

## Supporting Information

### A Pd(0)-Mediated Indole (Macro)cyclization Reaction

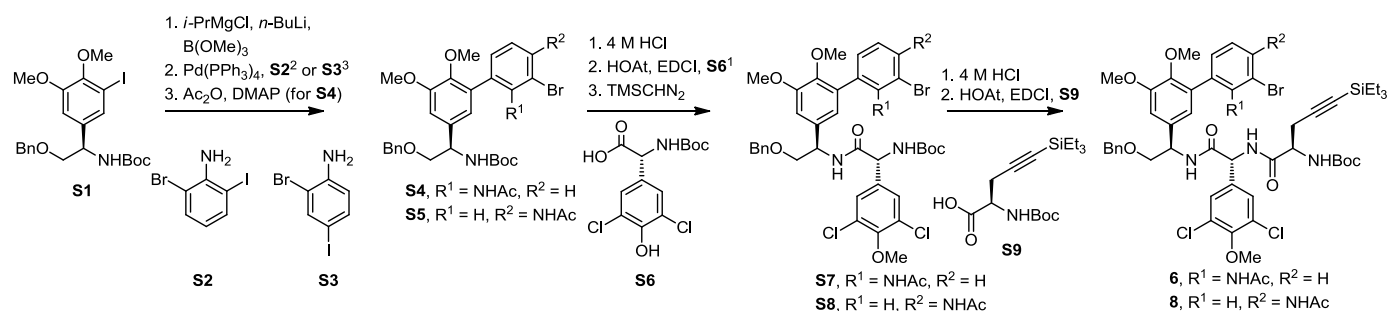
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#### General Methods

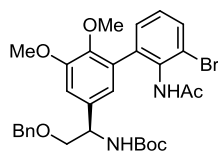
All reactions were carried out under a nitrogen atmosphere with anhydrous solvents under anhydrous conditions, unless otherwise noted. Anhydrous toluene, methylene chloride, diethyl ether (Et<sub>2</sub>O) and tetrahydrofuran (THF) were obtained by passing commercially available, pre-dried formulations through activated alumina columns. *N,N'*-Dimethylformamide (DMF), dimethylsulfoxide (DMSO), acetonitrile (CH<sub>3</sub>CN), methanol (MeOH), and ethanol (EtOH) were purchased in anhydrous form and used without further purification. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as the visualizing agent and aqueous ammonium cerium nitrate/ammonium molybdate. ZEOprep® 60 ECO silica gel (particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative TLC (PTLC) separations were carried out on 0.50 mm E. Merck silica gel plates (60F-254). NMR spectra were recorded on Bruker AV-400, DRX-500 or DRX-600 instruments and calibrated using residual undeuterated solvent as an internal reference [acetone-*d*<sub>6</sub>: 2.05/29.84, CDCl<sub>3</sub>: 7.26/77.0, DMSO-*d*<sub>6</sub>: 2.50/39.51, (<sup>1</sup>H/<sup>13</sup>C ppm)]. The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, br = broad. IR spectra were recorded on a Thermo Nicolet 380 FT-IR spectrometer. High-resolution mass spectra (HRMS) were recorded on an Agilent mass spectrometer using ESI-TOF (electrospray ionization-time of flight). Optical rotations were recorded on a Rudolph Autopol® III polarimeter at 589 nm, and are reported in units of 10<sup>-1</sup>(deg cm<sup>2</sup> g<sup>-1</sup>).

## Macrocyclizations Involving Isomers of Chloropeptin II.



**Scheme S1.** Preparation of macrocyclization precursors.

### Compound **S4**



Compound **S1**<sup>1</sup> (500 mg, 0.975 mmol) in anhydrous THF (15 mL) at 0 °C was treated dropwise with *i*-PrMgCl (2.0 M in THF, 1.0 mL, 2.0 mmol). After 1 h, the yellow solution was cooled to –78 °C and *n*-BuLi (2.5 M in hexane, 0.8 mL, 2.0 mmol) was added dropwise to the vigorously stirring solution. After 30 min, B(OMe)<sub>3</sub> (1.0 mL, excess) was added dropwise, and the reaction mixture was allowed to slowly warm to ambient temperature and left for 18 h. The white suspension was acidified to pH 3 with the addition of aqueous 1 N HCl, and the solution was stirred for 30 min. The resultant yellow solution was diluted with EtOAc (30 mL), and washed with H<sub>2</sub>O (3 × 20 mL) and saturated aqueous NaCl. The aqueous extracts were washed with EtOAc (3 × 10 mL) and the combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated to give the crude boronic acid product. This crude boronic acid product was combined with 2-bromo-6-iodoaniline<sup>2</sup> (**S2**, 435 mg, 1.46 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (180 mg, 0.156 mmol), aqueous 1 M NaHCO<sub>3</sub> (6.24 mL, 6.24 mmol) and dissolved by the addition of 1,2-dimethoxyethane (DME, 20 mL). The reaction solution was stirred at 80 °C for 24 h before being cooled to ambient temperature and filtered with EtOAc. The organic phase was washed with H<sub>2</sub>O (2 × 20 mL) and saturated aqueous NaCl. The combined aqueous phases were back extracted with EtOAc (2 × 20 mL), and the combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (SiO<sub>2</sub>, 5 × 15 cm, 10% EtOAc–hexanes) to afford the pure aniline (348 mg, 0.624 mmol, 64%), which was then immediately dissolved in CH<sub>2</sub>Cl<sub>2</sub> (15 mL). The solution was then treated with Ac<sub>2</sub>O (1 mL, excess) and 4-dimethylaminopyridine (5 mg, catalytic), and the mixture was stirred at room temperature for 16 h. Upon completion, the reaction mixture was diluted with additional CH<sub>2</sub>Cl<sub>2</sub> (20 mL), quenched with the addition of saturated aqueous NaHCO<sub>3</sub> (10 mL), and stirred vigorously for 15 min or until all bubbling ceased. The crude product was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 10 mL) and washed with saturated aqueous NaCl, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Flash chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes) provided **S4** as a white solid (336 mg, 58%, 2 steps).

[ $\alpha$ ]<sub>D</sub><sup>25</sup> –117 (*c* 0.09, CHCl<sub>3</sub>)

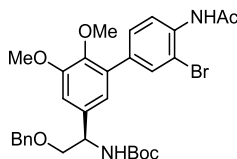
LC/MS *m/z* 597 ([M - H]<sup>-</sup>, C<sub>30</sub>H<sub>35</sub>BrN<sub>2</sub>O<sub>6</sub> requires 597)

IR (film)  $\nu_{\max}$  3256, 2940, 1670, 1489, 1254, 1166, 1004, 731 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.77 (s, 1H), 7.67 (s, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.26 – 7.33 (m, 6H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.93 (br s, 1H), 6.80 (s, 1H), 5.28 (br s, 1H), 4.83 (br s, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.48 (br s, 1H), 3.88 (s, 3H), 3.72 (m, 1H), 3.64 (m, 1H), 3.53 (s, 3H), 1.91 (s, 3H), 1.43 (s, 9H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  168.4, 155.7, 152.5, 144.5, 138.1, 137.9, 134.4, 133.06, 132.99, 128.6, 128.4, 128.0, 127.9, 127.9, 124.1, 111.2, 79.9, 73.4, 64.6, 61.4, 56.1, 54.1, 28.6, 23.5

## Compound S5



Compound **S1**<sup>1</sup> (400 mg, 0.80 mmol) in anhydrous THF (15 mL) at 0 °C was treated dropwise with *i*-PrMgCl (2.0 M in THF, 0.8 mL, 1.60 mmol). After 1 h, the yellow solution was cooled to -78 °C and *n*-BuLi (2.5 M in hexane, 0.64 mL, 1.60 mmol) was added dropwise to the vigorously stirring solution. After 30 min, B(OMe)<sub>3</sub> (0.8 mL, excess) was added dropwise, and the reaction mixture was allowed to slowly warm to ambient temperature and left for 18 h. The white suspension was acidified to pH 3 with the addition of aqueous 1 N HCl, and the solution was stirred for 30 min. The resultant yellow solution was diluted with EtOAc (30 mL), and washed with H<sub>2</sub>O (3 × 20 mL) and saturated aqueous NaCl. The aqueous extracts were washed with EtOAc (3 × 10 mL) and the combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated to give the crude boronic acid product. This crude boronic acid product was combined with 2-bromo-4-iodoaniline<sup>3</sup> (**S3**, 238 mg, 1.20 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (150 mg, 0.130 mmol), aqueous 1 M NaHCO<sub>3</sub> (6.24 mL, 6.24 mmol) and dissolved by the addition of 1,2-dimethoxyethane (DME, 20 mL). The reaction solution was stirred at 80 °C for 24 h before being cooled to ambient temperature and filtered with EtOAc. The organic phase was washed with H<sub>2</sub>O (2 × 20 mL) and saturated aqueous NaCl. The combined aqueous phases were washed with EtOAc (2 × 20 mL). The combined organic phases were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography (SiO<sub>2</sub>, 5 × 15 cm, 10% EtOAc–hexanes) to afford the pure aniline (348 mg, 0.624 mmol, 78%), which was then immediately dissolved in CH<sub>2</sub>Cl<sub>2</sub> (15 mL) and treated with Ac<sub>2</sub>O (1 mL, excess). The solution was stirred for 1 h at room temperature. The reaction mixture was diluted with additional CH<sub>2</sub>Cl<sub>2</sub> (20 mL), quenched with the addition of saturated aqueous NaHCO<sub>3</sub> (10 mL), and stirred for 15 min or until all bubbling ceased. The crude product was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 10 mL) and washed with saturated aqueous NaCl, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. Flash chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes) provided **S4** as a white solid (344 mg, 72%, 2 steps).

$[\alpha]_D^{25} +51$  (*c* 0.17, CHCl<sub>3</sub>)

LC/MS *m/z* 597 ([M - H]<sup>-</sup>, C<sub>30</sub>H<sub>35</sub>BrN<sub>2</sub>O<sub>6</sub> requires 597)

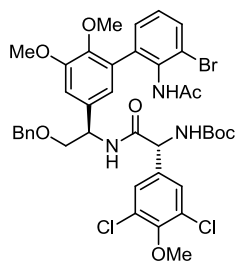
IR (film)  $\nu_{\max}$  3309, 2931, 1685, 1514, 1295, 1247, 1164, 728 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.34 (d, *J* = 8.4 Hz, 1H), 7.73 (s, 1H), 7.67 (s, 1H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.24 – 7.33 (m, 6H), 6.86 (s, 1H), 6.83 (s, 1H), 5.35 (br s, 1H), 4.82 (br s, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 3.85 (s, 3H), 3.72 (m, 1H), 3.63 (m, 1H), 3.57 (s, 3H), 2.25 (s, 3H), 1.43 (s, 9H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  168.2, 155.4, 152.9, 145.4, 137.6, 134.5, 133.3, 132.6, 129.2, 128.4, 128.3, 127.8, 127.6, 121.2, 120.0, 112.7, 110.4, 79.7, 73.1, 72.8, 60.5, 55.8, 54.2, 28.3, 24.8

Compounds **S7** and **S8** were prepared by the representative procedure below in similar yield and quantity.

## Compound S7



Compound **S4** (80 mg, 0.133 mmol) was dissolved in a commercially prepared solution of 4 M HCl in dioxane (5 mL) at room temperature and stirred for 1–2 h. The reaction mixture was analyzed by TLC to ensure

consumption of the starting material, and the reaction mixture condensed under a stream of nitrogen. The residue was then treated with a saturated solution of NaHCO<sub>3</sub> (5 mL) and EtOAc (5 mL). The organic layer was washed with water (1 × 20 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude mixture was used directly without purification and dissolved in a solution of CH<sub>2</sub>Cl<sub>2</sub> and DMF (10 mL, 3:1 v:v) at 0 °C. The solution was treated with solid EDCI (31 mg, 0.200 mmol), HOAt (27 mg, 0.200 mmol), and acid **S6** (67 mg, 0.200 mmol) and the resulting solution was allowed to slowly warm to room temperature and stirred overnight (12–16 h). The reaction mixture was quenched with the addition of water (10 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes), and provided the pure amide (78 mg, 72%, 0.960 mmol). This amide was dissolved in benzene:MeOH (12 mL, 3:2). The solution was treated dropwise with TMSCHN<sub>2</sub> (2.0 M in hexanes, 0.53 mL, 1.056 mmol). Upon completion (as indicated by a persistent yellow color in the solution and TLC), acetic acid (0.2 mL) was slowly added to quench the reaction until the yellow solution turned clear and bubbling ceased. The solvent was removed in vacuo to provide **S7** as a white solid (79 mg, 71%, 2 steps).

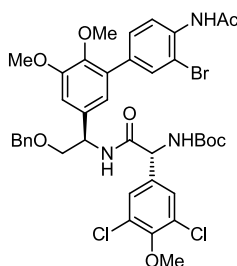
HRMS  $m/z$  830.1581 ([M + H]<sup>+</sup>, C<sub>39</sub>H<sub>42</sub>BrCl<sub>2</sub>N<sub>3</sub>O<sub>8</sub> requires 830.1605)

IR (film)  $\nu_{\max}$  3302, 2931, 1655, 1481, 1366, 1265, 1164, 998, 732, 670 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  7.67 (d,  $J$  = 7.2 Hz, 1H), 7.62 (br s, 1H), 7.37 (s, 2H), 7.27 – 7.35 (m, 4H), 7.21 (t,  $J$  = 7.8 Hz, 1H), 7.14 (m, 2H), 6.90 (s, 1H), 6.81 (s, 1H), 5.20 (br s, 1H), 5.10 (br s, 1H), 4.46 (d,  $J$  = 12.0 Hz, 1H), 4.40 (d,  $J$  = 12.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.64 (m, 2H), 3.54 (s, 3H), 1.91 (s, 3H), 1.39 (br s, 9H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  169.4, 169.3, 155.4, 152.6, 152.4, 144.9, 138.5, 137.5, 135.9, 134.3, 133.2, 133.1, 132.9, 129.9, 128.7, 128.6, 128.2, 128.0, 127.9, 124.2, 121.3, 119.3, 119.2, 80.8, 73.5, 72.0, 61.3, 61.0, 60.9, 56.1, 52.8, 28.5, 23.3

#### Compound **S8**



$[\alpha]_{\text{D}}^{25}$  –19 ( $c$  0.19, CHCl<sub>3</sub>)

HRMS  $m/z$  830.1609 ([M + H]<sup>+</sup>, C<sub>39</sub>H<sub>42</sub>BrCl<sub>2</sub>N<sub>3</sub>O<sub>8</sub> requires 830.1605)

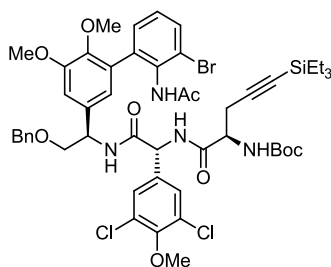
IR (film)  $\nu_{\max}$  3295, 2934, 1650, 1515, 1479, 1366, 1253, 1165, 998, 908, 729 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.37 (d,  $J$  = 8.4 Hz, 1H), 7.72 (d,  $J$  = 2.0 Hz, 1H), 7.65 (br s, 1H), 7.46 (dd,  $J$  = 1.2 Hz, 8.4 Hz, 1H), 7.41 (m, 1H), 7.35 (s, 2H), 7.27 – 7.35 (m, 4H), 7.13 – 7.15 (m, 2H), 6.87 (d,  $J$  = 2.0 Hz, 1H), 6.84 (d,  $J$  = 2.0 Hz, 1H), 6.59 (br s, 1H), 5.75 (br s, 1H), 5.07 (m, 2H), 4.47 (s, 1H), 4.46 (d,  $J$  = 12.0 Hz, 1H), 4.40 (d,  $J$  = 12.0 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.66 (m, 2H), 3.57 (s, 3H), 2.26 (s, 3H), 1.39 (br s, 9H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  168.9, 168.5, 153.4, 152.6, 151.5, 146.2, 137.5, 136.0, 135.5, 135.2, 134.9, 133.9, 132.9, 130.1, 129.50, 129.46, 128.8, 128.2, 127.91, 127.85, 121.5, 120.9, 120.7, 111.1, 80.8, 73.5, 72.0, 68.4, 60.9, 60.8, 56.2, 53.4, 28.4, 25.1

Macrocyclization precursors **6** and **8** were prepared by the representative procedure below in similar yield and quantity.

## Compound 6



Compound **S7** (120 mg, 0.144 mmol) was dissolved in a commercially prepared solution of 4 M HCl in dioxane (5 mL) at room temperature and stirred at this temperature for 1–2 h. The reaction mixture was analyzed by TLC to ensure consumption of the starting material, and the reaction mixture condensed under a stream of nitrogen. The residue was then treated with a saturated solution of NaHCO<sub>3</sub> (10 mL) and EtOAc (10 mL). The organic layer was washed with water (1 × 20 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude amine was used directly without purification and dissolved in a solution of DMF (5 mL) at 0 °C. This solution was treated with solid EDCI (45 mg, 0.288 mmol), HOAt (39 mg, 0.288 mmol), and **S9** (85 mg, 0.256 mmol) and the resulting solution was allowed to slowly warm to room temperature and stirred overnight. The reaction mixture was quenched with the addition of water (10 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes) and provided **6** (116 mg, 82%) as a white solid.

