

## Absolute Configuration and Total Synthesis of (-)-Cabeneigrin A-I

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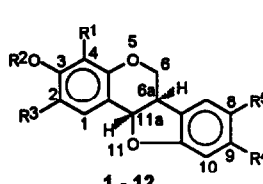
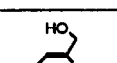
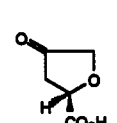
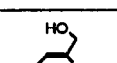

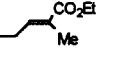
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**Abstract:** The total synthesis of (-)-cabeneigrin A-I [(-)-1] in five steps was achieved from (-)-6a*R*,11a*R*-maackiain [(-)-5], which in turn was prepared by the optical resolution of racemic (±)-5 using *S*-(-)-α-methylbenzyl isocyanate as the chiral auxiliary. The homochirality of (-)-maackiain [(-)-5] and (-)-cabeneigrin A-I [(-)-1] was proved by CD measurements. Synthesis of (±)-maackiain [(±)-5] is also presented, starting from the readily available phenol derivatives resorcinol and sesamol, which demonstrates the synthetic utility of the Heck-type oxyarylation process for obtaining pterocarpane derivatives on a multigram scale. A new ring-opening reaction of pterocarpanes (7 → 28) is described. © 1999 Elsevier Science Ltd. All rights reserved.

**Keywords:** Benzopyrans, biologically active compounds, flavanoids, resolution

Pterocarpanes are naturally occurring plant products carrying a *cis*-fused benzofuranyl-benzopyran ring system.<sup>1</sup> Many of them are phytoalexins possessing high antifungal and antibacterial activity,<sup>2,3</sup> and several of them have been reported to inhibit HIV-1 reverse transcriptase and the cytopathic effect of HIV-1 in cell cultures.<sup>4,5</sup> Furthermore, one of us has demonstrated that two representatives of these natural products, cabeneigrin A-I [(-)-1] and A-II [(-)-2] are the active components of a Brazilian folk medicine used against snake venoms.<sup>6</sup> Thus, both compounds have been found to be active in male beagle dogs (1 mg/kg i.v.) against the venom of *Bothrops atrox*.<sup>7</sup> These potent antidotes have been isolated by Nakanishi and co-workers<sup>6</sup> from the aqueous alcoholic extract of the root of a South American plant called “Cabeca de Negra”, and their structures have been elucidated by spectroscopic methods (UV, <sup>1</sup>H and <sup>13</sup>C NMR, CD, MS) and

substantiated by the synthesis of their racemates.<sup>8</sup> The CD spectra of (-)-cabeneigrin A-I [(-)-1], showing a large negative Cotton-effect ( $\Delta\epsilon = -9.84$ ) at 238 nm, allowed us to conclude that it is homochiral with (-)-6a*R*,11a*R*-

	R1	R2	R3	R4	R5	
		H	H	—OCH <sub>2</sub> O—		
1		H	H	—OCH <sub>2</sub> O—		13
2	H	H		—OCH <sub>2</sub> O—		
3	H	Me	H	OMe	H	
4	H	$\beta$ -D-Glup	H	OMe	H	
5	H	H	H	—OCH <sub>2</sub> O—		
6	H	Bn	H	—OCH <sub>2</sub> O—		
7	H	CH <sub>2</sub> =CH-CH <sub>2</sub> -	H	—OCH <sub>2</sub> O—		
8	CH <sub>2</sub> =CH-CH <sub>2</sub> -	H	H	—OCH <sub>2</sub> O—		
9	H	H	CH <sub>2</sub> =CH-CH <sub>2</sub> -	—OCH <sub>2</sub> O—		
10	—CH <sub>2</sub> -CHO	H	H	—OCH <sub>2</sub> O—		
11	—CH <sub>2</sub> -CHO	H	I	—OCH <sub>2</sub> O—		
12		H	H	—OCH <sub>2</sub> O—		

	R	X
14	BnO	O
15	H	NH

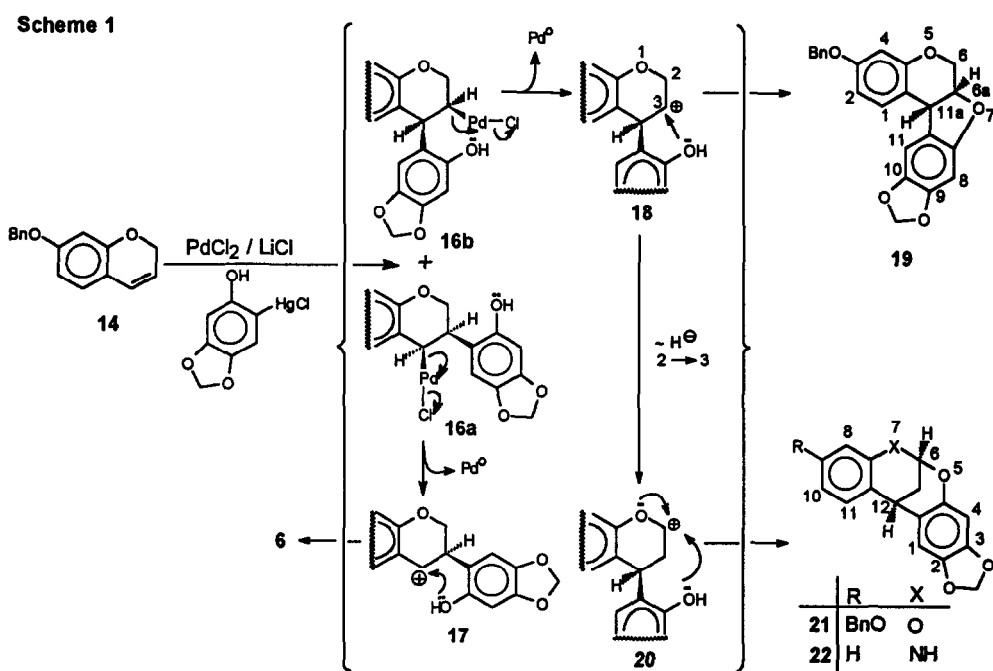
homopterocarpin [(-)-3] isolated by Rall *et al.*<sup>9</sup> from *Neorautanenia edulis*. However, it is to be noted that the CD-spectra of (-)-3 were not reported in that publication, but on the basis of the large negative optical rotation of (-)-3 at the sodium-D line ( $[\alpha]_D = -277.7$ ) Rall and co-workers supposed its homochirality with (-)-trifolirhizin [(-)-4], the 6a*R*,11a*R* absolute configuration of which had been established<sup>10</sup> by chemical correlation with (-)-paraconic acid [(-)-13] of known absolute configuration. Moreover, further doubt is presented by fact that the optical rotation value for (-)-1 at the sodium-D line was not published by Nakanishi *et al.*<sup>6</sup>

In order to unambiguously determine the absolute configuration of (-)-cabeneigrin A-I [(-)-1], and to examine its biological activity in comparison with that of its racemate, we set our sights on its total synthesis *via* (-)-maackiain [(-)-5], the 6a*R*,11a*R* absolute configuration of which had been deduced from chemical correlation with (-)-6a*R*,11a*R*-trifolirhizin [(-)-4].<sup>11</sup>

The strategy of our synthesis was based on the well-documented synthetic availability of racemic maackiain [(±)-5].<sup>12-15</sup> Its functionalizable hydroxyl group at C-3 offers a good chance to prepare diastereoisomers with a suitable chiral auxiliary, separable by chromatography or crystallization. Among the known syntheses of (±)-5, the one reported by Breytenbach and Rall<sup>12</sup> seemed to be useful to obtain (±)-5 on a multigram scale, from the commercially available starting materials resorcinol and sesamol (3,4-methylenedioxyphenol). Indeed, 7-benzyloxy-2*H*-1-benzopyran (14) could be obtained from resorcinol in four steps in an 18% overall yield, and reacted with 2-chloromercurio-3,4-methylenedioxyphenol (prepared from sesamol by a simple mercuriation) under the conditions of the Heck oxyarylation procedure, to afford the required 3-benzylmaackiain [(±)-6] in an acceptable yield (53%). However, it is to be noted that - in contrast to the reports of Breytenbach<sup>12</sup> and Harano<sup>15</sup> - our TLC examination showed that the oxyarylation reaction produced not only

( $\pm$ )-**6** in 66% yield, but also additional coupled products. Moreover, the m.p. of our product [( $\pm$ )-**6**, m.p. 143–144°C] was found to be characteristically different from that of Breytebach's compound (m.p. 173–174°C).

