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SYNTHESIS OF THE MONOTERPENE ALKALOID BAKANKOSIN FROM SECOLOGANIN[1]

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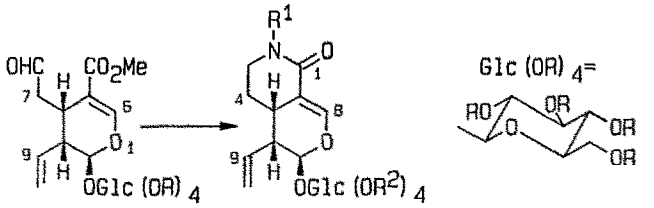
Abstract - Reduction of secologanin **1a** with sodium borohydride followed by acylation afforded 86% of sweroside tetraacetate **4** which was transformed to the 8-iodomethylester **5c** by treatment with trimethylsilyliodide, hydrolysis and addition of diazomethane in 92% yield. Reaction of **5c** with sodium azide gave 65% of the 8-azidomethylester **5d** which was reduced with 1,3-propanedithiol to give bakankosin **2a** after solvolysis in 80% yield.

The monoterpene alkaloid bakankosin **2a** was isolated by Bourquelot and Herissey from the seeds of *Strychnos Vacacoua Baillon* in 1908.[2] For the first time, Büchi and Manning[3] proposed the correct structure of bakankosin **2a** in 1960, which was confirmed independently by Inouye[4] and ourselves[5] with the presentation of the relative and absolute configuration.



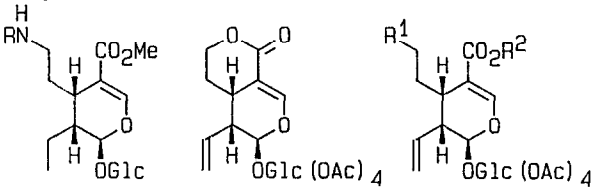
1	R
a	H
b	CH=N-OH instead of CH=O

2	R^1	R^2
a	H	H
b	$CH_2-C_6H_5$	H
c	$CH_2-C_6H_3$-3, 4-OCH_3	H
d	H; (8aS)-8, 8a-dihydro	H
e	H; 9, 10-dihydro	H
f	H	Ac

It can be assumed, that **2a** is biosynthetically dervied from secologanin[6] **1a** by a reductive amination followed by the formation of the lactam. **1a** is also a key intermediate in the biosynthesis of the secoiridoids, the monoterpenoid, indole, the ipecacuanha and the pyrroloquinoline alkaloids.[6,7] Since secologanin **1a** can be obtained in a good yield and with high purity from *Symphoricarpos albus (L.)* it may be used as starting material for the "enantioselective synthesis" of these compounds.[8]

All attempts so far however, to synthesize bakankosin **2a** from secologanin **1a** by a reductive amination resulted only in a low yield of **2a**.[4,5] Also, the reduction of the readily available oxime **1b** did not give **2a**.[5] In

contrast, primary amines can be used in a reductive amination. Thus, reaction of **1a** with benzylamine and 3,4-dimethoxybenzylamine, respectively in a mixture of tetrahydrofuran and a citrate buffer (pH 6) with sodium cyanoborohydride[9] resulted in the formation of the N-benzyl-bakankosin derivatives **2b** and **2c**, respectively in 60-70% yield. However, removal of the N-benzyl groups to give **2a** was not possible. Treatment of **2b** with sodium in liquid ammonia at -78°C led to a debenzylation at the nitrogen, but under these conditions the conjugated double bond was also reduced, whereas the vinyl group was left intact. After 4 h 8,8a-dihydrobakankosin **2d** was obtained in 55% yield as well as 7% of **2b** as the only product. The reaction seems to be completly stereoselective, providing only the (8aS)-diastereomer. Catalytic hydrogenation of **2b** at 45°C afforded 9,10-dihydrobakankosin **2e** in 70% yield after 4 h. **2e** could also be obtained in 94% yield by a reductive amination of **1a** with benzylamine under hydrogen using palladium on carbon as catalyst. In this case we assume that the secondary amine **3a** is formed first, which after debenzylation by hydrogenolysis gives **2e**. Since in both cases hydrogenation of the C-9,10-double bond is much faster than N-debenzylation, only the 9,10-dihydrobakankosin **2e** can be obtained. Finally, treatment of **2c** with dichlorodicyanobenzoquinone to obtain an oxidative removal[10] of the 3,4-dimethoxybenzyl group gave only unchanged starting material.



