159. Studies for a Diastereoselective Synthesis of the Tetracyclic Diterpenic Diol Stemarin: A Model Study for a New Preparation of the Key Intermediate and the Synthesis of (+)-18-Deoxystemarin

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Dedicated to Prof. *G. B. Marini-Bettolo* on the occasion of his 75th birthday

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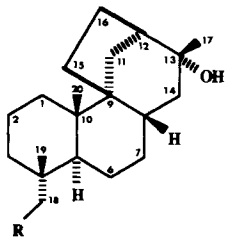
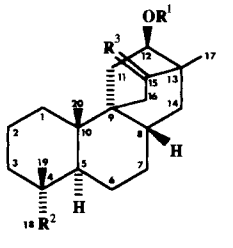
Methods for a stereoselective preparation of compounds of type **2b**, a key intermediate of a previous synthesis of the tetracyclic diterpene stemarin (**1a**), have been tested on model compounds **5a**, **5c**, and **8a**. Thus, (±)-(1*RS*,6*SR*,8*SR*,11*RS*)-11-hydroxytricyclo[6.2.2.0^{1,6}]dodecan-9-one (**5a**) was transformed by the *Mitsunobu* reaction into (±)-(1*RS*,6*SR*,8*SR*,11*SR*)-11-(benzoyloxy)tricyclo[6.2.2.0^{1,6}]dodecan-9-one (**6b**; *Scheme 2*). The latter was also obtained from (±)-(1*RS*,6*SR*,8*SR*,11*RS*)-11-[(4-toluenesulfonyloxy]tricyclo[6.2.2.0^{1,6}]dodecan-9-one (**5c**) by the action of Et_4N (PhCOO) in acetone. Compound **6b** was then converted into (±)-(1*RS*,6*RS*,8*RS*,9*RS*)-tricyclo[6.2.2.0^{1,6}]dodecan-9-ol (**8b**), a model for **2b**. Compound **8b** was also prepared from its epimer **8a** by the *Mitsunobu* reaction *via* ester **7b**. The inversion of configuration of bicyclo[2.2.2]octan-2-ols or derivates was not previously described. The model studies paved the way to the diastereoselective synthesis of (+)-18-deoxystemarin (**1b**) *via* 12β-hydroxy-13-methyl-9β,13β-ethano-9β-podocarpan-15-one (**10a**) and 13-methyl-9β,13β-ethano-9β-podocarpan-12α-ol (**11b**).

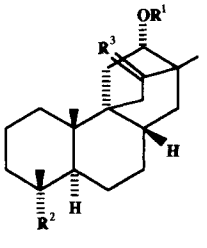
Introduction. – Having completed the synthesis of stemodin-type *Stemodia maritima* L. [1] constituents and of aphidicolin [2], we focussed our attention on another class of tetracyclic bicyclo[3.2.1]octane diterpenoids, represented by stemarin (**1a**; isolated from *Stemodia maritima* [3]) and 18-deoxystemarin (**1b**; obtained from **1a** during the work leading to its structure elucidation). Stemarin has been later synthesized in racemic form [4].



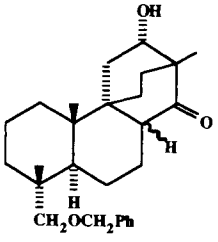
1a R = OH
b R = H



2a R^1 = H, R^2 = CO_2CH_3, R^3 = H,H
3a R^1 = H, R^2 = CO_2CH_3, R^3 = O
10a R^1 = H, R^2 = CH_3, R^3 = O
10c R^1 = Ts, R^2 = CH_3, R^3 = O
11a R^1 = H, R^2 = CH_3, R^3 = H,H
16a R^1 = COPh, R^2 = CH_3, R^3 = O
17a R^1 = COPh, R^2 = CH_3, R^3 = H,H



2b R^1 = H, R^2 = CO_2CH_3, R^3 = H,H
3b R^1 = H, R^2 = CO_2CH_3, R^3 = O
10b R^1 = H, R^2 = CH_3, R^3 = O
11b R^1 = H, R^2 = CH_3, R^3 = H,H
16b R^1 = COPh, R^2 = CH_3, R^3 = O
17b R^1 = COPh, R^2 = CH_3, R^3 = H,H



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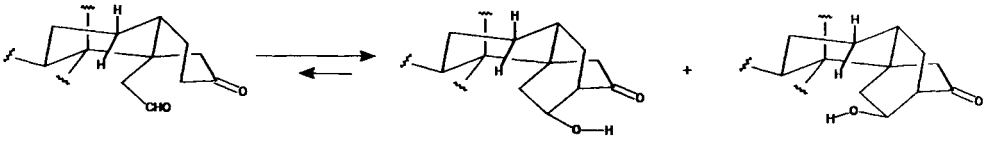
The problem of developing a new and efficient synthesis of compounds **1** is reduced to that of preparing an intermediate of type **2b**, since it has been shown [4] that the latter compound can be converted into (±)-**1a** stereospecifically and regioselectively. The reported preparation of **2b** [4], on the other hand, was not accomplished in a similarly selective manner. Thus, the development of a diastereoselective synthesis of a compound of type **2b** appeared to us to be a worthwile and challenging objective.

