# Total Synthesis of Diazonamide A

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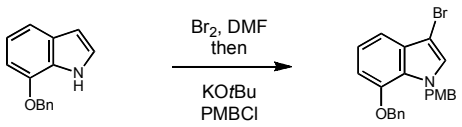
## *General Information*

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] All solvents were purified according to the method of Grubbs.[2] Non-aqueous reagents were transferred under nitrogen or argon via syringe or cannula. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator using a water bath. Chromatographic purification of products was accomplished using forced-flow chromatography on ICN 60 32-64 mesh silica gel 63 according to the method of Still.[3] Thin-layer chromatography (TLC) was performed on Silicycle 0.25 mm silica gel F-254 plates. Visualization of the developed chromatogram was performed by fluorescence quenching or by anisaldehyde, ceric ammonium molybdate, or potassium permanganate stain.

$^{1}$H and $^{13}$C NMR spectra were recorded on a Bruker 500 (500 MHz and 125 MHz) unless otherwise noted. Chemical shifts (δ) are reported from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26, $C_6D_6$: δ 7.15,

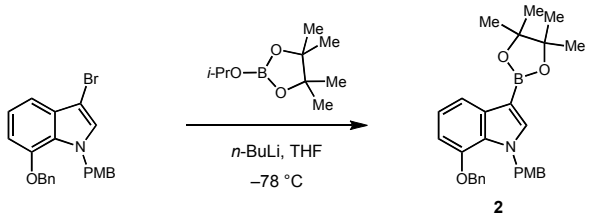
[1] Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals;* 3rd ed., Pergamon Press, Oxford, 1988.
[2] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen,R. K.; Timmers, F. J. *Organometallics,* **1996**, *15*, 1518.
[3] Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978,** *43*, 2923.

$CD_3OD$: δ 4.78, 3.31: CD3CN δ 1.94). Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, h = heptet, br = broad, m = multiplet), integration, coupling constants (Hz), and assignment. $^{13}C$ chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: δ 77.0, $C_6D_6$: δ 128.0, $CD_3OD$: δ 49.0: $CD_3CN$ δ 118.3). Unless noted otherwise, the reported $^1H$ NMR signals were assigned using standard 2D NMR techniques or by a direct comparison to the $^1H$ NMR spectra of corresponding starting materials. IR spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrometer and are reported in terms of frequency of absorption ($cm^{-1}$). Mass spectra were obtained from the Princeton University Mass Spectral facility, and from the California Institute of Technology Mass Spectral facility. Gas liquid chromatography (GLC) was performed on Hewlett-Packard 6850 and 6890 Series gas chromatographs equipped with a split-mode capillary injection system and flame ionization detectors using a J&W Scientific DB-1701 (30 m × 0.25 mm) column as noted. High performance liquid chromatography (HPLC) was performed on Hewlett-Packard 1100 Series chromatographs using a Chiralcel AD column (25 cm) and AD guard (5 cm) as noted. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D^{25}$ values reported in degrees; concentration (c) is in g/100 mL.



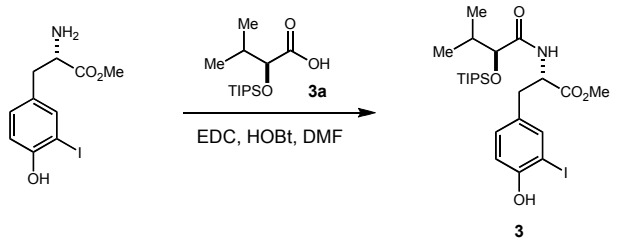

**7-(benzyloxy)-3-bromo-1-(4-methoxybenzyl)-1*H*-indole**: To a room temperature solution of 7-benzyloxyindole (5.0 g, 22.4 mmol) in 90 mL of DMF was added bromine (1.18 mL, 22.84 mmol) dropwise over the course of ten minutes. After 20 minutes the solution was cooled to 0 °C and KOtBu (5.78 g, 51.5 mmol) was added in a single portion. 30 minutes later PMBCl (3.65 mL, 26.88 mmol) was added dropwise over several minutes by syringe, after which the reaction mixture was allowed to warm to room temperature. After 6 hours the reaction was judged complete by TLC and the reaction mixture was diluted with 300 mL of diethyl ether and washed with 100 mL of 1% $Na_2S_2O_3$. The organic portions were washed three times with water and then once with brine before being dried over sodium sulfate. The organic portion was then concentrated *in vacuo* to yield a viscous yellow oil. These crude extracts could then be recrystallized from a hot mixture of 10% ethyl acetate in hexanes to afford 7.27 g (77%) of the title compound as a white crystalline solid. IR (Film): 2931, 1611, 1574, 1512, 1497, 1453, 1422, 1383, 1322, 1248, 1209, 1175, 1080, 1056, 1033, 988, 875, 818, 774, 727, 695, 625 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 7.38–7.25 (m, 5H, Ar**H**s), 7.19 (dd, 1H, J = 0.9, 7.8 Hz, Ar**H**), 7.07 (t, 1H, J = 7.8 Hz, Ar**H**), 7.04 (s, 1H, C(2)-**H**), 6.95–6.88 (m, 2H, Ar**H**), 6.80–6.72 (m, 3H, Ar**H**), 5.51 (s, 2H, PhC**H**$_2$), 5.12 (s, 2H, PMBC**H**$_2$), 3.77 (s, 3H, **Me**O-Ar) $^{13}C$ NMR: (300 MHz, $CDCl_3$) δ 158.9, 146.6, 136.7, 130.9, 129.9, 128.6, 128.1, 127.8, 125.7, 120.8, 114.0, 112.3, 104.6, 90.4,

70.5, 55.3, 52.2 HRMS (EI+) exact mass calculated for [M+•] ($C_{23}H_{20}NO_2Br$) requires *m/z* 421.0677, found *m/z* 421.0672.



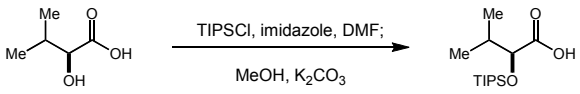

**7-(benzyloxy)-1-(4-methoxybenzyl)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-indole 2**: To a solution of *n*-butyllithium (7.34 mL, 10.65 mmol, 1.2 eq, 1.45M in hexanes) in 80 mL of THF at –78 °C was added 7-(benzyloxy)-3-bromo-1-(4-methoxybenzyl)-1*H*-indole (3.75 g, 8.88 mmol, 1.0 eq) in 10 mL of THF dropwise via syringe over 10 minutes. After 15 minutes, freshly distilled 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.62 mL, 17.76 mmol, 2.0 eq) was added via syringe. This reaction mixture was allowed to warm to ambient temperature over 3 hours. At this point, 100 mL of a saturated aqueous solution of $NH_4Cl$ was added to the reaction mixture and the layers were separated. The aqueous layer was washed 3 × 100 mL with EtOAc. The combined organic layer was washed with 100 mL of brine, dried over sodium sulfate, and concentrated *in vacuo*. The residual oil was then recrystallized from a hot solution of 10% EtOAc in hexanes to give the title compound as an off-white crystalline solid (3.40 g, 82% yield). The remaining mass was recovered as debrominated starting material. IR (Film): 2976, 1613, 1573, 1539, 1513, 1495, 1454, 1379, 1290, 1267, 1247, 1206, 1144, 1107, 1059, 1009, 783, 735, 696, 681 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 7.66 (dd, 1H, J = 0.6, 8.1 Hz, Ar**H**), 7.48 (s, 1H, C(2)-**H**), 7.35–7.22 (m, 5H, Ar**H**), 7.03 (t, 1H, J = 8.1Hz, Ar**H**), 6.91–6.87 (m, 2H, Ar**H**), 6.78–

6.65 (m, 3H, Ar**H**), 5.52 (s, 2H, PhC**H**$_2$), 5.09 (s, 2H, PMBC**H**$_2$), 3.75 (s, 3H, **Me**O-Ar), 1.35 (s, 12H, 4x**Me**) $^{13}$C NMR: (300 MHz, $CDCl_3$) δ 158.7, 146.6, 138.8, 137.0, 135.3, 131.3, 128.5, 128.4, 128.1, 127.9, 127.8, 126.9, 120.8, 115.7, 113.8, 104.1, 82.8, 70.3, 55.3, 52.2, 25.0 HRMS (EI+) exact mass calculated for [M+•] ($C_{29}H_{32}BNO_4$) requires *m/z* 469.2424, found *m/z* 469.2416.




**(*S*)-methyl3-(4-hydroxy-3-iodophenyl)-2-((*S*)-3-methyl-2-(triisopropylsilyloxy) butanamido)propanoate 3**: 3-Iodotyrosine methyl ester (15.4 g, 47.95 mmol), acid **3a** (11.96 g, 43.59 mmol), EDC (9.19 g, 47.95 mmol), and HOBt (6.47 g, 47.95 mmol) were combined in a 500 mL round bottom flask and 190 mL of DMF was added. After 12 hours the reaction mixture was diluted with 500 mL of ether and washed with 3 × 500 mL of water. The combined organic fractions were washed with brine and concentrated. The resulting oil was purified on silica gel (30% ethyl acetate in hexanes) to yield the title compound as a colorless oil (21.2 g, 82% yield). IR (Film): 3402, 2944, 2867, 1746, 1654, 1603, 1505, 1462, 1415, 1347, 1292, 1215, 1099, 1058, 882, 822, 684 cm$^{-1}$; $^1$H NMR: (300 MHz, $CDCl_3$) δ 7.44 (d, 1H, J = 2.1 Hz, Ar**H** ortho to iodide), 7.05 (br s, 1H, N**H**), 6.99 (dd, 1H, J = 2.1, 8.55 Hz, Ar**H** para to iodide), 6.87 (d, 1H, J = 8.5 Hz, Ar**H** meta to iodide), 5.82 (s, 1H, O**H**), 4.87 (m, 1H, NH**CH**), 4.15 (d, 1H, J = 3.3 Hz, C**H**OTIPS), 3.69 (s, 3H, $CO_2$**Me**), 2.91 (m, 2H,

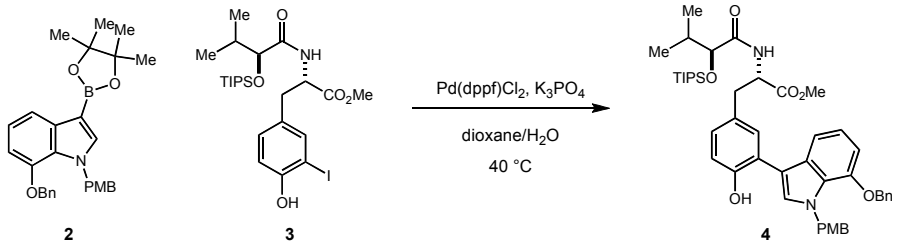
ArC**H**$_2$), 1.99 (m, 1H, C**H**$(CH_3)_2$), 1.1–1.0 (m, 21H, TIPS), 0.93 (d, 3H, J = 7.2 Hz, CH(C**H**$_3)_2$), 0.861 (d, 3H, J = 7.2 Hz, CH(C**H**$_3)_2$), $^{13}$C NMR: (75 MHz, $CDCl_3$) δ 172.88, 171.6, 154.5, 139.2, 131.0, 130.0, 115.3, 85.6, 78.3, 52.6, 52.4, 37.4, 34.2, 18.2, 18.1, 17.9, 17.5, 12.6 HRMS (FAB+) exact mass calculated for [M+H] ($C_{24}H_{41}NO_5SiI$) requires *m/z* 578.1799, found *m/z* 578.1791; $[\alpha]_D^{25}$ = –5.75 (c = 1.0 $CHCl_3$).




**3a**

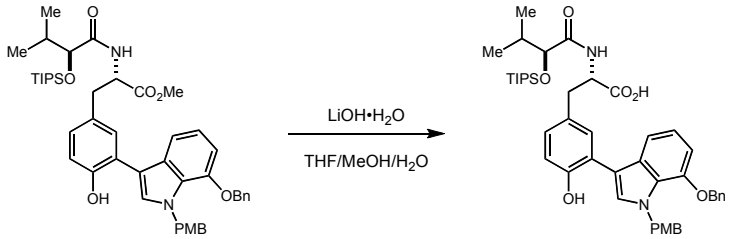
**(*S*)-3-methyl-2-(triisopropylsilyloxy)butanoic acid 3a**: To (*S*)-2-hydroxy valeric acid (5.0 g, 42.3 mmol) in a stirred solution of DMF (22 mL) was added triisopropylsilyl chloride (22 mL, 102 mmol) and imidazole (1.38 g, 204 mmol). After 24 hours, MeOH (210 mL) and 1M aqueous $K_2CO_3$ (64 mL) were added to this slurry, and after 4 h the resultant solution was diluted with 400 mL $H_2O$, acidified to pH 4, and extracted 3 × 300 mL with EtOAc. The combined organic fractions are washed with brine and concentrated. The resulting oil is purified of remaining TIPSOH by vacuum distillation of this impurity (85 °C, min. 10 mTorr) to yield the title compound as a colorless oil (9.7 g, 82% yield). IR (Film): 2963, 2945, 2869, 1723, 1465, 1388, 1234, 1152, 1068, 997, 882, 825, 681 cm$^{-1}$; $^1$H NMR: (300 MHz, $CDCl_3$) δ 4.26 (d, 1H, J = 3.6 Hz, C**H**OTIPS), 2.06 (m, 1H, C**H**$(CH_3)_2$), 1.10–0.97 (m, 27H, TIPS, CH(C**H**$_3)_2$), $^{13}$C NMR: (75 MHz, $CDCl_3$) δ 173.2, 65.9, 33.7, 17.9, 17.8, 17.7, 17.0,

15.3, 12.2; HRMS (FAB+) exact mass calculated for [M+H] ($C_{14}H_{31}O_3Si$) requires *m/z* 275.2043, found *m/z* 275.2041; $[\alpha]_D^{25} = -16.81$ (c = 1.0 $CHCl_3$).




**(*S*)-methyl3-(3-(7-(benzyloxy)-1-(4-methoxybenzyl)-1*H*-indol-3-yl)-4 hydroxy-phenyl)-2-((*S*)-3-methyl-2-(triisopropylsilyloxy)butanamido)propanoate 4**: A 100 mL round bottom flask with stirbar is charged with Pd(dppf)$Cl_2$ (0.633 g, 0.7755 mmol), $K_3PO_4$ (8.78 g, 41.36 mmol) and indole boronic ester **2** (8.74 g, 18.62 mmol) in a glove box. This flask was capped with a rubber septa and brought out of the box where in it was placed under a balloon of argon. To the flask is added aryl iodide **3** (5.976 g, 10.34 mmol) in 60 mL of degassed 1,4-dioxane. To this solution is then added 6 mL of degassed water and the resulting solution is stirred at 40 °C for 2 hours. After the reaction was judged complete by TLC analysis, the reaction mixture was diluted with 200 mL of diethyl ether and washed sequentially with 100 mL portions of water, saturated $NH_4Cl$ solution, and brine. The organic portion is dried over sodium sulfate and concentrated *in vacuo*. These crude extracts were purified by column chromatography (4% $Et_2O/CH_2Cl_2$) to yield the title compound (6.38 g, 78%) as a white amorphous solid. IR (Film): 3409, 2945, 2867, 2360, 1747, 1654, 1612, 1570, 1512, 1456, 1385, 1248, 1209, 1175, 1063, 882, 821 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 7.34–6.68 (m, 17H, Ar**H** and N**H**); 5.59 (s, 2H, OC**H₂**Ph), 5.34 (s, 1H,

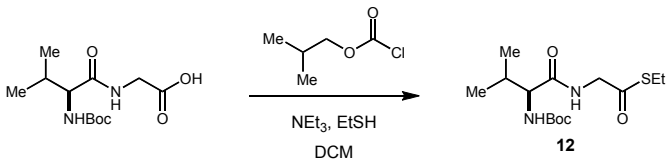
ArO**H**), 5.15 (s, 2H, OC**H**$_2$-*p*MeOPh), 4.90 (ddd, 1H, J = 6.0, 6.3 and 8.4 Hz, C**H**$CO_2$Me), 4.14 (d, 1H, J = 3.3 Hz, C**H**OTIPS); 3.77 (s, 3H, ArO**Me**); 3.66 (s, 3H, $CO_2$**Me**); 3.05 (m, 2H, *C***H**$_2$Ar); 1.93 (ddq, 1H, J = 3.6, 7.2, and 7.9 Hz, C**H**$Me_2$); 1.10–0.98 (m, 21H, TIPS); 0.88 (d, 3H, J = 6.9 Hz, CH(**Me**)Me); 0.79 (d, 3H, J = 6.9 Hz, CH(**Me**)Me) $^{13}$C NMR: (300 MHz, $CDCl_3$) δ 172.4, 171.8, 158.8, 152.5, 146.9, 136.7, 131.0, 129.2, 129.1, 128.6, 128.1, 128.0, 127.8, 127.5, 126.5, 121.1, 120.9, 115.4, 113.9, 112.7, 110.9, 104.6, 78.1, 76.6, 70.4, 55.2, 52.5, 52.2, 52.1, 37.7, 33.9, 18.0, 17.9, 17.7, 17.2, 12.3; HRMS (FAB+) exact mass calculated for [M+•] ($C_{47}H_{60}N_2O_7Si$) requires *m/z* 792.4170, found *m/z* 792.4175; $[\alpha]_D^{25}$: –9.39 (c = 1.03, $CHCl_3$).