$[\alpha]_D^{25}$  -14 (*c* 0.80, CHCl<sub>3</sub>)

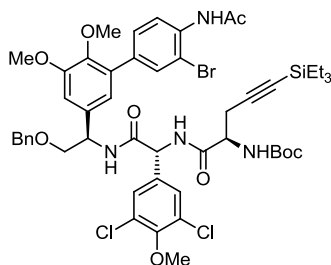
HRMS *m/z* 1039.2833 ([M + H]<sup>+</sup>, C<sub>50</sub>H<sub>61</sub>BrCl<sub>2</sub>N<sub>4</sub>O<sub>9</sub>Si requires 1039.2841)

IR (film)  $\nu_{\max}$  3258, 2952, 1648, 1520, 1367, 1272, 1167, 1001, 670 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  8.43 (br s, 1H), 7.61 (br s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.34 (s, 2H), 7.28 – 7.13 (m, 5H), 7.17 (d, *J* = 7.0 Hz, 2H), 6.87 (d, *J* = 10.0 Hz, 2H), 6.80 (br s, 1H), 5.38 (d, *J* = 6.5 Hz, 1H), 5.24 (br s, 1H), 5.11 (m, 1H), 4.59 (t, 2H), 4.21 (br s, 1H), 3.85 (s, 6H), 3.67 (d, *J* = 5.5 Hz, 2H), 3.64 (s, 3H), 2.74 (dd, *J* = 6.5, 11.5 Hz, 1H), 2.63 (dd, *J* = 6.5, 11.5 Hz, 1H), (s, 3H), 1.37 (s, 9H), 0.91 (t, *J* = 7.9 Hz, 9H), 0.50 (q, *J* = 7.9 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  170.4, 168.5, 168.3, 159.1, 153.3, 152.6, 146.1, 141.0, 140.1, 138.7, 137.7, 135.5, 135.4, 135.2, 134.4, 133.8, 132.0, 130.0, 128.7, 128.4, 128.1, 127.9, 126.6, 123.0, 120.6, 111.2, 86.34, 80.9, 73.4, 72.1, 61.1, 60.9, 56.6, 56.2, 53.4, 53.4, 28.6, 28.4, 25.1, 7.6, 4.5

## Compound 8



$[\alpha]_D^{25}$  -17 (*c* 0.22, CHCl<sub>3</sub>)

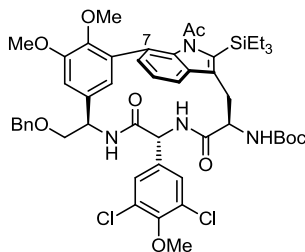
HRMS *m/z* 1039.2832 ([M + H]<sup>+</sup>, C<sub>50</sub>H<sub>61</sub>BrCl<sub>2</sub>N<sub>4</sub>O<sub>9</sub>Si requires 1039.2841)

IR (film)  $\nu_{\max}$  3628, 2921, 1649, 1519, 1267, 1171, 1001, 670 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  8.37 (br s, 1H), 7.72 (d, *J* = 1.8 Hz, 1H), 7.65 (br s, 1H), 7.49 (br s, 1H), 7.47 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.33 (s, 2H), 7.31 – 7.27 (m, 5H), 7.16 (d, *J* = 7.2 Hz, 2H), 6.86 (dd, *J* = 1.2, 10.0 Hz, 2H), 6.70 (br s, 1H), 5.30 (d, *J* = 6.0 Hz, 1H), 5.22 (br s, 1H), 5.10 (m, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.18 (br s, 1H), 3.860 (s, 3H), 3.858 (s, 3H), 3.67 (t, *J* = 4.2 Hz, 2H), 3.57 (s, 3H), 2.69 (dd, 6.5, 11.5 Hz, 2H), 2.27 (s, 3H), 1.39 (s, 9H), 0.91 (t, 9H, *J* = 7.8 Hz), 0.50 (q, 6H, *J* = 7.8 Hz)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  170.2, 168.5, 168.2, 153.4, 152.7, 146.2, 137.6, 135.4, 135.2, 135.1, 134.9, 133.9, 132.8, 130.2, 129.5, 128.77, 128.73, 128.2, 128.1, 127.9, 121.4, 120.7, 112.9, 111.1, 102.3, 86.6, 81.0, 80.1, 73.5, 71.9, 60.9, 60.8, 56.8, 56.2, 53.42, 53.36, 28.4, 25.2, 7.6, 4.4

## Macrocycle **7**



A solution of  $\text{Pd}(\text{OAc})_2$  (6 mg, 0.027 mmol) and *Dt*BPF ligand (15 mg, 0.031 mmol) in  $\text{CH}_3\text{CN}$ :toluene (5 mL, 1:1) was treated with distilled  $\text{Et}_3\text{N}$  (4.3  $\mu\text{L}$ , 0.031 mmol) at room temperature. This solution was slowly added to a refluxing solution of  $\text{CH}_3\text{CN}$ /toluene (15 mL, 1:1) in a three-necked flask equipped with a reflux condenser to give a clear orange solution. Compound **6** (25 mg, 0.024 mmol) in  $\text{CH}_3\text{CN}$ /toluene (5 mL, 1:1) was slowly added to the reaction vessel and the mixture was warmed at reflux. The reaction was complete after 1 h as indicated by the appearance of the products on TLC. The reaction solution was cooled to ambient temperature before the solvent was removed in vacuo. The crude product was purified by flash chromatography ( $\text{SiO}_2$ , 50% EtOAc–hexanes) and provided **6** (15 mg, 66%) as a single atropisomer.

$[\alpha]_D^{25} +41$  (*c* 0.017,  $\text{CHCl}_3$ )

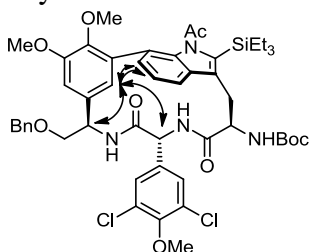
HRMS *m/z* 959.3585 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{50}\text{H}_{60}\text{Cl}_2\text{N}_4\text{O}_9\text{Si}$  requires 959.3579)

IR (film)  $\nu_{\text{max}}$  2930, 1699, 1650, 1480, 1369  $\text{cm}^{-1}$

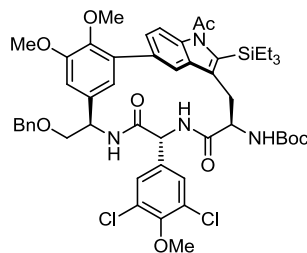
$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  7.63 (d, *J* = 8.4 Hz, 1H), 7.60 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.29 – 7.34 (m, 6H), 7.29 (s, 2H), 7.19 (m, 2H), 6.52 (d, *J* = 7.2 Hz, 1H), 6.48 (s, 1H), 6.20 (d, *J* = 7.8 Hz, 1H), 5.64 (s, 1H), 5.41 (d, *J* = 7.8 Hz, 1H), 5.12 (d, *J* = 8.4 Hz, 1H), 4.80 (m, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 4.10 (s, 3H), 3.90 (m, 1H), 3.85 (m, 1H, partially obstructed), 3.85 (s, 3H), 3.83 (s, 3H), 3.71 (dd, *J* = 3.0, 10.2 Hz, 1H), 3.62 (t, *J* = 10.2 Hz, 1H), 3.55 (t, *J* = 9.6 Hz, 1H), 3.08 (d, *J* = 13.2 Hz, 1H), 3.73 (s, 3H), 1.31 (s, 9H), 0.90 – 0.95 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  171.9, 169.0, 168.6, 154.4, 153.2, 152.3, 144.0, 138.9, 127.5, 134.7, 133.8, 132.1, 131.2, 130.5, 129.8, 129.1, 128.67, 128.58, 128.2, 127.9, 127.4, 123.4, 120.6, 117.1, 106.6, 80.0, 73.2, 69.4, 61.7, 60.6, 59.5, 56.6, 56.3, 53.3, 29.7, 28.1, 25.9, 8.3, 5.5

## Key ROESY correlations



## Macrocycle 9



A solution of Pd(OAc)<sub>2</sub> (2.1 mg, 0.0094 mmol) and DtBPF ligand (5.3 mg, 0.011 mmol) in CH<sub>3</sub>CN:toluene (5 mL, 1:1) was treated with distilled Et<sub>3</sub>N (1.5 μL, 0.011 mmol) at room temperature. This solution was slowly added to a refluxing solution of CH<sub>3</sub>CN/toluene (10 mL, 1:1) in a three-necked flask equipped with a reflux condenser to give a clear orange solution. Compound **6** (9 mg, 0.0086 mmol) in CH<sub>3</sub>CN/toluene (5 mL, 1:1) was slowly added to the reaction vessel and the mixture was warmed at reflux. The reaction was complete after 1 h as indicated by the appearance of the products on TLC. The reaction solution was cooled to ambient temperature before the solvent was removed in vacuo. The crude product was purified by flash chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes) and provided **6** (5.8 mg, 70%) as a single atropisomer.

$[\alpha]_D^{25}$  -3.0 (*c* 0.1, MeOH)

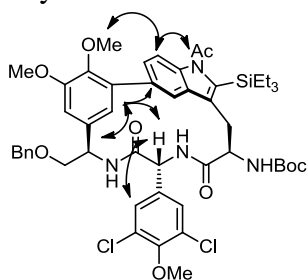
HRMS *m/z* 959.3577 ([M + H]<sup>+</sup>, C<sub>50</sub>H<sub>60</sub>Cl<sub>2</sub>N<sub>4</sub>O<sub>9</sub>Si requires 959.3579)

IR (film)  $\nu_{\max}$  2930, 1696, 1655, 1458, 1369, 1018 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  7.93 (d, *J* = 9.0 Hz, 1H), 7.63 (d, *J* = 9.0 Hz, 1H), 7.45 (s, 1H), 7.40 (s, 2H), 7.27 – 7.36 (m, 5H), 6.92 (s, 1H), 6.80 (d, *J* = 9.0 Hz, 1H), 6.71 (s, 1H), 5.61 (*J* = 8.4 Hz, 1H), 5.20 (m, 1H), 5.06 (d, *J* = 9.0 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.56 (d, *J* = 12.0 Hz), 4.29 (m, 1H), 4.02, (dd, *J* = 2.4, 10.8 Hz, 1H), 3.89 (s, 3H), 3.84 (s, 3H), 3.83 (dd, *J* = 2.4, 10.8 Hz, 1H), 3.82 (m, 1H, obstructed), 3.10 (dd, *J* = 3.6, 13.6 Hz, 1H), 2.85 (s, 3H), 1.38 (s, 9H), 0.91 – 0.97 (m, 15H)

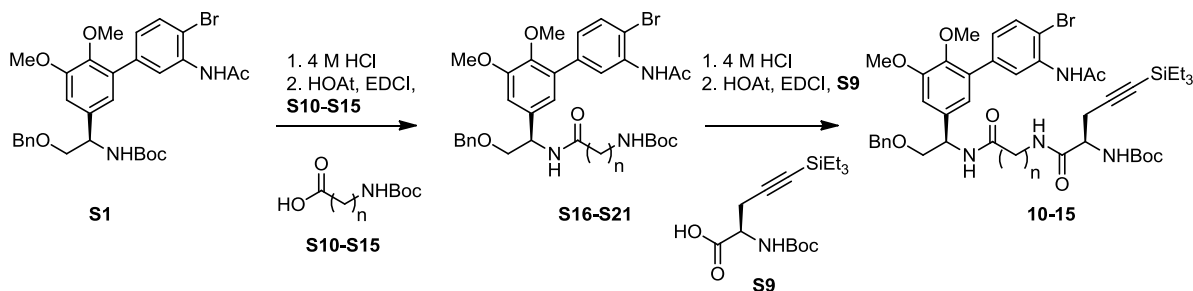
<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  172.1, 169.6, 169.5, 155.9, 154.9, 153.2, 152.5, 145.6, 138.1, 137.3, 136.5, 134.8, 134.2, 133.7, 133.1, 129.8, 128.6, 128.2, 128.1, 127.9, 126.2, 126.1, 121.9, 121.7, 121.2, 121.0, 113.3, 108.8, 80.7, 73.4, 70.0, 60.7, 60.4, 56.2, 56.0, 51.8, 50.1, 42.3, 29.7, 28.1, 26.6, 8.3, 6.2

### Key ROESY correlations



### Macrocyclization Reactions Forming Additional Cyclic Peptide Ring Sizes.

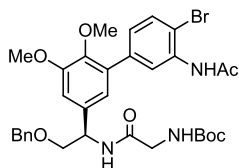
Boc-protected amino acid subunits were either commercially purchased (*n* = 1, 3, 4) or prepared in a single step from the commercially available amino acid (*n* = 2, 7, 11).



**Scheme S2.** Preparation of macrocyclic peptide precursors.

Compounds **S16–S21** were prepared by the representative procedure below in similar scale and yield (10–100 mg, 48–78% yield).

### Compound **S16**



Compound **S1**<sup>1</sup> (88 mg, 0.146 mmol) was dissolved in a commercially prepared solution of 4 M HCl in dioxane (5 mL) at room temperature and stirred at this temperature for 1–2 h. The reaction mixture was analyzed by TLC to ensure consumption of the starting material, and the reaction mixture was condensed under a stream of air. The residue was then treated with a saturated solution of NaHCO<sub>3</sub> (10 mL) and EtOAc (10 mL). The organic layer was washed with water (1 × 20 mL), dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude mixture was used directly without purification and dissolved in a solution of CH<sub>2</sub>Cl<sub>2</sub> and DMF (10 mL, 3:1 v:v) at 0 °C. This solution was treated with solid EDCI (34 mg, 0.219 mmol), HOAt (30 mg, 0.219 mmol), and **S10** (38 mg, 0.219 mmol) and the resulting solution was allowed to slowly warm to room temperature and stirred overnight. The reaction mixture was quenched with the addition of water (10 mL) and extracted with EtOAc (3 × 20 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes) and provided the pure amide **S16** (89 mg, 62%) as a white solid.

$[\alpha]_D^{25}$  –1.7 (*c* 0.28, CHCl<sub>3</sub>)

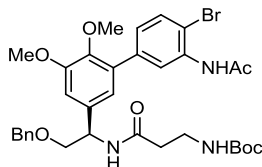
HRMS *m/z* 656.1965 ([M + H]<sup>+</sup>, C<sub>32</sub>H<sub>38</sub>BrN<sub>3</sub>O<sub>7</sub> requires 656.1966)

IR (film)  $\nu_{\max}$  2976, 2933, 1670, 1519, 1393, 1272, 1162 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.45 (s, 1H), 7.64 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.23 – 7.33 (m, 8H), 7.06 (br s, 1H), 6.87 (d, *J* = 9.6 Hz, 2H), 5.59 (br s, 1H), 5.14 (br s, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 3.91 (br s, 1H), 3.85 (s, 3H), 3.71 – 3.80 (m, 4H), 3.62 (s, 3H), 2.25 (s, 3H), 1.37 (s, 9H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  169.5, 168.3, 156.4, 155.8, 153.0, 145.7, 138.6, 137.6, 135.6, 135.3, 134.0, 131.7, 128.4, 127.8, 127.7, 126.4, 122.7, 120.3, 110.8, 80.1, 73.2, 72.2, 60.7, 56.0, 52.5, 44.6, 28.2, 24.9

### Compound **S17**



$[\alpha]_D^{25}$  –18 (*c* 0.39, CHCl<sub>3</sub>)

HRMS *m/z* 670.2099 ([M + H]<sup>+</sup>, C<sub>33</sub>H<sub>40</sub>BrN<sub>3</sub>O<sub>7</sub> requires 670.2122)

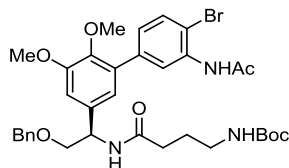


IR (film)  $\nu_{\max}$  2977, 1697, 1518, 1454, 1265, 1165, 732, 700  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  8.43 (s, 1H), 7.63 (s, 1H), 7.54 (d,  $J = 8.4$  Hz, 1H), 7.23 – 7.33 (m, 8H), 7.19 (d,  $J = 7.8$  Hz, 1H), 6.87 (d, 2H), 6.55 (br s, 1H), 5.37 (br s, 1H), 5.13 (dd,  $J = 4.8, 7.2$  Hz, 1H), 4.54 (d,  $J = 12.0$  Hz, 1H), 4.51 (d,  $J = 12.0$  Hz, 1H), 3.85 (br s, 1H), 3.68 – 3.70 (m, 1H), 3.72 – 3.74 (m, 1H), 3.62 (s, 3H), 3.35 – 3.41 (m, 1H), 2.46 (m, 2H), 2.24 (s, 3H), 1.36 (s, 9H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  171.2, 168.2, 156.2, 153.0, 145.7, 138.6, 137.6, 135.7, 135.3, 134.3, 131.7, 128.4, 127.86, 127.81, 126.4, 122.6, 120.3, 110.9, 79.2, 73.2, 72.4, 64.4, 60.7, 55.9, 36.6, 36.2, 28.3, 24.9

### Compound S18



$[\alpha]_{\text{D}}^{25} -22$  ( $c$  0.55,  $\text{CHCl}_3$ )

