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PHORBIC ACID FROM *ECHEVERIA ELEGANS*

RANDI KRINGSTAD

Department of Pharmacognosy, Institute of Pharmacy, University of Oslo, P.O. Box 1068, Oslo 3, Norway

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Key Word Index – *Echeveria elegans*, Crassulaceae, isolation, identification, lactone-forming acids, phorbic acid

Plant. *Echeveria elegans* Rose (Crassulaceae). *Source.* Fresh plant material was supplied by the Botanical Garden, University of Oslo, and Oslo Municipal Nursery, Oslo, Norway. The identification was carried out by Dr. Per Sunding, director of the Botanical Garden. *Previous work.* Phorbic acid, (1R·3R)-1,3-dihydroxypentane-1,3,5-tricarboxylic acid, was isolated from *Euphorbia resinifera* Berg [1,2] and *Euphorbia palustris* L. [3]. There are indications that the acid might be present also in a few other species [4,5].

Present work. Phorbic acid has now been isolated from *Echeveria elegans* in large quantities (2–4% of dry wt). The isolated acid corresponds in all the investigated properties with phorbic acid isolated from *Euphorbia resinifera* [1]. This is the first time that phorbic acid has been reported outside *Euphorbia* species.

EXPERIMENTAL

Isolation of dilactophorbic acid. Fr. leaves (2.45 kg) were extracted 2× H_2O, 100°, 3 l., 4 hr. The extract was passed through a column of Dowex 50-W × 8 [H^+], 20–50 mesh (600 ml), and then through a column of Dowex 1 × 8 [OH^-], 20–50 mesh (700 ml). The anion exchanger was eluted, first with 0.1 N HCl (7 l.), and then with 2 N HCl (8 l.). HCl was removed from the eluate as described earlier [5]. Upon treatment with activated charcoal, the residue was dried *in vacuo* over P_2O_5 for 2 days. This converted the residue into a crystalline mass, which after recrystallization from dry EtOH gave a white compound (dilactophorbic acid). Yield 2.21 g.

Identification of dilactophorbic acid. Mp 151–153°, lit. 151–154° [1]. The ethyl ester prepared by the method described earlier [6], was recrystallized from dry EtOH. Mp 90–92°, lit. 91.5–92° [1], $[\alpha]_D^{20}$ +33.2° (*c* = 10.18 EtOH), lit. $[\alpha]_D^{18}$ +33° (*c* = 10.18 EtOH) [1] (Found: C, 52.62; H, 5.51. Calc. for $C_{10}H_{12}O_6$: C, 52.62; H, 5.30%).

The IR spectrum was identical with that of authentic dilactophorbic acid monoethyl ester [7]. The preparation of the methyl ester, the GC–MS analysis of the methyl ester and the conditions for the TLC were the same as those described by Kringstad and Nordal [5]. TLC was carried out with the isolated acid and with the corresponding methyl and ethyl esters. All the obtained data were found identical with those of the reference compounds: dilactophorbic acid, phorbic acid monomethyl ester and phorbic acid monoethyl ester.

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SYNTHESIS OF EUPOMATENOID-7 AND EUPOMATENOID-12

RIAZ AHMED and ROBERT STEVENSON

Department of Chemistry, Brandeis University, Waltham, Massachusetts 02154, U.S.A.

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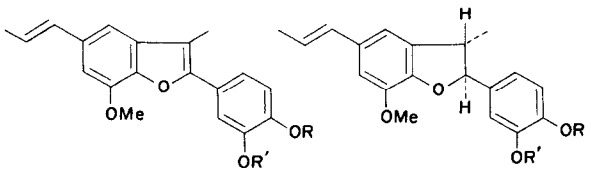
Key Word Index – *Eupomatia laurina*, Eupomatiaceae, lignans, neolignans, eupomatenoids, biogenetic-type synthesis, dehydrogenation of 5-propenyl-2-aryl-2,3-dihydrobenzofurans

From the bark, leaves and wood of *Eupomatia laurina* R.Br., Ritchie and Taylor and their coworkers [1–3] have identified 12 closely related products for which the generic name eupomatenoid has been introduced. Although these products do not conform strictly to the time-honoured Haworth definition [4] of lignan (a structure in which two *n*-propylbenzene units are united by the β-

carbon atom of the side chain), it was recognized that they could be formed by the same primary oxidation process incorporated by the brilliant biogenetic hypothesis of Erdtman [5]. Until a consensus on the conflicting proposals of definition [1,4,6,7] and distinction between the terms "lignan" and "neolignan" emerges, it is unfortunate that the classification of many bis-arylpropanoids (including the eupomatenoids) will remain arbitrary.



