Supplementary Material

for

Thio Acid/Azide Amidation: An Improved Route to N-Acyl Sulfonamides

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Full Citation: complete author list for reference 2c is given below.

Mader, M.; Shih, C.; Considine, E; De Dios, A.; Grossman, S.; Hipskind, P.; Lin, H.; Lobb, K.; Lopez, B.; Lopez, J.; Cabrejas, L. M. M.; Richett, M. E.; White, W. T.; Cheung, Y.-Y.; Huang, Z.; Reilly, J. E.; Dinn, S. R. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 617.

General procedure: Starting materials, reagents and solvents were purchased from commercial suppliers (Sigma-Aldrich and Fischer). All reactions were conducted in oven-dried (165 $^{\circ}$C) glassware under an inert atmosphere of dry argon. The progress of reactions was monitored by silica gel thin layer chromatography (TLC)[1] plates (pore size 60Å, 250 µm layer thickness, glass support, with fluorescent indicator, Sigma-Aldrich) visualized under 254 nm UV and charred using vanillin[2] or *p*-anisaldehyde stain[3]. Products were purified by flash column chromatography (FCC) on 230-400 mesh, pore size 60Å, Silicycle, ultra pure silica gel. Infrared (FTIR) spectra were recorded on an ATI MattsonGenesis Series FT-Infrared spectrophotometer. Characterized reactant products were homogeneous by TLC. Proton nuclear magnetic resonance spectra ^{1}H NMR were recorded on either a Varian-300 *Mercury* (300 MHz), or a Varian-400 *I-Nova* (400 MHz). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants in Hz. ^{13}C NMR were recorded on either a Varian-300 instrument (75 MHz) or a Varian-400 instrument (100 MHz). Chemical shifts are reported in ppm relative to tetramethylsilane (TMS) as the internal standard, for some insoluble N-acyl sulfonamides the introduction of acetic acid to the NMR sample was found to be beneficial for solubilization of the product. Mass spectra were recorded on a Finnigan LCQ-DUO.

[1] Acronyms: Boc = tert-Butoxycarbonyl, DCC = dicyclohexyl carbodiimide, DIC = diisopropyl carbodiimide, DIEA = diisopropyl ethyl amine, DMAP = 4-dimethylamino pyridine, DMF = N,N-dimethylformamide, DMSO = dimethyl sulfoxide, Fmoc = 9-Fluorenylmethoxycarbonyl, HMDT = hexamethyldisilthiane, IBCF = isobutyl chloroformate, SES-N_3 = trimethylsilylethyl sulfonylazide, TBAF = tetrabutyl ammonium fluoride, TLC = thin-layer chromatography, TMOB = trimethoxybenzyl

[2] LeRosen, A. L.; Moravek, R. T.; Carlton, J. K. *Anal. Chem*.,**1952**, *24*, 1335

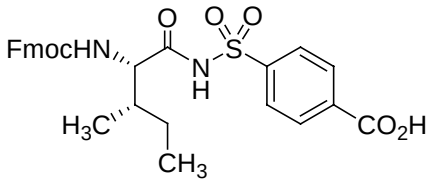
[3] Stahl, E.; Kaltenbach, U. *J. Chromatogr. A*, **1961**, *5*, 351

General protocol for thiolate formation:

Method A: Under an argon atmosphere a round bottom flask was charged with 2.50 mL of dry THF and bis(trimethylsilyl)sulfide (1.5 eq in relation to carboxylic acid). 1.2 eq of MeLi was added dropwise at -78 °C and allowed to warm to rt (approx. 30 min).

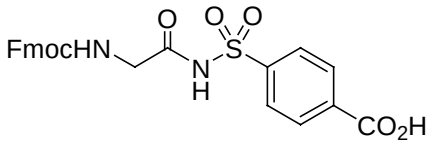
Method B: Under an argon atmosphere, a round bottom flask was charged with 2.50 mL of dry THF and bis(trimethylsilyl)sulfide (1.5 eq relative to carboxylic acid). 1.2 eq of anhydrous TBAF was added dropwise at -78 °C and the reaction was allowed to warm to rt (approx. 30 min).

