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Synthesis of Acyclic Analogues of Sesbanimides A and B

Jan C. van den Bos, Wilhelmus J. Vloon, Gerrit-Jan Koomen and Upendra K. Pandit*
Organic Chemistry Laboratory, University of Amsterdam,
Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands.

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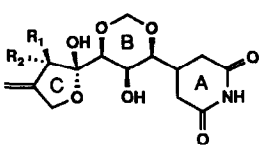
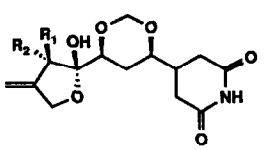
Abstract: The synthesis of sesbanimide analogues **3a** and **3b** is described. In these analogues the glutarimide and the hemiketal ring are separated by an acyclic carbohydrate moiety containing three carbon atoms with the same absolute configuration at the stereogenic centers, as in natural (+)-sesbanimide A.

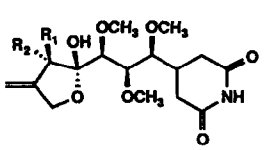
Sesbanimide A (**1a**) and sesbanimide B (**1b**), amongst other compounds, have been isolated from the seeds of *Sesbania drummondii*[1] and *Sesbania punicea*[2]. Sesbanimide A was found to be the most active component of the Sesbania alkaloids as evaluated in screening in experimental leukemias. Its novel structure consists of three rings linked by two single bonds. The high activity of **1** presumably originates from a combination of the structural features of all three rings[3]. In order to evaluate the role of ring B, we have synthesized two 8-deoxysesbanimides **2a,b**[4]. In this article we report the synthesis of the new sesbanimide analogues **3a** and **3b**, in which both the glutarimide ring and the cyclic hemiketal function of sesbanimide A are left intact, but they are separated by an acyclic carbohydrate moiety bearing three carbon atoms with identical absolute configurations as in sesbanimide A. This is of particular relevance to the question whether the notable activity of sesbanimide A is critically dependent upon the cyclic configuration of ring B.