(1) R, R′ = —CH_2—
(2) R = H, R′ = Me
(3) R = R′ = Me
(7) R = Ac, R′ = Me
(4) R = H R′ = Me
(5) R, R′ = —CH_2—
(6) R = Ac, R′ = Me
(8) R = R′ = Me

Eight of the *Eupomatia* constituents are 2-aryl-3-methyl-5-(E)-propenylbenzofurans as exemplified by eupomatenoid-1 (**1**), eupomatenoid-7 (**2**) and eupomatenoid-12 (**3**). In addition, from *Licaria aritu* Ducke, two analogous dihydrobenzofurans, licarin A (**4**, optically active dehydrodi-isoeugenol) and licarin B (**5**, same as eupomatenoid-8) have been isolated [8,9].

(±)-Dehydrodi-isoeugenol (**4**), readily obtained by $FeCl_3$ oxidation of *trans*-isoeugenol [10], is an obviously attractive starting material since dehydrogenation of the heterocyclic ring would complete an essential two-step "biogenetic-type" synthetic procedure for these benzofurans. It has been demonstrated, however, that despite considerable experimentation, this apparently simple transformation was unexpectedly recalcitrant [1]. We now report a procedure which overcomes this obstacle. Impressed by the observation that the dehydrogenation difficulty existed only when a conjugated ethylenic (propenyl sidechain) function was present, we find that dehydrogenation of the heterocyclic ring proceeds with facility after protection of the propenyl group by bromine addition.

Treatment of dehydrodi-isoeugenyl acetate (**6**) with an equivalent of Br_2 in $CHCl_3$, followed by solvent removal and refluxing the residual adduct with *N*-bromosuccinimide in CCl_4 yielded a product which on debromination with Zn dust gave eupomatenoid-7 acetate (**7**) in over 80% yield. Base hydrolysis of (**7**) gave eupomatenoid-7 (**2**). It should be noted that this dehydrogenation sequence (Br_2, NBS, Zn) does not require isolation and/or purification of the intermediates. The procedure is also applicable to the 2-veratryl-2,3-dihydrobenzofuran analogue. Thus, similar treatment of dehydrodi-isoeugenyl methyl ether (**8**) gave eupomatenoid-12 (**3**) in 70% yield.

EXPERIMENTAL

Si gel $PF_{254+366}$ was used for TLC and products were eluted with acetone UV, IR and PMR spectra were determined for all compounds and were in agreement with those reported [2,3]

Dehydrogenation of dehydrodi-isoeugenyl acetate (**6**) To a soln of the acetate (1·0 g) in $CHCl_3$ (100 ml), Br_2 (520 mg) was added in the same solvent Removal of solvent gave a residual oil (NMR spectrum showed absence of characteristic olefinic absorption at δ 6·0–6·2) which was dissolved in CCl_4 and heated under reflux with *N*-bromosuccinimide (500 mg) for 30 min Filtration and solvent evaporation gave a brown oil (NMR spectrum showed presence of benzofuran 3-methyl group at δ 2·4) Zn dust (2 g) was added to a soln of this oil in HOAc (50 ml), the mixture heated on the steam bath for 5 min, filtered and evaporated to give a crude product (0·98 g, estimated by NMR spectrum to contain 66% of eupomatenoid-7 acetate) Purification of a portion (400 mg) by TLC using C_6H_6–Me_2CO (9 1) and elution of the front running band gave 7-methoxy-3-methyl-2-(3′-acetoxy-4′-methoxyphenyl)-5-(E)-propenylbenzofuran (**7**), (250 mg), as needles mp 140–142° (lit. [2], mp 144°) from MeOH The multiplet pattern of the *trans*-vinyl protons bear a strong resemblance to that of *trans*-isoeugenol [11] In subsequent repeat experiments, yields surpassing 80% were obtained

Eupomatenoid-7 (**2**) A soln of KOH (3 g) in H_2O (50 ml) was added to a soln of eupomatenoid-7 acetate (100 mg) in MeOH (50 ml), the mixture refluxed for 1 hr, concentrated and acidified with dil HCl Several crystallizations of the ppt (78 mg) from light petrol gave 7-methoxy-3-methyl-2-(3′-hydroxy-4′-methoxyphenyl)-5-(E)-propenylbenzofuran (**2**), mp 104–106° (lit [2] mp 105–106°)

Eupomatenoid-12 (**3**) (a) Dehydrodi-isoeugenol methyl ether (**8**) (1·13 g) was treated successively with Br_2 (530 mg), NBS (652 mg) and Zn dust (2 g) as described above for the acetate Similar purification of a portion (400 mg) of crude product (1·05 g) by TLC yielded 7-methoxy-3-methyl-2-(3′,4′-dimethoxyphenyl)-5-(E)-propenylbenzofuran (**3**) as needles (245 mg), mp 114–115° (lit [3] mp 115–116°) A form mp 84–86° could also be obtained (b) To a soln of eupomatenoid-7 (50 mg) in Me_2CO (50 ml) was added anhydrous K_2CO_3 (1 g) and Me_2SO_4 (1 ml) The mixture was refluxed for 1 hr, acidified with dil HCl, and the precipitated oil crystallized from EtOH to give eupomatenoid-12 as needles (28 mg), mp 83–84° or 114–115°

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ACIDIC COMPOUNDS IN PATCHOULI OIL