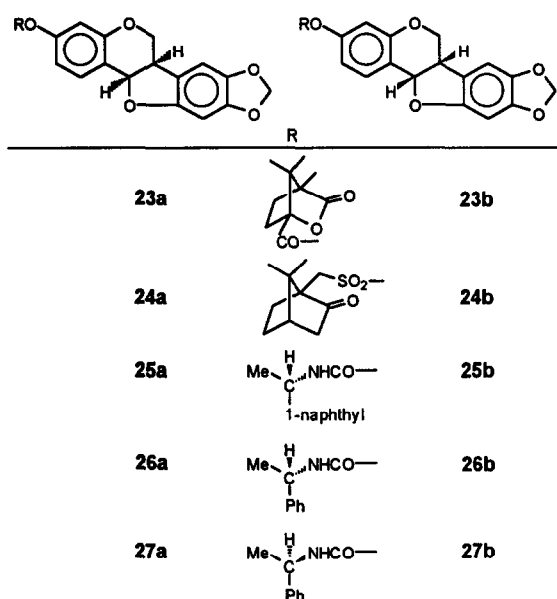
After isolation of ( $\pm$ )-**6** the side-products were separated by preparative TLC and their structures were elucidated by spectroscopic methods. On the basis of the comparison of the  $^1\text{H}$ -NMR and MS data of the less polar component of m.p. 199–200°C with those of the oxazocine derivative **22**, prepared by two of us<sup>16</sup> by the Heck-type coupling of 1,2-dihydroquinoline (**15**) with 2-chloromercurio-3,4-methylenedioxyphenol, a 6,12-methano-6H-dibenzo [d,g][1,3]dioxacine structure **21** has been unambiguously assigned. The HRMS and  $^1\text{H}$ -NMR spectra of the other unexpected compound clearly show that it is an isomer of ( $\pm$ )-**6** bearing the 3,4-methylenedioxyphenyl group at C-4 of the 7-benzoyloxychromane skeleton. Comparison of these data with our previous observations<sup>16</sup> suggests that (i) the Heck-type oxyarylation of 3-chromene derivatives did not take



place with complete regioselectivity ( $14 \rightarrow 16a \rightarrow 17 \rightarrow 6$ ) as published Breytenbach and others,<sup>12,15</sup> (ii) the ring closure of the corresponding organo-palladium intermediate **16b**, leading to the side products **19** and **21**, took place *via* a carbocation intermediate (**18**). This carbocation readily accepts not only an electron pair of the nucleophilic hydroxyl group to form the C-O bond of **19**, but it rearranges *via* a hydride shift to the more stable **20** which, upon reaction with the phenolic hydroxyl group, affords the dioxacine derivative **21** as depicted in Scheme 1.

Since our target molecule [(±)-6] could be separated from the side-products 19 and 21 by a very simple treatment with diethyl ether at room temperature, we developed this method for the multigram-scale preparation of (±)-6 to be used as the starting material for the synthesis of (-)-cabenegrin A-I [(-)-1].

In the first step the benzyl protecting group of (±)-6 was cleaved by catalytic hydrogenation over 10% palladium charcoal without cleavage of the C-11a—O-bond,<sup>17</sup> to give racemic maackiain [(±)-5] in 92% yield. In order to resolve (±)-5, the hydroxyl group at C-3 was acylated with both 1*S*-(-)-camphanic chloride and D-(+)-camphor-10-sulphonyl chloride under the conditions described by Lampe *et al.*<sup>18</sup> to give the diastereomeric mixtures 23a,b and 24a,b, respectively, in good yield. Although these were stable and crystalline compounds, their resolution by chromatography or crystallization, using various solvents was unsuccessful. Similar attempts with the carbonates 25a,b, prepared with *R*(-)-1-(1-naphthyl)ethyl isocyanate,<sup>19</sup> also failed. Finally, racemic maackiain [(±)-5] was treated with an equimolar amount of *R*(+)-α-methylbenzyl isocyanate in dry benzene at 80°C in the presence of *N,N*-dimethylethanolamine. The reaction was monitored by TLC, which clearly showed



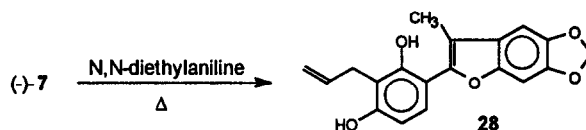
that a large amount of the starting material [(±)-5] was present after 13 h. Since addition of the isocyanate to the hydroxyl group of (±)-5 proceeded very slowly, a possibility of a kinetic resolution<sup>20</sup> could not be ruled out. Therefore, the reaction mixture was slowly cooled and a colourless crystalline product of m.p. 151–152°C was collected in 22% yield. Although this crystalline compound of sharp melting point seemed to be diastereomerically pure (26a or 26b) on the basis of its <sup>1</sup>H NMR data at 400 MHz, the cleavage of its carbamoyl function under the reported conditions<sup>21,22</sup> resulted in the racemic maackiain [(±)-5]. Therefore, the crystalline

product of m.p. 151–152°C proved to be a 1:1 diastereomeric mixture of 26a and 26b, but its repeated crystallization from methanol yielded (+)-26b of m.p. 209–210°C, whose diastereomeric purity was found to be 95.3% by HPLC analysis. From the combined mother liquors evaporation and repeated crystallization also gave (-)-26a of m.p. 199–200°C, whose HPLC analysis showed a 93% 26a and 7% 26b content. The establishment of the configuration of (-)-26a and (+)-26b at the pterocarpane nucleus was performed by chemical correlation with the maackiain enantiomers [(-)-5 and (+)-5], prepared by cleavage of the carbamoyl group of the diastereomers [(-)-26a → (-)-5, (+)-26b → (+)-5].

Since (-)-6a*R*,11a*R*-maackiain [(-)-5] has been found to be homochiral with (-)-cabenegrin A-I [(-)-1] on the basis of comparison of their CD-spectra, and its carbamoyl derivative [(-)-26a] was isolated from the mother liquors of the fractional crystallization of the 1:1 mixture of (-)-26a and (+)-26b, it seemed to be more expedient to repeat and optimize the resolution of (±)-5 with the enantiomeric chiral reagent *S*-(-)-α-methylbenzyl isocyanate. Thus, (±)-5 was treated with *S*-(-)-α-methylbenzyl isocyanate and a 1:1 diastereomeric mixture of the carbamates 27a + 27b (m.p. 147–149°C,  $[\alpha]_D = -80$ ) was isolated in 50% yield. The process of the fractional crystallization is given in the Experimental. It is to be noted that very modest yields [27a (5%), 27b (2%)] could be achieved due to very small differences in their solubilities. Such small differences both in the chemical shift values in their <sup>1</sup>H NMR spectra, and in their chromatographic behaviour on TLC (they were inseparable) also clearly indicated the absence of high second-order interactions, such as hydrogen bonds, *etc.*, between the molecules, which would be necessary to achieve a higher yield of separation of 27a and 27b by crystallization. Removal of the chiral auxiliary of (-)-27a by reduction with LiAlH<sub>4</sub> in a mixture of dry benzene and diethyl ether at r.t. gave the crude (-)-5, which was purified by chromatography to afford enantiomerically almost pure (-)-6a*R*,11a*R*-maackiain [(-)-5, ee = 99.5% by HPLC analysis]. It is noteworthy that the cleavage of the carbamoyl group of 27a or 26b with SiHCl<sub>3</sub> according to the methods reported by Messe<sup>21</sup> and Pirkle<sup>22</sup> resulted in a significantly lower yield.

