Total Synthesis of (±)-Haouamine A

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General Procedures. All reactions were carried out under a nitrogen atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dry tetrahydrofuran (THF), dichloromethane (DCM), methanol (MeOH), benzene, and toluene were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Yields refer to chromatographically and spectroscopically (¹H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and *p*-anisaldehyde in ethanol/aqueous H₂SO₄/CH₃CO₂H and heat as developing agents. NMR spectra were recorded on either a Bruker DRX 600, DRX 500 or an AMX 400 and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad. IR spectra were recorded on a Perkin-Elmer Spectrum BX spectrometer. High resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer (at Scripps) using ESI-TOF (electrospray ionization-time of flight) or a ThermoFinnigan Mass spectrometer (at UCSD) using FAB (fast atom bombardment), or EI (electron impact). Low resolution

mass spectra (LRMS) were recorded on an Agilent (at Scripps) or ThermoFinnigan Mass spectrometer (at UCSD) GC-MS. Melting points (m.p.) are uncorrected and were recorded on a Fisher-Johns 12-144 melting point apparatus. Microwave reactions were run in a Biotage “Initiator” system. Analytical HPLC was performed on an Agilent 1100 series using an Agilent Eclipse XBD-C8 5 μ m 4.6 x 150 mm column. Preparatory HPLC was performed on a Waters PrepLC system using a Waters Atlantis dC₁₈ OBD 10 μ m 30 x 250mm column.

Allylic alcohol 6a: To a solution of 3-methoxyphenylacetic acid (30.2 g, 182 mmol) in CH₂Cl₂ (250 mL) at 0° was added bromine (10.3 mL, 200 mmol, 1.1 equiv) dropwise. The solution was allowed to warm to room temperature and stirred for 2 h.

Saturated aqueous Na₂S₂O₃ (200 mL) was added and the aqueous layer further extracted with CH₂Cl₂ (2 x 200 mL). The combined organics were dried over MgSO₄, filtered, and concentrated. The crude mixture was dissolved in methanol (200 mL) and treated dropwise with thionyl chloride (39.8 mL, 546 mmol, 3.0 equiv). The solution was heated to reflux for 4 h and then cooled and concentrated. This material was dissolved in toluene (500 mL) and treated with tetrabutylammonium iodide (66.5 g, 180 mmol, 1.0 equiv), potassium carbonate (49.8 g, 360 mmol, 2.0 equiv), and paraformaldehyde (27.3 g, 900 mmol, 5.0 equiv). The resulting mixture was heated to reflux for 8 h and then cooled and diluted with EtOAc (500 mL) and washed with water (500 mL) and brine (500 mL). The organic was dried over MgSO₄, filtered, and concentrated. This crude mixture was dissolved in toluene (700 mL) and cooled to -78°. A toluene solution of

diisobutylaluminum hydride (345 mL, 1.5 M, 517 mmol, 3.0 equiv) was added and the solution stirred at -78° for 1 h. The reaction was quenched with EtOAc (200 mL) and allowed to warm to room temperature. Saturated aqueous potassium sodium tartrate (1.0 L) and Et₂O (1.0 L) were added and the solution stirred for 1 h. The layers were separated and the aqueous was further extracted with Et₂O (2 x 500 mL). The combined organics were dried over MgSO₄, filtered, and concentrated. Flash column chromatography (silica gel, 9:1 hexanes:EtOAc) afforded the allylic alcohol as a clear oil (23.4 g, 56% overall). **Allylic alcohol 6a**: R_f = 0.19 (silica gel, 4:1 hexanes:EtOAc); IR (film) $\nu_{\max}$ 3341 (br), 2360, 2341, 1590, 1567, 1464 (s), 1290, 1224 (s), 1039 (s), 1012, cm^{-1} ; ^1H NMR (500 MHz, CDCl₃) δ 7.42 (d, J = 8.8 Hz, 1 H), 6.75 (d, J = 3.1 Hz, 1 H), 6.71 (dd, J = 8.7 Hz, 3.1 Hz, 1 H), 5.51 (d, J = 1.5 Hz, 1 H), 5.13 (d, J = 1.3 Hz, 1 H), 3.77 (s, 3 H); ^{13}C -APT NMR (125 MHz, CDCl₃) δ 158.7, 149.1, 141.8, 133.3, 116.3, 115.0, 114.8, 112.6, 65.3, 55.4. Allylic alcohol **6a** (13.9 g, 57.1 mmol) was dissolved in CH₂Cl₂ (286 mL) and sequentially treated at 0° with triphenylphosphine (19.5 g, 74.2 mmol, 1.30 equiv), imidazole (5.44 g, 79.9 mmol, 1.4 equiv), and iodine (19.6 g, 77.1 mmol, 1.35 equiv). The solution was stirred at 0° for 30 min and quenched with saturated aqueous Na₂S₂O₃ (250 mL). Et₂O (500 mL) was added and the organic layer washed with water (200 mL) and brine (200 mL). The organic layer was dried over MgSO₄, filtered, concentrated, and passed through a plug of silica gel eluting with 9:1 hexanes:Et₂O (1 L) to give allyl iodide **6** (19.5 g, 97%) as an unstable oil which was used immediately.