SACHIKO NAKAHARA,* KEIKO KUMATANI* and HIROMU KAMEOKA†

* Yamamoto Perfumery Co, Ltd, 1-6, Kitakyuhojimachi, Higashiku, Osaka, 541, Japan, † Department of Applied Chemistry, Faculty of Science and Engineering, Kinki University, 1-4, 3-chome, Kowakae, Higashiosaka, 577, Japan

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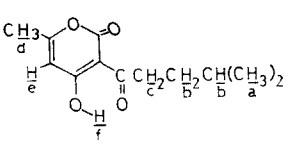
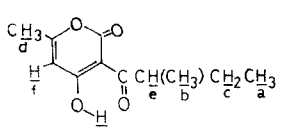
Key Word Index—*Pogostemon cablin*; Labiatae, patchouli oil, 3 - (4 - Methylpentanoyl -)3,4 - dihydro - 6 - methyl - 1,2 - pyran - 2,4 - dione, 3 - (2 - Methylbutyryl -)3,4 - dihydro - 6 - methyl - 1,2 - pyran - 2,4 - dione

Indonesian patchouli oil obtained from *Pogostemon cablin* Benth. by steam distillation gave a yellowish oil on treatment with 1N Na_2CO_3. The yellowish oil was separated by means of column chromatography and the 5% Et_2O-*n*-hexane fraction was examined. The gas chromatogram of this fraction has 2 main peaks at RT 12·4 min. (peak 1) and 7·6 min. (peak 2), the proportions of peak area being 85 and 12% respectively. Recrystallization with absolute ethanol gave needles of **1** (mp 34·5–35·5°), with the same retention time as peak 1. Semicarbazone mp 184·8–185·3° (dec.). On boiling with aq 0·5N NaOH, **1** yielded isoamylmethyl ketone as the main neutral product. IR spectrum of **1**; 3110, 1743, 1723, 1643, 1609, 1565, and 998 cm^{-1}. MS; *m/e* 224 (M^+, 4%), 209 (M^+–Me, 3%), 181(M^+-C_3H_7, 40%), 168(M^+-56, 100%), 153(M^+-71, 81%), 85($\overset{+}{O}\equiv$  , 28%), and 43($\overset{+}{C}_3H_7$, 44%). Elemental analysis of **1** Found; C 64·16%, H 7·25%, N 0·0%, calc. for $C_{12}H_{16}O_4$; C 64·28%, H 7·20%, O 28·54%. NMR ($\delta^{CCl_4}_{ppm}$); (a) 0·96 (*d*, 6H), (b) 1·55 (*m*, 3H), (c) 2·95 (*t*, 2H), (d) 2·23 (*s*, 3H), (e) 5·80 (*s*, 1H), and (f) 16·87 (*s*, 1H). From the above data structure **1** was deduced for this substance. The compound of peak(2) was isolated in the pure state by means of preparative GLC. IR of **2**; 3110, 1743, 1724, 1642, 1608, 1548, 1462, and 998 cm^{-1}. MS; *m/e* 210(M^+, 58%), 168(M^+-56, 15%), 153(M^+–C_4H_9, 100%), 126(M^+–$\overset{+}{O}\equiv C\cdot C_4H_9$, 26%), 85($\overset{+}{O}\equiv$  , 34%), 43($\overset{+}{C}_3H_7$, 29%), and 29($\overset{+}{C}_2H_5$, 10%). NMR ($\delta^{CCl_4}_{ppm}$); (a) 0·93 (*t*, 3H), (b) 1·12 (*d*, 3H), (c) 1·6 (*m*, 2H), (d) 2·25 (*s*, 3H), (e) 3·77 (*m*, 1H), (f) 5·81 (*s*, 1H), and (g) 17·18 (*s*, 1H). The structure assumed for peak(2) from these data is **2**. These two compounds were synthesized by the condensation of corresponding acid chloride with triacetic acid lactone in the presence of H_2SO_4[1]. IR, MS, and NMR of the synthetic specimens were completely in agreement with those of the natural compounds. The formal names for **1** and **2** are 3 - (4 - methylpentanoyl -)3,4 - dihydro - 6 - methyl - 1,2 - pyran - 2,4 - dione and 3 - (2 - methylbutyryl -)3,4 - dihydro - 6 - methyl - 1,2 - pyran - 2,4 - dione respectively. That these structures are in tautomerism with the corresponding enol form, 3 - (4 - methylpentanoyl -)4 - hydroxyl - 6 - methyl - α - pyrone and 3 - (2 - methylbutyryl -)4 - hydroxy - 6 - methyl - α - pyrone is indicated by the NMR spectra.



1



2

The presence of two compounds in the original oil was confirmed by the direct GLC of the oil.

EXPERIMENTAL

Analytical methods For column chromatography Kieselgel-G was used with *n*-hexane, 5%-Et_2O–*n*-hexane, 10%-Et_2O–*n*-hexane, 50%-Et_2O–*n*-hexane and Et_2O as elut-