol) and cyclohexanecarbonyl chloride (154 mg, 1.05 mmol) were dissolved in 20 mL THF. Pyridine (87 mg, 1.1 mmol) was added slowly *via* syringe and after stirring at room temperature for 4 h a white precipitate was removed by filtration. The filtrate was washed with water (10 mL) and brine (5 mL) and then dried over $MgSO_4$. The solvent was evaporated to give a yellow oil. Purification by flash chromatography (silica gel 10:1 hexanes:EtOAc) afforded the title compound as a clear oil (6:1 mixture of *E/Z* isomers, 268 mg, 92%). Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.34 (m, 4H), 3.96 (s, 3H), 2.62 (m, 1H), 2.11 (s, 3H), 1.97 (m, 2H), 1.81 (m, 2H), 1.52 (m, 2H), 1.30 (m, 4H); characteristic signals for minor isomer: ^{1}H NMR δ 3.78 (s, 3H), 2.08 (s, 3H); Major Isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 156.4, 142.2, 137.2, 129.8, 129.5, 129.2, 126.7, 62.0, 52.7, 29.7, 25.8, 25.6, 16.6; IR (neat, cm^{-1}): 3065 (m), 2934 (s), 1698 (s), 1633 (s); HRMS (FAB) Calcd for $C_{16}H_{22}O_2NS$ ($M+H^+$): 292.1365. Found: 292.1369.

2-(2-(1-(Methoxyimino)ethyl)phenylthio)-2-oxoethyl acetate (3e)



1-(2-Mercaptophenyl)ethanone *O*-methyloxime (181 mg, 1.0 mmol) and acetic acid chlorocarbonylmethyl ester (143 mg, 1.05 mmol) were dissolved in 20 mL THF. Pyridine (87 mg, 1.1 mmol) was added slowly *via* syringe and after stirring at room temperature for 4 h a white precipitate was removed by filtration. The filtrate was washed with water (10 mL) and brine (5 mL) and then dried over $MgSO_4$. The solvent was evaporated to give a yellow oil. Purification by flash chromatography (silica gel 10:1 hexanes:EtOAc) afforded the title compound as a clear oil (6:1 mixture of *E/Z* isomers, 256 mg, 91%). Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.39 (m, 4H), 4.81 (s, 2 H), 3.97 (s, 3 H), 2.20 (s, 3H), 2.12 (s, 3H); characteristic signals for minor isomer: ^{1}H NMR δ 3.79 (s, 3H), 2.09 (s, 3H); Major Isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 170.0, 155.9, 142.3, 137.3, 130.4, 129.7, 129.5, 124.5, 67.7, 62.1, 20.7, 16.5; IR (neat, cm^{-1}): 2937 (s), 1756 (s), 1710 (s); HRMS (FAB) Calcd for $C_{13}H_{16}O_4NS$ ($M+H^+$): 282.0797; Found: 282.0797.

(*2E*)-*S*-2-(1-(Methoxyimino)ethyl)phenyl but-2-enethioate (3f)



1-(2-Mercaptophenyl)ethanone *O*-methyloxime (181 mg, 1.0 mmol) and but-2-enoyl chloride (109 mg, 1.05 mmol) were dissolved in 20 mL THF. Pyridine (87 mg, 1.1 mmol) was added slowly *via* syringe and after stirring at room temperature for 4 h the white precipitate was removed by filtration. The filtrate was washed with water (10 mL) and brine (5 mL) and then dried over $MgSO_4$. The solvent was evaporated to give a yellow oil. Purification by flash chromatography (silica gel 10:1 hexanes:EtOAc) afforded the title compound as a clear oil (5:1 mixture of *E/Z* isomers, 226 mg, 90%). Major Isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.34 (m, 4H), 7.03-6.94 (m, 1H), 6.22-6.17 (m, 1H), 3.96 (s, 3H), 2.12 (s, 3H), 1.93 (dd, J = 6.8, 1.2 Hz, 3H); characteristic signals for minor isomer: ^{1}H NMR δ 3.77 (s, 3H), 2.09 (s, 3H); Major Isomer: ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.6, 156.4, 142.5, 142.1, 137.2, 129.9, 129.5, 129.4, 129.3, 126.4, 62.0, 18.3, 16.6; IR (neat, cm^{-1}): 3061 (m), 2937 (s), 1683 (s), 1637 (s); HRMS (FAB) Calcd for $C_{13}H_{16}O_2NS$ ($M+H^+$): 250.0896. Found: 250.0898.

