# Two New Triterpene and a New Nortriterpene Glycosides from *Phlomis viscosa*

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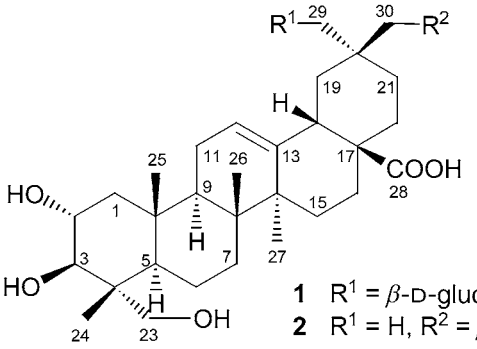
Dedicated to a very young collegue *Kürşat Avcı* (B.Sc., 1972–2003), who liked watching the world from the tops of high mountains

The isolation and structure elucidation of two new oleanane-type triterpene glycosides, 29-(β-D-glucopyranosyloxy)-2α,3β,23-trihydroxyolean-12-en-28-oic acid (=(2α,3β,4α,29α)-29-(β-D-glucopyranosyloxy)-2,3,23-trihydroxyolean-12-en-28-oic acid; **1**) and its C(20)-epimer, 30-(β-D-glucopyranosyloxy)-2α,3β,23-trihydroxyolean-12-en-28-oic acid (=(2α,3β,4α,29β)-29-β-D-glucopyranosyloxy)-2,3,23-trihydroxyolean-12-en-28-oic acid; **2**), and a novel nortriterpene glycoside, (17*S*)-2α,18β,23-trihydroxy-3,19-dioxo-19(18→17)-abeo-28-norolean-12-en-25-oic acid β-D-glucopyranosyl ester (=(1*R*,2*S*,4a*S*,4b*R*,6a*R*,7*R*,9*R*,10a*S*,10b*S*)-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11-tetradecahydro-1-hydroxy-7-(hydroxymethyl)-3′,4′,4a,4b,7-pentamethyl-2′,8-dioxospiro[chrysene-2(1*H*),1′-cyclopentane]-10a-carboxylic acid β-D-glucopyranosyl ester; **3**) from *Phlomis viscosa* (Lamiaceae) are reported. The structures of the compounds were asigned by means of spectroscopic (IR, 1D- and 2D-NMR, and LC-ESI-MS) and chemical (acetylation) methods.

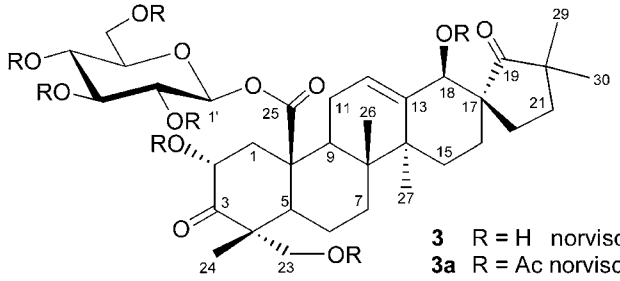
**1. Introduction.** – *Phlomis viscosa* POIRET (Lamiaceae) is one of the 34 species recorded in the Flora of Turkey [1]. During our systematic phytochemical examinations of *Phlomis* L. species, we have now investigated *Phlomis viscosa*. Chromatographic studies on the EtOH extract of the aerial parts of the plant led to the isolation of the two new oleanane-type triterpene glycosides **1** and **2** and the new nortriterpene glycoside **3**, which we call viscosides A (**1**) and B (**2**) and norviscoside (**3**). This is the first report of the isolation of triterpene glycosides from *Phlomis* species.

**2. Results and Discussion.** – The defatted EtOH extract of the aerial parts of the plant was chromatographed over polyamide (CC), *LiChroprep RP-18* (MPLC), and silica gel (CC) to furnish compounds **1**–**3** (see *Exper. Part*).

Compounds **1** and **2** had the same molecular formula $C_{36}H_{58}O_{11}$, as determined by $^{13}$C-NMR, DEPT experiments, and ESI-MS. The positive-ion ESI-MS of **1** and **2** showed the same quasimolecular-ion peak at *m*/*z* 689 ($[M+Na]^+$), while, in the negative-ion mode, a quasimolecular ion was detected at *m*/*z* 665 ($[M-H]^-$). In the negative-ion ESI-MS of both, the prominent fragment was observed at *m*/*z* 503 (cleavage of a hexose unit), indicating their monoglycosidic structures. Further spectral data established the structure of **1** and **2** to be the isomeric 29- and 30-(β-D-glucopyranosyloxy)-2α,3β,23-trihydroxyolean-12-en-18-oic acids, respectively.




