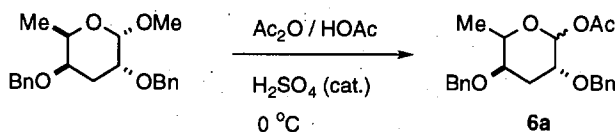
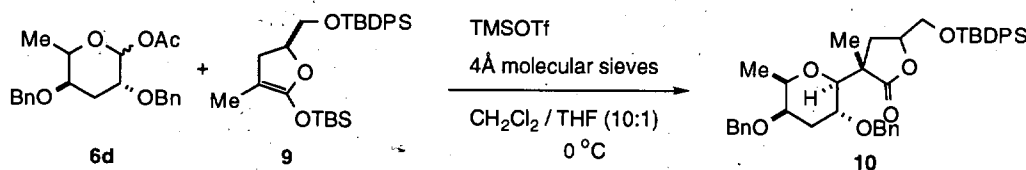


**General procedure:** Spectra of nuclear magnetic resonance of proton ( $^1\text{H-NMR}$ ) and carbon-13 ( $^{13}\text{C-NMR}$ ) were recorded in a deuterated solvent as indicated with  $\text{CHCl}_3$  (H,  $\delta=7.26$  ppm; C,  $\delta=77.00$  ppm) or  $\text{C}_6\text{H}_6$  (H,  $\delta=7.15$  ppm; C,  $\delta=128.00$  ppm) as the internal reference. Chemical shifts ( $\delta$ ) and coupling constants ( $J$ ) are expressed in ppm (part per million) and Hz (Hertz), respectively. The abbreviations used for the description of the peaks are as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad; dd, doublet of doublets; dt, doublet of triplets. Flash chromatography was carried out using E. Merck silica gel 60 (0.040-0.063 mm, 230-400 mesh). E. Merck precoated silica gel 60 F254 plates with a layer thickness of 250  $\mu\text{m}$  and of 500  $\mu\text{m}$  were used for thin layer chromatography (TLC) and for preparative TLC, respectively. A mixture of ethyl acetate-hexane on v/v basis, as indicated, was used as eluant. TLC plates were viewed by UV254-lamp for UV light active compounds and/or dipped into an anisaldehyde-EtOH-HOAc- $\text{H}_2\text{SO}_4$  stain solution and heated to develop the colored spots as indicated. All commercially available reagents and solvents were used without further purification, except where indicated. All anhydrous reactions were carried out under an atmosphere of dry nitrogen. The glass vessels, luer lock syringes and needles were oven-dried at 120-140  $^\circ\text{C}$  or flame-dried, and cooled to room temperature under a current of dry nitrogen. Micro-syringes were dried under vacuum using an oil pump at room temperature for at least 2 hours prior to use. Anhydrous solvents were dried and distilled over suitable drying agents: THF-sodium/benzophenone, dichloromethane-calcium hydride, toluene-sodium, benzene-sodium, xylenes-sodium.



To a solution of the methyl  $\alpha$ -glycoside (6.75 g, 19.7 mmol) in 150 mL of  $\text{Ac}_2\text{O}$  and 50 mL of  $\text{AcOH}$  at 0  $^\circ\text{C}$  was added dropwise 440  $\mu\text{l}$  conc.  $\text{H}_2\text{SO}_4$ . The resulting mixture was stirred for 50 min at this temperature, then poured in 1 L ether and 500 mL pH 7.0 buffer solution. The ether layer was washed with pH 7.0 buffer solution (2x250 mL). The aqueous phase was reextracted with  $\text{Et}_2\text{O}$  (3x300 mL), and the combined organics were dried over  $\text{Na}_2\text{SO}_4$ . The crude acetate **6a** (7.3 g) after removal of solvent under high vacuum was directly used for the next step.

$R_f = 0.62$ , E / H = 1:2.

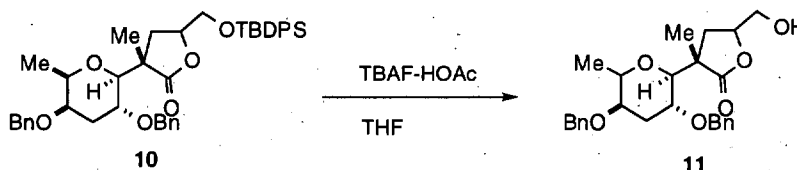


A stirred mixture of the crude acetate **6a** (7.3 g, 19.7 mmol) and the crude **9** (29.2 g, 60.5 mmol, 3 eq) was dried under vacuum for 1 h, then powder 4 Å molecular sieves (activated at 160  $^\circ\text{C}$  under high vacuum for 24 h, 12 g), dry  $\text{CH}_2\text{Cl}_2$  (200 mL) and dry THF (20 mL) were added, subsequently. The resulting mixture was cooled down to 0  $^\circ\text{C}$ , then TMSOTf (7.13 mL, 39.5 mmol, 2.0 eq) was added dropwise. The mixture was stirred at 0  $^\circ\text{C}$  for 1 hour and then quenched with sat.  $\text{NaHCO}_3$ . The layers were separated and the aqueous phase was extracted 3 times with  $\text{CH}_2\text{Cl}_2$  (100 mL). The combined organics

were dried over  $\text{Na}_2\text{SO}_4$ . The ratio of (*S*)- $\beta$  and (*S*)- $\alpha$  is approximately 3:1. The crude product was purified by chromatography (E/H = 1:20-1:10) to afford two fractions: (*S*)- $\beta$ -**10** (10.8 g, 65%) and (*S*)- $\alpha$ -anomer. The (*S*)- $\beta$ -**10** fraction was subjected to the next step directly.

(*S*)- $\beta$ -**10**:  $R_f = 0.39$ , E / H = 1:3 (red); (*S*)- $\alpha$ -isomer:  $R_f = 0.58$ , E / H = 1:3 (brown).

$^1\text{H-NMR}$  of (*S*)- $\beta$ -**10** ( $\text{CDCl}_3$ , 300 MHz):  $\delta = 7.69$ -7.66 (m, 4H), 7.42-7.32 (m, 16H), 4.60 (d,  $J = 12.3$  Hz, 1H), 4.56-4.37 (m, 3H), 4.39 (d,  $J = 11.5$  Hz, 1H), 3.85 (dd,  $J = 3.3, 11.4$  Hz, 1H), 3.73 (ddd,  $J = 4.4, 3.6, 4.3$  Hz, 1H), 3.65-3.53 (m, 3H), 3.4 (br, 1H), 2.54 (dt,  $J = 3.8, 13.3$  Hz, 1H), 2.42 (dd,  $J = 7.9, 12.8$  Hz, 1H), 1.95 (dd,  $J = 8.0, 12.8$  Hz, 1H), 1.52-1.43 (m, 1H), 1.38 (s, 3H), 1.13 (d,  $J = 6.3$  Hz, 3H), 1.06 (s, 9H).