General protocol for the conversion of a carboxylic acid to a thio acid: To a round bottom flask charged with dry CH_2Cl_2 under argon, 1 eq of carboxylic acid (azeotroped with toluene) was added, followed by the addition of 2,6-lutidine (3.0 eq) and isobutylchloroformate (1.2 eq) at 0 °C. The reaction mixture was stirred for 30 min then trimethylsilyl thiolate (see **Method A** or **Method B** above) was added via syringe. The reaction mixture was then stirred until TLC analysis indicated complete consumption of the mixed anhydride (30 min to 4 h). The reaction was then quenched with MeOH, dried *in vacuo,* and then azeotroped with MeOH (2 x 10 mL) to remove volatiles. The crude thio acid was taken up in 1.5 ml of MeOH, and to the mixture 2,6-lutidine (1 eq) then sulfonyl azide (0.8 eq) was added. Bubbling was observed after the addition of azide. The reaction was monitored by TLC. Upon completion the reaction was dried *in vacuo* and purified by FCC.



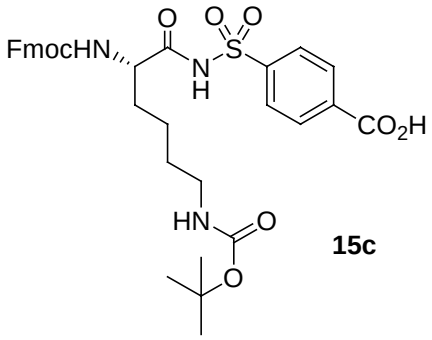
15a

15a: 200 mg (0.56 mmol) of Fmoc-Ile-OH, 92 mg (0.68 mmol) of isobutylchloroformate, 350 mg (3.0 mmol) of 2,6-lutidine, 0.152 mg (0.85 mmol) of bis(trimethylsilyl)sulfide , 0.68 mmol of MeLi, and 100 mg (0.44 mmol) of 4-carboxysulfonyl azide were used. FCC, eluted with 2.5:7.5 hexanes:ethyl acetate and 2% acetic acid, furnished 182 mg (86%) of a white solid. IR ν_{max}(KBr)/cm^{-1} 3374, 3068, 1720, δ_H δ_H (400 MHz, $CDCl_3$) 10.22-10.00 (1H, br), 8.17 (2H, d, J=8.0 Hz), 8.08 (2H, d, J=8.0 Hz), 7.76 (2H, d, J=7.2 Hz), 7.56 (2H, d, J=6.8 Hz), 7.40 (2H, t, J=7.2 Hz), 7.29 (2H, td J=7.2, 4.0 Hz), 5.45 (1H, d, J=8.8 Hz), 4.50-4.40 (2H, m), 4.20-4.10 (2H, m), 1.85-1.70 (1H, m), 1.45-1.30 (1H, m), 1.12-1.00 (2H, m), 0.90-0.70 (6H, m); δ_C (100 MHz, $CDCl_3$) 177.0, 169.6, 156.9, 141.3, 134.1, 130.6, 128.5, 127.9, 127.1, 125.0, 120.0, 67.7, 59.6, 46.9, 37.2, 24.6, 15.2, 11.0; *m/z* (ESI/MS) 559 $(M+23)^+$.



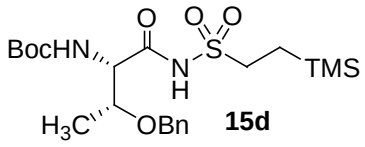
15b

15b: 250 mg (0.841 mmol) of Fmoc-Gly-OH, 137 mg (1.01 mmol) of isobutylchloroformate, 350 mg (3.3 mmol) of 2,6-lutidine, 0.265 mg (1.5 mmol) of bis(trimethylsilyl)sulfide , 1.01 mmol of MeLi, and 152 mg (0.80 mmol) of 4-carboxysulfonyl azide were used. FCC, eluted with 1:1 hexanes:ethyl acetate and 2% acetic acid, furnished 268 mg (83%) of a white solid. IR ν_{max}(KBr)/cm^{-1} 3374, 3068, 1715 δ_H (400 MHz, CD_3OD) 8.04 (2H, d, J=8.0 Hz), 7.95 (2H, d, J=8.0 Hz), 7.78 (2H, d, J=7.2 Hz), 7.65 (2H, d, J=7.2 Hz), 7.37 (2H, t, J=7.2 Hz), 7.29 (2H, t J=7.6 Hz), 4.28 (2H, d, J=7.2 Hz), 4.20 (1H, m), 3.73 (2H, s); δ_C (100 MHz, CD_3OD) 176.1, 171.4, 158.4, 144.8, 142.0, 129.8, 128.3, 127.7, 127.5, 125.8, 120.4, 67.5, 47.8, 46.3; *m/z* (ESI/MS) 479 $(M-1)^-$.



