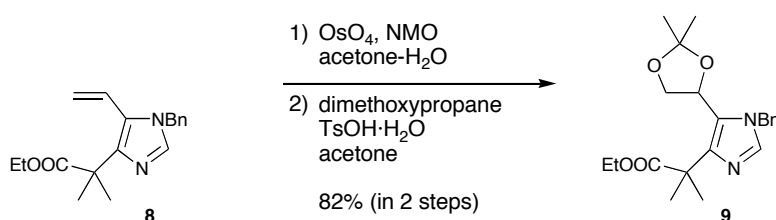


## Synthetic studies and biosynthetic speculation on marine alkaloid chartelline

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### Supplementary Information

#### Acetonide **9**;

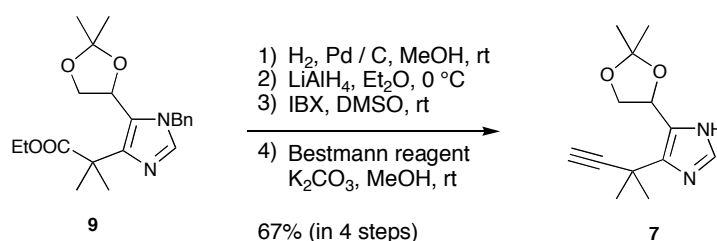


To a stirred solution of vinyl imidazole **8** (6.49 g, 21.7 mmol) and NMO (4.16 g, 23.9 mmol) in acetone (36 ml)- H<sub>2</sub>O (65 ml) was added a solution of 4% OsO<sub>4</sub> in H<sub>2</sub>O (6.9 ml, 1.1 mmol). After being stirred for 2 h at room temperature, the reaction was quenched with saturated Na<sub>2</sub>S<sub>2</sub>O<sub>4</sub> solution, and extracted with AcOEt (x2). The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The obtained crude product (6.15 g) was dissolved in acetone (118 ml), and 2, 2-dimethoxypropane (27 ml, 217 mmol) and TsOH·H<sub>2</sub>O (4.1 g, 22 mmol) were added. After being stirred for 10 h at room temperature, saturated NaHCO<sub>3</sub> solution was added, and the resulting mixture was extracted with AcOEt. The extract was washed with H<sub>2</sub>O and brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was purified by silica gel column chromatography (AcOEt:hexane= 1:2→ 1:1) to afford acetonide **9** (5.91 g, 73% in 2 steps) as a white amorphous solid.

IR (KBr)  $\nu_{\max}$  2984, 1725, 1499, 1380, 1253, 1138 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  1.23 (3H, t, *J* = 7 Hz, -OCH<sub>2</sub>-CH<sub>3</sub>), 1.36 (3H, s, acetonide), 1.44 (3H, s, acetonide), 1.60 (3H, s, -CH<sub>3</sub>), 1.64 (3H, s, -CH<sub>3</sub>), 3.68 (1H, t, *J* = 8 Hz, -CH<sub>A</sub>H<sub>B</sub>-O-), 4.03 (1H, t, *J* = 8 Hz, -CH<sub>A</sub>H<sub>B</sub>-O-), 4.11 (1H, dq, *J* = 10, 7 Hz, -O-CH<sub>C</sub>H<sub>D</sub>-CH<sub>3</sub>), 4.20 (1H, dq, *J* = 10, 7 Hz, -O-CH<sub>C</sub>H<sub>D</sub>-CH<sub>3</sub>), 5.21 (1H, d, *J* = 16 Hz, -CH<sub>E</sub>H<sub>F</sub>-Ph), 5.33 (1H, d, *J* = 16 Hz, -CH<sub>E</sub>H<sub>F</sub>-Ph), 5.34 (1H, t, *J* = 8 Hz, -CH-CH<sub>A</sub>H<sub>B</sub>-), 7.10 (2H, d, *J* = 7 Hz, phenyl), 7.28-7.38 (4H, m, aromatic). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  14.0, 23.6, 25.9, 26.6, 27.0, 43.3, 49.1, 60.9, 67.5, 69.1, 109.3, 121.8, 126.9, 128.0, 128.9, 136.8, 137.5, 144.6, 177.5. Anal. Calcd for C<sub>21</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>: C, 67.72; H, 7.58; N, 7.52. Found: C, 67.73; H,

7.68; N, 7.61.

