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C_{14} POLYACETYLENES FROM BRAZILIAN LOBELIOIDEAE

ADERBAL F. MAGALHÃES, DURVAL MARCOS VIEIRA, EVA G. MAGALHÃES and GEORGE J. SHEPHERD*

Instituto de Quimica; *Instituto de Biologia, Universidade Estadual de Campinas (UNICAMP) P.O. Box 6154, CEP 13081, Campinas, São Paulo, Brazil

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Key Word Index— *Lobelia*; *Siphocampylus*; Campanulaceae; Brazilian Lobelioideae; new C_{14} polyacetylenes; chemotaxonomy.

Abstract—Analysis of ethereal extracts from the roots of Brazilian species of *Lobelia* (*L. camporum*, *L. exaltata*, *L. fistulosa*, *L. langeana*, *L. numularioides*, *L. thapsoidea*) and *Siphocampylus* (*S. macropodus*, *S. sulfureus*, *S. verticilatus*, *S. westinianus*) gave acyclic C_{14} polyacetylenes containing ene-diyne or ene-yn-ene chromophores, of which four were unknown. The isolation of these acyclic polyacetylenes constitutes an important step in the chemotaxonomic characterization of these genera and, at the same time, confirms their position in the subfamily Lobelioideae as proposed by Wimmer and other authors.

INTRODUCTION

The genera *Lobelia* and *Siphocampylus* belong to the subfamily Lobelioideae. Although the major centres of diversity for the South American representatives of these genera are in the Andean region, a number of them are widely distributed in the highlands of central Brazil.

From a phytochemical viewpoint, several species of Campanulaceae have been characterized by the presence of C_{14} piranylacetylenes [1] while an acyclic C_{14} polyacetylene, represented by structure **1**, was isolated from a *Lobelia* species, *L. cardinalis* [2]. The genus *Siphocampylus*, however, is practically unexplored, although it was considered by Wimmer [3] to be close to *Lobelia* and was placed in the subfamily Lobelioideae.

In the present paper we report the polyacetylene composition of six species of *Lobelia* and four species of *Siphocampylus*, all from Brazil, and discuss the taxonomic significance of these compounds.

RESULTS AND DISCUSSION

From ethereal extracts of the roots, we isolated and identified five (**1**–**5**) polyacetylenes whose distributions and abundances are recorded in Table 1. The triol **1** was originally isolated and identified by Thaller *et al.* [2]. These authors demonstrated, by indirect means, that this triol possesses the 6*R*,7*R* configuration. It occurs in all of our species, and is almost always the most abundant polyacetylene component. The fact that our triol gave a very close optical rotation value suggested to us that it is the same stereoisomer, however, we did not rule out, initially, the possibility of it being the other diastereoisomer (6*R*,7*S* or 6*S*,7*R*). The above authors also postulated the occurrence of the aldehyde **2** in *L. cardinalis.*

We propose the structures **2**–**4** based on the ^{1}H NMR (Table 2), and other spectroscopic data, together with direct comparison of the mutual interconversion products, represented in Scheme 1.

In the transformation of the α-diol into its corresponding epoxide, in both *b* stages the tosylations occurred in a highly regioselective way. The subsequent cyclizations resulted in highly stereospecific products. The reverse reactions were also regioselective, providing the natural product **1**. Moreover, the *cis* configurations of these epoxides were confirmed by their ^{1}H NMR spectra data from the coupling constants measured for H-6 and H-7 ($J = 4.0$ Hz) [4]. Once epoxide cyclization occurs via the intramolecular S_N2 mechanism, resulting in the *cis* relative configuration product, the precursor (triol **1**) is necessarily *threo*. Therefore, we affirm that our triol **1** is the same (6*R*,7*R*) stereoisomer isolated by Thaller *et al.* and consequently the epoxides will possess 6*R*,7*R* configurations.

