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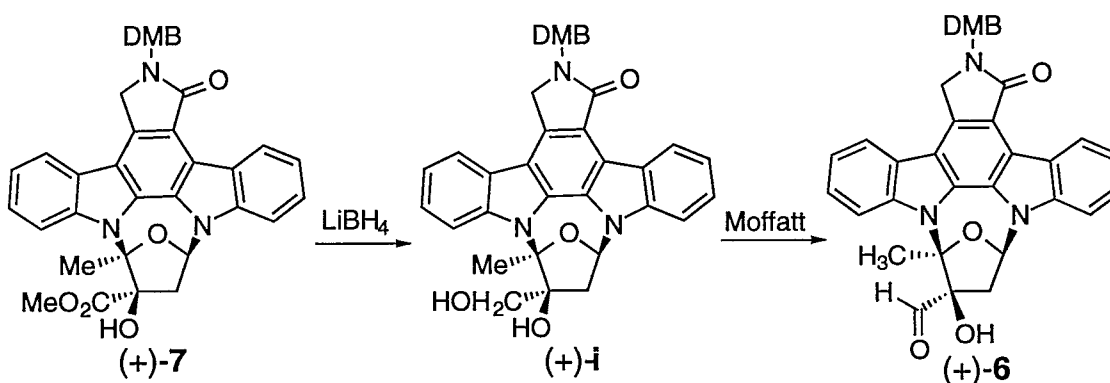
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**Experimental Section for
"The Total Synthesis of (+)-RK-286c,
(+)-MLR-52, (+)-Staurosporine, and (+)-K252a."**

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Preparation of aldehyde (+)-6



To a stirred solution of ester (+)-7 (150 mg, 0.243mmol) in THF (2.5 mL) was added LiBH_4 (12 mg, 0.535 mmol) at room temperature. After 20 min solvent was removed in vacuo. To the white residue, 10.0 mL 1.0 N HCl was added on an ice bath. The aqueous phase was extracted with CH_2Cl_2 (3x 20 mL). The combined organic phases were dried with Na_2SO_4 and chromatographed on silica gel using 1:1 hexanes:ethyl acetate as eluent to afford diol (+)-i (124mg, 89%) as a white solid.

^1H NMR (500 MHz, DMSO-d_6): δ 9.25 (d, $J=7.9$ Hz, 1H), 7.97 (d, $J=7.2$ Hz, 1H), 7.96 (d, $J=8.1$ Hz, 1H), 7.78 (d, $J=8.3$ Hz, 1H), 7.48 (app.t, $J=7.6$ Hz, 1H), 7.43 (app.t, $J=7.8$ Hz, 1H), 7.29 (app.t, $J=7.1$ Hz, 1H), 7.28 (app.t, $J=7.2$ Hz, 1H), 7.02 (s, 1H), 7.96 (dd, $J=5.2, 7.2$ Hz, 1H), 6.94 (s, 2H), 5.33 (s, 1H), 5.06 (t, $J=5.6$ Hz, 1H), 5.02 (d, $J=17.7$ Hz, 1H), 4.95 (d, $J=17.6$ Hz, 1H), 4.85 (d, $J=15.9$ Hz, 1H), 4.85 (d, $J=15.7$ Hz, 1H), 3.85-3.81 (m, 2H), 3.75 (s, 3H), 3.72 (s, 3H), 3.14 (dd, $J=7.6, 13.7$ Hz, 1H), 2.15 (s, 3H), 1.94 (dd, $J=4.8, 13.7$ Hz, 1H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 168.9, 148.9, 148.1, 140.0, 136.7, 130.5, 130.2, 128.7, 125.4, 125.3, 124.6, 124.3, 123.8, 122.4, 120.9, 120.0, 119.8, 119.2, 118.5, 115.2, 114.9, 114.0, 112.1, 111.8, 108.7, 100.2, 83.5, 64.7, 55.5, 55.5, 49.6, 45.4, 40.2, 40.1, 21.3.

IR (thin film/NaCl): 3343.8 (brm), 3001.5 (w), 2950.7 (m), 2926.1 (m), 1647.4 (s), 1588.0 (m), 1514.4 (m), 1459.7 (s), 1422.2 (m), 1399.6 (m), 1312.4 (m), 1138.0 (s), 744.7 (s) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{35}\text{H}_{32}\text{N}_3\text{O}_6$ (M+H): 590.2291. Found: 590.2289.

$[\alpha]_{\text{D}}^{20} +112^\circ$ (c=0.1, MeOH).

m.p.: >225 $^\circ\text{C}$ dec. (acetone)

To a stirred solution of diol (+)-**i** (395 mg, 0.67 mmol) in 1:1 benzene:DMSO (4.6 mL) was added pyridinium trifluoroacetate (130 mg, 0.67 mmol) followed by 1,3-dicyclohexylcarbodiimide (415 mg, 2.01 mmol). The flask was then quickly sealed with a septum, evacuated, and flushed with N_2 (3x). The heterogeneous mixture was stirred for 9h until reaction was complete as indicated by TLC. Benzene (5.0 mL) was added to the mixture and the 1,3-dicyclohexylurea (DCU) precipitate was filtered. The filtrate was washed with H_2O (3x 5.0 mL), and the combined aqueous layers were back extracted with CH_2Cl_2 (3x 10.0 mL). All organic layers were combined, dried with Na_2SO_4 , and evaporated to an oily residue. A minimum amount of acetone (2 mL) was added to precipitate the remaining DCU. Filtration and evaporation to a yellow oil, which was purified by MPLC (2:1 $\rightarrow$ 1:1 hexanes:ethyl acetate) gave aldehyde (+)-**6** (280 mg, 71%, 63% 2 steps) as a yellow powder.

