

## Photochemistry of Hecogenine Acetate Revisited

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*Dedicated to Professor Dr. Dr. h. c. mult. Karl-Heinz Büchel on the Occasion of his 65th Birthday*

**Abstract.** We were successful in optimizing the synthesis of the homoallylic alcohol **6** from hecogenine acetate **2** as an important precursor for our approach to cephalostatin analogues by doubling the yields. On this way we discovered that formation of homoallylic alcohol **6** proceeds *via* a diaste-

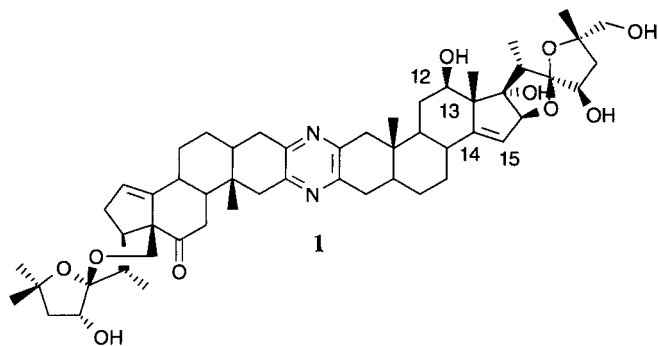
reoselective intramolecular Lewis acid catalysed ene reaction directly from lumihecogenine acetate **3**. Finally we were able to elucidate the structure of the already described but not clearly identified oxa-dimer **7**.

Cephalostatin **1** is the prototype of the cephalostatins and the ritterazines, a family of 30 trisdecacyclic pyrazines, isolated by Pettit and his co-workers since 1988 from the Indian Ocean marine worm *Cephalodiscus gilchristi* [1] and by the group of Fusetani from the tunicate *Riterella tokioka* [2]. This series of compounds are among the most potent cytostatics ever screened by the National Cancer Institute and therefore have potential applications as antitumor agents [3a)]. But the extremely poor availability of these marine natural products has even limited *in-vivo* tests [3a)].

Described cytostatic activity and limited availability [1a) in combination with the new and interesting structure of the cephalostatins immediately led to synthetic activities in various laboratories with different goals [3, 4, 5a)].

We embarked on a program to synthesize easily accessible and biologically active cephalostatin analogues to determine the essential substructures for cytostatic activity [5].

Within this program one essential was to establish the  $\Delta^{14,15}$ -double bond, a typical structural feature of most cephalostatins, which is an unusual structural element of natural steroids [6].

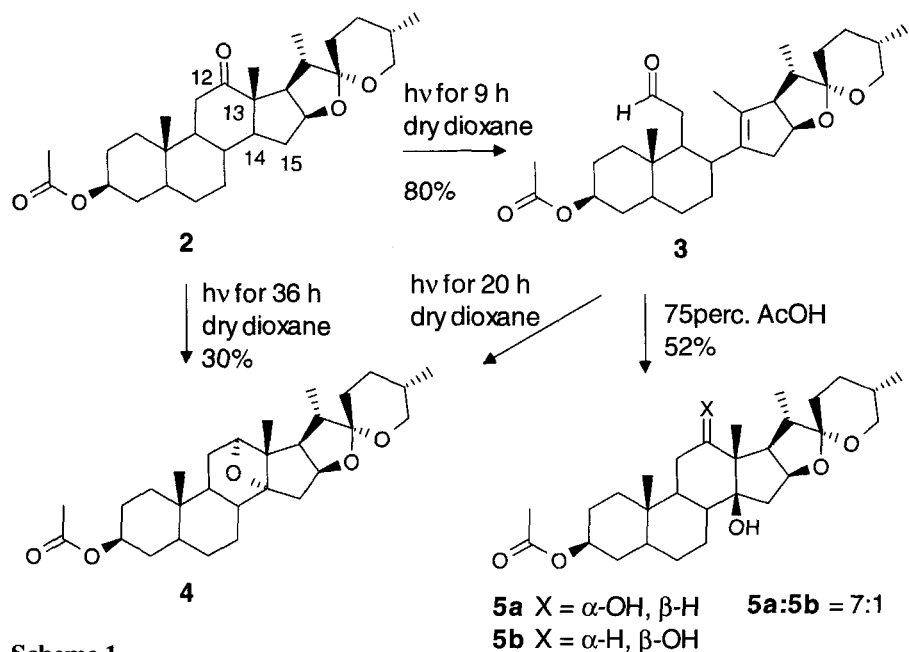


### Starting point

Looking for simple and efficient ways to introduce the  $\Delta^{14,15}$ -double bond led us to the photochemistry of hecogenine acetate **2**, which was established by Bladon and co-workers [7] and further investigated by other groups [8, 9].