In the same way we can also affirm that the aldehyde **2** possesses the same configuration of the **1** triol (6*R*,7*R*). The other natural product (**5**) containing the ene-yn-ene chromophore [5], of rare occurrence in plants, possesses a structure analogous to that of triol **1**. The α-diol cleavage, carried out with periodate ($NaIO_4$), resulted in a ene-yn-ene-one fragment, shown by the strong bathochromic shift observed in the UV spectrum, compared with that of the original chromophore. Furthermore, by comparing the ^{1}H NMR spectrum (Table 3) of the corresponding aldehyde **8** with that of the analogue **7** obtained from the triol **1**, we observe a doublet at $\delta 9.63$ ppm ($J = 7.0$ Hz), due to the aldehydic proton neighbouring the alkenic proton, while that of the ene-diyne-one analogue **7**, shows a singlet at $\delta 9.26$ ppm. The corresponding mass spectrum shows $[M]^+$ m/z 120 and $[M]^+$ m/z 118, respectively, for **8** and **7**.

Although other polyacetylenes were detected in *L. exaltata*, *L. fistulosa* and *S. macropodus*, their structures could not be determined due to their low concentration and structural instability. For one of them, however, occurring in *S. sulfureus*, we could postulate structure **6**. Its UV spectrum is superimposable on that of compound **5**, confirming the presence of the ene-yn-ene chromo-

Table 1. Distribution and abundances of polyacetylenes in *Lobelia* and *Siphocampylus* species

	Compounds (mg/kg fr roots)					
Species	**1**	**2**	**3**	**4**	**5**	**6**
Lobelia camporum Pohl	11				5,5	
L. exaltata Pohl*	21	2			4	
L. fistulosa Vell.	94	1,5	3	2,5	13	
L. numularioides Cham	40			125		
L. thapsoidea Schott	28	4			4	
L. langeana Dusen	24	6			9,5	
Siphocampylus sulfureus Winm*	2	3			19	1,5
S. macropodus (Billb.) G. Don*	250	1			6	
S. verticilatus (Cham) G. Don	10	2			5	
S. westinianus (Billb.) Pohl	5				3	

* Others polyacetylenes ene-diynes unidentified.

Table 2. ^{1}H NMR spectral data of compounds **2–5** (100 MHz, TMS int std)

	Compound/δ ppm			
H	**2**	**3**	**4**	**5**
1	9.76 *t*	3.62 *t*	9.73 *s*	3.65 *t*
2	2.4 *m*	1.6 *m*	2.5 *m*	1.6 *m*
3	2.4 *m*	2.20 *dt*	2.5 *m*	2.17 *dt*
4	6.31 *dt*	6.03 *dt*	5.96 *dt*	5.82 *dt*
5	5.54 *dd*	5.38 *dd*	5.39 *ddm*	5.42 *ddm*
6	4.06 *dd*	3.43 *dd*	3.34 *dd*	3.9 *m*
7	4.22 *d*	3.60 *d*	3.50 *d*	3.9 *m*
8	—	—	—	6.05 *dd*
9	—	—	—	5.79 *dd*
12	5.48 *dm*	5.49 *dq*	5.45 *dm*	5.55 *dm*
13	6.30 *dq*	6.34 *dq*	6.30 *dq*	6.15 *dq*
14	1.77 *dd*	1.78 *dd*	1.83 *dd*	1.76 *dd*
OH	2.9 *br*	*	—	*

* Signals not detected. Compounds in parenthesis; J in Hz: $J_{1,2} = J_{2,3} = J_{3,4} \approx 6{,}5$. **2**, $J_{1,2} = 1{,}5$; $J_{14,13} = J_{6,7}$ (**2**) $= 7{,}0$; $J_{14,12} = J_{5,8}$ (**5**) $= 2{,}0$; $J_{6,7}$ (**3** and **4**) $= 4{,}0$; $J_{13,12}$ (**5**) $= 16{,}0$; $J_{5,6}$ (**2** and **5**) $= 6{,}0$; $J_{5,6}$ (rest) $= 8{,}0$.

phore. The terminal aldehyde was suggested by TLC using dinitrophenylhydrazine (DNPH) as detector, besides the fact that the reduction product with sodium borohydride presented a mass spectrum identical that of the triol **5**.

Other ene-diyne and ene-diyne-one chromophores were also detected by UV. Although we cannot be certain that these constituents are not pyranylacetylenes, it seems clear that these species of *Lobelia* and *Siphocampylus* preferentially produce acyclic C_{14} polyacetylenes, whereas other Campanulaceae mainly produce pyranylacetylenes [1], indicating chemotaxonomic differences in spite of the small number of species studied up to now. These data are consistent with the division of the Campanulaceae into the subfamilies Lobelioideae and Campanuloideae and confirm the strong affinities between the genera *Lobelia* and *Simphocampylus*.