### Acetylene 7;

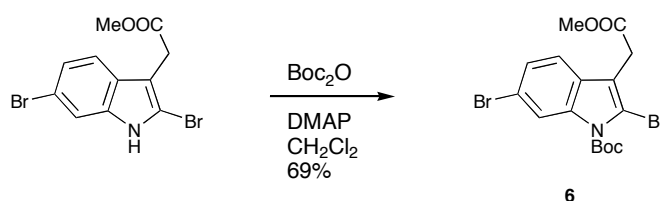


To a solution of *N*-benzylimidazole **9** (6.91 g, 18.6 mmol) in MeOH (169 ml) was added Pd/C (20%, 2.30 g). The mixture was vigorously stirred for 3.5 h at room temperature under an atmosphere of hydrogen. The reaction mixture was filtered through a pad of Super-Cel<sup>®</sup>, and the filtrate was concentrated to afford a crude product (4.76 g) as a colorless oil, which was used for the next step without purification. A solution of the crude product in Et<sub>2</sub>O (56.5 ml) was added dropwise over a period of 20 min to a stirred suspension of LiAlH<sub>4</sub> (961 mg, 25.3 mmol) in Et<sub>2</sub>O (56.5 ml) at 0 °C. After being stirred for 20 min, the reaction was quenched with H<sub>2</sub>O. Saturated Seignette's salt solution was added, the mixture was filtered, and NaCl salt was added to the filtrate to be saturated. The resulting solution was extracted with AcOEt (x3). The combined extracts were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to give a mixture of alcohol and aldehyde (3.89 g, alcohol:aldehyde= 64:36). This mixture was dissolved in DMSO (103 ml), and IBX (2.89 g, 10.3 mmol) was added at room temperature. After stirring for 1 h, an additional IBX (1.45 g, 5.16 mmol) was added and stirred for 1 h. Then, IBX (2.89 g, 10.3 mmol) was added again and a consumption of all alcohol was observed by TLC analysis (CH<sub>2</sub>Cl<sub>2</sub>:MeOH= 9:1). The reaction was quenched with saturated NaHCO<sub>3</sub> solution (0 °C), which was extracted with AcOEt (x3). The combined extracts were washed with brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated to afford a crude product (3.63 g). The product was dissolved in MeOH (127 ml), and K<sub>2</sub>CO<sub>3</sub> (1.14 g, 8.22 mmol) and Bestmann reagent (0.67 ml, 4.52 mmol) were added at room temperature. The mixture was stirred for 30 min, H<sub>2</sub>O was added and extracted with AcOEt (x2). The combined extracts were washed with H<sub>2</sub>O and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. The residue was purified by silica gel column chromatography (AcOEt:hexane= 1:1) to give acetylene **7** (2.90 g, 67% in 4 steps) as a waxy solid.

IR (KBr)  $\nu_{\max}$  3286, 2986, 2109, 1496, 1373, 1243, 1156 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400

MHz)  $\delta$  1.45 (3H, s, acetonide), 1.51 (3H, s, acetonide), 1.63 (3H, s, -Me), 1.65 (3H, s, -Me), 2.33 (1H, s, -C $\equiv$ CH), 3.89 (1H, t,  $J$  = 8 Hz, -CH<sub>A</sub>H<sub>B</sub>-O-), 4.32 (1H, dd,  $J$  = 8, 6 Hz, -CH<sub>A</sub>H<sub>B</sub>-O-), 5.72 (1H, dd,  $J$  = 8, 6 Hz, -CH-CH<sub>A</sub>H<sub>B</sub>-), 7.48 (1H, s, imidazole), 8.18 (1H, brs, NH). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  25.4, 26.6, 30.8, 31.0, 69.5, 69.6, 70.4, 90.3, 109.3, 125.0, 132.7, 138.9. Anal. Calcd for C<sub>13</sub>H<sub>18</sub>N<sub>2</sub>O<sub>2</sub>: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.63; H, 7.95; N, 11.87.

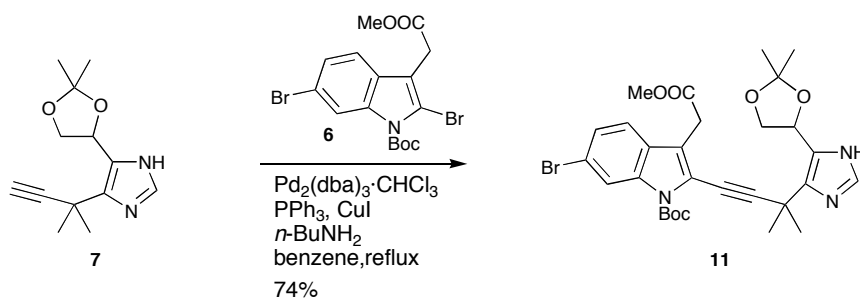
### ***N*-Boc indole 6;**



To a solution of dibromoindole (22.9 g, 66.1 mmol) and Boc<sub>2</sub>O (15.2 ml, 66.1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (350 ml) was added DMAP (81 mg, 0.66 mmol) at room temperature. After being stirred for 20 min, the solution was washed with H<sub>2</sub>O and concentrated under reduced pressure. The residue was recrystallized (Et<sub>2</sub>O-hexane) to afford *N*-Boc indole **6** (20.4 g, 69%) as a white solid.

Mp 89-90 °C. IR (KBr)  $\nu_{\max}$  2982, 1740, 1602, 1456, 1347, 1302, 1154 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  1.70 (9H, s, Boc), 3.69 (3H, s, -COOMe), 3.74 (2H, s, -CH<sub>2</sub>-), 7.32 (1H, d,  $J$  = 8 Hz, indole), 7.36 (1H, dd,  $J$  = 8, 2 Hz, indole), 8.31 (1H, d,  $J$  = 2 Hz, indole). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  28.0, 31.2, 52.2, 85.7, 111.4, 116.1, 118.5, 118.6, 119.4, 126.4, 127.4, 136.9, 148.6, 170.4. Anal. Calcd for C<sub>16</sub>H<sub>17</sub>Br<sub>2</sub>NO<sub>4</sub>: C, 42.98; H, 3.83; N, 3.13. Found: C, 42.78; H, 3.74; N, 3.29.

