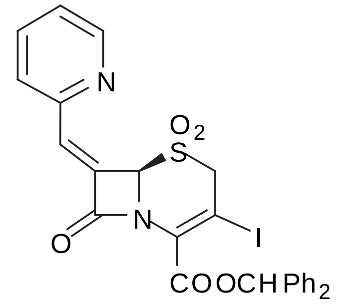
The Preparation and Utility of 3-Stannylated Cephalosporins

John D. Buynak,* Lakshminarayana Vogeti, and Hansong Chen

Department of Chemistry, Southern Methodist University, Dallas TX 75275-0314

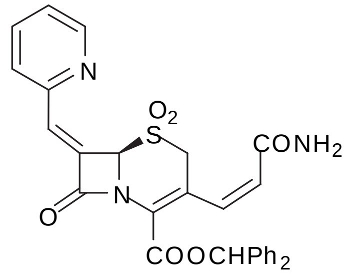
Supporting Material



12

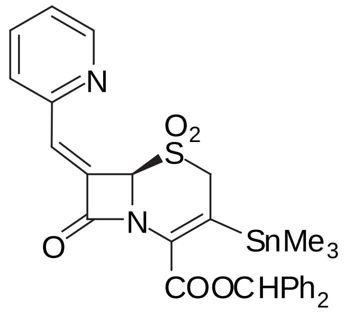
12. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.66 (d, J = 4.0 Hz, 1H), 7.71 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.49 – 7.25 (m, 13H), 7.03 (s, 1H), 5.96 (s, 1H), 4.38 (d, J = 18 Hz, 1H), 4.18 (d, J = 18 Hz, 1H). ^{13}C NMR ($CDCl_3$, 400 MHz) δ = 160.3, 160.2, 150.4, 150.2, 138.9, 138.6, 137.0, 132.7, 130.9, 128.6, 128.5, 128.4, 128.2, 128.0, 127.5, 127.2, 126.6, 126.4, 125.3, 80.5, 74.1, 64.2. HRMS calcd for $C_{26}H_{19}IN_2O_5S$ $[M+H]^+$ 599.0138, obsd 599.0135.

General Procedure for the Stille Couplings of iodide **12** with organostannanes as illustrated by the synthesis of **13d**.



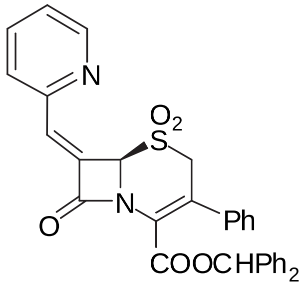
13d

To a solution of **12** (72 mg, 0.12 mmol) in anhydrous THF were added stannane **15** (25 mg, 0.11 mmol), $Pd_2(dba)_3$ (5 mg, 0.011 mmol) under an Ar atmosphere. The reaction mixture was stirred at 65 ^{0}C for 2.5 h and was monitored by ^{1}H NMR. After completion of the reaction, solvent was removed under reduced pressure and the product dissolved in CH_2Cl_2. The solution was then washed with water (10 mL) and brine (10 mL). the organic layer was concentrated and purified by column chromatogrphy using EtOAc / CH_2Cl_2 as eluent to obtain pure **13d**. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.67 (d, J = 4.0 Hz, 1H), 8.71 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.48 (d, J = 7.5 Hz, 2H), 7.41 – 7.26 (m, 11H), 6.90 (s, 1H), 6.81 (d, J = 11.8 Hz, 1H), 5.96 (s, 1H), 5.81 (d, J = 11.8 Hz, 1H), 5.5 (br s, 2H), 4.42 (d, J = 17.3 Hz, 1H), 3.99 (d, J = 17.3 Hz, 1H). ^{13}C NMR ($CDCl_3$, 400 MHz) δ = 166.2, 160.4, 159.4, 150.5, 150.3, 139.3, 139.2, 136.9, 133.2, 130.2, 129.6, 128.7, 128.6, 128.2, 127.4, 127.1, 126.2, 125.9, 125.1, 124.6, 124.4, 80.0, 73.5, 55.5.