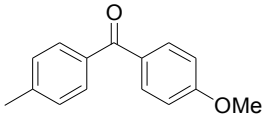
Table 1 Control Experiments

In the control experiments, the couplings of thiol esters with tributyl-(4-methoxyphenyl)stannane and 4-formylphenylboronic acid were conducted by the following general experimental procedure.

A Schlenk tube (entry 1-6) or microwave tube (entry 7-15) was charged with a stir bar. To the tube was added the thiol ester (0.1 mmol)[3], CuMeSal (0.02 mmol)[4] and organostannane (0.11 mmol)[5] or boronic acid (0.12 mmol).[5] After flushing with argon anhydrous and degassed DMF (1 mL) was added. The reaction mixture was stirred under the indicated reaction conditions. After cooling, ethyl ether (10 mL) was added to the mixture. The reaction mixture was washed with water, brine, dried over $MgSO_4$ and evaporated. The residue was purified by preparative plate silica chromatography using hexanes/EtOAc as the eluent.

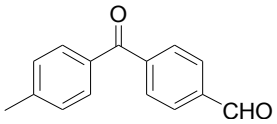
[3] In entries 1-13, thiol ester **3a** was employed; In entries 14 and 15, thiol ester *p*-tolyl(CO)S-*p*-tolyl was employed.
[4] In entries 11 and 12, CuMeSal was not added.
[5] In entry 13, neither oganostanane nor boronic acid was added.

4-Methyl-4'-methoxybenzophenone (entries 1, 3, 5, 7, 9 and 14)[6]



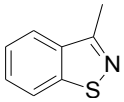
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid. Mp 91-92 °C (lit. {91.3-91.9 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.8 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3 H), 2.42 (s, 3 H); IR (neat, cm^{-1}) 1648 (s).

4-(4-Methyl-benzoyl)-benzaldehyde (entries 2, 4, 6, 8 and 10)[7]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid. Mp = 86-87 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13 (s, 1 H), 8.0 (d, *J* = 7.8 Hz, 2 H), 7.90 (d, *J* = 8.2 Hz, 2 H), 7.72 (d, *J* = 8.2 Hz, 2 H), 7.31 (d, *J* = 8.2 Hz, 2 H), 2.42 (s, 3 H); IR (neat, cm^{-1}) 1700 (s), 1640 (s).

3-Methyl-1,2-benzisothiazole [8]



Isolated along with the ketone product as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93-7.89 (m, 2H), 7.52-7.48 (m, 1H), 7.43-7.39 (m, 1H), 2.74 (s, 3 H); IR (neat, cm^{-1}): 3065 (m), 1733 (s), 1633 (s).

Scheme 1. Control Experiments with a Simple Thiol Ester

A dry microwave tube (10 mL) was charged with a stir bar. To the tube was added the thiol ester *p*-tolyl(CO)S-*p*-tolyl (0.1 mmol), CuMeSal (0.02 mmol), 1-phenyl-ethanone *O*-methyl-oxime (0.1 mmol) and tributyl-(4-methoxyphenyl)stannane (0.11 mmol) or 4-formylphenylboronic acid (0.12 mmol). The reaction tube was flushed with argon and sealed. Through the septum anhydrous and degassed DMF (1 mL) was added. The mixture was subsequently heated in a microwave reactor at 150 ^{o}C for 1 h. After cooling, ethyl ether (10 mL) was added to the mixture. The reaction mixture was washed with water (2×5 mL), brine (5 mL), dried over $MgSO_4$ and evaporated to afford a crude product. The ketone was *in situ* quantified (using pentamethylbenzene as an internal standard) by ^{1}H NMR.

