

SELECTIVE EXTRACTION OF  $\alpha$ -METHYLENE- $\gamma$ -LACTONES.  
REINVESTIGATION OF *VANILLOSMOPSIS ERYTHROPAPPA*<sup>1</sup>PATRICIA D.D.B. LIMA, MARCOS GARCIA,<sup>2</sup> and JAIME A. RABI\**Núcleo de Pesquisas de Produtos Naturais, Universidade Federal do Rio de Janeiro, Centro de Ciências da Saúde, Bloco H, 21941 Cidade Universitária, Rio de Janeiro, RJ, Brazil*

A frequent structural feature of biologically active sesquiterpenes is the presence of an unsaturated  $\gamma$ -lactone (1). This moiety undergoes facile 1,4-addition of nucleophiles, making it responsible for most if not all of the activities displayed by this group of compounds (1). This electrophilicity is the basis for the selective blocking of the exocyclic conjugated double bond of  $\gamma$ -lactones as exemplified in the synthesis of dehydro-saussurea lactone from the dimethylamine adduct of costunolide (2). Morpholine adducts, on the other hand, were used to facilitate the chromatographic separation of an otherwise difficult-to-purify mixture of lactones (3). Based upon the same reactivity, a nucleophilic polymer was developed for the selective removal of allergenic lactones from natural oils (4). More recently, the use of copper-containing polymeric supports was reported for the selective binding of diethylamine adducts of isovalantolactone and the lactones contained in the oil of *Saussurea lappa* C. (5).

We now wish to report that the acetates of the dimethylamine adducts of  $\alpha,\beta$ -unsaturated- $\gamma$ -lactones are sufficiently stable to allow their quantitative and selective isolation by simple extraction procedures from natural oils. The adducts thus obtained may liberate the lactones by reaction with methyl iodide followed by mild decomposition of the quaternary iodides.

The method, as developed in our lab-

oratory, is exemplified by the isolation of the unsaturated lactones of the previously investigated schistosomicidal oil of *Vanillosmopsis erythropappa* Sch. Bip. (Compositae) (6,7).

## EXPERIMENTAL

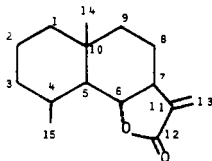
**PLANT MATERIAL.**—The plant material used in this study was collected in January 1981, in Itabira, State of Minas Gerais. A voucher specimen (RB-90739) collected in Diamantina, State of Minas Gerais, is deposited at the Herbarium of the Botanical Garden of Rio de Janeiro.

**EXTRACTION AND ISOLATION.**—Pulverized trunk wood of *V. erythropappa* (20.6 kg) was percolated twice with hexane (39 liters) and then with EtOH (30 liters). Evaporation of the hexane extract gave 289 g of oil. Concentration of the ethanolic extract gave a dark oil which was exhaustively extracted with hexane to give 344 g of oil. Aliquots of each oil (~60 g) were dissolved in EtOAc (100 ml) and dimethylamine added (33% aqueous solution, 20 ml). Tlc of the reaction mixtures (30% EtOAc in hexane) after 1 h showed the appearance of an elongated spot close to the origin. The mixture was diluted with EtOAc (50 ml) and washed with H<sub>2</sub>O (3 × 100 ml). The organic layer was concentrated (100 ml) and glacial HOAc (20 ml) added with continuous stirring. The acetates were extracted into H<sub>2</sub>O (6 × 100 ml), and the aqueous phase washed with EtOAc (6 × 100 ml), neutralized with a saturated solution of Na<sub>2</sub>CO<sub>3</sub>, and then reextracted with EtOAc (6 × 100 ml). The EtOAc extract was dried (MgSO<sub>4</sub>), filtered, and concentrated (~80 ml). Methyl iodide (~10 ml) was added and the mixture allowed to react for 2 h. A saturated solution of Na<sub>2</sub>CO<sub>3</sub> was added (pH~9) and the resulting mixture left at room temperature for 1 h. Then H<sub>2</sub>O (50 ml) was added and the mixture extracted with EtOAc (6 × 100 ml) to give, after drying (MgSO<sub>4</sub>) and evaporation, ~6 g of lactones. Repetition of the procedure with the remainder of the original oils gave a total lactone fraction of 29.7 g from the hexane extract and 53.8 g from the ethanolic extract. These mixtures of lactones were worked up separately by the normal chromatographic procedures to give:  $\alpha$ -cyclocostunolide (1) (8), eremanthin (2) (9), 4,15- $\alpha$ -epoxieremanthin (3) (10), 9,10- $\alpha$ -