To a solution of **10** (10.8 g, 15.9 mmol) in THF (125 mL) at room temperature was added TBAF-HOAc in THF (1:1 molar ratio, 0.95 M, 26.4 mL, 25 mmol, 2eq.). The resulting solution was stirred at room temperature for 2 h. The reaction mixture was diluted with EtOAc, washed with sat.  $\text{NaHCO}_3$  and brine, then dried over  $\text{Na}_2\text{SO}_4$ . The crude product was purified by chromatography to afford crystalline solid **11** (5.0 g, 60% from the methyl  $\alpha$ -glycoside).

$R_f = 0.20$ , E / H = 1:2.

mp = 127-129°C.

$[\alpha]_D -37.6^\circ$  ( $c$  0.4,  $\text{CH}_2\text{Cl}_2$ ).

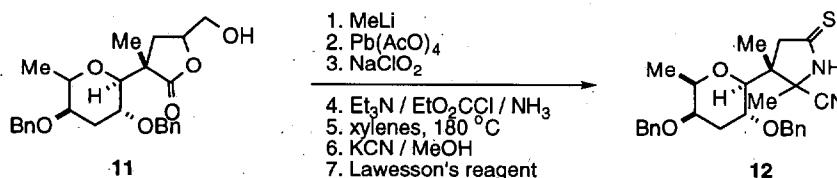
$^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  (ppm) = 7.38-7.26 (m, 10H), 4.59 (d,  $J = 12.1$  Hz, 1H), 4.56-4.53 (m, 1H), 4.50 (d,  $J = 11.9$  Hz, 1H), 4.47 (d,  $J = 12.5$  Hz, 1H), 4.38 (d,  $J = 11.5$  Hz, 1H), 3.83 (dd,  $J = 2.8, 12.5$  Hz, 1H), 3.73-3.69 (m, 1H), 3.57 (d,  $J = 9.3$  Hz, 1H), 3.56-3.48 (m, 2H), 3.41 (br, 1H), 2.55 (dt,  $J = 3.7, 13.4$  Hz, 1H), 2.45 (dd,  $J = 7.7, 13.0$  Hz, 1H), 1.89 (br, 1H), 1.75 (dd,  $J = 8.4, 12.9$  Hz, 1H), 1.49-1.44 (m, 1H), 1.37 (s, 3H), 1.14 (d,  $J = 6.2$  Hz, 3H).

$^{13}\text{C-NMR}$  ( $\text{C}_6\text{D}_6$ , 500 MHz):  $\delta$  (ppm) = 181.02, 139.19, 138.67, 128.59, 83.49, 78.33, 75.87, 75.44, 71.61, 71.50, 70.16, 68.83, 49.37, 33.02, 32.11, 23.05, 17.02.

IR (film,  $\text{cm}^{-1}$ ): 3460, 2932, 2854, 1762, 1454, 1202, 1092.

HRMS (FAB):  $\text{C}_{26}\text{H}_{32}\text{O}_6\text{Na}$  ( $\text{M}+\text{Na}$ ) $^+$ , calc. 463.2097, found 463.2117.

ORTEP drawing of **11**, see page 10.



To a solution of **11** (1.4 g, 3.2 mmol) in THF (32 mL) at  $-78^\circ\text{C}$  was added methyllithium in  $\text{Et}_2\text{O}$  (1.4 M, 22.7 mL, 10 eq.). The resulting suspension was stirred and the temperature was allowed to rise to  $-20^\circ\text{C}$  over a period of 1 h. The reaction was quenched with sat.  $\text{NaHCO}_3$ . The layers were separated and the aqueous phase was

extracted 3 times with  $\text{CH}_2\text{Cl}_2$ . The combined organics were dried over  $\text{Na}_2\text{SO}_4$ . The crude diol-ketone was dried and used for the next step directly.

$R_f = 0.50$ , E / H = 1:0.

To a solution of the crude diol-ketone in  $\text{CH}_2\text{Cl}_2$  (40 mL) were added  $\text{NaHCO}_3$  (8 g, 95.4 mmol, 30 eq.) and  $\text{Pb}(\text{OAc})_4$  (5.6 g, 12.7 mmol, 4.0 eq.) successively. The resulting mixture was stirred for 50 min. The reaction was quenched with sat.  $\text{NaHCO}_3$  and diluted with  $\text{CH}_2\text{Cl}_2$ , the layers were separated and the aqueous phase was extracted 3 times with  $\text{CH}_2\text{Cl}_2$ . The combined organics were dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated in vacuo. The crude product was subjected to the next step without purification.

$R_f = 0.70$ , E / H = 1:1.

To a solution of the crude aldehyde in *t*-BuOH (56 mL) and 2-methyl-2-butene (13.3 mL) was added a sodium chlorite stock solution (22.2 mL of a solution of 3 g  $\text{NaClO}_2$  and 3.96 g  $\text{NaH}_2\text{PO}_4$  in 30 mL  $\text{H}_2\text{O}$ ) at room temperature. The resulting mixture was stirred for 2 h, then diluted with  $\text{H}_2\text{O}$  (100 mL) and  $\text{CH}_2\text{Cl}_2$  (100 mL). The layers were separated and the aqueous phase was extracted 3 times with  $\text{CH}_2\text{Cl}_2$ . The combined organics were dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The crude ketone-acid was used directly for the next step.

$R_f = 0.3$ , E / H = 1:2=1.

To a solution of the crude ketone-acid in THF (60 mL) were added  $\text{Et}_3\text{N}$  (7.0 mL, 50.8 mmol) and  $\text{EtO}_2\text{CCl}$  (2.4 mL, 25.4 mmol) successively. The mixture was stirred 10 min and then dry  $\text{NH}_3$  gas was bubbled through the solution for 20 min. The resulting mixture was stirred for 30 min, then concentrated and purified directly by chromatography (E/H = 1:1 to 1:0) to afford a diastereomeric mixture (938 mg, 67%) of lactam.

$R_f = 0.47$ , E / H = 1:0.