Table 2. Cu-Catalyzed Desulfitative Coupling using a "Metallothionein Mimic"

General Procedure for Cu-Catalyzed Cross-Coupling of Thiol Esters with Boronic Acids. A dry microwave tube (10 mL) was charged with a stir bar. To the tube was added the corresponding thiol ester (0.1 mmol), boronic acid (0.12 mmol) and CuMeSal (0.02 mmol). The reaction tube was flushed with argon and sealed. Through the septum anhydrous and degassed DMF (1 mL) was added. The mixture was subsequently heated in a

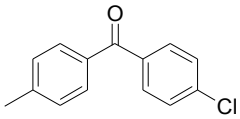
[6] Atkinson, G. E.; Fischer, P. M.; Chan, W. C. *J. Org. Chem.* **2000,** 65, 5048-5056.

[7] Ishiyama, T.; Kizaki, Hiroe.; Hayashi, T.; Suzuki, A.; Miyaura, N. *J. Org. Chem*., **1998**, *63*, 4726–4731.

[8] Buchwald, S. L.; Watson, B. T.; Lum, R. T. *J. Am. Chem. Soc.* **1987***, 109*, 7137-7141.

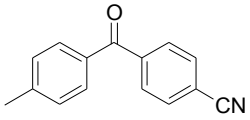
microwave reactor at 150 °C for 1 h. After cooling, ethyl ether (10 mL) was added to the mixture. The reaction mixture was washed with water (2×5 mL), brine (5 mL), dried over $MgSO_4$ and evaporated. The residue was purified by preparative plate silica chromatography using hexanes/EtOAc as the eluent.

4-Chloro-4'-methylbenzophenone (entry 1)[9]



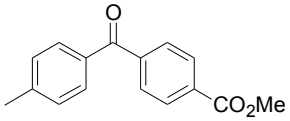
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (21 mg, 91%). Mp 126-127 °C (lit. {123-125°C}); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.0 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3 H); IR (neat, cm^{-1}) 1644 (s).

4-(4-methylbenzoyl)benzonitrile (entry 2)[10]



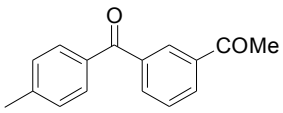
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (19 mg, 88%). Mp 160-161°C (lit. {165-167 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 2.46 (s, 3 H); IR (neat, cm^{-1}) 2227 (m), 1648 (s)

4-(4-methylbenzoyl)benzoic acid methyl ester (entry 3)[11]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (22 mg, 86%). Mp 119-120 °C (lit. {122-124 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.8 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 3.95 (s, 3H), 2.43 (s, 3 H); IR (neat, cm^{-1}) 1710 (s), 1660 (s).

1-[3-(4-methylbenzoyl)phenyl] ethanone (entry 4)[12]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (17 mg, 71%). Mp 72-73 °C (lit. {77.8-78 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (t, *J* = 1.2 Hz, 1H), 8.19 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.99 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.62 (t, *J* = 8.0 Hz,1H), 7.32 (d, *J* = 8.0 Hz, 2H), 2.66 (s, 3H), 2.46 (s, 3 H); IR (neat, cm^{-1}) 1687 (s), 1656 (s).

3-Benzoylbenzaldehyde (entry 5)[13]

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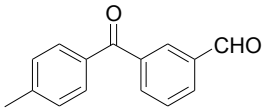
[9] Rao, M. L. N., Venkatesh, V. & Banerjee, D. *Tetrahedron* **2007**, *63*, 12917-12926.

[10] Wagner, G.; Voigt, B.; Steinbrueck, K.; Sekt. B. *Pharmazie* **1976**, *31*, 354-360.

[11] Gogoll, A.; Schaefer, H**.** *Liebigs Ann. Chem.* **1987**, *7,* 589-696.

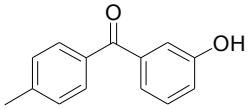
[12] Zhao, X.; Semenova, E. A.; Liao, C.; Nicklaus, M.; Pommier, Y.; Burke, T. R. *Bioorg. Med. Chem.* **2006**, *14*, 7816-7825.

[13] Miziak, P.; Zon, J.; Amrhein, N.; Gancarz, R. *Phytochemistry* **2007**, *68*, 407-415.