### **Coupling product 11;**

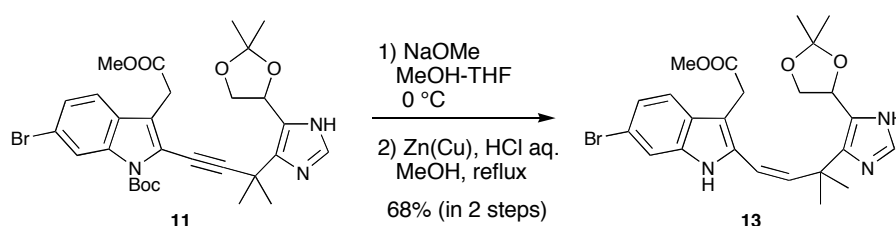


Acetylene **7** (780 mg, 3.33 mmol), dibromoindole **6** (4.47 g, 9.99 mmol), Pd<sub>2</sub>(dba)<sub>3</sub>·CHCl<sub>3</sub> (345 mg, 0.333 mmol), PPh<sub>3</sub> (349 mg, 1.33 mmol) and CuI (127 mg,

0.666 mmol) were placed in a two necked flask (200 ml) and the flask was charged with argon. Meanwhile, benzene in another flask was degassed by freeze/thaw cycle (3 times), benzene (111 ml) was added to the reaction vessel, and *n*-BuNH<sub>2</sub> (1.32 ml, 13.3 mmol) was then added. The reaction mixture was heated to reflux with stirring for 3 h, cooled to room temperature. A saturated NH<sub>4</sub>Cl solution was added and the mixture was extracted with AcOEt. The combined extracts were dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was purified by silica gel column chromatography (AcOEt:hexane= 2:1→ 1:0) to afford coupling product **11** (1.47 g, 74%) as a yellow amorphous solid.

IR (KBr)  $\nu_{\max}$  3304, 2981, 1736, 1458, 1356, 1246, 1146 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  1.45 (3H, brs, acetonide), 1.54 (3H, s, acetonide), 1.72 (9H, brs, -Boc), 1.78 (3H, s, -Me), 1.82 (3H, brs, -Me), 3.69 (3H, s, -COOMe), 3.81 (2H, s, -CH<sub>2</sub>-), 4.24 (1H, t, *J* = 7 Hz, -CH<sub>A</sub>H<sub>B</sub>-O-), 4.31 (1H, brt, *J* = 7 Hz, -CH<sub>A</sub>H<sub>B</sub>-O-), 5.33 (1H, brt, *J* = 7 Hz, -CH-CH<sub>2</sub>-), 7.39 (1H, d, *J* = 8 Hz, indole), 7.41 (1H, brd, *J* = 8 Hz, indole), 7.50 (1H, s, imidazole), 8.19 (1H, brs, indole). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  26.0, 26.7, 28.1, 28.2, 30.3, 30.7, 32.6, 52.3, 68.9, 71.3, 72.9, 86.0, 109.2, 119.0, 119.6, 119.9, 120.3, 120.5, 126.7, 127.5, 132.5, 135.6, 149.5, 170.6. Anal. Calcd for C<sub>29</sub>H<sub>34</sub>BrN<sub>3</sub>O<sub>6</sub>: C, 58.00; H, 5.71; N, 7.00. Found: C, 58.02; H, 5.55; N, 6.84.

### Z-Olefin **13**;

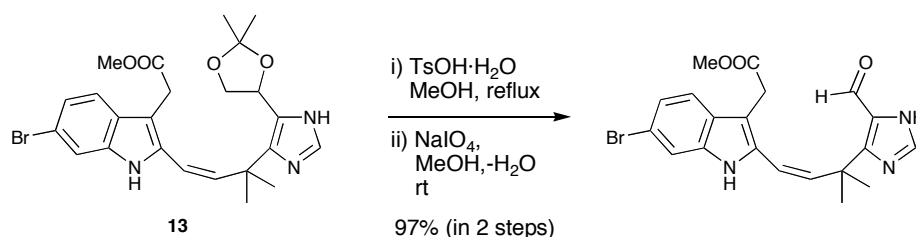


A solution of NaOMe (488 mg, 9.04 mmol) in MeOH (4.0 ml) was added to a solution of coupling product **11** (1.81 g, 3.01 mmol) in THF (56.2 ml) at 0 °C. After stirring for 15 min, the reaction mixture was poured into saturated NH<sub>4</sub>Cl solution. The solution was extracted with AcOEt. The extract was washed with H<sub>2</sub>O, dried over Na<sub>2</sub>SO<sub>4</sub>, and evaporated under reduced pressure to give a crude product (1.62 g) as a yellow amorphous solid. This product was dissolved in MeOH (151 ml) and a powder of Zn(Cu) (19.4 g) was added. After 12 N HCl (0.25 ml) was added, the mixture was heated to reflux with vigorous stirring for 15 min. The reaction mixture was cooled to

room temperature, then 12 N HCl (0.50 ml) was added and refluxed for 15 min; this procedure was repeated (5 times) until a complete consumption of acetylene was indicated by TLC (AcOEt:hexane= 2:1). The mixture was filtered through a pad of Super-Cel<sup>®</sup>, the filtrate was poured into saturated NaHCO<sub>3</sub> solution, at which point white precipitate was generated. The precipitate was removed by filtration, and the filtrate was extracted with AcOEt. The extract was washed with H<sub>2</sub>O and brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was purified by silica gel column chromatography (AcOEt:hexane= 1:1) to afford *Z*-olefin **13** (1.03 g, 68% in 2 steps) as a white amorphous solid.

