Pergamon

PII: S0031–9422(97)00906–0

Phytochemistry, Vol. 49, No. 3, pp. 801–804, 1998

SESQUITERPENE LACTONES FROM *SAUSSUREA LAPPA*

B. R. CHHABRA,* S. GUPTA, M. JAIN and P. S. KALSI

Department of Chemistry, Punjab Agricultural University, Ludhiana-141 004, India

(*Received in revised form* 21 *July* 1997)

Key Word Index—*Saussurea lappa*; Compositae; sequiterpene lactones; guaianoldies; α-methylene; γ-lactone; plant growth regulators.

Abstract—Three new guaianolides, namely 11,13 epoxydehydrocostuslactone, 11,13 epoxyisozaluzanin C and 11,13 epoxy-3-keto dehydrocostus-lactone were isolated from the petrol extract of powdered costus roots (*Saussurea lappa*). The structures of the new compounds have been deduced from spectral data and chemical transformations.© 1998 Elsevier Science Ltd. All rights reserved

---

INTRODUCTION

Sesquiterpene lactones having an α-methylene-γ-butyrolactone moiety, have been the subjects of many biological and chemical studies. Our bioassay oriented studies [1–4] on sesquiterpene lactones from the petrol extract of powdered costus (*Saussurea lappa* Clarke) roots have resulted in the isolation of some potent plant growth regulators like saussureal (**1**) [5] which has a new type of eudesmane skeleton in which ring A is five-membered. Costus roots are a rich source of two crystalline sesquiterpenes dehydro-costuslactone (**2**) and costunolide (**3**) [6]. In addition to these some other lactones have also been isolated such as 13-methoxy-11,13-dihydrodehydro-costuslactone [3], and the two aldehydo sesquiterpene lactones **4** and **5** [7]. In the present paper, we report on the isolation and structure elucidation of three new sesquiterpene lactones (**6**–**8**) which showed little bioactivity in terms of adventitious root formation in stem cuttings of *Vigna radiata*.

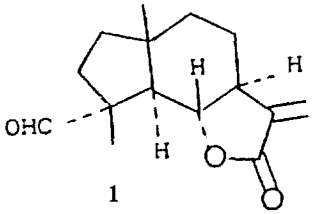
RESULTS AND DISCUSSION

The HR mass spectrum of compound **6** indicated a Mr of 246.288 consistent with molecular formula $C_{15}H_{18}O_3$. The spectral data showed the presence of a γ-lactone ring system/IR 1780 cm^{-1}, ^{13}C NMR δ180.3). The ^{1}H and ^{13}C NMR spectral data suggested that **6** had a guaianolide carbon skeleton (Tables 1 and 2). The multiplicity of various carbons was determined by DEPT experiments which showed the presence of four olefinic carbons (Table 2), one secondary carbon bearing oxygen (δ83.4, *d*) and one tertiary carbon bearing oxygen (δ60.0, *s*). The ^{1}H NMR spectrum showed the presence of two exomethylene double bonds [δ4.83 and 4.86 ea. 1H, *brs*) and δ5.02 and 5.6 (ea. 1H, *d*, $J = 2.5$ Hz)] which was supported by IR bands at 3080, 1640 and 895 cm^{-1}. A comparison of the chemical shifts and multiplicities of the ^{1}H and ^{13}C NMR signals (Tables 1 and 2) of compound **6** and dehydrocostuslactone (**2**) showed that the signals were closely related except for the absence of the signals for an exomethylene double bond in conjugation with the γ-lactone in compound **6** which showed instead a singlet for two hydrogens at δ2.91. This was further supported by the ^{13}C NMR spectral data which showed the presence of four olefinic carbons in compound **6** while there are six such carbons in dehydrocostuslactone. A survey of the literature revealed that the singlet at δ2.91 may be attributed to the presence of a 13-methylene when the 11,13 double bond is epoxidised with the oxirane ring α-placed at C-11 [8]. Hence the structure of this compound could be depicted as **6**. Confirmation of this structure was achieved when dehydrocostuslactone **2** was treated with H_2O_2/NaOH in THF for 72 h to yield a compound identical in all respects with the natural product **6**.