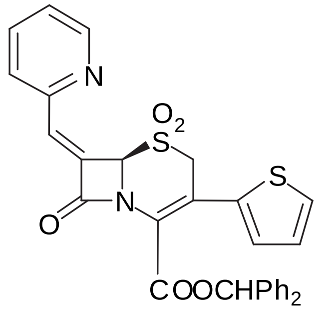
13e

Preparation of **13e**. To a solution of **12** (1.0 g, 1.71 mmol) in dry THF was added hexamethylditin (0.67 g, 2.0 mmol), $Pd_2(dba)_3$ (175 mg, 0.2 mmol) under an Ar atmosphere. The reaction mixture was stirred at 60 ^{0}C for 1.5 h, while monitoring by ^{1}H NMR. After completion of the reaction, solvent was removed under reduced pressure. The product was then dissolved in CH_2Cl_2 and washed with water (50 mL) and brine (30 mL). The organic layer was dried (Na_2SO_4), concentrated under reduced pressure, and purified by flash chromatography using EtOAc/ CH_2Cl_2 as eluent to obtain xx g (yy%) pure **13e**. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.66 (d, J = 3.9 Hz, 1H), 7.72 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.54 (d, J = 7.5 Hz, 2H), 7.43 to 7.26 (m, 11H), 6.92 (s, 1H), 5.88 (s, 1H), 4.07 (d, J = 18.5 Hz, 1H), 3.93 (d, J = 18.5 Hz, 1H), 0.15 (s, 9H). ^{13}C NMR ($CDCl_3$, 400 MHz) δ = 162.6, 158.4, 150.8, 150.3, 142.1, 139.6, 139.2, 136.8, 133.9, 130.6, 129.8, 128.6, 128.4, 128.2, 127.9, 127.5, 127.1, 126.0, 124.9, 80.3, 73.1, 57.6, -6.6. HRMS calcd for $C_{29}H_{29}N_2O_5SSn$ $[M+H]^+$ 637.0819, obsd 637.0823.



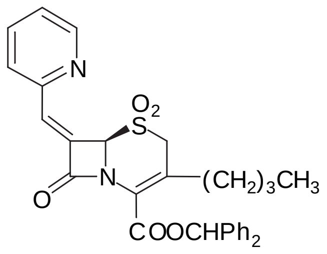
13b

13b. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.65 (d, J = 3.9 Hz, 1H), 7.7 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.34 – 7.13 (m, 16H), 6.92 (d, J = 6.7 Hz, 2H), 6.85 (s, 1H), 5.98 (s, 1H), 4.08 (s, 2H). ^{13}C NMR ($CDCl_3$, 400 MHz) δ = 160.8, 159.2, 150.2, 150.0, 138.6, 138.1, 136.5, 134.9, 132.8, 129.9, 128.9, 128.5, 128.09, 127.9, 127.7, 127.5, 127.2, 127.0, 126.9, 125.9, 124.7, 79.0, 73.0, 56.7.



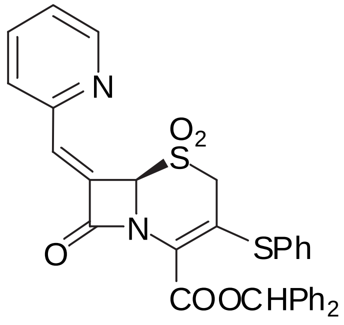
13c

13c. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.69 (d, J = 4.0 Hz, 1H), 7.72 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.4 – 7.21 (m, 12H), 7.07 – 7.05 (m, 2H), 6.96 (s, 1H), 6.84 (dd, J = 1 and 4 Hz, 1H), 6.75 (t, J = 4 Hz, 1H), 5.96 (s, 1H), 4.13 (, J = 18 Hz, 2H),



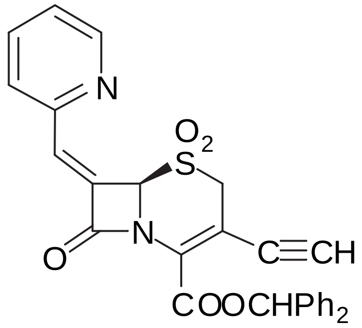
13f

13f. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.66 (d, J = 4.0 Hz, 1H), 7.71 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.47 – 7.25 (m, 13H), 6.98 (s, 1H), 5.75 (s, 1H), 3.81 (), 2.58 – 2.54 (m, 2H), 1.36 – 1.23 (m, 4H), 0.84 (t, J = 7 Hz, 3H). HRMS calcd for $C_{30}H_{29}N_2O_5S$ $[M+H]^+$ 529.1797 obsd 529.1831.