**4** **4a**

**(*S*)-3-(3-(7-(benzyloxy)-1-(4-methoxybenzyl)-1*H*-indol-3-yl)-4-hydroxyphenyl)-2-((*S*)-3-methyl-2-(triisopropylsilyloxy)butanamido)propanoic acid 4a:** To a solution of **4** (9.50 g, 11.98 mmol) in THF/MeOH/$H_2O$ (130 mL, 10:2:1) was added LiOH•$H_2O$ (2.01 g, 47.9 mmol) with stirring. After the reaction was judged complete by TLC analysis (4 h), the reaction mixture was diluted with 300 mL of diethyl ether, acidified with 1N HCl to pH 2, and washed with 100 mL of brine. The organic portion was dried over sodium sulfate and concentrated *in vacuo*. These crude extracts were purified by column chromatography (40% EtOAc/Hexanes with 1% AcOH) to yield the title compound (9.24 g, 99%) as a white amorphous solid. IR (Film): 3402, 2944,

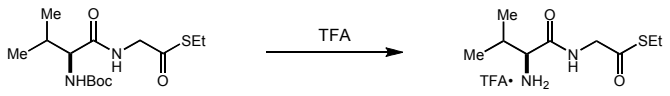
2867, 1723, 1641, 1613, 1572, 1513, 1454, 1385, 1248, 1209, 1176, 1063, 909, 882, 821, 732 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 7.35–6.73 (m, 17H, Ar**H** and N**H**); 5.57 (s, 2H, OC**H**$_2$Ph), 5.13 (s, 2H, OC**H**$_2$-pMeOPh), 4.89 (dd, 1H, J = 7.2, 12.9 Hz, C**H**$CO_2H$), 4.16 (d, 1H, J = 3.3 Hz, C**H**OTIPS); 3.76 (s, 3H, ArO**Me**); 3.17 (dd, 1H, J = 5.4, 14.7 Hz, C**H**$_2$Ar); 3.05 (dd, 1H, J = 7.2, 14.4 Hz, C**H**$_2$Ar); 1.92 (m, 1H, C**H**$Me_2$); 1.04–0.98 (m, 21H, TIPS); 0.83 (d, 3H, J = 6.9 Hz, CH(**Me**)Me); 0.74 (d, 3H, J = 6.9 Hz, CH(**Me**)Me); $^{13}C$ NMR: (75 MHz, $CDCl_3$) δ 175.8, 173.5, 158.8, 152.6, 146.9, 136.7, 131.3, 131.1, 129.2, 129.1, 128.6, 128.2, 128.0, 127.8, 127.2, 126.5, 121.3, 120.9, 115.6, 113.9, 112.7, 110.9, 104.5, 78.0, 70.4, 55.2, 52.6, 52.1, 37.0, 33.9, 18.0, 17.9, 17.6, 17.2, 12.3; HRMS (FAB+) exact mass calculated for [M+•] ($C_{46}H_{58}N_2O_7Si$) requires *m/z* 778.4013, found *m/z* 778.4034 $[\alpha]_D^{25} = -28.48$ (c = 0.53, $CHCl_3$)




**12**

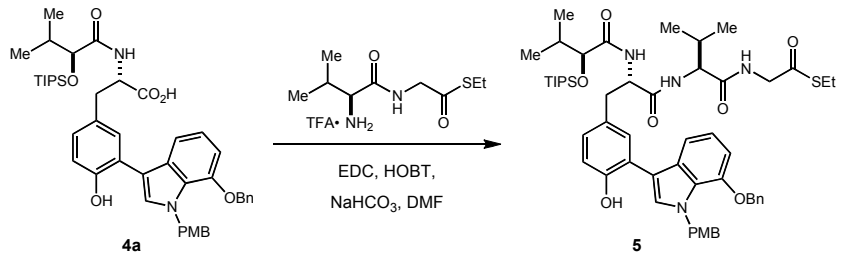
**(*S*)-*S*-ethyl2-(2-(*tert*-butoxycarbonylamino)-3-methylbutanamido) ethanethioate**: To a 0 °C solution of commercially available *N*-Boc-valinylglycine (2.96 g, 10.79 mmol) in 50 mL of $CH_2Cl_2$ under argon was added $NEt_3$ (3.91 mL, 28.054 mmol) followed by isobutyl chloroformate (1.66 mL, 12.95 mL). After 1 hour at 0 °C was added ethanethiol (1.67 mL, 2.0 mmol) and the reaction was warmed to room temperature and stirred for ten hours. The reaction mixture was then diluted with $NaHCO_3$ and extracted 3 × 100 mL of $CH_2Cl_2$. The combined organic layer was washed with 200 mL of brine and concentrated. The resulting oil was recrystallized

from a hot solution of 10% ethyl acetate in hexanes to give the title compound as a white crystalline solid in 85% yield (2.90 g). IR (Thin Film): 3310, 3077, 2968, 2932, 1688, 1663, 1525, 1392, 1366, 1298, 1247, 1170, 1094, 1043, 1016, 966 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 6.66 (br s, 1H, N**H**), 5.03 (br s, 1H, N**H**Boc), 4.19 (d, 2H, J = 5.4 Hz, NHC**H$_2$**), 4.00 (dd, 1H, J = 6.0, 8.4 Hz, C**H**NHBoc), 2.91 (q, 2H, J = 7.5 Hz, SC**H$_2$**), 2.21 (m, 1H, C**H**Me(Me)), 1.44 (s, 9H, O**tBu**), 1.25 (t, 3H, J = 7.5 Hz, $SCH_2$**C$H_3$**), 0.98 (d, 3H, J = 6.9 Hz, CH**Me**(Me)), 0.94 (d, 3H, J = 6.9 Hz, CHMe(**Me**)); $^{13}C$ NMR: (75 MHz, $CDCl_3$) δ 196.9, 172.2, 156.2, 80.3, 60.1, 49.2, 30.9, 28.5, 23.4, 19.6, 17.9, 14.8; HRMS: (FAB+) exact mass calculated for [M+H] ($C_{14}H_{27}N_2O_4S$) requires *m/z* 319.1702, found *m/z* 319.1692; $[\alpha]_D^{25}$ = –17.01 (c = 1.0 $CHCl_3$).



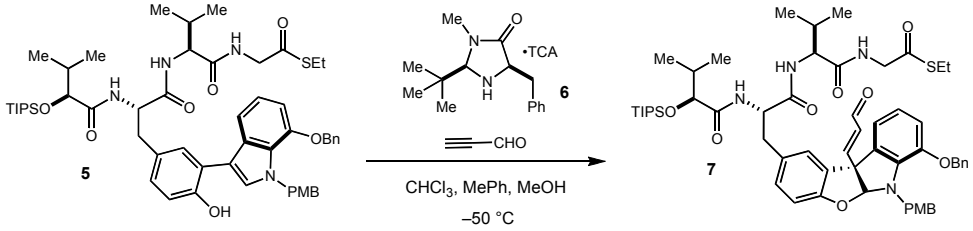

**(*S*)-*S*-ethyl 2-(2-amino-3-methylbutanamido)ethanethioate trifluoroacetate salt**: Trifluoroacetic acid (39.7 mL) was added to N-Boc-valine-glycine thioester (12.6 g, 39.7 mmol) with stirring at room temperature. After 30 minutes the solution was concentrated *in vacuo*. The resulting solid was repeatedly triturated with $Et_2O$ the dried *in vacuo* to yield the title compound as a white crystalline solid in 96% yield (12.0 g). IR (Thin Film): 2972, 2941, 1668, 1471, 1202, 1181, 1137, 971, 838, 799, 722 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CD_3OD$) δ 4.28 (d, 1H, J = 17.4 Hz, NHC**H**$_2$), 4.06 (d, 1H, J = 17.4 Hz, NHC**H**$_2$), 3.77 (d, 1H, J = 5.7 Hz, C**H**$NH_2$), 2.91 (q, 2H, J = 7.5 Hz, SC**H$_2$**),

2.25 (m, 1H, C**H**Me(Me)), 1.23 (t, 3H, J = 7.5 Hz, $SCH_2\mathbf{CH_3}$), 1.10 (d, 3H, J = 6.9 Hz, CH**Me**(Me)), 1.07 (d, 3H, J = 6.9 Hz, CHMe(**Me**)); $^{13}$C NMR: (75 MHz, $CD_3OD$) δ 196.8, 169.0, 156.2, 58.5, 30.3, 22.7, 17.7, 16.6, 13.9; HRMS: (EI+) exact mass calculated for [M+H] ($C_9H_{19}N_2O_2S$) requires *m/z* 219.1167, found *m/z* 219.1171; $[\alpha]_D^{25}$ = –0.95 (c = 1.0 MeOH)



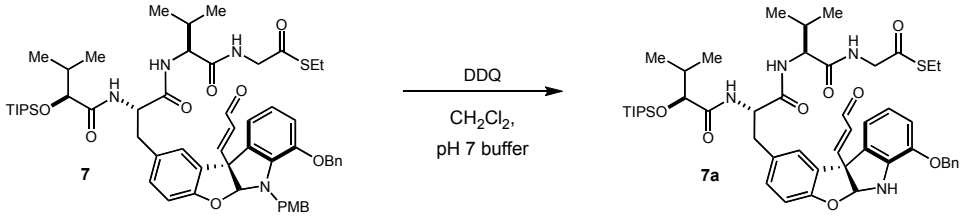

**Thioester 5**: To a solution of **4a** (8.96 g, 11.5 mmol) and valine-glycine-thioester •TFA (4.71 g, 15.0 mmol) in DMF (120 mL) was added HOBt (2.02 g, 15.0 mmol), EDC•HCl (2.87 g, 15.0 mmol), and $NaHCO_3$ (3.86 g, 46.0 mmol) with stirring. After the reaction was judged complete by TLC analysis (7 hours), the reaction mixture was diluted with 500 mL of diethyl ether and washed with 200 mL of saturated $NH_4Cl$, $H_2O$, and brine. The organic portion was dried over sodium sulfate and concentrated *in vacuo*. These crude extracts were purified by column chromatography (40% EtOAc/hexanes) to yield the title compound (10.7 g, 95% yield) as a white amorphous solid. IR (Film): 3288, 2962, 2943, 2868, 1642, 1612, 1513, 1455, 1385, 1262, 1248, 1209, 1176, 1064, 909, 882, 823, 732 $cm^{-1}$; $^1$H NMR: (300 MHz, $CDCl_3$) δ 7.35–6.49 (m, 19H, Ar**H** and N**H**); 5.57 (s, 2H, OC$\mathbf{H_2}$Ph); 5.15 (s, 2H, OC$\mathbf{H}_2$-pMeOPh); 4.62 (dd, 1H, J = 7.2, 12.9 Hz, $CH_2$C**H**CONH); 4.30 (dd, 1H, J = 5.6, 8.6 Hz, NHC**H**$CHMe_2$); 4.16 (d, 1H, J = 3.0 Hz, C**H**OTIPS); 3.98 (t, 2H, J = 4.8 Hz, NHC$\mathbf{H_2}$);

3.76 (s, 3H, ArO**Me**); 3.08 (m, 2H, C**H$_2$**Ar); 2.82 (q, 2H, J = 7.5 Hz, SC**H$_2$**); 2.21 (m, 1H, NHCHC**H**Me$_2$); 1.92 (m, 1H, OCHC**H**Me$_2$); 1.19 (t, 3H, J = 7.5 Hz, SCH$_2$C**H$_3$**); 1.04–0.98 (m, 21H, TIPS); 0.89–0.83 (m, 9H, OCHCH(**Me**)Me, NHCHCH(**Me**)**Me**); 0.74 (d, 3H, J = 6.9 Hz, OCHCH(**Me**)Me); $^{13}$C NMR: (300 MHz, $CDCl_3$) δ 196.9, 173.8, 171.0, 170.9, 158.8, 152.5, 146.9, 136.7, 131.2, 131.0, 128.9, 128.6, 128.3, 128.1, 127.8, 127.7, 126.5, 121.7, 120.9, 115.7, 113.9, 112.7, 110.8, 104.6, 78.0, 70.4, 58.5, 55.2, 54.8, 52.2, 48.9, 37.2, 34.0, 29.8, 23.0, 19.4, 18.0, 17.5, 17.0, 14.5, 12.4; HRMS (FAB+) exact mass calculated for [M+•] ($C_{55}H_{74}N_4O_8SiS$) requires *m/z* 978.4996, found *m/z* 978.4966; $[\alpha]_D^{25} = -17.13$ (c = 2.18, $CHCl_3$).



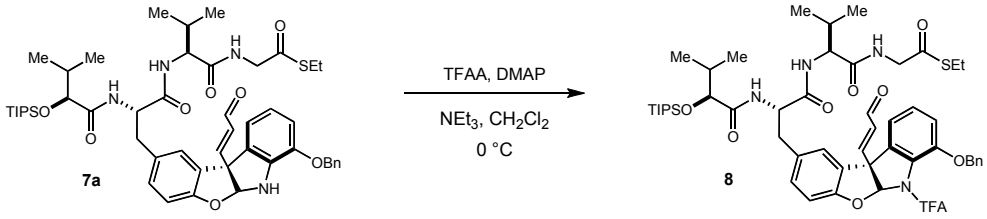

**Aldehyde 7**: (2*R,5R*)-2-*tert*-butyl-5-benzyl-3-methylimidazolidin-4-one•TCA **6** (1.88 g, 4.59 mmol) and phenol **5** (15.0 g, 15.3 mmol) were dissolved in 77 mL of $CHCl_3$/MePh/$CH_3OH$ (10:10:1). This mixture was cooled to –78 °C. To this cold solution was added freshly distilled propynal (8.1 g, 8.81 mL, 150 mmol). The reaction was warmed to –50 °C and stirred for 50 hours before being diluted with 200 mL $Et_2O$ and 50 mL of pH 7 buffer. The layers were separated and the organic portions were washed with brine and dried over sodium sulfate. Following concentration *in vacuo*, the crude reaction extracts were purified by flash chromatography (75% $Et_2O$ in pentane) to afford the title compound as an amorphous white solid as a >20:1 mixture

of diastereomers (13.6 g, 86%). IR (Film): 3409, 3300, 2962, 2942, 2868, 1692, 1648, 1512, 1494, 1466, 1385, 1248, 1175, 1100, 1064, 973, 911, 882, 822, 733, 683 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 9.45 (d, 1H, J = 7.5 Hz, C**H**O); 7.33–6.72 (m, 16H, Ar-**H**, C**H**=**C**HCHO); 6.46 (d, 1H, J = 8.1 Hz, CON**H**); 5.93 (s, 1H, OC**H**N); 5.88 (dd, 1H, J = 15.9, 7.8 Hz, CH=**C**H**C**HO); 5.22 (d, 1H, J = 15.3 Hz, NC**H₂**-pMeOPh); 5.01 (m, 2H, OC**H₂**Ph); 4.59–4.46 (m, 3H, C**H**NHCO, NC**H₂**-pMeOPh); 4.23 (dd, 1H, J = 8.2, 5.8 Hz, NHC**H₂**); 4.15 (d, 1H, J = 3.3 Hz, C**H**OTIPS); 4.03 (dd, 1H, J = 5.8, 1.0 Hz, NHC**H₂**); 3.76 (s, 3H, ArO**Me**); 3.11–2.82 (m, 4H, C**H₂**Ar, SC**H₂**); 2.18 (m, 1H, NHCHC**H**$Me_2$); 1.95 (m, 1H, OCHC**H**$Me_2$); 1.22 (t, 3H, J = 7.5 Hz, $SCH_2$**C**$H_3$); 1.05 (m, 21H, TIPS); 0.90–0.83 (m, 9H, OCHCH(**Me**)Me, NHCHCH(**Me**)**Me**); 0.71 (d, 3H, J = 6.9 Hz, OCHCH(**Me**)Me); $^{13}C$ NMR: (300 MHz, $CDCl_3$) δ 196.8, 196.6, 193.3, 173.8, 173.4, 171.0, 170.7, 158.9, 158.1, 155.3, 152.5, 146.9, 145.2, 137.3, 136.6, 136.5, 133.0, 131.8, 131.2, 130.3, 129.9, 129.7, 129.2, 129.0, 128.3, 128.0, 127.8, 127.5, 126.5, 121.7, 121.3, 121.0, 116.9, 115.7, 114.0, 113.9, 113.6, 112.7, 110.8, 110.3, 107.0, 104.6, 78.0, 70.8, 70.4, 61.6, 58.5, 55.2, 54.8, 51.1, 49.0, 37.5, 33.9, 30.3, 23.1, 19.3, 18.1, 17.5, 17.0, 14.6; HRMS (FAB+) exact mass calculated for [M+H] ($C_{58}H_{77}N_4O_9SiS$) requires *m/z* 1033.518, found *m/z* 1033.518; $[\alpha]_D^{25}$ = –46.19 (c = 1.20, $CHCl_3$).



