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

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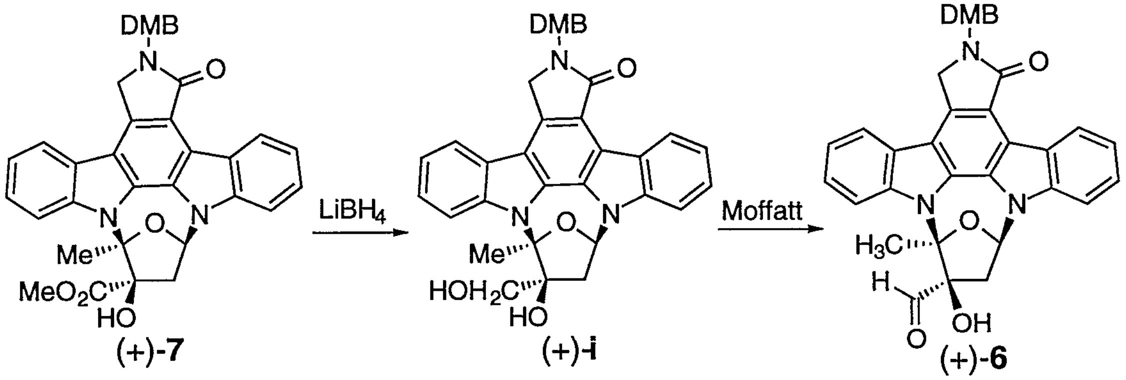
Preparation of aldehyde (+)-6



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$_2$Cl$_2$ (3x 20 mL). The combined organic phases were dried with Na$_2$SO$_4$ and chromatographed on silica gel using 1:1 hexanes:ethyl acetate as eluent to afford diol (+)-**i** (124mg, 89%) as a white solid.

^{1}H 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 $C_{35}H_{32}N_3O_6$ (M+H): 590.2291. Found: 590.2289.

$[\alpha]_D^{20}$ +112° (c=0.1, MeOH).

m.p.: >225 °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 puified by MPLC (2:1→1:1 hexanes:ethyl acetate) gave aldehyde (+)-**6** (280 mg, 71%, 63% 2 steps) as a yellow powder.

^{1}H 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.

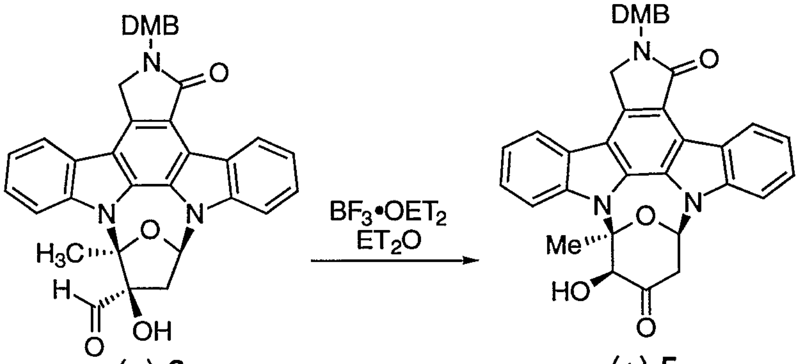
IR (thin film/NaCl): 3253.9 (brm), 3010.7 (m), 2953.6 (m), 2934.0 (m), 2833.9 (s), 1734.0 (s), 1646.2 (s), 1614.7 (w), 1589.9 (m), 1514.1 (m), 1399.1 (s), 1275.7 (m), 1138.4 (s), 1024.8 (m), 745.1 (s) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{35}H_{30}N_3O_6$ (M+H): 588.2135. Found: 588.2135.

$[\alpha]_D^{20}$ +48° (c=0.1, MeOH).

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

Preparation of hydroxy ketone (+)-5



(+)-**6** (+)-**5**

To a suspension of aldehyde (+)-**6** (100 mg, 0.170 mmol) in Et_2O (17.0 mL) was added $BF_3{\bullet}OEt_2$ (23 µL, 0.187 mmol) and the mixture stirred vigorously for 12h at 25-30 °C, when again was treated with $BF_3{\bullet}OEt_2$ (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.