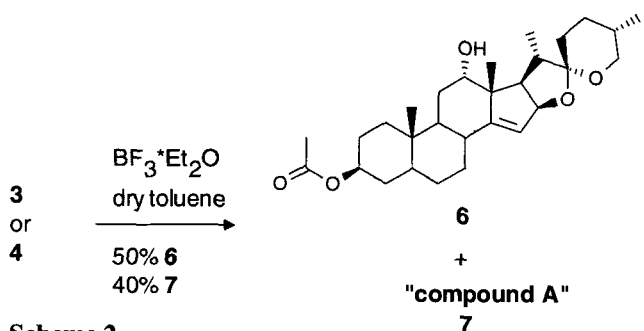
It was known that irradiation of hecogenine acetate **2** with light from a high-pressure mercury lamp in

dry, degassed dioxane generates the  $\delta,\epsilon$ -unsaturated aldehyde lumihecogenine acetate **3** via a Norrish-Type-1-cleavage of the 12,13-C-C-bond and a subsequent hydrogen shift. Lumihecogenine acetate **3** can be transformed in an intramolecular Paternò-Büchi reaction to the oxetane photohecogenine acetate **4** [7] or may be transformed in a Prins reaction into the 14-hydroxy compounds **5** [8] (see scheme 1).



Scheme 1

Treatment of pure lumihecogenine acetate **3** or of pure photohecogenine acetate **4** with catalytic amounts of boron trifluoride ether complex in absolute toluene at room temperature provided in all cases a 1:1 mixture of the  $\Delta^{14,15}$ -12 $\alpha$ -hydroxy derivative, called homoallylic



Scheme 2

alcohol **6**, and a less polar product, called „compound A“ **7**. The structure of „compound A“ **7** was not properly elucidated (see scheme 2) [7, 8].

There was a general belief [7], that in the presence of the Lewis acid boron trifluoride ether complex a fast

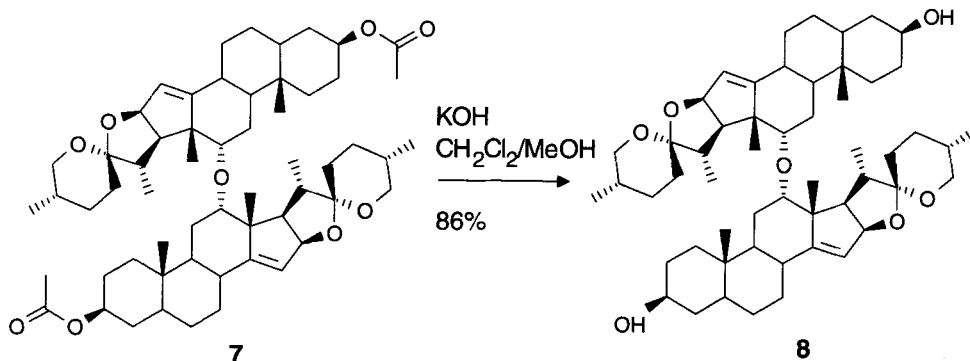
equilibration takes place between lumihecogenine acetate **3** and photohecogenine acetate **4** and, therefore, lumihecogenine acetate **3** was assumed to afford „compound A“ **7** while photohecogenine acetate **4** was believed to undergo an acid catalysed ring opening to the homoallylic alcohol **6**. This assumption was obviously supported by the stereocontrol in position 12.

## Results and Discussion

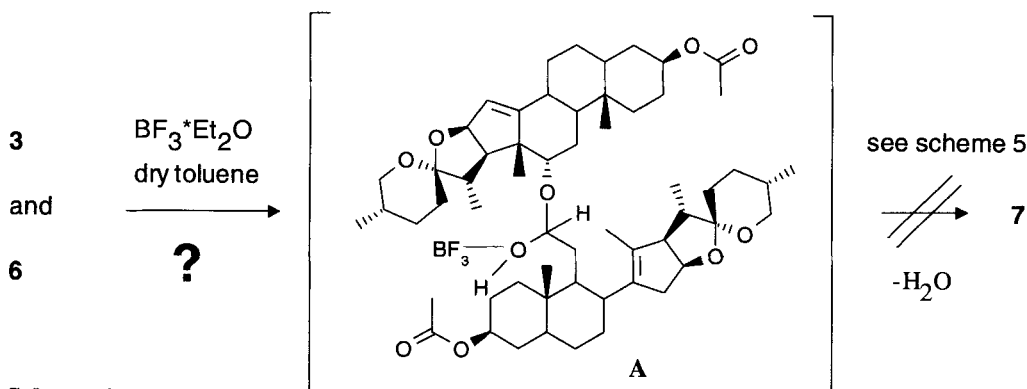
Since introduction of the  $\Delta^{14,15}$ -double bond *via* this process was the initial step in our synthesis of cephalostatin analogues [5] we had to improve the efficiency of the whole process.

