Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry. This journal is © The Royal Society of Chemistry 2016

## Supporting Information

## Asymmetric Synthesis of Crambescin A-C Carboxylic Acids and Their Inhibitory Activity on Voltage-Gated Sodium Channels

Atsuo Nakazaki, Yoshiki Nakane, Yuki Ishikawa, Mari Yotsu-Yamashita, and Toshio Nishikawa\*

Graduate School of Bioagricultural Sciences, Nagoya University Chikusa, Nagoya 464-8601, Japan, and Graduate School of Agricultural Science, Tohoku University Aoba, Sendai 981-8555, Japan

## **Table of Contents:**

General Experimental	S2
Experimental procedures and characterization data	S3-S36
Stability of crambescin B carboxylic acid (2) and	
its methyl ester (23)	S37
<sup>1</sup> H and <sup>13</sup> C NMR Spectra	S38-S127

## **General Experimental**

Infrared spectra (IR) were recorded on a JASCO FT/IR-8300 spectrophotometer and are reported in wave number (cm<sup>-1</sup>). Proton nuclear magnetic resonance (<sup>1</sup>H NMR) spectra were recorded on a Varian Gemini-2000 (300 MHz), a Bruker Avance-400 (400 MHz), or a Bruker Avance-600 (600 MHz) spectrometer. Chemical shifts of all compounds are reported in ppm relative to the residual undeuterated solvent (chloroform-*d* as  $\delta = 7.26$ , methanol-*d*<sub>4</sub> as  $\delta = 3.31$ ). Data were reported as follows: Chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broadened), coupling constant, and assignment. Carbon nuclear magnetic resonance (<sup>13</sup>C NMR) spectra were recorded on a Bruker Avance-400 (100 MHz) spectrometer. Chemical shifts of all compounds are reported in ppm relative to the solvent (chloroform-*d* as  $\delta = 77.0$ , methanol-*d*<sub>4</sub> as  $\delta = 49.0$ ). All NMR were measured at 300 K. High-resolution mass spectra (HRMS) were recorded on an Applied Biosystems Mariner ESI-TOF spectrometer for ESI-MS or a JEOL JMS-700 MStation for EI-MS, and reported in *m/z*. Elemental analyses were performed by the Analytical Laboratory of Graduate School of Bioagricultural Sciences, Nagoya University.

Reactions were monitored by thin layer chromatography (TLC) on 0.25 mm silica gel coated glass plates 60F<sub>254</sub> (Merck, #1.05715.0001). Visualization was achieved by using UV light (254 nm) and appropriate reagent (ethanolic phosphomolybdic acid, p-anisaldehyde solution in H<sub>2</sub>SO<sub>4</sub>/AcOH/EtOH, or ninhydrin solution in *n*-BuOH/H<sub>2</sub>O/AcOH), followed by heating. Silica gel 60 (particle size 0.063-0.200 mm, Merck, #1.07734.9025) was used for silica gel open column chromatography. Silica gel 60N (spherical, neutral, particle size 0.04-0.05 mm, Kanto, #37563-79) was used for neutral silica gel flash column chromatography. Silica gel 60 (spherical, particle size 0.04-0.05 mm, Kanto, #37562-84) was used for silica gel flash column chromatography. Chromatorex<sup>®</sup>-DNH (particle size MB100-75/200, Fuji Silysia Chemical Ltd. HU20792) was used for Chromatorex DNH silica gel column chromatography. Chromatorex<sup>®</sup> C8 (particle size MB100-75/200, Fuji Silysia Chemical Ltd. KU11202) was used for Chromatorex C8 silica gel column chromatography. Preparative TLC separations were carried out on 0.5 mm silica gel plates 60F254 (Merck). Dry THF, Et<sub>2</sub>O, and CH<sub>2</sub>Cl<sub>2</sub> were purchased from Kanto Chemical Co., Inc. Dry HMPA, DMF, toluene, Et<sub>3</sub>N, and pyridine were distilled from CaH<sub>2</sub>. Dry MeOH was distilled from Mg(OMe)<sub>2</sub>. Celite<sup>®</sup> (Hyflo Super-Cel Celite<sup>®</sup>) was purchased from Nacalai tesque Co., Inc. Florisil<sup>®</sup> was purchased from Kanto chemical Co., Inc. InI (anhydrous, powder, 99.999%) and CuI (powder and chunks, 99.999%) were purchased from sigma-Aldrich. All other commercially available reagents were as received.

<sup>1</sup>H-NMR, <sup>13</sup>C-NMR, and IR data for compounds **5**, **6**, **9** to **16**, and **2** were identical to those reported previously for the corresponding compounds (Nishikawa, T. *et al. Org. Biomol. Chem.* **2014**, *12*, 53).



**dodecanal S1**: This compound was synthesized according to the modified procedure of Anelli *et al.*<sup>1</sup> To a mixture of 1-dodecanol (12.5 g, 66.9 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (200 mL) and sat. NaHCO<sub>3</sub> solution (200 mL) were added TEMPO (106 mg, 0.678 mmol) and KBr (797 mg, 6.69 mmol) at 0 °C under N<sub>2</sub> atmosphere. To a vigorously stirred mixture was added dropwise ca. 6% aqueous solution of NaOCl (ca. 50 mL) until the color of reaction mixture became brown and the temperature was maintained below 0 °C. After completion of the reaction, the solution was filtered through a pad of Celite<sup>®</sup> (eluted with CH<sub>2</sub>Cl<sub>2</sub> (300 mL x 2). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/Et<sub>2</sub>O = 19/1 to 9/1) to afford dodecanal **S1** (11.7 g, 95%) as a colorless oil.

IR (film):  $v_{\text{max}}$  (cm<sup>-1</sup>) 2925, 2854, 1728, 1466. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 0.87 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.36 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.57-1.67 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>CHO), 2.41 (2H, td, J = 7.5, 2.0 Hz, -CH<sub>2</sub>CHO), 9.76 (1H, t, J = 2.0 Hz, -CHO). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 14.1, 22.1, 22.7, 29.2, 29.30, 29.34, 29.4, 29.6, 31.9, 43.9, 202.9. HRMS (EI, positive): calcd. For C<sub>12</sub>H<sub>24</sub>O, 184.1827; found, 184.1852.



**iodoalkyne S2**: This compound was synthesized according to the modified procedure of Rassat *et al.*<sup>2</sup> To a solution of CHI<sub>3</sub> (65.4 g, 0.166 mol) in anhydrous THF (600 mL) were added PPh<sub>3</sub> (43.5 g, 166 mmol) and then *t*-BuOK (18.6 g, 166 mmol) at room temperature under N<sub>2</sub> atmosphere. After being stirred for 15 min, to the reaction mixture was added a solution of dodecanal **S1** (20.4 g, 111 mmol) in THF (140 mL). After being stirred for 30 min, the reaction temperature was cooled to -78 °C, and then another portion of *t*-BuOK (62.0 g, 553 mmol) was added. The reaction temperature was warmed until the reaction was completed (ca. -60 °C) and then the reaction was quenched with brine (500 mL). The reaction mixture was filtered through a pad of Celite<sup>®</sup> (eluted with Et<sub>2</sub>O), and the resulting mixture was extracted with Et<sub>2</sub>O (500 mL x 2). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by

silica gel column chromatography (hexane) to afford iodoalkyne **S2** (32.2 g, 95%) as a yellow oil.

IR (film):  $v_{\text{max}}$  (cm<sup>-1</sup>) 2925, 2853, 1465. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 0.88 (3H, t, J = 6.5 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.42 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.47-1.55 (2H, m, I-C=CCH<sub>2</sub>CH<sub>2</sub>-), 2.35 (2H, t, J = 7.0 Hz, I-C=CCH<sub>2</sub>CH<sub>2</sub>-). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) -7.75, 14.1, 20.8, 22.7, 28.5, 28.8, 29.1, 29.3, 29.5, 29.6, 31.9, 94.9. HRMS (EI, positive): calcd. For C<sub>13</sub>H<sub>23</sub>I, 306.0844; found, 306.0834.



cis-iodoalkene S3: This compound was synthesized according to the modified procedure of Denmark et al.<sup>3</sup> A solution of BH<sub>3</sub>·SMe<sub>2</sub> (2.0 M in toluene, 54.7 mL, 109 mmol) in anhydrous and degassed Et<sub>2</sub>O (80 mL) was cooled to 5 °C. To the solution was added dropwise distilled cyclohexene (22.4 mL, 221 mmol) under N2 atmosphere and the temperature was maintained below 15 °C. After being stirred at 5 °C for 15 min, the solution was allowed to warm to room temperature and stirred for 1 h. The resulting white suspension was cooled to 2-3 °C and a solution of iodoalkyne (30.4 g, 99.4 mmol) in Et<sub>2</sub>O (30 mL) was added dropwise. After being stirred at 2-3 °C for 30 min, the reaction mixture was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was cooled to 2-3 °C and acetic acid (50 mL, 873 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. After completion of the reaction, the reaction mixture was washed with H<sub>2</sub>O (100 mL x 4). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane) to afford cis-iodoalkene **S3** (29.6 g, 97%) as a pale pink oil.

IR (film):  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 2921, 2854, 1608, 1465, 1377, 1284. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 0.88 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.22-1.36 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.36-1.48 (2H, m, ICH=CHCH<sub>2</sub>CH<sub>2</sub>-), 2.08-2.18 (2H, m, ICH=CHCH<sub>2</sub>-), 6.12-6.21 (2H, m, ICH=CHCH<sub>2</sub>-). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 14.1, 22.7, 28.0, 29.1, 29.3, 29.4, 29.55, 29.62, 31.9, 34.7, 82.1, 141.5. HRMS (EI, positive): calcd. For C<sub>13</sub>H<sub>25</sub>I, 308.1001; found, 308.0981.



**enyne 5:** A solution of *cis*-iodoalkene **S3** (10.0 g, 32.4 mmol) in benzene (231 mL) was cooled to 0 °C. To the solution were added 3-butyn-1-ol (7.3 mL, 97.3 mmol), CuI (1.24 g, 6.49 mmol), PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (0.683 g, 0.973 mmol) and Et<sub>3</sub>N (36 mL, 260 mmol) at 0 °C under Ar atmosphere. The resulting mixture was degassed by three freezed-thraw cycles, and the flask was filled with Ar. After being stirred at room temperature for 16 h, the reaction was quenched with sat. NH<sub>4</sub>Cl solution (200 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with Et<sub>2</sub>O (200 mL x 2). The combined organic layer was washed with H<sub>2</sub>O (200 mL x 2) and brine (200 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by column chromatography (flash silica gel and Florisil<sup>®</sup>, hexane/Et<sub>2</sub>O = 4/1) to afford enyne **5** (6.27 g, 77%) as a yellow oil.

IR (film):  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3350, 2925, 2854, 1466, 1044. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 0.88 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.35 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.35-1.45 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>CH=CH-), 1.74 (1H, br s, -OH), 2.28 (2H, qd, J = 7.5, 1.0 Hz, -CH<sub>2</sub>CH=CH-), 2.62 (2H, td, J = 6.0, 2.0 Hz, -CH<sub>2</sub>CH<sub>2</sub>OH), 3.75 (2H, t, J = 6.0 Hz, -CH<sub>2</sub>OH), 5.43 (1H, m, -CH<sub>2</sub>CH=CHC=C-), 5.86 (1H, dt, J = 10.5, 7.5 Hz, -CH<sub>2</sub>CH=CHC=C-). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 14.1, 22.7, 24.0, 28.8, 29.2, 29.3, 29.5, 29.59, 29.63, 29.7, 30.2, 31.9, 61.3, 79.4, 90.2, 108.7, 143.7. HRMS (EI, positive): calcd. For C<sub>17</sub>H<sub>30</sub>O, 250.2297; found, 250.2301.

<sup>&</sup>lt;sup>1</sup> Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. J. Org. Chem. 1987, 52, 2559.

<sup>&</sup>lt;sup>2</sup> Michel, P.; Rassat, A. *Tetrahedron Lett.* **1999**, *40*, 8579.

<sup>&</sup>lt;sup>3</sup> Denmark, S. E.; Wang, Z. Org. Synth. 2005, 81, 42.



(-)-epoxide 6: This compound was synthesized according to the modified procedure of Katsuki *et al.*<sup>4</sup> To a solution of (S,S)-salan ligand 7 (1.18 g, 2.20 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (30 mL) was added freshly distilled Ti(O-iPr)<sub>4</sub> (0.60 mL, 2.00 mmol) at room temperature under N<sub>2</sub> atmosphere. After being stirred at room temperature for 1 h, to the reaction mixture were added 4,4'-thiobis(6-tert-butyl-m-cresol) (470 mg, 1.30 mmol),<sup>5</sup> pH 7.4 phosphate buffer (2.5 mL), envne 5 (5.00 g, 20.0 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL), and 30% H<sub>2</sub>O<sub>2</sub> (4.5 mL, 40.0 mmol) under N<sub>2</sub> atmosphere. After being stirred at 40 °C for 7 h, the reaction mixture was allowed to cool to room temperature and to the reaction mixture was added solid NH<sub>4</sub>Cl (7.5 The resulting mixture was filtered through a pad of Celite<sup>®</sup> (eluted with hexane), and the g). filtrate was washed with sat. NH<sub>4</sub>Cl solution (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/Et<sub>2</sub>O = 2/1) to afford (-)-epoxide 6 (4.25 g, 80%, 95% ee) as a yellow solid. Recrystallization from hexane afforded (-)-epoxide 6 (3.14 g, 74% yield, >99% ee) as a pale yellow solid. Enantiomeric excess was determined by chiral HPLC analysis of the corresponding *p*-nitrobenzoate derived from (-)-epoxide 6. Chiral HPLC analysis (CHIRALPAK AS-H column, hexane/2-propanol = 9/1, flow rate = 0.50 mL/min, detection 270-nm light, 30 °C)  $t_{\rm R}$  = 16.5 min (major isomer), 18.3 min (minor isomer). The absolute configuration was determined by the modified Mosher method of MTPA esters S6a and S6b (vide infra).

mp: 48 °C.  $[\alpha]_D^{23}$  –9.27 (*c* 1.07, CHCl<sub>3</sub>) for >99% ee. IR (film):  $v_{max}$  (cm<sup>-1</sup>) 3272, 2919, 2848, 1465, 1046, 879, 855. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 0.88 (3H, t, *J* = 6.5 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.42 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.42-1.56 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.63-1.72 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.77 (1H, t, *J* = 6.0 Hz, -OH), 2.51 (2H, td, *J* = 6.0, 1.5 Hz, -CHC=CCH<sub>2</sub>-), 3.01 (1H, td, *J* = 6.0, 4.0 Hz, -CHCHC=C-), 3.42 (1H, dt, *J* = 4.0, 1.5 Hz, -CHCHC=C-), 3.73 (2H, q, *J* = 6.0 Hz, -CH<sub>2</sub>OH). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 14.1, 22.7, 23.2, 25.9, 29.31, 29.33, 29.4, 29.53, 29.55, 29.62, 29.63, 31.9, 45.3, 58.1, 60.9, 77.2, 82.8. Anal. Calcd for C<sub>17</sub>H<sub>30</sub>O<sub>2</sub>: C, 76.64; H, 11.35. Found: C, 76.38; H, 11.24.

<sup>&</sup>lt;sup>4</sup> Shimada, Y.; Kondo, S.; Ohara, Y.; Matsumoto, K.; Katsuki, T. Synlett 2007, 2445.

<sup>&</sup>lt;sup>5</sup> Jackson, K. L.; Li, W.; Chen, C.-L.; Kishi, Y. *Tetrahedron* **2010**, *66*, 2263.



silyl ether S4: To a solution of epoxide 6 (97.0 mg, 0.364 mmol) in dry  $CH_2Cl_2$  (3 mL) were added imidazole (56.9 mg, 0.836 mmol) and TBDPSCl (0.10 mL, 0.38 mmol) at 0 °C. After being stirred for 1 h at room temperature, to the reaction mixture were added imidazole (57.0 mg, 0.837 mmol) and TBDPSCl (0.10 mL, 0.38 mmol) at room temperature. After being stirred for 5 min at room temperature, the reaction was quenched with sat. NH<sub>4</sub>Cl solution (5 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic layer was washed with water (10 mL) and brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 9/1) to afford (–)-silyl ether S4 (182 mg, 99%) as a colorless oil.

[α]<sub>D</sub><sup>24</sup> -7.47 (*c* 0.25, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 2926, 2855, 1465, 1428, 1112. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.05 (9H, s, -Si-<sup>*t*</sup>Bu), 1.22-1.38 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.40-1.52 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.61-1.68 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.48 (2H, td, *J* = 7.0, 1.5 Hz, -CHC≡CCH<sub>2</sub>-), 2.97 (1H, td, *J* = 6.0, 4.0 Hz, -CHCHC≡C-), 3.38 (1H, dt, *J* = 4.0, 1.5 Hz, -CHCHC≡C-), 3.76 (2H, t, *J* = 7.0 Hz, -CH<sub>2</sub>OTBDPS), 7.36-7.46 (6H, m, Ph), 7.65-7.70 (4H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 19.2, 22.7, 23.0, 26.0, 26.8, 29.26, 29.34, 29.4, 29.5, 29.56, 29.63, 31.9, 45.4, 58.1, 62.3, 76.3, 83.4, 127.7, 129.7, 133.5, 135.5. HRMS (ESI, positive): calcd. For C<sub>33</sub>H<sub>48</sub>O<sub>2</sub>NaSi [M+Na]<sup>+</sup>, 527.3316; found, 527.3323.



**allene S5:** This compound was synthesized according to the modified procedure of Fürstner *et al.*<sup>6</sup> CuCN (38.1 mg, 0.425 mmol) was dried azeotropically with dry toluene (0.2 mL x3). To the residue were added dry THF (8 mL) and P(OPh)<sub>3</sub> (0.11 mL, 0.421 mmol) at room temperature under Ar atmosphere. After being stirred for 20 min at room temperature, to the reaction mixture was added a solution of MeMgBr (0.3 mL, 0.3 mmol, 3.0 M in Et<sub>2</sub>O) at -40 °C under Ar atmosphere. After being stirred for 30 min at -40 °C, to the reaction mixture was added a solution of silyl ether **S4** (177 mg, 0.350 mmol) in dry THF (4 mL). After being stirred for 3.5 h at -40 °C, the reaction mixture was warmed to 10 °C. After being stirred for 1 h at 10 °C, the reaction was quenched with sat. NH<sub>4</sub>Cl solution (10 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (10 mL x 2). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 14/1 to 9/1) to afford (+)-allene **S5** (174 mg, 95%, dr = >95:<5 determined by <sup>1</sup>H NMR analysis) as a colorless oil.

[α]<sub>D</sub><sup>24</sup> +26.4 (*c* 1.43, CHCl<sub>3</sub>). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3342, 2926, 2855, 1966, 1470, 1428, 1112. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.89 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.06 (9H, s, -Si-<sup>*t*</sup>Bu), 1.23-1.41 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.45-1.55 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.71 (3H, d, *J* = 2.5 Hz, -C=C=CCH<sub>3</sub>), 2.23 (2H, td, *J* = 6.5, 2.5 Hz, -CH<sub>2</sub>CH<sub>2</sub>OTBDPS), 3.76 (2H, t, *J* = 6.5 Hz, -CH<sub>2</sub>OTBDPS), 4.03 (1H, q, *J* = 6.0 Hz, -CHOH), 5.12 (1H, td, *J* = 6.0, 2.5 Hz, -CH=C=C-), 7.36-7.46 (6H, m, Ph), 7.66-7.70 (4H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 19.1, 19.4, 22.7, 25.4, 26.8, 29.3, 29.57, 29.60, 29.63, 29.7, 31.9, 37.0, 37.5, 62.5, 70.0, 95.2, 99.9, 127.6, 129.6, 133.8, 135.6, 199.7. HRMS (ESI, positive): calcd. For C<sub>34</sub>H<sub>52</sub>O<sub>2</sub>NaSi [M+Na]<sup>+</sup>, 543.3629; found, 543.3629.