Our strategy for the preparation of compounds of type **2b**, is based on the fact that, under thermodynamically controlled conditions, 3-oxocyclohexane-2-ethanals of type **I** give by intramolecular aldol condensation, the '*syn*'-6-hydroxybicyclo[2.2.2]octan-2-ones of type **IIa** as major products (*Scheme 1*) [2] [4] [5]. Since precursors of type **I** may be produced *via* the *Wiesner* photochemical annellation procedure [6] starting from a suitably substituted podocarp-9(11)-en-14-one, a compound of type **2b** could be obtained by inverting the configuration of the OH group of a hydroxyketone of type **3a**[1]) or of the corresponding deoxy derivative. The inversion of configuration of those bicyclo[2.2.2]octan-2-ol intermediates, for which no methods were described in the literature, is, therefore, the key step.

Scheme 1



1 **IIa** **IIb**

Furthermore, because of the well known tendency of properly substituted bicyclo[2.2.2]octanes to rearrange to the less strained bicyclo[3.2.1]octanes, the reactivity of the leaving group should be considered. Thus, a carbonyl group adjacent to the bridgehead C-atom should prevent the development of a positive charge on that C-atom and, therefore, allow to overcome this difficulty. To this end, 6-hydroxybicyclo[2.2.2]octan-2-ones **II** seem to be also suitable.

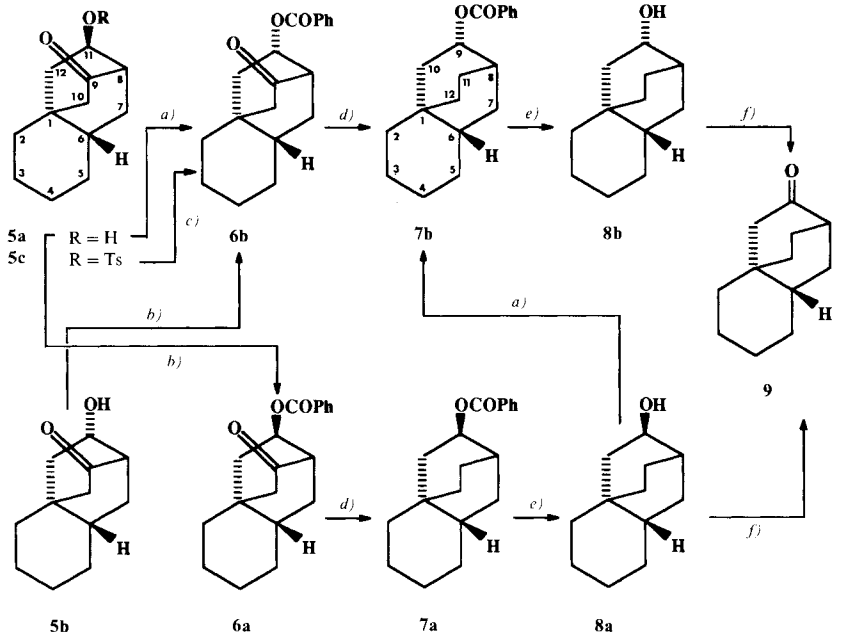
Alternatively, also in view of the empirical *Wiesner* photoaddition rule [7] and of a related precedent in the literature [8], it appears that applying the same photochemical annellation methodology to a properly substituted podocarp-8(9)-en-14-one, it should be possible to obtain a 6-hydroxybicyclo[2.2.2]octan-2-one of type **4** and then elaborate the latter into an intermediate of type **2b**.

In the present paper, we describe a model study focussing on the first approach and an application of these studies to the synthesis of optically active **1b**.

Results and Discussion. – The starting material for the model study was the known hydroxyketone **5**, obtained as an epimeric mixture at C(11) in five steps from commercially available 6-methoxy-1,2,3,4-tetrahydronaphthalene [5a]. The major epimer **5a** possesses the OH–C(9) '*syn*' to the carbonyl group. Compound **5a** was treated with diethyl

[1]) In the course of the cited synthesis of (±)-**1a**, compound **3a** was in fact obtained as a major epimer, along with **3b**. The synthesis of (±)-**1a** was then carried on with the minor epimer **3b** [4].

Scheme 2



azodicarboxylate (DEAD)/PPh_3 in the presence of benzoic acid [9] affording ester **6b** (*Scheme 2*). The latter was identical to the product prepared from the minor epimer **5b** by the action of benzoyl chloride in pyridine and different from the benzoate of **5a** obtained in the same manner. The inversion of configuration at C(11) was thus established. Whereas esters **6a** and **6b** displayed identical R_f values on TLC in several solvent systems, they could be separated by HPLC and distinguished by their ^{13}C-NMR spectra (C(11) of **6a** at 71.5 and of **6b** at 69.3 ppm).

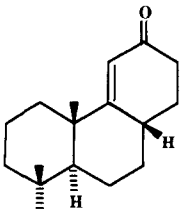
Inversion of configuration at C(11) could also be effected using a method similar to that developed by *Streitwieser* and coworkers [10] for acyclic secondary alcohols. Thus, tosylate **5c** (prepared from **5a**) was refluxed in acetone in the presence of $Et_4N(PhCOO)$ [11] to give **6b**, identical with the product obtained from the *Mitsunobu* reaction of **5a**. Deoxygenation of **6b** to **7b** was effected by *Raney*-Ni desulfurization in EtOH of the 5,5-acetal obtained from **6b** and ethanedithiol. Compound **7b** was then hydrolyzed with methanolic KOH to give **8b**, a model for **2b**. Similarly **6a** was converted into **8a**. The relationship of **8a** and **8b** was confirmed since both alcohols gave the same tricyclo-[6.2.2.$0^{1,6}$]dodecan-9-one **9** on pyridinium dichromate (PDC) oxidation in CH_2Cl_2.

