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NOVEL CYCLIZATION OF *trans*-1,2-DIVINYLCYCLOHEXANE-3,4-*trans*-γ-LACTONE UNIT

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Costunolide (I) displays anomalous ultraviolet absorption (λ_{max} 214.5 nm, ε11841)[*] which has been attributed to the transannular interaction of the double bonds in the medium ring[1,2]. Since the oxidative cyclization of an olefinic system is largely dependent upon its steric and conformational characteristics[3], the unique conformation[4] of the substrate (I) favours facile cyclization. When treated with N-bromosuccinimide (NBS) in aqueous acetone, costunolide (I) furnished the bromohydrin (II) and the bromolactones (III, IV) in 50, 18 and 23% yields, respectively[**].

In contrast, the olefinic substrates[5] (V, VI) differ from (I) in having freedom of rotation about the bonds carrying olefinic linkages. Despite this, the interaction of the double bonds in V (λ_{max} 211.5 nm, ε8630), as well as in VI (λ_{max} 209 nm, ε741), indicates the strong possibility of cyclization in these molecules, and the present communication deals with this aspect.

Treatment of dehydrosaussurea lactone (V) with NBS in aqueous acetone at room temperature gave a solid reaction mixture showing three distinct spots on TLC plates in several solvent systems. Column chromatography over silica gel gave the bromohydrin (II) and the bromolactones (III, IV) in 43, 15 and 15% yields, respectively[***]. The bromohydrin

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[*] Ultraviolet spectra were recorded in ethanol on Unicam Spectrophotometers, models SP.700 and SP.800.

[**] Briefly reported by T.C.J. in connection with another paper presented at the 158th National Meeting of the American Chemical Society, New York (see reference 8).

[***] All reported yields refer to the weights of the crystalline lactones isolated.

(II) [m.p. 186-188°, $[\alpha]_D^{25}$ + 12.7°* (c, 1.01); ν_{max}^{KBr}: 3535 cm^{-1} (hydroxyl), 1764, 1670 and 888 cm^{-1} (α,β-unsaturated γ-lactone); λ_{max} 206 nm, ε14800] analyzed for $C_{15}H_{21}O_3Br$; further confirmed by the high resolution mass spectrum, which displayed a significant peak due to M-CH_3 ($C_{14}H_{18}O_3{}^{79}Br$: observed mass 313.0437, calculated mass 313.0439). The N.M.R. spectrum in $CDCl_3$ exhibited two sharp three-proton singlets at 8.62 τ and 8.88 τ due to C-4 and C-10 methyls, respectively.** Additionally, the lone protons at C-1 and C-6 appeared as a multiplet centered at 5.90 τ, while the characteristic sets of doublets in the downfield region at 3.85 τ (1H, J=3.0 Hz) and 4.50 τ (1H, J=3.0 Hz) were ascribed to the >C=CH_2 unit in the lactone ring[6].

The bromolactone (III) [m.p. 116-118°, $[\alpha]_D^{25}$ + 49.9° (c, 1.12); λ_{max} 206 nm, ε17800; ν_{max}^{KBr}: 1765, 1679, 1624, 882, 844 and 810 cm^{-1} (α,β-unsaturated γ-lactone and a trisubstituted double bond)] analyzed for $C_{15}H_{19}O_2Br$, this being supported by high resolution mass measurement ($C_{15}H_{19}O_2{}^{79}Br$: observed mass 310.0563, calculated mass 310.0568, molecular ion). The *exo*-isomer, $C_{15}H_{19}O_2Br$, (IV) [m.p. 137-138°, $[\alpha]_D^{25}$ + 106.2° (c, 0.97); λ_{max} 206 nm, ε18400; ν_{max}^{KBr}: 1771 cm^{-1} (γ-lactone), 1673, 1650 and 920 cm^{-1} (exocyclic methylene)] displayed in its N.M.R. spectrum a set of broadened resonances at 4.97 and 5.09 τ (2H) due to exocyclic methylene at C-4, whereas the N.M.R. spectrum of the *endo*-isomer (III), in contrast, showed a broad band at 4.71 τ (1H) and a poorly split signal at 8.16 τ due to a trisubstituted double bond carrying a methyl group at C-4.

The bromolactones (II, III, and IV) were identical in all respects (mixed m.p., U.V., I.R., N.M.R. and mass spectra) with the corresponding compounds produced by NBS-induced oxidative carbocyclization of costunolide (I). Further evidence in favour of the stereostructures of II, III and IV was provided by their catalytic hydrogenation (ethanol-PtO_2) to VII, VIII and IX, respectively, which in turn have been rigorously tied up with molecules of well established stereochemistry[7,8].