IR (KBr)  $\nu_{\max}$  3376, 2986, 1734, 1458, 1373, 1215, 1157 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  1.42 (3H, brs, acetonide), 1.50 (3H, s, acetonide), 1.54 (3H, s, -Me), 1.63 (3H, brs, -Me), 3.54 (1H, brs, -CH<sub>A</sub>H<sub>B</sub>-O-), 3.65 (3H, s, -COOMe), 3.70 (2H, s, -CH<sub>2</sub>-), 4.14 (1H, dd,  $J = 8.5, 6$  Hz, -CH<sub>A</sub>H<sub>B</sub>-O-), 5.35 (1H, t,  $J = 6$  Hz, -CH-CH<sub>A</sub>H<sub>B</sub>-), 5.95 (1H, d,  $J = 12$  Hz, olefin), 6.39 (1H, d,  $J = 12$  Hz, olefin), 7.12 (1H, dd,  $J = 8, 2$  Hz, indole), 7.35 (1H, d,  $J = 8$  Hz, indole), 7.35 (1H, d,  $J = 2$  Hz, indole), 7.54 (1H, s, imidazole), 9.39 (1H, brs, NH). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  25.3, 26.7, 28.9, 30.2, 31.4, 36.9, 52.0, 69.0, 70.4, 107.9, 109.5, 113.8, 115.8, 117.1, 119.8, 122.7, 126.1, 132.3, 133.3, 136.9, 140.9, 172.1. Anal. Calcd for C<sub>24</sub>H<sub>28</sub>BrN<sub>3</sub>O<sub>4</sub>: C, 57.38; H, 5.62; N, 8.36. Found: C, 57.40; H, 5.63; N, 8.21.

### Aldehyde:

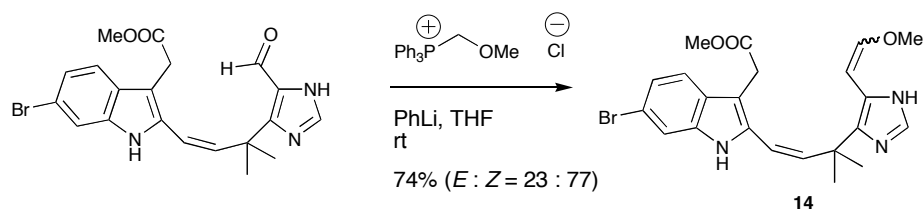


A solution of *Z*-olefin **13** (724 mg, 1.44 mmol) and TsOH·H<sub>2</sub>O (548 mg, 2.88 mmol) in MeOH (28.8 ml) was heated to reflux for 3 h. The reaction mixture was cooled to room temperature, and poured into saturated NaHCO<sub>3</sub> solution. The solution was extracted with AcOEt (x2), the combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated. The residue (737 mg) was dissolved in MeOH (21.6 ml) - H<sub>2</sub>O (7.2 ml), and NaIO<sub>4</sub> (616 mg, 2.88 mmol) was added. After being stirred for 5 min, H<sub>2</sub>O was added. The solution was extracted with AcOEt (x2). The combined

extracts were washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , and concentrated. The residue was purified by silica gel column chromatography (AcOEt: hexane = 1:2) to afford aldehyde (602 mg, 97% in 2 steps) as a white amorphous solid.

IR (KBr)  $\nu_{\text{max}}$  3407, 2971, 1733, 1656, 1458, 1340, 1264, 1173  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  1.70 (6H, s, dimethyl), 3.63 (3H, s, -COOMe), 3.69 (2H, s, - $\text{CH}_2$ -), 6.02 (1H, d,  $J = 12$  Hz, olefin), 6.49 (1H, d,  $J = 12$  Hz, olefin), 7.13 (1H, d,  $J = 8$  Hz, indole), 7.37 (1H, d,  $J = 8$  Hz, indole), 7.39 (1H, s, indole), 7.77 (1H, s, imidazole), 9.90 (1H, brs, NH of indole), 9.97 (1H, s, aldehyde), 10.62 (1H, brs, NH of imidazole).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  30.2, 31.0, 38.8, 52.0, 108.4, 113.6, 116.0, 117.9, 120.1, 122.9, 126.3, 127.8, 132.0, 136.7, 137.6, 140.0, 157.7, 171.8, 179.7. Anal. Calcd for  $\text{C}_{20}\text{H}_{20}\text{BrN}_3\text{O}_3$ : C, 55.83; H, 4.68; N, 9.77. Found: C, 55.83; H, 4.56; N, 9.65.

