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A FACILE *E,Z*-ISOMERIZATION OF α,β-UNSATURATED TERPENOID LACTONES AND ITS EFFECT ON PLANT GROWTH ACTIVITY

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Key Word Index—*E,Z* -isomer; conjugated terpenoid lactones; root promotors.

Abstract—Various synthetic C-16 lactones prepared in earlier work are the *Z*-isomers. These have been isomerized chemically to the corresponding *E*-isomers. It is observed that these isomers have different root initiating properties, which reflect the significance of the geometry of double bonds in conjugated γ-lactones which act as plant growth regulators.

INTRODUCTION

In our earlier work [1, 2] we reported the synthesis of several compounds containing an α,β-unsaturated lactone grouping (**1–4**). Interestingly the most active compound [3] as a root promotor from these series was **5** (*Z*-isomer). Therefore, we were interested to see if this biological activity could be further increased by the isomerization of the double bond in **5** (*E*-isomer). Interestingly however, it was found that the root forming potential of the isomerized product underwent a significant decrease. With this in mind the compounds of the type **1** were converted into the other isomer and it was found that upon this isomerization, the biological activity of the compound was changed. In the present paper the biological data on only four isomers are presented. The compounds (**6***E*, **6***Z*) and (**7***E*, **7***Z*) could not be tested due to paucity of the material.

Another reason for carrying out this isomerization was to fix the stereochemistry about the C=C rigorously. It has been reported [4] that α-methylene-γ-lactones can be purified by reaction with amines and subsequent elimination from the Michael addition product. We felt therefore, that this reaction would be useful for our isomerization work.

RESULTS AND DISCUSSION

Reaction of compound **5** (mp 74°) with diethylamine afforded a mixture of two products one of which was shown to be the starting compound (TLC and mmp). The other product (liquid) from its spectral data (IR bands at 1750, 1670 and 890 cm^{-1}; ^1H NMR see Table 1) was obviously the double bond isomer. Comparison of the olefinic proton region showed that the compound with mp 74° had its trisubstituted olefinic proton at δ5.93 as a doublet of quartets. In the isomerized product this proton appeared at 6.72. This clearly required the compound with mp 74° to be the *Z*-isomer whereas the isomerized compound is the *E*-isomer. These assignments were confirmed by looking at the allylic methyl group. In the compound with mp 74° this methyl appeared at δ2.1 as a doublet of doublets whilst in the isomerized product this methyl appeared at 1.91.

In our earlier paper [1] we had assigned the *E*-geometry to the compound with mp 74°. This was due to the fact that we had compared the signals of the olefinic proton of compounds of type **1** with that of the most down field proton of the compounds of type **4** without considering the expected down field shift due to increased substitution.

Isomerization of compounds **6**, **7** and **8** (mp 92°, liquid and mp 120° respectively) with dimethylamine afforded the isomeric compounds mp 96°, 131° and 110° respectively. Examination of the ^1H NMR spectra (Table 1) left no doubt that the isomerized compounds were the *E*-isomers whereas the starting compounds were the *Z*-isomers.

Similar isomerizations of aurones (**9**) have been reported [5] using pyridine as the reagent. Thus the reaction of compound **9***Z* (mp 185–7°) furnished the isomer **9***E* (mp 152°). It is interesting that here also the initial *Z*-isomer is converted with base into the *E*-isomer. A plausible mechanism of this reaction has been suggested [5].

The effects of compounds **5***E*, **5***Z*, **8***E* and **8***Z* on root initiation with *Phaseolus aureus* hypocotyl cuttings are shown in Table 2.

EXPERIMENTAL

An alcoholic soln of lactone (1 mol) in EtOH (15–20 ml/g) and diethylamine (3 mol) was stirred at 50–5° for several hr. The mixture was diluted with H_2O, extracted with Et_2O, neutralized and dried over Na_2SO_4. Evapn of the solvent afforded a mixture which was separated into its components by chromatography on Si gel. All the compounds gave satisfactory C,H analysis.

IR spectra (Table 1) were taken in nujol suspensions. ^1H NMR spectra (Table 1) were recorded in $CDCl_3$ with TMS as the internal standard. All values are recorded in δ. TLC was carried out using Si gel G supplied by BDH. Visualization of spots was by spraying with H_2SO_4–MeOH followed by heating at 120°.

