Supporting Information for the Paper entitled

**Synthetic Study of the Angular Tetracyclic Core Skeleton of Landomycin A via Masamune-Bergman Cyclization.**

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A. General Techniques

NMR spectra were recorded on a JEOL Model EX-270 (270 MHz for $^1$H, 67.8 MHz for $^{13}$C) or a JEOL Model ECP-400 (400 MHz for $^1$H, 100 MHz for $^{13}$C) instrument in the indicated solvent. Chemical shifts are reported in units parts per million (ppm) relative to the signal (0.00 ppm) for internal tetramethylsilane for solutions in CDCl$_3$. $^1$H NMR spectrum data is reported as follows: CDCl$_3$ (7.26 ppm). $^{13}$C NMR spectrum data is reported as follow: CDCl$_3$ (77.0 ppm). Multiplicities are reported by using the following abbreviations: s; singlet, d; doublet, t; triplet, q; quartet, m; multiplet, br; broad, $J$; coupling constants in Hertz.

IR spectra was recorded on a Perkin-Elmer Spectrum One FT-IR spectrophotometer. Only the strongest and/or structurally important peaks are reported as the IR data given in cm$^{-1}$.

All reactions were monitored by thin-layer chromatography carried out on 0.2 mm E. Merck silica gel plates (60F-254) with UV light, visualized by 10% ethanolic phosphomolybdic acid, p-anisaldehyde $\text{H}_2\text{SO}_4$ ethanol solution.

Merck silica gel was used for column chromatography.

ESI-TOF Mass spectra were measured with Waters LCT Premier™ XE.

Dry dichloromethane, dry THF, dry toluene, dry acetonitrile and dry triethylamine were obtained from solvent purification columns.
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B, Synthesis of Model Compound (3)

tert-butyl(2-ethynylphenethoxy)dimethylsilane (12)

To a stirred solution of NaBH₄ (1.36 g, 10.1 mmol) in EtOH (12.0 mL) was added 2-(2-ethynylphenyl)acetaldehyde¹ (11) (1.21 g, 8.41 mmol) in EtOH (12.0 mL) at 0 °C under argon. After being stirred at the same temperature for 1 h, the reaction mixture was poured into saturated aq. NH₄Cl. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was used for the next reaction without further purification.

To a stirred solution of the above residue in DMF (20.0 mL) was added TBSCl (1.52 g, 10.1 mmol) and imidazole (858 mg, 12.6 mmol) at 0 °C under argon. After being stirred at the same temperature for 1 h, the reaction mixture was poured into 1N HCl. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with saturated aq. NaHCO₃ and brine, dried over MgSO₄, filtered and concentrated in vacuo. The residue was chromatographed on silica gel with 90 : 10 hexane : ethyl acetate to give tert-butyl(2-ethynylphenethoxy)dimethylsilane (12) (1.69 g, 6.47 mmol, 2 steps 77%).

¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, 1H, J = 7.3 Hz), 7.30-7.24 (m, 2H), 7.17 (m, 1H), 3.87 (t, 2H, J = 7.3 Hz), 3.25 (s, 1H), 3.05 (t, 2H, J = 7.3 Hz), 0.89 (s, 9H), 0.00 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 141.6, 132.8, 130.1, 128.6, 126.1, 121.8, 82.3, 80.5, 63.3, 38.1, 25.9, 18.3, -5.43; IR (neat): 3305, 2929, 1472, 1256, 1100, 776, 757 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ calcd. 261.1675, found 261.1665.

2-((2-((2-(tert-butyldimethylsilyloxy)ethyl)phenyl)ethynyl)benzaldehyde (13)

To a stirred solution of PdCl₂(PPh₃)₂ (19.8 mg, 0.0282 mmol) and Cul (16.2 mg, 0.0846 mmol) was added DMF (5.60 mL), Et₂NH (583 µL, 5.64 mmol), 2-bromobenzaldehyde (9) (330 µL, 3.34 mmol) and tert-butyl(2-ethynylphenethoxy)dimethylsilane (12) (735 mg, 2.82 mmol) at room temperature under argon. After being stirred at 80 °C for 6 h, the reaction mixture was poured into 1N HCl. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was chromatographed on silica gel with 85 : 15 hexane : ethyl acetate to give 2-((2-(tert-butyldimethylsilyloxy)ethyl)phenyl)ethynyl)benzaldehyde (13) (678 mg, 1.86 mmol, 66%).

