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Supporting Information for "A Biomimetic Synthesis of Thiazolines Using Bis(triphenyl)oxodiphosphonium Trifluoromethanesulfonate"

Shu-Li You, Hossein Razavi and Jeffery W. Kelly*

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General Methods. Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purchased from Fisher and were dried prior to use. ^{1}H NMR spectra were measured at 500 MHz on a Bruker DRX spectrometer, and were referenced to internal TMS (0.0 ppm). ^{13}C NMR spectra were performed at 125 MHz on a Bruker DRX-500 instrument and were referenced to $CDCl_3$. The chemical shift assignments for the major diastereomer, not for the minor diastereomer, were reported. Flash chromatography was performed on silica gel 60 (230-400 mesh, E. Merck no. 9385).

General procedure for synthesis of fully protected Cysteine

[*] Prof. Jeffery W. Kelly
Department of Chemistry and The Skaggs Institute of Chemical Biology
The Scripps Research Institute
La Jolla, California 92037.
E-mail: jkelly@scripps.edu

derivatives. A solution of N^{α}-Fmoc-Cys(S-trityl)-OH (0.586 g, 1 mmol) in MeOH: Benzene (5 mL; 1:4) was treated with TMS-CHN_2 (600 µl of 2.0 M solution in hexanes, 1.2 mmol) at 25 °C and the reaction progress was monitored by TLC (usually complete after 0.5 h). The reaction mixture was concentrated *in vacuo* and the crude reaction mixture was used in the next step without purification.

Diethylamine (6 mL) was added to a solution of crude ester in CH_3CN (6 mL) and the resulting mixture was stirred at 25 °C for 30 min to ensure complete removal of the Fmoc protecting group. After concentration *in vacuo*, the reaction mixture was azetroped to dryness with CH_3CN (2 x 6 mL) and the residue was dissolved in DMF (4 mL). In another flask, a solution of desired Cbz-protected amino acid in DMF (4 mL) was treated with HOBT (1.1 mmol) and HTBU (1.1 mmol). After 10 min, the above free amino ester and DIEA (2.1 mmol) were sequentially added, the resulting mixture was stirred at 25 °C overnight. The reaction mixture was concentrated and the residue was dissolved in EtOAc and washed with 10% $NaHCO_3$ aqueous solution. The aqueous layer was dried over Na_2SO_4, filtered and concentrated. The resultant crude product was purified by flash chromatography using a mixture of EtOAc/hexanes.

***N*-Cbz-*L*-Phe-*L*-Cys(S-Trt)-OMe (7a).** ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.34-7.14 (m, 25H), 6.09 (d, *J* = 7.3 Hz, 1H), 5.30 (d, *J* = 6.3 Hz, 1H), 5.10 (AB, d, J_{AB} = 12.3 Hz, 1H), 5.07 (AB, d, J_{AB} = 12.3 Hz, 1H), 4.45 (m, 1H), 4.38 (m, 1H), 3.69 (s, 3H), 3.09-3.00 (m, 2H), 2.64 (dd, *J* = 12.5, 5.5 Hz, 1H), 2.55 (dd, *J* = 12.5, 4.8 Hz, 1H).

***N*-Cbz-*L*-Ala-*L*-Cys(S-Trt)-OMe (8a).** ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.39-7.19 (m, 20H), 6.26 (br, 1H), 5.31 (br, 1H), 5.12 (AB, d, J_{AB} = 12.1 Hz, 1H), 5.08 (AB, d, J_{AB} = 12.1 Hz, 1H), 4.52 (m, 1H), 4.19 (m, 1H), 3.69 (s, 3H), 2.69 (dd, *J* = 12.5, 5.9 Hz, 1H), 2.63 (dd, *J* = 13.5, 5.4 Hz, 1H), 1.35 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 170.7, 155.9, 144.4, 136.4, 129.6, 128.7, 128.3, 128.2 (d), 127.1, 67.2, 52.8, 51.4, 50.4, 33.7, 19.0; HRMS (MALDI-FTMS) calcd. for $C_{34}H_{34}N_2O_5S$ ($M+Na^+$) 605.2081, found 605.2076.

***N*-Cbz-*L*-Val-*L*-Cys(S-Trt)-OMe (9a).** ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.43-7.19 (m, 20H), 6.03 (d, *J* = 7.7 Hz, 1H), 5.33 (d, *J* = 7.7 Hz, 1H), 5.12 (AB, d, J_{AB} = 12.3 Hz, 1H), 5.10 (AB, d, J_{AB} = 12.3 Hz, 1H), 4.53 (m, 1H), 4.00 (m, 1H), 3.70 (s, 3H), 2.72 (dd, 1H, *J* = 12.8, 5.9 Hz), 2.61 (dd, 1H, *J* = 12.8, 4.8 Hz), 2.08 (m, 1H), 0.96 (d, 3H, *J* = 6.6

Hz), 0.89 (d, 3H, *J* = 6.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 170.7, 156.4, 144.4, 136.5, 129.6, 128.7, 128.3 (d), 127.1, 67.3, 67.2, 60.0, 52.8, 51.4, 50.4, 33.6, 31.7, 19.2, 17.6; HRMS (MALDI-FTMS) calcd. for $C_{36}H_{38}N_2O_5S$ ($M+Na^+$) 633.2393, found 633.2371.