15c

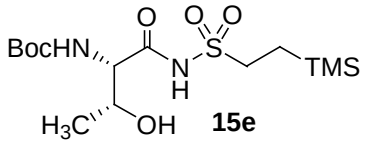
15c: 200 mg (0.43 mmol) of Fmoc-Lys-OH, 70 mg (0.52 mmol) of isobutylchloroformate, 200 mg (1.5 mmol) of 2,6-lutidine, 0.114 mg (0.65 mmol) of bis(trimethylsilyl)sulfide , 0.52 mmol of MeLi, and 121 mg (0.34 mmol) of 4-carboxysulfonyl azide were used. FCC, eluted with 5:5 hexanes:ethyl acetate and 2% acetic acid, furnished 217 mg (98%) of a white solid. IR ν_{max}(KBr)/cm^{-1} 3365, 3117, 1719, 1690 δ_H (300 MHz, acetone-d_6) 8.23 (2H, d, J=8.4 Hz), 8.14 (2H, d, J=8.7 Hz), 7.85 (2H, d, J=7.8 Hz), 7.67 (2H, d, J=7.2 Hz), 7.40 (2H, t, J=7.5 Hz), 7.34-7.27 (2H, m), 6.85 (1H, d, J=7.5 Hz), 5.90-6.02 (1H, m), 4.29 (2H, d, J=6.9 Hz), 4.28-4.16 (2H, m), 3.10-2.90 (3H, m), 1.90-1.60 (2H, m), 1.51-1.60 (4H), 1.39 (9H, s); δ_C (100 MHz, CD_3OD) 174.7, 172.9, 167.4, 157.9, 142.1, 136.2, 130.6, 128.8, 128.3, 127.7, 127.6, 125.7, 125.6, 120.4, 79.5, 67.5, 56.1, 47.8, 40.4, 31.5, 29.9, 28.3, 23.5; *m/z* (ESI/MS) 650 $(M-1)^-$.



15d

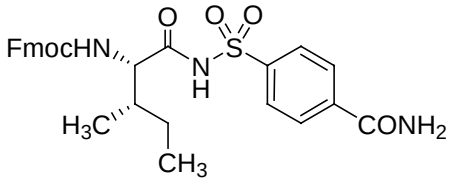
15d: 100 mg (0.323 mmol) of Boc-Thr-OH, 53 mg (0.39 mmol) of isobutylchloroformate, 121 mg (1.1 mmol) of 2,6-lutidine, 86 mg (0.49 mmol) of bis(trimethylsilyl)sulfide , 0.38 mmol of MeLi, and 53 mg (0.26 mmol) of SES-azide were used. FCC, eluted with 3:7 hexanes:ethyl acetate and 2% acetic acid, furnished 146 mg (96%) of a white solid. IR ν_{max}(neat)/cm^{-1} 3362, 3244, 1718; δ_H (400 MHz, $CDCl_3$) 9.18-8.82 (1H, br), 7.34-7.27 (5H, m), 5.39 (1H, d, J=6.8 Hz), 4.63 (1H, d, J=11.2 Hz),

4.54 (1H, d, J=11.2 Hz), 4.32 (1H, d, J=4.4 Hz), 4.20-4.12 (1H, m), 3.40-3.28 (2H, m), 1.45 (9H, s), 1.21 (3H, d, J=6.4 Hz), 1.02 (2H, dd, J=10.4, 7.6 Hz), 0.03 (9H, s); δ_C (100 MHz, $CDCl_3$) 170.0, 155.7, 137.1, 128.6, 128.1, 127.8, 81.0, 73.9, 71.7, 58.9, 50.1, 28.2, 15.6, 9.8, -2.1; *m/z* (ESIMS) 471 $(M-1)^-$.