A solution of the mixture of lactam (938 mg, 2.13 mmol) in xylenes (80 mL) and  $\text{Et}_3\text{N}$  (2 mL) was heated at 180 °C with a Dean-Stark apparatus and 90% xylenes was removed in 1 h. The remained 10% solution of high boiling-point xylenes was pyrolyzed for 1 h at 180 °C. The reaction mixture was cooled to room temperature and concentrated in vacuum to afford a crude enamide which was subjected to the next step directly.

$R_f = 0.71$ , E / H = 1:0.

To a solution of the crude enamide in dry MeOH (40 mL) was added solid KCN (1.4 g, 21.3 mmol) in one portion. The resulting mixture was stirred at 75 °C for 2.5 h, then cooled to room temperature. The reaction mixture was diluted with ether and poured in 50%  $\text{H}_3\text{PO}_4$  solution. The layers were separated, and the aqueous phase was extracted 3 times with ether. The combined organics were washed with brine and dried over  $\text{Na}_2\text{SO}_4$ . The crude product was purified by chromatography (E / H = 1:3-1:1) to provide a cyano-lactam (741 mg, 77%) as a mixture of 2 diastereomers (5:1).

$R_f = 0.69$ , E / H = 1:0.

$^1\text{H-NMR}$  of the major ( $\text{C}_6\text{D}_6$ , 400 MHz):  $\delta$  (ppm) = 7.52 (s, 1H), 7.42 (d,  $J = 7.1$  Hz, 2H), 7.28-7.12 (m, 7H), 4.76 (d,  $J = 11.9$  Hz, 1H), 4.32 (d,  $J = 12.2$  Hz, 1H), 4.16 (dd,  $J = 3.0, 12.2$  Hz, 2H), 3.97-3.91 (m, 1H), 3.73-3.67 (m, 1H), 3.06-2.97 (m, 2H), 2.93 (s, 1H), 2.34-2.23 (m+s, 4H), 1.69 (s, 1H), 1.48 (s, 3H), 1.14 (d,  $J = 6.3$  Hz, 3H), 0.97 (t, 1H).

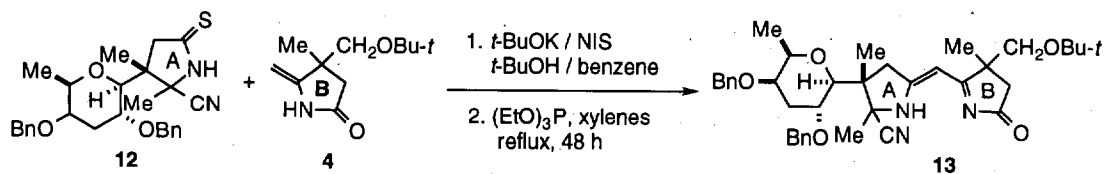
To a vigorously stirred solution of the cyano-lactam (741 mg, 1.65 mmol) in dry toluene (30 mL) was added Lawesson's reagent (400 mg, 0.99 mmol, 0.6 eq.). The mixture was heated at refluxing for 2.5 h, then cooled to room temperature and concentrated under vacuum. The crude product was purified by chromatography (E / H = 1:5) to provide **12** (648 mg, 84%) as a mixture of 2 diastereomers (5:1).

$R_f = 0.50$ , E / H = 1:2 (purple).

$^1\text{H-NMR}$  of the major isomer ( $\text{C}_6\text{D}_6$ , 400 MHz):  $\delta$  (ppm) = 7.45-7.13 (s, 10H), 4.69 (d,  $J = 11.9$  Hz, 1H), 4.30 (d,  $J = 12.2$  Hz, 1H), 4.16 (d,  $J = 12.2$  Hz, 1H), 4.11 (d,  $J =$

11.9 Hz, 1H), 3.98-3.91 (m, 1H), 3.71-3.60 (m, 1H), 3.03-2.89 (m, 3H), 2.67 (d,  $J = 18.0$  Hz, 1H), 2.25-2.20 (dt, 1H), 1.31 (s, 3H), 1.20 (s, 3H), 1.13 (d,  $J = 6.3$  Hz, 3H), 0.99-0.83 (m, 1H).

HRMS (FAB):  $C_{27}H_{33}N_2O_3SNa$  ( $M+H$ )<sup>+</sup>, calc. 465.2212, found 465.2214.



To a solution of **12** (234 mg, 0.504 mmol) and **4** (from its precursor of 542 mg, 2.52 mmol, 5 eq.) in benzene (3.0 mL) were added freshly prepared *t*-BuOK in *t*-BuOH (1.0 M, 3.0 mL, 3.0 mmol, 6.0 eq.) and NIS (282 mg, 1.26 mmol, 2.5 eq.). The resulting mixture was stirred at room temperature with protection from light for 3.5 h. The reaction mixture was quenched with 5% NaHCO<sub>3</sub> solution and diluted with EtOAc. The aqueous layer was extracted 3 times with EtOAc. The combined organics were washed with sat. NaHCO<sub>3</sub> and brine, then dried over Na<sub>2</sub>SO<sub>4</sub>. The crude product was purified by chromatography (E / H = 1:4-1:2) to provide coupled thioiminoether intermediate which was used directly in the next reaction.

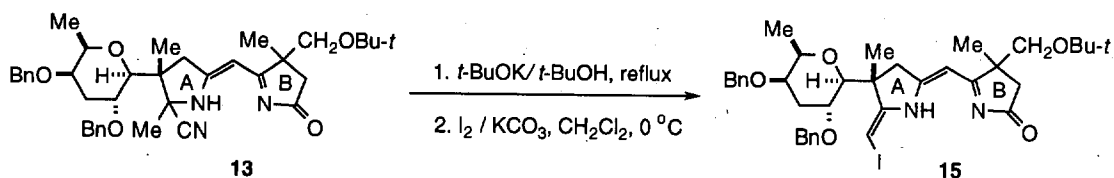
$R_f = 0.32$ , E / H = 1:2 (purple)

A solution of thioiminoether in xylenes (8 mL) and triethylphosphite (2 mL) was degassed (at room temperature, vacuum-nitrogen cycle) 4 times and heated at refluxing for 48 hours under nitrogen. The reaction was cooled to room temperature and concentrated in vacuo; the residue was subjected to chromatography (E / H = 1:4) to afford **13** (230 mg, 73%) as a mixture of 4 diastereomers.

$R_f = 0.60$ , E / H = 1:2 (red stream from top to baseline).

