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SESQUITERPENE LACTONES IN CHEMOTAXONOMY

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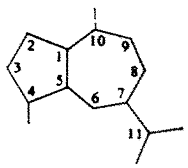
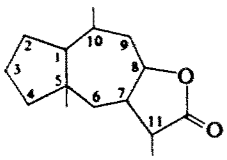
Abstract—The utilization of guaianolides in chemotaxonomy is discussed, and some biosynthetic considerations are advanced.

THE guaianolides, a class of sesquiterpene lactones with the guaiane skeleton (I) appear to possess potential application in the chemotaxonomy of higher plants.[1] In the course of an investigation of these compounds in the *Artemisia* species, we compiled a list of known guaianolides from several genera of the Compositae family† and noted taxonomically significant differences. Some of these findings are presented here.

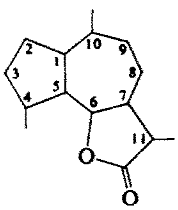
In Table 1 are listed 42 lactones, of which the first 27 are produced by the genera *Gaillardia* and *Helenium* and the last 15 by the genera *Achillea*, *Artemisia* and *Matricaria*. It is apparent that the former group all possess skeleton II (often designated as the pseudoguaianolide skeleton) with rearranged methyl group‡ and the lactone ring closed to C-8. In addition, there is rarely a functional group at C-10, whereas C-11 is unsaturated in about two-thirds of the compounds. Thus far, no guaianolide from either *Gaillardia* or *Helenium* has been reported to possess both a functional group at C-10 and a saturated C-11.



(I)



(II)



(III)

On the other hand, all guaianolides from the genera *Achillea*, *Artemisia* and *Matricaria* possess skeleton III with no rearranged methyl group and the lactone ring closed to C-6. In all but one compound (arbiglovin), a functional group is present at C-10. Only two compounds (arbiglovin and estafiatin) are unsaturated at C-11.

The Compositae family has been divided into thirteen tribes.[3] The genera *Gaillardia* and

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† All but one of the guaianolides reported have been isolated from Compositae species. Recently Šorm and his coworkers have found a new guaianolide in an Umbelliferae species.[2]

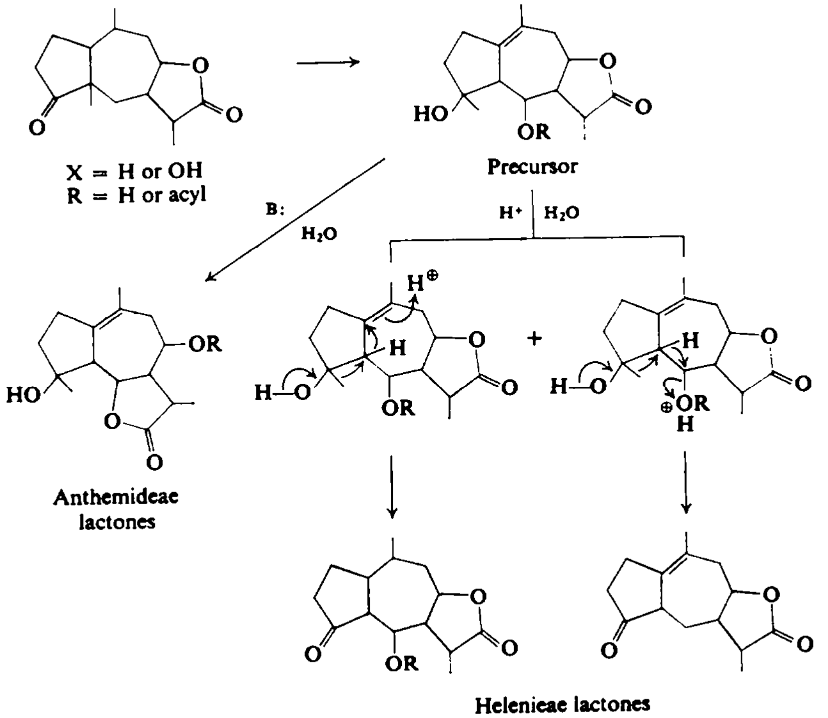
‡ Mexicanin E and its dihydro derivative have lost this methyl group entirely.

[1] See (*a*) H. ERDTMAN, *Chemistry of Natural Products* (International Symposium, Prague, 1962). Butterworths, London (1963) and (*b*) R. HEGNAUER, *Chemotaxonomie der Pflanzen*, Volume III, Birkhäuser Verlag, Basel (1964).

