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SESQUITERPENE LACTONES OF *BAILEYA* SPECIES. PLENIRADIN AND RADIATIN

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Abstract—Pleniradin (I) and radiatin (XI), new sesquiterpene lactones from *Baileya pleniradiata* Harv. and Gray, have structures related to those of the constituents of *Gaillardia* species. Both genera are members of the tribe Helenieae (fam. Compositae).

INTRODUCTION

FURTHER study of *Baileya pleniradiata* Harv. and Gray, from which the sesquiterpene lactone glucoside paucin has been isolated,[2] has revealed the presence of a number of additional constituents, the structures of which reveal their probable biosynthetic origins and interrelationships.

RESULTS AND DISCUSSION

Pleniradin

Pleniradin (I), m.p. 94–97°, $[\alpha]_D^{25} -35{\cdot}4^\circ$, was obtained in 0·01 % yield from the dried whole plant of *Baileya pleniradiata*, a showy annual of the south-western deserts of Arizona and California. It has the composition $C_{15}H_{20}O_4$, and shows the molecular ion at *m/e* 264 in the mass spectrometer. Its u.v. and i.r. spectra indicated that it was an α-methylene-γ-lactone, and this was confirmed by the NMR spectrum, which showed the characteristic pair of one-proton doublets ($J=3$ Hz) at δ 5·57 and 6·21. Other NMR signals were seen at 1·19 (3 H, s, C-4 CH_3); 1·82 (3 H, broadened singlet, C-10 CH_3); a septet at δ 4·30 (1 H, C*H*OH); and a complex multiplet between δ 5·24 and 5·59 (2 H, lactone proton and vinyl proton).

Pleniradin was easily acetylated with pyridine–acetic anhydride to yield a monoacetate (II). The i.r. spectrum of the acetate still showed hydroxyl absorption at 3500 cm^{-1}, an indication that a tertiary hydroxyl group was present. The NMR spectrum of the acetate showed the absence of a signal for the —C*H*OH proton of a secondary hydroxyl group, and contained a sharp three-proton singlet for a methyl group at δ 1·19, an indication that the hydroxyl group is attached to the carbon atom bearing the methyl group (at C-4). The mass spectrum of the acetate is nearly identical with that of gaillardin (III);[3] it shows the molecular ion at *m/e* 306, and prominent peaks at *m/e* 288 (M-18), 246 (M-60), 228 (M-18-60), 213, 188 (base peak), 105 and 91. These observations suggest that pleniradin acetate and gaillardin are stereoisomers, probably at C-2 or C-8 (or both).

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[1] Contribution No. 2399 from the Department of Chemistry, UCLA.

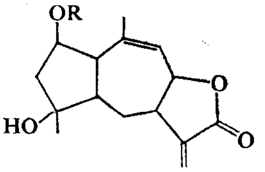
[2] T. G. WADDELL and T. A. GEISSMAN, *Tetrahedron Letters* 515 (1969).

[3] S. M. KUPCHAN, J. M. CASSADY, J. E. KELSEY, H. K. SCHNOES, D. H. SMITH and A. L. BURLINGAME, *J. Am. Chem. Soc.* **88**, 5292 (1966).

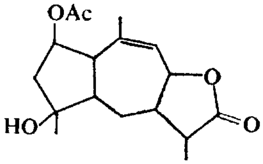
Reduction of pleniradin acetate with $NaBH_4$ yields the 11,13-dihydro compound (IV), as shown by the appearance in the NMR spectrum of a new three-proton doublet at δ 1·21 ($J = 6{\cdot}5$ Hz) and the disappearance of the pair of doublets at δ 5·54 and 6·19. The presence of a double bond in IV are shown by a signal for a vinyl proton at δ 5·62 (1 H, broad doublet, $J = 4$ Hz) and a broadened three-proton singlet for a vinyl methyl group at δ 1·73.

Epoxidation of dihydropleniradin acetate with *m*-chloroperbenzoic acid to yield V confirmed the presence of the double bond and established its relationship to the lactone grouping. The NMR signal for the lactonic proton (at C-8) in V appeared as a well-defined triplet at δ 4·97 ($J = 4$ Hz), coupled with the proton on the oxide ring (at C-9), which appeared as a doublet at δ 3·10 ($J = 4$ Hz).

