needles. The product was filtered and washed with cold methanol until the characteristic odor of methyl anisate could no longer be detected, yield 0.37 g (97%). The analytical sample was recrystallized from ethanol, mp 172–173°.

Anal. Calcd for $C_{25}H_{22}O_7$: C, 69.11; H, 5.10. Found C, 68.92; H, 5.05.

7-Benzyloxy-4′,5,6,8-tetramethoxyflavone (12b).—A mixture of 0.34 g of **12a**, 50 ml of acetone, 2 ml of dimethyl sulfate, and 2 g of anhydrous potassium carbonate was refluxed for 3 hr with stirring. The inorganic salts were filtered, the solvent was removed, and the residue was chromatographed over 25 g of silicic acid (solvent benzene–ethyl acetate, 4:1) in order to remove a green contaminant. Evaporation of the eluate afforded 0.25 g (70%) of the product. Recrystallization from benzene gave small, elongated prisms, mp 114–116°.

Anal. Calcd for $C_{26}H_{24}O_7$ C, 69.63; H, 5.39. Found: C, 69.14; H, 4.90.

5,7-Dihydroxy-4′,6,8-trimethoxyflavone (8a, Nevadensin).—On addition of 0.23 g of **12b** to a cold solution of 4 g of anhydrous aluminum chloride in 20 ml of dry ether, the ether-insoluble flavone dissolved gradually. After 3 hr the solvent was removed and the residue was treated with 50 ml of ice cold dilute hydrochloric acid (1:1). After heating for about 5 min on the water bath, the precipitate was filtered, dried, and chromatographed over 25 g of silicic acid (solvent benzene–ethyl acetate, 4:1). Evaporation of the less polar fraction yielded 95 mg of the almost pure product, mp 193–195°. Recrystallization from benzene raised the melting point to 197–198° (Kofler block); λ_{max} 284 mμ (log ε 4.38 and 334 mμ log ε 4.24). The mixture melting point with authentic nevadensin was undepressed and the infrared spectra were superimposable.

5,7-Diacetoxy-4′,6,8-trimethoxyflavone (8c, Nevadensin Diacetate).—The totally synthetic material was prepared in the manner previously described for the preparation of the derivative of nevadensin, mp 171–174°, mixture melting point undepressed.

5-Hydroxy-4′,6,7,8-tetramethoxyflavone (8d, 5-Desmethyltangeretin).—A solution of 22 mg of nevadensin in 5 ml of acetone containing 30 mg of anhydrous potassium carbonate and 8.5 mg of dimethyl sulfate was stirred under reflux for 1 hr. The inorganic salts were filtered, the solvent was evaporated, and the residue was recrystallized from ethanol. The product long yellow needles: mp 175–177° (lit.[32] mp 174–175°), λ_{max} 292 mμ (log ε 4.38) and 328 mμ (log ε 4.33).

Extraction of *I. Acerosa* (Nutt.) Jackson.—Above-ground material, collected in 1964 by members of the Agricultural Research Service of Utah State University in the vicinity of Logan, Utah, was made available through the courtesy of Professor F. R. Stermitz. Extraction of 950 g of ground plant in the usual manner[26] furnished 30.5 g of gum which was chromatographed over 225 g of silicic acid. Fractions 1–5 (400 ml of benzene each) yielded nothing, fractions 6–12 (benzene) yielded 0.2 g of what appeared to be triterpene mixture (positive Noller test), fractions 13–21 (benzene–chloroform, 3:1) yielded traces only, and fractions 22–26 (benzene–chloroform, 2:1) gave a residue which solidified on trituration with ether. Recrystallization from benzene yielded nevadensin, mp 186–188° and 193–195°, yield 0.15 g, mixture melting point undepressed, infrared and nmr spectra superimposable. Fractions 27–31 (benzene–chloroform, 2:1) gave gum; fractions 32–37 (benzene–chloroform, 1:1) gave a residue which solidified on trituration with ether. Recrystallization from acetone–ether–hexane afforded coronopilin, yield 0.3 g, mp 174–176°, mixture melting point undepressed, infrared and nmr spectra superimposable.

Acknowledgment.—We wish to thank the Research Council of the Florida State University for a grant which helped defray the cost of plant collections. L. F. gratefully acknowledges the hospitality of Professor H. M. Walborsky's laboratory during the period March 1965–February 1966.

(32) Chaliha, *et al.*,[23] prepared this flavone from *Citrus Jambhiri* and prepared it from tangeretin by demethylation with aluminum chloride and from 5,8-dihydroxy-4′,6,7-trimethoxyflavone (**8e**) by methylation with diazomethane. Compound **8e** in turn was prepared by nitric acid oxidation of tangeretin by reduction with sodium bisulfite. A previous preparation[33] of **8e** involved persulfate oxidation of 5-hydroxy-4′,6,7-trimethoxyflavone.