1a R_1=Me, R_2=H
1b R_1=H, R_2=Me

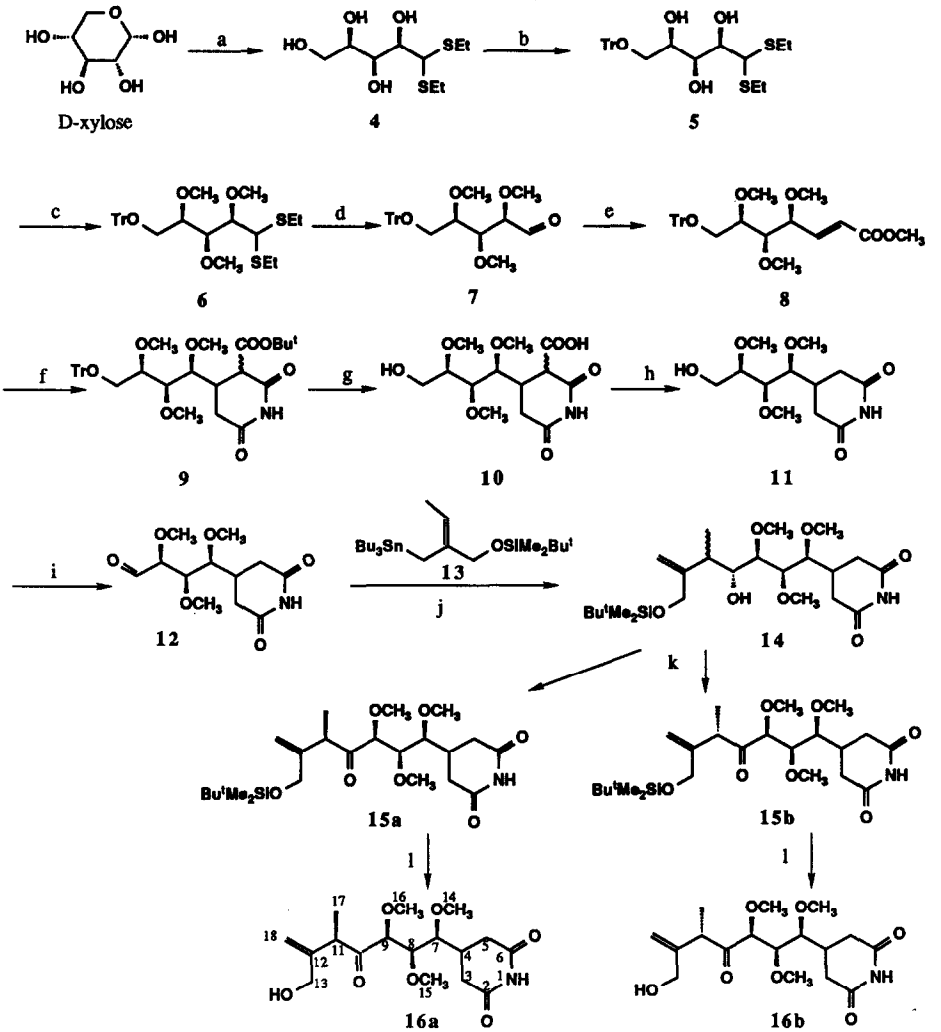


2a R_1=Me, R_2=H
2b R_1=H, R_2=Me



3a R_1=Me, R_2=H
3b R_1=H, R_2=Me

The synthetic approach to **3** was conceptually the same as that employed in the case of sesbanimide A[5,6]. In the sequence followed, D-xylose was converted into its diethyldithioacetal **4**[7]. The primary hydroxyl group in **4** was tritylated to afford derivative **5**. Methylation of the secondary hydroxyl groups of **5** gave the fully protected sugar **6**. Subsequently, the thioacetal function was cleaved with $HgCl_2$ by the procedure of Corey and Erickson[8] to yield aldehyde **7**. The latter compound was immediately treated with ylid



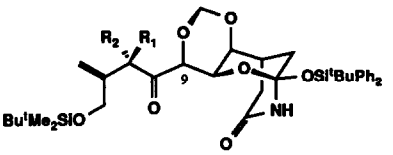
Reagents: (a) EtSH, conc. HCl; (b) TrCl, TEA, DMAP, CH_2Cl_2; (c) NaH, MeI; (d) $HgCl_2$, HgO, MeCN, H_2O; (e) $Ph_3PCHCOOMe$, Toluene; (f) $CH_2(CONH_2)COOBu^t$, $KOBu^t$, THF; (g) CF_3COOH; (h) ΔT, DMF; (i) $(COCl)_2$, DMSO, CH_2Cl_2; (j) **13**, $BF_3{\cdot}Et_2O$, CH_2Cl_2, (k) Dess-Martin periodinane, CH_2Cl_2; (l) HOAc, H_2O, THF.

$Ph_3P{=}CHCOOCH_3$ to give a 9:1 mixture of E- and Z-isomers of **8**. In the following step, the glutarimide ring was constructed in a one-pot reaction by a Michael addition of the enolate of $CH_2(CONH_2)COOBu^t$ to α,ß-unsaturated ester **8**, followed by cyclization. This reaction, leading to a diastereomeric mixture of **9**, was much slower than the comparable one in the synthesis of sesbanimide A. We believe this to be due to the flexible nature of the carbohydrate chain of **8**, which can rotate freely and thereby sterically hinder the Michael addition.

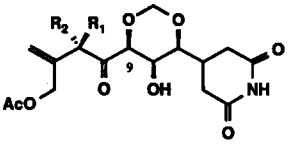
The mixture of glutarimides **9** was dissolved in pure trifluoroacetic acid whereby both the trityl- and *tert*-butyl groups were removed by acid-catalyzed fragmentation. Heating the resulting carboxylic acid mixture **10** in DMF led to decarboxylation, which furnished a single glutarimide alcohol **11**. After removal of the bulk of DMF, alcohol **11** was, without further purification, oxidized to aldehyde **12** by the Swern procedure[9].

In order to construct the hemiketal ring of the sesbanimide analogue, aldehyde **12** was subjected to a BF_3-catalyzed addition of crotylstannane **13**[10], whereupon alcohol **14** was formed as an inseparable mixture of C-11-epimers. Oxidation of this mixture with the Dess-Martin periodinane[11] gave the corresponding ketones **15a** and **15b** in a 3:1 ratio. These ketones were separated and their independent treatment with a 3:1:1 mixture of HOAc:THF:H_2O at room temperature, resulted in the formation of **16a** and **16b**, as colourless glasses, which are in fact the open hydroxy-ketone forms of the sesbanimide analogues **3a** and **3b**.

The ^1H NMR spectra of **15a** and **15b** were compared with the sets of spectra of **17a** and **17b**[12] and of **18a** and **18b**. The absolute configuration of C_{11} in the latter epimers is known, since they are derived from sesbanimide A and sesbanimide B respectively by Powell *et al*[1b].



