# Labdanes and Sucrose Esters from *Physalis sordida*

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Eight new compounds, labdanes **2**−**4**, homoergostane **10**, and sucrose esters **12**−**15**, were isolated from aerial parts of *Physalis sordida* together with several known compounds. Structures of the new compounds were elucidated using spectroscopic evidence and chemical transformations. The structure of **10** was confirmed by X-ray crystallographic analysis of its methyl ester. Anti-inflammatory activity of compounds **1**, **2**, **4**, **5**, and **12**−**15** was evaluated using the TPA-induced mouse ear edema test. Compounds **12** ($IC_{50}$ 0.26 $\mu$mol/ear) and **15** ($IC_{50}$ 0.24 $\mu$mol/ear) showed anti-inflammatory activity similar to that of indomethacin ($IC_{50}$ 0.24 $\mu$mol/ear).

The genus *Physalis* (Solanaceae), with about 90 species, is considered indigenous to America.[1] Mexico, with ca. 70 endemic species, is recognized as its center of diversity.[1,2] Chemical studies on *Physalis* sp., mainly of the aerial parts, have yielded withasteroids,[3−5] flavonoids,[6,7] sucrose esters,[8] and labdanes.[9] As part of a systematic investigation of Mexican *Physalis* species,[9−13] we studied the aerial parts of *Physalis sordida* Fernald (Solanaceae), a wild plant that grows from the center to the southeast of Mexico.[14] This investigation resulted in the isolation of three new labdane diterpenes (**2**−**4**), all possessing an oxygenated function at C-12, one 4-homoergostane (**10**), and four sucrose esters (**12**−**15**). Several known compounds were also isolated. To our knowledge, this is the second report on the presence of labdanes and 4-homosteroids in the genus *Physalis*.[9,15] Sucrose esters have been isolated from the aerial parts of *P. viscosa*[8] and from the fruits of *P. nicandroides* var. *attenuata*.[13] The anti-inflammatory activity of compounds **1**, **2**, **4**, **5**, and **12**−**15** was evaluated using the TPA-induced mouse ear edema test.

## Results and Discussion

The methanol extract of *P. sordida* was suspended in $H_2O$ and partitioned with hexane and EtOAc. Purification of the hexane fraction gave the known labdane physacoztomatin (**1**)[9] and the new compounds **2**−**4**, **10**, and **12**−**15**.

Compound **2**, $C_{22}H_{36}O_3$ (FABMS), showed bands at 3411 and 1736 $cm^{-1}$ in the IR spectrum, which, together with the fragments at *m/z* 331 $[M - OH]^+$ and 288 $[M - AcOH]^+$ observed in the FABMS, indicated the presence of OH and AcO groups in the molecule. Its NMR data were similar to those described for **1**, whose structure was confirmed by X-ray analysis.[9] Compound **2** showed signals for an acetoxy group. The H-12 signal with a downfield shift ($\delta$ 5.28) compared to that of **1** ($\delta$ 4.13) indicated that the AcO group was at C-12. The structural relationship between **1** and **2** was confirmed when compound **3** was obtained by acetylation of both compounds. Therefore, the new compound was named 12-*O*-acetylphysacoztomatin, and its structure and relative configuration is that depicted as **2**. Compound **3** was also isolated from *P. sordida*, and it was named 2,15-di-*O*-acetylphysacoztomatin.

Compound **4**, $C_{20}H_{34}O_3$ (HRFABMS), presented $^1H$ and $^{13}C$ NMR data (Tables 1 and 2) similar to those of **1**, mainly in the signals attributable to the side chain. A double bond at 8(17) was deduced from the chemical shifts of the H-17a ($\delta$ 5.08), H-17b ($\delta$ 4.62), and C-17 ($\delta$ 109.8) signals, and it was confirmed by the interactions of C-17 with H-7 ($\delta$ 4.39, t, $J = 3$ Hz) and H-9 ($\delta$ 2.45, d, $J = 11$ Hz) observed in the HMBC spectrum of **4**. The chemical shift and coupling constants of H-7 indicated the presence of an OH at C-7 and $\beta$-equatorial orientation of H-7. Therefore, the downfield shifts of H-5 and H-9 ($\delta$ 1.68 and 2.45, respectively) compared to those of **2** and **3** were caused by a deshielding effect of the $\alpha$-axial OH-7 group.

In order to confirm the structure of **4**, compound **3** was treated with MCPBA to give **6** and **7**. The $\alpha$-orientation of the epoxy group of **6** was deduced from the coupling constants of H-7 ($\delta$ 2.97, dd, $J = 2$, 1.5 Hz) and from its deshielding effect on H-9, which was downfield ($\delta$ 1.386) with respect to that of **7** ($\delta$ 1.28) (Table 1). A similar effect of the epoxy group of **7** on $CH_3$-20 was observed, suggesting the $\beta$-orientation of this group. TLC analysis of **7**, after two weeks at room temperature, showed the presence of a more polar compound (**8**). Compound **8** presented OH groups at C-7 and C-8. The chemical shifts of H-5 ($\delta$ 1.58), H-9 ($\delta$ 1.38), H-6$\beta$ ($\delta$ 2.15), and $CH_3$-20 ($\delta$ 0.93) in the $^1H$ NMR spectrum (Table 1) indicated a *trans*-diaxial relationship between the OH groups. Treatment of compound **6** with acid gave two products. The NMR spectra (Tables 1 and 2) of the less polar compound (**9**) showed the C-7 signal at $\delta$ 212.1 and that of $CH_3$-17 as a doublet at $\delta$ 1.11. An interaction between $CH_3$-20 and H-8 was observed in the NOESY spectrum. Therefore, the opening of the epoxide with the migration of H-7$\beta$ to C-8 and the formation of a ketone at C-7 afforded **9**. The more polar product of the acid treatment of **6** was acetylated to obtain a substance identical in all respects to **5**, the compound obtained by acetylation of **4**. The above confirmed the structure and relative configuration of **4**, which was named physordin.

Compound **10**, $C_{31}H_{48}O_5$ (HRFABMS), showed bands for carbonyl and OH groups (1724 and 3506 $cm^{-1}$, respectively) in the IR spectrum. The $^1H$ and $^{13}C$ NMR data (Table 3) were similar to those of 4$\alpha$-methylergost-8(14),24(28)-dien-3$\beta$-ol-23-one,[16] mainly in the signals attributed to the tetracyclic system. The positions of a methyl group ($CH_3$-29) at C-4 and an AcO at C-3 were deduced by the interactions of H-3 ($\delta$ 4.40) with C-29 ($\delta$ 15.1) and the acetoxy carbonyl ($\delta$ 171.0) and of C-3 ($\delta$ 78.5) with H-1b ($\delta$ 1.45), H-4 ($\delta$ 1.56), and $CH_3$-29 ($\delta$ 0.85) observed in the HMBC spectrum of **10**. In the same spectrum, the interactions of H-7 ($\delta$ 5.20) with C-5 ($\delta$ 46.7), C-9 ($\delta$ 49.4), and C-14 ($\delta$ 54.3) and of C-8 ($\delta$ 138.4) with $CH_2$-6 ($\delta$ 2.10 and 1.46), H-11a ($\delta$ 1.58), H-14 ($\delta$ 1.90), and H-15a ($\delta$ 1.64) were consistent with a double bond at C-7. The $\beta$-equatorial orientation of the AcO group at C-3 and the $\alpha$-equatorial orientation of $CH_3$-29 were deduced from the coupling constants of H-3 ($J = 11$, 11, 4 Hz), which indicated an anti-axial relationship of H-3 with H-4, and by the NOE effects of H-3 with H-1$\alpha$, H-2$\alpha$, H-5, and $CH_3$-29 observed in the NOESY spectrum. The side chain of **10** presented a carboxylic acid (C-21,