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\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \delta \ 10.7 \ (s, 1H), 7.96 \ (d, 1H, J = 7.7 \ Hz), 7.65 \ (d, 1H, J = 7.7 \ Hz), 7.56 \ (m, 2H), 7.45 \ (m, 1H), 7.31 \ (d, 2H, J = 3.9 \ Hz), 7.22 \ (m, 1H), 3.91 \ (t, 2H, J = 6.8 \ Hz), 3.11 \ (t, 2H, J = 6.8 \ Hz), 0.84 \ (s, 9H), 0.00 \ (s, 6H); \]

\[ ^13C \text{ NMR (100 MHz, CDCl}_3 \delta 191.5, 141.3, 135.7, 135.2, 133.7, 133.3, 132.4, 130.2, 128.9, 128.5, 127.3, 126.3, 121.8, 96.1, 88.3, 63.3, 38.2, 25.9, 18.2, -4.88; \]

IR (neat): 2929, 1699, 1593, 1472, 1257, 1095, 836, 758 cm\(^{-1}\); HRMS (ESI-TOF) [M+H\(^+\)] \text{calcd.} 365.1937, found 365.1937.

**tert-butyl(2-((2-ethynylphenyl)ethyl)phenethoxy)dimethylsilane**

To a stirred solution of 2-((2-((tert-butyldimethylsilyloxy)ethyl)phenyl)ethynyl)benzaldehyde (13) (543 mg, 1.49 mmol) in MeOH (4.00 mL) was added Ohira-Bestmann Reagent (14) (250 mg, 1.49 mmol) in MeOH (3.00 mL) and \( \text{K}_2\text{CO}_3 \) (596 mg, 4.31 mmol) at 0 °C under argon. After being stirred at room temperature for 3 h, the reaction mixture was poured into 1N HCl. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over MgSO\(_4\) and concentrated in vacuo. The residue was chromatographed on silica gel with 85 : 15 hexane : ethyl acetate to give tert-butyl(2-((2-ethynylphenyl)ethyl)phenethoxy)dimethylsilane (494 mg, 1.37 mmol, 92%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \delta 7.57-7.53 \ (m, 3H), 7.36-7.19 \ (m, 5H), 3.92 \ (t, 2H, J = 6.8 \ Hz), 3.41 \ (s, 1H), 3.18 \ (t, 2H, J = 6.8 \ Hz), 0.87 \ (s, 9H), 0.00 \ (s, 6H); \]

\[ ^13C \text{ NMR (100 MHz, CDCl}_3 \delta 141.2, 132.5, 131.9, 130.2, 128.5, 128.4, 127.8, 126.6, 126.1, 124.4, 122.8, 92.2, 91.1, 82.4, 81.4, 63.4, 38.2, 25.9, 18.3, -5.46; \]

IR (neat): 3296, 2929, 1729, 1472, 1256, 1093, 836, 777 cm\(^{-1}\); HRMS (ESI-TOF) [M+H\(^+\)] \text{calcd.} 361.1988, found 361.1988.

**2-(2-((2-ethynylphenyl)ethyl)phenyl)ethanol (15)**

To a stirred solution of tert-butyl(2-((2-ethynylphenyl)ethyl)phenethoxy)dimethylsilane (560 mg, 1.56 mmol) in DMF (7.50 mL) was added TBAF-xH\(_2\)O (608 mg, 2.34 mmol) at 0 °C under argon. After being stirred at room temperature for 1 h, the reaction mixture was poured into 1N HCl. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with saturated aq. NaHCO\(_3\) and brine, dried over MgSO\(_4\) and concentrated in vacuo. The residue was chromatographed on
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silica gel with 80 : 20 hexane : ethyl acetate to give 2-(2-((2-ethynylphenyl)ethynyl)phenyl)ethanol (15) (380 mg, 1.54 mmol, 99%).