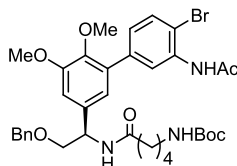
HRMS  $m/z$  684.2277 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{34}\text{H}_{42}\text{BrN}_3\text{O}_7$  requires 684.2279)

IR (film)  $\nu_{\max}$  3302, 2929, 1650, 1513, 1452, 1164, 907, 727  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  8.43 (s, 1H), 7.63 (s, 1H), 7.54 (d,  $J = 8.4$  Hz, 1H), 7.23 – 7.31 (m, 7H), 7.20 (d,  $J = 7.8$  Hz, 1H), 6.91 – 6.92 (m, 2H), 5.17 (m, 1H), 5.00 (br s, 1H), 4.54 (d,  $J = 12.0$  Hz, 1H), 4.50 (d,  $J = 12.0$  Hz, 1H), 3.85 (s, 3H), 3.71 – 3.73 (m, 2H), 3.63 (s, 3H), 3.16 (t,  $J = 6.0$  Hz, 2H), 2.25 (m, 5H), 1.81 (t,  $J = 6.0$  Hz, 2H), 1.41 (s, 9H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  172.2, 168.2, 156.5, 145.6, 138.7, 137.7, 136.0, 135.3, 134.2, 132.1, 132.0, 131.7, 128.45, 128.38, 127.7, 126.5, 122.6, 120.4, 112.2, 111.1, 79.2, 73.1, 72.6, 60.7, 55.9, 52.7, 39.7, 33.7, 28.4, 26.5, 24.8

### Compound S19



$[\alpha]_{\text{D}}^{25} -26$  ( $c$  0.19,  $\text{CHCl}_3$ )

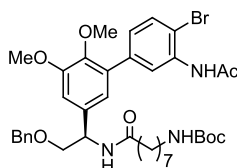
HRMS  $m/z$  698.2425 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{35}\text{H}_{44}\text{BrN}_3\text{O}_7$  requires 698.2435)

IR (film)  $\nu_{\max}$  3300, 2943, 2863, 1693, 1569, 1522, 1394, 1272, 1167  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  8.41 (s, 1H), 7.66 (s, 1H), 7.54 (d,  $J = 7.8$  Hz, 1H), 7.25 – 7.32 (m, 7H), 7.18 (d,  $J = 7.8$  Hz, 1H), 6.88 (s, 2H), 6.40 (br s, 1H), 5.16 (m, 1H), 4.78 (br s, 1H), 4.54 (d,  $J = 12.0$  Hz, 1H), 4.50 (d,  $J = 12.0$  Hz, 1H), 3.85 (s, 3H), 3.71 – 3.73 (m, 2H), 3.63 (s, 3H), 3.09 (m, 2H), 2.24 (m, 5H), 1.65 (m, 2H), 1.49 (m, 2H), 1.41 (s, 9H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  172.4, 168.3, 156.1, 152.9, 145.6, 138.6, 137.6, 135.9, 135.3, 134.3, 131.7, 128.4, 127.83, 127.79, 126.5, 122.6, 120.3, 111.1, 79.0, 73.2, 72.3, 60.7, 55.9, 52.8, 52.5, 39.9, 36.0, 29.4, 28.4, 22.7, 22.5

### Compound S20



$[\alpha]_{\text{D}}^{25} -27$  ( $c$  0.48,  $\text{CHCl}_3$ )

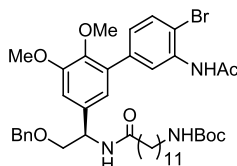
HRMS  $m/z$  740.2901 ( $[M + H]^+$ ,  $C_{38}H_{50}BrN_3O_7$  requires 740.2905)

IR (film)  $\nu_{max}$  3291, 2929, 2855, 1685, 1650, 1521, 1455, 1365, 1271, 729  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  8.41 (s, 1H), 7.69 (s, 1H), 7.54 (d,  $J = 7.8$  Hz, 1H), 7.25 – 7.32 (m, 7H), 7.15 (d,  $J = 7.8$  Hz, 1H), 6.88 (s, 2H), 6.29 (d,  $J = 7.2$  Hz, 1H), 5.16 (m, 1H), 4.54 (d,  $J = 12.0$  Hz, 1H), 4.54 (m, 1H, partially obstructed), 4.50 (d,  $J = 12.0$  Hz, 1H), 3.85 (s, 3H), 3.71 – 3.73 (m, 2H), 3.64 (s, 3H), 3.04 (m, 2H), 2.24 (s, 3H), 2.20 (t,  $J = 7.8$  Hz, 2H), 1.60 (m, 2H), 1.43 (s, 9H), 1.42 (m, 2H), 1.24 (m, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 150 MHz)  $\delta$  172.7, 168.2, 155.9, 152.9, 145.6, 138.6, 137.7, 136.0, 135.3, 134.2, 131.7, 128.4, 127.8, 127.7, 126.4, 122.9, 120.4, 111.2, 79.0, 73.1, 72.3, 64.3, 60.8, 55.9, 52.3, 40.5, 36.6, 29., 29.1, 28.9, 28.4, 26.5, 25.5, 24.8, 22.5

## Compound S21



$[\alpha]_D^{25}$   $-23$  ( $c$  0.16,  $CHCl_3$ )

HRMS  $m/z$  796.3527 ( $[M + H]^+$ ,  $C_{42}H_{58}BrN_3O_7$  requires 796.3531)

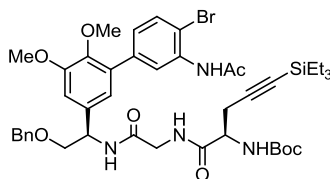
IR (film)  $\nu_{max}$  2924, 2852, 1648, 1456, 1271, 1166, 730  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  8.44 (s, 1H), 7.62 (s, 1H), 7.54 (d,  $J = 7.8$  Hz, 1H), 7.25 – 7.32 (m, 7H), 7.15 (d,  $J = 7.2$  Hz, 1H), 6.88 (s, 2H), 6.23 (d,  $J = 7.2$  Hz, 1H), 5.16 (m, 1H), 4.54 (d,  $J = 12.0$  Hz, 1H), 4.50 (d,  $J = 12.0$  Hz, 1H), 3.85 (s, 3H), 3.73 – 3.75 (m, 2H), 3.64 (s, 3H), 3.09 (m, 2H), 2.24 (s, 3H), 2.20 (t,  $J = 7.8$  Hz, 2H), 1.62 (m, 2H), 1.43 (s, 9H), 1.24 (m, 14H)

$^{13}C$  NMR ( $CDCl_3$ , 150 MHz)  $\delta$  172.7, 168.1, 156.0, 152.9, 145.6, 138.7, 137.7, 136.0, 135.3, 134.3, 131.7, 128.4, 127.81, 127.77, 126.4, 122.7, 120.4, 112.2, 111.1, 79.0, 73.2, 72.3, 60.8, 55.9, 52.3, 40.6, 36.8, 30.01, 29.46, 29.39, 29.31, 29.26, 29.24, 28.4, 26.8, 25.7, 24.8, 22.5

Macrocyclization precursors **10–15** were prepared by the representative procedure below in similar scale and yield (10–80 mg, 54–73% yield).

## Compound 10



Compound **S16** (50 mg, 0.0761 mmol) was dissolved in a commercially prepared solution of 4 M HCl in dioxane (5 mL) at room temperature and stirred at this temperature for 1–2 h. The reaction mixture was analyzed by TLC to ensure consumption of the starting material, and the reaction mixture was condensed under a stream of nitrogen. The residue was treated with a saturated solution of  $NaHCO_3$  (10 mL) and EtOAc (10 mL). The organic layer was washed with water (1  $\times$  20 mL), dried over  $Na_2SO_4$ , filtered, and concentrated in vacuo. The crude amine was used directly without purification and dissolved in a solution of DMF (5 mL) at 0  $^\circ C$ . This solution was then treated with solid EDCI (23.5 mg, 0.15 mmol), HOAt (21 mg, 0.15 mmol), and alkyne subunit **S9** (50 mg, 0.15 mmol) and the resulting solution allowed to slowly warm to room temperature and stirred overnight. The reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3  $\times$  20 mL). The organic layer was dried over  $Na_2SO_4$ , filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography ( $SiO_2$ , 100% EtOAc) and provided **10** (45 mg, 69%) as a white solid.

$[\alpha]_D^{25}$   $-8.6$  ( $c$  0.24,  $CHCl_3$ )

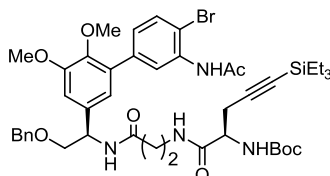
HRMS  $m/z$  865.3202 ( $[M + H]^+$ ,  $C_{43}H_{57}BrN_4O_8Si$  requires 865.3202)

IR (film)  $\nu_{max}$  3298, 2954, 2874, 1656, 1519, 1248, 1163, 1007, 727  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  8.43 (s, 1H), 7.64 (s, 1H), 7.54 (d,  $J = 8.4$  Hz, 1H), 7.24 – 7.33 (m, 8H), 7.02 (br s, 1H), 6.88 (s, 2H), 5.28 (br s, 1H), 5.14 (m, 1H), 4.55 (d,  $J = 12.0$  Hz, 1H), 4.50 (d,  $J = 12.0$  Hz, 1H), 4.20 (d,  $J = 6.0$  Hz, 1H), 3.99 (br s, 2H), 3.85 (s, 3H), 3.71 – 3.74 (m, 2H), 3.62 (s, 3H), 2.71 (dd,  $J = 7.2, 17.4$  Hz, 1H), 2.67 (dd,  $J = 7.2, 17.4$  Hz, 1H), 2.26 (s, 3H), 1.34 (s, 9H), 0.95 (t,  $J = 8.4$  Hz, 9H), 0.55 (q,  $J = 7.8$  Hz, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 150 MHz)  $\delta$  171.0, 168.4, 168.3, 155.7, 153.0, 145.7, 138.6, 137.7, 135.5, 135.2, 133.9, 131.7, 128.4, 127.77, 127.70, 126.5, 122.8, 120.3, 112.1, 111.0, 102.4, 85.9, 80.5, 73.2, 72.3, 60.7, 55.9, 52.8, 43.3, 28.3, 28.1, 24.9, 22.5, 7.4, 4.3

## Compound 11



$[\alpha]_D^{25}$   $-33$  ( $c$  0.63,  $CHCl_3$ )

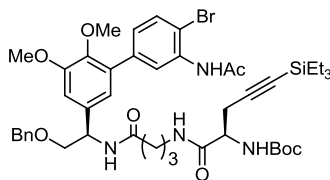
HRMS  $m/z$  901.3157 ( $[M + Na]^+$ ,  $C_{44}H_{59}BrN_4O_8Si$  requires 901.3178)

IR (film)  $\nu_{max}$  3290, 2931, 1653, 1521, 1366, 1247, 1166, 1010, 737, 670  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  8.43 (s, 1H), 7.63 (s, 1H), 7.54 (d,  $J = 7.8$  Hz, 1H), 7.24 – 7.33 (m, 8H), 7.16 (d,  $J = 7.8$  Hz, 1H), 6.95 (br s, 1H), 6.88 (s, 1H), 6.77 (br s, 1H), 5.25 (br s, 1H), 4.58 (d,  $J = 12.0$  Hz, 1H), 4.52 (d,  $J = 12.0$  Hz, 1H), 4.02 (d,  $J = 6.6$  Hz, 1H), 3.86 (s, 3H), 3.71 – 3.78 (m, 4H), 3.63 (s, 3H), 2.60 – 2.67 (m, 1H), 2.38 – 2.50 (m, 3H), 2.24 (s, 3H), 1.36 (s, 9H), 0.96 (t,  $J = 7.8$  Hz, 9H), 0.55 (q,  $J = 7.8$  Hz, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 150 MHz)  $\delta$  170.8, 168.4, 155.7, 153.2, 146.0, 138.8, 137.7, 135.5, 134.7, 131.9, 128.7, 128.3, 128.2, 128.1, 126.6, 122.9, 120.7, 112.4, 111.4, 102.8, 85.8, 80.4, 73.4, 72.6, 61.0, 56.2, 53.6, 52.7, 36.6, 36.2, 28.4, 25.1, 23.7, 7.7, 4.5

## Compound 12



$[\alpha]_D^{25}$   $-22$  ( $c$  0.13,  $CHCl_3$ )

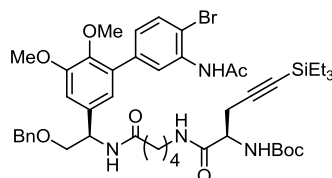
HRMS  $m/z$  893.3478 ( $[M + H]^+$ ,  $C_{45}H_{61}BrN_4O_8Si$  requires 893.3515)

IR (film)  $\nu_{max}$  3286, 1652, 1541, 1275, 760, 670  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  8.39 (s, 1H), 7.64 (s, 1H), 7.53 (d,  $J = 8.4$  Hz, 1H), 7.24 – 7.33 (m, 8H), 7.16 (d,  $J = 7.2$  Hz, 1H), 6.94 (s, 1H), 6.91 (s, 1H), 6.81 (br s, 1H), 6.26 (m, 1H), 5.35 (br s, 1H), 5.19 (br s, 1H), 4.55 (d,  $J = 12.0$  Hz, 1H), 4.52 (d,  $J = 12.0$  Hz, 1H), 4.41 (m, 1H), 3.84 (s, 3H), 3.73 (m, 2H), 3.62 (s, 3H), 3.29 (m, 2H), 3.25 (m, 1H), 2.72 (dd,  $J = 7.2, 18.6$  Hz, 1H), 2.56 (dd,  $J = 7.2, 18.6$  Hz, 1H), 2.23 (s, 3H), 1.84 (m, 2H), 1.39 (s, 9H), 0.94 (t,  $J = 7.8$  Hz, 9H), 0.53 (q,  $J = 7.8$  Hz, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 150 MHz)  $\delta$  172.6, 171.2, 168.6, 156.8, 153.1, 145.9, 138.8, 137.9, 136.0, 135.4, 134.5, 131.9, 128.6, 128.0, 127.9, 126.7, 123.0, 120.7, 112.6, 111.4, 99.4, 85.8, 80.6, 73.3, 72.9, 61.0, 56.1, 53.0, 38.7, 33.5, 29.9, 28.4, 25.0, 23.7, 21.4, 7.6, 4.5

## Compound 13



$[\alpha]_D^{25} -31$  (*c* 0.23, CHCl<sub>3</sub>)

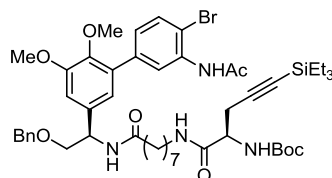
HRMS *m/z* 907.3649 ([M + H]<sup>+</sup>, C<sub>46</sub>H<sub>63</sub>BrN<sub>4</sub>O<sub>8</sub>Si requires 907.3671)

IR (film)  $\nu_{\max}$  3386, 2920, 2850, 1647, 671 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  8.42 (s, 1H), 7.63 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.27 – 7.33 (m, 8H), 7.16 (d, *J* = 7.8 Hz, 1H), 6.88 (s, 2H), 6.50 (br s, 1H), 5.31 (br s, 1H), 5.16 (m, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.15 (br s, 1H), 3.85 (s, 3H), 3.73 (d, *J* = 4.8 Hz, 2H), 3.63 (s, 3H), 3.30 (m, 1H), 3.16 (m, 1H), 2.73 (dd, *J* = 5.4, 16.8 Hz, 1H), 2.55 (dd, *J* = 5.4, 16.8 Hz, 1H), 2.24 (m, 4H), 1.40 (s, 9H), 0.95 (t, *J* = 7.8 Hz, 9H), 0.54 (q, *J* = 7.8 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  172.6, 170.7, 168.4, 155.7, 153.2, 145.9, 138.9, 137.8, 136.1, 135.5, 134.6, 131.9, 128.7, 128.11, 128.05, 126.7, 122.9, 120.7, 112.5, 111.4, 99.8, 85.7, 80.5, 73.4, 72.6, 61.0, 56.2, 52.7, 39.1, 35.9, 28.9, 28.5, 25.1, 23.9, 22.9, 7.7, 4.6

## Compound 14



$[\alpha]_D^{25} -39$  (*c* 0.05, CHCl<sub>3</sub>)

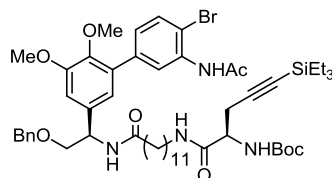
HRMS *m/z* 949.4126 ([M + H]<sup>+</sup>, C<sub>49</sub>H<sub>69</sub>BrN<sub>4</sub>O<sub>8</sub>Si requires 949.4141)

