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First Symmetrical Bicyclo[6.6.0]tetradecane Resveratrol Tetramer from Stalks of *Vitis vinifera* (Vitaceae)

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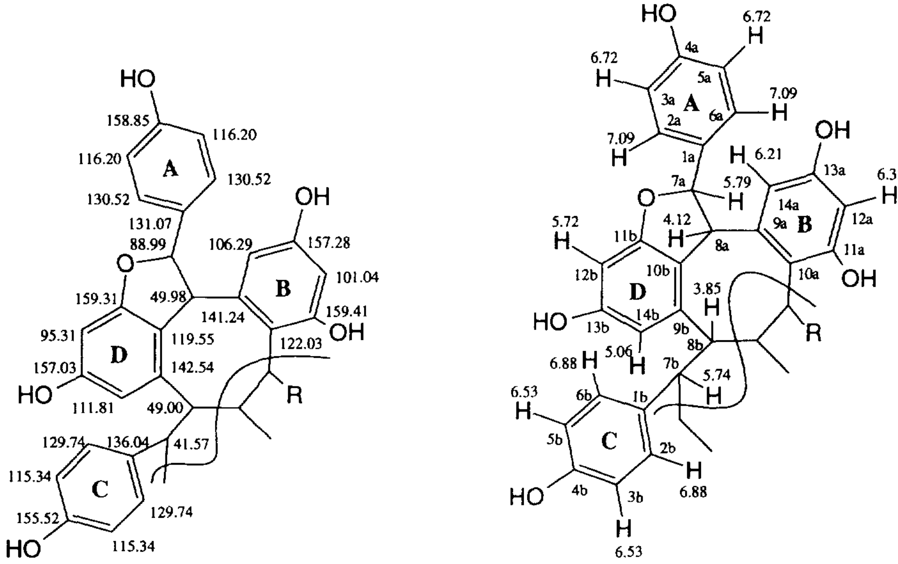
Abstract: A novel tetrastilbene with a symmetrical bicyclo[6.6.0]tetradecane structure has been isolated from stalks of *Vitis vinifera* (Vitaceae). Copyright © 1996 Published by Elsevier Science Ltd

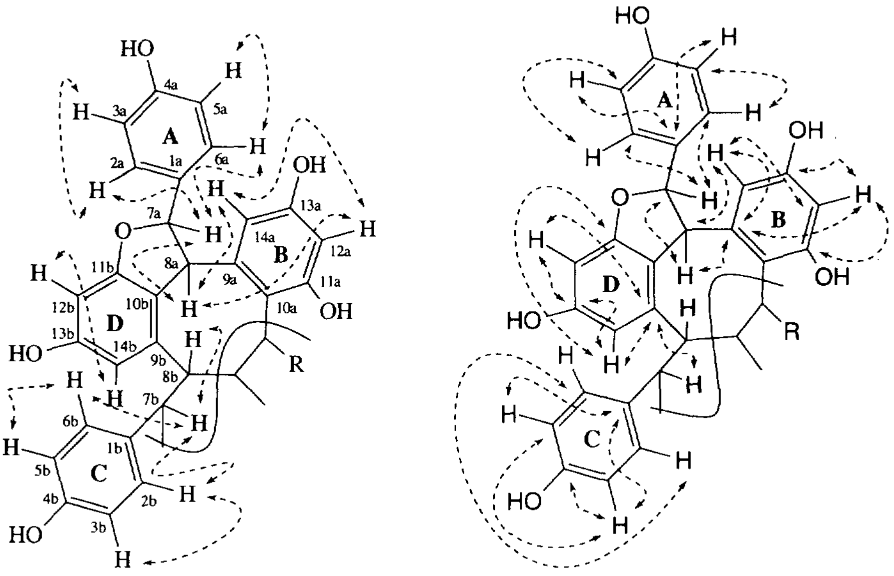
Resveratrol (3,5,4'-trihydroxystilbene) is claimed to be a stress metabolite produced by grapevine leaves[2]. The antihepatotoxic[3] and antifungal ε-viniferin was isolated from the same source[4]. Resveratrol was also found in grape berry skin and wine[5]. Pharmacological studies have established that *trans*-resveratrol inhibits the synthesis of eicosanoids by platelets[6], reducing incidence of coronary heart disease. Among by-products of wine harvest, grape seeds have been the subject of many studies[7], that resulted in the industrial exploitation of their flavonoidic content[8], but stalks have been neglected till now and a very few reports have concerned them[9]. However, a recent paper[10] describing oligostilbenes in the roots of genus *Vitis* prompts us to relate our results on the isolation and structural elucidation of a new resveratrol tetramer with the first symmetrical bicyclo[6.6.0]tetradecane structure, among other oligostilbenes (pallidol and ε-viniferin), from stalks.

