Synthetic Autocatalysts show Organocatalysis of other Reactions

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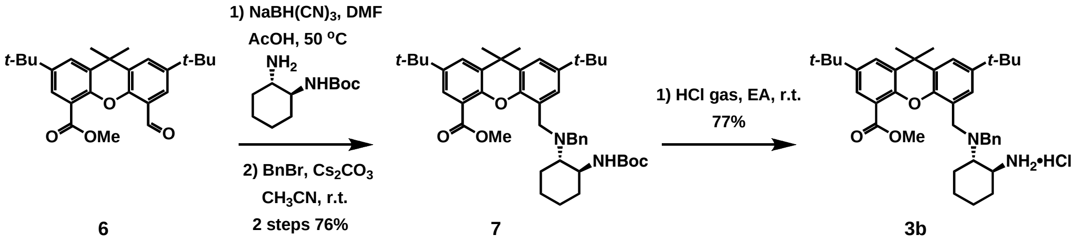
Supporting Information

General Experimental

All reagents were obtained from commercial suppliers and used without further purification. NMR spectra were recorded on a Bruker DRX-600 spectrometer at 300 K. Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. Reverse Phase High Performance Liquid Chromatography (HPLC) for analysis was performed on Hewlett Packard HP-1100 series system with following gradient: 5 to 40% over 7 min, 40 to 100% over 25 min and then 100% over 5 min CH_3CN in H_2O (0.1% TFA), with the flow rate of 0.5 mL/min on a GL Sciences Inc. Inertsil-ODS-1HO, 4.6 x 150 mm column. Peak areas were integrated with 254 nm. MALDI-FTMS experiments were performed on an IonSpec FTMS mass spectrometer.

Experimental Procedures and Characterization

Scheme S1. Synthesis of the amine **3b**



Boc-Protected Amine 7

1) $NaBH(CN)_3$ (446 mg, 7.10 mmol) and AcOH (812 μL, 14.2 mmol) was added to the aldehyde **6** (580 mg, 1.42 mmol) and trans-N-Boc-1,2-diaminocyclohexane (608 mg, 2.84 mmol) in DMF (14 mL) at 0 °C. After 24 h of stirring at 50 °C, the mixture was quenched with aqueous solution of the saturated NH_4Cl, and extracted with ethyl acetate. The extract was washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residue was used for the next reaction without further purification.

2) Benzyl bromide (338 μL, 2.84 mmol) and Cs_2CO_3 (1.39 g, 4.26 mmol) was added to the residue in CH_3CN (14 mL) at 0 °C. After 6 h of stirring at room temperature, the mixture was quenched with saturated aqueous NH_4Cl, and extracted with ethyl acetate. The extract was washed with saturated aqueous sodium bicarbonate and brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with 15% ethyl acetate in hexane to afford ester **7** (752 mg, 1.08 mmol, 76% in 2 steps) as a colorless oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 2.4 Hz, 1H), 7.62 (d, *J* = 2.4 Hz, 1H), 7.38 – 7.22 (m, 7H), 5.32 (s, 1H), 4.29 (d, *J* = 13.6 Hz, 1H), 4.03 (s, 3H), 3.93 – 3.85 (m, 1H), 3.58 – 3.52 (m, 1H), 3.45 (d, *J* = 13.6 Hz, 1H), 3.43 – 3.35 (m, 1H), 2.48– 2.42 (m, 1H), 2.37 (td, *J* = 3.0, 11.4 Hz, 1H), 2.32 – 2.25 (m, 1H), 1.84 – 1.80 (m, 1H), 1.76 – 1.57 (m, 1H), 1.67 (s, 3H), 1.61 (s, 3H), 1.48 (s, 9H), 1.45 – 1.33 (m, 1H), 1.38 (s, 9H), 1.37 (s, 9H), 1.29 – 1.26 (m, 1H), 1.18 – 1.07 (m, 1H), 0.97 – 0.91 (m, 1H);

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.0, 156.4, 148.6, 147.1, 145.0, 131.7, 129.3 x 2, 129.2, 128.3, 128.1, 127.1, 126.9, 126.8, 126.5, 125.7, 120.6, 118.6, 78.8, 62.0, 53.0, 52.3, 51.8, 46.8, 35.1, 34.7, 33.6, 32.0, 31.9, 31.6, 31.4, 28.8, 25.9, 24.8, 24.0, 23.8; **HRMS** (MALDI-FTMS: MH^+) calcd. for $C_{44}H_{61}N_2O_5^+$ 697.4581, found 697.4581.

Amine 3b

1) HCl gas was bubbled through a solution of the ester **7** (752 mg, 1.08 mmol) in

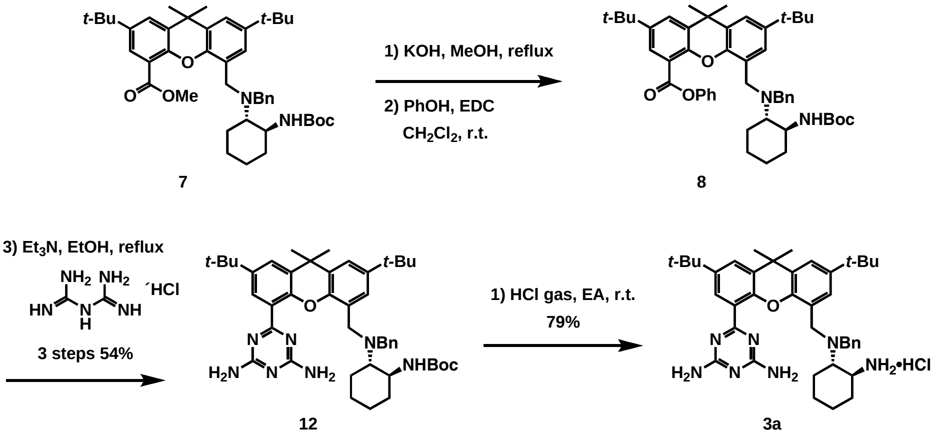
ethyl acetate (11 mL) for 2 min. at 0 °C. After being stirred at room temperature for 12 h, the mixture was concentrated *in vacuo*. The residue was diluted with diethyl ether and filtered. The filtrate was dried *in vavuo* to afford amine **3b** (526 mg, 0.83 mmol, 77%) as a white solid.

