# Uncommon Sesquiterpenoids and New Triterpenoids from *Jatropha neopauciflora* (Euphorbiaceae)

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Dedicated to Professor *Albert Eschenmoser* on the occasion of his 80th birthday

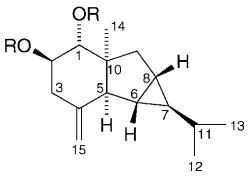
Eight new terpenoids (**1**–**8**) were isolated from the bark of *Jatropha neopauciflora*, together with eight known compounds. The new isolates include the sesquiterpenoids (1*R*,2*R*)-diacetoxycycloax-4(15)-ene (**1**); (1*R*,2*R*)-dihydroxycycloax-4(15)-ene (**2**), (2*R*)-δ-cadin-4-ene-2,10-diol (**3**), (2*R*)-δ-cadina-4,9-dien-2-ol (**4**), (1*R*,2*R*)-dihydroxyisodauc-4-en-14-ol (**5**) and its acetonide **6** (artifact), as well as the two triterpenoids (3β,16β)-16-hydroxylup-20(29)-en-3-yl (*E*)-3-(4-hydroxyphenyl)prop-2-enoate (**7**) and (3β,16β)-16-hydroxyolean-18-en-3-yl (*E*)-3-(4-hydroxyphenyl)prop-2-enoate (**8**). The structures of these compounds were established by extensive 1D- and 2D-NMR spectroscopic methods, and their *absolute* configurations were determined by circular-dichroism (CD) experiments, and by X-ray crystallographic analysis (compound **7**; *Fig. 3*). A plausible biosynthesis of the sesquiterpenoids **1**–**5** is proposed (*Scheme*), starting from (−)-germacrene D as the common biogenetic precursor.

**Introduction.** – The chemical constituents of *Jatropha* include diterpenoids with jatrophane, lathyrane, and ramnopholane skeletons, as well as lignans, cyclic peptides, and triterpenoids [1]. Some jatrophane-type diterpenes have shown relevant cytotoxic and antitumoral properties against leukemia and nasopharyngeal cells [2], and other constituents have shown antimicrobial and insecticidal activities [3].

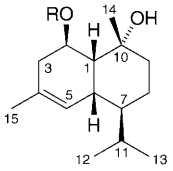
In the course of our systematic research of plants belonging to the Euphorbiaceae family, *J. neopauciflora*, an endemic plant of Mexico, was investigated. Recently, it was reported that some extracts from this plant display antibacterial activities [4]. In search of its chemical constituents, we herein report the isolation of eight new terpenoids from the dried bark of *J. neopauciflora*, the cycloax-4(15)-enes **1** and **2**, the cadinenes **3** and **4**, the isodaucenes **5** and **6**, and the pentacyclic triterpenoids **7** and **8**[2]), together with eight known compounds. Compound **4** was found to be the dehydration product of **3**, and **6** represents an artifact derived from **5**. This paper deals with the isolation and extensive structure elucidation of these compounds, which represent the first evidence of the unusual sesquiterpenoid chemistry in the Euphorbiaceae family and the high biosynthetic specificity of this species in synthesizing *cis*-fused bicyclic sesquiterpenoids. Additionally, a biosynthetic pathway is hypothesized to rationalize the biogenetic ori-

[1]) Taken, in part, from the Ph.D. thesis of *A. G.*

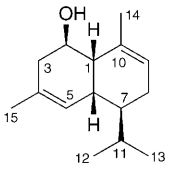
[2]) For systematic names, see *Exper. Part.*



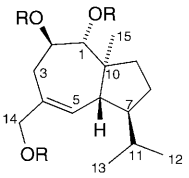
**1** R = Ac
**2** R = H
**2a** R = (*E*)-cinnamoyl



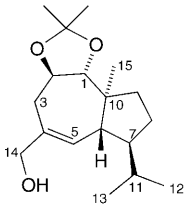
**3** R = H
**3a** R = 4-bromobenzoyl



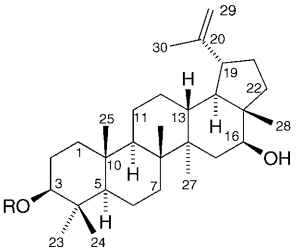
**4**



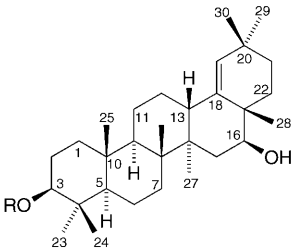
**5** R = H
**5a** R = 4-bromobenzoyl



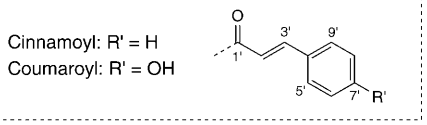
**6**



**7** R = (*E*)-*p*-coumaroyl



**8** R = (*E*)-*p*-coumaroyl




gin of the sesquiterpenoids **1**–**5** according to our results and those previously reported [5].

**Results and Discussion.** – Compound **1** was obtained as an optically active, yellow oil, with $[\alpha]_D^{25} = +23.5$. The molecular formula was deduced as $C_{19}H_{28}O_4$ by HR-FAB-MS (*m*/*z* 321.2074 ($[M+H]^+$; calc. 321.2066)). The $^{13}$C-NMR (DEPT) spectrum (*Table 1*) showed 19 signals, including seven $sp^3$ CH, one $sp^2$ $CH_2$, two $sp^3$ $CH_2$, and five Me groups, together with three $sp^2$ and one $sp^3$ quaternary C-atom(s). The IR absorptions at 1746 and 1245 $cm^{-1}$ indicated the presence of an AcO group, the absorptions at 1650 and 1040 $cm^{-1}$ suggested an *exo*-methylidene group, and those at 3076, 3017, and 1650 $cm^{-1}$ were attributed to a cyclopropyl unit. The $^1$H-NMR spectrum of **1** (*Table 1*) displayed signals for two CH (vicinal to an AcO group) at $\delta$(H) 5.38 (*d*, $J = 10.5$ Hz) and 4.84 (*ddd*, $J = 10.5$, 10.5, 5.5 Hz), which were attributed to $H_\beta$–C(1) and $H_\alpha$–C(2), respectively. In turn, $H_\beta$–C(1) and $H_\alpha$–C(2) showed long-range couplings to the C=O groups at $\delta$(C) 171.1 and 170.3, respectively. These correlated with Me groups at $\delta$(H) 2.06 and 2.01, establishing the presence of two AcO groups.

Further, $H_\alpha$–C(2) of **1** was $^1$H,$^1$H-correlated with $H_\alpha$–C(3) at $\delta$(H) 2.63 (*ddd*, $J = 13.0$, 5.5, 1.5 Hz) and with $H_\beta$–C(3) at $\delta$(H) 2.46 (*ddt*, $J = 13.0$, 11.0, 1.5 Hz), which exhibited a cross-peak to the $sp^2$-hybridized C(15) at $\delta$(C) 114.4. Thus, the $CH_2$(15) H-atoms at $\delta$(H) 4.89 (*t*, $J = 1.5$ Hz) and 4.86 (*t*, $J = 1.5$ Hz) exhibited $^3J$ corre-

Table 1. *$^1$H- and $^{13}$C-NMR Data of* **1** *and* **2**. At 500 ($^1$H) and 125 MHz ($^{13}$C); $\delta$ in ppm, $J$ in Hz. Arbitrary atom numbering (see chemical formulae).

| Position | **1** (in $CDCl_3$) | | **2** (in $C_6D_6$) | |
|---|---|---|---|---|
| | $^1$H | $^{13}$C | $^1$H | $^{13}$C |
| $H_\beta$–C(1) | 5.38 (*d*, *J* = 10.5) | 75.4 | 3.63 (*d*, *J* = 9.5)[a]) | 77.7 |
| $H_\alpha$–C(2) | 4.84 (*ddd*, *J* = 11.0, 10.5, 5.5) | 72.0 | 3.47 (*ddd*, *J* = 11.0, 9.5, 4.5)[a]) | 72.1 |
| $H_\alpha$–C(3) | 2.63 (*ddd*, *J* = 13.0, 5.5, 1.5) | 36.5 | 2.48 (*ddd*, *J* = 13.0, 5.0, 1.5) | 39.8 |
| $H_\beta$–C(3) | 2.46 (*ddt*, *J* = 13.0, 11.0, 1.5) | | 2.36 (*ddt*, *J* = 13.0, 11.0, 1.5) | |
| C(4) | | 141.4 | | 144.8 |
| $H_\alpha$–C(5) | 1.95 (*d*, *J* = 3.5) | 60.5 | 1.90 (*d*, *J* = 3.0) | 61.2 |
| $H_\beta$–C(6) | 1.18 (*dt*, *J* = 7.5, 3.5) | 31.2 | 1.06 (*dt*, *J* = 7.0, 3.5) | 32.1 |
| $H_\alpha$–C(7) | 0.55 (*dt*, *J* = 7.5, 3.0) | 47.7 | 0.41 (*dt*, *J* = 9.0, 3.0) | 48.1 |
| $H_\beta$–C(8) | 1.31–1.35 (*m*) | 24.5 | 1.08–1.13 (*m*) | 25.1 |
| $H_\beta$–C(9) | 1.88 (*dd*, *J* = 13.5, 6.5) | 42.3 | 2.45 (*dd*, *J* = 13.5, 6.0) | 42.7 |
| $H_\alpha$–C(9) | 0.90–0.93 (*m*) | | 0.91–0.94 (*m*) | |
| C(10) | | 58.4 | | 58.6 |
| $H_\alpha$–C(11) | 0.90–0.93 (*m*) | 32.1 | 0.74 (*d* × *sept.*, *J* = 8.5, 6.5) | 32.5 |
| Me(12) | 0.91 (br. *s*)[b]) | 21.8[c]) | 0.94 (*d*, *J* = 6.5) | 22.0 |
| Me(13) | 0.91 (br. *s*)[b]) | 21.6[c]) | 0.93 (*d*, *J* = 6.5) | 21.9 |
| Me(14) | 0.86 (*s*) | 17.9 | 0.91 (*s*) | 17.8 |
| $H_a$–C(15) | 4.89 (*t*, *J* = 1.5) | 114.3 | 4.78 (*d*, *J* = 1.5) | 112.6 |
| $H_b$–C(15) | 4.86 (*t*, *J* = 1.5) | | 4.78 (*d*, *J* = 1.5) | |
| 1-AcO | 2.06 (*s*) | 171.1 | | |
| 2-AcO | 2.01 (*s*) | 170.3 | | |