3	R
a	CH_2-C_6H_5
b	H

4

5	R^1	R^2
a	I	$SiMe_3$
b	I	H
c	I	CH_3
d	N_3	CH_3
e	NH_2	CH_3
f	OH	CH_3
g	OTos	CH_3

As all these attempts to achieve a practical transformation of secologanin **1a** to bakankosin **2a** failed we introduced the amino function in **2a** via an azido moiety. Starting from sweroside tetraacetate **4**, which can be obtained from secologanin **1a** by treatment with sodium borohydride followed by acylation in 86% yield, the 8-iodomethylester **5c** was synthesized according to the procedure of McLean.[11] Reaction of **4** with trimethylsilyl iodide in chloroform afforded the 8-iodotrimethylsilylester **5a**, an unstable product, which was trapped after fast hydrolysis to **5b** with an excess of diazomethane in diethyl ether to give **5c** in 92% yield. At this stage, it is possible to introduce an azido moiety which can be reduced to an amino function without effecting the C-5,6- and C-9,10-double bonds. Treatment of **5c** with sodium azide in dimethylformamide gave the 8-azidomethylester **5d** in 65% yield. The use of azide derivatives which are soluable in organic solvents such as trimethylsilyl azide or the employment of phase transfer catalysts,[12] did not improve the yields. Also, it was not possible to transform secologanol tetraacetate **5f**, the first product in the reduction of secologanin tetraacetate, to a *p*-toluenesulfonate **5g** or a methanesulfonate in order to introduce the azido moiety by a nucleophilic substitution, since the cyclization to sweroside tetraacetate **4** predominates. The

hydrogenation of the azido moiety in **5d** with hydrogen using palladium on calcium carbonate (5%) as catalyst[13] in ethyl acetate followed by cyclization afforded bakankosin tetraacetate **2f** in only 30% yield, in addition 10% of **4** and 30% of the starting material **5d** were isolated. Better results in the reduction of **5d** were obtained by treatment with triphenylphosphine[14] in tetrahydrofuran, which led after hydrolysis of the intermediately formed phosphineamide to **2f** in 51% yield. The best yields however were achieved by reduction of **5d** with propanedithiol in methanol in the presence of triethylamine,[15] which afforded 89% of **2f**. Solvolysis of **2f** with sodium ethanolate in methanol yielded 90% of bakankosin **2a**.

EXPERIMENTAL

Melting points: Kofler micro-melting point apparatus (uncorrected values). - IR: Perkin Elmer 297. - UV: Varian Cary 219. - Optical rotations: Perkin Elmer 241. - ^1H and ^{13}C NMR: Varian XL 200 (internal TMS). - Thin layer chromatography: SIL G/UV_{254} (Macherey, Nagel & Co.). - Column chromatography: Silica gel 60 (Macherey, Nagel & Co.). - Elementar analyses were carried out in the analytical laboratory of the University of Göttingen.

Isolation of secologanin **1a**: Berries (105 kg) of *Symphoricarpos albus (L.)* were collected around Göttingen in September/October, cut to pieces together with the same volumina of aceton/chloroform (10:1) and the obtained slurry was filtered. The filtrate was centrifuged to remove suspended particles, concentrated in vacuo at 30°C and freeze-dried. The yellow residue (6 kg) was mixed with silica gel together with a small amount of water and filtered with ethyl acetate/isopropanol (3:1). Chromatography on silica gel with the same solvent afforded 178 g (0.17%) secologanin **1a**. - R_f = 0.39. - IR (KBr): ν = 3400 cm^{-1} (OH), 1710 (C=O), 1635 (C=C). - UV (methanol): λ_{max} (lg ϵ) = 234 nm (4.34). - ^1H NMR (CD_3OD): δ = 2.47 (ddd, J = 1 Hz, J = 6 Hz, J = 12 Hz, 1 H; 7-H), 2.64-2.86 (m, 2 H; 3-H, 7-H), 2.94-3.02 (m, 1 H; 4-H), 3.04-3.98 (m, 6 H; 2'-H, 3'-H, 4'-H, 5'-H, 6'-H_2), 3.66 (s, 3 H; OCH_3), 4.66 (d, J= 8 Hz, 1 H; 1'-H), 5.18-5.44 (m, 2 H; 10-H_2), 5.49 (d, J = 4 Hz, 1 H; 2-H), 5.46-5.80 (m, 1 H; 9-H), 7.51 (d, J = 2 Hz, 1 H; 6-H), 9.69 (d, J = 1 Hz; 1 H; 8-H).