When compound **8a** was submitted to the *Mitsunobu* reaction, ester **7b** was the only product obtained. Thus, the carbonyl group present in **5a**, is not essential to prevent skeletal rearrangement when *Mitsunobu* conditions are used for the inversion of bicyclo-[2.2.2]octan-2-ols, and it should be possible, in principle, to develop other methods to this end.

On successful conclusion of the model study, we applied the diastereoselective conversions **5a**→**8b**, **8a**→**7b**→**8b** and **5c**→**8b** to compounds of type **2a** or **3a** which would allow

a diastereoselective entry into the stemarin system. Hydroxy ketone **10a** [12] and its 15-deoxy derivative **11a** [12], differing from **3a** and **2a**, respectively, only for the substitution at C(18), were chosen as starting materials. But **10a** and **11a** failed to react, probably because of steric hindrance, under *Mitsunobu*'s conditions which had been effective on model compounds **5a** and **8a**. Therefore, the optically active hydroxy ketone **10a**, available in about eleven steps from the preformed system of podocarpic acid[2]), was transformed by standard methods into tosylate **10c**. The latter, on refluxing with $Et_4N(PhCOO)$ in acetone, afforded benzoate **16b**, identical in all respects with the compound obtained by direct benzoylation of hydroxy ketone **10b** and different from **16a** obtained by benzoylation of **10a**. The difference in chemical shifts (2.5 ppm) between the C(12) resonances of **10b** and **16b** was comparable with that of C(11) in the corresponding model compounds **5b** and **6b** (3 ppm), thus confirming the 12α-configuration in **16b**. *Raney*-Ni desulfurization of the 5,5-acetal from **16b** and ethanedithiol gave benzoate **17b**, and $LiAlH_4$ reduction of the latter in THF produced **11b**, which differs from **2b** only for the substitution at C(4).

Compound **11b** was refluxed in benzene in the presence of TsOH to give in high yield olefin **18b** which was converted into **1b** by the procedure described for **18a**→**1a** [4]:



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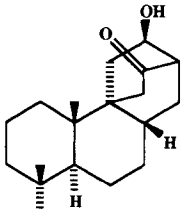

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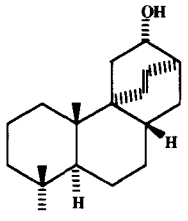

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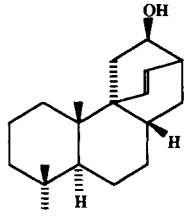

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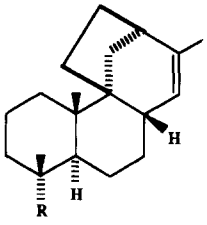
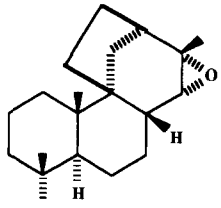


18a R = CO_2CH_3
b R = CH_3



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[2]) We previously used podocarpic acid as starting material and an analogous approach for the synthesis of 17-noraphidicolan-16-one and 17-norstemodan-16-one, *via* podocarp-9(11)-en-12-one (**12**), hydroxy ketone **13**, and bicyclo[2.2.2]oct-5-en-2-ols **14** and **15**, respectively [2a]. This approach was quite convenient since the conversion **13**→**15** was straightforward, and **13** could be diastereoselectively transformed into **14** exploiting steric hindrance in the reduction of the C=O group of **13**. These studies followed those by *Wiesner* and coworkers which culminated with the syntheses of some diterpene alkaloids [5b] [13a] [14] with bicyclo[3.2.1]octane moieties, the latter being obtained by rearrangement of a substituted bicyclo[2.2.2]octane intermediate. The basic approach described in [5] [13] [14] was later adopted also by us, who had previously the privilege to contribute to the *Wiesner* work, for the syntheses described in [2] and by other groups for the syntheses of the same or related compounds [12] [15] [16] and **1a** [4].

Thus, epoxidation of **18b** with 3-chloroperbenzoic acid at −20° in CH_2Cl_2, followed by $LiAlH_4$ reduction in THF of the resulting epoxide **19** yielded 18-deoxystemarin (**1b**).

Conclusions. – The possibility of manipulating the OH group of 6-hydroxybicyclo-[2.2.2]octan-2-ones into the '*anti*'- or '*syn*'-configuration, as confirmed by the diastereoselective synthesis of **1b**, should widen the number of terpenoids available simply and stereoselectively by the *Wiesner* photochemical method [6].

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Experimental Part

General. See [2]. Differing from that: ^{1}H- and ^{13}C-NMR: also *Varian-Gemini-200* spectrometer.

(±)-(1RS,6SR,8SR,11RS)-11-(Benzoyloxy)tricyclo[6.2.2.0^{1,6}]dodecan-9-one (**6a**). To a stirred soln. of **5a**[3]) (55 mg, 0.28 mmol) in pyridine (3 ml), benzoyl chloride (42 mg, 0.30 mmol) was added. After 15 min, H_2O (1 ml) was added and the whole stirred for additional 10 min. Et_2O (50 ml) was then added, the aq. layer separated and the org. one washed with 2N HCl, H_2O, $NaHCO_3$ soln., H_2O till neutral, and brine, dried (Na_2SO_4), and evaporated. The residue was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 9:1): **6a** in 75% yield. TLC (petroleum ether (40–70°)/Et_2O 8:2): R_f (**6a**) > R_f (**5a**); I_2 chamber for visualization. M.p. (pentane) 125–127°. IR (CCl_4): 1728, 1740 (sh). ^{1}H-NMR ($CDCl_3$): 1.94 (*dd*, *J* = 3, 19, 1 H); 2.23 (*d*, *J* = 19, 1H); 2.56 (br. *s*, 1 H); 2.72 (*m*, 1 H); 5.27 (*m*, 1 H); 7.30–7.60 (*m*, 3 H); 7.80–8.00 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 21.0, 25.8, 28.8, 30.6 (C(2), C(3), C(4), C(5)); 33.4, 36.4 (C(7), C(12)); 35.3 (C(1)); 36.2 (C(6)); 47.5 (C(8)); 52.5 (C(10)); 71.5 (C(11)); 128.5, 129.8 (C_o, C_m); 130.0 (C_{ipso}); 133.3 (C_p); 165.9 (*O*COPh); 213.8 (C(9)). MS: 105 (100), 132 (11), 149 (10), 176 (9), 193 (17), 298 (4). Anal. calc. for $C_{19}H_{22}O_3$ (298.37): C 76.48, H 7.43; found: C 77.05, H 7.55.