These observations left undecided the position of the secondary hydroxyl group, which could have been placed at C-2, C-3 or C-6. The signal for the proton on this carbon atom was a deformed septet (δ 4·30), an indication that it was coupled with at least three protons. In the epoxyacetate, the signal for this proton was also a septet at δ 5·30. These observations are consistent only with the C-2 position for the hydroxyl group, a conclusion that was substantiated in the following way. Oxidation of pleniradin with chromic acid gave a non-crystalline ketone (VI), which showed a strong, broad absorption at 1755 cm^{-1} in the i.r., consistent with the presence of a cyclopentanone moiety. When the ketone VI was treated with *p*-toluene-sulfonic acid in benzene solution there was formed a mixture of two compounds which were separated by preparative TLC. The higher R_f component of the mixture showed absorption at 1765 and 1705 cm^{-1} in the i.r. and intense end absorption in the u.v., both consistent with the presence of the cyclopentenone structure (VII). The lower R_f component of the mixture (VIII) showed u.v. absorption at 210 and 255 nm and i.r. absorption at 1765, 1690 and 1623 cm^{-1}; all these data are in accord with the presence of the cross-conjugated dienone (VIII), and agree with the spectral properties described for virginolide,[4] lactucin,[5] matricarin,[6] and other lactones in which this structure is found.



(I) R = H
(II) R = Ac
(III) R = Ac (stereoisomeric)



(IV)

The foregoing evidence leads to the formulation of the gross structure of pleniradin as I but does not define the stereochemistry of the molecule. The circular dichroism curve of pleniradin acetate shows a strong positive Cotton effect; this defines[7] the configuration of the C-7/C-8 lactone grouping as *trans*-fused. The configuration of the hydroxyl group at C-2 was

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[4] W. HERZ and P. S. SANTHANAM, *J. Org. Chem.* **32**, 507 (1967).

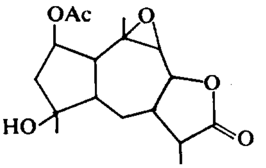
[5] L. DOLEJS, M. SOUCHY, M. HORAK, V. HEROUT and F. SORM, *Coll. Czech. Chem. Commun.* **23**, 2195 (1958).

[6] Z. CEKAN, V. PROCHASKA, V. HEROUT and F. SORM, *Coll. Czech. Chem. Commun.* **24**, 1554 (1959); W. HERZ and K. UEDA, *J. Am. Chem. Soc.* **83**, 1139 (1961).

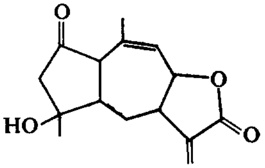
[7] T. G. WADDELL, W. STÖCKLIN and T. A. GEISSMAN, *Tetrahedron Letters*, in press (1969).

established by the use of the method of Horeau,[8–10] and was found to be α-oriented. Biogenetic considerations lead to the conclusion that the stereochemistry of the A/B ring junction and of the C-4 position are as shown, for oxidative ring closure of a germacranolide progenitor would be expected to proceed in a stereospecific manner to lead to these configurations. The complete structure of pleniradin is thus represented as IX.

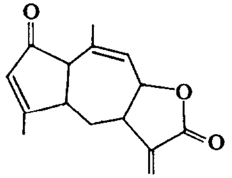
A convincing confirmation of these structural (but not stereochemical) conclusions is found in a color reaction[11] shown by pleniradin (and dihydropleniradin) and by xanthinin.[12] When xanthinin (X) is treated with conc. HCl in ethanol, the originally colorless solution assumes a deep rose-red color when heated. This color is stable and persists upon standing for many hours. When the red solution is diluted with an excess of water, ether extracts a yellow material which regenerates the red color when acidified.



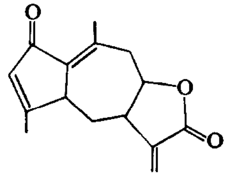
(V)



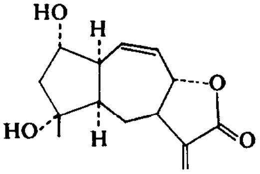
(VI)



(VII)



(VIII)



(IX)

Pleniradin and its acetate give the same color test when treated with HCl; in this case, however, the color appears in the cold and heating is not required. Not only are the colors identical to visual observation, but the absorption spectra are nearly identical: both show a principal maximum at 542 nm (ε 17,000), and other peaks at 500, 360 and 310 nm.