IR (film)  $\nu_{\max}$  3294, 2931, 2873, 1651, 1521, 1456, 1366, 1239, 1164 1053, 1008, 727 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  8.41 (s, 1H), 7.70 (s, 1H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.24 – 7.30 (m, 8H), 7.15 (d, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 1.8 Hz, 2H), 6.37 (br s, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 5.40 (br s, 1H), 5.36 (d, *J* = 7.8 Hz, 1H), 5.16 (m, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.43 (m, 1H), 4.19 (br s, 1H), 3.84 (s, 3H), 3.71 – 3.76 (m, 4H), 3.64 (s, 3H), 3.17 – 3.23 (m, 2H), 2.78 – 2.82 (m, 2H), 2.59 (dd, *J* = 17.4, 6.6 Hz, 1H), 2.24 (s, 3H), 2.20 (m, 2H), 1.61 (m, 2H), 1.43 (s, 9H), 1.22 – 1.28 (m, 8H), 0.96 (m, 9H), 0.55 (m, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  173.4, 173.0, 168.5, 155.5, 153.1, 145.9, 138.8, 137.9, 136.1, 135.5, 134.5, 131.9, 128.6, 128.03, 127.99, 126.7, 123.1, 120.6, 112.7, 111.4, 102.2, 85.8, 80.2, 73.4, 72.5, 61.0, 56.1, 52.6, 39.8, 36.8, 29.6, 29.2, 29.0, 28.47, 28.45, 26.7, 25.7, 25.0, 24.1, 24.0, 7.6, 4.5

## Compound 15



$[\alpha]_D^{25} -23$  (*c* 0.025, CHCl<sub>3</sub>)

HRMS *m/z* 1005.4785 ([M + H]<sup>+</sup>, C<sub>53</sub>H<sub>77</sub>BrN<sub>4</sub>O<sub>8</sub>Si requires 1005.4767)

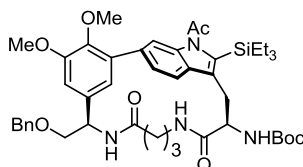
IR (film)  $\nu_{\max}$  2920, 2849, 1736, 1652, 1459, 1237, 1016, 720, 671 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  8.43 (s, 1H), 7.65 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.24 – 7.30 (m, 8H), 7.16 (t, *J* = 7.2 Hz, 1H), 6.88 (s, 2H), 6.37 (br s, 1H), 6.29 (d, *J* = 7.8 Hz, 1H), 5.39 (br s, 1H), 5.34 (d, *J* = 7.8 Hz, 1H), 5.16 (m, 1H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.45 (m, 1H), 4.20 (br s, 1H), 3.85 (s, 3H),

3.71 – 3.76 (m, 4H), 3.64 (s, 3H), 3.17 – 3.23 (m, 2H), 2.78 – 2.85 (m, 3H), 2.59 (dd,  $J = 15.6, 6.0$  Hz, 1H), 2.25 (s, 3H), 2.22 (m, 2H), 1.61 (m, 2H), 1.44 (s, 9H), 1.22 – 1.28 (m, 14H), 0.96 (m, 9H), 0.57 (m, 6H)  
 $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  173.8, 173.2, 170.4, 155.6, 153.1, 145.9, 138.9, 137.9, 136.1, 135.5, 134.5, 131.9, 129.2, 128.6, 128.4, 128.04, 128.00, 126.7, 123.0, 120.6, 111.4, 102.0, 86.0, 80.4, 73.4, 72.5, 61.0, 56.1, 52.6, 39.9, 36.9, 29.73, 29.66, 29.64, 29.55, 29.49, 29.46, 28.5, 27.0, 25.9, 25.0, 24.1, 7.6, 4.5

Macrocyclization products **16–21** were prepared by the representative procedure below.

### Macrocycle **18**



A solution of  $\text{Pd}(\text{OAc})_2$  (6.1 mg, 0.027 mmol) and *Dt*BPF ligand (15 mg, 0.032 mmol) in  $\text{CH}_3\text{CN}$ :toluene (5 mL, 1:1) was treated with distilled  $\text{Et}_3\text{N}$  (4.5  $\mu\text{L}$ , 0.032 mmol) at room temperature. This solution was slowly added to a refluxing solution of  $\text{CH}_3\text{CN}$ /toluene (15 mL, 1:1) in a three-necked flask equipped with a reflux condenser to give a clear orange solution. Compound **12** (22 mg, 0.025 mmol) in  $\text{CH}_3\text{CN}$ /toluene (5 mL, 1:1) was slowly added to the reaction vessel and the mixture was warmed at reflux. The reaction was complete after 1 h as indicated by the appearance of the products on TLC. The reaction solution was cooled to ambient temperature before the solvent was removed in vacuo. The crude product was purified by flash chromatography ( $\text{SiO}_2$ , 100% EtOAc) and provided **16** (13.0 mg, 65%) as a white solid.

$[\alpha]_D^{25}$   $-12.6$  ( $c$  0.29,  $\text{CHCl}_3$ )

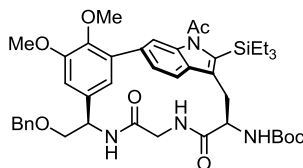
HRMS  $m/z$  813.4226 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{45}\text{H}_{60}\text{N}_4\text{O}_8\text{Si}$  requires 813.4253)

IR (film)  $\nu_{\text{max}}$  2923, 1650, 1513, 1452, 1270, 1164, 907, 727, 647  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  7.81 (s, 1H), 7.59 (d,  $J = 8.4$  Hz, 1H), 7.31 – 7.36 (m, 5H), 7.27 (s, 1H), 6.61 (d,  $J = 1.8$  Hz, 1H), 6.39 (s, 1H), 6.38 (s, 1H), 5.48 (d,  $J = 9.0$  Hz, 1H), 4.95 (m, 1H), 4.87 (m, 1H), 4.61 (d,  $J = 12.0$  Hz, 1H), 4.53 (d,  $J = 12.0$  Hz, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 3.82 (app t,  $J = 4.2$  Hz, 2H), 3.22 – 3.29 (m, 2H), 2.94 (m, 1H), 2.79 (s, 3H), 2.41 (m, 1H), 2.12 (d,  $J = 3.6$  Hz, 1H), 2.05 (m, 1H), 1.61 (m, 1H), 1.37 (m, 1H), 1.45 (s, 9H), 0.92 – 0.98 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  172.6, 172.4, 169.8, 154.9, 153.4, 144.8, 137.5, 136.6, 136.4, 135.1, 133.7, 132.0, 130.8, 128.8, 128.3, 128.1, 123.6, 123.0, 120.5, 115.8, 108.4, 80.0, 73.3, 71.6, 61.6, 58.8, 56.2, 53.0, 39.6, 34.7, 30.2, 28.5, 28.4, 26.7, 26.5, 8.6, 5.7

### Macrocycle **16**



$[\alpha]_D^{25}$   $+30$  ( $c$  0.030,  $\text{CHCl}_3$ )

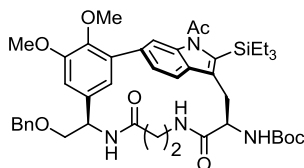
HRMS  $m/z$  785.3941 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{43}\text{H}_{56}\text{N}_4\text{O}_8\text{Si}$  requires 785.3940)

IR (film)  $\nu_{\text{max}}$  2930, 1698, 1650, 1518, 1370, 1246, 1164, 670  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  7.59 (d,  $J = 9.0$  Hz, 1H), 7.56 (br s, 1H), 7.32 – 7.38 (m, 5H), 7.25 (partially obstructed), 6.75 (s, 1H), 6.02 (d,  $J = 7.8$  Hz, 1H), 5.84 (d,  $J = 5.4$  Hz, 1H), 5.60 (s, 1H), 5.29 (d,  $J = 10.2$  Hz, 1H), 4.83 (m, 1H), 4.60 (d,  $J = 12.6$  Hz, 1H), 4.53 (br s, 1H), 4.51 (d,  $J = 12.6$  Hz, 1H), 4.35 (dd,  $J = 8.4, 16.8$  Hz, 1H), 4.10 (s, 3H), 3.91 (dd,  $J = 3.3, 10.2$  Hz, 1H), 3.84 (s, 3H), 3.78 (dd,  $J = 3.3, 10.2$  Hz, 1H), 3.64 (m, 1H), 3.59 (m, 2H), 2.72 (s, 3H), 1.44 (s, 9H), 0.91 – 0.96 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  172.4, 169.2, 168.6, 156.3, 154.5, 153.3, 144.2, 139.2, 137.6, 137.4, 135.9, 133.9, 131.6, 130.7, 129.7, 128.8, 128.4, 128.2, 123.4, 120.7, 117.3, 106.9, 80.2, 79.3, 73.7, 70.1, 61.9, 56.5, 53.9, 43.5, 40.9, 28.6, 8.5, 5.7

Macrocycle (*R*)-**17** – “natural” (*R*)-atropisomer



TLC: ((*R*)-atropisomer  $R_f = 0.5$ , (*S*)-atropisomer  $R_f = 0.6$ , 100% EtOAc).

Equilibration of the natural atropisomer in toluene took place very slowly at room temperature. At 50 °C, a 3:1 ratio of (*R*)-**17** to (*S*)-**17** was observed after 30 min and after 8 h, a 1:1 ratio of atropisomers was present.

$[\alpha]_D^{25} +12$  ( $c$  0.050,  $\text{CHCl}_3$ )

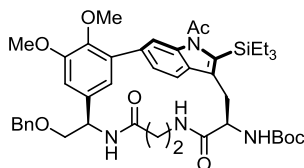
HRMS  $m/z$  799.4079 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{44}\text{H}_{58}\text{N}_4\text{O}_8\text{Si}$  requires 799.4096)

IR (film)  $\nu_{\text{max}}$  2933, 1700, 1520, 1369, 1310, 1242, 1165, 737, 700  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.61 (m, 1H), 7.60 (s, 1H), 7.35 – 7.40 (m, 4H), 7.28 – 7.34 (m, 5H), 6.63 ( $J = 2.4$  Hz, 1H), 6.45 (d,  $J = 7.2$  Hz, 1H), 6.21 (d,  $J = 7.2$  Hz, 1H), 5.32 (d,  $J = 7.8$  Hz, 1H), 4.85 (m, 1H), 4.60 (d,  $J = 12.0$  Hz, 1H), 4.56 (d,  $J = 12.0$  Hz, 1H), 3.98 (s, 3H), 3.88 (s, 3H), 3.79 (dd,  $J = 3.6, 9.6$  Hz, 1H), 3.74 (dd,  $J = 3.6, 9.6$  Hz, 1H), 3.39 (m, 1H), 3.18 (t,  $J = 12.0$  Hz, 1H), 2.76 (s, 3H), 2.71 (m, 1H), 1.88 (m, 1H), 1.46 (s, 9H), 1.43 (m, partially obstructed, 1H), 0.96 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  173.6, 171.7, 169.6, 154.7, 153.1, 144.4, 138.0, 137.6, 137.3, 134.8, 134.6, 128.8, 128.3, 128.2, 126.4, 123.1, 121.3, 116.3, 109.2, 80.1, 73.6, 71.3, 61.9, 58.3, 56.3, 54.0, 39.0, 38.0, 30.8, 28.5, 26.3, 8.8, 5.7

Macrocycle (*S*)-**17** – “unnatural” (*S*)-atropisomer



$[\alpha]_D^{25} +43$  ( $c$  0.025,  $\text{CHCl}_3$ )

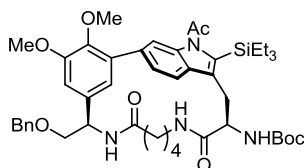
HRMS  $m/z$  799.4100 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{44}\text{H}_{58}\text{N}_4\text{O}_8\text{Si}$  requires 799.4096)

IR (film)  $\nu_{\text{max}}$  2934, 1701, 1650, 1493, 1369, 1231, 1160, 729, 670  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.70 (m, 1H), 7.61 (s, 1H), 7.30 – 7.34 (m, 5H), 7.20 – 7.23 (m, 3H), 6.64 (d,  $J = 2.4$  Hz, 1H), 5.87 (d,  $J = 6.0$  Hz, 1H), 5.84 (s, 1H), 5.27 (br s, 1H), 5.06 (m, 1H), 4.55 (d,  $J = 12.0$  Hz, 1H), 4.46 (d,  $J = 12.0$  Hz, 1H), 3.93 (s, 3H), 3.86 (s, 3H), 3.77 (dd,  $J = 9.6, 3.6$  Hz, 1H), 3.73 (m, 1H), 3.56 (d,  $J = 1.2$  Hz), 3.31 (m, 1H), 3.03 (m, 1H), 2.78 (s, 3H), 2.57 (m, 1H), 1.75 (m, 1H), 1.42 (s, 9H), 1.34 (m, partially obstructed, 1H), 0.96 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 150 MHz)  $\delta$  172.03, 172.00, 169.6, 155.0, 154.7, 152.9, 144.2, 138.4, 137.5, 137.3, 136.9, 134.7, 128.8, 128.3, 128.2, 126.3, 124.8, 121.3, 115.0, 108.3, 80.8, 73.6, 70.4, 61.8, 56.3, 53.3, 52.6, 35.7, 30.8, 28.4, 26.5, 8.5, 6.5

Macrocycle **19**



$[\alpha]_D^{25} +9.9$  (*c* 0.23, CHCl<sub>3</sub>)

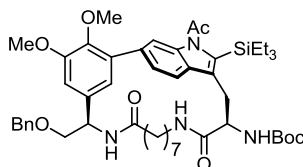
HRMS  $m/z$  827.4395 ( $[M + H]^+$ , C<sub>46</sub>H<sub>62</sub>N<sub>4</sub>O<sub>8</sub>Si requires 827.4409)

IR (film)  $\nu_{\max}$  2928, 1647, 1522, 1369, 1237, 1162, 670 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  7.91 (s, 1H), 7.60 (d, *J* = 9.0 Hz, 1H), 7.31 – 7.36 (m, 5H), 7.22 – 7.24 (m, 2H), 6.88 (d, *J* = 1.8 Hz, 1H), 6.56 (d, *J* = 1.8 Hz, 1H), 6.15 (d, *J* = 7.0 Hz, 1H), 5.14 (m, 1H), 4.62 (d, *J* = 12.5 Hz, 1H), 4.49 (d, *J* = 12.5 Hz, 1H), 4.29 (s, 1H), 3.98 (dd, *J* = 4.5, 10.0 Hz, 1H), 3.85 (s, 3H), 3.80 (dd, *J* = 4.5, 10.0 Hz, 1H), 3.67 (s, 3H), 3.83 (m, 1H), 2.87 (m, 1H), 2.79 (s, 3H), 2.45 (m, 1H), 2.25 (m, 1H), 1.92 (m, 1H), 1.42 (s, 9H), 0.92 – 0.98 (m, 15H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  172.8, 172.3, 169.9, 155.1, 153.2, 145.0, 137.6, 136.9, 136.3, 135.5, 134.1, 131.4, 128.8, 128.4, 128.2, 124.0, 122.9, 121.3, 114.6, 108.6, 104.4, 80.6, 73.5, 71.0, 61.2, 56.2, 52.1, 40.9, 36.4, 29.9, 28.5, 27.0, 23.3, 22.9, 8.6, 6.4

## Macrocycle 20



$[\alpha]_D^{25} -8.7$  (*c* 0.14, CHCl<sub>3</sub>)

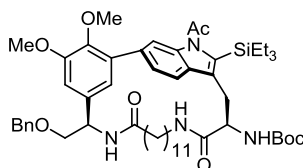
HRMS  $m/z$  869.4845 ( $[M + H]^+$ , C<sub>49</sub>H<sub>68</sub>N<sub>4</sub>O<sub>8</sub>Si requires 869.4879)

IR (film)  $\nu_{\max}$  2931, 1697, 1651, 1521, 1367, 1162, 729, 670 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz)  $\delta$  7.74 (s, 1H), 7.72 (br s, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.32 – 7.37 (m, 5H), 7.28 – 7.29 (m, 3H), 6.85 (s, 1H), 6.83 (s, 1H), 5.40 (m, 1H), 5.20 (m, 1H), 4.82 (m, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.40 (br s, 1H), 3.88 (s, 3H), 3.83 (m, 2H), 3.60 (s, 3H), 3.42 (dd, *J* = 4.2, 15 Hz, 1H), 3.21 (app t, *J* = 12.6 Hz, 1H), 2.85 (m, 2H), 2.75 (s, 3H), 2.33 (m, 1H), 2.09 – 2.14 (m, 3H), 1.75 (m, 1H), 1.57 (s, 6H), 1.48 (s, 9H), 1.43 (m, 1H), 0.91 – 1.03 (m, 15H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  172.7, 171.0, 169.9, 155.3, 153.2, 145.8, 137.8, 137.3, 135.9, 135.8, 131.5, 128.8, 128.3, 128.0, 124.7, 120.4, 120.0, 114.4, 110.3, 80.1, 73.5, 72.4, 61.0, 56.2, 52.5, 39.5, 36.6, 29.9, 29.3, 28.8, 28.6, 28.4, 27.0, 26.6, 25.9, 8.6, 6.2

## Macrocycle 21



Note: This reaction required approximately 4 h to proceed to completion.