(33) V. V. S. Murti, K. V. Rao, and T. R. Seshadri, *Proc. Indian Acad. Sci.*, **26A**, 182 (1947).

Constituents of *Iva* Species. VII. New Guaianolides from *Iva axillaris* Pursh. ssp. *robustior*[1,2]

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The structure of three new guaianolides which were isolated from *Iva axillaris* Pursh. ssp. *robustior* has been established.

In earlier parts of our systematic study of the genus *Iva*, we reported the isolation of eudesmanolides from *Iva microcephala* Nutt.,[3,4] *I. imbricata* Walt.,[3] *I. asperifolia* Less.,[5] and *I. texensis* Jackson,[5] the isolation of guaianolides from a variety of *I. microcephala*,[6] and the isolation of pseudoguaianolides from *I. acerosa* (Nutt.) Jackson, *I. nevadensis* M. E. Jones, and *I. xanthifolia* Nutt.[7] We now describe the isolation and structure determination of new guaianolides from *I. axillaris* Pursh. ssp. *robustior*.[8]

Extraction of *I. axillaris* ssp. *robustior* collected in Reno, Nev., furnished three new guaianolides, which we have called axivalin, ivaxillin, and ivaxillarin, and the eudesmanolide microcephalin (**1**).[6] Material collected at Montgomery Pass, Mineral Co., Nev., yielded axivalin, ivaxillin, ivaxillarin, a fourth guaianolide anhydroivaxillarin, and a new flavone axillarin (**2**) which we have described elsewhere.[2] Structures of axivalin, ivaxillarin, and anhydroivaxillarin have been determined and are reported in this paper.

The physical properties of the most plentiful and relatively polar material ivaxillarin (**3**), $C_{15}H_{18}O_4$, mp 186–188°, $[\alpha]^{27}D$ −240.8° (*c* 0.72, CH_3OH), high intensity ultraviolet absorption at 207 mμ (ε 10,050), and infrared bands at 1775 and 1665 cm^{-1}, suggested

(1) Supported in part by a grant from the U. S. Public Health Service (GM-05814).

(2) Previous paper: W. Herz, L. Farkas, V. Sudarsanam, H. Wagner, L. Hörhammer, and R. Rüger, *Chem. Ber.*, in press.

(3) W. Herz and G. Högenauer, *J. Org. Chem.*, **27**, 905 (1962).

(4) W. Herz, G. Högenauer, and A. Romo de Vivar, *ibid.*, **29**, 1700 (1964).

(5) W. Herz and N. Viswanathan, *ibid.*, **29**, 1012 (1964).

(6) W. Herz, A. Romo de Vivar, and M. V. Lakshmikantham, *ibid.*, **30**, 118 (1965).

(7) L. Farkas, M. Nogradi, V. Sudarsanam, and W. Herz, *ibid.*, **31**, 3228 (1966).

(8) Evidence for the existence of two subspecies, ssp. *robustior* and ssp. *axillaris*, has been presented recently.[9] Our material came from western Nevada where ssp. *axillaris* does not occur.

(9) I. J. Bassett, G. A. Mulligan, and C. Frankton, *Can. J. Botany*, **40**, 1243 (1962).

TABLE I

NMR SPECTRA OF IVAXILLARIN AND DERIVATIVES[a]

Compd	H_6	H_7	H_8	H_9	C_4-CH_3	C_{10}-CH_3	C_{11}-CH_3	Misc
3[b]	4.35 d (6)	3.51 d br (6)	1.45 m	0.58 m	1.21 d (6.5)	1.06	...	6.23 d,[c] 5.81 d (1)[d]
4	4.22 d (4)			0.63 m	1.17 d (6.5)	1.07	1.31 d (6.5)	
5a	4.15[e]			0.55 m	1.01 d (7)	0.98	1.30 d (6)	4.15 m,[f]
5b	4.07 d (4)			0.5 m	1.04 d (7)	1.00	1.33 d (6.5)	5.21 m,[f] 2.0[g]
6	5.35 d m	3.2 m		0.57 m	1.87 t (1.5)	0.90	...	6.29 d (2),[c] 5.77 d (2)[d,h]
7	5.26 m			0.43 m	1.85 t (1)	0.83	1.36 d (7)	
8				0.45 m	1.00 d (7)	1.05	1.22 d (7)	
9	4.17 d (6)	3.43 d br (6)		0.5 m	1.09 d (6.5)	1.02	...	6.25 d (1),[c] 5.79 d (1),[d] 5.26 m,[f] 2.10[g]