[a]) In the presence of $D_2O$, these signals collapsed to $\delta$(H) 2.72 (br. *s*, 2 H). [b]) Signals may be interchanged.

lations with C(3) at $\delta$(C) 36.5 and C(5) at $\delta$(C) 60.5. In the HSQC spectrum, $H_\alpha$–C(5) appeared at $\delta$(H) 1.95 (*d*, *J* = 3.5 Hz), and showed an $^1$H,$^1$H correlation with $H_\beta$–C(6) at $\delta$(H) 1.18. Thus, inspection of the $^1$H,$^1$H-COSY spectrum revealed that $H_\beta$–C(6) was part of a cyclopropyl system because of its correlations with $H_\alpha$–C(7) at $\delta$(H) 0.55 and $H_\beta$–C(8) at 1.33. The latter, in turn, correlated with $H_\beta$–C(9) at $\delta$(H) 1.88 and with $H_\alpha$–C(9) at 0.90. The uncoupled Me(14) group at $\delta$(H) 0.86 exhibited cross-peaks with C(9) ($\delta$(C) 42.3), C(1) (75.4), C(10) (58.4), and C(5) (60.5), establishing the perhydroindane skeleton of **1**.

The analysis of the COSY, HSQC, and HMBC spectra of **1** revealed an i-Pr group, based on cross-peaks between $H_\alpha$–C(7) and C(12) ($\delta$(C) 21.8) and C(13) (21.6), and due to an $^1$H,$^1$H correlation with H–C(11) ($\delta$(C) 0.90). This information indicated the presence of a cycloax-4(15)-ene-type sesquiterpenoid, as further corroborated by 1D difference homo-decoupling experiments: irradiation of $H_\alpha$–C(5) resulted in $H_\beta$–C(6) appearing as a *dd* (*J* = 7.5, 3.0 Hz), irradiation of $H_\beta$–C(6) induced $H_\alpha$–C(7) to appear similarly as a *dd* (*J* = 7.0, 3.5 Hz), and irradiation of $H_\beta$–C(8) gave rise to a *d* and a *dd* for $H_\beta$–C(9) (*J* = 12.5 Hz) and $H_\alpha$–C(7) (*J* = 7.5, 3.0 Hz), respectively.

The magnitude of the vicinal coupling constants of the cyclopropyl H-atoms did not allow us to assign the configuration of the fused three-membered ring, so the relative configuration of **1** was established with the aid of NOESY and 1D-NOE difference

spectra. Relevant NOE interactions were observed between $H_\beta$–C(1) and $H_\beta$–C(3), $H_\beta$–C(6), $H_\beta$–C(8), and $H_\beta$–C(9); between $H_\alpha$–C(5) and Me(14) as well as $H_\alpha$–C(7); and between $H_\alpha$–C(2) and $H_\alpha$–C(3) as well as Me(14), which determined the *cis*-perhydroindane fusion of **1** (*Fig. 1*). Additionally, the orientation of the i-Pr group was established by the observed interactions between H–C(11) and $H_\beta$C(6) and $H_\beta$–C(8), as shown in *Fig. 1*. The absolute configuration of **1**, determined chemically, was established as (1*R*,2*R*), since acetylation of **2** afforded **1** (see below).

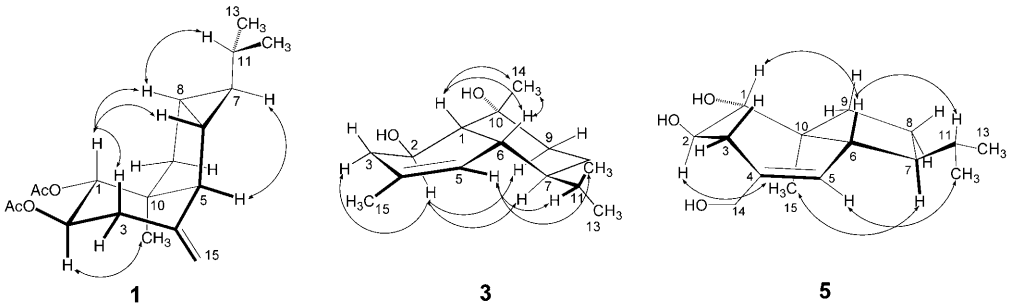



Fig. 1. *Preferred solution conformations of* **1**, **3**, *and* **5** *according to NOESY experiments*

Compound **2** had the molecular formula $C_{15}H_{24}O_2$ based on HR-FAB-MS (*m*/*z* 237.1848 ($[M+H]^+$; calc. 237.1855)), which implies four degrees of unsaturation. The $^{13}$C-NMR (DEPT) spectrum (*Table 1*) showed 15 signals, including seven $sp^3$ CH, one $sp^2$ $CH_2$, two $sp^3$ $CH_2$, and three Me groups, together with one $sp^2$ and one $sp^3$ quaternary C-atom each. The IR spectrum indicated the presence of OH groups (3379 $cm^{-1}$), an olefinic group (1647 and 1048 $cm^{-1}$), and a cyclopropyl system (3073, 3010, and 1647 $cm^{-1}$). The $^1$H-NMR spectrum of **2** (*Table 1*) displayed spin systems similar to those of **1**, except for the two AcO functions.

Inspection of the $^1$H-NMR spectrum of **2** revealed the presence of two geminal vinyl H-atoms at $\delta$(H) 4.78 ($CH_2$(15)), two oxygenated CH at $\delta$(H) 3.63 (*d*, *J* = 9.5 Hz, $H_\beta$–C(1)) and 3.47 (*ddd*, *J* = 11.0, 9.5, 4.5 Hz, $H_\alpha$–C(2)), two Me groups ($\delta$(H) 0.93 and 0.94), one H–C(11) ($\delta$(H) 0.74) due to an i-Pr functionality, and a cyclopropyl system formed by $H_\beta$–C(6)/$H_\alpha$–C(7)/$H_\beta$–C(8) at $\delta$(H) 1.06/0.41/1.10, as confirmed by $^1$H,$^1$H-COSY and HMBC correlations. Additionally, the uncoupled Me(14) group showed cross-peaks with $H_\beta$–C(9) and $H_\alpha$–C(9) at $\delta$(H) 2.45 and 0.92, respectively, with HO–C(1) at $\delta$(C) 77.7, and with C(5) at $\delta$(C) 61.2, which established the connectivity of the perhydroindane skeleton of **2**.

The relative configuration of **2** was determined by a NOESY experiment, which showed relevant interactions between $H_\beta$–C(1) and $H_\beta$–C(3), $H_\beta$–C(6), $H_\beta$–C(8), and $H_\beta$–C(9), between $H_\alpha$–C(2) and Me(14), and between $H_\alpha$–C(5) and both $H_\alpha$–C(7) and Me(14), confirming the *cis*-indane fusion, as established before for **1**. The absolute configuration of **2** was derived by circular dichroism (CD), with the aid of the exciton-chirality method of the corresponding 1,2-dibenzoate [6]. Thus, **2** was reacted with (*E*)-cinnamoyl chloride to afford the ester derivative **2a**, which exhibited a negative *Cotton* effect in the CD spectrum. The associated $\pi \rightarrow \pi^*$ intramolecular charge-transfer band at 297 nm constitutes the negative contribution between the