^1H NMR (500 MHz, DMSO-d_6): δ 10.07 (s, 1H), 9.31 (d, $J=7.9$ Hz, 1H), 8.02 (d, $J=8.5$ Hz, 1H), 7.99 (d, $J=7.7$ Hz, 1H), 7.87 (d, $J=8.2$ Hz, 1H), 7.50 (app.t, $J=8.1$ Hz, 1H), 7.47 (app.t, $J=8.2$ Hz, 1H), 7.32 (app.t, $J=8.1$ Hz, 1H), 7.17 (dd, $J=7.2, 4.8$ Hz, 1H), 7.04 (s, 1H), 6.94 (d, $J=9.6$ Hz, 1H), 6.93 (d, $J=8.1$ Hz, 1H), 6.57 (bs, 1H), 5.02 (d, $J=17.6$ Hz, 1H), 4.98 (d, $J=17.7$ Hz, 1H), 4.87 (d, $J=15.2$ Hz, 1H), 4.83 (d, $J=15.2$ Hz, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.24 (dd, $J=7.6, 14.0$ Hz, 1H), 2.22 (s, 3H), 2.00 (dd, $J=4.5, 14.0$ Hz, 1H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 202.2, 168.7, 148.9, 148.1, 139.9, 136.9, 130.4, 130.2, 128.2, 125.5, 125.1, 123.9, 123.9, 122.5, 121.1, 120.4, 119.9, 119.6, 119.1, 115.8, 114.6, 114.4, 112.1, 111.8, 109.0, 98.7, 86.8, 84.3, 55.5, 55.5, 49.6, 45.5, 39.4, 22.7.

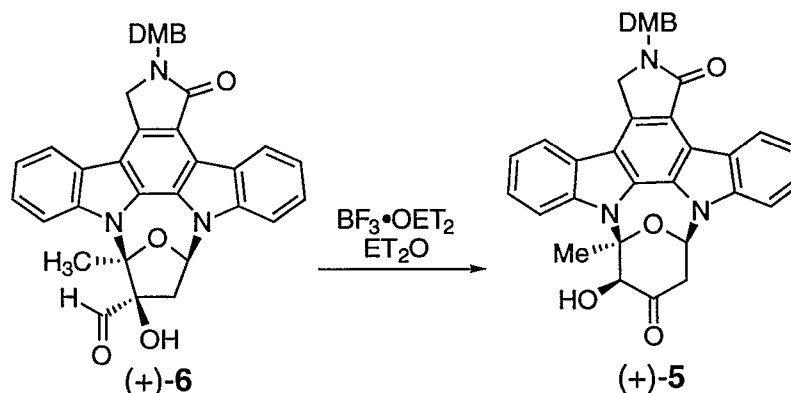
IR (thin film/NaCl): 3253.9 (brm), 3010.7 (m), 2953.6 (m), 2934.0 (m), 2833.9 (s), 1734.0 (s), 1646.2 (s), 1614.7 (w), 1589.9 (m), 1514.1 (m), 1399.1 (s), 1275.7 (m), 1138.4 (s), 1024.8 (m), 745.1 (s) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{35}\text{H}_{30}\text{N}_3\text{O}_6$ (M+H): 588.2135. Found: 588.2135.

$[\alpha]_{\text{D}}^{20} +48^\circ$ (c=0.1, MeOH).

m.p.: >205 °C dec. (ethyl acetate / hexanes)

Preparation of hydroxy ketone (+)-5



To a suspension of aldehyde (+)-6 (100 mg, 0.170 mmol) in Et_2O (17.0 mL) was added $\text{BF}_3 \cdot \text{OEt}_2$ (23 μL , 0.187 mmol) and the mixture stirred vigorously for 12h at 25-30 °C, when again was treated with $\text{BF}_3 \cdot \text{OEt}_2$ (23 μL , 0.187 mmol) and stirred for an additional 12 h at the same temperature. The reaction mixture was filtered to provide ketone (+)-5 (85 mg, 85%) as a white powder.

^1H NMR (500 MHz, $\text{DMSO}-d_6$, 310 K): δ 9.35 (d, $J=7.9$ Hz, 1H), 8.06 (d, $J=8.6$ Hz, 1H), 7.92 (d, $J=7.7$ Hz, 1H), 7.72 (d, $J=8.2$ Hz, 1H), 7.53 (app.t, $J=7.6$ Hz, 1H), 7.43 (app.t, $J=8.1$ Hz, 1H), 7.40 (d, $J=6.6$ Hz, 1H), 7.35 (app.t, $J=7.5$ Hz, 1H), 7.29 (app.t, $J=7.4$ Hz, 1H), 7.02 (s, 1H), 6.93 (s, 2H), 6.12 (d, $J=5.1$ Hz, 1H), 5.23 (d, $J=4.5$ Hz, 1H), 4.96 (s, 2H), 4.85 (d, $J=15.1$ Hz, 1H), 4.81 (d, $J=15.1$ Hz, 1H), 3.97 (dd, $J=6.7, 14.1$ Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 2.66 (d, $J=14.1$ Hz, 1H), 2.54 (s, 3H).

^{13}C NMR (500 MHz, $\text{DMSO}-d_6$): δ 201.1, 168.6, 148.9, 148.1, 140.3, 136.0, 130.4, 129.8, 126.9, 125.6, 125.5, 124.9, 124.0, 123.6, 122.8, 120.7, 120.4, 119.9, 119.9, 118.8, 115.9, 115.1, 114.3, 112.1, 111.8, 109.2, 100.5, 84.4, 80.0, 55.5, 55.5, 49.6, 45.4, 44.9, 29.4.

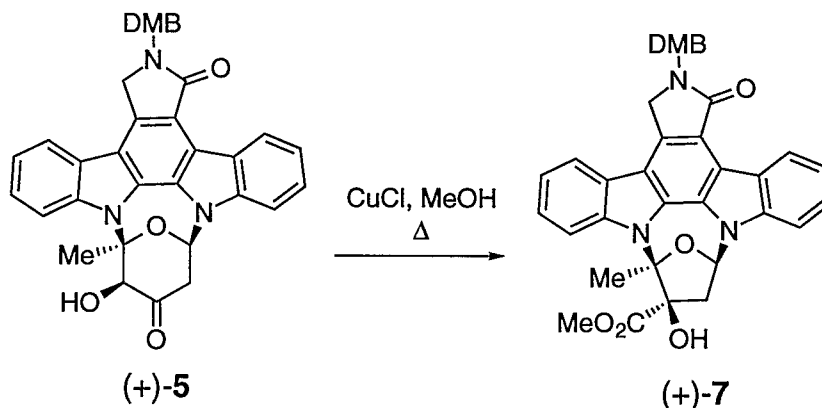
IR (thin film/ NaCl): 3300.0 (brs), 2999.5 (brm), 2848.6 (m), 1728.9 (m), 1665.5 (s), 1503.3 (m), 1451.2 (s), 1406.8 (m), 1132.8 (s), 1021.9 (m), 750.6 (s) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{35}\text{H}_{30}\text{N}_3\text{O}_6$ ($\text{M}+\text{H}$): 588.2135. Found: 588.2135.

$[\alpha]_{\text{D}}^{20} +83^{\circ}$ ($c=0.1$, DMSO).