Indanone 5: To 7-methoxyindanone¹ (37 g, 228 mmol) in THF (500 mL) at 0° was added a solution of 3-(methoxyphenyl)magnesium bromide (500 mL, 319 mmol). The reaction mixture was allowed to warm to room temperature and stirred for 1 h. Saturated aqueous NH₄Cl (200 mL) was added and

the mixture was extracted with Et₂O (3 x 250 mL), dried over MgSO₄, filtered, and concentrated. The resultant oil was dissolved in CH₃CN (500 mL), treated with H₂SO₄ (10%, 50 mL), and heated to 60° for 1 h. The reaction mixture was cooled to room temperature and stirred overnight. The mixture was then diluted with brine (200 mL) and extracted with CH₂Cl₂ (3 x 250 mL); the combined extracts were dried over MgSO₄, filtered, and concentrated. Flash column chromatography (silica gel, 2:1 to 1:1 hexanes/CH₂Cl₂) afforded 4-methoxy-3-(3-methoxyphenyl)-1*H*-indene (43 g, 170 mmol) as an unstable oil that was immediately dissolved in 9:1 acetone/H₂O (550 mL) and cooled to 0°. 4-Methylmorpholine-*N*-oxide (34.5 g, 255 mmol, 1.5 equiv) was added followed by osmium tetroxide (2.5% in *t*-BuOH; 21 mL, 1.7 mmol, 0.01 equiv) and the solution was warmed to room temperature and stirred for 7.5 h. Saturated aqueous Na₂S₂O₃ (100 mL) was added and the mixture was stirred for 1 h. Saturated aqueous NaHCO₃ (500 mL) was added and the aqueous mixture extracted with EtOAc (3 x 500 mL); the extracts were dried over MgSO₄, filtered, and concentrated. The dark oil was dissolved in benzene (500 mL) and treated with *p*-toluenesulfonic acid (3.2 g, 17.0 mmol, 0.1 equiv). The flask was equipped with a Dean-Stark trap and refluxed for 6 h. The

¹ Commercially available or synthesized in 2 steps from phenol: Nguy, N. M.; Chiu, I.-C.; Kohn, H. *J. Org. Chem.* **1987**, 52, 1649 – 1655.

reaction was cooled, diluted with EtOAc (500 mL) and washed subsequently with saturated aqueous NaHCO₃ (100 mL) and brine (100 mL). The combined aqueous washings were back-extracted with EtOAc (500 mL), and the combined organic extracts were dried over MgSO₄, filtered, and concentrated. Flash column chromatography (silica gel, 9:1 hexanes/EtOAc) afforded the indanone as an off-white solid (40.4 g, 66% overall). **Indanone 5**: m.p. 104 – 105 °C; R_f = 0.35 (silica gel, 4:1 hexanes:EtOAc); IR (film) ν_{max} 2939, 2359, 1749 (s), 1598 (s), 1484 (s), 1290, 1265, 1135, 1047 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.35 (t, *J* = 7.9 Hz, 1 H), 7.20 (t, *J* = 7.9 Hz, 1 H), 7.00 (d, *J* = 7.5 Hz, 1 H), 6.83 (d, *J* = 8.3 Hz, 1 H), 6.78 (dd, *J* = 8.3, 2.2 Hz, 1 H), 6.70 – 6.67 (m, 2 H), 4.64 (s, 1 H), 3.77 (s, 3 H), 3.73 – 3.67 (m, 1 H), 3.66 (s, 3 H); ¹³C-APT NMR (150 MHz, CDCl₃) δ 213.2, 159.6, 156.6, 138.9, 138.8, 129.4, 129.3, 128.4, 119.7, 116.9, 113.4, 112.1, 109.4, 57.3, 55.3, 55.1, 42.8; HRMS (ESI) calcd. for C₁₇H₁₇O₃ [M + H⁺] 269.1172, found 269.1171.