The regioselective introduction of the hydroxyisoprene unit at C-4 of (-)-5 was developed according to the method of Ishiguro *et al.*<sup>8</sup> In the first step (-)-maackiain [(-)-5] was alkylated with allyl bromide in the presence of potassium carbonate to give (-)-7 in 77% yield, whose thermal Claisen rearrangement in *N,N*-diethylaniline at 208°C (in contrast to Ishiguro's result) did not give regioselectively the corresponding 4-allyl-derivative [(-)-8], but was followed by cleavage of the C-O bond of the benzopyrane moiety and loss of hydrogens at C-6a and C-11a to result in 42% of 28 as depicted in Scheme 2. This unexpected transformation of the pterocarpane skeleton could be avoided when the reaction was executed in a sealed tube in xylene at 192°C. At this temperature the Claisen rearrangement takes place rather slowly, but without considerable side-reaction. Although the reaction mixture still contained the starting material [(-)-7] in a considerable amount (20%) after 24 h, the desired product [(-)-8] could be isolated by preparative TLC in 68%

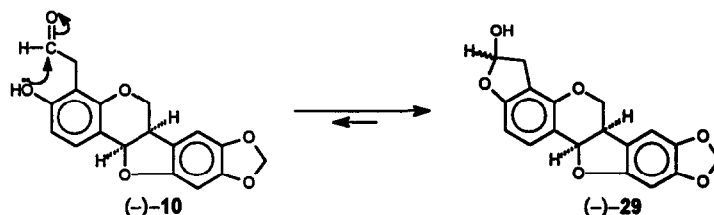
Scheme 2



yield, beside the isomeric C-allyl derivative [(-)-9], characterised by <sup>1</sup>H NMR measurements. In the next step of the synthesis we observed a rather different transformation of (-)-8 than in case of its racemic form. Thus, treatment of (-)-8 with osmium tetroxide, followed by oxidation with sodium metaperiodate in dioxan at room temperature resulted in a mixture of (-)-10 and (-)-11, which could be readily separated by preparative TLC. This side-reaction occurred due to the good solubility of (-)-10, which did not precipitate from the solution in

contrast to the racemic aldehyde [(±)-10], and therefore its iodo derivative [(–)-11] was also produced. It is noteworthy, that on the basis of the  $^1\text{H}$  NMR measurements of (–)-10, it exists in  $\text{CDCl}_3$  in its hemiacetal form [(–)-29], due to a rapid intramolecular cyclization as shown in Scheme 3.

Scheme 3



The *E*-olefinic side-chain of (–)-1 was stereoselectively introduced by the Wittig reaction of (–)-10 with  $\alpha$ -ethoxycarbonylethyltriphenylphosphonium bromide<sup>23</sup> in ethanol at room temperature in the presence of potassium ethoxide to give 48% of (–)-12, whose enantiomeric purity (ee% = 99.1%) was determined by HPLC on a Chiracel-OD column using a mixture of hexane and ethanol (82:18) as eluent. In the last step of the synthesis, the *E*-ester [(–)-12] was reduced with lithium aluminium hydride in diethyl ether at room temperature to afford (–)-1 in 31% yield. The UV, NMR and CD-data of this *levo*-rotatory enantiomer were identical with those reported for cabenegrin-AI,<sup>6</sup> and therefore this allows the assignment of the 6a*R*,11a*R* configuration for (–)-cabenegrin-AI [(–)-1].

Furthermore, it is to be noted that in our hands reduction of the ester (–)-12 or its racemate [(±)-12] did not result in the corresponding allyl alcohol (–)-1 or (±)-1, respectively, under the conditions ( $\text{LiAlH}_4$ , THF,  $-40^\circ\text{C}$ ) reported by Ishiguro et al.<sup>8</sup> Instead, no transformation of these compounds could be detected.

In summary, we accomplished the total synthesis of (–)-6a*R*,11a*R*-cabenegrin-AI [(–)-1] via (–)-6a*R*,11a*R*-maackiain [(–)-5], which was prepared by the optical resolution its racemic form [(±)-5] using *S*-(–)- $\alpha$ -methylbenzyl isocyanate as the chiral auxiliary. We showed that the Heck-type oxyarylation of 7-benzyloxy-2*H*-1-benzopyran (14) with 2-chloromercurio-3,4-methylenedioxyphenol offers a suitable, direct route to racemic maackiain [(±)-5] on a multigram scale. A notable feature of this strategy is that in contrast to previous observations<sup>12,15</sup> the palladium chloride-catalysed coupling reaction did not proceed with full regioselectivity to give the pterocarpane ring system, but it also furnished other O-heterocycles as side-products. A new thermal ring opening reaction of pterocarpanes (7  $\rightarrow$  28) was also observed.

### Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. 200-MHz  $^1\text{H}$ -NMR spectra were recorded with a Bruker WP 200 SY (marked by an asterisk\*) and XLAA 400 Varian instrument in  $\text{CDCl}_3$  with TMS as internal standard. MS spectra were obtained with a VG-7035 GC/MS/DS spectrometer (ion current 0.1 mA, direct insertion technique). IR spectra were recorded on a Perkin Elmer FT IR spectrometer. Elemental analyses were carried out with a Carlo Erba 1106 analyser. Optical rotation was

measured with Perkin-Elmer 241 polarimeter at the sodium-D line. CD spectra were recorded with a Jobin-Yvon Mark VI dichrograph at room temperature. (1*S*)-(-)-Campanic chloride, (1*S*)-(+)-camphorsulfonyl chloride, (R)-(-)-1-(1-naphthyl)ethyl isocyanate, (S)-(+)- $\alpha$ -methylbenzyl isocyanate, (S)-(-)- $\alpha$ -methylbenzyl isocyanate and osmium tetroxide were purchased from Sigma-Aldrich, 7-benzyloxy-2*H*-1-benzopyran (**14**), 2-chloromercury-4,5-methylenedioxy-phenol and triphenyl-(1-ethoxycarbonyl)ethyl-phosphonium bromide were prepared by known methods.<sup>12,13</sup> Pre-coated silica gel plates (Kieselgel 60 F254, 0.25 mm, Merck) were used for analytical and preparative TLC. For workup the solutions were dried (MgSO<sub>4</sub>) and concentrated in vacuo.