^{1}H NMR (600 MHz, DMSO-d_6, mixture of rotamers) δ 9.02 (s, 0.5H), 8.86 (s, 1H), 8.21 (d, J = 1.9 Hz, 0.5H), 7.87 – 7.65 (m, 3.5H), 7.61 (d, J = 2.1 Hz, 0.5H), 7.60 (d, J = 2.1 Hz, 0.5H), 7.44 – 7.36 (m, 2H), 7.35 (d, J = 2.1 Hz, 0.5H), 7.26 (t, J = 7.3 Hz, 2H), 7.21 (t, J = 7.2 Hz, 1H), 4.91 (d, J = 10.6 Hz, 0.5H), 4.78 (dd, J = 8.8, 12.5 Hz, 0.5H), 4.64 (dd, J = 7.9, 13.6 Hz, 0.5H), 4.29 (dd, J = 2.3, 13.0 Hz, 0.5H), 4.08 – 3.74 (m, 5H), 3.56 (d, J = 13.9 Hz, 1H), 3.27 (t, J = 9.8 Hz, 0.5H), 3.10 – 3.02 (s, 0.5H), 2.63 (td, J = 2.8, 11.1 Hz, 0.5H), 2.45 (d, J = 10.3 Hz, 0.5H), 2.20 – 2.13 (m, 0.5H), 2.07 – 1.90 (m, 1H), 1.86 – 1.80 (m, 0.5H), 1.77 – 1.50 (m, 7H), 1.50 – 1.24 (m, 19H), 1.23 – 1.09 (m, 1H), 1.09 – 0.88 (m, 2H);

^{13}C NMR (151 MHz, DMSO-d_6, mixture of rotamers) δ 166.0, 165.4, 147.0, 146.4, 146.1, 145.6, 145.4, 145.2, 144.8, 139.3, 131.8, 131.2, 131.1, 130.7, 129.5, 129.4, 128.9, 128.8, 128.8, 128.5, 128.2, 127.2, 126.9, 125.5, 125.4, 125.3, 125.0, 121.1, 118.3, 117.6, 115.4, 62.6, 62.1, 59.7, 53.4, 52.4, 52.2, 52.2, 50.1, 48.0, 47.0, 40.1, 34.6, 34.4, 34.3, 34.3, 34.2, 32.9, 32.2, 32.1, 31.3, 31.2, 31.1, 31.1, 31.0, 30.3, 29.8, 24.7, 23.6, 23.3, 23.3, 22.6, 22.4, 20.7;

HRMS (MALDI-FTMS: MH$^+$) calcd. for $C_{39}H_{53}N_2O_3^+$ 597.4055, found 597.4053.

Scheme S2. Synthesis of amine **3a**



Boc-Protected Amine 12

1) KOH (806 mg, 14.3 mmol) was added to a solution of the ester **7** (1.00 g, 1.43 mmol) in MeOH (14 mL) at 0 ^oC. After 12 h of stirring at reflux, the mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The extract was washed with brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residue was used for the next reaction without further purification.

2) To a stirred solution of the residue in CH_2Cl_2 (28 mL) was added Phenol (403 mg, 4.29 mmol), DCC (443 mg, 2.15 mmol) and DMAP (263 mg, 2.15 mmol) at 0 ^oC. After 6 h of stirring at room temperature, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with 10% ethyl acetate in hexane to afford semi-pure phenyl ester **8**. The residue was used for the next reaction without further purification.

3) Biguanide•2HCl (979 mg, 7.15 mmol) and triethylamine (1.4 mL) was added to the residue in EtOH (14 mL) at room temperature. After 2 days of stirring at reflux, the mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with 20% acetone in CH_2Cl_2 to afford triazine **12** (576 mg, 0.78 mmol, 54% in 3 steps) as a white solid.

^{1}H NMR (600 MHz, DMSO-*d₆*) δ 8.31 (s, 1H), 7.52 (d, *J* = 2.4 Hz, 1H), 7.37 (d, *J* = 2.3 Hz, 1H), 7.29 – 7.22 (m, 3H), 7.20 – 7.13 (m, 3H), 6.85 – 6.65 (m, 4H), 5.45 (s, 1H), 3.97 (d, *J* = 13.6 Hz, 1H), 3.66 (d, *J* = 11.2 Hz, 1H), 3.38 – 3.32 (m, 1H), 3.25 – 3.20 (m, 1H), 3.22 (d, *J* = 13.6 Hz, 1H), 2.12 (td, *J* = 3.0, 11.4 Hz, 1H), 2.08 – 2.04 (m, 1H), 1.82– 1.76 (m, 1H), 1.71 – 1.65 (m, 1H), 1.60 (s, 3H), 1.55 (s, 3H), 1.51 – 1.44 (m, 1H), 1.36 (s, 9H), 1.31 (s, 9H), 1.25 (s, 9H), 1.20 – 1.09 (m, 2H), 0.96 – 0.79 (m, 2H);

^{13}C NMR (151 MHz, DMSO-*d₆*) δ 172.3, 167.2, 155.1, 146.5, 145.9, 144.6, 144.2, 140.6, 130.4, 128.9, 128.6, 127.8, 127.0, 126.5, 126.4, 124.7, 124.5, 123.1, 120.3, 79.2, 77.5, 62.1, 52.5, 50.7, 46.9, 34.5, 34.2, 34.1, 33.0, 31.6, 31.4, 31.3, 28.2, 25.3, 24.3, 23.0;
HRMS (MALDI-FTMS: MH^+) calcd. for $C_{45}H_{62}N_7O_3^+$ 748.4908, found 748.4904.