Reductive amination: To a solution of **1a** (1.00 g, 2.58 mmol) and the amine as hydrochloride (3.87 mmol) in tetrahydrofuran/citrate-buffer (pH 6) was added sodium cyanoborohydride (264 mg, 4.40 mmol). After stirring for 24 h at room temperature sodium carbonate was added until pH 9 was obtained. The solvent was removed in vacuo and a solution of the residue in methanol was filtered over silica gel with methanol as solvent. Purification was achieved by chromatography on silica gel (chloroform : methanol = 4:1).

(4aS,5R,6S)-N-benzylbakankosin **2b**: Reaction of **1a** (1.00 g, 2.58 mmol) and benzylamine (415 mg, 387 mmol); yield 786 mg (68%) of **2b**. - Mp 189°C. - R_f = 0.52. - IR (KBr): ν = 3400 cm^{-1} (OH), 1660 (C=O), 1595 (C=C). - UV (methanol): λ_{max} (lg ϵ) = 238 nm (4.23). - $[\alpha]^{20}_D$ = -163.5° (c = 1 in methanol). - ^1H NMR (CD_3OD): δ = 1.40-1.80 (m, 2 H; 4-H_2), 2.64 (ddd, J = 2 Hz, J = 6 Hz, J = 9.5 Hz, 1 H; 5-H), 2.96-3.10 (m, 1 H; 4a-H), 3.12-3.46 (m, 6 H; 3-H_2, 2'-H, 3'-H, 4'-H, 5'-H), 3.67 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'a-H), 3.90 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'b-H), 4.55-4.74 (m, 3 H; 1-H, 11-H_2), 5.24 (dd, J = 2.5 Hz, J = 10 Hz, 1 H; 10a-H), 5.28 (dd, J = 2.5 Hz, J = 17.5 Hz, 1 H; 10b-H), 5.49 (d, J = 2 Hz, 1 H; 6-H), 5.60 (ddd, J = 9.5 Hz, J = 10 Hz, J = 17.5 Hz, 1 H; 9-H), 7.23-7.42 (m, 5 H; aromat. H), 7.46 (d, J = 2.5 Hz, 1 H; 8-H). - ^{13}C NMR (CD_3OD): δ = 26.04 (C-4), 29.02 (C-4a), 44.51 (C-5), 47.48 (C-3), 51.32 (C-11), 62.61 (C-6'), 71.47 (C-4'), 74.66 (C-2'), 77.86 (C-3'), 78.22 (C-5'), 97.32 (C-6), 99.60 (C-1'), 109.21 (C-8a), 120.33 (C-10), 128.46 (C-4"), 128.94 (C-3"), 129.64 (C-2"), 134.03 (C-9), 138.40 (C-1"), 148.88 (C-8), 166.42 (C-1).

(4aS,5R,6S)-N-(3,4-dimethoxy)benzylbakankosin **2c**: Reaction of **1a** (1.00 g, 2.58 mmol) and 3,4-dimethoxybenzylamine (650 mg, 387 mmol); yield 906 mg (67%) of **2c**. - Mp 115°C. - R_f = 0.66. - IR (KBr): ν = 3400 cm^{-1} (OH), 1660 (C=O), 1590 (C=C). - UV (methanol): λ_{max} (lg ϵ) =

236 nm (4.35), 278 (3.67). - $[\alpha]^{20}_D$ = -144.0° (c = 1 in methanol). - ^{1}H NMR (CD_3OD): δ = 1.40-1.62 (m, 1 H; 4-H_{ax}), 1.64-1.78 (m, 1 H; 4-H_{eq}), 2.62 (ddd, J = 2 Hz, J = 6 Hz, J = 10 Hz, 1 H; 5-H), 2.94-3.10 (m, 1 H; 4a-H), 3.11-3.44 (m, 6 H; 3-H_2, 2'-H, 3'-H, 4'-H, 5'-H), 3.65 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'a-H), 3.78 (2s, 6 H; OCH_3), 3.89 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'b-H), 4.54 (m, 2 H; 11-H_2), 4.66 (d, J = 8 Hz, 1 H; 1'-H), 5.22 (dd, J = 2.5 Hz, J = 10 Hz, 1 H; 10a-H), 5.26 (dd, J = 2.5 Hz, J = 17.5 Hz, 1 H; 10b-H), 5.47 (d, J = 2 Hz, 1 H; 6-H), 5.56 (ddd, J = 10 Hz, J = 10 Hz, J = 17.5 Hz, 1 H; 9-H), 6.81 (dd, J = 2 Hz, J = 10 Hz, 1 H; 6"-H), 6.88 (s, 1 H; 2"-H), 6.89 (d, J = 10 Hz, 1 H; 5"-H), 7.43 (d, J = 2.5 Hz, 1 H; 8-H). - ^{13}C NMR (CD_3OD): δ = 26.04 (C-4), 28.99 (C-4a), 44.48 (C-5), 47.25 (C-3), 51.00 (C-11), 56.41 (O-CH_3), 56.45 (O-CH_3), 62.61 (C-6'), 71.47 (C-4'), 74.66 (C-2'), 77.87 (C-3'), 78.23 (C-5'), 97.24 (C-6), 99.55 (C-1'), 109.24 (C-8a), 112.84 (C-5"), 112.98 (C-2"), 120.32 (C-10), 121.69 (C-6"), 131.13 (C-1"), 134.02 (C-9), 148.85 (C-8), 149.91 (C-4"), 150.56 (C-3"), 166.28 (C-1). - Anal. Calcd for $C_{25}H_{34}O_{11}N$ (523.53): C, 57.36; H, 6.35; N, 2.68. Found: C, 57.90; H, 6.64; N, 2.76%.