15e

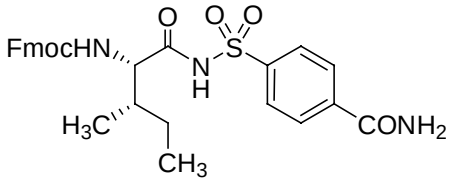
15e: 100 mg (0.46 mmol) of Boc-Thr-OH, 75 mg (0.55 mmol) of isobutylchloroformate, 171mg (1.6 mmol) of 2,6-lutidine, 121 mg (0.69 mmol) of bis(trimethylsilyl)sulfide , 0.55 mmol of MeLi, and 78 mg (0.36 mmol) of SES-azide were used. FCC, eluted with 5:5 hexanes:ethyl acetate and 2% acetic acid, furnished 131 mg (94%) of a white solid. **:** IR ν_{max}(neat)/cm^{-1} 3376, 3253, 1716, 1701 δ_H (400 MHz, $CDCl_3$) 5.64 (1H, d, J=6.8 Hz), 4.34 (1H, m), 4.17 (1H, d, J=6.0 Hz), 3.37-3.23 (2H, m), 1.45 (9H, s), 1.21 (3H, d, J=6.0 Hz), 1.05-1.00 (2H, m), 0.04 (9H, s); δ_C (100 MHz, $CDCl_3$) 170.9, 156.5, 81.2, 66.5, 59.3, 50.0, 28.2, 18.5, 9.8, -2.1; *m/z* (ESI/MS) 381 $(M-1)^-$.



18

From **15a**

Wang amide resin (105 mg, 0.11 mmol) was swelled in DMF (4 mL) for 4 h and then treated with 113 mg (0.21 mmol) of **15a**, HOBt 121 mg (4.1 mmol), and DIC 113 mg (4.1 mmol). The mixture was shaken for 8 h, at which time a sample of the derivatized support gave a negative Kaiser test. The solid support was then rinsed with excess CH_2Cl_2, and the sulfonamide was then cleaved from the support using cleavage cocktail K.[1] FCC (1:3 hexanes:ethyl acetate and 2% acetic acid) furnished 52 mg of a white solid [92% yield based on Wang amide resin (0.8 mmol/g); 46% yield based on **15a**].

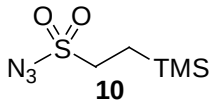


18

From **14a**

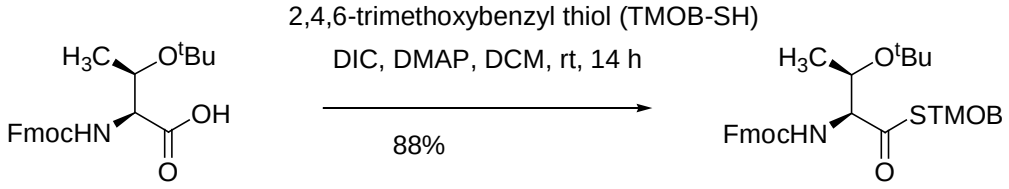
18: 317 mg (0.9 mmol) of Fmoc-Ile-OH, 184 mg (1.36 mmol) of isobutylchloroformate, 350 mg (3.0 mmol) of 2,6-lutidine, 228 mg (1.35 mmol) of bis(trimethyl)sulfide, and 1.00 mmol of MeLi were used to prepare the thio acid as per Procedure A. Wang amide resin (550 mg, 0.45 mmol) was swelled in DMF (8 mL) for 4 h and then treated with 200 mg (0.9 mmol) of 4-carboxybenzenesulfonazide (**14a**), HOBt 241 mg (1.8 mmol), and DIC 226 mg (1.8 mmol). The mixture was shaken for 8 h, at which time a sample of the derivatized support gave a negative Kaiser test. The solid support was then rinsed with excess CH_2Cl_2. The resin was then treated with 2 mL of 1:1 (v/v) acetic anhydride:pyridine and shaken for one hour. The solid support was then rinsed with excess CH_2Cl_2. The immobilized azide was then treated with the crude Fmoc-Ile-SH (prepared above) and lutidine (0.35 mL) in CH_2Cl_2 (8 mL). Bubbling ensued, and the reaction mixture was shaken for 4h. The sulfonamide was cleaved from solid support using cleavage cocktail K.[4] FCC (1:3 hexanes:ethyl acetate and 2% acetic acid) furnished 169 mg of a white solid, 72%, yield [based on Wang amide resin (0.8 mmol/g)]. IR ν_{max}(neat)/cm^{-1} 3316, 1716, 1651. δ_H (400 MHz, CD_3CN) 7.98 (2H, d, J=9.5 Hz), 7.87 (2H, d, J=9.5 Hz), 7.83 (2H, d, J=6.1 Hz), 7.64 (2H, d, J=6.0 Hz), 7.40 (2H, t, J=7.3 Hz), 7.31 (2H, td J=7.0, 4.0 Hz), 6.85 (1H, br), 6.14 (1H, br), 5.72 (1H, d, J=7.8Hz), 4.37-4.14 (3H, m), 3.38 (1H, t, J=7.69), 1.75 (1H, m), 1.37-1.29 (1H, m), 1.12-1.00 (2H, m), 0.90-0.78 (6H, m); δ_C (100 MHz, $CDCl_3$) 171.1, 168.5, 156.9, 143.7, 143.2, 141.6, 141.3, 138.0, 128.5, 128.1, 127.8, 127.2, 125.0, 120.0, 67.6, 59.6, 46.9, 37.4, 24.5, 15.3, 11.0; *m/z* (ESI/MS) 558 $(M+23)^+$.