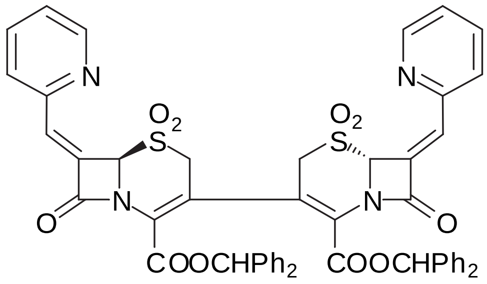
13g

13g. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.63 (d, J = 3.9 Hz, 1H), 7.71 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.53 – 7.26 (m, 19H), 7.02 (s, 1H), 5.75 (s, 1H), 3.75 (d, J = 15.6 Hz, 1H), 3.59 (d, J = 15.6 Hz, 1H), 3.59 (d, J = 15.6 Hz, 1H).



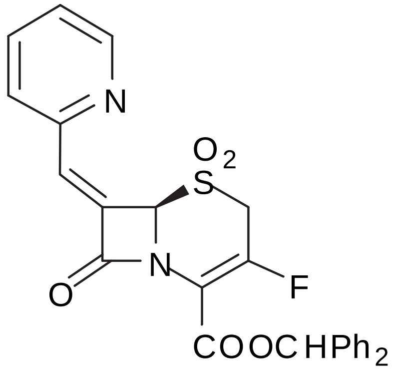
13h

13h. ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.66 (d, J = 4 Hz, 1H), 7.72 (t of d, J = 1.6 and 7.7 Hz, 1H), 7.51 – 7.26 (m, 13H), 7.03 (s, 1H), 5.94 (s, 1H), 4.09 (d, J = 17.6 Hz, 1H), 3.86 (d, J = 17.6 Hz, 1H), 3.41 (s, 1H).



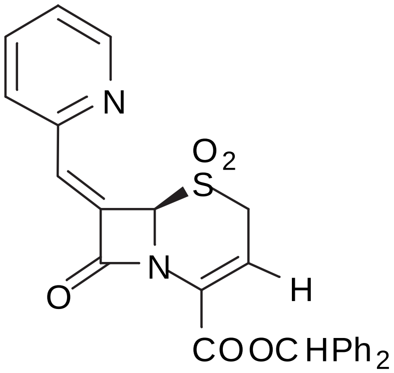
16

16. ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 8.70 (d, J = 4.0 Hz, 2H), 7.74 (t of d, J = 1.5 and 7.7 Hz, 2H), 7.44 – 7.16 (26 H, m), 6.82 (s, 2H), 5.04 (s, 2H), 4.18 (d, J = 18.5 Hz, 2H), 3.56 (d, J = 18.5 Hz, 2H). ^{13}C NMR (CDCl$_3$, 400 MHz) δ = 138.5, 136.9, 132.0, 131.5, 129.6, 128.8, 128.7, 128.3, 128.1, 127.8, 126.8, 126.2, 125.9, 120.2, 81.1, 73.2, 52.6. HRMS calcd for $C_{52}H_{39}N_4O_{10}S_2$ [M+H]$^+$ 943.2108 obsd 943.2055.



13j

13j. ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 8.65 (d, J = 4.0 Hz, 1H), 7.71 (t of d, J = 1.5 and 7.7 Hz, 1H), 7.47 – 7.27 (m, 13H), 7.04 (s, 1H), 5.84 (s, 1H), 4.23 (d of d, J = 5.4 and 20 Hz, 1H), 4.08 (d of d, J = 5.4 and 20 Hz, 1H).



13k

13k. ^{1}H NMR (CDCl$_3$, 400 MHz) δ = 8.66 (d, J = 4.0 Hz, 1H), 7.76 (t of d, J = 1.5 and 7.7 Hz, 1H), 7.48 – 7.25 (m, 13H), 6.99 (s, 1H), 6.34 (d of d, J = 3.5 and 2.0 Hz), 5.94 (s, 1H), 4.04 (d of d, 1.5 and 17.5 Hz, 1H), 3.83 (d of d, J = 5.6 and 17.5 Hz, 1H). HRMS calcd for $C_{26}H_{21}N_2O_5S$ [M+H]$^+$ 473.1171, obsd 473.1148.