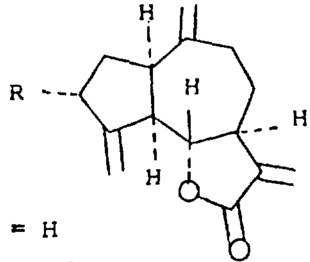
Compound **7** was assigned the molecular formula $C_{15}H_{18}O_4$, 262.291 (HRMS). The guaianolide nature of this compound was established by a triplet at δ3.90 ($J = 10$ Hz) and supported by an IR band at 1760 cm^{-1}. The presence of a hydroxyl group was confirmed by the IR (3550 cm^{-1}) and ^{1}H and ^{13}C NMR data (Tables 1 and 2). A comparison of the ^{13}C NMR data of **7** with those of dehydrocostuslactone **2** and **6** revealed the absence of a signal due to a C-2 methylenic carbon around δ36 and a doublet at δ74.8. This suggested the presence of a hydroxyl group at C-2. The position and stereochemistry of the hydroxyl

---

* Author to whom correspondence should be addressed.

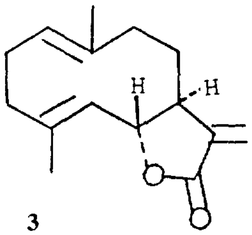


1

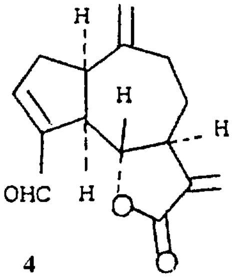


2, R = H

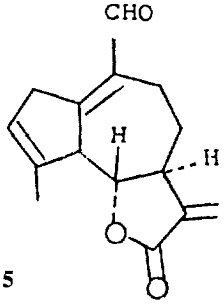
9, R= -OH



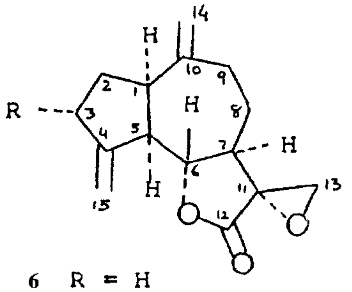
3



4

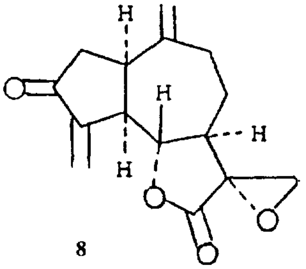


5



6 R = H

7 R= -OH



8

Table 1. ^1H NMR spectra data of compounds **6**–**8**.

	C_3H	C_6-H	C_{13}-H and C'_{13}-H	C_{14}-H's	C_{15}-H's
6	-	4.1, 1H, *t* (J = 9.1 Hz)	2.91, 2H, *s*	4.83, 1H, *brs* 4.86, 1H, *brs*	5.02, 1H, *d*(J = 2.5 Hz) 5.6, 1H, *d*(J = 2.5 Hz)
7	3.90, 1H, *t* J = 10 Hz	4.68, 1H, *t* (J = 8.0 Hz)	3.07, 1H 3.1, 1H	5.35, 1H, *brs* 5.45, 1H, *brs*	5.56, 1H, *d*(J = 2 Hz) 6.20, 1H, *d*(J = 2 Hz)
8	-	4.1, 1H, *t* (J = 9 Hz)	3.1, 2H, *s*	4.9, 1H, *brs* 5.0, 1H, *brs*	5.63, 1H, *d*(J = 3 Hz) 6.25, 1H, *d*(J = 3 Hz)

group was confirmed when isozaluzanin C (**9**) [9], a compound of known structure and stereochemistry, on reaction with H_2O_2/NaOH in THF yielded the natural product **7**.