<sup>1</sup>H-NMR of the mixture (C<sub>6</sub>D<sub>6</sub>, 300 MHz):  $\delta$  (ppm) = 7.49-7.06 (m, 10H), 4.91-4.86 (d), 4.80-4.75 (d+d), 4.37-4.22 (m, 2H), 4.18-4.08 (m, 2H), 3.91-3.85 (m, 1H), 3.80-3.70 (m, two sets), 3.20=3.00 (m, two sets), 3.0-2.95 (m), 2.58-2.20 (m), 1.93-1.86 (d, two sets), 1.39-1.29 (m), 1.20-1.17 (m), 0.97-0.87 (m), 0.80-0.76 (d).

HRMS (FAB):  $C_{38}H_{49}O_5N_3Na$  ( $M+Na$ )<sup>+</sup>, calc. 650.3570, found 650.3588.



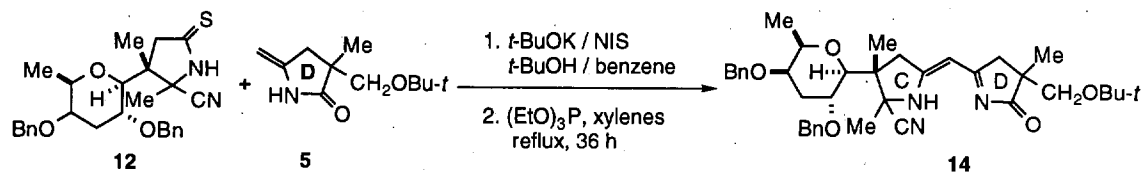
To a solution of **13** (227 mg, 0.36 mmol) in doubly distilled *t*-BuOH (10 mL) was added *t*-BuOK in *t*-BuOH (1.0 M, 2.2 mL, 2.2 mmol, 6 eq.), the resulting solution was degassed (vacuum-nitrogen cycle) four times at room temperature, then heated at gentle refluxing under nitrogen for 3.5 h and the color turned from yellow to orange. The reaction mixture was cooled to room temperature and poured into toluene. The organic layer was washed three times with brine, and the combined aqueous phases were extracted three times with toluene. The organics were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo to provide crude enamine which was subjected to the next step directly.

To a solution of the crude enamine in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at 0 °C were added excess solid K<sub>2</sub>CO<sub>3</sub>, and then a solution of I<sub>2</sub> (110 mg, 0.434 mmol, 1.2 eq.) in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) dropwise over 1 h. The reaction mixture was stirred for additional 20 min, then filtered through a plug of glass wool and concentrated. The crude product was purified by

chromatography (hexanes:  $\text{CH}_2\text{Cl}_2 = 2:1:1$ ) on deactivated neutral alumina (6% water) to provide **15** (170 mg, 46% from **12**) as a mixture of 2 diastereomers.

$R_f = 0.75$ , E / H = 1:1 (grey spot at top).

$^1\text{H-NMR}$  of the mixture ( $\text{C}_6\text{D}_6$ , 400 MHz):  $\delta$  (ppm) = 7.70 (br, major), 7.60 (br, minor), 7.54 (d,  $J = 8.6$  Hz, minor), 7.34-7.06 (m), 6.54 (d,  $J = 8.7$  Hz, minor), 6.10 (d,  $J = 4.8$  Hz, major), 4.85 (d), 4.53 (s), 4.27-4.21 (m), 4.13 (d,  $J = 13.9$  Hz), 4.04-3.98 (m), 3.80-3.70 (m), 3.60 (d,  $J = 8.7$  Hz, major), 3.56 (d,  $J = 9.3$  Hz, minor), 3.13-3.07 (m), 2.93-2.85 (m), 2.77-2.72 (m), 2.52-2.46 (m), 2.27 (dd), 2.25-2.05 (m), 2.17-1.92 (d+d, major+minor), 1.5-0.5 (overlap).



To a solution of **12** (232 mg, 0.50 mmol) and **5** (from its precursor of 540 mg, 2.5 mmol) in benzene (2.5 mL) were added freshly prepared  $t\text{-BuOK}$  in  $t\text{-BuOH}$  (1.0 M, 2.5 mL, 2.5 mmol, 5.0 eq.) and NIS (280 mg, 1.3 mmol, solid). The mixture was stirred at room temperature with protection from light for 5.5 h. The reaction mixture was quenched with 5%  $\text{NaHCO}_3$  solution and diluted with  $\text{EtOAc}$ . The aqueous layer was extracted 3 times with  $\text{EtOAc}$ . The combined organics were washed with sat.  $\text{NaHCO}_3$  and brine, then dried over  $\text{Na}_2\text{SO}_4$ . The crude product was purified by chromatography (E / H = 1:4-1:2) to provide a coupled thioiminoether intermediate which was used directly in the next reaction.

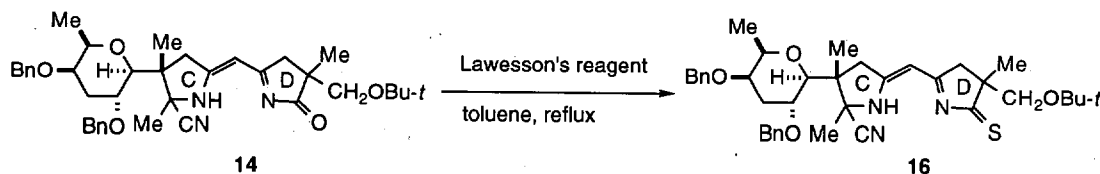
$R_f = 0.2-0.5$ , E / H = 1:2 (three red spots).

A solution of the thioiminoether in xylenes (8 mL) and triethylphosphite (2.0 mL) was degassed 4 times and heated at refluxing for 36 hours under nitrogen. The reaction was cooled to room temperature and concentrated under vacuum, the crude material was purified by chromatography (E/H = 1:10-1:4) to afford **14** (222 mg, 71%) as a mixture of 4 diastereomers

$R_f = 0.75$ , E / H = 1:1 (red stream from top to baseline).

$^1\text{H-NMR}$  of the mixture ( $\text{C}_6\text{D}_6$ , 400 MHz):  $\delta$  (ppm) = 7.56-7.07 (m), 4.90 (d,  $J = 11.9$  Hz), 4.69-4.65 (dd), 4.44-4.22 (m), 4.17-4.05 (m), 3.90-3.87 (m), 3.75 (m), 3.64 (m), 3.48-3.43 (m), 3.18-2.94 (m), 2.51-2.26 (m), 2.05 (d,  $J = 18$  Hz), 1.63 (s), 1.39 (s), 1.34 (s), 1.33 (s), 1.19-1.13 (m), 1.01-0.97 (s+m, overlap), 0.8 (d).