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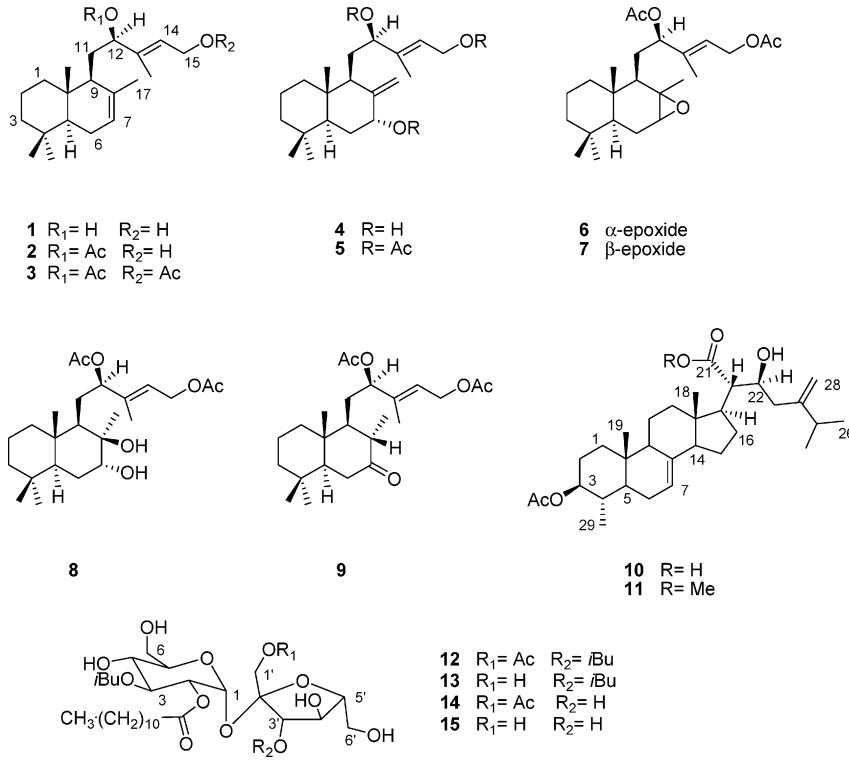
**Chart 1**




$\delta$ 177.3) and a carbinol (C-22, $\delta_C$ 68.6, $\delta_H$ 3.90). The chemical shifts of C-24 ($\delta$ 151.8) and C-28 ($\delta$ 110.4) were consistent with a double bond between these atoms. Interactions of H-22 with C-24, C-21, C-20 ($\delta$ 51.3), and C-17 ($\delta$ 49.1), of C-24 with $CH_3$-27 ($\delta$ 1.04), and of C-28 with $CH_2$-23 ($\delta$ 2.26) and H-25 ($\delta$ 2.24) observed in the HMBC spectrum confirmed the positions of the three functions on the side chain. The formation of **11** by treatment of **10** with $CH_2N_2$ corroborated the presence of the carboxylic acid, and X-ray crystallographic analysis of **11** (Figure 1) confirmed the structure and relative configuration proposed for **10**, which was named physordic acid.

Compound **12** had the molecular formula $C_{34}H_{58}O_{15}$ (HRFABMS) and absorption bands for OH (3619 and 3472 $cm^{-1}$) and ester (1741 $cm^{-1}$) groups in the IR spectrum. The sucrose unit in **12** was deduced from the $^1H$, $^{13}C$, $^1H-^1H$ COSY, and HMBC spectra (Tables 4 and 5). The anomeric hydrogen signal of the glucopyranose was observed at $\delta$ 5.56 (d, $J = 3.5$ Hz), and the $^1H-^1H$ COSY spectrum led to assignment of the H-2, H-3, H-4, H-5, and $CH_2$-6 signals of this sugar moiety. The $^1H$ NMR spectrum displayed the $CH_2$-1′ signals of the fructofuranose as an AB system ($\delta$ 4.07 and 3.94), which showed interactions with C-3′ ($\delta$ 78.6) and the anomeric carbon C-2′ ($\delta$ 102.1) in the HMBC spectrum. Interaction of C-2′ with H-1 of the glucose was also observed. The esterification degree of sucrose was deduced by the chemical shifts of H-2, H-3, $CH_2$-1′, and H-3′ and by the characteristics signals of four acyl groups: an acetyl, two isobutyryl, and a lauroyl. The MS of **12** showed fragments at *m*/*z* 43, 71, and 183 consistent with the acyl groups. Interactions of the acetyl carbonyl ($\delta$ 170.0) with $CH_2$-1′ of the fructose, the carbonyl of one of the isobutyryl groups ($\delta$ 177.4) with H-3′ of the ketose, and the carbonyl of the other isobutyryl group ($\delta$ 178.2) with H-3 of the glucose observed in the HMBC spectrum indicated the positions of these acyl groups. No interaction of the lauroyl carbonyl with the sucrose hydrogens was observed; however, the chemical shift of H-2 was in agreement with it being geminal to an *O*-acyl group. Therefore, the *O*-lauroyl group was placed at C-2 of the new sucrose derivative **12**, which was named physordinose A.

Compounds **13** and **14** presented NMR features similar to those of **12** (Tables 4 and 5). The main differences were the upfield shift of the $CH_2$-1′ signals ($\delta$ 3.58 and 3.50) of **13** compared to those of **12** and the absence of signals attributable to an acetyl group. Compound **14** showed the H-3′ signal at $\delta$ 4.19, and those attributable to the isobutyryl group at C-3′ of **12** were absent. These facts and the molecular formulas (**13**: $C_{32}H_{56}O_{14}$; **14**: $C_{30}H_{52}O_{14}$) indicated that **13** and **14** were the 1′-*O*-deacetyl and the 3′-*O*-deisobutyryl derivatives of **12**, respectively. These new sucrose esters were named physordinoses B (**13**) and C (**14**).

Compound **15**, like **12**, showed NMR signals (Tables 4 and 5) of isobutyryl and lauroyl groups attached to the glucopyranose, but those of the acyl groups attached to the ketose of **12** were absent. The chemical shifts of H-1′a ($\delta$ 3.58), H-1′b ($\delta$ 3.45), and H-3′ ($\delta$ 4.32) of **15** as well as its molecular formula ($C_{28}H_{50}O_{13}$) indicated that **15**, named physordinose D, was the 1′,3′-di-*O*-deacyl derivative of **12**.

Fractionation of the EtOAc fraction afforded compound **1**, the flavonoids 3,7,3′,4′-tetra-*O*-methylmyricetin[17] and 3,7,3′,5′-tetra-*O*-methylmyricetin,[18] and the amides *N*-*trans*-feruloyl 3′-*O*-methyldopamine[19] and *N*-*trans*-feruloyltyramine.[20] These compounds were identified by comparison of their spectroscopic data with those described in the literature, and compound **1** was also identified by direct comparison with an authentic sample.