[4] Procedure for preparation of cleavage cocktail K: King. D; Fields, C. G.; Fields, G. B. *Int. J. Peptide Protien Res.*, ***1990**, 36, 255-266.* consists of TFA 82.5 % v/v, phenol 5 % v/v, water 5% v/v, thioanisole 5 % v/v, 1,2-ethanedithiol 2.5 % v/v



10

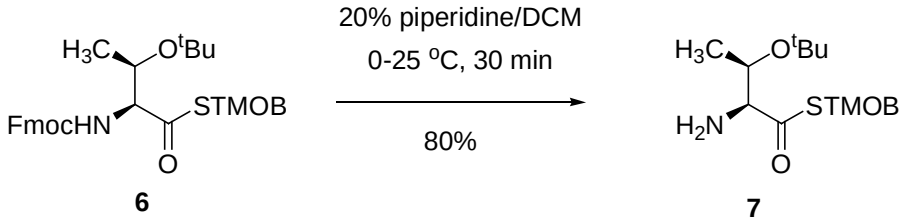
10: SES-Cl[5] 809 mg (4 mmol) was added to 3 eq of sodium azide (720 mg) and stirred in acetone (10 mL), for 3 h. The reaction mixture then washed with water (3 x 50 mL) and back-extracted with 50 mL of ethyl ether. The crude product [pale yellow oil 837 mg (89%)] was then dried *in vacuo* and used without further purification. δ_H (400 MHz, $CDCl_3$) 3.27-3.22 (2H, m), 1.17-1.13 (2H, m), 0.09 (9H, s); δ_C (100 MHz, $CDCl_3$) 53.0, 10.4, -2.1.



