Chemistry of Natural Compounds, Vol. 31, No. 2, 1995

PHLOMOSIDE A — AN IRIDOID GLYCOSIDE FROM *Phlomis thapsoides*

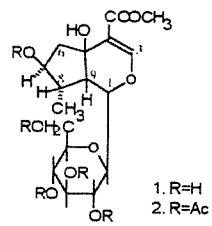
M. S. Maksudov, E. S. Maksimov, R. U. Umarova, Z. Saatov, and N. D. Abdullaev

UDC 547.918:547.192+548.737

The presence of three compounds of iridoid nature has been detected in the epigeal organs of the plant Phlomis thapsoides. *A spectral and chemical investigation has shown the identity of the structure of one of them with that of 5-hydroxy-8-epiloganin, obtained previously from the iridoid glycoside strictoloside by catalytic hydrogenation. Thus, 5-hydroxy-8-epiloganin has been isolated from this plant for the first time. In view of its natural origin it has been named phlomoside A.*

We have investigated the epigeal organs of *Phlomis thapsoides* (fam. Lamiaceae), which is distributed on the territory of Uzbekistan. Qualitative chromatography of the butanolic fraction of an extract of the plant revealed the presence of at least three substances of iridoid nature, two of them being the main components of the total iridoids. By a stagewise procedure we isolated an amorphous compound (**1**) with the composition $C_{17}H_{26}O_{11}$, $[\alpha]_D^{22}$ −115.7° (*c* 0.62; methanol). The UV spectrum had an absorption maximum at 231 nm, which is characteristic for an enol−ether system conjugated with a carbonyl group at C-4 [1, 2]. The IR spectrum of the glycoside contained characteristic bands at 1705 cm^{-1} (C=O) and 1635 cm^{-1} (C=C).

The acid hydrolysis of (**1**) led to *D*-glucose and a black product of the decomposition of the aglycon moiety of the iridoid. Analysis by the GLC method of the products of the methanolysis of the glycoside showed that it was a monoside of *D*-glucose.



NMR spectroscopy is very effectively and widely used in chemical investigations of iridoids and their glycosides. In view of this, we made a detailed investigation of the ^1H and ^{13}C NMR spectra of compound (**1**) and its pentaacetyl derivative (**2**). The characteristics of the resonance lines of the protons and the isotopic carbon atoms are given in Tables 1 and 2. The assignment of the resonance lines in the proton resonance spectra (at H_0 = 500 MHz) was made on the basis of an analysis of the 2D COSY spectra of compound (**1**).

In the identification of the signals of the carbon atoms we compared spectra taken under conditions of complete decoupling and conditions of the retention of spin−spin interaction of the nuclei of the ^{13}C isotope with protons. Analysis of the information given in Tables 1 and 2 revealed closeness of the resonance characteristics of the spectra of compound (**1**) and those of 5-OH-8-epilognin [3, 4].

In some positions the chemical shifts of the protons and of the ^{13}C nuclei differed somewhat. However, the observed differences may be due to the influence of the nature of the solvent (D_2O in the case of compound (**1**), and CD_3OD for (**3**)). On the basis of the spectral results given, we came to the conclusion of the structural identity of compound (**1**) and 5-OH-epiloganin, previously obtained synthetically by reducing the iridoid glycoside strictoloside [3]. This was also indicated by the configuration of the substituents at C-7 and C-8 determined from the SSCCs of the interacting protons (Table 1) along the chain $-H_2C_6-HC_7(OH)-HC_8(CH_3)-HC_9-HC_1-O-$ in dihedral angular relationship. In this situation the chemical shift of the

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 89 14 75. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 243-246, March-April, 1995. Original article submitted November 28, 1994.

