RECENT STUDIES ON SESQUITERPENES

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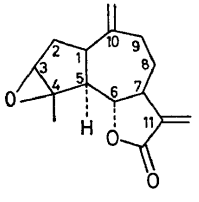
ABSTRACT

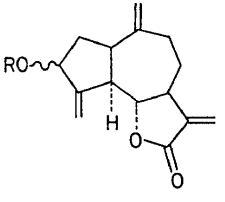
The structure of several guaianolides have been recently determined in our laboratory. The configuration of the asymmetric centres at C-5, C-6 and C-7 of estafiatin (I), zaluzanins C and D (IIa and IIb), ligustrin (III), cumambrins A and B (IVa and IVb) and bahías I and II (VIIIa and VIIIb) have been established by correlation between them and with a derivative of isophoto-α-santonic lactone. Two sesquiterpene lactones found as constituents of *Artemisia klotzchiana* were identified as matricarin (XIIb) and desacetylmatricarin (XIIa). A new guaianolide named chrysartemin was isolated from the same source. The structure XIII was proposed for this lactone 2. The known eudesmanolides arglanin (XVIII) and douglanin (XIX) were isolated from *A. mexicana* 3. A recent study of several species in the genus *Helenium, Ambrosia, Franseria* and *Hymenoxis* led to the isolation of several sesquiterpene lactones. The structure of franserin (XXX), confertin (XXXI), odoratin (XXXII) and canambrin was established 4. A transformation of a furoeremophylane into a furonaphtalene derivative is described.

INTRODUCTION

This paper is concerned with a description of our recent studies on terpenoids isolated from Compositae. Earlier work in our laboratory led to the isolation and structure elucidation of several guaianolides found as



(I)



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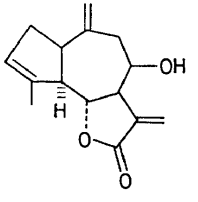
b, R=Ac



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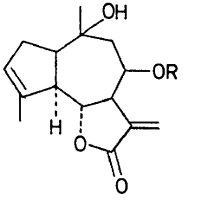

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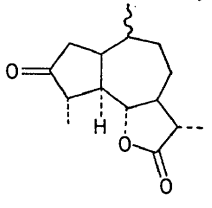

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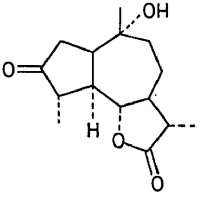

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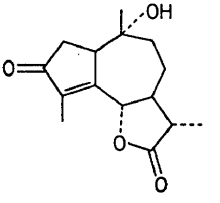
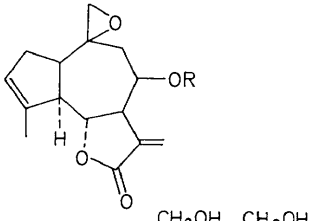


(VII)

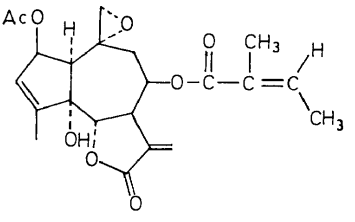
constituents of the genus *Artemisia*, *Zaluzania*, *Eupatorium* and *Ambrosia*. These lactones are estafiatin (I)[1], zaluzanins C and D (IIa and IIb)[2], ligustrin (III)[3] and cumambrins A and B (IVa and IVb).[4] Their stereochemistry at C-5, C-6 and C-7 was established by correlation with the ketone (V)[5], a derivative of isophotosantonic lactone (VII)[5,6], of known configuration at the C-5, C-6 and C-11 asymmetric centres.

The guaianolides bahía I (VIIIa) and bahía II (VIIIb) recently isolated from *Bahia pringlei*[7] contain the espiroepoxide grouping like euparotin acetate (IX)[8]. The stereochemistry at C-5, C-6 and C-7 in both guaianolides were deduced from their correlation with ligustrin (III)[3].

The zaluzanins A and B (Xa and Xb)[9] are triciclic guaianolides containing a six membered lactone easily isomerized to the five membered lactone compounds (XI). The latter are found also in nature[10].



