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PSILOSTACHYIN, A NEW TYPE OF SESQUITERPENE LACTONE

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We wish to report the structure of psilostachyin, I, a new sesquiterpene lactone from *Ambrosia psilostachyia*, and its synthesis from coronopilin, VIII. Herz and Hogenauer (1) previously established the structure of coronopilin, a sesquiterpene lactone isolated from *A. psilostachyia* obtained in Kansas. More recently, Geissman and Turley (2) described the acid-catalyzed dehydration-rearrangement of coronopilin to coronopilic acid, IX, which argued for the stereochemical features of VIII, previously proposed by Herz and co-workers(3) on the basis of the tentative absolute configuration of parthenin which had been directly correlated to coronopilin.

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We obtained three new sesquiterpene lactones,* psilostachyin, psilostachyin B, $C_{15}H_{18}O_4$, m.p. 123°, and psilostachyin C, $C_{15}H_{20}O_4$, m.p. 223-225°, from A. psilostachyia collected on Galveston Island, Texas in the summer and fall of 1963 and 1964. No coronopilin was detected in the terpenoid extracts from any of the collections. Evidence is now presented to support structure I for psilostachyin.

Psilostachyin (I), $C_{15}H_{20}O_5$, m.p. 215°, $[\alpha]_D^{24°}$ -125.2 (c=4.76, $CHCl_3$), displayed a carbonyl absorption in the infrared at 1764 cm^{-1} which corresponded roughly to two carbonyl groups on comparison with the infrared spectra of related compounds of known structure. A weak IR band at 1660 cm^{-1} and the UV absorption at λ max 212 mμ, ϵ 12,600 were in good agreement with the presence of one α,β-unsaturated lactone. An IR signal at 3570 cm^{-1} could be assigned to a tertiary hydroxyl group on the basis of a sharp singlet at δ 5.29 in the NMR spectrum of I in deuterated dimethylsulfoxide (DMS), which disappeared on the addition of D_2O (4). Moreover, psilostachyin did not form an acetate.

The NMR spectrum of I in $CDCl_3$ showed a singlet at δ 1.22 and a doublet at δ 1.04, (J = 7 cps) for one tertiary and one secondary methyl group, respectively. A doublet, integrating for one proton, at δ 4.96, (J = 10 cps) and a pair of doublets (intensity one proton each) at δ 5.53 and δ 6.29, (J = 3 cps), were typical for the γ-lactone with a conjugated C_{11} methylene of the type found in coronopilin. Furthermore, a multiplet, centered at δ 3.43, could be assigned to the proton at C-7; the complexity

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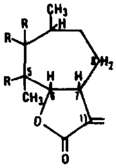
* Elemental and mass spectrographic analyses for all the compounds described in this paper were in close agreement with the theoretical values.

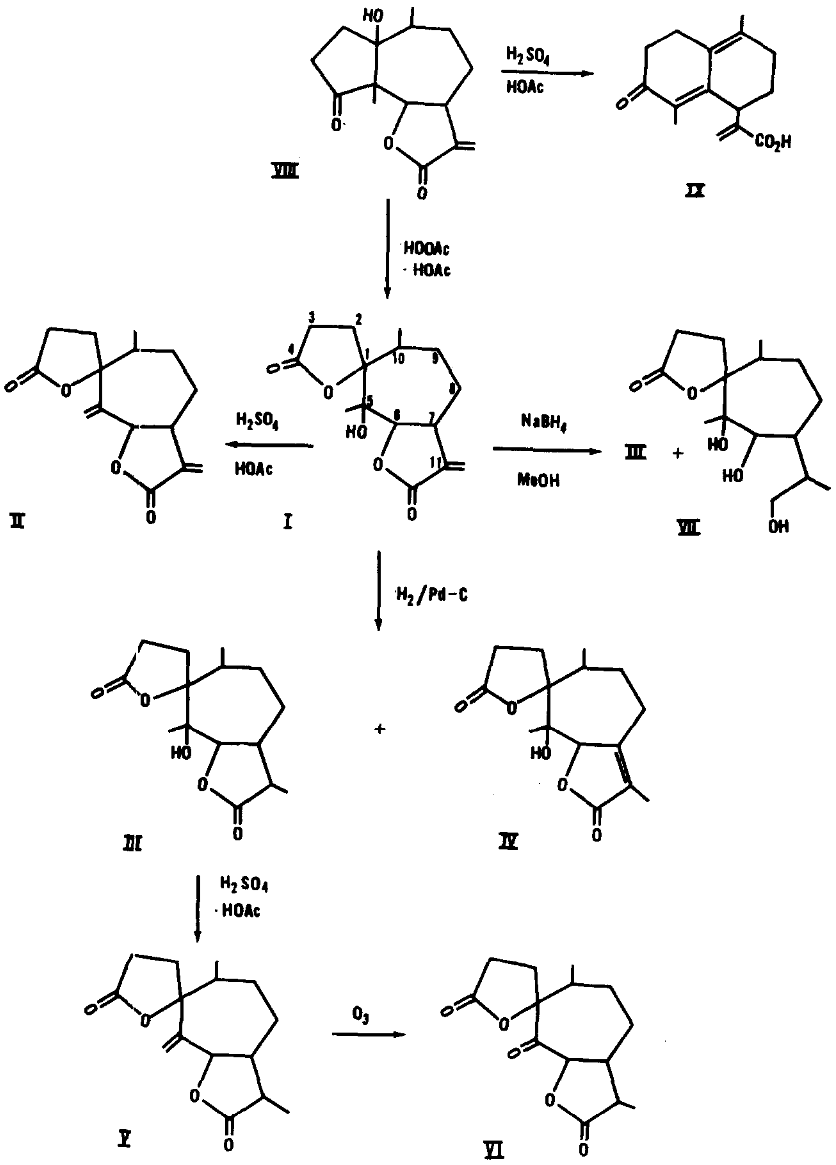
of the signal even after spin-spin decoupling the interaction with the C-6 lactonic proton was in accord with a methylene group at C-8.