A detailed account of the study of this color reaction will be given later,[11] and for the present purpose the following formulation will suffice to show how xanthinin (X) and pleniradin acetate (II) can undergo acid-catalyzed transformation to lead to a common intermediate:

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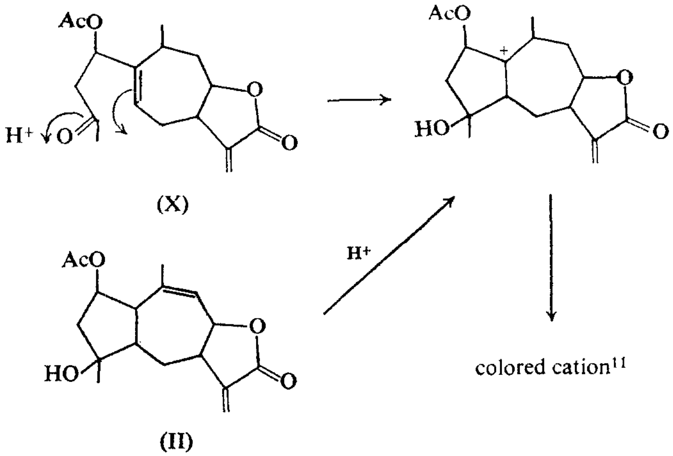
[8] A. Horeau, *Tetrahedron Letters* 506 (1961).

[9] A. Horeau and H. B. Kagan, *Tetrahedron* **20**, 2431 (1964).

[10] T. J. Mabry, W. Renold, H. E. Miller and H. B. Kagan, *J. Org. Chem.* **31**, 681 (1966).

[11] T. A. Geissman, T. E. Winters and T. S. Griffin, unpublished. Studies on this reacton are nearing completion and will be described in a forthcoming communication.

[12] T. E. Winters, T. A. Geissman and D. Safir, *J. Org. Chem.* **34**, 153 (1969).



(X)

(II)

It is clear from this formulation that because pleniradin, pleniradin acetate and dihydropleniradin all give substantially identical colors in this test, the α-methylene group of the lactone is not involved and elimination of the acetyl and hydroxyl groups is a part of the overall process.

Radiatin

Radiatin (XI), m.p. 202–204°, $[\alpha]_D^{25} -84°$, was obtained in 0·15 per cent yield from *B. pleniradiata*. It has the composition $C_{19}H_{24}O_6$, and shows the molecular ion at *m/e* 348. Bands at 3570, 1770, 1725 (strong), 1640 and 1580 cm^{-1} in the i.r. suggested the presence of a hydroxyl group, a γ-lactone, a cyclopentenone of the type found in the fastigilins,[13] and an α,β-unsaturated ester. The ester grouping could be regarded as containing four carbon atoms and in the event was found to be a methacrylyl grouping.

The NMR spectrum of radiatin showed the low-field doublets of doublets at δ 7·22 (J = 6·2 Hz) and 6·08 (J = 6·3 cps) characteristic of the cyclopent-2-ene-4-one structure found in the fastigilins as well as in numerous other sesquiterpene lactones.[13] These signals disappeared upon reduction of radiatin to tetrahydroradiatin (XII). Two additional signals in the NMR spectrum of radiatin (XI) were at low-field (δ 5·41, broad singlet; and 4·89, quartet, J = 6·2 Hz), and were ascribed to the protons of —C*H*—O— at C-6 and C-8, respectively. The proton at C-6, the point of attachment of the methacrylyl grouping, retains its multiplicity in all of the derivatives of XI, while that of C-8, the point of attachment of the lactone ring, appears as a well-defined doublet (δ 4·86, J = 6·5 Hz) in 9-dehydrotetrahydroradiatin (XIII). A signal at 3·50 (1 H, mult.) in the spectrum of radiatin is found at δ 4·97 (1 H, doublet of doublets) in radiatin acetate, and is assigned to the proton at C-9, which bears the secondary hydroxyl group.

These observations revealed that radiatin is closely related to the fastigilins, differing in the presence of the methacrylyl group in XI rather than the senecioyl or angelyl groupings in fastigilins C and A.[13] Indeed, the near identity of the NMR spectra of radiatin with that of fastigilin A in all respects save those signals due to the acyl groupings suggests the identity of deacyl-fastigilin A and deacyl-radiatin.