[2] M. HOLUB, D. P. POPA, V. HEROUT and F. ŠORM, *Collection Czech. Chem. Commun.* **29**, 938 (1964).

[3] N. A. SORENSEN, *Chemistry of Natural Products* (International Symposium, Australia, 1960), p. 569. Butterworths, London (1961).

Helenium belong to the Helenieae tribe; *Achillea, Artemisia* and *Matricaria* are in the Anthemideae tribe. Thus, the above chemical features may be characteristic of the two tribes rather than just the above-mentioned genera. If this is true, as these results suggest, the two classes of sesquiterpene lactones might originate from a precursor common to both tribes. The divergence from the precursor should be explicable on the basis of one or two simple gene-controlled steps. One possible mechanism is shown in scheme I.

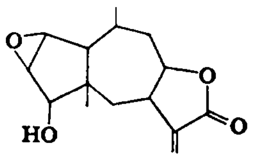


SCHEME I. Possible biosynthetic routes to guaianolides from a common precursor.

The critical step for the Anthemideae lactones is a transesterification of the precursor, catalyzed by a nucleophile (B); for the Helenieae lactones, an acid-catalyzed rearrangement is proposed. Oxidation levels of the compounds are generally the same for all genera in these two tribes and are apparently not taxonomically significant.

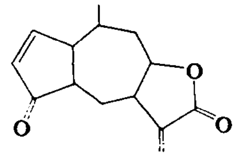
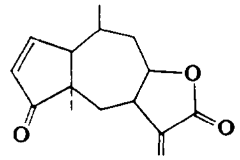
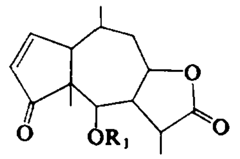
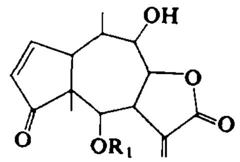
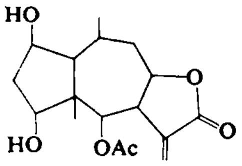
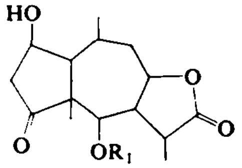
Such a mechanism is purely speculative, but it may provide a basis for future experiments and search for precursors such as depicted above.

TABLE 1. GUAIANOLIDES FROM *Helenieae* AND *Anthemideae* TRIBES

Name	Structure	Genera	Reference
Amarilin		*Helenium*	4

[4] R. A. LUCAS, S. ROVINSKI, R. J. KIESEL, L. DORFMAN, and H. B. MACPHILLAMY, *J. Org. Chem.* **29**, 1549 (1964).

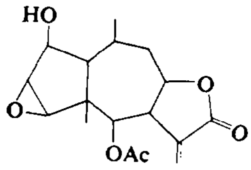
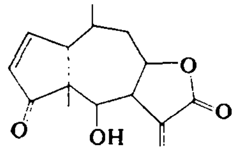
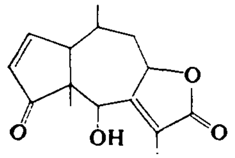
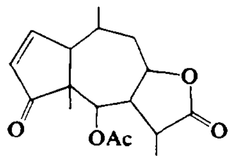
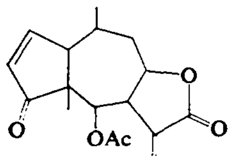
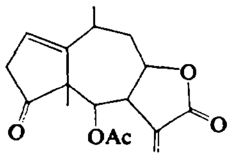
TABLE 1.—*continued*

Name	Structure	Genera	Reference
Aromaticin,* Aromatin		*Helenium*	5
Dihydro mexicanin E		*Helenium*	6
Fastigilin A,* Fastigilin B		*Gaillardia*	7
Fastigilin C†		*Gaillardia*	7
Flexuosin A		*Helenium*	8
Flexuosin B†		*Helenium*	8

* These two compounds possess the same formula but are stereoisomers.
† R_1 = —COCH=C(CH$_3$)$_2$

[5] J. ROMO, P. JOSEPH-NATHAN, and F. DIAZ, *Chem. & Ind.* (*London*) 1839 (1963).
[6] R. A. LUCAS, R. G. SMITH, and L. DORFMAN, *J. Org. Chem.* **29**, 2101 (1964).
[7] W. HERZ, Personal communication.
[8] W. HERZ, Y. KISHIDA, and M. V. LAKSHINIKANTHAN, *Tetrahedron* **20**, 969 (1964).