(±)-(1RS,6SR,8SR,11SR)-11-(Benzoyloxy)tricyclo[6.2.2.0^{1,6}]dodecan-9-one (**6b**) *from* **5a**. To a stirred soln. of **5a** (231 mg, 1.2 mmol) and PPh_3 (320 mg, 1.2 mmol) in anh. benzene (5 ml), benzoic acid (150 mg, 1.2 mmol) and diethyl azodicarboxylate (DEAD; 0.25 ml, 1.6 mmol) in anh. benzene (2 ml) were added in this order at r.t. After a few min, the reaction was complete. The solvent was evaporated and the residue purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 8:2): **6b** in 76% yield. TLC: same R_f as **6a**. HPLC (*μ-Porasil*, hexane/AcOEt 95:5, 2.0 ml/min): t_R (**6b**) 10.6 min, t_R (**6a**) 11.6 min. M.p. (pentane) 75–77°. IR (CCl_4): 1730, 1740 (sh). ^{1}H-NMR ($CDCl_3$): 2.62 (*m*, 1 H); 5.28 (*m*, 1 H); 7.38–7.62 (*m*, 3 H); 7.98–8.10 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 21.0, 25.6, 25.9, 30.0 (C(2), C(3), C(4), C(5)); 33.4, 36.5 (C(7), C(12)); 35.4 (C(1)); 37.2 (C(6)); 48.5 (C(8)); 52.4 (C(10)); 69.3 (C(11)); 128.4, 129.5 (C_o, C_m); 130.1 (C_{ipso}); 133.1 (C_p); 165.6 (*O*COPh); 213.1 (C(9)). MS: 105 (100), 132 (33), 176 (17), 193 (2), 270 (2). Anal. calc. for $C_{19}H_{22}O_3$ (298.37): C 76.48, H 7.43; found: C 76.88, H 7.58.

6b *from* **5b**. Compound **6b** was prepared from **5b**[4]) as described for the preparation of **6a** from **5a**.

(±)-(1RS,6SR,8SR,11RS)-11-[(4-Toluenesulfonyl)oxy]tricyclo[6.2.2.0^{1,6}]dodecan-9-one (**5c**). To a stirred soln. of **5a** (85 mg, 0.44 mmol) in pyridine (5 ml), TsCl (100 mg, 0.52 mmol) was added. After stirring for 18 h at r.t., H_2O (1 ml) was added, followed, after additional 10 min, by Et_2O (80 ml). The aq. layer was separated and the org. one washed with 2N HCl, H_2O, $NaHCO_3$ soln., H_2O till neutral, and brine, dried (Na_2SO_4), and evaporated. The

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[3]) M.p. (Et_2O/CH_2Cl_2) 127–129° ([5a]: 128.5–130°). IR ($CHCl_3$): 1720, 3410, 3580. ^{1}H-NMR ($CDCl_3$): 1.87 (*dd*, *J* = 19, 3, (1 H); 2.02 (*m*, 1 H); 2.23 (*d*, *J* = 19, 1 H); 2.41 (*s*, 2 H); 2.57 (*m*, 1 H); 4.18 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 21.2, 26.0, 28.9, 30.8 (C(2), C(3), C(4), C(5)); 35.1, 36.6 (C(7), C(12)); 35.4 (C(1)); 36.3 (C(6)); 51.4 (C(8)); 52.5 (C(10)); 69.0 (C(11)); 215.8 (C(9)). MS: 91 (40), 92 (56), 105 (12), 108 (4), 134 (100), 151 (2), 194 (4).

[4]) IR ($CHCl_3$): 1718, 3410, 3600. ^{1}H-NMR ($CDCl_3$): 2.35 (*m*, 1 H); 4.20 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 21.0, 24.2, 25.8, 29.8 (C(2), C(3), C(4), C(5)); 35.4, 36.7 (C(7), C(12)); 35.5 (C(1)); 37.4 (C(6)); 52.1 (C(10)); 52.3 (C(8)); 66.3 (C(11)); 215.7 (C(9)). MS: 91 (49), 92 (42), 105 (15), 108 (32), 134 (100), 151 (30), 166 (6), 194 (14), 195 (2).

residue was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 9:1): **5c** in 90% yield. TLC (Et_2O/petroleum ether (40–70°) 1:1): R_f(**5c**) > R_f(**5a**). M.p. (pentane) 117–118.5°. IR (CCl_4): 1740. ^{1}H-NMR ($CDCl_3$): 2.42 (*s*, 3 H); 2.60 (*m*, 1 H); 4.87 (*m*, 1 H); 7.30 (*XX'* of *AA'XX'*, *J* = 8, 2 H); 7.72 (*AA'* of *AA'XX'*, *J* = 8, 2 H). MS: 91 (17), 105 (6), 119 (11), 132 (25), 134 (100), 135 (15). HR-MS: 348.1376 ($C_{19}H_{24}O_4S$, M^+, calc. 348.1395).

