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THE EFFECTS OF A TERPENE ALDEHYDE-ESTER FROM *ERYNGIUM PANICULATUM* AND ANALOGS ON VELVETLEAF GERMINATION

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In a continuing effort to discover and evaluate natural growth and germination inhibitors (1-3), the hexane extract of seeds from *Eryngium paniculatum* Cav. and Comby ex. Delar L. was found to inhibit germination of velvetleaf (*Abutilon theophrasti* Medic.). Fractionations, monitored by bioassay, gave **1**, (-)-2,4,4-trimethyl-3-formyl-2,5-cyclohexadienyl angelate, as the only active component. Ester **1** has been reported as a constituent of the roots of *Bupleurum gibraltaricum* Lam. (4), and several isomeric and analogous terpene aldehyde-esters have been found in other Umbelliferae (5-8). These compounds have remained biosynthetic curiosities, and no functional role has yet been ascribed to them. Observations that one member of the series has antigermination properties aroused curiosity about their structural-activity relationships. In an attempt to gain insight into this question, several analogs of **1** were prepared and bioassayed.

RESULTS AND DISCUSSION

The compounds tested and responses of velvetleaf to them are given in Table 1. The structure of **1** was established by comparison of its nmr with the published spectrum (4) and capillary gc/ms of its methanolysis product, which was confirmed to be methyl angelate. Compounds **2** and **3** have been successfully synthesized (9), and **2** is active, albeit less so than **1**. It is not known whether or not this difference is due to the location of the ring-methyl group, the nature of the acyl group, or stereochemistry (**1** is optically active, and **2** is racemic). Compound **3**, the positional isomer of **2**, was inactive at five times the concentration.

The alcohol portion of **1** is strikingly similar to **4**, a precursor in the synthesis of strigol, and a compound that is very active in promoting germination of witchweed (*Striga asiatia*) (10). The difference is only that of the 5,6-double bond. The activity of **4** versus velvetleaf was about the same as that of **2**, and both compounds are racemic. Acetylation of **4** (yielding **5**) negated activity.

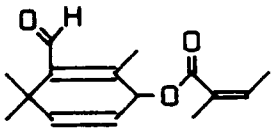
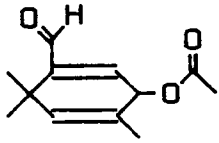
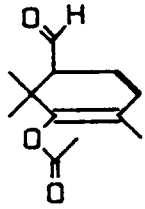
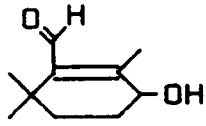
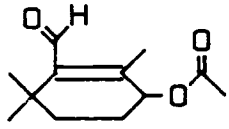
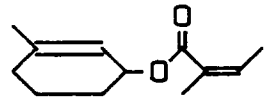
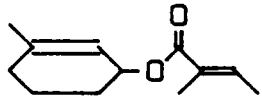
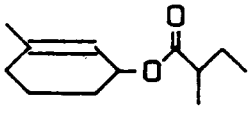
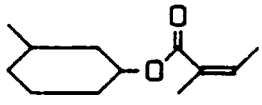
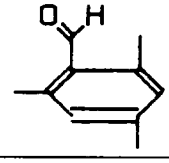
The responses of velvetleaf to **1**, **2**, **4**, and **5** is somewhat incongruous. Considering the similarity of activity between **2** and **4** it is surprising that acetylation would decrease the activity of **4**. Actually, results for the free alcohol from **2** or **1** might have helped clarify this point, but they are far too labile (9) to make the bioassay results reliable. Additionally, the angelate ester of **4** was not forthcoming by the esterification methods used. At this point, the reason for the lack of inhibition shown by **5** remains unexplainable.

It is known that **1** and **2** are somewhat unstable and, when subjected to even mild heat, undergo elimination and rearrangement to give 2,3,6-trimethylbenzaldehyde (6). Although this compound was not available for bioassay, its isomer **10** was not active, suggesting that the effects of **1** or **2** are not due to their degradation product.

Bioassay results from **1-5** rouse curiosity about what kind of functional-

[1]The mention of firms names of trade products does not imply that they are endorsed or recommended by the U.S. Department of Agriculture over other firms or similar products not mentioned.

TABLE 1. Germination Response of Velvetleaf (*Abutilon theophrasti*) Seeds

Compound	Concentration (mM)/Percent Germination[a]				
	2	4	6	8	10
1 	92	41	0		
2 		90	30	10	0
3 					100
4 		70	52	22	0
5 					100
6 			100	28	0
7 		100	16	5	0
8 					100
9 					100
10 					100

[a]Relative to controls; control rate = 36-40 seeds/40. Values below 85 significantly different from controls.

ity is necessary to cause inhibition. In order to improve upon these speculations, esters **6-9** were prepared and assayed. (Each of the alcohols was tested prior to esterification, and none showed any effect at 10 mM.) Results from compounds **6** and **7** indicate that activity is diminished by removing the formyl group from the ring and that the orientation of the acyl double bond is not really important. Moreover, **8** and **9** are inactive, an outcome which seems to suggest that the cyclic double bond(s) is required.

Whether or not terpene aldehyde-esters play a role in allelopathy is unknown. Certainly, as root constituents, they are prime candidates. Finally, because these compounds are closely related to **4**, their activity towards stimulation of witchweed germination could prove to be interesting.

EXPERIMENTAL

Seeds of *E. paniculatum* were collected by Uruguayan botanists and shipped to the Beltsville Agricultural Research Center, Beltsville, Maryland, for identification. Thus, no voucher specimen is available. A 100-g sample was finely ground and extracted overnight with hexane in a soxhlet apparatus. The extract was concentrated, placed on a silica column, and eluted with 400 ml batches of: hexane, 2% Et_2O in hexane, and 20% Et_2O in hexane. Fractions (10 ml) were collected, and progess was monitored by tlc. The biologically active fractions consisted of a mixture of triglycerides and **1**. The triglycerides were removed by hplc on a Partisil 10 PAC column (Whatman) with hexane-EtOAc (85:15) as the eluent. In this way, 200 mg of pure (tlc, hplc) **1** was finally procured. Its nmr spectrum was identical to that given by Bohlmann *et al.* (4) and its $[\alpha]^{27}D$ $-67°$ $c=1.44$ in hexane.

A 10 mg sample of **1** was stirred for 30 min in 5% NaOMe in MeOH. The reaction mixture was analyzed by gc/ms in a 25 m CP®SIL (Chrompak Inc., Bridgewater, New Jersey) capillary column held isothermal at 40°.

Compounds **2** and **3** were prepared and isolated by the procedure of Bohlmann and Weickgenannt (9). The strigol precursor **4** was synthesized as described by He and Wu (11) and was acetylated in Ac_2O/pyridine (2:1) to yield **5**. The method House and Rasmussen (12) provided angelic acid. The alcohols used to prepare compounds **6-9**, and tiglic acid, 2-methyl butyric acid, and mesitaldehyde **10** were purchased from Aldrich Chemical Co. Esters **6-9** were synthesized by mixing the acid chloride (made from the appropriate acid and oxalyl chloride) and the alcohol in pyridine. These products were purified by hplc (Partisil 10 PAC, 5% EtOAc in hexane).

The bioassay procedure has been described previously (3). Each treatment was duplicated. Results given in Table 1 are an average of the two, and every two treatments were accompanied by a control. In the control sets, 36 to 40 seeds out of 40 germinated. Germination tallies were made 7 days after treatment.

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