$[\alpha]_D^{25} -27$  (*c* 0.21, CHCl<sub>3</sub>)

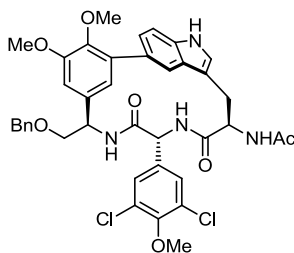
HRMS  $m/z$  925.5506 ( $[M + H]^+$ , C<sub>53</sub>H<sub>76</sub>N<sub>4</sub>O<sub>8</sub>Si requires 925.5505)

IR (film)  $\nu_{\max}$  2928, 1652, 1493, 1367, 1161, 908, 728 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  7.96 (s, 1H), 7.72 (br s, 1H), 7.41 (d, *J* = 6.6 Hz, 1H), 7.28 – 7.31 (m, 8H), 6.85 (s, 1H), 7.00 (s, 1H), 6.97 (s, 1H), 6.20 (d, *J* = 6.6 Hz, 1H), 5.38 (br s, 1H), 5.25 (br s, 1H), 5.20 (m, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.36 (br s, 1H), 3.89 (s, 3H), 3.78 (m, 2H), 3.57 (s, 3H), 3.42 (m, 2H), 3.09 (m, 1H), 2.93 (m, 1H), 2.77 (s, 3H), 2.29 (m, 1H), 2.15 (m, 1H), 1.69 (m, 1H), 1.56 (m, 1H), 1.44 (m, 2H), 1.41 (s, 9H), 1.21 – 1.25 (m, 6H), 1.05 – 1.11 (m, 8H), 0.92 – 0.98 (m, 15H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$  172.9, 171.2, 169.9, 153.2, 145.8, 138.1, 137.8, 137.2, 136.8, 135.6, 135.1, 131.9, 128.8, 128.70, 128.65, 128.2, 128.0, 124.3, 120.8, 119.9, 115.0, 111.1, 80.2, 73.6, 72.5, 60.8, 56.1, 52.6, 39.3, 36.9, 28.9, 28.83, 28.75, 28.66, 28.59, 28.50, 28.45, 27.0, 26.22, 25.79, 8.6, 6.3

## Compound S22

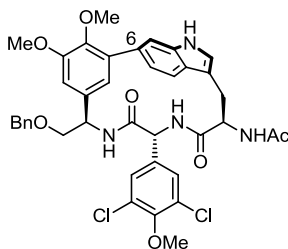


Compound **9** (8.0 mg, 8.33  $\mu\text{mol}$ ) was dissolved in a commercially prepared solution of 4 M HCl in dioxane (5 mL) at room temperature and stirred for 12 h. The reaction mixture was analyzed by TLC to ensure consumption of the starting material, and the reaction mixture condensed under a stream of nitrogen. The residue was treated with saturated aqueous  $\text{NaHCO}_3$  (5 mL) and EtOAc (5 mL). The organic layer was washed with water ( $1 \times 20$  mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude product was dissolved in a solution of  $\text{CH}_2\text{Cl}_2$  (5 mL), and treated with  $\text{Ac}_2\text{O}$  (10  $\mu\text{L}$ , excess) at room temperature. After 1 h, the reaction mixture was diluted with additional  $\text{CH}_2\text{Cl}_2$  (20 mL), quenched with the addition of saturated aqueous  $\text{NaHCO}_3$  (10 mL), and stirred for 15 min or until all bubbling ceased. The crude product was extracted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 10$  mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude product was dissolved in a freshly prepared solution of 1 M LiOH in THF (15 mL, 9:1 v:v) at room temperature and stirred for 6 h. Upon completion, the reaction was diluted with EtOAc (10 mL) and  $\text{H}_2\text{O}$  (10 mL), extracted with EtOAc ( $3 \times 20$  mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude mixture was purified by preparative thin-layer chromatography ( $\text{SiO}_2$ , 100% EtOAc) and provided **S22** (2.7 mg, 43%) as a white solid.

LCMS  $m/z$  746 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{39}\text{H}_{38}\text{Cl}_2\text{N}_4\text{O}_7$  requires 746)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  8.09 (s, 1H), 7.71 (m, 2H), 7.54 (m, 2H), 7.33 – 7.41 (m, 3H), 7.15 (d,  $J = 6.0$  Hz, 1H), 6.98 (s, 1H), 6.78 (s, 1H), 6.63 (s, 1H), 6.47 (d,  $J = 4.2$  Hz, 1H), 6.36 (d,  $J = 7.2$  Hz, 1H), 5.65 (d,  $J = 7.8$  Hz, 1H), 5.04 (m, 1H), 4.78 (m, 1H), 4.51 (d,  $J = 12.0$  Hz, 1H), 4.46 (d,  $J = 12.0$  Hz, 1H), 4.22 (m, 1H), 3.92 (s, 3H), 3.85 (s, 3H), 3.65 (m, 2H), 3.60 (s, 3H), 3.25 (m, 1H), 2.05 (s, 3H)

## Compound S23



This compound was prepared from (*S*)-**2** in the same manner as compound **S22**.

$[\alpha]_D^{25}$   $-41$  ( $c$  0.09,  $\text{CHCl}_3$ )

HRMS  $m/z$  745.2197 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{39}\text{H}_{38}\text{Cl}_2\text{N}_4\text{O}_7$  requires 745.2190)

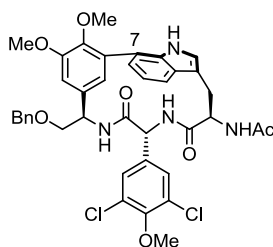
IR (film)  $\nu_{\text{max}}$  2938, 1636, 1481, 1246, 1122, 671  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  8.03 (br s, 1H), 7.64 (d,  $J = 8.4$  Hz, 1H), 7.43 (s, 1H), 7.29 – 7.34 (m, 5H), 7.17 (d,  $J = 6.6$  Hz, 2H), 7.11 (s, 2H), 7.01 (d,  $J = 8.4$  Hz, 1H), 6.89 (s, 1H), 6.83 (d,  $J = 5.4$  Hz, 1H), 6.51 (d,  $J = 2.4$  Hz, 1H), 6.21 (d,  $J = 6.6$  Hz, 1H), 5.88 (d,  $J = 9.0$  Hz, 1H), 5.37 (m, 1H), 5.15 (d,  $J = 1.8$  Hz, 1H), 4.79 (m, 1H), 4.56 (d,  $J = 7.2$  Hz, 1H), 4.43 (d,  $J = 12.6$  Hz, 1H), 4.40 (d,  $J = 12.6$  Hz, 1H), 4.15 (s, 3H), 3.85 (s, 3H), 3.81 (dd,  $J = 3.6, 9.6$  Hz, 1H), 3.79 (s, 3H), 3.65 (dd,  $J = 3.6, 9.6$  Hz, 1H), 3.40 (dd,  $J = 6.0, 13.8$  Hz, 1H), 2.89 (t,  $J = 12.6$  Hz, 1H), 1.95 (s, 3H)

$^{13}\text{C}$  NMR (acetone- $d_6$ , 150 MHz)  $\delta$  170.7, 169.7, 169.4, 153.3, 152.2, 144.1, 139.3, 139.2, 138.1, 136.6, 135.7, 131.5, 129.6, 129.1, 128.9, 128.4, 128.3, 127.8, 126.9, 126.1, 124.2, 119.3, 114.8, 111.6, 109.2, 73.6, 71.6, 61.3, 60.9, 56.5, 56.5, 53.9, 53.4, 28.7, 22.6



## Compound S24



Compound **S23** (7.0 mg, 9.39  $\mu\text{mol}$ ) was treated with trifluoroacetic acid (neat, 200  $\mu\text{L}$ ), and warmed to 50  $^{\circ}\text{C}$  for 15 min. The reaction mixture was analyzed by TLC to ensure consumption of the starting material, and the reaction mixture was condensed under a stream of nitrogen. The residue was purified by preparative thin-layer chromatography ( $\text{SiO}_2$ , 100% EtOAc) to provide **S24** (3.8 mg, 55%) as a white solid.

$[\alpha]_{\text{D}}^{25}$   $-150$  ( $c$  0.05,  $\text{CHCl}_3$ )

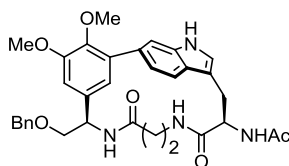
HRMS  $m/z$  745.2191 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{39}\text{H}_{38}\text{Cl}_2\text{N}_4\text{O}_7$  requires 745.2190)

IR (film)  $\nu_{\text{max}}$  2937, 1742, 1637, 1481, 1363, 1270, 669  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 600 MHz)  $\delta$  7.99 (s, 1H), 7.59 (d,  $J = 7.8$  Hz, 1H), 7.43 (m, 3H), 7.34 – 7.39 (m, 3H), 7.22 (d,  $J = 7.2$  Hz, 1H), 7.16 (m, 2H), 6.95 (d,  $J = 2.4$  Hz, 1H), 6.59 (d,  $J = 1.8$  Hz, 1H), 6.53 (d,  $J = 8.4$  Hz, 1H), 6.24 (d,  $J = 2.4$  Hz, 1H), 6.18 (d,  $J = 6.6$  Hz, 1H), 5.96 (d,  $J = 7.8$  Hz, 1H), 4.98 (d,  $J = 8.4$  Hz, 1H), 4.86 (d,  $J = 6.6$  Hz, 1H), 4.68 (d,  $J = 12.0$  Hz, 1H), 4.59 (d,  $J = 12.0$  Hz, 1H), 4.37 (m, 1H), 4.17 (dd,  $J = 2.4, 10.2$  Hz, 1H), 3.99 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.68 (dd,  $J = 3.0, 9.6$  Hz, 1H), 3.42 (dd,  $J = 4.8, 12.6$  Hz, 1H), 3.02 (t,  $J = 12.0$  Hz, 1H), 1.99 (s, 3H)

$^{13}\text{C}$  NMR (acetone- $d_6$ , 150 MHz)  $\delta$  173.0, 170.1, 169.8, 154.3, 152.2, 145.9, 139.3, 138.2, 138.2, 133.9, 132.1, 129.6, 129.25, 129.10, 128.70, 128.51, 128.43, 128.20, 127.8, 126.6, 125.6, 122.45, 120.20, 118.2, 109.5, 73.7, 70.5, 61.4, 60.9, 57.1, 56.5, 52.1, 30.4, 22.7

## Compound S25



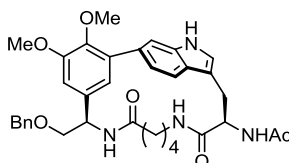
Compound (*R*)-**17** (5.4 mg, 6.70  $\mu\text{mol}$ ) was dissolved in a freshly prepared solution of 10% TFA in  $\text{CH}_2\text{Cl}_2$  (5 mL) at room temperature and stirred at this temperature for 1–2 h. The reaction mixture was analyzed by TLC to ensure consumption of the starting material, and the reaction mixture condensed under a stream of nitrogen. The residue was treated with saturated aqueous  $\text{NaHCO}_3$  (10 mL) and  $\text{CH}_2\text{Cl}_2$  (10 mL). The organic layer was washed with water (1  $\times$  20 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude product was dissolved in a freshly prepared solution of 1 M LiOH in THF (10 mL, 9:1 v:v) at room temperature and stirred for 6 h. Upon completion, the reaction mixture was diluted with EtOAc (10 mL) and  $\text{H}_2\text{O}$  (10 mL), and extracted with EtOAc (3  $\times$  20 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude product was dissolved in a solution of  $\text{CH}_2\text{Cl}_2$  (5 mL), and treated with  $\text{Ac}_2\text{O}$  (10  $\mu\text{L}$ , excess) at room temperature. After 1 h, the reaction mixture was diluted with additional  $\text{CH}_2\text{Cl}_2$  (20 mL), quenched with the addition of saturated aqueous  $\text{NaHCO}_3$  (10 mL), and stirred for 15 min or until all bubbling ceased. The crude product was extracted with  $\text{CH}_2\text{Cl}_2$  (2  $\times$  10 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography ( $\text{SiO}_2$ , 10% MeOH–  $\text{CH}_2\text{Cl}_2$ ) and provided **S25** (2.0 mg, 51%) as a white solid.

HRMS  $m/z$  585.2708 ( $[M + H]^+$ ,  $C_{33}H_{36}N_4O_6$  requires 585.2708)

IR (film)  $\nu_{max}$  2923, 1650, 1509, 1263, 1117, 671  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  7.94 (s, 1H), 7.76 (d,  $J = 6.0$  Hz, 1H), 7.31 – 7.38 (m, 5H), 7.15 (d,  $J = 8.4$  Hz, 1H), 7.00 (s, 1H), 6.64 (m, 1H), 6.57 (d,  $J = 2.4$  Hz, 1H), 5.92 (d,  $J = 7.2$  Hz, 1H), 5.85 (d,  $J = 2.4$  Hz, 1H), 5.40 (m, 1H), 5.07 (m, 1H), 4.96 (m, 1H), 4.59 (d,  $J = 12.0$  Hz, 1H), 4.48 (d,  $J = 12.0$  Hz, 1H), 4.02 (s, 3H), 3.84 (s, 3H), 3.71 (dd,  $J = 3.6, 10.2$  Hz, 1H), 3.60 (dd,  $J = 3.6, 10.2$  Hz, 1H), 3.18 (m, 1H), 2.89 (m, 1H), 2.35 (m, 1H), 2.01 (s, 3H)

## Compound S26



This compound was prepared from **19** in the same manner as compound **S25**.

$[\alpha]_D^{25}$   $-4$  ( $c$  0.025,  $CHCl_3$ )

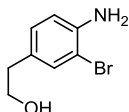
HRMS  $m/z$  613.3022 ( $[M + H]^+$ ,  $C_{33}H_{36}N_4O_6$  requires 613.3020)

IR (film)  $\nu_{max}$  2925, 1636, 1540, 1262, 1085, 748  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 600 MHz)  $\delta$  8.16 (s, 1H), 7.58 (s, 2H), 7.31 – 7.38 (m, 3H), 7.12 – 7.16 (m, 3H), 6.64 (s, 1H), 6.50 (d,  $J = 2.4$  Hz, 1H), 6.13 (d,  $J = 7.2$  Hz, 1H), 5.10 (m, 1H), 4.63 (d,  $J = 12.0$  Hz, 1H), 4.51 (d,  $J = 12.0$  Hz, 1H), 3.96 (dd,  $J = 4.8, 10.8$  Hz, 1H), 3.84 (s, 3H), 3.81 (dd,  $J = 4.8, 10.8$  Hz, 1H), 3.71 (s, 3H), 3.06 (m, 1H), 3.00 (s, 1H), 2.35 (m, 2H), 2.19 (m, 1H), 2.03 (s, 3H), 1.25 (m, 4H)

## Carbon Chain-based Macrocycles.

### Compound S27



A solution of 2-(4-aminophenyl)ethanol (1.96 g, 14.28 mmol, 1 equiv) in DMF (71 mL) at 0 °C was treated with a solution of NBS (N-bromosuccinimide, 2.5 g, 14.28 mmol, 1.0 equiv) in DMF (2 mL) and the cold bath was removed. The solution was stirred for 2 h at room temperature. Upon completion, the reaction mixture was washed with water ( $3 \times 20$  mL) and the organic layer dried over  $Na_2SO_4$ , filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography ( $SiO_2$ , 30% EtOAc–hexanes) and provided **S27** (3.15 g, 96%) as white solid.

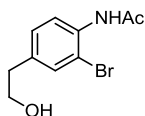
LC/MS  $m/z$  217 ( $[M + H]^+$ ,  $C_8H_{11}BrNO$  requires 217)

IR (film)  $\nu_{max}$  3335, 2936, 1702, 1619, 1502, 1411, 1291, 1184, 1038, 816, 671  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  7.28 (br s, 1H), 6.98 – 6.95 (m, 1H), 6.72 (d,  $J = 8.0$  Hz, 1H), 4.00 (br s, 1H) 3.78 (t,  $J = 6.4$  Hz, 2H), 2.73 (t,  $J = 6.4$  Hz, 2H), 1.66 (br s, 2H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  142.4, 132.7, 129.9, 129.0, 115.9, 109.3, 63.4, 37.8

### Compound S28



A solution of **S27** (1.69 g, 6.89 mmol, 1 equiv) in DMF (3.4 mL) at room temperature was treated sequentially with imidazole (938 mg, 13.8 mmol, 2.0 equiv), DMAP (84 mg, 0.68 mmol, 0.1 equiv), and TBSCl (1.50 g,

10.3 mmol, 1.5 equiv) and stirred for 4 h. The reaction mixture was quenched with the addition of water (10 mL) and extracted with 20% EtOAc in hexanes (3 × 10 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude mixture was used directly without further purification and dissolved in CH<sub>2</sub>Cl<sub>2</sub> (34 mL) and treated sequentially with pyridine (1.6 mL, 20.7 mmol, 1.5 equiv) and acetic anhydride (975 μL, 10.33 mmol, 1.5 equiv). The mixture was stirred overnight (12–16 h) at room temperature and quenched by the addition of saturated aqueous NaHCO<sub>3</sub> (50 mL) and stirred vigorously for 1 h. The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (10 mL × 3). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude amide in THF (50 mL) was treated with a 1 M solution of Bu<sub>4</sub>NF in THF (11 mL, 11 mmol, 2 equiv) at room temperature. The mixture was stirred for 2 h and quenched by the addition of water (10 mL). The layers were separated and the aqueous layer extracted with EtOAc (10 mL × 3). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes to 75% EtOAc–hexanes) and provided **S28** (1.5 g, 85% over 3 steps) as a white solid.