Compound **8** was shown to have the molecular formula $C_{15}H_{16}O_4$ (HRMS, $[M]^+ = m/z$ 260.278). The IR spectrum shows the presence of a carbonyl band (1725 cm^{-1}) together with a band at 1765 cm^{-1} (guaianolide). The presence of two carbonyls and four olefinic carbons in addition to three oxygen-bearing carbons was revealed by the ^{13}C NMR data. These spectral features suggested that this compound was an oxidation product of compound **7**. When compound **7** was oxidised with PCC, it gave compound **8** in

Table 2. ^{13}C NMR spectral data of compounds **2**, **6**, **7** and **8**

C	**2**	**6**	**7**	**8**
1	45.2 (*d*)	44.7 (*d*)	44.4 (*d*)	43.4 (*d*)
2	32.6 (*t*)	36.8* (*t*)	37.6 (*t*)	34.8 (*t*)
3	36.2 (*t*)	35.4* (*t*)	74.8 (*d*)	210.4 (*s*)
4	149.3 (*s*)	150.5 (*s*)	154.4 (*s*)	148.3 (*s*)
5	52.0 (*d*)	51.0 (*d*)	50.8 (*d*)	49.4 (*d*)
6	85.2 (*d*)	83.4 (*d*)	82.8 (*d*)	84.6 (*d*)
7	47.6 (*d*)	45.6 (*d*)	44.6 (*d*)	43.4 (*d*)
8	31.0* (*t*)	27.3 (*t*)	28.9 (*t*)	29.8 (*t*)
9	30.3* (*t*)	33.6 (*t*)	34.9 (*t*)	32.9 (*t*)
10	139.8 (*s*)	145.4 (*s*)	146.8 (*s*)	144.5 (*s*)
11	151.2 (*s*)	60.0 (*s*)	60.7 (*s*)	59.8 (*s*)
12	170.2 (*s*)	180.3 (*s*)	174.7 (*s*)	178.4 (*s*)
13	120.1* (*t*)	49.5 (*t*)	50.1 (*t*)	50.8 (*t*)
14	109.6 (*t*)	113.6 (*t*)	114.8 (*s*)	118.4 (*s*)
15	112.6 (*t*)	110.2 (*t*)	111.7 (*s*)	112.4 (*s*)

* Interchangeable within the same column.

almost quantitative yield and identical in all respects with the natural product.

EXPERIMENTAL

MPs: uncorr; IR: nujol mull; ^1H and ^{13}C NMR: 90 MHz and 67.8 MHz, respectively, $CDCl_3$, TMS as int. standard. All chromatographic separations were performed on silica gel.

Plant material

Roots of *Saussurea lappa* Clarke were procured from the Lahaul and Spiti region of India, and plant specimen no. 1067 was deposited in the herbarium of the Botany Department of this University.

Isolation of compounds 6, 7 and 8

Powdered costus roots (1 kg) were packed in a glass column and eluted with petrol (40–60°) (5l). The total extract was evaporated under red pres to yield a semi-solid golden yellow material (25 g). This was dissolved in the minimum quantity of petrol (40–60°) and kept at 4° for 48 h when a solid mixture of dehydrocostuslactone and costunolide was obtained. It was filtered and washed thoroughly with cold petrol. Evaporation of petrol gave an oil (2.3 g). The ^1H NMR spectrum of this crude liquid showed signals in the region around 3δ. It was treated with an excess of an ethereal sol of CH_2N_2 followed by CC on silica gel (100 g) and elution of the column with solvents of increasing polarity: petrol-Et_2O (20:1) yielded with a less polar fraction (0.8 g) of at least three compounds (TLC, silica gel-$AgNO_3$ 10%) followed by highly polar pyrazolines of sesquiterpene lactones. The ^1H NMR spectrum of the less polar fraction showed signal around δ2.5. This fraction was further chromatographed over silica gel-$AgNO_3$ 10% (100 g). Elution of the column with petrol-Et_2O (10:1) gave **6** as a solid (230 mg): mp 78°; HRMS 246.288 ($C_{15}H_{18}O_3$ requires 246.298); IR ν_{max}^{nujel} cm^{-1}: 3080, 1780, 1640, 1120, 895 and 820. It was followed by (70 mg) **7**: mp 148°; HRMS 262.291 ($C_{15}H_{18}O_4$ requires 262.298); IR ν_{max}^{nujel} cm^{-1}: 3550, 3082, 1760, 1640, 1600, 1140 and 890. Further elution of the column with the same solvent (1.5 l) followed by crystallization from Et_2O yielded **8** (150 mg): mp 115°; HRMS 260.278 ($C_{15}H_{16}O_4$ requires 260.283); IR ν_{max}^{nujel} cm^{-1}: 3075, 1760, 1725, 1623, 1130 and 880.