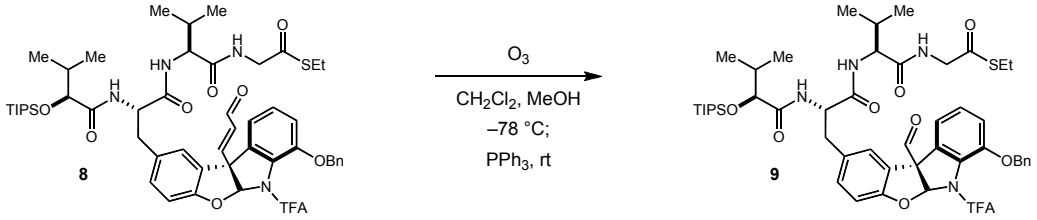
**Amine 7a**: To a vigorously stirred solution of aldehyde **7** (4.8 g, 4.64 mmol) in a 1:1 mixture of dichloromethane and pH 7 phosphate buffer (75 mL each) at 0 °C was added freshly recrystallized DDQ (2.10 g, 9.29 mmol). The resulting dark heterogeneous reaction mixture was allowed to warm to ambient temperature over the course of two hours, after which time it was diluted with ethyl acetate and washed with a saturated solution of $Na_2SO_3$, followed by a saturated solution of $NaHCO_3$ and brine. The layers were separated and the aqueous layer wash washed with three times with 50 mL of ethyl acetate. The combined organic layer was washed with brine and dried over sodium sulfate. Purification by flash chromatography on silica gel (35%–40% EtOAc in hexanes) gave the desired product as an amorphous off-white solid in 84% yield (3.54 g). IR (Film): 3301, 2962, 2942, 2868, 1691, 1648, 1498, 1466, 1387, 1206, 1058, 975, 882, 823, 749, 683 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 9.61 (d, 1H, J = 7.5 Hz, C**H**O); 7.41–6.67 (m, 12H, Ar-**H**, C**H**=**C**HCHO); 6.56 (d, 1H, J = 8.7 Hz, CON**H**); 6.24 (d, 1H, J = 2.4 Hz, OC**H**N); 6.14 (dd, 1H, J = 15.6, 7.5 Hz, CH=**C**HCHO); 5.04 (s, 2H, OC**H₂**Ph); 4.59 (m, 1H, CONHC**H**CH); 4.24 (dd, 1H, J = 8.6, 5.6 Hz, NHC**H₂**); 4.14 (m, 1H, CONHC**H**$CH_2$); 4.03 (d, 1H, J = 5.7 Hz, C**H**OTIPS); 3.93 (m, 1H, NHC**H₂**); 3.15–2.80 (m, 4H, C**H₂**Ar, SC**H₂**); 2.17 (m, 1H, NHCHC**H**$Me_2$); 1.92 (m, 1H, OCHC**H**$Me_2$); 1.22 (t, 3H, J = 7.5 Hz, $SCH_2$**C**$H_3$); 1.05 (m, 21H, TIPS); 0.90–0.82 (m, 9H, OCHCH(**Me**)Me, NHCHCH(**Me**)**Me**); 0.72 (d, 3H, J = 6.9 Hz, OCHCH(**Me**)Me); $^{13}C$ NMR: (300 MHz, $CDCl_3$) δ 196.6, 193.5, 173.3, 170.7, 170.4, 158.2, 155.4, 137.1, 136.6, 133.1, 130.2, 129.7, 129.5, 129.4, 129.3, 129.2, 128.6, 128.1, 127.6, 125.0, 121.0, 116.4, 112.3, 110.4, 103.0, 78.0, 70.4, 63.7, 58.5, 54.6, 49.0, 37.5, 33.9, 30.3, 23.1, 19.0, 18.1, 18.0, 17.9, 17.5, 17.0, 14.6, 12.4; HRMS

(FAB+) exact mass calculated for [M+H] ($C_{50}H_{69}N_4O_8SiS$) requires *m/z* 913.4605, found *m/z* 913.4632; $[\alpha]_D^{25} = -61.30$ (c = 3.08, $CHCl_3$).



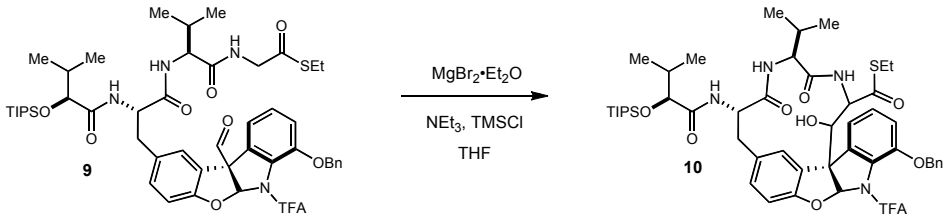

**Aldehyde 8**: To a solution of amino aldehyde **7a** (3.54 g, 3.87 mmol), pyridine (0.78 mL, 9.68 mmol) and DMAP (165 mg, 1.35 mmol) in 77 mL of dichloromethane at 0 °C was added trifluoroacetic anhydride (0.82 mL, 5.81 mmol) dropwise by syringe under argon. After 30 minutes the reaction was diluted with 200 mL of ethyl acetate and washed with 60 mL of saturated sodium bicarbonate solution. The layers were separated and the organic fraction was washed with brine and dried over sodium sulfate. Purification by flask chromatography on silica gel (40% ethyl acetate in hexanes) gave the title compound product as an amorphous yellow solid in 87% yield (354 mg). IR (Film): 3406, 3306, 2962, 2868, 1731, 1695, 1650, 1492, 1463, 1387, 1292, 1204, 1183, 1154, 1058, 981, 882, 823, 738, 684 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$) δ 9.65 (d, 1H, J = 7.2 Hz, C**H**O); 7.47–6.54 (m, 13H, Ar-**H**, C**H**=**C**HCHO, OC**H**N); 6.24 (dd, 1H, J = 15.9, 7.2 Hz, CH=**C**HCHO); 5.19 (dd, 2H, J = 18.6, 6.4 Hz, OC**H₂**Ph); 4.59 (m, 1H, CONHC**H**CH); 4.24–4.03 (m, 4H, NHC**H₂**, C**H**OTIPS, CONHC**H**$CH_2$); 3.12–2.86 (m, 4H, C**H₂**Ar, SC**H₂**); 2.13 (m, 1H, NHCHC**H**$Me_2$); 1.95 (m, 1H, OCHC**H**$Me_2$); 1.23 (t, 3H, J = 7.5 Hz, $SCH_2$**C**$H_3$); 1.05 (m, 21H, TIPS); 0.90–0.86 (m, 9H, OCHCH(**Me**)Me, NHCHCH(**Me**)**Me**); 0.75 (d, 3H, J = 6.6 Hz,

OCHCH(**Me**)Me); $^{13}$C NMR: (300 MHz, $CDCl_3$) δ 196.2, 192.7, 173.2, 170.5, 170.1, 157.3, 151.6, 149.6, 136.3, 135.2, 131.0, 130.8, 129.2, 128.6, 128.2, 128.0, 127.0, 124.9, 116.3, 114.4, 110.5, 100.4, 78.0, 70.8, 63.3, 58.5, 54.4, 49.0, 37.6, 33.9, 30.6, 23.1, 18.9, 18.1, 18.0, 17.5, 17.1, 14.6, 12.4; $^{19}$F NMR: (75 MHz, $CDCl_3$) δ –70.0 (s, 3F, $CF_3$); HRMS (FAB+) exact mass calculated for [M+H] ($C_{52}H_{68}N_4O_9F_3SiS$) requires *m/z* 1009.443, found *m/z* 1009.444; $[\alpha]_D^{25}$ = –133.69 (c = 0.37, $CHCl_3$).



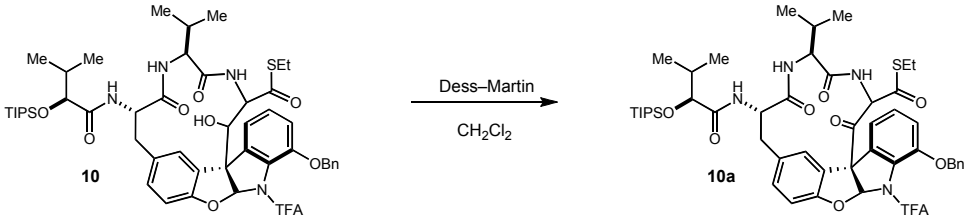

**Aldehyde 9**: A stream of ozone was passed through a solution of α,β-unsaturated aldehyde **8** (601 mg, 0.59 mmol) in 14 mL of dichloromethane and 1.4 mL of methanol at –78 °C for 45 minutes. The solution was bubbled through with oxygen for ten minutes and then quenched by the addition of triphenylphospine (0.44 g, 1.67 mmol). After warming to room temperature overnight the reaction mixture was concentrated *in vacuo* and loaded directly onto a silica gel column. Elution with 35% ethyl acetate in hexanes afforded the desired product (517 mg, 88%) as an amorphous white solid. IR (Film): 3301, 2963, 2868, 1729, 1649, 1492, 1464, 1406, 1292, 1252, 1204, 1182, 1159, 985, 882, 823, 738, 684 $cm^{-1}$; $^1$H NMR: (300 MHz, $CDCl_3$) δ 10.1 (s, 1H, C**H**O); 7.46–6.42 (m, 12H, Ar-**H**, OC**H**N); 5.18 (dd, 2H, J = 17.7, 12.0 Hz, OC**H**$_2$Ph); 4.59 (m, 1H, CONHC**H**CH); 4.24–3.96 (m, 4H, NHC**H**$_2$, C**H**OTIPS, CONHC**H**$CH_2$); 3.14–2.87 (m, 4H, C**H**$_2$Ar, SC**H**$_2$); 2.14 (m, 1H, NHCHC**H**$Me_2$); 1.92

(m, 1H, OCHC**H**$Me_2$); 1.24 (t, 3H, J = 7.5 Hz, $SCH_2$**C$H_3$**); 1.04 (m, 21H, TIPS); 0.93–0.84 (m, 9H, OCHCH(**Me**)Me, NHCHCH(**Me**)**Me**); 0.69 (d, 3H, J = 6.6 Hz, OCHCH(**Me**)Me); $^{13}$C NMR: (300 MHz, $CDCl_3$) δ 196.4, 191.7, 173.4, 170.6, 170.4, 156.7, 149.5, 136.2, 132.1, 131.4, 130.7, 129.0, 128.5, 128.0, 127.0, 125.2, 124.0, 115.7, 115.0, 114.0, 110.8, 100.0, 78.0, 70.8, 58.6, 54.4, 49.0, 37.5, 33.9, 30.4, 23.2, 19.2, 18.0, 17.9, 17.8, 17.5, 17.0, 14.6, 12.3; $^{19}$F NMR: (75 MHz, $CDCl_3$) δ –70.3 (s, 3F, $CF_3$); HRMS (FAB+) exact mass calculated for [M+H] ($C_{50}H_{66}N_4O_9F_3SiS$) requires *m/z* 983.4272, found *m/z* 983.4238; $[\alpha]_D^{25}$ = –93.42 (c = 0.47, $CHCl_3$).



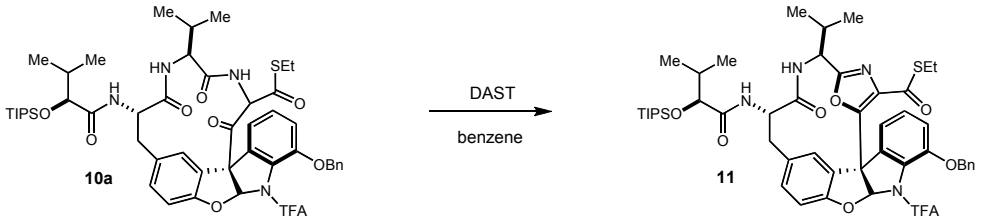

**Alcohol 10**: A flame-dried 1000 mL flask was charged with aldehyde **9** (2.1 g, 2.14 mmol) and $MgBr_2$•$Et_2O$ (1.65 g, 6.41 mmol) under Ar. To this flask was then added THF (425 mL) followed by $Et_3N$ (2.98 mL, 21.4 mmol) and TMSCl (0.68 mL, 5.34 mmol) with stirring. After 75 minutes 1N HCl (100 mL) was added and stirred for 10 minutes. The solution was diluted with EtOAc and pH 7 buffer, and washed with brine. The organic fractions were concentrated and the resulting oil purified by column chromatography (33% ethyl acetate in hexanes) to afford 1.49 g of the title compound (67%) as an off-white solid. IR (Film): 3401, 2962, 2868, 1732, 1681, 1644, 1490, 1462, 1288, 1204, 1181, 1160, 1125, 1099, 1057, 982, 881, 832, 752, 736, 684 $cm^{-1}$; $^1$H NMR: (300 MHz, $CDCl_3$) δ 7.50–6.86 (m, 10H, Ar-**H**); 6.77 (d, 1H, J = 8.4 Hz, Ar-**H**); 6.63 (s, 1H, OC**H**N); 5.36 (d, 1H, J = 10.2 Hz, CON**H**); 5.16 (dd, 2H, J

= 17.7, 12.3 Hz, OC**H**$_2$Ph); 4.89 (d, 1H, J = 9.3 Hz, C**H**C(O)SEt); 4.48 (d, 1H, J = 6.0 Hz, C**H**OH); 4.36 (m, 1H, CONHC**H**CH); 4.18–4.10 (m, 2H, C**H**OTIPS, CONHC**H**CH$_2$); 3.04 (dd, 1H, J = 12.3, 4.6 Hz, C**H**$_2$Ar); 2.85 (q, 2H, J = 7.5 Hz, SC**H**$_2$CH$_3$); 2.65 (t, 1H, J = 12.3 Hz, C**H**$_2$Ar); 2.05 (m, 1H, NHCHC**H**Me$_2$); 1.92 (m, 1H, OCHC**H**Me$_2$); 1.20 (t, 3H, J = 7.5 Hz, SCH$_2$C**H**$_3$); 1.06–0.94 (m, 30H, TIPS, OCHCH(**Me**)Me, NHCHCH(**Me**)**Me**); 0.84 (d, 3H, J = 6.6 Hz, OCHCH(**Me**)Me); $^{13}$C NMR: (300 MHz, $CDCl_3$) δ 199.8, 172.3, 170.4, 169.9, 158.6, 149.4, 136.7, 136.4, 129.8, 129.7, 128.5, 128.4, 128.3, 127.9, 127.3, 127.1, 126.4, 126.2, 117.9, 114.2, 110.9, 97.8, 77.9, 72.5, 70.8, 64.6, 58.9, 55.8, 40.2, 33.8, 30.1, 23.9, 19.3, 18.2, 18.0, 17.9, 17.8, 17.6, 17.5, 14.2, 12.2; $^{19}$F NMR: (75 MHz, $CDCl_3$) δ –69.7 (s, 3F, $CF_3$); HRMS (FAB+) exact mass calculated for [M+H] ($C_{50}H_{66}N_4O_9F_3SiS$) requires *m/z* 983.4272, found *m/z* 983.4243; $[\alpha]_D^{25}$ = –129.17 (c = 0.27, $CHCl_3$).



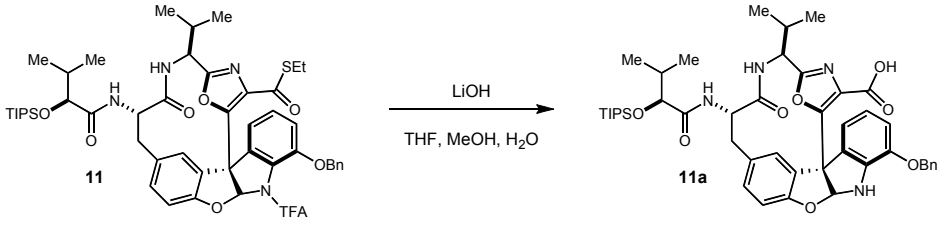

**Ketone 10a**: To a solution of **10** (46 mg, 0.047 mmol) in 1.0 mL of $CH_2Cl_2$ was added Dess–Martin periodinane (59 mg, 0.14 mmol). After 30 minutes the solution was diluted with EtOAc and washed with a saturated solution of $NaHCO_3$. The organic fractions were concentrated and the resulting oil purified by column chromatography to afford 37 mg of the title compound (80%) as an off-white solid. IR (Film): 3408, 3272, 2925, 2868, 1735, 1651, 1516, 1492, 1465, 1293, 1204, 1184, 1163, 1057, 967, 881, 737, 682 cm$^{-1}$; $^1$H NMR: (300 MHz, $CDCl_3$) δ 7.56–6.78 (m, 12H, Ar-**H**, OC**H**N); 5.76

(m, 2H, CON**H,** C**H**C(O)SEt); 5.16 (dd, 2H, J = 18.3, 12.3 Hz, OC**H$_2$**Ph); 4.45 (m, 1H, CONHC**H**CH); 4.18 (d, 1H, J = 3.3 Hz, C**H**OTIPS); 4.02 (m, 1H, CONHC**H**CH$_2$); 2.95–2.75 (m, 4H, C**H$_2$**Ar, SC**H$_2$**CH$_3$); 2.05 (m, 1H, NHCHC**H**Me$_2$); 1.92 (m, 1H, OCHC**H**Me$_2$); 1.20 (t, 3H, J = 7.5 Hz, SCH$_2$C**H$_3$**); 1.06 (m, 24H, TIPS, NHCHCH(Me)**Me**); 1.01–0.95 (m, 6H, OCHCH(**Me**)Me, NHCHCH(Me)**Me**); 0.88 (d, 3H, J = 6.3 Hz, OCHCH(**Me**)Me); $^{13}$C NMR: (300 MHz, $CDCl_3$) δ 196.3, 195.9, 172.4, 170.9, 169.8, 158.6, 149.0, 136.4, 132.2, 131.2, 130.3, 128.5, 128.4, 128.3, 128.2, 127.9, 127.0, 125.0, 124.2, 118.0, 114.5, 111.4, 96.7, 78.0, 73.7, 70.8, 61.8, 59.2, 55.2, 39.2, 33.8, 29.9, 23.8, 19.1, 18.4, 18.1, 18.0, 17.7, 17.5, 14.1, 12.4; $^{19}$F NMR: (75 MHz, $CDCl_3$) δ –70.0 (s, 3F, $CF_3$); HRMS (FAB+) exact mass calculated for [M+H] ($C_{50}H_{64}N_4O_9F_3SiS$) requires *m/z* 981.4115, found *m/z* 981.4107; $[\alpha]_D^{25}$ = –179.9 (c = 0.30, $CHCl_3$).