**1** $R^1$ = β-D-glucopyranosyloxy, $R^2$ = H viscoside A
**2** $R^1$ = H, $R^2$ = β-D-glucopyranosyloxy viscoside B




**3** R = H norviscoside
**3a** R = Ac norviscoside heptaacetate

The $^{13}$C-NMR spectra of **1** and **2** each showed 36 signals, of which 30 were assigned to a triterpenoid moiety and six to a hexose unit. The $^1$H-NMR spectra revealed anomeric-proton signals at $\delta$ 4.84 (*d*, $^3J = 7.8$ Hz) and 4.75 (*d*, $^3J = 7.8$ Hz), respectively. Full assignments of the $^1$H- and $^{13}$C-NMR data (*Tables 1* and *2*) of the hexose units and the aglycone moieties of **1** and **2** were corroborated by 2D-NMR experiments. The multiplicities and the coupling constants were consistent with the presence of a β-D-glucopyranose unit for both, the D-configuration being assumed according to those most often encountered among the plant glycosides. Significant proton resonances were observed for five tertiary Me, two OCH, and two $CH_2O$ groups and for an olefinic proton, all arising from the aglycone moieties. The DQF-COSY experiments clearly established the *trans*-diaxial positions of H–C(2) and H–C(3) ($\delta$(H) 4.24 (*m*) and 4.19 (*d*, $^3J = 9.4$ Hz for **1**; $\delta$(H) 4.18 (*m*) and 4.19 (*d*, $^3J =$ 9.4 Hz) for **2**). Additional $CH_2$ signals ($\delta$(H) 2.29 (*dd*, $^3J = 12.4$, 4.1 Hz) and 1.37 (overlapped) for **1**; $\delta$(H) 2.28 (*dd*, $^3J = 12.5$, 4.8 Hz and 1.38 (overlapped) for **2**) were assigned to $H_\beta$–C(1) (equatorial) and $H_\alpha$–C(1) (axial). The $^{13}$C-NMR signals at $\delta$(C) 122.6 and 144.8 for **1** and $\delta$(C) 122.5 and 144.9 for **2**, attributable to C(12) and C(13), suggested an olean-12-ene skeleton. The olefinic H–C(12) was observed at $\delta$(H) 5.42 (*t*, $^3J = 3.3$ Hz) for **1** and 5.57 (*t*, $^3J = 3.3$ Hz) for **2**. A combination of 1D- and 2D-NMR techniques allowed to assign the $\delta$(H) and $\delta$(C) to a tetrahydroxyolean-12-ene unit [2] for **1** and **2**.

The two $CH_2O$ groups of **1** were observed as two *AX* systems at $\delta$(H) 4.21 and 3.72 ($^2J = 10.4$ Hz) and 3.90 and 3.39 ($^2J = 9.2$ Hz) and assigned to C(23) or C(24) ($\delta$(C) 66.6) and C(29) or C(30) ($\delta$(C) 81.5), respectively, by HMBC experiments (*Table 1*). The locations of the two $CH_2O$ groups were established by the HMBC correlations C(4)/$CH_2$(23) and C(20) $CH_2$(29) and confirmed by a ROESY experiment. The NOEs for H–C(3)/$CH_2$(23), H–C(3)/H–C(5), H–C(5)/H–C(9), and H–C(9)/Me(27) indicated that these protons are situated on the same side ($\alpha$) of the triterpene moiety. On the other hand, an NOE for H–C(18)/Me(30) suggested their position on the β-side and the magnitude of the coupling constants is indicative for a chair conformation of ring E. The $\delta$(C) 81.5 of the $CH_2O$ group assigned to C(29) showed a HMBC correlation to the anomeric H–C(1′) of the glucose unit establishing the site of glycosidation at ring E; this was confirmed by the long-range correlation between the anomeric C(1′) ($\delta$(C) 105.5) and C*H*$_2$O ($\delta$(H) 3.90 and 3.39). The $\delta$(C) at 180.1 suggested the occurrence of a free COOH functionality at C(17).

The NMR data of **2** closely resembled those of **1** (*Tables 1* and *2*). Significant differences were observed only for the chemical-shift values of H–C(18), Me(29), C(29), $CH_2$(30), and C(30). The HMBC correlation

Table 1. *$^1$H- and $^{13}$C-NMR Data for Viscoside A* (**1**) *and HMBC Correlations in ($D_5$)Pyridine.* $\delta$ in ppm, $J$ in Hz.