Amine 3a

1) HCl gas was bubbled through a solution of the diaminotriazine **12** (250 mg,

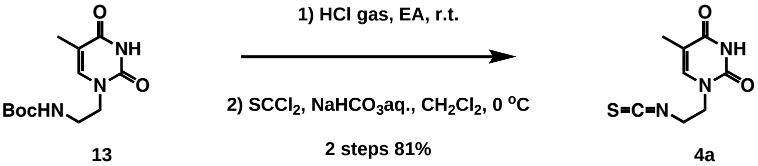
335 μmol) in ethyl acetate (3.4 mL) for 2 min. at 0 ^{o}C. After 6 h of stirring at room temperature, the mixture was concentrated *in vacuo*. The residue was diluted with ethyl acetate and filtered. The filtrate was dried *in vavuo* to afford amine **3a** (181 mg, 265 μmol, 79%) as a white solid.

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.88 – 8.35 (m, 4H), 7.80 (s, 1H), 7.78 (s, 1H), 7.62 – 7.58 (m, 3H), 7.58 (s, 1H), 7.38 – 7.34 (m, 2H), 7.36 (s, 1H), 7.27 – 7.20 (m, 3H), 4.89 (d, *J* = 11.9 Hz, 1H), 4.60 (d, *J* = 11.9 Hz, 1H), 3.77 – 3.72 (m, 2H), 3.40 – 3.35 (m, 1H), 3.15 – 3.05 (m, 1H), 2.49 – 2.40 (m, 1H), 2.05 – 1.98 (m, 1H), 1.80 – 1.72 (m, 2H), 1.67 (s, 3H), 1.60 (s, 3H), 1.38 – 1.33 (m, 1H), 1.34 (s, 9H), 1.30 (s, 9H), 1.23 – 1.16 (m, 1H), 1.02 – 0.91 (m, 1H), 0.89 – 0.75 (m, 1H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.0, 162.0, 145.7, 145.7, 145.3, 144.9, 138.9, 130.6, 128.9, 128.7, 128.2, 128.1, 127.9, 126.9, 125.4, 125.2, 121.2, 118.3, 79.3, 49.8, 34.5, 34.4, 34.3, 32.8, 31.6, 31.3, 31.3, 31.1, 29.7, 24.6, 23.5, 22.3, 21.1.

HRMS (MALDI-FTMS: MH^{+}) calcd. for $C_{40}H_{54}N_7O^{+}$ 648.4384, found 648.4386.

Scheme S3. Synthesis of thymine derived thioisocyanate **4a**



Thymine Derived Thioisocyanate 4a

1) HCl gas was bubbled through a solution of the **13** (1.50 g, 5.57 mmol) in ethyl acetate (60 mL) for 2 min. at 0 ^{o}C. After 12 h of stirring at room temperature, the mixture was concentrated *in vacuo*. The residue was diluted with ethyl acetate and filtered. The filtrate was dried *in vavuo* to afford amine as a white solid. The amine was used for the next reaction without further purification.

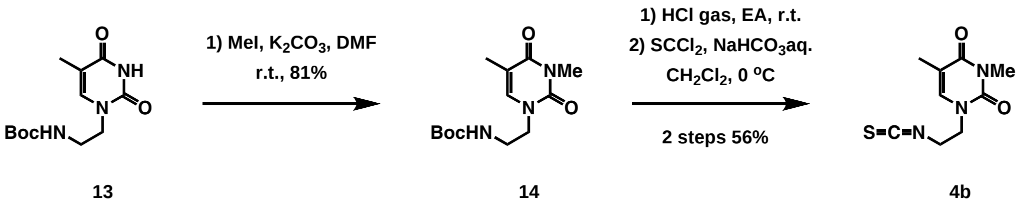
2) Thiophosgene (849 μL, 11.2 mmol) was added to a solution of the amine in CH_2Cl_2 (50 mL) and saturated aqueous sodium bicarbonate (5 mL) at 0 °C. After 6 h of stirring at same temperature, the mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The extract was washed with brine, dried over magnesium sulfate, filtered and concentrated *in vacuo.* The residue was purified by column chromatography on silica gel, eluting with 3% methanol in CH_2Cl_2 to afford thioisocyanate **4a** (952 mg, 4.51 mmol, 81% in 2 steps) as a pale yellow solid.

^{1}H NMR (600 MHz, DMSO-d_6) δ 11.40 (s, 1H), 7.56 (s, 1H), 3.99 – 3.88 (m, 4H), 1.76 (s, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 164.2, 150.8, 141.2, 129.8, 108.8, 46.4, 43.7, 11.9.

HRMS (MALDI-FTMS: MH^+) calcd. for $C_8H_{10}N_3O_2S^+$ 212.0488, found 212.0485.

Scheme S4. Synthesis of thymine derived thioisocyanate **4b**



Thymine Derived Boc-Protected Amine 14

1) Methyl iodide (691 mL, 11.2 mmol) and K_2CO_3 (2.31 g, 16.7 mmol) was added to a solution of **13** (1.50 g, 5.57 mmol) in DMF (60 mL) at 0 °C. After 6 h of stirring at room temperature, the mixture was quenched with 1M HCl and extracted with ethyl acetate. The extract was washed with saturated aqueous sodium bicarbonate, H_2O and brine, dried over magnesium sulfate, filtered and concentrated *in vacuo.* The residue was purified by column chromatography on silica gel, eluting with 2% methanol in chloroform to afford **14** (1.28 g, 4.51 mmol, 81%) as pale yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 6.93 (s, 1H), 5.17 (s, 1H), 3.80 (t, *J* = 5.7 Hz, 2H), 3.36 – 3.29 (m, 2H), 3.26 (s, 3H), 2.13 – 2.07 (m, 1H), 1.84 (s, 3H), 1.34 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.7, 156.2, 151.9, 139.2, 109.4, 79.8, 49.1, 39.4, 28.4, 28.0, 13.1.

HRMS (MALDI-FTMS: MH^+) calcd. for $C_{13}H_{22}N_3O_4^+$ 284.1605, found 284.1602.

Thymine Derived Thioisocyanate 4b

1) HCl gas was bubbled through a solution of **14** (1.28 g, 4.51 mmol) in ethyl acetate (45 mL) for 2 min. at 0 °C. After 10 h of stirring at room temperature, the mixture was concentrated *in vacuo*. The residue was used for the next reaction without further purification.