EXPERIMENTAL

Polyacetylene extraction. In a typical procedure, fr. roots were cut and percolated with Et_2O at 5° for 10 days (3 successive extractions). The exts were dried (Na_2SO_4) and the solvent evapd in a rotary evaporator in the dark at room temp. The residue* obtained was immediately redissolved in CH_2Cl_2–hexane (1 : 1) and subjected to silica gel CC eluting with 4 successive portions (50–200 ml, depending on the quantity of crude ext) of CH_2Cl_2–hexane (1 : 1), CH_2Cl_2, CH_2Cl_2–Et_2O (1 : 1) and Et_2O. The fractions containing polyacetylenes (generally those most polar) were concd and rechromatographed on Chromatotron (gradient elution CH_2Cl_2–Et_2O, 5 ml/min) providing pure compounds.

Lobelia camporum Pohl. Plants were collected in January 1984 in Poços de Caldas (MG-Brazil). A voucher specimen is deposited in the Herbarium under Shepherd 15865 (UEC). Fr roots (93 g) provided **1** (1 mg) and **5** (0.5 mg).

L. exaltata Pohl. Plants were collected in Campinas (SP) in January 1984. A voucher specimen is deposited in the Herbarium under Shepherd & Vieira 15860 (UEC). Fr roots (1.2 kg) afforded **1** (25 mg) **2** (2.5 mg) and **5** (5.0 mg), besides others highly unstable unidentified-diyne-ene-one polyacetylenes†.

L. fistulosa Vell. Plants were collected in July 1984, in Poços de Caldas. A voucher specimen is deposited in the Herbarium under Shepherd 1586 3 (UEC). From fr. roots (680 g) were isolated **1** (64 mg), **2** (1.0 mg), **3** (2.0 mg), **4** (1.7 mg) and **5** (9.0 mg).

L. langeana Dusen. Plants were collected in January 1985, in Londrina (PR). A voucher specimen is deposited in the Herbarium under Vieira 16811 (UEC). Fr. roots (87 g) afforded **1** (2.0 mg), **2** (0.5 mg) and **5** (0.8 mg).

L. numularioides Cham. Plants were collected in January 1984 in Andradas (MG). A voucher specimen is deposited in the Herbarium under Shepherd & Vieira 16811 (UEC). Whole plants (20 g) were extd with Et_2O in the same way as the roots of other species, providing **1** (0.8 mg) and **5** (2.5 mg).

L. thapsoidea Schott. Plants were collected in February 1984 in Petropolis (RJ).‡ Fr. roots (380 g) provided **1** (10.6 g), **2** (1.5 mg) and **5** (1.5 mg).

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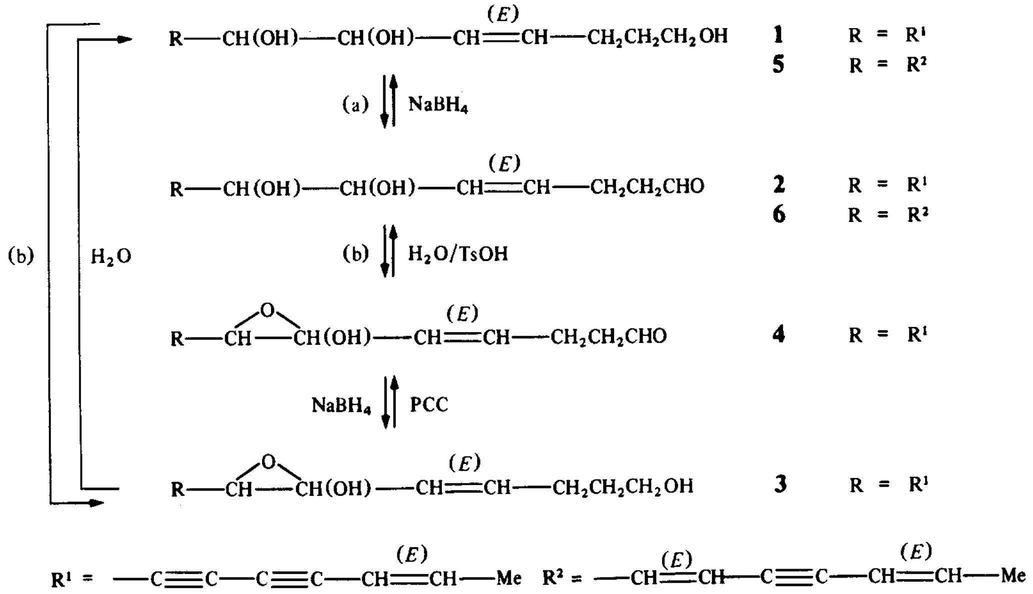
* A large amount of non-polyacetylenic material precipitated.