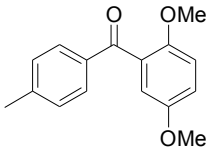
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (16 mg, 69%). Mp 88-90 °C (lit. {91-99 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.10 (s, 1H), 8.27 (s, 1H), 8.13-8.07 (m, 2H), 7.74-7.67 (m, 3H), 7.34 (d, *J* = 8.4 Hz, 2H), 2.47 (s, 3 H); IR (neat, cm^{-1}) 1702 (s), 1656 (s).

3-Hydroxy-4'-methylbenzophenone (entry 6)[14]



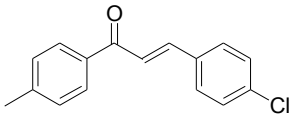
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (15 mg, 70%). Mp 120-122 °C (lit. {126 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.31-7.25 (m, 5H), 7.07-7.04 (m, 1H), 2.42 (s, 3 H); IR (neat, cm^{-1}) 1644 (s)

2,5-Dimethoxy-1-(4-methylbenzoyl)benzene (entry 7)[15]



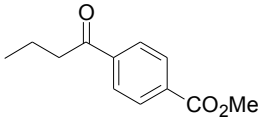
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (17 mg, 68%). Mp 60-61 °C (lit. {63°C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.67-6.86 (m, 3H), 3.76 (s, 3H), 3.66 (s, 3H), 2.39 (s, 3H); IR (neat, cm^{-1}) 1660 (s)

(*E*)-3-(4-chlorophenyl)-1-p-tolylprop-2-en-1-one (entry 8)[16]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (13 mg, 52%). Mp 146-147 °C (lit. {148-150 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 15.6 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 15.6 Hz, 1H), 7.41-7.39 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3H); IR (neat, cm^{-1}) 1656 (s).

4-Butyrylbenzoic acid methyl ester (entry 9)[17]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (17mg, 82%); Mp 81-82 °C (lit. {84°C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 3.93 (s, 3H), 2.96 (t, *J* = 7.6 Hz, 2H), 1.78-1.75 (m, 2H), 1.01 (t, *J* = 7.6 Hz, 3H); IR (neat, cm^{-1}) 1722 (s), 1675

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[14] Astoin, J.; Lepage, F.; Fromantin, J. P.; Poisson, M. *Eur. J. Med. Chem.* **1980**, *15*, 457-462.

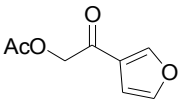
[15] Waterlot, C.; Hasiak, B.; Couturier, D.; Rigo, B. *Tetrahedron* **2001**, *57*, 4889-4902.

[16] Madapa, S.; Sridhar, D.; Yadav, G. P.; Maulik, P. R.; Batra, S. *Eur. J. Org. Chem.* **2007**, *26*, 4343-4351.

[17] Sumida, Y.; Takada, Y.; Hayashi, S.; Hirano, K.; Yorimitsu, H.; Oshima, K. *Chem. Asian J.* **2008**, *3,* 119-125.

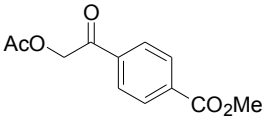
(s).

Acetoxymethyl 2-furyl ketone (entry 10)[18]



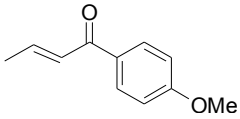
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a clear oil (12 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (t, *J* = 0.8 Hz, 1H), 7.46 (t, *J* = 2.0 Hz, 1H), 6.78 (dd, *J* = 2.0, 0.8 Hz, 1H), 5.01 (s, 2H), 2.20 (s, 3H); IR (neat, cm^{-1}) 1729 (s), 1629 (s).

4-Carbomethoxyphenacyl acetate (entry 11)[19]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (18 mg, 78%). Mp 78-80 °C (lit. {80-82 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.8 Hz, 2H), 7.98 (d, *J* = 8.8 Hz, 2H), 5.35 (s, 2H), 3.96 (s, 3H), 2.24 (s, 3H); IR (neat, cm^{-1}) 1752 (s), 1698 (s).