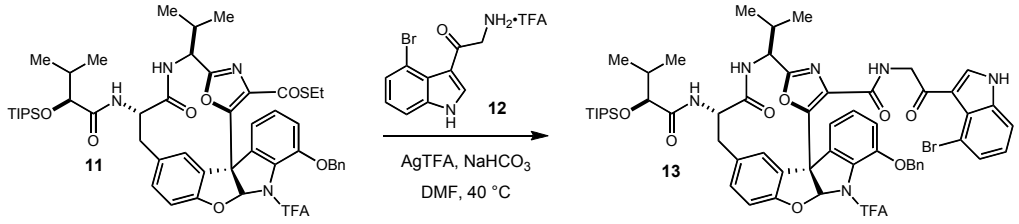

**Oxazole 11**: To a solution of **10a** (125 mg, 0.127 mmol) in benzene (11 mL) was added DAST (1.1 mL) dropwise by syringe. The solution was stirred at room temperature for 3 hours before being diluted with EtOAc and a saturated solution of $NaHCO_3$. The layers were separated and the aqueous layer was washed with ethyl acetate 3 × 50 mL. The combined organics were washed with brine and concentrated. The resulting oil was purified on silica gel (20% EtOAc in hexanes) to yield the title

compound (99 mg, 81%) as a pale yellow solid. IR (film): 3405, 3286, 2926, 2868, 1739, 1656, 1494, 1463, 1291, 1251, 1201, 1157, 990, 879 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CDCl_3$): δ 7.63 (d, 1H, J = 1.5 Hz, Ar-**H**), 7.40–7.26 (m, 5H, Ar-**H**), 7.18–7.08 (m, 2H, Ar-**H**), 6.99–6.93 (m, 2H, Ar-**H**), 6.84 (s, 1H, OC**H**N), 6.78 (d, 1H, J = 8.4 Hz, Ar-**H**), 5.26–5.11 (m, 3H, OC**H**$_2$Ph, CONHC**H**CH), 4.71 (m, 1H, CONHC**H**$CH_2$), 3.96 (d, 1H, J = 3.0 Hz, C**H**OTIPS), 3.42 (t, 1H, J = 12.3 Hz, C**H**$_2$Ar), 2.99–2.75 (m, 2H, SC**H**$_2$$CH_3$), 2.64 (dd, 1H, J = 12.3, 3.3 Hz, C**H**$_2$Ar), 2.43 (m, 1H, NHCHC**H**$(CH_3)_2$), 1.72 (m, 1H, OCHC**H**$(CH_3)_2$), 1.18 (t, 3H, J = 7.5 Hz, $SCH_2C$**H**$_3$), 1.07 (m, 24H, TIPS and NHCHCH(**C**$H_3)_2$), 0.91–0.87 (m, 6H, NHCHCH(**C**$H_3)_2$, OCHCH(**Me**)Me), 0.63 (d, 3H, J = 7.2 Hz, OCHCH(**Me**)Me); $^{13}C$ NMR: (75 MHz, $CDCl_3$) δ 186.2, 172.4, 171.7, 160.8, 156.8, 150.2, 149.7, 136.8, 136.2, 134.0, 130.4, 130.2, 129.4, 129.2, 128.8, 128.7, 128.6, 128.1, 127.6, 127.4, 115.0, 114.6, 110.7, 100.3, 77.9, 71.0, 60.9, 55.3, 53.5, 39.0, 34.0, 28.9, 23.0, 19.8, 18.3, 18.2, 18.0, 17.5, 17.0, 14.4, 12.6; HRMS: (FAB+) exact mass calculated for [M+H] ($C_{50}H_{62}F_3N_4O_8SiS$) requires *m/z* 963.4010, found *m/z* 963.3998; $[\alpha]_D^{25} = -61.01$ (c = 0.55, $CHCl_3$).



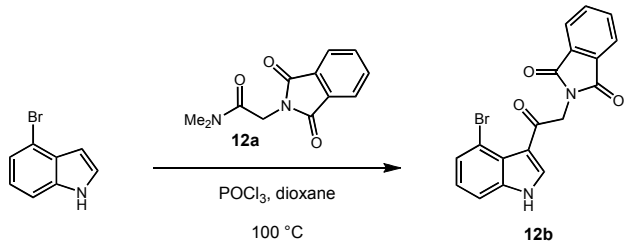

**Acid 11a**: To a solution of **11** (84 mg, 0.087 mmol) in THF/MeOH/$H_2O$ (4.4 mL, 10:2:1) was added LiOH•$H_2O$ (36.5 mg, 0.87 mmol) with stirring. After the reaction was judged complete by TLC analysis (2 hours), the reaction mixture was

diluted with 50 mL of diethyl ether, acidified with 1N HCl to pH 2, and washed with 20 mL of brine. The organic portion was dried over sodium sulfate and concentrated *in vacuo*. These crude extracts were purified by column chromatography (50% EtOAc/Hexanes to 10% MeOH in $CH_2Cl_2$) to yield the title compound (71 mg, 99%) as a white amorphous solid. IR (Film): 3405, 2917, 2849, 1654, 1498, 1464, 1289, 1251, 1209, 1068, 882, 754, 684 $cm^{-1}$; $^1H$ NMR: (300 MHz, $CD_3OD$): δ 7.54–7.26 (m, 6H, Ar-**H**), 7.18 (dd, 1H, J = 8.2, 1.6 Hz, Ar-**H**), 6.94 (s, 1H, OC**H**N), 6.87–6.65 (m, 4H, Ar-**H**), 5.08 (s, 2H, OC**H**$_2$Ph), 4.93 (m, 1H, CONHC**H**CH), 4.53 (m, 1H, CONHC**H**$CH_2$), 4.16 (d, 1H, J = 3.9 Hz, C**H**OTIPS), 3.15 (t, 1H, J = 12.3 Hz, C**H**$_2$Ar), 2.85 (dd, 1H, J = 12.3, 3.8 Hz, C**H**$_2$Ar), 2.36 (m, 1H, NHCHC**H**$(CH_3)_2$), 2.05 (m, 1H, OCHC**H**$(CH_3)_2$), 1.09 (m, 24H, TIPS and NHCHCH(**C**$\mathbf{H_3}$)$_2$), 1.04–1.01 (m, 6H, NHCHCH(**C**$\mathbf{H_3}$)$_2$, OCHCH(**Me**)Me), 0.87 (d, 3H, J = 6.9 Hz, OCHCH(**Me**)Me); $^{13}C$ NMR: (75 MHz, $CD_3OD$) δ 172.7, 172.6, 165.9, 160.0, 157.2, 154.0, 144.0, 138.3, 137.0, 133.0, 130.6, 130.1, 130.0, 128.7, 128.2, 127.9, 127.6, 127.4, 127.3, 120.3, 114.9, 112.1, 110.2, 103.9, 70.2, 61.5, 55.6, 53.8, 38.6, 33.8, 28.6, 19.1, 17.6, 17.5, 17.1, 17.0, 16.6, 12.2; HRMS: (FAB+) exact mass calculated for [M+Na] ($C_{46}H_{58}N_4O_8SiNa$) requires *m/z* 845.3921, found *m/z* 845.3914; $[\alpha]_D^{25}$ = –100.66 (c = 0.493, $CHCl_3$).



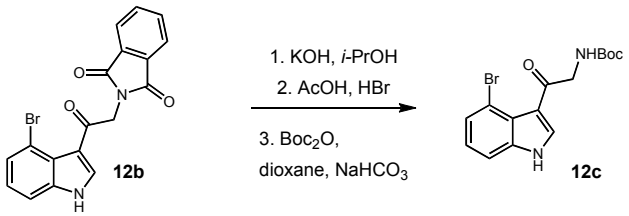
**Ketoamide 13**: To a flame-dried flask wrapped in foil to protect from light were combined thioester **11** (200 mg, 0.208 mmol), indole **12** (229 mg, 0.623 mmol), silver trifluoroacetate (276 mg, 1.248 mmol), and $NaHCO_3$ (114 mg, 1.352 mmol). The flask was sealed and degassed DMF (4.2 mL) was added via syringe. The reaction was heated to 40 °C in the dark for 2 hours and then diluted with EtOAc (100 mL) and $H_2O$ (20 mL). The collected organic layer was further washed with sat. aq. $NaHCO_3$ and brine (20 mL each), dried over $Na_2SO_4$ and solvent removed *in vacuo*. The resulting crude solids were purified by chromatography on silica gel (10% EtOAc:DCM) to yield the title compound as a white solid (211 mg, 88%). IR (Film): 3403, 3287, 2930, 2868, 1732, 1655, 1609, 1514, 1494, 1463, 1409, 1292, 1200, 1182, 1158, 1101, 1059, 995, 929, 880, 814, 740, 716, 684 $cm^{-1}$; $^1H$ NMR: (400 MHz, $CD_3CN$) δ 10.12 (br s, 1H, N-H), 8.10 (d, 1H, J = 3.2 Hz, Ar-H), 7.73 (app t, 1H, J = 5.2 Hz, Ar-H), 7.55-7.43 (m, 5H, Ar-H), 7.40-7.30 (m, 3H, Ar-H), 7.24 (app t, 1H, J = 8.0 Hz, Ar-H), 7.18-7.12 (m, 6H, Ar-H), 7.07 (app t, 2H, J = 8.0 Hz, Ar-H), 6.82 (d, 1H, J = 8.4 Hz, Ar-H), 5.20 (s, 2H, OC**H$_2$**Ph), 5.11 (dd, 1H, J = 12.0, 5.2, C(O)NHC**H**CH), 4.53 (dq, 2H, J = 13.2, 5.6 Hz, C**H$_2$**CO), 4.38 (dt, 1H, J = 8.4, 3.6 Hz, CONHC**H**$CH_2$), 4.10 (d, 1H, J = 3.6 Hz, C**H**OTIPS), 3.21 (t, 1H, J = 12.0 Hz, C**H**$_2$Ar), 2.79 (dd, 1H, J = 12.0, 3.2 Hz, C**H**$_2$Ar), 2.35 (m, 1H, NHCHC**H**$(CH_3)_2$), 1.97 (m, 1H, OCHC**H**$(CH_3)_2$), 1.09 (m, 24H, TIPS and NHCHCH(**CH$_3$**)$_2$), 0.98–0.87 (m, 9H, NHCHCH(**CH$_3$**)$_2$, OCHCH(**Me**)$_2$); $^{13}C$ NMR: (125 MHz, $CD_3CN$) δ 188.0, 172.0, 170.8, 160.4, 160.0, 156.05, 150.1, 149.0, 136.7, 135.2, 133.7, 132.0, 130.0, 129.7, 128.2, 127.5, 127.1, 124.2, 114.8, 113.8, 111.5, 109.7, 100.8, 77.8, 70.2, 55.6, 53.1, 46.5, 38.3, 33.6, 28.7, 18.6, 17.2, 16.7, 12.0. HRMS (ESI+) exact mass calc. for

$[M+H]^+$ ($C_{58}H_{65}BrF_3N_6O_9Si$) requires *m/z* 1153.3712, found *m/z* 1153.3705; $[\alpha]_D^{25}$ = – 74.4 (c = 1.0, EtOAc).




**2-(2-(4-bromo-1*H*-indol-3-yl)-2-oxoethyl)isoindoline-1,3-dione 12b**: To an oven-dried 100 mL flask equipped with a stirbar was added 4.20 g (18.10 mmol) of **12a**. After being capped with a rubber septa, the flask was charged with 45 mL of dioxane introduced via syringe under argon. Next, 1.687 mL (18.10 mmol) of $POCl_3$ was added via syringe under argon. The flask was then fitted with a condenser, and heated to 95 °C under argon for one hour. The reaction mixture was then allowed to cool to room temperature. Next, 1.135 mL (9.05 mmol) of 4-bromoindole was added via syringe through the septa on the condenser, and the resulting mixture was heated to reflux at 105 °C for 24 hours. After cooling to room temperature, 45 mL of water was added to the reaction mixture, followed by the dropwise addition of 1.0 M NaOH solution until the solution was pH 8. The resulting solution was heated to 100 °C for 20 minutes, then cooled in an ice bath. The product precipitated as a light brown powder, which was then washed 3 × 100 mL with $Et_2O$ and dried under vacuum for 24 hours to give 76% (2.65 g) of the title compound as a free-flowing tan powder. IR (Solid): 3312, 1769, 1704, 1673, 1657, 1513, 1426, 1396, 1317, 1314, 1200, 1143, 1100, 1087, 953, 777, 739 $cm^{-1}$; $^1H$ NMR: (500 MHz, $d_6$-DMSO) δ 12.49 (br s, 1H, N-H), 8.75 (s,

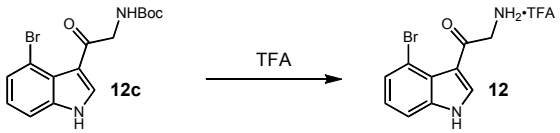
1H, C-2 Ar-H), 7.85–7.98 (m, 4H, phthalimide Ar-H), 7.54 (d, 1H, J = 8.1 Hz, C7 Ar-H), 7.40 (d, 1H, J = 8.1 Hz, J = 7.5 Hz, C-5 Ar-H), 7.15 (app t, 1H, J = 7.9 Hz, C-6 Ar-H) 5.08 (s, 1H, C**H**$_2$N); $^{13}$C NMR: (125 MHz, $CDCl_3$) δ 184.6, 167.7, 138.7, 136.1, 134.7, 131.7, 127.1, 124.3, 124.2, 123.3, 113.7, 111.9, 45.3; HRMS (FAB+) exact mass calc. for [M+•] ($C_{18}H_{12}N_2O_3Br$) requires *m/z* 383.0031, found *m/z* 383.0048.




***tert*-butyl 2-(4-bromo-1*H*-indol-3-yl)-2-oxoethylcarbamate 12c**: To a solution of bromide **12b** (4.0 g, 10.5 mmol) in 200 mL of 4:1 a mixture of water and isopropanol was added 650 mg (11.6 mmol) of KOH pellets. The reaction was heated to 100 °C for three hours, then cooled to room temperature. The resulting solution was acidified to pH 4 with 1.0 M HCl and concentrated in vacuo. The resulting solids were then dissolved in 42 mL of water and 42 mL of 33% HBr in AcOH and the solution was heated to 75 °C for two hours. After cooling to room temperature the crude reaction mixture was concentrated and suspended in 250 mL of a 5:1 mixture of $CH_2Cl_2$ and hexanes. The suspension was filtered through a sintered glass frit, and the resulting solids were washed with 4 × 100 mL of a 5:1 mixture of $CH_2Cl_2$ and hexanes.

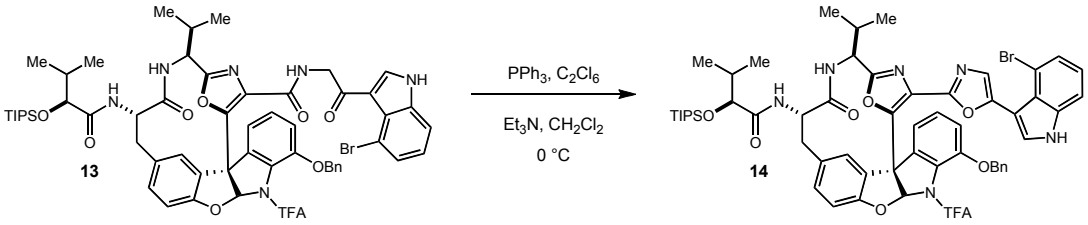
The resulting solid was then dissolved in 30 mL of dioxane and 15 mL of saturated aqueous $NaHCO_3$. Solid $Boc_2O$ (2.8 g 12.8 mmol) was then added in a single portion and the resulting solution was stirred at room temperature for 3.5 hours. The reaction

was diluted with 500 ml EtOAc and washed with $NaHCO_3$, and brine (100 mL each). The combined aqueous washings were further extracted with EtOAc (3 × 100 mL). The organics were dried over $Na_2SO_4$ and solvent removed *in vacuo*. The resulting solid was purified by flash chromatography (15% EtOAc in $CH_2Cl_2$) to yield 1.7 g of the title compound as an off-white solid, a total of 60% yield over the three-step sequence. IR (Film): 3257, 2978, 2931, 1667, 1613, 1564, 1516, 1444, 1411, 1393, 1367, 1331, 1309, 1288, 1250, 1199, 1163, 1108, 1048, 1027, 908, 863, 778, 736 $cm^{-1}$; $^1H$ NMR: (400 MHz, $CDCl_3$) δ 9.47 (s, 1H, C=CN**H**), 7.83 (d, 1H, J = 4.0 Hz, Ar-**H**), 7.48 (d, 1H, J = 8.0 Hz, Ar-**H**), 7.38 (d, 1H, J = 8.0 Hz, Ar-**H**), 7.13 (app t, 1H, J = 8.0 Hz, Ar-**H**), 5.68 (br s, 1H, $CH_2N$**H**), 4.49 (d, 2H, J = 4.0 Hz, COC$\mathbf{H}_2$), 1.49 (s, 9H, C(C$\mathbf{H}_3)_3$); $^{13}C$ NMR: (125 MHz, $CDCl_3$) δ 189.0, 156.3, 138.2, 134.2, 131.7 128.1, 125.0, 124.9, 123.6, 116.2, 114.6, 111.1, 49.1, 28.4; HRMS (ESI+) exact mass calc. for $[M+H]^+$ ($C_{15}H_{18}BrN_2O_3$) requires *m/z* 353.0495, found *m/z* 353.0498.