6b *from* **5c**. To a stirred soln. of **5c** (68 mg, 0.19 mmol) in CH_3COCH_3 (3 ml), Et_4N(PhCOO) (55 mg, 0.22 mmol) was added. After refluxing for 22 h, the soln. was cooled, diluted with Et_2O (60 ml), washed with $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. The residue was then purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 9:1): **6b** in 96% yield. TLC (petroleum ether (40–70°)/Et_2O 1:1): R_f(**6b**) > R_f(**5c**).

*(±)-(1*RS,*6*RS,*8*RS,9SR*)-Tricyclo[6.2.2.0^{1,6}]dodec-9-yl Benzoate* (**7a**). Oily compound **7a** was prepared from **6a** as described for **7b** (see below). TLC (petroleum ether (40–70°)/Et_2O 9:1). R_f (**7a**) > R_f (**6a**). IR ($CHCl_3$): 1713. ^{1}H-NMR ($CDCl_3$): 2.51 (*m*, 1 H); 5.05 (*m*, 1 H); 7.36–7.60 (*m*, 3 H); 7.98–8.10 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 20.0, 21.7, 26.2, 31.5 (C(2), C(3), C(4), C(5)); 29.2 (C(6)); 30.9 (C(1)); 32.2, 34.1, 35.3 (C(7), C(11), C(12)); 36.6 (C(8)); 37.6 (C(10)); 73.2 (C(9)); 128.4, 129.6 (C_o, C_m); 131.1 (C_{ipso}); 132.8 (C_p); 166.5 (*O*C*O*Ph). MS: 77 (83), 105 (100), 133 (53), 134 (73), 147 (7), 162 (79), 163 (11), 179 (3), 284 (2). HR-MS: 284.1778 ($C_{19}H_{24}O_2$, M^+, calc. 284.1776).

*(±)-(1*RS,*6*RS,*8*RS,*9*RS*)-Tricyclo[6.2.2.0^{1,6}]dodec-9-yl Benzoate* (**7b**). To a soln. of **6b** (100 mg, 0.34 mmol) in CH_2Cl_2 (10 ml), an excess of $HSCH_2CH_2SH$ and a catalytic amount of $BF_3 \cdot Et_2O$ were added and stirred at r.t. for 2 h (TLC: petroleum ether (40–70°)/Et_2O 9:1): R_f (**7b**) > R_f (**6b**). Then the mixture was washed with $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated. The residue was taken up in abs. EtOH (10 ml) and refluxed for 2 d in the presence of a large excess of *Raney*-Ni (*Fluka AG*; washed several times with abs. EtOH until it would ignite, after drying, on filter paper). The soln. was then filtered under vacuum through a *Celite* pad and evaporated. The residue was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 95:5): **7b** in 94% yield. Clear viscous oil. IR ($CHCl_3$): 1711. ^{1}H-NMR ($CDCl_3$): 5.15 (*m*, 1 H); 7.35–7.65 (*m*, 3 H); 8.00–8.20 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 21.9, 23.5, 26.3, 28.5 (C(2), C(3), C(4), C(5)); 29.7 (C(6)); 31.2 (C(1)); 30.9, 33.9, 34.7 (C(7), C(11), C(12)); 37.4 (C(8)); 37.8 (C(10)); 74.2 (C(9)); 128.2, 129.5 (C_o, C_m); 131.0 (C_{ipso}); 132.6 (C_p); 166.2 (*O*C*O*Ph). MS: 77 (87), 105 (100), 133 (50), 134 (58), 162 (67), 163 (10), 284 (2). HR-MS: 284.1725 ($C_{19}H_{24}O_2$, M^+, calc. 284.1776).

*(±)-(1*RS,*6*RS,*8*RS,*9*RS*)-Tricyclo[6.2.2.0^{1,6}]dodecan-9-ol* (**8b**). A soln. of **7b** (30 mg, 0.11 mmol) in 1% methanolic KOH was stirred at r.t. under N_2 until TLC (petroleum ether (40–70°)/Et_2O 6:4; R_f (**8b**) < R_f (**7b**)) indicated complete disappearance of **7b**. The mixture was then neutralized with 2N HCl, the org. solvent evaporated, and the residue thoroughly extracted with Et_2O, dried (Na_2SO_4), and evaporated to give, after CC (SiO_2, petroleum ether (40–70°)/Et_2O 6:4), oily **8b** in 72% yield, which crystallized on standing. IR ($CHCl_3$): 3440, 3618. ^{1}H-NMR ($CDCl_3$): 3.93 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 21.9, 23.8, 26.1, 27.5 (C(2), C(3), C(4), C(5)); 31.4 (C(1)); 33.1 (C(6)); 30.8, 34.6, 36.7 (C(7), C(11), C(12)); 37.4 (C(8)); 38.1 (C(10)); 70.6 (C(9)). MS: 92 (100), 105 (16), 119 (14), 134 (80), 135 (31), 136 (4). HR-MS: 180.1509 ($C_{12}H_{20}O$, M^+, calc. 180.1514).