^{1}H NMR (500 MHz, 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, 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.

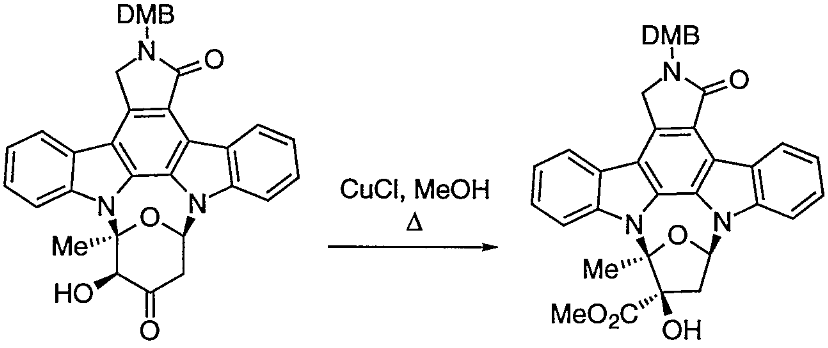
IR (thin film/NaCl): 3300.0 (brs), 2999.5 (brm), 2848.6 (m), 1728.9 (m), 1665.5 (s), 1503.3 (m), 1451.2 (s), 1406.8 (m), 1132.8 (s), 1021.9 (m), 750.6 (s) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{35}H_{30}N_3O_6$ (M+H): 588.2135. Found: 588.2135.

$[\alpha]_D^{20}$ +83° (c=0.1, DMSO).

m.p.: >220 °C dec. (diethyl ether)

Preparation of Ester (+)-7

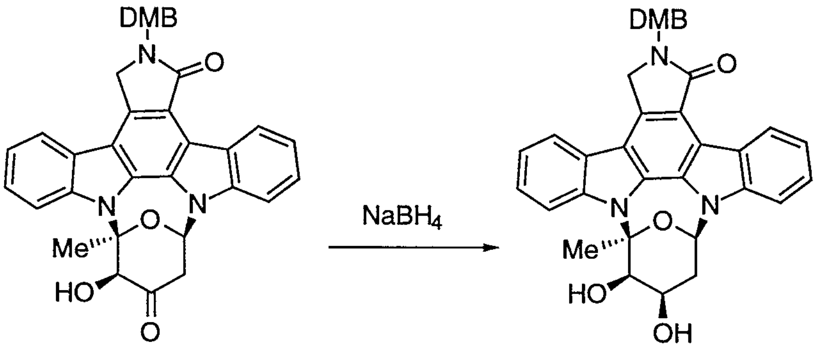


(+)-**5**

(+)-**7**

To a solution of ketone (+)-**5** (10 mg, 0.017 mmol) in 1:1 $MeOH/CH_2Cl_2$ (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



(+)-**5**

(+)-**10**

To a stirred solution of ketone (+)-**5** (85 mg, 0.15 mmol) in 1:1:2 MeOH:CH_2Cl_2:$CHCl_3$ (20.0 mL), $NaBH_4$ (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 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 alcohol (+)-**10** (81 mg, 95%) as a white solid.

^{1}H NMR (500 MHz, acetone-d_6): 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=.85 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).

^{13}C NMR (125 MHz, acetone-d_6): 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.

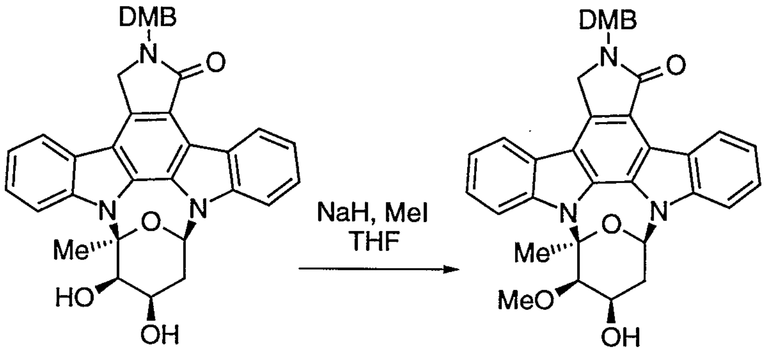
IR (thin film/NaCl)**:** 3355.5 (brm), 2922.9 (m), 2847.8 (m), 1654.5 (s), 1501.5 (w), 1449.3 (s), 1254.5 (s), 1136.8 (s), 1025.7 (m), 747.1 (s) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{35}H_{32}N_3O_6$ (M+H): 590.2291. Found: 590.2289.