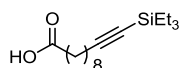
LC/MS *m/z* 258 ([M + H]<sup>+</sup>, C<sub>10</sub>H<sub>12</sub>BrNO<sub>2</sub> requires 258)

IR (film)  $\nu_{\max}$  3274, 1664, 1517, 1395, 1293, 1019, 679, 583, 530, 439 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.22 (d, *J* = 8.4 Hz, 1H), 7.53 (br s, 1H), 7.42 (d, *J* = 1.6 Hz, 1H), 7.17 (dd, *J* = 1.6, 8.4 Hz, 1H), 3.83 (q, *J* = 6.4 Hz, 2H), 2.80 (t, *J* = 6.4 Hz, 2H), 2.22 (s, 3H), 1.48 (br s, 1H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  168.5, 136.4, 134.1, 132.7, 129.1, 122.4, 113.7, 63.4, 38.3, 24.9

### Compound **S29**



A solution of undec-10-ynoic acid (1 g, 5.48 mmol, 1 equiv) in THF (54 mL) at –78 °C was treated with 2.5 M *n*-BuLi (4.6 mL, 11.5 mmol, 2.1 equiv) dropwise by syringe. The mixture was stirred at –78 °C for 30 min before chlorotriethylsilane (2 mL) was added. The cold bath was removed and the mixture was allowed to warm to room temperature and was stirred for an additional 2 h. The reaction was quenched by the addition of saturated aqueous NaCl (20 mL). The layers were separated and the aqueous layer was extracted with ether (3 × 10 mL). The combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was used without further purification, and dissolved in a solution of THF:MeOH:H<sub>2</sub>O (50 mL, 3:1:1) and treated with K<sub>2</sub>CO<sub>3</sub> (3.78 g, 27.4 mmol, 5 equiv). The mixture was stirred at room temperature for 30 min and diluted with both CH<sub>2</sub>Cl<sub>2</sub> (20 mL) and saturated aqueous NaCl (50 mL each), and acidified to pH 2 by slow addition of aqueous 1 N HCl. The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 10 mL). The combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (SiO<sub>2</sub>, 10% EtOAc–hexanes to 60% EtOAc–hexanes) and provided **S29** as a colorless oil (1 g, 63%).

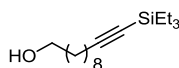
LC/MS *m/z* 295 ([M – H]<sup>+</sup>, C<sub>17</sub>H<sub>32</sub>O<sub>2</sub>Si requires 296)

IR (film)  $\nu_{\max}$  2171, 1707, 1458, 1413, 1277, 1236, 1015, 943, 722 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  2.34 (t, *J* = 7.6 Hz, 2H), 2.22 (t, *J* = 7.2 Hz, 2H), 1.63 (quin, *J* = 7.2 Hz, 2H), 1.51 (quin, *J* = 6.4 Hz, 2H), (m, 1.43 – 1.18, 8H), 0.97 (t, *J* = 7.6 Hz, 9H), 0.56 (q, *J* = 7.2 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  180.1, 108.8, 81.5, 34.2, 29.3, 29.1, 29.0, 28.8, 24.8, 19.9, 7.5, 4.7

### Compound **S30**



A solution of carboxylic acid **S29** (305 mg, 1.02 mmol, 1 equiv) in THF (5 mL) at 0 °C was treated with a 1 M solution of LiAlH<sub>4</sub> in hexanes (1.5 mL, 1.5 mmol, 1.5 equiv) dropwise by syringe. The mixture was stirred at 0 °C for 2 h and slowly quenched with the addition of water (5 mL). The reaction was diluted with 1 M NaOH (5

mL) and the layers were separated. The aqueous layer was extracted with ether (3 × 5 mL). The combined organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by a flash column chromatography (SiO<sub>2</sub>, 5% EtOAc–hexanes to 20% EtOAc–hexanes) and provided the desired compound **S30** as colorless oil (245 mg, 86%).

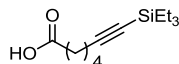
LC/MS *m/z* 283 ([M + H]<sup>+</sup>, C<sub>17</sub>H<sub>35</sub>OSi requires 283)

IR (film)  $\nu_{\text{max}}$  2925, 2873, 2171, 1458, 1015, 722, 466 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  3.64 (t, *J* = 6.8 Hz, 2H), 2.38 (t, *J* = 6.8 Hz, 2H), 1.60 – 1.48 (m, 5H), 1.42 – 1.30 (m, 10H), 0.99 (t, *J* = 8.0 Hz, 9H), 0.57 (q, *J* = 8.0 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  108.9, 81.4, 62.9, 32.8, 29.6, 29.5, 29.1, 28.8, 28.8, 25.8, 19.9, 7.5, 4.6

### Compound **S31**



This compound was prepared from 6-heptynoic acid in a manner similar to that of compound **S29**.

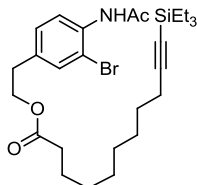
LC/MS *m/z* 239 ([M – H]<sup>+</sup>, C<sub>17</sub>H<sub>23</sub>O<sub>2</sub>Si requires 239)

IR (film)  $\nu_{\text{max}}$  2179, 2022, 1708, 1654, 1408, 941, 720, 699 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  10.36 (br s, 1H), 2.38 (t, *J* = 7.6 Hz, 2H), 2.27 (t, *J* = 6.8 Hz, 2H), 1.76 (quin, *J* = 7.2 Hz, 2H), 1.58 (quin, *J* = 7.6 Hz, 2H), 0.97 (t, *J* = 7.6 Hz, 9H), 0.56 (q, *J* = 7.2 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  180.3, 107.8, 82.2, 33.7, 28.1, 23.8, 19.7, 7.6, 4.7

### Compound **22**



A mixture of alcohol **S28** (100 mg, 0.38 mmol, 1 equiv) and carboxylic acid **S29** (114 mg, 0.38 mmol, 1 equiv) in THF (1 mL) was treated with DMAP (5 mg, 0.038 mmol, 0.1 equiv) and EDCI (180 mg, 1.16 mmol, 3 equiv). The mixture was stirred overnight (12–16 h) at room temperature, and upon completion, diluted with saturated aqueous NaHCO<sub>3</sub> (5 mL) and EtOAc (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (SiO<sub>2</sub>, 25% EtOAc–hexanes) and provided **22** (172 mg, 83%) as white solid.

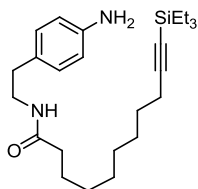
HRMS *m/z* 536.2190 [M + H]<sup>+</sup>, C<sub>27</sub>H<sub>43</sub>BrNO<sub>3</sub>Si requires 536.2195)

IR (film)  $\nu_{\text{max}}$  2021, 1712, 1518, 1360, 1222, 721, 683, 699 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.25 (d, *J* = 8.0 Hz, 1H), 8.25 (d, *J* = 8.0 Hz, 1H), 7.53 (br s, 1H), 7.39 (d, *J* = 2.0 Hz, 1H), 7.17 – 7.15 (m, 1H), 4.24 (t, *J* = 6.8 Hz, 2H), 2.89 (t, *J* = 6.8 Hz, 2H), 2.73 (t, *J* = 7.6 Hz, 2H), 2.73 (q, *J* = 6.8 Hz, 4H), 1.58 – 1.47 (m, 5H), 1.37 – 1.20 (m, 8H), 0.97 (t, *J* = 7.6 Hz, 9H), 0.56 (q, *J* = 7.2 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  173.7, 168.3, 135.4, 134.3, 132.5, 128.9, 122.2, 113.4, 108.8, 81.5, 64.3, 34.3, 34.2, 29.2, 29.1, 28.9, 28.8, 28.7, 25.0, 24.8, 19.9, 7.5, 4.6

### Compound S32



This compound was prepared from the commercially available diamine and carboxylic acid **S29** in a manner similar to that of compound **22**.

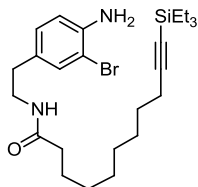
LC/MS  $m/z$  414 ( $[M + H]^+$ ,  $C_{25}H_{42}BrN_2OSi$  requires 414)

IR (film)  $\nu_{max}$  2038, 1547, 1437, 1253, 815, 640, 580  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  6.93 (d,  $J = 8.4$  Hz, 2H), 6.78 (d,  $J = 8.4$  Hz, 2H), 5.63 (t,  $J = 4.8$  Hz, 1H), 3.41 (q,  $J = 6.8$  Hz, 2H), 2.66 (t,  $J = 6.8$  Hz, 2H), 2.20 (t,  $J = 7.2$  Hz, 2H), 2.07 (t,  $J = 7.2$  Hz, 2H), 1.57 – 1.34 (m, 6H), 1.25 (s, 6H), 0.96 (t,  $J = 7.6$  Hz, 9H), 0.54 (q,  $J = 7.2$  Hz, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  173.1, 145.0, 129.6, 128.7, 115.4, 108.8, 81.5, 40.8, 36.8, 34.8, 29.3, 28.9, 28.8, 28.74, 25.8, 19.9, 7.57, 4.6

### Compound S33



A solution of **S32** (60 mg, 0.14 mmol, 1 equiv) in DMF (0.5 mL) at 0 °C was treated with a solution of NBS (N-bromosuccinimide, 28 mg, 0.15 mmol, 1.1 equiv) in DMF (0.5 mL) and the cold bath was removed. The solution was stirred for 2 h at room temperature. Upon completion, the reaction mixture was diluted with EtOAc (5 mL) and washed with water ( $3 \times 5$  mL) and the organic layer dried over  $Na_2SO_4$ , filtered, and concentrated in vacuo. The crude mixture was purified by column chromatography ( $SiO_2$ , 20% EtOAc–hexanes) and provided **S33** (54 mg, 76%) as yellow oil.

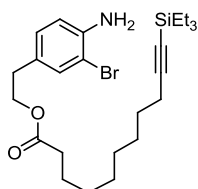
LC/MS  $m/z$  493 ( $[M + H]^+$ ,  $C_{25}H_{42}BrN_2OSi$  requires 493)

IR (film)  $\nu_{max}$  2201, 2017, 1977, 1714, 1519, 670  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  7.21 (d,  $J = 1.6$  Hz, 1H), 6.90 (dd,  $J = 2.0, 8.0$  Hz, 1H), 6.69 (d,  $J = 8.8$  Hz, 1H), 5.55 (t,  $J = 4.4$  Hz, 2H), 4.02 (br s, 1H), 3.41 (q,  $J = 6.8$  Hz, 2H), 2.65 (t,  $J = 7.2$  Hz, 2H), 2.22 (t,  $J = 7.2$  Hz, 2H), 1.60 – 1.45 (m, 4H), 1.41 – 1.25 (m, 9H), 0.96 (t,  $J = 7.6$  Hz, 9H), 0.55 (q,  $J = 7.2$  Hz, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  173.2, 142.7, 132.7, 130.1, 128.8, 116.0, 109.4, 108.9, 81.5, 40.7, 36.9, 34.5, 31.7, 29.4, 29.07, 28.8, 28.8, 25.9, 22.8, 19.9, 14.2, 7.6, 4.7

### Compound S34



This compound was prepared from alcohol **S27** and carboxylic acid **S29** in a manner similar to that of compound **22**.

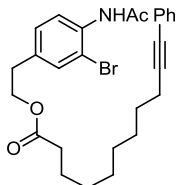
HRMS  $m/z$  494.2084 ( $[M + H]^+$ ,  $C_{25}H_{41}BrNO_2Si$  requires 494.2084)

IR (film)  $\nu_{max}$  2166, 2034, 2020, 1716, 1621, 1503, 719, 669, 654  $cm^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.27 (d,  $J = 1.6$  Hz, 1H), 6.95 (dd,  $J = 8.0, 2.0$  Hz, 1H), 6.70 (d,  $J = 8.0$  Hz, 1H), 4.21 (t,  $J = 7.2$  Hz, 2H), 4.02 (bs, 1H), 2.89 (t,  $J = 6.8$  Hz, 2H), 2.80 (t,  $J = 7.2$  Hz, 2H), 2.28 (t,  $J = 7.2$  Hz, 2H), 2.23 (t,  $J = 7.2$  Hz, 2H), 1.59 (q,  $J = 7.6$  Hz, 2H), 1.40–1.37 (m, 2H), 1.28–1.26 (m, 6H), 0.98 (t,  $J = 7.6$  Hz, 9H), 0.57 (q,  $J = 7.2$  Hz, 6H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  173.9, 142.7, 132.9, 129.0, 115.9, 109.3, 108.9, 81.6, 64.9, 34.5, 34.0, 29.3, 29.2, 29.0, 28.8, 28.8, 25.1, 20.0, 7.6, 4.7

### Compound S35



This compound was prepared from alcohol **S28** and the corresponding aryl-substituted alkyne<sup>4</sup> in a manner similar to that of compound **22**.

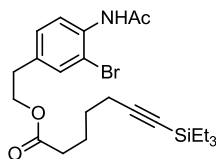
HRMS  $m/z$  498.1639 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{27}\text{H}_{33}\text{BrNO}_3$  requires 498.1638)

IR (film)  $\nu_{\text{max}}$  2024, 1570, 1501, 1329, 1228, 999, 731, 671, 651  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  8.30 (d,  $J = 6.8$  Hz, 1H), 7.64 (br s, 1H), 7.47 – 7.44 (m, 3H), 7.36 – 7.32 (m, 3H), 7.22 (dd,  $J = 1.6, 6.8$  Hz, 1H), 2.93 (t,  $J = 5.6$  Hz, 2H), 2.47 (t,  $J = 5.6$  Hz, 2H), 2.35 (t,  $J = 6.0$  Hz, 2H), 2.29 (s, 3H), 1.66 (q,  $J = 6.0$  Hz, 4H), 1.51 (q,  $J = 5.6$  Hz, 4H), 1.38 – 1.33 (m, 6H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  173.8, 168.3, 135.4, 134.3, 132.5, 131.6, 129.0, 128.3, 127.6, 124.2, 122.1, 113.4, 9.5, 80.7, 64.3, 34.4, 34.3, 29.2, 29.2, 29.1, 28.9, 28.8, 25.0, 24.9, 19.5

### Compound S36



This compound was prepared from alcohol **S28** and carboxylic acid **S31** in a manner similar to that of compound **22**.

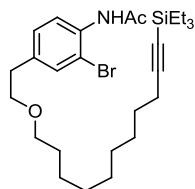
HRMS  $m/z$  480.1564 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{23}\text{H}_{35}\text{BrNO}_3\text{Si}$  requires 480.1564)

IR (film)  $\nu_{\text{max}}$  2213, 2166, 2030, 1963, 1573, 1513, 1396, 1296, 1265, 733, 671, 653  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  8.25 (d,  $J = 6.4$  Hz, 1H), 7.55 (br s, 1H), 7.40 (d,  $J = 1.6$  Hz, 1H), 7.16 (dd,  $J = 2.0, 8.4$  Hz, 1H), 4.25 (t,  $J = 6.8$  Hz, 2H), 2.87 (t,  $J = 7.2$  Hz, 2H), 2.32 (t,  $J = 7.6$  Hz, 2H), 2.25 (t,  $J = 6.8$  Hz, 2H), 2.23 (s, 3H), 1.72 (quin,  $J = 7.6$  Hz, 2H), 1.54 (quin,  $J = 6.8$  Hz, 2H), 0.98 (t,  $J = 7.6$  Hz, 9H), 0.57 (q,  $J = 8.0$  Hz, 6H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  173.3, 168.3, 135.3, 134.3, 132.5, 128.9, 122.2, 113.4, 107.9, 82.0, 64.4, 34.2, 33.7, 28.1, 24.8, 24.0, 19.6, 7.5, 4.6

### Compound S37



A mixture of alcohol **S30** (245 mg, 0.86 mmol, 1 equiv) and pyridine (200  $\mu\text{L}$ , 2.6 mmol, 3 equiv) in  $\text{CH}_2\text{Cl}_2$  (5 mL) was treated with Dess–Martin periodinane (441 mg, 1.04 mmol, 1.2 equiv) at 0  $^\circ\text{C}$ . The mixture was stirred

at 0 °C for 2 h and upon completion, diluted with saturated aqueous NaHCO<sub>3</sub> (5 mL) and CH<sub>2</sub>Cl<sub>2</sub> (5 mL). The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 5 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by a rapid silica gel column chromatography (SiO<sub>2</sub>, 20% EtOAc–hexanes) and provided the corresponding aldehyde (148 mg, 61%) as colorless oil, which tended to polymerize during purification. A solution of this freshly prepared aldehyde (20 mg, 0.071 mmol, 1 equiv) and alcohol **S28** (22 mg, 0.085 mmol, and 1.2 equiv) in CH<sub>2</sub>Cl<sub>2</sub> (700 μL) was treated with triethylsilane (23 μL, 0.14 mmol, 2 equiv) and TMSOTf (19 μL, 0.10 mmol, 1.5 equiv) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and quenched with the addition of saturated aqueous NaHCO<sub>3</sub> (5 mL). The mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub> (5 mL) and the layers were separated. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 5 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude product was purified by column chromatography (SiO<sub>2</sub>, 20% EtOAc–hexanes) and provided the corresponding ether (16 mg, 43%) as colorless oil.