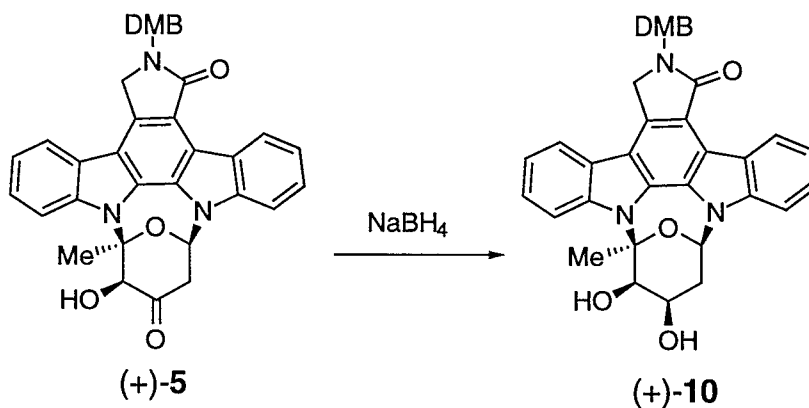
m.p.: $>220^{\circ}\text{C}$ dec. (diethyl ether)

Preparation of Ester (+)-7



To a solution of ketone (+)-5 (10 mg, 0.017 mmol) in 1:1 $\text{MeOH}/\text{CH}_2\text{Cl}_2$ (1.0 mL) was added Copper (I) chloride (30 mg, 0.30 mmol), and the mixture warmed to reflux for 15 min. Solvent was removed *in vacuo* and the resulting residue subjected to silica gel chromatography (1:1, hexanes:ethyl acetate) to afford (+)-7 (10 mg, 95%) as a colorless solid.

Preparation of diol (+)-10



To a stirred solution of ketone (+)-**5** (85 mg, 0.15 mmol) in 1:1:2 MeOH:CH₂Cl₂:CHCl₃ (20.0 mL), NaBH₄ (20 mg, 0.53 mmol) was added at room temperature. After 5 minutes solvent was removed under reduced pressure. To the white residue, 10 mL 1.0 N HCl was added on an ice bath. The mixture was stirred for 15 min at 25 °C and extracted with CH₂Cl₂ (3x 20 mL). The combined organic phases were dried with Na₂SO₄ and chromatographed on silica gel using 1:1 hexanes:ethyl acetate as eluent to afford alcohol (+)-**10** (81 mg, 95%) as a white solid.

¹H NMR (500 MHz, acetone-d₆): δ 9.53 (d, J=7.9 Hz, 1H), 8.11 (d, J=8.5 Hz, 1H), 7.88 (d, J=7.7 Hz, 1H), 7.51 (d, J=8.2 Hz, 1H), 7.46 (app.t, J=7.2 Hz, 1H), 7.36 (app.t, J=7.9 Hz, 1H), 7.29 (app.t, J=7.4 Hz, 1H), 7.22 (app.t, J=7.4 Hz, 1H), 7.08 (s, 1H), 6.98 (d, J=8.3 Hz, 1H), 6.91 (d, J=8.2 Hz, 1H), 6.76 (d, J=5.1 Hz, 1H), 4.95 (d, J=17.1 Hz, 1H), 4.90 (d, J=71.1 Hz, 1H), 4.89 (d, J=15.2 Hz, 1H), 4.85 (d, J=15.2 Hz, 1H), 4.24 (d, J=8.5 Hz, 1H), 4.23 (bs, 1H), 4.14 (d, J=8.6 Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.64 (bs, 1H), 2.76 (d, J=15.1 Hz, 1H), 2.65 (d, J=15.1 Hz, 1H), 2.35 (s, 3H).

¹³C NMR (125 MHz, acetone-d₆): δ 170.4, 150.6, 149.7, 141.2, 137.7, 132.0, 130.7, 130.4, 127.6, 127.1, 125.8, 125.3, 125.0, 124.3, 121.5, 121.0, 120.6, 120.0, 119.8, 116.6, 116.0, 115.0, 112.8, 108.9, 93.3, 80.6, 74.7, 65.4, 56.1, 50.4, 46.6, 35.4, 30.4.

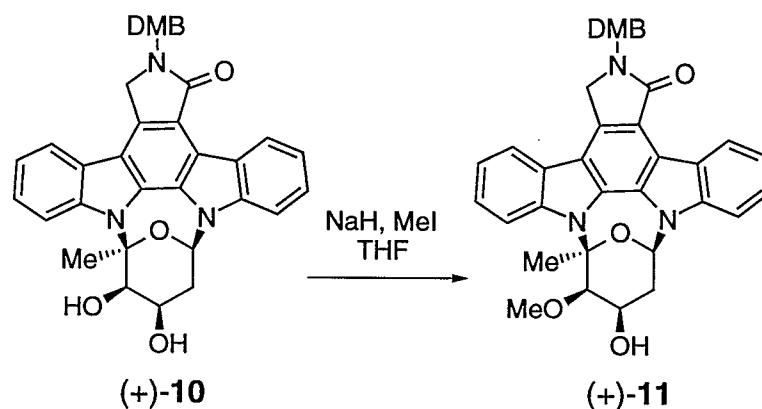
IR (thin film/NaCl): 3355.5 (brm), 2922.9 (m), 2847.8 (m), 1654.5 (s), 1501.5 (w), 1449.3 (s), 1254.5 (s), 1136.8 (s), 1025.7 (m), 747.1 (s) cm⁻¹.

HRMS (FAB) *m/z* Calc'd for C₃₅H₃₂N₃O₆ (M+H): 590.2291. Found: 590.2289.

[α]_D²⁰ +37° (c=0.1, MeOH).

m.p.: 174-176 °C dec. (acetone)

Preparation of methyl ether (+)-**11**



To a stirred suspension of NaH (14 mg, 0.58 mmol) in THF (1.0 mL) was added a solution of alcohol (+)-**10** (81 mg, 0.138 mmol) in THF (7 mL). The resulting mixture was stirred for 10 min with the visible evolution of gas, and for an additional 15 min thereafter. Addition of MeI (9.5 μ L, 0.15 mmol) produced a single product by TLC (2.5:1 hexanes:acetone). After approximately 50 min the reaction was quenched by addition of 1.0 mL 1.0N HCl followed by 2.0 mL H₂O. Extraction of the solution with CH₂Cl₂ (3x 10 mL), drying over Na₂SO₄ and evaporation to a residue which could be purified by MPLC (2.5:1 hexanes:acetone) provided methyl ether (+)-**11** (67 mg, 80%) as a yellow foam.