#### Vinyl ether **14**:

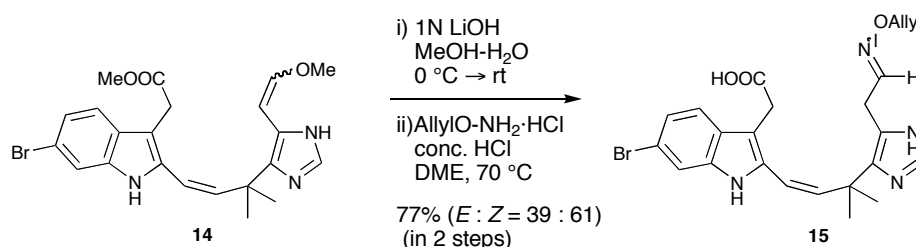


A solution of phenyllithium (1.08 M in  $\text{Et}_2\text{O}$ -cyclohexane, 4.41 ml, 4.76 mmol) was added dropwise over a period of 5 min to a stirred suspension of (methoxymethyl)-triphenylphosphonium chloride (1.63 g, 4.76 mmol) in THF (17.1 ml) at 0 °C. The mixture was stirred for 5 min, then allowed to warm to room temperature. After being stirred for 1 h, a solution of aldehyde (410 mg, 0.953 mmol) in THF (5.7 ml) was cannulated into the dark red ylide solution. After stirring for 2.5 h at room temperature, the reaction was quenched with saturated  $\text{NH}_4\text{Cl}$  and extracted with AcOEt. The extract was washed with  $\text{H}_2\text{O}$ , brine, dried over  $\text{Na}_2\text{SO}_4$ , and concentrated. The residue was purified by silica gel column chromatography (AcOEt:hexane= 1:2) to afford vinyl ether **14** (341 mg, 74%,  $E:Z = 23:77$ ) as a yellow oil.

IR (KBr)  $\nu_{\text{max}}$  3372, 2970, 1734, 1655, 1459, 1337, 1266, 1162  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz) ( $E$  isomer)  $\delta$  1.56 (6H, s, dimethyl), 3.61 (2H, s, - $\text{CH}_2$ -), 3.62 (3H, s, -COOMe), 3.69 (3H, s, -OMe), 5.80 (1H, d,  $J = 12.5$  Hz, - $\text{CH}=\text{CH}-\text{OMe}$ ), 5.95 (1H, d,  $J = 12.5$  Hz, - $\text{CH}=\text{CH}$ -), 6.39 (1H, d,  $J = 12.5$  Hz, - $\text{CH}=\text{CH}$ -), 6.73 (1H, brd,  $J = 12.5$  Hz, - $\text{CH}=\text{CH}-\text{OMe}$ ), 7.11 (1H, dd,  $J = 8, 2$  Hz, indole), 7.35 (1H, d,  $J = 2$  Hz, indole), 7.36 (1H, d,  $J = 8$  Hz, indole), 7.64 (1H, s, imidazole), 9.55 (1H, brs, NH of indole). ( $Z$

isomer)  $\delta$  1.59 (6H, s, dimethyl), 3.62 (3H, s, -COOMe), 3.63 (2H, s, -CH<sub>2</sub>-), 3.74 (3H, s, -OMe), 5.50 (1H, d,  $J = 6.5$  Hz, -CH=CH-OMe), 5.94 (1H, d,  $J = 6.5$  Hz, -CH=CH-OMe), 5.99 (1H, d,  $J = 12.5$  Hz, -CH=CH-), 6.38 (1H, d,  $J = 12.5$  Hz, -CH=CH-), 7.11 (1H, dd,  $J = 8, 2$  Hz, indole), 7.35 (1H, d,  $J = 2$  Hz, indole), 7.36 (1H, d,  $J = 8$  Hz, indole), 7.64 (1H, s, imidazole), 9.55 (1H, brs, NH of indole). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  29.9, 30.1, 30.3, 37.0, 37.2, 51.9, 52.0, 56.8, 60.7, 95.3, 107.8, 113.7, 115.6, 115.7, 116.4, 119.8, 122.5, 122.6, 123.0, 126.2, 132.0, 132.7, 132.8, 136.8, 140.4, 140.6, 142.7, 144.2, 171.9, 172.1. Anal. Calcd for C<sub>22</sub>H<sub>24</sub>BrN<sub>3</sub>O<sub>3</sub>: C, 57.65; H, 5.28; N, 9.17. Found: C, 57.64; H, 5.16; N, 8.98.