Anti-inflammatory activity of diterpenes **1**, **2**, **4**, and **5** and of sucrose esters **12**−**15** was evaluated in vivo using the 12-*O*-tetradecanoylphorbol 13-acetate (TPA)-induced mouse ear edema test. The percentage of inhibition values of **2** and **5**, using a dose of 1 $\mu$mol/ear, were low (25.4% and 29.4%, respectively). Compounds **1** and **4** had significant activity (65.8% and 64.3%, respectively), with $IC_{50}$ values of 0.49 and 0.63 $\mu$mol/ear. These results indicate that activity is decreased when the OH groups are esterified. The $IC_{50}$ values of sucrose esters **12**−**15** ($IC_{50}$ 0.26, 0.35, 0.34, and 0.24 $\mu$mol/ear, respectively) showed that **12** and **15** were very similar in activity to indomethacin (reference compound, $IC_{50}$ 0.24 $\mu$mol/ear) and slightly higher than that of **13** and **14**. Anti-inflammatory activity of the major fraction of an ether extract of calyxes of *Physalis peruviana* was recently described.[21] The fraction, primarily a mixture of two sucrose esters (82%), showed activity similar to that of indomethacin. Considering that sucrose esters have been found in the aerial parts,[8] fruits,[13] and calyxes of

**Table 1.** $^1$H NMR Data ($CDCl_3$, 500 MHz) for Compounds **4** and **6**−**9**[a]

| position | **4** | **6**[b] | **7**[b] |
|---|---|---|---|
| 1α | 1.16 ddd (13, 13, 4) | 0.83 m | 0.76 ddd (14, 13, 3) |
| 1*β* | 1.72 brd (13) | 1.77 m | 1.81 brd (13) |
| 2α | 1.65 m | 1.45 m | 1.38 m |
| 2*β* | 1.65 m | 1.45 m | 1.48 dtt (14, 14, 3) |
| 3α | 1.25 ddd (13, 13, 4.5) | 1.11 ddd (13, 11, 7) | 1.11 ddd (14, 14, 5) |
| 3*β* | 1.43 brd (13) | 1.39 m | 1.40 m |
| 5 | 1.68 dd (14, 3) | 1.07 dd (13, 4.5) | 0.94 dd (13.5, 5) |
| 6α | 1.87 ddd (14, 3, 3) | 2.11 brdd (15, 4.5) | 1.97 ddd (15, 6.5, 5) |
| 6*β* | 1.57 ddd (14, 14, 3) | 1.69 ddd (15, 13, 2) | 1.78 m |
| 7 | 4.39 t (3) | 2.97 dd (2, 1.5) | 3.01 d (6.5) |
| 9 | 2.45 d (11) | 1.386 brd (10) | 1.28 dd (7, 1) |
| 11a | 1.63 m | 1.79 ddd (15, 11, 1.5) | 1.86 ddd (15.5, 11, 1) |
| 11b | 1.55 m | 1.53 ddd (15, 10, 3) | 1.74 ddd (15.5, 7, 3) |
| 12 | 4.05 dd (10, 3) | 5.21 brdd (11, 3) | 5.38 dd (11, 3) |
| 14 | 5.63 t (7) | 5.61 tquint (7, 1) | 5.61 tquint (7, 1) |
| 15 | 4.18 d (7) | 4.61 d (7) | 4.61 d (6.5) |
| 16 | 1.70 s | 1.73 brs | 1.75 d (0.5) |
| 17 | 5.08, 4.62 brs | 1.34 s | 1.32 s |
| 18 | 0.89 s | 0.86 s | 0.88 s |
| 19 | 0.81 s | 0.87 s | 0.83 s |
| 20 | 0.66 s | 0.74 s | 0.81 s |

| position | **8**[b] | **9**[b,c] |
|---|---|---|
| 1α | 0.90 m | 0.91 ddd (14, 13, 4) |
| 1*β* | 1.77 m | 1.89 brd (13) |
| 2α | 1.46 dquint (17, 4) | 1.55 m |
| 2*β* | 1.60 m | 1.60 tt (14, 3.5) |
| 3α | 1.22 ddd (14, 13, 4) | 1.18 ddd (14, 14, 4) |
| 3*β* | 1.42 brd (14) | 1.49 brd (13) |
| 5 | 1.58 dd (13, 2) | 1.27 dd (14, 3.5) |
| 6α | 1.80 ddd (15, 3, 2) | 2.42 dd (14, 3.5) |
| 6*β* | 2.15 ddd (15, 13, 3) | 2.30 ddd (14, 14, 1) |
| 7 | 4.00 t (3) | |
| 9 | 1.38 dd (7, 2) | 1.05 ddd (12, 6.5, 2) |
| 11a | 1.70 m | 1.94 ddd (15, 10.5, 2) |
| 11b | 1.63 m | 1.32 ddd (15, 6.5, 3) |
| 12 | 5.18 dd (10, 4) | 5.12 dd (10.5, 3) |
| 14 | 5.58 tquint (7, 1) | 5.57 tquint (6.5, 1) |
| 15 | 4.60 d (7) | 4.59 d (6.5) |
| 16 | 1.72 brs | 1.71 d (1) |
| 17 | 1.34 s | 1.11 d (7) |
| 18 | 0.87 s | 0.87[d] s |
| 19 | 0.82 s | 0.86[d] s |
| 20 | 0.93 s | 1.00 s |

[a] *δ* in ppm; coupling constants (*J*) in Hz are given in parentheses. [b] AcO-12: *δ* 2.08 (**6**), 2.09 (**7**, **8**), 2.06 (**9**); AcO-15: *δ* 2.06 (**6**−**9**). [c] H-8 *δ* 2.27, dq (12, 7). [d] Signals are interchangeable.

*Physalis* species, their presence can be related to the anti-inflammatory activity described for some plants of this genus.[22]

## Experimental Section

**General Experimental Procedures.** Optical rotations were measured on a Perkin-Elmer 343 polarimeter. IR spectra were recorded on a Bruker Tensor 27 spectrophotometer. 1D and 2D NMR spectra were obtained on a Varian-Unity Inova 500 spectrometer with tetramethylsilane (TMS) as internal standard. EIMS (70 eV) were obtained on a JEOL JMS-AX505HA mass spectrometer. FABMS and HRFABMS were obtained on a JEOL JMS-SX102A mass spectrometer. Elemental analysis was obtained on a CE-440 elemental analyzer, Exeter Analytical Inc. Column chromatography (CC) was operated with vacuum using silica gel 60 G Merck, and flash chromatography utilized silica gel 60 (230−400 mesh, Macherey-Nagel). Preparative TLC was performed on precoated Sil G-100UV$_{254}$ plates (Macherey-Nagel) or Sil RP-18W/UV$_{254}$ plates of 1.0 mm thickness (Macherey-Nagel). X-ray crystallographic analysis was carried out on a Bruker Smart Apex CCD diffractometer with graphite-monochromated Mo Kα radiation ($\lambda$ = 0.71073 Å). The structure was solved by direct methods using the SHELXS program. Non-hydrogen atoms were refined with anisotropic displacement parameters using the SHELXTL program. Hydrogen atoms, except those bonded to oxygen atoms, were included at calculated positions and were not refined.