Compound **1** was obtained as an amorphous powder which decomposed above 300°C. The ultraviolet and infrared spectra were the same as those of polyphenols, showing a maximum at 285 nm and strong absorptions at ν 3400 and 1613 cm^{-1} (hydroxyl and aromatic C=C respectively). **1** displayed a positive FABMS ion *m/z* 907 $[MH]^+$ and a significant peak at m/z 453 $[M-453]^+$. ^{13}C and ^{1}H NMR spectra signals displayed only one half of the molecule (Scheme 1a and 1b), allowing to deduce the molecular formula $C_{56}H_{42}O_{12}$ of a symmetrical compound. COSY and HMBC correlations (Scheme 1c and 1d) have shown two resveratrol entities indicated by signals for two phenols, two resorcinols and two two-carbon linkages. So, a two-carbon link between either phenol (**A**) and resorcinol (**B**) or phenol (**C**) and resorcinol (**D**), led to two resveratrol entities **A**-C7a-C8a-**B** and **C**-C7b-C8b-**D** respectively (Scheme 1c and 1d). A correlation study showed that a furan nucleus resulted from bonding between the two resveratrol entities making unit 1 (Scheme 2, solid curve). The symmetrical unit 2 have superimposed NMR signals.



a (half molecule, unit 1)

b (half molecule, unit 1)



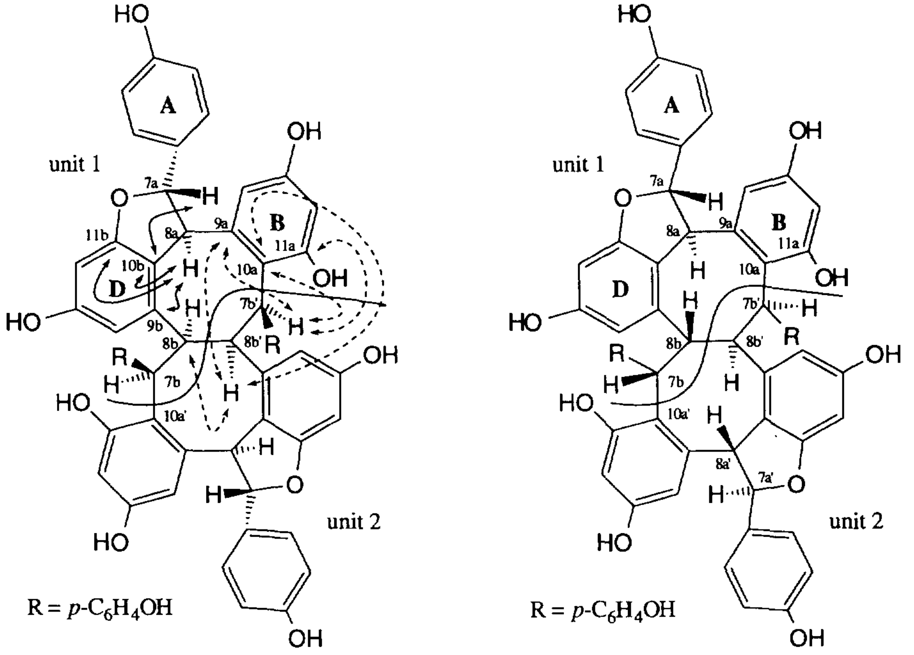
c (half molecule, unit 1)

d (half molecule, unit 1)