$[\alpha]_D^{20}$ +37° (c=0.1, MeOH).

m.p.: 174-176 °C dec. (acetone)

Preparation of methyl ether (+)-11



(+)-**10** (+)-**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 µL, 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 H_2O. Extraction of the solution with CH_2Cl_2 (3x 10 mL), drying over Na_2SO_4 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.

^{1}H NMR (500 MHz, $CDCl_3$): 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).

^{13}C NMR (125 MHz, $CDCl_3$, 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.

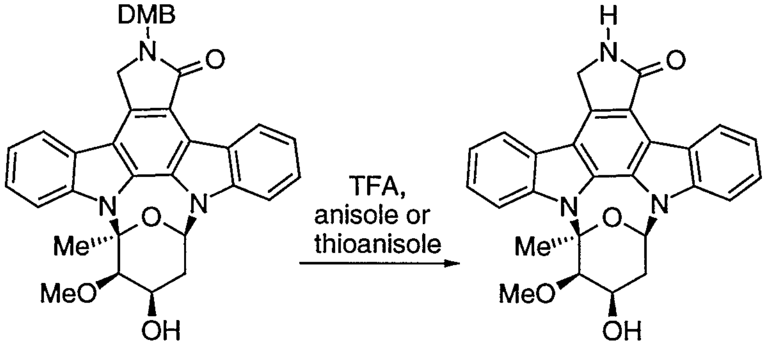
IR (thin film/NaCl): 3423.7 (brm), 2923.2 (s), 2848.1 (m), 2636.2 (m), 1647.2 (s), 1514.3 (m), 1462.9 (s), 1258.0 (m), 1235.3 (m), 1136.9 (m), 1026.9 (w), 743.3 (s) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{36}H_{34}N_3O_6$ (M+H): 604.2448. Found: 604.2449.

$[\alpha]_D^{20}$ +48° (c=0.1, MeOH).

m.p.: >235 °C dec. (acetone)

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



(+)-**11** (+)-**3**

To a stirred solution of ether (+)-**11** (10 mg, 0.017 mmol) in anisole or thioanisole (80 µL, ≈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 H_2O was added, followed by extraction with CH_2Cl_2 (3x 5mL). Combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried over Na_2SO_4, and evaporated to a residue, which was purified by preparative TLC (5% MeOH:CH_2Cl_2) to provide (+)-RK-286c (**3**, 6 mg, 75%).

^{1}H NMR (500 MHz, DMSO-d_6): 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).

^{13}C NMR (125 MHz, DMSO-d_6): 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 [illegible]

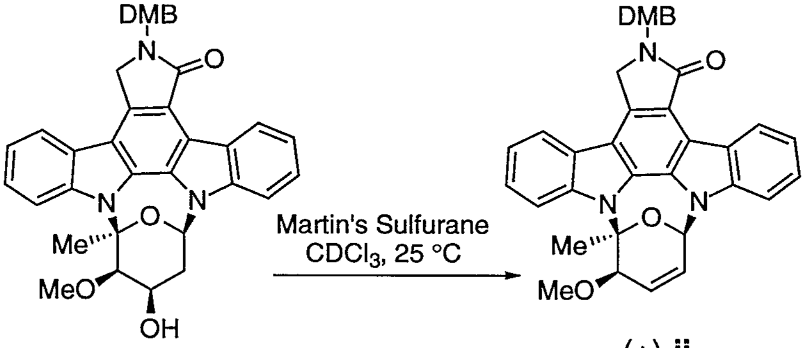
743.8 (s) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{27}H_{24}N_3O_4$ (M+H): 454.1767. Found: 454.1766.