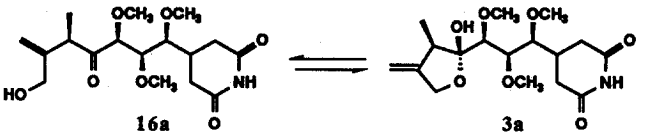
17a R_1=Me, R_2=H
17b R_1=H, R_2=Me

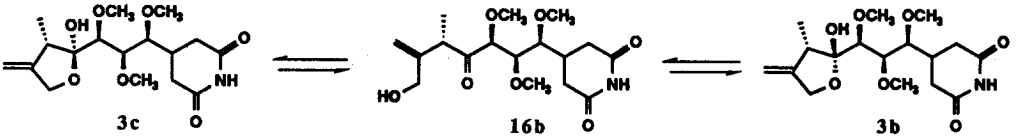


18a R_1=Me, R_2=H
18b R_1=H, R_2=Me

The C_9 protons in **17a** and **18a** appear as doublets at δ 4.12 and δ 4.29 respectively, while the same protons in **17b** and **18b** exhibit doublets at δ 4.31 and δ 4.40. Thus in both sets of compounds, the ketone with the R-configuration at C_{11} shows the signal of the C_9 proton at a higher field. Of the two epimeric ketones **15**, one exhibits the C_9 proton as a doublet at δ 3.67, whereas the other gives a doublet at δ 4.06 for the analogues proton. Based upon analogy with the chemical shift displacement in the spectra of **17a,b** and **18a,b**, the ketone with the C_9 proton at δ 3.67 is assigned structure **15a**, while the epimer which shows its C_9 proton at δ 4.06 is assigned the isomeric structure **15b**.

This assignment is supported by a comparison of the sesbanimide analogues derived from **15a** and **15b** with sesbanimide A and B. In $CDCl_3$, sesbanimide A is found in only *one* hemiketal form, whereas sesbanimide B exists as an equilibrium of the *two* possible hemiketal forms. Apparently, the configuration of the methyl group has a notable influence on the stereochemistry of hemiketal formation. In $CDCl_3$, the hydroxy-ketone **16a** was found to be in equilibrium with *one* hemiketal form **3a** . On the other hand, the hydroxy-ketone **16b**, was observed to be in equilibrium with *two* hemiketals, **3b** and **3c**, epimeric at C_{10}.





In conclusion, this article reports the synthesis of the sesbanimide analogues **3a** and **3b** from D-xylose. Biological evaluation of these and other sesbanimide analogues, which is in progress, is expected to contribute to the study of the structure-activity relationship in this class of alkaloids.

Acknowledgement. Financial support from the Dutch Cancer Society (Nederlandse Kankerbestrijding, Koningin Wilhelmina Fonds) is gratefully acknowledged.

Experimental

General information

Thin layer chromatography was performed using silicagel coated plastic sheets (Merck 60 F_{254}) and UV and *p*-anisaldehyde-sulphuric acid reagent[13] for detection. Infrared spectra were recorded on a Perkin Elmer 1310 spectrophotometer. Nuclear magnetic resonance spectra were recorded on Bruker AC 200, Bruker WM 250 and Bruker AMX 300 instruments. The numbering used in the description of the NMR spectra of structures **3** and **9-15** is given in structure **16a**. Mass spectra were obtained on a Varian MAT 711 instrument. Melting points were determined on a Leitz melting point microscope and are uncorrected. Optical rotations were measured on a Perkin Elmer 241 polarimeter.

Thioacetal 5

To a solution of D-xylose diethyldithioacetal[8] (15 g, 58.6 mmol) in CH_2Cl_2 (225 ml) was added Et_3N (30 ml), trityl chloride (18 g, 64.5 mmol) and 100 mg DMAP. After stirring the reaction mixture for 48 h at room temperature, it was poured into cold water and stirred vigorously. The organic layer was washed with satd. NH_4Cl, water and brine, concentrated *in vacuo*, and the residue was chromatographed on silica to give 24.4 g (83%) of **5**. R_f = 0.4 (EtOAc:PE (1:1); detection with H_2SO_4-spray reagent). $[\alpha]_D$ = +27.4° (c 1.17; $CHCl_3$). **IR** ($CHCl_3$) : 3560-3460(broad), 3040, 3000, 2975, 2930, 2875, 1590, 1490, 1445, 1380, 695, 630 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 1.26 and 1.27 (2 x t, 2 x 3H, 2 x $SCH_2\underline{CH_3}$), 2.70 (m, 2 x 2H, $SC\underline{H_2}CH_3$), 3.21-3.37 (AB, J = 9.62 Hz, 2H, $C\underline{H_2}OTr$), 3.54 (d, J = 8.83 Hz, 1H), 3.90 (m, 1H), 4.05 (m, 1H), 4.19 (s, 1H), 7.19-7.33 (m, 9H, aromatic protons), 7.43-7.50 (m, 6H, aromatic protons).

