Supplementary Information for

Synthesis of the Core Structure of Phalarine

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General Remarks.

All non-aqueous reactions were carried out under an inert atmosphere of N_2 gas in oven-dried glassware unless otherwise noted. Dehydrated CH₂Cl₂, DMSO were purchased from Kanto Chemicals Co., and were used after passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. DMA for dearomatization were distilled over CaH₂. All other reagents were commercially available and used without further purification unless otherwise noted. Analytical thin layer chromatography (TLC, 0.25 mm), high performance thin layer chromatography (HPTLC, 0.20 mm) and preparative thin layer chromatography (pTLC, 0.50 mm) were performed on Merck precoated analytical plates, silica gel 60 F₂₅₄. Preparative flash chromatography was performed using Silica Gel (AP-300, irregular, 38-75 µm) purchased from Toyotakako Co., Ltd, and neutral Silica Gel 60 (spherical, average 75 µm) purchased from Nacalai Tesque, Inc. All sample spots which recorded in retension factor (Rf) on TLC plate were detected by ultraviolet (UV) lamp at 254 nm and cerium sulfate-phosphomolybdic acid (Ce-PMA) which was prepared by Ce₂(SO₄)₃·nH₂O (12.5 g), phosphomolybdic acid (35.0 g), and 2 M H₂SO₄ aq (500 mL). ¹H and ¹³C NMR were recorded on a JEOL JNM-ECA 600 or JNM-ECA 600II spectrometer. All ¹H NMR spectra are reported in delta (δ) units, parts per million (ppm) downfield from tetramethylsilane as the internal standard (0.00 ppm) and coupling constants (J) are indicated in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t =triplet, q = quartet, m = multiplet, br = broad. All ¹³C NMR spectra are reported in ppm relative to the central line of the triplet for CDCl₃ (77.0 ppm). Infrared spectra (IR) were recorded on a FT/IR-6100 Fourier Transform Infrared Spectrophotometer, and are reported in wavenumbers (cm-¹). High resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF-QII in positive electrospray ionization (ESI) method using PEG as the internal standard.

Catalytic Dearomatization of Indole: General Procedure



A 10-mL Schlenk tube equipped with a J. YOUNG valve cock and a magnetic stir bar was charged under Ar gas with 6 (50.7 mg, 100 μ mol), palladium catalyst (Pd: 10 μ mol), NaOAc (12.3 mg, 150 μ mol) and DMA (1.0 mL), which was degassed twice by freeze-thaw process. The resulting mixture was stirred at 100 °C for 18 h, and quenched with sat NH₄Cl aq (4.0 mL). The mixture was partitioned between Et₂O (4.0 mL) and water (4.0 mL). The organic phase was collected and the aqueous phase was extracted with Et₂O (4.0 mL) twice. The combined organic extract was dried over anhydrous MgSO₄ (ca. 1.0 g), filtered and concentrated *in vacuo*.

To the mixture was added dimethyl sulfone (33.3 mM CDCl₃ solution; 0.500 mL, 16.7 μ mol). An aliquot of the solution (0.500 mL) was transferred to a NMR tube. The solution was subjected to ¹H-NMR analysis (ca. 200 mM, 25 °C) with 10 sec relaxation delay. The yields were determined by the comparison of the ratio of the signal intensities of the product **7** (δ 5.53 (s, 1H, C=CH)) and dimethyl sulfone (δ 2.98 (s, 6H, CH₃ x 2)). [KD08122]

Catalytic Cascade Cyclization of Amide: General Procedure



A 10-mL Schlenk tube equipped with a J. YOUNG valve cock and a magnetic stir bar was charged with **10** (25.8 mg, 50 μ mol), Pd(OAc)₂ (1.12 mg, 5.0 μ mol), H₂O (x equiv), NaIO₄ (1.5 equiv) and dehydrated DMSO (1.0 mL). The resulting mixture was stirred under CO atmosphere (1 atm) at 40 °C for 18 h, and quenched with sat NH₄Cl aq (4.0 mL). The mixture was partitioned between Et₂O (4.0 mL) and water (4.0 mL). The organic phase was collected and the aqueous phase was extracted with Et₂O (4.0 mL) twice. The combined organic extract was dried over anhydrous MgSO₄ (ca. 1.0 g), filtered and concentrated *in vacuo*.