$[\alpha]_D^{25}$ +41.1° (c=0.18, EtOAc); natural RK-286c $[\alpha]_D^{20}$ +45.3° (c=0.22, EtOAc).

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

Preparation of Olefin (+)-ii



(+)-**11**

(+)-**ii**

To a stirred solution of ether (+)-**11** (112 mg, 0.186 mmol) in $CDCl_3$ (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 reidue subjected to silica gel chromatography (2:1 hexanes:ethyl acetate) to provide olefin (+)-**ii** (96 mg, 88%) as a white solid.

^{1}H NMR (500 MHz, DMSO-d_6, 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).

^{13}C NMR (125 MHz, acetone-d_6): 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.

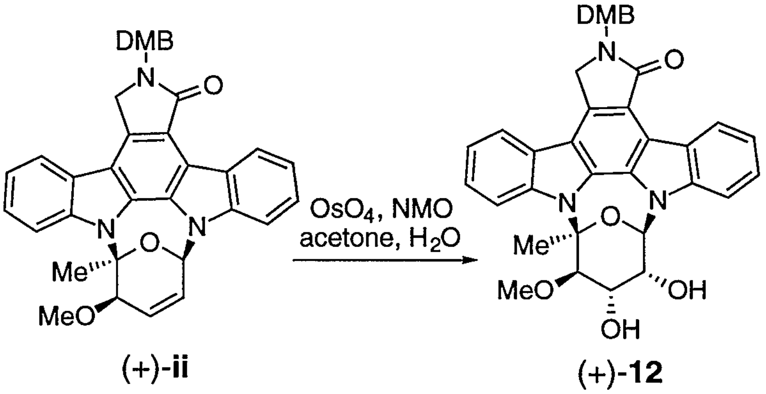
IR (thin film/NaCl): 2920.5 (s), 2851.5 (s), 1709.8 (m), 1674.3 (s), 1589.0 (m), 1513.7 (m), 1457.5 (s), 1222.9 (m), 1026.6 (m), 745.3 (m) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{36}H_{32}N_3O_5$ (M+H): 586.2342. Found: 586.2343.

$[\alpha]_D^{20}$ +36° (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.

^{1}H NMR (500 MHz, 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, 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}.

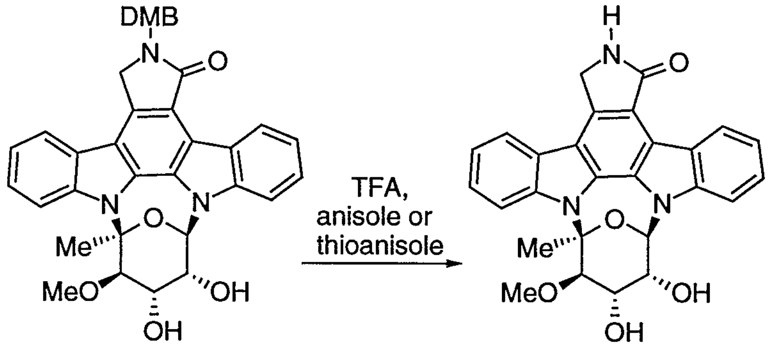
HRMS (FAB) *m/z* Calc'd for $C_{36}H_{34}N_3O_7$ (M+H): 620.2397. Found:

620.2390.

$[\alpha]_D^{20}$ +17° (c=0.1, MeOH).

m.p.: 227-230 °C (acetone)

Preparation of (+)-MLR-52 (4)



(+)-**12** (+)-**4**

To a stirred solution of diol (+)-**12** (10 mg, 0.016 mmol) in anisole or thioanisole (80 µL, ≈50 equiv) was added TFA (0.5 mL). The reaction was monitored by TLC, and after 16 h had proceeded to completion, whereupon 1.0 mL H_2O was added, followed by extraction with CH_2Cl_2 (3x 5mL). Combined organic layers were washed with saturated aqueous $NaHCO_3$ (5 mL), dried over Na_2SO_4, and evaporated to a residue, which was purified by preparative TLC (5% MeOH:CH_2Cl_2) to provide (+)-MLR-52 (**4**, 6 mg, 77%).