¹H NMR (500 MHz, CDCl₃): δ 9.54 (d, J=7.9 Hz, 1H), 7.90 (d, J=8.5 Hz, 1H), 7.81 (d, J=7.7 Hz, 1H), 7.48 (app.t, J=7.6 Hz, 1H), 7.41 (app.t, J=7.2 Hz, 1H), 7.38 (app.t, J=7.2 Hz, 1H), 7.28 (m, 2H), 6.97 (d, J=8.2 Hz, 1H), 6.95 (s, 1H), 6.86 (d, J=8.1 Hz, 1H), 6.60 (d, J=5.8 Hz, 1H), 4.96 (d, J=15.0 Hz, 1H), 4.89 (d, J=15.0 Hz, 1H), 4.84 (d, J=16.7 Hz, 1H), 4.79 (d, J=16.6 Hz, 1H), 4.38 (d, J=2.6 Hz, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.71 (d, J=2.6 Hz, 1H), 3.57 (s, 3H), 2.76 (dd, J=3.1, 15.1 Hz, 1H), 2.50 (bd, J=14.7 Hz, 1H), 2.3 (s, 3H).

¹³C NMR (125 MHz, CDCl₃, 315 K): δ 170.3, 149.6, 148.7, 140.1, 136.8, 130.8, 129.4, 127.0, 126.4, 125.3, 124.8, 124.3, 123.7, 120.7, 120.4, 120.2, 120.0, 119.6, 116.0, 115.5, 114.5, 111.6, 111.5, 107.1, 90.7, 83.2, 79.5, 60.6, 57.4, 56.1, 56.0, 49.9, 46.5, 33.6, 30.1.

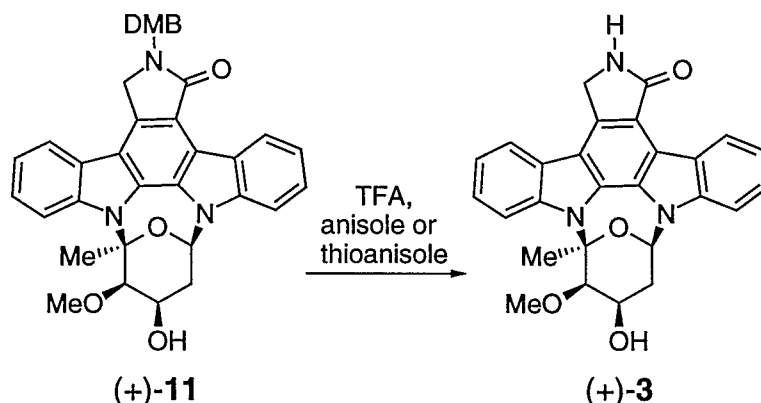
IR (thin film/NaCl): 3423.7 (brm), 2923.2 (s), 2848.1 (m), 2636.2 (m), 1647.2 (s), 1514.3 (m), 1462.9 (s), 1258.0 (m), 1235.3 (m), 1136.9 (m), 1026.9 (w), 743.3 (s) cm^{-1} .

HRMS (FAB) m/z Calc'd for C₃₆H₃₄N₃O₆ (M+H): 604.2448. Found: 604.2449.

$$[\alpha]_D^{20} +48^{\circ} \text{ (c=0.1, MeOH).}$$

m.p.: >235 °C dec. (acetone)

Preparation of (+)-RK-286c (3)



To a stirred solution of ether (+)-11 (10 mg, 0.017 mmol) in anisole or thioanisole (80 μ L, $\approx$ 50 equiv) was added TFA (0.5 mL). The reaction was monitored by TLC, and after 24 h had proceeded to completion, whereupon 1.0 mL H₂O was added, followed by extraction with CH₂Cl₂ (3x 5mL). Combined organic layers were washed with saturated aqueous NaHCO₃ (5 mL), dried over Na₂SO₄, and evaporated to a residue, which was purified by preparative TLC (5% MeOH:CH₂Cl₂) to provide (+)-RK-286c (3, 6 mg, 75%).

¹H NMR (500 MHz, DMSO-d₆): δ 9.27 (d, *J*=7.9 Hz, 1H), 8.47 (bs, 1H), 7.99 (d, *J*=8.5 Hz, 1H), 7.94 (d, *J*=7.7 Hz, 1H), 7.59 (d, *J*=8.2 Hz, 1H), 7.45 (app.t, *J*=7.4 Hz, 1H), 7.40 (app.t, *J*=7.5 Hz, 1H), 7.26 (app.t, *J*=7.5 Hz, 1H), 6.78 (d, *J*=5.3 Hz, 1H), 4.95 (d, *J*=17.6 Hz, 1H), 4.89 (d, *J*=17.7 Hz, 1H), 4.25 (bs, 1H), 4.17 (bs, 1H), 3.83 (d, *J*=2.7 Hz, 1H), 3.41 (s, 3H), 2.60 (ddd, *J*=3.2, 5.6, 14.8 Hz, 1H), 2.41 (dd, *J*=3.3, 14.8 Hz, 1H), 2.31 (s, 3H).

¹³C NMR (125 MHz, DMSO-d₆): δ 139.7, 136.1, 129.5, 125.5, 124.7, 124.1, 123.9, 122.6, 120.6, 119.5, 118.9, 118.6, 115.7, 108.6, 90.9, 82.3, 79.5, 58.8, 56.4, 45.3, 33.9, 29.9.

IR (thin film/NaCl): 3354.0 (brm), 2920.4 (s), 2851.6 (m), 1677.2 (s), 1636.0

1575.5 (s), 1476.2 (s), 1379.8 (s), 1327.7 (s), 1291.7 (s), 1177.2 (s), 1117.2 (s), 1077.2 (s), 1037.2 (s), 1017.2 (s), 977.2 (s), 937.2 (s), 897.2 (s), 857.2 (s), 817.2 (s), 777.2 (s), 737.2 (s), 697.2 (s), 657.2 (s), 617.2 (s), 577.2 (s), 537.2 (s), 497.2 (s), 457.2 (s), 417.2 (s), 377.2 (s), 337.2 (s), 297.2 (s), 257.2 (s), 217.2 (s), 177.2 (s), 137.2 (s), 97.2 (s).