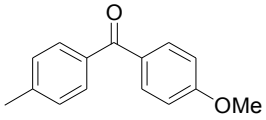
(*E*)-1-(4-Methoxyphenyl)-2-buten-1-one (entry 12)[20]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a clear oil (14 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.94 (m, 2H), 7.09-7.02 (m, 1H),6.97-6.90 (m, 3H), 3.88 (s, 3H), 2.01 (dd, *J* = 6.8, 1.6 Hz, 3H); IR (neat, cm^{-1}) 1668 (s).

General Procedure for Cu-Catalyzed Cross-Coupling of Thiol Esters with Organostananes. A dry microwave tube (10 mL) was charged with a stir bar. To the tube was added the corresponding thiol ester (0.1 mmol) and CuMeSal (0.02 mmol). The reaction vessel was flushed with argon and sealed. Through the septum the organostanane (0.11 mmol) and anhydrous and degassed DMF (1 mL) was added. The mixture was subsequently heated in a microwave reactor at 150 ^{o}C for 1 h. After cooling, ethyl ether (10 mL) was added to the mixture. The reaction mixture was washed with water (2×5 mL), brine (5 mL), dried over $MgSO_4$ and evaporated. The residue was purified by preparative plate silica chromatography using hexanes/EtOAc as the eluent.

4-Methyl-4'-methoxybenzophenone (entry 13)[6]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded title compound as a white solid (22 mg, 95%). Mp 91-92 °C (lit. {91.3-91.9 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.8 Hz, 2H), 7.67 (d, *J* = 8.0 Hz,

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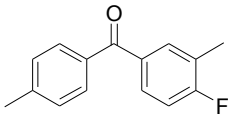
[18] Allcock, H. W.; Kipnis, F.; Ornfelt, J.; Allen, P. *J. Am. Chem. Soc.* **1948***, 70,* 3949-3950.

[19] Liebeskind, L. S.; Srogl, J. *J. Am. Chem. Soc.* **2000***, 122,*11260-11261.

[20] Ochiai, M.; Yoshimura, A.; Mori, T.; Nishi, Y.; Hirobe, M. *J. Am. Chem. Soc.* **2008***, 130,* 3742-3743.

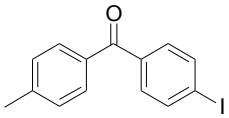
2H), 7.27 (d, *J* = 8.0 Hz, 2H), 6.95 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3 H), 2.42 (s, 3 H); IR (neat, cm^{-1}) 1648 (s).

4-Fluoro-3-methyl-4'-methylbenzophenone (entry 14)



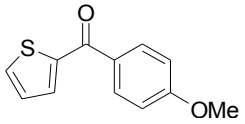
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (19 mg, 81%). Mp 92-93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.67 (m, 3H), 7.63-7.59 (m, 1H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 8.8 Hz, 1H), 2.45 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 165.3 (d, *J* = 251 Hz), 143.4, 135.1, 134.0, 133.9 (d, *J* = 6.0 Hz), 130.3, 130.1 (d, *J* = 8.9 Hz), 129.2, 125.4 (d, *J* = 18 Hz), 115.1 (d, *J* = 22 Hz), 21.8, 14.8; ^{19}F NMR (375 MHz, $CDCl_3$) δ -120.8; IR (neat, cm^{-1}) 1648 (s); HRMS (FAB) Calcd for $C_{15}H_{14}OF$ ($M+H^+$): 229.1023. Found: 229.1024.

4-Iodo-4'-methylbenzophenone (entry 15)[21]



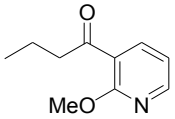
Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (22 mg, 68%). Mp 149-150 °C (lit. {157.5-158 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 2.45 (s, 3 H); IR (neat, cm^{-1}) 1644 (s).

2-(4-Methoxybenzoyl)thiophene (entry 16)[22]



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (19 mg, 86%). Mp 73-74 °C (lit. {74-75 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.2 Hz, 2H), 7.63 (dd, *J* = 4.8, 1.2 Hz, 1H), 7.58 (dd, *J* = 4.0, 1.2 Hz, 1H), 7.10 (dd, *J* = 4.8, 4.0 Hz, 1H), 6.93 (d, *J* = 9.2 Hz, 2H), 3.82 (s, 3H); IR (neat, cm^{-1}) 1656 (s).