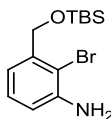
LC/MS *m/z* 523 ([M + H]<sup>+</sup>, C<sub>27</sub>H<sub>45</sub>BrNO<sub>2</sub>Si requires 523)

IR (film)  $\nu_{\max}$  1729, 1695, 1417, 1344, 1322, 1228, 1208, 1127, 1078, 738 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.20 (d, *J* = 8.4 Hz, 1H), 7.52 (br s, 1H), 7.41 (d, *J* = 1.2 Hz, 1H), 7.22 (dd, *J* = 1.6, 8.4 Hz, 1H), 3.58 (t, *J* = 6.8 Hz, 2H), 3.4 (t, *J* = 6.8 Hz, 2H), 2.81 (t, *J* = 6.8 Hz, 2H), 2.22 (s, 3H), 1.54 – 1.47 (m, 4H), 1.40 – 1.36 (m, 2H), 1.28 – 1.25 (m, 10H), 0.97 (t, *J* = 7.6 Hz, 9H), 0.56 (q, *J* = 7.2 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  168.3, 136.9, 133.9, 132.6, 129.2, 128.9, 122.0, 71.4, 71.3, 38.7, 35.5, 29.8, 29.6, 29.2, 28.9, 28.9, 26.3, 25.0, 20.0, 7.6, 4.7

### Compound **S38**



A solution of 2-bromo-3-nitrobenzoic acid (1 g, 4.0 mmol, 1 equiv) in 10 mL THF at 0 °C was treated with a 1 M solution of BH<sub>3</sub>•THF in THF (8.1 mL, 8.1 mmol, 2 equiv) slowly by syringe that resulted in the evolution of gas. The cold bath was then removed and the mixture was stirred at room temperature for 3 h. The reaction was quenched by the slow addition of water (5 mL) and excess solid K<sub>2</sub>CO<sub>3</sub> (ca. 1 g). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. The crude alcohol was taken to the next step without further purification. The crude alcohol was dissolved in a mixture of ethanol and glacial acetic acid (10 mL, 1:1 v:v) and concentrated HCl (0.5 mL) was added. This mixture was treated with iron powder (1.0 g, 16.25 mmol, 4 equiv) and warmed at reflux at 100 °C for 3 h. The reaction mixture was neutralized by the addition of K<sub>2</sub>CO<sub>3</sub> powder and extracted with Et<sub>2</sub>O (3 × 50 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and concentrated in vacuo. The crude amine was taken to the next step without further purification. This crude amine was dissolved in DMF (20 mL) and treated sequentially with imidazole (500 mg, 8.12 mmol, 2 equiv) and DMAP (50 mg, 0.4 mmol, 0.1 equiv). TBSCl (1 g, 6.0 mmol, 1.5 equiv) was added and the resulting solution was stirred overnight (12–16 h) at room temperature. The reaction was quenched with the addition of water (30 mL) and diluted with EtOAc (50 mL). The layers were separated and the organic layer was washed with water (3 × 20 mL). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> filtered, and concentrated in vacuo. The crude product was purified by column chromatography (SiO<sub>2</sub>, 20% EtOAc–hexanes) and provided **S38** (780 mg, 61% over 3 steps) as a yellow oil.

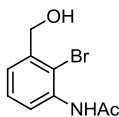
LC/MS *m/z* 316 ([M + H]<sup>+</sup>, C<sub>13</sub>H<sub>22</sub>BrNOSi requires 316)

IR (film)  $\nu_{\max}$  2926, 1716, 1619, 1450, 1338, 1234, 1168, 1003, 723, 696 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.13 (t, *J* = 7.6 Hz, 1H), 6.93 (br s, 1H), 6.67 (br s, 1H), 4.69 (s, 2H), 0.96 (s, 9H), 0.12 (s, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  143.8, 141.0, 127.7, 117.2, 114.4, 108.1, 65.2, 26.0, 18.4, –5.2

### Compound S39



Compound **S38** (300 mg, 0.94 mmol, 1 equiv) was dissolved in  $\text{CH}_2\text{Cl}_2$  (1 mL) and was treated with pyridine (150  $\mu\text{L}$ , 1.9 mmol, 2 equiv) and acetic anhydride (100  $\mu\text{L}$ , 1.0 mmol, 1.1 equiv) at room temperature. The mixture was stirred overnight (12–16 h) and quenched by the addition of saturated aqueous  $\text{NaHCO}_3$  (3 mL). The layers were separated and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 5$  mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude amide was taken to next step without further purification. A solution of the crude acetamide in THF (5 mL) was treated with a 1 M solution of  $\text{Bu}_4\text{NF}$  in THF (1.4 mL, 1.42 mmol, 1.5 equiv), and stirred at room temperature for 1 h. The reaction was quenched by the addition of saturated aqueous  $\text{NaCl}$  (5 mL) and extracted with EtOAc ( $3 \times 5$  mL). The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ , filtered, and concentrated in vacuo. The crude product was purified by column chromatography ( $\text{SiO}_2$ , 50% EtOAc–hexanes) to provide the desired alcohol.

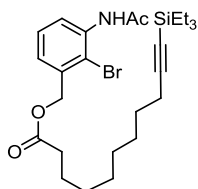
LC/MS  $m/z$  244 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_9\text{H}_{10}\text{BrNO}_2$  requires 244)

IR (film)  $\nu_{\text{max}}$  3276, 1660, 1537, 1468, 1416, 1370, 1302, 669  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 600 MHz)  $\delta$  8.50 (br s, 1H), 7.94 (d,  $J = 6.6$  Hz, 1H), 7.34 – 7.39 (m, 3H), 4.67 (d,  $J = 6.0$  Hz, 2H), 4.49 (t,  $J = 6.0$  Hz, 1H), 2.18 (s, 3H)

$^{13}\text{C}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 150 MHz)  $\delta$  167.0, 142.8, 137.4, 128.2, 124.3, 123.5, 115.3, 64.8, 24.1

### Compound S40



This compound was prepared from alcohol **S39** and carboxylic acid **S29** in a manner similar to that of compound **22**.

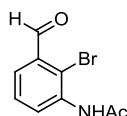
HRMS  $m/z$  522.2016 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{26}\text{H}_{41}\text{BrNO}_3\text{Si}$  requires 522.2033)

IR (film)  $\nu_{\text{max}}$  2135, 2010, 1668, 1507, 1387, 1092, 659  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  8.26 (d,  $J = 7.6$  Hz, 1H), 7.71 (br s, 1H), 7.30 (t,  $J = 8.0$  Hz, 1H), 7.14 (d,  $J = 7.6$  Hz, 1H), 5.16 (s, 2H), 2.36 (t,  $J = 7.6$  Hz, 2H), 2.23 (s, 3H), 2.20 (t,  $J = 6.8$  Hz, 2H), 1.64 (q,  $J = 7.6$  Hz, 2H), 1.49 (q,  $J = 6.8$  Hz, 2H), 1.38–1.35 (m, 2H), 1.29–1.23 (m, 6H), 0.96 (t,  $J = 7.6$  Hz, 9H), 0.54 (q,  $J = 7.2$  Hz, 6H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  173.4, 168.4, 136.2, 136.0, 128.1, 125.2, 122.0, 114.6, 108.8, 81.5, 66.1, 34.3, 29.2, 29.2, 28.4, 28.8, 28.7, 25.8, 19.9, 7.6, 4.7

### Compound S41



Compound **S39** was dissolved in THF (6 mL) and treated with  $\text{MnO}_2$  (273 mg, 5.15 mmol, 5 equiv) at room temperature. The mixture was stirred at room temperature for 2 h and an additional 5 equiv of  $\text{MnO}_2$  was added. After 1 h, the mixture was filtered and the filtrate concentrated in vacuo. The crude product was purified by column chromatography ( $\text{SiO}_2$ , 50% EtOAc–hexanes) and provided **S41** (135 mg, 92% over 3 steps) as a white solid.



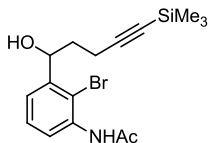
LC/MS  $m/z$  240 ( $[M - H]^+$ ,  $C_9H_8BrNO_2$  requires 240)

IR (film)  $\nu_{max}$  1673, 1512, 1414, 1234, 787, 670  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 500 MHz)  $\delta$  10.37 (s, 1H), 8.58 (d,  $J = 8.5$  Hz, 1H), 7.77 (br s, 1H), 7.68 (dd,  $J = 1.5, 7.5$  Hz, 1H), 7.45 (t,  $J = 8.0$  Hz, 1H), 2.30 (s, 3H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  191.4, 168.7, 136.6, 133.8, 128.2, 128.1, 125.8, 118.2, 24.7

#### Compound **S42**



A solution of (4-iodobut-1-ynyl)trimethylsilane (62 mg, 0.24 mmol, 3 equiv) in  $Et_2O$  (0.5 mL) at  $-78$  °C was treated with a 1.7 M solution of *t*-BuLi in pentane (290  $\mu$ L, 0.49 mmol, 6 equiv) by syringe and stirred for 30 min at  $-78$  °C. This mixture was then treated with a solution of aldehyde **S41** (20 mg, 0.082 mmol, 1 equiv) in  $Et_2O$  (0.5 mL) and stirred at  $-78$  °C for an additional 30 min. The reaction was quenched by the addition of water (0.5 mL) and the solution was extracted with  $EtOAc$  ( $3 \times 5$  mL). The organic layers were combined and the solvent was removed in vacuo. The crude product was purified by preparative thin-layer chromatography ( $SiO_2$ , 50%  $EtOAc$ -hexanes) to provide **S42** (10.2 mg, 34%) as a white solid.

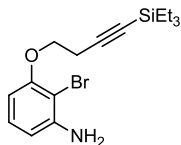
HRMS  $m/z$  368.0676 ( $[M + H]^+$ ,  $C_{16}H_{23}BrNO_2Si$  requires 368.0671)

IR (film)  $\nu_{max}$  2161, 1593, 1523, 1249, 842, 762, 669, 648  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  8.21 (t,  $J = 4.8$  Hz, 1H), 7.68 (br s, 1H), 7.35 – 7.33 (m, 2H), 5.23 (ddd,  $J = 3.2, 3.2, 8.8$  Hz, 1H), 2.54 – 2.38 (m, 3H), 2.24 (s, 3H), 2.04 – 1.93 (m, 1H), 1.83 – 1.74 (m, 1H), 0.16 (s, 9H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  168.5, 144.1, 135.5, 128.3, 122.9, 121.5, 113.3, 106.7, 5.8, 72.5, 36.2, 25.0, 16.9, 0.29

#### Compound **S43**



A mixture of 4-(trimethylsilyl)but-3-yn-1-ol (10 mg, 0.054 mmol, 1 equiv), 3-amino-2-bromophenol (20 mg, 0.108 mmol, 2 equiv), and triphenylphosphine (18 mg, 0.07 mmol, 1.3 equiv) in THF (0.5 mL) was cooled to 0 °C and treated with diisopropyl azodicarboxylate (14  $\mu$ L, 0.07 mmol, 1.3 equiv) dropwise by syringe and the reaction mixture was slowly warmed to room temperature over 2 h. The solvent was removed and the crude product was purified by column chromatography ( $SiO_2$ , 10%  $EtOAc$ -hexanes) to provide **S43** (10.7 mg, 56%) as a yellow oil.

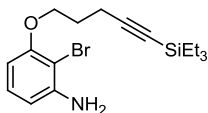
HRMS  $m/z$  354.0889 ( $[M + H]^+$ ,  $C_{16}H_{25}BrNOSi$  requires 354.0883)

IR (film)  $\nu_{max}$  1679, 1465, 1397, 1265, 1174, 1102, 668  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  7.03 (t,  $J = 8.4$  Hz, 1H), 6.43 (dd,  $J = 8.0, 3.2$  Hz, 1H), 6.33 (dd,  $J = 8.4, 3.2$  Hz, 1H), 4.16 (br s, 1H), 4.13 (t,  $J = 7.6$  Hz, 2H), 2.79 (t,  $J = 7.2$  Hz, 2H), 0.99 (t,  $J = 8.0$  Hz, 9H), 0.59 (q,  $J = 7.6$  Hz, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  155.8, 145.8, 128.2, 108.8, 103.6, 103.0, 99.5, 83.9, 67.6, 21.0, 7.6, 4.6

## Compound S44



This compound was prepared from 3-amino-2-bromophenol and the corresponding alcohol in a manner similar to that of compound **S43**.

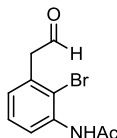
HRMS  $m/z$  368.1041 ( $[M + H]^+$ ,  $C_{17}H_{27}BrNOSi$  requires 368.1040)

IR (film)  $\nu_{max}$  2025, 1971, 1570, 1330, 1229, 1002, 668  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  7.02 (t,  $J = 8.4$  Hz, 1H), 6.41 (dd,  $J = 8.0, 3.2$  Hz, 1H), 6.31 (dd,  $J = 3.2, 8.4$  Hz, 1H), 4.15 (br s, 1H), 4.12 (t,  $J = 7.6$  Hz, 2H), 2.52 (t,  $J = 7.2$  Hz, 2H), 2.04 (q,  $J = 6.4$  Hz, 2H), 0.98 (t,  $J = 8.0$  Hz, 9H), 0.57 (q,  $J = 7.6$  Hz, 6H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  155.1, 145.6, 128.2, 108.4, 107.5, 102.5, 99.3, 82.4, 67.4, 28.6, 16.8, 7.6, 4.6

## Compound S45



A solution of (methoxymethyl)triphenylphosphonium chloride (764 mg, 2.23 mmol, 1 equiv) in THF (5 mL) was treated with a solution of potassium *tert*-butoxide (250 mg, 2.23 mmol, 5 equiv) in THF (1 mL) at room temperature. The bright red solution was stirred for 10 min and a solution of aldehyde **S41** in THF (1 mL) was added by syringe. The reaction was stirred for 15 min and quenched by the addition of water (5 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3  $\times$  5 mL). The combined organic layers were dried over  $Na_2SO_4$ , filtered, and concentrated in vacuo. The crude product was purified by column chromatography ( $SiO_2$ , 50% EtOAc–hexanes) and provided the methyl enol ether (103 mg, 86%) as a white solid. This methyl enol ether was dissolved in THF (3 mL) and treated with 10% aqueous HCl (6 mL), and stirred overnight (12–16 h) at room temperature. The reaction mixture was neutralized by the addition of saturated aqueous  $NaHCO_3$  (10 mL) and extracted with EtOAc (3  $\times$  5 mL). The combined organic layers were dried over  $Na_2SO_4$ , filtered, and concentrated in vacuo. The crude product was purified by column chromatography ( $SiO_2$ , 50% EtOAc–hexanes to 100% acetone) to provide aldehyde **S45** (54 mg, 47% over 2 steps) as a white solid.

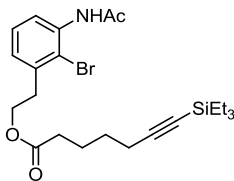
LC/MS  $m/z$  256 ( $[M - H]^+$ ,  $C_{10}H_{10}BrNO_2$  requires 256)

IR (film)  $\nu_{max}$  1676, 1590, 1518, 1466, 1401, 1293, 1028, 668  $cm^{-1}$

$^1H$  NMR ( $CDCl_3$ , 400 MHz)  $\delta$  9.78 (s, 1H), 8.27 (d,  $J = 6.0$  Hz, 1H), 7.83 (s, 1H), 7.35 (t,  $J = 6.4$  Hz, 1H), 7.05 (d,  $J = 5.6$  Hz, 1H), 2.93 (s, 2H), 2.29 (s, 3H)

$^{13}C$  NMR ( $CDCl_3$ , 100 MHz)  $\delta$  198.0, 168.5, 136.5, 133.3, 128.3, 127.2, 121.8, 116.5, 51.3, 24.8

## Compound S46



A mixture of aldehyde **S45** (189 mg, 0.74 mmol, 1 equiv) in MeOH (5 mL) was treated with  $NaBH_4$  (56 mg, 1.48 mmol, 2 equiv) at 0  $^{\circ}C$ . The reaction mixture was stirred at 0  $^{\circ}C$  for 1 h after which it was brought to room temperature. Upon completion, the excess MeOH was evaporated and the mixture was diluted with saturated

aqueous NaCl (5 mL) and CH<sub>2</sub>Cl<sub>2</sub> (5 mL). The layers were separated and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 × 5 mL). The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in vacuo. The crude product was taken to the next step without further purification, and the esterification of the alcohol with carboxylic acid **S31** was carried out according to the procedure similar to that for **22**.

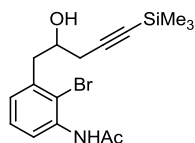
LC/MS *m/z* 481 ([M + H]<sup>+</sup>, C<sub>23</sub>H<sub>35</sub>BrNO<sub>3</sub>Si requires 481)

IR (film)  $\nu_{\max}$  1731, 1698, 1519, 1464, 1408, 1265, 1235, 1173, 1143, 1014, 722 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.17 (d, *J* = 7.6 Hz, 1H), 7.73 (br s, 1H), 7.23 (t, *J* = 8 Hz, 1H), 6.99 (d, *J* = 7.2, 2.0 Hz, 1H), 4.28 (t, *J* = 6.8 Hz, 2H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.81 – 2.21 (m, 4H), 1.78 – 1.66 (m, 2H), 1.60 – 1.47 (m, 2H), 0.96 (t, *J* = 7.6 Hz, 9H), 0.55 (q, *J* = 8.0 Hz, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  173.4, 168.4, 137.8, 136.2, 127.9, 126.5, 120.8, 107.9, 82.1, 63.1, 36.2, 33.8, 28.2, 24.9, 24.0, 23.9, 19.6, 7.6, 4.6

#### Compound **S47**



A solution of (3-bromoprop-1-ynyl)trimethylsilane (45 mg, 0.23 mmol, 3 equiv) in THF (0.5 mL) was treated with indium powder (27 mg, 0.23 mmol, 5 equiv) and indium tribromide (5.5 mg, 0.015 mmol, 0.2 equiv) at room temperature. The mixture was stirred at room temperature for 15 min. This mixture was subsequently treated with a solution of aldehyde **S45** (45 mg, 0.23 mmol, 3 equiv) in THF (0.5 mL) and warmed to reflux at 80 °C overnight. Upon completion, the reaction mixture was cooled to room temperature and the solvent was removed in vacuo. The crude product was purified by preparative thin-layer chromatography (SiO<sub>2</sub>, 50% EtOAc–hexanes) to provide the desired alcohol **S47** (13 mg, 46%) as a white solid.