**Table 2.** $^{13}$C NMR Data (*δ*) ($CDCl_3$, 125 MHz) for Compounds **4**, **6**−**9**

| position | **4** | **6**[a] | **7**[a] | **8**[a] | **9**[a,b] |
|---|---|---|---|---|---|
| 1 | 38.7 $CH_2$ | 38.9 $CH_2$ | 40.6 $CH_2$ | 39.3 $CH_2$ | 38.9 $CH_2$ |
| 2 | 19.3 $CH_2$ | 18.6 $CH_2$ | 18.1 $CH_2$ | 18.3 $CH_2$ | 18.5 $CH_2$ |
| 3 | 42.1 $CH_2$ | 42.0 $CH_2$ | 42.3 $CH_2$ | 41.9 $CH_2$ | 41.8 $CH_2$ |
| 4 | 33.1 qC | 33.1 qC | 33.0 qC | 32.8 qC | 33.8 qC |
| 5 | 47.8 CH | 45.5 CH | 49.9 CH | 47.2 CH | 53.9 CH |
| 6 | 31.4 $CH_2$ | 22.9 $CH_2$ | 22.0 $CH_2$ | 26.6 $CH_2$ | 38.8 $CH_2$ |
| 7 | 74.2 CH | 60.9 CH | 62.7 CH | 68.4 CH | 212.1 C |
| 8 | 149.6 C | 58.3 C | 60.4 C | 76.1 C | 48.4 CH |
| 9 | 46.8 CH | 50.7 CH | 49.7 CH | 48.3 CH | 53.8 CH |
| 10 | 39.7 qC | 35.7 qC | 36.6 qC | 38.7 qC | 38.1 qC |
| 11 | 29.5 $CH_2$ | 30.4 $CH_2$ | 31.5 $CH_2$ | 28.9 $CH_2$ | 34.0 $CH_2$ |
| 12 | 74.7 CH | 78.0 CH | 78.2 CH | 78.9 CH | 78.3 CH |
| 13 | 141.7 C | 139.6 C | 139.7 C | 139.8 C | 139.4 C |
| 14 | 123.7 CH | 120.7 CH | 120.6 CH | 120.7 CH | 121.0 CH |
| 15 | 58.9 $CH_2$ | 60.7 $CH_2$ | 60.7 $CH_2$ | 60.6 $CH_2$ | 60.6 $CH_2$ |
| 16 | 12.1 $CH_3$ | 12.9 $CH_3$ | 12.9 $CH_3$ | 12.7 $CH_3$ | 12.8 $CH_3$ |
| 17 | 109.8 $CH_2$ | 23.4 $CH_3$ | 22.3 $CH_3$ | 29.1 $CH_3$ | 13.0 $CH_3$ |
| 18 | 33.2 $CH_3$ | 32.6 $CH_3$ | 33.2 $CH_3$ | 32.8 $CH_3$ | 32.7[c] $CH_3$ |
| 19 | 21.5 $CH_3$ | 22.0 $CH_3$ | 21.8 $CH_3$ | 22.0 $CH_3$ | 21.2[c] $CH_3$ |
| 20 | 13.6 $CH_3$ | 14.3 $CH_3$ | 15.0 $CH_3$ | 15.3 $CH_3$ | 13.6 $CH_3$ |

[a] AcO-12: *δ* 170.2 (**6**), 170.6 (**7**), 170.3 (**8**), 170.1 (**9**), 21.2 (**6**, **9**), 21.3 (**7**), 22.3 (**8**); AcO-15: *δ* 170.9 (**6**, **9**), 170.3 (**8**), 21.0 (**6**−**9**). [b] Measured at 75 MHz on a Varian Unity 300 spectrometer. [c] Signals are interchangeable.

**Table 3.** NMR Data ($CDCl_3$, 500 MHz) for Compound **10a**

| position | $\delta_H$ (*J* in Hz) | $\delta_C$, mult. | HMBC[b] |
|---|---|---|---|
| 1 | 1.84, 1.45 m | 27.1 $CH_2$ | 5 |
| 2 | 1.81, 1.16 m | 36.7 $CH_2$ | |
| 3 | 4.40 ddd (11, 11, 4) | 78.5 CH | 1a, 1b, 2a, 4, 6b, 29 |
| 4 | 1.56 m | 37.0 CH | 2a, 29 |
| 5 | 1.09 ddd (11.5, 11.5, 4.5) | 46.7 CH | 1a, 4, 6b, 7, 19, 29 |
| 6 | 2.10, 1.46 m | 26.6 $CH_2$ | 5, 7 |
| 7 | 5.20 ddd (4.5, 2, 1.5) | 117.8 CH | 6a, 14 |
| 8 | | 138.4 C | 6a, 6b, 11a, 14, 15a |
| 9 | 1.67 m | 49.4 CH | 7, 11a, 12a, 19 |
| 10 | | 34.7 C | 1a, 1b, 2a, 5, 6a, 6b, 11b, 19 |
| 11 | 1.58, 1.42 m | 21.2 $CH_2$ | |
| 12 | 1.78, 1.20 m | 36.9 $CH_2$ | 11b, 17, 18 |
| 13 | | 42.8 C | 11a, 12b, 14, 15a, 16a, 16b, 18 |
| 14 | 1.90 brs | 54.3 CH | 7, 12a, 15b, 16b, 18 |
| 15 | 1.64, 1.48 m | 22.1 $CH_2$ | |
| 16 | 2.12, 1.62 m | 26.6 $CH_2$ | 15b, 20 |
| 17 | 2.11 m | 49.1 CH | 18, 20, 22 |
| 18 | 0.61 s | 11.7 $CH_3$ | 12b, 14, 17 |
| 19 | 0.82 s | 13.9 $CH_3$ | 1a, 2a, 2b |
| 20 | 2.39 dd (11, 2) | 51.3 CH | 17, 22, 23 |
| 21 | | 177.3 C | 20, 22 |
| 22 | 3.90 ddd (9, 5, 2) | 68.6 CH | 23, 28 |
| 23 | 2.26 m | 41.3 $CH_2$ | 20, 22, 25, 28a, 28b |
| 24 | | 151.8 C | 22, 23, 25, 26, 27, 28 |
| 25 | 2.24 m | 33.5 CH | 23, 26, 27, 28a, 28b |
| 26 | 1.06 d (7) | 21.7 $CH_3$ | 25, 27 |
| 27 | 1.04 d (6.5) | 21.9 $CH_3$ | 25, 26, 28a |
| 28 | 4.96 t (1), 4.83 d (1.5) | 110.4 $CH_2$ | 23, 25 |
| 29 | 0.85 d (7) | 15.1 $CH_3$ | 3, 4 |

[a] AcO: $\delta_H$ 2.05, $\delta_C$ 171.0 and 21.3. [b] HMBC correlations are from carbon(s) stated to the indicated hydrogens. AcO carbonyl group coupled to H-3.

**Plant Material.** *P. sordida* was collected in Cerro del Azteca, State of Querétaro, México, in July 2004. A voucher specimen of the plant (QMEX 6531) was identified by one of the authors (M.M.) and deposited at the Herbarium of the Universidad Autónoma de Querétaro.

