Superacid-Catalyzed Cyclization of Methyl (6*Z*)-Geranylfarnesoates

by **Marina Grinco**[a]), **Veaceslav Kulciţki**[a]), **Nicon Ungur**[a]), **Wieslaw Jankowski**[b]), **Tadeusz Chojnacki**[b]), and **Pavel F. Vlad***[a])

[a]) Institutul de Chimie al Academiei de Ştiinţe a Moldovei, str. Academiei, 3, MD 2028, Chişinău, Republic of Moldova (phone/fax: +373-22-739-775; e-mail: vlad_p@mail.md)

[b]) Institute of Biochemistry and Biophysics, Polish Academy of Sciences, A. Pawiñskiego 5a, 02-106 Warszawa, Poland

Methyl (2*Z*,6*Z*,10*E*,14*E*)- (**3**) and methyl (2*E*,6*Z*,10*E*,14*E*)-geranylfarnesoate (**4**) were prepared, and then individually cyclized in the presence of the superacid FSO_3H. In the case of substrate **3**, the scalaranic ester **9** (26%) and the cheilanthanic ester **10** (39%) were isolated. Under the same conditions, substrate **4** afforded a mixture of the corresponding stereoisomers **11** (25%) and **12** (63%). The observed product selectivity supports that the internal, (6*Z*)-configured C=C bond in these and other biologically relevant substrates plays an essential role in the cyclization process.

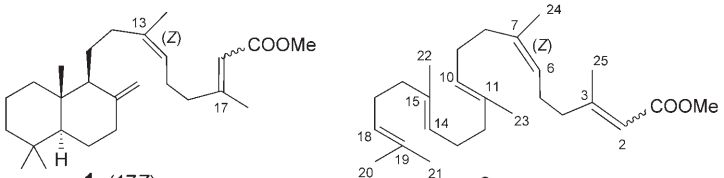
Introduction. – Prenols represent a large class of natural, linear isoprenoids that occur abundantly in plant kingdom. Their diversity is due to the (*E*/*Z*)-configuration of the C=C bonds and their chain length, which may vary from two (in monoterpenols) to several thousand (in natural rubber) isoprene units [1]. Terpenols with short chain lengths (up to five isoprene units) having all their C=C bonds in (*E*)-configuration are regarded as biogenetic precursors of the corresponding cyclic isoprenoids. Based on this notion, many biomimetic syntheses of cyclic terpenoids have been elaborated, which turned out to serve not only as demonstrations of the biogenetic origin of cyclic isoprenoids, but also as very efficient synthetic tool for their *in vitro* preparation. Superacid-catalyzed cyclization of regular-structured, short-chain terpenoids is one of the most-successful biomimetic procedures to establish a link between the cyclic compounds and their aliphatic precursors [2].

Biomimetic cyclization of long-chain polyprenols has also been investigated, and successful attempts of both enzymatic [3] and superacidic [4] cyclization have been reported; but only prenols with (all-*E*)-configuration have been used as substrates. On the other hand, it is known that most of the natural long-chain polyprenols possess the so-called 'di-*trans*-poly-*cis*' or 'tri-*trans*-poly-*cis*' configuration[1]). To the best of our knowledge, none of these compounds have been used as substrates for biomimetic cyclizations.

We have shown in recent papers [5][6] that the presence of an internal (13*Z*)-configured C=C bond in the bicyclic, stereoisomeric compounds methyl (13*Z*,17*Z*)- (**1**) and methyl (13*Z*,17*E*)-bicyclogeranylfarnesoate (**2**) influences the selectivity of the

[1]) In the older literature, *cis* and *trans* refer to (*Z*) and (*E*), resp.

cyclization process, leading to a mixture of tri- and tetracyclic products. Thereby, cyclization proceeds in a stepwise manner, involving a protonation–deprotonation sequence to provide *trans*-fused cyclic systems. Consequently, long-chain polyprenols with the 'di-' or 'tri-*trans*-poly-*cis*' configuration could be considered as potential biogenetic precursors of bi-, tri-, and tetracyclic compounds, with lateral chains of different lengths and of condensed polycyclic compounds [4]. These latter type of compounds are found in fossil sediments, and are still regarded as 'orphans' in biogenetic terms.



