*Phytochemistry*, Vol. 24, No. 11, pp. 2728–2730, 1985.
Printed in Great Britain.

0031–9422/85 $3.00 + 0.00


# TWO GUAIANOLIDES FROM *CALEA SOLIDAGINEA*

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(*Revised received* 20 *March* 1985)

**Key Word Index**—*Calea solidaginea*; Asteraceae; Heliantheae; sesquiterpene lactones; guaianolides; solidaginolides A and B.

**Abstract**—The isolation and structure elucidation of two new guaianolides, solidaginolides A (**1**) and B (**5**), from *Calea solidaginea* are reported. The structures of the new compounds were established by spectroscopic methods.

## INTRODUCTION

Among the 40 *Calea* species that have so far been chemically investigated [1], guaianolides were found only in *C. subcordata* [2], *C. berteriana* [1], *C. prunifolia* [1] and *C. solidaginea* [1]. In continuation of our biochemical systematic investigations of the genus *Calea* we have further analysed *C. solidaginea* from Venezuela for its sesquiterpene lactone constituents. Previous studies of the same collection of this species [1] afforded the two guaianolides 8-epi-8-tiglylrupicolin A and desacyl-8-tiglylsubcordatolide A. We now report the isolation and structure determination of two new guaianolides, solidaginolide A (**1**) and solidaginolide B (**5**). The structures of the new compounds were established by spectroscopic and chemical methods.

## RESULTS AND DISCUSSION

Solidaginolide A (**1**), $C_{20}H_{24}O_7$, is a gum with an IR spectrum showing the presence of hydroxyl group(s) (3640 and 3600 $cm^{-1}$), a $\gamma$-lactone (1760 $cm^{-1}$), an unsaturated ester (1700 $cm^{-1}$), and carbon–carbon double bond(s) (1650 and 1605 $cm^{-1}$). The $^1H$ NMR spectrum corroborated the presence of an $\alpha$-methylene-$\gamma$-lactone moiety by exhibiting two one-proton doublets at $\delta$ 6.24 (H-13a) and 5.47 (H-13b), and a one-proton multiplet at $\delta$ 3.74 (H-7). The unsaturated ester side chain was identified as a tiglate group on the basis of the characteristic $^1H$ NMR signals (a one-proton quartet of quartets at $\delta$ 6.86, and two three-proton vinyl methyl signals at $\delta$ 1.76 and 1.79), together with strong mass spectral peaks at *m/z* 83 ($A^1$) and 55 ($A^2$). Detailed spin decoupling experiments in $CDCl_3$ and benzene-$d_6$ allowed the assignments of all $^1H$ NMR signals (Table 1). The mass spectrum of **1** showed no molecular ion peak and only very weak high-mass peaks. The spectrum was dominated by a base peak at *m/z* 111 which was assigned to $C_6H_7O_2^+$ (**B**). The formation of this ion can be accounted for by fragmentation of a diepoxycyclopentane moiety, thus suggesting structural features in **1** similar to canin (**4**) [3] and artecanin (**2**) [4].

The chemical shifts and multiplicities of H-5 ($\delta$ 2.86, *d*, $J_{5,6}$ = 10.5 Hz) and H-6 (4.72, *t*, $J_{5,6} = J_{6,7}$ = 10.5 Hz), together with the absence of angular methyl signals in the $^1H$ NMR spectrum, suggested a guaianolide-type skeleton with a tiglate ester side chain. Assuming that H-7 is $\alpha$-oriented as in all known lactones from higher plants [5], H-6 should be $\beta$-oriented since the coupling constant ($J_{6,7}$ = 10.5 Hz) clearly indicated an antiperiplanar arrangement of H-6 and H-7. Similarly, the coupling constant $J_{5,6}$ = 10.5 Hz also supported an antiperiplanar arrangement of H-5 and H-6, and therefore an $\alpha$-orientation for H-5. On the basis of chemical shift arguments, the ester side chain must be attached to C-8. Furthermore, the small coupling constant ($J_{7,8}$ = 2.5 Hz) suggested a $\beta$-orientation of the C-8 ester sidechain. The chemical shifts of the methyl signals at $\delta$ 1.12 (H-14) and 1.58 (H-15) were in accord with the presence of a hydroxyl group at C-10 and an epoxide function at C-4, respectively. A narrow doublet ($J$ = 1 Hz) at $\delta$ 3.60 (H-2) which was coupled to a broadened one-proton singlet at 3.30 (H-3) suggested epoxide functions at C-1 and C-3 as in canin (**4**) [3] and artecanin (**2**) [4], further corroborating the mass spectral conclusions. The stereochemistry of the epoxide functions and the orientation of the hydroxyl at C-10 in **1** were assigned by NMR spectral correlations of H-5 and H-6 with those reported for artecanin (**2**) [4] and 10-epicanin [6]. The chemical shift of H-5 in compound **1** ($\delta$ 2.86) is comparable with that of artecanin (**2**) (2.83), and appears 0.31 ppm and 0.24 ppm downfield from the respective H-5 signals of canin (**4**) and 10-epicanin [6]. It must therefore be concluded that the epoxide functions at C-1 and C-3 in **1** are $\alpha$-oriented as in artecanin (**2**).