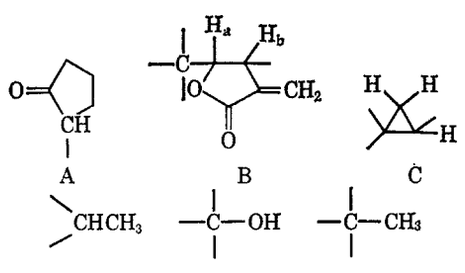
[a] Spectra were determined in deuteriochloroform solution on a Varian A-60 spectrometer using tetramethylsilane as internal standard. Chemical shifts are given in ppm; signals are denoted in the usual way: d, doublet; t, triplet; br, broadened signal; m, complex multiplet. Unmarked signals are singlets. Figures in parentheses are line separations in cps. Signals in first three columns correspond to one proton, in fourth column to two protons, in fifth, sixth, and seventh columns to three protons. [b] In $CDCl_3$–pyridine mixture. [c] H_{13a}. [d] H_{13b}. [e] Superimposed on H_8. [f] H_8. [g] Acetate. [h] Long-range coupling to H_6 or H_8 superimposed on doublet.

the presence of an exocyclic methylene group conjugated with a lactone function which is also found in other constituents of *Iva* species.[3-7] This was confirmed by the formation of a pyrazoline derivative on treatment with diazomethane. The presence of a hydroxyl group was inferred from infrared bands at 3500 and 3680 cm^{-1}; this was assumed to be tertiary since it could not be acetylated and since ivaxillarin was not oxidized on treatment with chromium oxide–pyridine.

The presence of a five-membered ring ketone was suggested by an infrared band at 1750 cm^{-1} which disappeared on reduction with sodium borohydride. That a methylene group was adjacent to the carbonyl was indicated by an infrared band at 1405 cm^{-1} and a positive Zimmerman test. The functional groups shown to be present (one double bond, lactone, hydroxyl, and ketone) in conjunction with the empirical formula required that ivaxillarin be tricyclic.

Hydrogenation of ivaxillarin in the presence of palladium resulted in the uptake of 1 mole equiv of hydrogen. The product, dihydroivaxillarin (**4**), exhibited no ultraviolet maximum in the region 200–250 mμ (due to reduction of the double bond conjugated with the lactone function), but displayed a near-infrared band at 1.62 mμ characteristic of a methylene group in a cyclopropane ring;[10] other bands were found at 3500 (OH), 1775 (lactone), and 1745 cm^{-1} (cyclopentanone). Catalytic reduction of ivaxillarin with platinum oxide–acetic acid furnished tetrahydroivaxillarin (**5a**) by reduction of the double bond and ketone (disappearance of ultraviolet maximum at 207 mμ and infrared band at 1750 cm^{-1}). The formation of a new secondary hydroxyl group was demonstrated by acetylation of **5a** to **5b**. (See Scheme I.)

Consideration of the nmr spectra of ivaxillarin and its derivatives (Table I) supported the deductions made so far and permitted description of the various structural units as follows.



Ivaxillarin had one methyl singlet, one methyl doublet, and two slightly split doublets at 6.23 and 5.81 ppm characteristic of an exocyclic methylene group conjugated with the lactone. A sharp doublet at 4.35 ppm must be ascribed to hydrogen (H_a) on carbon carrying the lactone ether oxygen which was obviously spin coupled to only one proton. A broad doublet at 3.5 ppm was assigned to the hydrogen (H_b) allylically placed to the exocyclic methylene group of the lactone system as this signal moved upfield on conversion of **3** to **4**. Simultaneously the signals of the exocyclic methylene group were replaced by a second methyl doublet. A two-proton multiplet at 0.58 ppm was attributed to the methylene group of the cyclopropane ring and one broad signal at 1.45 ppm was thought likely to be the methine proton of C.

In the nmr spectrum of **5a** the usual two methyl doublets and one methyl singlet were present as were the signals of two protons on carbon atoms carrying lactone and hydroxyl oxygen which were superimposed at 4.15 ppm. In the nmr spectrum of **5b** these were cleanly separated as expected, the downfield shift of the acetate hydrogen revealing its multiplicity which indicated that it must be coupled to more than two protons, probably three. The chemical shift of a one-proton signal superimposed on the methyl peaks and signals near 0.5 ppm in **5a** and **5b** gave additional evidence for the presence of three cyclopropane protons.

The relative positions of the cyclopentanone, tertiary hydroxyl group, and the lactone function were established by the facile dehydration of **3** with methanesulfonyl chloride–pyridine to anhydroivaxillarin (**6**) which turned out to be identical with a minor and least polar constituent of *I. axillaris*. This showed ultraviolet absorption, λ_{max} 234 mμ (ϵ 16,500), characteristic of chromophore D[11] and infrared bands at 1770 and 1655 (conjugated lactone) and 1705 cm^{-1} (cyclopentenone).[12] In the nmr spectrum of **6**, the signal due to H_a, formerly a sharp doublet at 4.35, had moved downfield to 5.35 ppm which indicated that it was now allylically placed with respect to the newly introduced double bond. Broadening of the doublet suggested long-range coupling to several protons near the other

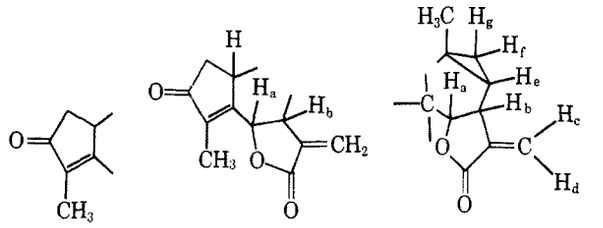
(10) W. w. Washburn and M. w. Mahoney, *J. Am. Chem. Soc.*, **80**, 504 (1958).