HRMS (FAB):  $\text{C}_{38}\text{H}_{50}\text{N}_3\text{O}_5$  ( $\text{M}+\text{H}^+$ ), calc. 628.3751, found 628.3751.

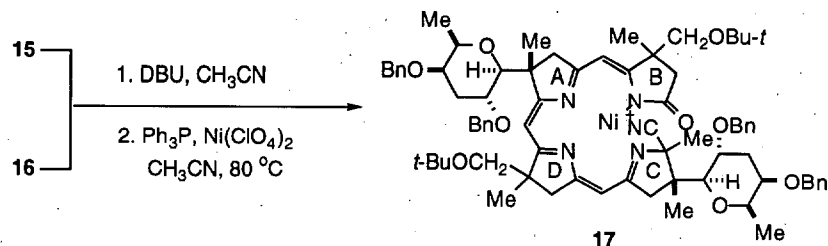


To a vigorously stirred solution of **14** (222 mg, 0.35 mmol) in toluene (15 mL) was added Lawesson's reagent (86 mg, 0.212 mmol). The mixture was heated at refluxing for 3 h. After partially removal of solvent, the crude product was purified by chromatography (benzene, then  $\text{Et}_2\text{O}$ ) to afford **16** (220 mg, 68% from thiolactam **12**) as a mixture of 4 diastereomers.

$R_f = 0.62$ , E / H = 1:2 (purple).

$^1\text{H-NMR}$  of the mixture ( $\text{C}_6\text{D}_6$ , 400 MHz):  $\delta$  (ppm) = 7.5-7.0 (m), 4.87 (d), 4.65 (d), 4.35-4.30 (m), 4.25-4.20 (m), 4.20-4.10 (m), 4.10-4.00 (dd), 3.90-3.80 (m), 3.77-3.70 (m), 3.65-3.60 (m), 3.55-3.45 (m), 3.25-2.90 (m), 2.50-2.0 (m), 1.40-0.7 (m).

HRMS (FAB):  $\text{C}_{38}\text{H}_{50}\text{N}_3\text{O}_4\text{S}$  ( $\text{M}+\text{H}$ ) $^+$ , calc. 644.3522, found 644.3506.



To a solution of **15** (170 mg, 0.234 mmol) and **16** (220 mg, 0.342 mmol) in  $\text{CH}_3\text{CN}$  (5 mL) was added DBU (350  $\mu\text{L}$ , 2.34 mmol, 10 eq.) dropwise. The resulting mixture was stirred at room temperature for 3 h with protection from light. The reaction mixture was then diluted with EtOAc and washed with 5%  $\text{NaHCO}_3$  solution. The aqueous phase was extracted 3 times with EtOAc, and the combined organics were dried over  $\text{Na}_2\text{SO}_4$ . The crude material was purified by chromatography (E/H = 1:2) to give a thioether intermediate which was used immediately in the next reaction.

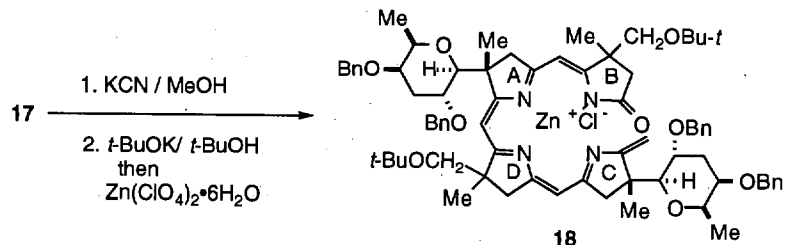
$R_f$  = 0.58, 0.70, E/H = 1:1 (two purple spots).

$\text{Ni}(\text{ClO}_4)_2 \cdot \text{H}_2\text{O}$  (428 mg, 1.2 mmol, 5 eq.) was azeotroped by evaporation of  $\text{CH}_3\text{CN}$  (2 mL) four times (became purple-blue) and then dissolved in  $\text{CH}_3\text{CN}$  (3 mL) and transferred dropwise via cannula to a solution of the thioether and  $\text{PPh}_3$  (429 mg, 1.6 mmol, 7 eq) in  $\text{CH}_3\text{CN}$  (5 mL). The initially yellow-orange solution turns dark red upon addition of  $\text{Ni}(\text{ClO}_4)_2$ . The resulting mixture was heated at  $75\text{ }^\circ\text{C}$  for 3 h, then cooled to room temperature. The reaction mixture was poured into  $\text{CH}_2\text{Cl}_2$  and 10%  $\text{NaClO}_4$  and washed 3 times with brine, the aqueous phase was extracted 3 times with  $\text{CH}_2\text{Cl}_2$  and the combined organics were dried over  $\text{Na}_2\text{SO}_4$ . The crude material was purified by chromatography (E/H = 1:2) on a mixture of Celite / Silica = 2:1 to give **17** (180 mg, 65%) as a mixture of 8 diastereomers.

$R_f$  = 0.5-0.6, E/H = 1:0 (pink stream, blue after stain).

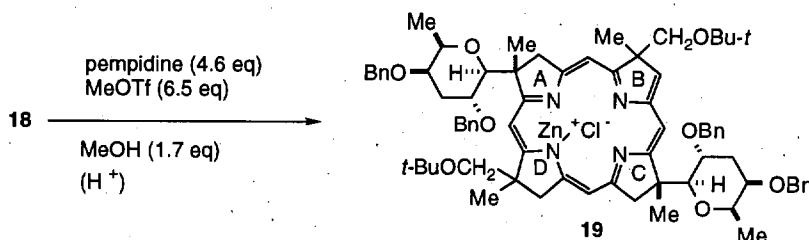
$^1\text{H-NMR}$  of the mixture ( $\text{C}_6\text{D}_6$ , 400 MHz):  $\delta$  (ppm) = 6.65-5.20 (several doublet and singlet as characteristic peaks).

MS (FAB):  $\text{C}_{75}\text{H}_{94}\text{O}_9\text{N}_5\text{Ni}^+$ , 1266, 1011, 903, 881.



To a solution of **17** (66 mg, 0.049 mmol) in MeOH (10 mL) was added KCN (100 mg) and the reaction was stirred at room temperature for 40 min with protection from light. The mixture was diluted with  $\text{CH}_2\text{Cl}_2$  and washed 3 times with brine. The aqueous phases were extracted 3 times with  $\text{CH}_2\text{Cl}_2$ . The combined organics were dried over  $\text{Na}_2\text{SO}_4$  and filtered through a plug of glass wool and concentrated in vacuo.

