

A Stilbene from the Roots of *Leuzea carthamoides*

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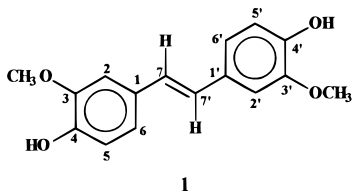
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From the roots of *Leuzea carthamoides*, (*E*)-3,3'-dimethoxy-4,4'-dihydroxystilbene (**1**) has been isolated and its structure elucidated by means of NMR spectroscopy, including HMQC and HMBC measurements, mass spectrometry, and X-ray crystallography.

Leuzea carthamoides DC. [syn. *Rhaponticum carthamoides* (Willd.) Iljin] (Asteraceae) is a medicinal plant of Siberian origin that possesses stimulant and tonic activity.¹ It belongs to the group of adaptogenic plants.² The roots are used in both traditional and official medicine in the countries of the former Soviet Union, and the above-ground parts are used as fodder material.^{3,4} The plant has been introduced into cultivation in several European countries.

Previous chemical studies on *L. carthamoides* have revealed the presence of ecdysteroids, flavonoids, and polyacetylenes.^{5–9} The present paper describes the isolation of a stilbene derivative and its structure elucidation. This is the first report on the isolation of this compound from *L. carthamoides* and on its occurrence in the family Asteraceae.

The benzene-soluble fraction of a methanol extract of the roots of *L. carthamoides* was subjected to repeated chromatography to afford compound **1**. The ¹H NMR spectrum



of **1** contained signals at δ_{H} 7.02 d ($J = 2$ Hz), 7.00 dd ($J = 2$ and 8 Hz), and 6.90 d ($J = 8$ Hz), corresponding to an ABX aromatic system. The singlet signal at δ_{H} 3.95, with three-proton intensity, revealed the presence of a methoxy group. Additionally, two singlet signals could be observed in the ¹H NMR spectrum at δ_{H} 6.89 and 5.61. The HMQC spectrum of **1** demonstrated the presence of five protonated carbons at δ_{C} 126.9, 120.4, 114.8, 108.5, and 56.1 and indicated that the singlet signal at δ_{H} 5.61, which did not exhibit any correlations, corresponded to a hydroxyl group. The HMQC correlations permitted the unambiguous assignments of the ¹H and ¹³C NMR spectra of **1**. The two- and three-bond long-range correlations observed in the HMBC spectrum pointed to the presence of three quaternary carbons (δ_{C} 146.8, 145.4, and 130.6), and the HMBC correlation signals suggested the partial structure of

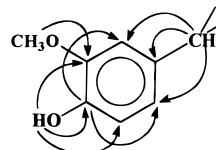


Figure 1. Observed main couplings of an HMBC experiment of **1** (H(C)).

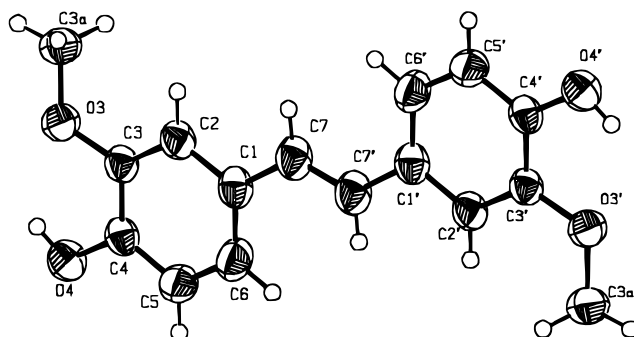


Figure 2. Perspective view of the molecule using thermal ellipsoids with 50% probability level. (Symmetry-equivalent atoms are marked with a prime).

compound **1** depicted in Figure 1. The EIMS of **1** exhibited a molecular peak at m/z 272, and the high-resolution mass spectrum led to the elemental formula for **1** of $\text{C}_{16}\text{H}_{16}\text{O}_4$. These data suggested that the molecule of **1** is formed from two of the units elucidated by means of the NMR studies above. Thus, this compound was identified as a symmetric stilbene with 3,3'-dimethoxy-4,4'-dihydroxy substitution. The *Z* or *E* stereochemistry of the olefinic protons was investigated by means of X-ray analysis. The crystallographic data confirmed the structure of **1** as (*E*)-4,4'-dihydroxy-3,3'-dimethoxystilbene (Figure 2). The molecule has a center of symmetry at the C-7–C-7' double bond of 1.305(4) Å. Other relevant distances (Å) are as follows: C-1–C-7 1.473(2); C-4–O-4, 1.370(2); C-3–O-3, 1.373(2); and O-3–C-3a 1.418(2). The average C–C bond distance in the benzene ring is 1.386(2) Å. In the crystal lattice, there is an O-4–H-4 \cdots O-3 intermolecular hydrogen bond O-4–H-4 \cdots O-3ⁱ (O \cdots Oⁱ, 2.932 Å, H \cdots Oⁱ, 2.146 Å; O–H \cdots Oⁱ, 160.6°; the symmetry operatorⁱ, $-x, y, 0.5 - z$). The corresponding parameters for the intramolecular O-4–H-4 \cdots O-3 hydrogen connection are 2.668 Å, 2.216 Å, and 115.0°.