To the mixture was added dimethyl sulfone (16.7 mM CDCl₃ solution; 0.500 mL, 8.3 μ mol). An aliquot of the solution (0.500 mL) was transferred to a NMR tube. The solution was subjected to ¹H-NMR analysis (ca. 100 mM, 25 °C) with 10 sec relaxation delay. The yields were determined by the comparison of the ratio of the signal intensities of the product **11** (δ 3.52 (d, 1H, C–CH–C)) and dimethyl sulfone (δ 2.98 (s, 6H, CH₃ x 2)). [KD08125, KD08127]

3-Methyl-1*H*-indole-2-carboxylic acid (14)



A 300-mL, one-necked round-bottomed flask equipped with a three-way cock, a bubbler, a glass stopper and a magnetic stir bar was charged under N₂ gas with methyl-2-oxo-butyrate (14) (10.9 mL, 100 mmol), EtOH (20 mL) and phenylhydrazine (9.83 mL, 100 mmol). The resulting mixture was evaporated under reduced pressure. EtOH (90 mL) and H₂SO₄ (10 mL, 53 mmol) were added and the mixture was stirred at 80 °C for 7 h. The reaction was cooled to room temperature and partitioned between Et₂O (100 mL) and water (200 mL). The organic phase was collected and the aqueous phase was extracted with Et₂O (100 mL). The combined organic extract was washed with sat. NaHCO₃ aq. (200 mL) and concentrated *in vacuo* to give a crude product, which was used in the next step without further purification.

A 300-mL, one-necked round-bottomed flask equipped with a three-way cock, a bubbler, a glass stopper and a magnetic stir bar was charged under N₂ gas with the crude product, EtOH (200 mL) and 5 M NaOH aq (100 mL, 500 mmol). The reaction mixture was stirred at 40 °C for 16 h, and Et₂O (100 mL) was added. The organic phase was collected and the aqueous phase was extracted with Et₂O (100 mL). The organic phase was discarded. The aqueous phase was neutralized with 12 M HCl aq (45 mL, 540 mmol) at 0 °C (pH \approx 3). The aqueous phase was extracted with CH₂Cl₂ (200 mL) twice. The combined organic extract was dried over anhydrous Na₂SO₄ (ca. 20 g), filtered and concentrated *in vacuo*. Recrystallization from *n*-hexane/EtOAc = 1/1 (100 mL) gave **15** (5.87 g, 33.5 mmol, 34%) as yellow crystals. The concentrated mother liquor was dissolved in *n*-hexane/EtOAc = 1/1 (50 mL), cooled to 0 °C, and filtered to afford the second crop of crystals of **15** (5.08 g, 29.0 mmol, 29%). [KD07196]

Rf = 0.38 (toluene/HCO₂H/HCO₂Et = 4/1/1, UV, Ce-PMA);

IR (neat, cm⁻¹) 1663, 1556, 1449, 1335, 1241, 1187;

¹H NMR (CDCl₃, 600 MHz) δ 8.75 (br, 1H), 7.69 (d, *J* = 8.3 Hz, 1H), 7.37 (t, *J* = 8.3 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.16 (t, *J* = 8.3 Hz, 1H), 2.67 (s, 1H);

¹³C NMR (CDCl₃, 150 MHz) δ 168.0 (C), 136.4 (C), 128.5 (C), 126.3 (CH), 123.0 (C), 122.3 (C), 121.0 (CH), 120.1 (CH), 111.8 (CH), 10.0 (CH₃);

HRMS (ESI) calcd for $C_{10}H_9NO_2Na([M + Na]^+)$ 198.0531, found 198.0510.

