Cuprous Chloride Accelerated Stille Reactions. A General and Effective Coupling System for Sterically Congested Substrates and for Enantioselective Synthesis.

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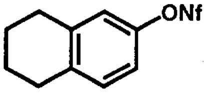
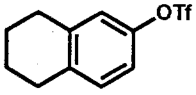
Supplementary Material



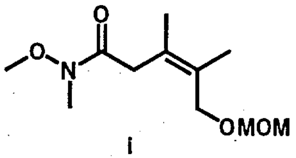
10a

Nonaflate 10a. To a solution of tetrahydro-2-naphthol (1.5 g, 10.1 mmol) and Et$_3$N (1.7 mL, 12.1 mmol) in CH$_2$Cl$_2$ (80 mL) at room temperature was added Nonaflyl fluoride (2.2 mL, 12.1 mmol) in a dropwise fashion. The resulting solution was stirred for 28 h, washed with 5% NaOH (2 x100 mL), water (2 x 100 mL), and brine (2 x 100 mL), then dried over Na$_2$SO$_4$, and evaporated *in vacuo*. The residue was purified by flash chromatography (hexanes eluent) to afford **10a** (3.61 g, 83% yield) as a colorless liquid: ^{1}H NMR (400 MHz) δ 7.11 (d, J = 8.4 Hz, 1H), 6.99 (dd, J = 8.4, 2.5 Hz, 1H), 6.97 (s, 1H), 2.79 - 2.76 (m, 4H), 1.82 - 1.78 (m, 4H); ^{13}C NMR (100 MHz) δ 147.5, 139.6, 137.6, 130.6, 121.3, 118.1, 119 - 109 (m), 29.4, 28.8, 22.7, 22.5.



10b

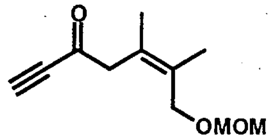
Triflate 10b. To a solution of 5,6,7,8-tetrahydro-2-naphthol (4.0 g, 27.0 mmol) and DMAP (0.33 g, 2.7 mmol) in pyridine (20 mL) at 0 °C was added Tf$_2$O (5.45 mL, 32.4 mmol) in a dropwise fashion. The mixture was stirred at 0 °C for 10 min, allowed to warm to room temperature, and stirred for 12 h. The reaction mixture was poured into water (150 mL), and extracted with Et_2O (3 x 100 mL). The combined organic layers were washed with water (100 mL), 10% HCl (2 x 100 mL), water (100 mL) and brine (100 mL), dried over Na_2SO_4, and evaporated *in vacuo*. The residue was purified by flash chromatography (1:30 EtOAc/hexanes eluent) to afford **10b** as a colorless liquid (6.42 g, 85% yield): ^{1}H NMR (500 MHz) δ 7.10 (d, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 1H), 6.96 (s, 1H), 2.78 - 2.75 (m, 4H), 1.81 - 1.78 (m, 4H); ^{13}C NMR (125 MHz) δ 147.3, 139.6, 137.6, 130.7, 121.4, 118.8 (q, *J* = 1278 Hz), 118.1, 29.4, 28.9, 22.8, 22.5.



i

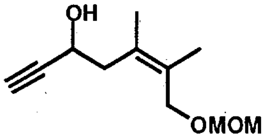
Amide i. A cooled (0 °C) suspension of *N*, *O*-dimethylhydroxylamine hydrochloride (8.3 g, 85.3 mmol) in CH_2Cl_2 (340 mL) was treated with solution of Me_3Al (8.2 mL, 85.3 mmol) in toluene (80 mL) in a dropwise fashion over 10 min. The resulting solution was treated with 4,5-dimethyl-3,6-dihydropyran-2-one[1] (4.3 g, 34.1 mmol) as a solution in CH_2Cl_2 (68 mL). After stirring for 3.5 h, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (350 mL), and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 200 mL), and the combined organic layers were washed with brine, dried over Na_2SO_4, and evaporated to a yellow oil which was used in the next step without purification.