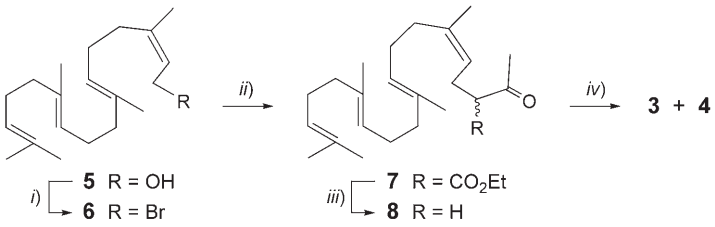
1 (17*Z*)
2 (17*E*)

3 (2*Z*)
4 (2*E*)

In the previously investigated bicyclic sesterterpenoid esters **1** and **2** [5], the lateral chain contains two isoprene units with an internal, (*Z*)-configured C=C bond. Taking into consideration that the bicyclic cores of **1** and **2** can be derived from linear precursors with (*E*,*E*)-configuration, the hypothetic precursors of these bicyclic esters could be linear sesterterpenoids with a polyprenol-like configuration of their C=C bonds. To confirm this hypothesis, we decided to synthesize the new, linear congeners **3** and **4**, and to investigate their behavior in classical superacid-catalyzed cyclization.

Results and Discussion. – The synthesis of the sesterterpenic esters **3** and **4**, based on sequential homologation [7] of (2*Z*)-geranylgeraniol (**5**)[2]) [8], is outlined in *Scheme 1*. Bromination of **5** with phosphorus tribromide (PBr_3) provided the known bromide **6** [9], which was submitted to alkylation with the Na salt of ethyl acetoacetate (=ethyl 3-oxobutanoate). The obtained keto ester **7** was decarboxylated in KOH/

Scheme 1



i) PBr_3, pyridine, Et_2O, 0° → r.t.; 97%. *ii*) $MeC(O)CH_2CO_2Et$, Na, toluene, reflux, 2 h; 87%. *iii*) 10% KOH in EtOH, reflux, 2 h; 64%. *iv*) $(MeO)_2P(O)CH_2CO_2Me$, MeONa, C_6H_6, reflux, 3 h; 82% (**3**/**4** 1:3).

[2]) For sysematic names, see *Exper. Part.*

EtOH solution upon heating. The resulting ketone **8** was 'olefinated' with trimethyl phosphonoacetate to provide a mixture of the desired esters **3** and **4**, which was separated by semipreparative HPLC to provide the pure target compounds.

We decided to investigate the superacid-catalyzed cyclization of **3** and **4**, instead of their corresponding alcohols. The reason for this was based on our earlier observation that long-chain terpenic alcohols tend to sediment at low temperature, *i.e.*, under standard conditions of superacidic cyclization. Evolving of the biphasic system also favors local temperature rises, so that elimination reactions prevail, which negatively affects both yield and selectivity of the cyclization process. Modification of the cyclization procedure, *i.e.*, changing the order of addition of the reagents (addition of substrate to a solution of the superacid), did not improve the overall performance.