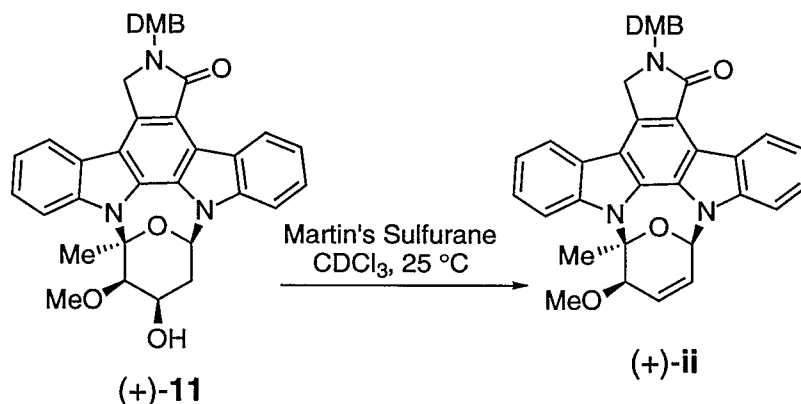
743.8 (s) cm⁻¹.

HRMS (FAB) *m/z* Calc'd for C₂₇H₂₄N₃O₄ (M+H): 454.1767. Found: 454.1766.

[α]_D²⁵ +41.1° (*c*=0.18, EtOAc); natural RK-286c [α]_D²⁰ +45.3° (*c*=0.22, EtOAc).

m.p.: >255 °C dec. (acetone); natural RK-286c **m.p.:** >265 °C dec.

Preparation of Olefin (+)-ii



To a stirred solution of ether (+)-**11** (112 mg, 0.186 mmol) in CDCl₃ (2.0 mL) was added Martin's sulfurane (187 mg, 0.28 mmol). The reaction rapidly proceeded to a less polar product as monitored by TLC, and after 20 min was complete. Solvent was evaporated and the residue subjected to silica gel chromatography (2:1 hexanes:ethyl acetate) to provide olefin (+)-**ii** (96 mg, 88%) as a white solid.

¹H NMR (500 MHz, DMSO-d₆, 315 K): δ 9.31 (d, J=7.9 Hz, 1H), 8.11 (d, J=8.6 Hz, 1H), 7.91 (d, J=7.7 Hz, 1H), 7.86 (d, J=8.2 Hz, 1H), 7.50 (td, J=1.0, 7.34 Hz, 1H), 7.43 (app.t, J=7.8 Hz, 1H), 7.31 (app.t, J=7.0 Hz, 1H), 7.28 (app.t, J=7.1 Hz, 1H), 7.13 (d, J=1.9 Hz, 1H), 7.02 (s, 1H), 6.93 (d, J=8.6 Hz, 1H), 6.92 (d, J=8.6 Hz, 1H), 6.09 (d, J=10.4 Hz, 1H), 5.77 (dt, J=2.3, 10.4 Hz, 1H), 4.95 (s, 2H), 4.85 (d, J=15.1 Hz, 1H), 4.81 (d, J=15.1 Hz, 1H), 4.48 (d, J=1.4 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 3.57 (s, 3H), 2.20 (s, 3H).

¹³C NMR (125 MHz, acetone-d₆): δ 169.9, 150.5, 149.7, 141.3, 137.4, 131.8, 131.2, 130.5, 127.7, 127.1, 126.4, 126.2, 125.5, 125.3, 124.3, 121.5, 121.2, 121.1, 120.5, 120.4, 118.0, 117.1, 115.9, 112.8, 112.8, 109.1, 91.5, 80.8, 78.8, 57.7, 56.0, 56.0, 50.5, 46.5, 28.0.

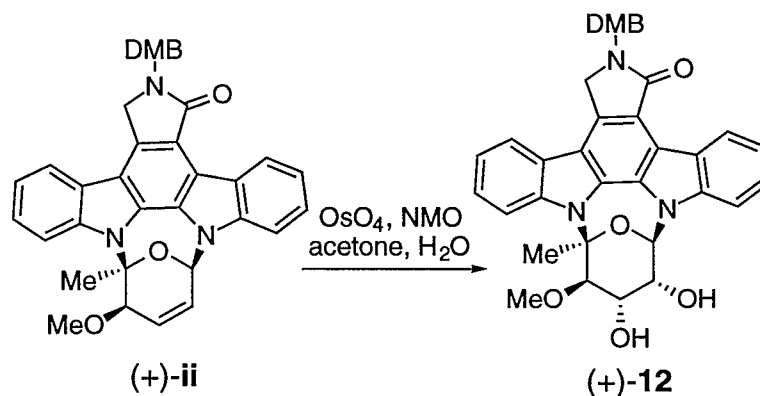
IR (thin film/NaCl): 2920.5 (s), 2851.5 (s), 1709.8 (m), 1674.3 (s), 1589.0 (m), 1513.7 (m), 1457.5 (s), 1222.9 (m), 1026.6 (m), 745.3 (m) cm⁻¹.

HRMS (FAB) m/z Calc'd for C₃₆H₃₂N₃O₅ (M+H): 586.2342. Found: 586.2343.

$$[\alpha]_D^{20} +36^\circ \text{ (c=0.1, MeOH).}$$

m.p.: 185-187 °C (acetone)

Preparation of Diol (+)-12



To a stirred solution of 4-methylmorpholine N-oxide (6 mg, 0.05 mmol) and OsO_4 (0.6 mL of a 2.5% solution in *t*-BuOH, 0.05 mmol) in 4:1 acetone: H_2O (2 mL) was added solution of olefin (+)-ii (25 mg, 0.043 mmol) in acetone (1 mL). The reaction was monitored by TLC, and after 16 h had proceeded to completion, whereupon 100 mg NaHSO_3 was added in 1.0 mL H_2O , and the black solution was stirred for 20 min and filtered, followed by extraction with CH_2Cl_2 (3x 15mL). Combined organic layers were dried over Na_2SO_4 , and evaporated to a residue, which was purified by MPLC (1:1 hexanes:ethyl acetate) to provide diol (+)-12 (23 mg, 84%) as a white powder.

^1H NMR (500 MHz, $\text{DMSO}-d_6$): δ 9.36 (d, $J=7.9$ Hz, 1H), 7.95 (d, $J=8.6$ Hz, 1H), 7.94 (d, $J=7.6$ Hz, 1H), 7.64 (d, $J=8.1$ Hz, 1H), 7.55 (app.t, $J=7.6$ Hz, 1H), 7.45 (app.t, $J=7.7$ Hz, 1H), 7.35 (app.t, $J=7.5$ Hz, 1H), 7.29 (app.t, $J=7.5$ Hz, 1H), 7.02 (s, 1H), 6.94 (s, 2H), 6.59 (d, $J=1.6$ Hz, 1H), 6.13 (d, $J=3.8$ Hz, 1H), 5.07 (d, $J=6.0$ Hz, 1H), 4.99 (d, $J=17.8$ Hz, 1H), 4.95 (d, $J=17.8$ Hz, 1H), 4.83 (s, 2H), 4.12 (d, $J=10.1$ Hz, 1H), 4.12 (dd, $J=2.3, 3.8$ Hz, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.62 (s, 3H), 3.55 (ddd, $J=2.3, 6.1, 10.1$ Hz, 1H), 2.37 (s, 3H).