^{1}H NMR (500 MHz, DMSO-d_6): δ 9.31 (d, J=7.9 Hz, 1H), 8.61 (bs, 1H), 7.99 (d, J=7.7 Hz, 1H), 7.96 (d, J=8.7 Hz, 1H), 7.62 (d, J=8.2 Hz, 1H), 7.53 (app.t, J=7.5 Hz, 1H), 7.45 (td, J=0.8, 7.7 Hz, 1H), 7.32 (app.t, J=7.4 Hz, 1H), 7.32 (app.t, J=7.4 Hz, 1H), 6.58 (d, J=1.6 Hz, 1H), 6.12 (d, J=4.0 Hz, 1H), 5.06 (d, J=5.9 Hz, 1H), 4.99 (d, J=17.6 Hz, 1H), 4.95 (d, J=17.5 Hz, 1H), 4.13 (d, J=10.3 Hz, 1H), 4.12 (dd, J=1.6, 2.6 Hz, 1H), 3.62 (s, 3H), 3.56 (ddd, J=2.6, 6.2, 10.3 Hz, 1H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 171.8, 140.2, 136.4, 132.6, 127.8, 125.8, 125.5, 124.8, 124.6, 123.6, 122.7, 120.9, 120.1, 119.7, 119.3, 115.4, 114.9, 114.3, 108.7, 95.6, 87.2, 83.1, 71.7, 65.6, 61.6, 45.4, 29.0.

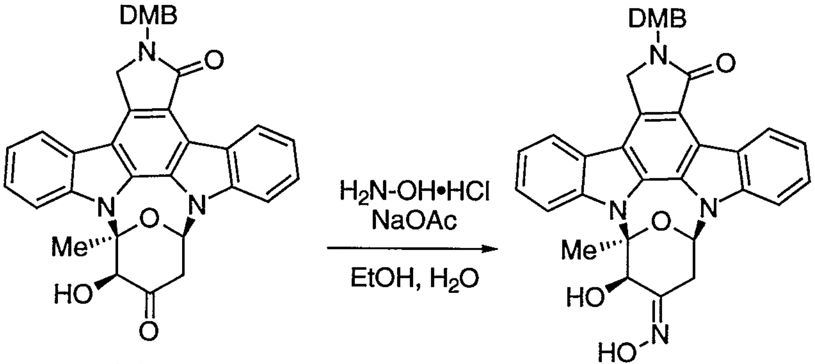
IR (thin film/NaCl): 3348.5 (brm), 2922.9 (s), 2851.9 (m), 1638.2 (s), 1586.6 (m), 1455.5 (s), 1373.5 (m), 1336.6 (m), 1320.8 (m), 1275.0 (m), 1224.7 (m), 1200.3 (w), 1119.5 (s), 740.8 (s,) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{27}H_{24}N_3O_5$ (M+H): 470.1716. Found: 470.1717.

$[\alpha]_D^{25}$ +65° (c=0.1, MeOH); natural MLR-52 $[\alpha]_D$ +68° (c=0.093, MeOH).

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

Preparation of oxime (-)-13



(+)-**5** (-)-**13**

A suspension of ketone (+)-**5** (100 mg, 0.17 mmol), hydroxylamine hydrochloride (165 mg, 2.38 mmol), and NaOAc (167 mg, 2.04 mmol) in 80% aqueous EtOH (35.0 mL) was heated gently to reflux for 30 min. Following cooling to room temperature, sovent was removed *in vacuo*, and the residue purified by MPLC (1:1 hexanes:ethyl acetate) to provide oxime (-)-**13** (98 mg, 95%) as a yellow powder.