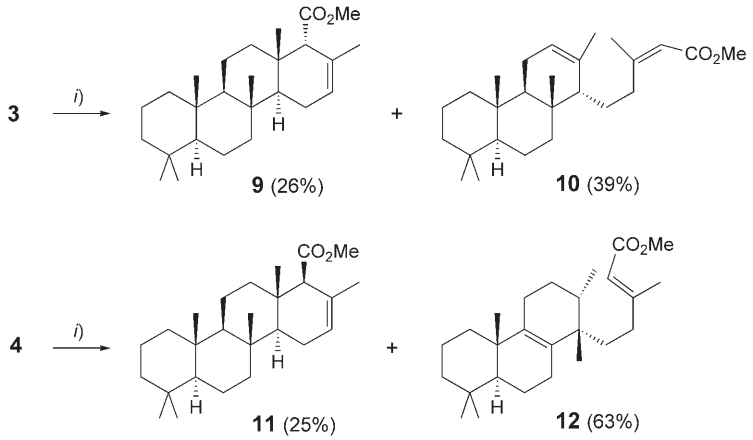
As expected, the solubility of the esters **3** and **4** at low temperature was satisfactory. Most likely, in classical prenols, H-bonding interactions in combination with the hydrophobic properties of the aliphatic chain usually gives rise to substrate precipitation at low temperature. In the case of the above two esters, the possibility of H-bonding was eliminated, and the compounds did not sediment, even at temperatures as low as $-78°$. Although esters can tolerate superacidic media at temperatures of up to $-40°$ [10], more-elevated reaction temperatures may cause selectivity problems. Therefore, we performed the cyclizations of **3** and **4** at $-78°$.

Treatment of a solution of **3** in 2-nitropropane in the presence of 5 equiv. of fluorosulfuric acid (FSO_3H) provided a product that appeared to be homogeneous according to TLC (*Scheme 2*). However, its NMR spectrum was rather complex, showing that a mixture of compounds had been obtained. At this point, we decided to separate the mixture by means of selective saponification. We have reported before the selective hydrolysis of cheilanthanic compounds in the presence of tetracyclic scalaranes [5]. Application of this procedure (10% KOH in EtOH, 2 h reflux) proved to be successful. Now, TLC showed a mixture of compounds, consisting of a non-polar spot (unsaponified ester) and a polar compound, with the characteristic tailoring on the TLC plate (acid). This hydrolysis mixture was submitted to flash chromatography on silica gel, which resulted in the isolation of two compounds. According to NMR analysis, the non-polar product was the known scalarane **9** [5][11]. The polar compound (acid), was methylated with an ethereal solution of diazomethane, and the resulting Me ester was identified by NMR as the known cheilanthane **10** [5][12]. The overall yield of the two esters **9** and **10** was *ca.* 65%, and the ratio **9**/**10** was *ca.* 2:3.

The above observed product selectivity indicates that the (6*Z*)-configured C=C bond in the original substrate **3** plays an essential role in the cyclization. Further, the above data are in agreement with our previous results on the cyclization of the bicyclic substrate **1**: Both the structures and relative amounts of the products **9** and **10** were found to be nearly identical in both cases.

The superacid-catalyzed cyclization of the congener **4**, performed under the same reaction conditions as above, also led to two products, which were submitted to selective hydrolysis. After short reflux in 5% KOH in EtOH, workup, and chromatographic separation, the scalaranic ester **11** (25%) was identified by comparison of its spectroscopic data (IR, ^{1}H- and ^{13}C-NMR) with those of an authentic sample [10–12]. The second, polar compound (acid) was methylated, and then purified by column

Scheme 2



i) 1. FSO_3H (5 equiv.), 2-nitropropane, – 78°, 15 min; 2. Et_3N.

chromatography, which afforded the rearranged cheilanthanic ester **12** (63%), as identified by spectroscopic comparison with an authentic sample [5].

Conclusions. – The present paper demonstrates that low-temperature superacidic cyclization represents an efficient method for the conversion of sesterterpenic, aliphatic (2*E*,6*Z*)- and (2*Z*,6*Z*)-configured esters to scalarane- and cheilanthane-based compounds. The presence of the internal (6*Z*)-configured C=C bond is a characteristic feature of polyprenols, which represents a large class of plant isoprenoids. The behavior of these aliphatic esters on treatment with a superacid constitutes a simulation of the biogenetic transformations of aliphatic pentaprenols into condensed polycyclic compounds found in Nature. Our results indicate that, on cyclization of sesterterpenoids, a bicyclic carbocation acts as key intermediate [13], determining the overall yield of the resulting tri- and tetracyclic products. These results provide additional support of a biogenetic relationship between long-chain polyprenols found in plants and polycyclic compounds isolated from different natural sources, including fossil sediments.