(*E*)-3,3'-Dimethoxy-4,4'-dihydroxystilbene has not been reported previously as a natural product. To date, **1** has been described only as a synthetic product and as one of the degradation products of lignin.¹⁰

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Experimental Section

General Experimental Procedures. The melting point was uncorrected. Spectral data: UV, MeOH; IR, KBr; EIMS, 70 eV, direct inlet; ^1H NMR and 2D correlation spectra, 400 MHz (^1H) and 100 MHz (^{13}C), CDCl_3 , with TMS as internal standard. Column chromatography: silica gel (Kieselgel 60, Merck). TLC: silica gel (Kieselgel 60F₂₅₄, Merck).

Plant Material. The roots of *L. carthamoides*, supplied by the University of the Horticultural and Food Industry, Budapest, Hungary, originated from a large-scale culture at the university and were collected in October 1996. A reference sample and voucher specimen have been deposited at the Department of Pharmacognosy, Albert Szent-Györgyi Medical University, Szeged, Hungary.

Extraction and Isolation. The dried pulverized roots (3.2 kg) of *L. carthamoides* were extracted at room temperature with MeOH (50 L). The MeOH extract was evaporated under reduced pressure to give 300 g of residue, which was partitioned between water and C_6H_6 . The C_6H_6 extract was evaporated under reduced pressure in a fumehood to give an oil-like material, which was chromatographed over a silica gel column by elution with a gradient system of C_6H_6 and C_6H_6 -EtOAc (49:1 \rightarrow 48:2). From the fractions obtained with C_6H_6 -EtOAc 48:2, compound **1** was purified after preparative TLC, using C_6H_6 -EtOAc (4:1) as the solvent system.

(E)-3,3'-Dimethoxy-4,4'-dihydroxystilbene (1): colorless crystals from CH_2Cl_2 -MeOH (1:1); mp 212–215 °C; UV λ_{max} (log ϵ) 224, 239 (sh), 309 (sh), 338, 350 (sh) nm; IR ν_{max} 3400, 2940, 1590, 1460, 1430, 1370, 1290, 1260, 1220, 1160, 1110, 1020, 960, 930, 870, 850, 820, 790, 720, 630 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 3.95 (3H, s, OCH_3), 5.61 (1H, s, OH), 6.89 (1H, s, H-7), 6.90 (1H, d, $J = 8$ Hz, H-5), 7.00 (1H, dd, $J = 8, 2$ Hz, H-6), 7.02 (1H, d, $J = 2$ Hz, H-2); ^{13}C NMR (100 MHz, CDCl_3) δ 56.1 (OCH_3), 108.5 (C-2), 114.8 (C-5), 120.4 (C-6), 126.9 (C-7), 130.6 (C-1), 145.4 (C-4), 146.8 (C-3); EIMS m/z 272 [M]⁺ (100), 257 [$\text{M} - \text{CH}_3$]⁺ (1), 242 [$\text{M} - 2 \times \text{CH}_3$]⁺ (1), 211 [$\text{M} - \text{CH}_3 - \text{CO} - \text{H}_2\text{O}$] (10), 207 (6), 197 (7), 169 (6); HREIMS m/z 272.10480 [M]⁺ $\text{C}_{16}\text{H}_{16}\text{O}_4$ required 272.10486.

Crystal data for 1: $M = 272.29$, monoclinic, space group $C2/c$; $a = 20.689(1)$ Å, $b = 5.327(1)$ Å, $c = 12.924(1)$ Å, $\beta = 99.74(1)^\circ$. $V = 1403.8(3)$ Å³, $Z = 4$, $D_c = 1.288$ Mg m^{-3} , $\mu(\text{Cu K}\alpha$ radiation, $\lambda = 1.5418$ Å) = 0.759 mm^{-1} . Crystal dimensions: 0.20 \times 0.15 \times 0.02 mm. Intensity data ($-25 \leq 2\theta \leq 25$, $-6 \leq h \leq 6$, $-16 \leq k \leq 16$, $\theta_{\text{max}} = 75.05$) were collected on an Enraf-Nonius CAD4 diffractometer. The crystal structure was solved by direct methods. Full-matrix least-squares refinement of atomic parameters based on F_o^2 converged at $R1 = 0.038$ for 998 $F_o^2 > 2\sigma(F_o^2)$ unique reflections ($R_{\text{tot}} = 0.0717$ for 1442 reflections). Atomic parameters, bond lengths, bond angles and torsion angles have been deposited at the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.

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