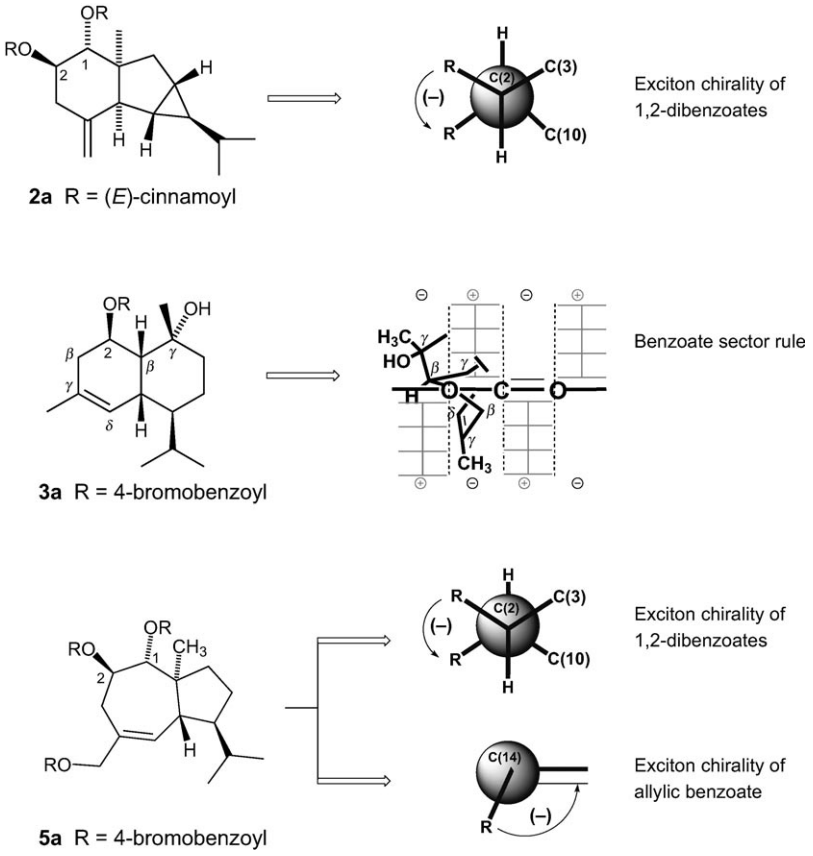



Fig. 2. *Circular-dichroism exciton-chirality method for the determination of the absolute configurations of* **2a**, **3a**, *and* **5a**

two coupled electric-dipole transition moments of the dibenzoate system of **2a**, which, according to the 'dibenzoate chirality rule' [6], corresponds to the (1*R*,2*R*) absolute configuration (*Fig. 2*).

Compound **3** had the molecular formula $C_{15}H_{26}O_2$ (*m*/*z* 239.2030 ($[M+H]^+$; calc. 239.2011)), as determined by HR-FAB-MS, and confirmed by $^{13}$C-NMR (DEPT) analysis. The IR spectrum exhibited absorption bands for OH group (3413 $cm^{-1}$) and an olefinic function (1673 and 1041 $cm^{-1}$). The $^{13}$C-NMR spectrum (*Table 2*) revealed 15 signals, which were assigned to four CH, one oxygenated CH, one $sp^2$ CH, three $CH_2$, and four Me groups, including one Me group attached to an aromatic system, together with one $sp^2$ and one $sp^3$ quaternary C-atom each. The $^1$H-NMR spectrum of **3** (*Table 2*) displayed characteristic signals for an i-Pr group [$\delta$(H) 0.82 (*d*), 0.87 (*d*), 1.90 (*m*)], an oxymethine H-atom at $\delta$(H) 4.13, and a Me group at $\delta$(H) 1.45 (*s*) attached to an oxygenated CH ($\delta$(C) 72.4). A vinylic Me group at $\delta$(C) 1.66 and a vinylic CH at $\delta$(H) 5.50 were attributed to a trisubstituted olefin, which pointed to a cadinene-type skeleton for compound **3**. The olefinic H–C(5) exhibited $^1$H,$^1$H correlations with $H_\alpha$–C(6)

Table 2. *$^1$H- and $^{13}$C-NMR Data of* **3** *and* **5**. At 500 ($^1$H) and 125 MHz ($^{13}$C), resp., in $CDCl_3$; $\delta$ in ppm, $J$ in Hz. Arbitrary atom numbering (see chemical formulae).

| Position | **3** | | Position | **5** | |
|---|---|---|---|---|---|
| | $^1$H | $^{13}$C | | $^1$H | $^{13}$C |
| $H_\beta$–C(1) | 1.58–1.62 (*m*) | 52.3 | $H_\beta$–C(1) | 3.25 (*d*, *J* = 9.0) | 87.7 |
| $H_\alpha$–C(2) | 4.13 (*ddd*, *J* = 10.5, 8.0, 6.5) | 67.3 | $H_\alpha$–C(2) | 3.57 (*ddd*, *J* = 12.0, 9.0, 3.0) | 69.5 |
| $H_\beta$–C(3) | 1.87–1.94 (*m*) | 42.7 | $CH_2$(3) | 2.39–2.49 (*m*) | 35.6 |
| $H_\alpha$–C(3) | 2.43 (*dd*, *J* = 17.5, 6.5) | – | C(4) | – | 137.7 |
| C(4) | | 131.1 | H–C(5) | 5.48 (*d*, *J* = 4.5) | 132.1 |
| H–C(5) | 5.50 (*dt*, *J* = 5.5, 2.0) | 125.1 | $H_\beta$–C(6) | 2.11 (*dd*, *J* = 9.5, 5.5) | 48.8 |
| $H_\beta$–C(6) | 2.55 (*ddd*, *J* = 10.5, 5.5, 5.0) | 36.7 | $H_\alpha$–C(7) | 1.72–1.80 (*m*) | 50.3 |
| $H_\alpha$–C(7) | 1.16–1.22 (*m*) | 44.2 | $CH_2$(8) | 1.72–1.80, 1.32–1.38 (2*m*) | 24.8 |
| $CH_2$(8) | 1.39–1.46 (*m*) | 19.7 | $CH_2$(9) | 1.94–1.98 (*m*), 1.49–1.53 (*m*) | 40.0 |
| $CH_2$(9) | 1.58–1.62 (*m*) | 35.1 | C(10) | – | 49.3 |
| C(10) | – | 72.4 | H–C(11) | 1.49–1.53 (*m*) | 32.1 |
| H–C(11) | 1.87–1.94 (*m*) | 27.1 | Me(12) | 0.88 (*d*, *J* = 6.5) | 21.9 |
| Me(12) | 0.82 (*d*, *J* = 7.0) | 15.4 | Me(13) | 0.84 (*d*, *J* = 7.0) | 19.2 |
| Me(13) | 0.87 (*d*, *J* = 7.0) | 21.5 | $CH_2$(14) | 3.95 (*s*) | 67.8 |
| Me(14) | 1.45 (*s*) | 31.3 | Me(15) | 0.96 (*s*) | 14.8 |
| Me(15) | 1.66 (*s*) | 22.9 | | | |

($\delta$(H) 2.55) and long-range couplings with C(1) ($\delta$(C) 52.3), C(3) (42.7), and C(15) (22.9). In turn, $H_\beta$–C(6) showed HMBC correlations with C(1) (δ(C) 52.3), C(2) (67.3), C(4) (131.1), and C(7) (44.2), which established the decalin skeleton of **3**.

The HSQC and HMBC correlations between Me(14) ($\delta$(H) 1.45) and C(1) ($\delta$(C) 52.3) and C(9) (35.1) allowed us to position the remaining OH function of **3** at C(10). On the basis of HMBC and COSY correlations, the signal at $\delta$(H) 1.21 was assigned to $H_\alpha$–C(7), based on its correlations with the i-Pr group. The relative configuration of **3**, determined on the basis of coupling constants and NOESY interactions, was found to be different than in its isomers khusinodiol and isokhusinodiol [7]. In this context, H–C(5) exhibited a coupling constant of 5.5 Hz, suggesting a dihedral angle H–C(5)–C(6)–H of *ca*. 50° and establishing the $\beta$-orientation of H–C(6) in a *cis*-decalin skeleton. Additionally, $H_\beta$–C(6) exhibited a pseudoaxial-axial coupling constant (10.5 Hz) with $H_\alpha$–C(7), and a pseudoaxial-equatorial one (5.0 Hz) with $H_\beta$–C(1). Finally, $H_\alpha$–C(2) showed coupling constants of 10.5, 8.5, and 6.5 Hz, indicating two *trans*-diaxial and an axial-equatorial coupling pattern (*s*), which established the $\beta$-orientation of HO–C(2) and of $H_\beta$–C(1). The NOESY interactions between $H_\alpha$–C(2) ($\delta$(H) 4.13) and $H_\alpha$–C(3) (2.43), $H_\alpha$–C(7) (1.21), and $H_\alpha$–C(9) (1.60), between $H_\beta$–C(6) ($\delta$(H) 2.55) and $H_\beta$–C(1) (1.61), and between $H_\beta$–C(1) and $\beta$-Me(14) ($\delta$(H) 1.45) further established the *cis*-decalin fusion of **3**. The observed NOESY interactions between H–C(5) and H–C(11) ($\delta$(H) 1.90) and Me(12) ($\delta$(H) 0.82) determined the relative orientation of the i-Pr group, as shown in *Fig. 1*.