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Experimental Part

General. Workup of reaction mixtures included exhaustive extraction with Et_2O and washing neutral with H_2O, drying (Na_2SO_4), filtration, and solvent removal *in vacuo.* Thin-layer chromatography (TLC): *Merck Kieselgel 60 F-254* or *Merck RP-18 F254s* plates. The chromatograms were sprayed with 0.1% $Ce(SO_4)_2$ in 2N aq. H_2SO_4, and then heated at 80° for 5 min. Flash chromatography (FC): *Merck Kieselgel 60* (0.040–0.063 mm). HPLC: *Gilson* system, with reverse-phase (RP) *Nova-Pack* column ($MeOH/H_2O$ gradient; UV detection) or with normal-phase (NP) *Silasorb* column (1% AcOEt in hexane; RI detection). IR Spectra: *Bio-Rad FTS-7* spectrophotometer; in cm^{-1}. ^1H- and ^{13}C-NMR

Spectra: *Bruker AM-400* (400/100 MHz, resp.) and *Varian Gemini-300* (300/75 MHz, resp.) spectrometers, in $CDCl_3$ soln.; chemical shifts δ in ppm rel. to residual solvent signals ($CHCl_3$: δ(H) 7.26; δ(C) 77.0). HR-ESI-MS: *Bruker Daltonics APEX-II* mass spectrometer; in *m/z*.

(5Z,9E,13E)-Geranylgeranylacetone (= *Ethyl (4Z,8E,12E)-2-Acetyl-5,9,13,17-tetramethyloctadeca-4,8,12,16-tetraenoate*; **7**). a) To an ice-cooled soln. of (2*Z*,6*E*,10*E*)-geranylgeraniol (**5**; 527 mg, 1.82 mmol) in anh. Et_2O (31 ml) and pyridine (0.2 ml) was added a soln. of PBr_3 (0.24 ml, 2.48 mmol) in Et_2O (1.0 ml). The mixture was stirred for 2 h at 0°, and then at r.t. for 12 h. Usual workup yielded 597 mg (97%) of the crude bromide **6** (= *(2Z,6E,10E)-1-bromo-3,7,11,15-tetramethylhexadeca-2,6,10,14-tetraene*), which was used in the next step without purification.

b) To a soln. of ethyl acetoacetate (0.27 ml, 2.10 mmol) in anh. toluene (4.2 ml), Na (48 mg, 2.09 equiv.) was added under Ar atmosphere. When the Na was dissolved, a soln. of **6** (543 mg, 1.54 mmol) in anh. toluene (2.6 ml) was added. The mixture was heated at reflux for 2 h, and the reaction was then quenched by addition of H_2O (10 ml). Usual workup yielded a crude residue (1.06 g), which was purified by FC (30 g SiO_2; AcOEt/petroleum ether (PE) gradient) to afford 538.2 mg (87%) of **7**. Colorless oil. IR (film): 1730, 1710, 1440, 1230, 1140, 840. ^{1}H-NMR (400 MHz): 1.24 (*t*, *J* = 7, 3 H); 1.58 (*s*, 3 H), 1.59 (*s*, 6 H); 1.66 (*s*, 6 H); 2.03 (*m*, 12 H); 2.19 (*s*, 3 H); 2.52 (*t*, *J* = 7, 2 H); 3.39 (*t*, *J* = 7, 1 H); 4.15 (*q*, *J* = 7, 2 H); 5.00 (*t*, *J* = 7, 1 H); 5.09–5.02 (*m*, 3 H). ^{13}C-NMR (100 MHz): 14.2 (*q*); 16.0 (*q*); 16.1 (*q*); 17.7 (*q*); 23.5 (*q*); 25.7 (*q*); 26.5 (*t*); 26.7 (*t*); 26.8 (*t*); 26.8 (*t*); 29.1 (*q*); 32.0 (*t*); 39.8 (*t*); 60.1 (*t*); 61.3 (*d*); 120.4 (*d*); 123.9 (*d*); 124.3 (*d*); 124.5 (*d*); 131.3 (*s*); 135.6 (*s*); 138.6 (*s*); 169.6 (*s*); 203.1 (*s*). HR-ESI-MS. 425.3031 ($[M + Na]^+$, $C_{26}H_{42}NaO_3^+$; calc. 425.3032).