**Extraction and Isolation.** Dried and ground aerial parts (606 g) of *P. sordida* were extracted with MeOH. The extract was suspended in $H_2O$ and partitioned with hexane and EtOAc to obtain hexane (46.0 g) and EtOAc (5.6 g) fractions. The hexane fraction was separated by CC (hexane−EtOAc, 100:0 → 30:70, $Me_2CO$, and MeOH). Fractions 4−29 (eluted with hexane−EtOAc, 98:2 and 95:5) gave a mixture of *β*-sitosterol and stigmasterol (48 mg). Fractions 30−50 (eluted with

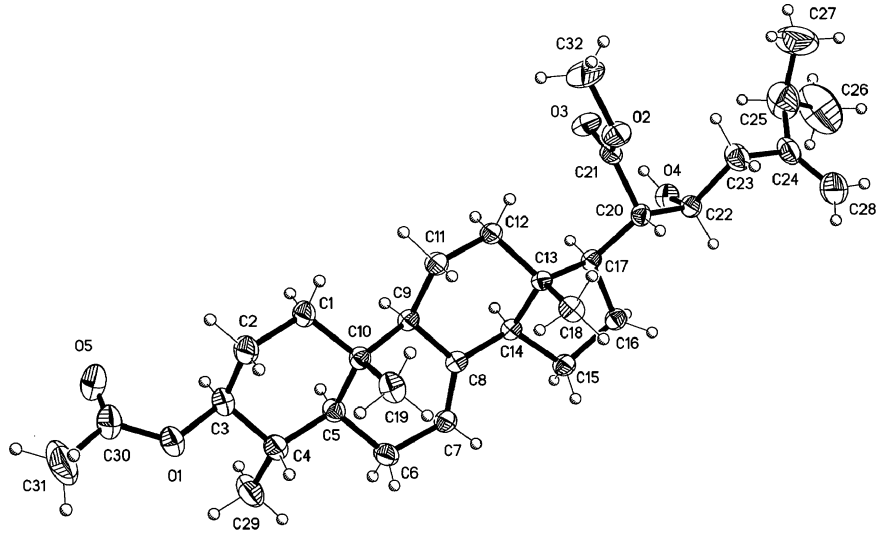



**Figure 1.** ORTEP projection of **11** (crystallographic numbering).

**Table 4.** $^1$H NMR Data ($CDCl_3$, 500 MHz) for Compounds **12**−**15**[a]

| position | **12**[b,c] | **13**[b] | **14**[c] | **15** |
|---|---|---|---|---|
| 1 | 5.56 d (3.5) | 5.55 d (3.5) | 5.59 d (3.5) | 5.55 d (3) |
| 2 | 4.93 dd (10.5, 3.5) | 4.89 dd (10.5, 3.5) | 4.89 dd (10, 3.5) | 4.87 dd (10, 3) |
| 3 | 5.17 dd (10.5, 9.5) | 5.22 dd (10.5, 9.5) | 5.36 dd (10, 9.5) | 5.39 t (10) |
| 4 | 3.55 ddd (9.5, 9.5, 4.5) | 3.54 m | 3.50 dd (10.5, 9.5) | 3.49 t (10) |
| 5 | 4.05 m | 4.05 m | 3.80 m | 4.16 m |
| 6a | 3.97 brd (13) | 3.98 m | 3.95 m | 3.99 brd (12) |
| 6b | 3.70 dd (13, 6) | 3.76 m | 3.74 m | 3.74 dd (12, 5) |
| 1′a | 4.07 d (11.5) | 3.58 m | 4.09 d (12) | 3.58 d (12) |
| 1′b | 3.94 d (11.5) | 3.50 m | 3.97 d (12) | 3.45 d (12) |
| 3′ | 5.23 d (8.5) | 5.19 d (8) | 4.19 d (9) | 4.32 m |
| 4′ | 4.61 ddd (8.5, 8.5, 2.5) | 4.54 t (8) | 4.33 t (9) | 4.30 m |
| 5′ | 3.95 m | 3.94 m | 4.13 m | 3.86 m |
| 6′a | 3.94 brd (11.5) | 3.90 m | 3.90 brd (11) | 3.89 brd (12) |
| 6′b | 3.72 brd (11.5) | 3.76 m | 3.75 m | 3.79 brd (12) |
| | | lauroylO-2 | | |
| 2″a | 2.36 dt (16, 8) | 2.29 dt (16, 8) | 2.38 dt (16, 8) | 2.33 dt (16, 8) |
| 2″b | 2.29 dt (16, 8) | 2.24 dt (16, 8) | 2.29 dt (16, 8) | 2.26 dt (16, 8) |
| 3″ | 1.58 quint (8) | 1.55 quint (8) | 1.57 quint (8) | 1.55 quint (8) |
| 4″−11″ | 1.25 brs | 1.25 brs | 1.25 brs | 1.25 brs |
| 12″ | 0.88 t (7) | 0.88 t (7) | 0.88 t (7) | 0.88 t (7) |
| | | *i*BuO-3 | | |
| 2‴ | 2.57 hept (7) | 2.56 hept (7) | 2.59 hept (7) | 2.56 hept (7) |
| 3‴ | 1.16 d (7) | 1.15 d (7) | 1.15 d (7) | 1.14 d (7) |
| 4‴ | 1.15 d (7) | 1.13 d (7) | 1.13 d (7) | 1.12 d (7) |

[a] $\delta$ in ppm; coupling constants (*J*) in Hz are given in parentheses. [b] HO-4: $\delta$ 2.93 brd (4.5) (**12**), 2.97 brs (**13**); HO-4′: $\delta$ 3.35 brs (**12**), 3.36 brs (**13**); *i*BuO-3′: H-2‴″ $\delta$ 2.74 hept (7) (**12**, **13**), H-3‴″ $\delta$ 1.30 d (7) (**12**), 1.28 d (7) (**13**), H-4‴″ $\delta$ 1.27 d (7) (**12**), 1.25 d (7) (**13**). [c] AcO-1′: $\delta$ 2.10 s (**12**), 2.09 s (**14**).