The presence of the methacrylyl grouping in XI was revealed by the NMR signals at

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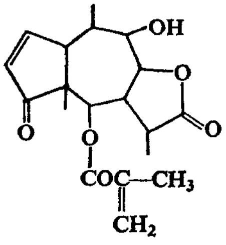
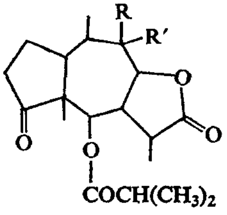
[13] W. HERZ, S. RAJAPPA, S. K. ROY, J. J. SCHMID and R. N. MIRRINGTON, *Tetrahedron* **22**, 1907 (1966).

δ 5·42 and 5·82 for the protons of the methylene grouping and a broad singlet (δ 1·80, 3 H) for the vinyl methyl group. Reduction of radiatin to tetrahydroradiatin (XII) provided confirmation of this: the tetrahydro compound showed two new doublets at δ 1·06 and δ 1·07 (each 3 H, $J=7$ Hz) for the methyl groups of the isobutyryl residue.

The mass spectrum of radiatin showed prominent peaks at m/e 279 (loss of $COC(CH_3)=CH_2$) and 262 (loss of $CH_2=C(CH_3)COOH$), while that of tetrahydroradiatin showed peaks at m/e 281 (M-isobutyryl) and 264 (M-isobutyric acid).



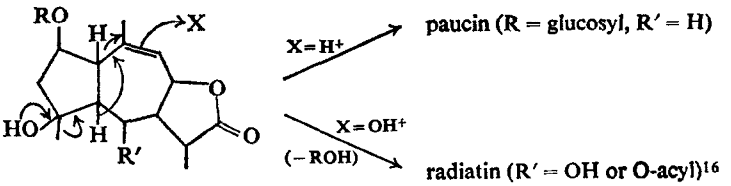
(XI)



(XII) R, R′ = H, OH
(XIII) R, R′ = O

In order to establish the complete stereochemistry of radiatin, 3-bromoradiatin (XIV) and 3-bromoradiatin acetate (XV) have been prepared for study by X-ray crystallography.[14] The results of this work will be reported in due course.

The biosynthetic implications seen in the co-occurrence of pleniradin, a guaianolide, and paucin and radiatin, pseudoguaianolides, deserve comment. The probable course of biosynthesis of the sesquiterpene lactones by way of a farnesol-derived germacranolide through a guaianolide and thence, by methyl migration from C-4 to C-5, to a pseudoguaianolide, finds support in a number of examples of the occurrence of two or more members of these structural types in a single genus or species.[4, 15] It is mechanistically quite reasonable to assume that the origins of paucin and radiatin from a precursor of the type represented by pleniradin can be by way of a methyl migration in the latter initiated by acid catalysis (to give the paucin structure), or by oxidative attack at C-9 or by way of epoxidation at C-9/C-10 (to give radiatin).



paucin (R = glucosyl, R′ = H)

radiatin (R′ = OH or O-acyl)[16]

The presumptive germacranolide precursor of pleniradin is also known in *Baileya*. This compound, baileyin, will be described in a forthcoming communication.[17]

It is finally to be noted that radiatin gives no color when treated with mineral acid as

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[14] Dr. M. T. Emerson, University of Hawaii, has undertaken this investigation.

[15] S. Griffin, T. G. Waddell, H. Chen and T. A. Geissman, *Phytochem.* **8**, 145 (1969).

[16] The use of OH^+ is a formal device. It is clear that acid-catalyzed openings of a 9,10-epoxide could be the actual biosynthetic process.

[17] T. G. Waddell and T. A. Geissman, to be published.

described above for pleniradin and xanthinin. This observation is quite in accord with our view of the course of this color reaction.[11]

EXPERIMENTAL

M.ps. were taken in capillaries and are corrected. In Tables 1 and 2 are summarized the NMR data (measured with a Varian A-60 instrument). TLC was carried out with Merck pre-coated silica gel plates; the usual solvent system was acetone–$CHCl_3$ (3:7).