( $\pm$ )-3-Benzyloxy-8,9-methylenedioxypterocarpan [( $\pm$ )-**6**], ( $\pm$ )-6,11-methano-2,3-methylenedioxy-6*H*-dibenzo[d,g][1,3]dioxacin (**21**) and ( $\pm$ )-6a,12b-dihydro-6*H*-benzo[4,5]furo[2,3-*c*]chromene (**19**). Palladium chloride (17.1 g, 9.6 mmol) and lithium chloride (8.52 g, 20.2 mmol) were stirred in dry acetone (300 ml) for 15 min and 5-benzyloxy-2*H*-1-benzopyran (**14**)<sup>12</sup> (22.85 g, 9.6 mmol) was added, stirred again for 15 min, followed by dilution of the mixture with dry acetone (300 ml) and addition of 2-chloromercury-4,5-methylenedioxyphenol<sup>12</sup> (38 g, 10.1 mmol). Stirring was continued for 150 min, and then the reaction mixture was poured into brine (1500 ml), extracted with benzene, washed with brine, dried and concentrated in vacuo to a viscous crude product (60g), which became a gray to white solid on addition of a small quantity of methanol. After filtration the crude product was purified by stirring with diethyl ether (200 ml) at room temperature to give rac. **6** of m.p. 143–144°C (19 g, 53%).  $\nu_{\max}$  (KBr): 1620, 1584, 1506, 1474, 1462, 1180, 1166, 1144, 1036 cm<sup>-1</sup>. <sup>1</sup>H NMR\*: 7.50–7.30 (m, 6H, C1-H), 6.72 (s, 1H, C10-H), 6.70 (d, *J* = 2.5 Hz, C2-H), 6.56 (d, *J* = 2.5 Hz, C4-H), 6.42 (s, 1H, C7-H), 5.90 (d, 1H, O-CH<sub>2</sub>-O), 5.50 (d, *J* = 7.5 Hz, 1H, C11a-H), 5.08 (s, 2H, benzyl-CH<sub>2</sub>), 4.23 (dd, *J* = 3 and 12 Hz, 1H, C6<sub>eq</sub>-H), 3.64 (t, *J* = 12 Hz, 1H, C6<sub>ax</sub>-H), 3.50 (m, 1H, C6<sub>a</sub>-H); Anal. Calcd. for C<sub>23</sub>H<sub>18</sub>O<sub>5</sub> (374.39): C, 73.78; H, 4.84; found C, 73.52; H, 4.81. Evaporation of the mother liquor gave a thick oil (27 g). A small quantity (100 mg) of this oil was purified on preparative TLC using benzene as eluent to result in **21** (10 mg) and **19** (4 mg). **21**: colourless needles from acetone, m.p. 199–200°C;  $\nu_{\max}$  (KBr): 1624, 1580, 1500, 1480, 1442, 1240, 1172, 1144, 1088 cm<sup>-1</sup>. <sup>1</sup>H NMR\*: 2.20 (t, *J* = 2 Hz, 2H, C13-H<sub>2</sub>), 3.68 (s, 1H, C6-H), 4.99 (s, 2H, benzyl-CH<sub>2</sub>), 5.82 (d, 2H, O-CH<sub>2</sub>-O), 6.05 (s, 1H, C12-H), 6.42 (s, 1H, C4-H), 6.55–6.49 (m, 2H, C8,10-H), 6.60 (s, 1H, C12-H), 7.03 (d, *J* = 8 Hz, 1H, C11-H), 7.25–7.41 (m, 5H, Ph); Anal. Calcd. for C<sub>23</sub>H<sub>18</sub>O<sub>5</sub> (374.39): C, 73.78; H, 4.84; found C, 73.49; H, 4.90; **19**: colourless oil;  $\nu_{\max}$  (KBr): 1620, 1580, 1502, 1482, 1460, 1198, 1180, 1146, 932 cm<sup>-1</sup>. <sup>1</sup>H NMR\*: 4.10–4.25 (m, 2H, C6-H<sub>2</sub>), 4.28 (t, *J* = 3.5 Hz, 1H, C6a-H), 5.01 (s, 2H, benzyl-CH<sub>2</sub>), 5.22 (d, *J* = 3.5 Hz, 1H, C11a-H), 5.38 (s, 2H, O-CH<sub>2</sub>-O), 5.82 (d, *J* = 3 Hz, 1H, C4-H), 6.47 and 6.49 (s, 2H, C8,11-H), 6.50–6.60 (m, 2H, C2,4-H), 6.82 (d, *J* = 7.5 Hz, 1H, C1-H), 7.32–7.50 (m, 5H, Ph); HRMS: Calcd. for C<sub>23</sub>H<sub>18</sub>O<sub>5</sub> (374.1154), found *m/z*: 374.1147 (*M*<sup>+</sup>).

**(±)-3-Hydroxy-8,9-methylenedioxypterocarpan [rac.-maackiain, (±)-5].** (±)-6 (9.6 g, 26.2 mmol) was dissolved in a mixture of acetone-tetrahydrofuran (3:1, 480 ml) and hydrogenated in the presence of 10% palladium-charcoal (2.5 g) until the uptake of 680 ml of hydrogen. Usual workup resulted in rac. maackiain (6.8 g, 92%) of m.p. 194–196°C. Lit.<sup>24</sup> m.p. 195–196°C; Anal. Calcd. for C<sub>16</sub>H<sub>12</sub>O<sub>3</sub> (284.26): C, 67.60; H, 4.25; found C, 67.50; H, 4.49.

**(-)-3(1*S*-Camphanic)-maackiain (23a,b).** (±)-5 (500 mg, 1.75 mmol) was dissolved in dry pyridine (10 ml) and (1*S*)-(-)-camphanic chloride (605 mg, 2.8 mmol) was added at room temperature. After stirring for 24 hrs the reaction mixture was poured into ice-water, when the colourless solid product was precipitated (625 mg, 77 %), and it was crystallized from methanol yielding 527 mg (50%) of 23a,b (diastereomeric mixture), m.p. 190–191°C,  $[\alpha]_D^{24} = -5$  (c = 0.9 in chloroform).  $\nu_{\max}$  (KBr): 1788, 1754, 1618, 1474, 1460, 1260, 1116, 1046, 992 cm<sup>-1</sup>. <sup>1</sup>H NMR: 1.09, 1.15 and 1.17 (s, 3x3H, C4'-H<sub>3</sub>, C8'-H<sub>3</sub>, C9'-H<sub>3</sub>), 1.77 and 1.99 (m, 2H, C5'-H<sub>2</sub>), 2.20 and 2.56 (m, 2H, C6'-H<sub>2</sub>), 3.53 (m, *J* = 10.3, 7.0 and 4.8 Hz, 1H, C6a-H), 3.66 and 3.67 (2xt, *J* = 10.3 Hz, 1H, C6-H<sub>ax</sub>), 4.28 (d, *J* = 10.3 and 4.5 Hz, 1H, C6-H<sub>eq</sub>), 5.51 (d, *J* = 7.0 Hz, 1H, C11a-H), 5.91 and 5.93 (*J* = 1.5 Hz, 2H, O-CH<sub>2</sub>-O), 6.73 and 6.75 (2xd, *J* = 2.2 Hz, 1H, C4-H), 6.83 (dd, *J* = 8.1 and 2.2 Hz, 1H, C2-H), 7.54 (d, *J* = 8.1 Hz, 1H, C1-H); Anal. Calcd. for C<sub>26</sub>H<sub>24</sub>O<sub>8</sub> (464.45): C, 67.23; H, 5.20; found C, 67.21; H 5.27.

**(+)-3(1*S*-Camphor-10-sulfonyl)-maackiain (24a,b).** 500 mg (1.76 mmol) of [(±)-5], abs. pyridine (10 ml) and 700 mg (2.8 mmol) of (1*S*)-(+)-10-camphorsulfonyl chloride was stirred at room temperature for 24 h. The reaction mixture was poured into ice-water. The product precipitated was filtered off and washed with water. 680 mg 75 % of colourless solid was obtained, m.p. 136°C, which was crystallized from methanol, yielding 400 mg (44 %) of 24a,b (diastereomeric mixture), m.p. 142–143°C,  $[\alpha]_D^{24} = +21$  (c = 1 in acetone).  $\nu_{\max}$  (KBr): 1746, 1614, 1494, 1474, 1460, 1374, 1180, 1146, 1110 cm<sup>-1</sup>. <sup>1</sup>H NMR: 0.92 and 1.18 (s, 2x3H, C8'-H<sub>3</sub>, C9'-H<sub>3</sub>), 1.47 and 1.72 (m, 2H, C5'-H<sub>2</sub>), 1.98 (d, *J* = 18.3 Hz, 1H, C3'-H<sub>A</sub>), 2.09 (m, *J* = 18.3, 4.3 and 3.5 Hz, 1H, C3'-H<sub>B</sub>), 2.14 (dd, *J* = 4.5 and 4.3 Hz, 1H, C4'-H), 2.42 and 2.55 (m, 2H, C6'-H<sub>2</sub>), 3.53 and 3.54 (m, *J* = 10.5, 7.0 and 4.9 Hz, 1H, C6a-H), 3.64 and 3.66 (2xt, *J* = 10.5 Hz, 1H, C6-H<sub>ax</sub>), 4.29 (dd, *J* = 10.5 and 4.9 Hz, 1H, C6-H<sub>eq</sub>), 5.50 (d *J* = 7.0 Hz, 1H, C11a-H), 5.90 and 5.93 (*J* = 1.4 Hz, 2H, O-CH<sub>2</sub>-O), 6.43 (s, 1H, C10-H), 6.72 (s, 1H, C7-H), 6.92 and 6.94 (2xd, *J* = 2.2 Hz, 1H, C4-H), 7.03 (dd, *J* = 8.2 and 2.2 Hz, 1H, C2-H), 7.55 (d, *J* = 8.2 Hz, 1H, C1-H); Anal. Calcd. for C<sub>26</sub>H<sub>26</sub>O<sub>8</sub>S (498.56): C, 62.63; H, 5.25; S, 6.43; found C, 62.75; H, 5.10; S, 6.35.

