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STUDIES ON THE BIOLOGICAL ACTIVITIES OF RARE PHENYLPROPANOIDS OF THE GENUS *PIMPINELLA*

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ABSTRACT.—Several rare phenylpropanoids of the genus *Pimpinella* were tested for biological activity. Compounds with epoxy groups have a negative effect on the growth of plants, and they also show insecticidal and acaricidal activities.

The genus *Pimpinella* produces phenylpropanoids with an unusual substitution pattern at the phenyl ring (1–6). We called the (1*E*)-propenyl-2-hydroxy-5-methoxybenzene skeleton of these compounds pseudoisoeugenol (2). Beyond the pseudoisoeugenols, derivatives of (1*E*)-propenyl-4-hydroxybenzene have been identified in some *Pimpinella* species (4, 5). In a wide screening program, the phenylpropanoids of Table 1 were tested with regard to their insecticidal, acaricidal, herbicidal, and fungicidal activities. Of special interest was the determination of whether biological activity is general in scope or directed against a particular organism or organism group. Compounds **1** and **3** (see Table 1) are mainly found in *Pimpinella peregrina*; **2**, **4**, and **5** dominate in *Pimpinella major* (6). Isoeugenol [**8**] and its derivatives **6** and **7** are totally absent in the genus *Pimpinella*. Nevertheless, they were integrated into the screening program to obtain information about structure-activity relationships.

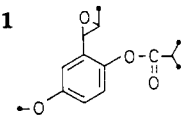
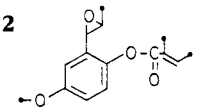
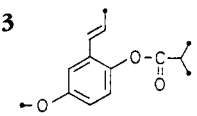
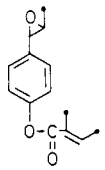
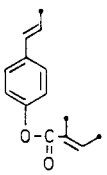
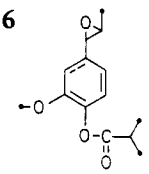
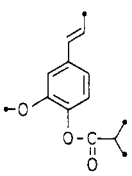
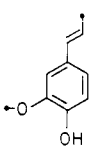
The results in Table 1 show that the phenylpropanoids of the genus *Pimpinella* have significant biological activities. They have an evident effect on plant growth, and they also show insecticidal and acaricidal activities. On the other hand they are ineffective against the phytopathogenic fungi that we have tested. In a contact assay with *Musca domestica*, compounds **1**, **4**, and **6** (0.2 mg) showed a 100% result. With a ten times higher concentration, **2** and **3** had an efficiency of 100% and 90%, respectively. For the present, the conspicuously lower activity of **2** as opposed to the other epoxyphenylpropane derivatives cannot be explained. The other insects were not impaired by these substances.

In the contact assay with *Tetranychus telarius*, **4** was particularly effective. A concentration of 100 ppm had a 100% result. At the same concentration **1**, **2**, **3**, and **6** showed an 80 to 90% result.

In the plant-assay systems compounds **1–6** showed an evident growth inhibitory effect. The most effective growth retardation was noticed in *Azolla filiculoides* and a cell culture of *Zea mays*.

Comparison with the biological activities of the isoeugenol derivatives shows that there were no differences between the activities of epoxy-pseudoisoeugenolisobutyrate [**1**] and epoxy-isoeugenolisobutyrate [**6**], but the olefinic derivatives of these compounds were practically ineffective. On the other hand, pseudoisoeugenolisobutyrate [**3**] presented a relatively wide spectrum of activity. Furthermore, the results show that for a strong biological activity the epoxy-group represents the most important part of the molecule. If it is absent, the potency of the substances is obviously lower. In this respect, our results confirm those of Kleiman *et al.* (4), who

TABLE 1. Insecticidal, Acaricidal, and Phytotoxic Activities of Phenylpropanoids.[a]

Compound	Test System					
	Musca domestica (0.2 mg)	*Tetranychus telarius* (100 ppm)	*Scenedesmus acutus* (10^{-4} M)	*Lemna paucicostata* (10^{-4} M)	*Zea mays* cell culture (10^{-4} M)	*Azolla filiculoides* (10^{-4} M)
1 	+++	++	(+)	+++	+++	+++
2 	—	++	+	(+)	+++	+++
3 	—	++	—	++	+	+++
4 	+++	+++	+	—	+++	+++
5 	—	—	++	+	—	+
6 	+++	++	+	+	+++	++
7 	—	—	—	+	—	—
8 	—	—	—	—	—	—

[a] — = not active (0–25%); (+) = little activity (26–50%); + = active (51–80%); ++ = strong activity (81–94%); +++ = very strong activity (95–100%).