TABLE 1. NMR SIGNALS OF PLENIRADIN AND ITS DERIVATIVES

Compound	C-2 H	C-4 H	C-8 H	C-9 H	C-13 H	C-4 Me	C-10 Me	C-2 OAc
I	4·30 m[a]	3·16–3·83 br-m	5·24–5·59 br-m[b]	5·24–5·59 br-m[b]	5·57 d (3) 6·21 d (3)	1·19 s	1·82 br-s	
II	5·10–5·55 br-m[c]	3·10–3·85 br-m	5·10–5·55 m[c]	5·10–5·55 m[c]	5·54 d (3) 6·19 d (3)	1·19 s	1·68 br-s	2·00 s
IV	4·92–5·40 br-m[d]		4·92–5·40 br-m[d]	5·62 d (4)[e]	1·21 d (6·5)[f]	1·19 s	1·73 br-s	2·01 s
V	5·30 m[g]		4·97 t (4)	3·10 d (4)	1·19 d (6·5)[f]	1·12 s	1·31 s	2·09 s

Values are given in δ units. Numbers in parentheses denote coupling constants in cps. Multiplets are described as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br-s broad singlet; br-m, broad multiplet. [a]Deformed septet. [b]C-8 H and C-9 H overlap. [c]C-2 H, C-8 H and C-9 H overlap. [d]C-2 H and C-8 H overlap. [e]Broad doublet. [f]Three protons. [g]Septet.

TABLE 2. NMR SIGNALS OF RADIATIN AND ITS DERIVATIVES

Compound	C-2 H	C-3 H	C-6 H	C-8 H	C-9 H	C-5 Me	C-10 Me	C-11 Me	C-6 acyl group
XI	7·22 dd (6,2)	6·08 dd (6,3)	5·41 brs[a]	4·89 dd (6,2)	3·50 m	1·02 s	1·38 d (6·5)	1·52 d (6·5)	5·82 m[b] 5·45 m[a,b] 1·80 brs[c]
Fastigilin A[d]	7·55 dd (6,2)	6·10 dd (6,3)	5·45 brs[e]	4·92 dd (6,2)	3·50 m[f]	1·02 s	1·38 d (6·5)	1·52 d (6·5)	6·1[g] 1·90 dd (6·5, 1)[h] 1·71 m (1·5)[h]
Radiatin acetate	7·72 dd (6,2)	6·12 dd (6,3)	5·47 brs[a]	4·70 dd (6,2)	4·97 dd (10,2)	1·08 s	1·21 d (6·5)	1·55 d (6·5)	5·87 m[b] 5·51 m[a,b] 1·84 brs[c], 2·15 s[i]
XII	—	—	5·17 d (1·5)	4·86 dd (6,2)	3·52 m	0·80 s	1·18 d (6·5)	1·45 d (6·5)	1·04 d[j] (7) 1·06 d[j] (7)
XIII	—	—	5·37 brs[k]	4·86 d (6·5)	—	1·02 s	1·21 d (6·5)	1·51 d (6·5)	1·05 d[j] (7) 1·07 d[j] (7)
XIV	7·48 d (2)	—	5·48 brs[a]	4·92 dd (6,2)	3·52 m	1·08 s	1·39 d (6·5)	1·55 d (6·5)	5·86 m[b] 5·52 m[a,b] 1·81 brs[c]

Values are given in ppm (δ). Numbers in parentheses denote coupling constants in Hz. Signals are described as follows: s, singlet; d, doublet; m, multiplet; brs, broad singlet. [a] C-6 H and methylene of C_6 side-chain overlap. [b] End methylene (narrowly splitted). [c] Vinyl methyl. [d] See Ref. 13. [e] $W_{1/2}=3·5$. [f] Center. [g] Vinyl H. [h] Vinyl methyl. [i] Acetyl. [j] Isopropyl methyl. [k] $W_{1/2}=2$.

Extraction of Plant Material

A sample of 4·98 kg of *Baileya pleniradiata* Harv. and Gray[18] was dried, ground in a Wiley mill, and extracted exhaustively with $CHCl_3$ at ordinary temperature. After removal of the solvent the tarry residue was dissolved in 800 ml of ethanol and the solution diluted with 2 l. of hot water. The aqueous solution was clarified by filtration through celite and extracted with $CHCl_3$. The dried $CHCl_3$ solution was evaporated to yield 151 g of an oily material. A portion of 93 g of the crude material was subjected to chromatography on 1·7 kg of silica gel; elution was carried out with solvents ranging from benzene to $CHCl_3$ to a final $CHCl_3$–acetone (20:80) mixture. The eluted fractions were examined by LTC and grouped into fractions I (most rapidly eluted) to VI.

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[18] Collected by Mr. R. J. BARR (voucher no. 67358-9367 BP), near Wilcox, Arizona (Cochise County), at 4200 ft elevation, 3 September, 1967.