| | $\delta$(H) | $\delta$(C)[a] | HMBC (from C to H) | ROESY |
|---|---|---|---|---|
| $CH_2$(1) | 1.37[b]) | 47.8 | Me(25) | |
| | 2.29 (*dd*, $J$ = 12.4, 4.1) | | | H–C(9), $CH_2$(23) |
| H–C(2) | 4.24 (*m*) | 68.9 | H–C(3), $H_a$–C(1) | Me(25) |
| H–C(3) | 4.19 (*d*, $J$ = 9.4) | 78.3 | $H_a$–C(1) | H–C(5), $CH_2$(23) |
| C(4) | – | 43.7 | H–C(5), $CH_2$(23), Me(24) | |
| H–C(5) | 1.80[b]) | 48.0 | $CH_2$(23), Me(24), $H_a$–C(1) | H–C(9), $CH_2$(23) |
| $CH_2$(6) | 1.73[b]) | 18.6 | H–C(5) | |
| | 1.44[b]) | | | |
| $CH_2$(7) | 1.63 (*m*) | 32.9 | Me(26) | Me(27) |
| | 1.30[b]) | | | |
| C(8) | – | 39.9 | Me(26), Me(27), H–C(9) | |
| H–C(9) | 1.86[b]) | 48.2 | H–C(12), Me(25), Me(26) | Me(27) |
| C(10) | – | 38.4 | $CH_2$(1), H–C(5), H–C(9), Me(25) | |
| $CH_2$(11) | 2.00 (*m*) | 24.0 | H–C(9) | |
| H–C(12) | 5.42 (*t*, $J$ = 3.3) | 122.6 | H–C(18), $CH_2$(11) | H–C(18), $CH_2$(11), H–C(9) |
| C(13) | – | 144.8 | $CH_2$(11), Me(27) | |
| C(14) | – | 42.2 | H–C(9), H–C(12), Me(26), Me(27) | |
| $CH_2$(15) | 2.14 (*ddd*, $J$ = 12.5, 13.2, 2.5) | 28.3 | Me(26) | Me(26) |
| | 1.10[b]) | | | |
| $CH_2$(16) | 2.05[b]), 1.88 (*m*) | 23.8 | | |
| C(17) | – | 47.0 | H–C(18), $H_a$–C(22), $H_b$–C(19) | |
| H–C(18) | 3.32 (*dd*, $J$ = 13.4, 3.5) | 41.1 | H–C(12), $H_a$–C(19) | H–C(12), $H_a$–C(16), Me(30) |
| $CH_2$(19) | 1.96 (*t*, $J$ = 13.4) | 41.2 | $CH_2$(29), Me(30) | Me(27), $H_a$–C(29) |
| | 1.41 (*dd*, $J$ = 13.4, 3.5) | | | Me(30) |
| C(20) | – | 35.7 | $CH_2$(19), $CH_2$(29) | |
| $CH_2$(21) | 1.70[b]) | 29.4 | Me(30) | $CH_2$(29) |
| | 1.41[b]) | | | Me(30) |
| $CH_2$(22) | 2.05[b]), 1.81[b]) | 32.4 | | |
| $CH_2$(23) | 4.21 (*d*, $J$ = 10.4) | 66.6 | H–C(5), $CH_2$(24) | H–C(5), Me(24) |
| | 3.72 (*d*, $J$ = 10.4) | | | H–C(5), Me(24) |
| Me(24) | 1.07 (*s*) | 14.4 | H–C(3), $CH_2$(23) | $CH_2$(23) |
| Me(25) | 1.07 (*s*) | 17.4 | $CH_2$(1), H–C(5) | |
| Me(26) | 1.04 (*s*) | 17.6 | H–C(9) | |
| Me(27) | 1.17 (*s*) | 26.1 | $H_a$–C(15) | |
| C(28) | – | 180.1 | | |
| $CH_2$(29) | 3.90 (*d*, $J$ = 9.2) | 81.5 | H–C(1′), Me(30) | Me(30) |
| | 3.39 (*d*, $J$ = 9.2) | | | H–C(1′) |
| Me(30) | 1.19 (*s*) | 19.8 | $CH_2$(29), $H_a$–C(19), $H_a$–C(21) | H–C(18), $CH_2$(29) |
| H–C(1′) | 4.84 (*d*, $J$ = 7.8) | 105.5 | $CH_2$(29), H–C(2′) | $H_b$–C(29) |
| H–C(2′) | 4.07 (*dd*, $J$ = 7.8, 9.5) | 75.4 | H–C(3′) | |
| H–C(3′) | 4.26 (*t*, $J$ = 9.5) | 78.6 | | |
| H–C(4′) | 4.27 (*t*, $J$ = 9.5) | 71.8 | H–C(3′) | |
| H–C(5′) | 3.99 (*m*) | 78.7 | | |
| $CH_2$(6′) | 4.59 (*dd*, $J$ = 11.8, 2.4), | 62.9 | | |
| | 4.43 (*dd*, $J$ = 11.8, 5.3) | | | |

[a]) Multiplicity was obtained from DEPT experiments. [b]) Signal patterns undetermined due to overlapping.

Table 2. *$^1$H- and $^{13}$C-NMR Data of Viscoside B* (**2**) *and HMBC Correlations in ($D_5$)Pyridine.* $\delta$ in ppm, $J$ in Hz.

| | $\delta$(H) | $\delta$(C)[a]) | HMBC (from C to H) |
|---|---|---|---|
| $CH_2$(1) | 1.38[b]) | 47.8 | Me(25) |
| | 2.28 (*dd*, $J$ = 12.5, 4.8) | | |
| H–C(2) | 4.18[b]) | 68.9 | H–C(3), $CH_2$(1) |
| H–C(3) | 4.19 (*d*, $J$ = 9.4) | 78.3 | $H_a$–C(1), $CH_2$(23), Me(24) |
| C(4) | – | 43.7 | H–C(5), $CH_2$(23), Me(24) |
| H–C(5) | 1.81[b]) | 48.0 | $CH_2$(23), Me(24), Me(25) |
| $CH_2$(6) | 1.73[b]), 1.44[b]) | 18.6 | |
| $CH_2$(7) | 1.64 (*m*) | 32.9 | Me(26) |
| | 1.30[b]) | | |
| C(8) | – | 39.8 | H–C(9), Me(26), Me(27) |
| H–C(9) | 1.88 (*t*, $J$ = 9.5) | 48.2 | H–C(12), Me(25), Me(26) |
| C(10) | – | 38.5 | $CH_2$(1), H–C(9), Me(25) |
| $CH_2$(11) | 1.98 (*m*) | 24.0 | |
| H–C(12) | 5.57 (*t*, $J$ = 3.3) | 122.5 | |
| C(13) | – | 144.9 | Me(27) |
| C(14) | – | 42.2 | H–C(12), Me(26), Me(27) |
| $CH_2$(15) | 2.19[b]) | 28.4 | Me(27) |
| | 1.13[b]) | | |
| $CH_2$(16) | 2.09 (*ddd*, $J$ = 13.2, 12.5, 2.5), 1.98 (*m*) | 24.2 | |
| C(17) | – | 46.5 | $CH_2$(19) |
| H–C(18) | 3.51 (*dd*, $J$ = 8.5, 9.5) | 41.4 | H–C(12) |
| $CH_2$(19) | 1.71[b]) | 42.3 | Me(29) |
| C(20) | – | 35.2 | $CH_2$(19), $CH_2$(30) |
| $CH_2$(21) | 1.71[b]) | 30.2 | Me(29) |
| | 1.38[b]) | | |
| $CH_2$(22) | 2.19[b]), 1.80[b]) | 33.3 | |
| $CH_2$(23) | 4.18 (*d*, $J$ = 10.7) | 66.6 | H–C(5), Me(24) |
| | 3.72 (*d*, $J$ = 10.7) | | |
| Me(24) | 1.07 (*s*) | 14.4 | H–C(3), $CH_2$(23) |
| Me(25) | 1.06 (*s*) | 17.4 | $CH_2$(1), H–C(5), H–C(9) |
| Me(26) | 1.02 (*s*) | 17.6 | H–C(9) |
| Me(27) | 1.21 (*s*) | 26.2 | |
| C(28) | – | n.d. | |
| Me(29) | 1.09 (*s*) | 28.6 | $CH_2$(30) |
| $CH_2$(30) | 4.27 (*d*, $J$ = 9.4) | 74.2 | H–C(1′), Me(29) |
| | 3.73 (*d*, $J$ = 9.4) | | |
| H–C(1′) | 4.75 (*d*, $J$ = 7.8) | 105.5 | $CH_2$(30) |
| H–C(2′) | 4.06 (*dd*, $J$ = 7.8, 9.5) | 75.5 | |
| H–C(3′) | 4.26[b]) | 78.5 | |
| H–C(4′) | 4.27[b]) | 71.9 | |
| H–C(5′) | 3.99 (*m*) | 78.6 | |
| $CH_2$(6′) | 4.57 (*dd*, $J$ = 11.8, 2.4), 4.41 (*dd*, $J$ = 11.8, 5.3) | 63.1 | |