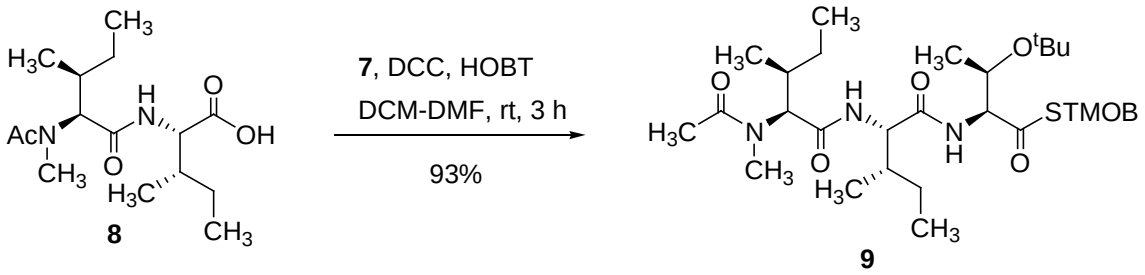
5 **6**

6: To a solution of FmocThr(^{t}Bu)-OH **5** (476 mg, 1.2 mmol) in DCM (8 mL) was added DIC (151 mg, 1,22 mmol; 0.186 mL) under nitrogen atmosphere and stirred for 5 minutes at rt. Tmob thiol (214 mg, 1 mmol) was added to the resulting suspension and then catalytic amount of DMAP (15 mg, 0.05 mmol) was added and the reaction was continued at rt overnight (14 h). Precipitated DIU was removed by filtration and the precipitate was washed with DCM. The filtrate was concentrated and the residue was purified by gravity driven silica gel chromatrography. Elution with 10% ethyl acetate-hexanes gave the unreacted thiol (20 mg, 9%). Continued elution gave the thioester **6** (525 mg, 88%). Spectral data: δ_H (400 MHz, $CDCl_3$) 7.76 (2H, d, J=7.6 Hz), 7.65 (2H, dd, J=7.6, 2.4 Hz), 7.38 (2H, t, J=7.2 Hz), 7.29-7.24 (2H, m), 6.09 (2H, s), 5.75 (1H, d, J=9.2 Hz), 4.48 (1H, dd, J=9.6, 6.4 Hz), 4.35-4.13 (6H, m), 3.81 (3H, s), 3.77 (6H, s), 1.21 (3H, d, J=6.4 Hz), 1.16 (9H, s).

[5] Preparation of SES-Cl see: Weinreb, S. M.; Chase, C. E.; Wipf, P.; Venkatraman, S. *Org. Syn*. **1997**, *75*, 161.

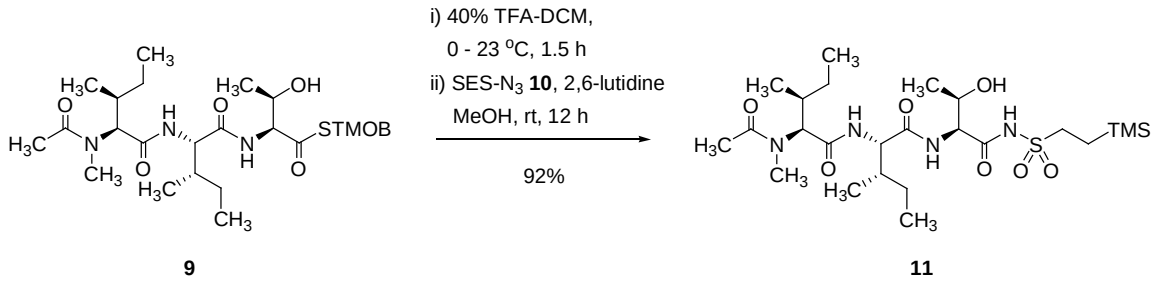


7: To a solution of thioester **6** (200 mg, 0.336 mmol) in DCM (2.4 ml) was added dropwise 0.6 mL of piperidine at 0 ^{o}C. The reaction was allowed to warm to rt over 30 minutes, the solvent was evaporated, and the residue was purified by FCC (SiO_2). Elution with 30% ethyl acetate-hexanes removed less polar compounds. Continued elution with 50% ethyl acetate-hexanes gave amine **7** (100 mg, 80%). Spectral data: δ_H (400 MHz, $CDCl_3$) 6.09 (2H, s), 4.14 (2H, s), 4.18-4.10 (1H, m), 3.80 (3H, s), 3.79 (6H, s), 3.26 (1H, bs), 1.78-1.62 (2H, bs), 1.23 (3H, d, J=6.0 Hz), 1.14 (9H, s); δ_C (100 MHz, $CDCl_3$) 206.3, 160.7, 159.2, 104.8, 90.4, 73.6, 68.4, 67.5, 55.7, 55.3, 28.5, 22.1, 21.2.