1-(2-Methoxy-pyridin-3-yl)-butan-1-one (entry 17)



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a clear oil (13 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 2.8 Hz, 1H), 8.07-8.05 (m, 1H), 6.99-6.96 (m, 1H), 4.05 (s, 3H), 3.00 (t, *J* = 7.2 Hz, 2H), 1.74-1.68 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 162.0, 150.5, 139.9, 122.2, 117.2, 53.9, 45.4, 17.7, 14.0; IR (neat, cm^{-1}) 1679 (s); HRMS (FAB) Calcd for $C_{10}H_{14}O_2N$ ($M+H^+$): 180.1019. Found: 180.1017.

Cyclohexyl *p*-methoxyphenyl ketone (entry 18)[23]

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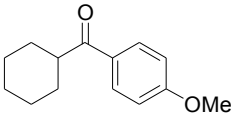
[21] Kikukawa, K.; Idemoto, T.; Katayama, A.; Kono, K.; Wada, F.; Matsuda, T, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1511-1514.

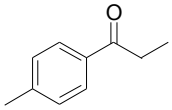
[22] Zhao, W.; Carreira, E. M. *Chem. Eur. J.* **2007***, 13*, 2671-2685.



Purification by preparative TLC (hexanes/EtOAc 4:1) afforded the title compound as a white solid (14 mg, 62%). Mp 60-62 °C (lit. {61-63 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 9.2 Hz, 2H), 6.92 (d, *J* = 9.2 Hz, 2H), 3.85 (s, 3H), 3.23-3.16 (m, 1H), 1.85-1.20 (m, 10H); IR (neat, cm^{-1}) 1671 (s).

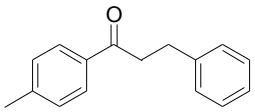
Figure 1. Cu-Catalyzed Desulfitative Couplings: Aliphatic Transfer Reagents and Peptidyl Ketone Synthesis

Ethyl 4-methylphenyl ketone [24]



A dry microwave tube (10 mL) was charged with a stir bar. To the tube was added *S*-2-(1-(methoxyimino)ethyl)phenyl 4-methylbenzothioate (**3a**) (30 mg, 0.1 mmol) and CuMeSal (4 mg, 0.02 mmol). The reaction tube was flushed with argon and sealed. Through the septum triethylborane (11 mg, 0.11 mmol) and anhydrous and degassed DMF (1 mL) was added. The mixture was subsequently heated in a microwave reactor at 150 ^{o}C for 1 h. After cooling, the reaction mixture was diluted with ethyl ether (10 mL), washed with (2×5 mL), brine (5 mL), dried over $MgSO_4$ and evaporated. The residue was purified by preparative plate silica chromatography using CH_2Cl_2 as the eluent to afford the title compound as a clear oil (12 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.8 Hz, 2H), 3.01 (q, *J* = 7.2 Hz, 2H), 2.41 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); IR (neat, cm^{-1}) 1683 (s).

4-Methylphenyl phenethyl ketone [25]



A dry microwave tube (10 mL) was charged with a stir bar. To the tube was added *S*-2-(1-(methoxyimino)ethyl)phenyl 4-methylbenzothioate (**3a**) (30 mg, 0.1 mmol) and CuMeSal (4 mg, 0.02 mmol). The reaction tube was flushed with argon and sealed. Through the septum *B*-2-phenylethyl-9-BBN (0.22 mL [0.5 M in THF], 0.11 mmol) and anhydrous and degassed DMF (1 mL) was added. The mixture was subsequently heated in a microwave reactor at 150 ^{o}C for 1 h. After cooling, the reaction mixture was diluted with ethyl ether (10 mL), washed with water (2×5 mL), brine (5 mL), dried over $MgSO_4$ and evaporated. The residue was purified by preparative plate silica chromatography using hexanes/EtOAc (4:1) as the eluent to afford the title compound as a white solid (16 mg, 71%). Mp 64-65 °C (lit. {62-64 °C}); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.32-7.20 (m, 7H), 3.39 (t, *J* = 8.0 Hz, 2H), 3.08 (t, *J* = 8.0 Hz, 2H), 2.40 (s, 3H); IR (neat, cm^{-1}) 1683 (s).