*(±)-(1*RS,*6*RS,*8*RS,*9*SR*)-Tricyclo[6.2.2.0^{1,6}]dodecan-9-ol* (**8a**). As described for **8b**, **8a** was obtained in 75% yield as an oil which crystallized on standing. TLC (petroleum ether (40–70°)/Et_2O 1:1; 3 developments): R_f (**8a**) > R_f (**8b**). IR ($CHCl_3$): 3440, 3610. ^{1}H-NMR ($CDCl_3$): 2.34 (*m*, 1 H); 3.86 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 18.9, 21.7, 26.2, 31.6 (C(2), C(3), C(4), C(5)); 31.2 (C(1)); 32.4 (C(6)); 32.6, 35.4, 36.6 (C(7), C(11), C(12)); 36.7 (C(8)); 37.6 (C(10)); 69.5 (C(9)). MS: 41 (100), 67 (57), 91 (68), 95 (31), 120 (40), 133 (53), 162 (51), 180 (4), 181 (1). HR-MS: 180.1517 ($C_{12}H_{20}O$, M^+, calc. 180.1514).

*(±)-(1*RS,*6*RS,*8*RS*)-Tricyclo[6.2.2.0^{1,6}]dodecan-9-one* (**9**). To a soln. of **8** (20 mg, 0.11 mmol) in CH_2Cl_2 (2 ml), and excess of PDC was added and the whole stirred for 24 h. After filtration through a *Celite* pad and evaporation of the solvent, the residue was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 9:1): **9** in 80% yield. Viscous oil. TLC (petroleum ether (40–70°)/Et_2O 2:1): R_f (**9**) > R_f (**8**); 0.3% soln. of 2,4-dinitrophenylhydrazine in 2N HCl for visualization of **9**. IR (CCl_4): 1725. MS: 41 (100), 67 (56), 79 (57), 107 (23), 135 (76), 160 (13), 178 (38), 179 (5). HR-MS: 178.1392 ($C_{12}H_{18}O$, M^+, calc. 178.1358).

13-Methyl-15-oxo-9β,13β-ethano-9β-podocarpan-12β-yl 4-Toluenesulfonate (**10c**). As described for **5c**, **10c** was prepared from **10a**[5]). The crude product was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 9:1): **10c** in 90% yield. TLC (petroleum ether (40–70°)/Et_2O 2:1): R_f (**10c**) > R_f (**10a**). M.p. (pentane) 110–112°. IR (CCl_4): 1738. ^{1}H-NMR ($CDCl_3$): 0.70 (*s*, 3 H); 0.81 (*s*, 3 H); 0.85 (*s*, 3 H); 0.90 (*s*, 3 H); 2.13 (*s*, 2 H); 2.41 (*s*, 3 H); 2.63 (*m*, 1 H);

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[5]) M.p. (petroleum ether (40–70°)/Et_2O) 150–150.5° ([12]: 149°). IR (CCl_4): 1728, 3440, 3620. ^{1}H-NMR ($CDCl_3$): 0.80 (*s*, 3 H); 0.82 (*s*, 3 H); 0.90 (*s*, 3 H); 0.94 (*s*, 3 H); 2.08 ('*s*', 2 H); 2.37 (br. *s*, 1 H); 2.55 (*m*, 1 H); 3.75 (br. *d*, 1 H). ^{13}C-NMR ($CDCl_3$): 15.8, 22.1 (C(18), C(19), C(20)); 18.4, 21.8, 32.3, 33.0, 37.6, 41.8, 43.9 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(16)); 32.6, 34.0, 46.0 (C(5), C(8), C(17)); 33.4, 38.3, 43.0, 48.7 (C(4), C(9), C(10), C(13)); 73.9 (C(12)); 216.9 (C(15)).

4.63 (*dd*, J = 2.5, 9.1, 1 H); 7.31 (*XX'* of *AA'XX'*, J = 8, 2 H); 7.74 (*AA'* of *AA'XX'*, J = 8, 2 H). MS: 91 (20), 106 (26), 120 (16), 147 (7), 172 (10), 215 (10), 229 (18), 244 (72), 258 (10), 271 (32), 286 (100). HR-MS: 286.2317 ($C_{20}H_{30}O$, $[M - TsOH]^+$, calc. 286.2297).

13-Methyl-15-oxo-9β,13β-ethano-9β-podocarpan-12α-yl Benzoate (**16b**) *from* (**10b**). As described for **6a** from **5a**, **16b** was prepared from **10b**[6]). Purification of the crude product by CC (SiO_2, petroleum ether (40–70°)/Et_2O 9:1) gave **16b** in 75% yield. TLC (Et_2O/petroleum ether (40–70°) 8:2): R_f (**16b**) > R_f (**10b**). M.p. (pentane) 182–182.5°. IR (CCl_4): 1732. ^{1}H-NMR ($CDCl_3$): 0.80 (*s*, 6 H); 0.93 (*s*, 3 H); 0.96 (*s*, 3 H); 2.12 (*s*, 2 H); 4.95 (*d*, J = 8.5, 1 H); 7.40–7.70 (*m*, 3 H); 8.00–8.20 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 15.5, 15.8, 22.0 (C(18), C(19), C(20)); 18.3, 21.9, 30.7, 31.2, 32.8, 41.6, 44.0 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(16)); 33.0, 38.5, 41.9, 47.2 (C(4), C(9), C(10), C(13)); 32.6, 33.8, 45.6 (C(5), C(8), C(17)); 72.7 (C(12)); 128.6, 128.9, 129.6, 130.3 (C_o, C_m); 130.6 (C_{ipso}); 133.2 (C_p); 166.0 (*O*C*O*Ph); 215.1 (C(15)). MS: 105 (57), 176 (6), 244 (19), 286 (100), 287 (26), 364 (26), 390 (1), 408 (1), 409 (1). HR-MS: 408.2658 ($C_{27}H_{36}O_3$, M^+, calc. 408.2664).