0009-3130/95/3102-0200$12.50

TABLE 1. Chemical Shifts (ppm), Multiplicities, and SSCCs (J, Hz) of the Signals in the PMR Spectrum of Compound (**1**) in D_2O, of Its 2′,3′,4′,6′,7-Pentaacetate (**2**) in $CDCl_3$, and of 5-OH-8-Epiloganin (**3**) in CD_3OD [3, 4]

H_i	Compound		
	1	2	3
H−1	5.78 br.d $^3J \leq 1$	5.30 d	5.74 d $^3J=1.6$
H−3	7.56 s	7.32 s	7.47 s
H−6	2.05 dd $^2J=13.8$, $^3J=6.2$	2.24 dd	2.03 dd $^2J=13.6$, $^3J=5.6$
H−6	2.59 dd $^2J=13.8$, $^3J=5.5$	2.58 dd	2.55 dd $^2J=13.6$, $^3J=6.7$
H−7	3.68 m $^3J=6.2,5.5$, 4.8	4.58–5.20	3.54 m
H−8	2.35 m $^3J=10.0$, 7.4, 4.8		2.26 m
H−9	2.87 br.d $^3J=10.0$, ≤1	2.88 dd	2.79 dd $^3J=10.3$, 1.4
CH_3−10	0.91 d $^3J=7.4$	0.91	0.95 d $^3J=7.4$
$COOCH_3$	3.77 s	3.76	3.72 s
H−1′	4.75 d $^3J=8.3$	4.58–5.20	4.55 d $^3J=7.9$
H−2′	3.30 m $^3J=9.5$, 8.3	4.58–5.20	
H−3′	3.51 $^3J=9.5$, 6.0	4.58–5.20	
H−4′	3.74 dd $^3J=12.0$, 6.0	4.58–5.20	
H−5′	3.94 br.dd $^3J=12.0$, 1.8	3.73 m	
H−6′	3.42 m $\Sigma J=19.0$	4.09 dd	
H−6′	3.51 m $\Sigma J=17.5$	4.25 dd	
$OCOCH_3$		1.96, 1.99, 2.02, 2.04, 2.09	

TABLE 2. Chemical Shifts (ppm), Multiplicities, and SSCCs ($^1J_{CH}$, Hz — in parenthesis) in the ^{13}C NMR Spectrum of Compound (**1**) in D_2O and of 5-OH-Epiloganin (**3**) in CD_3OD [3, 4]

Carbon atom	Compound	
	1	3
1	95.35 d (175.9)	95.7
3	153.25 d (190.3)	153.4
4	113.68 s	115.3
5	70.34 s	71.5
6	46.56 t (132.8)	48.0
7	76.65 d (143.6)	77.9
8	42.02 d (132.8)	43.6
9	50.10 d (129.3)	51.6
10	13.10 q (125.7)	13.8
11	168.52 s	168.1
OMe	52.12 q (147.2)	51.6
1′	98.72 d (165.2)	99.7
2′	72.74 d (147.2)	74.4
3′	75.68 d (143.6)	77.5
4′	69.97 d (147.2)	71.7
5′	76.88 d (154.4)	78.4
6′	61.06 t (143.6)	62.8

C-9 carbon atom of compound (**1**) is significant: its value of 50.1 ppm shows the α-configuration of the methyl group at C-8. This also agrees with the value of $^1J_{CH}$ for C-8, 132.8 Hz, which is characteristic for a 8α-CH_3 substituent [5].

Thus, 5-hydroxy-8-epiloganin has been isolated from the epigeal organs of the plant *Phlomis thapsoides* for the first time. In view of the natural origin of compound (**1**), we have called it phlomoside A.

EXPERIMENTAL

TLC was conducted on Silufol plates. For column chromatography we used silica gels KSK and L 100/160 μm (Czechoslovakia). In TLC, the iridoid glycosides were revealed by spraying with vanillin—sulfuric acid followed by heating at 110-120°C for 2-5 min [6].