Based on the above information and by analogy with the structure of coronopilin, a partial formula could now be offered for psilostachyin:



Additional support for an α ,β-unsaturated γ-lactone system was provided by the catalytic hydrogenation of I which afforded a mixture of the reduced product, dihydropsilostachyin (III), ($C_{15}H_{22}O_5$, m.p. 222-223°) and isomerized psilostachyin, IV ($C_{15}H_{20}O_5$, m.p. 194-195°).

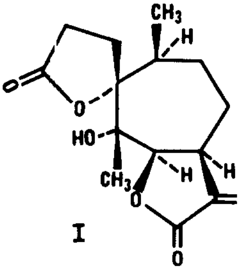
In contrast with coronopilin, which dehydrates with rearrangement giving coronopilic acid (IX), both psilostachyin and dihydropsilostachyin (III) smoothly dehydrated when treated with glacial acetic acid - concentrated sulfuric acid to II, $C_{15}H_{18}O_4$, m.p. 158°, and V, $C_{15}H_{20}O_4$, m.p. 173-175°, respectively, suggesting that the tertiary hydroxyl group might be at the C-5 position in the starting materials, I and III. The NMR data support structures II and V. In the vinyl proton region of the NMR spectra of II and V, a new pair of doublets, each representing one proton, were observed. They appeared to be coupled to the C-6 lactonic proton which now occurred as two triplets. In the NMR spectrum of VI, obtained from ozonolysis of V, the signal for the C-6 proton was again a doublet. Compound VI, $C_{14}H_{18}O_5$, m.p. 170-172°, showed a weak UV absorption at λmax 295 mμ, ϵ 42 for the keto group.


HO
VIII
H₂SO₄
HOAc
IX
CO₂H
HOOAc
HOAc
3
2
4
1
10
9
8
5
6
7
11
HO
II
H₂SO₄
HOAc
I
NaBH₄
MeOH
III +
HO
HO
OH
VII
H₂/Pd-C
HO
III
+
HO
IV
H₂SO₄
HOAc
V
O₃
VI

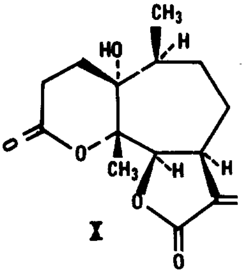
The interpretation of the fourth and fifth oxygen atoms in I now remained. The absence of a keto group in I was concluded when no low intensity UV absorption near 290 mμ was observed. In addition, the ORD curve of I did not show a Cotton-effect in this region. That the remaining two oxygen atoms belonged to a γ-lactone was suggested by the analysis of the sodium borohydride reduction products. Sodium borohydride treatment of I in methanol reduces the α,β-unsaturated γ-lactone, giving initially III, and finally VII. To our knowledge, this is the first example of the total reduction of an α,β-unsaturated γ-lactone with sodium borohydride although other workers (5) have observed the reduction of this carbon-carbon double bond with this reagent. The NMR analysis of VII in DMS confirmed the presence of three hydroxyl groups: one primary (triplet, δ 4.88); one secondary (doublet, δ 5.14); and one tertiary (singlet, δ 4.47). All three hydroxyl proton signals disappeared on the addition of D_2O. Compound VII, $C_{15}H_{26}O_5$, m.p. 115-117°, still showed a carbonyl band at 1760 cm^{-1}, which could be either a γ-lactone or cyclopentanone. The γ-lactone is favored since VII did not show either a UV signal or Cotton-effect near 290 mμ. The γ-lactone must be lactonized to a tertiary position since no NMR signal was detected for a lactonic proton.

All of the above data supported structure I for psilostachyin. Final proof of structure was provided by the synthesis of psilostachyin when coronopilin was treated with peracetic acid. The synthetic product was identical in all respects with the natural psilostachyin. The Baeyer-Villiger peracid oxidation of ketones is known to cleave stereospecifically (6).

Therefore the absolute configuration of coronopilin at C-5 should be retained in the oxidized product. The initial product should be the δ - lactone lactonized to C-5 but the conditions of the reaction would be expected to allow equilibration to the more stable product. We favor structure I over X since the dehydrated product V cannot contain a δ - lactone and the infrared spectra in the carbonyl region of I and V are similar and in accord with one γ - and one α,β-unsaturated γ -lactone. The absolute configuration of psilostachyin (I) can therefore be formulated, on the basis of the stereochemistry proposed for coronopilin (2, 3).



I



X

The facile conversion of coronopilin to psilostachyin suggests the biogenesis of I, photochemically and/or enzymatically, from VIII.

The structures of psilostachyin B and C will be the subject of a later communication.

Acknowledgements

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