^{13}C (a), ^{1}H (b) chemical shifts (δ ppm), COSY (c) and HMBC (d) correlations in resveratrol entities of **1**

Scheme 1

Two symmetry elements must be considered : a twofold axis with a *cis*-relationship between H-8b and H-8b' (Scheme 2, **1a**) and a center of symmetry imposing a *trans*-relationship between these equivalent protons (Scheme 2, **1b**). The study can be limited to sixteen diastereomers. Energy minimized modeling using the MM2 Force Field (CSC) and ROESY experiment correlations[11] allowed us to exclude fourteen symmetrical stereoisomers. However, these data are compatible with structures **1a** or **1b** as well (Scheme 2).



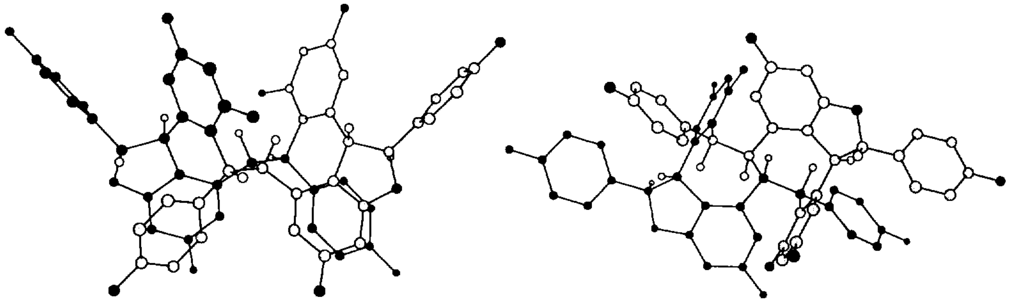
1a : twofold axis symmetry

1b : symmetry center

$^{13}C,^{1}H$ long range correlations between resveratrol entities (solid curve) and dimer units (dotted curve) of **1a**. Identical curves could be drawn in the case of structure **1b**

Scheme 2

The junction between unit 1 (two resveratrol entities) and unit 2 (symmetrical two resveratrol entities) ensued from HMBC correlations (Scheme 2, dotted curve) of C-10a with H-8b and H-7b (^4J and ^5J respectively if considered within the same unit 1). Also, C-9a and C-11a would correlate (^5J and ^6J) with H-8b and H-7b. Actually, these correlations of carbons of unit 1 are due to the equivalent proton H-7b' and H-8b' from unit 2. Units 1 and 2 are linked by symmetrical bonds C-10a,C-7b' and C-7b,C-10a'. But there is still a third linkage between units 1 and 2. It was materialized by the apparent HMBC correlation between C-8b and the corresponding proton H-8b, which actually concerned the H-8b' equivalent proton; this crucial bond between C-8b and C-8b' led to two fused cyclooctane rings. A resveratrol tetramer named vaticaffinol, showing a bicyclo[6.6.0]tetradecane structure, had precedently been isolated from a Dipterocarpaceae[12]; however, this molecule was not symmetrical. In our case, the symmetry element cut right accross the middle of the C-8b,C-8b' bond. 3D molecular studies allowed us to display the two generated models **1a** and **1b** (Scheme 3).



Stereostructure of **1a** Stereostructure of **1b**

(Only the interesting H are represented).

Scheme 3

Thus, for the first time, a biologically active stilbenoidic polyphenol (ε-viniferin) and a new resveratrol tetramer showing a symmetrical bicyclo[6.6.0]tetradecane framework have been isolated from stalks of *Vitis vinifera*.

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