First of all structure elucidation of „compound A“ **7** led us to a  $C_2$ -symmetric substance that we named oxa-dimer **7** (see scheme 3). This oxa-dimer **7** is a formal condensation product of two homoallylic alcohols **6**. The fact that the oxa-dimer **7** „kept“ the  $\alpha$ -configuration in both 12-positions was a significant hint that its formation does not proceed via a simple Lewis acid catalysed condensation of two molecules of homoallylic alcohol **6** and, as expected, homoallylic alcohol **6** proved to be stable under these reaction conditions.

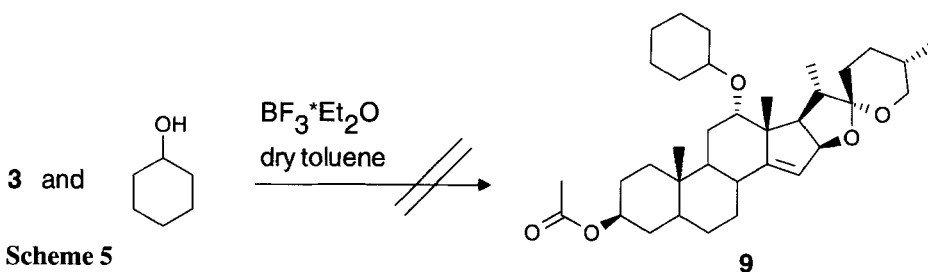
A possible mechanism for the formation of oxa-dimer **7** was a Lewis acid catalysed intramolecular dehydration of semiacetal **A** formed from one molecule of lumihecogenine acetate **3** and one of homoallylic alcohol **6** as depicted in scheme 4. The rationalisation of the stereoselectivity of this process is depicted in Fig. 1. But mixing 1 eq. of lumihecogenine acetate **3** and one of homoallylic alcohol **6** under standard reaction



Scheme 3



Scheme 4



Scheme 5

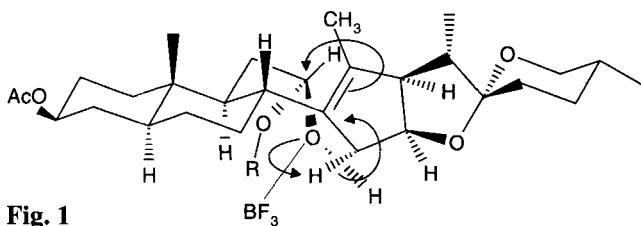


Fig. 1

conditions failed to increase the yield of oxa-dimer **7**, but slowed down the reaction of lumihecogenine acetate **3** and gave numerous by-products. Mixing 1 eq. of lumihecogenine acetate **3** and one of cyclohexanol as a mimic of homoallylic alcohol **6** did not provide product **9** under standard reaction conditions (see scheme 5) [10].

No further assumptions were made for the formation of the oxa-dimer **7** and since our ultimate goal was to

avoid the formation of oxa-dimer **7** altogether we terminated for the moment investigations at this point. The structure of the oxa-dimer **7** was proven particularly by MS ( $MH^+ = 928$ ), NMR-measurement and chemical investigations. As expected, the attempt to acetylate the oxa-dimer **7** failed and saponification afforded the oxa-endiol **8** ( $MH^+ = 844$ ) (see scheme 3). Although crystallisation of **7** and **8** was tried with various solvents and under a manifold of conditions we were unable to get satisfactory X-ray data from the obtained crystalline material.

Referring to results from Bladon and co-workers that lumihecogenine acetate **3** and photohecogenine acetate **4** had afforded similar results on treatment with boron trifluoride ether complex [7] we used in our initial experiments a mixture of both, called photomixture, which was the crude product of long irradiation of hecogenine acetate **2** and therefore rich in photohecogenine

acetate **4**. To avoid the formation of oxa-dimer **7** we ran the boron trifluoride reaction with the photomixture at higher dilution and indeed suppressed its formation significantly. Homoallylic alcohol **6** was formed in 56% yield from hecogenine acetate **2** compared to the reported yields around 43% [7].