[a]) Multiplicity was obtained from DEPT experiments. [b]) Signal patterns undetermined due to overlapping.

between the $CH_2O$ group at $\delta$(C) 74.2, assigned to C(30), and the anomeric H–C(1′) of the glucose unit and *vice versa* supported the site of glycosidation at ring E of **2**. In contrast to **1**, the coupling constants of H–C(18) suggested that ring E of **2** rather adopts a boat or twist-boat conformation with the $CH_2O$ group in the sterically favored pseudo-axial position. Furthermore, no NOE for H–C(18)/Me(30) as in **1** but a weak NOE for H–C(18)/$CH_2$(30)O located at ring E was observed. Moreover, the signal of this $CH_2O$ group of **2** is

paramagnetically shifted with respect to that of **1**, which additionally confirms the relative configuration at C(20) [3][1]). These results evidenced that compound **2** is the C(20) epimer of viscoside A (**1**).

Compound **3** was isolated as an amorphous colorless powder. The IR absorptions at 3420, 1717, 1652, and 1073 $cm^{-1}$ indicated the presence of hydroxy, ester carbonyl, ketone, double-bond, and acetal functionalities. Its FAB-MS (positive mode) displayed a $[M+Na]^+$ and $[M+K]^+$ pseudomolecular ion at *m/z* 687.5 and 703.4, respectively. FAB-MS and NMR data (*Table 3*) were in accordance with the molecular formula $C_{35}H_{52}O_{12}$. Acetylation of **3** yielded the heptaacetate **3a** (ESI-MS (pos.): *m/z* 981.4 ($[M+Na]^+$, $C_{49}H_{66}NaO_{19}^+$)). The spectral data of **3** and **3a** established the structure of **3** to be (17*S*)-2$\alpha$,18$\beta$,23-trihydroxy-3,19-dioxo-19(18 → 17)-abeo-28-norolean-12-en-25-oic acid $\beta$-D-glucopyranosyl ester.