**(+)-3[1*S*-N-(1-Naphthyl)ethylcarbamoyl]-maackiain (25a,b).** A stirred solution of 100 mg (0.35 mmol) of (±)-5, 69 mg (0.35 mmol) of (*R*)-(-)-1-(1-naphthyl)ethyl isocyanate 20 ml of dry benzene, and 1 drop of *N,N*-dimethylethanolamine catalyst was heated under reflux for 9.5 h. The solvent was removed in vacuo and the crude diastereomeric carbamates were crystallized from methanol. A total of 75 mg (45 %) of colourless crystalline product was collected, m.p. 152–153°C,  $[\alpha]_D^{24} = +25$  (c = 0.8 in acetone) (diastereomeric mixture).  $\nu_{\max}$  (KBr): 1736, 1728,



1618, 1494, 1474, 1460, 1256, 1180, 1144  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR: 1.73 (d,  $J = 7.2$  Hz, 3H,  $\text{CH}_3$ ), 3.48 and 3.50 (m, 1H, C6a-H), 3.62 and 3.65 (2xt,  $J = 10.6$  Hz, 1H, C6-H<sub>ax</sub>), 4.22 (dd,  $J = 10.6$  and 5.0 Hz, 1H, C6-H<sub>eq</sub>), 5.33 (d,  $J = 8$  Hz, 1H, NH), 5.48 (d,  $J = 7.0$  Hz, 1H, C11a-H), 5.73 (m, 1H, CH), 5.89 and 5.93 ( $J = 1.5$  Hz, 2H, O-CH<sub>2</sub>-O), 6.42 (s, 1H, C10-H), 6.71 (s, 1H, C7-H), 6.73 and 6.75 (2xd,  $J = 2.2$  Hz, 1H, C4-H), 6.84 and 6.88 (dd,  $J = 7.0$  and 2.1 Hz, 1H, C2-H), 7.40 and 7.60 (m, 5H, C3'-H, C6'-H, C7'-H, C1-H, C2'-H), 7.82 and 7.88 (dd,  $J = 7.0$  and 1.5 Hz, 2H, C4'-H, C5'-H), 8.12 (dd,  $J = 7.4$  and 1.3 Hz, 1H, C8'-H); Anal. Calcd. for  $\text{C}_{29}\text{H}_{23}\text{NO}_6$  (481.49): C, 72.34; H, 4.81; N, 2.90; found C, 72.51; H, 4.79; N, 2.89.

(-)-3[1-*R*-N(1-Methyl)benzylcarbamoyl]-6a*R*,11a*R*-maackiain (26a) and (+)-3[1'-*R*-N(1'-methyl)benzyl-carbamoyl]-6a*S*,11a*S*-maackiain (26b). A mixture of ( $\pm$ )-5 (2.5 g, 8.75 mmol), (*R*)-(+)- $\alpha$ -methylbenzyl isocyanate (1.4 g, 1.75 mmol), *N,N*-dimethylethanolamine (3 drop), and dry benzene (225 ml) was heated at 80°C for 18 h. After cooling 875 mg (22 %) of colourless crystalline product was obtained; m.p. 151–152°C;  $[\alpha]_{\text{D}}^{24} = +67$  ( $c = 1$ , chloroform), (1:1 mixture of diastereomeric carbamates);  $^1\text{H}$  NMR: 1.52 (d,  $J = 7.2$  Hz, 3H,  $\text{CH}_3$ ), 3.47 and 3.49 (m, 1H, C6a-H), 3.64 and 3.66 (2xt,  $J = 10$  Hz, 1H, C6-H<sub>ax</sub>), 4.22 (dd,  $J = 10.6$  and 5.0 Hz, 1H, C6-H<sub>eq</sub>), 4.92 (m, 1H, CH), 5.28 (d,  $J = 7.8$  Hz, 1H, NH), 5.48 (d,  $J = 7.0$  Hz, 1H, C11a-H), 5.88 and 5.93 ( $J = 1.4$  Hz, 2H, O-CH<sub>2</sub>-O), 6.43 (s, 1H, C10-H), 6.71 (s, 1H, C7-H), 6.72 and 6.73 (2xd,  $J = 2.1$  Hz, 1H, C4-H), 6.81 and 6.83 (2xdd,  $J = 7.8$  and 2.1 Hz, 1H, C2-H), 7.26 and 7.35 (m, 5H, C2'-H, C6'-H), 7.44 (d,  $J = 7.8$  Hz, 1H, C1-H); MS (70 eV)  $m/z$  %: 431 [ $\text{M}^+$ ] (100), 413, 386, 368; HPLC (Chiracel-OD; eluent; *n*-hexane:ethanol = 82:18):  $R_t = 16.54$  and 21.30 min. Fractional crystallization of the diastereomeric carbamates from methanol yielded (+)-26b (120 mg, 6%); m.p. 209–210°C,  $[\alpha]_{\text{D}}^{24} = +243$  ( $c = 1$  in acetone); HPLC:  $R_t = 16.52$  min;  $\nu_{\text{max}}$  (KBr): 1708, 1618, 1546, 1530, 1496, 1460, 1454, 1180, 1146  $\text{cm}^{-1}$ . Anal. Calcd. for  $\text{C}_{25}\text{H}_{21}\text{NO}_6$  (431.42) C, 69.60; H, 4.90; N, 3.24; found C, 69.51; H, 4.87; N, 3.15. Fractional crystallization of the product obtained by evaporation of the combined mother liquors of the above mentioned crystallization resulted in (-)-26a (45 mg, 3%), m.p. 199–200°C,  $[\alpha]_{\text{D}}^{24} = -45$  ( $c = 1$  in acetone); HPLC:  $R_t = 21.30$  min;  $\nu_{\text{max}}$  (KBr): 1702, 1618, 1562, 1530, 1498, 1474, 1456, 1160, 1146  $\text{cm}^{-1}$ . Anal. Calcd. for  $\text{C}_{25}\text{H}_{21}\text{NO}_6$  (431.42) C, 69.60; H, 4.90; N, 3.24; found C, 69.15; H, 4.88; N, 3.40.

(-)-3[1-*S*-N(1-Methyl)benzylcarbamoyl]-6a*R*,11a*R*-maackiain (27a) and (+)-3[1-*S*-N(1-methyl)benzyl-carbamoyl]-6a*S*,11a*S*-maackiain (27b). 5 g (17.5 mmol) of ( $\pm$ )-5 and *S*-(-)- $\alpha$ -methylbenzyl isocyanate (5 ml, 34 mmol), in dry benzene (300 ml) in presence of 5 drops of *N,N*-dimethylethanolamine was boiled for 15 h. After cooling to room temperature 3.8 g (50 %) 27a,b (1:1 mixture of diastereomeric carbamates) was obtained, m.p. 147–149°C,  $[\alpha]_{\text{D}}^{24} = -80$  ( $c = 0.9$  in acetone); HPLC:  $R_t = 16.88$  and 18.62 min. The diastereomeric mixture was dissolved in ethanol (150 ml) under reflux and cooled slowly to room temperature to give a colourless precipitate (840 mg), whose crystallization from ethanol (100 ml) resulted in a crystalline product (420 mg,  $[\alpha]_{\text{D}} = -178$ ). Its crystallization from ethanol afforded (-)-27a of m.p. 209–210°C (210 mg,  $[\alpha]_{\text{D}} = -240$ ), whose melting point increased to 214–215°C (190 mg, 5%),  $[\alpha]_{\text{D}} = -262$ ,  $c = 1$  in acetone) by a repeated crystallization from ethanol; HPLC:  $R_t = 18.62$

min.  $\nu_{\max}$  (KBr): 1708, 1618, 1592, 1528, 1496, 1474, 1456, 1232, 1146  $\text{cm}^{-1}$ . Anal. Calcd. for  $\text{C}_{25}\text{H}_{21}\text{NO}_6$  (431.45): C, 69.62; H, 4.92; N, 3.24; found C, 69.84; H, 4.91; N, 3.24.