<sup>&</sup>lt;sup>6</sup> Larivée, A.; Unger, J. B.; Thomas, M.; Wirtz, C.; Dubost, C.; Handa, S.; Fürstner, A. Angew. Chem. Int. Ed. 2011, 50, 304.



**MTPA ester S6a:** To dry pyridine (0.1 mL, 1.24 mmol) were added (+)-MTPACl (ca. 25  $\mu$ L, 0.13 mmol) and a solution of allene **S5** (20.1 mg, 0.0386 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) at room temperature. After being stirred for 1 h, to the reaction mixture was added (+)-MTPACl (ca. 10  $\mu$ L, 0.053 mmol) at room temperature. After being stirred for 3 h at room temperature, the reaction was quenched with 3-dimethyl-amino-1-propylamine (20  $\mu$ L). After being stirred for 5 min at room temperature, the resulting mixture was diluted with EtOAc (5 mL) and then washed with cold 1 M HCl (5 mL), cold sat. Na<sub>2</sub>CO<sub>3</sub> solution (5 mL) and brine (5 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 20/1) to afford MTAP ester **S6a** (26.3 mg, 93%) as a colorless oil.

[α]<sub>D</sub><sup>26</sup> +35.4 (*c* 1.30, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 2927, 1969, 1746, 1466, 1428, 1258, 1170, 1112, 1017. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ (ppm) 0.89 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.04 (9H, s, -Si-<sup>*t*</sup>Bu), 1.20-1.33 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.58 (1H, m, -CH<sub>*a*</sub>H<sub>*b*</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.66 (3H, d, *J* = 2.5 Hz, -C=C=CCH<sub>3</sub>), 1.68 (1H, m, -CH<sub>*a*</sub>H<sub>*b*</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.13-2.26 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>OTBDPS), 3.54 (3H, s, -OMe), 3.71 (2H, t, *J* = 7.0 Hz, -CH<sub>2</sub>OTBDPS), 4.97 (1H, m, -CH=C=C-), 5.34 (1H, q, *J* = 7.0 Hz, -CH<sub>2</sub>CH-), 7.35-7.44 (9H, m, Ph), 7.50-7.54 (2H, m, Ph), 7.64-7.68 (4H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 18.9, 19.2, 22.7, 25.2, 26.8, 29.2, 29.3, 29.46, 29.54, 29.6, 31.9, 34.0, 36.7, 55.4, 62.3, 76.4, 89.2, 99.1, 127.5, 127.6, 128.3, 129.4, 129.6, 132.5, 133.9, 135.5, 165.8, 203.0 (CF<sub>3</sub> carbon peak is missing due to its very low intensity). HRMS (ESI, positive): calcd. For C<sub>44</sub>H<sub>59</sub>O<sub>4</sub>F<sub>3</sub>NaSi [M+Na]<sup>+</sup>, 759.4027; found, 759.4029.



**MTPA ester S6b:** To dry pyridine (0.1 mL, 1.24 mmol) were added (+)-MTPACl (ca. 25  $\mu$ L, 0.13 mmol) and a solution of allene **S5** (20.1 mg, 0.0386 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) at room temperature. After being stirred for 1 h, to the reaction mixture was added (+)-MTPACl (ca. 10  $\mu$ L, 0.053 mmol) at room temperature. After being stirred for 3 h at room temperature, the reaction was quenched with 3-dimethyl-amino-1-propylamine (20  $\mu$ L). After being stirred for 5 min at room temperature, the resulting mixture was diluted with EtOAc (5 mL) and then washed with cold 1 M HCl (5 mL), cold sat. Na<sub>2</sub>CO<sub>3</sub> solution (5 mL) and brine (5 mL). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 20/1) to afford MTPA ester **S6b** (17.6 mg, 87%) as a colorless oil.

[α]<sub>D</sub><sup>25</sup> –19.4 (*c* 0.88, CHCl<sub>3</sub>). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 2927, 1747, 1472, 1270, 1186, 1111, 1019. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>): δ (ppm) 0.89 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.04 (9H, s, -Si-<sup>*I*</sup>Bu), 1.12-1.34 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.53 (1H, dt, *J* = 14.5, 6.0 Hz, -CH<sub>a</sub>H<sub>b</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.61 (1H, dt, *J* = 14.5, 7.5 Hz, -CH<sub>a</sub>H<sub>b</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.66 (3H, d, *J* = 2.5 Hz, -C=CCH<sub>3</sub>), 2.16-2.30 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>OTBDPS), 2.26 (1H, dtd, *J* = 14.5, 7.0, 2.5 Hz, -CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>OTBDPS), 3.55 (3H, s, -OMe), 3.73 (2H, t, *J* = 6.5 Hz, -CH<sub>2</sub>OTBDPS), 5.08 (1H, m, -CH=C=C-), 5.36 (1H, q, *J* = 6.5 Hz, -CH<sub>2</sub>CH-), 7.35-7.44 (9H, m, Ph), 7.52-7.56 (2H, m, Ph), 7.65-7.68 (4H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 18.9, 19.2, 22.7, 25.0, 26.8, 29.1, 29.3, 29.4, 29.5, 29.6, 31.9, 33.9, 36.7, 55.4, 62.3, 76.1, 89.4, 99.3, 127.3, 127.6, 128.3, 129.4, 129.6, 132.7, 133.82, 133.84, 135.5, 165.8, 203.0 (CF<sub>3</sub> carbon peak is missing due to its very low intensity). HRMS (ESI, positive): calcd. For C<sub>44</sub>H<sub>59</sub>O<sub>4</sub>F<sub>3</sub>NaSi [M+Na]<sup>+</sup>, 759.4027; found, 759.4029.





(-)-aziridine 9: To a solution of epoxide 6 (2.0 g, 7.5 mmol) in dry MeOH (90 mL) was added NaN<sub>3</sub> (4.0 g, 62 mmol) at room temperature. After being stirred vigorously for 37.5 h at room temperature, to the reaction mixture was added water (90 mL). The resulting mixture was extracted with EtOAc (100 mL x 3). The combined organic layer was washed with brine (200 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure to provide crude azide. The crude azide was dried azeotropically with toluene (20 mL x 2), and dissolved in dry DMF (110 mL), and then PPh<sub>3</sub> (4.0 g, 15 mmol) was added to the solution. After being stirred for 5 h at 80 °C, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (60 mL), and then to the solution were added imidazole (1.1 g, 16 mmol) and TBDPSCl (2.2 mL, 12 mmol) at 0 °C. After being stirred for 20 min at room temperature, the reaction was quenched with sat. NH<sub>4</sub>Cl solution (60 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (60 mL x 2). The combined organic layer was washed with water (120 mL) and brine (120 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced The residue was purified by neutral silica gel flash column chromatography pressure. (hexane/EtOAc/CH<sub>2</sub>Cl<sub>2</sub> = 30/1/1 with 1% *i*-Pr<sub>2</sub>NH to 20/1/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (-)-aziridine 9 (2.07 g, 55% in 3 steps) as a colorless oil.

 $[α]_D^{29}$  –6.10 (*c* 1.03, CHCl<sub>3</sub>). IR (film): *v*<sub>max</sub> (cm<sup>-1</sup>) 2926, 2855, 1465, 1428, 1112. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 6.5 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.05 (9H, s, -Si<sup>-t</sup>Bu), 1.21-1.35 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.40-1.49 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.49-1.57 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.01 (1H, br, -CHCHC≡C-), 2.40-2.48 (3H, m -CHC≡CCH<sub>2</sub>-, -CHCHC ≡C-), 3.75 (2H, t, *J* = 7 Hz, -CH<sub>2</sub>OTBDPS), 7.35-7.45 (6H, m, -Si-Ph), 7.64-7.70 (4H, m, -Si-Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 19.2, 22.7, 23.0, 24.4, 26.8, 27.4, 29.3, 29.4, 29.57, 29.60, 29.63, 29.7, 30.6, 31.9, 37.0, 62.6, 77.2, 78.8, 127.6, 129.6, 133.6, 135.5. HRMS (ESI, positive): calcd. For C<sub>33</sub>H<sub>50</sub>NOSi [M+H]<sup>+</sup>, 504.3656; found, 504.3646.



(+)-guanidino-aziridine 10: To a solution of aziridine 9 (2.07 g, 4.17 mmol), Boc,Cbz-methylisothiourea (1.5 g, 4.6 mmol), and dry Et<sub>3</sub>N (5.8 mL, 42 mmol) in dry DMF (42 mL) was added HgCl<sub>2</sub> (1.2 g, 4.6 mmol) at room temperature. After being stirred for 1h at room temperature, the reaction mixture was diluted with EtOAc (40 mL), and then filtered through a pad of Celite<sup>®</sup> (eluted with EtOAc). The filtrate was washed with water (40 mL x 3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was diluted with EtOAc (20 mL) filtered through a pad of Celite<sup>®</sup> (eluted with EtOAc) and concentrated under reduced pressure. The filtrate was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 19/1 with 1% *i*-Pr<sub>2</sub>NH) and concentrated under reduced pressure. The residue was diluted with hexane/Et<sub>2</sub>O = 1/1 (20 mL) and then filtered through a pad of Celite<sup>®</sup> (eluted with hexane/Et<sub>2</sub>O = 1/1) to afford (+)-guanidino-aziridine **10** (2.88 g, 90%) as a yellow oil.

[α]<sub>D</sub><sup>30</sup> +43.4 (*c* 1.00, CHCl<sub>3</sub>). IR (film): *v*<sub>max</sub> (cm<sup>-1</sup>) 2926, 2855, 1766, 1651, 1596, 1111. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.04 (9H, s, -Si-<sup>*t*</sup>Bu), 1.20-1.34 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.35-1.55 (3H, m, -CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.47 (9H, s, -O-<sup>*t*</sup>Bu), 2.10 (1H, m, -CH<sub>a</sub>H<sub>b</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.48 (2H, td, *J* = 7.5, 1.5 Hz, -CHC≡CCH<sub>2</sub>-), 2.69 (1H, ddd, *J* = 8.5, 6.0, 4.0 Hz, -CHCHC≡CCH<sub>2</sub>-), 3.22 (1H, dt, *J* = 6.0, 1.5 Hz, -CHC≡ CCH<sub>2</sub>-), 3.76 (2H, t, *J* = 7.5 Hz, -CH<sub>2</sub>OTBDPS), 5.15 (2H, s, -CH<sub>2</sub>Ph), 7.27-7.44 (11H, m, -Si-Ph, -CH<sub>2</sub>Ph), 7.63-7.69 (4H, m, -Si-Ph), 10.94 (1H, br, -NHBoc). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 19.2, 22.7, 23.0, 26.1, 26.8, 28.0, 28.7, 29.3, 29.4, 29.51, 29.54, 29.6, 29.7, 31.9, 34.7, 46.8, 62.4, 67.6, 75.5, 81.4, 82.5, 127.7, 128.2, 128.5, 129.7, 133.5, 135.5, 136.2, 148.5, 163.7. Anal. Calcd for C<sub>47</sub>H<sub>65</sub>N<sub>3</sub>O<sub>5</sub>Si: C, 72.36; H, 8.40; N, 5.39. Found: C, 72.19; H, 8.47; N, 5.58.



(-)-alcohol 11: To a mixture of guanidino-aziridine 10 (2.88 g, 3.69 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (213 mg, 0.185 mmol), and InI (1.33 g, 5.50 mmol) were added a degassed solution of dry THF (25 mL), dry HMPA (6.3 mL), and formalin (0.48 mL, 6.4 mmol, 37% solution) at room temperature under the argon atmosphere. After being stirred for 1 h at room temperature, the solution was passed through a short pad of neutral flash silica gel (eluted with EtOAc with 1% *i*-Pr<sub>2</sub>NH), and the resulting solution was washed with water (100 mL x 3) and brine (100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/Et<sub>2</sub>O = 4/1 with 1% *i*-Pr<sub>2</sub>NH) to hexane/Et<sub>2</sub>O = 1/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (-)-alcohol 11 (2.45 g, 82%, dr = >95:<5 determined by <sup>1</sup>H NMR analysis of diol 13) as a yellow oil.

[α]<sub>D</sub><sup>29</sup> –4.25 (*c* 1.08, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 3319, 2927, 2855, 1723, 1646, 1618, 1132, 1057. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.05 (9H, s, -Si-<sup>*t*</sup>Bu), 1.20-1.33 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.49 (9H, s, -O-<sup>*t*</sup>Bu), 1.49-1.61 (1H, m, -CH<sub>a</sub>CH<sub>b</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.02 (1H, m, -CH<sub>a</sub>CH<sub>b</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.36 (1H, m, -CHCH<sub>2</sub>OH), 2.49 (2H, td, J = 7.0, 2.0 Hz, -CH<sub>2</sub>CH<sub>2</sub>OTBDPS), 3.55-3.66 (2H, m, -CH<sub>2</sub>OH), 3.76 (2H, t, J = 7.0 Hz, -CH<sub>2</sub>OTBDPS), 4.12 (1H, qd, J = 9.0, 2.5 Hz, -NHCH-), 5.07 (1H, d, J = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 5.13 (1H, d, J = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 7.27-7.44 (11H, m, -Si-Ph, -CH<sub>2</sub>Ph), 7.64-7.70 (4H, m, -Si-Ph), 8.32 (1H, d, J = 8.5 Hz, -NH(=NCbz)NHBoc), 11.33 (1H, br s, -NHBoc). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 19.2, 22.7, 23.1, 25.7, 26.8, 28.0, 28.1, 29.2, 29.3, 29.4, 29.5, 29.62, 29.64, 31.9, 33.0, 41.1, 51.3, 61.9, 62.7, 67.0, 79.7, 80.9, 83.9, 127.7, 127.8, 128.4, 129.6, 133.7, 135.5, 136.5, 153.0, 157.3, 163.1. Anal. Calcd for C<sub>48</sub>H<sub>69</sub>N<sub>3</sub>O<sub>6</sub>Si: C, 70.99; H, 8.56; N, 5.17. Found: C, 71.17; H, 8.51; N, 5.27.



(+)-alcohol 12: To a solution of alcohol 11 (2.45 g, 3.02 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (75 mL) were added Et<sub>3</sub>N (6.8 mL), Ac<sub>2</sub>O (6.8 mL), and DMAP (37 mg, 0.303 mmol) at room temperature. After being stirred for 1 h at room temperature, the reaction mixture was concentrated under reduced pressure with toluene/MeOH (2/1, 20 mL), and then dried azeotropically with toluene/MeOH (2/1, 20 mL x3) to provide crude acetate. The residue of the acetate was dissolved in dry THF (75 mL), and then TBAF (9.0 mL, 9.0 mmol, 1.0 M solution in THF) was added at room temperature. After being stirred for 13 h at room temperature, to the reaction mixture was added TBAF (2.0 mL, 2.0 mmol). After being stirred for 4.5 h at room temperature, to the reaction mixture was added TBAF (1.0 mL, 1.0 mmol). After being stirred for 3 h at room temperature, the reaction was quenched with brine (70 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (70 mL x The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under 3). reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 3/1 with 1% *i*-Pr<sub>2</sub>NH) and then repurified by neutral silica gel flash column chromatography (hexane/EtOAc = 6/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (+)-alcohol 12 (1.70 g, 91% in 2 steps) as a pale yellow oil.

[α]<sub>D</sub><sup>29</sup> +35.4 (*c* 1.08, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 3319, 2925, 2854, 1724, 1640, 1619, 1250, 1056. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.17-1.45 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.50 (9H, s, -O-<sup>*t*</sup>Bu), 1.53-1.63 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.06 (3H, s, -CO-CH<sub>3</sub>), 2.44 (2H, td, J = 5.5, 2.5 Hz, -CH<sub>2</sub>CH<sub>2</sub>OH), 3.04 (1H, m, -CHCH<sub>2</sub>OAc), 3.69 (2H, t, J = 5.5 Hz, -CH<sub>2</sub>OH), 4.04 (1H, dd, J = 10.5, 6.5 Hz, -CH<sub>a</sub>H<sub>b</sub>OAc), 4.23 (1H, dd, J = 10.5, 6.5 Hz, -CH<sub>a</sub>H<sub>b</sub>OAc), 4.42 (1H, ddd, J = 14, 9.5, 5.5 Hz, -NHCH-), 5.11 (1H, d, J = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 5.15 (1H, d, J = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 7.26-7.41 (5H, m, Ph), 8.57 (1H, d, J = 9.5 Hz, -NH(=NCbz)NHBoc), 11.44 (1H, br s, -NHBoc). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 20.8, 22.7, 23.4, 25.6, 28.0, 28.2, 29.3, 29.49, 29.52, 29.56, 29.61, 30.5, 31.9, 36.6, 50.2, 61.1, 63.8, 67.0, 78.1, 82.0, 83.7, 127.8, 127.9, 128.4, 136.9, 153.2, 156.2, 163.7, 170.9. HRMS (ESI, positive): calcd. For C<sub>34</sub>H<sub>53</sub>N<sub>3</sub>O<sub>7</sub>Na [M+Na]<sup>+</sup>, 638.3776; found, 638.3778.



(+)-*spiro*-hemiaminal 14: A solution of guanidino-alcohol 12 (1.70 g, 2.76 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (50 mL) and TFA (5 mL) was stirred for 2.5 h at room temperature and then the reaction mixture was concentrated under reduced pressure with toluene/MeOH (2/1, 40 mL). The residue was dried azeotropically with toluene/MeOH (2/1, 20 mL x3) to provide crude alcohol 13. The residue was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub>/H<sub>2</sub>O (330 mL, 1/1), and then K<sub>2</sub>CO<sub>3</sub> (2.29 g, 16.6 mmol) was added. To a vigorously stirred mixture was added PyHBr<sub>3</sub> (2.64 g, 8.25 mmol). After being stirred for 30 min at room temperature, the reaction was quenched with sat. Na<sub>2</sub>SO<sub>3</sub> solution (150 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (200 mL x 2). The combined organic layer was washed with water (400 mL) and brine (400 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 5/1 with 1% i-Pr<sub>2</sub>NH) to afford (+)-*spiro*-hemiaminal 14 (1.35 g, 73%, dr = >95:<5 determined by <sup>1</sup>H NMR analysis) as a pale yellow oil.

[α]<sub>D</sub><sup>29</sup> +115 (*c* 1.04, CHCl<sub>3</sub>). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 2925, 2853, 1744, 1635, 1241, 1030. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.19-1.48 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.54-1.72 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.02 (3H, s, -CO-CH<sub>3</sub>), 2.67 (1H, dt, *J* = 5.5, 3.5 Hz, -CHCH<sub>2</sub>OAc), 3.17 (1H, ddd, *J* = 14.5, 7.0, 2.0 Hz, -CH<sub>a</sub>H<sub>b</sub>CBr<sub>2</sub>-), 3.27 (1H, m, -CH<sub>a</sub>H<sub>b</sub>CBr<sub>2</sub>-), 3.93-4.01 (2H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-, -NHCH-), 4.06 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 4.33 (1H, dd, *J* = 12.5, 5.5 Hz, -CH<sub>a</sub>H<sub>b</sub>OAc), 4.54 (1H, dd, *J* = 12.5, 3.5 Hz, -CH<sub>a</sub>H<sub>b</sub>OAc), 5.10 (2H, s, -CH<sub>2</sub>Ph), 7.26-7.40 (5H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 20.9, 22.7, 25.9, 29.3, 29.4, 29.5, 29.6, 31.4, 31.9, 41.3, 49.0, 50.6, 58.5, 62.2, 63.4, 66.5, 93.2, 127.75, 127.82, 128.3, 136.8, 157.0, 163.1, 170.5. Anal. Calcd for C<sub>29</sub>H<sub>43</sub>N<sub>3</sub>O<sub>5</sub>Br<sub>2</sub>: C, 51.72; H, 6.44; N, 6.24. Found: C, 52.01; H, 6.59; N, 6.33.