Oxime 4: To indanone **5** (12.3 g, 46.0 mmol) in 5:1 THF/DMPU (206 mL) at 0° was added a solution of KHMDS in toluene (0.5 M, 101 mL, 1.1 equiv). The reaction mixture was warmed to room temperature and stirred for 1 h. This was cooled to –78° and treated rapidly with a solution of allyl iodide **6** (19.5 g, 55.2 mmol, 1.2 equiv) in THF (50 mL). The reaction mixture was warmed to room temperature and stirred for 1 h. Saturated aqueous NH₄Cl (100 mL) and Et₂O (100 mL) were added, and the aqueous layer was further extracted with Et₂O (2 x 200 mL). The combined organics were dried

over MgSO_4 , filtered, and concentrated. Flash column chromatography (silica gel, 9:1 $\rightarrow$ 4:1 hexanes/ Et_2O) afforded alkylated ketone as a thick oil (12.3 g, 24.8 mmol, 54%). This material was dissolved in EtOH (236 mL), treated with hydroxylamine hydrochloride (49.1 g, 0.71 mol, 20.0 equiv) and sodium acetate (43.5 g, 0.53 mol), and heated to reflux for 15 h. After being cooled to room temperature, the reaction mixture was diluted with aqueous NaHCO_3 (5%, 200 mL) and extracted with CH_2Cl_2 (3 x 200 mL). The combined organics were dried over MgSO_4 , filtered, and concentrated. Flash column chromatography (silica gel, 9:1 $\rightarrow$ 4:1 hexanes/ EtOAc) afforded the title oxime as a white solid (9.47 g, 75%). **Oxime 4:** m.p. 134 – 137 °C; R_f = 0.19 (silica gel, 4:1 hexanes: EtOAc); IR (film) ν_{max} 3274, 2936, 1587 (s), 1480 (s), 1288, 1224 (s), 1079, 1042 cm^{-1} ; ^1H NMR (600 MHz, CDCl_3) δ 8.23, (br s, 1 H), 7.22 (d, J = 8.6 Hz, 1 H), 7.76 (t, J = 7.6 Hz, 1 H), 7.15 (t, J = 8.1 Hz, 1 H), 6.88 (d, J = 7.5 Hz, 1 H), 6.81 – 6.72 (m, 2 H), 6.71 (d, J = 7.1 Hz, 1 H), 6.50 (dd, J = 8.6, 3.0 Hz, 1 H), 6.39 (d, J = 7.0 Hz, 1 H), 5.64 (d, J = 3.0 Hz, 1 H), 5.29 (s, 1 H), 4.91 (s, 1 H), 3.98 (d, J = 13.0 Hz, 1 H), 3.84 (d, J = 13.0 Hz, 1 H), 3.73 (s, 3 H), 3.69 (d, J = 22.4 Hz, 1 H), 3.58 (s, 3 H), 3.57 (d, J = 21.8 Hz, 1 H), 3.36 (s, 3 H), ; ^{13}C -APT NMR (150 MHz, CDCl_3) δ 167.4, 159.3, 157.9, 156.7, 147.5, 146.7, 144.3, 139.9, 132.3, 131.8, 129.5, 128.9, 120.4, 118.7, 116.7, 115.3, 114.3, 112.7, 112.3, 110.1, 108.7, 59.1, 55.0 (2 C), 54.4, 42.3, 34.1; HRMS (ESI) calcd. For $\text{C}_{27}\text{H}_{27}\text{BrNO}_4$ [$\text{M} + \text{H}^+$] 508.1118, found 508.1110.