(VIII) a, R=H
b, R=O=C–C=C(CH2OH)(CH2OH)–C(H)



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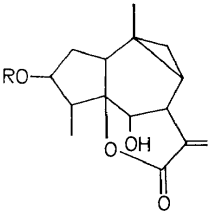
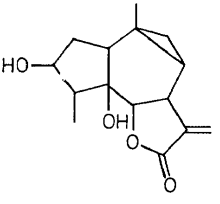
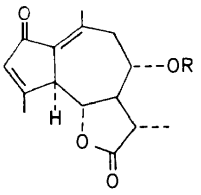


(X) a, R=H
b, R=Ac

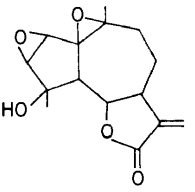


(XI)

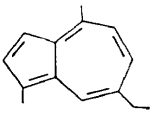
The chemical study of *Artemisia klotzchiana* led to the isolation of three guaianolides. Two of them were identified as matricarin (XIIb)[11,12] and desacetylmatricarin (XIIb)[12]. Both lactones have been recently synthesized starting from isophotosantonic lactone (VII)[13] and their stereochemistry at C-5, C-6, C-7 and C-11 has been established[13]. A third lactone ($C_{15}H_{18}O_5$) named chrysartemin was found as a constituent of *Artemisia klotzchiana*[14]. This lactone (XIII) is a guaianolide which yielded chamazulene (XIV) by aromatization in the presence of palladium on charcoal. Hydrogenation of chrysartemin (XIII) afforded a dihydroderivative (XV). Chemical and spectral data indicates that chrysartemin possess structure (XIII). Chysartemin (XIII) contains two epoxide functions. The epoxide function attached at the secondary carbon atoms adds selectively the elements of *p*-toluene sulphonic



(XII) a, R = H
b, R = Ac



(XIII)



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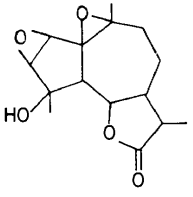

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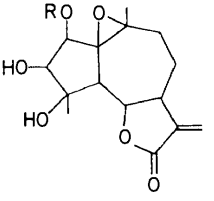
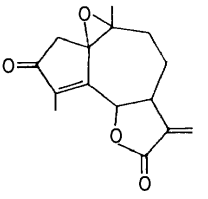


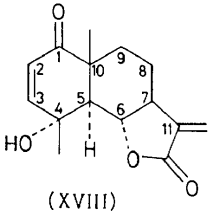
(XVI) R = $CH_3-C_6H_5-SO_2$



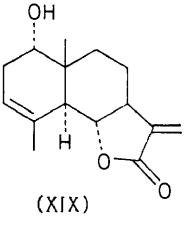
(XVII)

acid. Treatment of the resulting *p*-toluene sulphonate (XVI) with formic acid produced a pinacolic rearrangement with simultaneous dehydration of the tertiary hydroxyl group yielding an α,β-unsaturated cyclopentanone ($C_{15}H_{16}O_4$). The spectral data of this ketone are in accord with structure (XVII).

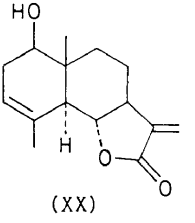
In the previous examination of *Artemisia mexicana* we isolated the guaianolide estafiatin (I)[1]. In a recent study of a collection of the same species we found as a minor constituent chrysartemin (XIII)[14] and in relative large amounts the known eudesmanolides arglanin (XVIII)[15] and douglanin



(XVIII)



(XIX)



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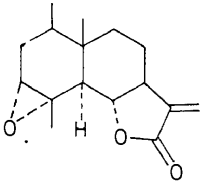
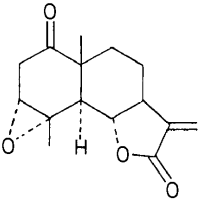
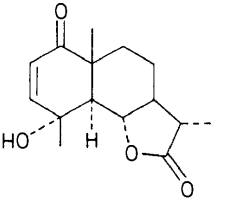


(XXI)



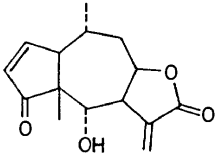
(XXII)



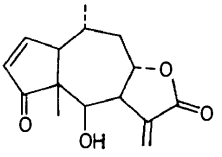
(XXIII)

(XIX)[16]. Santamarin (XX), a santanolide isolated from *Chrysanthemum parthenium*[17], differing from douglanin (XIX) in the configuration of the hydroxyl group was correlated with arglanin (XVIII)[14]. Chromium trioxide oxidation of the epoxide of santamarin (XX)[17] gave the ketoepoxide (XXII). Treatment of the latter with pyridine and *p*-toluene sulphonic acid afforded arglanin (XVIII). The stereochemistry of arglanin was previously established by correlation with vulgarin (tauremisin) (XXIII)[18,19].