(+)-spiro-hemiaminal 15: To a solution of spiro-hemiaminal 14 (1.35 g, 2.00 mmol) and *n*-Bu<sub>3</sub>SnH (2.7 mL, 10 mmol) in dry toluene (22 mL) were added Et<sub>3</sub>B (1.0 mL, 1.0 mmol, 1.0 M solution in hexane) and air (1 mL) at room temperature. After being stirred for 2.5 h at room temperature, the solution was passed through a short pad of neutral flash silica gel (eluted with EtOAc) and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 5/1 with 1% *i*-Pr<sub>2</sub>NH to 1/1with 1% i-Pr<sub>2</sub>NH) to afford (+)-spiro-hemiaminal 15 (990 mg, 96%) as a pale yellow oil.  $[\alpha]_D^{31}$  +81.9 (c 1.00, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 2925, 2854, 1744, 1628, 1228.  $^{1}H$ NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 0.88 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.45 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.53-1.66 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.96-2.24 (5H, m, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -CHCH<sub>2</sub>OAc), 2.03 (3H, s, -CO-CH<sub>3</sub>), 3.85 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 3.91-4.01 (2H, m, -OCH<sub>a</sub> $H_b$ CH<sub>2</sub>-, -NHCH-), 4.05 (1H, dd, J = 12, 4.5 Hz, -CH<sub>a</sub>H<sub>b</sub>OAc), 4.12 (1H, dd, J = 12, 5.5 Hz, -CH<sub>a</sub>H<sub>b</sub>OAc), 5.05 (1H, d, J = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 5.09 (1H, d, J = 12.5 Hz, -CH<sub>a</sub>*H*<sub>b</sub>Ph), 7.23-7.40 (5H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 20.9, 22.7, 24.7, 25.8, 29.3, 29.40, 29.43, 29.5, 29.6, 31.6, 31.9, 35.2, 42.1, 49.7, 60.7, 66.2, 66.5, 90.3, 127.6, 127.7, 128.3, 137.3, 157.9, 163.9, 170.6. HRMS (ESI, positive): calcd. For  $C_{29}H_{46}N_{3}O_{5}[M+H]^{+}$ , 516.3432; found, 516.3450.



(+)-common intermediate 16: To a solution of *spiro*-hemiaminal 15 (990 mg, 1.91 mmol) in MeOH (50 mL) was added  $K_2CO_3$  (265 mg, 1.92 mmol) at room temperature. After being stirred for 1 h at room temperature, the reaction was quenched with sat. NH<sub>4</sub>Cl solution (50 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (50 mL x 2). The combined organic layer was washed with water (100 mL) and brine (100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (EtOAc with 1% *i*-Pr<sub>2</sub>NH to CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (+)-common intermediate 16

(866 mg, 95%) as a pale yellow oil.

[α]<sub>D</sub><sup>30</sup> +83.4 (*c* 1.02, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 3262, 2925, 2854, 1619, 1541, 1456, 1392, 1326, 1257, 1101, 1050. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.46 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.53-1.70 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.90 (1H, td, *J* = 5.0, 4.0 Hz, -CHCH<sub>2</sub>OH) 1.93-2.20 (4H, m, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-), 3.52 (1H, dd, *J* = 11.5, 5.0 Hz, -CH<sub>a</sub>H<sub>b</sub>OH), 3.72 (1H, dd, *J* = 11.5, 5.0 Hz, -CH<sub>a</sub>H<sub>b</sub>OH), 3.78-3.96 (3H, m, -OCH<sub>2</sub>CH<sub>2</sub>-, -NHCH-), 5.02 (1H, d, *J* = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 5.08 (1H, d, *J* = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 7.23-7.39 (5H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 22.7, 24.7, 26.0, 29.3, 29.4, 29.5, 29.6, 31.6, 31.9, 35.0, 44.9, 49.9, 59.0, 66.2, 66.3, 90.7, 127.6, 127.9, 128.3, 137.2, 158.0, 163.7.

Anal. Calcd for C<sub>27</sub>H<sub>43</sub>N<sub>3</sub>O<sub>4</sub>: C, 68.47; H, 9.15; N, 8.87. Found: C, 68.26; H, 9.12; N, 8.78.



(+)-crambescin B carboxylic acid (2): To a solution of common intermediate 16 (30.2 mg, 0.0638 mmol) in acetone (3 mL) was added 2.5 M Jones reagent (100  $\mu$ L) at 0 °C. After being stirred for 15 min at 0 °C, the reaction was quenched with 2-propanol (0.5 mL) and H<sub>2</sub>O (3 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 with 1% *i*-Pr<sub>2</sub>NH) to afford carboxylic acid (41.2 mg) as a white solid. Carboxylic acid (41.2 mg), 10% Pd-C (10.0 mg), and MeOH (5 mL) were placed in a recovery flask (20 mL) connected to an inlet adaptor with three way-stopcock. The atmosphere of the reaction vessel was replaced by hydrogen (1.0 atm). After being stirred for 20 min at room temperature, the catalyst was filtered off through a pad of Celite<sup>®</sup> (eluted with MeOH), and then the filtrate was concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 1/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (+)-crambescin B carboxylic acid (2) (16.8 mg, 75% in 2 steps) as a colorless oil.

 $[\alpha]_D^{30}$  +89.9 (*c* 0.64, MeOH). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3247, 2924, 2853, 1683, 1616, 1568, 1403, 1040. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded as trifluoroacetic acid salts. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  (ppm) 0.90 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.23-1.42 (16H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.42-1.53 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>) 1.57-1.71 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>),

2.01-2.23 (4H, m, -OCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-), 2.89 (1H, d, J = 4.0 Hz, -CHCO<sub>2</sub>H), 3.84 (1H, td, J = 7.0, 4.0 Hz, -NHCH-), 3.93 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 4.02 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD):  $\delta$  (ppm) 14.4, 23.7, 25.7, 26.5, 30.4, 30.5, 30.6, 30.7, 32.8, 33.1, 36.2, 49.6, 49.9, 68.8, 90.0, 155.2, 171.4. HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>36</sub>N<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup>, 354.2751; found, 354.2750.



(+)-crambescin B decarboxylate (17): A solution of crambescin B carboxylic acid (2) (21.2 mg, 0.0600 mmol) in MeOH (10 mL) was stirred for 24 h at room temperature and then to the reaction mixture was added *i*-Pr<sub>2</sub>NH (1 mL). After being stirred for 24 h at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by Chromatorex DNH silica gel column chromatography (EtOAc to  $CH_2Cl_2/MeOH =$ 9/1 to MeOH) to afford (+)-crambescin B decarboxylate (17) (17.8 mg, 80 %) as a colorless oil. The relative stereochemistry of 17 could not be determined by NOESY analysis.  $[\alpha]_D^{25}$  +70.9 (c 0.40, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 3234, 2925, 2854, 1682, 1613, 1465, 1399, 1350, 1195, 1028. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded as carbonic acid <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 0.87 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.54 salts.  $(19H, m, -CH_aH_b(CH_2)_9CH_3), 1.54-1.68 (2H, m, -CH_aH_b(CH_2)_9CH_3 -CHCH_aH_bCO-, -CH_2-),$ 1.84-2.04 (3H, m, -CHCH<sub>a</sub>H<sub>b</sub>CO-, -CH<sub>2</sub>-), 2.07-2.28 (2H, m), 3.59 (1H, m, -NHCH-), 3.85 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 3.97 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 22.7, 24.7, 25.1, 29.3, 29.45, 29.50, 29.56, 29.62, 31.9, 34.8, 36.8, 37.5, 47.2, 67.3, 88.0, 154.2, 179.3. HRMS (ESI, positive): calcd. For  $C_{18}H_{36}N_{3}O$  [M+H]<sup>+</sup>, 310.2853; found, 310.2856.



(-)-enal 18: To a solution of common intermediate 16 (303 mg, 0.640 mmol) and TEMPO (20 mg, 0.13 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (40 mL) was added PhI(OAc)<sub>2</sub> (517 mg, 1.61 mmol) at room temperature. After being stirred for 6.5 h at room temperature, the reaction was quenched with sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (40 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (40 mL x 3). The combined organic layer was washed with water (120 mL) and brine (120 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 2/1 with 1% *i*-Pr<sub>2</sub>NH to 1/1 with 1% *i*-Pr<sub>2</sub>NH to EtOAc with 1% *i*-Pr<sub>2</sub>NH) to afford (–)-enal 18 (240 mg, 80%) as a brown oil.

[α]<sub>D</sub><sup>28</sup> –17.8 (*c* 0.97, CHCl<sub>3</sub>). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3283, 2925, 2854, 1747, 1652, 1457, 1255, 1067. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.19-1.37 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.44-1.52 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.68-1.78 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>OH), 2.58 (1H, dt, *J* = 14.5, 6.5 Hz, -CH<sub>a</sub>CH<sub>b</sub>CH<sub>2</sub>CH<sub>2</sub>OH), 2.69 (1H, dt, *J* = 14.5, 7.0 Hz, -CH<sub>a</sub>CH<sub>b</sub>CH<sub>2</sub>CH<sub>2</sub>OH), 3.58 (2H, t, *J* = 5.5 Hz, -CH<sub>2</sub>OH), 4.44 (1H, t, *J* = 5.5 Hz, -NHC*H*-), 5.04 (1H, d, *J* = 12 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 5.15 (1H, d, *J* = 12 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 7.27-7.38 (5H, m, Ph), 9.69 (1H, s, -CHO). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 22.6, 24.1, 24.4, 29.25, 29.29, 29.5, 29.57, 29.64, 30.6, 31.9, 36.2, 48.2, 60.2, 67.0, 113.4, 128.2, 128.3, 128.5, 136.2, 154.2, 156.0, 163.0, 185.3. HRMS (ESI, positive): calcd. For C<sub>27</sub>H<sub>42</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup>, 472.3170; found, 472.3190.



(+)-guanidine 19: To a solution of enal 18 (29.2 mg, 0.0619 mmol) in MeOH (6 mL) was added distilled DBU (ca. 20  $\mu$ L, 0.134 mmol) at room temperature. After being stirred for 12 h, the reaction was quenched with 1 M HCl (10 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 3). The combined

organic layer was washed with brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (EtOAc to  $CH_2Cl_2/MeOH = 1/1$ ) to afford (+)-guanidine **19** (20.0 mg) as a yellow oil.

[α]<sub>D</sub><sup>27</sup> +27.2 (*c* 1.69, CHCl<sub>3</sub>). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3295, 2925, 2853, 1694, 1661, 1548, 1460, 1366, 1258, 1063. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ (ppm) 0.90 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.25-1.42 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.45-1.62 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>) 1.88 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>OH), 2.86 (2H, t, *J* = 7.5 Hz, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH), 3.64 (2H, t, *J* = 6.0 Hz, -CH<sub>2</sub>OH), 4.44 (1H, dd, *J* = 6.5, 4.5 Hz, -NHCH-), 9.86 (1H, s, -CHO). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ (ppm) 14.4, 23.7, 25.0, 25.4, 30.3, 30.5, 30.58, 30.64, 30.73, 30.74, 32.2, 33.1, 36.9, 49.3, 61.8, 115.7, 153.4, 153.9, 188.0. HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>36</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>, 338.2802; found, 338.2800.

(+)-crambescin C carboxylic acid (3): To a solution of guanidine 19 (20.0 mg) in *t*-BuOH (6 mL) and 2-methyl-2-butene (0.40 mL, 3.76 mmol) was added a solution of NaClO<sub>2</sub> (54.0 mg, 0.597 mmol) and NaH<sub>2</sub>PO<sub>4</sub> (138 mg, 1.15 mmol) in H<sub>2</sub>O (2 mL) at room temperature. After being stirred for 22.5 h, the reaction was quenched with sat. NaHSO<sub>3</sub> (10 mL) and brine (10 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (30 mL x 2). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by HPLC on Nomura Chemical ODS-HG-5 monitored by UV detector (4.6 x 250 mm, 0.013M TFA/MeCN, 1.0 mL/min, 220 nm) to afford (+)-crambescin C carboxylic acid (3) (8.6 mg, 39% in 2 steps) as a colorless oil.

[α]<sub>D</sub><sup>26</sup> +46.3 (*c* 0.43, MeOH). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3735, 3191, 2924, 2853, 1687, 1557, 1247, 1059. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded as trifluoroacetic acid salts. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ (ppm) 0.90 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.23-1.50 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.53-1.64 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>) 1.80 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>OH), 2.75-2.92 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH), 3.60 (2H, t, *J* = 6.0 Hz, -CH<sub>2</sub>OH), 4.44 (1H, t, *J* = 5.0 Hz, -NHC*H*-). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ (ppm) 14.4, 23.7, 25.1, 28.5, 30.3, 30.5, 30.60, 30.64, 30.7, 30.8, 31.9, 33.1, 36.9, 51.4, 62.0, 106.8, 148.1, 153.5, 168.0. HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>36</sub>N<sub>3</sub>O<sub>3</sub>[M+H]<sup>+</sup>, 354.2751; found, 354.2740.



(+)-pyrrolidine 20: To a solution of enal 18 (49.5 mg, 0.105 mmol) and Et<sub>3</sub>N (Ca. 30  $\mu$ L, 0.22 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was added MsCl (ca. 15  $\mu$ L, 0.19 mmol) at room temperature. After being stirred for 10 min at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 2/1 to EtOAc) and then repurified by neutral silica gel flash column flash column chromatography (hexane/EtOAc = 3/1 to 2/1) to afford (+)-pyrrolidine 20 (30.3 mg, 64%) as a colorless oil.

[α]<sub>D</sub><sup>28</sup> +13.2 (*c* 1.52, CHCl<sub>3</sub>). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 2925, 2853, 1653, 1602, 1243. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 6.5 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.20-1.40 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.44-1.61 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.99-2.21 (2H, m, -NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-), 3.04 (1H, dt, *J* = 17, 9.0 Hz, -NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>H<sub>b</sub>-), 3.16 (1H, ddd, *J* = 17, 8.5, 4.0 Hz, -NCH<sub>2</sub>CH<sub>2</sub>CH<sub>4</sub>H<sub>b</sub>-), 3.80-3.94 (2H, m, -NCH<sub>2</sub>CH<sub>2</sub>-), 4.48 (1H, m, -NHCH-), 5.11 (1H, d, *J* = 12 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 5.17 (1H, d, *J* = 12 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 7.26-7.43 (5H, m, Ph), 9.51 (1H, br, -NH-), 9.55 (1H, s, -CHO). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 21.4, 22.7, 24.5, 28.0, 29.25, 29.31, 29.5, 29.6, 31.9, 36.8, 48.1, 49.3, 67.1, 110.2, 127.9, 128.2, 128.4, 136.7, 155.2, 157.1, 163.8, 185.2. HRMS (ESI, positive): calcd. For C<sub>27</sub>H<sub>40</sub>N<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup>, 454.3064; found, 454.3085.



(+)-guanidine 21: To a solution of pyrrolidine 20 (30.3 mg, 0.0668 mmol) in glyme (3.6 mL) and H<sub>2</sub>O (2.4 mL) was added to Ba(OH)<sub>2</sub>·8H<sub>2</sub>O (276 mg, 0.875 mmol) at room temperature. After being stirred for 8.5 h at 80 °C, the reaction mixture was added H<sub>2</sub>O (5 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (10 mL x 2). The combined organic layer was washed with brine (20 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (EtOAc to CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 5/1 to MeOH to MeOH with 1% CH<sub>3</sub>COOH) to afford (+)-guanidine 21 (11.3 mg) as a pale yellow oil.

[α]<sub>D</sub><sup>28</sup> +50.0 (*c* 0.56, CHCl<sub>3</sub>). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 3152, 2925, 2854, 1692, 1655, 1520, 1458, 1401, 1269, 1190. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded as acetic acid salts. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD):  $\delta$  (ppm) 0.90 (3H, t, *J* = 6.5 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.22-1.43 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.46-1.61 (2H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.90 (3H, s, *CH*<sub>3</sub>COO, overlap with residual acetic acid), 2.18 (1H, m, -NCH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 2.31 (1H, m, -NCH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 3.09 (1H, dt, *J* = 17, 9.0 Hz, -NCH<sub>2</sub>CH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>-), 3.31 (1H, m, -NCH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>-), 3.72 (1H, td, *J* = 9.0, 7.5 Hz, -NCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 3.87 (1H, td, *J* = 9.0, 3.0 Hz, -NCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 4.43 (1H, t, *J* = 5.5 Hz, -NHC*H*-), 9.61 (1H, s, -CHO). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD):  $\delta$  (ppm) 14.4, 23.1, 23.7, 24.0, 25.1, 28.1, 30.4, 30.5, 30.6, 30.66, 30.74, 30.8, 33.1, 37.3, 49.5, 49.7, 112.8, 153.3, 158.6, 180.9, 188.2. HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>34</sub>N<sub>3</sub>O [M+H]<sup>+</sup>, 320.2696; found, 320.2692.

(+)-crambescin A carboxylic acid (1): To a solution of guanidine 21 (11.3 mg) in *t*-BuOH (2.7 mL) and 2-methyl-2-butene (ca. 225  $\mu$ L, 2.12 mmol) was added a solution of NaClO<sub>2</sub> (32.0 mg, 0.354 mmol) and NaH<sub>2</sub>PO<sub>4</sub> (85 mg, 0.71 mmol) in H<sub>2</sub>O (0.9 mL) at room temperature. After being stirred for 29.5 h, the reaction was quenched with sat. NaHSO<sub>3</sub> (2 mL) and brine (2 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by HPLC on Nomura Chemical ODS-HG-5 monitored by UV detector (4.6 x 250 mm, 0.013 M TFA/MeCN, 1.0 mL/min, 220 nm) to afford (+)-crambescin A carboxylic acid (1) (2.8 mg, 12% in 2 steps) as a colorless oil.

[α]<sub>D</sub><sup>27</sup> +51.9 (*c* 0.14, MeOH). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3393, 2925, 2853, 1684, 1543, 1433, 1264, 1187, 1139, 1033. <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded as trifluoroacetic acid salts. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ (ppm) 0.90 (3H, t, J = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.25-1.48 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.59 (2H, q, J = 6.0 Hz,-CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.10 (1H, m, -NCH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 2.23 (1H, m, -NCH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 2.97 (1H, dt, J = 18, 9.0 Hz, -NCH<sub>2</sub>CH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>-), 3.35 (1H, ddd, J = 18, 9.5, 3.0 Hz,-NCH<sub>2</sub>CH<sub>2</sub>CH<sub>a</sub>H<sub>b</sub>-), 3.66 (1H, td, J = 9.5, 7.5 Hz, -NCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 3.81 (1H, td, J = 9.5, 2.5 Hz, -NCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 4.38 (1H, t, J = 6.0 Hz, -NHCH-). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ (ppm) 14.4, 23.0, 23.7, 25.2, 30.3, 30.5, 30.6, 30.66, 30.74, 30.8, 31.8, 33.1, 37.3, 49.5, 51.5, 103.9, 152.3, 153.1, 167.8. HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>34</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>, 336.2646; found, 336.2642.



To a solution of common intermediate 16 (37.1 mg, 0.0783 mmol) in (+)-methyl ester 22: acetone (3.0 mL) was added 2.5 M Jones reagent (100 µL) at 0 °C. After being stirred for 15 min at 0 °C, the reaction was quenched with 2-propanol (0.3 mL) and  $H_2O$  (3 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure to provide crude carboxylic acid. The residue of the carboxylic acid was dissolved in MeOH (6.0 mL), and then TMSCHN<sub>2</sub> (0.6 M in Hex, 0.6 mL, 0.4 mmol) was added at 0 °C. After being stirred for 10 min at 0 °C, to the reaction mixture were added TMSCHN<sub>2</sub> (0.6 mL, 0.4 mmol). After being stirred for 20 min at 0 °C, to the reaction mixture were added TMSCHN<sub>2</sub> (0.3 mL, 0.2 mmol). After being stirred for 40 min at 0 °C, the reaction was quenched with AcOH (0.3 mL). The resulting mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography (Hexane/EtOAc = 1/1) to afford (+)-methyl ester 22 (18.4 mg, 47% in 2 steps) as a colorless oil.