### Oxime **15**;

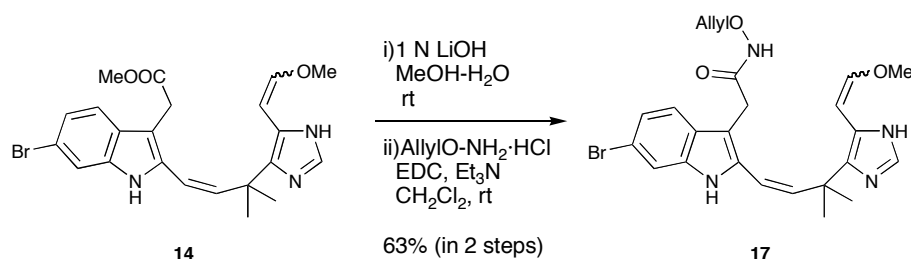


To a solution of vinyl ether **14** (33.4 mg, 72.9  $\mu$ mol) in MeOH (2.4 ml) – H<sub>2</sub>O (1.0 ml) was added LiOH (1 N, 0.22 ml, 0.219 mmol) at 0 °C. After being stirred for 15 min, the mixture was allowed to warm to room temperature and stirred for 4 h. The reaction was quenched with saturated NH<sub>4</sub>Cl solution, the mixture was extracted with AcOEt (x3). The combined extracts were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated to afford carboxylic acid, which was used for a next step without purification. This material was dissolved in DME (2.4 ml), *O*-allylhydroxylamine hydrochloride (39.9 mg, 0.365 mmol) and HCl (12 N, 30.4  $\mu$ l, 0.365 mmol) was added. The mixture was stirred for 20 min at 70 °C, then cooled to room temperature followed by dilution with H<sub>2</sub>O. The product was extracted with AcOEt (x2), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was purified by silica gel column chromatography (CH<sub>2</sub>Cl<sub>2</sub> : MeOH =19:1) to afford oxime **15** (27.3 mg, 77% in 2 steps, *E*:*Z*= 39: 61) as a yellow amorphous solid.

IR (KBr)  $\nu_{\max}$  3244, 2973, 1717, 1559, 1458, 1374, 1269, 1188 cm<sup>-1</sup>. <sup>1</sup>H NMR (CD<sub>3</sub>OD, 400 MHz) (*E* isomer)  $\delta$  1.52 (6H, s, dimethyl), 3.56 (2H, s, -CH<sub>2</sub>-COOH), 3.71 (2H, d,  $J = 5$  Hz, -CH<sub>2</sub>-CH=N-), 4.57 (2H, d,  $J = 5.5$  Hz, -CH<sub>2</sub>-CH=CH<sub>2</sub>), 5.18 (1H, dd,  $J = 10, 2$  Hz, -CH=CH<sub>A</sub>H<sub>B</sub>), 5.26 (1H, dd,  $J = 17, 2$  Hz, -CH=CH<sub>A</sub>H<sub>B</sub>), 5.83-6.03

(1H, m,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ ), 6.01 (1H, d,  $J = 12$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.45 (1H, d,  $J = 12$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.64 (1H, t,  $J = 5$  Hz,  $-\text{CH}=\text{N}-$ ), 7.05 (1H, dd,  $J = 8, 2$  Hz, indole), 7.27 (1H, d,  $J = 2$  Hz, indole), 7.35 (1H, d,  $J = 8$  Hz, indole), 7.48 (1H, s, imidazole). (*Z* isomer)  $\delta$  1.53 (6H, s, dimethyl), 3.58 (2H, s,  $-\text{CH}_2-\text{COOH}$ ), 3.60 (2H, d,  $J = 4.5$  Hz,  $-\text{CH}_2-\text{CH}=\text{N}-$ ), 4.45 (2H, d,  $J = 5.5$  Hz,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ ), 5.12 (1H, dd,  $J = 10, 2$  Hz,  $-\text{CH}=\text{CH}_A\text{H}_B$ ), 5.18 (1H, dd,  $J = 17, 2$  Hz,  $-\text{CH}=\text{CH}_A\text{H}_B$ ), 5.83-6.03 (1H, m,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ ), 5.97 (1H, d,  $J = 12$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.46 (1H, d,  $J = 12$  Hz,  $-\text{CH}=\text{CH}-$ ), 7.06 (1H, dd,  $J = 8, 2$  Hz, indole), 7.24 (1H, d,  $J = 2$  Hz, indole), 7.36 (1H, d,  $J = 8$  Hz, indole), 7.36 (1H, s, imidazole), 7.52 (1H, t,  $J = 4.5$  Hz,  $-\text{CH}=\text{N}-$ ).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ , 100 MHz)  $\delta$  24.6, 28.0, 30.0, 30.2, 32.5, 32.7, 38.1, 38.4, 75.5, 76.0, 109.8, 114.2, 114.3, 116.0, 116.1, 117.9, 118.6, 118.8, 121.0, 121.0, 123.2, 125.4, 126.3, 127.8, 127.9, 133.4, 133.5, 133.8, 133.9, 135.4, 135.5, 136.7, 137.2, 138.1, 143.7, 149.0, 149.9, 177.9, 178.5. Anal. Calcd for  $\text{C}_{23}\text{H}_{25}\text{BrN}_4\text{O}_3$ : C, 56.91; H, 5.19; N, 11.54. Found: C, 56.92; H, 5.18; N, 11.38.