Pleniradin (*I*)

Rechromatography of fraction V on neutral alumina (100 g) with ethyl acetate as eluant yielded 815 mg of pleniradin. Recrystallized from ethyl acetate, it formed colorless needles, m.p. 94–97°; $[\alpha]_D^{26}$ −35·4° (*c* 1·01, $CHCl_3$). It had λ_{max} (EtOH) 210 nm (end absorption), ϵ 14,300. The i.r. spectrum showed 3590, 3425, 1765, 1665, 1625 cm^{-1}. The mass spectrum showed the molecular ion at *m*/*e* 264. (Found: C, 66·01; H, 7·70. Calc. for $C_{15}H_{20}O_4$; $\frac{1}{4}H_2O$: C, 65·93; H, 7·66%.)

Pleniradin Acetate (*II*)

Acetylation of pleniradin with acetic anhydride-pyridine yielded the acetate; recrystallized from ethanol, it formed colorless needles, m.p. 221–222°; $[\alpha]_D^{25}$ −49° (*c* 1·01, $CHCl_3$). The u.v. spectrum showed end absorption (ϵ 14,000 at 209 nm) and the i.r. spectrum had peaks at 3500, 1765, 1720, 1670 cm^{-1}. The mass spectrum showed *m*/*e* 306 (M^+), 246 (M-60), 228 (M-60-18), 213, 188 (base peak), 105, 91. The circular dichroism curve showed a maximum at 260 nm ($[\theta]+4680$). (Found: C, 66·49; H, 7·43. Calc. for $C_{17}H_{22}O_5$: C, 66·65; H, 7·24%.)

Dihydropleniradin Acetate (*IV*)

To a solution of 100 mg of pleniradin acetate in 15 ml of methanol was added 200 mg $NaBH_4$ and the solution was kept at room temperature for 48 hr, then poured into water, acidified with dilute H_2SO_4 and extracted with $CHCl_3$. Removal of the $CHCl_3$ left an oil (98 mg) which was purified by passage over silica gel (5 g). A homogeneous fraction (by TLC) in the eluate was crystallized from ethyl acetate as colorless needles, m.p. 245–247°; $[\alpha]_D^{25}$ −8°. The i.r. spectrum showed peaks at 3500, 1775, 1720 and 1675 cm^{-1}, and the mass spectrum showed the molecular ion at *m*/*e* 308. (Found: C, 66·34; H, 7·95. Calc. for $C_{17}H_{24}O_5$: C, 66·21; H, 7·85%.)

Epoxidation of Dihydropleniradin Acetate (*V*)

A solution of 40 mg of *m*-chlorobenzoperacid and 37 gm of dihydropleniradin acetate in 5 ml $CHCl_3$ was kept at room temperature overnight. The solution was washed with 5% aqueous $NaHCO_3$ and water, dried and evaporated. The crystalline residue (38 mg) was recrystallized from ethyl acetate, and formed colorless crystals, m.p. 241–243°. Its i.r. spectrum showed peaks at 3550, 1775, 1720 cm^{-1}. (Found: C, 63·08; H, 7·63. Calc. for $C_{17}H_{24}O_6$: C, 62·95; H, 7·46%.)

Oxidation of Pleniradin; 2-Dehydropleniradin (*VI*)

A solution of 50 mg of pleniradin in 5 ml of acetone was cooled in ice and treated with 0·8 ml of Jones' reagent (CrO_3 in dil. H_2SO_4). After 10 min the solution was diluted with 100 ml of water containing a few ml of methanol and extracted with $CHCl_3$. The dried extract was evaporated to yield an oil (37 mg), which was passed through a column of silica gel (2 g). The eluted material showed a single spot on TLC and gave a positive Zimmerman test. It could not be crystallized. Its i.r. spectrum showed a strong, broad absorption at 1755 cm^{-1} and hydroxyl absorption at 3580 cm^{-1}.

Dehydration of 2-Dehydropleniradin

The oily pleniradin oxidation product was dissolved in 20 ml benzene, 3 mg of *p*-toluenesulfonic acid was added, and the solution was heated and allowed to reduce in volume to about 5 ml for 30 min. The solution was added to aqueous $NaHCO_3$ and $CHCl_3$ and the $CHCl_3$ layer dried and evaporated. The oily product was subjected to chromatography on five 5 × 10-cm silica gel plates. An upper band showed intense end absorption at 215 nm, and i.r. absorption at 1765 and 1705 cm^{-1}. A lower band had a u.v. spectrum with end absorption at 210 nm and a second maximum at 255 nm. It showed i.r. absorption at 1765, 1690, 1620 cm^{-1}.