1-(tert-Butyl)-2-(2-iodo-5-methoxyphenyl)-3-methyl-1H-indole-1,2-dicarboxylate (5)



A 100-mL, one-necked round-bottomed flask equipped with a three-way cock, a bubbler, a glass stopper and a magnetic stir bar was charged under N₂ gas with **15** (3.15 g, 18 mmol), CH₂Cl₂ (36 mL) 2-iodo-5-methoxyphenol (**16**)¹ (4.95 g, 19.8 mmol), DMAP (219.9 mg, 1.8 mmol). EDCI·HCl (3.80 g, 19.8 mmol) was added and the reaction mixture was stirred at 40 °C for 3 h, and quenched with 1 M NaOH aq (50 mL). The mixture was poured into separatory funnel, diluted with CH₂Cl₂ (50 mL), and partitioned. The organic phase was collected and the aqueous phase was extracted with CH₂Cl₂ (50 mL). The combined organic extract was washed with brine (50 mL) and filtered through a short pad of silica gel (20 mL of silica gel, diameter = 5 cm, height = 1 cm) and washed with CH₂Cl₂ (50 mL). The solution was concentrated *in vacuo* to afford the crude material as a yellow solid, which was used in the next step without further purification.

A 100-mL, one-necked round-bottomed flask equipped with a three-way cock, a bubbler, a glass stopper and a magnetic stir bar was charged under N₂ gas with the crude product, CH₂Cl₂ (36 mL), DMAP (219.9 mg, 1.8 mmol). Boc₂O (4.55 mL, 19.8 mmol) was added and the reaction mixture was stirred at 40 °C for 12 h. The reaction was quenched with water (50 mL), and the mixture was poured into separatory funnel, diluted with CH₂Cl₂ (50 mL), and partitioned. The organic phase was collected and the aqueous phase was extracted with CH₂Cl₂ (50 mL). The combined organic extract was washed with brine (50 mL), dried over anhydrous Na₂SO₄ (ca. 10 g), filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (500 mL of silica gel, diameter = 5 cm, height = 25 cm, *n*-hexane/EtOAc = 9/1) to afford crude **6** as a white solid. Recrystallization from *n*-hexane/EtOAc = 1/1 (50 mL) gave **6** (7.55 g, 14.9 mmol, 83%) as white crystals. [KD07198]

Rf = 0.42 (*n*-hexane/EtOAc = 5/1, UV, Ce-PMA);

IR (neat, cm⁻¹) 1728, 1395, 1234, 1188, 1151, 1086;

¹H NMR (CDCl₃, 600 MHz) δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.46 (dd, *J* = 8.3, 7.6 Hz, 1H), 7.32 (dd, *J* = 8.3, 7.6 Hz, 1H), 7.04 (d, *J* = 2.8 Hz, 1H), 6.65 (dd, *J* = 9.0, 2.8 Hz, 1H), 3.83 (3H), 2.61 (3H), 1.66 (9H);

¹³C NMR (CDCl₃, 150 MHz) δ 160.9 (C), 159.6 (C), 152.0 (C), 149.6 (C), 139.1 (CH), 136.8 (C), 129.4 (C), 127.3 (CH), 125.9 (C), 125.7 (C), 123.0 (CH), 120.5 (CH), 114.8 (CH), 114.2 (CH), 108.9 (CH), 84.6 (C), 78.7 (C), 55.5 (CH₃), 28.0 (CH₃), 10.0 (CH₃);

HRMS (ESI) calcd for $C_{22}H_{22}NO_5INa([M + Na]^+) 530.0440$, found 530.0413.