Since formation of the homoallylic alcohol **6** is triggered by a Lewis acid we investigated various acid catalysts. The assumed precursor photohecogenine acetate **4**, which was prepared in an improved procedure in 71% yield from hecogenine acetate **2**, was treated under various conditions with boron trifluoride ether complex and three acid-exchange resins in dry dioxane and dry toluene. Except for the original conditions using boron trifluoride ether complex in dry toluene, all these experiments yielded no homoallylic alcohol **6** whatsoever. Either no reaction took place when proceeding in dry toluene, or a quantitative yield of lumihecogenine acetate **3** was obtained when we ran the process in dry dioxane or dry toluene/dioxane 3:1 (see table 1). The conversion of photohecogenine acetate **4** to lumihecogenine acetate **3** was first reported by Bladon and co-workers, who isolated traces of lumihecogenine acetate **3** after the boron trifluoride reaction of photohecogenine acetate **4** [7]. Under different circumstances Welzel *et al.* observed formation of lumihecogenine acetate **3** by treating photohecogenine acetate **4** with 75 perc. acetic acid [8]. With these results in mind we

**Table 1** Reaction of **4** with different acids in different solvents

Educt	Acid <sup>a)</sup>	Solvent <sup>b)</sup>	Product
<b>4</b>	Lewatit CNP80	toluene	no reaction
<b>4</b>	Amberlite IR-120	toluene	no reaction
<b>4</b>	Nafion NR 50	toluene	no reaction
<b>4</b>	Nafion NR 50	toluene/ dioxane 3:1	<b>3</b>
<b>4</b>	Nafion NR 50	dioxane	<b>3</b>
<b>4</b>	BF <sub>3</sub> •Et <sub>2</sub> O	dioxane	<b>3</b>
<b>4</b>	BF <sub>3</sub> •Et <sub>2</sub> O	toluene	fast formation of <b>3</b> , then <b>6</b> and <b>7</b>

<sup>a)</sup> Lewatit CNP80 is a weak acid-exchange resin, Amberlite IR-120 and Nafion NR 50 are strong ones <sup>b)</sup> all solvents were dry

readdressed the original reaction conditions and discovered that photohecogenine acetate **4** gives in the presence of catalytic amounts of boron trifluoride ether complex in dry toluene in a very fast reaction quantitatively lumihecogenine acetate **3** which then continues to the homoallylic alcohol **6** and the oxa-dimer **7**.

This result strongly questioned the mechanism for formation of homoallylic alcohol **6** postulated by Bladon *et al.* [7] which contains as the crucial step a fast

Lewis acid catalyzed equilibrium between lumihecogenine acetate **3** and photohecogenine acetate **4**. Knowing that the (Lewis) acid catalysed ring opening reaction from photohecogenine acetate **4** to lumihecogenine acetate **3** proceeds very fast we had to make sure of the reverse step – the Lewis acid catalysed intramolecular 2 $\pi$ –2 $\pi$ -cycloaddition of lumihecogenine acetate **3**. A literature search revealed that Lewis acid catalysed 2 $\pi$ –2 $\pi$ -cycloadditions forming oxetanes from alkenes and aldehydes are well established [11] but known to proceed only with electron-rich alkenes, e.g. ketene acetals, and with long reaction times [12] – especially when using boron trifluoride ether complex as the Lewis acid catalyst [12b)]. Therefore one can safely state that the boron trifluoride catalysed formation of lumihecogenine acetate **3** from photohecogenine acetate **4** is irreversible under the reaction conditions generating homoallylic alcohol **6**.

These facts left no doubt that rather than photohecogenine acetate **4** lumihecogenine acetate **3** is the precursor of the homoallylic alcohol **6** and this led to a new experimental approach for the large scale synthesis of homoallylic alcohol **6**. Drastic reduction of the irradiation time from 36 h to 3 h afforded a photomixture, which mainly contained lumihecogenine acetate **3**. This lumihecogenine acetate **3**-rich photomixture was dissolved in dry toluene and added slowly to a 0 °C cold solution of an excess of boron trifluoride ether complex in dry toluene. The basic ideas were that lowering the temperature from room temperature to 0 °C favours the intramolecular formation of homoallylic alcohol **6** over the intermolecular dimerization process and use of excess boron trifluoride ether complex enhances the formation of homoallylic alcohol **6** and therefore lowers the concentration of the available lumihecogenine acetate **3** for dimerization. This reaction cascade, which avoided long irradiation times in the first and high stationary lumihecogenine acetate **3** concentrations in the second step, afforded the homoallylic alcohol **6** in 80% yield from hecogenine acetate **2** after crystallisation compared to the reported yields of 43% [7].