Trimethyl ether 6

A NaH 55% dispersion (2.6 g, 59.6 mmol) in a three neck flask under nitrogen was washed with dry pentane. To this DMF (20 ml) was added and the suspension was cooled in ice. A solution of acetal **5** (9.2 g, 18.4 mmol) in 90 ml DMF was added dropwise and the mixture was allowed to warm up to room temperature. After 20-30 min, the reaction mixture was cooled again and methyl iodide (3.8 ml, 61.0 mmol) was added. The resulting mixture was stirred for 2 hours at 0 °C to room

temperature. The reaction was quenched with MeOH/H_2O. Extraction with Et_2O/H_2O, drying with $MgSO_4$ and concentration *in vacuo* gave 9.9 g (99%) of **6** as a yellow oil, which crystallized upon standing. R_f = 0.56 (EtOAc:PE (1:2); detection with H_2SO_4- or *p*-anisaldehyde-reagent). M.p. 88-90 °C. $[\alpha]_D$ = -7.2° (c 1.98; $CHCl_3$). **IR** ($CHCl_3$): 3050, 3000-2960(broad), 2920, 2820, 1490, 1090, 695, 630 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 1.20-1.29 (m, 2 x 3H, 2 x SCH_2CH_3), 2.56-2.76 (m, 2 x 2H, SCH_2CH_3), 3.15-3.22 (m, 1H, C_1H), 3.3-3.6 (m, 12H, 3 x OCH_3, C_2H, C_3H, C_4H), 3.88-3.92 (m, 2H, C_5H_2), 7.18-7.32 (m, 9H, aromatic protons), 7.45-7.52 (m, 6H, aromatic protons). **MS** (EI): 540 (M^+; 1 %), 244 (23 %), 243 (Ph_3C^+; 100 %), 191 (11 %), 165 (25 %), 135 (56 %).

α,ß-Unsaturated ester 8

To a stirred solution of $HgCl_2$ (7.15 g, 26.3 mmol) in 360 ml MeCN:H_2O (4:1) was added HgO (2.85 g, 13.2 mmol) and a solution of thioacetal **6** (6.6 g, 12.2 mmol) in 180 ml MeCN:H_2O (4:1). This mixture was stirred for 15 min at room temperature, followed by refluxing for 4.5 h. Subsequently, the reaction mixture was cooled, filtered off over hyflo, the hyflo washed with $CHCl_3$:hexane (1:1) and the combined filtrates washed with 5 M NH_4OAc. The organic layer was washed with water and brine, and dried (Na_2SO_4). Concentration *in vacuo* gave 6.0 g residue consisting of **7**. R_f = 0.33 (EtOAc:PE (1:2); detection with *p*-anisaldehyde reagent). **IR** ($CHCl_3$): 3660, 3500, 3020, 3000, 2930, 2860, 2820, 2240, 1720, 1665, 1595, 1490, 1450, 1365 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 3.21-3.43 (m, 11H, 3 x OCH_3 and C_5H_2), 3.48-3.53 (m, 1H, C_4H), 3.70-3.86 (2 x m, 2 x 1H, C_2H and C_3H), 7.21-7.36 (m, 9H, aromatic protons), 7.46-7.50 (m, 6H, aromatic protons), 9.69 (s, 1H, CHO). The crude aldehyde **7** (6.0 g, from 12.2 mmol acetal) was dissolved in toluene (90 ml). To this solution was added Ph_3P=$CHCOOCH_3$ (4.8 g, 14.4 mmol) and this reaction mixture was stirred for 24 h. The mixture was concentrated and the residue chromatographed to yield 4.9 g (83% over 2 steps) of α,ß-unsaturated ester **8** as a mixture of E- and Z-isomers. One column fraction with pure E-isomer was concentrated and identified. $[\alpha]_D$ = +0.30° (c 1.65; $CHCl_3$). **IR** ($CHCl_3$): 3590, 3055, 3000, 2930, 2895, 2820, 1720, 1650, 1590, 1490, 1440 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 3.10 (s, 3H, $COOCH_3$), 3.10-3.45 (m, 4H, C_5H, C_6H and C_7H_2), 3.35 (s, 3H, OCH_3), 3.46 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.76-3.81 (m, 1H, C_4H), 5.97 (dd, J = 15.8 and 1.24 Hz, 1H, C_2H), 6.83 (dd, J = 15.8 and 6.45 Hz, 1H, C_3H), 7.19-7.35 (m, 9H, aromatic protons), 7.42-7.49 (m, 6H, aromatic protons). **MS** (FD): 243 (Ph_3C^+), 490(M^+).