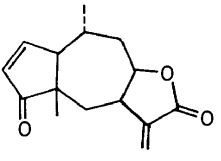
In connection with our investigation in the genus *Helenium* we recently examined two collections of *Helenium quadridentatum*.[20] Helenalin (XXIV), mexicanin I (XXV) and aromatin (XXVI) were found as constituents in



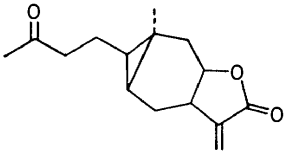
(XXIV)



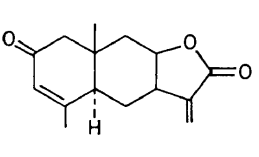
(XXV)



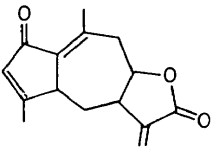
(XXVI)



(XXVII)



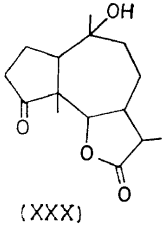
(XXVIII)



(XXIX)

one of them. From the other one we isolated helenalin (XXIV) and carabrone (XXVII)[21]. The finding of the latter as constituent in a species of the genus *Helenium* is unusual since pseudoguaianolides are the typical constituents of that genus. Previously, the eudesmanolide, pinnatifidin (XXVIII)[22] and the guaianolide, virginolide (XXIX)[23] were isolated from the genus *Helenium*.

In a study of several *Ambrosia* and *Franseria* species we have isolated several sesquiterpenes whose structures were established. Cumambrins A and B (IVa and IVb),[4] franserin (XXX)[24] and confertin (XXXI)[24]. From *Hymenoxis odorata* was isolated the pseudoguaianolide odoratin (XXXII)[25], closely related to the lactones found in the genus *Helenium*.



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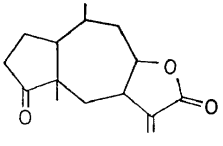
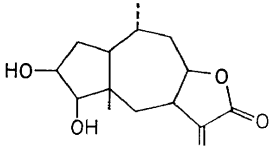
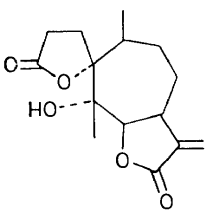


(XXXI)



(XXXII)

From *Ambrosia canescens* there was isolated a dilactone named canambrin (XXXIV)[26] which differs from psilostachyin (XXXIII)[27] in stereochemistry. Isomerization of canambrin (XXXIV) in an atmosphere of hydrogen in the presence of palladium on charcoal afforded the isoderivative XXXV. Chemical reduction of canambrin (XXXIV) with sodium borohydride takes a similar course as in the reduction of psilostachyin (XXXIII)[27]. The dihydro derivative and the triol (XXXVII) are obtained. Oxidation of the



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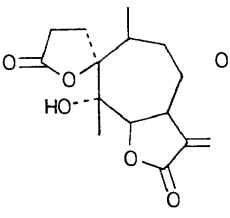
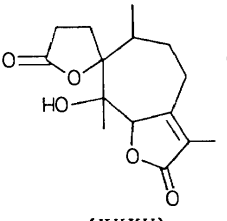


(XXXIV)



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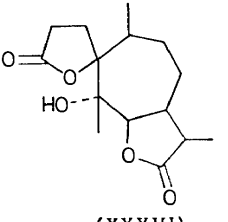
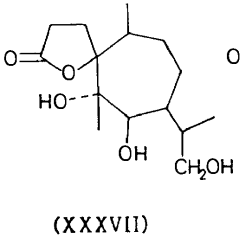


(XXXVI)



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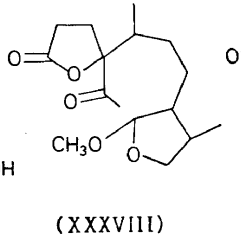

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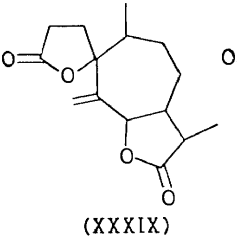