\[ \text{1}^1\text{H NMR (400 MHz, CDCl}_3\text{)} \delta 7.58-7.53 (m, 3H), 7.35-7.21 (m, 5H), 3.95 (t, 2H, } J = 6.8 \text{ Hz), 3.41 (s, 1H), 3.20 (t, 2H, } J = 6.8 \text{ Hz); } \text{13C NMR (100 MHz, CDCl}_3\text{)} \delta 140.6, 132.7, 131.9, 129.7, 128.7, 128.6, 127.9, 126.4, 126.3, 124.2, 122.9, 92.0, 91.4, 82.6, 81.2, 63.1, 1042, 751, 624 \text{ cm}^{-1}; \text{ IR (neat)}: 3558, 3370, 3287, 2930, 1716, 1490, 1042, 751, 624 \text{ cm}^{-1}; \text{ HRMS (ESI-TOF) [M+H]}^+ \text{ calcd. 247.1113, found 247.1123.} \]

2-2-(2-((iodoethynyl)phenyl)ethynyl)phenyl)ethanol

To a stirred solution of 2-(2-((2-ethynylphenyl)ethynyl)phenyl)ethanol (15) (361 mg, 1.47 mmol) in toluene (22.0 mL) was added morpholine (1.92 mL, 22.1 mmol, 15.0 eq.) and I\(_2\) (1.87 g, 7.35 mmol) at room temperature under argon. After being stirred at 50 °C for 1 h, the reaction mixture was poured into 10% aq. Na\(_2\)S\(_2\)O\(_3\). The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over MgSO\(_4\) and concentrated in vacuo. The residue was chromatographed on silica gel with 80 : 20 hexane : ethyl acetate to give 2-(2-((iodoethynyl)phenyl)ethynyl)phenyl)ethanol (492 mg, 1.32 mmol, 90%).

\[ \text{1}^1\text{H NMR (270 MHz, CDCl}_3\text{)} \delta 7.59-7.45 (m, 3H), 7.33-7.21 (m, 5H), 4.00 (t, 2H, } J = 6.6 \text{ Hz), 3.21 (t, 2H, } J = 6.6 \text{ Hz); } \text{13C NMR (67.8 MHz, CDCl}_3\text{)} \delta 140.7, 132.9, 132.8, 131.8, 129.7, 128.7, 128.5, 127.9, 126.6, 126.4, 125.4, 122.9, 93.1, 92.1, 91.4, 63.1, 38.1, 10.7; \text{ IR (neat): 3370, 2952, 2167, 1490, 1041, 757 cm}^{-1}; \text{ HRMS (ESI-TOF) [M+H]}^+ \text{ calcd. 373.0089, found 373.0089.} \]

2-2-(2-((iodoethynyl)phenyl)ethynyl)phenyl)acetaldehyde (8)

To a stirred solution of 2-(2-((iodoethynyl)phenyl)ethynyl)phenyl)ethanol (150 mg, 0.403 mmol) in CH\(_2\)Cl\(_2\) (2.00 mL) was added Dess-Martin Periodinane (256 mg, 0.605 mmol) at 0 °C under argon. After being stirred at room temperature for 1 h, the reaction mixture was poured into saturated aq. NaHCO\(_3\). The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with
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brine, dried over MgSO₄ and concentrated in vacuo. The residue was chromatographed on silica gel with 80 : 20 hexane : ethyl acetate to give 2-(2-((2-(iodoethynyl)phenyl)ethynyl)phenyl)acetaldehyde (8) (140 mg, 0.379 mmol, 94%).

¹H NMR (400 MHz, CDCl₃) δ 9.86 (t, 1H, J = 2.0 Hz), 7.64 (m, 1H), 7.54-7.45 (m, 2H), 7.37-7.25 (m, 5H), 4.06 (d, 2H, J = 2.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 199.1, 134.4, 132.9, 132.8, 131.8, 130.1, 129.1, 128.6, 128.1, 127.5, 126.2, 125.4, 123.5, 93.1, 92.3, 91.5, 49.3, 10.9; IR (neat): 3426, 3060, 2826, 2167, 1723, 1491, 1036, 757 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ calcd. 370.9933, found 370.9933.