### *O*-Allylhydroxamic acid **17**;



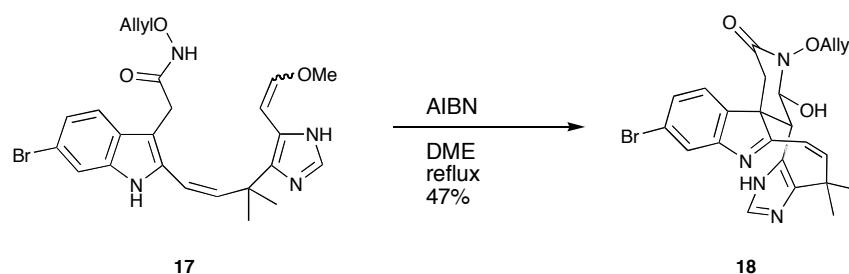
To a solution of vinyl ether **14** (60.7 mg, 0.132 mmol) in MeOH (3.3 ml) – H<sub>2</sub>O (0.7 ml) was added LiOH (1 N, 0.40 ml, 0.397 mmol) at room temperature. After being stirred for 11 h, the reaction was quenched with saturated NH<sub>4</sub>Cl solution. The solution was extracted with AcOEt (x3), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated to afford carboxylic acid, which was used for a next step without purification. The crude product was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (4.4 ml), followed by additions of *O*-allylhydroxylamine hydrochloride (29.0 mg, 0.265 mmol), Et<sub>3</sub>N (36.7  $\mu$ l, 0.265 mmol) and EDC (50.8 mg, 0.265 mmol). The mixture was stirred for 1.5 h, and the reaction was quenched with H<sub>2</sub>O. The product was extracted with CH<sub>2</sub>Cl<sub>2</sub> (x2), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated. The residue was purified by silica gel column chromatography (AcOEt : hexane = 1:1  $\rightarrow$  2:1) to afford *O*-allylhydroxamic acid **17** (41.4 mg, 63% in 2 steps) as a white amorphous solid.



(*Z*)-*O*-Allylhydroxamic acid **17**; IR (KBr)  $\nu_{\max}$  3368, 2972, 1659, 1461, 1337, 1266, 1101  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  1.61 (6H, s, dimethyl), 3.67 (2H, brs,  $-\text{CH}_2-$ ), 3.75 (3H, s, -OMe), 4.27 (2H, brd,  $J = 6.5$  Hz,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ ), 5.16 (1H, brd,  $J = 17$  Hz,  $-\text{CH}=\text{CH}_A\text{H}_B$ ), 5.17 (1H, brd,  $J = 10$  Hz,  $-\text{CH}=\text{CH}_A\text{H}_B$ ), 5.49 (1H, d,  $J = 7$  Hz,  $-\text{CH}=\text{CH}-\text{OMe}$ ), 5.82 (1H, ddt,  $J = 17, 10, 6.5$  Hz,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ ), 5.99 (1H, d,  $J = 7$  Hz,  $-\text{CH}=\text{CH}-\text{OMe}$ ), 6.01 (1H, d,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.28 (1H, brd,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-$ ), 7.13 (1H, dd,  $J = 8, 2$  Hz, indole), 7.30 (1H, d,  $J = 8$  Hz, indole), 7.40 (1H, d,  $J = 2$  Hz, indole), 7.62 (1H, s, imidazole), 8.05 (1H, brs, NH of indole), 9.71 (1H, brs, NH of imidazole).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  30.1, 30.3, 37.5, 60.8, 95.0, 106.5, 113.9, 115.7, 116.0, 119.5, 120.8, 123.0, 125.8, 128.6, 131.7, 132.1, 133.1, 137.0, 141.8, 144.6, 168.2. HRMS (FAB) ( $\text{M}+\text{H}$ ) $^+$  calcd for  $\text{C}_{24}\text{H}_{28}\text{BrN}_4\text{O}_3$  501.1324, found 501.1300.

(*E*)-*O*-Allylhydroxamic acid **17**; IR (KBr)  $\nu_{\max}$  3363, 2969, 1655, 1460, 1334, 1217, 1156  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  1.56 (6H, s, dimethyl), 3.63 (5H, s,  $-\text{CH}_2-$  and -OMe), 4.25 (2H, brd,  $J = 6.5$  Hz,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ ), 5.16 (1H, brd,  $J = 17$  Hz,  $-\text{CH}=\text{CH}_A\text{H}_B$ ), 5.17 (1H, brd,  $J = 10$  Hz,  $-\text{CH}=\text{CH}_A\text{H}_B$ ), 5.75-5.87 (1H, m,  $-\text{CH}_2-\text{CH}=\text{CH}_2$ ), 5.81 (1H, d,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-\text{OMe}$ ), 5.96 (1H, d,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.29 (1H, brd,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.75 (1H, brd,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-\text{OMe}$ ), 7.12 (1H, d,  $J = 8$  Hz, indole), 7.28 (1H, d,  $J = 8$  Hz, indole), 7.37 (1H, brs, indole), 7.45 (1H, brs, imidazole).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  29.9, 30.1, 37.3, 57.0, 94.6, 106.3, 114.0, 116.0, 116.2, 119.5, 121.0, 123.0, 125.9, 131.7, 132.4, 133.0, 136.9, 142.0, 149.0, 168.5. HRMS (FAB) ( $\text{M}+\text{H}$ ) $^+$  calcd for  $\text{C}_{24}\text{H}_{28}\text{BrN}_4\text{O}_3$  501.1324, found 501.1338.