^{1}H NMR (500 MHz, DMSO-d_6): δ 10.3 (s, 1H), 9.34 (d, J=7.9 Hz, 1H), 8.08 (d, J=8.6 Hz, 1H), 7.90 (d, J=7.6 Hz, 1H), 7.71 (d, J=8.3 Hz, 1H), 7.51 (app.t, J=7.6 Hz, 1H), 7.42 (app.t, J=7.9 Hz, 1H), 7.32 (app.t, J=7.7 Hz, 1H), 7.28 (app.t, J=7.4 Hz, 1H), 7.04 (d, J=6.3 Hz, 1H), 7.03 (s, 1H), 6.95 (d, J=8.4 Hz, 1H), 6.93 (d, J=8.2 Hz, 1H), 5.56 (m, 2H), 4.97 (d, J=18.1 Hz, 1H), 4.93 (d, J=16.9 Hz, 1H), 4.85 (d, J=15.0 Hz, 1H), 4.45 (d, J=15.0 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.61 (d, J=13.9 Hz, 1H), 3.01 (dd, J=5.8, 14.3 Hz, 1H), 2.46 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6): δ 168.8, 148.9, 148.1, 147.4, 140.2, 136.1, 130.5, 129.6, 128.1, 125.4, 125.3, 124.7, 124.6, 123.6, 122.8, 120.5, 120.1, 119.9, 119.6, 118.5, 116.0, 114.8, 113.9, 112.1, 111.9, 108.9, 97.4, 82.0, 74.9, 55.5, 55.5, 49.5, 45.5, 29.6, 28.6.

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

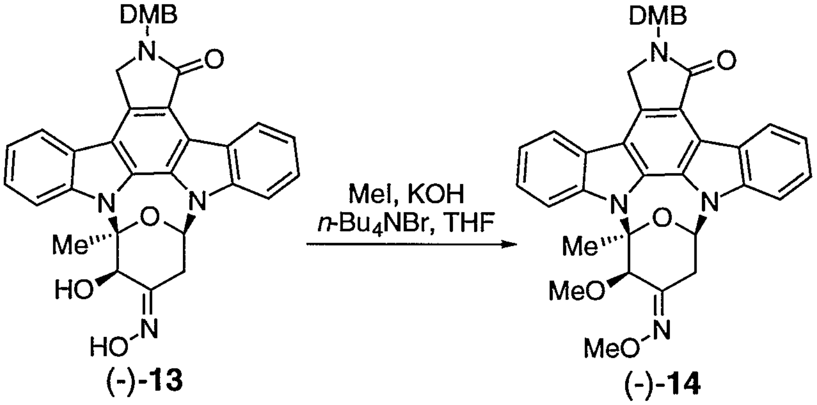
(m), 1513.5 (s), 1461.1 (s), 1417.9 (m), 1399.0 (m), 1349.2 (s), 1315.5 (m), 1260.0 (s), 1234.6 (m), 1124.4 (m), 1027.2 (m), 741.7 (s) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{35}H_{31}N_4O_6$ (M+H): 603.2244. Found: 603.2238.

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

m.p.: >270 °C dec. (EtOH)

Preparation of methoxy oxime (-)-14



To a mixture of oxime (-)-**13** (90 mg, 0.15 mmol), MeI (88µL, 1.42 mmol), and powdered KOH (88 mg, 1.58 mmol) in 15 mL THF was added *n*-Bu_4NBr (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.

^{1}H 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.

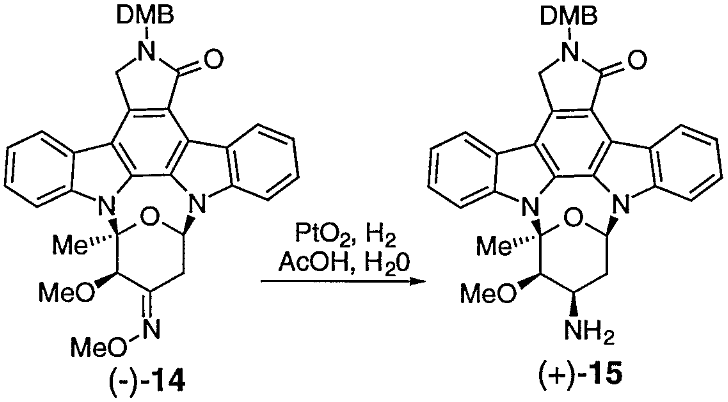
IR (thin film/NaCl): 2998.0 (w), 2926.3 (m), 1674.1 (s), 1590.0 (m), 1513.7 (s), 1460.9 (s), 1418.2 (m), 1397.9 (s), 1349.4 (s), 1316.2 (s), 1262.1 (m), 1225.6 (m), 1044.3 (m), 743.5 (m) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{37}H_{35}N_4O_6$ (M+H): 631.2557. Found: 631.2564.