Fractional crystallization of the product (1920 mg,  $[\alpha]_D = -67$ ) obtained from the methanol liquors of the first crystallization of the diastereomeric carbamates of m.p. 147–149°C resulted in (+)-**27b** (75 mg, 2%),  $[\alpha]_D^{24} = +79$  ( $c = 0.9$  in acetone), m.p. 203–204°C; HPLC:  $R_t = 16.88$  min.  $\nu_{\max}$  (KBr): 1706, 1618, 1592, 1526, 1494, 1474, 1454, 1158, 1144  $\text{cm}^{-1}$ . Anal. Calcd. for  $\text{C}_{25}\text{H}_{21}\text{NO}_6$  (431.45): C, 69.62; H, 4.92; N, 3.24; found C, 69.92; H, 4.94; N, 3.25.

(+)-**6aS,11aS-Maackiain** [(+)-**5**]. a) To a stirred solution of **26b** (43 mg, 0.1 mmol) and 1 drop of triethylamine in 7 ml of dry benzene was added 0.15 ml (0.12 mmol) of  $\text{SiHCl}_3$  in 5 ml of dry benzene over a 10-min period. The reaction mixture was heated at reflux under argon for 4 h. For completion of the decomposition of the diastereomer carbamate a further 0.5 ml (0.4 mmol) of  $\text{SiHCl}_3$  was added in dry benzene (5 ml) and boiled for 2 hrs. After being cooled, the reaction mixture was poured with stirring into 50 ml of saturated aqueous  $\text{NH}_4\text{Cl}$ . The insoluble silicon-containing solid was removed by filtration and washed with benzene. The organic phase was washed with water, dried over  $\text{MgSO}_4$  and concentrated. The residue was purified on preparative TLC yielding 10 mg (35 %) of (+)-**5**. M.p. 181–182°C,  $[\alpha]_D^{24} = +179$  ( $c = 0.1$  in acetone), its enantiomeric purity was 83.5 % as checked by HPLC analysis. b) Starting from **27b** ( $[\alpha]_D^{24} = +79$ ) (+)-**5** was obtained, with  $\text{LiAlH}_4$  as described below, m.p. 179–181°C,  $[\alpha]_D^{24} = +258$  ( $c = 0.1$  in acetone).  $\text{CD}(\text{CH}_3\text{CN}) \lambda_{\text{nm}} (\Delta\epsilon)$ : 211 (28.60), 237 (11.02), 313 (-2.23);  $ee = 99\%$  (HPLC: Chiralpak OT(+), methanol,  $R_t = 9.43$  min); Anal. Calcd. for  $\text{C}_{16}\text{H}_{12}\text{O}_5$  (284.26): C, 67.60; H, 4.25; found C, 67.65; H, 4.25.

(-)-**6aR,11aR-Maackiain** [(-)-**5**]. To a stirred solution of **27a** (340 mg, 0.8 mmol), ( $[\alpha]_D = -262$ ) in a mixture of dry ether (100 ml) and dry benzene (100 ml) 150 mg (4 mmol) of  $\text{LiAlH}_4$  was added. After 20 min the excess of  $\text{LiAlH}_4$  was decomposed with water. The organic phase was separated and washed with water (2x50 ml). The aqueous phase was acidified with 5 % of  $\text{HCl}$  to pH = 6 and extracted with benzene. Drying over  $\text{MgSO}_4$  and concentration of the combined organic phase afforded crude (-)-**5** which was purified by column chromatography on silica gel (toluene:acetone = 4:1) yielding 200 mg (90 %) of (-)-**5** as colourless prisms. M.p. 181–187°C,  $[\alpha]_D^{24} = -267$  ( $c = 0.1$  in acetone).  $\text{CD}(\text{CH}_3\text{CN}) \lambda_{\text{nm}} (\Delta\epsilon)$ : 208 (-28.51), 238 (-10.06), 309 (+2.66),  $ee = 99.5\%$  (HPLC: Chiralpak OT(+), methanol,  $R_t = 11.37$  min).  $\nu_{\max}$  (KBr): 3428, 1620, 1598, 1510, 1476, 1312, 1286, 1180, 1146  $\text{cm}^{-1}$ .  $^1\text{H NMR}^*$ : 7.40 (d,  $J = 10$  Hz, 1H, C1-H), 6.70 (s, 1H, C10-H), 6.55 (dd,  $J = 10$  Hz, 4 Hz, 1H, C2-H), 6.45 (s, 1H, C7-H), 6.40 (d,  $J = 4$  Hz, 1H, C4-H), 5.90 (d, 2H, O-CH<sub>2</sub>-O), 5.50 (d,  $J = 10$  Hz, 1H, C11a-H), 5.0 (br.s, 1H, C3-OH), 4.20 (dd,  $J = 5$  Hz and 10 Hz, 1H, C6<sub>eq</sub>-H), 3.60 (t,  $J = 10$  Hz, 1H, C6<sub>a</sub>-H), 3.45 (m, 1H, C6<sub>ax</sub>-H); Anal. Calcd. for  $\text{C}_{16}\text{H}_{12}\text{O}_5$  (284.26): C, 67.60; H, 4.25; found C, 67.61; H, 4.24. Starting from **27a** ( $[\alpha]_D^{24} = -262$ ) (-)-**5** was obtained with  $\text{SiHCl}_3$  only in 40% yield.

**(-)-3-Allyloxy-8,9-methylenedioxypterocarpan [(-)-7].** To a solution of (-)-5 (250 mg, 0.88 mmol) in acetone (30 ml),  $K_2CO_3$  (500 mg) and allyl bromide (0.2 ml) were added and the mixture was stirred at 50°C for 10 h. After filtration of the salt the filtrate was evaporated to give a colourless oil (261 mg), whose crystallization from *n*-hexane afforded 193 mg (77 %) of (-)-7 as colourless needles of m.p. 138–139°C,  $[\alpha]_D^{24} = -224$  ( $c = 0.1$  in acetone),  $CD(CH_3CN) \lambda_{nm} (\Delta\epsilon)$ : 312 (3.35), 239 (-14.79), 212 (-32.53);  $\nu_{max}$  (KBr): 1620, 1614, 1586, 1504, 1478, 1330, 1288, 1266, 1242  $cm^{-1}$ .  $^1H$  NMR: 3.40 (m,  $J = 11.0, 6.8$  and  $5.1$  Hz, 1H, C6a-H), 3.57 (t,  $J = 11.0$  Hz, 1H, C6-H<sub>ax</sub>), 4.15 (dd,  $J = 11$  and  $5.1$  Hz, 1H, C6-H<sub>eq</sub>), 4.45 (m,  $J = 5.2, 1.3$  and  $1.3$  Hz, 2H, C1'-H<sub>2</sub>), 5.20 (m,  $J = 10.8, 1.5, 1.3$  and  $1.3$  Hz, 1H, C3'-H<sub>A</sub>), 5.32 (m,  $J = 17.0, 1.5, 1.3$  and  $1.3$  Hz, 1H, C3'-H<sub>B</sub>), 5.40 (d,  $J = 6.8$  Hz, 1H, C11a-H), 5.82 and 5.84 ( $J = 1.5$  Hz, 2H, O-CH<sub>2</sub>-O), 5.96 (m, 1H, C2'-H), 6.37 (s, 1H, C10-H), 6.41 (d,  $J = 2.5$  Hz, 1H, C4-H), 6.57 (dd,  $J = 8.5$  and  $2.5$  Hz, 1H, C2-H), 6.63 (s, 1H, C7-H), 7.33 (d,  $J = 8.5$  Hz, 1H, C1-H). Anal. Calcd. For  $C_{19}H_{16}O_5$  (324.32): C, 70.36; H, 4.97; found C, 70.43; H, 5.01.