(5Z,9E,13E)-Geranylgeranylacetone (= *(5Z,9E,13E)-6,10,14,18-Tetramethylnonadeca-5,9,13,17-tetraen-2-one*; **8**). To a soln. of **7** (727 mg, 1.81 mmol) in EtOH (4.0 ml) was added 10% KOH in EtOH (8.5 ml). The mixture was heated at reflux for 2 h. After usual workup, a crude residue (597 mg) was obtained, which was purified by FC (15 g SiO_2; AcOEt/PE 3:7) to afford 382 mg (64%) of **8**. Colorless oil. IR (film): 1720, 1440, 1360, 1216, 1110, 850. ^{1}H-NMR (400 MHz): 1.57 (*s*, 9 H); 1.66 (*s*, 6 H), 1.96–1.95 (*m*, 4 H); 2.08–2.06 (*m*, 8 H); 2.10 (*s*, 3 H); 2.26–2.23 (*m*, 2 H); 2.42 (*t*, *J* = 7, 2 H); 5.10–5.03 (*m*, 4 H). ^{13}C-NMR (100 MHz): 16.0 (*q*); 16.0 (*q*); 17.5 (*q*); 17.7 (*q*); 22.3 (*t*); 23.4 (*t*); 25.7 (*q*); 26.5 (*t*); 26.7 (*t*); 26.8 (*t*); 29.9 (*q*); 31.8 (*t*); 31.9 (*t*); 39.8 (*t*); 123.3 (*d*); 124.0 (*d*); 124.2 (*d*); 124.4 (*d*); 131.3 (*s*); 135.0 (*s*); 135.4 (*s*); 136.6 (*s*); 207.8 (*s*). HR-ESI-MS. 353.2819 ($[M + Na]^+$, $C_{23}H_{38}NaO^+$; calc. 353.2820).

Methyl (2Z,6Z,10E,14E)- (**3**) *and Methyl (2E,6Z,10E,14E)-Geranylfarnesoate* (**4**). A soln. of MeONa in MeOH, prepared by dissolving Na (64.0 mg, 2.79 equiv.) in MeOH (2.7 ml), was slowly added to a stirred soln. of **8** (306 mg, 0.93 mmol) and 'trimethyl phosphonoacetate' (0.45 ml, 2.79 mmol)[3]) in benzene (15.0 ml). The mixture was heated at reflux for 3 h, cooled down, treated with ice-water (15 ml), and extracted with Et_2O (3 × 10 ml). After usual workup, the solvent was removed *in vacuo* to afford a 1:3 mixture (by ^{1}H-NMR) of **3**/**4**. Yield: 347 mg (97%). This mixture was separated by semiprep. normal-phase HPLC (1% AcOEt in hexane).