[α]<sub>D</sub><sup>28</sup> +79.9 (*c* 0.92, CHCl<sub>3</sub>). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 2925, 1744, 1631, 1546, 1457, 1391, 1243, 1098, 1029. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 0.88 (3H, t, *J* = 6.5 Hz, -CH<sub>2</sub>C*H*<sub>3</sub>), 1.21-1.45 (18H, m, -CH<sub>2</sub>(C*H*<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.48-1.56 (2H, m, -C*H*<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.95-2.16 (4H, m, -OCH<sub>2</sub>C*H*<sub>2</sub>C*H*<sub>2</sub>-), 2.81 (1H, d, *J* = 4.0 Hz, -C*H*CO<sub>2</sub>CH<sub>3</sub>), 3.67 (3H, s, -CO<sub>2</sub>C*H*<sub>3</sub>), 3.81-3.90 (2H, m, -OC*H*<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-, -NHC*H*-), 3.97 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 5.06 (1H, d, *J* = 12.5 Hz, -C*H*<sub>a</sub>H<sub>b</sub>Ph), 5.10 (1H, d, *J* = 12.5 Hz, -CH<sub>a</sub>H<sub>b</sub>Ph), 7.23-7.40 (5H, m, Ph). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 14.1, 22.6, 24.7, 25.6, 29.2, 29.3, 29.4, 29.6, 31.9, 32.1, 35.6, 48.5, 49.3, 51.9, 66.2, 67.0, 88.5, 127.5, 127.7, 128.2, 137.2, 157.6, 163.5, 168.8. HRMS (ESI, positive): calcd. For C<sub>28</sub>H<sub>44</sub>N<sub>3</sub>O<sub>5</sub> [M+H]<sup>+</sup>, 502.3276; found, 502.3282.

(+)-crambescin B methyl ester (23): Methyl ester 22 (4.3 mg, 8.57  $\mu$ mol), 10% Pd-C (7.0 mg), and MeOH (2 mL) were placed in a recovery flask (10 mL) connected to an inlet adaptor with three way-stopcock. The atmosphere of the reaction vessel was replaced by hydrogen (1.0 atm). After being stirred for 10 min at room temperature, the resulting mixture was added TFA (25  $\mu$ L). The catalyst was filtered off through a pad of Celite<sup>®</sup> (eluted with MeOH), and then the filtrate was concentrated under reduced pressure. The residue was purified by Chromatorex C8 silica gel column chromatography (MeOH/H<sub>2</sub>O = 1/2 with 0.1% TFA to MeOH with 0.1% TFA) to afford (+)-crambescin B methyl ester (23) (4.0 mg, 97%) as a colorless oil.

[α]<sub>D</sub><sup>28</sup> +74.7 (*c* 0.22, MeOH). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3411, 2925, 2855, 1675, 1203, 1136. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ (ppm) 0.90 (3H, t, *J* = 6.5 Hz, -CH<sub>2</sub>C*H*<sub>3</sub>), 1.23-1.41 (16H, m, -CH<sub>2</sub>(*CH*<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.41-1.51 (2H, m, -*CH*<sub>2</sub>(CH<sub>2</sub>)<sub>8</sub>CH<sub>3</sub>), 1.51-1.62 (2H, m, -*CH*<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.98-2.20 (4H, m, -OCH<sub>2</sub>C*H*<sub>2</sub>C*H*<sub>2</sub>-), 3.01 (1H, d, *J* = 4.0 Hz, -*CH*CO<sub>2</sub>CH<sub>3</sub>), 3.73 (3H, s, -CO<sub>2</sub>C*H*<sub>3</sub>), 3.86 (1H, td, *J* = 7.0, 4.0 Hz, -NHC*H*-), 3.93 (1H, m, -OC*H*<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 4.02 (1H, m, -OCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ (ppm) 14.4, 23.7, 25.7, 26.4, 30.4, 30.5, 30.6, 30.7, 32.7, 33.1, 36.1, 50.1, 52.5, 68.9, 89.9, 155.2, 170.3. HRMS (ESI, positive): calcd. For C<sub>20</sub>H<sub>38</sub>N<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup>, 368.2908; found, 368.2922.



(+)-crambescin B alcohol (24): Common intermediate 16 (13.7 mg, 0.0289 mmol), 10% Pd-C (5.0 mg), and MeOH (2 mL) were placed in a recovery flask (10 mL) connected to an inlet adaptor with three way-stopcock. The atmosphere of the reaction vessel was replaced by hydrogen (1.0 atm). After being stirred for 20 min at room temperature, the catalyst was filtered off through a pad of Celite<sup>®</sup> (eluted with MeOH), and then the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (MeOH/H<sub>2</sub>O = 9/1 with 0.1% AcOH) and then the residue was purified by Chromatorex DNH silica gel column chromatography (EtOAc to CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 9/1 to MeOH) to afford (+)-crambescin B alcohol (26) (7.9 mg, 81%) as a colorless oil.

[α]<sub>D</sub><sup>30</sup> +53.4 (*c* 0.40, MeOH). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3328, 2853, 2360, 1674, 1607, 1559, 1407, 1033. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were recorded as acetic acid salts. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ (ppm) 0.90 (3H, t, J = 7.0 Hz,  $-CH_2CH_3$ ), 1.25-1.50 (18H, m,  $-CH_2(CH_2)_9CH_3$ ), 1.57-1.81 (2H, m,  $-CH_2(CH_2)_9CH_3$ ), 1.90 (3H, s,  $CH_3COO$ ), 1.93 (1H, m,  $-CHCH_2OH$ ), 1.95-2.22 (3H, m), 2.24-2.38 (1H, m), 3.52 (1H, dd, J = 11.5, 4.5 Hz,  $-CH_aH_bOH$ ), 3.67 (1H, dd, J = 11.5, 5.0 Hz,  $-CH_aH_bOH$ ), 3.81-3.93 (2H, m), 3.98 (1H, m). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ (ppm) 14.4, 23.7, 24.2, 25.7, 26.8, 30.4, 30.5, 30.6, 30.66, 30.71, 30.73, 32.0, 33.1, 35.6, 45.7, 49.5, 51.3, 58.8, 68.1, 92.1, 155.3, 180.4. HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>38</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>, 340.2959; found, 340.2961.



(+)-crambescin C methyl ester (25): Methyl ester 22 (10.9 mg, 0.0217 mmol), 10% Pd-C (3.6 mg), and MeOH (2 mL) were placed in a recovery flask (20 mL) connected to an inlet adaptor with three way-stopcock. The atmosphere of the reaction vessel was replaced by hydrogen (1.0 atm). After being stirred for 20 min at room temperature, the catalyst was filtered off through a pad of Celite<sup>®</sup> (eluted with MeOH), and then the filtrate was concentrated under reduced pressure. The residue was purified by Chromatorex DNH silica gel column chromatography (EtOAc to MeOH) to afford (+)-crambescin B methyl ester (23) (8.8 mg) as a colorless oil. To a solution of crambescin B methyl ester (23) (8.8 mg) in MeOH (4 mL) was added *i*-Pr<sub>2</sub>NH (0.5 mL) at room temperature. After being stirred for 41 h at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by Chromatorex C8 silica gel column chromatography (MeOH/H<sub>2</sub>O = 1/2 to MeOH) to afford (+)-crambescin C methyl ester (25) (6.5 mg, 85% in 2 steps) as a colorless oil.

[α]<sub>D</sub><sup>29</sup> +106 (*c* 0.33, MeOH). IR (film):  $\nu_{max}$  (cm<sup>-1</sup>) 3341, 2925, 2854, 1697, 1434, 1241, 1203, 1186, 1140, 1088. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ (ppm) 0.90 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.23-1.65 (20H, m, -(CH<sub>2</sub>)<sub>10</sub>CH<sub>3</sub>), 1.79 (2H, m, -CH<sub>2</sub>CH<sub>2</sub>OH), 2.71 (1H, dt, *J* = 12.5, 7.5 Hz, -CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>CH<sub>2</sub>OH), 2.79 (1H, dt, *J* = 12.5, 7.5 Hz, -CH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>CH<sub>2</sub>OH), 3.71 (3H, s, -CO<sub>2</sub>CH<sub>3</sub>), 4.32 (1H, dd, *J* = 7.0, 3.5 Hz, -NHC*H*-). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ (ppm) 14.4, 23.7, 25.1, 30.4, 30.5, 30.6, 30.7, 30.75, 30.77, 32.3, 33.1, 37.4, 51.0, 51.7, 62.5, 103.3, 155.4, 156.4, 167.8. HRMS (ESI, positive): calcd. For C<sub>20</sub>H<sub>38</sub>N<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup>, 368.2908; found, 368.2904.



(-)-crambescin A methyl ester (1b): To a solution of (-)-crambescin A carboxylic acid (*ent*-1) (5.4 mg, 0.016 mmol) in MeOH (1 mL) and Et<sub>2</sub>O (0.5 mL) was added TMSCHN<sub>2</sub> (0.6 M in Hex, 0.5 mL, 0.3 mmol) at 0 °C. After being stirred for 2 h at room temperature, the reaction was quenched with CH<sub>3</sub>COOH (0.5 mL) and sat. NaHCO<sub>3</sub> solution (1 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (3 mL x2). The combined organic layer was washed with water (5 mL) and brine (5 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by preparative TLC (MeOH/CH<sub>2</sub>Cl<sub>2</sub>/H<sub>2</sub>O/HCOOH = 15/85/1/1) to afford (-)-crambescin A methyl ester (1b) (5.7 mg, 89%) as a colorless oil.

[α]<sub>D</sub><sup>25</sup> –56.2 (*c* 0.28, MeOH). IR (film):  $v_{max}$  (cm<sup>-1</sup>) 3145, 2925, 2854, 1699, 1593, 1536, 1436, 1348, 1268, 1194, 1095. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD): δ (ppm) 0.90 (3H, t, *J* = 7.0 Hz, -CH<sub>2</sub>CH<sub>3</sub>), 1.25-1.48 (18H, m, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 1.57 (2H, q, *J* = 6.0 Hz, -CH<sub>2</sub>(CH<sub>2</sub>)<sub>9</sub>CH<sub>3</sub>), 2.10 (1H, m, -NCH<sub>2</sub>CH<sub>*a*H<sub>b</sub>CH<sub>2</sub>-), 2.23 (1H, m, -NCH<sub>2</sub>CH<sub>*a*H<sub>b</sub>CH<sub>2</sub>-), 2.97 (1H, dt, *J* = 18, 9.0 Hz, -NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>H<sub>b</sub>-), 3.32 (1H, ddd, *J* = 18, 8.5, 3.0 Hz, -NCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>H<sub>b</sub>-), 3.66 (1H, dt, *J* = 9.5, 7.5 Hz, -NCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 3.76 (3H, s, -CO<sub>2</sub>CH<sub>3</sub>), 3.81 (1H, m, -NCH<sub>a</sub>H<sub>b</sub>CH<sub>2</sub>-), 4.39 (1H, t, *J* = 5.5 Hz, -NHCH-), 8.53(1H, br s, -NH-). <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD): δ (ppm) 14.4, 22.9, 23.7, 25.1, 30.3, 30.5, 30.6, 30.66, 30.74, 31.8, 33.1, 37.4, 48.9, 51.3, 52.1, 103.2, 152.7, 153.1, 166.6. HRMS (ESI, positive): calcd. For C<sub>20</sub>H<sub>36</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>, 350.2802; found, 350.2809.</sub></sub>



(+)-epoxide *ent*-6: This reaction was performed according to the reported procedure. To a solution of (R,R)-salan ligand (ent-7) (1.80 g, 3.34 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (45 mL) were added freshly distilled Ti(O-*i*Pr)<sub>4</sub> (0.90 mL, 3.0 mmol) at room temperature under N<sub>2</sub> atmosphere. After being stirred at room temperature for 1 h, to the reaction mixture was added 4,4'-thiobis(6-tert-butyl-m-cresol) (704 mg, 1.96 mmol), pH 7.4 phosphate buffer (3.8 mL), envne 5 (7.61 g, 30.4 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (31 mL), and 30% H<sub>2</sub>O<sub>2</sub> (7.0 mL, 61 mmol) under N<sub>2</sub> atmosphere. After being stirred at 40 °C for 5 h, the reaction mixture was allowed to cool to room temperature and to the reaction mixture was added solid NH<sub>4</sub>Cl (11 g). The resulting mixture was filtered through a pad of Celite<sup>®</sup> (eluted with hexane), and the filtrate was washed with sat. NH<sub>4</sub>Cl solution (50 mL x 3). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/Et<sub>2</sub>O = 2/1) to afford (+)-epoxide ent-6 (6.85 g, 85%, 95% ee) as a yellow solid. Recrystallization from hexane afforded (+)-epoxide ent-6 (5.00 g, 73% yield, >99% ee) as a pale yellow solid. Enantiomeric excess was determined by chiral HPLC analysis of the corresponding *p*-nitrobenzoate derived from (+)-epoxide ent-6. Chiral HPLC analysis (CHIRALPAK AS-H column, hexane/2-propanol = 9/1, flow rate = 0.50 mL/min, detection 270-nm light, 30 °C)  $t_{\rm R}$  = 16.5 min (minor isomer), 18.3 min (major isomer).

mp: 48 °C.  $[\alpha]_D^{30}$  +8.96 (*c* 1.01, CHCl<sub>3</sub>) for >99% ee. Anal. Calcd for C<sub>17</sub>H<sub>30</sub>O<sub>2</sub>: C, 76.64; H, 11.35. Found: C, 76.61; H, 11.20. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (–)-epoxide **6**.



To a solution of epoxide ent-6 (2.0 g, 7.5 mmol) in dry MeOH (80 mL) (+)-aziridine *ent*-9: was added NaN<sub>3</sub> (4.0 g, 62 mmol) at room temperature. After being stirred vigorously for 44 h at room temperature, to the reaction mixture was added water (80 mL). The resulting mixture was extracted with EtOAc (100 mL x 3). The combined organic layer was washed with brine (200 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure to provide crude azide. The crude azide was dried azeotropically with toluene (20 mL x 2), and dissolved in dry DMF (110 mL), and then PPh<sub>3</sub> (4.0 g, 15 mmol) was added to the solution. After being stirred for 5 h at 80 °C, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (60 mL), and then to the solution were added imidazole (1.1 g, 16 mmol) and TBDPSCI (2.2 mL, 12 mmol) at 0 °C. After being stirred for 20 min at room temperature, the reaction was quenched with sat.  $NH_4Cl$  solution (60 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (60 mL x 2). The combined organic layer was washed with water (120 mL) and brine (120 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced The residue was purified by neutral silica gel flash column chromatography pressure. (hexane/EtOAc/CH<sub>2</sub>Cl<sub>2</sub> = 30/1/1 with 1% *i*-Pr<sub>2</sub>NH to 20/1/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (+)-aziridine ent-9 (1.89 g, 50% in 3 steps) as a colorless oil.

 $[\alpha]_D^{31}$  +5.65 (*c* 1.26, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>33</sub>H<sub>50</sub>NOSi [M+H]<sup>+</sup>, 504.3656; found, 504.3681. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (–)-aziridine **9**.



(-)-guanidino-aziridine *ent*-10: To a solution of aziridine *ent*-9 (1.89 g, 3.77 mmol), Boc,Cbz-methylisothiourea (1.3 g, 4.0 mmol), and dry  $Et_3N$  (5.3 mL, 38 mmol) in dry DMF (38 mL) was added HgCl<sub>2</sub> (1.1 g, 4.1 mmol) at room temperature. After being stirred for 3h at room temperature, the reaction mixture was diluted with EtOAc (40 mL), and then filtered

through a pad of Celite<sup>®</sup> (eluted with EtOAc). The filtrate was washed with water (40 mL x 3), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was diluted with EtOAc (20 mL) filtered through a pad of Celite<sup>®</sup> (eluted with EtOAc) and concentrated under reduced pressure. The filtrate was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 19/1 with 1% *i*-Pr<sub>2</sub>NH) and concentrated under reduced pressure. The residue was diluted with hexane/Et<sub>2</sub>O = 1/1 (20 mL) and then filtered through a pad of Celite<sup>®</sup> (eluted with hexane/Et<sub>2</sub>O = 1/1) to afford (–)-guanidino-aziridine *ent*-**10** (2.80 g, 96%) as a yellow oil.

 $[\alpha]_D^{30}$  –45.5 (*c* 1.27, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>47</sub>H<sub>66</sub>N<sub>3</sub>O<sub>5</sub>Si [M+H]<sup>+</sup>, 780.4766; found, 780.4761. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-guanidino-aziridine **10**.



(+)-alcohol *ent*-11: To a mixture of guanidino-aziridine *ent*-10 (2.80 g, 3.59 mmol), Pd(PPh<sub>3</sub>)<sub>4</sub> (207 mg, 0.179 mmol), and InI (1.3 g, 5.4 mmol) were added a degassed solution of dry THF (25 mL), dry HMPA (6.3 mL), and formalin (0.48 mL, 6.4 mmol, 37% solution) at room temperature under the argon atmosphere. After being stirred for 1 h at room temperature, the solution was passed through a short pad of neutral flash silica gel (eluted with EtOAc with 1% *i*-Pr<sub>2</sub>NH), and the resulting solution was washed with water (100 mL x 3) and brine (100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified twice by neutral silica gel flash column chromatography (hexane/Et<sub>2</sub>O = 4/1 with 1% *i*-Pr<sub>2</sub>NH to hexane/Et<sub>2</sub>O = 1/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (+)-alcohol *ent*-11 (2.33 g, 80%, dr = >95:<5 determined by <sup>1</sup>H NMR analysis of diol *ent*-13) as a yellow oil.

 $[\alpha]_D^{30}$  +5.21 (*c* 1.01, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>48</sub>H<sub>69</sub>N<sub>3</sub>O<sub>6</sub>SiNa [M+Na]<sup>+</sup>, 834.4848; found, 834.4855. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (–)-alcohol **11**.



(-)-alcohol ent-12: To a solution of alcohol ent-11 (2.33 g, 2.87 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (75 mL) were added Et<sub>3</sub>N (6.4 mL), Ac<sub>2</sub>O (6.4 mL), and DMAP (35 mg, 0.286 mmol) at room temperature. After being stirred for 1 h at room temperature, the reaction mixture was concentrated under reduced pressure with toluene/MeOH (2/1, 20 mL), and then dried azeotropically with toluene/MeOH (2/1, 20 mL x2) to provide crude acetate. The residue of the acetate was dissolved in dry THF (75 mL), and then TBAF (8.6 mL, 8.6 mmol, 1.0 M solution in THF) was added at room temperature. After being stirred for 13 h at room temperature, to the reaction mixture was added TBAF (1.0 mL, 1.0 mmol). After being stirred for 4.5 h at room temperature, to the reaction mixture was added TBAF (1.0 mL, 1.0 After being stirred for 15 min at room temperature, the reaction was quenched with mmol). brine (70 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (70 mL x 3). The combined organic layer was dried over anhydrous  $Na_2SO_4$ , and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 3/1 with 1% *i*-Pr<sub>2</sub>NH) and then repurified by neutral silica gel flash column chromatography (hexane/EtOAc = 6/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (-)-alcohol ent-12 (1.61 g, 91% in 2 steps) as a pale yellow oil.

 $[\alpha]_D^{31}$  –36.8 (*c* 1.04, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>34</sub>H<sub>53</sub>N<sub>3</sub>O<sub>7</sub>Na [M+Na]<sup>+</sup>, 638.3776; found, 638.3767. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-alcohol **12**.



(-)-*spiro*-hemiaminal *ent*-14: A solution of alcohol *ent*-12 (1.69 g, 2.74 mmol) in dry  $CH_2Cl_2$  (50 mL) and TFA (5 mL) was stirred for 2.5 h at room temperature and then the reaction mixture was concentrated under reduced pressure with toluene/MeOH (2/1, 40 mL).

The residue was dried azeotropically with toluene/MeOH (2/1, 20 mL x2) to provide crude alcohol *ent*-**13**. The residue was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub>/H<sub>2</sub>O (330 mL, 1/1), and then K<sub>2</sub>CO<sub>3</sub> (2.24 g, 16.2 mmol) was added. To a vigorously stirred mixture was added PyHBr<sub>3</sub> (2.59 g, 8.09 mmol). After being stirred for 30 min at room temperature, the reaction was quenched with sat. Na<sub>2</sub>SO<sub>3</sub> solution (150 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (200 mL x 2). The combined organic layer was washed with water (400 mL) and brine (400 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 5/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (–)-*spiro*-hemiaminal *ent*-**14** (1.12 g, 62%, dr = >95:<5 determined by <sup>1</sup>H NMR analysis) as a pale yellow oil.