The $^{13}$C-NMR spectrum of **3** revealed 35 signals of which six were assigned to a glucose unit. The anomeric H–C(1′) of the latter at $\delta$(H) 6.47 (*d*, $^3J$ = 8.3 Hz) indicated the $\beta$-D-configuration (D assumed, *cf.* **1** and **2**). The NMR signals of the glucose unit, particularly the $\delta$ of H–C(1′) and C(1′) were in agreement with an ester linkage to the aglycone. In the $^{13}$C-NMR spectrum, the aglycone moiety gave rise to five Me, nine $CH_2$, and five CH groups and to ten quaternary C-atoms, as established by DEPT experiments. Thus, the formula $C_{29}H_{42}O_8$ was attributed to the aglycone, implying nine degrees of unsaturation, *i.e.*, a C=C bond ($\delta$(C) 142.1 (C), 119.9 (CH)), three C=O groups ($\delta$(C) 226.9, 215.0, 175.6) and a pentacyclic aglycone structure. The $\delta$(H) 5.22 (*dd*, $^3J$ = 13.0, 5.7 Hz) and 4.82 (br. *s*) and the correlated $\delta$(C) 71.3 (CH) and 72.3 (CH) indicated the presence of two OCH groups, and an *AB* system at $\delta$(H) 4.48 and 3.69 ($^2J$ = 11.0 Hz) correlated to $\delta$(C) 65.0 ($CH_2$) was suggesting the presence of a $CH_2O$ group in the aglycone moiety. The complete structure of **3** was determined after extensive 2D-NMR measurements (COSY, HMQC and HMBC). In addition to a glucose unit, COSY experiments revealed the five main molecular fragments *a*–*e*, besides five tertiary Me groups and a primary alcohol (*Fig. 1*). The connectivities and the ester glycosidic linkage were established by HMBC experiments (*Table 3*). In particular, $^1$H,$^{13}$C correlations from the C=O at $\delta$(C) 175.6 to the anomeric H–C(1′), $H_\alpha$–C(1), H–C(5), and H–C(9) enabled us to position the COOH group at C(10). Similarly, correlations from one of the ketone C=O ($\delta$(C) 215.0) to $CH_2$(1), H–C(2), $CH_2$(23), and Me(24) established the C(3)=O and $CH_2$(23)OH moieties. Additional long-range interactions from C(23) ($\delta$(C) 65.0) to Me(24) and H–C(5), from C(9) to $H_\alpha$–C(1), H–C(5), H–C(12), and Me(26), as well as from C(8) to H–C(9), Me(26), and Me(29) allowed to connect the fragments *a*–*c* and to generate the rings A, B, and C. The two isolated $CH_2CH_2$ fragments *d* and *e* were attributed to rings D and E, respectively. The weak COSY cross-peak for the olefinic proton at $\delta$(H) 6.30 (br. *d*, $^3J$ = 2.5 Hz) and the OCH at $\delta$(H) 4.82 (br. *s*) located the secondary OH function at C(18). The remaining ketone C=O ($\delta$(C) 226.9), assigned to C(19)=O, exhibited long range correlations to the $CH_2CH_2$ fragment *e* and to the tertiary Me(29) and Me(30), hence suggesting that ring E is five-membered. The quaternary C-atom at $\delta$(C) 46.3 supported this assumption: it was assigned to C(20) and showed long-range correlations with Me(29), Me(30), and the $CH_2CH_2$ fragment *e*. The remaining quaternary C-atom ($\delta$(C) 57.6) was attributed to a spiro atom, *i.e.*, to C(17). Long-range correlations of $H_\alpha$–C(16), $CH_2$(21), and $CH_2$(22) to C(17) as well as the lack of a resonance for C(28) (of the oleanane skeleton) corroborated this interpretation.

In the $^1$H-NMR spectrum of heptaacetate **3a**, the resonances of H–C(2) ($\delta$(H) 5.51 (*dd*, $^3J$ = 13.7, 5.5 Hz)), H–C(18) ($\delta$(H) 5.60 (*d*, $^3J$ = 2.4 Hz)), and $CH_2$(23) ($\delta$(H) 4.34 and 4.04 (*AB*, $^2J$ = 11.4 Hz)) were shifted downfield (*Table 4*). All signal assignments of **3a** were based on a series of 2D-NMR experiments and strongly supported the proposed structure of **3**. The relative configuration of **3** was established by 2D-NMR experiments with **3** and **3a**. The NOEs for H–C(2)/Me(24) and H–C(2)/$H_\beta$–C(1) suggested that these protons are on the same side ($\beta$) of the nortriterpene moiety, where H–C(2) is axial ($^3J$(2,1$\alpha$) = 13.0 Hz for **3** and 13.7 Hz for **3a**), while NOEs for H–C(5)/$CH_2$(23), H–C(5)/H–C(9), H–C(9)/Me(27), and Me(27)/H–C(18) indicated their

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[1]) It has been established for the di- and triterpenoid series that the relative configuration at C(4) can be assigned by the $^1$H-NMR-shift differences of the respective $CH_2OH$ or $CH_2OAc$ groups at C(4) [3]. Generally, the $CH_2$ of axial groups are paramagnetically shifted with respect to their equatorial counterparts. The same argument seems to hold also for the relative configuration at C(20) of triterpenoids; however, the conformation of the *cis*-fused ring E of **2** is not a chair.

Table 3. *$^1$H- and $^{13}$C-NMR Data of Norviscoside* (**3**) *and HMBC Correlations in ($D_5$)Pyridine.* $\delta$ in ppm, $J$ in Hz.