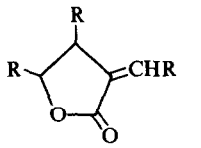
Table 1. Spectral data for the isomerized compounds

Compound	IR (cm^{-1})	NMR			
		C-6H	C-15H	C-15 Me	Others
5*Z*	1760, 1640, 890	3.73, 1H, *t* $J = 9$	5.93, *dq*, $J = 3, 7.5$	2.12, *dd* $J = 2, 7.5$	4.73, *bs* 4.8, *bs*, 1H each 4.97, *d*, $J = 2$ 5.23, *d*, $J = 2$
5*E*	1750, 1670, 890	3.83, 1H, *t* $J = 9$	6.72, *dq* $J = 3, 7.5$	1.91, *dd* $J = 3, 7.5$	4.8 *bs*, 2H 5.02 *bs*, 1H 5.27 *bs*, 1H C-11 and C-12 H
6*Z*	3050, 1750, 1675, 895, 865	3.97, *t* $J = 11$	6.0, *m* $J = 2, 7$	2.12, *dd* $J = 2, 7$	4.85 *bs*, 1H 5.0 *bs*, 1H 0.85 *s*, C-10 CH_3
6*E*	1750, 1675, 1650, 880	3.8, 1H, *t* $J = 10.5$	6.5, *dq* $J = 3, 8$	1.9, *dd* $J = 2, 8$	4.8 *bs*, 1H 4.88 *bs*, 1H C-12 H. 0.8 *s*, 3H C-11 H
7*Z*	1750, 1670	3.9, *t* $J = 11$	6.1, *dq* $J = 3, 8$	2.17, *dd* $J = 3, 8$	0.9 *s*, C-10 CH_3 5.5 *nm*, C-3 H 1.87 *bs* C-4 CH_3
7*E*	1750, 1675, 840	3.72, 1H, *t* $J = 11$	6.51, *dq* $J = 3, 8$	1.9, *dd* $J = 2, 8$	5.32 *bs*, 1H, C-3 H 1.82 *bs*, 3H, C-12 H 0.9 *s*, 3H, C-11 H
8*Z*	1750, 1650, 1660, 1010, 920, 890	4.13, *t* $J = 11.5$	6.13, *dq* $J = 3, 7$	2.2, *dd*	1.81 *bs*, 3H 1.07 *s*, 3H, C-1 H 5.83 *m*, C-2 and C-3 H 5.0 *m*, 4H
8*E*	1750, 1675, 1640, 980, 905, 880	3.98, 1H, *t* $J = 11$	6.57, *dq* $J = 3, 8$	1.92, *dd* $J = 2, 8$	4.95 *dd*, 1H $J = 1.5, 10$ 4.90 *dd*, 1H $J = 1.5, 8$, C-2 H 4.69 *bs*, 1H 5.02 *bs*, 1H, C-3 H 1.8 *bs*, 3H, C-12 H 1.08 *s*, 3H, C-11 H 5.82, sextet, 1H $J = 10, 18$

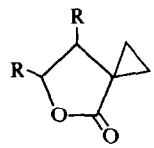
Table 2. Effect of different concentrations of terpenoids on the number of roots per rooted segment produced on hypocotyl cuttings of *Phaseolus aureus* after 7 days

Treatment mg/l.*	Number of roots			
	10	20	30	40
5*Z*	14.7 ± 1.3	27.7 ± 2.27	34.5 ± 2.59	—
5*E*	13.0 ± 0	12.7 ± 1.3	14.6 ± 0.94	17.0 ± 0.70
8*Z*	7.7 ± 1.09	8.7 ± 0.83	6.5 ± 0.86	8.0 ± 1.22
8*E*	9.8 ± 1.32	11.8 ± 0.4	12.2 ± 2.04	13.2 ± 1.6

* Control experiment, water = 9.3 ± 1.18.



1 R = Me
4 R = H



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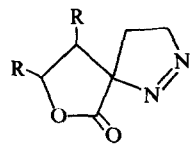

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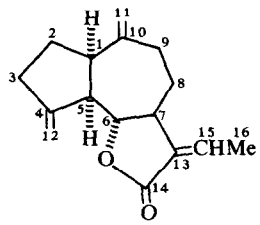
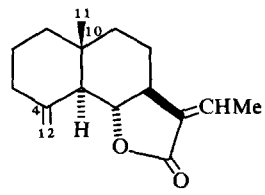


5Z, 5E



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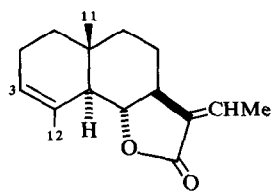
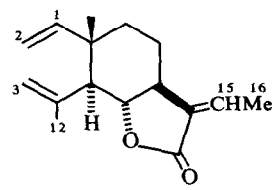
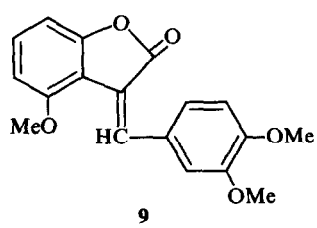


7Z,7E



8Z, 8E



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Isomerization of **5Z** *to* **5E**. The compound **5Z** (mp 74°) on isomerization (42 hr at 55°) afforded a mixture of two major components. The product mixture was chromatographed (petrol–Et_2O, 9:1) to furnish compound **5Z** (mp 74°). IR and ^1H NMR (Table 1). Compound **5E** (liquid) was eluted in petrol–Et_2O (17:3).