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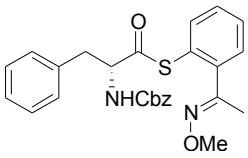
[23] Rao, M. L. N.; Venkatesh, V.; Banerjee, D. *Tetrahedron* **2007***, 63*, 12917-12926.

[24] Olah, G. A.; Forsyth, D. A. *J. Am. Chem. Soc.* **1975***, 97,* 3137-3141.

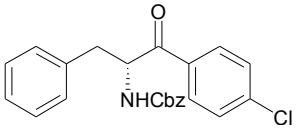
[25] Li, J-P.; Zhang, Y-X.; Ji, Y. *J. Chin. Chem. Soc.* **2008***, 55*, 390-393.

(+)-(*R,E*)-*S*-2-(1-(Methoxyimino)ethyl)phenyl 2-(benzyloxycarbonylamino)-3-phenylpropanethioate



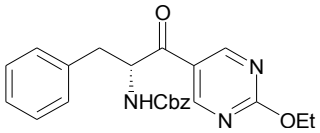
To a solution of 1-(2-mercaptophenyl)ethanone *O*-methyloxime (181 mg, 1.0 mmol) and *N*-Cbz-D-phenylalanine (299 mg, 1.0 mmol) in ethyl acetate (10 mL) was added EDC (192 mg, 1.0 mmol in 10 mL CH_2Cl_2) dropwise at 0 ºC. After addition of EDC, the ice bath was removed and the reaction was stirred at room temperature overnight. The reaction crude was washed by 1M HCl (10 mL), $NaHCO_3$ (10 mL) and brine (5 mL). The organic layer was dried over $MgSO_4$ and concentrated. Purification by flash chromatography (silica gel 6:1 hexanes:EtOAc) afforded the title compound as a white solid (286 mg, 62%). Mp 50-51 °C; HPLC Chiral OJ-RH, λ= 254 nm, Method: Flow: 1.0 mL/min; T = 30 °C; Gradient: 50% H_2O in CH_3CN during 25 min to 75% CH_3CN, during 28 min to 100% CH_3CN hold for 2 min, D-isomer t_R =13.8 min, L-isomer t_R =15.3 min, ee > 99%. ^{1}H NMR (400 MHz, $CDCl_3$) 7.48-7.27 (m, 12H), 7.18 (d, *J* = 8.4 Hz, 2H), 5.19-5.09 (m, 3H), 4.83-4.81 (m, 1H), 3.95 (s, 3H), 3.18-3.13 (m, 2H), 2.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 156.2, 155.8, 142.3, 137.1, 136.2, 135.5, 130.2, 129.7, 129.6, 129.4, 129.0, 128.8, 128.5, 128.3, 127.5, 125.8, 67.5, 62.1, 61.7, 38.3, 16.7; IR (neat, cm^{-1}): 3327 (m), 3034 (m), 2937 (m), 1698 (s); HRMS (FAB) Calcd for $C_{26}H_{27}O_4N_2S$ ($M+H^+$): 463.1686. Found: 463.1692; $[\alpha]_D^{20}$ +57.7 (*c* 2.1, $CHCl_3$).