¹ M. W. Carson, M. W. Giese and M. J. Coghlan, Org. Lett., 2008, **10**, 2701-2704.

tert-Butyl-6-methoxy-3'-methylene-2-oxo-2*H*-spiro[benzofuran-3,2'-indoline]-1'-carboxylate (6)



A 1-L Schlenk tube equipped with a glass stopper, a cold finger, and a magnetic stir bar was charged under Ar gas with recrystallized Pd₂(dba)₃·CHCl₃ (517.6 mg, 0.50 mmol),²¹ NaOAc (1.23 g, 15 mmol), **6** (5.07 g, 10 mmol) and DMA (100 mL) which was degassed twice by freeze–thaw process. The reaction mixture was stirred at 100 °C for 18 h, then quenched with sat NH₄Cl aq (200 mL) at 0 °C. The mixture was poured into separatory funnel, diluted with Et₂O (100 mL), and partitioned. The organic phase was collected and the aqueous phase was extracted with Et₂O (100 mL), dried over anhydrous Na₂SO₄ (ca. 10 g), filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (400 mL of silica gel, diameter = 5 cm, height = 20 cm, *n*-hexane/EtOAc = 20/1 to 5/1) to afford **7** as a white solid. Recrystallization from *n*-hexane/Et₂O = 5/1 (50 mL) gave **7** (2.09 g, 5.51 mmol, 55%) as white crystals. The concentrated mother liquor was dissolved in *n*-hexane/Et₂O = 5/1 (20 mL), cooled to 0 °C, and filtered to afford the second crop of crystals (620.0 mg, 1.63 mmol, 16%). [KD08031]

Rf = 0.39 (*n*-hexane/EtOAc = 5/1, UV, Ce-PMA);

IR (neat, cm⁻¹) 1820, 1719, 1501, 1477, 1370, 1285, 1154, 1132, 1070, 751;

¹H NMR (CDCl₃, 600 MHz, 60 °C) δ 8.05 (br, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 7.06 (t, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 8.3 Hz, 1H), 6.73 (s, 1H), 6.67 (d, *J* = 8.3 Hz, 1H), 5.53 (s, 1H), 4.69 (s, 1H), 3.84 (s, 3H), 1.25 (s, 9H);

¹³C NMR (CDCl₃, 150 MHz, 60 °C) *δ* 173.0 (C), 161.6 (C), 154.8 (C), 149.8 (C), 145.8 (C), 144.8 (C), 130.9 (CH), 126.0 (C), 123.8 (CH), 123.4 (CH), 122.3 (C), 120.8 (CH), 115.5 (CH), 110.7 (CH), 104.7 (CH₂), 97.7 (CH), 83.2 (C), 71.9 (C), 55.8 (CH₃), 27.8 (CH₃);

HRMS (ESI) calcd for $C_{22}H_{21}NO_5Na([M + Na]^+) 402.1317$, found 402.1287.

² S. S. Zalesskiy and V. P. Ananikov, *Organometallics*, 2012, **31**, 2302-2309.

tert-Butyl 2-(2-hydroxy-4-methoxyphenyl)-2-((4-methoxybenzyl)carbamoyl)-3-methylene indoline-1-carboxylate (9)



A 500-mL, one-necked round-bottomed flask equipped with a three-way cock, a bubbler, a glass stopper and a magnetic stir bar was charged under N₂ gas with 7 (1.90 g, 5.0 mmol), toluene (10 mL), CH₃OH (10 mL) and PMBNH₂ (2.59 mL, 20 mmol). The reaction mixture was stirred at rt for 30 min, then concentrated *in vacuo*. The residue was purified by column chromatography on neutral silica gel (200 mL of silica gel, diameter = 5 cm, height = 10 cm, *n*-hexane/EtOAc = 9/1) to afford **10** (2.09 g, 4.0 mmol, quant) as a white foam. [KD08112]

Rf = 0.39 (*n*-hexane/EtOAc = 3/1, UV, Ce-PMA);

IR (neat, cm⁻¹) 1713, 1612, 1600, 1514, 1475, 1464, 1366, 1250, 1161, 1116, 751;

¹H NMR (CDCl₃, 600 MHz) δ 8.01 (br, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 8.3 Hz, 2H), 6.70 (d, *J* = 9.0 Hz, 1H), 6.53 (br, 1H), 6.50 (d, *J* = 2.8 Hz, 1H), 6.26 (dd, *J* = 9.0, 2.8 Hz, 1H) 5.56 (s, 1H), 5.54 (s, 1H), 4.59 (dd, *J* = 14.5, 6.9 Hz, 1H), 4.23 (dd, *J* = 14.5, 4.8 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 1.22 (s, 9H);