TABLE 1.—*continued*

Name	Structure	Genera	Reference
Gaillardilin		*Gaillardia*	7
Helenalin,* Mexicanin I		*Helenium*,§ *Gaillardia*	9, 10
Isohelenalin		*Helenium*	9
Isotenulin		*Helenium*	11
Linifolin A		*Helenium*	12
Linifolin B		*Helenium*	12

§ Helenalin has also been found in *Balduina* and *Leptopoda*; tenulin has been found in *Leptopoda*.

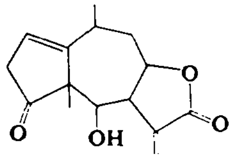
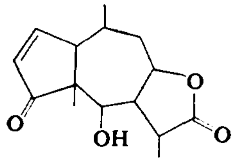
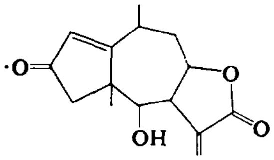
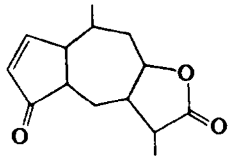
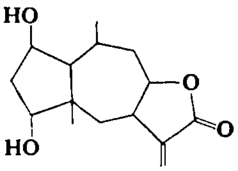
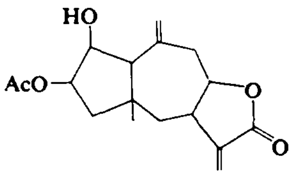
9 W. HERZ, A. R. DE VIVAR, J. ROMO, and N. VISWANATHAN, *J. Am. Chem. Soc.* **85**, 19 (1963).

10 E. DOMINGUEZ and J. ROMO, *Tetrahedron* **19**, 1415 (1963).

11 W. HERZ, W. A. ROHDE, K. RABINDRAN, P. JAYARAMAN, and N. VISWANATHAN, *J. Am. Chem. Soc.* **84**, 3857 (1962).

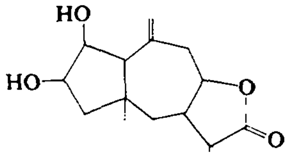
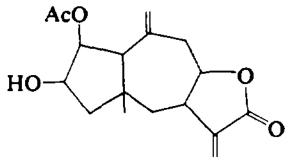
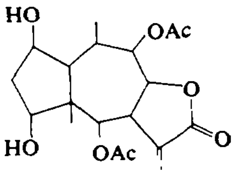
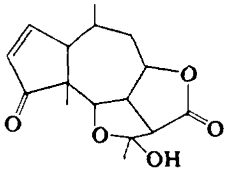
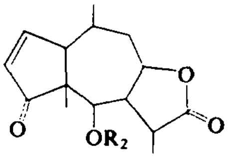
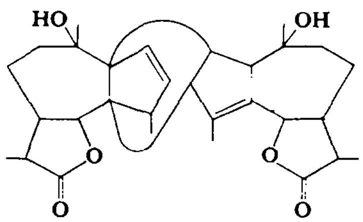
12 W. HERZ, *J. Org. Chem.* **27**, 4043 (1962).

TABLE 1.—*continued*

Name	Structure	Genera	Reference
Mexicanin A		*Helenium*	9
Mexicanin C		*Helenium*	13
Mexicanin D		*Helenium*	9
Mexicanin E		*Helenium*	14
Pulchellin		*Gaillardia*	15
Pulchellin B		*Gaillardia*	16

[13] W. HERZ, A. R. DE VIVAR, J. ROMO, and N. VISWANATHAN, *Tetrahedron* **19**, 1359 (1963).
[14] J. ROMO, A. R. DE VIVAR, and W. HERZ, *Tetrahedron* **19**, 2318 (1963).
[15] W. HERZ, K. UEDA, and S. INAYAMA, *Tetrahedron* **19**, 483 (1963).
[16] W. HERZ and S. INAYAMA, *Tetrahedron* **20**, 3461 (1964).