The absolute configuration of **3** was determined by CD as (2*R*) by applying the 'benzoate sector rule' [8] on the basis of the observed negative molar ellipticity ($[\theta]_{252} = -9489.27$ deg cm$^2$ dmol$^{-1}$) for its 4-bromobenzoyl derivative **3a**. The observed negative *Cotton* effect is due to the dominant contribution of the $\gamma$,$\delta$-double bond to

the stereogenic C(2) center, and also due to the rotatory contribution of the $\beta,\gamma$-bond bearing the Me and OH groups (*Fig. 2*).

A check of the recovered NMR sample of **3** (in $CDCl_3$ solution) showed that it had undergone spontaneous dehydration to (2*R*)-$\delta$-cadin-4,9-diene-2-ol (**4**). This compound is a diastereoisomer of (+)-amorpha-4,9-diene-2-ol, which has a different relative configuration at C(2) and C(7) [9].

Compound **5** had the molecular formula $C_{15}H_{26}O_3$ (*m/z* 255.1967 ($[M+H]^+$; calc. 255.1960)), as deduced by HR-FAB-MS analysis. The $^{13}$C-NMR (DEPT) spectrum (*Table 2*) revealed 15 signals, including three $sp^3$ CH, one $sp^2$ CH, two oxygenated $sp^3$ CH, one oxygenated $sp^3$ $CH_2$, three $sp^3$ $CH_2$, and three Me groups, together with one $sp^3$ and one $sp^2$ quaternary C-atom. The IR spectrum of **5** showed OH absorption bands (3622 and 3457 $cm^{-1}$) and an olefinic functionality (1449 and 1046 $cm^{-1}$). The $^1$H-NMR spectrum (*Table 2*) exhibited a vinylic H-atom at $\delta$(H) 5.48 (H−C(5)), which showed allylic couplings with $H_\beta$−C(6) ($\delta$(H) 2.11) and cross-peaks with both $CH_2$(3) at $\delta$(H) 2.46 and $CH_2$(14) at 3.95. In turn, $CH_2$(3) was $^1$H,$^1$H-correlated with $H_\alpha$−C(2) ($\delta$(H) 3.57), which correlated with $H_\beta$−C(1) at $\delta$(H) 3.25. The oxymethine resonance for $H_\beta$−C(1) showed cross-peaks with an uncoupled $\alpha$-Me group at $\delta$(C) 14.8 (Me(15)), with C(10) at 49.31, and with C(6) at 48.81, which established a seven-membered ring within the sesquiterpene skeleton. The HMBC spectrum of **5** revealed long-range correlations between C(11) and both $H_\beta$−C(6) and $H_\alpha$−C(7). The characteristic methine H-atom of an i-Pr group coupled with Me(12) at $\delta$(H) 0.88 and Me(13) at 0.84. The C(8)- and C(9) atoms at $\delta$(H) 24.8 and 40.0, respectively, showed cross-peaks with H−C(11) at $\delta$(H) 1.52 and H−C(1) at 3.25, respectively, confirming the isodaucane skeleton of **5**.

The relative configuration of **5** was established by analysis of its NOESY spectrum, which showed relevant interactions between $H_\beta$−C(1) and both $H_\beta$−C(6) and $H_\beta$−C(3); between $H_\alpha$−C(2) and $\alpha$-Me(15); and between $H_\alpha$−C(7) and $\alpha$-Me(15), indicating a *trans*-fused [5.3.0]bicyclodecene. Additionally, the NOE interactions between $H_\beta$−C(6) and Me(12), and between H−C(5) and Me(12) indicated the relative orientation of the i-Pr group, as shown in *Fig. 1*. The absolute configuration of **5** was assigned to be (1*R*,2*R*) on the basis of the observed negative *Cotton* effect in the CD spectrum of its tribenzoyl derivative **5a** (*Fig. 2*). The dominant negative contributions are due to the exciton chirality of the 1,2-dibenzoate [6] and the allylic benzoate [10], as shown in *Fig. 2*. The cumulative contributions due to chiral exciton coupling between the allylic benzoate and the 1,2-dibenzoate systems were neglected. This was possible since the interchromophoric coupling angles between the allylic chromophore and the 2- and 1-benzoate, respectively, is *ca.* 35° and 0°, values that constitute only small contributions to the sign of the overall *Cotton* effect [11].

After the isolation and purification process, another compound, the acetonide **6** (*m/z* 295.2268 ($[M+H]^+$; calc. 295.2273)) was obtained as an artifact, and characterized by NMR (see *Exper. Part*).

Compound **7** had the molecular formula $C_{39}H_{56}O_4$ (*m/z* 588.4187 ($M^+$; calc. 588.4179)), as determined by HR-FAB-MS, indicating twelve degrees of unsaturation. The $^{13}$C-NMR (DEPT) spectrum (*Table 3*) showed 39 signals, including 13 CH (with six $sp^2$ and two $sp^3$ oxymethines), ten $CH_2$ (one terminal $sp^2$), and seven Me groups (one at an olefinic moiety), together with nine quaternary C-atoms (four $sp^2$ and five $sp^3$). The

IR spectrum of **7** suggested the presence of an OH group (3423 and 3143 $cm^{-1}$), an $\alpha,\beta$-unsaturated C=O group (1681 $cm^{-1}$), and an aromatic moiety (1598 and 1512 $cm^{-1}$). These data were in accord with a pentacyclic triterpenoid and an attached coumaroyl[3]) group.

The $^1$H-NMR spectrum of **7** revealed six Me *singlet*s, Me(23)–Me(28), a Me group in vinylic position ($\delta$(C) 1.79 (Me(30)) coupled with two geminal vinylic H-atoms at $\delta$(H) 4.78 and 4.94 ($CH_2$(29)), which indicated an isopropenyl functionality of a lupane-type triterpene. These assignments were inferred from long-range correlations between the vinylic H-atoms and the $sp^2$ quaternary C(20) atom at $\delta$(H) 151.1. Inspection of the $^1$H-NMR spectrum of **7** (*Table 3*) showed two oxygenated CH groups at $\delta$(H) 3.96 ($H_\alpha$–C(16)) and 4.90 ($H_\alpha$–C(3)). The low-field region of the spectrum was in accord with a coumaroyloxy function, based on two olefinic H-atoms at $\delta$(C) 6.70 ($d$, $J$ = 16.0 Hz, H–C(2′)) and 8.02 ($d$, $J$ = 16.0 Hz, H–C(3′)), an aromatic $AA'MM'$ system at $\delta$(H) 7.17 ($d$, $J$ = 9.0 Hz, H–C(6′,8′)) and 7.65 ($d$, $J$ = 9.0 Hz, H–C(5′,9′)), and an exchangeable OH H-atom at $\delta$(H) 12.3.

The information of COSY, HMQC, and HMBC spectra were combined to ascertain the location of the coumaroyloxy and OH functionalities. The key starting point were the geminal Me(23) Me(24) groups, which showed cross peaks with C(3), suggesting that this fragment was attached to C(4), a feature characteristic for most triterpenes. These two Me groups showed cross-peaks with C(5) at $\delta$(C) 56.1, which showed a third HMBC correlation with Me(25) at $\delta$(C) 16.8. In turn, $H_\alpha$–C(3) exhibited a long-range correlation with the Me groups of the $Me_2$C(4) unit, and with the C=O group at $\delta$(C) 167.4 of the coumaroyl function. The OH function was located at C(16), since $H_\alpha$–C(16) exhibited a long-range coupling with Me(28) at $\delta$(H) 12.8. Finally, both the constitution and relative configuration of **7** were confirmed by an X-ray crystal-structure analysis (*Fig. 3*).

The minor component **8** (3 mg), isolated as a colorless film, had the molecular formula $C_{39}H_{56}O_4$ ($m/z$ 589.4257 ($[M+H]^+$; calc. 589.4257)) according to HR-FAB-MS and $^{13}$C-NMR (DEPT) experiments. The $^1$H- and $^{13}$C-NMR spectra (*Table 3*) of **8** were very similar to those of **7**. However, in **8**, there was no isopropenyl group present, in contrast to the OH and coumaroyl functions. Surprisingly, we found that **8** was converted into two components, when dissolved in $CDCl_3$ and stored at room temperature for 24 h. $^1$H-NMR Analysis indicated that the major component, the one with an (*E*)-configured coumaroyl group, was in equilibrium with the corresponding (*Z*)-configured compound, giving rise to an (*E*/*Z*) mixture of 3:1[4]). Due to the low intensity and absence of some H- and C-atom signals of (*Z*)-**8**, it was not possible to assign all of its atoms. Full NMR assignment of (*E*)-**8** was possible through a combination of COSY, HMQC, and HMBC experiments, and by considering the two pairs of geminal Me groups, *i.e.*, Me(23, 24) and Me(29, 30) as starting fragments. The observed homo- and heteronuclear correlations for (*E*)-**8** were similar to those of **7**, with the coumaroyloxy group at position 3. Working in a similar fashion as for **7**, it was possible to determine that **8** had an oleanene skeleton, because the vinylic H–C(19) at $\delta$(H) 4.98 exhibited long-range couplings with Me(29) and Me(30) at $\delta$(C) 31.0 and 29.1, respectively,

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[3]) Coumaroyl = (*E*)-4-(hydroxyphenyl)prop-2-enoyl.

[4]) For a similar precedent, see [12].