^{13}C NMR (125 MHz, $\text{DMSO}-d_6$): δ 168.8, 148.9, 148.1, 140.3, 136.5, 130.4, 129.9, 127.8, 125.7, 125.0, 124.7, 123.5, 122.7, 120.8, 120.2, 119.9, 119.9, 118.7, 115.5, 114.8, 114.1, 112.0, 111.7, 108.8, 95.6, 87.3, 83.1, 71.7, 65.6, 61.6, 55.5, 55.5, 49.6, 45.5, 29.0.

IR (thin film/ NaCl): 3411.2 (brm), 2929.3 (m), 2849.4 (w), 2656.3 (m), 1590.0 (m), 1514.0 (m), 1461.2 (s), 1350.9 (m), 1273.6 (s), 1127.1 (s), 1025.0 (m), 743.3 (s) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{36}\text{H}_{34}\text{N}_3\text{O}_7$ ($\text{M}+\text{H}$): 620.2397. Found:

m.p.: 227-230 °C (acetone)

IR (thin film/NaCl): 3348.5 (brm), 2922.9 (s), 2851.9 (m), 1638.2 (s), 1586.6 (m), 1455.5 (s), 1373.5 (m), 1336.6 (m), 1320.8 (m), 1275.0 (m), 1224.7 (m), 1200.3 (w), 1119.5 (s), 740.8 (s), cm^{-1} .

m.p.: >260 °C dec. (acetone); natural MLR-52 **m.p.:** 263 -268 °C

Chemical reaction scheme showing the conversion of (+)-5 to (-)-13. The reaction involves the treatment of (+)-5 with $\text{H}_2\text{N-OH}\cdot\text{HCl}$ and NaOAc in EtOH , H_2O .

IR (thin film/NaCl): 3324.0 (brm), 2995.0 (w), 2911.3 (m), 1660.0 (s), 1589.7

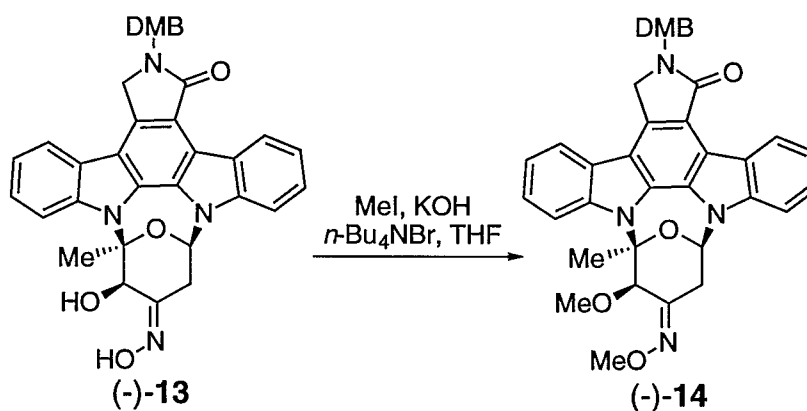
(m), 1513.5 (s), 1461.1 (s), 1417.9 (m), 1399.0 (m), 1349.2 (s), 1315.5 (m), 1260.0 (s), 1234.6 (m), 1124.4 (m), 1027.2 (m), 741.7 (s) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{35}\text{H}_{31}\text{N}_4\text{O}_6$ ($\text{M}+\text{H}$): 603.2244. Found: 603.2238.

$[\alpha]_{\text{D}}^{20}$ -18° ($c=0.1$, CH_2Cl_2).

m.p.: $>270^\circ\text{C}$ dec. (EtOH)

Preparation of methoxy oxime (-)-14



To a mixture of oxime (-)-13 (90 mg, 0.15 mmol), MeI (88 μL , 1.42 mmol), and powdered KOH (88 mg, 1.58 mmol) in 15 mL THF was added $n\text{-Bu}_4\text{NBr}$ (10 mg, 0.03 mmol). The mixture was stirred under N_2 for 30 min, solvent was removed *in vacuo*, and the residue was subjected to silica gel chromatography (1:1 hexanes:ethyl acetate) to provide methoxime (-)-14 (85 mg, 90%) as a yellow powder.

^1H NMR (500 MHz, DMSO-d_6 , 345 K): δ 9.36 (d, $J=8.0$ Hz, 1H), 7.99 (d, $J=8.6$ Hz, 1H), 7.93 (d, $J=7.8$ Hz, 1H), 7.68 (d, $J=8.3$ Hz, 1H), 7.51 (app.t, $J=7.6$ Hz, 1H), 7.44 (app.t, $J=7.8$ Hz, 1H), 7.33 (app.t, $J=7.2$ Hz, 1H), 7.30 (app.t, $J=7.1$ Hz, 1H), 7.04 (s, 1H), 7.02 (d, $J=5.6$ Hz, 1H), 6.97 (d, $J=9.4$ Hz, 1H), 6.94 (d, $J=8.1$ Hz, 1H), 4.97 (s, 2H), 4.86 (d, $J=15.5$ Hz, 1H), 4.85 (d, $J=15.7$ Hz, 1H), 4.76 (s, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.54 (d, $J=14.4$ Hz, 1H), 3.45 (s, 3H), 3.16 (dd, $J=5.9, 14.4$ Hz, 1H), 3.14 (s, 3H), 2.46 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 168.7, 148.9, 148.1, 147.3, 139.8, 136.1, 130.4, 129.5, 128.0, 125.4, 125.3, 124.7, 124.6, 123.6, 122.7, 120.6, 120.2, 119.9, 119.6, 118.6, 115.5, 114.9, 113.8, 112.2, 112.0, 108.9, 96.1, 83.3, 82.0, 60.8, 58.4, 55.5, 55.5, 49.5, 45.4, 30.4, 28.5.