Amine 3: To a solution of the above oxime (1.07 g, 2.11 mmol) in 1,2-dichloroethane (21.1 mL) at 0° was added 2,4,4,6-tetrabromo-2,5-cyclohexadienone

(1.73 g, 4.22 mmol, 2.2 equiv) at once. Stirring was continued for 30 min at 0° C and EtOH (21.1 mL) was then added followed by sodium borohydride (399 mg, 10.5 mmol, 5.0 equiv). The reaction mixture was heated to 50° for 1 h and then poured into 1:1 5% aqueous NaHCO₃/brine (100 mL) and extracted with CH₂Cl₂ (3 x 100 mL). The combined organics were dried over MgSO₄, filtered, concentrated and diluted with EtOH (14.0 mL). The solution was heated to reflux and indium powder (484 mg, 4.22 mmol, 2.0 equiv) was added followed by saturated aqueous NH₄Cl (7.0 mL). The reaction was heated to reflux for 3.5 h then cooled and diluted with EtOAc (100 mL) and 5% aqueous NaHCO₃ (100 mL). The aqueous layer was further extracted with EtOAc (3 x 100 mL) and the combined organics were dried over MgSO₄, filtered, and concentrated. Flash column chromatography (silica gel, 4:1 → 2:1 hexanes/EtOAc) afforded the amine as a white foam (592 mg, 57%). **Amine 3**: m.p. 57 – 61 °C; R_f = 0.25 (silica gel, 1:1 hexanes:EtOAc); IR (film) ν_{max} 2935, 1587 (s), 1478 (s), 1463 (s), 1288, 1263 (s), 1080, 1051, 1028 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.43 (d, *J* = 8.7 Hz, 1 H), 7.26 (t, *J* = 8.7 Hz, 1 H), 7.18 (t, *J* = 7.9 Hz, 1 H), 6.94 (d, *J* = 7.4 Hz, 1 H), 6.83 (s, 1 H), 6.79 – 6.67 (m, 5 H), 6.36 (s, 1 H), 3.82 (d, *J* = 17.0 Hz, 1 H), 3.77 (s, 3 H), 3.76 (s, 3 H), 3.68 (dd, *J* = 6.8, 4.6 Hz, 1 H), 3.60 (s, 3 H), 3.53 (d, 17.0 Hz, 1 H), 3.17 (dd, *J* = 16.0, 6.9 Hz, 1 H), 2.95 (dd, *J* = 16.0, 4.3 Hz, 1 H), 2.31 (brs, 1 H); ¹³C-APT NMR (150 MHz, CDCl₃) δ 159.5, 158.8, 157.4, 147.2, 143.6, 143.5, 139.0, 133.2, 132.3, 130.0, 129.1, 129.0, 119.4, 117.8, 116.0, 114.2, 113.1, 112.8, 111.3, 109.6, 66.4, 55.6, 55.5, 55.2, 55.1, 45.1, 36.0; HRMS (ESI) calcd. For C₂₇H₂₇BrNO₃ [M + H⁺] 491.1169, found 492.1163.

Stannyl pyrone 12: To a solution of 4-bromo-3-hydroxy-2-pyrone² (300 mg, 1.57 mmol) in Et₂O (15 mL) was added diazomethane in Et₂O (0.3 M, 5.5 mL) until a yellow color showed complete methylation.

Concentration afforded pure 4-bromo-3-methoxy-2-pyrone (322 mg, 100%). A flask was charged with 4-bromo-3-methoxy-2-pyrone (106.9 mg, 0.52 mmol), hexamethylditin (0.162 mL, 0.78 mmol, 1.5 equiv), and tetrakis(triphenylphosphine)palladium(0) (60 mg, 0.052 mmol, 0.1 equiv) under argon. Toluene (5.2 mL) was added and the solution was degassed by argon bubbling for 30 min. The reaction mixture was heated to reflux for 5 h then cooled and passed through 10% KF/silica gel with EtOAc. Flash column chromatography (silica gel, 19:1 hexanes:EtOAc) afforded the title compound as a colorless oil (116 mg, 77%). **Stannyl pyrone 12:** $R_f = 0.45$ (silica gel, 4:1 hexanes:EtOAc); IR (film) $\nu_{\max}$ 2916, 2362, 1709 (s), 1604, 1271, 1171, 1066, 777 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.24 (d, $J = 4.9$ Hz, 1 H), 6.14 (d, $J = 4.9$ Hz, 1 H), 3.89 (s, 3 H), 0.31 (s, 9 H); ¹³C-APT NMR (125 MHz, CDCl₃) δ 157.3, 149.9, 144.5, 144.0, 110.7, 59.6, -9.1.