2) Thiophosgene (688 μL, 9.02 mmol) was added to a solution of the residue in CH_2Cl_2 (50 mL) and saturated aqueous sodium bicarbonate (5 mL) at 0 °C. After 6 h of stirring at same temperature, the mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The extract was washed with brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with 1% methanol in CH_2Cl_2 to afford thioisocyanate **4b** (568 mg, 2.52 mmol, 56% in 2 steps) as a pale yellow solid.

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.63 (s, 1H), 4.01 (t, *J* = 5.8 Hz, 2H), 3.95 (t, *J* = 5.8 Hz, 2H), 3.19 (s, 3H), 1.82 (s, 3H).

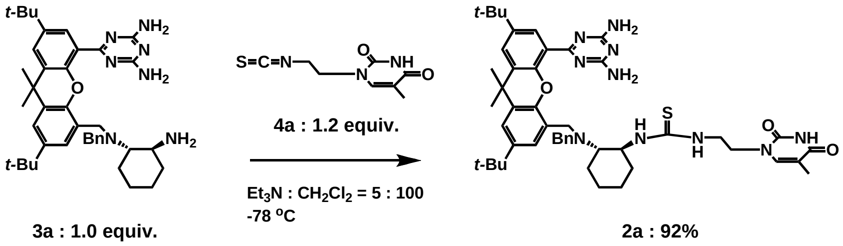
^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 164.1, 151.9, 140.6, 130.8, 108.7, 48.4, 44.6, 28.4, 13.4.

HRMS (MALDI-FTMS: MH^+) calcd. for $C_9H_{12}N_3O_2S^+$ 226.0645, found 226.0648.

General procedure for coupling reaction of amine 3a or 3b with thymine derived thioisocyanate 4a or 4b:

Thymine derived thioisocyanate **4a** or **4b** (1.2 equiv.) was treated with a solution of amine **3a** or **3b** (1.0 equiv.) in CH_2Cl_2 (7.6 mM) and triethylamine (0.4 mM) at -78 ^{o}C in an acetone dry ice bath. After 24 h of stirring at -78 ^{o}C, the reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel, eluting with 20% acetone in chloroform to afford the thiourea.

Scheme S5. Coupling reaction of amine **3a** and thymine derived thioisocyanate **4a**



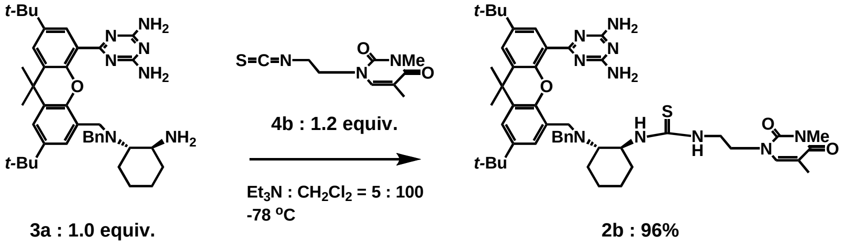
Thiourea 2a

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 7.70 (d, *J* = 2.4 Hz, 1H), 7.58 (d, *J* = 2.4 Hz, 1H), 7.35 – 7.26 (m, 3H), 7.25 – 7.18 (m, 3H), 7.13 (t, *J* = 7.3 Hz, 1H), 7.03 (s, 1H), 6.60 – 6.48 (m, 2H), 4.06 – 3.90 (m, 3H), 3.94 (s, 3H), 3.91 – 3.68 (m, 4H), 3.72 (d, *J* = 13.9 Hz, 1H), 3.60 (d, *J* = 13.7 Hz, 1H), 3.27 (s, 3H), 2.56 (t, *J* = 9.8 Hz, 1H), 2.25 (s, 1H), 2.06 (d, *J* = 9.9 Hz, 1H), 1.85 – 1.73 (m, 1H), 1.79 (s, 3H), 1.73 – 1.65 (m, 1H), 1.58 (s, 6H), 1.51 – 1.38 (m, 1H), 1.38 – 1.16 (m, 1H), 1.32 (s, 9H), 1.30 (s, 9H), 1.14 – 1.01 (m, 1H), 1.02 – 0.90 (m, 1H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 182.4, 167.4, 164.2, 152.7, 149.1, 147.3, 146.4, 145.4, 141.0, 139.2, 132.2, 129.5, 129.3, 128.6, 127.4, 127.2, 127.0, 126.6, 126.6, 120.9, 118.3, 110.3, 62.8, 55.5, 53.4, 52.6, 48.7, 44.2, 35.3, 35.0, 34.9, 33.5, 32.00, 31.9, 31.8, 31.7, 30.1, 28.3, 26.0, 25.1, 14.5, 13.3.

HRMS (MALDI-FTMS: MH$^+$) calcd. for $C_{48}H_{63}N_{10}O_3S^+$ 859.4805, found 859.4792.

Scheme S6. Coupling reaction of amine **3a** and thymine derived thioisocyanate **4b**