Configuration of C-2 in Pleniradin

A solution of 100 mg of pleniradin and 260 mg of (±)-2-phenylbutanoic anhydride in 3 ml of pyridine was kept at room temperature overnight. After working up the reaction mixture by the usual procedure[8–10] there was recovered 148 mg of 2-phenylbutanoic acid with $[\alpha]_D^{25}$ −10·3° (*c* 2·96, $CHCl_3$).

Radiatin (*XI*)

Fraction III of the column upon which the crude plant extract was separated yielded 11·2 g of a crystalline material which was recrystallized from ethyl acetate to give 7·6 g of radiatin, colorless leaflets, m.p. 202–204°; $[\alpha]_D^{25}$ −84·0° (*c* 1·03, $CHCl_3$). It showed a maximum in the u.v. at 215 nm (ϵ 12,800), and i.r. absorption at 3570, 1770, 1725, 1640 and 1580 cm^{-1}. The mass spectrum showed the molecular ion at *m*/*e* 348, and the CD curve showed $[\theta]-5190$ at 326 nm. (Found: C, 65·60; H, 6·99. Calc. for $C_{19}H_{24}O_6$: C, 65·50; H, 6·94%.)

Radiatin Acetate

Prepared in the usual way (acetic anhydride-pyridine), radiatin acetate had m.p. 187–188° (from ethanol). I.r. spectrum: 1780, 1735, 1725, 1645, 1580 cm^{-1}; mass spectrum, *m/e* 390 (molecular ion). (Found: C, 64·77; H, 6·61. Calc. for $C_{21}H_{26}O_7$: C, 64·60; H, 6·71%.)

Tetrahydroradiatin (XII)

Hydrogenation of 200 mg of radiatin (ethanol; Pd–C, 200 mg) resulted in the uptake of 2 mole equivalents of H_2 in 1 hr, at which point H_2 uptake ceased. The filtered solution was evaporated to give 176 mg of crystals, which were recrystallized from ethyl acetate to give 121 mg of the pure tetrahydrocompound, m.p. 150–151°. It gave a positive Zimmerman test and showed i.r. absorption at 3575, 1780 ,1750 and 1735 cm^{-1}. The mass spectrum showed the molecular ion at *m/e* 352. (Found: C, 64·70; H, 7·86. Calc. for $C_{19}H_{28}O_6$: C, 64·75; H, 8·01%.)

Tetrahydrodehydroradiatin (XIII)

To a solution of 100 mg of tetrahydroradiatin in 2 ml HOAc was added a solution of 100 mg of chromic acid in 2 ml HOAc (containing a few drops of water). After 20 hr at room temperature the excess oxidant was destroyed with methanol and the solution evaporated to dryness. The residue was taken up in $CHCl_3$ and the solution passed through a column of silica gel. The eluted material (57 mg) crystallized upon removal of solvent after recrystallization from ether–petroleum ether had m.p. 137–138°; i.r. spectrum 1785, 1750, 1735, 1720 cm^{-1}. (Found: C, 65·28; H, 7·40. Calc. for $C_{19}H_{26}O_6$: C, 65·12; H, 7·48%.)

3-*Bromoradiatin (XIV)*

A solution of 95 mg Br_2 in 10 ml EtOAc was added slowly to a solution of 348 mg of radiatin in 20 ml EtOAc. The solution was evaporated under reduced pressure and the residue taken up in 50% aqueous ethanol. The product crystallized and was collected and recrystallized from ethanol to give 222 mg of colorless leaflets of the bromo compound, m.p. 222–223°. (Found: C, 53·61; H, 5·64. Calc. for $C_{19}H_{23}O\ Br_6$ C, 53·39; H, 5·39%.)

The structure of the compound as the 3-bromo derivative was established by the NMR spectrum, which showed the C-2 proton as a low-field doublet and the absence of the proton at C-3.

3-*Bromoradiatin Acetate (XV)*

Radiatin acetate was brominated in the manner described for radiatin. The product formed colorless platelets, m.p. 223–224°. (Found: C, 53·68; H, 5·15. Calc. for $C_{21}H_{25}O_7Br$: C, 53·74; H, 5·37%.)

The NMR spectrum showed the expected signals, in particular the C-2 proton as a low-field doublet and the three-proton signal for the acetyl methyl group.

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