Pyrone 14: To a solution of the above amine (492 mg, 1.0 mmol) in CH₂Cl₂ (10 mL) was added di-*tert*-butyl dicarbonate (262 mg, 1.2 mmol, 1.2 equiv) and the solution was stirred at room temperature for 30 min. Concentration

² Komiyama, T.; Takaguchi, Y.; Gubaidullin, A. T.; Mamedov, V. A.; Litvinov, I. A.; Tsuboi, S. *Tetrahedron* **2005**, *61*, 2541 – 2547.

and flash column chromatography (silica gel, 4:1 hexanes/EtOAc) afforded Boc-protected amine (563 mg, 95%). To a mixture of Boc-protected amine (50.9 mg, 0.086 mmol), stannyl-pyrone **12** (41.1 mg, 0.14 mmol, 1.65 equiv), tetrakis(triphenylphosphine)palladium(0) (9.9 mg, 0.0086 mmol, 0.1 equiv), and copper(I) iodide (3.3 mg, 0.017 mmol, 0.2 equiv) under argon was added toluene (3.0 mL) and the solution was subjected to five freeze-pump-thaw cycles. The mixture was then heated to 110° for 15 h. After cooling to room temperature, the reaction mixture was passed through 10% KF/silica gel and eluted with EtOAc. Flash column chromatography (silica gel, 4:1 hexanes/EtOAc) afforded coupled pyrone **13** (25.2 mg, 46%) which was dissolved in 10:1 CH₂Cl₂/TFA (2.2 mL) and stirred at room temperature for 3 h. After concentration, 3-butynyl *p*-toluenesulfonate (45.0 mg, 0.2 mmol, 5.0 equiv), potassium carbonate (27.6 mg, 0.2 mmol, 5.0 equiv), and CH₃CN (0.4 mL) were added and the resultant mixture was heated to 80° in a sealed vessel for 6h. After cooling, EtOAc (5 mL) was added and the reaction was filtered through a cotton plug. Concentration and flash column chromatography (silica gel, 4:1 hexanes/EtOAc) afforded pyrone **14** as an off-white foam (16.5 mg, 70%). **Pyrone 14**: m.p. 66 – 70 °C; R_f = 0.28 (silica gel, 2:1 hexanes:EtOAc); IR (film) ν_{max} 3284, 2935, 2836, 1705 (s), 1601, 1479, 1289, 1264 (s), 1210, 1170, 1079, 1064, 1046, 777 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.22 (t, *J* = 8.0 Hz, 1 H), 7.18 (d, *J* = 8.6 Hz, 1 H), 7.11 (t, *J* = 8.0 Hz, 1 H), 6.97 (d, *J* = 2.5 Hz, 1 H), 6.85 (dd, *J* = 8.6, 2.5 Hz, 1 H), 6.81 (d, *J* = 7.5 Hz, 1 H), 6.75 – 6.71 (m, 2 H), 6.67 (dd, *J* = 8.2, 1.2 Hz, 1 H), 6.64 (d, *J* = 8.2 Hz, 1 H), 6.53 (d, *J* = 5.1 Hz, 1 H), 5.77 (s, 1 H), 5.58 (d, *J* = 5.1 Hz, 1 H), 3.86 (s, 3 H), 3.74 – 3.71 (m, 4 H), 3.64 – 3.61 (m, 4 H), 3.42 (s, 3 H), 3.35 (dd, *J* = 16.8, 1.7 Hz, 1 H), 2.92 (dd, *J* = 15.6, 9.5 Hz, 1 H), 2.84 – 2.70 (m, 3

H), 2.26 (bt, $J = 7.0$ Hz, 2 H), 1.87 (t, $J = 2.6$ Hz, 1 H); ^{13}C -APT NMR (125 MHz, CDCl_3) δ 159.8, 159.7, 159.0, 155.9, 148.7, 143.9, 142.5, 141.2, 140.7, 133.5, 131.3, 131.1, 129.93, 129.86, 129.2, 128.2, 128.0, 125.4, 119.4, 117.5, 114.1, 113.5, 112.5, 110.2, 109.6, 108.9, 70.2, 69.1, 59.2, 56.6, 55.4, 55.1, 54.8, 54.2, 49.6, 28.0, 18.1; HRMS (ESI) calcd. for $\text{C}_{37}\text{H}_{36}\text{NO}_6$ $[\text{M} + \text{H}^+]$ 590.2535, found 590.2535.