¹³C NMR (CDCl₃, 150 MHz) δ 173.3 (C), 160.4 (C), 159.1 (C), 155.5 (C), 151.0 (C), 147.9 (C), 143.0 (C), 130.5 (CH), 129.2 (CH), 129.1 (CH), 128.0 (C), 126.0 (C), 123.9 (CH), 121.3 (CH), 119.1 (C), 115.5 (CH), 114.0 (CH), 106.5 (CH), 105.0 (CH₂), 104.0 (CH), 83.1 (C), 77.9 (C), 55.2 (CH₃), 55.1 (CH₃), 43.7 (CH₂), 27.7 (CH₃);

HRMS (ESI) calcd for $C_{30}H_{32}N_2O_6Na([M + Na]^+)$ 539.2158, found 539.2130.

tert-Butyl 7-methoxy-12-(4-methoxybenzyl)-11,13-dioxo-10*H*-4b,9b-(ethanoiminomethano) benzofuro[3,2-*b*]indole-10-carboxylate (10)



A 150-mL Schlenk tube equipped with a glass stopper and a magnetic stir bar was charged with **10** (516.6 mg, 1.0 mmol), Pd(OAc)₂ (11.2 mg, 0.05 mmol), NaIO₄ (320.8 mg, 1.5 mmol), H₂O (18.0 μ L, 1.0 mmol) and DMSO (10 mL). The resulting mixture was stirred under CO atmosphere (Tedlar[®] bag, 1 atm) at 40 °C. After 18 h, the reaction mixture was quenched with sat NaHCO₃ aq (50 mL) and water (50 mL) at 0 °C, then the mixture was poured into separatory funnel, diluted with Et₂O (50 mL), and partitioned. The organic phase was collected and the aqueous phase was extracted with Et₂O (50 mL) twice. The combined organic extract was washed with brine (50 mL), dried over anhydrous Na₂SO₄ (ca. 5.0 g), filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (200 mL of silica gel, diameter = 5 cm, height = 10 cm, *n*-hexane/EtOAc = 20/1 to 3/1) to afford **11** (392.6 mg, 72.4 mmol, 72%) as a white solid. [KD08126]

Rf = 0.36 (*n*-hexane/EtOAc = 3/1, UV, Ce-PMA);

IR (neat, cm⁻¹) 1715, 1692, 1361, 1248, 1156, 753;

¹H NMR (CDCl₃, 600 MHz) δ 7.81 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 9.0 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.38 (dd, *J* = 8.3, 7.6 Hz, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 8.3 Hz, 2H), 6.70 (d, *J* = 8.3 Hz, 2H), 6.47 (d, *J* = 9.0 Hz, 1H), 6.34 (s, 1H), 4.84 (d, *J* = 13.8 Hz, 1H), 4.75 (d, *J* = 13.8 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.52 (d, *J* = 15.8 Hz, 1H), 3.12 (d, *J* = 15.8 Hz, 1H), 1.53 (s, 9H); ¹³C NMR (CDCl₃, 150 MHz) δ 167.2 (C), 166.8 (C), 162.7 (C), 161.1 (C), 158.7 (C), 151.0 (C), 143.3 (C), 131.5 (CH), 131.1 (CH), 129.5 (CH), 128.0 (C), 126.0 (C), 123.6 (CH), 123.4 (CH), 116.6 (CH), 113.6 (C), 113.5 (CH), 107.4 (CH), 95.8 (CH), 90.8 (C), 82.8 (C), 77.2 (C), 55.3 (CH₃), 54.9 (CH₃), 43.9 (CH₂), 40.0 (CH₂), 28.1 (CH₃);

HRMS (ESI) calcd for $C_{31}H_{30}N_2O_7Na([M + Na]^+)$ 565.1951, found 565.1921.



