| | $\delta$(H) | $\delta$(C)[a]) | HMBC (from C to H) |
|---|---|---|---|
| $CH_2$(1) | 1.74 (*dd*, *J* = 12.5, 13.0) | 46.8 | H–C(2), H–C(9) |
| | 3.64 (*dd*, *J* = 12.5, 5.7) | | |
| H–C(2) | 5.22 (*dd*, *J* = 13.0, 5.7) | 71.3 | $CH_2$(1) |
| C(3) | – | 215.0 | $CH_2$(1) |
| C(4) | – | 54.2 | H–C(5), $CH_2$(23), Me(24) |
| H–C(5) | 2.67 (*dd*, *J* = 11.2, 1.5) | 49.4 | $CH_2$(23), Me(24), $H_\beta$–C(1) |
| $CH_2$(6) | 2.96[b]) | 19.5 | |
| | 1.83[b]) | | |
| $CH_2$(7) | 1.84[b]) | 34.3 | Me(26) |
| | 1.63[b]) | | |
| C(8) | – | 40.7 | H–C(9), Me(26), Me(27) |
| H–C(9) | 2.09 (*dd*, *J* = 12.3, 4.9) | 47.4 | $CH_2$(1), H–C(5), H–C(12), Me(26) |
| C(10) | – | 48.6 | $CH_2$(1), H–C(5), H–C(9) |
| $CH_2$(11) | 2.66 (*dm*, *J* = 15.6) | 26.0 | H–C(9), H–C(12) |
| | 2.99 (*m*) | | |
| H–C(12) | 6.30 (br. *d*, *J* = 2.5) | 119.9 | |
| C(13) | – | 142.1 | Me(27) |
| C(14) | – | 44.9 | H–C(9), H–C(12), Me(26) |
| $CH_2$(15) | 1.78[b]) | 27.2 | $CH_2$(16), Me(27) |
| | 1.12[b]) | | |
| $CH_2$(16) | 1.92 (*ddd*, *J* = 13.7, 13.7, 1.40) | 30.7 | $CH_2$(15), $CH_2$(22) |
| | 1.40 (*m*) | | |
| C(17) | – | 57.6 | $CH_2$(16), $CH_2$(21), $CH_2$(22) |
| H–C(18) | 4.82 (br. *s*) | 72.3 | H–C(12), $CH_2$(22) |
| C(19) | – | 226.9 | $CH_2$(21), $CH_2$(22), Me(29), Me(30) |
| C(20) | – | 46.3 | $CH_2$(21), $CH_2$(22), Me(29), Me(30) |
| $CH_2$(21) | 2.00 (*ddd*, *J* = 12.2, 7.5, 7.5) | 36.5 | $CH_2$(22), Me(29), Me(30) |
| | 1.69 (*ddd*, *J* = 12.2, 7.5, 6.3) | | |
| $CH_2$(22) | 2.23 (*ddd*, *J* = 13.3, 6.3, 7.5) | 24.6 | $CH_2$(21) |
| | 1.57 (*ddd*, *J* = 13.3, 7.5, 7.5) | | |
| $CH_2$(23) | 4.48 (*d*, *J* = 11.0) | 65.0 | H–C(5), Me(24) |
| | 3.69 (*d*, *J* = 11.0) | | |
| Me(24) | 1.24 (*s*) | 19.3 | H–C(5), $CH_2$(23) |
| C(25) | – | 175.6 | H–C(1′), $CH_2$(1), H–C(5), H–C(9) |
| Me(26) | 1.39 (*s*) | 17.0 | H–C(9) |
| Me(27) | 1.07 (*s*) | 23.1 | $CH_2$(15) |
| Me(29) | 1.22 (*s*) | 23.9 | $CH_2$(21) |
| Me(30) | 1.12 (*s*) | 25.6 | $CH_2$(21) |
| OH–C(18)[c]) | 6.63 (*d*, *J* = 5.1) | | |
| H–C(1′) | 6.47 (*d*, *J* = 8.3) | 96.3 | |
| H–C(2′) | 4.21 (*dd*, *J* = 8.3, 9.0) | 74.0 | |
| H–C(3′) | 4.30[b]) | 79.5 | |
| H–C(4′) | 4.30[b]) | 71.7 | |
| H–C(5′) | 4.48 (*m*) | 79.7 | |
| $CH_2$(6′) | 4.45 (*dd*, *J* = 11.8, 2.5), 4.33 | 62.9 | |
| | (*dd*, *J* = 11.8, 4.5) | | |

[a]) Multiplicity was obtained from DEPT experiments. [b]) Signal patterns undetermined due to overlapping. [c]) Disappeared after adding $D_2O$.

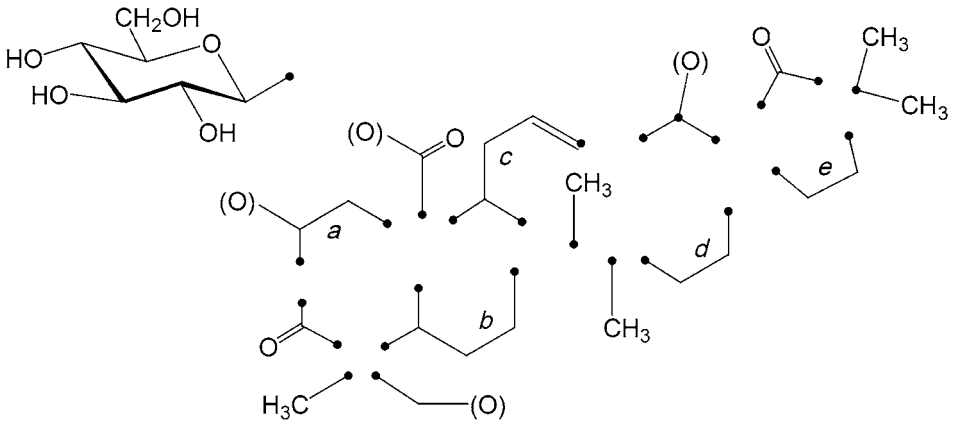


Fig. 1. *Fragments of* **3** *deduced from 2D-NMR measurements*

$\alpha$-position. The NOE for H–C(18)/$H_{ax}$–C(16) ($\delta_H$ 1.92) and the absence of NOEs for H–C(18) and the protons of ring E suggested the $\alpha$-position of the keto function at C(19) ((*S*)-configuration at C(17)). Furthermore, assuming the occurrence of a spiro-type cyclization from oleanolic acid (= 3$\beta$-hydroxyolean-12-en-28-oic acid) by oxidative decarboxylation supported this proposal.

To the best of our knowledge, no *ent*-oleananes have been known from Lamiaceae species; thus, the absolute configurations of compounds **1**–**3** was assigned for biogenetic reasons in terms of the normal oleanane skeleton. In one of the previous studies performed on *Phlomis spectabilis*, 28-noroleana-16,21-diene triterpenes had also been reported [4]. This is the second report of nortriterpene glycosides from the genus *Phlomis*. Recently, the first representative nortriterpenoids having the same skeleton were reported from *Notochaete hamosa* (Lamiaceae) [5].