UV spectra were taken on a Hitachi instrument, and IR spectra on a UR-20 in KBr. ^1H and ^{13}C NMR spectra were recorded on a WM-500 spectrometer (Bruker) at H_0 = 500 MHz for ^1H and 125 MHz for ^{13}C, and the PMR spectrum of the pentaacetate (**2**) on a BS-567A (Tesla) at H_0 = 100 MHz.

Isolation of Iridoid Fractions from the Epigeal Part. The epigeal part of *Phlomis thapsoides* was gathered in June, 1989, in the Ordzhonikidze region of Tashkent province, environs of Chimgan. The dried and comminuted raw material (1 kg) was exhaustively extracted with methanol (6 × 5 liters). The methanolic extracts were combined and were concentrated to a volume of 0.5 liter, the residue was diluted with water, and the resulting precipitate was separated off. The methanol was evaporated, and the aqueous residue was extracted, first with hexane and then with butanol. After the butanol had been distilled off, 165 g of a light brown powder was obtained, part of which (30 g) was chromatographed on a column of silica gel (800 g).

On elution with the chloroform—methanol—water (70:23:4) system, 100-ml fractions were collected, and these were analyzed by TLC. Combined fractions (**8-15**) contained 8.8 g of a yellowish amorphous substance. Rechromatography on a column, using the same solvent system, gave 7.82 g (yield calculated on the air-dry raw material 4.3%) of amorphous phlomoside A (**1**), $C_{17}H_{26}O_{11}$, $[\alpha]_D^{22} -115.7°$ (s 0.62; methanol), λ_{max} (C_2H_5OH, nm) 231 nm ($lg\varepsilon = 3.85$), ν_{max} (KBr, cm^{-1}); 3400-3600 (OH), 1705 (C=O), 1635 (C=C).

Acid Hydrolysis. A solution of 20 mg of glycoside (**1**) in 5 ml of 5% sulfuric acid was heated on the water bath for an hour. The black-violet precipitate that deposited was filtered off. The filtrate was neutralized with barium acetate and was filtered again, after which it was concentrated in vacuum to 0.5 ml and chromatographed on paper with a marker — glucose. Glucose was detected in the hydrolysate.

Methanolysis of Phlomoside A (1). A solution of 5.0 mg of glycoside (**1**) in 5 ml of absolute methanol containing 5% HCl was boiled for 16 h. Then an equal volume of water was added to the reaction mixture, the acid was neutralized with silver carbonate, the precipitate was filtered off, and the filtrate was evaporated to dryness. *D*-Glucose was detected by GLC [7]. For the quantitative determination of the product of the methanolysis of phlomoside A we used *D*-glucose as internal standard. According to the results of the quantitative determination, phlomoside A contains one molecule of *D*-glucose.

Acetylation of Phlomoside A. A solution of 200 mg of phlomoside A (**1**) in 2 ml of pyridine was acetylated with 1.5 ml of acetic anhydride at room temperature for a day. Then the solution was poured into cold water, and the precipitate that deposited was filtered off and chromatographed on a column of silica gel. Elution with the ethyl acetate—toluene (3:5) system yielded 118 mg of the pentaacetate (**2**), $C_{27}H_{41}O_{16}$, mp 130-132°C (methanol), $[\alpha]_D^{22} -104°$ (c 0.90; methanol).

REFERENCES

1. A. Bianco, M. Guiso, C. Lavarone, and C. Trogolo, Gazz. Chim. Ital., **105**, 185 (1975).
2. V. A. Mnatsakanyan, Natural Iridoids [in Russian], Izd. ArmSSR, Erevan (1986), p. 57.
3. P. Junior, Planta Med., **51**, 229 (1985).
4. C. A. Boros and F. R. Stermitz, J. Nat. Prod., **53**, 105 (1990).
5. S. Damtoft, S. R. Jensen, and B. J. Nielsen, Phytochemistry, **20**, 2717 (1981).
6. M. N. Galbraith and D. H. S. Horn, Aust. J. Chem., **22**, 1045 (1969).
7. T. T. Gorovits, Khim. Prir. Soedin., 263 (1970).