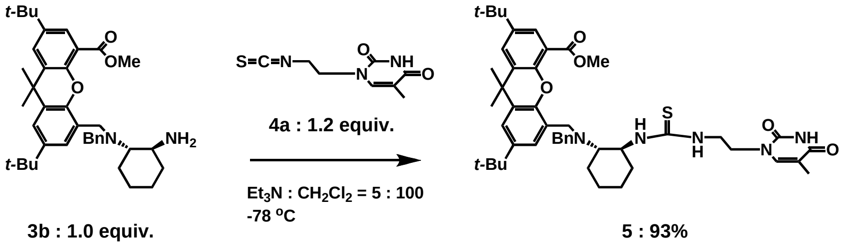
Thiourea 2b

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 11.25 (s, 1H), 7.69 (d, *J* = 2.1 Hz, 1H), 7.67 – 7.61 (m, 1H), 7.59 (d, *J* = 2.1 Hz, 1H), 7.38 (s, 1H), 7.30 – 7.24 (m, 3H), 7.20 – 7.13 (m, 4H), 6.83 (s, 1H), 4.05 – 3.88 (m, 1H), 3.93 (s, 3H), 3.86 – 3.77 (m, 1H), 3.76 – 3.69 (s, 2H), 3.65 – 3.45 (m, 3H), 3.32 (s, 2H), 2.56 – 2.46 (m, 1H), 2.16 – 2.00 (m, 2H), 1.76 – 1.69 (m, 1H), 1.63(s, 3H), 1.62 – 1.57 (m, 1H), 1.59 (s, 3H), 1.53 (s, 3H), 1.30 (s, 9H), 1.29 – 1.15 (m, 2H), 1.28 (s, 9H), 1.10 – 0.85 (m, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 166.4, 164.3, 151.0, 146.9, 145.5, 145.2, 144.6, 141.5, 140.0, 131.1, 128.4, 128.2, 128.0, 127.0, 126.5, 126.3, 125.6, 125.2, 120.5, 118.4, 108.1, 62.3, 52.9, 52.3, 46.9, 46.1, 42.2, 40.1, 34.3, 34.2, 32.9, 32.3 31.3, 31.2, 31.1, 25.1, 24.5, 11.8.

HRMS (MALDI-FTMS: MH$^+$) calcd. for $C_{49}H_{65}N_{10}O_3S^+$ 873.4961, found 873.4950.

Scheme S7. Coupling reaction of amine **3b** and thymine derived thioisocyanate **4a** was done as described above.



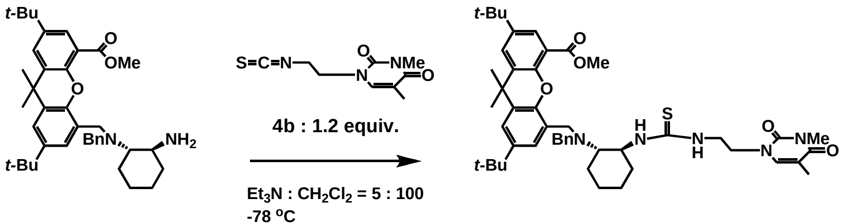
Thiourea 5

^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 11.24 (s, 1H), 7.64 – 7.57 (m, 1H), 7.51 (d, *J* = 2.2 Hz, 1H), 7.42 (d, *J* = 2.2 Hz, 1H), 7.35 – 7.27 (m, 1H), 7.24 (d, *J* = 2.2 Hz, 1H), 7.23 – 7.11 (m, 6H), 6.93 – 6.74 (m, 4H), 6.59 (s, 1H), 3.83 – 3.77 (m, 1H), 3.81 (d, *J* = 12.9 Hz, 1H), 3.77 – 3.68 (m, 2H), 3.62 – 3.43 (m, 2H), 3.38 – 3.32 (m, 2H), 3.21 (d, *J* = 14.1 Hz, 1H), 2.31 – 2.21 (m, 1H), 2.07 – 2.01 (m, 1H) 1.95 – 1.89 (m, 1H), 1.81 – 1.70 (m, 1H), 1.62 (s, 6H), 1.54 – 1.47 (m, 1H), 1.50 (s, 3H), 1.30 (s, 9H), 1.27 (s, 9H), 1.24 – 1.13 (m, 2H), 0.95 – 0.80 (m, 2H).

^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 173.3, 168.1, 165.3, 151.9, 147.5, 146.9, 145.6, 145.1, 142.4, 141.0, 131.4, 129.6, 129.3, 128.8, 128.0, 127.3, 127.1, 126.8, 125.1, 123.8, 121.0, 120.9, 109.0, 63.0, 54.2, 53.5, 47.8, 46.4, 43.2, 35.4, 35.1, 35.1, 33.7, 33.2, 32.3, 32.2, 30.9, 26.0, 25.5, 23.7, 12.7.

HRMS (MALDI-FTMS: MH$^+$) calcd. for $C_{48}H_{64}N_5O_5S^+$ 822.4628, found 822.4620.

Scheme S8. Coupling reaction of amine **3b** and thymine derived thioisocyanate **4b** was done as described above.



3b : 1.0 equiv.

15 : 95%

Thiourea 15

^{1}**H NMR** (600 MHz, $CDCl_3$) δ 7.63 – 7.54 (s, 1H), 7.50 (s, 1H), 7.34 (s, 1H), 7.33 – 7.29 (m, 1H), 7.28 – 7.01 (m, 7H), 6.94 – 6.73 (s, 4H), 6.60 (s, 1H), 3.92 – 3.76 (m, 4H), 3.60 – 3.52 (m, 1H), 3.46 (d, *J* = 12.4 Hz, 1H), 3.40 – 3.32 (s, 2H), 3.21 (d, *J* = 14.1 Hz, 1H), 3.15 (s, 3H), 2.30 – 2.22 (s, 1H), 2.10 – 1.97 (m, 1H), 1.97 – 1.88 (m, 1H), 1.82 – 1.71 (m, 1H), 1.69 (s, 3H), 1.62 (s, 3H), 1.59 – 1.51 (m, 1H), 1.50 (s, 3H), 1.30 (s, 9H), 1.26 (s, 9H), 1.22 – 1.09 (m, 2H), 0.98 – 0.76 (m, 2H).

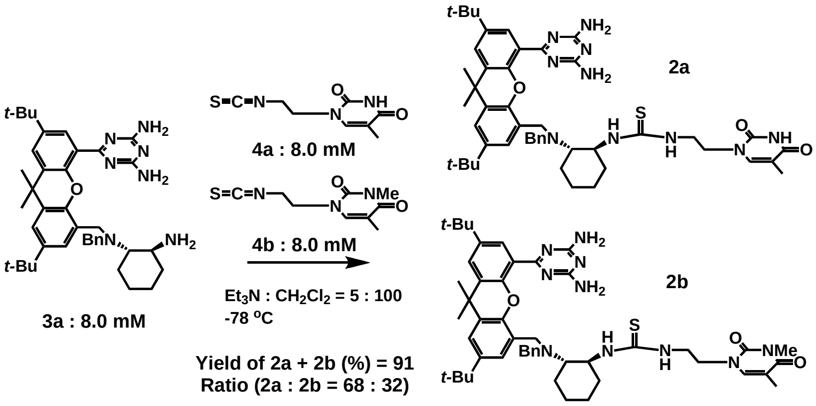
^{13}**C NMR** (151 MHz, $CDCl_3$) δ 172.4, 167.2, 163.4, 151.1, 146.6, 146.0, 144.7, 144.2, 140.1, 139.9, 130.6, 128.7, 128.4, 127.9, 127.1, 126.4, 126.2, 125.9, 124.2, 122.9, 120.1, 107.2, 62.1, 53.3, 52.6, 48.1, 45.5, 42.2, 40.1, 34.4, 34.2, 34.2, 32.8, 32.3, 31.4, 31.3, 30.0, 27.4, 25.1, 24.6, 22.9, 12.5.