**(-)-4-Allyl-8,9-methylenedioxypterocarpan [(-)-8], (-)-2-allyl-8,9-methylenedioxypterocarpan [(-)-9] and 2-(2',4'-dihydroxy-3'-allyl)phenyl-3-methyl-5,6-methylenedioxybenzo[b]furan (28).** 600 mg (1.4 mmol) of (-)-7 was dissolved in dry xylene (10 ml) and kept in a sealed tube at 192°C for 24 h. After cooling the solvent was evaporated in vacuo and the residue was purified by preparative TLC on silica gel to result in (-)-8, (-)-9, 27 and unchanged (-)-7 (120 mg, 20%); (-)-8: 413 mg (68%), colourless prisms of m.p. 122–123°C,  $[\alpha]_D^{24} = -223$  ( $c = 0.17$  in acetone);  $\nu_{max}$  (KBr): 3358, 1620, 1602, 1496, 1474, 1188, 1144, 1220, 1036  $cm^{-1}$ .  $^1H$  NMR: 3.38 (m, 2 H, C1'-H<sub>2</sub>), 3.41 (m,  $J = 11.0, 6.6$  and  $5$  Hz, 1H, C6a-H), 3.54 (t,  $J = 11.0$  Hz, 1H, C6-H<sub>ax</sub>), 4.20 (dd,  $J = 11$  and  $5.0$  Hz, 1H, C6-H<sub>eq</sub>), 5.02 (m,  $J = 10.3, 1.6$  and  $1.4$  Hz, 1H, C3'-H<sub>A</sub>), 5.02 (s, 1H, OH), 5.04 (m,  $J = 17.2, 1.8$  and  $1.4$  Hz, 1H, C3'-H<sub>B</sub>), 5.41 (d,  $J = 6.6$  Hz, 1H, C11a-H), 5.82 and 5.84 ( $J = 1.4$  Hz, 2H, O-CH<sub>2</sub>-O), 5.90 (m, 1H, C2'-H), 6.37 (s, 1H, C10-H), 6.48 (d,  $J = 8.3$  Hz, 1H, C2-H), 6.63 (s, 1H, C7-H), 7.21 (d,  $J = 8.3$  Hz, 1H, C1-H); Anal. Calcd. for  $C_{19}H_{16}O_5$  (324.32) C, 70.36; H, 4.97; found C, 70.61; H, 4.62; (-)-9: 20 mg (3 %) colourless prisms, m.p. 174–175°C,  $[\alpha]_D^{24} = -249$  ( $c = 0.2$  in acetone);  $\nu_{max}$  (KBr): 3358, 1620, 1602, 1496, 1472, 1216, 1144, 1120, 936  $cm^{-1}$ .  $^1H$  NMR: 3.29 (m,  $J = 5.9, 1.4$  and  $1.5$ , 2 H, C1'-H<sub>2</sub>), 3.37 (m,  $J = 10.9, 5.0$  and  $7.0$  Hz, 1H, C6a-H), 3.53 (t,  $J = 10.9$  Hz, 1H, C6-H<sub>ax</sub>), 4.12 (dd,  $J = 10.9$  and  $5.0$  Hz, 1H, C6-H<sub>eq</sub>), 5.02 (s, 1H, OH), 5.08 (m,  $J = 10.0, 1.4$  and  $1.7$  Hz, 1H, C3'-H<sub>A</sub>), 5.11 (m,  $J = 17.1, 1.5$  and  $1.7$  Hz, 1H, C3'-H<sub>B</sub>), 5.38 (d,  $J = 7.0$  Hz, 1H, C11a-H), 5.80 and 5.82 ( $J = 1.4$  Hz, 2H, O-CH<sub>2</sub>-O), 5.93 (m, 1H, C2'-H), 6.36 (s, 1H, C10-H), 6.38 (s, 1H, C4-H), 6.61 (s, 1H, C7-H), 7.14 (s, 1H, C1-H). 28: 3 mg (0.5 %), colourless rhombic prisms of m.p. 90–92°C;  $\nu_{max}$  (KBr): 3434, 3346, 1626, 1606, 1496, 1462, 1376, 1310, 1170  $cm^{-1}$ .  $^1H$  NMR\*: 7.18 (d,  $J = 7$  Hz, 6'-H), 7.00 and 6.95 (s, 2H, 4,7-H), 6.51 (d,  $J = 7$  Hz, 4'-H), 6.01 (s, 2H, 5,6-OCH<sub>2</sub>O-), 6.10–5.90 (m, 1H, -CH=), 5.19 (m, 2H, =CH<sub>2</sub>), 3.55 (d,  $J = 5.5$  Hz, 2H, 3'-allyl-CH<sub>2</sub>), 2.30 (s, 3H, 3-Me); Anal. calcd. for  $C_{19}H_{16}O_5$  (324.32) C, 70.36; H, 4.97; found C, 70.10; H, 4.81. This compound as a sole product was also obtained in 42% yield, when (-)-7 was heated in *N,N*-diethylaniline at 208°C.

**(-)-3-Hydroxy-4-(2-oxo)ethyl-8,9-methylendioxypterocarpan [(-)-10] and 3-hydroxy-2-iodo-4-(2-oxo)ethyl-8,9-methylendioxy-pterocarpan [(-)-11].** To a stirred solution of (-)-8 (305 mg, 0.94 mmol) in dioxane (19.2 ml) OsO<sub>4</sub> (43 mg, 0.15 mmol) was added at room temperature. After 30 min a solution of NaIO<sub>4</sub> (450 mg) in water (50 ml) was added dropwise and stirred overnight. After addition of water the product was extracted with CHCl<sub>3</sub>. The organic phase was washed with aqueous NaHSO<sub>3</sub>, dried over MgSO<sub>4</sub> and evaporated in vacuo. The syrupy residue was purified on preparative TLC with toluene:ethyl acetate (4:1) as the eluent, yielding 104 mg (34 %) of (-)-10 as colourless needles, m.p. 150–151°C,  $[\alpha]_D^{24} = -175$  (c = 0.1 in acetone).  $R_f = 0.54$ ;  $\nu_{\max}$  (KBr): 3470, 1716, 1624, 1496, 1474, 1144, 1072, 1038, 1008 cm<sup>-1</sup>. <sup>1</sup>H NMR: 2.93 (dd,  $J = 16.6$  and 2.1 Hz, 1H, C1'-H<sub>A</sub>), 3.04 and 3.05 (2xd,  $J = 6.0$  and 5.7 Hz, 1H, 2xOH), 3.23 (dd,  $J = 16.6$ , and 6.4, 1 H, C1'-H<sub>B</sub>), 3.39 and 3.41 (m, 1H, C6a-H), 3.63 and 3.64 (2xt,  $J = 10.8$  Hz, 1H, C6-H<sub>ax</sub>), 4.17 and 4.18 (2xdd,  $J = 10.8$  and 5.0 Hz, 1H, C6-H<sub>eq</sub>), 5.42 and 5.43 (2xd,  $J = 6.9$  Hz, 1H, C11a-H), 5.80 and 5.82 (d,  $J = 1.4$  Hz, 2H, O-CH<sub>2</sub>-O), 6.02 and 6.04 (m, 1H, C2'-H), 6.37 (s, 1H, C10-H), 6.52 (d,  $J = 8.4$  Hz, 1H, C2-H), 6.61 (s, 1H, C7-H), 7.22 (d,  $J = 8.4$  Hz, 1H, C1-H); Anal. Calcd. for C<sub>18</sub>H<sub>14</sub>O<sub>6</sub> (326.30): C, 66.25; H, 4.32; found C, 66.10; H, 4.28; (-)-11 was also isolated (29 mg, 7 %);  $R_f = 0.85$ ; m.p. 175°C,  $[\alpha]_D^{24} = -180$  (c = 0.1 in acetone);  $\nu_{\max}$  (KBr): 3428, 1722, 1642, 1618, 1474, 1460, 1254, 1234, 1200 cm<sup>-1</sup>. <sup>1</sup>H NMR: 2.90 (dd,  $J = 16.6$  and 2.1 Hz, 1H, C1'-H<sub>A</sub>), 3.06 and 3.07 (2xd,  $J = 6.0$  and 5.7 Hz, 1H, 2xOH), 3.25 (dd,  $J = 16.6$ , and 6.4, 1 H, C1'-H<sub>B</sub>), 3.40 and 3.41 (m, 1H, C6a-H), 3.63 and 3.65 (2xt,  $J = 10.8$  Hz, 1H, C6-H<sub>ax</sub>), 4.17 and 4.18 (2xdd,  $J = 10.8$  and 5.0 Hz, 1H, C6-H<sub>eq</sub>), 5.42 and 5.44 (2xd,  $J = 6.9$  Hz, 1H, C11a-H), 5.80 and 5.82 (d,  $J = 1.4$  Hz, 2H, O-CH<sub>2</sub>-O), 6.02 and 6.04 (m, 1H, C2'-H), 6.38 (s, 1H, C10-H), 6.40 (s, 1H, C4-H), 6.62 (s, 1H, C7-H), 7.24 (s, 1H, C1-H). Anal. Calcd. for C<sub>18</sub>H<sub>13</sub>IO<sub>6</sub> (452.19): C, 47.81; H, 2.89; I, 28.06; found C, 47.55; H, 2.79; I, 28.51.