13-Methyl-15-oxo-9β,13β-ethano-9β-podocarpan-12β-yl Benzoate (**16a**) *from* **10a**. Oily **16a** was obtained in 93% yield from **10a** as described for **16b**. TLC (petroleum ether (40–70°)/Et_2O 1:1): R_f (**16a**) > R_f (**10a**). IR (CCl_4): 1730. ^{1}H-NMR ($CDCl_3$): 0.81 (*s*, 3 H); 0.84 (*s*, 3 H); 0.94 (*s*, 3 H); 0.99 (*s*, 3 H); 2.21 (*s*, 2 H); 2.85 (*dd*, 1 H); 5.07 (*dd*, J = 9.2, 3, 1 H); 7.30–7.60 (*m*, 3 H); 7.80–8.00 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 15.9, 16.1, 22.2 (C(18), C(19), C(20)); 18.3, 21.8, 31.1, 32.3, 33.5, 37.6, 41.6, 43.9 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(16)); 33.0, 38.4, 43.1, 46.5 (C(4), C(9), C(10), C(13)); 32.5, 33.9, 45.8 (C(5), C(8), C(17)); 76.5 (C(12)); 128.5, 129.7 (C_o, C_m); 129.9 (C_{ipso}); 133.3 (C_p); 166.1 (*O*C*O*Ph); 215.1 (C(15)). MS: 77 (11), 105 (67), 244 (71), 286 (100), 303 (65), 364 (43), 408 (53). HR-MS: 408.2659 ($C_{27}H_{36}O_3$, M^+, calc. 408.2664).

16b *from* **10c**. As described for **6b** from **5c**, **16b** was prepared from **10c**. The crude product was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 9:1): **16b** in 96% yield. TLC (petroleum ether (40–70°)/Et_2O 1:1): R_f (**16b**) > R_f (**10c**).

13-Methyl-9β,13β-ethano-9β-podocarpan-12α-yl Benzoate (**17b**). As described for **7b**, **17b** was prepared from **10b**. The crude product was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 95:5): **17b** in 94% yield. Clear viscous oil. IR (CCl_4): 1721. ^{1}H-NMR ($CDCl_3$): 0.78 (*s*, 3 H); 0.79 (*s*, 3 H); 0.80 (*s*, 3 H); 0.90 (*s*, 3 H); 4.86 (*m*, 1 H); 7.38–7.60 (*m*, 3 H); 8.00–8.15 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 15.5, 24.0 (C(18), C(19), C(20)); 18.6, 22.2, 25.3, 30.6, 31.4, 32.0, 32.8, 35.8, 41.9 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(15), C(16)); 30.9, 33.1, 38.7, 38.8 (C(4), C(9), C(10), C(13)); 33.0, 34.0, 46.4 (C(5), C(8), C(17)); 77.6 (C(12)); 128.5, 129.6 (C_o, C_m); 131.1 (C_{ipso}); 132.8 (C_p); 166.6 (*O*C*O*Ph). MS: 105 (16), 116 (28), 118 (28), 190 (16), 244 (35), 257 (25), 272 (100), 273 (27), 274 (3). HR-MS: 272.2509 ($C_{20}H_{32}$, $[M - PhCOOH]^+$, calc. 272.2504).

13-Methyl-9β,13β-ethano-9β-podocarpan-12α-ol (**11b**). To a stirred soln. of **17b** (75 mg, 0.27 mmol) in THF (5 ml), $LiAlH_4$ was added in excess at 0°. When the reaction was complete, the mixture was hydrolyzed with aq. NH_4Cl soln., extracted several times with $CHCl_3$, the extract washed with brine, dried (Na_2SO_4), and evaporated and the residue purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 4:1): **11b** in 48% yield. TLC (Et_2O/petroleum ether (40–70°) 8:2): R_f (**11**) < R_f (**17b**). M.p. (pentane) 82–83°. IR (CCl_4): 3630. ^{1}H-NMR ($CDCl_3$): 0.74 (*s*, 3 H); 0.79 (*s*, 3 H); 0.80 (*s*, 3 H); 0.86 (*s*, 3 H); 3.495 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 15.6, 23.8 (C(18), C(19), C(20)); 18.6, 22.2, 25.3, 31.7, 32.1, 32.5, 33.0, 34.7, 42.1 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(15), C(16)); 31.9, 33.1, 38.7, 38.9 (C(4), C(9), C(10), C(13)); 32.8, 34.1, 46.3 (C(5), C(8), C(17)); 74.6 (C(12)). MS: 41 (20), 55 (15), 69 (16), 81 (17), 95 (17), 123 (27), 134 (15), 187 (45), 206 (26), 229 (21), 245 (65), 257 (69), 272 (88), 290 (100), 291 (22). HR-MS: 290.2596 ($C_{20}H_{34}O$, M^+, calc. 290.2610).