Since there was no doubt, that lumihecogenine acetate **3** is the precursor of homoallylic alcohol **6**, a new explanation for formation of this material was necessary. Acid catalysed cyclisation reactions of  $\delta,\epsilon$ -unsaturated aldehydes, like lumihecogenine acetate **3**, to cyclohexane-1,3-diols [13] or cyclohexenols [14] are well known and reactions carried out in polar solvents with proton acid catalysts are postulated to follow a cationic, stepwise Prins-reaction mechanism, often going along with low diastereoselectivity. This postulation is in line with the results reported by Welzel *et al.* [8], that Prins-reaction of lumihecogenine acetate **3** in aqueous medium with protic acid catalysis afforded a mixture of the cyclohexane-1,3-diols **5** (see scheme 1).

However Lewis acid-catalysed cyclisation reactions of *d,e*-unsaturated aldehydes in unpolar, aprotic solvents follow a type I [15] or type II [16] intramolecular oxygen analogue ene reaction [17], depending on the structure of the substrate, and proceed with high regio- and diastereoselectivity. Reaction conditions, substrate structure and selectivity of the process call for a type II ene reaction of lumihecogenine acetate **3** as depicted in Fig. 2.

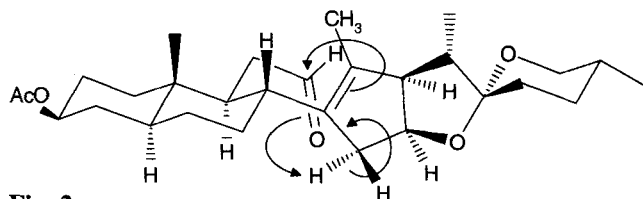


Fig. 2

The exclusive  $\alpha$ -attack of the aldehyde group is controlled by the steric demand of the  $\beta$ -orientated spiroether [8], which governs the diastereoselectivity of the ene reaction *via* concave–convex folding [18] and determines the  $\alpha$ -configuration of the 12-hydroxy group in our final product.

An X-ray analysis gave final proof of the  $\alpha$ -orientated hydroxy group in 12-position of the homoallylic alcohol **6** (see Fig. 3).

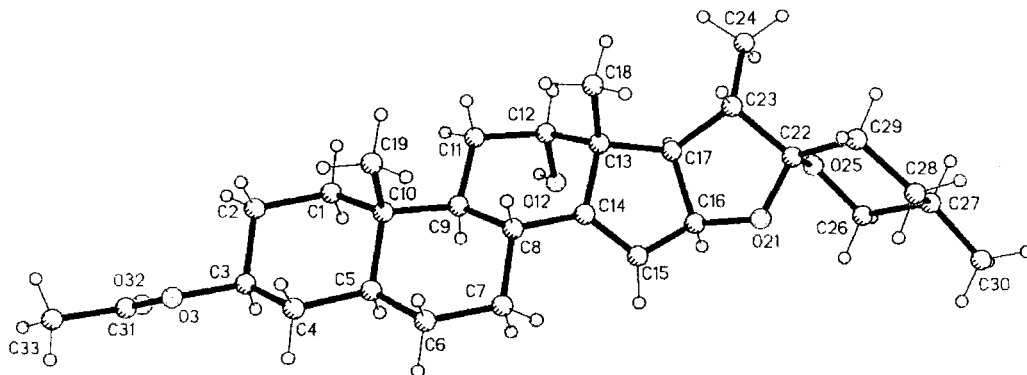


Fig. 3 Crystal structure of homoallylic alcohol **6** showing the  $\alpha$ -orientated hydroxy group in position 12

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## Experimental

Melting points were recorded on a Büchi melting point microscope. IR spectra were measured on a Perkin–Elmer 581 spectrometer.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra were recorded on a Bruker WP 200 (200 MHz) and AM 400 (400 MHz) and  $\delta$  values are given relative to tetramethylsilane. Mass spectra

were determined with a Finnigan MAT 312 instrument at 70 eV and FAB spectra with a VG Autospec in an *m*-NBA matrix. Elemental analysis were obtained using a Heraeus CHN rapid analyser.

## Lumihecogenine acetate **3** from photohecogenine acetate **4**

**A.** 100 mg (0.212 mmol) of photohecogenine acetate **4** were dissolved in 14 ml of dry toluene and 4 ml dry dioxane under an argon atmosphere and 700 mg of acid exchange resin Nafion NR 50 were added. After 24 hours the resin was removed by filtration and the solvent was slowly evaporated to afford 98 mg (98%) of lumihecogenine acetate **3** as a colorless crystalline solid.

