EUPHORBIN E, A HYDROLYZABLE TANNIN DIMER OF HIGHLY OXIDIZED STRUCTURE, FROM EUPHORBIA HIRTA

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A novel dimeric hydrolyzable tannin, euphorbin E, was isolated from the leaves of Euphorbia hirta. Its structure (**1**), having two dehydrohexahydroxydiphenoyl groups, and a dehydroeuphorbinoyl group as a novel connecting unit between two polyaroylglucose cores, was determined based on spectral and chemical evidence.

KEYWORDS Euphorbia hirta; Euphorbiaceae; tannin; dimeric hydrolyzable tannin; euphorbin E; dehydroeuphorbinoyl group

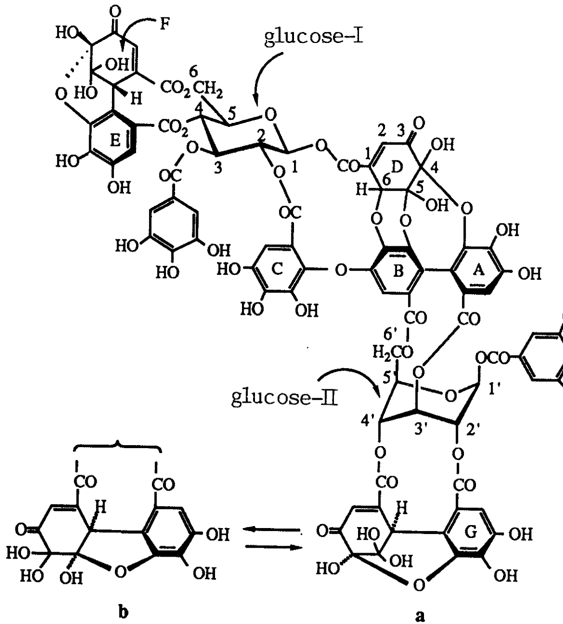
Besides the dimeric dehydroellagitannins, euphorbins A, B[1)] and C,[2)] previously isolated from the leaves of Euphorbia hirta L. (Euphorbiaceae), an additional novel dimer, named euphorbin E (**1**), $C_{82}H_{52}O_{54}\cdot 8H_2O$, $[\alpha]_D$ -48° (c=1.0, MeOH), has been isolated and its unique structure was found to be **1** as follows.