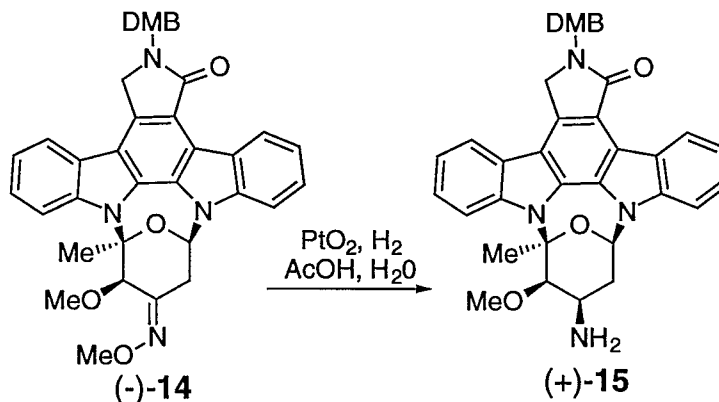
IR (thin film/NaCl): 2998.0 (w), 2926.3 (m), 1674.1 (s), 1590.0 (m), 1513.7 (s), 1460.9 (s), 1418.2 (m), 1397.9 (s), 1349.4 (s), 1316.2 (s), 1262.1 (m), 1225.6 (m), 1044.3 (m), 743.5 (m) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{37}\text{H}_{35}\text{N}_4\text{O}_6$ ($\text{M}+\text{H}$): 631.2557. Found: 631.2564.

$[\alpha]_{\text{D}}^{20}$ -22° ($c=0.1$, CH_2Cl_2).

m.p.: $>270^\circ\text{C}$ dec. (acetone)

Preparation of amine (+)-15



A mixture of oxime (+)-14 (85 mg, 0.13 mmol) and PtO_2 (28 mg) in a 60% aqueous acetic acid (15.0 mL) was treated with H_2 , and the reaction was monitored by TLC (1:1 hexanes:ethyl acetate). Upon completion, the mixture was filtered through celite and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2 (40 mL) and washed with 8.0 mL 1.0N NaOH. The aqueous layer was then back-extracted with CH_2Cl_2 (2x 15 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to a residue (79 mg), which was used in the next step without further purification.

An analytically pure sample of primary amine (+)-15 could be obtained by preparative TLC of the above residue using 5% MeOH: CH_2Cl_2 as eluent.

^1H NMR (500 MHz, CDCl_3 , 310 K): δ 9.55 (d, $J=7.9$ Hz, 1H), 7.95 (d, $J=8.5$ Hz, 1H), 7.83 (d, $J=7.7$ Hz, 1H), 7.51 (app.t, $J=7.6$ Hz, 1H), 7.42 (app.t, $J=8.2$ Hz, 1H), 7.40 (app.t, $J=7.5$ Hz, 1H), 7.30 (app.t, $J=7.8$ Hz, 2H), 6.99 (d, $J=9.4$ Hz, 2H), 6.87 (d, $J=8.0$ Hz, 1H), 6.59 (d, $J=4.9$ Hz, 1H), 4.98 (d, $J=14.9$ Hz, 1H), 4.92 (d, $J=14.9$ Hz, 1H), 4.87 (d, $J=16.7$ Hz, 1H), 4.82 (d, $J=16.7$ Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.75 (m, 2H), 3.46 (s, 3H), 2.63 (m, 2H), 2.32 (s, 3H), 1.27 (bs, 2H).

^{13}C NMR (125 MHz, CDCl_3 , 315 K): δ 170.2, 149.6, 148.7, 140.1, 137.0, 130.8, 129.6, 129.5, 127.0, 126.2, 125.4, 124.7, 124.5, 123.8, 120.8, 120.5, 120.2, 120.2, 119.6, 116.0, 115.4, 114.6, 111.6, 111.6, 107.4, 91.3, 84.2, 80.2, 57.5, 56.1, 56.1, 49.9, 46.5, 42.6, 34.6, 30.0.

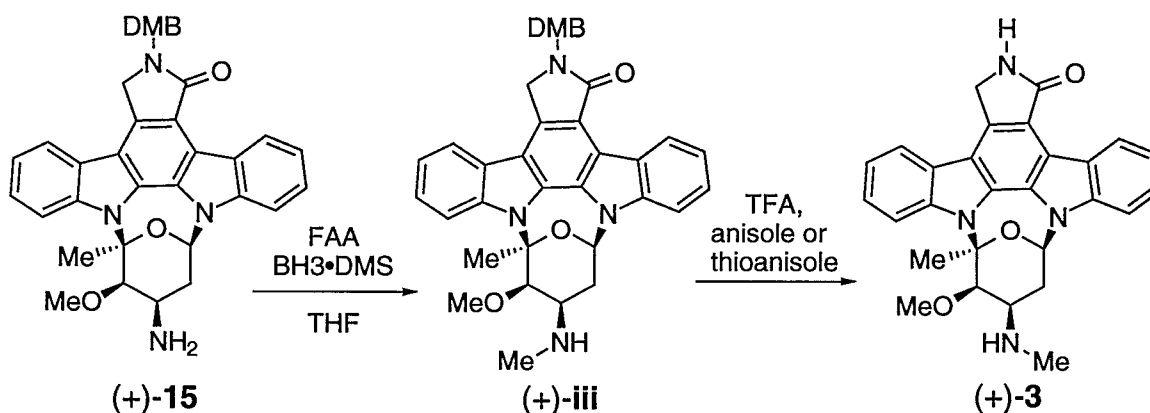
IR (thin film/ NaCl): 3414.7 (brw), 2920.8 (s), 2851.7 (s), 1733.7 (w), 1672.8 (s), 1636.0 (w), 1588.1 (m), 1513.5 (s), 1352.7 (s), 1259.3 (s), 1136.7 (m), 744.2 (m) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{36}\text{H}_{35}\text{N}_4\text{O}_5$ ($\text{M}+\text{H}$): 603.2610. Found: 603.2229.