**B.** 100 mg (0.212 mmol) of photohecogenine acetate **4** were dissolved in 14 ml of dry dioxane and treated as described under **A** to yield 97 mg (97%) of lumihecogenine acetate **3** as a colorless crystalline solid.

**C.** 50 mg (0.106 mmol) of photohecogenine acetate **4** were dissolved in 7 ml of dry dioxane under an argon atmosphere and 7  $\mu\text{l}$  (0.053 mmol) of boron trifluoride ether complex were added. After 20 hours the reaction was quenched by adding saturated sodium bicarbonate solution. The aqueous layer was extracted with ether and the combined organic layer was dried over sodium sulfate, and then slow removal of the solvent yielded 47 mg (94%) of lumihecogenine acetate **3** as a colorless crystalline solid (*m.p.* 142 °C from ether/petrolether) – IR (KBr): 2929 vs (C–H), 2860 s (C–H),

2720 vw (–CHO), 1734 vs (C=O), 1645 vw (C=C), 1244 vs (C–O), 1062 s (C–O). –  $^1\text{H}$  NMR (200 MHz/ $\text{CDCl}_3$ ):  $\delta$  9.48 (s br, 1 H), 4.68 (m, 1 H), 4.47 (m, 1 H), 3.43 (m, 2 H), 2.67 (m br, 1 H), 2.50–2.05 (m, 4 H), 2.02 (s, 3 H), 1.06 (d, 3 H,  $J = 7$  Hz), 0.85 (s, 3 H), 0.80 (d, 3 H,  $J = 6$  Hz). –  $^{13}\text{C}$  NMR (50 MHz/ $\text{CDCl}_3$ ):  $\delta$  12.07, 12.74, 14.18, 17.14, 21.34, 27.17, 28.16, 30.31, 30.87, 31.10, 33.86, 36.36, 37.31, 43.21, 43.74, 46.24, 48.60, 61.28, 65.80, 66.79, 73.08, 77.56, 106.10, 134.98, 135.50, 170.41, 201.04. – MS (70 eV, 130 °C): 472 ( $\text{M}^+/\text{12}$ ), 358 (40), 183 (25), 139 (93), 126 (100). – Anal. calcd. for  $\text{C}_{29}\text{H}_{44}\text{O}_5$  (472.66), C 73.69, H 9.38, found C 73.39, H 9.34

*Photohecogenine acetate 4*

12.00 g (25.4 mmol) of hecogenine acetate **2** dissolved in 230 ml of dry, degassed dioxane were irradiated under an argon atmosphere for 24 hours at room temperature with of a high-pressure mercury lamp (125 W) in a photoreactor. The 125 W high-pressure mercury lamp was placed into a double-walled quartz cooling finger inside the reaction flask. The dioxane solvent was evaporated and the crude product was recrystallized from petrolether/ether to afford 8.524 g (71%) of photohecogenine acetate **4** as a colorless crystalline solid (*m.p.* 205 °C). – IR (KBr): 2930 vs (C–H), 2859 (C–H), 1728 vs (C=O), 1243 vs (C–O), 1070 s (C–O). – <sup>1</sup>H NMR (200 MHz/CDCl<sub>3</sub>): δ 4.99 (q, 1 H, *J* = 8 Hz), 4.69 (m, 1 H), 4.39 (dd, 1 H, *J* = 5.7 Hz), 3.47 (m, 2 H), 2.75 (dd, 1 H, *J* = 8, 12 Hz), 2.20 – 1.90 (m, 6 H), 1.32 (s, 3 H), 1.03 (d, 3 H, *J* = 7 Hz), 0.93 (s, 3 H), 0.80 (d, 3 H, *J* = 6 Hz). – <sup>13</sup>C NMR (50 MHz/CDCl<sub>3</sub>): δ 11.20, 13.39, 17.14, 20.57, 21.33, 27.04, 28.56, 28.82, 29.07, 30.32, 32.63, 33.18, 35.05, 35.57, 37.50, 38.10, 38.76, 43.67, 44.23, 56.19, 58.20, 59.84, 67.11, 73.44, 80.86, 85.03, 91.02, 107.73, 170.33 – MS (70 eV, 130 °C): 472 (M<sup>+</sup>), 358 (41), 183 (100), 126 (57), 126 (57), 107 (31) – Anal. calcd. for C<sub>29</sub>H<sub>44</sub>O<sub>5</sub> (472.66), C 73.69, H 9.38, found C 73.73, H 9.20