Table 3. *$^1$H- and $^{13}$C-NMR Data of* **7** *and* **8**. At 500 ($^1$H) and 125 MHz ($^{13}$C), resp., $\delta$ in ppm, $J$ in Hz.

| Position | **7** (in $C_5D_5N$) | | Position | **8** (in $CDCl_3$) | |
|---|---|---|---|---|---|
| | $^1$H | $^{13}$C | | $^1$H | $^{13}$C |
| $CH_2$(1) | 1.56–1.68, 0.97–1.01 (2*m*) | 39.1 | $CH_2$(1) | 1.66–1.79, 1.06–1.10 (2*m*) | 38.7 |
| $CH_2$(2) | 1.81–1.88, 1.74–1.79 (2*m*) | 24.7 | $CH_2$(2) | 1.66–1.79, 1.00–1.04 (2*m*) | 23.8 |
| $H_\alpha$–C(3) | 4.90 (*dd*, *J* = 11.5, 4.5) | 81.0 | $H_\alpha$–C(3) | 4.62 (*dd*, *J* = 11.0, 5.5) | 80.8 |
| C(4) | | 38.7 | C(4) | | 38.1 |
| $H_\alpha$–C(5) | 0.83–0.86 (*m*) | 56.1 | $H_\alpha$–C(5) | 0.84–0.86 (*m*) | 55.6 |
| $CH_2$(6) | 1.40–1.47, 1.31–1.39 (2*m*) | 18.9 | $CH_2$(6) | 1.49–1.64, 1.34–1.45 (2*m*) | 18.2 |
| $CH_2$(7) | 1.40–1.47 (*m*) | 35.0 | $CH_2$(7) | 1.49–1.64, 1.34–1.45 (2*m*) | 34.5 |
| C(8) | | 41.7 | C(8) | | 40.7 |
| $H_\alpha$–C(9) | 1.31–1.39 (*m*) | 50.6 | $H_\alpha$–C(9) | 1.27–1.32 (*m*) | 50.5 |
| C(10) | | 37.7 | C(10) | | 37.1 |
| $CH_2$(11) | 1.81–1.88, 1.15–1.20 (2*m*) | 21.6 | $CH_2$(11) | 1.49–1.64 (*m*) | 21.1 |
| $CH_2$(12) | 1.40–1.47, 1.15–1.20 (2*m*) | 25.7 | $CH_2$(12) | 1.49–1.64 (*m*) | 25.9 |
| $H_\beta$–C(13) | 1.74–1.79 (*m*) | 38.1 | $H_\beta$–C(13) | 2.29 (br. *dd*, *J* = 8.5, 2.0) | 37.9 |
| C(14) | – | 44.6 | C(14) | – | 42.5 |
| $CH_2$(15) | 1.91–2.00, 1.56–1.68 (2*m*) | 38.3 | $CH_2$(15) | 1.66–1.79, 1.34–1.45 (2*m*) | 36.7 |
| $H_\alpha$–C(16) | 3.96 (*dd*, *J* = 11.5, 4.5) | 76.4 | $H_\alpha$–C(16) | 3.47 (*dd*, *J* = 11.5, 5.0) | 76.5 |
| C(17) | – | 50.0 | C(17) | – | 40.1 |
| $H_\alpha$–C(18) | 1.66–1.68 (*m*) | 48.7 | C(18) | – | 141.1 |
| $H_\beta$–C(19) | 2.67 (*td*, *J* = 11.0, 6.0) | 48.5 | H–C(19) | 4.98 (br. *d*, *J* = 2.0) | 132.2 |
| C(20) | – | 151.1 | C(20) | | 32.1 |
| $CH_2$(21) | 2.05–2.13, 1.56–1.68 (2*m*) | 30.8 | $CH_2$(21) | 1.34–1.45 (*m*) | 33.0 |
| $CH_2$(22) | 1.91–2.00, 1.49–1.53 (2*m*) | 39.2 | $CH_2$(22) | 1.66–1.79, 1.49–1.64 (2*m*) | 33.4 |
| Me(23) | 0.98 (*s*) | 28.6 | Me(23) | 0.89 (*s*) | 28.0 |
| Me(24) | 1.01 (*s*) | 17.4 | Me(24) | 0.92 (*s*) | 16.7 |
| Me(25) | 0.87 (*s*) | 16.8 | Me(25) | 0.93 (*s*) | 16.7 |
| Me(26) | 1.08 (*s*) | 16.6 | Me(26) | 1.10 (*s*) | 16.1 |
| Me(27) | 1.12 (*s*) | 16.9 | Me(27) | 0.79 (*s*) | 15.9 |
| Me(28) | 1.13 (*s*) | 12.8 | Me(28) | 0.99 (*s*) | 18.0 |
| $H_a$–C(29) | 4.94 (*d*, *J* = 2.0) | 110.5 | Me(29) | 0.96 (*s*) | 31.0 |
| $H_b$–C(29) | 4.94 (*d*, *J* = 2.0) | | Me(30) | 0.96 (*s*) | 29.1 |
| Me(30) | 1.79 (*s*) | 19.9 | C(4′) | – | 127.6 |
| C(4′) | – | 126.7 | H–C(5′,9′) | 7.43 (*d*, *J* = 8.5) | 129.9 |
| H–C(5′,9′) | 7.65 (*d*, *J* = 9.0) | 131.1 | H–C(6′,8′) | 6.83 (*d*, *J* = 8.5) | 115.8 |
| H–C(6′,8′) | 7.17 (*d*, *J* = 9.0) | 117.3 | C(7′) | – | 157.4 |
| C(7′) | – | 161.9 | H–C(3′) | 7.60 (*d*, *J* = 16.0) | 143.8 |
| H–C(3′) | 8.02 (*d*, *J* = 16.0) | 145.5 | H–C(2′) | 6.30 (*d*, *J* = 15.5) | 116.5 |
| H–C(2′) | 6.70 (*d*, *J* = 16.0) | 116.3 | C(1′) | – | 167.1 |
| C(1′) | – | 167.4 | | | |
| 16-OH | 5.76 (*d*, *J* = 4.0) | | | | |
| 7′-OH | 12.25 (*s*) | | | | |

with C(13) at 37.9, and with C(17) at 40.1. In turn, the HMBC spectrum showed a $^2J$ correlation between C(17) and Me(28) at $\delta$(H) 0.99, which correlated with C(16) at $\delta$(C) 76.5. The OH group was placed again at C(16) by considering the last observed correlations and cross-peaks between $H_\alpha$–C(16) at $\delta$(H) 3.47 and Me(28) at $\delta$(C) 18.0. The configurations at C(3) and C(16) were found to be $\beta$ each, and the C=C

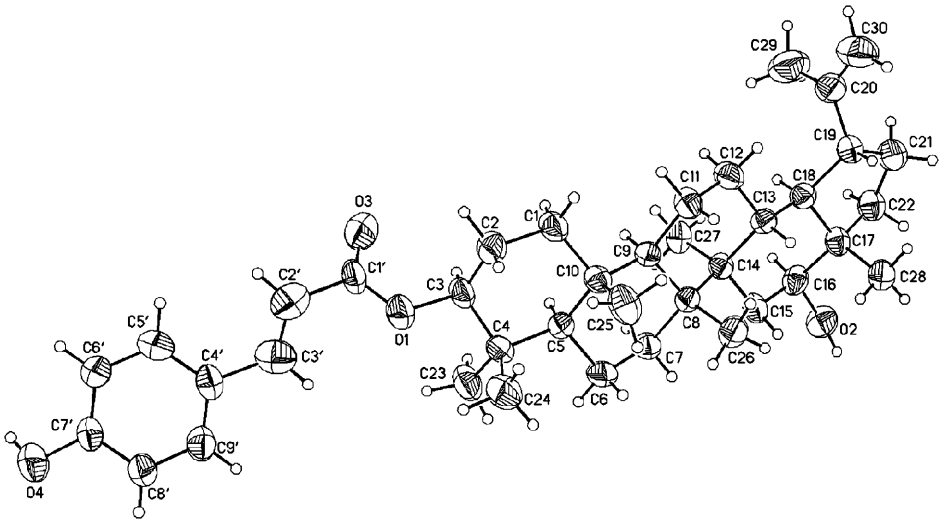


Fig. 3. *X-Ray Analysis of compound* **7** (ORTEP view)

bond was placed at C(18) of the oleane. These assignments were confirmed by NOESY interactions of $H_\alpha$–C(3) with Me(23), $H_\alpha$–C(16) with Me(27), and $H_\beta$–C(13) with both Me(26) and Me(28).

The following known compounds were also isolated from *J. neopauciflora*, and identified by comparison of their spectroscopic data with those published: $\beta$-sitosterol [13], lupeol [14], a lupeol/germanicol mixture [15], calenduladiol [16], 6,7-dimethoxycoumarin [17], 5-hydroxy-6,7-dimethoxycoumarin [18], $\beta$-sitosteryl $\beta$-D-glucopyranoside [19], and sucrose [20].