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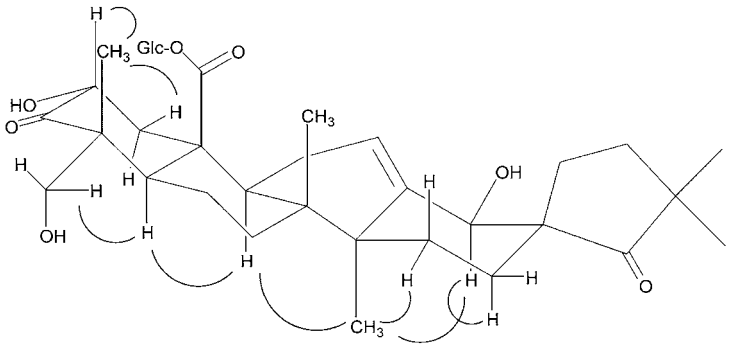


Fig. 2. *Key NOEs of norviscoside* (**3**)

Table 4. *$^1$H- and $^{13}$C-NMR Data of Norviscoside Heptaacetate* (**3a**) *and HMBC Correlations in $CDCl_3$.* $\delta$ in ppm, $J$ in Hz.

| | $\delta$(H) | $\delta$(C)[a]) | HMBC (from C to H) |
|---|---|---|---|
| $CH_2$(1) | 1.51 (*dd*, *J* = 12.6, 13.7) | 42.3 | |
| | 2.91 (*dd*, *J* = 12.5, 5.5) | | |
| H–C(2) | 5.51 (*dd*, *J* = 13.7, 5.5) | 71.2 | $CH_2$(1) |
| C(3) | – | 204.0 | $CH_2$(1), H–C(2), $CH_2$(23), Me(24) |
| C(4) | – | 52.0 | H–C(5), $CH_2$(23), Me(24) |
| H–C(5) | 1.83[b]) | 45.9 | Me(24) |
| $CH_2$(6) | 2.53 (*ddd*, *J* = 13.1, 2.7, 3.4), 1.42[b]) | 18.6 | |
| $CH_2$(7) | 1.59[b]) | 33.5 | Me(26) |
| | 1.55[b]) | | |
| C(8) | – | 44.9 | Me(26), Me(27) |
| H–C(9) | 1.80[b]) | 49.4 | $CH_2$(1), H–C(5), Me(26) |
| C(10) | – | 48.0 | $CH_2$(1), H–C(9), Me(26) |
| $CH_2$(11) | 2.16[b]), 1.75[b]) | 24.9 | |
| H–C(12) | 5.12[b]) | 119.9 | |
| C(13) | – | 137.3 | Me(27) |
| C(14) | – | 40.1 | Me(26), Me(27) |
| $CH_2$(15) | 1.79[b]) | 26.5 | Me(27) |
| | 1.24[b]) | | |
| $CH_2$(16) | 1.77[b]), 1.46[b]) | 29.5 | |
| C(17) | – | 56.0 | $CH_2$(21) |
| H–C(18) | 5.60 (br. *d*, *J* = 2.4) | 74.5 | |
| C(19) | – | 224.0 | $CH_2$(21), Me(29), Me(30) |
| C(20) | – | 45.8 | $CH_2$(21), Me(29), Me(30) |
| $CH_2$(21) | 1.78[b]) | 35.5 | Me(29), Me(30) |
| | 1.72[b]) | | |
| $CH_2$(22) | 1.95[b]), 1.69[b]) | 24.1 | |
| $CH_2$(23) | 4.34 (*d*, *J* = 11.4) | 64.9 | Me(24) |
| | 4.04 (*d*, *J* = 11.4) | | |
| Me(24) | 1.02 (*s*) | 17.8 | |
| C(25) | – | 173.2 | |
| Me(26) | 1.01 (*s*) | 16.2 | |
| Me(27) | 1.07 (*s*) | 22.6 | |
| Me(29) | 1.22 (*s*) | 23.9 | Me(30) |
| Me(30) | 0.99 (*s*) | 25.1 | Me(29) |
| H–C(1′) | 5.83 (*d*, *J* = 8.3) | 91.7 | |
| H–C(2′) | 5.28[b]) | 70.0 | |
| H–C(3′) | 5.29[b]) | 73.0 | |
| H–C(4′) | 5.11[b]) | 68.3 | |
| H–C(5′) | 3.87 (*ddd*, *J* = 10.0, 5.4, 2.3) | 72.9 | |
| $CH_2$(6′) | 4.19 (*dd*, *J* = 12.4, 2.3), 4.10 | 61.9 | |
| | (*dd*, *J* = 12.4, 5.4) | | |

[a]) Multiplicity was obtained from DEPT experiments. [b]) Signal patterns undetermined due to overlapping. Additional signals: 173.19, 170.75, 170.67, 170.37, 169.30, 169.08, 168.90 (7 Me*C*O); 21.01–20.68 (7 *Me*CO).