The ^{1}H-NMR spectrum (500 MHz, acetone-d_6-D_2O) of **1**, in which each signal is duplicated in a ratio of 2:1, exhibited the allylic methine and vinyl proton signals, characteristic of a dehydrohexahydroxydiphenoyl (DHHDP) group existing in an equilibrium mixture between six- and five-membered hemiacetal forms (a-form $\rightleftarrows$ b-form),[3)] at δ 5.33 (2/3H, s), 5.06 (1/3H, d, J=1.5 Hz), 6.88 (2/3H, s) and 6.58 (1/3H, d, J=1.5 Hz). The presence of another DHHDP group forming a six-membered hemiacetal form in **1** was also indicated by a pair of singlets due to an additional allylic methine proton, at δ 4.63 (2/3H, s) and 4.59 (1/3H, s). The presence of two galloyl groups was revealed by the signals at δ 7.14 (2H, s), 7.16 (4/3H, s), and 7.13 (2/3H, s). The following aromatic proton singlets (rings A-C and E-G) were also observed: δ 5.96, 6.22, 6.47, 6.77, 7.03, 7.25 (each 2/3H, s), 6.03, 6.18, 6.42, 6.76, 6.97, 7.29 (each 1/3H, s). The ^{13}C-NMR spectrum of **1** disclosed signals due to three α, β-unsaturated ketone systems and six hemiacetal or gem-diol carbons, indicating the presence of the third hydrated cyclohexene trione moiety, in addition to those in two DHHDP groups. A pair of doublets (J=2 Hz) attributable to an olefinic proton (2-H of ring D) at δ 6.35 (2/3H) and 6.41 (1/3H) were related to oxygen-bearing allylic methine signals at δ 5.54 and 5.53 (each d, J=2 Hz, 6-H of ring D), in the ^{1}H-^{1}H shift correlation spectrum. Upon condensation with o-phenylenediamine in acidic medium followed by methylation, **1** gave a methylated phenazine derivative which was methanolyzed with sodium methoxide to afford methyl tri-O-methylgallate, a phenylphenazine derivative (**2**),[4)] and the dodecamethyl derivative (**3**), $[\alpha]_D$ +8° (acetone), which showed an $[M+Na]^+$ ion peak at m/z 935 in FAB-MS. The optically inactive character of **2** $[\alpha]_D$ 0° (acetone) indicated that **2** consists of an equimolar mixture of (R) and (S)-atropisomers. Since the absolute configuration at the methine carbon of the DHHDP group is associated with the atropisomerism of the phenylphenazine derivative,[4)] those of the two DHHDP groups in 1 could be (R) and (S). Acid hydrolysis of the phenazine derivative produced from **1** by condensation with o-phenylenediamine, and subsequent methylation yielded glucose, methyl tri-O-methylgallate, dilactonized congener of **2**,[4)] methyl hexa-O-methylvaloneate dilactone (**5**)[5)] and a trimethylated phenazine derivative (**6**). Since the compounds (**5**) and (**6**) can be regarded as the products from cleavage of an aryl ether bond of **4**, which is the parent acid of **3**, the new constituent unit in **1** is considered to be an oxidized analogue (dehydroeuphorbinoyl group) of the euphorbinoyl (tetrameric galloyl) group.[2)] Euphorbin E (**1**) is thus a dimer consisting of a dehydroeuphorbinoyl group, and of glucose, galloyl and DHHDP groups, two of each. The formation of hemiacetals, not gem-diols, at C-4 and C-5 of ring D was evident from the FAB-MS data of **1** [m/z 1923 $(M+Na)^+$], which is consistent with the molecular formula $C_{82}H_{52}O_{54}$. The proton signals[6)] ascribable to two glucose cores adopting the $^4C_1$ and $^1C_4$ conformation, are closely similar to those of the monomeric dehydroellagitannins, such as isoterchebin (**7**)[7)] and geraniin (**8**).[3)] The chemical shifts of glucose carbons in the ^{13}C-NMR spectrum of **1** are also almost identical with those of **7** and **8**, although those due to C-3 and C-4 in glucose-I of **1** are somewhat different from the corresponding signals in **7** (Table I). Euphorbin E (**1**) thus appeared to have the partial structures associated with **7** and **8**, and was regarded as an oxidized analogue of euphorbin C (**9**)[2)] which is the main tannin constituent of this plant.

Table I. ^{13}C-NMR Spectral Data[a)] for the Glucose Moieties of **1**, **7** and **8** (126 MHz, Acetone-d_6)

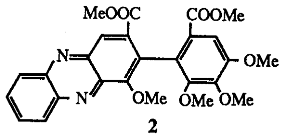
		Glucose-I						Glucose-II					
		C-1	C-2	C-3	C-4	C-5	C-6	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'
1	a-form	91.9	72.2	73.7	72.5	69.5	65.2	91.0	71.8	63.1	66.1	72.5	64.0
		92.0	71.8	73.5	72.7	69.6	65.2						
	b-form							91.9	72.2	62.4	66.9	73.1	64.2
7[8)]	a-form	92.9	71.1	72.9	73.4	69.2	65.9						
8[9)]	a-form							90.8	69.9	63.3	65.9	72.6	63.6
	b-form							91.8	70.4	62.3	66.8	73.1	63.8

a) Assignments were made by the ^{1}H-^{13}C COSY spectra.



b a

1



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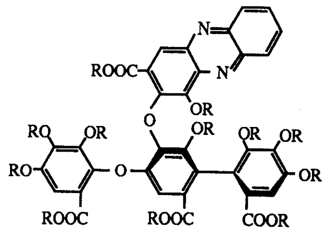
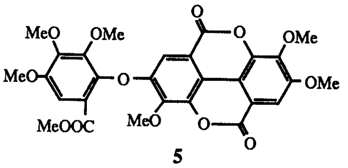


3 R=Me
4 R=H



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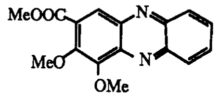

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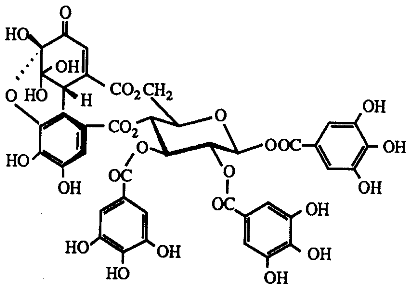