The above crude oil was dissolved in CH_2Cl_2 (340 mL), cooled to -78 °C, and sequentially treated with *i*-Pr_2NEt (60 mL, 341 mmol) and chloromethyl methyl ether (13 mL, 170.5 mmol). The resulting solution was allowed to warm to room temperature and stirred for 10 h. The reaction mixture was poured into 1M HCl (500 mL), layers were separated and the aqueous layer extracted with CH_2Cl_2 (3 x 200 mL). The combined organic layers were washed with $NaHCO_3$ (300 mL) and brine (300 mL), dried over $NaSO_4$, and evaporated to an oil which was purified by flash chromatography (3:1 → 3:5 hexane/EtOAc eluent) to provide amide **i** (5.1 g, 65% yield) as a slightly yellow oil: FTIR (film) 2937, 1665 cm^{-1}; ^1H NMR (500MHz, $CDCl_3$) δ 4.56 (s, 2H), 4.02 (s, 2H), 3.66 (s, 3H), 3.33 (s, 3H), 3.29 (bs, 2H), 3.14 (s, 3H), 1.76 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 128.5, 128.0, 95.0, 67.6, 61.0, 55.1, 36.9, 32.2, 19.4, 17.1; HRMS (CI) for $[C_{11}H_{21}NO_4 + H]^+$ calcd 232.1549, found 232.1558.



ii

A solution of amide **i** (500 mg, 2.16 mmol) in THF (2.2 mL) at 0 °C was treated with ethynyl magnesium bromide (8.7 mL, 0.5 M solution in THF, 4.33 mmol), allowed to warm to room temperature, and stirred for 4 h. The reaction mixture was quenched by addition of saturated aqueous NH_4Cl (15 mL), and extracted with Et_2O (3 x 15 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, and evaporated to an oil which was purified by flash chromatography (6:1 hexane/EtOAc eluent) to give ketone **ii** (342 mg, 81% yield) as a colorless oil: FTIR (film) 3246, 2932, 2092, 1683 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 4.52 (s, 2H), 3.98 (s, 2H), 3.38 (s, 2H), 3.32 (s, 3H), 3.25 (s, 1H), 1.75 (s, 3H), 1.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.5, 130.6, 125.6, 95.0, 81.3, 78.8, 67.3, 55.1, 50.3, 19.6, 17.1; HRMS (CI) for $[C_{11}H_{16}O_3 + NH_4]^+$ calcd 214.1443, found 214.1442.



iii

A solution of ketone **ii** (230 mg, 1.17 mmol) in MeOH (12 mL) at 0 °C was treated with $CeCl_3{\bullet}7H_2O$ (523 mg, 1.40 mmol) followed by $NaBH_4$ (177 mg, 4.68 mmol) in three portions over 2 min. The reaction mixture was stirred for 15 min, quenched by addition of 1N NaOH (15 mL), and extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, and evaporated to an oil which was purified by flash chromatography (6:1 → 1:1 hexane/EtOAc eluent) to provide alcohol **iii** (228 mg, 98% yield) as a colorless oil: FTIR (film) 3425, 3289, 3933 cm^{-1}; ^1H NMR (400MHz, $CDCl_3$) δ 4.62 (d, J = 6.7 Hz, 1H), 4.58 (d, J = 6.6 Hz, 1H), 4.41 (ddd, J = 2.0, 4.9, 8.8 Hz, 1H), 4.19 (d, J = 10.8 Hz, 1H), 3.90 (d, J = 10.8 Hz, 1H), 3.38 (s, 3H), 3.30 (bs, 1H), 2.71 (dd, J = 8.9, 13.8 Hz, 1H), 2.42 (dd, J = 4.8, 13.7 Hz, 1H), 2.42 (d, J = 2.2Hz, 1H), 1.75 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 130.2, 129.2, 95.3, 85.3, 72.2, 67.7, 59.9, 55.3, 42.4, 18.8, 17.9; HRMS (CI) for $[C_{11}H_{18}O_3 + NH_4]^+$ calcd 216.1600, found 216.1590.

References:

(1) Aumann, R.; Ring, H.; Krüger, C.; Goddard, R. *Chem. Ber.* **1979**, *112*, 3644.