Isomerization of **6Z** *to* **6E**. Compound **6Z** (mp 92°) on isomerization (40 hr at 50–2°) afforded a mixture. The product was chromatographed in petrol–Et_2O (19:1) to furnish compound **6Z** (mp 92°). Compound **6E** (mp 96°) was eluted in petrol–Et_2O (19:1).

Isomerization of **7Z** *to* **7E**. Compound **7Z** (liquid) on isomerization (45 hr at 55°) afforded a mixture which was chromatographed in petrol–Et_2O (49:1) to furnish compound **7Z** (liquid). Compound **7E** (mp 131°) was eluted in petrol–Et_2O (19:1).

Isomerization of **8Z** *to* **8E**. Compound **8Z** (mp 120°) on isomerization (42 hr at 55°) afforded a mixture which was chromatographed in petrol–Et_2O (19:1) to furnish compound **8Z** (mp 120°). Compound **8E** (mp 110°) was eluted in petrol–Et_2O (19:1).

Biologiçal testing. For root initiation studies on hypocotyl cuttings of *Phaseolus aureus* the seedlings were raised under continuous illumination. After 4 days, when the hypocotyls were 5–6 cm long, cuttings were made by excision 4 cm below the cotyledonary node leaving the cotyledonary leaves and apex intact. In all, 4 compounds at 4 concentrations (10, 20, 30 and 40 mg/l.) along with H_2O as control were tested. For all treatments 10 replicates were cultured in vials each containing 30 ml of test soln. All the solns were replaced with fresh ones after 4 days. The final observations were recorded on the 8th day. The experiment was repeated three times at 26 ± 2°.

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EUDESMANOLIDES FROM *DIMEROSTEMMA LIPPIOIDES**

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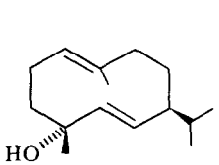
Key Word Index—*Dimerostemma lippioides*; Heliantheae; Compositae; sesquiterpene lactones; eudesmanolides.

The Brazilian genus *Dimerostemma* is placed by Stuessy [1] in the subtribe Verbesininae (tribe Heliantheae, Compositae). So far nothing is known about the chemistry of this small genus.

We have now investigated *D. lippioides* (Baker) Blake. The aerial parts afforded germacrene D, α-humulene, bicyclogermacrene, 4α-hydroxygermacra-1(10),5-diene (**1**), spathulenol (**2**) and the isomeric acids **3** and **4**. The polar fractions gave three sesquiterpene lactones, the eudesmanolides **5**–**7**. The structures followed from the ^{1}H NMR data (Table 1), though **6** and **7** could not be separated even by HPLC. Compounds **5**–**7** are closely related to the β-cyclocostunolides from *Zexmenia phyllocephala* [2]. The small couplings of 1-H required an α-position of the ester residues, while the stereochemistry at C-5 through C-8 followed from the sequence of axial, axial-couplings. The presence of the 4,15-epoxide was deduced from the typical doublets in the spectrum of **6** at δ 3.42 and 2.44. The large difference in the chemical shifts of the epoxide protons and the chemical shift of the 10-methyl group favoured a β-epoxide. As could be seen from models one of the epoxide protons is deshielded by the lactone oxygen, while the 10-methyl group is deshielded by the epoxide oxygen. The relative position of the ester groups in **6** and **7** was supported by the differences in the chemical shifts of 6-, 7- and 8-H, which were typical for compounds with saturated and unsaturated ester groups. However, the signal of 1-H was identical in both compounds. We therefore assign the structures as **6** and **7**, though the relative position of the ester groups could not be established by partial saponification. The diol, which is derived from the esters **5**–**7**, we have named dimerostemmolide.

The roots afforded only bicyclogermacrene. The



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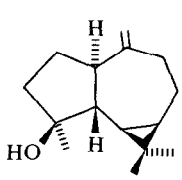

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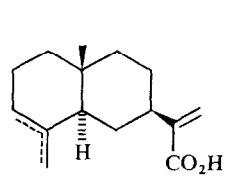
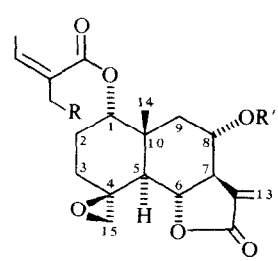


3 Δ4(15)
4 Δ3(4)



5 R = H, R′ = H
6 R = OH, R′ = Ang
7 R = OH, R′ = Mebu

*Part 313 in the series 'Naturally Occurring Terpene Derivatives'. For Part 312 see: Bohlmann, F., Zdero, C., Robinson, H. and King, R. M. (1981) *Phytochemistry* **20**, 739.