 $[\alpha]_D^{31}$  –116 (*c* 1.06, CHCl<sub>3</sub>). Anal. Calcd for C<sub>29</sub>H<sub>43</sub>N<sub>3</sub>O<sub>5</sub>Br<sub>2</sub>: C, 51.72; H, 6.44; N, 6.24. Found: C, 52.01; H, 6.27; N, 6.31. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-*spiro*-hemiaminal 14.



(-)-*spiro*-hemiaminal *ent*-15: To a solution of *spiro*-hemiaminal *ent*-14 (1.12 g, 1.66 mmol) and *n*-Bu<sub>3</sub>SnH (2.2 mL, 8.18 mmol) in dry toluene (18 mL) were added Et<sub>3</sub>B (0.85 mL, 0.85 mmol, 1.0 M solution in hexane) and air (1 mL) at room temperature. After being stirred for 4.5 h at room temperature, the solution was passed through a short pad of neutral flash silica gel (eluted with EtOAc) and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 5/1 with 1% *i*-Pr<sub>2</sub>NH to 1/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (-)-*spiro*-hemiaminal *ent*-15 (830 mg, 97%) as a pale yellow oil.

 $[\alpha]_D{}^{31}$  –79.7 (*c* 0.98, CHCl<sub>3</sub>). Anal. Calcd for C<sub>29</sub>H<sub>45</sub>N<sub>3</sub>O<sub>5</sub>: C, 67.54; H, 8.80; N, 8.15. Found: C, 67.46; H, 8.70; N, 8.28. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-*spiro*-hemiaminal **15**.



(-)-common intermediate *ent*-16: To a solution of *spiro*-hemiaminal *ent*-15 (829 mg, 1.61 mmol) in MeOH (50 mL) was added K<sub>2</sub>CO<sub>3</sub> (222 mg, 1.61 mmol) at room temperature. After being stirred for 1 h at room temperature, the reaction was quenched with sat. NH<sub>4</sub>Cl solution (50 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (50 mL x 2). The combined organic layer was washed with water (100 mL) and brine (100 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (EtOAc with 1% *i*-Pr<sub>2</sub>NH to CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (–)-common intermediate *ent*-16 (692 mg, 91%) as a pale yellow oil.

 $[\alpha]_D^{30}$  –82.6 (*c* 0.99, CHCl<sub>3</sub>). Anal. Calcd for C<sub>27</sub>H<sub>43</sub>N<sub>3</sub>O<sub>4</sub>: C, 68.47; H, 9.15; N, 8.87. Found: C, 68.22; H, 9.21; N, 8.86. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-common intermediate **16**.



(-)-crambescin B carboxylic acid (*ent-2*): To a solution of common intermediate *ent-16* (33.5 mg, 0.0707 mmol) in acetone (3 mL) was added 2.5 M Jones reagent (100  $\mu$ L) at 0 °C. After being stirred for 15 min at 0 °C, the reaction was quenched with 2-propanol (0.5 mL) and H<sub>2</sub>O (3 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 20/1 with 1% *i*-Pr<sub>2</sub>NH) to afford carboxylic acid (45.3 mg) as a white solid. Carboxylic acid (45.3 mg), 10% Pd-C (19.2 mg), and MeOH (6 mL) were placed in a recovery flask (20 mL) connected to an inlet adaptor with three way-stopcock. The atmosphere of the reaction vessel was replaced by hydrogen (1.0 atm). After being stirred for 15 min at room temperature, the catalyst was filtered off through a pad of Celite<sup>®</sup> (eluted with MeOH), and then the filtrate was concentrated under reduced pressure. The residue gel flash

column chromatography (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 1/1 with 1% *i*-Pr<sub>2</sub>NH) to afford (–)-crambescin B carboxylic acid (*ent*-**2**) (23.6 mg, 94% in 2 steps) as a colorless oil.

 $[\alpha]_D{}^{30}$  –75.9 (*c* 1.06, MeOH). HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>36</sub>N<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup>, 354.2751; found, 354.2738. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-crambescin B carboxylic acid (**2**).



(-)-crambescin B decarboxylate (*ent*-17): A solution of crambescin B carboxylic acid (*ent*-2) (7.1 mg, 0.020 mmol) in MeOH (4 mL) was stirred for 24 h at room temperature and then to the reaction mixture was added *i*-Pr<sub>2</sub>NH (0.5 mL). After being stirred for 24 h at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by Chromatorex DNH silica gel column chromatography (EtOAc to CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 9/1 to MeOH) to afford (–)-crambescin B decarboxylate (*ent*-17) (7.2 mg, 96 %) as a colorless oil.

 $[\alpha]_D^{26}$  -76.1 (*c* 0.11, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>18</sub>H<sub>36</sub>N<sub>3</sub>O [M+H]<sup>+</sup>, 310.2853; found, 310.2856. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-crambescin B decarboxylate (**17**).



(+)-enal *ent*-18: To a solution of common intermediate *ent*-16 (295 mg, 0.623 mmol) and TEMPO (20 mg, 0.13 mmol) in dry  $CH_2Cl_2$  (40 mL) was added  $PhI(OAc)_2$  (501 mg, 1.56 mmol) at room temperature. After being stirred for 7 h at room temperature, the reaction was quenched with sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution (40 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (40 mL x 3). The combined organic layer was washed with water (120 mL) and brine (120 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash

column chromatography (hexane/EtOAc = 2/1 with 1% *i*-Pr<sub>2</sub>NH to 1/1 with 1% *i*-Pr<sub>2</sub>NH to EtOAc with 1% *i*-Pr<sub>2</sub>NH) to afford (+)-enal *ent*-**18** (242 mg, 82%) as a brown oil.

 $[\alpha]_{D}^{29}$  +19.9 (*c* 1.00, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>27</sub>H<sub>42</sub>N<sub>3</sub>O<sub>4</sub> [M+H]<sup>+</sup>, 472.3170; found, 472.3186. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (–)-enal **18** (242 mg, 82%).



(-)-guanidine *ent*-19: To a solution of enal *ent*-18 (50.6 mg, 0.107 mmol) in MeOH (10 mL) was added distilled DBU (ca. 30  $\mu$ L, 0.20 mmol) at room temperature. After being stirred for 18 h, the reaction was quenched with 1 M HCl (10 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic layer was washed with brine (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (EtOAc to CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 1/1) to afford (-)-guanidine *ent*-19 (34.1 mg) as a yellow oil.

 $[\alpha]_D^{28}$  –24.7 (*c* 1.71, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>36</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>, 338.2802; found, 338.2808. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-guanidine **19**.

(–)-crambescin C carboxylic acid (*ent-3*): To a solution of guanidine *ent-19* (34.1 mg) in *t*-BuOH (9 mL) and 2-methyl-2-butene (0.65 mL, 6.12 mmol) was added a solution of NaClO<sub>2</sub> (91.4 mg, 1.01 mmol) and NaH<sub>2</sub>PO<sub>4</sub> (242 mg, 2.02 mmol) in H<sub>2</sub>O (3 mL) at room temperature. After being stirred for 12 h, the reaction was quenched with sat. NaHSO<sub>3</sub> (10 mL) and brine (10 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (30 mL x 2). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by HPLC on Nomura Chemical ODS-HG-5 monitored by UV detector (4.6 x 250 mm, 0.013 M TFA/MeCN, 1.0 mL/min, 220 nm) to afford (–)-crambescin C carboxylic acid (*ent-3*) (9.5 mg, 25% in 2 steps) as a colorless oil.

 $[\alpha]_D^{26}$  –46.3 (*c* 0.48, MeOH). HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>36</sub>N<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup>, 354.2751; found, 354.2757. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-crambescin C carboxylic acid (**3**).



(-)-pyrrolidine *ent*-20: To a solution of enal *ent*-18 (157 mg, 0.333 mmol) and Et<sub>3</sub>N (100  $\mu$ L, 0.717 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (16 mL) was added MsCl (50  $\mu$ L, 0.65 mmol) at room temperature. After being stirred for 10 min at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (hexane/EtOAc = 2/1) to afford (-)-pyrrolidine *ent*-20 (77.7 mg, 51%) as a colorless oil.

 $[\alpha]_D^{28}$  –12.7 (*c* 0.86, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>27</sub>H<sub>40</sub>N<sub>3</sub>O<sub>3</sub> [M+H]<sup>+</sup>, 454.3064; found, 454.3071. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-pyrrolidine **20**.



(-)-guanidine *ent*-21: To a solution of pyrrolidine *ent*-20 (17.2 mg, 0.0379 mmol) in glyme (2 mL) and H<sub>2</sub>O (1.3 mL) was added to Ba(OH)<sub>2</sub>·8H<sub>2</sub>O (157 mg, 0.498 mmol) at room temperature. After being stirred for 7.5 h at 80 °C, the reaction mixture was added H<sub>2</sub>O (5 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (10 mL x 2). The combined organic layer was washed with brine (20 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by neutral silica gel flash column chromatography (EtOAc to CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 5/1 to MeOH to MeOH with 1% CH<sub>3</sub>COOH) to afford (–)-guanidine *ent*-21 (7.0 mg) as a pale yellow oil.  $[\alpha]_D^{27}$  –50.6 (*c* 0.33, CHCl<sub>3</sub>). HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>34</sub>N<sub>3</sub>O [M+H]<sup>+</sup>, 320.2696; found, 320.2708. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-guanidine 21.

(-)-crambescin A carboxylic acid (*ent*-1): To a solution of guanidine *ent*-21 (7.0 mg) in *t*-BuOH (1.5 mL) and 2-methyl-2-butene (130  $\mu$ L, 1.22 mmol) was added a solution of NaClO<sub>2</sub> (18.4 mg, 0.203 mmol) and NaH<sub>2</sub>PO<sub>4</sub> (48.4 mg, 0.403 mmol) in H<sub>2</sub>O (0.5 mL) at

room temperature. After being stirred for 12 h, the reaction was quenched with sat. NaHSO<sub>3</sub> (2 mL) and brine (2 mL). The resulting mixture was partitioned, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The residue was purified by HPLC on Nomura Chemical ODS-HG-5 monitored by UV detector (4.6 x 250 mm, 0.013 M TFA/MeCN, 1.0 mL/min, 220 nm) to afford (–)-crambescin A carboxylic acid (*ent*-1) (2.2 mg, 17% in 2 steps) as a colorless oil.

 $[\alpha]_D^{28}$  –53.9 (*c* 0.11, MeOH). HRMS (ESI, positive): calcd. For C<sub>19</sub>H<sub>34</sub>N<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>, 336.2646; found, 336.2654. IR, <sup>1</sup>H-NMR, and <sup>13</sup>C-NMR data were in agreement with those of (+)-crambescin A carboxylic acid (1).


Stability of crambescin B carboxylic acid (2) and its methyl ester (23)

Decarboxylation of **2** (ca. 5 mg) into crambescin B decarboxylate **17** was monitored by <sup>1</sup>H NMR analysis at room temperature in CD<sub>3</sub>OD (0.75 mL) in the presence of 6-10% of H<sub>2</sub>SO<sub>4</sub>, CH<sub>3</sub>COOH, or i-Pr<sub>2</sub>NH.



## Stability of crambescin B methyl ester (23)

Transformation of **23** (ca. 5 mg) into crambescin C methyl ester **25** was monitored by <sup>1</sup>H NMR analysis at room temperature in CD<sub>3</sub>OD (0.75 mL) in the presence of 6-10% of CF<sub>3</sub>COOH, CH<sub>3</sub>COOH, or Et<sub>3</sub>N.



Current Data Parameters NAME nakane-B400 EXPNO 157 PROCNO 2	F2 - Acquisition Parameters Date 20160316 Time 19.40 NISTRUM spect PROBHD 5 mm QNP 1H/13 PULPROG 2gpg30 TD 65536 SOLVENT CDC13 NS 200 DS 2 SWH 23980.814 Hz FIDRES 0.365918 Hz AQ 1.3664256 sec RG 2580.3 DW 20.850 usec DE 6.50 usec DE 6.50 usec D1 2.0000000 sec D11 0.03000000 sec D11 0.03000000 sec D11 0.03000000 sec D11 2.0000000 sec D11 2.0000000 sec D11 2.0000000 sec D11 2.0000000 sec D11 1.30 usec D11 1.30 usec D11 1.200 usec P1 1.50 dB	SFOI         100.6228298 MHz           CPDPRG[2         waltz16           CPDPRG[2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL2         10.30 dB           PL12         25.00 dB           PL13         25.00 dB           PL13         25.00 dB           PL13         25.00 dB	F2 - Processing parameters SI 32768 SF 100.6127706 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	H <sub>3</sub> C <sub>V</sub>	aldehyde <b>S1</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
					udd
60 <sup>-</sup> 77 20 <sup>-</sup> 27 00 <sup>-</sup> 77					20
51'62 56'30 56'30 56'30 56'30					30
88.15 88.15				and the second state of th	40
00 27					50
				in one internet in the second	09
89'94 ~					
00'LL ZE'LL					08
					06
				y na shan sha sha	001
				الم من الم من الم عن الم الم من الم الم الم الم الم الم الم من الم الم الم الم الم الم الم	011
				and the first second	
					130
					140
					151

	160
	170
	180
بببطيب	<i>061</i>
	200

ren e d'Ara (d'Ara a d'Ara d'Ara d'Ara d'Ara d'Ara d'A Ara de Ara de







_	160
	170
_	180
	190
	200
	210

المراجعة ال محمد مراجعة المراجعة ا



exp9 std1h

. .

MPLE	Jan 31 14	CDC13	exp	NOILIS	299.967	H1	3.748	33728	4499.5	2250	316	11.0	0.252	149.3	16	16	¢	not used	AGS	ជ	ជ	ጽ	PLAY	-300.0	3599.5	1344	•	400	9.00	9206.30	2777.7	2177.8	7	1.000	цц
SAU	date	solvent	file	ACQUI	sfrq		at	đr	MS	ţ	þs	мđ	đl	tof	пt	ct	alock	gain	FL	Γŗ	in	đp	DIS	đs	đim	VS	50	MC	mmzd	18	rfl	rfp	tћ	ins	ai cđc

& VT	299.957	HI	-10000.0	uuu	υ	200	<b>SNISS</b>		ft	not used	react	olist('ent~	process_J~	2132')		
DEC.	đfrq	đn	dof	din	dmn	dmf	PROCI	wtfile	proc	fn	WOLL	wexp auto	erJ', 'hl.		wbs	writ



S42

Current Data Parameters NAME nakane-B400 EXPNO 163 PROCNO 2	F2 - Acquisition Parameters         Date       20160406         Time       17.39         INSTRUM       spect         PROBHD       5 mm QNP 1H/13         PULPROG       zgpg30         TD       65536         SOLVENT       CDCl3         NS       20         SOLVENT       CDCl3         NS       200         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664256 sec         RG       2580.3         DW       20.850 usec         DW       20.850 usec         DI       1.00000000 sec         D1       0.03000000 sec         D1       0.03000000 sec	CHANNEL f1 NUC1 13C P1 12.00 usec PL1 7.50 dB SFO1 100.6228298 MHz	CHANNEL f2         CHANNEL f2           CPDPRG[2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL12         10.30 dB           PL12         25.00 dB           PL13         25.00 dB           PL13         25.00 dB           PL13         25.00 dB           PL13         25.00 dB	F2 - Processing parameters SI 32768 SF 100.6127706 MHz WDW EM SSB 0 1.00 Hz GB 0 1.40 PC 1.40	H <sub>3</sub> C + M	<i>cis</i> -iodoalkene <b>S3</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						<i>mdd</i>
						,
01.41						<i>01</i>
55.68 50.33 50.33 50.33 50.33						0 20
\$5'62 29'62 06'18 69'78				<u> </u>		40 3
						50
						0 00
L9'9L 66'9L 15'LL 90'78			· _, · · ———	<u></u>		50 Z
<i>y</i> , <i>c</i>						06
					and in the second of the se	100
					a a de la constante de la const La constante de la constante de	110 20 110
						130 1.
64.141						140







Current Data Parameters NAME nakane-A400 EXPNO 106 PROCNO 2	F2 - Acquisition ParametersDate20160407Time11.08Diste20160407Time11.08INSTRUMspectPROBHD5 mm QNP 1H/13PULPROG55336SOLVENT65536SOLVENT65536SOLVENT0.365918 HzNS300DS2SWH23980.814 HzFIDRES0.365918 HzAQ1.3664256 secRG16384DW20.850 usecDI1.3664256 secRG16384DW20.850 usecDI1.0000000 secDI1.00000000 secDI1.0000000 secDI10.000000 secPLW1-1.00000000 WSFO2400.1316005 MHzNUC21HCPDPRG[2waltz16PCPD280.00 usec	PLW2 -1.0000000 W PLW12 -1.0000000 W PLW13 -1.00000000 W F2 - Processing parameters SI 32768 SF 100.6127704 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	enyne <b>5</b> <sup>0H</sup> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
01.41			الم	udd 0 0I
23.97 29.65 20.65 20.55				0 40 30 20
			a (table to be a state of the s	70 60 50
91.06 —			and the second secon	08 06
£7.801 ——			وها ها المراجعة ا ما ما ما مواجعة المراجعة المراجع	120 110 100
٤٢.٤٩١			المحاطية ال محمد المحاطية	140 130

ببياييت	160
	170
	180
	190
	200
وتقاربهم والمحمد	210





	Current Data Parameters NAME nakane-n400 EXPNO 210 PROCNO 2	F2 - Acquisition Parameters Date 20150206 Time 16.56 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG zgpg30 TD 65536 SOLVENT CDCl3 NS 262	DS2SWH23980.814 HzSWH23980.814 HzFIDRES0.365918 HzAQ1.3664756 secRG1.3664756 secBW20.850 usecDW20.850 usecDE30.00 usecTE300.0 KD11.0000000 secd110.03000000 secd120.0002000 sec	CHANNEL f1	CHANNEL f2           CPDPRG2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL2         -4.50 dB           PL12         14.87 dB           PL13         14.80 dB           PL13         14.80 dB           PL13         14.80 dB           PL13         14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	OH (–)-epoxide <b>6</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
	01'+1 257.67					· 	الم الح الحالي الم	mdd 01 0;
29.62	16 65 16 65 16 65 26 65 27 67 25 67 29 67 06 18				<b></b>			0 30 2
	££.23						edult a set of the set	50 4
	¢6'09 ——							09
	69 <sup>.9</sup> <i>L</i> 00 <sup>.</sup> <i>LL</i>						A B A A A A A A A A A A A A A A A A A A	0 70
	87.28							8 06
								6 001
							्रम् हे जन्म हो हो है प्रस्तित के प्रसिद्ध के स्टब्स्	011
							يان من المارينيانيانيانيانيانيانيانيانيانيانيانيانيا	120
								130
							المريد المريد محمد المريد ال محمد المريد ال	140
							in the second	
								0 100
							भारतात्वा क्यांत्वा होते. संस्थानिक स्थापनि स्थिति संस्थानिक स्थापनि स्थापनि स्थापनि स्थापनि स्थापनि स्थापनि स्थापनि स्थापनि स्थापनि स्थाप	80 17
							in a dia ang ina dia ang in Ang ina dia ang ina dia ang Ang ina dia ang	RI 061
							ta parts and that had	200 1
					,		العام المالية المالية والمالية المالية المالية والمالية المالية المالي	210
				S47				