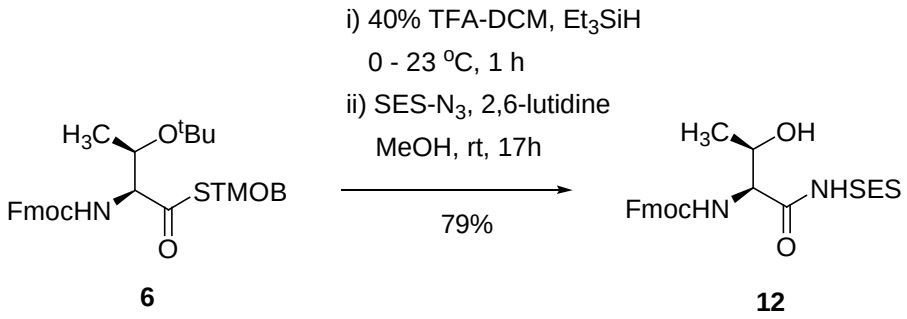
9: To a solution of dipeptide acid (98 mg, 0.325 mmol) and amine **8** (122 mg, 0.328 mmol) in dry DCM (3 mL) was added HOBT (87 mg, 0.651 mmol). DMF (0.6 mL, with stirring) was added dropwise until HOBT was dissolved. DCC (74 mg, 0.357 mmol) was added and the reaction mixture was stirred at rt for 1.5 h. TLC showed the reaction was complete. To the reaction mixture was added 30 mL of ethyl acetate and stirred. The precipitate was removed by filtration through a cotton plug. The filtrate was washed successively with 10% $NaHCO_3$ (5 mL X2), water and brine and dried over $MgSO_4$.

Solvent was evaporated and the crude material was purified by FCC (SiO_2). Elution with 20% ethyl acetate-hexanes removed DCC and less polar impurities. Continued elution with 60% ethyl acetate-hexanes gave the tripeptide thioester **9** (200 mg, 93%) as a colorless viscous liquid. Spectral data: δ_H (400 MHz, $CDCl_3$) 6.70 (1H, d, J=8.8 Hz), 6.57 (1H, d, J=8.4 Hz), 6.07 (2H, s), 4.66 (1H, d, J=11.6 Hz), 4.46 (1H, d, J=9.2 Hz), 4.41 (1H, dd, J=8.4, 6.0 Hz), 4.36-4.26 (1H, m), 4.18-4.07 (2H, m), 3.80 (3H, s), 3.76 (6H, s), 2.94 (3H, s), 2.10 (3H, s), 2.10-1.20 (6H, series of m), 1.17-0.81 (15H, series of m), 1.12 (9H, s); δ_C (100 MHz, $CDCl_3$) 201.5, 171.9, 171.4, 170.1, 160.8, 159.2, 104.3, 90.3, 74.0, 67.3, 64.3, 61.0, 57.5, 55.6, 55.3, 36.4, 34.0, 31.6, 31.4, 28.3, 25.6, 25.0, 24.6, 24.1, 22.4, 22.0, 21.0, 15.8, 15.6, 11.0, 10.4.



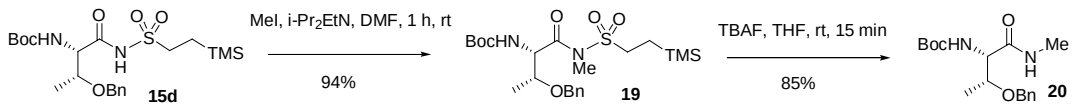
9 **11**

11: To a solution of thioester (100 mg, 0.153 mmol), Et_3SiH (0.2 mL) at 0 °C was added 40% TFA-DCM (2 mL) dropwise and after 5 minutes, the reaction mixture was continued at rt. After 1.5 h, solvent was evaporated and the residue was azeotroped with benzene and dried. To this crude thioacid was added a solution of SES-azide (77 mg, 0.370 mmol) in MeOH (0.5 ml) and then 2,6-lutidine (59 mg, 0.555 mmol; 64 μL) was added dropwise at 0 °C. The reaction mixture was stirred at rt for 14 h. Solvent was evaporated and azeotroped with benzene. The crude material was purified by FCC (SiO_2). Elution with 50% ethyl acetate-hexanes removed Tmob derived compounds. Continued elution with 70-100% ethyl acetate-hexanes gave SES-amide product (80 mg, 92%). Spectral data: δ_H (400 MHz, $CDCl_3$) 7.57 (1H, d, J=7.2 Hz), 7.21 (1H, d, J=8.4 Hz), 4.72-4.22 (4H, series of m), 3.37-3.31 (2H, m), 3.02 (3H, s), 2.15 (3H, s), 2.10-0.90 (8H, series of m), 1.18 (3H, d, J=6.3 Hz), 0.92-0.86 (12H, m), 0.05 (9H, s).