**(-)-3-Hydroxy-4-[(E)-2-ethoxycarbonyl-2-buten-4-yl]-8,9-methylendioxypterocarpan [(-)-12].** To a solution of (-)-10 (120 mg, 0.37 mmol) and triphenyl-(1-ethoxycarbonyl)ethylphosphonium bromide (200 mg, 0.45 mmol) in abs. ethanol (5 ml) 0.91 ml of 1N NaOC<sub>2</sub>H<sub>5</sub> was added at room temperature. After 3 h the reaction mixture was partially evaporated, acidified slightly with 10% HCl and diluted with water. The product was extracted with dichloromethane, washed with water, dried and evaporated to give the crude product which was purified by preparative TLC (toluene:acetone = 20:1) affording 72 mg (48 %) of (-)-12 as rhombic prisms, m.p. 175–176°C,  $[\alpha]_D^{24} = -73$  (c = 0.1 in chloroform);  $\nu_{\max}$  (KBr): 3386, 1704, 1640, 1614, 1474, 1292, 1260, 1144, 1074 cm<sup>-1</sup>. <sup>1</sup>H NMR: 1.17 (t,  $J = 6.8$  Hz, 3H, CH<sub>3</sub>), 1.91 (s, 3H, C5'-H<sub>3</sub>), 3.39 (m,  $J = 11.0$ , 7.0 and 5.0 Hz, 1H, C6a-H), 3.46 (d,  $J = 7.4$  Hz, 2H, C1'-H<sub>2</sub>), 3.54 (d,  $J = 11.0$  Hz, 1H, C6-H<sub>ax</sub>), 4.08 (q,  $J = 8$  Hz, 2H, OCH<sub>2</sub>), 4.21 (dd,  $J = 11.0$  and 5.0 Hz, 1H, C6-H<sub>eq</sub>), 5.08 (s, 1H, OH), 5.41 (d,  $J = 7.0$  Hz, 1H, C11a-H), 5.82 and 5.85 ( $J = 1.5$  Hz, 2H, O-CH<sub>2</sub>-O), 6.35 (s, 1H, C10-H), 6.42 (d,  $J = 8.3$  Hz, 1H, C2-H), 6.62 (s, 1H, C7-H), 6.68 (t,  $J = 7.4$  Hz, 1H, C2'-H), 7.14 (d,  $J = 8.3$  Hz, 1H, C1-H); HPLC (Chiracel-OD, n-hexane:ethanol=82:18);  $R_t = 13.51$  and 11.17 min for (-)-12 and (+)-12 resp., ee = 99.1%; Anal. Calcd. for C<sub>23</sub>H<sub>22</sub>O<sub>7</sub> (410.41): C, 67.31; H, 5.40; found C, 67.17; H, 5.52.

**(-)-3-Hydroxy-4[(E)-2-hydroxymethyl-2-buten-4-yl]-8,9-methylenedioxypterocarpan; (-)-cabeneegrin-AI [(-)-1].** 36 mg (0.99 mmol) (-)-12 was dissolved in diethyl ether, cooled to 0°C and LiAlH<sub>4</sub> (20 mg) was added in four portions. After stirring for 2 hrs the reaction mixture was poured into NH<sub>4</sub>Cl solution. The product was extracted with ethyl acetate, dried and evaporated to give an amorphous powder (30 mg) which was purified by means of preparative TLC (toluene:ethyl acetate=4:1) resulting in (-)-1 (11 mg, 31 %) as colourless prisms, m.p. 165–167°C,  $[\alpha]_D^{24} = -127$  (c=0.1 in chloroform); CD(EtOH)  $\lambda_{nm}$  ( $\Delta\epsilon$ ): 214 (-30.53), 240 (-13.31), 309 (+3.54);  $\nu_{max}$  (KBr): 3550, 1614, 1500, 1474, 1144, 1094, 1074, 1016, 940 cm<sup>-1</sup>. <sup>1</sup>H NMR: 1.22 (t, *J* = 4.4 Hz, 1H, OH), 1.76 (s, 3H, C5'-H<sub>3</sub>), 3.33 (d, *J* = 7.3 Hz, 2H, C1'-H<sub>2</sub>), 3.41 (m, *J* = 11.0, 6.5 and 5.0 Hz, 1H, C6a-H), 3.55 (dd, *J* = 11.0 and 10.9 Hz, 1H, C6-H<sub>ax</sub>), 3.92 (d, *J* = 4.4 Hz, 2H, C4'-H<sub>2</sub>), 4.22 (dd, *J* = 10.9 and 5.0 Hz, 1H, C6-H<sub>eq</sub>), 5.41 (d, *J* = 6.5 Hz, 1H, C11a-H), 4.95 (s, 1H, OH), 5.42 (t, *J* = 7.3 Hz, 1H, C2'-H), 5.82 and 5.85 (*J* = 1.4 Hz, 2H, O-CH<sub>2</sub>-O), 6.36 (s, 1H, C10-H), 6.46 (d, *J* = 8.4 Hz, 1H, C2-H), 6.64 (s, 1H, C7-H), 7.17 (d, *J* = 8.4 Hz, 1H, C1-H); <sup>13</sup>C NMR: 13.77 ((C5')), 21.84 (C1'), 40.14 (C6a), 66.71 (C6), 68.68 (C4'), 79.07 (C11a), 93.78 (C10), 101.26 (OCH<sub>2</sub>O), 104.73 (C-7), 109.60 (C2), 112.63 (C4), 115.02 (C1a), 118.03 (C7a), 123.31 (C2'), 129.15 (C1), 136.09 (C3'), 141.65 (C8), 148.06 (C9), 154.20 (C4a,10a), 155.06 (C3); MS (70eV) *m/z*, %: 368 [M<sup>+</sup>] (100), 350 (80), 335 (95), 295 (18), 175 (27). Anal. Calcd. for C<sub>21</sub>H<sub>20</sub>O<sub>6</sub> (368.36): C, 68.47; H, 5.47; found C, 68.27; H, 5.31.

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