**Homoallylic alcohol 6 from hecogenine acetate 2**

25.120 g (53.14 mmol) of hecogenine acetate **2** dissolved in 520 ml dry, degassed dioxane were irradiated under an argon atmosphere for 175 minutes at room temperature with a high-pressure mercury lamp (125 W) in a photochemical reaction apparatus (description of this apparatus: see above). The dioxane solvent was evaporated and the crude product was dried for three days in high vacuum at 45 °C to afford 25.889 g (103%) of a mixture of mainly lumihecogenine acetate **3**, some photohecogenine acetate **4** and little of unchanged starting material hecogenine acetate **2**, called the „photomixture“, as a white, crystalline solid.

1.000 g of the crude photomixture were dissolved in 6 ml of 0 °C cold, dry toluene and added within 25 min to a 0 °C cold solution of 0.31 ml (2.54 mmol) of boron trifluoride ether complex in 15 ml of dry toluene. After 40 min the reaction was quenched by adding 10 ml (5.0 mmol) of a 0.5 M sodium bicarbonate solution. The mixture was diluted with ethyl acetate, the organic layer was separated and washed with saturated sodium chloride solution. The organic solution was dried, evaporated and recrystallized from ether/petrolether to afford 773 mg (80% from hecogenine acetate **2**) of homoallylic alcohol **6** as a colorless crystalline solid (*m.p.* 224 °C). – IR (KBr): 3499 vs br (O–H), 3060 vw (O–H), 2947 vs (C–H), 2873 s (C–H), 1733 vs (C=O), 1650 vw (C=C), 1244 vs (C–O), 1063 s (C–O). – <sup>1</sup>H NMR (200 MHz/CDCl<sub>3</sub>): δ 5.54 (s br, 1 H), 4.87 (dd, 1 H, *J* = 1.6, 8 Hz), 4.67 (m, 1 H), 3.69 (m, 1 H), 3.46 (m, 2 H), 2.66 (dd, 1 H, *J* = 8, 10 Hz), 2.15 (m, 1 H), 2.02 (s, 3 H), 1.11 (s, 3 H), 1.01 (d, 3 H, *J* = 7 Hz), 0.89 (s, 3 H), 0.80 (d, 3 H, *J* = 6 Hz). – <sup>13</sup>C NMR (50 MHz/CDCl<sub>3</sub>): δ 11.98, 14.19, 17.15, 18.59, 21.39, 27.29, 28.17, 28.62,

28.70, 29.47, 30.39, 31.07, 33.85, 34.39, 35.78, 36.37, 44.51, 44.71, 49.76, 52.31, 53.61, 67.05, 73.34, 76.16, 84.99, 106.40, 121.10, 153.85, 170.57. – MS (70 eV, 130 °C): 472 (M<sup>+</sup>), 454 (41), 358 (100), 147 (33), 126 (81), 107 (38). – Anal. calcd. for C<sub>29</sub>H<sub>44</sub>O<sub>5</sub> (472.66), C 73.69, H 9.38, found C 73.47, H 9.32

*Oxa-dimer 7*

Oxa-dimer **7** was prepared according to ref. [7] by reaction of lumihecogenine acetate **3** or photohecogenine acetate **4** with boron trifluoride ether complex in dry toluene (instead of dry benzene) (*m.p.* 290 °C from ether/petrolether). – IR (KBr): 2932 vs (C–H), 2861 s (C–H), 1735 vs (C=O), 1652 w (C=C), 1242 vs (C–O), 1065 s (C–O). – <sup>1</sup>H NMR (200 MHz/CDCl<sub>3</sub>): δ 5.31 (s br, 2 H), 4.70 (m, 4 H), 3.55–3.35 (m, 4 H), 3.26 (s br, 2 H), 2.47 (dd, 2 H, *J* = 8, 10 Hz), 2.02 (s, 6 H), 1.04 (s, 6 H), 0.97 (d, 6 H, *J* = 7 Hz), 0.88 (s, 6 H), 0.82 (d, 6 H, *J* = 6 Hz). – <sup>13</sup>C NMR (50 MHz/CDCl<sub>3</sub>): δ 11.78, 14.04, 17.33, 18.50, 21.46, 22.92, 27.34, 28.40, 28.76, 29.93, 30.44, 31.20, 33.86, 34.01, 35.81, 35.92, 44.05, 44.64, 49.93, 50.95, 53.88, 66.95, 73.39, 80.42, 85.62, 106.11, 120.86, 152.61, 170.48. – FAB [exact mass <sup>12</sup>C<sub>58</sub><sup>1</sup>H<sub>86</sub><sup>16</sup>O<sub>9</sub> = 926.627]: 928 (MH<sup>+</sup>/100), 455 (65). – Anal. calcd. for C<sub>58</sub>H<sub>86</sub>O<sub>9</sub> (927.31), C 75.12, H 9.35, found C 75.13, H 9.39