With the absolute configurations of the sesquiterpenoids **1**–**5** being known, and based on earlier considerations by *Bülow* and *König* [5], a plausible biosynthetic pathway for these compounds could start from (−)-germacrene D as the biogenetic precursor (*Scheme*). (−)-Germacrene D is first protonated to form the germacrenyl cation **A**, which, after a conformational change to **B**, allows two cyclizations through the cycloaxene cation **C** to the cycloax-4(15)-ene **D**. Then, **D** would be transformed into **1** and **2** through a sequence of hydroxylations and esterifications. Similarly, **A** might also be converted to the conformer **E**, which could cyclize to the isodaucenyl cation **F**, which, after isomerization and several hydroxylations, affords **5**. Finally, **3** and **4** may be formed by the isomerization of (−)-germacrene D. The resulting isomer is protonated to the germacrenyl cation **G**, which then isomerizes to **H**. Then, rotation of the C(1)=C(10) bond in **H** allows the cyclization to the cadinenyl cation **I**, which can be converted to **3** *via* cyclization to **J**, followed by hydroxylation, or to **4** by loss of $H^+$ and hydroxylation (not shown).

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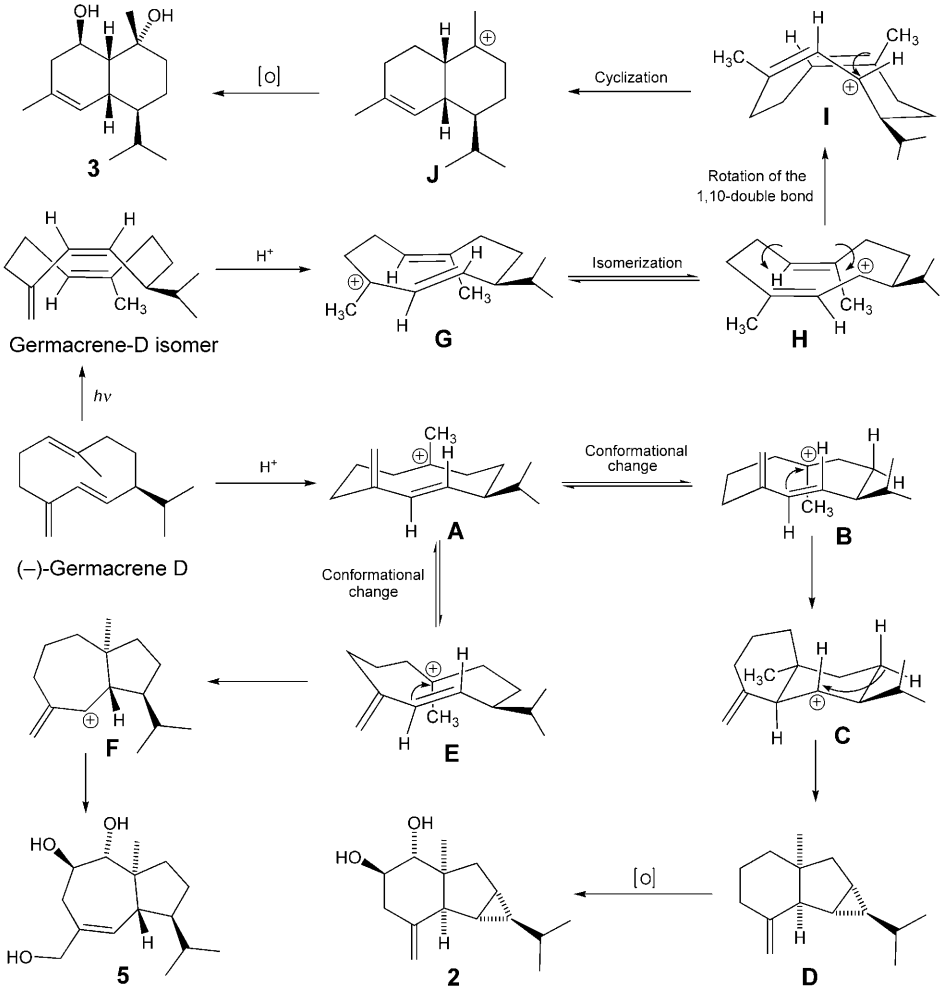
Scheme. *Hypothetical Biogenetic Pathway for the Sesquiterpenoids* **1**–**5**




## Experimental Part

*General*. Column Chromatography (CC): silica gel (70–230 and 230–400 mesh). Anal. and prep. TLC: silica gel *60* $F_{254}$ (*Merck*) plates. M.p.: *Fisher Johns* apparatus; uncorrected. UV Spectra: *Shimadzu UV-160* spectrophotometer; $\lambda_{max}$ (log $\varepsilon$) in nm. Optical rotation: *Perkin-Elmer 341* polarimeter. CD Spectra: *Jasco J720* spectropolarimeter. IR Spectra: *Nicolet Magna FT-IR 750* spectrometer; in $cm^{-1}$. $^1$H-and $^{13}$C-NMR Spectra: *Bruker ARX-500* spectrometer, at 500 and 125 MHz, resp.; $\delta$ in ppm, *J* in Hz. EI- and HR-FAB-MS: *Jeol JMS-AX505HA* and *JMX-SX102A* mass spectrometers, resp.

*Plant Material*. *J. neopauciflora* PAX was collected in Totomuchil, Estado de México on April 2003, and authenticated by Dr. Jaime Jiménez Ramírez (Facultad de Ciencias, UNAM). A voucher specimen (No. 089165) was deposited at the Herbario Facultad de Ciencias, UNAM.

*Extraction and Isolation*. The bark of *Jatropha neopauciflora* (500 g) was dried at r.t. and then repeatedly extracted (3×) with a mixture of $CH_2Cl_2$/MeOH 1:1. The crude extract (17.0 g) was dissolved in EtOH, heated at 50°, and treated with activated carbon. The obtained brown residue (10.1 g) was dis-

solved in a mixture of $CH_2Cl_2$/MeOH, adsorbed on silica gel, and subjected to CC (petroleum ether (PE), PE/$Me_2CO$, $Me_2CO$/MeOH, and MeOH): *Fractions 1–13*. *Fr. 1* and *2* contained lipidic material. *Fr. 3* (0.5 g) afforded lupeol (38 mg) and $\beta$-sitosterol (25 mg; PE/AcOEt 8:2). From *Fr. 4* (1.54 g) were obtained: a mixture of lupeol/germanicol 3:4 in the form of the acetylated derivatives (66 mg; PE/AcOEt 9:1), 6,7-dimethoxycoumarin (3.9 mg; prep. TLC, PE/$Me_2CO$ 7:3), 5-hydroxy-6,7-dimethoxycoumarin (3 mg; PE/$Me_2CO$ 6:4), and **3** (10 mg; prep. TLC, PE/$Me_2CO$ 7:3). *Fr. 5* afforded calenduladiol (4 mg; PE/$Me_2CO$ 7:3), **1** (14 mg; PE/$Me_2CO$ 8:2), **8** (3 mg; PE/$CHCl_3$/$Me_2CO$ 6:1:3), **7** (300 mg; PE/$CHCl_3$/$Me_2CO$ 6:1:3), and **2** (23 mg; PE/$Me_2CO$ 7:3). From *Fr. 6* were isolated lupeol (12 mg) and **7** (28 mg). *Fr. 7* and *8* afforded **5** (51 mg; prep. TLC, $CHCl_3$/MeOH 85:15) and **6** (15 mg; prep. TLC, PE/$CHCl_3$/$Me_2CO$ 5:2.5:2.5). *Fr. 9* and *10* afforded $\beta$-sitosteryl $\beta$-D-glucopyranoside (120 mg) and sucrose (50 mg).

*(1*R*,1a*R*,1b*S*,4*R*,5*R*,5a*S*,6a*R*)-Decahydro-5a-methyl-1-(1-methylethyl)-2-methylidenecyclopropa[*a*]-indene-4,5-diyl Diacetate* (**1**). Yellow oil. $[\alpha]_D^{25} = +23.5$ ($c = 0.085$, $CHCl_3$). IR (film): 3076, 3017, 2956, 2872, 1746, 1650, 1460, 1368, 1245, 1040, 905. $^1$H- and $^{13}$C-NMR: see *Table 1*. FAB-MS: 321 (9, $[M+H]^+$), 261 (20), 218 (17), 201 (79), 145 (100), 43 (53). HR-FAB-MS: 321.2074 ($[M+H]^+$, $C_{19}H_{29}O_4^+$; calc. 321.2066).

*(1*R*,1a*R*,1b*S*,4*R*,5*R*,5a*S*,6a*R*)-Decahydro-5a-methyl-1-(1-methylethyl)-2-methylidenecyclopropa[*a*]-indene-4,5-diol* (**2**). Transparent oil. $[\alpha]_D^{25} = +17.06$ ($c = 0.17$, MeOH). IR (film): 3379, 3073, 3010, 2955, 2929, 2872, 1647, 1462, 1379, 1048, 895, 659. $^1$H- and $^{13}$C-NMR: see *Table 1*. EI-MS: 236 (32, $M^+$), 218 (20), 203 (23), 175 (40), 161 (39), 147 (58), 139 (100), 121 (69), 105 (55), 91 (56), 41 (44). HR-FAB-MS: 237.1848 ($[M+H]^+$, $C_{15}H_{25}O_2^+$; calc. 237.1855).