Glutarimide alcohol 11

To a stirred suspension of amide $CH_2(CONH_2)COOBu^t$ (615 mg, 3.86 mmol) in 5 ml THF at -10 °C was added $KOBu^t$ (355 mg, 3.16 mmol). After 20 min, a solution of ester **8** (1.6 g, 3.26 mmol) in 8 ml THF was added dropwise. This mixture was stirred for 15 min, allowed to warm up to room temperature and concentrated to a syrup by a continuous stream of dry nitrogen. After 4 h, an additional amount of $KOBu^t$ (20 mg) was added, followed, after one day stirring, by a second portion of $KOBu^t$ (10 mg). After a total reaction time of 3 days the reaction was quenched with 400 µl HOAc. This mixture was concentrated *in vacuo* and dichloromethane (20 ml) was added to the residue to dissolve the organic material. The insoluble KOAc was removed by filtration. Concentration of the filtrate resulted in 2.1 g of a residue, which after chromatography gave 0.26 g of a mixture of starting material and product and 1.53 g (76%) of product **9** (as a 3:1 mixture of isomers). R_f = 0.39 and 0.24 (EtOAc:PE (1:2); characteristic blue colour with *p*-anisaldehyde reagent). One of the isomers (R_f = 0.39) was obtained as a crystalline compound. M.p. 78-80 °C. **IR** (CHC'_3): 3370, 3080, 3050, 3020, 3000, 2980, 2930, 2900, 2825, 1730-1690 (broad), 1590, 1488, 1445, 1365, 1245, 1145, 1090, 895, 840, 695, 645, 630 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 1.50 (s, 9H, Bu^t), 2.4-2.75 (m, 3H, glutarimide protons), 2.97 (t, J = 5.9 Hz, 1H, glutarimide proton), 3.28-3.60 (m, 5H, C_7H, C_8H, C_9H, $C_{10}H_2$), 3.28, 3.38 and 3.47 (3 x s, 3 x 3H, 3 x OCH_3), 7.21-7.36 (m, 9H, aromatic protons), 7.43-7.48 (m, 6H, aromatic protons), 7.82 (s, 1H, NH). To glutarimide **9** (1.53 g) was added CF_3COOH (10 ml) and the resulting yellow mixture was stirred for 1.5 h at room temperature. Concentration, followed by coevaporation with MeOH, gave a mixture, which was triturated with pentane to remove the trityl alcohol. The residue obtained after removal of the trityl

alcohol was coevaporated several times with MeOH/H_2O until the peak at 1785 cm^{-1} in the IR-spectrum had disappeared. **IR** ($CHCl_3$): 3370, 2985, 2935, 2825, 1705(broad), 1170, 1090, 1035 cm^{-1}. The thus obtained carboxylic acid **10** (0.73 g) was dissolved in 5 ml DMF and heated for 6 min. at reflux temperature to cause decarboxylation. Concentration *in vacuo* gave 770 mg of crude **11**, which still contained DMF. This was subjected to a Swern oxidation without further purification. R_f = 0.29 (EtOAc:MeOH (9:1)). **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 2.45-2.65 (m, 5H, glutarimide protons), 3.30-3.55 (m, 12H, 3 x OCH_3, C_7H, C_8H and C_9H), 3.77 (AB, J = 11.6 Hz, 2H, $C_{10}H_2$), 8.00 (s, 1H, NH). **MS** (EI): 275 (M^+; 0.5 %), 258 (2 %), 245 (6 %), 243 (4 %), 188 (10 %), 169 (19 %), 156 (46 %), 119 (49 %), 87 (100 %).