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

m.p.: >270 °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.

^{1}H 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.

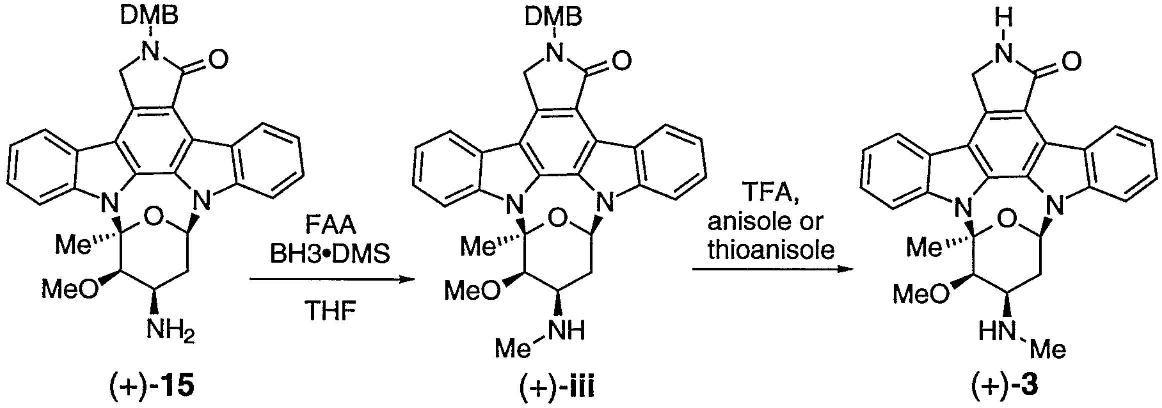
IR (thin film/NaCl): 3414.7 (brw), 2920.8 (s), 2851.7 (s), 1733.7 (w), 1672.8 (s), 1636.0 (w), 1588.1 (m), 1513.5 (s), 1352.7 (s), 1259.3 (s), 1136.7 (m), 744.2 (m) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{36}H_{35}N_4O_5$ (M+H): 603.2610. Found: 603.2229.

$[\alpha]_D^{20}$ +14.3° (c=0.14, $CHCl_3$).

m.p.: >275 °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 BH_3•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 CH_2Cl_2 followed by 1.0 N NaOH (5.0 mL), layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3x 7.0 mL). Combined organic layers were dried over Na_2SO_4, evaporated, and purified by MPLC (5% MeOH:CH_2Cl_2) to give methyl amine (+)-**iii** (80 mg, 91% 2 steps from **14**) as a yellow foam.

^{1}H NMR (500 MHz, $CDCl_3$, 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).

^{13}C NMR (125 MHz, $CDCl_3$): 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 $C_{37}H_{37}N_4O_5$ (M+H): 617.2764. Found: 617.2764.

$[\alpha]_D^{20}$ +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 H_2O was added, and the solution was adjusted to pH10 with 5.0 N NaOH, followed by extraction with CH_2Cl_2 (3x 5mL). Combined organic layers were dried over Na_2SO_4, and evaporated to a residue, which was purified by preparative TLC (5% MeOH:CH_2Cl_2) to provide (+)-staurosporine (**3**, 6 mg, 70%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.43 (d, J=7.9 Hz, 1H), 7.94 (8.5, 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).

^{13}C NMR (125 MHz, $CDCl_3$): 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.