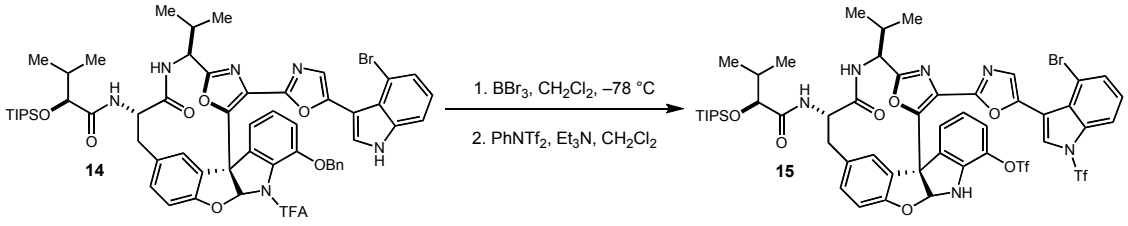

**2-amino-1-(4-bromo-1*H*-indol-3-yl)ethanone•TFA 12**: Trifluoroacetic acid (14 mL) was added to a flask containing **12c** (495 mg, 1.40 mmol). After stirring for 20 minutes, the reaction was diluted with toluene (20 mL) and volatiles removed *in vacuo*. The solids were further azeotroped with toluene (3 × 10 mL) and then triturated with $Et_2O$ to give the title compound as a light pink solid (510 mg, 99%). IR (Film): 3112, 2420, 1667, 1560, 151, 420, 1368, 1330, 1304, 1199, 1137, 903, 839, 800, 780,

739, 723 $cm^{-1}$; $^{1}H$ NMR: (400 MHz, $CD_3OD$) δ 8.32 (s, 1H, C=C**H**NH), 7.50 (d, 1H, J = 8.0 Hz, Ar-**H**), 7.46 (d, 1H, J = 8.0 Hz, Ar-**H**), 7.16 (app t, 1H, J = 8.0 Hz, Ar-**H**), 4.45 (s, 2H, COC**H**$_2$); $^{13}C$ NMR: (125 MHz, $CD_3OD$) δ 186.1, 140.5, 136.3, 128.9, 125.9, 115.4, 115.1, 112.6, 46.7; $^{19}F$ NMR: (75 MHz, $CD_3OD$) –77.39 (s, 3F, $CF_3$); HRMS (ESI+) exact mass calc. for $[M+H]^+$ ($C_{10}H_{10}BrN_2O$) requires *m/z* 252.9971, found *m/z* 252.9977.




**Bisoxazole 14**: To a solution of $PPh_3$ (795 mg, 3.03 mmol) in $CH_2Cl_2$ (30.3 mL) was added $C_2Cl_6$ (708 mg, 3.03 mmol). The solution was stirred at room temperature for 10 minutes at which time $Et_3N$ (0.842 mL, 6.06 mmol) was added dropwise. The resultant solution was stirred for 10 minutes and then added dropwise via cannula to a stirred $CH_2Cl_2$ (12.1 mL) solution of **13** (699 mg, 0.606 mmol) at 0 °C and held at this temperature for 1.5 hours. The solution was then diluted with 100 mL EtOAc, washed with 50 mL saturated aqueous $NaHCO_3$, and brine (2 × 20 mL), dried over $Na_2SO_4$ and concentrated. The resulting yellow solid was purified on silica gel (30–45% EtOAc in hexanes) to yield the title compound (604 mg, 88%) as a white solid. IR (Film): 3399, 3290, 2962, 2869, 1736, 1686, 1654, 1608, 1519, 1494, 1464, 1390, 1292, 1250, 1202, 1180, 1159, 1124, 1061, 1012, 983, 953, 918, 882, 842, 759, 739, 717, 684 $cm^{-1}$; $^{1}H$ NMR: (400 MHz, $CDCl_3$) δ 8.33 (d, 1H, *J* = 4.0 Hz, Ar-**H**),

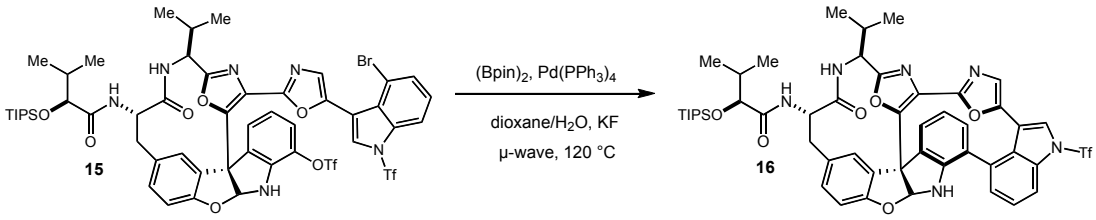
7.45 (m, 2H, Ar-**H**), 7.39 (app t, 1H, J = 4.0 Hz, Ar-**H**), 7.34 (d, 1H, J = 8.0 Hz, Ar-**H**), 7.31 (d, 1H, J = 4.0 Hz, Ar-**H**) 7.24 (app t, 1H, J = 8.0 Hz, Ar-H), 7.15-7.13 (m, 1H, Ar-**H**), 7.11 (s, 1H, Ar-H), 7.06 (dt, 2H, J = 12.0, 8.0 Hz, Ar-H), 6.93 (d, 1H, J = 4.0 Hz, Ar-**H**), 6.84 (d, 1H, J = 8.0 Hz, Ar-**H**), 6.77 (d, 1H, J = 8.0 Hz, Ar-**H**), 5.97 (d, 1H, J = 8.0 Hz, CON**H**CHCH), 5.07 (dd, 1H, J = 12.0, 8.0 Hz, CONHC**H**CH), 4.98 (dd, 2H, 16.0, 8.0 Hz, OC**H**$_2$Ph), 4.37 (dt, 1H, J = 12.0, 4.0 Hz, CONHC**H**CH$_2$), 4.18 (d, 1H, J = 4.0 Hz, C**H**OTIPS), 3.39 (t, 1H, J = 12.0 Hz, C**H**$_2$Ar), 2.74 (dd, 1H, J = 12.0, 4.0 Hz, C**H**$_2$Ar), 2.49 (m, 1H, NHCHC**H**(CH$_3$)$_2$), 2.06 (m, 1H, OCHC**H**(CH$_3$)$_2$), 1.09 (m, 24H, TIPS and NHCHCH(**CH$_3$**)$_2$), 1.04–0.94 (m, 9H, NHCHCH(**CH$_3$**)$_2$, OCHCH(**Me**)$_2$);$^{13}$C NMR: (125 MHz, $CDCl_3$) δ 172.3, 171.7, 161.5, 156.8, 153.1, 149.1, 147.5, 145.6, 136.7, 134.4, 130.4, 130.0, 129.1, 128.6, 128.3, 128.0, 127.9, 127.2, 125.3, 125.0, 123.6, 115.1, 114.1, 114.0, 110.7, 104.3, 100.4, 78.1, 70.5, 61.1, 56.1, 54.3, 38.1, 33.8, 29.2, 19.5, 12.4; $^{19}$F NMR: (75 MHz, $CDCl_3$) –70.42 (s, 3F, $CF_3$); HRMS (ESI+) exact mass calc. for $[M+H]^+$ ($C_{58}H_{63}BrF_3N_6O_8Si$) requires *m/z* 1135.3607, found *m/z* 1135.3578; $[\alpha]_D^{25} = -81.5$ (c = 1.4, $CHCl_3$).




**Bromo-bistriflate 15**: To a –78 °C solution of **14** (141.0 mg, 0.124 mmol) in $CH_2Cl_2$ (12.4 mL), was added $BBr_3$ solution (1.0 M in $CH_2Cl_2$, 0.497 mL, 0.497 mmol). The reaction was stirred at –78 °C for 1.5 hours at which point 5.0 mL pH 7 phosphate buffer and 5.0 mL EtOAc were added and the reaction allowed to achieve

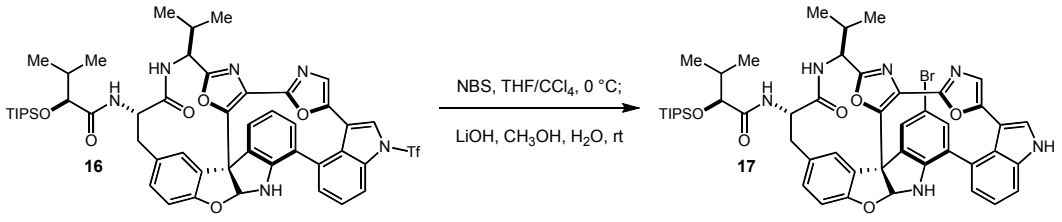
room temperature. The reaction mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$, brine, dried over $Na_2SO_4$ and concentrated. The resultant solid was taken up in 6.2 mL of $CH_2Cl_2$ and $Et_3N$ (172.0 μL, 1.240 mmol) then $PhNTf_2$ (221.0 mg, 0.620 mmol) were added sequentially. After 24 hours at room temperature the reaction was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$, brine, dried over $Na_2SO_4$ and concentrated *in vacuo*. The crude reaction mixture was purified on silica gel (25% EtOAc in hexanes) to yield 120.0 mg of the title compound as a white solid (80% yield over the two-step process). IR (Film): 3406, 3292, 2962, 2963, 2869, 1658, 1516, 1496, 1471, 1428, 1412, 1300, 1253, 1213, 1141, 1114, 1063, 1048, 987, 905, 881, 811, 676, 608 $cm^{-1}$; $^1H$ NMR: (500 MHz, $CDCl_3$) δ 7.94 (d, 1H, J = 8.5 Hz, Ar-**H**), 7.59 (d, 1H, J = 8.0 Hz, Ar-**H**), 7.51 (s, 1H, Ar-**H**), 7.36-7.34 (m, 2H, Ar-**H**), 7.20 (app t, 1H, J = 8.5 Hz, Ar-**H**), 7.16 (s, 1H, Ar-**H**), 7.12 (d, 1H, J = 7.0 Hz, Ar-**H**), 6.94 (d, 1H, J = 4.0 Hz, OC**H**NH), 6.88 (app t, 1H, J = 8.0 Hz, Ar-**H**), 6.67 (d, 1H, J = 7.5 Hz, Ar-**H**), 5.81 (d, 1H, J = 8.5 Hz, CON**H**CHCH), 5.50 (d, 1H, J = 4.0 Hz, OCHN**H**) 5.00 (dd, 1H, J = 8.0, 5.0 Hz CONHC**H**CH), 4.37 (m, 1H, CONHC**H**$CH_2$), 4.19 (d, 1H, J = 4.0 Hz, C**H**OTIPS), 3.34 (t, 1H, J = 12.5 Hz, C**H**$_2$Ar), 2.80 (dd, 1H, J = 12.5, 3.5 Hz, C**H**$_2$Ar), 2.45 (m, 1H, NHCHC**H**$(CH_3)_2$), 2.08 (m, 1H, OCHC**H**$(CH_3)_2$), 1.09 (m, 24H, TIPS and NHCHCH(**CH$_3$**)$_2$), 1.04–0.89 (m, 9H, NHCHCH(**CH$_3$**)$_2$, OCHCH(**Me**)$_2$); $^{13}C$ NMR: (125 MHz, $CDCl_3$) δ 171.9, 171.8, 161.6, 157.4, 155.0, 150.0, 141.4, 141.3, 136.2, 132.9, 132.6, 130.5, 130.4, 130.0, 129.5, 128.8, 128.1, 128.0, 127.8, 127.7, 127.6, 122.8, 121.7, 120.8, 120.7, 119.8, 118.1, 117.2, 114.7, 113.2, 112.6, 111.0, 103.2, 77.8, 61.2, 55.5, 54.2, 38.6, 33.9, 29.3, 19.5, 18.0, 18.0, 17.9, 17.3, 17.2, 12.3; $^{19}F$ NMR: (75 MHz, $CDCl_3$) –74.77 (s, 3F,

$CF_3$), –76.54 (s, 3F, $CF_3$); HRMS (ESI+) exact mass calc. for $[M+H]^+$ ($C_{51}H_{56}BrF_6N_6O_{11}S_2Si$) requires *m/z* 1213.2300, found *m/z* 1213.2296; $[\alpha]_D^{25} = -97.6$ (c = 0.5, $CHCl_3$).




**Macrocycle 16**: A microwave reactor vessel was charged with 20.0 mg of bromo-bistriflate **15** (16.47 μmol), 12.4 mg of $Pd(PPh_3)_4$ (10.70 μmol), 3.8 mg of bis(pinacolato)diboron (14.82 μmol) and 2.4 mg of LiCl (41.18 μmol) inside a glove box. The flask was sealed and charged with 3.6 mL of freshly distilled/degassed dioxane and 0.18 mL degassed $H_2O$ via syringe. The reaction was then heated to 120 °C in a CEM Discover microwave (200W) in 20 minute intervals while monitering the reaction progress by LCMS. The reaction was complete after three 20 minute heating cycles. The crude solution was cooled to room temperature and diluted with 25 mL of EtOAc and 15 mL of saturated $NH_4Cl$ solution. The layers were separated and the organic was washed 2 × 10 mL with brine and dried over sodium sulfate. Following concentration, the resulting residue was purified by flash chromatography on silica gel (25% EtOAc in hexanes) to yield the title compound as an amorphous solid (8.1 mg, 50%). IR (Film): 3405, 3296, 2962, 2925, 2869, 1655, 1519, 1491, 1462, 1426, 1410,

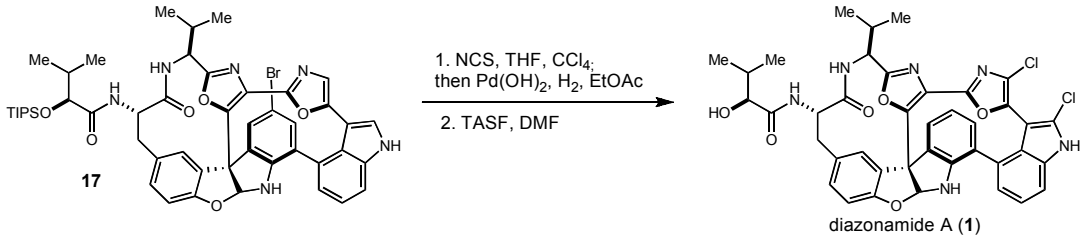
1260, 1234, 1209, 1095, 1066, 1022, 881, 801, 755, 666, 612 $cm^{-1}$; $^1H$ NMR: (500 MHz, $CDCl_3$) δ 7.97 (d, 1H, J = 8.5 Hz, Ar-**H**), 7.60 (d, 1H, J = 8.0 Hz, Ar-**H**), 7.59 (d, 1H, J = 8.0 Hz, Ar-**H**) 7.54 (app t, 1H, J = 8.0 Hz, Ar-**H**), 7.48-7.40 (m, 2H, Ar-**H**), 7.15 (d, 1H, J = 4.0 Hz Ar-**H**), 7.10 (dd, 1H, J = 8.0, 4.0 Hz, Ar-**H**), 7.00 (s, 1H, Ar-**H**), 6.98 (s, 1H, Ar-**H**), 6.77 (app t, 1H, J = 8.0 Hz, Ar-**H**), 6.60 (app t, 1H, J = 8.0 Hz, Ar-**H**), 6.35 (d, 1H, J = 4.0 Hz, OC**H**NH), 5.86 (d, 1H, J = 8.5 Hz, CON**H**CHCH), 5.11 (d, 1H, J = 4.0 Hz, OCHN**H**) 4.95 (dd, 1H, J = 8.0, 4.0 Hz CONHC**H**CH), 4.33 (m, 1H, CONHC**H**$CH_2$), 4.14 (d, 1H, J = 4.0 Hz, C**H**OTIPS), 3.46 (t, 1H, J = 12.0 Hz, C**H**$_2$Ar), 2.67 (dd, 1H, J = 12.0, 4.0 Hz, C**H**$_2$Ar), 2.36 (m, 1H, NHCHC**H**$(CH_3)_2$), 2.08 (m, 1H, OCHC**H**$(CH_3)_2$), 1.03 (m, 24H, TIPS and NHCHCH(**CH$_3$**)$_2$), 0.98–0.95 (m, 6H, NHCHCH(**CH$_3$**)$_2$), 0.82 (d, 3H, J = 8.0 Hz, OCHCH(**Me**)$_2$); $^{13}C$ NMR: (125 MHz, $CDCl_3$) δ 172.4, 171.9, 161.0, 158.2, 155.6, 152.3, 149.2, 143.5, 136.1, 132.8, 130.3, 130.2, 130.0, 128.4, 127,4, 127.2, 126.9, 126.1, 123.8, 120.8, 120.1, 113.8, 112.6, 110.6, 104.1, 78.1, 75.1, 61.3, 60.5, 56.2, 54.8, 37.8, 33.8, 30.2, 29.8, 24.9, 19.2, 18.1, 17.8, 17.4, 12.4; HRMS (ESI+) exact mass calc. for $[M+H]^+$ ($C_{50}H_{56}F_3N_6O_8Si$) requires *m/z* 985.3596, found *m/z* 985.3607; $[\alpha]_D^{25}$ = –80.0 (c = 0.40, $CHCl_3$).