HRMS (MALDI-FTMS: MH^+) calcd. for $C_{47}H_{62}N_5O_5S^+$ 808.4471, found 808.4470.

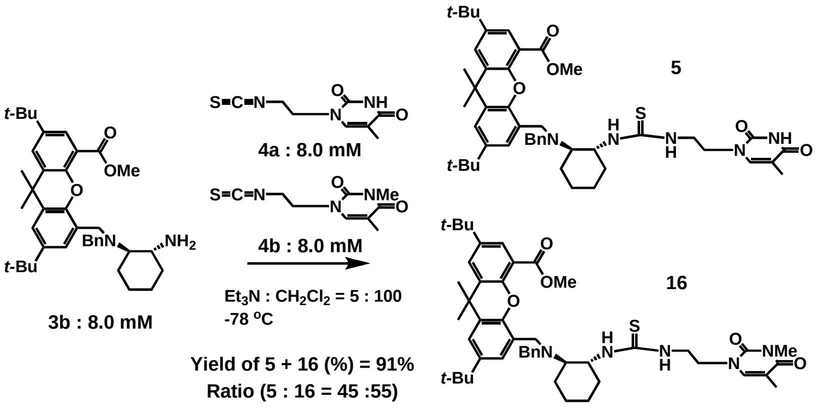
General procedure of competition studies for coupling reaction of amine 3a or 3b with thymine derived thioisocyanates 4a and 4b

Thymine derived thioisocyanates **4a** and **4b** (8.0 mM) were mixed with a solution of amine **3a** or **3b** (8.0 mM) in Et_3N/CH_2Cl_2 (5/95) at -78 ^oC as described above. After 24 h of stirring at -78 ^oC, the mixture was analyzed by HPLC using the peak areas [254 nm].

Scheme S9. Coupling reaction of amine **3a** and thymine derived thioisocyanates **4a** and **4b** was done as described above.



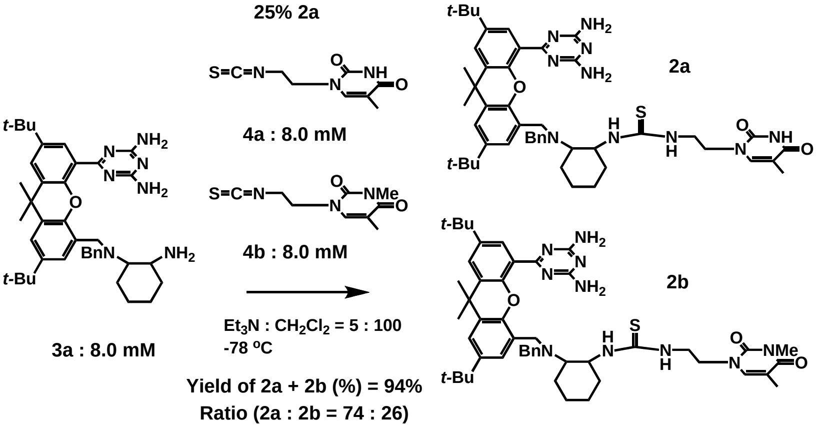
Scheme S10. Coupling reaction of amine **3b** and thymine derived thioisocyanates **4a** and **4b** was done as described above.



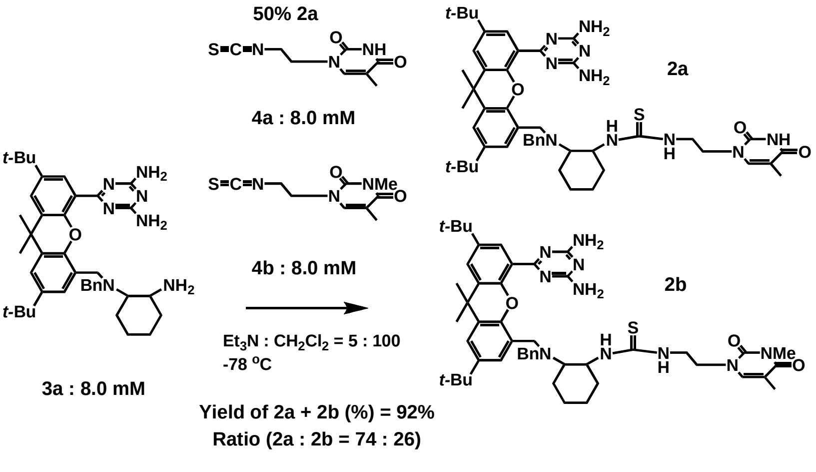
General procedure of competition studies in the presence of thiourea 2a for coupling reaction of amine 3a with thymine derived thioisocyanates 4a and 4b

A solution of amine **3a** (8.0 mM) and thymine derived thioisocyanates **4a** and **4b** (8.0 mM) in Et_3N/CH_2Cl_2 (5/95) was treated with thiourea **2a** (2.0 mM or 4.0 mM) at -78 °C. After 24 h of stirring at -78 °C, the mixture was analyzed by HPLC using the peak areas [254 nm].