Data of **3**. Colorless, viscous oil. IR (film): 1728, 1640, 1440, 1380, 1220, 1150, 840. ^{1}H-NMR (400 MHz): 1.58 (*s*, 9 H); 1.67 (*s*, 6 H); 1.87 (*s*, 3 H); 1.97–1.95 (*m*, 4 H); 2.04 (br. *s*, 8 H); 2.18–2.13 (*m*, 2 H); 2.62 (*t*, *J* = 7.8, 2 H); 3.66 (*s*, 3 H); 5.16–5.08 (*m*, 4 H); 5.64 (*s*, 1 H). ^{13}C-NMR (75 MHz): 16.1 (*q*); 17.8 (*q*); 23. 5 (*q*); 25.5 (*q*); 25.8 (*q*); 26.7 (*q*); 26.8 (*t*); 26.9 (*t*); 29.8 (*t*); 32.0 (*t*); 33.7 (*t*); 33.8 (*t*); 39.7 (*t*); 39.8 (*t*); 50.8 (*q*); 115.9 (*d*); 124.27 (*d*); 124.3 (*d*); 124.4 (*d*); 124.5 (*d*); 131.3 (*s*); 135.0 (*s*); 135.3 (*s*); 136.0 (*s*); 160.5 (*s*); 166.8 (*s*). HR-ESI-MS: 409.3079 ($[M + Na]^+$, $C_{26}H_{42}NaO_2^+$; calc. 409.3083).

Data of **4**. Colorless, viscous oil. IR (film): 1726, 1648, 1438, 1222, 1156, 856. ^{1}H-NMR (400 MHz; selected signals): 1.58 (*s*, 9 H); 1.67 (*s*, 6 H); 1.95–2.07 (*m*, 10 H); 2.14 (br. *s*, 8 H); 3.67 (*s*, 3 H); 5.08–5.11 (*m*, 4 H); 5.66 (*s*, 1 H). ^{13}C-NMR (100 MHz): 16.0 (*q*); 16.0 (*q*); 17.7 (*q*); 18.8 (*q*); 23.4 (*q*); 25.7 (*q*); 25.8 (*t*); 26.5 (*t*); 26.6 (*t*); 26.8 (*t*); 29.7 (*t*); 32.0 (*t*); 39.7 (*t*); 41.2 (*t*); 50.8 (*q*); 115.2 (*d*); 123.6 (*d*); 124.0 (*d*); 124.2 (*d*); 124.4 (*d*); 131.2 (*s*); 135.0 (*s*); 135.4 (*s*); 136.3 (*s*); 160.1 (*s*); 167.3 (*s*). HR-ESI-MS: 409.3081 ($[M + Na]^+$, $C_{26}H_{42}NaO_2^+$; calc. 409.3083).

Cyclization of **3**. A soln. of **3** (150 mg, 0.39 mmol) in 2-nitropropane (5 ml), cooled at −78°, was treated with a pre-cooled (−78°) soln. of FSO_3H (390 mg, 3.90 mmol) in 2-nitropropane (0.9 ml) under stirring. After 15 min, the reaction was stopped by adding Et_3N (0.5 ml) in light petroleum ether (PE;

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[3]) Systematic name: methyl (dimethoxyphosphoryl)acetate ($(MeO)_2P(O)CH_2COOMe$).

0.5 ml). Usual workup afforded 147 mg of a crude residue, which was dissolved in EtOH (1 ml). Then, 10% KOH in EtOH (3 ml) was added, and the mixture was heated at reflux for 2 h. Usual workup yielded 142 mg of crude product, which was purified by FC (4.5 g SiO_2; AcOEt/PE gradient). This afforded 39.2 mg (26%) of **9**, whose IR, ^{1}H-NMR, and ^{13}C-NMR data were identical with those reported in the literature [5][10][11], together with 101.5 mg (70.2%) of an acid-containing fraction. The latter was treated with a sat. soln. of CH_2N_2 in Et_2O (3 ml). After 20 min, the solvent was removed *in vacuo*. The residue was purified by FC (3 g SiO_2; PE) to afford 100.6 mg of a mixture, which was purified by semiprep. RP-HPLC (*Nova-Pack C18*; MeOH/H_2O 95 : 5, 1.5 ml/min) to afford pure **10** (58.5 mg, 39%), as identified by comparison of its spectroscopic data (IR, ^{1}H-NMR, ^{13}C-NMR) with those reported previously [5].