hexane−EtOAc, 90:10) were further fractionated by CC (hexane−EtOAc, 80:20) to give fractions A, B, C, and D. Fraction A was separated by two CC (hexane−EtOAc, 80:20 and 90:10) to yield subfractions $A_1$, and $A_2$. Fraction B was submitted to CC ($C_6H_6$−$Me_2CO$, 85:15) to give subfractions $B_1$, $B_2$, and $B_3$. Subfraction $B_2$ gave **1** [73 mg, mp 98−101 °C, $[\alpha]_D$ +19.6 (*c* 0.24, MeOH); lit:[9] oil, $[\alpha]_D$ +12.5 (*c* 0.24, MeOH)]. Subfractions $A_1$ and $B_1$ were mixed and submitted to three successive CC separations ($C_6H_6$−$Me_2CO$, 95:5; $C_6H_6$−EtOAc, 95:5 and 98:2) to afford **2** (980 mg). Fraction C and subfractions $A_2$ and $B_3$ were mixed and fractionated by CC ($C_6H_6$−$Me_2CO$, 93:7) to give **1** (1.48 g). Fraction D was fractionated into $D_1$, $D_2$, and $D_3$ by CC (hexane−$Me_2CO$, 90:10 → 80:20). CC of fractions $D_1$, $D_2$, and $D_3$ yielded **10** (13 mg), **3** (13 mg), and **4** (104 mg), respectively. Fractions 62−63 from the first CC (eluted with hexane−EtOAc, 30:70) were separated by CC ($CH_2Cl_2$−MeOH, 100:0 → 0:100). Eluate $CH_2Cl_2$−MeOH, 99:1, was purified by two CC ($CHCl_3$−$Me_2CO$, 75:25; then hexane−$Me_2CO$, 70:30) to give **12** (176 mg). Eluate $CH_2Cl_2$−MeOH, 90:10, gave **13** (125 mg) after purification by CC ($CHCl_3$−$Me_2CO$, 60:40). Fractions 64−72 (eluted with hexane−EtOAc, 30:70, and $Me_2CO$) from the first CC were further separated by CC ($CH_2Cl_2$−MeOH, 100:0 → 80:20) to yield fractions E and F. Two consecutive CC separations ($CHCl_3$−$Me_2CO$, 65:35; hexane−$Me_2CO$, 50:50) of fraction E gave 430 mg of **13**. $\beta$-Sitosterol glucopyranoside (28 mg) crystallized from fraction F, and its mother liquors were purified by CC (hexane−$Me_2CO$, 50:50) to give subfractions $F_1$ and $F_2$. Subfraction $F_1$ (2.19 g) was submitted to successive CC runs (hexane−$Me_2CO$, 50:50; $CH_2Cl_2$−$Me_2CO$, 50:50) to yield **13** (722 mg) and **14** (782 mg). Compound **15** (451 mg) was obtained after CC ($CH_2Cl_2$−$Me_2CO$, 40:60) of subfraction $F_2$. Purification of the EtOAc fraction (5.63 g) by several CC and preparative TLC separations yielded compound **1** (35 mg); 3,7,3′,4′-tetra-*O*-methylmyricetin[17] (6 mg), mp 154−155 °C (MeOH), lit. mp 149−151 °C ($C_6H_6$); 3,7,3′,5′-tetra-*O*-methylmyricetin[18] (6 mg), mp 188−192 °C (MeOH), lit. mp 183−185 °C (MeOH); *N-trans*-feruloyl 3′-*O*-methyldopamine[19] (10 mg); and *N-trans*-feruloyltyramine (19 mg).[20]

**12-*O*-Acetylphysacoztomatin (2):** colorless oil; $[\alpha]_D$ +2.7 (*c* 0.11, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3411, 2925, 1736, 1673, 1242 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$ 5.64 (1H, tquint, $J$ = 6.5, 1.5 Hz, H-14), 5.41 (1H, brs, H-7), 5.28 (1H, dd, $J$ = 11, 2 Hz, H-12), 4.18 (2H, dd, $J$ = 6.5, 1.5 Hz, H-15), 2.08 (3H, s, $CH_3CO_2$), 1.97 (1H, brd, $J$ = 17 Hz, H-6$\beta$), 1.87 (1H, brd, $J$ = 13 Hz, H-1$\beta$), 1.85 (1H, m, H-6$\alpha$), 1.77 (1H, dd, $J$ = 15, 11 Hz, H-11a), 1.72 (3H, dd, $J$ = 2.5, 1 Hz, H-17), 1.72 (1H,

**Table 5.** $^{13}C$ NMR Data ($CDCl_3$, 125 MHz) for Compounds **12**−**15**

| position | **12**[a,b,c] | **13**[a,c] | **14**[a,b] | **15**[a] |
|---|---|---|---|---|
| 1 | 89.6 CH | 89.7 CH | 89.5 CH | 89.1 CH |
| 2 | 69.3 CH | 69.8 CH | 69.9 CH | 70.3 |
| 3 | 73.0 CH | 72.6 CH | 72.2 CH | 72.6 CH |
| 4 | 69.9 CH | 69.9 CH | 69.9 CH | 69.7 CH |
| 5 | 74.5 CH | 73.9 CH | 74.4 CH | 74.4 CH |
| 6 | 62.3 $CH_2$ | 62.2 $CH_2$ | 62.4 $CH_2$ | 60.4 $CH_2$ |
| 1′ | 64.5 $CH_2$ | 64.2 $CH_2$ | 63.3 $CH_2$ | 64.2 $CH_2$ |
| 2′ | 102.1 C | 103.9 C | 102.3 C | 103.6 C |
| 3′ | 78.6 CH | 78.9 CH | 77.4 CH | 77.9 CH |
| 4′ | 70.6 CH | 71.2 CH | 72.0 CH | 73.1 CH |
| 5′ | 82.3 CH | 82.2 CH | 81.4 CH | 81.6 CH |
| 6′ | 59.5 $CH_2$ | 60.1 $CH_2$ | 59.7 $CH_2$ | 60.4 $CH_2$ |

[a] LauroylO-2: C-1″ δ 173.1 (**12**, **15**), 173.3 (**13**, **14**), $CH_2$-2″ δ 33.9 (**12**−**14**), 33.8 (**15**), $CH_2$-3″ δ 24.6 (**12**−**15**), $CH_2$-4″ δ 29.1 (**12**−**15**), $CH_2$-5″ to $CH_2$-11″ δ 29.4, 29.3, 29.2, 29.6, 31.9, 22.7 (**12**−**15**), $CH_3$-12″ δ 14.1 (**12**−**15**); *i*BuO-3: C-1‴ δ 178.2 (**12**, **15**), 177.9 (**13**, **14**), CH-2‴ δ 34.1 (**12**−**15**), $CH_3$-3‴ δ 18.7 (**12**), 18.8 (**13**−**15**), $CH_3$-4‴ δ 18.9 (**12**, **14**, **15**), 19.0 (**13**). [b] AcO-1′: δ C 170.0 (**12**), 170.5 (**14**), $CH_3$ δ 20.7 (**12**, **14**). [c] *i*BuO-3′: C-1⁗ δ 177.4 (**12**), 178.0 (**13**), CH-2⁗ δ 33.9 (**12**, **13**), $CH_3$-3⁗ δ 18.7 (**12**, **13**), $CH_3$-4⁗ δ 19.2 (**12**, **13**).

m, H-9), 1.69 (3H, d, $J$ = 1.5 Hz, H-16), 1.54 (1H, dtt, $J$ = 13.5, 13.5, 3.5 Hz, H-2$\beta$), 1.45 (1H, dtt, $J$ = 13.5, 3.5, 3.5 Hz, H-2α), 1.41 (2H, m, H-3$\beta$ and H-11b), 1.19 (1H, dd, $J$ = 14, 5 Hz, H-5), 1.16 (1H, ddd, $J$ = 13, 13, 3.5 Hz, H-3α), 0.91 (1H, ddd, $J$ = 13, 13, 4 Hz, H-1α), 0.88 (3H, s, H-19), 0.86 (3H, s, H-18), 0.74 (3H, s, H-20); $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 170.6 (C, $CH_3CO_2$), 137.8 (C, C-13), 134.4 (C, C-8), 125.1 (CH, C-14), 123.0 (CH, C-7), 78.6 (CH, C-12), 59.0 ($CH_2$, C-15), 50.3 (CH, C-9), 50.0 (CH, C-5), 42.3 ($CH_2$, C-3), 39.3 ($CH_2$, C-1), 36.4 (qC, C-10), 33.1 ($CH_3$, C-18), 33.0 (qC, C-4), 31.6 ($CH_2$, C-11), 23.8 ($CH_2$, C-6), 22.3 ($CH_3$, C-17), 21.9 ($CH_3$, C-19), 21.3 ($CH_3$, $CH_3CO_2$), 18.8 ($CH_2$, C-2), 13.5 ($CH_3$, C-20), 12.8 ($CH_3$, C-16); FABMS *m*/*z* 331 $[M - 17]^+$, 288 $[M - AcOH]^+$, 270, 204, 190, 164, 133, 119, 109, 83, 81, 69, 55, 43.