Scheme S11. Coupling reaction of amine **3a** and thymine derived thioisocyanates **4a** and **4b** in the presence of 25% thiourea **2a**



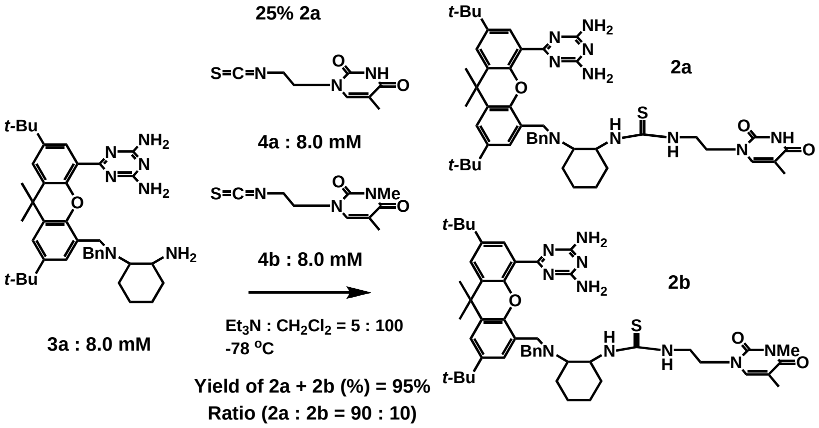
Scheme S12. Coupling reaction of amine **3a** and thymine derived thioisocyanate **4a** and **4b** in the presence of 50% thiourea **2a**



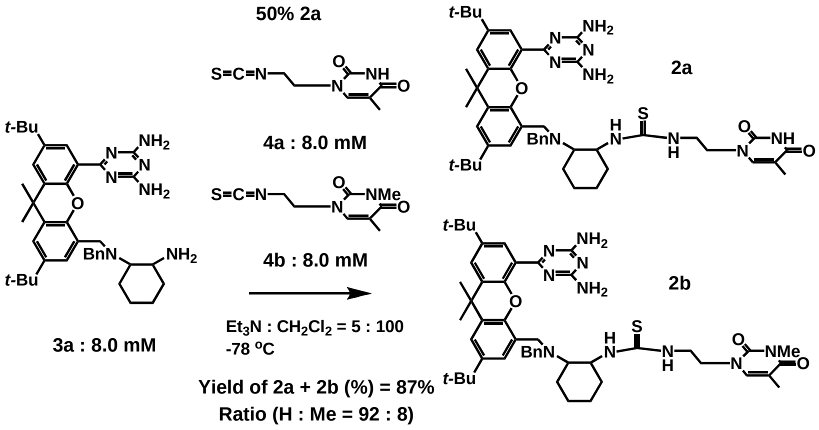
General procedure of competition studies in the presence of thiourea 2a for coupling reaction of amine 3a with thymine derived thioisocyanates 4a and 4b utilizing high dilution condition

Thymine derived thioisocyanates **4a** and **4b** (8.0 mM) were added very slowly to a solution of amine **3a** (8.0 mM) and thiourea **2a** (2.0 mM or 4.0 mM) in Et_3N/CH_2Cl_2 (5/95) at -78 °C over 6 h. After 24 h of stirring at -78 °C, the mixture was analyzed by HPLC using the peak areas [254 nm].

Scheme S13. Coupling reactions of amine **3a** and thymine derived thioisocyanates **4a** and **4b** in the presence of 25% thiourea **2a** under high dilution



Scheme S14. Coupling reactions of amine **3a** and thymine derived thioisocyanates **4a** and **4b** in the presence of 50% thiourea **2a** under high dilution.



General procedure for Organocatalytic Hydride Reduction

The *trans*-β-nitrostyrene **16** (1.0 equiv.) was added to a solution of thiourea **2a** (0.5 equiv.), and Hantzch ester **17** (10.0 equiv.) in $CDCl_3$ (5.0 mM) at 0 °C. The bath was removed and the solution was allowed to come to room temperature. The mixture was analyzed by ^1H NMR as shown in Figure S1 below.