$[\alpha]_{\text{D}}^{20} +14.3^\circ$ ($c=0.14$, CHCl_3).

m.p.: $>275^\circ\text{C}$ dec. (acetone)

Preparation of (+)-staurosporine (2)



Crude amine (+)-15 was dissolved in THF (2.0 mL) and treated with formic acetic anhydride in THF (1.3 μL of a 1.3 M solution in THF, 0.17 mmol)(FAA prepared by treatment of 1.0 equiv acetic anhydride with 1.2 equiv formic acid followed by reflux for 2 h). TLC analysis showed rapid formation of a less polar substance. A stream of N_2 was used to evaporate the solvent, followed by high vacuum for 15 min. THF (1.3 mL) was added to dissolve the residue, the reaction vessel was cooled to 0°C , and $\text{BH}_3\cdot\text{DMS}$ (193 μL of a 2.0 N solution in toluene, 0.39 mmol) was introduced. The solution was heated to reflux for 2h at which point it was again cooled to 0°C . Methanolic HCl (1.0 mL) was added along with excess MeOH (1.3 mL) and the solution was refluxed for an additional hour. Following cooling, volatiles were removed *in vacuo*, and the solid residue was azeotroped with MeOH (5x 5.0 mL). To the remaining residue

was added 7.0 mL CH₂Cl₂ followed by 1.0 N NaOH (5.0 mL), layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3x 7.0 mL). Combined organic layers were dried over Na₂SO₄, evaporated, and purified by MPLC (5% MeOH:CH₂Cl₂) to give methyl amine (+)-**iii** (80 mg, 91% 2 steps from **14**) as a yellow foam.

¹H NMR (500 MHz, CDCl₃, 320 °K): δ 9.55 (d, J=7.9 Hz, 1H), 7.89 (d, J=8.5 Hz, 1H), 7.82 (d, J=7.3 Hz, 1H), 7.48 (td, J=1.0, 7.5 Hz, 1H), 7.39 (td, J=1.0, 7.4 Hz, 1H), 7.38 (app.t, J=7.3 Hz, 1H), 7.27 (m, 2H), 7.01 (m, 2H), 6.88 (d, J=8.7 Hz, 1H), 6.57 (dd, J=1.4, 6.0 Hz, 1H), 4.98 (d, J=14.9 Hz, 1H), 4.91 (d, J=14.9 Hz, 1H), 4.84 (s, 2H), 3.92 (d, J=3.0 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.37 (dd, J=3.8, 7.7 Hz, 1H), 3.33 (bs, 3H), 2.72 (ddd, J=1.3, 4.6, 14.5 Hz, 1H), 2.46 (m, 1H), 2.35 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ 170.4, 149.3, 148.4, 139.6, 136.7, 130.6, 130.4, 129.3, 127.1, 126.6, 125.1, 124.5, 124.3, 123.5, 120.7, 120.4, 120.0, 119.8, 119.1, 115.5, 114.9, 114.0, 111.2, 111.2, 107.0, 91.2, 83.9, 80.2, 57.5, 56.0, 55.9, 50.7, 49.9, 46.4, 33.2, 30.1, 29.9.

IR (thin film/NaCl): 2954.1 (m), 2915.1 (m), 1673.2 (s), 1635.8 (m), 1462.7 (s), 1399.0 (s), 1352.6 (s), 1258.7 (m), 1136.5 (m), 1026.9 (m), 745.2 (s) cm⁻¹.

HRMS (FAB) *m/z* Calc'd for C₃₇H₃₇N₄O₅ (M+H): 617.2764. Found: 617.2764.

[α]_D²⁰ +22° (c=0.1, MeOH).

m.p.: 225-230 °C dec. (acetone)

To a stirred solution of amine (+)-**15** (10 mg, 0.016 mmol) in anisole or thioanisole (80 μL, ≈50 equiv) was added TFA (0.5 mL). The sluggish reaction was monitored by TLC, and after 48 h had proceeded to completion, whereupon 1.0 mL H₂O was added, and the solution was adjusted to pH10 with 5.0 N NaOH, followed by extraction with CH₂Cl₂ (3x 5mL). Combined organic layers were dried over Na₂SO₄, and evaporated to a residue, which was purified by preparative TLC (5% MeOH:CH₂Cl₂) to provide (+)-staurosporine (**3**, 6 mg, 70%).

¹H NMR (500 MHz, CDCl₃): δ 9.43 (d, J=7.9 Hz, 1H), 7.94 (s, 1H), 7.90 (d, J=7.7 Hz, 1H), 7.49 (app.t, J=7.6 Hz, 1H), 7.43 (app.t, J=7.7 Hz, 1H), 7.37 (app.t, J=7.5 Hz, 1H), 7.33 (app.t, J=7.4 Hz, 1H), 7.30 (d, J=8.0 Hz, 1H), 6.57 (d, J=5.6 Hz, 1H), 6.33 (bs, 1H), 5.05 (d, J=15.8 Hz, 1H), 5.01 (d, J=15.8 Hz, 1H), 3.89 (bs, 1H), 3.42 (s, 3H), 3.37 (d, 3.2H), 2.76 (dd, J=3.9, 14.7 Hz, 1H), 2.41 (bd, J=15.4 Hz, 1H), 2.37 (s, 3H), 1.59 (bs, 1H), 1.57 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ 173.6, 139.8, 136.7, 132.2, 130.8, 126.6, 125.0, 124.6, 124.2, 123.4, 120.6, 120.0, 119.8, 115.3, 114.1, 106.9, 91.1, 84.2,

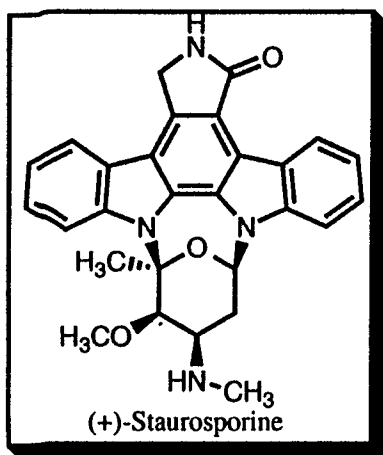
80.1, 57.2, 50.4, 45.9, 33.3, 30.3, 30.1.

IR (thin film/NaCl): 3316.6 (m), 2925.0 (m), 2850.8 (m), 1678.7 (s), 1636.2 (m), 1584.2 (m), 1457.5 (s), 1352.2 (s), 1316.7 (s), 1281.3 (m), 1115.5 (m), 744.8 (s) cm^{-1} .

HRMS (FAB) m/z Calc'd for $\text{C}_{28}\text{H}_{27}\text{N}_4\text{O}_3$ (M+H): 467.2083. Found: 467.2085.

$[\alpha]_{\text{D}}^{25} +35^\circ$ (c=0.1, MeOH); natural staurosporine $[\alpha]_{\text{D}}^{25} +35^\circ$ (c=1.0, MeOH).

m.p.: 273-280 °C dec. (MeOH); natural staurosporine **m.p.:** >270 °C dec. (MeOH)



Top-Danishefsky Synthetic
 Bottom-Wood Synthetic

¹H NMR Comparison (500 MHz, CDCl₃)