**Bromoindoline 17**: 157 µL of a freshly prepared (5.3 mg/mL) *N*-bromosuccinimide stock solution (0.84 mg, 4.72 µmol) was added to a 0 °C solution of macrocycle **16** (4.6 mg, 4.67 µmol) in 3.9 mL of 1:1 THF/$CCl_4$. After 1 hour at 0 °C,

$CH_3OH$ (0.78 mL), $H_2O$ (0.39 mL), and $LiOH•H_2O$ (2.0 mg, 46.73 μmol) were added sequentially and the reaction was allowed to achieve room temperature. The reaction was determined to be complete by TLC analysis (1:1 EtOAc:hexanes) after four hours at room temperature. The reaction mixture was diluted with 25 mL of EtOAc and 15 mL of saturated $NaHCO_3$ solution. The layers were separated and the organic was washed 2 × 10 mL with brine and dried over sodium sulfate. Following concentration, the resulting residue was purified by flash chromatography on silica gel (50–60% EtOAc in hexanes) to yield the title compound as an amorphous solid (3.6 mg, 83%). IR (Film): 3401, 3294, 2926, 2867, 1712, 1655, 1516, 1492, 1464, 1344, 1297, 1260, 1206, 1182, 1115, 1096, 1072, 1014, 917, 882, 852, 805, 751, 685 $cm^{-1}$; $^1H$ NMR: (500 MHz, $CDCl_3$) δ 8.58 (s, 1H, Ar-**H**), 7.46 (m, 3H, Ar-**H**), 7.30 (m, 3H, Ar-**H**) 7.17 (s, 1H, Ar-**H**), 7.10 (m, 3H, Ar-**H**), 6.99 (d, 2H, J = 4.0 Hz, Ar-**H**), 6.92 (s, 1H, Ar-**H**), 6.75 (d, 1H, J = 8.0 Hz, Ar-**H**), 6.34 (d, 1H, J = 4.0 Hz, OC**H**NH), 5.91 (d, 1H, J = 8.5 Hz, CON**H**CHCH), 5.19 (d, 1H, J = 4.0 Hz, OCHN**H**) 5.00 (dd, 1H, J = 8.0, 4.0 Hz CONHC**H**CH), 4.35 (m, 1H, CONHC**H**$CH_2$), 4.14 (d, 1H, J = 4.0 Hz, C**H**OTIPS), 3.49 (t, 1H, J = 12.0 Hz, C**H**$_2$Ar), 2.68 (dd, 1H, J = 12.0, 4.0 Hz, C**H**$_2$Ar), 2.44 (m, 1H, NHCHC**H**$(CH_3)_2$), 2.03 (m, 1H, OCHC**H**$(CH_3)_2$), 1.03 (m, 24H, TIPS and NHCHCH(**C**$\mathbf{H_3}$)$_2$), 0.98–0.95 (m, 6H, NHCHCH(**C**$\mathbf{H_3}$)$_2$), 0.81 (d, 3H, J = 8.0 Hz, OCHCH(**Me**)$_2$); $^{13}C$ NMR: (125 MHz, $CDCl_3$) δ 172.4, 171.9, 160.6, 158.2, 154.1, 151.0, 148.5, 147.0, 136.9, 132.5, 130.6, 130.1, 129.9, 128.7, 128.5, 128.3, 126.9, 126.5, 125.6, 125.1, 124.3, 124.0, 123.7, 122.2, 112.0, 111.7, 110.6, 104.6, 103.8, 78.1, 61.1, 60.5, 56.2, 54.7, 37.9, 33.8, 29.8, 19.3, 18.1, 18.0, 17.8, 17.6, 17.4, 12.4; HRMS

(ESI+) exact mass calc. for $[M+H]^+$ ($C_{49}H_{56}BrN_6O_6Si$) requires *m/z* 931.3208, found *m/z* 91.3214; $[\alpha]_D^{25} = -65.8$ (c = 0.30, $CHCl_3$).




**Diazonamide A 1**: 137.6 μL of a freshly prepared (6.25 mg/mL) *N*-chlorosuccinimide stock solution (0.86 mg, 6.45 μmol) was added to a solution of macrocycle **17** (2.4 mg, 2.58 μmol) in 1.3 mL of 1:1 THF/$CCl_4$ and the reaction was heated to 40 °C for 12 hours until complete by LCMS analysis. To this reaction was added 30 mg $Pd(OH)_2$, 0.5 mL EtOAc and fitted with a balloon of $H_2$. After an additional 20 hours at 40 °C the reaction was filtered through celite (flushed with EtOAc 4 × 2 mL) and solvent removed *in vacuo*. The residue was dissolved in 1.3 mL DMF and a freshly prepared solution of TASF was added via syringe (70 μL of 20 mg/mL stock solution; 1.4 mg, 5.16 μmol). After 20 minutes the reaction was diluted with 5 mL of EtOAc and 2.5 mL of saturated $NaHCO_3$ solution. The organic layer was further washed with H2O and brine, dried over $Na_2SO_4$. Following concentration, the resulting residue was purified by preparative TLC (60% EtOAc in hexanes) to yield

diazonamide A (**1**) as an amorphous solid (1.2 mg, 60% over 2 steps). All spectral data were found to be in accord with those of the natural isolate.[4]

| **Diazonamide A $^{13}$C NMR signals in $CDCl_3$ (125 MHz)** | | |
|---|---|---|
| | **Natural diazonamide A** | **Synthetic diazonamide A** |
| **Position** | **$\partial$ in ppm** | **$\partial$ in ppm** |
| **1** | **174.8** | **174.8** |
| **2** | **57.2** | **57.1** |
| **3** | **38.9** | **38.9** |
| **4** | **129.9** | **129.9** |
| **5** | **131.1** | **131.1** |
| **6** | **111.3** | **111.3** |
| **7** | **159.7** | **159.7** |
| **8** | **129.6** | **129.7** |
| **9** | **131.1** | **131.0** |
| **10** | **62.3** | **62.3** |
| **11** | **106.1** | **106.1** |
| **12** | **127.8** | **127.8** |
| **13** | **123.9** | **123.9** |
| **14** | **120.9** | **120.9** |
| **15** | **131.2** | **131.2** |
| **16** | **123.2** | **123.2** |
| **17** | **151.0** | **151.1** |
| **18** | **131.6** | **131.7** |
| **19** | **122.7** | **122.7** |
| **20** | **124.3** | **124.3** |
| **21** | **112.2** | **112.2** |
| **22** | **136.9** | **136.9** |
| **23** | **127.6** | **127.5** |
| **24** | **98.2** | **98.2** |
| **25** | **141.7** | **141.8** |
| **26** | **130.1** | **130.0** |
| **27** | **129.2** | **129.1** |
| **28** | **155.1** | **155.1** |
| **29** | **128.4** | **128.3** |
| **30** | **155.4** | **155.4** |

[4] Lindquist, N.; Fenical, W.; Van Duyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1991**, *113*, 2303.

| | | |
|---|---|---|
| **31** | **163.1** | **163.1** |
| **32** | **56.6** | **56.6** |
| **33** | **33.2** | **33.2** |
| **34** | **19.4** | **19.4** |
| **35** | **16.4** | **16.4** |
| **36** | **175.5** | **175.7** |
| **37** | **76.9** | **76.9** |
| **38** | **31.7** | **31.7** |
| **39** | **19.6** | **19.6** |
| **40** | **18.9** | **18.9** |

# *Crystal Structure Analysis for Intermediate 11a*

## *Contents*

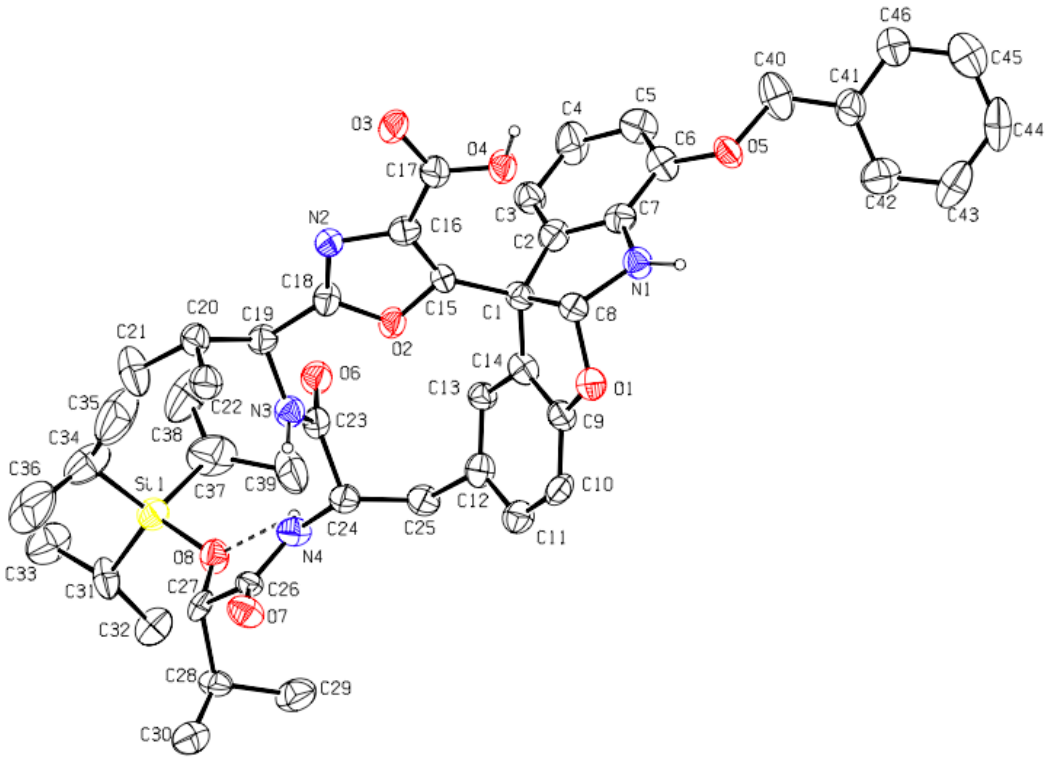



*Table 1. Crystal data and structure refinement for k08308.*

| | | |
|---|---|---|
| Identification code | k08308 | |
| Empirical formula | C47 H59 Cl3 N4 O8 Si | |
| Formula weight | 942.42 | |
| Temperature | 200(2) K | |
| Wavelength | 0.71073 Å | |
| Crystal system | Monoclinic | |
| Space group | C 2 | |
| Unit cell dimensions | a = 19.546(4) Å | a= 90°. |
| | b = 17.360(4) Å | b= 105.63(3)°. |
| | c = 19.889(4) Å | g = 90°. |
| Volume | 6499(2) Å$^3$ | |
| Z | 4 | |

| | |
|---|---|
| Density (calculated) | 0.963 $Mg/m^3$ |
| Absorption coefficient | 0.201 $mm^{-1}$ |
| F(000) | 1992 |
| Crystal size | 0.40 x 0.30 x 0.20 $mm^3$ |
| Theta range for data collection | 2.58 to 24.38°. |
| Index ranges | -22<=h<=21, -19<=k<=20, 0<=l<=22 |
| Reflections collected | 8612 |
| Independent reflections | 5228 [R(int) = 0.0623] |
| Completeness to theta = 24.38° | 94.3 % |
| Absorption correction | Semi-empirical from equivalents |
| Max. and min. transmission | 0.958 and 0.516 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 5228 / 22 / 568 |
| Goodness-of-fit on $F^2$ | 1.111 |
| Final R indices [I>2sigma(I)] | R1 = 0.1136, wR2 = 0.2908 |
| R indices (all data) | R1 = 0.1515, wR2 = 0.3174 |
| Largest diff. peak and hole | 0.532 and -0.316 $e.Å^{-3}$ |

*Table 2. Atomic coordinates ( x $10^4$) and equivalent isotropic displacement parameters ($Å^2$x $10^3$) for k08308. U(eq) is defined as one third of the trace of the orthogonalized $U^{ij}$ tensor.*

| | x | y | z | U(eq) |
|---|---|---|---|---|
| Si(1) | 1845(2) | 3815(2) | 3117(2) | 86(1) |
| O(1) | 5341(4) | 6479(4) | 8038(3) | 84(2) |
| O(2) | 4264(3) | 4519(4) | 7182(3) | 74(2) |
| O(3) | 4873(4) | 3366(4) | 9303(4) | 95(2) |

| | | | | |
|---|---|---|---|---|
| O(4) | 4828(4) | 4640(4) | 9345(3) | 90(2) |
| O(5) | 3925(4) | 6989(4) | 9838(3) | 84(2) |
| O(6) | 3075(4) | 4378(4) | 5698(3) | 89(2) |
| O(7) | 4400(4) | 4544(5) | 4089(3) | 96(2) |
| O(8) | 2523(4) | 4450(4) | 3373(3) | 84(2) |
| N(1) | 4737(4) | 6468(5) | 8959(4) | 77(2) |
| N(2) | 4535(4) | 3426(5) | 7809(4) | 72(2) |
| N(3) | 4217(4) | 3991(5) | 5953(4) | 78(2) |
| N(4) | 3459(4) | 4850(6) | 4450(4) | 82(2) |
| C(1) | 4347(5) | 5596(6) | 7972(5) | 68(2) |
| C(2) | 3777(3) | 5765(4) | 8318(3) | 82(3) |
| C(3) | 3073(4) | 5524(4) | 8153(3) | 84(3) |
| C(4) | 2631(3) | 5770(5) | 8553(4) | 115(4) |
| C(5) | 2893(3) | 6257(5) | 9119(4) | 103(4) |
| C(6) | 3597(3) | 6498(4) | 9284(3) | 83(3) |
| C(7) | 4039(3) | 6252(4) | 8883(3) | 74(3) |
| C(8) | 5021(5) | 6000(6) | 8474(5) | 75(3) |
| C(9) | 4915(3) | 6467(4) | 7393(3) | 80(3) |
| C(10) | 5075(3) | 6780(4) | 6811(4) | 87(3) |
| C(11) | 4634(4) | 6639(4) | 6147(3) | 88(3) |
| C(12) | 4031(3) | 6185(4) | 6066(2) | 86(3) |
| C(13) | 3871(3) | 5872(4) | 6649(3) | 69(2) |
| C(14) | 4312(3) | 6013(4) | 7312(3) | 82(3) |
| C(15) | 4431(5) | 4739(5) | 7877(4) | 68(2) |
| C(16) | 4599(5) | 4081(6) | 8251(5) | 80(3) |
| C(17) | 4785(6) | 4019(7) | 9008(6) | 87(3) |
| C(18) | 4330(5) | 3747(6) | 7175(6) | 81(3) |
| C(19) | 4144(6) | 3381(6) | 6452(5) | 78(3) |
| C(20) | 4505(6) | 2632(6) | 6395(6) | 85(3) |
| C(21) | 4205(10) | 2282(10) | 5696(8) | 142(6) |
| C(22) | 5294(7) | 2748(7) | 6515(6) | 100(4) |
| C(23) | 3676(5) | 4452(6) | 5644(5) | 69(2) |
| C(24) | 3845(6) | 5069(6) | 5170(5) | 79(3) |
| C(25) | 3649(7) | 5894(7) | 5352(5) | 91(3) |
| C(26) | 3766(5) | 4603(5) | 3983(4) | 63(2) |

| | | | | |
|---|---|---|---|---|
| C(27) | 3207(5) | 4388(5) | 3273(5) | 77(3) |
| C(28) | 3303(6) | 4908(7) | 2691(5) | 79(3) |
| C(29) | 3230(8) | 5764(9) | 2859(8) | 120(4) |
| C(30) | 3945(8) | 4778(9) | 2474(8) | 123(4) |
| C(31) | 1501(6) | 3781(5) | 2157(5) | 100(4) |
| C(32) | 1296(6) | 4541(6) | 1791(7) | 104(4) |
| C(33) | 918(8) | 3193(10) | 1901(8) | 145(6) |
| C(34) | 2145(8) | 2839(9) | 3485(7) | 141(7) |
| C(35) | 2535(15) | 2780(13) | 4250(9) | 219(13) |
| C(36) | 2648(15) | 2402(11) | 3171(17) | 227(14) |
| C(37) | 1160(8) | 4262(11) | 3478(11) | 164(8) |
| C(38) | 476(10) | 3899(14) | 3531(14) | 208(11) |
| C(39) | 1327(16) | 5070(12) | 3745(14) | 212(12) |
| C(40) | 3560(7) | 7265(10) | 10317(8) | 126(5) |
| C(41) | 3812(5) | 7972(4) | 10655(4) | 95(3) |
| C(42) | 4089(5) | 8546(6) | 10317(4) | 118(4) |
| C(43) | 4276(5) | 9254(5) | 10640(7) | 138(6) |
| C(44) | 4187(5) | 9389(5) | 11300(7) | 142(6) |
| C(45) | 3910(6) | 8815(7) | 11638(4) | 134(5) |
| C(46) | 3723(5) | 8106(6) | 11315(4) | 110(4) |
| Cl(1) | 2755(5) | 3628(4) | 878(3) | 133(3) |
| Cl(2) | 2424(5) | 5208(5) | 639(4) | 141(3) |
| Cl(3) | 3492(4) | 4592(6) | 157(7) | 172(4) |
| C(1S) | 2698(7) | 4385(6) | 316(8) | 125(11) |
| Cl(4) | 1845(5) | 5304(7) | 5786(6) | 164(4) |
| Cl(5) | 1064(6) | 5554(7) | 6790(5) | 165(3) |
| Cl(6) | 346(4) | 5406(7) | 5310(5) | 152(3) |
| C(2S) | 1091(6) | 5649(15) | 5944(6) | 174(17) |