Glutarimide aldehyde 12

To a solution of oxalyl chloride (220 µl) in 10 ml CH_2Cl_2 at -75°C under nitrogen was added a solution of DMSO (220 µl) in 5 ml CH_2Cl_2. After stirring for 3 min, a solution of **11** (488 mg) in 3 ml CH_2Cl_2 was added. This reaction mixture was stirred for 3 h at -75 °C. Subsequently, Et_3N (880 µl) was added and the mixture was warmed up to 0 °C, water (400 µl) wasadded and the mixture was stirred for 15 min followed by concentration *in vacuo*. Purification by flash chromatography gave 363 mg of aldehyde **12**. (90% over 3 steps). R_f = 0.42 (EtOAc:MeOH (9:1); detection with *p*-anisaldehyde-H_2SO_4-reagent gave a characteristic dark orange-brown colour). **IR** ($CHCl_3$): 3370, 3030, 2995, 2930, 2820, 1725, 1700 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 2.0-2.8 (m, 5H, glutarimide protons), 3.28 (m, 1H, C_7H), 3.37 (s, 3H, C_9OCH_3), 3.51 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 3.65 (m, 1H, C_8H), 3.77 (m, 1H, C_9H), 8.07 (s, 1H, NH), 9.76 (s, 1H, CHO).

Alcohol 14

To a solution of aldehyde **12** (156 mg, 0.57 mmol) in 4 ml CH_2Cl_2 at -75 °C was added freshly destilled $BF_3{\cdot}Et_2O$ (360 µl). A yellow complex was formed immediately. After 10 min, crotylstannane **13**[10] (380 µl) was added. Within 5 min the yellow colour disappeared. After stirring for 1.5 h at -75 °C the reaction was quenched with Et_3N (1.4 ml), satd. $NaHCO_3$ (1.5 ml) was added and the mixture was allowed to warm up to room temperature under vigorous stirring for 25 min. This mixture was diluted with CH_2Cl_2, the organic layer was separated, washed with H_2O and satd. NaCl, dried on Na_2SO_4 and concentrated. Chromatography gave 235 mg (87%) of a mixture of diastereomeric alcohols, represented by structure **14**. R_f = 0.18 (EtOAc:PE (1:1)). **IR** ($CHCl_3$): 3380, 2960, 2930, 2850, 1700 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 250 MHz, 1.6/1 mixture of diastereomers): δ 0.06 (s, 6H, $SiMe_2$), 0.90 (s, 9H, $SiBu^t$), 1.08 (d, 3H, $C_{17}H_3$), 1.15 (d, 3H, $C_{17}H_3$), 2.35 (m, 1H, $C_{11}H$), 2.50-2.65 (m, 5H, glutarimide protons), 3.14 (m, 1H, C_7H), 3.33-3.52 (m, 12H, 3 x OCH_3, C_8H, C_9H), 3.6-3.7 (m, 1H, $C_{10}H$), 4.02-4.25(m, 2H, $C_{13}H_2$) 4.8-5.2 (m, 2H, $C_{18}H_2$), 7.82 and 7.87 (s, 1H, NH).

Ketones 15a and 15b

To a solution of alcohol **14** (230 mg, 0.48 mmol) in 6 ml dichloromethane was added Dess-Martin periodinane (225 mg). After stirring for 75 min, 20 ml Et_2O, 10 ml PE 40/60 and 20 ml of a 4:1 mixture of $Na_2S_2O_3$ (0.4 M) and satd. $NaHCO_3$ was added. After 20 min of vigorous stirring, the layers were separated, the water layer washed with Et_2O and satd. NaCl. The combined organic layers were dried on Na_2SO_4 and concentrated to give 203 mg of a residue, **IR** ($CHCl_3$): 3370, 2960, 2930, 2850, 1705 cm^{-1}, which was chromatographed on silica, to yield two diastereomeric alcohols: 76 mg **15a** (34%), R_f = 0.22 (EtOAc:PE (1:1)). $[\alpha]_D$= -70.5°. **^{1}H-NMR** ($CDCl_3$, 250 MHz): δ 0.06 (s, 6H, $SiMe_2$), 0.90 (s, 9H, $SiBu^t$), 1.19 (d, J = 6.94 Hz, 3H, $C_{17}H_3$), 2.3 (m, 1H, glutarimide proton), 2.2.5-2.7 (m, 4H, glutarimide protons), 3.29 (dd, J = 7.46 and 3.70 Hz, 1H, C_7H), 3.37 and 3.39 (s, 2 x 3H, $OC_{14}H_3$ and $OC_{15}H_3$), 3.47 (s, 3H, $OC_{16}H_3$), 3.55(dd, J = 7.47 and 3.1 Hz, 1H, C_8H), 3.62 (q, J = 6.93 Hz, $C_{11}H$), 3.67 (d, J = 3.1 Hz, C_9H), 4.15 (AB, J = 15.3 and 16.9 Hz, 2H, $C_{13}H_2$), 4.84 (s, 1H, $C_{18a}H$), 5.21 (d, J = 1.26 Hz, 1H, $C_{18b}H$), 7.92 (s, 1H, NH). **MS** (EI): 471 (M^+; 0.5 %), 414 (19 %), 382 (60 %), 272 (10 %), 244 (3 %), 227 (66 %), 200 (79 %), 199 (46 %), 126 (100 %), 73 (94 %).