*In situ* acylation of **1** with trichloroacetyl isocyanate [7] yielded the trichloroacetyl carbamate derivative **3**, the $^1H$ NMR spectrum of which showed one NH signal at $\delta$ 8.47 which confirmed the presence of one hydroxyl group in compound **1**. The assignment of the $^1H$ NMR signals of **3** were deduced by double irradiation experiments (Table 1). The paramagnetic acylation shift of the C-10 methyl protons (H-14) from $\delta$ 1.12 in **1** to 1.40 in the trichloroacetyl carbamate **3** ($\Delta\delta$ = 0.28) was in agreement with the presence of a hydroxyl group at C-10. Absence of

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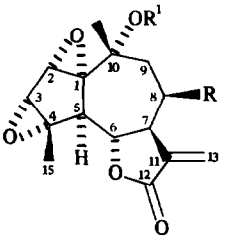
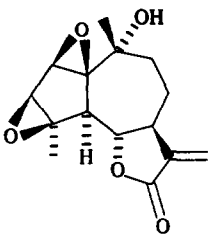


**1** R = OTiglate, $R^1$ = H
**2** R = H , $R^1$ = H
**3** R = OTiglate, $R^1$ = $CONHCOCCl_3$



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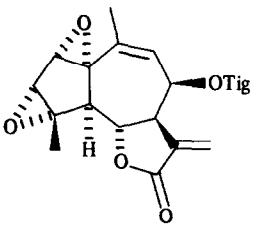

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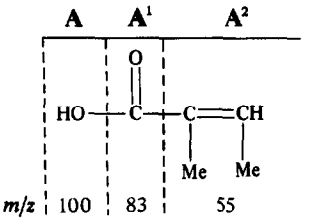


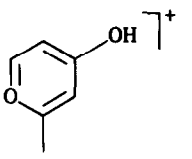

**B**

Table 1. $^1$H NMR spectral data* of solidaginolide A (**1**) and B (**5**) and derivative **3** (200 MHz, $CDCl_3$[$C_6D_6$], TMS)

| H | 1 | 3 | 5 |
|---|---|---|---|
| 2 | 3.60 [2.83] *d* (1.0) | 3.77 *br s* | 3.78 [3.37] *br s* |
| 3 | 3.30 [2.62] *br s* | 3.39 *br s* | 3.72 [3.29] *br s* |
| 5 | 2.86 [2.58] *d* (10.5) | 2.36 *d* | 2.40 [2.09] *d* (10.0) |
| 6 | 4.72 [4.95] *dd* (10.5; 10.5) | 4.75 *t* | 5.01 [5.18] *dd* (10.0; 10.0) |
| 7 | 3.74 [3.47] *m* | 3.35 *m* | 4.26 [4.14] *m* |
| 8 | 5.65 [5.62] *ddd* (9.0; 2.5; 2.5) | 5.71 *dt* | 6.08 [6.10] *m* (narrow) |
| 9α | 2.36 [1.98] *dd* (16.0; 9.0) | 2.79 *dd* | |
| 9β | 1.86 [1.88] *dd* (16.0; 2.5) | 1.92 *m* | 5.48 [5.40] *m* |
| 13a | 6.24 [6.14] *d* (4.0) | 6.28 *d* | 6.30 [6.28] *d* (4.0) |
| 13b | 5.47 [5.20] *d* (3.3) | 5.53 *d* | 5.54 [5.26] *d* (3.3) |
| 14 | 1.12 [0.57] *s* | 1.40 *s* | 1.85 [1.52] *br s* |
| 15 | 1.58 [1.41] *s* | 1.58 *s* | 1.60 [1.36] *s* |
| Tig | 6.86 [6.96] *qq* (7.5; 2.0) | 6.88 *m* | 6.78 [6.82] *qq* (7.5; 2.0) |
| | 1.79 [1.71] *br* | 1.81 *br* | 1.76 [1.69] *br* |
| | 1.76 [1.67] *br* | 1.80 *br* | 1.75 [1.64] *br* |
| NH | — | 8.47 *s* | — |