† Sample of plants collected in January 1985 showed different proportions of polyacetylenic compounds.

‡ Specimen identified by Ana Odete Vieira (University of Londrina, Paraná).



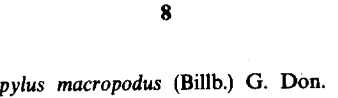
(a) Me_2CO/TsOH, then PCC, then H_3O^+; (b) TsCl, then base

Scheme 1. Mutual interconversions of the polyacetylenes of *Lobelia* and *Siphocampylus* species.

Table 3. ^1HNMR spectral data of compound **7** and **8** (100 MHz)

Proton	7	8[2]
H-1	9.63 *d*	9.26 *s*
H-2	6.44 *dd*	—
H-3	6.76 *dd*	—
H-6	5.76 *ddq*	5.61 *dq*
H-7	6.34 *dq*	6.53 *dq*
H-8	1.91 *dd*	1.86 *dd*

J (Hz): $J_{1,2}=J_{7,8}=7{,}0$; $J_{2,3}=J_{6,7}=16.0$; $J_{3,6}=J_{6,8}=2.0$; compound **8**: $J_{6,8}=1.6$.



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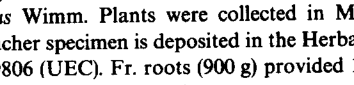

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Simphocampylus macropodus (Billb.) G. Don. Plants were collected in July 1984, in Poços de Caldas. A voucher specimen is deposited in the Herbarium under Shepherd 19808 (UEC). Fr. roots (3.0 kg) afforded **1** (750 mg), **2** (3.0 mg) and **5** (18 mg).

S. sulfureus Wimm. Plants were collected in Monte Verde (MG). A voucher specimen is deposited in the Herbarium under Shepherd 19806 (UEC). Fr. roots (900 g) provided **1** (2.0 mg), **2** (3.0 mg), **5** (17 mg) and **6** (1.5 mg).

S. verticilatus (Cham.) G. Don. Plants were collected in January 1984, in Poços de Caldas. A voucher specimen is deposited in the Herbarium under Shepherd 15864 (UEC). Fr. roots (900 g) provided **1** (9.0 mg), **2** (2.0 mg) and **5** (4.5 mg).

S. westinianus (Billb) Pohl. Plants were collected in January 1984, in Poços de Caldas. A voucher specimen is deposited in the Herbarium under Shepherd 19807 (UEC). Fr. roots (470 g) afforded **1** (2.4 mg) and **5** (1.5 mg).

Conversion of **1** *into* **2**. The triol **1** was transformed into dioxolan [(4*R*,5*R*)-4(hept-5*E*-ene-1,3-diynyl-5-(5-hydroxypent-1-ynyl)-2,2-dimethyl-1,3-dioxolan]; spectral data and procedure described in ref. [2]. The dioxolan (206 mg) was dissolved in CH_2Cl_2 (10 ml) at 0° under N_2 in the dark, and PCC (480 mg) and NaOAc (*ca* 50 mg) added. The reaction was completed in 20 min (assayed by TLC). The crude product after being filtered and chromatographed on Chromatotron afforded the corresponding dioxolan-aldehyde (160 mg, 78% yield). Part (123 mg) was dissolved in THF–H_2O (5 : 1, 3 ml) containing a few crystals of TsOH and left overnight at 25°. The reaction product was extd with Et_2O, dried and purified on Chromatotron, affording the aldehyde **2** (47 mg, 44% yield). Conversion of **5** into **6** was performed in the same way. All reductions (**2** into **1**; **6** into **5**; **4** into **3**) were performed in Et_2O using excess $NaBH_4$. The products were compared with the corresponding natural alcohols by TLC.