Stemar-13-ene (= *13-Methyl-9β,12β-ethano-9β-podocarp-13-ene;* **18b**). A soln. of **11b** (85 mg, 0.29 mmol) in anh. benzene (10 ml) was refluxed for 3 h in the presence of a catalytic amount of TsOH. After cooling to r.t., the mixture was diluted with Et_2O, washed with $NaHCO_3$, soln. H_2O, and brine, dried (Na_2SO_4), and evaporated. The residue was purified by CC (SiO_2, petroleum ether/Et_2O 99:1): **18b** in 96% yield. Oil. TLC (petroleum ether (40–70°)/Et_2O 98:2): R_f (**18b**) > R_f (**11b**). ^{1}H-NMR ($CDCl_3$): 0.80 (*s*, 3 H); 0.82 (*s*, 3 H); 0.93 (*s*, 3 H); 1.60 (*t*, J = 1.4, 3 H); 2.16 (*t*, J = 4, 1 H); 4.93 ('*d*', 1 H). ^{13}C-NMR ($CDCl_3$): 16.4, 21.8, 22.1 (C(18), C(19), C(20)); 22.0, 18.5, 29.6, 31.4, 31.6, 32.2, 33.1, 42.3 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(15), C(16)); 33.2, 38.6, 50.8 (C(4), C(9), C(10)); 33.7, 43.0, 44.2, 48.9 (C(5), C(8), C(12), C(17)); 124.1 (C(14)); 138.8 (C(13)). MS: 187 (7), 229 (20), 257 (100), 258 (20), 272 (61), 273 (13). HR-MS: 272.2502 ($C_{20}H_{32}$, M^+, calc. 272.2504).

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[6]) M.p. (petroleum ether (40–70°)/Et_2O) 214–215° ([12]: 215°). IR (CCl_4): 1725, 3420, 3630. ^{1}H-NMR ($CDCl_3$): 0.80 (*s*, 3 H); 0.83 (*s*, 3 H); 0.90 (*s*, 3 H); 0.91 (*s*, 3 H); 3.65 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 15.5, 15.6, 22.1 (C(18), C(19), C(20)); 18.4, 21.9, 31.1, 31.6, 32.8, 41.8, 43.8 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(16)); 33.0, 33.9, 45.6 (C(5), C(8), C(17)); 32.1, 38.4, 41.9, 49.0 (C(4), C(9), C(10), C(13)); 70.2 (C(12)); 217.8 (C(15)).

13α,14α-Epoxystemarane (= *13α,14α-Epoxy-13β-methyl-9β,12β-ethano-9β-podocarpane*; **19**). A soln. of **18b** (30 mg, 0.11 mmol) and 3-chloroperbenzoic acid (50 mg, 0.29 mmol) in anh. CH_2Cl_2 (2 ml) was stirred at −20° for 2 h. The mixture was then diluted with CH_2Cl_2, washed with a Na_2SO_3 soln., H_2O, and brine, dried (Na_2SO_4), and evaporated. The residue was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 98:2): **19** in 73% yield. Oil. TLC (petroleum ether (40–70°)/Et_2O 9:1): R_f (**19**) < R_f (**18b**). IR (CCl_4): 1120. ^{1}H-NMR ($CDCl_3$): 0.79 (*s*, 3 H); 0.81 (*s*, 3 H); 0.88 (*s*, 3 H); 1.27 (*s*, 3 H); 2.22 (*t*, *J* = 4.7, 2 H); 2.75 (*dd*, *J* = 1, 5.1, 1 H). ^{13}C-NMR ($CDCl_3$): 16.4, 20.1, 22.2 (C(18), C(19), C(20)); 18.4, 21.0, 25.1, 27.7, 28.3, 31.8, 32.1, 42.2 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(15), C(16)); 33.1, 38.3, 49.4 (C(4), C(9), C(10)); 33.5, 41.1, 42.3, 48.4 (C(5), C(8), C(12), C(17)); 61.3, 61.4 (C(13), C(14)). MS: 93 (6), 107 (11), 135 (8), 175 (7), 217 (12), 247 (30), 260 (19), 288 (100), 289 (29). HR-MS: 288.2459 ($C_{20}H_{32}O$, M^+, calc. 288.2453).

Stemaran-13α-ol (= *13β-Methyl-9β,12β-ethano-9β-podocarpan-13α-ol*; **1b**). To a soln. of **19** (35 mg, 0.12 mmol) in anh. THF (10 ml), $LiAlH_4$ (40 mg) was added portionwise and the mixture stirred at r.t. for 15 h. Excess $LiAlH_4$ was then quenched with wet Et_2O and the mixture filtered through a *Celite* pad. The soln. was evaporated and the residue taken up with $CHCl_3$. The org. soln. was washed with H_2O and brine, dried (Na_2SO_4), and evaporated. The residue was purified by CC (SiO_2, petroleum ether (40–70°)/Et_2O 95:5): **1b** in 68% yield, which crystallized on standing. TLC (petroleum ether (40–70°)/Et_2O 8:2): R_f (**1b**) < R_f (**19**). $[\alpha]_D^{18}$ = +10.8 (*c* = 1.2, CH_2Cl_2). IR (CCl_4): 3620. ^{1}H-NMR ($CDCl_3$): 0.77 (*s*, 3 H); 0.81 (*s*, 3 H); 0.88 (*s*, 3 H); 1.11 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 16.3, 21.9, 29.5 (C(18), C(19), C(20)); 18.8, 22.6, 26.7, 26.8, 29.3, 30.7, 32.0, 39.5, 42.3 (C(1), C(2), C(3), C(6), C(7), C(11), C(14), C(15), C(16)); 29.6, 33.4, 51.4 (C(4), C(9), C(10)); 33.6, 38.7, 48.4, 48.9 (C(5), C(8), C(12), C(17)); 73.8 (C(13)). MS: 161 (6), 176 (10), 187 (11), 229 (14), 231 (24), 232 (24), 244 (10), 247 (8), 257 (35), 258 (7), 272 (100), 273 (24), 275 (37), 276 (8), 290 (42), 291 (10). HR-MS: 290.2619 ($C_{20}H_{34}O$, M^+, calc. 290.2610).

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