Masamune-Bergmann Cyclization

To a stirred solution of 2-(2-((2-(iodoethynyl)phenyl)ethynyl)phenyl)acetaldehyde (8) in THF was added CrCl₂ and NiCl₂ at room temperature under argon. After being stirred at the same temperature for 10 min, the reaction mixture was poured into H₂O. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was used for the next reaction without further purification.

To a stirred solution of the residue in CH₃CN was added a large amount of halogen source at room temperature under argon. After being stirred at 60 °C for 1 h, the reaction mixture was concentrated in vacuo. The residue was chromatographed on silica gel with 80 : 20 hexane : ethyl acetate to give product.

(entry 1) Br source : CBr₄

2-(2-((2-(iodoethynyl)phenyl)ethynyl)phenyl)acetaldehyde (8) (43.6 mg, 0.118 mmol)
THF (20.0 mL)
CrCl₂ (130 mg, 1.06 mmol) and NiCl₂ (9.80 mg, 0.0755 mmol)
CH₃CN (10.0 mL)
CBr₄ (392 mg, 1.18 mmol)
Product : 7,12-dibromo-5,6-dihydrotetraphen-6-ol (4a) (17.2 mg, 0.0437 mmol, 2 steps 37%)

¹H NMR (400 MHz, CDCl₃) δ 8.52 (m, 1H), 8.40-8.32 (m, 2H), 7.70-7.62 (m, 2H), 7.40-7.35 (m, 3H), 5.64 (t, 1H, J = 2.9 Hz), 3.20 (dd, 1H, J = 15.0 Hz, J = 2.9 Hz), 3.11 (dd, 1H, J = 15.0 Hz, J = 2.9 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 137.3, 134.6, 134.3, 133.8, 133.8, 132.6, 132.2, 130.8, 129.6, 129.12, 129.05, 128.6, 128.24, 128.18, 126.2, 124.8, 121.5, 68.9, 37.2; IR (neat): 3407, 2932, 1489, 1247, 1045, 761 cm⁻¹.
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(entry 2) **Source:** I$_2$

2-(2-(2-(iodoethynyl)phenyl)ethynyl)phenyl)acetaldehyde (8) (57.8 mg, 0.156 mmol)

THF (31.2 mL)

CrCl$_2$ (172 mg, 1.40 mol) and NiCl$_2$ (12.8 mg, 0.0998 mmol)

CH$_3$CN (15.6 mL)

I$_2$ (396 mg, 1.56 mmol)

**Product:** 7,12-diiodo-5,6-dihydrotetraphen-6-ol (4b) (decomposed)

(entry 3) **Source:** NIS

2-(2-(2-(iodoethynyl)phenyl)ethynyl)phenyl)acetaldehyde (8) (90.8 mg, 0.245 mmol)

THF (49.0 mL)

CrCl$_2$ (271 mg, 2.21 mmol) and NiCl$_2$ (20.3 mg, 0.157 mmol)

CH$_3$CN (24.5 mL)

NIS (700 mg, 3.93 mmol)

**Product:** 7,12-diiodo-5,6-dihydrotetraphen-6-ol (4b) (trace)

(entry 4) **Source:** ICH$_2$CH$_2$I

2-(2-(2-(iodoethynyl)phenyl)ethynyl)phenyl)acetaldehyde (8) (87.0 mg, 0.235 mmol)

THF (47.0 mL)

CrCl$_2$ (259 mg, 2.11 mmol) and NiCl$_2$ (19.5 mg, 0.150 mmol)

CH$_3$CN (23.5 mL)

ICH$_2$CH$_2$I (excess)

**Product:** 7,12-diiodo-5,6-dihydrotetraphen-6-ol (4b) (61.4 mg, 0.123 mmol, 2 steps 52 %)

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.40 (m, 1H), 8.26-8.20 (m, 2H), 7.64-7.56 (m, 2H), 7.36-7.32 (m, 3H), 5.46 (t, 1H, $J = 2.9$ Hz), 3.15 (dd, 1H, $J = 2.9$ Hz, $J = 15.4$ Hz), 3.10 (dd, 1H, $J = 2.9$ Hz, $J = 15.4$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 140.8, 139.0, 136.8, 135.40, 135.16, 134.66, 134.33, 133.9, 132.9, 132.7, 131.6, 130.2, 129.3, 129.1, 129.0, 128.7, 128.4, 127.6, 127.1, 126.0, 108.5, 102.4, 74.6, 49.4, 37.4; IR (neat): 3437, 3019, 1722, 1216, 1045, 753, 667 cm$^{-1}$; HRMS (ESI-TOF) [M+H]$^+$ calcd. 498.9056, found 498.9035.
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7,12-dimethoxy-5,6-dihydrotetraphen-6-ol (16)