Debenzylation of 2b: To a solution of 2b (600 mg, 1.34 mmol) in liquid ammonia was added sodium (616 mg, 26.8 mmol) at -78°C. After stirring for 4 h, ammonium chloride was added, and the solution was warmed to room temperature. Chromatography of the residue on silica gel (chloroform : methanole = 4:1) afforded 263 mg (55%) of (4aS,5R,6S,8aS)-8,8a-dihydrobakankosin 2d and in addition 42 mg (7%) of the starting material 2b. - R_f = 0.20. - IR (KBr): ν = 3400 cm^{-1} (OH), 1640 (C=O). - $[\alpha]^{20}_D$ = -69.0° (c = 1 in methanol). - ^{1}H NMR (CD_3OD): δ = 1.54-1.98 (m, 2 H; 4-H_2), 2.39-2.55 (m, 2H; 4a-H, 5-H), 3.10-3.42 (m, 7 H; 3-H_2, 2'-H, 3'-H, 4'-H, 5'-H, NH), 3.70 (m, 1 H; 6'a-H), 3.94 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'b-H), 3.96 (dd, J = 5 Hz, J = 12 Hz, 1 H; 8-H_{ax}), 4.12 (dd, J = 6 Hz, J = 12 Hz, 1 H; 8-H_{eq}), 4.62 (d, J = 8 Hz, 1 H; 1'-H), 5.09 (d, J = 6.5 Hz, 1 H; 6-H), 5.12-5.28 (m, 2 H; 10-H_2), 5.87 (ddd, J = 7.5 Hz, J = 10 Hz, J = 17.5 Hz, 1 H; 9-H). - ^{13}C NMR (CD_3OD): δ = 21.65 (C-4), 35.58 (C-4a), 41.88 (C-3), 42.01 (C-5), 47.54 (C-8a), 62.63 (C-6'), 62.77 (C-8), 71.49 (C-4'), 74.76 (C-2'), 78.00 (C-3'), 78.18 (C-5'), 97.58 (C-6), 99.19 (C-1'), 111.18 (C-10), 137.33 (C-9), 174.67 (C-1). - Anal. Calcd for $C_{16}H_{25}O_8N$ (359.38): C, 53.48; H, 7.01. Found: C, 53.42; H, 7.08%.

9,10-Dihydrobakankosin 2e: To a solution of 1a (200 mg, 0.5 mmol) in methanol (25 ml) were added benzylamine hydrochloride (95 mg, 0.7 mmol) and palladium/carbon (10 %; 20 mg). After stirring for 4 h at 45°C (p H_2 = 1 atm) sodium carbonate solution was added until pH 9 was obtained. The solvent was removed in vacuo and a solution of the residue in methanol was filtered over silica gel with methanol as solvent. Purification by chromatography on silica gel (chloroform : methanol = 3:1) afforded 184 mg (94%) of 2e. - Mp. 227°C. - R_f = 0.32. - $[\alpha]^{20}_D$ = -181.0° (c = 1 in methanol. - ^{1}H NMR (CD_3OD): δ = 1.00 (dd, J = 5 Hz, J = 5 Hz, 3 H; 10-H_2), 1.20-1.96 (m, 5 H; 4-H_2, 5-H, 9-H_2), 2.90-3.40 (m, 7 H; 2'-H, 3'-H, 4'-H, 5'-H, 3-H_2, 4a-H), 3.65-3.90 (m, 2 H; 6'-H_2), 4.70 (d, J = 8 Hz, 1 H; 1'-H), 5.28-5.60 (m, 3 H; 9-H, 10-H_2), 5.63 (d, J = 1.5 Hz, 1 H; 6-H), 7.33 (d, J = 2.5 Hz, 1 H; 8-H).