The crude yellow demetallated compound was placed in a 10-mL Schlenk flask and dried under vacuum for 1 h. Under nitrogen, *t*-BuOK in *t*-BuOH (1.0 M, 3.0 mL) was introduced and the mixture was heated at 80 °C for 30 min. Upon cooling to room temperature, a solution of Zn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O (900 mg, excess) in MeOH (10 mL) was quickly added to the rapidly stirred dark red reaction mixture. After 20 min the violet-red solution was diluted with CH<sub>2</sub>Cl<sub>2</sub> and washed 3 times with brine. The aqueous phases were extracted 3 times with CH<sub>2</sub>Cl<sub>2</sub>. The combined organics were dried over Na<sub>2</sub>SO<sub>4</sub> and filtered through a plug of glass wool and concentrated. The crude product **18** was dried under vacuum for 20 h and used in the next step.



To a solution of the crude zinc-complex **18** in CH<sub>2</sub>Cl<sub>2</sub> (600 μL) were added freshly distilled (over CaH<sub>2</sub>) 1,2,2,6,6-pentamethylpiperidine (39.9 μL, 0.22 mmol, 4.5 eq.) and freshly distilled (over CaH<sub>2</sub>) methyl trifluoromethanesulfonate (36.1 μL, 0.318 mmol, 6.5 eq.) successively at room temperature under nitrogen. The resulting solution was sealed with plastic cap and teflon sealing tape, and stirred with protection of light for 24 h.

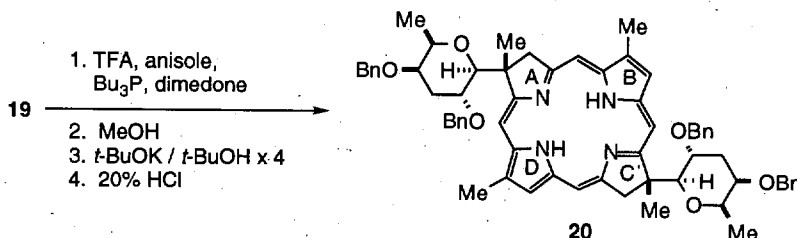
Dry MeOH (3.3 μL, 1.7 eq.) was added under nitrogen, and the solution was sealed again and stirred with protection of light for an additional 24 h.

The reaction solution was diluted with 9:1 benzene:MeOH and washed one time with half-saturated NaCl (with dropwise addition of 3% NaHCO<sub>3</sub> till a basic aqueous phase was attained). The organic layer was then successively washed with half-saturated NaCl/1% ZnCl<sub>2</sub>, half-saturated NaCl/1% ZnCl<sub>2</sub> (with dropwise addition of 1 N HCl until an acidic solution was obtained), half-saturated NaCl/1% ZnCl<sub>2</sub> (2 times), half-saturated NaCl (with dropwise addition of 3% NaHCO<sub>3</sub> till a basic aqueous phase was attained). The dark-red-orange organic layer was dried over Na<sub>2</sub>SO<sub>4</sub> and filtered and concentrated. The crude product was purified by chromatography (E/H = 1:10-1:5-1:1) on deactivated and modified silica (173 g silica was treated by a solution of 2.59 g Zn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O and 2.59 g NaCl in 8.65 mL H<sub>2</sub>O) to afford **19** as a violet-red solid (30 mg, 48% from **17**).

UV spectrum is the most reliable method to characterize this compound.

UV (benzene), nm (relative absorbance): 552 (br) (1.0), 367 (4.4), 308 (4.8).

MS (FAB): C<sub>74</sub>H<sub>91</sub>O<sub>8</sub>N<sub>4</sub>Zn<sup>+</sup>, 1227, 1140, 916, 829.



Note: Up to the third stage, the strict exclusion of oxygen was essential. During the third stage, oxygen was slowly introduced by using aged *t*-BuOK.

A solution of TFA (2 mL), anisole (30 μL), and PBu<sub>3</sub> (30 μL), in a 100-mL two-necked flask with rubber septum and connection to a vacuum/nitrogen line, was degassed 4

times via freeze (liquid nitrogen)-pump (5 min)-nitrogen-thaw cycle. In a separate Schlenk flask was placed **19** (13.5 mg) along with dimedone (40 mg) and the mixture was placed under vacuum for 1 h. The degassed TFA solution was added via cannula to the Schlenk flask containing **19** and dimedone. The resulting brown mixture was stirred 30 min and then concentrated in vacuo to give a dark brown sludge.

Dry MeOH (2 mL) was placed in a two-necked flask with rubber septum and connection to a vacuum/nitrogen line and degassed 3 times via a freeze (liquid nitrogen)-pump (5 min)-nitrogen-thaw cycle. The degassed MeOH was then added via cannula to the dark brown sludge in the Schlenk flask, and the mixture became violet-red. After 10 min of stirring, the mixture was concentrated in vacuo.

Separately, freshly prepared *t*-BuOK/*t*-BuOH (1.0 M, 3.0 mL) was degassed at room temperature three times via a pump-nitrogen cycle and then added via cannula to the reaction Schlenk flask. The mixture turned to a deep blue color and concentrated in vacuo. (After this stage no degassing process was necessary and an aged *t*-BuOK/*t*-BuOH was used). After 10 min, dry MeOH (1.5 mL) was added, and the mixture was concentrated. After 10 min an additional 2 mL of *t*-BuOK/*t*-BuOH solution was added and concentrated. Three more portions of *t*-BuOK/*t*-BuOH (2 mL) were added and concentrated. The color of the reaction mixture turned from deep blue to dark purple or deep burgundy through this process.

After the final addition of *t*-BuOK/*t*-BuOH, the reaction was quenched by rapid addition of 10 mL of 20% HCl solution. The reaction mixture was poured into H<sub>2</sub>O (50 mL) and CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The layers were separated and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub>, the combined organics (dark green) were washed with sat. NaHCO<sub>4</sub> and dried over Na<sub>2</sub>SO<sub>4</sub>. The crude product was purified by chromatography (E/H = 1:10-1:5) to give bright green **20** containing impurity. Further purification by preparative TLC (silica gel, E / H = 1:2 (buffered with 1% Et<sub>3</sub>N)) afforded pure **20** as a bright green solid (4.2 mg, 40%).