Data of **9** (= *Methyl (1*R*,4a*S*,4b*R*,6a*S*,10a*S*,10b*R*,12a*S*)-1,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-2,4b,7,7,10a,12a-hexamethylchrysene-1-carboxylate*). Colorless, viscous oil. ^{1}H-NMR (300 MHz; selected signals): 0.79 (*s*, Me(20)); 0.83 (*s*, Me(21), Me(22)); 0.89 (*s*, Me(23)); 0.91 (*s*, Me(24)); 1.60 (*s*, Me(25)); 2.47 (br. *s*, H–C(18)); 3.69 (*s*, MeO); 5.58 (br. *s*, H–C(16)). ^{13}C-NMR (75 MHz): 16.5 (*q*); 17.0 (*q*); 17.4 (*q*); 18.2 (*t*); 18.6 (*t*); 21.3 (*q*); 22.4 (*q*); 22.6 (*t*); 22.9 (*t*); 33.3 (*q*); 33.4 (*s*); 36.4 (*s*); 37.4 (*s*); 37.5 (*s*); 39.2 (*t*); 39.7 (*t*); 41.6 (*t*); 42.1 (*t*); 46.7 (*d*); 51.4 (*q*); 56.1 (*d*); 60.8 (*d*); 61.9 (*d*); 124.6 (*d*); 128.5 (*s*); 174.8 (*s*). Anal. calc. for $C_{26}H_{42}O_2$: C 80.77, H 10.94; found: C 80.68, H 10.97.

Data of **10** (= *Methyl (2*Z*)-5-[(14α)-8,13-Dimethylpodocarp-12-en-14-yl]-3-methylpent-2-enoate*). Colorless, viscous oil. IR (film): 1726, 1658, 1380, 1238, 1152, 859. ^{1}H-NMR (300 MHz; selected signals): 0.84 (*s*, Me(20)); 0.88 (*s*, Me(23)); 0.887 (*s*, Me(21)); 0.893 (*s*, Me(22)); 1.71 (*s*, Me(24)); 1.91 (*s*, Me(25)); 2.53 (*ddd*, *J* = 12, 12, 6, CH_2(16)); 2.75 (*ddd*, *J* = 12, 12, 4, 1 H); 3.67 (*s*, MeO); 5.23 (br. *s*, H–C(12)); 5.63 (br. *s*, H–C(18)). ^{13}C-NMR (75 MHz): 15.6 (*q*); 18.5 (*t*); 18.6 (*t*); 21.9 (*q*); 23.1 (*t*); 23.2 (*q*); 23.4 (*q*); 25.3 (*q*); 30.4 (*t*); 33.1 (*s*); 33.6 (*q*); 35.5 (*t*); 37.1 (*t*); 37.2 (*s*); 37.2 (*s*); 40.1 (*t*); 42.0 (*t*); 47.2 (*d*); 50.7 (*q*); 54.9 (*d*); 56.5 (*d*); 115.8 (*d*); 119.7 (*d*); 136.1 (*s*); 160.3 (*s*); 166.2 (*s*). Anal. calc. for $C_{26}H_{42}O_2$: C 80.77, H 10.94; found: C 80.83, H 10.87.