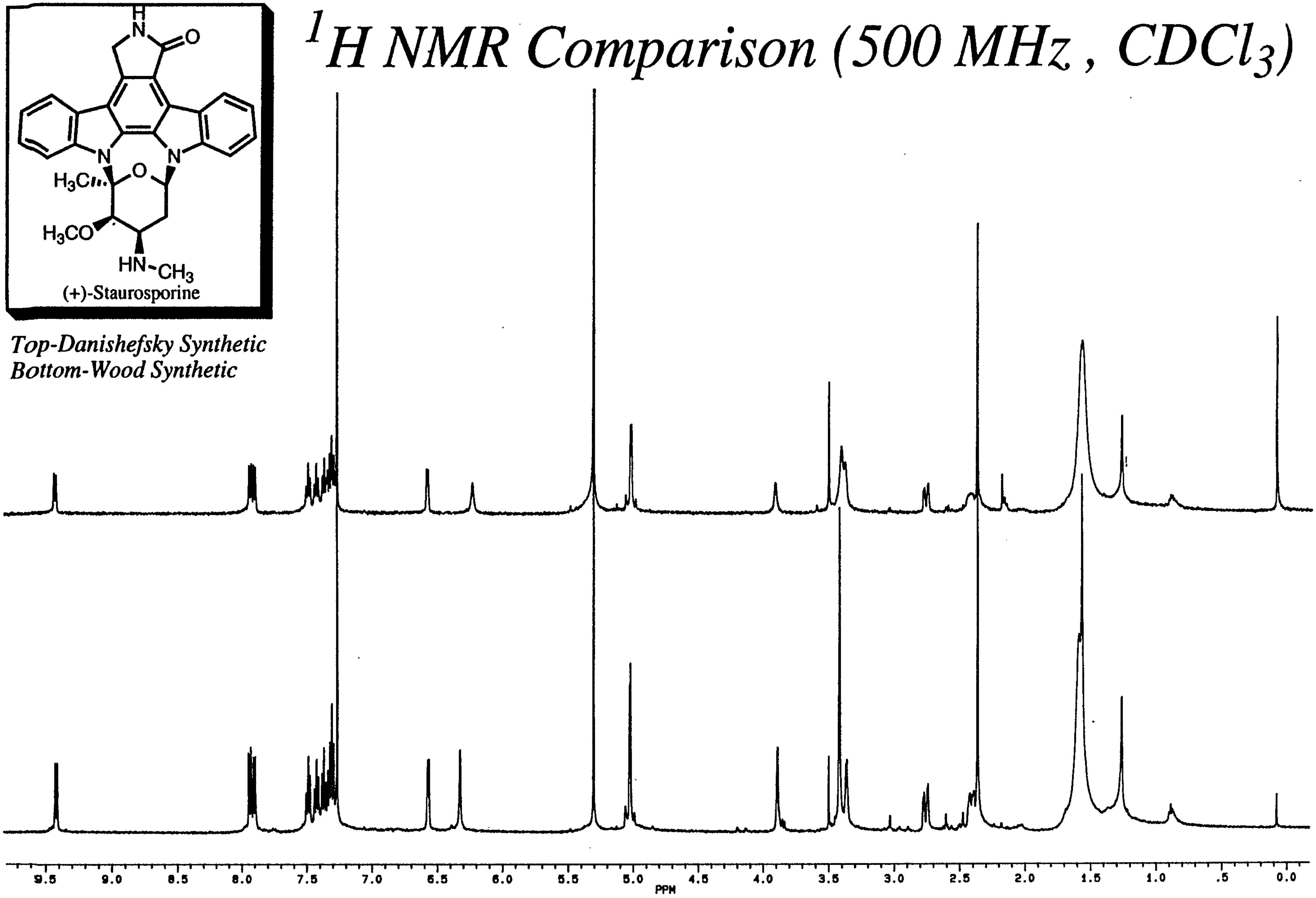
IR (thin film/NaCl)**:** 3316.6 (m), 2925.0 (m), 2850.8 (m), 1678.7 (s), 1636.2 (m), 1584.2 (m), 1457.5 (s), 1352.2 (s), 1316.7 (s), 1281.3 (m), 1115.5 (m), 744.8 (s) cm^{-1}.

HRMS (FAB) *m/z* Calc'd for $C_{28}H_{27}N_4O_3$ (M+H): 467.2083. Found: 467.2085.

$[\alpha]_D^{25}$ +35° (c=0.1, MeOH); natural staurosporine $[\alpha]_D^{25}$ +35° (c=1.0, MeOH).

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

^1H NMR Comparison (500 MHz, $CDCl_3$)


(+)-Staurosporine

Top-Danishefsky Synthetic
Bottom-Wood Synthetic