### Indolenine **19**;

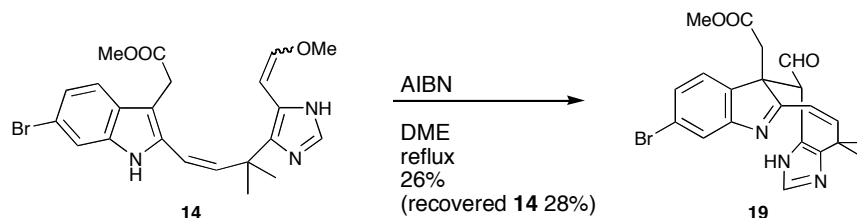


To a solution of *O*-allylhydroxamic acid **17** (8.9 mg, 17.9  $\mu\text{mol}$ ) in DME (1.1 ml) was added AIBN (2.9 mg, 17.9  $\mu\text{mol}$ ), and heated to reflux for 2.5 h. The mixture was cooled to room temperature, and concentrated under reduced pressure. The residue

was purified by PTLC ( $\text{CH}_2\text{Cl}_2$  : MeOH = 9:1) to afford indolenine **18** (4.1 mg, 47%) as a colorless oil.

IR (KBr)  $\nu_{\text{max}}$  3229, 2965, 1654, 1456, 1363, 1293, 1091  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ , 400 MHz)  $\delta$  1.42 (3H, s, -Me), 1.53 (3H, s, -Me), 2.11 (1H, d,  $J = 16$  Hz,  $-\text{CH}_A\text{H}_B^-$ ), 3.21 (1H, d,  $J = 16$  Hz,  $-\text{CH}_A\text{H}_B^-$ ), 3.98 (1H, d,  $J = 9$  Hz,  $-\text{CH}-$ ), 4.72 (1H, ddt,  $J = 10.5, 6, 1$  Hz,  $-\text{CH}_C\text{H}_D-\text{CH}=\text{CH}_2$ ), 4.79 (1H, ddt,  $J = 10.5, 6, 1$  Hz,  $-\text{CH}_C\text{H}_D-\text{CH}=\text{CH}_2$ ), 5.32 (1H, ddt,  $J = 10, 2, 1$  Hz,  $-\text{CH}=\text{CH}_E\text{H}_F$ ), 5.44 (1H, ddt,  $J = 17, 2, 1$  Hz,  $-\text{CH}=\text{CH}_E\text{H}_F$ ), 6.03 (1H, d,  $J = 9$  Hz,  $-\text{CH}-$ ), 6.16 (1H, ddt,  $J = 17, 10, 6$  Hz,  $-\text{CH}=\text{CH}_2$ ), 6.17 (1H, d,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.25 (1H, d,  $J = 12.5$  Hz,  $-\text{CH}=\text{CH}-$ ), 7.12 (1H, s, imidazole), 7.25 (1H, d,  $J = 8$  Hz, indolenine), 7.39 (1H, d,  $J = 2$  Hz, indolenine), 7.43 (1H, dd,  $J = 8, 2$  Hz, indolenine).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{OD}$ , 100 MHz)  $\delta$  28.9, 32.0, 38.8, 39.3, 44.8, 61.7, 78.9, 84.6, 117.5, 120.3, 123.3, 124.3, 125.9, 130.4, 133.8, 134.0, 138.5, 148.1, 157.0, 167.4, 185.1. HRMS (FAB) ( $\text{M}+\text{H}$ ) $^+$  calcd for  $\text{C}_{23}\text{H}_{24}\text{BrN}_4\text{O}_3$  485.1020, found 485.1011.

### Aldehyde **19**;



The reaction was conducted with vinyl ether **14** (17.0 mg, 37.1  $\mu\text{mol}$ ) following the procedure described for the preparation of compound **18**. The crude material was purified by silica gel column chromatography (AcOEt:hexane= 2:1) to afford aldehyde **19** (4.2 mg, 26%) as a yellow amorphous solid and vinyl ether (4.8 mg, 28%) was recovered.

IR (KBr)  $\nu_{\text{max}}$  3323, 2929, 1736, 1664, 1567, 1436  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  0.94 (3H, s, -Me), 1.37 (3H, s, -Me), 3.68 (3H, s,  $-\text{COOMe}$ ), 3.75 (1H, d,  $J = 15$  Hz,  $-\text{CH}_A\text{H}_B^-$ ), 3.79 (1H, d,  $J = 15$  Hz,  $-\text{CH}_A\text{H}_B^-$ ), 5.57 (1H, brs,  $-\text{CH}-$ ), 5.83 (1H, d,  $J = 10$  Hz,  $-\text{CH}=\text{CH}-$ ), 6.67 (1H, d,  $J = 10$  Hz,  $-\text{CH}=\text{CH}-$ ), 7.18 (1H, dd,  $J = 8, 2$  Hz, indolenine), 7.37 (1H, d,  $J = 8$  Hz, indolenine), 7.56 (1H, d,  $J = 2$  Hz, indolenine), 7.85 (1H, s, imidazole), 9.15 (1H, d,  $J = 2$  Hz, aldehyde).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$

21.4, 25.4, 29.8, 43.0, 52.2, 94.1, 98.9, 108.5, 115.5, 115.7, 117.1, 120.1, 124.0, 128.9,  
132.1, 133.7, 138.4, 151.9, 161.6, 171.4, 189.1. HRMS (FAB) (M+H)<sup>+</sup> calcd for  
C<sub>21</sub>H<sub>21</sub>BrN<sub>3</sub>O<sub>3</sub> 442.0766, found 442.0786.