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THE STEREOCHEMISTRY OF GERMACRANOLIDE SESQUITERPENES

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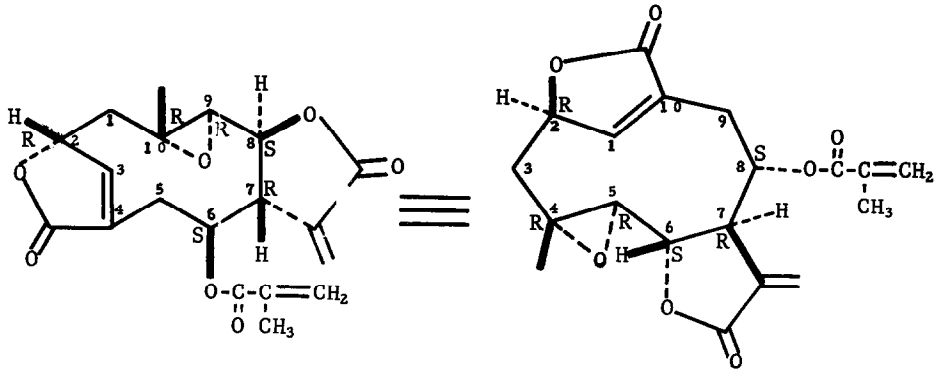
All non-germacranolide sesquiterpene lactones with rigorously established absolute configurations appear to have C-7β-oriented substituents (1-11). In contrast, germacranolides of rigorously established configurations have been represented with C-7 substituents oriented either α or β.

We note here that the presently-used convention for describing germacranolides is not unambiguous, because of the symmetry of the germacranolide carbon skeleton about the C-2, C-7 axis. Consequently, each germacranolide may be represented by two configurationally equivalent structural formulae. Furthermore, those germacranolides which have heretofore been represented as bearing C-7α-substituents may be equally well portrayed by equivalent formulae with C-7β-substituents, and therefore fit the proposed biogenetic generalization that all sesquiterpenes bear C-7β-substituents (9).

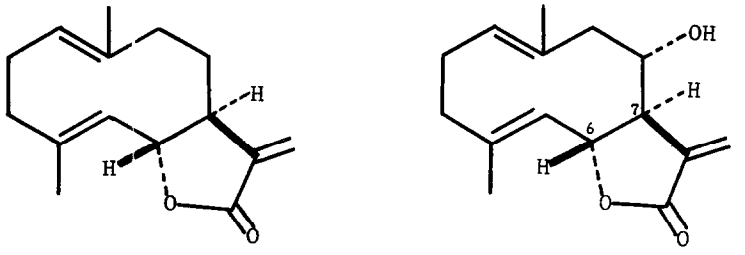
A convention is advanced to define a unique and consistent representation for germacranolide sesquiterpenes; namely, that each germacranolide be represented with C-7 in the lower right corner and bearing a β-substituent. The convention thus defines (a) the face of the molecule which is under observation and (b) a unique and consistent numbering system for the carbon skeleton.

A Dreiding model of elephantopin (Ia, 12) was rotated 180° about the C-2,C-7 axis and rotomer Ib, bearing a C-7β-substituent was obtained. The proposed convention defines structure and numbering Ib as the preferred representation of elephantopin. The absolute configuration at each asymmetric center is indicated (13).

Costunolide (II, 14) and balchanolide (III, 4,15) have well-established absolute configurations. By a series of reactions involving epimerization at C-7, balchanolide (III) and eupatoriopicrin (IVa, 4,16) were correlated (via tetrahydroacetylbalchanolide (VII)), and eupatoriopicrin has been designated as bearing a C-7α-substituent (cf. IVa). However, it is proposed that, under the new convention, eupatoriopicrin's structure should be represented by the equivalent formula, IVb. Although epimerization at C-7 was possible in the interrelation of III and IV, both compounds bear C-7β-substituents. Balchanolide (III) is a 6,7-lactone, whereas eupatoriopicrin (IVb) is a 7,8-lactone.

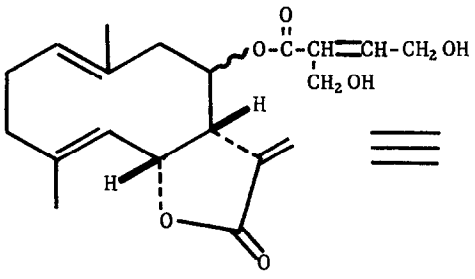


Ia Ib

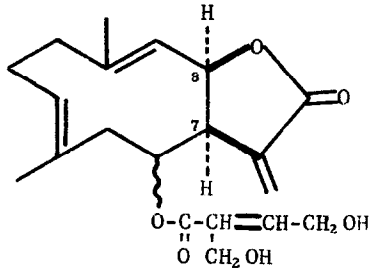


II III

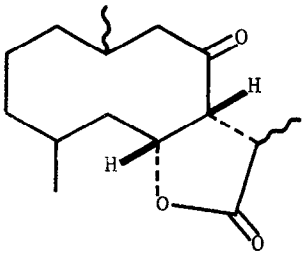
Germacranolides of established configuration may, indeed, be regarded as conforming to the noteworthy biogenetic correlation that C-7 substituents in sesquiterpenes have a common absolute β-configuration (9b). If there is a common biogenetic origin for the guaianolides, santanolides, and germacranolides (cf. 9), then the numbering convention suggested here probably correctly identifies those carbons in the 10-membered ring compounds which become C-4 and C-10, respectively, in the guaianolides and santanolides. No detailed biosynthetic information is yet available to test the hypothesis that the carbon atom designated as C-10 by this convention arises in all these compounds from a unique position in a farnesol-like precursor.



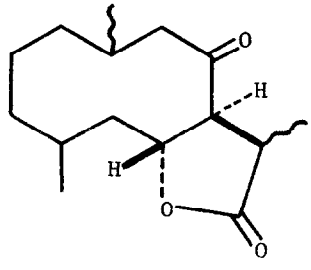
IVa



IVb

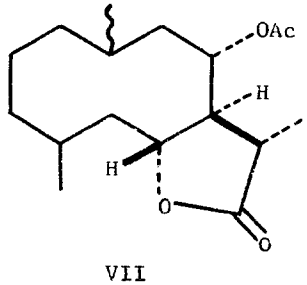


V



VI

III



VII

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