[b] Tested compounds: epoxy-pseudoisoeugenolisobutyrate [**1**]; epoxy-pseudoisoeugenoltiglate [**2**]; pseudoisoeugenolisobutyrate [**3**]; epoxy-anoltiglate [**4**]; anoltiglate [**5**]; epoxy-isoeugenolisobutyrate [**6**]; isoeugenolisobutyrate [**7**]; isoeugenol [**8**].

tested pseudoisoeugenol and other phenylpropanoid derivatives for their antigermination activities. They found that epoxyphenylpropanoid esters were active (10^{-2} to 10^{-3} M) against seeds from several different plant species, whereas compounds with olefinic groups are either inactive or had minimal activity.

EXPERIMENTAL

HERBICIDE TESTS IN VITRO.—Lemna *test.*—Plants of *Lemna paucicostata* were cultivated autotrophically under sterile conditions and permanent illumination. Compounds were dissolved in a small amount of Me_2CO and added to the inorganic nutrient medium. Eight days after starting, the newly formed plants and leaves were counted.

Azolla *test.*—Plants of *Azolla filiculoides* were cultivated autotrophically in an organic nutrient medium. The substances (dissolved in Me_2CO) were added to the nutrient medium; 14 days after starting, the growth retardation was estimated visually and the increase of fresh wt was determined.

Alga test.—*Scenedesmus acutus* was cultivated at 22° under permanent illumination in an autotroph shaking-culture. Twenty-four hours after adding the test substances, the increase of the algae (fresh wt) was recorded.

Cell culture test.—Cell suspensions of *Zea mays* and other plants were cultivated in sterile disposable test-tubes. The substances, in a solution of Me_2CO, were added to the nutrient medium and, after 8 days of incubation, the conductivity of the culture medium was measured to estimate the increase in growth.

All results of the herbicidal experiments were noted as percentages of controls.

FUNGICIDE TEST IN THE GREENHOUSE.—Suitable plants susceptible to fungi were cultivated in greenhouses as pot-plants and treated with the test substances before (protective) or after (curative) an artificial fungus infection. Then the plants were placed in optimal climatic conditions for the development of the fungi. The dimension of fungal infection was estimated on a scale from 0 = no effect (total infestation) to 8 = very good effect (without infestation), and the results were evaluated as a percentage of controls. The following test systems were used: *Alternaria solani* (on tomatoes), *Botrytis cinera* (on pepper), *Erysiphe cichoracearum* (on cucumber), *Erysiphe graminis* (on wheat), *Plasmopara viticola* (on vines), *Puccinia recondita* (on wheat), *Pyrenophora teres* (on barley), *Pyricularia oryzae* (on rice), and *Septoria nodorum* (on wheat).

INSECTICIDAL AND ACARICIDAL EFFECTS.—The insecticidal activity was tested by contact assay on *Musca domestica, Aedes aegypti, Plutella maculipennis,* and *Prodenia litura* and by breeding assay on *Heliothis virescens, Aedes aegypti* (mosquito larvae), and *Prodenia litura.*

For the contact assay, a defined amount of the test substance was given in lockable dishes. After 4–24 h, the dead insects were evaluated as a percentage of controls. In the breeding assay, a special diet (containing a defined concentration of the test substances) was fed to the caterpillars or the larvae. The development to the imago was observed and evaluated as a percentage of controls.

The acaricidal activity was checked in a contact assay with *Tetranychus telarius*; the dead animals were evaluated as a percentage of controls.

ISOLATION AND SYNTHESIS OF THE TEST SUBSTANCES.—Compounds **1**, **3**, **6**, and **7** were synthesized as described earlier (2); **4**, **5**, and **2** were isolated from fruits of *Pimpinella major* and their structures ascertained spectroscopically (6). Isoeugenol was supplied by Fa. Roth, Karlsruhe.

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