*Table 3. Bond lengths [Å] and angles [°] for k08308.*

| | |
|---|---|
| Si(1)-O(8) | 1.694(8) |
| Si(1)-C(31) | 1.847(10) |
| Si(1)-C(37) | 1.852(18) |

| | |
|---|---|
| Si(1)-C(34) | 1.875(16) |
| O(1)-C(9) | 1.328(8) |
| O(1)-C(8) | 1.458(12) |
| O(2)-C(18) | 1.347(13) |
| O(2)-C(15) | 1.387(11) |
| O(3)-C(17) | 1.266(13) |
| O(4)-C(17) | 1.260(13) |
| O(5)-C(6) | 1.404(8) |
| O(5)-C(40) | 1.419(15) |
| O(6)-C(23) | 1.215(10) |
| O(7)-C(26) | 1.205(11) |
| O(8)-C(27) | 1.407(12) |
| N(1)-C(7) | 1.383(9) |
| N(1)-C(8) | 1.479(12) |
| N(2)-C(18) | 1.336(13) |
| N(2)-C(16) | 1.423(13) |
| N(3)-C(23) | 1.337(13) |
| N(3)-C(19) | 1.485(13) |
| N(4)-C(26) | 1.306(12) |
| N(4)-C(24) | 1.477(13) |
| C(1)-C(14) | 1.485(10) |
| C(1)-C(2) | 1.488(10) |
| C(1)-C(15) | 1.515(14) |
| C(1)-C(8) | 1.585(14) |
| C(2)-C(3) | 1.3900 |
| C(2)-C(7) | 1.3900 |
| C(3)-C(4) | 1.3900 |
| C(4)-C(5) | 1.3900 |
| C(5)-C(6) | 1.3900 |
| C(6)-C(7) | 1.3900 |
| C(9)-C(10) | 1.3900 |
| C(9)-C(14) | 1.3900 |
| C(10)-C(11) | 1.3900 |
| C(11)-C(12) | 1.3900 |
| C(12)-C(13) | 1.3900 |

| | |
|---|---|
| C(12)-C(25) | 1.503(11) |
| C(13)-C(14) | 1.3900 |
| C(15)-C(16) | 1.354(14) |
| C(16)-C(17) | 1.454(14) |
| C(18)-C(19) | 1.523(15) |
| C(19)-C(20) | 1.499(15) |
| C(20)-C(21) | 1.485(17) |
| C(20)-C(22) | 1.509(17) |
| C(23)-C(24) | 1.521(14) |
| C(24)-C(25) | 1.551(16) |
| C(26)-C(27) | 1.580(13) |
| C(27)-C(28) | 1.520(13) |
| C(28)-C(30) | 1.451(17) |
| C(28)-C(29) | 1.54(2) |
| C(31)-C(32) | 1.508(10) |
| C(31)-C(33) | 1.512(10) |
| C(34)-C(36) | 1.506(11) |
| C(34)-C(35) | 1.511(11) |
| C(37)-C(38) | 1.505(11) |
| C(37)-C(39) | 1.505(11) |
| C(40)-C(41) | 1.422(17) |
| C(41)-C(42) | 1.3900 |
| C(41)-C(46) | 1.3900 |
| C(42)-C(43) | 1.3900 |
| C(43)-C(44) | 1.3900 |
| C(44)-C(45) | 1.3900 |
| C(45)-C(46) | 1.3900 |
| Cl(1)-C(1S) | 1.711(9) |
| Cl(2)-C(1S) | 1.711(10) |
| Cl(3)-C(1S) | 1.704(10) |
| Cl(4)-C(2S) | 1.696(10) |
| Cl(5)-C(2S) | 1.706(10) |
| Cl(6)-Cl(6)#1 | 1.564(18) |
| Cl(6)-C(2S) | 1.704(10) |

| | |
|---|---|
| O(8)-Si(1)-C(31) | 111.6(4) |
| O(8)-Si(1)-C(37) | 101.5(5) |
| C(31)-Si(1)-C(37) | 108.3(7) |
| O(8)-Si(1)-C(34) | 109.5(5) |
| C(31)-Si(1)-C(34) | 111.3(6) |
| C(37)-Si(1)-C(34) | 114.2(8) |
| C(9)-O(1)-C(8) | 108.0(7) |
| C(18)-O(2)-C(15) | 106.6(7) |
| C(6)-O(5)-C(40) | 121.7(8) |
| C(27)-O(8)-Si(1) | 127.1(6) |
| C(7)-N(1)-C(8) | 108.2(7) |
| C(18)-N(2)-C(16) | 101.8(8) |
| C(23)-N(3)-C(19) | 121.8(8) |
| C(26)-N(4)-C(24) | 124.2(9) |
| C(14)-C(1)-C(2) | 116.8(7) |
| C(14)-C(1)-C(15) | 110.4(7) |
| C(2)-C(1)-C(15) | 111.7(8) |
| C(14)-C(1)-C(8) | 100.0(7) |
| C(2)-C(1)-C(8) | 102.8(7) |
| C(15)-C(1)-C(8) | 114.4(8) |
| C(3)-C(2)-C(7) | 120.0 |
| C(3)-C(2)-C(1) | 130.4(6) |
| C(7)-C(2)-C(1) | 109.5(6) |
| C(2)-C(3)-C(4) | 120.0 |
| C(5)-C(4)-C(3) | 120.0 |
| C(4)-C(5)-C(6) | 120.0 |
| C(7)-C(6)-C(5) | 120.0 |
| C(7)-C(6)-O(5) | 114.4(5) |
| C(5)-C(6)-O(5) | 125.6(5) |
| N(1)-C(7)-C(6) | 127.0(5) |
| N(1)-C(7)-C(2) | 113.0(5) |
| C(6)-C(7)-C(2) | 120.0 |
| O(1)-C(8)-N(1) | 111.8(8) |
| O(1)-C(8)-C(1) | 107.1(7) |
| N(1)-C(8)-C(1) | 105.0(7) |

| | |
|---|---|
| O(1)-C(9)-C(10) | 125.1(5) |
| O(1)-C(9)-C(14) | 114.3(5) |
| C(10)-C(9)-C(14) | 120.0 |
| C(9)-C(10)-C(11) | 120.0 |
| C(10)-C(11)-C(12) | 120.0 |
| C(11)-C(12)-C(13) | 120.0 |
| C(11)-C(12)-C(25) | 119.3(6) |
| C(13)-C(12)-C(25) | 119.3(6) |
| C(14)-C(13)-C(12) | 120.0 |
| C(13)-C(14)-C(9) | 120.0 |
| C(13)-C(14)-C(1) | 128.5(6) |
| C(9)-C(14)-C(1) | 109.8(5) |
| C(16)-C(15)-O(2) | 105.8(8) |
| C(16)-C(15)-C(1) | 141.1(8) |
| O(2)-C(15)-C(1) | 113.0(8) |
| C(15)-C(16)-N(2) | 111.5(7) |
| C(15)-C(16)-C(17) | 126.0(10) |
| N(2)-C(16)-C(17) | 122.5(9) |
| O(4)-C(17)-O(3) | 122.5(9) |
| O(4)-C(17)-C(16) | 116.7(10) |
| O(3)-C(17)-C(16) | 120.7(10) |
| N(2)-C(18)-O(2) | 114.2(9) |
| N(2)-C(18)-C(19) | 130.6(10) |
| O(2)-C(18)-C(19) | 115.1(9) |
| N(3)-C(19)-C(20) | 115.8(9) |
| N(3)-C(19)-C(18) | 107.0(8) |
| C(20)-C(19)-C(18) | 115.8(9) |
| C(21)-C(20)-C(19) | 110.5(10) |
| C(21)-C(20)-C(22) | 109.3(11) |
| C(19)-C(20)-C(22) | 110.8(10) |
| O(6)-C(23)-N(3) | 124.1(10) |
| O(6)-C(23)-C(24) | 120.4(9) |
| N(3)-C(23)-C(24) | 115.4(8) |
| N(4)-C(24)-C(23) | 106.3(8) |
| N(4)-C(24)-C(25) | 111.7(8) |

| | |
|---|---|
| C(23)-C(24)-C(25) | 113.4(8) |
| C(12)-C(25)-C(24) | 116.1(9) |
| O(7)-C(26)-N(4) | 123.5(9) |
| O(7)-C(26)-C(27) | 124.5(8) |
| N(4)-C(26)-C(27) | 112.0(9) |
| O(8)-C(27)-C(28) | 112.3(8) |
| O(8)-C(27)-C(26) | 108.0(8) |
| C(28)-C(27)-C(26) | 110.0(7) |
| C(30)-C(28)-C(27) | 115.4(10) |
| C(30)-C(28)-C(29) | 110.7(11) |
| C(27)-C(28)-C(29) | 111.7(9) |
| C(32)-C(31)-C(33) | 110.4(10) |
| C(32)-C(31)-Si(1) | 116.5(7) |
| C(33)-C(31)-Si(1) | 113.6(9) |
| C(36)-C(34)-C(35) | 100(2) |
| C(36)-C(34)-Si(1) | 117.7(11) |
| C(35)-C(34)-Si(1) | 118.3(13) |
| C(38)-C(37)-C(39) | 118.5(19) |
| C(38)-C(37)-Si(1) | 126.9(16) |
| C(39)-C(37)-Si(1) | 114.6(11) |
| O(5)-C(40)-C(41) | 115.8(13) |
| C(42)-C(41)-C(46) | 120.0 |
| C(42)-C(41)-C(40) | 121.4(10) |
| C(46)-C(41)-C(40) | 118.4(10) |
| C(43)-C(42)-C(41) | 120.0 |
| C(42)-C(43)-C(44) | 120.0 |
| C(45)-C(44)-C(43) | 120.0 |
| C(44)-C(45)-C(46) | 120.0 |
| C(45)-C(46)-C(41) | 120.0 |
| Cl(3)-C(1S)-Cl(2) | 106.7(8) |
| Cl(3)-C(1S)-Cl(1) | 112.4(9) |
| Cl(2)-C(1S)-Cl(1) | 111.6(8) |
| Cl(6)#1-Cl(6)-C(2S) | 165.6(9) |
| Cl(4)-C(2S)-Cl(6) | 112.8(9) |
| Cl(4)-C(2S)-Cl(5) | 114.1(11) |

Cl(6)-C(2S)-Cl(5) 117.3(10)

Symmetry transformations used to generate equivalent atoms: #1 -x,y,-z+1

*Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for k08308.*

| | $U^{11}$ | $U^{22}$ | $U^{33}$ | $U^{23}$ | $U^{13}$ | $U^{12}$ |
|---|---|---|---|---|---|---|
| Si(1) | 81(2) | 86(2) | 92(2) | -4(2) | 24(1) | -9(2) |
| O(1) | 90(4) | 82(4) | 81(4) | -8(4) | 22(4) | -6(4) |
| O(2) | 91(4) | 55(4) | 74(4) | 2(3) | 19(3) | 6(3) |
| O(3) | 134(6) | 58(4) | 94(5) | 9(4) | 31(4) | 4(4) |
| O(4) | 134(6) | 61(4) | 70(4) | 1(3) | 19(4) | 9(4) |
| O(5) | 90(4) | 90(5) | 80(4) | -22(4) | 38(4) | 2(4) |
| O(6) | 101(5) | 78(4) | 87(4) | 0(4) | 22(4) | 1(4) |
| O(7) | 81(5) | 126(6) | 86(4) | -7(4) | 31(3) | -2(4) |
| O(8) | 77(4) | 79(4) | 96(4) | -18(4) | 21(3) | -8(3) |
| N(1) | 71(5) | 80(5) | 77(5) | -12(4) | 17(4) | -6(4) |
| N(2) | 78(5) | 65(5) | 80(5) | -4(4) | 32(4) | -6(4) |
| N(3) | 77(5) | 76(5) | 84(5) | -2(4) | 24(4) | 3(4) |
| N(4) | 79(5) | 98(6) | 71(5) | 8(4) | 21(4) | -7(5) |
| C(1) | 73(5) | 70(6) | 63(5) | 4(4) | 21(4) | 14(5) |
| C(2) | 86(7) | 77(7) | 77(6) | 2(5) | 11(5) | -4(6) |
| C(3) | 85(7) | 85(7) | 87(6) | -3(6) | 30(6) | 7(6) |
| C(4) | 73(7) | 123(11) | 143(10) | -49(9) | 16(7) | -28(7) |
| C(5) | 81(7) | 128(10) | 96(7) | 0(8) | 18(6) | -4(7) |
| C(6) | 69(6) | 96(8) | 78(6) | -7(6) | 10(5) | 14(6) |
| C(7) | 74(6) | 70(6) | 75(6) | 19(5) | 16(5) | 16(5) |
| C(8) | 86(6) | 76(6) | 66(5) | -1(5) | 23(5) | -4(5) |
| C(9) | 99(7) | 74(6) | 74(6) | -5(5) | 32(6) | 9(6) |
| C(10) | 96(7) | 53(6) | 118(8) | 1(5) | 40(7) | -15(5) |
| C(11) | 96(8) | 74(7) | 96(8) | 9(6) | 28(6) | 11(6) |

| | | | | | | |
|---|---|---|---|---|---|---|
| C(12) | 83(7) | 74(6) | 96(7) | -4(6) | 18(6) | 6(6) |
| C(13) | 76(6) | 68(6) | 63(5) | 4(4) | 21(5) | 5(5) |
| C(14) | 83(7) | 87(7) | 76(7) | -7(5) | 22(5) | 9(6) |
| C(15) | 83(6) | 62(6) | 63(5) | -13(4) | 27(4) | -4(5) |
| C(16) | 89(7) | 78(7) | 71(6) | 14(6) | 18(5) | 5(5) |
| C(17) | 106(8) | 73(8) | 86(7) | 0(6) | 33(6) | 7(6) |
| C(18) | 90(7) | 62(6) | 88(7) | -5(5) | 17(5) | 3(5) |
| C(19) | 98(7) | 68(6) | 63(5) | 8(5) | 15(5) | 0(5) |
| C(20) | 103(8) | 67(6) | 87(7) | 3(5) | 30(6) | 15(6) |
| C(21) | 170(14) | 127(12) | 109(9) | -48(9) | 5(9) | 33(10) |
| C(22) | 117(10) | 84(8) | 107(8) | 4(6) | 44(7) | 22(7) |
| C(23) | 42(5) | 71(6) | 97(6) | -23(5) | 24(4) | -11(5) |
| C(24) | 93(7) | 76(7) | 66(6) | 3(5) | 21(5) | -5(5) |
| C(25) | 117(8) | 93(8) | 57(5) | 5(5) | 14(5) | -6(7) |
| C(26) | 72(6) | 61(5) | 65(5) | 5(4) | 34(4) | 8(5) |
| C(27) | 88(7) | 47(5) | 97(7) | -7(5) | 25(5) | -28(5) |
| C(28) | 90(7) | 91(7) | 61(5) | 17(5) | 27(5) | 7(5) |
| C(29) | 132(11) | 101(10) | 138(11) | 38(8) | 54(9) | 10(8) |
| C(30) | 142(11) | 103(9) | 141(11) | 8(8) | 68(9) | -16(9) |
| C(31) | 119(9) | 84(7) | 83(6) | -30(6) | 3(6) | 16(7) |
| C(32) | 81(7) | 92(8) | 127(9) | 19(7) | 9(6) | 2(6) |
| C(33) | 124(11) | 159(15) | 128(11) | 12(11) | -9(9) | -51(11) |
| C(34) | 115(10) | 129(13) | 151(13) | 47(11) | -13(10) | -38(10) |
| C(35) | 280(30) | 132(17) | 189(19) | -1(15) | -39(19) | -86(18) |
| C(36) | 230(20) | 91(12) | 410(40) | 46(18) | 170(30) | 64(14) |
| C(37) | 93(9) | 220(20) | 178(14) | -7(15) | 40(9) | -56(12) |
| C(38) | 180(20) | 129(15) | 280(30) | 9(18) | 8(18) | -58(15) |
| C(39) | 290(30) | 153(18) | 260(20) | -100(18) | 190(20) | -51(19) |
| C(40) | 92(8) | 146(13) | 128(10) | -45(10) | 8(7) | 37(8) |
| C(41) | 96(8) | 75(7) | 115(9) | -6(7) | 32(7) | 17(6) |
| C(42) | 114(9) | 131(13) | 102(8) | 5(9) | 16(7) | -24(9) |
| C(43) | 102(10) | 77(10) | 226(19) | 1(11) | 29(11) | -12(7) |
| C(44) | 126(12) | 92(11) | 191(17) | -65(12) | 13(11) | 13(9) |
| C(45) | 117(10) | 158(16) | 118(10) | -24(12) | 15(8) | 23(11) |
| C(46) | 116(9) | 107(10) | 105(9) | -14(8) | 25(7) | 2(8) |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cl(1) | 193(7) | 94(5) | 96(4) | 2(3) | 9(4) | -40(5) |
| Cl(2) | 173(7) | 119(6) | 134(5) | 1(5) | 49(5) | 5(5) |
| Cl(3) | 110(5) | 146(8) | 286(12) | 46(8) | 99(7) | 26(5) |
| C(1S) | 101(16) | 200(30) | 67(11) | -22(16) | 14(11) | -80(20) |
| Cl(4) | 132(6) | 144(7) | 220(9) | -50(7) | 54(6) | -5(6) |
| Cl(5) | 180(8) | 179(9) | 137(6) | -20(6) | 41(6) | -18(7) |
| Cl(6) | 107(5) | 177(8) | 171(7) | 11(7) | 36(4) | 3(5) |
| C(2S) | 180(30) | 130(30) | 260(40) | -90(30) | 140(30) | -40(20) |