Cyclization of **4**. A soln. of **4** (210 mg, 0.54 mmol) in 2-nitropropane (7 ml), cooled at −78°, was treated with a pre-cooled (−78°) soln. of FSO_3H (270 mg, 2.70 mmol) in 2-nitropropane (1.2 ml) under stirring. After 15 min, the reaction was stopped by adding Et_3N (2.5 ml) in petroleum ether (2.5 ml). Usual workup gave 207 mg of a crude residue, which was dissolved in EtOH (1.2 ml) and treated with 5% KOH in EtOH (4.5 ml). The mixture was heated at reflux for 2 h. Usual workup yielded 203 mg of crude product, which was purified by FC (5 g SiO_2; PE/AcOEt gradient). This yielded 52.5 mg (25%) of **11**, as identified by IR, ^{1}H-NMR, and ^{13}C-NMR [5][8][9], together with 128.2 mg of an acid fraction. To the latter was added a sat. soln. of CH_2N_2 in Et_2O (1 ml). After 20 min, the solvent was removed *in vacuo* to afford 133.0 mg of a residue, which was purified by FC (0.5 g SiO_2; PE) to afford 132.3 mg (63%) of **12**. The IR, ^{1}H- and ^{13}C-NMR data of **12** were identical with those reported in the literature [5].

Data of **11** (= *Methyl (1*S*,4a*S*,4b*R*,6a*S*,10a*S*,10b*R*,12a*S*)-1,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11,12,12a-Hexadecahydro-2,4b,7,7,10a,12a-hexamethylchrysene-1-carboxylate*). Colorless crystals. M.p. 166–168° (PE) (lit. 167–169° (PE) [8]). ^{1}H-NMR (400 MHz; selected signals): 0.80 (*s*, Me(20)); 0.83 (*s*, Me(21), Me(22)); 0.91 (*s*, Me(23)); 0.92 (*s*, Me(24)); 1.59 (br. *s*, Me(25)); 2.89 (br. *s*, H–C(18)); 3.66 (*s*, MeO); 5.51 (br. *s*, H–C(16)). ^{13}C-NMR (100 MHz): 15.4 (*q*); 16.4 (*q*); 16.9 (*q*); 17.5 (*q*); 18.2 (*t*); 18.6 (*t*); 21.2 (*q*); 21.4 (*t*); 22.6 (*t*); 33.2 (*q*); 33.3 (*s*); 36.3 (*s*); 37.4 (*s*); 37.7 (*s*); 39.9 (*t*); 41.8 (*t*); 41.9 (*t*); 42.1 (*t*); 51.0 (*q*); 54.8 (*d*); 56.5 (*d*); 61.3 (*d*); 62.7 (*d*); 124.1 (*d*); 128.7 (*s*); 174.4 (*s*). Anal. calc. for $C_{26}H_{42}O_2$: C 80.77, H 10.94; found: C 80.72, H 10.83.

Data of **12** (= *Methyl (2*E*)-5-[(13α,14α)-13,14-Dimethylpodocarp-8-en-14-yl]-3-methylpent-2-enoate*). Colorless crystals. M.p. 109–111° (PE) (lit. 110–111° (PE) [5]). IR (film): 1722, 1648, 1436, 1379, 1225, 1151, 865. ^{1}H-NMR (400 MHz; selected signals): 0.83 (*s*, Me(20)); 0.85 (*d*, *J* = 7, Me(24)); 0.87 (*s*, Me(21)); 0.96 (*s*, Me(22)); 1.04 (*s*, Me(23)); 2.17 (br. *s*, Me(25)); 3.67 (*s*, MeO); 5.68 (br. *s*, H–C(18)). ^{13}C-NMR (100 MHz): 14.7 (*q*); 19.2 (*q*); 19.2 (*t*); 19.4 (*t*); 19.8 (*q*); 20.0 (*t*); 21.8 (*q*); 26.1 (*t*); 26.6 (*q*); 27.2 (*t*); 33.2 (*q*); 33.2 (*s*); 34.1 (*t*); 34.7 (*d*); 35.5 (*t*); 37.0 (*t*); 38.3 (*s*); 39.0 (*s*); 41.6 (*t*); 50.6 (*q*); 51.5 (*d*); 114.6 (*d*); 130.8 (*s*); 137.3 (*s*); 162.0 (*s*); 167.3 (*s*). Anal. calc. for $C_{26}H_{42}O_2$: C 80.77, H 10.94; found: C 80.84, H 10.92.

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