(-)-(*R*)-benzyl 1-(4-chlorophenyl)-1-oxo-3-phenylpropan-2-ylcarbamate



A dry microwave tube (10 mL) was charged with a stir bar. To the tube was added (+)-(*R,E*)-*S*-2-(1-(methoxyimino)ethyl)phenyl 2-(benzyloxycarbonylamino)-3-phenylpropanethioate (**4**) (46 mg, 0.1 mmol), 4-chlorophenylboronic acid (17 mg, 0.11 mmol) and CuMeSal (4 mg, 0.02 mmol). The reaction tube was flushed with argon and sealed. Through the septum anhydrous and degassed DMF (1 mL) was added. The mixture was subsequently heated in a microwave reactor at 90 ^{o}C for 1 h. After cooling, reaction mixture was diluted with ethyl ether (10 mL), washed with water (2×5 mL), brine (5 mL), dried over $MgSO_4$ and evaporated. The residue was purified by preparative plate silica chromatography using hexanes/EtOAc (4:1) as the eluent to afford the title compound as a white solid (33 mg, 82%). Mp 87-88 °C; HPLC Chiral OJ-RH, λ= 254 nm, Method: Flow: 1.0 mL/min; T = 30 °C; Gradient: 50% H_2O in CH_3CN during 25 min to 75% CH_3CN, during 28 min to 100% CH_3CN hold for 2 min, D-isomer t_R =18.3 min, L-isomer t_R =23.7 min, ee > 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.8 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.39-7.31 (m, 5H), 7.21-7.18 (m, 3H), 6.98-6.96 (m, 2H), 5.65 (d, *J* = 8.0 Hz, 1H), 5.57-5.53 (m, 1H), 5.15 (AB q, *J* = 12 Hz, 2H), 3.26 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.10 (dd, *J* = 14.0, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 155.8, 140.5, 136.4, 135.5, 133.2, 130.2, 129.6, 129.4, 128.7, 128.6, 128.4, 128.2, 127.3, 67.1, 56.5, 39.2; IR (neat, cm^{-1}) 1722 (s), 1687 (s), 1498 (s); HRMS (FAB) Calcd for $C_{23}H_{21}O_3NCl$ ($M+H^+$): 394.1204. Found: 394.1209. $[\alpha]_D^{20}$ -21.0 (*c* 0.4, $CHCl_3$).

(-)-(*R*)-benzyl 1-(2-ethoxypyrimidin-5-yl)-1-oxo-3-phenylpropan-2-ylcarbamate



A dry microwave tube (10 mL) was charged with a stir bar. To the tube was added (+)-(*R,E*)-*S*-2-(1-(methoxyimino)ethyl)phenyl 2-(benzyloxycarbonylamino)-3-phenylpropanethioate (**4**) (46 mg, 0.1 mmol) and CuMeSal (4 mg, 0.02 mmol). The reaction tube was flushed with argon and sealed. Through the septum 2-ethoxyl-5-(tributylstannyl)pyrimidine (45 mg, 0.11 mmol) and anhydrous and degassed DMF (1 mL) was added. The mixture was subsequently heated in a microwave reactor at 150 ^{o}C for 1 h. After cooling, reaction mixture was diluted with ethyl ether (10 mL), washed with water (2×5 mL), brine (5 mL) dried over $MgSO_4$ and evaporated. The residue was purified by preparative plate silica chromatography using hexanes/EtOAc (4:1) as the eluent to afford the title compound as a white solid (31 mg, 76%). Mp 91-92 °C; HPLC Chiral OJ-RH, λ= 254 nm, Method: Flow: 1.0 mL/min; T = 30 °C; Gradient: 50% H_2O in CH_3CN during 25 min to 75% CH_3CN, during 28 min to 100% CH_3CN hold for 2 min, D-isomer t_R =15.3 min, L-isomer t_R =12.1 min, ee > 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 2H), 7.37-7.33 (m, 5H), 7.24-7.19 (m, 3H), 7.05-7.03 (m, 2H), 5.62 (d, *J* = 8.4 Hz, 1H), 5.41-5.36 (m, 1H), 5.14 (AB q, *J* = 12 Hz, 2H), 4.54 (q, *J* = 7.2 Hz, 2H), 3.20 (dd, *J* = 13.6, 5.6 Hz, 1H), 3.10 (dd, *J* = 13.6, 5.6 Hz, 1H), 1.48 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 167.0, 160.7, 155.8, 136.2, 135.2, 129.5, 128.9, 128.7, 128.5, 128.3, 127.5, 123.0, 67.3, 65.0, 56.8, 39.3, 14.5; IR (neat, cm^{-1}) 1718 (s), 1687 (s), 1590 (s) 1498 (s); HRMS (FAB) Calcd for $C_{23}H_{24}O_4N_3$ ($M+H^+$): 406.1761. Found: 406.1765. $[\alpha]_D^{20}$ -36.4 (*c* 0.5, $CHCl_3$).