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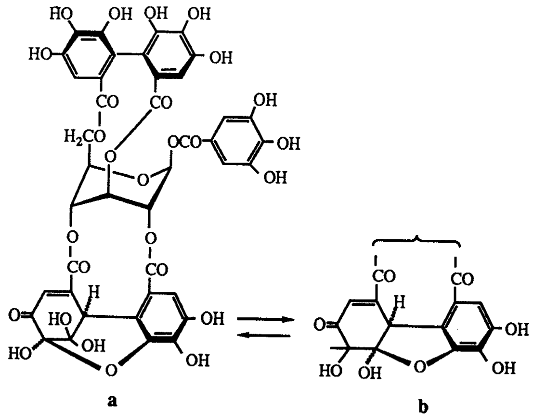

a b

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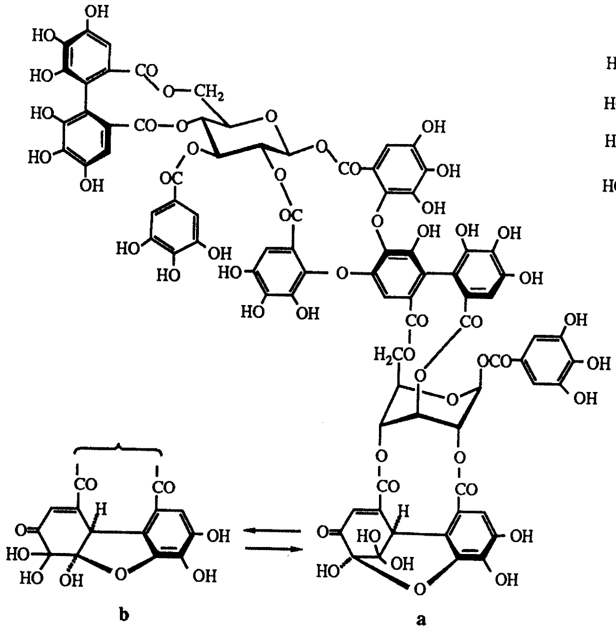
The structure (**1**) thus proposed was confirmed by its catalytic hydrogenation over Pd-C to yield a product, which was identical in all respects (HPLC, ^{1}H-NMR, CD) with **10** prepared by similar hydrogenation of **9**. Based on these data, the structure of euphorbin E, including absolute stereochemistry except that of ring D, was determined to be **1**. This is the first known example of highly oxidized hydrolyzable tannin dimer which has two DHHDP groups and a dehydroeuphorbinoyl group in a molecule.



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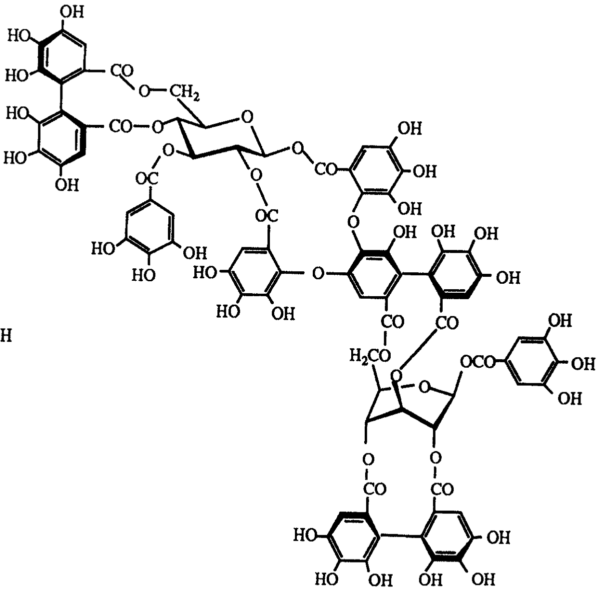

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6) Glucose proton signals for the predominant a-form of **1** : δ 6.51 (d, J=8.5 Hz, H-1), 5.63 (dd, J=8.5, 10 Hz, H-2), 5.83 (t, J=10 Hz, H-3), 5.65 (t, J=10 Hz, H-4), 4.28 (m, H-5), 5.03 (dd, J=4, 11 Hz, H-6), 3.97 (t, J=11 Hz, H-6), 6.59 (br s, H-1'), 5.58 (br s, H-2'), 5.53 (br s, H-3'), 5.84 (br s, H-4'), 4.88 (dd, J=8, 11 Hz, H-5'), 4.80 (t, J=11 Hz, H-6'), 4.18 (dd, J=8, 11 Hz, H-6').

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