Reaction of dehydrocostuslactone 2 with H_2O_2/NaOH

Dehydrocostuslactone (100 mg) (**2**) was dissolved in THF (15 ml) and to this was added H_2O_2 (30 Vol, 5 ml) followed by NaOH soln (10%, 2 ml). The reaction mixture was kept at 4° for 72 h. The usual work up involving dilution with H_2O, neutralization with dil. HCl and extraction with Et_2O yielded a two component mixture (85 mg). This upon chromatography over silica gel (15 g) yielded unreacted starting material (50 mg) followed by pure solid compound (30 mg) identical in all respects to the natural product **6**.

Reaction of isozaluzanic-C 9 with H_2O_2/NaOH

Izosaluzanic C (100 mg) **9** was reacted as above under same conditions to yield compound **7** (40 mg).

Reaction of compound 7 with PCC

Compound **7** (50 mg) was dissolved in CH_2Cl_2 (15 ml) and to this was added PCC (0.5 g). After stirring for 1 h at room temp., the mixture was filtered through a small bed of celite, which was washed with CH_2Cl_2 (20 ml). The combined CH_2Cl_2 was washed with a sat. soln. of $CuSO_4$ followed by H_2O and dried. Evaporation of solvent yielded after, crystallization from CH_2Cl_2, a solid compound (40 mg) identical in all respects to compound **8**.

Acknowledgements—The authors thank the Punjab Government for financial support under the project 'Chemistry of some natural products and their significance in agriculture'. Thanks are also due to Prof. H. Etoh of Shizuoka University, Department of Applied and Agricultural Chemistry, Japan, for his help in providing spectral data.

REFERENCES

1. Kalsi, P. S., Kaur, P. and Chhabra, B. R., *Phytochemistry*, 1979, **18**, 1877.
2. Dhillon, R. S., Kalsi, P. S., Singh, W. P., Gautam, V. K. and Chhabra, B. R., *Phytochemistry*, 1987, **26**, 1209.

3. Kalsi, P. S., Kaur, G., Sharma, S. and Talwar, K. K., *Phytochemistry*, 1984, **23**, 2855.
4. Kalsi, P. S., Chhabra, B. R., Chhabra, A. and Wadia, M. S., *Tetrahedron*, 1979, **35**, 1993.
5. Singh, I. P., Talwar, K. K., Arora, J. K., Chhabra, B. R. and Kalsi, P. S., *Phytochemistry*, 1992, **31**, 2529.
6. Govindan, S. V. and Bhattacharyya, S. C., *Indian J. Chem.*, 1977, **15B**, 956.
7. Kalsi, P. S., Kumar, S., Jawanda, G. S. and Chhabra, B. R., *Phytochemistry*, 1995, **40**, 1713.
8. Reis, L. V., Tavares, M. R., Palma, F. M. S. B. and Marcelo-Curto, M. J., *Phytochemistry*, 1992, **31**, 1285.
9. Kalsi, P. S., Sharma, S. and Kaur, G., *Phytochemistry*, 1983, **22**, 1993.