S48

Current Data Parameters NAME nakane-n400 EXPNO 242 PROCNO 2	F2 - Acquisition Parameters         Date       20150210         Time       9.53         INSTRUM       av400         PROBHD       5 mm QNP 1H/13         PULPROG       zgpg30         TD       65536         SOLVENT       CDCl3         NS       760         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         RG       1.3664756 sec         DW       20.850 usec         DW       20.850 usec         DI       1.0000000 sec         d11       0.03000000 sec         d12       0.00002000 sec	CHANNEL fl NUC1 13C P1 9.00 usec PL1 -3.00 dB SFO1 100.6228298 MHz	CHANNEL f2           CHANNEL f2           CPDPRG2         waltz16           NUC2         1H         P           PCPD2         80.00 usec         PL2         -4.50 dB           PL12         14.87 dB         PL13         14.80 dB           PL13         14.80 dB         PL13         SFO2         400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )9	(–)-epoxide <b>S4</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
11.41						<i>10</i>
537.68 57.68 57.68 57.68 57.68 57.74 57.74						20
567 567 567 567 567 567 567						30 30
						40
٢٥.8٤						0 50
65.26				<del></del>		9 0 <u>/</u>
27.67 27						80
96.68						06
					and the second se	<b>100</b>
						110
					a la provincia de la companya de la La companya de la comp	120
89'LZI 89'6ZI 1S'SEI †S'SEI						130
						140
						150

		и 1.1.1.4.1.4.4.4.4.4. мрия прия лачи 2.00
	S49	



Current Data Parameters NAME nakane-n400 EXPNO 175 PROCNO 2	F2 - Acquisition Parameters         Date       20150113         Time       21.26         INSTRUM       av400         PROBHD       5 mm QNP 1H/13         PULPROG       230536         SOLVENT       cS536         SOLVENT       CDC13         NS       125         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         RG       16384         DW       20.850 usec         DW       20.850 usec         DW       20.850 usec         DI       2.0000000 sec         d11       0.03000000 sec         d12       0.00002000 sec	CHANNEL fi	CHANNEL f2           CPDPRG2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL12         -4.50 dB           PL12         14.87 dB           PL13         14.80 dB           PL13         14.80 dB           SFO2         400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127722 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )	<ul> <li>OTBDPS</li> <li>(+)-allene S5</li> <li><sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)</li> </ul>
01'\$1 16'10 10'\$0						50 40 30 20 10 Ppn
22.22 76.68 76.68 76.68 76.68 76.68		· · · · · ·				09 02 08 06
68'66 —			 			

ļ

₱*L*'661 ——



Current Data Parameters NAME nakane-n400 EXPNO 181 PROCNO 2	F2 - Acquisition Parameters         Date       20150115         Time       13.13         INSTRUM       av400         PROBHD       5 mm QNP 1H/13         PULPROG       zgpg30         TD       65536         SOLVENT       CDCl3         NS       703         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         DW       20.850 usec         DW       20.850 usec         DW       20.00 usec         DI       2.0000000 sec         d11       0.0300000 sec         d12       0.00002000 sec	CHANNEL f1	CHANNEL f2           CPDPRG2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL2         -4.50 dB           PL12         14.87 dB           PL13         14.80 dB           PL13         14.80 dB           SFO2         400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127715 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	OTBDPS (+)-MTPA ester <b>S6a</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						udd
11'†1 - \$8'81 -						10
- 16'19 - 55'98 - 52'55 - 52'55 - 56'85						20
567 567 567 567 567 567						30
16.1E E0.4E 17.9E						40
۲٤.٤٤						50
				_		609
96.97 89.97 00.77 22.77		- <u>-</u>				80 × 20
				-		06
tl.99.14						<i>001</i>
						110
57.721						120
90 801 50 201 50 200 50 200						130
es sei						) 140
					Ĩ	150





				•		
Current Data Parameters NAME nakane-n400 EXPNO 178 PROCNO 2	F2 - Acquisition Parameters         Date       20150115         Time       11.37         NNSTRUM       av400         PROBHD       5 mm QNP 1H/13         PULPROG       zgpg30         TD       65536         SOLVENT       CDCl3         NS       1220         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         RG       16384         DW       20.850 usec         DE       30.00 usec         TE       300.00 sec         d11       0.03000000 sec         d12       0.0000000 sec	CHANNEL f1 NUC1 13C P1 9.00 usec PL1 -3.00 dB SF01 100.6228298 MHz	CPDPRG2         waltz16           CPDPRG2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL2         -4.50 dB           PL12         14.87 dB           PL13         14.80 dB           PL13         14.80 dB           PL13         14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> E <sub>3</sub> C OMe	(+)-MTPA ester <b>S6b</b>
						<i>udd</i>
11.41 68.61						<b>0</b> 1
						20
51.62 52.25.24 52.25.24 50.25 50.			_			30
19.67						40
						50
22.38						09
11'92 -						<b>0</b> 2
00'LL 2E'LL						80
68						06
SZ 66 ———						00I
						011
- 157.31 						120
12751 12751 12751 12751						
78 221 -/ ES'SEI -						0 140





Current Data Parameters NAME nakane-n400 EXPNO 216 PROCNO 2	F2 - Acquisition Parameters Date 20150209 Time 20104 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG 2336 SOLVENT 655356 SOLVENT 076 SOLVENT 07	OTBDPS (-)-aziridine 9 <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
01'+1 16'10 25'62 55'62 59'28 50'78 50'78		50 40 30 20 10 ppm
05.50 09.29 09.29 00.77 02.77 02.77 78.83 78.83		0 100 90 80 70 60
+9.721 +9.721 +133.69 +21 +2.25.65 +2.25 +		0 140 130 120 110





Current Data Parameters NAME nakane-n400 EXPNO 218 PROCNO 2	F2 - Acquisition Parameters         Date       20150206         Time       23.13         INSTRUM       av400         PROBHD       5 mm QNP 1H/13         PULPROG       zgpg30         TD       65536         SOLVENT       CDCl3         NS       2400         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         NK       20.850 usec         DW       20.850 usec         DW       20.850 usec         DI       1.0000000 sec         d11       0.03000000 sec         d12       0.00002000 sec	CHANNEL fl NUC1 13C Pl 9.00 usec PL1 -3.00 dB SFO1 100.6228298 MHz	CPDPRG2         waltz16           CPDPRG2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL2         -4.50 dB           PL12         14.87 dB           PL13         14.80 dB           PL13         14.80 dB           SFO2         400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127715 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CbzN NHBoc CH <sub>3</sub> (CH <sub>2</sub> )9	OTBDPS	(+)-guanidino-aziridine <b>10</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
							wdd
- 14.11 - 19.15 - 23.00		· _			and the second		10
50'92 82'92 56'22 29'82							20
26 0C 15 0C 50 27 79 20 79 20							0 30
01.42 0.					and the second se		50 4
Str.79			· · · · · · · · · · · · · · · · · · ·	,	and the second se		60
59°L9					an at a factor of the second secon		70
00 <sup>°</sup> <i>LL</i> 07 <sup>°</sup> <i>LL</i> 76 <sup>°</sup> <i>LL</i> 96 <sup>°</sup> 18		<u> </u>					80
07 68					العامين المراجع المراجع المراجع المراجع		06
					المالية المالي مناطقة المالية ا		100
					الله الله الله الله الله الله الله الله		011 04
							30 12
							140 1
15.841					attanti attanti attanti attanti attanti attanti (†		150

أ تداياتك أ منتظي 160 59.691 -----170 180 190 200 210 (/ S59



Current Data Parameters NAME nakane-n400 EXPNO 224 PROCNO 2	F2 - Acquisition Parameters         Date       20150207         Time       10.58         InsTRUM       av400         PROBHD       5 mm QNP 11H/13         PULPROG       zgpg30         TD       65536         SOLVENT       CDC13         NS       1300         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         DW       20.850 usec         DW       20.850 usec         DE       30.00 usec         TE       300.00 sec         d11       0.0000000 sec         d12       0.00002000 sec	CHANNEL f1	CHANNEL f2           CHANNEL f2           CPDPRG2         waltz16           NUC2         1H         P           PCPD2         80.00 usec         P           PL2         -4.50 dB         P           PL12         14.87 dB         P           PL13         14.80 dB         P           PL13         14.80 dB         P           SFO2         400.1316005 MHz         P	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )9 OH HN CbzN BocHN	OTBDPS (–)-alcohol <b>11</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
11.41 11.41 11.41 11.41 11.41 11.42 11						30 20 10 ppm
97.02 97.02 29.02 10.15 20.02 80.15 20.25 80.15 20.25 80.15 20.25 80.15 20.25 80.15 20.25						60 50 40
12.29 56.99 89.92 00.77 00.77 07.77 0.						90 80 × 70
	· · · · · · · · · · · · · · · · · · ·					(20 <i>110 100</i>
59'ZZI 58'ZZI 19'6ZI 89'EEI 55'5EI 55'9EI						50 140 130 J
00.621						I.



Current Data Parameters NAME nakane-n400 EXPNO 227 PROCNO 227 PROCNO 227 Time 17.14 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG 2g30 TD 65536 SOLVENT CDC13 NS 8 SOLVENT CDC13 NS 8 DS 2 SWH 8278.146 Hz FIDRES 0.126314 Hz AQ 3.9584243 sec RG 3.255 DW 60.400 usec TE 300.0 K D1 1.0000000 sec	CHANNEL f1	F2 - Processing parameters SI 32768 SF 400.1300094 MHz WDW EM SSB 0 LB 0.30 Hz GB 0	PC 1.40 CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> QAc	CbzN	 ppm <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> )
					<u>34.740</u>
		·			<u> 3.452</u> 3.452 3.452 3.452
					<u>1.226</u> w
					<u>11243</u>
					<u>ع.365</u> س
					- - - - - -
					- <u></u> - <u></u> →9£.9
					- ω



	Current Data Parameters NAME nakane-n400 EXPNO 228 PROCNO 2	F2 - Acquisition Parameters Date 20150207 Time 14.19 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG zgpg30 TD 65536 SOLVENT CDC13 NS 500	DS 2 SWH 23980.814 Hz FIDRES 0.365918 Hz AQ 1.3664756 sec RG 1.3664756 sec 16384 DW 20.850 usec 16384 30.00 usec TE 30.00 usec d11 0.03000000 sec d12 0.00002000 sec	CHANNEL fl	CHANNEL f2           CHANNEL f2           CPDPRG2         waltz16           NUC2         1H         H           PCPD2         80.00 usec         PL2         -4.50 dB           PL12         14.87 dB         PL13         14.80 dB           PL13         14.80 dB         PL13         14.80 dB           PL13         14.80 dB         PL13         14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127722 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> OAc HN CbzN BocHN	⊖H (+)-alcohol <b>12</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
							and a set of the set o	udd
	- 14.09							<i>10</i>
	- 23.36							20
	67 67 75 67 95 67 19 67	-						30 30
	ες·οε -// 68·ΙΕ -/ 25·9ε -							40
	20.20							50
	60'19 82'£9 70'29				<del>-</del>			09
	89'9L 00'LL							<i>0</i> 2
	27.£8 79.87 79.87							80
								66
								1001
							and the second se	<i>JII 6</i>
₹ 8 8 6	8'221 8'221 8'271 8'221		s 					9 120
9' L. Z	2.821 7.821 9.821							0 13,
								50 I4

1 P. 1998



Current Data Parameters	NAME nakane-n400 EXPNO 231 PROCNO 2	F2 - Acquisition Parameters Date 20150210 Time 21.17 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG zg30	TD 65536 SOLVENT CDCl3 NS 16 DS 2 SWH 8278.146 Hz FIDRES 0.126314 Hz AQ 3.9584243 sec RG 322.5	DW 60.400 usec DE 6.00 usec TE 300.0 K D1 1.0000000 sec	CHANNEL II           NUC1         1H           P1         8.60 usec           PL1         -4.50 dB           SFO1         400.1324710 MHz	F2 - Processing parameters SI 32768 SF 400.1300094 MHz WDW EM SSB 0	LB 0.30 HZ GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	CbzNNNOBr	(+)-spiro-aminal 14       Ppm       1H NMR (400 MHz, CDCl <sub>3</sub> )
										- 0
										<u>1.637</u> <u>1.124</u> <u>1.124</u> <u>1.124</u> <u>1.124</u>
			х - -							815.0
										<u>0.534</u>
										<u>1.040</u> <u>4</u> <u>1.040</u> <u>4</u>
						-				μΩ <u>(000. T</u>
										<u>863.5</u>



Current Data Parameters NAME nakane-n400 EXPNO 232 PROCNO 2	F2 - Acquisition Parameters         Date       20150207         Time       20.16         INSTRUM       av400         PROBHD       5 mm QNP 1H/13         PULPROG       5 gspg30         TD       65536         SOLVENT       CDCl3         NS       4000         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         RG       16384         DW       20.850 usec         DI       1.00000000 sec         d11       0.03000000 sec         d12       0.00002000 sec	CHANNEL fl NUC1 13C P1 9.00 usec PL1 -3.00 dB SFO1 100.6228298 MHz	CHANNEL f2         CHANNEL f2           CPDPRG2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL12         -4.50 dB           PL12         14.87 dB           PL13         14.80 dB           PL13         14.80 dB           PL13         14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127722 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )9 OAc HN Br CbzN H OAc	(+)- <i>spiro</i> -aminal <b>14</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
					and the second secon	10
						20
						30
25.14						40
\$6`87 L\$`0\$						50
98 <sup>.</sup> 80			• <u>1</u>			<b>09</b>
2010/						2 <b>0</b>
$\begin{array}{c} 00^{\circ}LL \\ 07^{\circ}LL \\ 15^{\circ}LL \end{array} =$						80
						06
L1°E6 ———						001
					and the second secon	, <b>01</b>
						20 1
52.721						) I
15.821						13(
08'9£1						140
						50





10 9

Current Data Parameters NAME nakane-n400 EXPNO 236 PROCNO 2	F2 - Acquisition Parameters         Date       20150209         Time       12.26         INSTRUM       av400         PROBHD       5 mm QNP 1H/13         PULPROG       zgpg30         TD       65536         SOLVENT       CDC13         NS       700         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         RG       16384         DW       20.850 usec         DW       20.850 usec         DI       1.00000000 sec         d11       0.03000000 sec         d12       0.00002000 sec	CHANNEL fl NUC1 13C P1 9.00 usec PL1 -3.00 dB SFO1 100.6228298 MHz	CPDPRG2         Waltz16           CPDPRG2         waltz16           NUC2         1H           PCPD2         80.00 usec           PL2         -4.50 dB           PL12         14.87 dB           PL13         14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127715 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> OAc HN CbzN H CbzN H CbzN H 15	<sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
01'+1 68'07 99'77 29'+7 58'57 15'67 05'67 85'67 95'15 68'15 91'55 60'7+ +2'6+ 						0 50 40 30 20 10 ppm
\$9'09         \$1'99         \$25'99         \$89'92         \$00'22         \$25'22         \$00'24         \$25'24						90 80 20 60
95°LZ1 29°LZ1 29°LZ1 28°Z1					بالمراجع المراجع المراجع والمراجع المراجع المراجع والمراجع المراجع	130 120 110 100
52.751 29.521 26.722					a de la constante de la constan La seconda de la constante de la La seconda de la constante de la	70 160 150 140
						0 200 190 180 13
		S67				210





Current Data Parameters NAME nakane-n400 EXPNO 240 PROCNO 2 F2 - Acquisition Parameters	Date       20150209         Time       12.59         INSTRUM       av400         PROBHD       5 mm QNP 1H/11         PULPROG       zgpg30         TD       65536         SOLVENT       CDC13         NS       500         DS       2         SWH       23980.814 Hz         FIDRES       0.365918 Hz         AQ       1.3664756 sec         RG       16384         DW       20.850 usec         DW       20.850 usec         DE       300.00 usec         DI       1.0000000 sec	d11 0.0300000 sec d12 0.00002000 sec muc1 0.00002000 sec NUC1 13C P1 9.00 usec PL1 -3.00 dB SF01 100.6228298 MHz	CHANNEL f2 == CPDPRG2 waltz16 NUC2 1H PCPD2 80.00 usec PL2 -4.50 dB PL12 14.87 dB PL13 14.80 dB PL13 14.80 dB SFO2 400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127722 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )
					and the second secon
			· · · · · · · · · · · · · · · · · · ·		t tai hita a tai a ta
16 62 67 67 75 67 65 67 95 16					
06.44					
t0.e2					a pi a a han a a su
99.18					
69.97 00.77 22.77					
72.06					
					and a state of the
157.62					
1.761					
0.861				· · · · · · · · · · · · · · · · · · ·	
0.02.601					





Current Data Parameters NAME nakane-n400 EXPNO 252 PROCNO 2	F2 - Acquisition Parameters         Date       20150220         Time       16.48         INSTRUM       av400         PNDLPROG       2gpg30         PULPROG       55536         SOLVENT       CD30D         NS       1000         NS       1000         NS       1000         DS       2         SWH       23980.814 Hz         AQ       1.3664756 sec         RG       16.384         DW       20.850 usec         DI       1.0000000 sec         d11       0.03000000 sec         d11       0.03000000 sec	CHANNEL f1	CHANNEL f2	F2 - Processing parameters SI 32768 SF 100.6126276 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> H <sub>1</sub> H <sub>2</sub> N H	(+)-crambescin B carboxylic acid 2 <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
						udd
C+'+1						<i>10</i>
- 53.73						20
- 30.47 - 30.61 - 20.61 - 20.77 - 32.75						30
L0.5.84 - 91.95 25.84 - 25.84						<b>40</b>
48.79 49.00 12.94 49.00						50
55.67 - 88.67 -						<i>60</i>
18.89						20 20
						80
96.68						<b>6</b> 6
						100
						011
						120
						<b>130</b>
						140
						150





8278.146 Hz 0.126314 Hz 3.9583745 sec 161.3 60.400 usec 6.50 usec 297.2 K 1.0000000 sec F2 - Acquisition Parameters Date\_\_\_\_\_\_20150227 Time\_\_\_\_\_\_\_15.43 INSTRUM spect PROBHD 5 mm QNP 1H/13 PULPROG 2g30 TD 65536 SOLVENT CDC13 NS SOLVENT CDC13 NS DS 227 15.00 usec 10.30 dB 400.1324710 MHz ======= CHANNEL f1 ======= Processing parameters 32768 400.1300095 MHz EM ΗZ 0.30 Current Data Parameters NAME nakane-B400 EXPNO 104 PROCNO 2  $1 \mathrm{H}$ 1.00  $\leftarrow$ 0 0 TD SOLVENT NS DS SWH FIDRES AQ CW D1 TE D1 TD0 I NUC1 PL1 SF01 Р1

10.5 10.0 9.5 9.0 8

S72
Current Data Parameters NAME nakane-B400 EXPNO 105 PROCNO 2	F2 - Acquisition ParametersDate20150227Time15.48InsTRUMspectPROBHD5 mm QNP 11H/13PULPROGzgpg30FD65536SOLVENTCDC13NS538SOLVENT538NS538SOLVENT0.365918 HzAQ1.3664256 secRG2580.3DW20.850 usecDE6.50 usecD11.0000000 secD10.03000000 secTD01	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG[2       waltz16         NUC2       1H       1H         PCPD2       80.00 usec       1L         PL2       10.30 dB       1L12       25.00 dB         PL13       25.00 dB       25.00 dB       2500 dB         PL13       25.00 dB       700.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127709 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	(+)-crambescin B decarboxylate 17 <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						<i>mdd</i>
						0 01
14'10 25'92 57'92 57'92 57'92 58'94						20
05.62 95.62 79.62 18.74 18.74 18.74 18.74 19.70 10.70 10.70 10.70 10.70 10.70 10.70 10.70 10.70 10.70						40 30
87'LE						, 50
۶۵:۵ <i>۷</i>						20 00 L
20°2L 20°2L 20°2S						80
0.00						06 001
						<i>011</i>
						0 120
						140 I3
						20

----- 124.23



يتنبينايين





Current Data Parameters NAME nakane-n400 EXPNO 244 PROCNO 2	F2 - Acquisition Parameters       Date     20150212       Time     17.21       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       FID     65536       SOLVENT     CDC13       NS     1569       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       RG     16384       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       P         PCPD2       80.00 usec       PL         PL2       -4.50 dB       PL         PL12       14.87 dB       PL         PL13       14.80 dB       PL         PL13       14.80 dB       PL         SFO2       400.1316005 MHz       PL	F2 - Processing parameters SI 32768 SF 100.6127744 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> HN	OH (–)-enal <b>18</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
/0.41						<i>10</i>
- 57.64						20
25°52 25°52 25°52 49°62						30
69 06 - 98 16 - 98 -						40
						50
81.09						<i>60</i>
26 <sup>.</sup> 99						2 <b>0</b>
00 <sup>.</sup> <i>LL</i> 02 <sup>.</sup> <i>LL</i>						80
						06
						<b>100</b>
				_		011
						120
128.45						130
136.21						140
						150