*Coupling constants (*J*) or line separations in Hz are given in parentheses. Multiplets are given by the usual symbols.

a paramagnetic acylation shift of H-6$\beta$ in the carbamate derivative 3 ($\delta$4.75), when compared with H-6 in 1 (4.72), suggested an C-10 $\alpha$-hydroxyl group. More significantly, the paramagnetic shift of H-5$\alpha$ and H-7$\alpha$ was 0.50 and 0.39, respectively. This permitted the unambiguous assignment of the stereochemistry as C-10$\alpha$-hydroxyl and an overall stereostructure for solidaginolide A as shown in 1.

Solidaginolide B (5), $C_{20}H_{22}O_6$, exhibited in the $^1$H NMR spectrum two one-proton doublets at $\delta$6.30 (H-13a) and 5.54 (H-13b), and a one-proton multiplet at 4.26 (H-7) suggesting an $\alpha$-methylene-$\gamma$-lactone. A strong IR band at 1760 cm$^{-1}$ corroborated the presence of a $\gamma$-lactone moiety. Further IR absorption bands at 1700, 1650 and 1605 cm$^{-1}$ indicated the presence of an unsaturated ester side chain and double bonds. As in the case of compound 1, the ester side chain was identified as a tiglic ester on the basis of the diagnostic $^1$H NMR and mass spectral signals. Exhaustive spin decoupling experiments in $CDCl_3$ and benzene-$d_6$ allowed the assignments of the skeletal protons (Table 1).

Comparison of the $^1$H NMR spectra of compounds 1 and 5 showed major differences only for the signals of H-9 and H-14. Instead of the H-9 proton absorptions, which in 1 were represented by two one-proton doublet of doublets at $\delta$2.36 (H-9a) and 1.86 (H-9b), in compound 5 a one-proton multiplet appeared at $\delta$5.48 clearly indicating its olefinic nature. Furthermore, the H-14 signal which in 1 was a three-proton singlet at $\delta$1.12, appeared in 5 as a broadened three-proton singlet at $\delta$1.85 which sharpened upon irradiation of the H-9 signal at 5.48. The downfield shift of H-7 ($\delta$4.26) in compound 5, when compared to 1 (3.74), can be explained if deshielding of this proton by the carbonyl of the ester group at C-8 is assumed. Inspection of stereomodels revealed that this is the case when the seven-membered ring adopts a conformation with the C-8 ester group being in the more favored equatorial position. Based on the above arguments, we postulated stereostructure 5 for solidaginolide B.

## EXPERIMENTAL

*Calea solidaginea* Kunth was collected on December 12, 1979 in Salom, Venezuela (L. Urbatsch No. 3466, voucher deposited at L.S.U., U.S.A.). The air-dried plant material (728 g) was extracted and worked up as previously described [8, 9]. For the isolation of minor constituents, portions of fractions 23–24 (51 mg) were rechromatographed on silica gel plates using $CHCl_3$–$Me_2CO$ (9:1), yielding 8 mg of solidaginolide A (1) and 7 mg of solidaginolide B (5).

*Solidaginolide A* (1), $C_{20}H_{24}O_7$, gum; UV $\lambda^{MeOH}$ nm: strong end absorption; IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 3640 (OH), 3600 (OH, broad), 1760 ($\gamma$-lactone), 1700 (unsaturated ester), 1650 (double bond), 1605 (double bond); EIMS (probe) (rel. int.): 276 $[M-A]^+$ (0.2), 258 $[M-A-H_2O]^+$ (0.3), 230 $[M-A-H_2O-CO]^+$ (0.5), 202 $[M-A-H_2O-2CO]^+$ (1.0), 111 $[B]^+$ (100.0), 83 $[A']^+$ (68.6), 55 $[A'']^+$ (18.4).

*Solidaginolide B* (5). $C_{20}H_{22}O_6$, gum; UV $\lambda^{MeOH}$ nm: strong end absorption; IR $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 1760 ($\gamma$-lactone), 1700 (unsaturated ester), 1650 (double bond), 1605 (double bond); EIMS (probe) (rel. int.): 258 $[M-A]^+$ (0.1), 240 $[M-A-H_2O]^+$ (0.1), 83 $[A]^+$ (100.0), 55 $[A'']^+$ (24.7).

*Acknowledgements*—We thank Helga D. Fischer for technical assistance. A.G.O. thanks the Universidad Tecnica Santa Maria, Valparaiso, Chile for educational leave.

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