***N*-Cbz-*L*-Ile-*L*-Cys(S-Trt)-OMe (10a).** ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.32-7.19 (m, 20H), 6.10 (d, *J* = 7.7 Hz, 1H), 5.32 (d, *J* = 8.4 Hz, 1H), 5.12 (AB, d, J_{AB} = 11.7 Hz, 1H), 5.09 (AB, d, J_{AB} = 11.7 Hz, 1H), 4.54 (m, 1H), 4.04 (m, 1H), 3.69 (s, 3H), 2.69 (dd, *J* = 12.5, 6.2 Hz, 1H), 2.62 (dd, *J* = 12.5, 4.4 Hz, 1H), 1.82 (m, 1H), 1.47 (m, 1H), 1.12 (m, 1H), 0.93-0.88 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 170.7, 156.4, 144.4, 136.5, 129.6, 128.7, 128.3 (d), 127.1, 67.3, 67.2, 60.0, 52.8, 51.4, 50.4, 33.6, 31.7, 19.2, 17.6; HRMS (MALDI-FTMS) calcd. for $C_{37}H_{40}N_2O_5S$ ($M+Na^+$) 647.2550, found 647.2536.

General procedure for synthesis of thiazolines. To a solution of triphenylphosphine oxide (167 mg, 0.6 mmol) in dry CH_2Cl_2 (2 mL), trifluoromethanesulfonic anhydride (50 μl, 0.3 mmol) was added slowly at 0 °C. The reaction mixture was stirred for 10 min at 0 °C and then adjusted to the desired reaction temperature enabling addition of the fully protected cysteine *N*-amide (0.2 mmol). The reaction

progress was monitored by TLC. The reaction mixture was quenched with 10 % aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The resultant crude product was purified by flash chromatography using a mixture of EtOAc/hexanes.

4-Carbomethoxy-2-(*N*-Cbz-*L*-Phe)-Δ^2-thiazoline (7b). ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.36-7.15 (m, 10H), 5.43 (d, *J* = 8.1 Hz, 1H), 5.09-5.03 (m, 3H), 4.89 (dd, *J* = 13.2, 6.6 Hz, 2H), 3.77 (s, 3H), 3.62 (dd, *J* = 11.4, 9.8 Hz, 1H), 3.51 (t, *J* = 9.8 Hz, 1H), 3.23 (dd, *J* = 13.9, 5.9 Hz, 1H), 3.09 (dd, *J* = 13.9, 6.6 Hz, 1H).

4-Carbomethoxy-2-(*N*-Cbz-*L*-Ala)-Δ^2-thiazoline (8b). ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.36-7.29 (m, 5H), 5.60 (br, 1H), 5.14-5.07 (m, 3H), 4.65 (m, 1H), 3.80 (s, 3H), 3.60 (dd, *J* = 11.0, 9.2 Hz, 1H), 3.55 (dd, *J* = 10.6, 9.9 Hz, 1H), 1.55 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 170.7, 155.9, 144.4, 136.4, 129.6, 128.7, 128.3, 128.2 (d), 127.1, 77.8, 67.2, 52.8, 51.4, 50.4, 33.7, 19.0; HRMS (MALDI-FTMS) calcd. for $C_{15}H_{18}N_2O_4S$ ($M+H^+$) 323.1060, found 323.1068.

4-Carbomethoxy-2-(*N*-Cbz-*L*-Val)-Δ^2-thiazoline (9b). ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.37-7.36 (m, 5H), 5.48 (d, *J*

= 8.8 Hz, 1H), 5.15-5.09 (m, 3H), 4.56 (dd, *J* = 9.2, 4.4 Hz, 1H), 3.79 (s, 3H), 3.61 (dd, *J* = 11.4, 7.7 Hz, 1H), 3.55 (t, *J* = 11.0 Hz, 1H), 2.20 (m, 1H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.7, 171.1, 156.3, 136.4, 128.6, 128.3, 128.2, 128.0, 77.6, 67.1, 58.7, 52.8, 35.9, 32.5, 19.5, 16.7; HRMS (MALDI-FTMS) calcd. for $C_{17}H_{22}N_2O_4S$ ($M+Na^+$) 373.1192, found 373.1184.

4-Carbomethoxy-2-(*N*-Cbz-*L*-Ile)-Δ^2-thiazoline (10b). ^{1}H NMR (500 MHz, $CDCl_3$, 25°C, TMS) δ 7.36-7.31 (m, 5H), 5.47 (d, *J* = 8.1 Hz, 1H), 5.14-5.08 (m, 3H), 4.58 (dd, *J* = 8.5, 4.8 Hz, 1H), 3.79 (s, 3H), 3.60 (dd, *J* = 11.4, 7.7 Hz, 1H), 3.53 (t, *J* = 10.3 Hz, 1H), 1.93 (m, 1H), 1.53 (m, 1H), 1.14 (m, 1H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 171.2, 156.2, 136.5, 128.7, 128.3 (d), 77.7, 58.4, 52.9, 39.3, 35.8, 24.3, 15.7, 11.9; HRMS (MALDI-FTMS) calcd. for $C_{18}H_{24}N_2O_4S$ ($M+H^+$) 365.1529, found 365.1526.