*(1*R*,1a*R*,1b*S*,4*R*,5*R*,5a*S*,6a*R*)-Decahydro-5a-methyl-1-(1-methylethyl)-2-methylidenecyclopropa[*a*]-indene-4,5-diyl Dicinnamate* (**2a**). Compound **2** (7 mg) was reacted with (*E*)-cinnamoyl chloride in anh. pyridine (dried over 4-Å molecular sieves) to afford crude **2a** (1 mg), which was purified by HPLC (*Lichrosorb-5 RP-18* column, 250×4.0 mm, 5 µm; gradient elution: 1. $H_2O$/MeCN 3:7 at a flow rate of 1 ml/6 min, 2. $H_2O$/MeCN 3:7 → 1:9 at a flow of 1 ml/14 min). Colorless oil. UV ($c = 12.1$ µM, MeOH): 217 (4.40), 232 (3.69), 278 (4.59). CD ($c = 12.1$ µM, MeOH): $[\theta]_{267} = +62664$, $[\theta]_{297} = -43986$.

*(1*R*,4*S*,4a*R*,8*R*,8a*R*)*-1,2,3,4,4a,7,8,8a-*Octahydro-1,6-dimethyl-4-(1-methylethyl)naphthalene-1,8-diol* (**3**). Yellow oil. $[\alpha]_D^{25} = -34.28$ ($c = 0.07$, $CHCl_3$). IR (film): 3413, 2957, 2928, 2870, 1673, 1460, 1377, 1195, 1041. For $^1$H- and $^{13}$C-NMR data in $CDCl_3$, see *Table 2*. $^1$H-NMR (500 MHz, $C_6D_6$): 5.38 (*dt*, $J = 5.5$, 2.0, H–C(5)); 3.90 (*ddd*, $J = 11.0$, 8.5, 6.5, $H_\alpha$–C(2)); 3.24 (*s*, OH); 2.72 (*ddd*, $J = 10.5$, 5.0, 4.5, $H_\beta$–C(6)); 2.11 (*dd*, $J = 16.5$, 6.0, $H_\alpha$–C(3)); 1.96 (*d*×*sept.*, $J = 7.0$, 3.5, H–C(11)); 1.63–1.68 (*m*, $CH_2$(9), H–C(3)); 1.56 (*s*, Me(15)); 1.48 (*dd*, $J = 9.0$, 3.5, $H_\beta$–C(1)); 1.42 (*s*, Me(14)); 1.28–1.34 (*m*, $CH_2$(8)); 1.14–1.18 (*m*, H–C(7)); 0.87 (*d*, $J = 7.0$, Me(12)); 0.86 (*d*, $J = 7.0$, Me(13)). $^{13}$C-NMR (125 MHz, $C_6D_6$): 131.1 (C(4)); 125.7 (C(5)); 71.8 (C(10)); 66.9 (C(2)); 52.4 (C(1)); 44.7 (C(7)); 43.1 (C(3)); 37.0 (C(6)); 35.2 (C(9)); 32.0 (C(14)); 27.5 (C(11)); 23.0 (C(15)); 21.7 (C(13)); 20.0 (C(8)); 15.5 (C12)). FAB-MS: 239 (3, $[M+H]^+$), 154 (100), 221 (7, $[M+H-H_2O]^+$), 203 (10), 154 (100, $[M-C_{10}H_{18}O]^+$), 136 (90, $[M-C_{20}H_{34}O]^+$), 55 (98, $C_4H_7^+$), 43 (89, $C_3H_7^+$). HR-FAB-MS: 239.2030 ($[M+H]^+$, $C_{15}H_{27}O_2^+$, calc. 239.2011).

*(1*R*,4*S*,4a*R*,8*R*,8a*R*)*-1,2,3,4,4a,7,8,8a-*Octahydro-1-hydroxy-1,6-dimethyl-4-(1-methylethyl)naphthalen-8-yl 4-Bromobenzoate* (**3a**). Compound **3** (5 mg) was reacted with 4-bromobenzoyl chloride in anh. pyridine (as above) to afford **3a** (4 mg). Colorless oil. UV ($c = 47.6$ µM, MeOH): 206 (4.30), 218 (3.94), 244 (4.40). CD ($c = 47.6$ µM, MeOH): $[\theta]_{252} = -9489$.

*(1*R*,4a*R*,5*S*,8a*S*)-1,2,4a,5,6,8a-Hexahydro-3,8-dimethyl-5-(1-methylethyl)naphthalen-1-ol* (**4**). Yellow oil. $[\alpha]_D^{25} = -6.6$ ($c = 0.075$, MeOH). IR (film): 3420, 2957, 2925, 2855, 1460, 1378, 1052. $^1$H-NMR ($C_6D_6$, 500 MHz): 5.38 (*d*×*quint.*, $J = 4.5$, 1.5, H–C(9)); 5.24 (*dt*, $J = 5.0$, 1.5, H–C(5)); 3.97 (*dd*, $J = 11.5$, 5.0, $H_\alpha$–C(2)); 2.43 (br. *s*, $H_\beta$–C(6)); 2.14 (*t*, $J = 6.0$, $H_\beta$–C(1)); 2.04–2.08 (*m*, $H_\alpha$–C(3)); 1.94–2.01 (*m*, $H_\alpha$–C(8)); 1.74–1.83 (*m*, $H_\beta$–C(8)); 1.74–1.83 (*m*, H–C(11)); 1.74–1.83 (*m*, H–C(3)); 1.73 (*d*, $J = 1.5$, Me(14)); 1.56 (*s*, Me(15)); 1.28–1.33 (*m*, H–C(7)); 0.90 (*d*, $J = 6.5$, Me(13)); 0.83 (*d*, $J = 6.5$, Me(12)). $^{13}$C-NMR ($C_6D_6$, 125 MHz): 133.8 (C(10)); 131.0 (C(4)); 125.5 (C(5)); 123.1 (C(9)); 69.0 (C(2)); 43.1 (C(1)); 43.1 (C(7)); 37.9 (C(3)); 35.0 (C(6)); 27.2 (C(11)); 24.91 (C(8)); 23.7 (C(15)); 23.4 (C(14)); 21.2 (C(13)); 18.8 (C12)). EI-MS: 220 (5, $M^+$), 219 (10, $[M-1]^+$), 149 (40), 71 (70), 57 (100), 43 (60), 41 (32). HR-FAB-MS: 221.1902 ($[M+H]^+$, $C_{15}H_{25}O^+$; calc. 221.1905).

*(1*S*,3a*S*,4*R*,5*R*,8a*R*)-1,2,3,3a,4,5,6,8a-Octahydro-7-(hydroxymethyl)-3a-methyl-1-(1-methylethyl)-azulene-4,5-diol* (**5**). Yellow oil. $[\alpha]_D^{25} = -40$ ($c = 0.055$, $CHCl_3$). IR (film): 3622, 3457, 2975, 2927, 2895,

1449, 1391, 1046, 877. $^1$H- and $^{13}$C-NMR: see *Table 2*. EI-MS: 254 (4, $M^+$), 253 (3, $[M-1]^+$), 236 (50, $[M-H_2O]^+$), 193 (49), 178 (68), 175 (65), 123 (100), 95 (78), 43 (66), 41 (59). HR-FAB-MS: 255.1967 ($[M+H]^+$, $C_{15}H_{27}O_3^+$; calc. 255.1960).

*(1*S*,3a*S*,4*R*,5*R*,8a*R*)-1,2,3,3a,4,5,6,8a-Octahydro-7-(hydroxymethyl)-3a-methyl-1-(1-methylethyl)-azulene-4,5-diyl Bis(4-bromobenzoate)* (**5a**). Compound **5** (10 mg) was reacted with 4-bromobenzoyl chloride in anh. pyridine (as above) to afford **5a**. Colorless solid (8 mg). UV ($c=5.5$ μM, MeOH): 207 (4.67), 220 (4.37), 244 (4.75). CD ($c=5.5$ μM, MeOH): $[\theta]_{237}=+73587$, $[\theta]_{254}=-121296$.