30 mg **15b** (15%), R_f = 0.28 (EtOAc:PE (1:1)). $[\alpha]_D$= +94.5°. **^{1}H-NMR** ($CDCl_3$, 200 MHz): δ 0.07 (s, 6H, $SiMe_2$), 0.92 (s, 9H, $SiBu^t$), 1.19 (d, J = 6.8 Hz, 3H, $C_{17}H_3$), 2.46-2.70 (m, 5H, glutarimide protons), 3.10 (m, 1H, C_7H), 3.30

and 3.34 (s, 2 x 3H, $OC_{14}H_3$ and $OC_{15}H_3$), 3.39-3.57 (m, 2H, C_8H and $C_{11}H$), 3.50 (s, 3H, $OC_{16}H_3$), 4.06 (d, J = 3.85 Hz, C_9H), 4.13 (s, 2H, $C_{13}H_2$), 4.92 (s, 1H, $C_{18a}H$), 5.26 (s, 1H, $C_{18b}H$), 7.90 (s, 1H, NH). **MS** (EI): 471 (M^+; 0.5 %), 414 (18 %), 382 (52 %), 272 (9 %), 244 (3 %), 227 (67 %), 200 (78 %), 199 (45 %), 126 (89 %), 73 (100 %).

Note: In addition, 35 mg of a mixture of both diastereomers and starting alcohol was obtained.

Sesbanimide analog 3a

A solution of silylether **15a** (75 mg, 0.16mmol) in a 3:1:1 mixture of HOAc:H_2O:THF (1.6 ml) was stirred for 5 h. at room temperature. Toluene was added, and the mixture was coevaporated. This was repeated several times. Removal of the residual solvents *in vacuo* gave 64 mg of a residue. This was chromatographed to yield 45 mg of pure **3a** and 4 mg impure **3a** (86%). $[\alpha]_D$ = -0.66° (c 2.265; $CHCl_3$). **IR** ($CHCl_3$): 3600-3100(broad), 3380, 2950, 2930, 1700, 1250 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 300 MHz, mixture of *one* hemiketal and the open hydroxy-ketone form): δ 1.20 (d, 3H, $C_{17}H_3$ hemiketal), 1.25 (d, 3H, $C_{17}H_3$ open), 2.5-2.8 (m, 5H, glutarimide protons), 3.21-3.74 (m, 13H, 3 x OCH_3, C_7H, C_8H, C_9H hemiketal, $C_{11}H$), 3.82 (d, J = 3.4 Hz, 1H, C_9H open), 4.17 (m, 2H, $C_{13}H_2$ open), 4.43 (AB, J = 12.9 Hz, 2H, $C_{13}H_2$ hemiketal), 4.92-5.0 (m, 2H, $C_{18}H_2$ hemiketal and $C_{18a}H$ open), 5.22 (s, 1H, $C_{18b}H$ open), 8.12 (s, 1H, NH). **^{1}H-NMR** (CD_3OD, 250 MHz, mixture of hemiketal and open form): δ 1.15 (d, J = 6.8 Hz, 3H, $C_{17}H_3$ hemiketal), 1.21 (d, J = 7.0 Hz, 3H, $C_{17}H_3$ open), 2.42-2.88 (m, 5H, glutarimide protons), 3.18-3.76 (m, 12H, 3 x OCH_3, C_7H, C_8H, $C_{11}H$), 3.91 (d, J = 3.14 Hz, 1H, C_9H open), 4.11 (s; 2H, $C_{13}H_2$ open), 4.25 (s, 2H, $C_{13}H_2$ hemiketal), 4.95 (m, 1H, $C_{18b}H$ hemiketal), 5.20 (d, J = 1.04 Hz, 1H, $C_{18b}H$ open). **MS** (FD): 359 (M^+).