**12,15-Di-*O*-acetylphysacoztomatin (3):** colorless oil; $[\alpha]_D$ +7.9 (*c* 0.33, $CHCl_3$); IR (film) $\nu_{max}$ 2950, 1742, 1673, 1234 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) δ 5.58 (1H, tquint, $J$ = 7, 1.5 Hz, H-14), 5.45 (1H, brs, H-7), 5.30 (1H, dd, $J$ = 11, 1.5 Hz, H-12), 4.60 (2H, d, $J$ = 7 Hz, H-15), 2.08 (3H, s, $CH_3CO_2$-15), 2.05 (3H, s, $CH_3CO_2$-12), 1.97 (1H, brd, $J$ = 18 Hz, H-6$\beta$), 1.87 (1H, brd, $J$ = 13 Hz, H-1$\beta$), 1.85 (1H, m, H-6α), 1.76 (1H, brdd, $J$ = 15, 12 Hz, H-11a), 1.722 (3H, brd, $J$ = 1.5 Hz, H-16), 1.72 (3H, brs, H-17), 1.71 (1H, brd, $J$ = 12 Hz, H-9), 1.55 (1H, dtt, $J$ = 13.5, 13.5, 4 Hz, H-2$\beta$), 1.47 (1H, dtt, $J$ = 13.5, 4, 4 Hz, H-2α), 1.41 (2H, m, H-3$\beta$, H-11b), 1.19 (1H, dd, $J$ = 12, 5 Hz, H-5), 1.17 (1H, ddd, $J$ = 13.5, 13.5, 4 Hz, H-3α), 0.90 (1H, ddd, $J$ = 13, 13, 4 Hz, H-1α), 0.88 (3H, s, H-19), 0.86 (3H, s, H-18), 0.74 (3H, s, H-20); $^{13}C$ NMR ($CDCl_3$, 125 MHz) δ 170.9 (C, $CH_3CO_2$-12), 170.5 (C, $CH_3CO_2$-15), 140.0 (C, C-13), 134.3 (C, C-8), 123.0 (CH, C-7), 120.2 (CH, C-14), 78.3 (CH, C-12), 60.7 ($CH_2$, C-15), 50.3 (CH, C-9), 50.0 (CH, C-5), 42.3 ($CH_2$, C-3), 39.3 ($CH_2$, C-1), 36.4 (qC, C-10), 33.1 ($CH_3$, C-18), 33.0 (qC, C-4), 31.5 ($CH_2$, C-11), 23.8 ($CH_2$, C-6), 22.3 ($CH_3$, C-17), 21.9 ($CH_3$, C-19), 21.3 ($CH_3$, $CH_3CO_2$-15), 21.0 ($CH_3$, $CH_3CO_2$-12), 18.8 ($CH_2$, C-2), 13.5 ($CH_3$, C-20), 12.9 ($CH_3$, C-16); EIMS *m*/*z* 331 $[M - AcO]^+$ (3), 270 $[M - 2AcOH]^+$ (36), 255 (7), 190 (54), 175 (14), 146 (55), 131 (52), 119 (57), 109 (51), 83 (50), 81 (44), 69 (32), 55 (42), 43 (100).

**Physordin (4):** white crystals (hexane−EtOAc); mp 155−158 °C; $[\alpha]_D$ −8 (c 0.1, MeOH); IR ($CHCl_3$) $\nu_{max}$ 3603, 3415, 2931 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 1 and 2; EIMS *m*/*z* 304 $[M - H_2O]^+$ (2), 286 $[M - 2H_2O]^+$ (2), 273 (5), 248 (8), 233 (34), 204 (9), 189 (9), 123 (27), 109 (31), 88 (61), 83 (27), 81 (19), 55 (32), 44 (49), 43 (38), 41 (26), 30 (100); FABMS *m*/*z* 321 $[M - H]^+$, 287; HRFABMS *m*/*z* 322.2498 (calcd for $C_{20}H_{34}O_3$, 322.2508).

**Physordic acid (10):** pale yellow crystals (hexane−EtOAc); mp 233−240 °C; $[\alpha]_D$ −14 (*c* 0.1, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3506, 2964, 1724, 1643 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Table 3; FABMS *m*/*z* 523 $[M + Na]^+$, 500 $[M]^+$, 483 $[M - HO]^+$, 441 $[M - AcO]^+$, 417, 399, 357, 327, 269, 113, 95, 69, 55, 43; HRFABMS *m*/*z* 500.3491 (calcd for $C_{31}H_{48}O_5$, 500.3502).

**Physordinose A (12):** colorless oil; $[\alpha]_D$ +36.2 (*c* 0.32, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3619, 3472, 2974, 2929, 1741 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 4 and 5; FABMS *m*/*z* 729 $[M + Na]^+$, 415, 327, 275, 215, 197, 183, 127, 97, 71, 57, 55, 43; HRFABMS *m*/*z* 729.3669 (calcd for $C_{34}H_{58}O_{15}Na$, 729.3673).

**Physordinose B (13):** colorless oil; $[\alpha]_D$ +28 (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3480, 2929, 1736 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 4 and 5; FABMS *m*/*z* 687 $[M + Na]^+$, 415, 327, 233, 215, 183, 167, 127, 97, 71, 57, 55, 43; HRFABMS *m*/*z* 687.3576 (calcd for $C_{32}H_{56}O_{14}Na$, 687.3568).

**Physordinose C (14):** colorless oil; $[\alpha]_D$ +29 (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3489, 2928, 1741 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 4 and 5; FABMS *m*/*z* 659 $[M + Na]^+$, 415, 205, 183, 97, 83, 57, 55, 43; HRFABMS *m*/*z* 659.3265 (calcd for $C_{30}H_{52}O_{14}Na$, 659.3255).

**Physordinose D (15):** colorless oil; $[\alpha]_D$ +36.3 (*c* 0.295, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 3463, 2929, 1732 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 4 and 5; FABMS *m*/*z* 617 $[M + Na]^+$, 415, 327, 183, 163, 154, 145, 127, 83, 71, 57, 55, 43; HRFABMS *m*/*z* 617.3146 (calcd for $C_{28}H_{50}O_{13}Na$, 617.3149).