## Experimental Part

*General*. Column chromatography (CC): silica gel (70–230 mesh, *Merck*) and polyamide (*Fluka*). Medium-pressure liquid chromatography (MPLC): *Labomatic* glass column (2.6 × 46 cm, i.d.), packed with *LiChroprep RP-18*; *Büchi 681* chromatography pump. TLC: precoated silica gel *60 $F_{254}$* (*Merck*) plates; $CHCl_3$/MeOH/$H_2O$ mixtures; visualization by spraying with 1% vanillin in conc. $H_2SO$ soln. followed by heating at 105° for 1–2 min. Optical rotations: *Autopol IV* polarimeter; in MeOH at 20°. NMR Spectra: *Bruker DRX-600* FT spectrometer operating at 600 and 500 ($^1H$) and 150.9 and 125 ($^{13}C$) MHz; $\delta$ in ppm rel. to $SiMe_4$ coupling constants $I$ in Hz; multiplicities for $^{13}C$ by DEPT experiments. MS: *Finnigan 311-A* (for FAB) and *Finnigan-MAT TSQ-7000* spectrometer (for ESI); in *m/z*.

*Plant Material. Phlomis viscosa* POIRET was collected from Osmaniye, Düziçi (Haruniye), above Çitli Village (Turkey) on July 1, 2001. The plant specimen was identified by Dr. *Ali A. Dönmez*. The voucher specimen (AAD 9493) has been deposited at the Herbarium of the Department of Biology, Faculty of Science, Hacettepe University, Ankara, Turkey.

*Extraction and Isolation*. The powdered herb of *Phlomis viscosa* (350 g) was extracted with EtOH (90°, 2 × 2.5 l, 5 h) and then filtered. The filtrate was evaporated: 65 g (18.7%) of crude extract. The residue of the EtOH extract was suspended in $H_2O$ (0.1 l) and washed with $CHCl_3$ (3×). The remaining $H_2O$ phase was evaporated: 41.9 g of crude extract. An aliquot of the latter (39.9 g) was separated by CC (polyamide (200 g), 0 → 100% MeOH/$H_2O$): 17 fractions (*Frs. A–R*). *Fr. I* (763 mg) was subjected to reversed-phase MPLC (*LiChroprep C-18*; 20 → 100% MeOH/$H_2O$): eight major fractions (*Frs. $I_1$–$I_8$*). *Fr. $I_8$* yielded pure **3** (16 mg). *Fr. J* (2737 mg) was also subjected to MPLC (conditions as for *Fr. J*): verbascoside (1380 mg), **1** (38 mg), **2** (15 mg), and **3** (13 mg) as crude compounds. Their purification by CC (silica gel, $CH_2Cl_2$/MeOH/$H_2O$ 40:10:1) afforded pure **1** (11 mg), **2** (4 mg), and **3** (3 mg).

*Viscoside A* (= *(2α,3β,4α,29α)-29-(β-D-Glucopyranosyloxy)-2,3,23-trihydroxyolean-12-en-28-oic Acid*; **1**). $[\alpha]_D^{20} = +19.9$ ($c = 0.05$, MeOH). IR (KBr): 3405, 1694, 1652, 1077, 1048. $^1H$- (600 MHz) and $^{13}C$-NMR (150.9 MHz): *Table 1*. ESI-MS: 689.4 ($[M+Na]^+$, $C_{36}H_{58}NaO_{11}^+$).

*Viscoside B* (= *(2α,3β,4α,29β)-29-(β-D-Glucopyranosyloxy)-2,3,23-trihydroxyolean-12-en-28-oid Acid*; **2**). $[\alpha]_D^{20} = +19.9$ ($c = 0.05$, MeOH). IR (KBr): 3444, 1652, 1122. $^1H$- (600 MHz) and $^{13}C$-NMR (150.9 MHz): *Table 2*. ESI-MS: 689.4 ($[M+Na]^+$, $C_{36}H_{58}NaO_{11}^+$).

*Norviscoside* (= *(1*R*,2*S*,4a*S*,4b*R*,6a*R*,7*R*,9*R*,10a*S*,10b*S*)-3,4,4a,4b,5,6,6a,7,8,9,10,10a,10b,11-Tetradecahydro-1-hydroxy-7-(hydroxymethyl)-3′,3′,4a,4b,7-pentamethyl-2′,8-dioxospiro[chrysene-2(1*H*),1′-cyclopentane]-10a-carboxylic Acid β-D-Glucopyranosyl Ester*; **3**). $[\alpha]_D^{20} = -19.9$ ($c = 0.1$, MeOH). IR (KBr): 3420, 1717, 1652, 1073. $^1H$- (600 MHz) and $^{13}C$-NMR (150.9 MHz): *Table 3*. ESI-MS: 687.5 ($[M+Na]^+$, $C_{35}H_{52}NaO_{12}^+$), 703.4 ($[M+K]^+$).

*Norviscoside Heptaacetate* (**3a**). Treatment of **3** (5 mg) with $Ac_2O$ (0.5 ml) and pyridine (0.5 ml) at r.t. overnight followed by the usual workup yielded **3a**. $^1H$- (600 MHz) and $^{13}C$-NMR (150.9 MHz): *Table 4*.

## REFERENCES

[1] A. Huber-Morath, in 'Flora of Turkey and the East Aegean Islands', Ed. P. H. Davis, University Press, Edinburgh, 1982, Vol. 7, p. 102.
[2] S. B. Mahato, A. P. Kundu, *Phytochemistry* **1994**, *37*, 1517.
[3] A. Gaudemer, J. Polonsky, E. Wenkert, *Bull. Soc. Chim. Fr.* **1964**, 407.
[4] R. Kumar, S. Bhan, A. K. Kalla, K. L. Dhar, *Phytochemistry* **1992**, *31*, 2797.
[5] Y. Luo, C. Feng, Y. Tian, B. Li, G. Zhang, *Tetrahedron* **2003**, *59*, 8227.

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