Sweroside tetraacetate 4: To a solution of sodium borohydride (287 mg, 7.60 mmol) in dry ethanol (50 ml) was added 1a (2.00 g, 5.2 mmol) in ethanol (50 ml). After stirring for 2 h at room temperature, strong acidic ion exchanger was added and stirring was continued for 1 h. After filtration, the solvent was removed in vacuo; chromatography of the residue on silica gel (chloroform : methanol = 4.1) afforded 1.82 g (94%) sweroside.[16,17]
To a solution of sweroside (2.00 g, 5.6 mmol) in dry pyridine (40 ml) was added freshly distilled acetanhydride (20 ml) at 0°C. After stirring 12 h at room temperature, diethyl ether (200 ml) was added, and the solution was washed with 2n hydrochloric acid (3 x 50 ml), saturated sodium hydrogencarbonate solution (3 x 50 ml) and brine (2 x 50 ml), and then dried (sodium sulfate). The solvent was removed in vacuo and the residue purified by chromatography on silica gel (ethyl acetate) to give 2.68 g (91%) sweroside tetraacetate 4.[16,17]

Methyl (2S,3R,4S)-2-(2',3',4',6'-tetraacetyl-ß-D-glucopyranosyloxy)-4-(2-azidoethyl)-3-vinyl-3,4-dihydro-2H-pyran-5-carboxylate 5d: To a solution of 5c (340 mg, 0.51 mmol) in dimethylformamide (20 ml) was added sodium azide (332 mg, 5.10 mmol). After stirring for 12 h at room temperatur, the solvent was removed in vacuo. Chromatography of the residue on silica gel (ethyl acetate) afforded 190 mg (65%) of 5d. - R_f = 0.59. - IR (KBr): ν = 2100 cm^{-1} (N_3), 1750 (acetyl-C=O), 1705 (C=O), 1630 (C=C). - UV (acetonitril): λ_{max} (lg ε) = 230

nm (4.27). - $[\alpha]^{20}_D$ = -80.1° (c = 1 in chloroform). - ^{1}H NMR ($CDCl_3$): δ = 1.52-1.68 (m, 2 H; 7-H_2), 1.93, 2.01, 2.03, 2.10 (4s, 12 H; O=CCH_3), 2.58 (m, 2 H; 3-H, 8a-H), 3.18 (dd, J = 8 Hz, J = 16 Hz, 1 H; 8b-H), 3.18-3.38 (m, 1 H; 4-H), 3.72 (s, 3 H; CO_2CH_3), 3.66-3.89 (m, 1 H; 5'-H), 4.16 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'a-H), 4.30 (dd, J = 4 Hz, J = 12 Hz, 1 H; 6'b-H), 4.89 (d, J = 8 Hz, 1 H; 1'-H), 4.84-5.38 (m, 5 H; 10-H_2, 2'-H, 3'-H, 4'-H), 5.29 (d, J = 2 Hz, 1 H; 2-H), 5.63 (ddd, J = 10 Hz, J = 10 Hz, J = 17 Hz, 1 H; 9-H), 7.39 (d, J = 2 Hz, 1 H; 6-H).