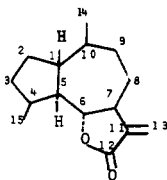
<sup>1</sup>Taken, in part, from the M.S. thesis of Patricia D.D.B. Lima, NPPN-UFRJ, 1983.

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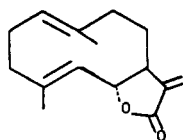
epoxieranthin (**4**) (11), dehydrocostuslactone (**5**) (11), costunolide (**6**) (12), reynosin (**7**) (13), santamarin (**8**) (14), magnolialide (**9**) (15), arbusculin A (**10**) (16), 4-*epi*-arbusculin A (**11**) (17), trifloculoside (**12**, H-1 $\alpha^3$ ) (18), estafiatone (**13**) (19), and eregogazin (**14**) (20) which showed physical properties in complete agreement with those reported.



- 1**  $\Delta^{3,4}$   
**7**  $\Delta^{3,4}$ -1- $\beta$ -OH  
**8**  $\Delta^{4,15}$ -1- $\beta$ -OH  
**9**  $\Delta^{4,5}$ -1- $\beta$ -OH  
**10** 4- $\alpha$ -OH  
**11** 4- $\beta$ -OH



- 2**  $\Delta^{4,15,9,10}$   
**3**  $\Delta^{9,10}$ -4,15- $\alpha$ -epoxy  
**4**  $\Delta^{4,15}$ -9,10- $\alpha$ -epoxy  
**5**  $\Delta^{4,15,10,14}$   
**12**  $\Delta^{4,15}$ -10- $\alpha$ -OH  
**13**  $\Delta^{10,14}$ -3-oxo-4- $\alpha$ -Me  
**14**  $\Delta^{9,10}$ -3-oxo-4- $\alpha$ -Me



**6**

## DISCUSSION

It is relevant to note that the conditions of the isolation procedure were first tested using previously isolated **2** and **6** which are, as reported (6, 7), the most

abundant lactones of the oil. Both compounds were reisolated in 95% yield. No other components were detected. This result is relevant since **6** is known to undergo acid catalyzed cyclizations (21) and could therefore be the source of some of the eudesmanolides isolated. Further, compounds **3**, **4**, **10**, **11**, and **12** were found to be stable under the conditions of the isolation procedure.

Although the epoxides **3** and **4** had already been obtained in our laboratory from the reaction of **2** with *m*-chloroperbenzoic acid (9, 10), this is their first isolation from a natural source.

The significance of the selective method of extraction of  $\alpha$ -methylene- $\gamma$ -lactones as reported here may be assessed by considering previous studies of the oil of *V. erythropappa*, which led to the isolation of only **2** (6, 7) and **6** (6). Thus, the use of sesquiterpene lactones as markers in biochemical systematic studies as well as the search for new alkylating agents should be greatly facilitated.

## ACKNOWLEDGMENTS

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<sup>3</sup>The stereochemistry at C-1 is not correct as reported by Bohlmann and Zdero (18) according to a personal communication by F. Bohlmann. Comparison of the  $^1\text{H}$ -nmr spectrum of compound **12** with that isolated from *Vernonia trifloculosa* suggested their identity.

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