To a stirred solution of 7,12-diiodo-5,6-dihydrotetraphen-6-ol (4b) (12.7 mg, 0.0254 mmol) in MeOH (2.00 mL) was added t-BuOK (7.15 mg, 0.0637 mmol), CuI (0.484 mg, 0.00254 mmol) and 1,10-phenanthroline (0.915 mg, 0.00508 mmol) at room temperature under argon. After being stirred at 150 °C, 300 W for 60 min under micro-wave irradiation, the reaction mixture was poured into diethyl ether and H₂O. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was chromatographed on silica gel with 70 : 30 hexane : ethyl acetate to give 7,12-dimethoxy-5,6-dihydrotetraphen-6-ol (16) (5.98 mg, 0.0196 mmol, 77%).

¹H NMR (400 MHz, CDCl₃) δ 8.64 (d, 1H, J = 7.7 Hz), 8.24 (m, 1H), 7.12 (m, 1H), 7.58-7.52 (m, 2H), 7.41-7.27 (m, 3H), 5.53 (t, 1, J = 3.4 Hz), 4.08 (s, 3H), 3.72 (s, 3H), 3.21 (dd, 1H, J = 3.4 Hz, J = 15.0 Hz), 3.09 (dd, 1H, J = 3.4 Hz, J = 15.0 Hz); ¹³C NMR (100 MHz, CDCl₃) δ 150.5, 149.7, 133.5, 131.5, 130.0, 128.6, 128.45, 128.42, 128.0, 127.5, 126.7, 126.6, 123.1, 122.5, 121.8, 63.7, 62.4, 60.9, 37.8; IR (neat): 3446, 2933, 1647, 1452, 1353, 1217, 1069, 763 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ calcd. 307.1334, found 307.1348.

Model compound : 6-hydroxy-5,6-dihydrotetrathene-7,12-dione (3)

To a stirred solution of 7,12-dimethoxy-5,6-dihydrotetraphen-6-ol (16) (4.40 mg, 0.0144 mmol) in CH₃CN (1.00 mL) and H₂O (0.500 mL) was added CAN (17.4 mg, 0.0316 mmol) at room temperature under argon. After being stirred at the same temperature for 10 min, the reaction mixture was poured into diethyl ether and H₂O. The aqueous layer was extracted with two portions of diethyl ether. The combined extract was washed with brine, dried over MgSO₄ and concentrated in vacuo. The residue was chromatographed on silica gel with 70 : 30 hexane : ethyl acetate to give model compound:6-hydroxy-5,6-dihydrotetrathene-7,12-dione (3) (3.00 mg, 0.0109 mmol, 75%).

¹H NMR (400 MHz, CDCl₃) δ 8.24 (m, 1H), 8.18 (m, 1H), 8.14 (m, 1H), 7.82-7.74 (m, 2H), 7.44-7.35 (m,
3H), 5.30 (t, 1H, \( J = 4.8 \) Hz), 3.23 (dd, 1H, \( J = 4.8 \) Hz, \( J = 15.5 \) Hz), 3.11 (dd, 1H, \( J = 4.8 \) Hz, \( J = 15.5 \) Hz);
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 185.5, 185.1, 139.8, 138.6, 135.8, 134.0, 133.8, 132.9, 131.8, 130.8, 130.6, 129.3, 127.9, 127.2, 126.9, 126.0, 61.5, 35.5; IR (neat): 3446, 2927, 1652, 1305, 1054, 763 cm\(^{-1}\); HRMS (ESI-TOF) [M+H]\(^+\) calcd. 277.0865, found 277.0860.
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