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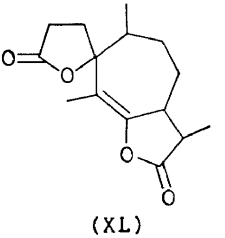
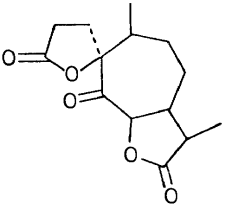
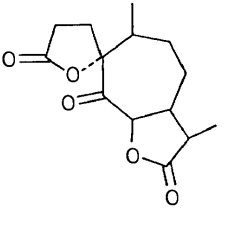


(XL)



(XLI)



(XLII)

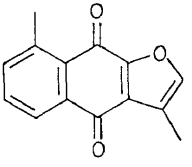
triol (XXXVII) with periodic acid in methanol solution gave the keto-lactone (XXXVIII). Dehydration of canambrin (XXXIV) with thionyl chloride in pyridine solution furnished two anhydro derivatives (XXXIX) and (XL). Ozonolysis of the anhydro derivative (XXXIX) gave the ketone (XLI). The latter differs from the same derivative of the psilostachyin series. However treatment of (XLI) with zinc in acetic acid resulted in a product identical with the ketolactone (XLII) obtained from psilostachyin. This correlation established the structure and configuration at C-7 and C-10 of canambrin. Biogenetic considerations and careful spectral examination render very probable that canambrin (XXXIV) only differs from psilostachyin (XXXIII) in the asymmetrical centre at C-1.

APPENDIX

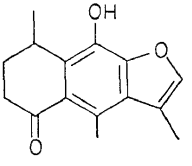
The position of the aromatic methyl group of maturinone (XLIII)[28] was deduced from the obtention of 3-methyl phthalic acid by alkaline hydrogen peroxide oxidation of (XLIII)[28] and the non-existence of hydrogen bonding between the hydroxyl and the carbonyl groups in cacalone (XLIV)[29,30] which was correlated to maturinone by degradations. However the evidence reported in this communication permit to revise the structure of maturinone to (XLV).

The n.m.r. spectrum ($CDCl_3$) of the cyclopropyl derivative (XLVI)[31] did not show a signal at 6·91 ppm corresponding to a proton substituted at C-5, shielded by the cyclopropane ring. The presence of a signal with the above chemical shift has been demonstrated for similar products.[32] Therefore the methyl group must be attached at C-5.

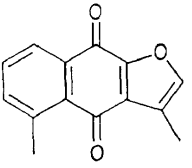
Furthermore, treatment of desacetyl-6-epi-decompostin (XLVIIa)[33] with mesyl chloride in pyridine gave an oily mesylate (XLVIIb) which without



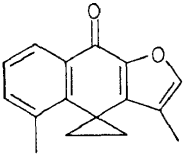
(XLIII)



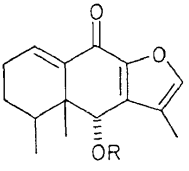
(XLIV)



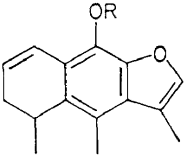
(XLV)



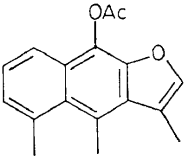
(XLVI)



(XLVII) a, R=H
b, R=Mesyl



(XLVIII) a, R=H
b, R=Me



(XLIX)

purification was treated with collidine. The resulting crystalline product (XLVIIIa) m.p. 124–125° had a n.m.r. spectrum ($CDCl_3$) identical to that of the methyl ether of dehydrocacalol (XLVIIIb) except for the signal corresponding to the methyl ether. It showed the following signals: at 7·23 (quadruplet, C-2 proton), at 6·91 (quadruplet, $J_A = 10$ cps, $J_B = 3$ cps, C-8 proton), at 5·88 (multiplet, C-7 hydrogen), at 4·87 (broad singlet, disappears on equilibration with D_2O, phenolic proton) at 2·48 (singlet,

C-4 methyl group), at 2·35 (doublet, J = 1·5 cps, C-2 methyl group) and at 1·06 (doublet J = 7 cps, C-5 methyl group). Treatment of (XLVIIIa) in benzene solution with D.D.Q. yielded a fully aromatic product which was identified as the acetate (XLIX)[27]. The mixed m.p. showed no depression and the i.r. spectra were superimposable. This correlation suggests a biogenetic relationship of the furanoeremophilane series with the furonaphtalene derivatives.

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