*[(3a*R*,6a*R*,7*S*,9a*S*,9b*R*)-3a,4,6a,7,8,9,9a,9b-Octahydro-2,2,9a-trimethyl-7-(1-methylethyl)azuleno[4,5-*d*][1,3]dioxol-5-yl]methanol* (**6**). Yellow oil. $[\alpha]_D^{25}=-47.5$ ($c=0.12$, MeOH). IR (film): 3421, 2956, 2934, 2872, 1457, 1374, 1233, 1170, 1125, 1067, 1046, 856, 797. $^1$H-NMR (500 MHz, $C_6D_6$): 5.45 (*dd*, $J=3.5$, 1.5, H–C(5)); 3.66 (*s*, $CH_2$(14)); 3.58 (*ddd*, $J=11.0$, 8.5, 2.0, $H_\alpha$–C(2)); 3.30 (*d*, $J=9.0$, $H_\beta$–C(1)); 2.51 (*ddd*, $J=14.0$, 2.0, 1.0, $H_\alpha$–C(3)); 2.22 (*td*, $J=13.5$, 1.5, $H_\beta$–C(3)); 1.84–1.92 (*m*, H–C(6)); 1.84–1.92 (*m*, H–C(9)); 1.68–1.75 (*m*, H–C(7)); 1.52–1.58 (*m*, H–C(11)); 1.49, 1.42 (2*s*, $Me_2$C–O); 1.39–1.44 (*m*, H–C(9)); 1.29–1.35 (*m*, $CH_2$(8)); 0.91 (*s*, Me(15)); 0.87 (*d*, $J=6.5$, Me(13)); 0.80 (*d*, $J=6.5$, Me(12)). $^{13}$C-NMR (125 MHz, $C_6D_6$): 137.8 (C(4)); 129.7 (C(5)); 106.8 ($Me_2C$–O); 92.8 (C(1)); 72.5 (C(2)); 67.8 (C(14)); 49.4 (C(6)); 49.3 (C(7)); 46.4 (C(10)); 38.8 (C(9)); 31.3 (C(11)); 30.7 (C(3)); 27.5, 27.1 ($Me_2$-C–O); 24.8 (C(8)); 22.1 (C(13)); 18.5 (C(12)); 14.1 (C(15)). EI-MS: 294 ($M^+$, not obs.), 279 (13, $[M-Me]^+$), 236 (14), 219 (86), 201 (45), 81 (73), 69 (100), 55 (75), 43 (85), 28 (51), 18 (43). HR-FAB-MS: 295.2268 ($[M+H]^+$, $C_{18}H_{31}O_3^+$; calc. 295.2273).

*(3β,16β)-16-Hydroxylup-20(29)-en-3-yl (*E*)-3-(4-Hydroxyphenyl)prop-2-enoate* (**7**). Colorless powder. M.p. 288–290°. $[\alpha]_D^{25}=+33$ ($c=0.1$, pyridine). IR (KBr): 3423, 3143, 2941, 2877, 2763, 2695, 2623, 2526, 1681, 1598, 1512, 1455, 1383, 1272, 1173, 1012, 530. $^1$H- and $^{13}$C-NMR: see *Table 3*. EI-MS: 588 (17, $M^+$), 570 (21), 406 (15), 147 (100). HR-FAB-MS: 588.4187 ($M^+$, $C_{39}H_{56}O_4^+$; calc. 588.4179).

*(3β,16β)-16-Hydroxyolean-18-en-3-yl (*E*)-3-(4-Hydroxyphenyl)prop-2-enoate* (**8**). Colorless film. M.p. 275–277°. $[\alpha]_D^{25}=+32.5$ ($c=0.04$, $CHCl_3$). IR (film): 3388, 2947, 2869, 1684, 1604, 1514, 1450, 1373, 1276, 1169, 1012, 981, 757. $^1$H- and $^{13}$C-NMR: see *Table 3*. EI-MS: 588 (19, $M^+$), 570 (20), 439 (7), 424 (12), 409 (9), 353 (4), 147 (100). HR-FAB-MS: 589.4257 ($[M+H]^+$, $C_{39}H_{57}O_4^+$; calc. 589.4257).

*X-Ray Crystallography*[5]). Crystallographic measurements were made on a *Bruker Smart Apex* automatic diffractometer with a CCD area detector using graphite-monochromated Mo$K_\alpha$ (0.71073 Å) radiation. A clear, colorless prism of **7** ($C_{39}H_{56}O_4$) was slowly grown from a hot mixture of acetone/MeOH 1:9. A crystal of dimension $0.30\times0.18\times0.18$ mm was mounted on a glass fiber, fixed on a goniometer head, and then placed in the X-ray diffractometer. The *SMART 5.625* program [21] was used for centering, indexing, and data collection. Unit-cell dimensions were obtained by a least-squares fit of 5987 carefully centered reflections in the range of $1.95°\leq\theta\leq25.00°$. Cell constants corresponded to the monoclinic system $P2_1$, with cell dimensions (at 291(2) K) of $a=10.4619(8)$, $b=12.5842(9)$, $c=13.0219(9)$ Å; $V=1707(2)$ Å$^3$. For $Z=2$ and $M_r$ 588.84, the calculated density was 1.145 g/cm$^3$. Data were collected at 291(2) K using the $\omega$-scan technique. The space group was determined by considering systematic absences, packing, statistical analysis of intensity distributions, and successful solution and refinement of the structure. Data were collected to a maximum $\theta$ value of 25.00° (100% completeness to $\theta$), and no significant decay was observed. The structure was solved by direct methods, and refined by full-matrix least squares on $F^2$ with the *SHELXTL97* program [22]. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* [23]. Non-H-atoms were refined anisotropically. H-Atoms were placed at calculated positions, and refined as riding atoms on their respective attached atom, with the exception of that ligated to O(16), which was located and refined as the non-H-atoms, with a thermal isotropic factor $U$ of 1.2 Å$^2$ from the attached O-atom. At convergence, the final discrepancy indices on $F$ were $R(F)$ 0.0476, $Rw(F^2)$ 0.0690, and goodness-of-fit on $F^2$ 0.834 for the 5987 reflections, with $I=2\sigma(I)$ and 401 parameters refined with restraints and constraints of 1 each. The largest difference peak and hole was 0.178 and $-0.112$ eÅ$^{-3}$, resp.

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[5]) The crystallographic data of **7** have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication number CCDC-281733. Copies of the data can be obtained, free of charge, via the internet (http://www.ccdc.cam.ac.uk/data_request/cif).

## REFERENCES


[1] 'Dictionary of Natural Products', Vers. 13:2, Chapman & Hall, CRC Press, 2004.
[2] G. R. Pettit, C. L. Herald, C. R. Smith, 'Biosynthetic Products for Cancer Chemotherapy', Elsevier Science Publishers, Amsterdam, 1989, Vol. 6, p. 12.
[3] C. Auvin-Guette, C. Baraguey, A. Blond, H. Xavier, H. Pousset, B. Bodo, *Tetrahedron Lett.* **1999**, *55*, 11495; C. M. Chariandy, C. E. Seaforth, R. H. Phelps, G. V. Pollard, B. P. S. Khambay, *J. Ethnopharmacol.* **1999**, *64*, 265.
[4] M. Canales, T. Hernández, J. Caballero, A. Romo de Vivar, G. Avila, A. Duran, R. Lira, *J. Ethnopharmacol.* **2005**, *97*, 429.
[5] N. Bülow, W. A. König, *Phytochemistry* **2000**, *55*, 141.
[6] N. Harada, K. Nakanishi, *Acc. Chem. Res.* **1972**, *5*, 257.
[7] K. Yueh-Hsiung, C. Chiou-Fung, L. Hsiu-Chuan, *Chem. Pharm. Bull.* **2003**, *51*, 986.
[8] N. Harada, Mo. Ohashi, K. Nakanishi, *J. Am. Chem. Soc.* **1968**, *90*, 7349.
[9] C. Paul, W. A. König, C.-L. Wu, *Phytochemistry* **2001**, *58*, 789.
[10] N. Harada, J. Iwabuchi, Y, Yokota, H, Uda, *J. Am. Chem. Soc.* **1981**, *103*, 5590.
[11] S. Lai Chen, N. Harada, K. Nakanishi, *J. Am. Chem. Soc.* **1974**, *96*, 7352; N. Harada, S. Lai Chen, K. Nakanishi, *J. Am. Chem. Soc.* **1975**, *97*, 5345.
[12] S. McLean, F. W. Reynolds, J.-P. Yang, H. Jacobs, L. L Jean-Pierre, *Magn. Reson. Chem.* **1994**, *32*, 422.
[13] 'Aldrich Library of $^{13}C$ and $^{1}H$ FT NMR Spectra', *Aldrich Chemical Co.*, 1993, *Vol. 3*, 569 A.
[14] C. Seger, B. Jandl, G. Brader, W. Robien, O. Hofer, H. Greger, *Fresenius' J. Anal. Chem.* **1997**, *359*, 42.
[15] S. B. Mahato, A. P. Kundu, *Phytochemistry* **1994**, *37*, 1517.
[16] E. Wenkert, G. V. Baddeley, I. R. Burfitt, L. N. Moreno, *Org. Magn. Reson.* **1978**, *11*, 337.
[17] H. Günter, J. Priestien, P. Joseph-Nathan, *Org. Magn. Reson.* **1975**, *7*, 339.
[18] M. Kanlayavattanakul, N. Ruangrungsi, T. Watanabe, T. Ishikawa, *Heterocycles* **2003**, *61*, 183.
[19] S. Faizi, M. Ali, R. Saleem, S. Bibi, *Magn. Reson. Chem.* **2001**, *39*, 399.
[20] A. Bruyn, P. A. Alvarez, *Carbohydr. Res.* **1992**, *235*, 303.
[21] SMART (5.625), *Bruker AXS, Inc.*, Madison, WI, 2000.
[22] G. M. Sheldrick, 'SHELXTL97, An Integrated System for Solving, Refining and Displaying Crystal Structures from Diffraction Data', University of Göttingen, Germany, 1997.
[23] 'International Tables for X-ray Crystallography', Kynoch Press, Birmingham, 1974, Vol. IV.


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