HRMS *m/z* 368.0668 ([M + H]<sup>+</sup>, C<sub>16</sub>H<sub>23</sub>BrNO<sub>2</sub>Si requires 368.0676)

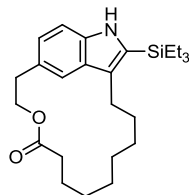
IR (film)  $\nu_{\max}$  1664, 1520, 1297, 1246, 1079, 844, 668 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  8.10 (d, *J* = 8.0 Hz, 1H), 7.71 (s, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 7.6 Hz, 1H), 4.05 (ddd, *J* = 6.0, 5.2, 5.2 Hz, 1H), 3.12 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.95 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.51 (dd, *J* = 16.8, 5.2 Hz, 1H), 2.44 (dd, *J* = 16.8, 5.2 Hz, 1H), 2.22 (s, 2H), 0.17 (s, 9H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  168.4, 138.4, 136.2, 127.9, 127.3, 120.8, 116.4, 102.8, 88.4, 69.3, 43.5, 28.5, 25.0, 0.2

Macrocyclic and cyclic indole products **23–34** were prepared by the representative procedure shown below.

#### Compound **24**



A solution of alkyne **S36** (70.2 mg, 0.14 mmol, 1 equiv), Pd<sub>2</sub>(dba)<sub>3</sub> (19 mg, 0.021 mmol, 0.15 equiv) and *Dt*BPF (20 mg, 0.042 mmol, 0.3 equiv) in DMF (0.02 M, 7 mL) in a sealed tube was purged with argon for 5 min. This solution was treated with triethylamine (100  $\mu$ L, 0.70 mmol, 5.0 equiv) and the tube was sealed. The reaction mixture was heated at 130 °C for 3 h. Upon completion, the reaction mixture was cooled to room temperature and filtered through a short silica gel column. The reaction mixture was diluted with Et<sub>2</sub>O (10 mL). Excess DMF was removed by washing with water (3 × 10 mL) and the organic layer was dried with Na<sub>2</sub>SO<sub>4</sub>.

The crude product was purified by preparative thin-layer chromatography (SiO<sub>2</sub>, 20% EtOAc–hexanes) to provide **24** (40.9 mg, 70%) as a colorless oil.

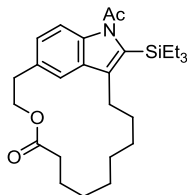
HRMS  $m/z$  414.2832 ( $[M + H]^+$ , C<sub>25</sub>H<sub>40</sub>NO<sub>2</sub>Si requires 414.2828)

IR (film)  $\nu_{\max}$  1718, 1648, 1619, 1514, 1263, 1088, 735 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.84 (s, 1H), 7.41 (s, 1H), 7.32 (d,  $J = 8.4$  Hz, 1H), 7.03 (dd,  $J = 1.6, 8.4$  Hz, 1H), 4.49 (t,  $J = 5.6$  Hz, 2H), 3.10 (t,  $J = 5.2$  Hz, 2H), 2.80 (t,  $J = 7.2$  Hz, 2H), 2.31 (t,  $J = 6.8$  Hz, 2H), 1.70 – 1.65 (m, 4H), 1.48 – 1.45 (m, 4H), 1.37 – 1.33 (m, 4H), 1.04 – 0.99 (m, 9H), 0.92 – 0.86 (m, 6H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  171.3, 136.3, 136.0, 134.8, 133.7, 133.0, 125.3, 119.5, 114.1, 64.9, 34.8, 33.2, 30.6, 27.8, 27.3, 26.8, 26.5, 24.8, 24.7, 8.4, 5.9

### Compound **23**



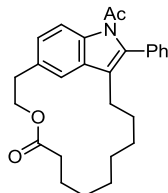
HRMS  $m/z$  456.2939 ( $[M + H]^+$ , C<sub>27</sub>H<sub>42</sub>NO<sub>3</sub>Si requires 456.2934)

IR (film)  $\nu_{\max}$  1735, 1695, 1119, 995, 764, 669, 592 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.58 (d,  $J = 8.4$  Hz, 1H), 7.34 (s, 1H), 7.17 (d,  $J = 8.8$  Hz, 1H), 4.46 (t,  $J = 5.2$  Hz, 2H), 3.09 (t,  $J = 5.2$  Hz, 2H), 2.79 (s, 3H), 2.95 (t,  $J = 6.4$  Hz, 2H), 1.67 (t,  $J = 6.0$  Hz, 2H), 1.45 (br s, 4H), 1.31 (br s, 5H), 1.25 (br s, 4H), 0.97 – 0.86 (m, 15H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  174.3, 169.4, 136.3, 136.0, 134.8, 133.7, 133.0, 125.3, 119.5, 114.1, 64.9, 34.8, 33.9, 30.6, 27.8, 27.6, 27.3, 26.8, 26.5, 24.8, 24.7, 8.48, 5.94

### Compound **25**



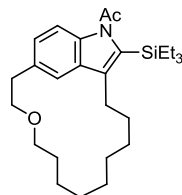
HRMS  $m/z$  418.2372 ( $[M + H]^+$ , C<sub>27</sub>H<sub>32</sub>NO<sub>3</sub> requires 418.2382)

IR (film)  $\nu_{\max}$  2928, 1726, 1695, 1446, 1369, 1339, 1305, 1264, 1208, 731 cm<sup>-1</sup>

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.39 (d,  $J = 8.4$  Hz, 1H), 7.50 – 7.41 (m, 3H), 7.39 – 7.35 (m, 3H), 7.23 (dd,  $J = 2.0, 8.8$  Hz, 1H), 4.48 (t,  $J = 5.6$  Hz, 2H), 3.11 (t,  $J = 5.6$  Hz, 2H), 2.51 (t,  $J = 7.2$  Hz, 2H), 2.89 (t,  $J = 6.4$  Hz, 2H), 1.92 (s, 3H), 1.64 (quin,  $J = 6.0$  Hz, 2H), 1.52 (quin,  $J = 7.2$  Hz, 2H), 1.36 – 1.25 (m, 8H)

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz)  $\delta$  174.3, 171.1, 135.7, 135.2, 134.0, 133.9, 130.5, 130.0, 128.8, 128.7, 125.9, 123.0, 118.9, 116.9, 65.1, 35.1, 33.5, 28.9, 27.8, 27.7, 27.7, 27.4, 26.9, 24.9, 23.8

### Compound **26**



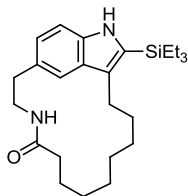
HRMS  $m/z$  442.3140 ( $[M + H]^+$ , C<sub>27</sub>H<sub>44</sub>NO<sub>2</sub>Si requires 442.3141)

IR (film)  $\nu_{\max}$  1694, 1372, 1294, 1264, 1118, 1073, 1033, 799, 736, 670 cm<sup>-1</sup>

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.58 (d,  $J = 8.4$  Hz, 1H), 7.34 (s, 1H), 7.17 (d,  $J = 8.8$  Hz, 1H), 4.46 (t,  $J = 5.2$  Hz, 2H), 3.09 (t,  $J = 5.2$  Hz, 2H), 2.79 (s, 3H), 2.95 (t,  $J = 6.4$  Hz, 2H), 1.67 (t,  $J = 6.0$  Hz, 2H), 1.45 (br s, 4H), 1.31 (br s, 5H), 1.25 (br s, 4H), 0.97 – 0.86 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  174.5, 137.4, 130.9, 129.2, 129.1, 126.5, 123.0, 118.8, 111.1, 65.4, 35.1, 33.5, 30.9, 28.0, 27.5, 27.1, 25.8, 25.0, 7.6, 3.9

### Compound 27



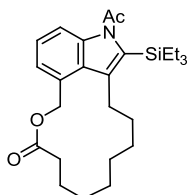
HRMS  $m/z$  413.2996 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{25}\text{H}_{41}\text{N}_2\text{OSi}$  requires 413.2988)

IR (film)  $\nu_{\text{max}}$  1618, 1262, 1110, 837, 750, 667  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  7.85 (br s, 1H), 7.33 (t,  $J = 8.5, 1.5$  Hz, 2H), 5.46 (t,  $J = 5.5$  Hz, 2H), 3.62 (dd,  $J = 5.5, 11.0$  Hz, 2H), 2.92 (t,  $J = 5.5$  Hz, 2H), 2.78 (t,  $J = 7.0$  Hz, 2H), 2.22 (t,  $J = 7.0$  Hz, 1H), 2.08 (t,  $J = 6.0$  Hz, 2H), 1.69 – 1.60 (m, 4H), 1.46 – 1.41 (m, 4H), 1.33 – 1.28 (m, 4H), 0.99 (t,  $J = 8.5$  Hz, 9H), 0.88 (q,  $J = 8.0$  Hz, 6H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  173.3, 137.3, 131.3, 129.4, 126.6, 122.7, 119.6, 111.5, 40.8, 36.0, 35.9, 31.6, 29.9, 28.3, 28.3, 27.9, 27.7, 25.7, 25.4, 7.6, 3.9

### Compound 28



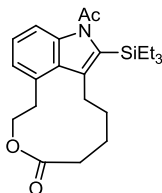
HRMS  $m/z$  442.2772 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{26}\text{H}_{40}\text{NO}_3\text{Si}$  requires 442.2777)

IR (film)  $\nu_{\text{max}}$  1729, 1690, 1363, 1264, 1127, 1079, 995, 734, 696  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.69 (d,  $J = 8.4$  Hz, 1H), 7.30 (dd,  $J = 7.6, 8.4$  Hz, 1H), 7.19 (d,  $J = 7.6$  Hz, 1H), 5.45 (s, 2H), 3.01 (s, 1H), 2.88 (t,  $J = 8$  Hz, 2H), 2.79 (s, 3H), 2.44 (t,  $J = 6.8$  Hz, 2H), 2.76 – 2.75 (m, 2H), 1.59 (s, 1H), 1.51 – 1.46 (m, 4H), 1.35 (br s, 4H), 1.00 – 0.87 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  171.2, 170.0, 139.0, 136.9, 126.4, 130.8, 128.6, 128.3, 127.8, 124.4, 114.5, 63.8, 32.5, 30.0, 28.5, 27.3, 27.0, 26.3, 24.5, 23.8, 22.6, 8.4, 6.2

### Compound 29



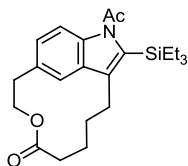
HRMS  $m/z$  400.2304 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{23}\text{H}_{34}\text{NO}_3\text{Si}$  requires 400.2308)

IR (film)  $\nu_{\text{max}}$  1730, 1693, 1416, 1368, 1284, 1235, 1133, 1085, 997, 731, 694  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  7.54 (d,  $J = 8.5$  Hz, 1H), 7.23 (t,  $J = 7.5$  Hz, 1H), 7.04 (d,  $J = 7.0$  Hz, 1H), 4.51 (t,  $J = 7.5$  Hz, 2H), 3.41 (t,  $J = 8.0$  Hz, 2H), 2.88 (t,  $J = 8.0$  Hz, 2H), 2.78 (s, 3H), 2.34 (t,  $J = 6.0$  Hz, 2H), 1.75 – 1.53 (m, 2H), 1.46 – 1.31 (m, 2H), 1.00 – 0.88 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  174.6, 170.0, 138.8, 136.9, 136.1, 131.1, 130.5, 124.4, 122.9, 119.2, 112.3, 64.2, 34.7, 31.6, 31.0, 28.2, 28.0, 27.3, 27.2, 26.9, 24.7, 8.4, 6.3

### Compound 30



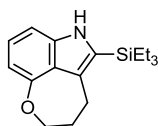
HRMS  $m/z$  400.2310 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{23}\text{H}_{34}\text{NO}_3\text{Si}$  requires 400.2308)

IR (film)  $\nu_{\text{max}}$  1698, 1521, 1373, 1325, 1264, 1116, 736, 670  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.61 (br s, 1H), 7.50 (d,  $J = 8.4$  Hz, 1H), 7.10 (dd,  $J = 1.2, 8.4$  Hz, 1H), 4.37 (t,  $J = 5.2$  Hz, 2H), 3.00 (t,  $J = 5.2$  Hz, 2H), 2.93 (t,  $J = 6.0$  Hz, 2H), 2.78 (s, 3H), 2.52 (t,  $J = 6.8$  Hz, 2H), 1.65 – 1.57 (m, 4H), 0.98 – 0.86 (m, 15H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  173.9, 169.3, 136.0, 135.9, 134.8, 133.9, 132.2, 125.2, 121.1, 114.1, 64.5, 34.5, 33.3, 30.1, 26.5, 22.9, 22.3, 8.4, 5.8

### Compound 31



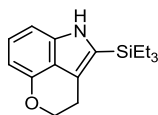
HRMS  $m/z$  288.1792 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{17}\text{H}_{26}\text{NOSi}$  requires 288.1784)

IR (film)  $\nu_{\text{max}}$  1602, 1138, 1069, 1030, 870, 669  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.98 (br s, 1H), 7.07 (t,  $J = 7.6$  Hz, 1H), 6.98 (d,  $J = 7.6$  Hz, 1H), 4.38 (t,  $J = 4.4$  Hz, 2H), 3.05 (t,  $J = 6.0$  Hz, 2H), 2.26 – 2.21 (m, 2H), 1.56 (s, 3H), 1.03 (t,  $J = 8.0$  Hz, 9H), 0.90 (q,  $J = 7.6$  Hz, 6H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  153.1, 141.2, 128.9, 124.1, 123.1, 118.7, 105.9, 103.5, 72.9, 30.9, 28.2, 7.6, 3.5

### Compound 32



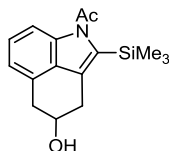
HRMS  $m/z$  274.1629 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{16}\text{H}_{24}\text{NOSi}$  requires 274.1626)

IR (film)  $\nu_{\text{max}}$  1649, 1602, 1326, 1330, 728  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.85 (br s, 1H), 7.07 (dd,  $J = 8.4, 7.6$  Hz, 1H), 6.49 (d,  $J = 7.6$  Hz, 1H), 6.44 (t,  $J = 5.6$  Hz, 2H), 3.14 (t,  $J = 5.6$  Hz, 2H), 1.03 (t,  $J = 8$  Hz, 9H), 0.87 (q,  $J = 8$  Hz, 6H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  151.1, 138.2, 126.9, 124.4, 119.3, 118.1, 103.5, 101.9, 68.6, 25.0, 7.6, 3.8, 3.5

### Compound 33



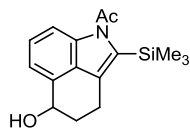
HRMS  $m/z$  288.1415 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{16}\text{H}_{22}\text{NO}_2\text{Si}$  requires 288.1420)

IR (film)  $\nu_{\text{max}}$  1684, 1439, 1394, 1337, 1264, 1052, 759, 671, 652, 616  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.43 (d,  $J = 8.0$  Hz, 1H), 7.26 (dd,  $J = 7.2, 8.4$  Hz, 1H), 7.02 (d,  $J = 6.8$  Hz, 1H), 4.41 (br s, 1H), 3.23 – 3.13 (m, 2H), 3.02 – 2.95 (m, 2H), 2.77 (s, 3H), 0.34 (s, 9H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  169.3, 136.0, 135.2, 130.6, 129.8, 128.5, 126.0, 121.5, 112.0, 68.0, 36.1, 33.5, 26.2, 2.4

### Compound 34



HRMS  $m/z$  288.1415 ( $[\text{M} + \text{H}]^+$ ,  $\text{C}_{16}\text{H}_{22}\text{NO}_2\text{Si}$  requires 288.1420)

IR (film)  $\nu_{\text{max}}$  1691, 1376, 1329, 1264, 1245, 1144, 1040, 880, 814  $\text{cm}^{-1}$

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.50 (d,  $J = 8.0$  Hz, 1H), 7.33 (dd,  $J = 7.2, 7.2$  Hz, 1H), 7.27 (d,  $J = 7.2$  Hz, 1H), 5.03 (br s, 1H), 3.14 – 3.06 (m, 1H), 2.99 – 2.92 (m, 1H), 2.78 (s, 3H), 2.21 – 2.04 (m, 2H), 1.76 (br s, 1H), 0.34 (s, 9H)

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  169.3, 135.6, 135.3, 134.8, 130.8, 130.2, 125.7, 119.7, 119.0, 113.3, 67.4, 33.2, 26.3, 20.8, 2.4

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