Scheme S15. Organocatalytic Hydride Reduction

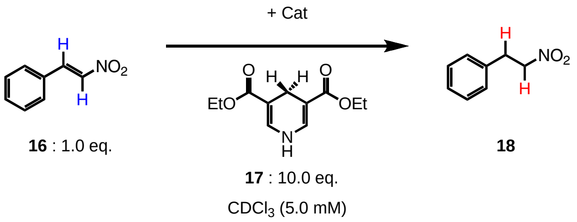


Figure S1. ^1H NMR spectra of the reaction in the presence of 50% **2a**

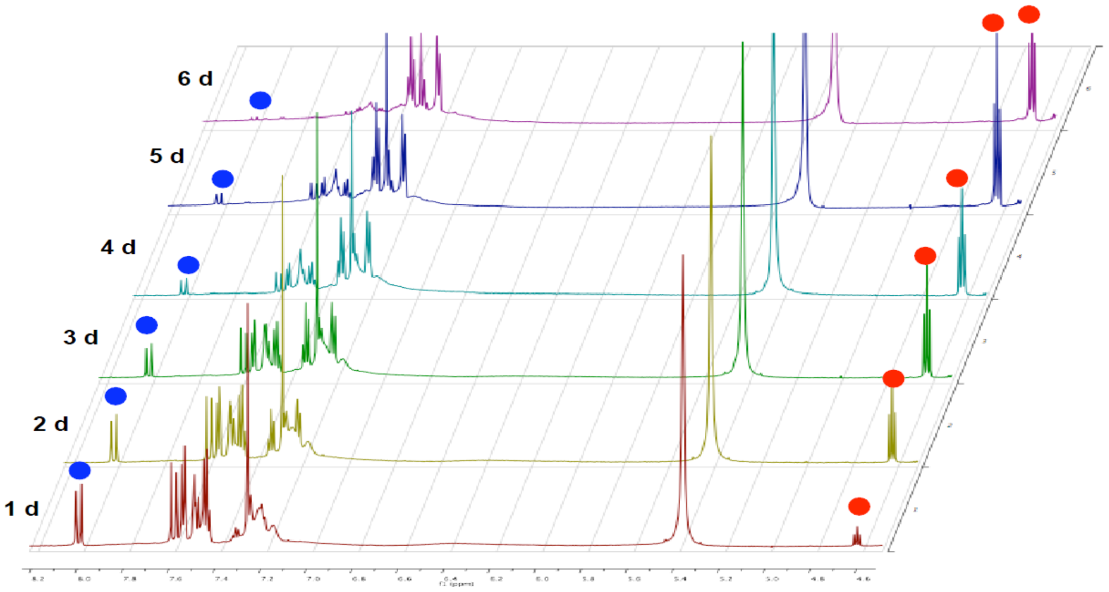


Table S1. Concentrations of **18** in the Organocatalytic Hydride Reduction

	Concentration of **18** (50% **2a**)	Concentration of **18** (no **2a**)	Concentration of **18** (50% **3a** + 50% **4b** + 5eq. Et_3N)	Concentration of **18** (50% **2b**)	Concentration of **18** (50% **3a**)	Concentration of **18** (50% **4a**)	Concentration of **18** (5eq. Et_3N)
1 d	0.77	0.01	1.79	2.07	-	0.18	0.16
2 d	1.76	0.03	2.79	3.38	-	-	0.25
3 d	2.86	0.05	3.60	4.30	0.24	0.35	0.46
4 d	3.90	0.05	4.05	4.74	0.27	0.45	0.95
5 d	3.96	0.08	4.69	4.88	0.32	0.49	1.36
6 d	4.70	0.10	4.86	4.90	0.43	0.54	1.55

General procedure of Organocatalytic Michael addition

The *trans*-β-nitrostyrene **16** (1.0 equiv.) was added to a solution of thiourea **2a** (0.5 equiv.), 2,5-pentanedione **19** (5.0 equiv.) and Et_3N (5 equiv) in $CDCl_3$ (5.0 mM) at 0 °C. The bath was removed and the solution was allowed to come to room temperature. The mixture was analyzed by ^1H NMR as shown in Figure S2 below.

Scheme S16. Organocatalytic Michael addition

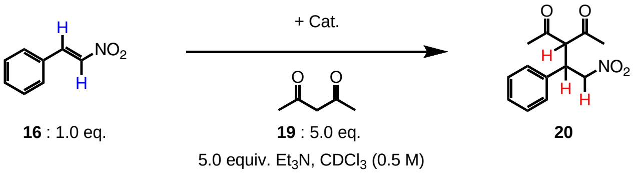


Figure S2. ^1H NMR spectrum of the reaction, in the presence of 50% **2a**

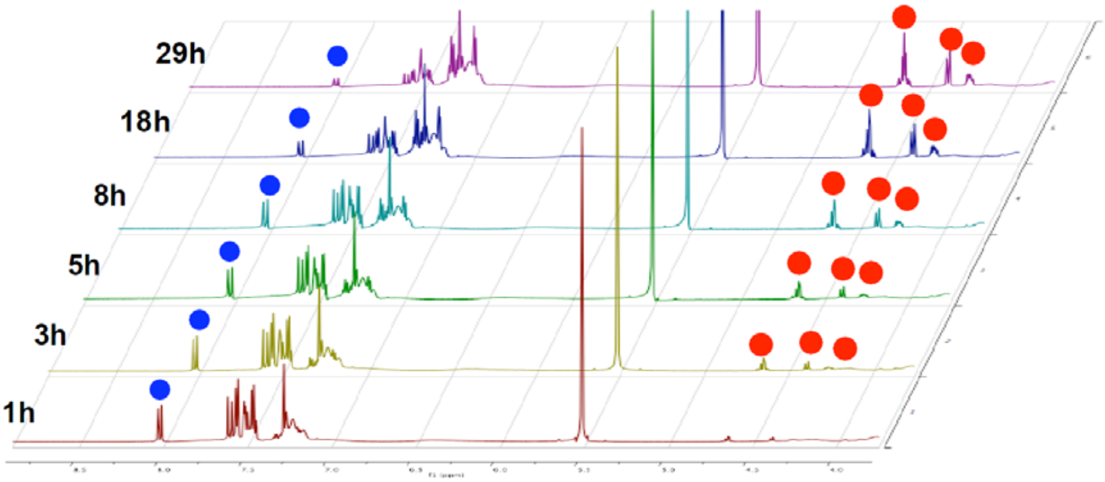


Table S2. Concentrations of **20** in the Organocatalytic Michael addition

	Concentration of **20** (50% **2a**)	Concentration of **20** (no **2a**)	Concentration of **20** (50% **3a** + 50% **4b**)	Concentration of **20** (50% **2b**)	Concentration of **20** (50% **3a**)	Concentration of **20** (50% **4a**)
0h	0	0	0	0	0	0
1h	0.724	0.229	0.91	0.86	0.383	0.034
3h	1.377	0.532	1.441	1.77	0.745	0.378
5h	1.731	0.791	1.881	2.37	1.078	0.73
8h	2.52	1.206	2.56	3.16	1.466	1.151
18h	3.97	2.549	4.00	4.50	2.392	2.473
29h	4.481	3.316	4.51	4.94	3.099	3.162

General procedure of Organocatalytic Michael addition using thiophenol

The *trans*-β-nitrostyrene **16** (1.0 equiv.) was added to a solution of thiourea **2a** (0.2 equiv.) and thiophenol **21** (2.0 equiv.) in CD_2Cl_2 (5.0 mM) at 0 ^{o}C. The bath was removed and the solution was allowed to come to room temperature. The mixture was analyzed by ^{1}H NMR as shown in Figure S3 below.

Scheme S17. Organocatalytic Michael addition using thiophenol

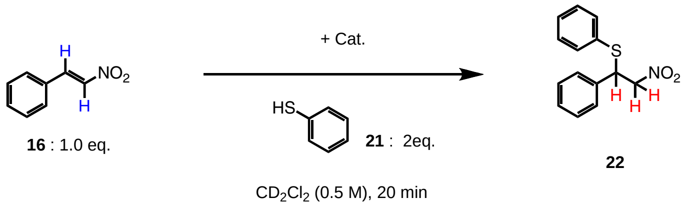


Figure S3. Organocatalytic Michael addition