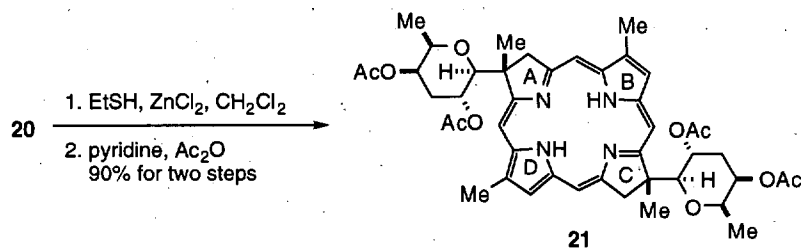
$R_f = 0.70$ , E / H = 1:2.

$[\alpha]_D -47.6^\circ$  (*c* 0.06, CH<sub>2</sub>Cl<sub>2</sub>).

<sup>1</sup>H-NMR (C<sub>6</sub>D<sub>6</sub>, 500 MHz):  $\delta$  (ppm) = 9.61 (s, 1H), 9.46 (s, 1H), 8.65 (s, 1H), 8.61 (s, 1H), 8.45 (s, 1H), 8.38 (s, 1H), 7.21-6.91 (m, 10H), 6.61-6.55 (m, 2H), 6.42-6.37 (m, 4H), 5.94 (d, *J* = 7.6 Hz, 2H), 5.85 (d, *J* = 7.7 Hz, 2H), 5.39 (d, *J* = 16.0 Hz, 1H), 5.33 (d, *J* = 16.0 Hz, 1H), 4.25 (d, *J* = 16.0 Hz, 1H), 4.21 (d, *J* = 16.0 Hz, 1H), 4.12-4.02 (m, 8H), 3.83-3.77 (m, 1H), 3.55-3.50 (m, 2H), 3.41 (s, 3H), 3.22 (s, 3H), 3.05 (d, *J* = 17.4 Hz, 1H), 2.98 (d, *J* = 11.2 Hz, 1H), 2.90 (d, *J* = 10.8 Hz, 1H), 2.31 (d, *J* = 10.9 Hz, 1H), 2.22 (s, 3H), 2.15 (s, 3H), 2.11-1.87 (m, 4H), 1.51 (d, *J* = 6.2 Hz, 3H), 1.45 (d, *J* = 6.3 Hz, 3H), -1.92 (s, 1H), -1.95 (s, 1H).

UV (CH<sub>2</sub>Cl<sub>2</sub>), nm ( $\epsilon$ ): 716 (86,446), 681(7,908), 656(4,090), 489 (23,179), 461 (7,635), 434 (5,454), 371 (109,352), 344 (91,627).

HRMS (FAB): C<sub>64</sub>H<sub>70</sub>N<sub>4</sub>O<sub>6</sub> (M+H)<sup>+</sup>, calc. 990.5295, found 990.5303.



To a solution of **20** (3.5 mg, 3.5  $\mu$ mol) in CH<sub>2</sub>Cl<sub>2</sub> (1.5 mL) and EtSH (1 mL) was added excess anhydrous ZnCl<sub>2</sub> as solid in one portion, the solution immediately turns



from deep green to pink-red. The mixture was stirred at room temperature for 24 h, then poured in a solution of  $\text{CH}_2\text{Cl}_2$  and  $\text{Et}_3\text{N}$  (10:1) meanwhile the green color of the original solution was restored. The resulting mixture was concentrated, and the residual was dissolved in  $\text{CH}_2\text{Cl}_2$  and washed three times with a solution of brine/1N HCl (1:1). The aqueous phase was extracted 3 times with  $\text{CH}_2\text{Cl}_2$ , and the combined organics were dried over  $\text{Na}_2\text{SO}_4$ . TLC showed a green spot (dark, 366 nm) at  $R_f = 0.15$  (EtOAc). The crude product was dried under vacuum for 2 h.

To the crude product were added freshly distilled pyridine (1 mL) and  $\text{Ac}_2\text{O}$  (1 mL), the resulting solution was stirred for 18 h at room temperature. The crude product after removal solvent under high vacuum was purified by chromatography (E / H = 1:5-1:2) to afford **21** (2.6 mg, 90%).

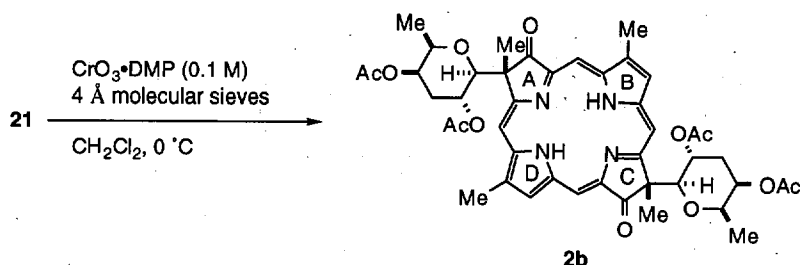
$R_f = 0.10$ , E / H = 1:2.

$[\alpha]_D -35.0^\circ$  (c 0.1,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H-NMR}$  ( $\text{C}_6\text{D}_6$ , 500 MHz):  $\delta$  (ppm) = 9.09 (s, 1H), 8.96 (s, 1H), 8.72 (s, 1H), 8.61 (s, 1H), 8.44 (s, 1H), 8.37 (s, 1H), 5.28-5.24 (m, 1H), 4.97 (d,  $J = 16.1$  Hz, 1H), 4.93 (d,  $J = 16.1$  Hz, 1H), 4.80 (br, 1H), 4.28-4.26 (m, 2H), 4.09-4.06 (m, 2H), 3.40 (s, 3H), 3.26 (s, 3H), 2.21-2.18 (m, 1H), 2.06 (s, 3H), 1.97 (s, 3H), 1.56 (d,  $J = 15.3$  Hz, 3H), 0.91 (d,  $J = 6.2$  Hz, 3H), -0.01 (br, 2H).

UV ( $\text{CH}_2\text{Cl}_2$ ), nm ( $\epsilon$ ): 713 (79,600), 678 (6,880), 655 (3,370), 597 (1,172), 488 (19,636), 460 (5,568), 434 (92,857), 369 (108,440), 343 (89,537), 242 (12,309).

HRMS (EI):  $\text{C}_{44}\text{H}_{55}\text{O}_{10}\text{N}_4$  (M+H) $^+$ , calc. 799.3918, found 799.3888.