*Table 5. Hydrogen coordinates ( x $10^4$) and isotropic displacement parameters (Å$^2$x $10^3$) for k08308.*

| | x | y | z | U(eq) |
|---|---|---|---|---|
| H(3) | 4976 | 3425 | 9738 | 143 |
| H(4) | 4938 | 4543 | 9775 | 135 |
| H(1A) | 4971 | 6823 | 9246 | 92 |
| H(3B) | 4628 | 4051 | 5858 | 94 |
| H(4B) | 2993 | 4888 | 4328 | 99 |
| H(3A) | 2894 | 5191 | 7766 | 101 |
| H(4A) | 2150 | 5605 | 8440 | 139 |
| H(5A) | 2592 | 6425 | 9392 | 123 |
| H(8A) | 5367 | 5608 | 8735 | 91 |
| H(10A) | 5487 | 7091 | 6866 | 105 |
| H(11A) | 4744 | 6853 | 5749 | 106 |
| H(13A) | 3459 | 5562 | 6593 | 82 |
| H(19A) | 3625 | 3261 | 6338 | 93 |
| H(20A) | 4426 | 2270 | 6758 | 102 |
| H(21A) | 4455 | 1800 | 5663 | 213 |
| H(21B) | 4265 | 2640 | 5334 | 213 |
| H(21C) | 3699 | 2177 | 5629 | 213 |

| | | | | |
|---|---|---|---|---|
| H(22A) | 5521 | 2251 | 6482 | 150 |
| H(22B) | 5495 | 2969 | 6979 | 150 |
| H(22C) | 5379 | 3100 | 6160 | 150 |
| H(24A) | 4366 | 5053 | 5212 | 94 |
| H(25A) | 3745 | 6254 | 5002 | 109 |
| H(25B) | 3132 | 5910 | 5306 | 109 |
| H(27A) | 3287 | 3842 | 3153 | 93 |
| H(28A) | 2898 | 4791 | 2275 | 95 |
| H(29A) | 2791 | 5841 | 3000 | 180 |
| H(29B) | 3214 | 6075 | 2444 | 180 |
| H(29C) | 3638 | 5921 | 3241 | 180 |
| H(30A) | 4014 | 4223 | 2427 | 184 |
| H(30B) | 4354 | 4992 | 2823 | 184 |
| H(30C) | 3902 | 5030 | 2023 | 184 |
| H(31A) | 1908 | 3591 | 1987 | 120 |
| H(32A) | 1133 | 4456 | 1286 | 156 |
| H(32B) | 1708 | 4885 | 1897 | 156 |
| H(32C) | 912 | 4775 | 1952 | 156 |
| H(33A) | 775 | 3189 | 1389 | 218 |
| H(33B) | 509 | 3328 | 2073 | 218 |
| H(33C) | 1093 | 2682 | 2074 | 218 |
| H(34A) | 1708 | 2516 | 3413 | 169 |
| H(35A) | 2650 | 2239 | 4371 | 329 |
| H(35B) | 2233 | 2980 | 4531 | 329 |
| H(35C) | 2974 | 3081 | 4344 | 329 |
| H(36A) | 2753 | 1899 | 3401 | 340 |
| H(36B) | 3090 | 2695 | 3237 | 340 |
| H(36C) | 2429 | 2326 | 2671 | 340 |
| H(37A) | 913 | 4468 | 3006 | 197 |
| H(38A) | 194 | 4282 | 3701 | 312 |
| H(38B) | 583 | 3465 | 3857 | 312 |
| H(38C) | 207 | 3716 | 3069 | 312 |
| H(39A) | 922 | 5280 | 3888 | 318 |
| H(39B) | 1420 | 5392 | 3375 | 318 |
| H(39C) | 1748 | 5065 | 4147 | 318 |

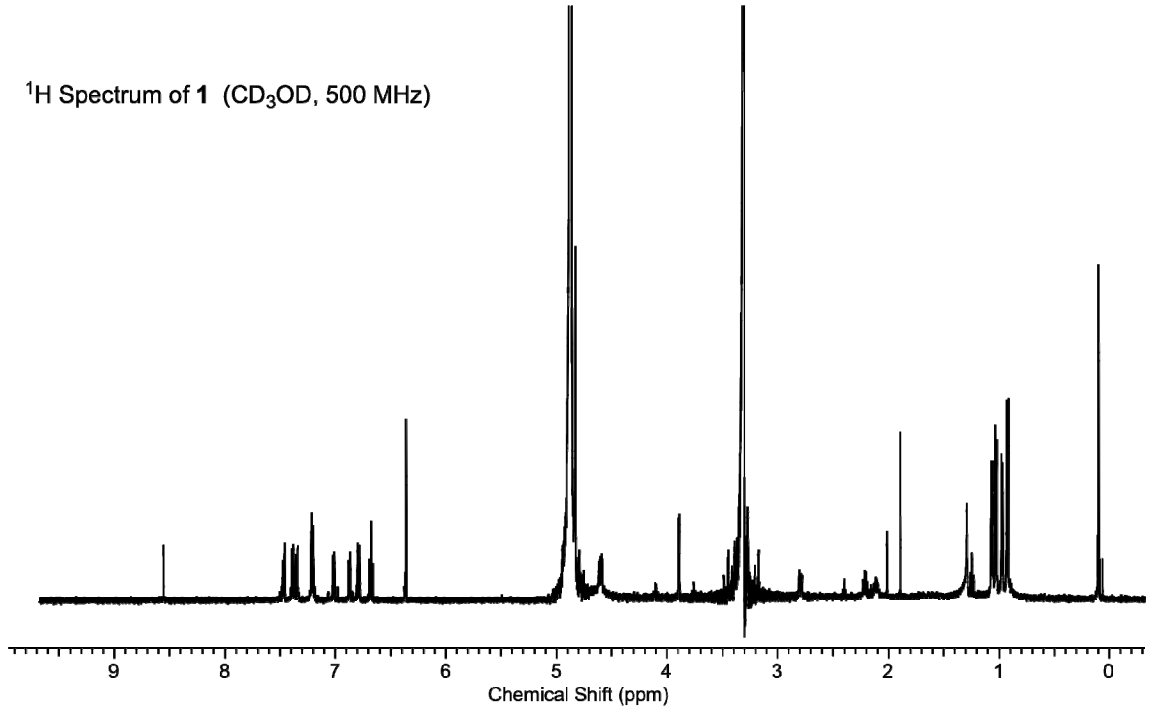
| | | | | |
|---|---|---|---|---|
| H(40A) | 3589 | 6866 | 10680 | 152 |
| H(40B) | 3053 | 7329 | 10065 | 152 |
| H(42A) | 4150 | 8454 | 9866 | 142 |
| H(43A) | 4465 | 9647 | 10409 | 165 |
| H(44A) | 4315 | 9873 | 11521 | 171 |
| H(45A) | 3849 | 8906 | 12089 | 161 |
| H(46A) | 3534 | 7714 | 11546 | 133 |
| H(1S) | 2346 | 4254 | -136 | 150 |
| H(2S) | 1129 | 6218 | 5886 | 209 |

*Table 6. Hydrogen bonds for k08308 [Å and °].*

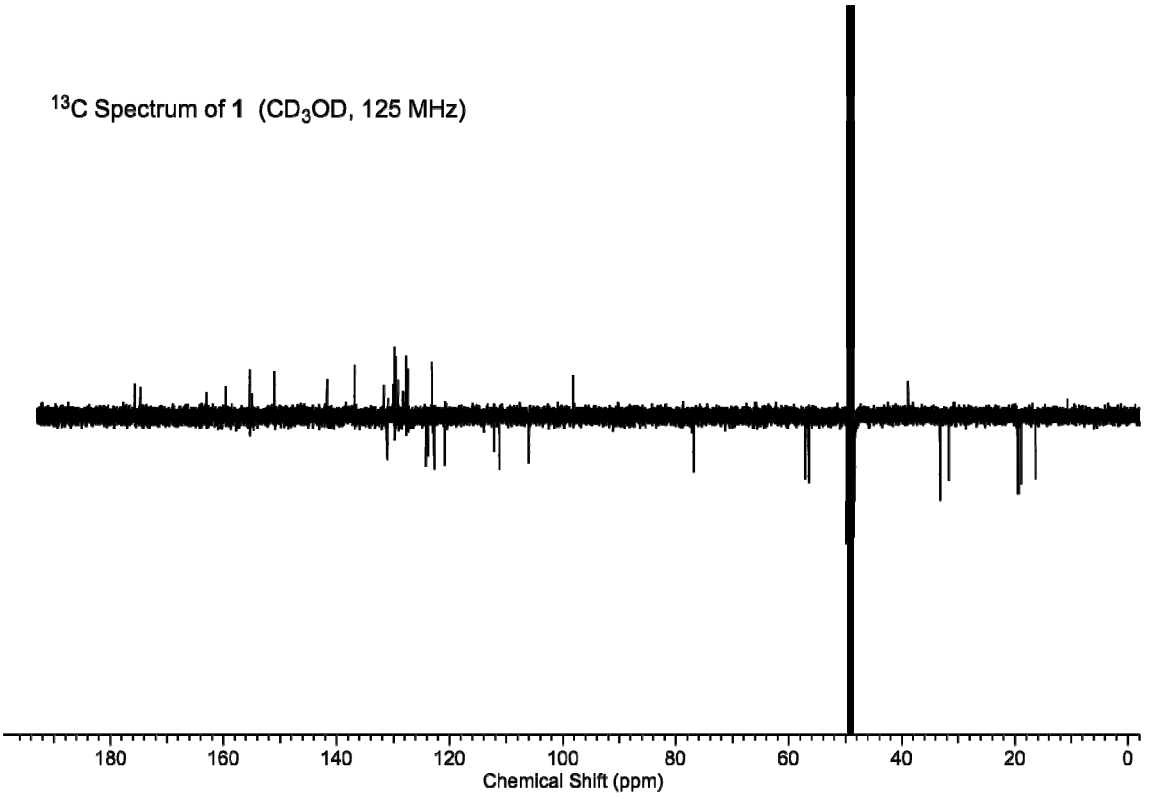
| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(3)-H(3)...O(3)#2 | 0.84 | 1.85 | 2.681(15) | 168.8 |
| O(4)-H(4)...O(4)#2 | 0.84 | 1.69 | 2.507(13) | 162.8 |
| N(1)-H(1A)...O(5)#2 | 0.88 | 2.44 | 3.164(10) | 140.3 |
| N(3)-H(3B)...O(7)#3 | 0.88 | 2.06 | 2.891(12) | 157.1 |
| N(4)-H(4B)...O(8) | 0.88 | 2.02 | 2.511(10) | 113.9 |

Symmetry transformations used to generate equivalent atoms:
#1 -x,y,-z+1 #2 -x+1,y,-z+2 #3 -x+1,y,-z+1

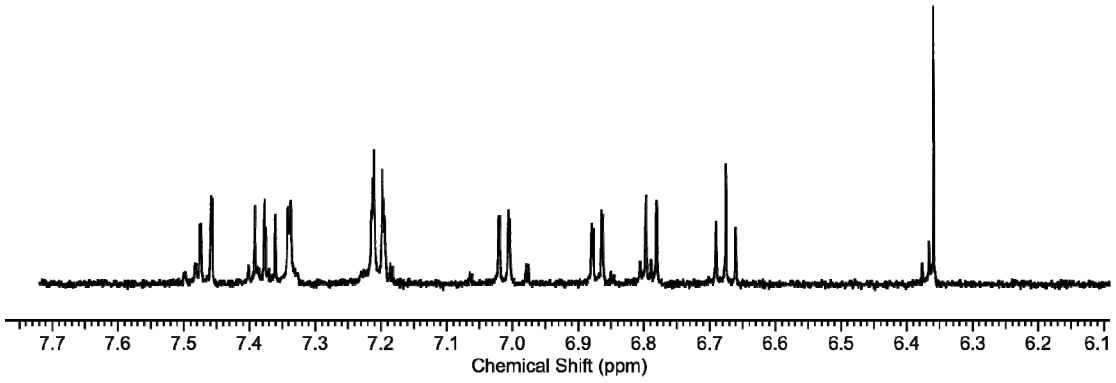
$^{1}$H Spectrum of **1** ($CD_3OD$, 500 MHz)

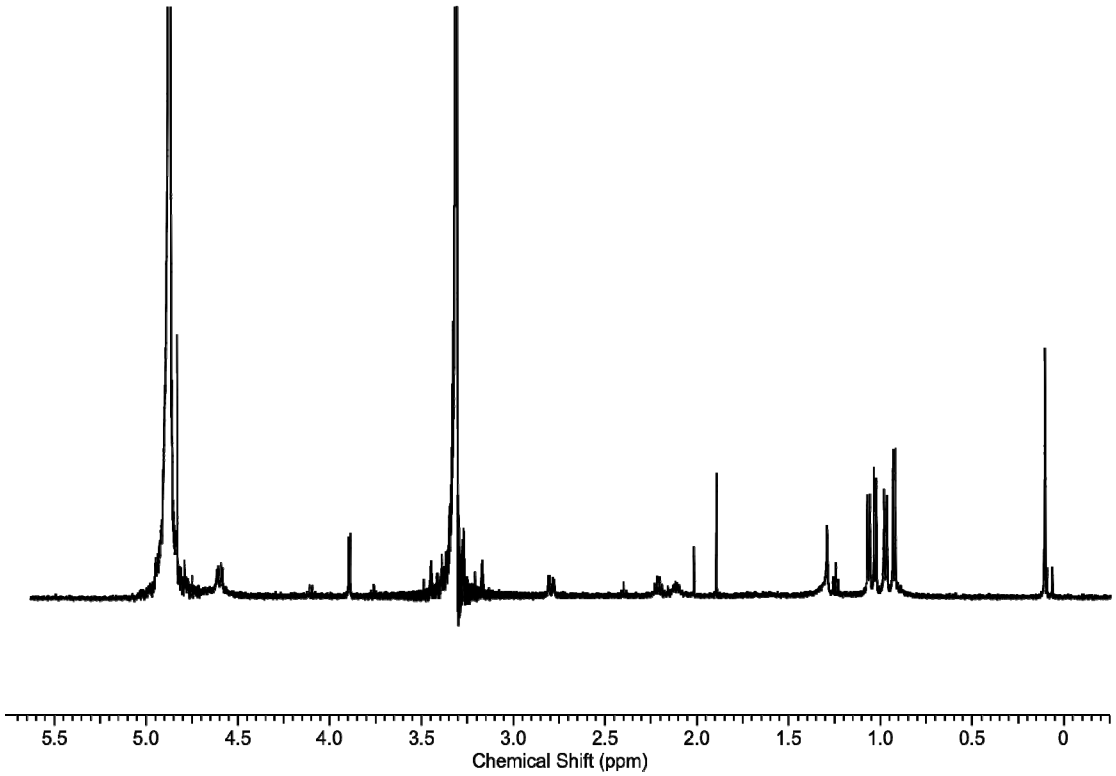



$^{13}$C Spectrum of **1** ($CD_3OD$, 125 MHz)



Expanded Views of $^{1}$H Spectrum of **1** ($CD_3OD$, 500 MHz)



Expanded Views of $^{13}C$ Spectrum of **1** ($CD_3OD$, 125 MHz)