*Oxa-enediol 8*

200 mg (0.216 mmol) of oxa-dimer **7** and 70 mg (1.0 mmol) of potassium hydroxide were dissolved in 3 ml of methanol/dichloromethane 1:1 and stirred for 2 hours at room temperature. The reaction was quenched with water and the aqueous layer was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, concentrated, and the crude product was recrystallized from ether to afford 174 mg (87%) of oxa-enediol **8** as a colorless crystalline solid (*m.p.* >300 °C). – IR (KBr): 3476 m br (O–H), 2929 vs (C–H), 2860 s (C–H), 1651 vw (C=C), 1243 m (C–O), 1060 s (C–O). – <sup>1</sup>H NMR (400 MHz/CDCl<sub>3</sub>/CD<sub>3</sub>OD 5:1): δ 5.34 (s, 2 H), 4.74 (d, 2 H, *J* = 8 Hz), 3.7–3.5 (m, 2 H), 3.50–3.30 (m, 4 H), 3.25 (s br, 2 H), 2.42 (dd, 2 H, *J* = 8, 10 Hz), 1.04 (s, 6 H), 0.94 (d, 6 H, *J* = 7 Hz), 0.87 (s, 6 H), 0.81 (d, 6 H, *J* = 6 Hz). – <sup>13</sup>C NMR (100 MHz/CDCl<sub>3</sub>/CD<sub>3</sub>OD 5:1): δ 11.31, 13.28, 16.68, 17.83, 22.64, 28.11, 28.24, 29.75, 30.02, 30.48, 30.70, 33.52, 35.58, 35.73, 37.24, 43.96, 44.27, 49.97, 50.66, 53.61, 66.57, 70.10, 80.36, 85.51, 105.86, 120.19, 152.54. – FAB [exact mass <sup>12</sup>C<sub>54</sub><sup>1</sup>H<sub>82</sub><sup>16</sup>O<sub>7</sub> = 842.606]: 844 (MH<sup>+</sup>/100), 414 (55). – Anal. calcd. for C<sub>54</sub>H<sub>82</sub>O<sub>7</sub> (843.24), C 76.92, H 9.80, found C 76.91, H 9.85

**Structure Analysis and Refinement**<sup>1)</sup>

All calculations were performed using the Siemens SHELXTL+ (VMS) program. The structure was solved by direct methods. The hydrogen atom belonging to the hydroxyl group was located from a difference Fourier map and the remaining hydrogens were included in calculated positions. One overall temperature factor was refined for all hydrogen

<sup>1)</sup> The atomic coordinates and anisotropic displacement coefficients for this work are available on request of CSD404922 from the Fachinformationszentrum Karlsruhe, 76344 Eggenstein-Leopoldshafen.

atoms. Convergence for the full-matrix least-squares refinement using anisotropic displacement coefficients for all carbon and oxygen atoms was achieved at  $R = 5.50\%$ , data-to-parameter ratio = 5.4:1.

### Crystal data of homoallylic alcohol 6

$C_{29}H_{44}O_5$ ,  $M = 472.665$  g/mol, colourless crystals from acetonitrile,  $0.55 \times 0.35 \times 0.1$  mm<sup>3</sup>, orthorhombic, space group  $P_{12121}$ ,  $a = 6.724(5)$ ,  $b = 11.67(1)$ ,  $c = 33.05(3)$  Å,  $V = 2597(4)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.209$  g/cm<sup>3</sup>,  $\mu = 0.081$  mm<sup>-1</sup>,  $F(000) = 1032$ , graphite monochromated MoK $\alpha$  radiation from a fine focus sealed tube ( $\lambda = 0.71073$  Å), 3067 reflections measured ( $3^\circ \leq 2\theta \leq 47.5$ ,  $-1 \leq h \leq 7$ ,  $-13 \leq k \leq 13$ ,  $-37 \leq l \leq 1$ ), 2626 unique reflections ( $R_{int} = 4.34\%$ ), 1658 observed reflections ( $F \leq 2.0 \sigma(F)$ ). The data collected on a Siemens P4 four-circle diffractometer were corrected for Lorentz and polarisation effects. Three standard reflections measured every 97 reflections revealed no decay due to radiation damage.

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