Hydrogenation of **5d** *with palladium/calcium carbonate*: To a solution of **5d** (100 mg, 0.17 mmol) in ethyl acetate (10 ml) was added palladium/calcium carbonate (5%; 200 mg). After stirring for 36 h at room temperature (p H_2 = 1 atm) the slurry was filtered and the solvent was removed in vacuo. Chromatography on silica gel (ethyl acetate) afforded three fractions. - A: R_f = 0.59. - 34 mg (30%) of **5d**. - B: R_f = 0.56. - 9 mg (10%) of sweroside tetraacetate **4**. - C: R_f = 0.12. - 27 mg (30%) of bakankosin tetraacetate **2f**. - IR (KBr): ν = 3600-3200 cm^{-1} (NH), 1750 (acetyl-C=O), 1670 (C=O), 1620 (C=C).- UV (acetonitril): λ_{max} (lg ϵ) = 236 nm (4.36). - $[\alpha]^{20}_D$ = -158.6° (c = 0.5 in chloroform). - ^{1}H NMR ($CDCl_3$): δ = 1.48-1.80 (m, 2 H; 4-H_2), 1.97, 2.00, 2.03, 2.10 (4s, 12 H; O=CCH_3), 3.66-3.80 (m, 1 H; 5'-H), 4.14 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'a-H), 4.31 (dd, J = 4 Hz, J = 12 Hz, 1 H; 6'b-H), 4.92-5.61 (m, 8 H; 6-H, 9-H, 10-H_2, 1'-H, 2'-H, 3'-H, 4'-H), 5.94 (s, 1 H; NH), 7.38 (d, J = 2 Hz, 1 H; 8-H). - ^{13}C NMR ($CDCl_3$): δ = 20.48, 20.59, 20.68, 20.75 ($CO_2\underline{C}H_3$),24.62 (C-4), 27.66 (C-4a), 40.90 (C-3), 42.66 (C-5), 61.71 (C-6'), 68.15 (C-4'), 70.44 (C-2'), 72.25 (C-3'), 95.77 (C-6), 96.25 (C1''), 108.23 (C-8a), 120.44 (C-10), 131.91 (C-9), 146.80 (C-8), 165.68 (C-1), 169.49, 169.57, 170.05, 170.63 ($\underline{C}O_2CH_3$).

Reduction of **5d** *with trimetylphosphine*: To a solution of **5d** (200 mg, 0.34 mmol) in tetrahydrofuran (5 ml) was added triphenylphospine (90 mg, 0.34 mmol) in tetrahydrofuran (5 ml). After stirring for 24 h at room temperature water (5 ml) was added and stirring was continued for 24 h. The solvent was removed in vacuo and the residue was purified by chromatography (ethyl acetate) on silica gel to give 91 mg (51%) of bakankosin tetraacetate **2f**.

Reduction of **5d** *with propanedithiol*: To a solution of **5d** (200 mg, 0.34 mmol) in dry methanol (2 ml) were added under nitrogen freshly distilled propanedithiol (186 mg, 1.72 mmol) and dry triethylamine (174 mg, 1.72 mmol). After stirring for 20 h at room temperatur, the solvent was removed in vacuo. Chromatography of the residue on silica gel (ethyl acetate) afforded 159 mg (89%) bakankosin tetraacetate **2f**.

Bakankosin **2a**: To a solution of **2f** (150 mg, 0.29 mmol) in dry methanol (30 ml) was added sodium ethanolate in methanol (10 %; 0.3 ml). After stirring for 6 h at room temperature, the solvent was removed in vacuo. Chromatography of the residue on silica gel (chloroform : methanol = 4:1) afforded 93 mg (90%) of **2a**. - R_f = 0.21. - IR (KBr): ν =3650-3100 cm^{-1} (NH, OH), 1665 (C=O), 1605 (C=C). - UV (methanol): λ_{max} (lg ϵ) = 235 nm (4.35). - $[\alpha]^{20}_D$ = -178.0° (c = 0.5 in chloroform). - ^{1}H NMR (CD_3OD): δ = 1.40-1.64 (m, 1 H; 4-H_{ax}), 1.67-1.82 (m, 1 H; 4-H_{eq}), 2.67 (ddd, J = 2 Hz, J = 5.5 Hz, J = 10 Hz, 1 H; 5-H), 2.94-3.12 (m, 1 H; 4a-H), 3.14-3.45 (m, 6 H; 3-H_2, 2'-H, 3'-H, 4'-H, 5'-H), 3.68 (dd, J = 2 Hz, J = 12 Hz, 1 H; 6'a-H), 3.91 (dd, J = 4 Hz, J = 12 Hz, 1 H; 6'b-H), 4.69 (d, J = 8 +z, 1 H; 1'-H), 5.26 (dd, J = 2.5 Hz, J = 10 Hz, 1 H; 10a-H), 5.30 (dd, J = 2.5 Hz, J = 17.5 Hz, 1 H; 10b-H), 5.50 (d, J = 2 Hz, 1 H; 6-H), 5.60 (ddd, J = 9.5 Hz, J = 10 Hz, J = 17.5 Hz, 1 H; 9-H), 7.39 (d, J = 2.5 Hz, 1 H; 8-H), 7.94 (s, 1 H; NH). - Anal. Calcd for $C_{18}H_{23}O_8N$ (381.38): C,56.69; H,6.08; N,3.67. Found: C,56.83; H,5.96; N,3.62%.

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