6 **12**

12: To a solution of thioester (110 mg, 0.185 mmol), Et_3SiH (0.2 mL) at 0 ^oC was added 40% TFA-DCM (2 mL) dropwise and the reaction mixture was stirred at rt. After 1 h, solvent was evaporated and the residue was azeotroped with benzene and dried. To this crude thioacid was added a solution of SES-azide (83 mg, 0.4 mmol) in MeOH (2 mL) and then 2,6-lutidine (64 mg, 0.6 mmol; 70 µL) was added dropwise at 0 ^oC. The reaction mixture was stirred at rt for 17 h. Solvent was evaporated and azeotroped with benzene. The crude material was purified by FCC (SiO_2). Elution with 30-50% ethyl acetate-hexanes removed Tmob derived compounds. Continued elution with 50% ethyl acetate-DCM gave SES-amide product (74 mg, 79%). Spectral data: Spectral data: δ_H (400 MHz, $CDCl_3$) 7.77 (2H, d, J=7.2 Hz), 7.59 (2H, d, J=6.8 Hz), 7.41 (2H, t, J=7.2 Hz), 7.32 (2H, t, J=7.2 Hz), 5.94 (1H, d, J=7.6 Hz), 4.51-4.20 (5H, series of m), 3.40-3.36 (2H, m), 1.20 (3H, d, J=6.4 Hz), 1.05 (2H, t, J=8.4 Hz), 0.05 (9H, s); δ_C (100 MHz, $CDCl_3$) 170.5, 156.9, 143.5, 143.4, 141.3, 127.8, 127.1, 125.05, 125.0, 121.0, 120.0, 67.6, 66.8, 59.8, 50.2, 47.0, 23.5, 18.4, 9.8, -2.0



21: To a solution of BocThr(Bn)NHSES **20** (50 mg, 0.106 mmol) in dry DMF (0.5 mL) was added ethyldiisopropylamine (137 mg, 1.06 mmol) and stirred under argon. After 5 min, MeI (300 mg, 2.12 mmol) was added and stirred under argon for 1 h. The reaction mixture was taken up in ethyl acetate (20 mL) and washed with water (10 mL x 6) and then brine (20 mL) and then dried over anhydrous sodium sulfate. Evaporation of solvent gave pure *N*-methyl sulfonamide **19** (40 mg, 94%), which was used as such in the next step. IR ν_{max}(neat)/cm^{-1} 3442, 1712, 1704, 1494, 1359; δ_H (300 MHz, $CDCl_3$) 7.40-7.20 (5H, m), 5.50 (1H, d, J=9.3 Hz), 4.91 (1H, dd, J=9.3, 2.4 Hz), 4.53 (1H, d, J=12.0 Hz), 4.39 (1H, d, J=11.7 Hz), 4.04-3.97 (1H, m), 3.45-3.38 (2H, m), 3.23 (3H, s), 1.42 (9H, s), 1.28 (3H, d, J=6.3 Hz), 1.04-0.98 (2H, m), 0.06 (6H, s).

To a solution of above sulfonamide **19** (9 mg, 0.018 mmol) in dry THF (0.3 mL) was added TBAF (0.04 mL of 1M solution in THF) and stirred at rt. After 15 min, solvent was evaporated and the residue was purified (FCC, SiO_2). Elution with 75% ethyl acetate-hexanes buffered with acetic acid (0.05%) furnished *N*-methylamide **20** (5 mg, 85%) as a clear viscous liquid. δ_H (300 MHz, $CDCl_3$) 7.40-7.26 (5H, m), 6.50-6.38 (1H, br), 5.55-5.40 (1H, br), 4.62-4.53 (2H, m), 4.30-4.10 (2H, m), 2.82 (3H, d, J=4.8 Hz), 1.45 (9H, s), 1.16 (3H, d, J=6.3 Hz); *m/z* (ESI/MS) 323 $(M+1)^+$.