Current Data Parameters NAME nakane-n400 EXPNO 246 PROCNO 2	F2 - Acquisition Parameters       Date     20150216       Time     13.21       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CD30D       NS     4480       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       RG     16384       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL fl NUC1 13C P1 9.00 usec PL1 -3.00 dB SFO1 100.6228298 MHz	CPDPRG2 waltz16 CPDPRG2 waltz16 NUC2 1H PCPD2 80.00 usec PL2 -4.50 dB PL12 14.87 dB PL13 14.80 dB SFO2 400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6130243 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )9 HN H2N HN HN H	OH (+)-guanidine <b>19</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
					a statistica da anti-	<b>u</b> dd
- 14.42						<i>01</i>
- 32.43 - 22.43 - 30.45 - 30.58				· · · · · · · · · · · · · · · · · · ·		20
**************************************						30
90'EE - 90'EE - 98'9E - 9E'87 - (5'87 -			-	· · · · · · · · · · · · · · · · · · ·		40
€23 67 						50
27'67 - 67'67 - 81'19 -						60
					arte kaj Kontrak Kontrak Kontrak	02
		3				80
					i porta	06
						<b>100</b>
02.211				_		110
						120
						130 130
						140
04.821						150

86.781 -----معيدارير S77





 $\infty$ 

Current Data Parameters NAME nakane-n400 EXPNO 203 PROCNO 2	F2 - Acquisition Parameters       Date     20150131       Time     17.41       NSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     5536       PULPROG     5536       SOLVENT     CD30D       NS     1293       NS     1293       SOLVENT     CD30D       NS     1293       DS     2       SWH     23980.814 Hz       AQ     1.293       DS     2       SWH     23980.814 Hz       AQ     1.3664756 sec       RG     16384       DW     20.850 usec       DW     20.850 usec       DI     1.20000005 sec       d11     0.03000000 sec       d12     0.0002000 sec       MUC1     13C	PL1     -3.00 dB       SF01     100.6228298 MHz	$CH_{3}(CH_{2})_{9} \xrightarrow{\vdots} 0 \xrightarrow{i} 0 $
\$\mathbf{E}^+ \vee 1\$       \$\mathbf{Z} 23^2 \mathbf{Z} 23^2 \mathb			40 30 20 10 Ppm
25.84 12.04 12.04 14.15 14			Aud by the second state of the product of the product of the second state of the product of the product of the product of the second state of the
78'901			
60'8†I 05'E\$I			Indef       Indef <td< td=""></td<>
86'.291			1900 I 001 01100000000000000000000000000
		S79	210 200



Current Data Parameters NAME nakane-n400 EXPNO 248 PROCNO 2	F2 - Acquisition Parameters       Date     20150216       Time     16.27       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CDCl3       NS     565       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.0300000 sec       d12     0.00002000 sec	CHANNEL fl	CHANNEL f2         CPDPRG2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       -4.50 dB         PL12       14.87 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127729 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub>	(+)-pyrrolidine <b>20</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
60'†1					and a sub-	<i>01</i>
51.143						20
52.62 15.62 54.62 25.62						30
52.9E					and the second se	40
49.29						50
11:76						60
89'9L 00'LL						0L
0777 18.77						80
						<i>06</i>
						<i>001</i>
110.21						<i>011</i>
16'221						120
t/ '961						<b>130</b>
						140
						150



Current Data Parameters NAME nakane-n400 EXPNO 147 PROCNO 2 F2 - Acquisition Parameters Date 20141023 Time 16.36 Date 20141023 Time 16.36 SOLVENT 16.36 SOLVENT 16.36 SOLVENT 16.3536 SOLVENT 16.3536 SOLVENT 16.3536 SOLVENT 16.3536 SOLVENT 16.3536 SOLVENT 16.3536 SOLVENT 16.5336 SOLVENT 16.5336 SOLVENT 16.5336 SOLVENT 16.5336 SOLVENT 16.500 usec E. 3000 K D1 1.0000000 sec T 2. Processing parameters SI 4.500 usec D1 1.0000000 sec T 4.500 usec D1 1.0000000 sec T 4.500 Hz SI 4.00.1324710 MHz SI 4.00.1324710 MHz SI 4.00.1324710 MHz SI 0.030 Hz SI 0.030 Hz CH3CO <sup>2</sup> H <sub>2</sub> N <sup>+</sup> <sup></sup>	<sup>1</sup> H NMR (400 MHz, CD <sub>3</sub> OD)
	unda
	<u>3,5773</u>
	<u>5.207</u>
	3.612 w
	<u>650.1</u>



Current Data Parameters NAME nakane-n400 EXPNO 148 PROCNO 2	F2 - Acquisition Parameters       Date     20141023       Time     16.51       INSTRUM     av400       PROBHD     5 mm QNP 11H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CD30D       NS     2865       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       DW     20.865 usec       DW     20.850 usec       DW     20.00 usec       TE     30.00 usec       DI     2.0000000 sec       d11     0.03000000 sec	CHANNEL f1	CPDPRG2       Waltz16         CPDPRG2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       -4.50 dB         PL12       14.87 dB         PL13       14.80 dB         PL13       14.80 dB         SFO2       400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6126276 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	$CH_3(CH_2)_9$ HN $HN$ $HN$ $HN$ $HN$ $HN$ $HN$ $HN$	(+)-guanidine <b>21</b> <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
57°71 -						<i>mdd</i>
- 53.05 - 23.05 - 24.04 - 25.06					A state of the sta	10
- 38.15 - 30.37 - 30.47 - 30.59						20
99'06 +L'06 9L'06 						30
20 22 - 67.12 - 98.34 - 85.84 -						40
00.64 90.64 12.64						50
42.242					in production of the second	60
12 67 -					a da de ser d	20 20
						80
					a solar s	06
						<i>001</i>
115.82						<i>011</i>
						120
					an a	130
						140
52'851				_		150







Current Data Parameters NAME nakane-n400 EXPNO 170 PROCNO 2	F2 - Acquisition Parameters       Date     20150105       Time     17.18       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       FULPROG     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CD30D       NS     5282       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       NS     5282       DW     20.850 usec       DW     20.850 usec       DW     20.850 usec       DI     2.0000000 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       H         PCPD2       80.00 usec       PL2         PL2       -4.50 dB       PL12       14.87 dB         PL13       14.80 dB       PL13       14.80 dB         PL13       14.80 dB       PL13       SFO2	F2 - Processing parameters SI 32768 SF 100.6126269 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9 H <sub>2</sub> N H <sub>1</sub> O	(+)-crambescin A carboxylic acid <b>1</b> a <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
					and the first of the	mdd
- 17.45						<b>0</b> I
91 92 - 91 92 - 92 - 30 - 30 - 30 - 30 - 30 - 30 - 30 - 3						20
42.0ε 52.0ε 92.1ε 20.εε						30
27.34 82.84 82.84 95.84 97.84 97.84 97.84						40
98'87 00'67 20'67 77'67						50
- +6 - 50 - +6 - 50 - +6 - 50 - +0 - 50 - +0 - 50					المراجع المراجع المراجع المراجع	60
12.64 -] 15.15 -						<b>20</b>
						80
					ng kasing n Kasing ng kasing ng ka	06
98.E01				-		<i>001</i>
					المراجعة ال المراجعة المراجعة الم	<i>011</i>
						120
						130
					a da da serie da ser Serie da serie da ser	140
123.27						150

160 08.761 -----170 180 التحطائة فللغط 190 للممريفة إراض حروا كالأنزيان يوارك معتال الكردي المتكريك 200 210 S85









S87

LS.T21 -----

£5.£ð1 ——

LL'891 -----









Current Data Parameters NAME nakane-B400 EXPNO 143 PROCNO 2	F2 - Acquisition Parameters Date 20151019 Time 16.26 INSTRUM speet PROBHD 5 mm QNP 1H/13 PULPROG zgpg30 TD 65536 SOLVENT MeOD NS 8200 DS 2 SWH 23980.814 Hz FIDRES 0.365918 Hz AQ 1.3664256 sec RG 11585.2 DW 20.850 usec DE 6.50 usec DI 1.0000000 sec D11 0.03000000 sec	CHANNEL f1	CPDPRG[2 waltz16 CPDPRG[2 waltz16 NUC2 1H PCPD2 80.00 usec PL2 10.30 dB PL12 25.00 dB PL13 25.00 dB PL13 25.00 dB PL13 25.00 dB PL13 25.00 dB	F2 - Processing parameters SI 32768 SF 100.6126265 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9 H <sub>2</sub> N H H <sub>2</sub> N H	(+)-crambescin B methyl ester 23 <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
						mdd
					بالمراجعة المراجع ماليان المراجعة المراجع	0
					ی دارید. ۱۹۰۹ این میرا میلو ۱۹۰۹ این میرا میلو را دارد.	01
52°.43 - 20°.43 - 20°.43						20
65.05 89.25 60.05						40 30
00.04 12.04 70.05		<u> </u>	<u> </u>			50
84.25 ->					जनसम्बद्धाः विद्युत्ति हि	<i>09</i>
76 <sup>-</sup> 89 <del></del>					and a state of the	20
					يا باريني وي المراجع مواليا وي المراجع مواليا وي المراجع	80
£6 <sup>-</sup> 68 ——					يارين ويروني ويروني موريا الماليانية، موريا الماليانية،	)6 06
		/				110 11
		1			and a state of the s	120
					و مارو بالمارين و مارو بالمارين المارين و مارو بالمارين المارين	130
					يونيا بي المراجع المراجع . وقالم المراجع المراجع . وقالم المراجع .	140
01/071						150

81.221				
				160
				<i>170</i>
				180
				061
				200
				210
	7			
	$\bigcirc$	S89	$\bigcirc$	



11.0 10.5 10.0 9.5 9.0 8.5

 $\left( \right)$ 

S90



S91

 

 Date
 20151002

 Time
 15.24

 INSTRUM
 spect

 PROBHD
 5 mm QNP 1H/13

 PULPROG
 zgpg30

 TD
 65536

 SOLVENT
 McOD

 NS
 3500

 DS
 2

 SWH
 23980.816 Hz

 FIDRES
 0.365918 Hz

 AQ
 1.3664255 sec

 RG
 16384

 DW
 20.850 usec

 DW
 20.850 usec

 DE
 6.50 usec

 TE
 299.3 K

 D1
 1.0000000 sec

 10.00 usec -1.00000000 W 400.1316005 MHz 1H 23980.816 Hz 23980.816 Hz 0.365918 Hz 1.3664255 sec 16384 20.850 usec 6.50 usec 299.3 K 1.0000000 sec 0.03000000 sec 0.03000000 sec 100.6228328 MHz F2 - Processing parameters SI 32768 SF 100.6126275 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40 [2 waltz16 80.00 usec -1.0000000 W -1.0000000 W -1.0000000 W F2 - Acquisition Parameters Date 20151002 Current Data Parameters NAME nakane-A400 2

52.221

150

НО

180.44



Current Data Parameters NAME nakane-B400 EXPNO 146 PROCNO 22 F2 - Acquisition Parameters Date 20151022 Time 20151022 Time 20151022 Time 20151022 TinsTRUM 5 mm QNP 1H/13 PULPROG 5 m QNP 1H/13 PULPROG 5536 SOLVENT 8278.146 Hz AQ 5336 SOLVENT 8278.146 Hz AQ 5336 SOLVENT 0.126314 Hz AQ 5336 SOLVENT 0.126314 Hz AQ 5336 SOLVENT 8278.146 Hz AQ 5336 SOLVENT 8278.146 Hz AQ 5336 SOLVENT 16 16 D1 1.00000 sec 75 D1 1.000000 sec 75 D1 1.000000 sec 75 D1 1.00000 sec 75 D1 1.00000 sec 75 P1 10.30 dB F1 400.1324710 MHz SF 400.1320074 MHz MDW EM SSB 0 0.30 Hz GB 0 1.00 FC 10 0.30 Hz GB 0 1.00 10.5 10.0 9.5 9.0

8.5

Current Data Parameters	NAME nakane-B400 EXPNO 147 PROCNO 2	F2 - Acquisition ParametersDate20151022Time20151022Time20151022Time21.49INSTRUMspectPROBHD5 mm QNP 1H/13PULPROGzgpg30TD65536SOLVENTMcODNS4500DS2SWH23980.814 HzFIDRES0.365918 HzAQ1.3664256 secRG1.3664256 secRG1.3664256 secDW20.850 usecDI1.00000000 secD10.03000000 secTD01	CHANNEL fl NUC1 13C Pl 12.00 usec PL1 7.50 dB SFO1 100.6228298 MHz	CPDPRG[2 waltz16 CPDPRG[2 waltz16 NUC2 1H PCPD2 80.00 usec PL2 10.30 dB PL12 25.00 dB PL13 25.00 dB PL13 25.00 dB PL13 25.00 dB	F2 - Processing parameters SI 32768 SF 100.6126272 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	H OH (+)-crambescin C methyl ester <b>25</b> <sup>13</sup> C NMR (100 MHz CD <sub>2</sub> OD)
						المعالمين ومناطق المحمد المعالمين المحمد المعالمين. محمد على المحمد المعالمين المحمد المعالمين المحمد المحمد المحمد المحمد المحمد المحمد المحمد المحمد المحمد المحم	mdd 0
20.42 - 25.07 - 25.43			_			internet in the second se	0 10
- 30'49 - 30'28 - 30'22 - 30'12 - 30'12 - 30'22 - 30'31							30 2
233.07 95.84 72.84 72.84 87.84							0 40
43 00 46 71 46 71 46 64 20 66 21 60							60 5
74.23						العام المراجع المراجع المراجع . وقد العام المراجع المراجع . وقد العام المراجع المراجع .	0 20
						مثلور به مراجع المراجع كانتها المراجع المراجع كانتها المراجع من المراجع	8 06
62.201 -			i j			العاملية الالتانية العاملية برايج الالتانية برايج التاريخ الإليانية	001 01
			1			r statistister en fite Afrika en statister fite	120 I.
						and the second secon	i0 130
24.251-	>			·		ا المحمد المحمد الم المحمد المحمد	150 14
85.921 -							E o

160 190 180 170 Ш والمقادر والمستحدا فأردأوا وأركا 200 للبالك ف 210 Ē

Û

S93

sl:191 -----





Current Data Parameters NAME nakane-B400 EXPNO 101 PROCNO 2	F2 - Acquisition ParametersDate20150205Time20150205Time20.08INSTRUMspectPROBHD5 mm QNP 1H/13PULPROG55356SOLVENTMeODNS479DS2SWH23980.814 HzAQ1.3664256 secRG23980.814 HzAQ1.365918 HzAQ1.365918 HzDW20.850 usecDE6.50 usecD11.0000000 secD10.0300000 secD10.0300000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CHANNEL f2         CPDPRG[2       waltz16         NUC2       1H       P         PCPD2       80.00 usec       P       P         PL2       10.30 dB       P       P       P         PL12       25.00 dB       P       P       P       P         PL13       25.00 dB       P	F2 - Processing parameters SI 32768 SF 100.6126273 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> HN H <sub>2</sub> N N	(–)-crambescin A methyl ester <b>1</b> b <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
						udd
						0
£†`†I				-		10
-23.01						20
LS'0E 99'0E #L'0E 6L'1E						) 30
16.84					and the second se	0 40
27.12	· · · ·					0 5(
						0 0
					a da	08
					runi fizzaten e	90 8
						5 00,
103.21						1 011
						120
						130
						140
						50



Current Data Parameters NAME nakane-n400 EXPNO 211 PROCNO 21 F2 - Acquisition Parameters Date 20150206 Time 17.07 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG 2g30 TD 65536 SOLVENT 2GC13 NS 8 SOLVENT 20126314 Hz FIDRES 0.126314 Hz FIDRES 0.126314 Hz FIDRES 0.126314 Hz FIDRES 0.126314 Hz MV 60.400 usec DE 6.00 usec TE 300.0 K D1 1.0000000 sec TE 300.0 K D1 1.0000000 sec	F2 - Processing parameters SI 32768 SF 400.130094 MHz WDW EM SSB 0 LB 0.30 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub>	0 ppm <sup>1</sup> H NMR (400 MHz, CDCl <sub>3</sub> )
			$ \frac{961}{1.000} \frac{961}{1.$
			2 2



Current Data Parameters NAME nakane-n400 EXPNO 212 PROCNO 2	F2 - Acquisition Parameters       Date     20150206       Time     17.09       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CDC13       NS     300       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       1H         NUC2       80.00 usec       1H         PCPD2       80.00 usec       80.00 usec         PL2       -4.50 dB       14.87 dB         PL12       14.87 dB       14.80 dB         PL13       14.80 dB       810.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127715 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	DH (+)-epoxide <i>ent-</i> <b>6</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
					and the second sec	0 10
52°52 53°55 14°57 55°57 55°57						30 21
75 00 19:02 						40
01.85					niji i ve konstanti je konstanti Konstanti je konstanti je konstant Konstanti je konstanti je konstant	60 50
69.94					1) a fior a fin an an an an an	02
00'LL 25'LL 18'78 						80
					and the second	06 0
						91 011
					a an	120
					a Bartan ang tang tang tang tang tang tang ta	130
						0 140
						<b>S</b> <sup>⊥</sup>





S98

, , ,	Current Data Parameters NAME nakane-n400 EXPNO 214 PROCNO 2	F2 - Acquisition Parameters Date 20150209 Time 19.40 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG zgpg30 TD 65536 SOL VENT CDC13	SULVENT CLOCIS NS 3000 DS 2 SWH 23980.814 Hz FIDRES 0.365918 Hz AQ 1.3664756 sec RG 16384 DW 20.850 usec DE 300.00 usec d11 0.0300000 sec d12 0.00002000 sec	CHANNEL fl NUC1 13C Pl 9.00 usec PL1 -3.00 dB SFO1 100.6228298 MHz	CHANNEL f2         CPDPRG2       waltz16         CPDPRG2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       -4.50 dB         PL12       14.87 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.20	CH <sub>3</sub> (CH <sub>2</sub> )9	OTBDPS (+)-aziridine <i>ent-</i> <b>9</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
								mdd
411 81.6 89.2						-		01
26°2 07'7 95'9 82'9	- 52 - 7 - 7 - 7 - 7 - 7 - 7 - 7 - 7 - 7 - 7							20
95.9 24.9 25.9 25.9								30
99.6 29.0 26.1 96.9								
,,,,								20 20
19.2	<u> </u>							09
89'9 00'2 07'/								- U.L.
48.8 7.32						-		80
							and the second se	06
								001
								011
00.77	71							120
29.62 29.62 29.62								130
25 52	21 -							140 Jan
								150



Current Data Parameters NAME nakane-n400 EXPNO 220 PROCNO 2	F2 - Acquisition Parameters       Date     20150206       Time     20150206       Time     23.54       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CDCl3       NS     14300       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       RG     1.3664756 sec       RG     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CPDPRG2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL12       14.87 dB         PL13       14.80 dB         PL13       14.80 dB         SFO2       400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CbzNNHBoc CH <sub>3</sub> (CH <sub>2</sub> )9N	OTBDPS (-)-guanidino-aziridine <i>ent</i> - <b>10</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
11.71 - 91.61 -					भूक में हिस्स स्थान की स्थान है। अपने स्थान स्थान स्थान की स्थान की स्थान की	<i>mdd 01</i>
- 55.68 - 59.09 - 59.09 - 59.09 - 59.79 - 58.67 - 28.67						2007
25'62 95'62 25'62 55'62 55'62						30
99.62 12.75 12.75 76.95						
tt <sup>.7</sup> 9						90 2 1
69.763 69.763 69.67 75.27 89.67 00.777 00.777 00.777 00.777 00.777 00.777 00.777 00.777 00.777 00.777 00.772 0						02
07 LL 76 LL 61 LL 86 18 64 78						80 81
0, 60					al de la companya de La companya de la comp La companya de la comp	06
					te di seconda di second Seconda di seconda di s Seconda di seconda di s	
89:121-7						120 I.
60 821 L1 821 S7 821 S9 621 S5 ° 521						130
81.9E1						140
12.841						20