**Acetylation of 1 and 2.** Compound **1** (230 mg), acetic anhydride (2.3 mL), and pyridine (2.3 mL) were mixed and held at rt for 5 h. The reaction mixture was worked up in the usual manner and purified by CC (hexane−EtOAc, 90:10) to afford 123 mg of **3**, $[\alpha]_D$ +9.26 (*c* 0.27, $CHCl_3$). Acetylation of **2** (45 mg) was carried out in the same manner (0.5 mL of acetic anhydride and 0.5 mL of pyridine) to give 26 mg of **3**, $[\alpha]_D$ +9.2 (*c* 0.164, $CHCl_3$); *anal*. C 73.65%, H 9.75%, calcd for $C_{24}H_{38}O_4$, C 73.81%, H 9.81%.

**Epoxidation of 3.** A solution of MCPBA (61 mg) in $CH_2Cl_2$ (2 mL) was added to a solution of **3** (108 mg) in $CH_2Cl_2$ (4 mL). The reaction mixture was stirred at rt for 2.5 h. After, it was separated into two fractions by flash CC (hexane−$Me_2CO$, 92:8). The more polar fraction (TLC: hexane−$Me_2CO$, 90:10, 3×) yielded 61 mg of **6**. The less polar fraction gave 22 mg of **7** (TLC: hexane−EtOAc, 90:10, 7×). Preparative TLC (hexane−EtOAc, 85:15, 3×) performed on **7** after two weeks of standing at rt gave **8** (5.7 mg) and **7** (9 mg). Compound **6**: colorless oil; IR ($CHCl_3$) $\nu_{max}$ 2930, 1734, 1235 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 1 and 2; EIMS *m*/*z* 405 $[M - H]^+$ (1), 347 (21), 287 (17), 221 (66), 207 (12), 189 (17), 149 (28), 135 (37), 123 (59), 109 (79), 97 (84), 83 (55), 69 (48), 55 (43), 43 (100). Compound **7**: colorless oil; IR ($CHCl_3$) $\nu_{max}$ 2931, 1731, 1240 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 1 and 2; EIMS *m*/*z* 406 $[M]^+$ (1), 347 (5), 346 (5), 287 (10), 286 (13), 221 (38), 207 (44), 189 (36), 163 (16), 149 (30), 123 (56), 119 (49), 109(72), 97 (71), 95 (58), 83 (67), 81 (65), 69 (72), 55 (60), 43 (100). Compound **8**: colorless oil; IR ($CHCl_3$) $\nu_{max}$ 3527, 2931, 1730, 1241 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 1 and 2; EIMS *m*/*z* 382 $[M - CH_2CO]^+$ (3), 364 (2), 322 (87), 309 (12), 286 (14), 225 (68), 208 (23), 189 (35), 149 (37), 123 (45), 109 (44), 97 (34), 95 (36), 83 (57), 69 (53), 55 (42), 43 (100).

**Acetylation of 4.** Compound **4** (24.5 mg), acetic anhydride (0.25 mL), and pyridine (0.25 mL) were mixed. After 8 h at rt, the reaction mixture was worked up in the usual manner and then purified by preparative TLC ($C_6H_6$−EtOAc, 95:5, 3×) to give 14 mg of **5**, mp 58−60 °C (hexane−EtOAc); $[\alpha]_D$ +0.8 (*c* 0.25, $CHCl_3$); IR ($CHCl_3$) $\nu_{max}$ 2931, 1729, 1250, 1242 $cm^{-1}$; NMR and MS data in the Supporting Information.

**Treatment of 6 with Acid.** Aqueous $HClO_4$ (0.5%, 0.12 mL) was added to a solution of **6** (49.6 mg) in isopropyl ether (5 mL). The mixture was stirred for 3 h at rt. After, it was washed with water and $NaHCO_3$, dried over anhydrous $Na_2SO_4$, and purified by preparative TLC ($C_6H_6$−EtOAc, 90:10, 2×) and CC ($C_6H_6$−EtOAc, 90:10) to give 7.9 mg of **9** and 9.6 mg of the second product, which was acetylated (0.25 mL of pyridine and 0.25 mL of acetic anhydride). After 3 h at rt, the reagents were eliminated with an air flow. The mixture was purified by CC ($C_6H_6$−EtOAc, 90:10) to give 4.3 mg of **5**, mp 58−60 °C (hexane−EtOAc), $[\alpha]_D$ +0.9 (*c* 0.33, $CHCl_3$). Compound **9**: colorless oil; IR ($CHCl_3$) $\nu_{max}$ 3534, 2931, 1732, 1242 $cm^{-1}$; $^1H$ and $^{13}C$ NMR data Tables 1 and 2; EIMS *m*/*z* 406 $[M]^+$ (1), 347 (8), 346 (5), 286 (19), 207 (97), 189 (12), 165 (14), 151 (19), 140 (64), 137 (33), 123 (100), 109 (27), 95 (22), 83 (27), 81 (18), 69 (29), 55 (22), 43 (47).

**Methylation of 10.** Treatment of **10** (5 mg in ethyl ether, 3 mL) with $CH_2N_2$ yielded compound **11** (3.3 mg); mp 163−165 °C ($Me_2CO$−MeOH); IR ($CHCl_3$) $\nu_{max}$ 3624, 3485, 2973, 1719 $cm^{-1}$; NMR and MS data in the Supporting Information.

**X-ray Crystal Data of 11.** [23] $C_{32}H_{50}O_5$, MW = 514.72, triclinic, space group $P1$, $a$ = 5.995(1) Å, α = 85.5253°, $b$ = 6.617(1) Å, $\beta$ = 83.748(3)°, $c$ = 19.465(4) Å, $\gamma$ = 81.907(3)°, $V$ = 758.3(3) $Å^3$, $Z$ =

1, $D_c$ 1.127 Mg/m$^3$, $F(000) = 282$; crystal dimensions 0.296 × 0.272 × 0.156 mm; reflections collected 7738, independent reflections 3716.

**Anti-inflammatory Activity.** The assay of TPA-induced ear edema in mice was performed as previously reported.[24] A group of 5−8 male NIH mice were anaesthetized with Sedaphorte, and a solution of 12-*O*-tetradecanoylphorbol 13-acetate (2.5 $\mu$g) dissolved in EtOH (10 $\mu$L) was topically applied to both faces of the right ear of the mice (5 $\mu$L each face). The left ear received only EtOH (10 $\mu$L). After 10 min, doses of 0.1 to 1.0 $\mu$mol of the test compounds, or indomethacin as reference, dissolved in 20 $\mu$L of $Me_2CO-CH_2Cl_2$ (1:1) were applied to the right ear (10 $\mu$L each face). Control animals received only $Me_2CO-CH_2Cl_2$ (1:1). Four hours later the animals were sacrificed by cervical dislocation, and a plug (7 mm diameter) was removed from each ear. The edematous response was measured as the weight difference between the two plugs. The percent inhibition of edema was calculated by the equation: % = [(edema A − edema B)/edema A] × 100. Edema A = edema induced by TPA alone and edema B = edema induced by TPA plus sample. Data were analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's test. The $IC_{50}$ values ($\mu$mol/ear) were estimated from the linear regression equation.

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**Supporting Information Available:** The NMR spectra of compounds **2**−**15** and the $^1$H and $^{13}$C NMR and MS data of compounds **5** and **11** are available free of charge via the Internet at http://pubs.acs.org.

## References and Notes

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