Phytochemistry, 1973, Vol. 12, pp. 631 to 632. Pergamon Press. Printed in England.

SESQUITERPENOID LACTONES FROM THE LIVERWORT *FRULLANIA TAMARISCI*

J. D. CONNOLLY and I. M. S. THORNTON
Department of Chemistry, University of Glasgow, Glasgow G12 8QQ

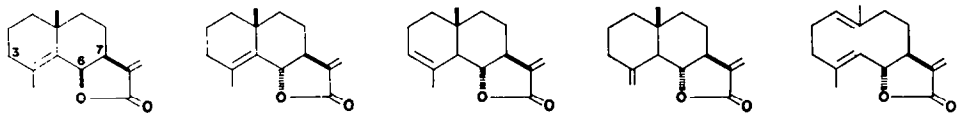
(*Received* 27 *September* 1972. *Accepted* 15 *October* 1972)

Key Word Index—*Frullania tamarisci*; liverwort; sesquiterpenoid lactones; eudesmanolides; costunolide.

Abstract—Four isomeric sesquiterpenoid lactones have been isolated from the liverwort *Frullania tamarisci* They have been identified as the simple eudesmanolides (I–III) and costunolide (IV).

AS PART of a screening programme[1] of liverworts growing in the West of Scotland we investigated the terpenoids of *Frullania tamarisci* (L.)Dum. The major component, the *cis*-lactone* was assigned the structure (I) on the basis of the evidence presented below. In addition three other related isomeric sesquiterpenoids, the *trans*-lactones (II) and (III) and costunolide (IV) were isolated.

The *cis*-lactone (I), $C_{15}H_{20}O_2$, $\nu_{max}^{CCl_4}$ 1770 cm^{-1}, had signals in the NMR at τ 8·93 (tertiary methyl), 8·25 (vinyl methyl), 7·03 (*bm*, H-7), 4·77 (*d*, *J* 5 Hz, H-6) and 4·42, 3·84 (both *d*, *J* 1 Hz, CH_2=). Irradiation at τ 4·77 (H-6) changed the signal at τ 7·03 (H-7) to a broadened triplet (J_{obs} 9 Hz) consistent with the presence of an adjacent methylene group. The reverse experiment caused H-6 to collapse to a broad singlet. The residual broadening of H-6 is due to homoallylic coupling with the vinyl methyl group and this was demonstrated by irradiating H-6 whereupon the intensity of the vinyl methyl signal increased. From the magnitude of this residual coupling the stereochemistry of the lactone ring junction was deduced[4] to be *cis*, as in (I).



(I) (II) (III) (V) (IV)

The second compound, the *trans*-lactone (II) had an NMR spectrum which was very similar to that of (I). The major differences were in the coupling of the exomethylene protons (τ 4·57, 3·87, both *d*, *J* 3Hz) and in the signal for H-6 which appeared as a diffuse doublet at higher field (τ 5·46). Irradiation at this frequency sharpened the vinyl methyl signal at τ 8·16 by the removal of a relatively large homoallylic coupling. This is consistent[4] with the presence of a *trans*-fused lactone as in (II). The *trans*-lactone (II), is in fact, γ-cyclocostunolide.†

* During the course of our work Ourisson reported[2] the isolation of both enantiomeric forms of (I) from *Frullania* species. The results of an investigation of the allergenic activity of these and related sesquiterpenoid lactones has also appeared.[3]

† The same compound has been recently isolated, as arbusculin-*B*, from *Artemesia arbuscula* by Geissman.[5]

[1] I. M. S. THORNTON, Ph.D. Thesis, Glasgow (1971).
[2] H. KNOCHE, G. OURISSON, G. W. PEROLD, J. FOUSSEREAU and J. MALEVILLE, *Science* **166**, 239 (1969).
[3] J. C. MITCHELL, B. FRITIG, B. SINGH and G. H. N. TOWERS, *J. Invest. Derm.* **54**, 233 (1970).
[4] S. STERNHELL, *Pure Appl. Chem.* **14**, 15 (1964).

The two remaining lactones were readily identified from spectroscopic data as α-cyclocostunolide (III) and costunolide (IV). Confirmation of the structures of (II) and (III) was obtained by cyclization[6] of authentic costunolide (from *Saussurea lappa*).[7] This yielded α-cyclocostunolide (III) and γ-cyclocostunolide (II), identical with the natural compounds and, in addition, β-cyclocostunolide (V). No trace of the latter was found in the extract. The isolation, from a natural source, of costunolide and two of its *in vitro* cyclization products is of biogenetic interest. Recently Ourisson has reported[8] the synthesis of γ-cyclocostunolide (arbusculin-*B*).

EXPERIMENTAL

Extraction. Dried *F. tamarisci* was powdered and extracted with $CHCl_3$ in a Soxhlet. The extract was chromatographed over deactivated Spence Grade H alumina and the sesquiterpenoid lactones separated and purified by preparative TLC. The most abundant component, the *cis*-lactone (I) was recrystallised from methanol as needles, m.p. 74–76°, $[\alpha]_D$ −109° (lit.[2] m.p. 77°, $[\alpha]_D$ −113°), *m/e* 232 ($C_{15}H_{20}O$ *m/e* 232). γ-Cyclocostunolide (II) was recrystallized from MeOH as needles, m.p. 86–87°, $[\alpha]_D$ + 27° (lit.[6] m.p. 87–88°, $[\alpha]_D$ + 22°), *m/e* 232. α-Cyclocostunolide (III) was obtained as needles (ex MeOH) m.p. 82–83°, $[\alpha]_D$ +108° (lit.[7] m.p. 83–84°, $[\alpha]_D$ +118°), *m/e* 232, NMR τ 6·16 (*t*, $J_{6,6a}$ 12 Hz, H-6) 4·65 (*bd*, H-3 and one exomethylene proton), 3·97 (*d*, *J* 3 Hz, exomethylene proton). Costunolide, the most polar compound, was crystallized from MeOH as needles m.p. 103–105°, $[\alpha]_D$ + 121° (lit.[7] m.p. 106–107°, $[\alpha]_D$ + 128), *m/e* 232.

Cyclization of Costunolide (IV). Costunolide (200 mg) was allowed to stand in $CHCl_3$ containing redistilled $SOCl_2$(0·1 ml) according to the method of Doskotch *et al.*[6] Removal of solvent left a residue containing three components. Separation by preparative TLC afforded pure samples of α-, β- and γ-cyclocostunolides. The α- and γ-cyclocostunolides were identical (m.p., m.m.p., NMR, TLC, and $[\alpha]_D$) with II and III isolated from *F. tamarisci*.

Acknowledgements—We are grateful to Professors G. Ourisson and G. H. N. Towers for informing us of their results prior to publication.

[5] T. A. GEISSMAN and M. A. IRWIN, *Phytochem.* **8**, 2411 (1969).
[6] R. W. DOSKOTCH and F. S. EL-FERABY, *J. Org. Chem.* **35**, 1928 (1970).
[7] A. S. RAS, G. R. KELKER and S. C. BHATTACHARYYA, *Tetrahedron* **9**, 275 (1960).
[8] A. E. GREEN, J.-C. MULLER and G. OURISSON, *Tetrahedron Letters* 3375 (1972).