Sesbanimide analog 3b

A solution of silylether **15b** (28 mg, 0.06 mmol) in a 3:1:1 mixture of HOAc:H_2O:THF (0.75 ml) was stirred for 3 h at room temperature. Toluene was added, and the mixture was coevaporated. This was repeated several times. Removal of the residual solvents *in vacuo* gave a residue, which was chromatographed to yield 17 mg of pure **3b** and 4 mg impure **3b** (98%). $[\alpha]_D$ = +52.3 (c 0.6; $CHCl_3$). **IR** ($CHCl_3$): 3600-3200(broad), 3370, 2930, 2820, 1725(shoulder), 1700, 1250 cm^{-1}. **^{1}H-NMR** ($CDCl_3$, 300 MHz, mixture of *two* hemiketals and the open hydroxy-ketone form): δ 1.12 (d, J = 6.8 Hz, 3H, $C_{17}H_3$ hemiketal), 1.20 and 1.25 (2 x d, J = 6.8 Hz, 2 x 3H, $C_{17}H_3$ hemiketal and open form), 2.49-2.69 (m, 4H, C_3H_2 and C_5H_2), 2.82 (m, 1H, C_4H), 3.21-3.69 (m, 13H, 3 x OCH_3, C_7H, C_8H, C_9H hemiketal, $C_{11}H$), 4.09-4.13 (m, 1H, C_9H open), 4.17 (m, 2H, $C_{13}H_2$ open), 4.44 (m, 2H, $C_{13}H_2$ ketal), 4.88-5.21 (m, 2H, $C_{18}H_2$ ketal and open), 7.86 and 7.96 (s, 1H, NH). **^{1}H-NMR** (CD_3OD, 250 MHz, mixture of hemiketal and open form): δ 1.24 (d, J = 6.88 Hz, 3H, $C_{17}H_3$ hemiketal), 1.28 (d, J = 6.80 Hz, 3H, $C_{17}H_3$ open), 2.60-2.76 (m, 5H, glutarimide protons), 3.30-3.80 (m, 12H, 3 x OCH_3, C_7H, C_8H, $C_{11}H$), 4.16 (m, 2H, $C_{13}H_2$ open), 4.27 (d, J = 3.44 Hz, 1H, C_9H open), 4.53 (m, 2H, $C_{13}H_2$ hemiketal), 5.31 (m, 1H, $C_{18b}H$ hemiketal). **MS** (FD): 359 (M^+).

References and Notes

1. (a) Powell, R.G., Smith, Jr.,C.R., Weisleder, D., Matsumoto, G.K., Clardy, J. Kozlowski, J. *J. Am. Chem. Soc.*, **1983**, *105*, 3739-41. (b) Powell, R.G., Smith, Jr.,C.R., Weisleder, D. *Phytochemistry*, **1984**, *23*, 2789-96.
2. Gorst-Allman, C.P., Steyn, P.S., Vleggaar, R. *J. Chem. Soc. Perkin Trans 1*, **1984**, 1311-4.
3. A number of AB- and BC-ring systems of sesbanimide 1 have been tested for antitumour activity, but none of these exhibited a cytotoxicity comparable to that of (+)-sesbanimide A. (a) Matsuda, F., Ohsaki, M., Yamada,K., Tereshima, S. *Bull. Chem. Soc. Jpn.*, **1988**, *61*, 2123-31. (b) Unpublished results from this laboratory.
4. To be reported in a forthcoming paper.

5. (a) Wanner, M.J., Koomen, G.-J., Pandit, U.K. *Heterocycles*, **1984**, *22*, 1483. (b) Wanner, M.J., Willard, N.P. Koomen, G.-J., Pandit, U.K. *J. Chem. Soc., Chem. Commun.*, **1986**, 396. (c) Wanner, M.J., Willard, N.P., Koomen, G.-J., Pandit, U.K. *Tetrahedron*, **1987**, *43*, 2549-56.
6. In the coupling reaction with crotylsilanes, silyl enol ethers were formed as major byproducts.The use of crotylstannanes instead of crotylsilanes avoided the formation of enol ethers. This will be described in a forthcoming paper.
7. Rollin, P., Pougny, J.-R. *Tetrahedron*, **1986**, *42*, 3479-90.
8. Corey ,E.J., Erickson, B.W. *J. Org. Chem.*, **1971**, *36*, 3553-60.
9. Mancuso, A.J., Huang, S.-L., Swern, D. *J.Org. Chem.*, **1978**, *43*, 2480-2.
10. Schlessinger, R.H., Wood, J.L. *J. Org. Chem.*, **1986**, *51*, 2621-3.
11. Dess, D.B., Martin, J.C. *J. Org. Chem.*, **1983**, *48*, 4155-6.
12. Wood, J.L., Thesis, University of Rochester, **1986**. The structure assignement of **17** by Wood was not correct. See: Vloon, W.J., Bos, J.C. van den, Willard, N.P., Koomen, G.-J., Pandit, U.K. *Recl. Trav. Chim. Pays-Bas*, **1989**, *108*, 393-4.
13. Lisboa, B.P. *J. Chromatog.*, **1964**, *16*, 136-51.