A suspension of tetra-Ac **21** (1.2 mg) and activated powder 4Å molecular sieves in  $\text{CH}_2\text{Cl}_2$  (1.5 mL) at 0 °C was titrated with a solution of 0.1 M  $\text{CrO}_3 \cdot \text{DMP}$  in  $\text{CH}_2\text{Cl}_2$  (freshly prepared from  $\text{CrO}_3$  and 3,5-dimethylpyrazole in  $\text{CH}_2\text{Cl}_2$  at -25 °C). The progress of reaction was monitored by TLC (E/H = 2:1). The green tetra-Ac was first transformed to a more polar green monoketone, then the green monoketone to a slightly less polar dark-purple diketone. The reaction was quenched with 50  $\mu\text{L}$  isopropanol when reaction completion. The reaction mixture was diluted with  $\text{CH}_2\text{Cl}_2$  and washed with brine. The crude product was purified by preparative TLC (silica gel, E / H = 1:1, two developments) to afford **2b** (0.38 mg, 30%) as a purple solid.

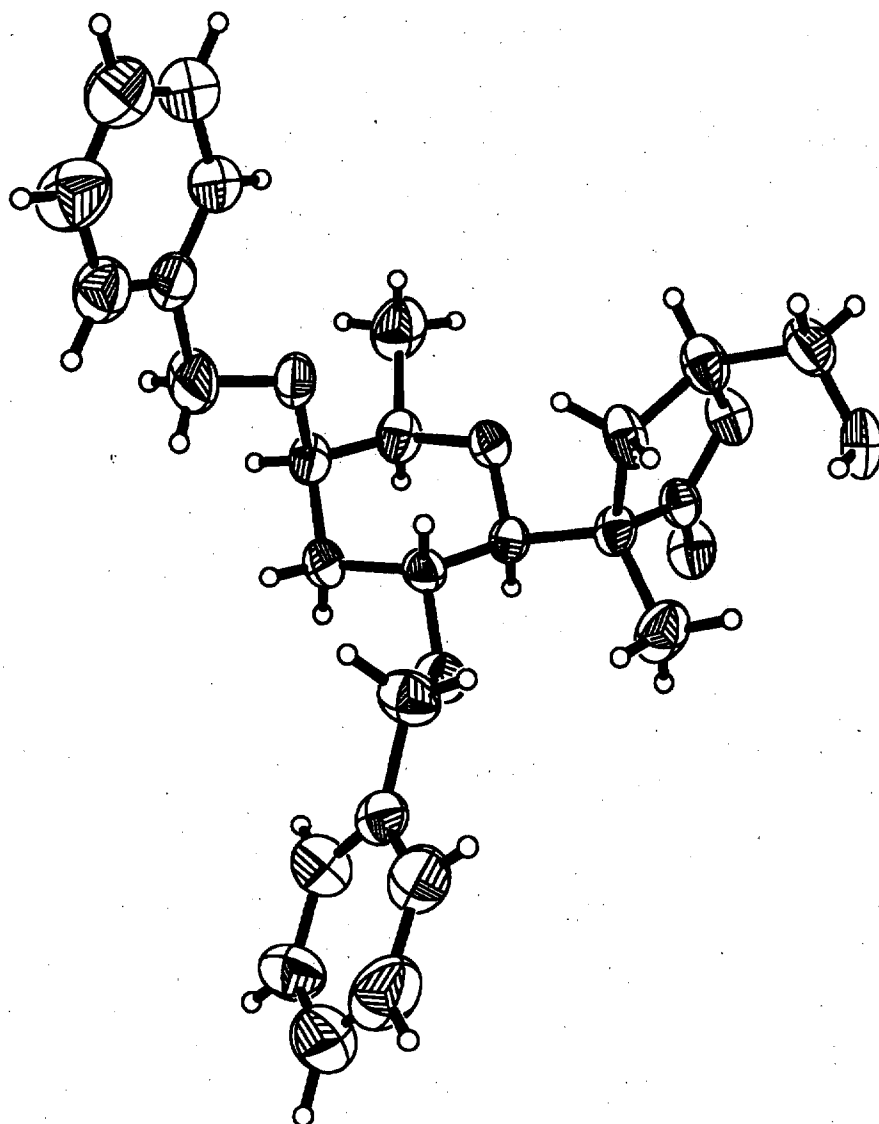
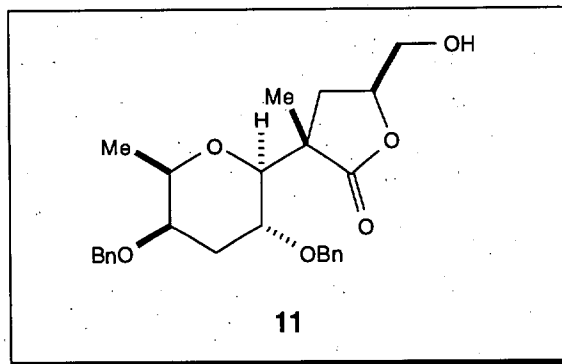
$R_f = 0.50$ , E / H = 2:1.

$^1\text{H-NMR}$  ( $\text{C}_6\text{D}_6$ , 500 MHz):  $\delta$  (ppm) = 10.06 (s, 1H), 9.97 (s, 1H), 9.68 (s, 1H), 9.54 (s, 1H), 8.50 (s, 1H), 8.33 (s, 1H), 5.30 (s, 2H), 4.73-4.54 (m, 6H), 3.39-3.37 (m, 3H), 3.28 (s, 3H), 3.15 (s, 3H), 2.24 (d,  $J = 9.5$  Hz, 6H), 1.84-1.76 (m, 2H), 1.56 (s, 3H), 1.50 (s, 3H), 1.35-1.14 (m, 4H), -0.60 (s, 3H), -0.65 (s, 3H), -2.66 (s, 1H), -2.69 (s, 1H). See also Figure 2.

UV ( $\text{CH}_2\text{Cl}_2$ ), nm ( $\epsilon$ ): 678 (44,600), 645 (2,837), 614 (2,482), 545 (3,812), 504 (3,812), 480 (3,305), 406 (107,463).

CD ( $\text{CH}_2\text{Cl}_2$ ), nm ( $\Delta\epsilon$ ): 400 (+8.8), 381 (+4.4), 316 (-1.3). See also Figure 3.

HRMS (EI):  $\text{C}_{44}\text{H}_{51}\text{O}_{12}\text{N}_4$  (M+H) $^+$ , calc. 827.3503, found 827.3535.



ORTEP Drawing of 11