In short, this chemical correlation confirms the predicted course of cyclization

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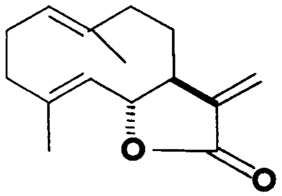
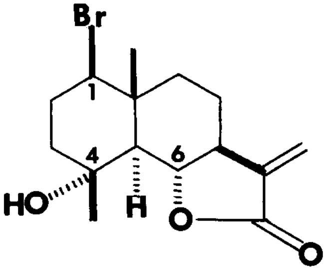
* Unless otherwise stated, specific rotations were determined in $CHCl_3$ solution on a Perkin Elmer model 141 polarimeter.

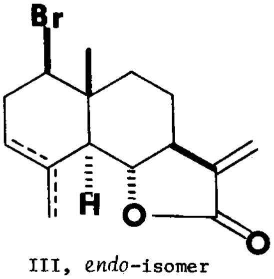
** N.M.R. spectra were obtained with a Varian Associates HA-60 spectrometer using TMS as internal standard.



I

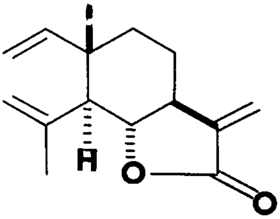


II

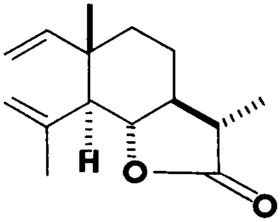


III, *endo*-isomer

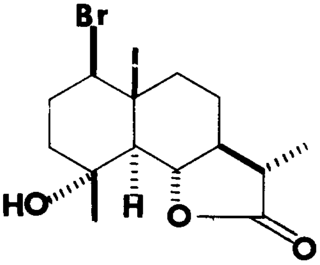
IV, *exo*-isomer



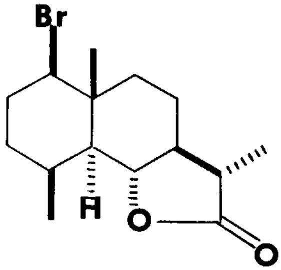
V



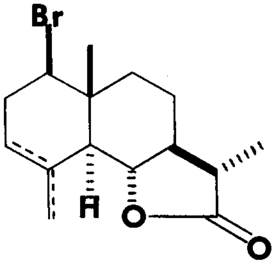
VI



VII

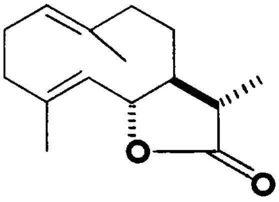


VIII



IX, *exo*-isomer

X, *endo*-isomer



XI

of dehydrosaussurea lactone (V), which now represents a new and especially mild means of cyclizing a *trans*-1,2-divinylcyclohexane-3,4-*trans*-γ-lactone - a system commonly encountered in the chemistry of germacranolides[9]. To the best of our knowledge, neither naturally occurring, nor synthetic, sesquiterpene lactones based on the elemane framework have hitherto been converted to bicyclic sesquiterpene lactones*. This present reaction now affords mild means for effecting such a carbocyclization.

The reaction was further tested on the naturally occurring sesquiterpene lactone (VI) which, under identical conditions, yielded VII, IX and X in 48.2, 21.7 and 15.3% yields, respectively**.

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REFERENCES

1. For quantum chemical study of transannular interaction, see J. Paldus and J. Koutecký, Coll. Czech. Chem. Commun., **27**, 2139 (1962).
2. R. V. H. Jones and M. D. Sutherland, Aust. J. Chem., **21**, 2255 (1968).
3. E. E. van Tamelen, Accounts Chem. Res., **1**, 111 (1968) and references cited therein.
4. For conformation of ten-membered ring sesquiterpenes (a) by X-ray crystallography, see R. J. McClure, G. A. Sim, P. Coggon and A. T. McPhail, Chem. Commun., 128 (1970); (b) by Nuclear Overhauser Effects, see N. S. Bhacca and N. H. Fischer, *ibid.*, 68 (1969).
5. T. C. Jain, C. M. Banks and J. E. McCloskey, Tetrahedron Letters, 841 (1970) and references cited therein.
6. T. C. Jain and J. E. McCloskey, Tetrahedron Letters, 2917 (1969).
7. T. C. Jain, C. M. Banks and J. E. McCloskey, Experientia, **25**, 906 (1969).
8. T. C. Jain, C. M. Banks and J. E. McCloskey, Abstracts of Papers, AGFD-49, 158th National Meeting, American Chemical Society, New York, September 7-12, 1969.
9. F. Šorm and L. Dolejs, "Guaianolides and Germacranolides", Hermann, Paris (1965).
10. A. S. Rao, A. Paul, Sadgopal and S. C. Bhattacharyya, Tetrahedron, **13**, 319 (1961).

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* In light of our recent work[5] on the reversibility in the germacranolide-Cope reaction, an earlier report[10] on acid catalyzed cyclization of saussurea lactone (VI) at elevated temperature would presumably involve the substrate (XI).

** Full details of this reaction on substrates (V) and (VI) will be reported in due course.