Current Data Parameters NAME nakane-n400 EXPNO 222 PROCNO 2	F2 - Acquisition Parameters       Date     20150207       Time     9.52       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     55356       SOLVENT     cZgpg30       NS     700       DS     2       SOLVENT     CDC13       NS     700       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       RG     16384       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.03000000 sec       d11     0.03000000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       NUC2       1H         PCPD2       80.00 usec       90.00 usec       91.2       4.50 dB         PL12       14.87 dB       91.13       14.80 dB       91.13       91.4.80 dB         SFO2       400.1316005 MHz       90.01316005 MHz       91.2	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> OH CbzNH BocHN	OTBDPS (+)-alcohol <i>ent</i> - <b>11</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						<b>u</b> dd
- 17'11 - 16'18 - 17'12 - 17'12 - 17'12						<i>01</i>
- 52:10 - 52:1						20
2767 26733 26707 26707 2677						30
20.65 19.05 20.65 70.15 70.15 70.15 70.15 70.15						0 40
LZ.12						50 S
\$8 19 12:79 \$6:99 89:92						20
00 <sup>°</sup> <i>LL</i> 17 <sup>°</sup> <i>LL</i> 0 <sup>°</sup> <i>CL</i> 0 <sup>°</sup> <i>CL</i>		- <u></u>				
88.68					to a second s	06
						<b>100</b>
						011
						120
77.851 13.661 13.681 13.681						) 130
₽S <sup>-</sup> 9EI -∕						150 14(





Current Data Parameters NAME nakane-n400 EXPNO 226 PROCNO 2	F2 - Acquisition Parameters       Date     20150207       Time     13.39       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     cDC13       NS     500       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DW     20.00 usec       DI     1.00000000 sec       d11     0.03000000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       1H         PCPD2       80.00 usec       90.01         PL2       -4.50 dB       91.13       14.87 dB         PL12       14.87 dB       91.13       14.80 dB         PL13       14.80 dB       91.13       91.00	F2 - Processing parameters SI 32768 SF 100.6127707 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> OAc CbzN BocHN	OH (–)-alcohol <i>ent</i> - <b>12</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
01'71 - 58'02 - 70'82					and the second se Second second s	<i>01</i>
23.28 53.28 53.28 58.02 58.02						20
25'62 05'62 +5'62 85'62 			·			30
\$\$`0£ _// 06`1£ _/ 6\$`9£ _/						0 40
20:22						0 5
6L'E9 90'L9						70 6
89'92 00'22 75'22 01'82 86'18						80
+L'E8						<i>06</i>
						<i>001</i>
	•					<i>011</i>
58.721						120
te.ast						9 130
						141 19
123.25						Ĩ

92.951 -----160 -SL.Ed1 -----170 88.071 -----180 190 للطريطة بالليه 200 210  $\bigcirc$ S105





Current Data Parameters NAME nakane-n400 EXPNO 230 PROCNO 2	F2 - Acquisition Parameters       Date     20150209       Time     20150209       Time     21.35       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     65536       SOLVENT     CDC13       NS     16500       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DI     1.20000005 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CPDPRG2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       -4.50 dB         PL12       14.87 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB	F2 - Processing parameters SI 32768 SF 100.6127715 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9 OAC HN Br	
						mdd
		•				01
			_		-	20
15.92. 14.23. 14.23. 14.23. 14.23. 14.25. 14						30
06'0E						40
t6.87						50
67.85						09
89.92 95.101						20 20
						80
91`€6						06
						100
						011
62-221 -						120
128.32						130
72 921						) 140






	Current Data Parameters NAME nakane-n400 EXPNO 234 PROCNO 2	F2 - Acquisition Parameters       Date     20150209       Time     11.31       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CDC13       NS     500       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       RG     16384       DW     20.850 usec       DW     20.850 usec       DI     1.0000000 sec       d11     0.03300000 sec       d12     0.00002000 sec	CHANNEL f1 — CHANNEL f1 — CHANNEL f1 13C P1 9.00 usec PL1 -3.00 dB SFO1 100.6228298 MHz	CPDPRG2 waltz16 CPDPRG2 waltz16 NUC2 1H PCPD2 80.00 usec PL2 -4.50 dB PL12 14.87 dB PL13 14.87 dB PL13 14.80 dB SFO2 400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127722 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )9 OAc	(–)- <i>spiro</i> -aminal <i>ent</i> - <b>15</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
3							<i>udd</i>
							<b>0</b> ,
	- 17.09					ter ( trajet)	6
	5976						5
	55.15 - 29.50 - 29.50 - 29.50			·····			30
	42.02						40
	£2.64						50
	99.09				<u></u>		<i>09</i>
	64.00						<b>6</b> 2
							80
	LZ.06						<b>06</b>
							00
						and the second secon	0 1
							II (
	95'/21 -						120
	69'121						130
					_		140
						and the state of the	150





Current Data Parameters NAME nakane-n400 EXPNO 238 PROCNO 2	F2 - Acquisition Parameters       Date     20150209       Time     12.40       NNSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     65536       SOLVENT     cZppg30       TD     65536       SOLVENT     CDCl3       NS     408       DS     2       SWH     23980.814 Hz       AQ     1.3664756 sec       RG     0.365918 Hz       AQ     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.03000000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       P         NUC2       1H       P       P         PCPD2       80.00 usec       PL2       -4.50 dB         PL12       14.87 dB       PL13       14.80 dB         PL13       14.80 dB       PL13       SFO2       400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127737 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> OH CbzN HN OH	(–)-common intermediate <i>ent</i> - <b>16</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
						<b>0</b> I
25.65 - 22.65 - 24.67				<u> </u>	the second se	20
52.99 29.30 29.30 12.29						30
85'6Z					the second s	40
68.64						20
L6 <sup>.</sup> 85						0
21'99						0 9
89 <sup>.</sup> 9 <i>L</i>						12 <b>(</b>
78712					and the second se	
02.06						06
						<i>001</i>
					and the second secon	110
+0.71 -						120
98.721			<u> </u>			130
₩1.7£I						140
					a kontraktion Second Second	· [50







Current Data Parameters NAME nakane-n400 EXPNO 250 PROCNO 2	F2 - Acquisition Parameters       Date     20150221       Time     15.24       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CDCl3       NS     2121       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       RG     16384       DW     20.850 usec       DW     20.850 usec       DI     1.00000000 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       NUC2       1H         PCPD2       80.00 usec       PL2       -4.50 dB         PL12       14.87 dB       PL13       14.80 dB         PL13       14.80 dB       SFO2       400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6126276 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub>	(–)-crambescin B carboxylic acid <i>ent-</i> <b>2</b> <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
						<i>udd</i>
£†`†1					an a	<i>10</i>
- 23 23 - 22 69 - 52 - 86 52 - 15 92 - 20:45					A good and the second	20
27 06 27 06 19 06 27 06 27 06 27 75		<u>_</u>				30
20:22 91:92 95:87 25:87				·		40
00'67 12'67 12'67 12'67						50
27.67 05.67 79.67 17.64						09
67.88 ———						<b>0</b> 2
						80 8
20.02					and the second se	06
					and the second secon	<b>100</b>
					al de la constant de La constant de la cons La constant de la cons	011
						120
						130
					and the second secon	140
					en construction of the second s	150





8.5 F2 - Acquisition Parameters Date\_ 20150227 Time 16.10 INSTRUM 5 mm QNP 1H/13 PULPROG 5536 SOLVENT 5 mm QNP 1H/13 PULPROG 65536 SOLVENT 2030 SOLVENT 2030 SOLVENT 8278.146 Hz FIDRES 3.9583745 sec RG 60.400 usec RG 60.400 usec TE 297.2 K D1 1.0000000 sec 1H 15.00 usec 10.30 dB 400.1324710 MHz ======= CHANNEL f1 ======== NUC1 1H Processing parameters 32768 400.1300095 MHz EM 9.0 *II6*.0 0.30 Hz Current Data Parameters NAME nakane-B400 EXPNO 106 PROCNO 2 1.00 9.5 10.0 0 0 10.5 Time Trime PROBHD PULPROG TD SOLVENT NS SOLVENT NS SWH FIDRES AQ RG DM DM DM DM TE D1 TD TD D1 PL1 SF01 Р.

S114

Current Data Parameters NAME nakane-B400 EXPNO 107 PROCNO 2	F2 - Acquisition Parameters Date 20150227 Time 16.25 INSTRUM spect PROBHD 5 mm QNP 1H/13 PULPROG 5536 SOLVENT CDC13 NS 1139 DS 2 SWH 23980.814 Hz FIDRES 0.365918 Hz AQ 1.3664256 sec RG 1290.2 DW 20.850 usec DE 6.50 usec DI 1.0000000 sec D1 1.0000000 sec D1 1.0000000 sec	CHANNEL f1	CHANNEL f2       CHANNEL f2         CPDPRG[2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       10.30 dB         PL12       25.00 dB         PL13       25.00 dB         PL13       25.00 dB         PL13       25.00 dB         PL13       25.00 dB	F2 - Processing parameters SI 32768 SF 100.6127704 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> )9	H₂ <sup>N</sup> N ō √ (–)-crambescin B decarboxylate <i>ent-</i> 1 <sup>1</sup> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd
						0
14'10 55'98 72'91						20 10
70'5C 50'34 50'5C 50'5C 50'5C 50'5C						30
54.75 71.90 71.90 71.90 71.90 71.90 72.00 72						40
<i>PC LP</i>						50 50
1† <sup>-</sup> 29 ——						20
00 <sup>.</sup> <i>LL</i>						80
20 88						06 00
						1 011
						120
						40 130
						150 14





Current Data Parameters NAME nakane-B400 EXPNO 98 PROCNO 2	F2 - Acquisition ParametersDate20150131Time12.06NISTRUMspectPROBHD5 mm QNP 11H/13PULPROGzgpg30F0ULPROG55536SOLVENTCDC13NS2600DS2SWH23980.814 HzFIDRES0.365918 HzAQ1.3664256 secRG1024DW20.850 usecDE6.50 usecD11.20000005 secD110.03000005 secTD01	CHANNEL f1	CHANNEL f2       CHANNEL f2         CPDPRG[2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       10.30 dB         PL12       25.00 dB         PL13       25.00 dB         SFO2       400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6127711 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub>	OH OH (+)-enal <i>ent</i> - <b>18</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						mdd 0
 11'۲۱ 89'۲۲ م						01
54'10 54'30 53'30 53'30 53'20						30 20
19.62 19.62 26.05 29.67 29.79 20.79						40
48'33						0 50
\$0°29 89°92 ->						<b>9</b> <b>0</b> <b>0</b>
						80
						100 001
97.511						110
L1.821						30 120
136'50						140 I







Current Data Parameters NAME nakane-n400 EXPNO 142 PROCNO 2	F2 - Acquisition Parameters Date 20141003 Time 20141003 Time 10.22 INSTRUM av400 PROBHD 5 mm QNP 1H/13 PULPROG zgpg30 TD 65536 SOLVENT CD30D NS 3200 DS 2 SWH 23980.814 Hz FIDRES 0.365918 Hz AQ 1.3664756 sec RG 16384 DW 20.850 usec DE 30.00 usec TE 300.0 K	D1       2.0000000 sec         d11       0.0300000 sec         d12       0.00002000 sec         muc1       0.00002000 sec         P1       9.00 usec         PL1       -3.00 dB         SF01       100.6228298 MHz	CHANNEL f2         CPDPRG2       waltz16         CPDPRG2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       -4.50 dB         PL12       14.87 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB	F2 - Processing parameters SI 32768 SF 100.6126276 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub> H <sub>1</sub> N <sup>H</sup> H	DH (-)-guanidine <i>ent</i> - <b>19</b> (100 MHz, CD <sub>3</sub> OD)
52.52     52.52 <t< td=""><td></td><td></td><td>- </td><td></td><td></td><td>60 50 40 30 20 10 pp</td></t<>			- 			60 50 40 30 20 10 pp
					स्वति का स्वतुम्धा होते. स्वतुम्धा स्वतुम्धा स स्वतुम्धा स्वतुम्धा स्	02 08 06 001 0
۷9'S11					સુકાર જે છે. તે કે	50 140 130 120 11
40.781 20.421 20.421 20.421 20.4221						90 180 170 160 1
	·	S11	9		માં મુખ્યત્વે કે આવ્યાં છે. આ ગામમાં આવ્યાં છે. આ ગામમાં આવ્યાં છે. આ ગામમાં આવ્યાં છે. આ ગામમાં આવ્યાં છે. આ ગામમાં આવ્યાં છે. આ ગામમાં આવ્યાં છે. આ ગામમાં આવ્યાં છે. આ ગામમાં આવ્યાં છે.	210 200 15





Current Data Parameters NAME nakane-n400 EXPNO 172 PROCNO 2	F2 - Acquisition Parameters       Date     20150113       Time     13.50       Time     13.50       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CD30D       NS     2800       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       RG     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DW     20.850 usec       DW     20.30500000 sec       d11     0.03000000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       1H         PCPD2       80.00 usec       80.00 usec         PL12       14.87 dB       14.87 dB         PL13       14.80 dB       8PL13         SFO2       400.1316005 MHz	F2 - Processing parameters SI 32768 SF 100.6126269 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	$CH_3(CH_2)_9$ $H_2^{(H)}$ $H_1^{(H)}$ $H_2^{(H)}$ $H$	OH (–)-crambescin C carboxylic acid <i>ent</i> - <b>3</b> <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
					a bet the second se	mdd
- 14.43					la ser anna a laidhean air	<i>01</i>
- 52.14 - 28.47 - 30.32					a di telanda Telanda di telanda Telanda di telanda Telanda di telanda Telanda di telanda Telanda di telanda Telanda di telanda	<b>20</b>
- 30.64 - 30.64 - 30.76						30
28.1ε 20.εε 56.9ε Δε.8μ					A set of the set of th	40
48'35 10'67 10'67 76'79						50
62 67 - 57 67 - 79 67 - 79 67 -						<i>09</i>
10.23						<i>0</i> ∠
						<b>06</b>
					مراجعها المراجعة الم مراجعة المراجعة المراج مراجعة المراجعة المراج	001
1.701						011
						120
					بالمراجع المراجع المراج	130
					li vili la construction de la co	140
42.741 42.521						150





Current Data Parameters NAME nakane-B400 EXPNO 94 PROCNO 2	F2 - Acquisition Parameters Date 20150129 Time 10.51 INSTRUM spect PROBHD 5 mm QNP 1H/13 PULPROG 2gpg30 TD 65536 SOLVENT CDCl3 NS 339 DS 2 SWH 23980.814 Hz FIDRES 0.365918 Hz AQ 1.3664256 sec RG 2298.8 DW 200850 usec DI 1.20000005 sec D1 1.20000005 sec D11 0.03000000 sec	CHANNEL f1	CHANNEL f2       CHANNEL f2         CPDPRG[2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       10.30 dB         PL12       25.00 dB         PL13       25.00 dB         PL13       25.00 dB         PL13       25.00 dB         PL13       25.00 dB	F2 - Processing parameters SI 32768 SF 100.6127725 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.40	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub>	(–)-pyrrolidine <i>ent-</i> <b>20</b> <sup>13</sup> C NMR (100 MHz, CDCl <sub>3</sub> )
						udd 0
01:41						10
57,43						20
97.62 75.62 97.62 85.62 68.15						30
60'87						40
62 67						0 50
					and the second se Second second se	9 02
89'9L 00'LL 2E'LL						80
					a da serie de la companya de la comp	06
					a regeneration of the second	001
110.21						110
158.24						9 120
£7.851 <u>~</u>						(0 I3(
						14



Current Data Parameters NAME nakane-n400 EXPNO 199 PROCNO 2	F2 - Acquisition ParametersDate20150130Time18.20INSTRUMav400PROBHD5 mm QNP 11H/13PULPROGzg30TD65536SOLVENTCD30DNS8SOLVENTCD30DNS8SWH8278.146 HzFIDRES0.126314 HzAQ3.9584243 secRG90.5DW60.400 usecDE6.00 usecTE300.0 KD11.0000000 sec	CHANNEL f1 NUC1 1H P1 8.60 usec PL1 -4.50 dB SFO1 400.1324710 MHz	F2 - Processing parameters SI 32768 SF 400.1300074 MHz WDW EM SSB 0 LB 0.30 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )9	CH <sub>3</sub> CO <sub>2</sub> H <sub>2</sub> N <sup>M</sup> N <sup>H</sup>	(–)-guanidine <i>ent</i> - <b>21</b>	
							4.803 2.654 2.654 2.412 7.002 1.002
				-			<u>7.073</u> 7.073 7.073
						9 L	



	Current Data Parameters NAME nakane-n400 EXPNO 200 PROCNO 2	F2 - Acquisition Parameters       Date     20150130       Time     18.22       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CD30D       NS     376       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DW     20.850 usec       DW     20.850 usec       DW     1.3664756 sec       d11     0.030000005 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CHANNEL f2         CPDPRG2       waltz16         NUC2       1H       1H         PCPD2       80.00 usec       90.00 usec         PL2       -4.50 dB       9112         PL12       14.87 dB       9113         PL13       14.80 dB       91316005 MHz	F2 - Processing parameters SI 32768 SF 100.6126298 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> )	(−)-guanidine <i>ent</i> -21 <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
						is a state for the state of the	mdd
- 14'44 - 23'06 - 23'06 - 23'06							0 10
99.06 99.06 99.06							30 2
90.55 92.75 92.75 95.84 95.84						and the second	40
25 87 82.87 90.67 12.67							<i>50</i>
69.94 - 69.94 - 24.94 -						an a	09
						and the decision of the second se	02 0
						भित्र सम्प्रद्धाः सम्पत्ताः सम्पत्ताः सम्पत्ताः सम्पत्ताः सम्पत्ताः सम्पत्ताः सम्पत्ताः सम्पत्ताः सम्पत्ताः सम सम्पत्न सम्पत्न	<i>8 06</i>
						and the second secon	100
						and the first of the second	<i>011</i>
						une, kuntuk dan	120
						and the second secon	130
						is van de de ser	0 140





Current Data Parameters NAME nakane-n400 EXPNO 208 PROCNO 2	F2 - Acquisition Parameters       Date     20150203       Time     18.00       INSTRUM     av400       PROBHD     5 mm QNP 1H/13       PULPROG     zgpg30       TD     65536       SOLVENT     CD30D       NS     4000       NS     4000       NS     20       SOLVENT     CD30D       NS     4000       DS     2       SWH     23980.814 Hz       FIDRES     0.365918 Hz       AQ     1.3664756 sec       NG     1.3664756 sec       DW     20.850 usec       DW     20.850 usec       DI     1.20000005 sec       d11     0.030300000 sec       d12     0.00002000 sec	CHANNEL f1	CHANNEL f2         CPDPRG2       waltz16         NUC2       1H         PCPD2       80.00 usec         PL2       -4.50 dB         PL12       14.87 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB         PL13       14.80 dB	F2 - Processing parameters SI 32768 SF 100.6126269 MHz WDW EM SSB 0 LB 1.00 Hz GB 0 PC 1.00	CH <sub>3</sub> (CH <sub>2</sub> ) <sub>9</sub>	(–)-crambescin A carboxylic acid <i>ent-</i> <b>1a</b> <sup>13</sup> C NMR (100 MHz, CD <sub>3</sub> OD)
						mdd
- 14.42						<i>10</i>
- 30.46 - 30.46 - 30.33 - 25.15						20
99'0E 52'1E 90'EE						30
00.64 0.						) 40
17.64 17.64 17.64 17.64 17.64 1.64 1.64 1.64 1.64 1.64 1.64 1.64 1						50 5(
15.12 -						0 02
						80 8
					ale et plant de la companya de la co Nota de la companya d Nota de la companya d	06
98.601						<i>001</i>
						0110
						80 I26
					and the second se	( <b>40</b> <i>I</i> 3
LZ.221						150 1
20 851						<i>160</i>
08.781						<i>170</i>
					Allive and the second	180
						061 (
						10 201
		S127	,			2.