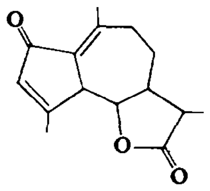
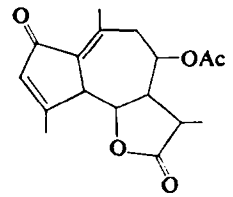
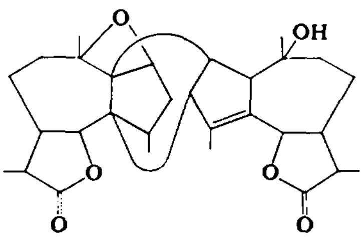
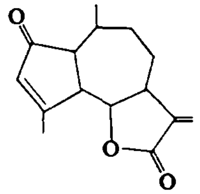
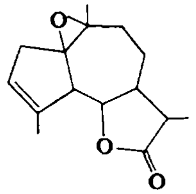
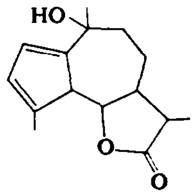
TABLE 1.—*continued*

Name	Structure	Genera	Reference
Pulchellin C		*Gaillardia*	16
Pulchellin E		*Gaillardia*	7
Spathulin		*Gaillardia*	7
Tenulin		*Helenium*§	11
Thurberilin‡		*Helenium*	7
Absinthin		*Artemisia*	17

‡ $R_2 = -COC(CH_3){=}CH-CH_3$

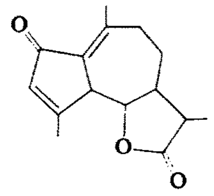
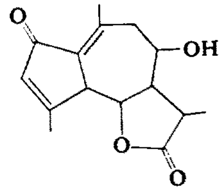
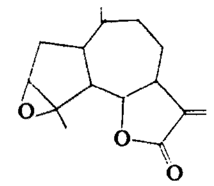
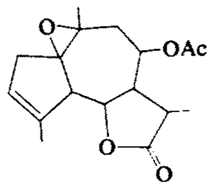
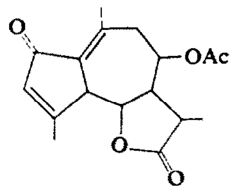
[17] L. NOVOTNÝ, V. HEROUT, and F. ŠORM, *Collection Czech. Chem. Commun.*, **25**, 1492 (1960).

TABLE 1.—*continued*

Name	Structure	Genera	Reference
Achillin		*Achillea*	18
Acetoxyachillin		*Achillea*	18
Anabsinthin		*Artemisia*	17
Arbiglovin		*Artemisia*	7
Arborescin		*Artemisia*, *Matricaria*	19
Artabsin		*Artemisia*	20

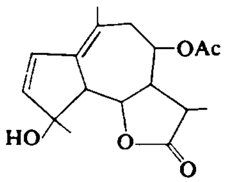
[18] E. H. WHITE and R. E. K. WINTER, *Tetrahedron Letters* **17**, 137 (1963).
[19] R. B. BATES, Z. ČEKAN, V. PROCHÁZKA, and V. HEROUT, *Tetrahedron Letters* **17**, 1127 (1963).
[20] M. SUCHÝ, V. HEROUT, and F. ŠORM, *Collection Czech. Chem. Commun.* **29**, 1829 (1964).

TABLE 1.—*continued*

Name	Structure	Genera	Reference
Desacetoxy-matricarin* Leucomysin		*Artemisia*	21, 22
Desacetyl-matricarin* Hydroxyachillin		*Achillea, Artemisia*	23, 18
Estafiatin		*Artemisia*	24
Globicin		*Matricaria*	25
Matricarin		*Achillea, Artemisia, Matricaria*	23

[21] M. HOLUB and V. HEROUT, *Collection Czech. Chem. Commun.* **27**, 2980 (1962).
[22] K. S. RYBALKO, *Z. Obshchei Khim.* **33**, 2734 (1963).
[23] W. HERZ and K. UEDA, *J. Am. Chem. Soc.* **83**, 1139 (1961).
[24] F. SÁNCHEZ-VIESCA and J. ROMO, *Tetrahedron* **19**, 1285 (1963).
[25] V. PROCHÁZKA, Z. ČEKAN, and R. B. BATES, *Collection Czech. Chem. Commun.* **28**, 1202 (1963).

TABLE 1.—*continued*

Name	Structure	Genera	Reference
Matricin		*Artemisia*, *Matricaria*	26, 27

Acknowledgement—We are indebted to Professor Robert Bates of this Department for his valuable comments and suggestions.

[26] Z. ČEKAN, V. HEROUT, and F. ŠORM, *Chem. & Ind.* (*London*) 1234 (1956).
[27] C. STEELINK and J. C. SPITZER, unpublished results. See also C. STEELINK and E. PENUNURI, *J. Pharm. Sci.* **51**, 598 (1962).