Haouamine A (1): To a solution of **3** (46.0 mg, 0.078 mmol) in CH_2Cl_2 (1.0 mL) at -78° was added boron tribromide in CH_2Cl_2 (0.78 mL, 1.0 M, 0.78 mmol, 10.0 equiv) and the solution was allowed to warm to room temperature and stirred for 1.5 h. Aqueous $\text{KH}_2\text{PO}_4/\text{K}_2\text{HPO}_4$ (2.0 mL, 0.5 M, pH 7.0) was added and the solution extracted with EtOAc (3 x 15 mL). The combined organics were dried over MgSO_4 , filtered, and concentrated. Acetic anhydride (0.5 mL) and pyridine (0.5 mL) were immediately added to the crude polyphenol and the reaction was stirred at room temperature for 3 h. After concentration, the material was purified by flash column chromatography (silica gel, 4:1 hexanes:EtOAc) to give **15** (37 mg, 67%). A portion of this material (5.0 mg, 0.0071 mmol) was dissolved in *o*-dichlorobenzene (7.1 mL) and 2,5-di-*tert*-butyl-4-methylphenol (12.1 mg, 0.055 mmol, 7.7 equiv) was added. The clear solution was then irradiated in a microwave at 250° for 10 h. After cooling to room temperature, the solution was passed through silica gel eluting first with hexanes to remove *o*-dichlorobenzene and subsequently with EtOAc. The crude reaction was concentrated and purified by preparatory TLC (silica gel, 2:1 hexanes:EtOAc, run twice)

to give recovered **15** (1.5 mg, 30%) as well as peracetyl haouamine A contaminated with its atropisomer (1.0 mg, 21%) which was dissolved in 1:1 MeOH:CH₂Cl₂ (0.6 mL) and treated with potassium carbonate (1.0 mg, 0.0072 mmol, 4.7 equiv). Stirring at room temperature was continued for 30 min, and aqueous KH₂PO₄/K₂PO₄ (1.0 mL, 0.5 M, pH 7.0) was added. The aqueous layer was extracted with EtOAc (3 x 10 mL) and the combined organics were dried over MgSO₄, filtered, and concentrated. Purification by preparatory HPLC (42.5 mL/min, solvent A: H₂O with 0.1% TFA; solvent B: CH₃CN with 0.1% TFA; 0 min- 7:3 A:B, 30 min- 6:4 A:B) afforded the TFA salt of haouamine A which was neutralized with aqueous KH₂PO₄/K₂PO₄ (1.0 mL, 0.5 M, pH 7.0) and extracted with EtOAc (3 x 10 mL). The combined organics were dried over MgSO₄, filtered, and concentrated to afford pure haouamine A as a white film (0.7 mg, corresponding to *ca.* 21% from **15**); R_f = 0.26 (silica gel, 1:1 hexanes:EtOAc); IR (film) ν_{max} 3247 (br), 1594, 1410, 1281, 1182 cm⁻¹; ¹H NMR (500 MHz, 10% D₂O/CD₃COCD₃) δ See comparison below; HRMS (ESI) calcd. For C₃₂H₂₈NO₄ [M + H⁺] 490.2013, found 490.2009. Analytical HPLC comparison and co-injection, shown below, (1.0 mL/min, solvent A: H₂O with 0.1% TFA; solvent B: CH₃CN with 0.1% TFA; 0 min- 9:1 A:B, 10 min- 2.85:1 A:B, 15 min- 2:3 A:B, 20 min- 0:1 A:B) showed synthetic haouamine A to be identical to a natural sample. The tentatively assigned atropisomer of **1** was not fully characterized due to the minute and varying quantities formed, see Ref. 12 for further details.