Conversion of **1** *into* **3** (*epoxidation*). The triol **1** (86 mg) and TsCl (77 mg) were dissolved in CH_2Cl_2 (2 ml). A drop of satd aq KOH soln was then added with stirring. The reaction was complete in 5 min and the mixt. dil with Et_2O (4 ml). The organic layer was sepd and washed with H_2O. The crude material was purified by prep. TLC affording the epoxide **3** (77 mg, 97% yield). The conversion of **2** into **4** was performed in the same way.

(6R,7R)-*Tetradeca*-4E,12E-*diene*-6,7-*diol*-8,10-*diyneal* (**2**). Very unstable liquid; $[\alpha]_D^{25}+19$ ($CHCl_3$; *c* 0.32); $\lambda_{max}^{Et_2O}$ nm (ε) 283 (8500), 268 (11 200), 254 (8000), 240 (4500), 215 (28 600); $\nu_{max}^{CHCl_3}$ cm^{-1} 3550, 3400, 3000, 2920, 2850, 2730, 2230, 1725, 1385, 1265, 1040, 975, 955; MS *m/z* (rel. int.) 232 ([M]$^+$, 2), 120 (100), 119 (88), 113 (33), 95 (24), 91 (61), 67 (100); ^1HNMR see Table 2.

Tetradeca-4E,12E-*diene*-cis-8,10-*epoxide*-1-*ol* (**3**). Very unstable liquid; $\lambda_{max}^{Et_2O}$ nm (ε) 289 (10 300), 173 (12 570), 258 (10 540), 228 (15 900); $\nu_{max}^{CHCl_3}$ cm^{-1} 3620, 3450, 3000, 2940, 2880, 2230, 1655, 1620, 1440, 1360, 1300, 1230, 1040, 970, 950, 930, 840; MS *m/z* (rel. int.) ([M]$^+$ absent), 119 (3), 117 (2), 115 (5), 102 (100), 89 (4), 85 (18), 59 (44), 76 (26); ^{1}H NMR see Table 2.

Tetradeca-4E,12E-*diene*-cis-8,10-*epoxide*-1-*al* (**4**). Very unstable liquid; $\lambda_{max}^{Et_2O}$ nm (ε): 289.5 (10 300), 273 (12 570), 258 (10 540), 228 (15 900); ^{1}H NMR see Table 2.

Tetradeca-4*E*,8*E*,12*E*-*triene*-10-*yne*-1,6,7-*triol* (**5**). Colourless oil, very unstable, $[\alpha]_D^{CHCl_3}$ +34 (CHCl$_3$; *c* 0.433); $\lambda_{max}^{Et_2O}$ 280 (14 000), 266 (18 100), 253 (14 100), 241 (9150); $\nu_{max}^{CHCl_3}$ cm^{-1}: C≡C not observed), 3500, 3400, 3000, 2940, 1380, 1220, 1050, 975, 960, 720, 670; MS *m/z* (rel. int.): ([M]$^+$ absent), 122 (70), 121 (75), 120 (53), 119 (25), 115 (39), 97 (84), 91 (8), 79 (100), 77 (68), 67 (42).

REFERENCES

1. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973). *Naturally Occurring Acetylenes*, pp. 486 and 503. Academic Press, London.
2. Bentley, R. K., Jones, E. R. H., Ross, R. A. M. and Thaller, V. (1973) *J. Chem. Soc. Perkin Trans. I*, 140.
3. Wimmer, F. G. (1957) *Campanulaceae-Lobelioideae*, in *Das Planzenieich IV*, 276*B*. Academie, Berlin.
4. Bentley, R. K., Higham, C. A., Jenkins, J. K., Jones, E. R. H. and Thaller, V. (1974) *J. Chem. Soc. Perkin Trans. I* 1987 (see also ref. 1 p. 243).
5. Bohlmann, F., Thefeld, W. and Zdero, C. (1970) *Chem. Ber.* **103**, 2245.