(11) R. L. Frank, R. Armstrong, J. Kwiatek, and H. A. Price, *ibid.*, **70**, 1379 (1948).

(12) *Cf.* the ultraviolet and infrared spectrum of geigerin: D. H. R. Barton and J. E. D. Levisalles, *J. Chem. Soc.*, 4518 (1958).

terminus of the unsaturated system; the source of this long-range coupling could be identified as a vinyl methyl group (triplet at 1.87 ppm) which had taken the place of the secondary methyl group present in ivaxillarin. Other clearly visible resonances occurred at 3.2 which was identified as the signal of the proton (H_b) placed allylically to the exocyclic methylene group, at 0.90 (methyl singlet), and at 0.58 ppm (cyclopropane methylene).

Dehydration of dihydroivaxillarin (**4**) furnished **7**, λ_{max} 236 mμ (ε 16,900), infrared bands at 1780 (γ-lactone) and 1705 and 1645 cm^{-1} (cyclopentenone), whose nmr spectrum indicated that an analogous transformation had taken place (vinyl methyl triplet at 1.85, H_b—broadened doublet at 5.26 ppm). Consideration of these features of **6** and **7** allowed expansion of partial structure D to E where a proton was placed at C_1 because of the triplet nature of the vinyl methyl signal.



D E F

Confirmation for the presence of structural unit E in **6** was obtained by hydrogenolytic cleavage of the lactone group with platinum oxide to the acid **8**, infrared bands at 1745 (cyclopentanone) and 1710 cm^{-1} (carboxyl). The nmr spectrum of this substance did not show the presence of the lactone proton (H_a), but exhibited two methyl doublets, one methyl singlet, and the cyclopropane multiplet.

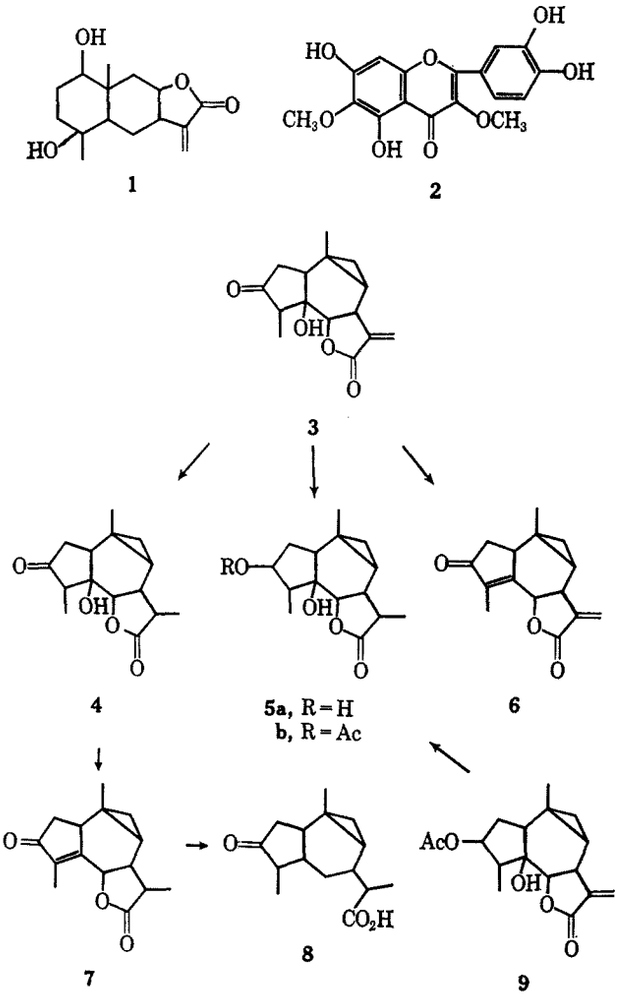
The combination of C_4H_6 lacking from E to complete the structure of anhydroivaxillarin must include a quaternary methyl group, a cyclopropane methylene, and a cyclopropane methine. If a "biogenetically normal" carbon skeleton be assumed, the only structure which can be written for anhydroixavillarin is **6**. Since the precursor ivaxillarin contains a tertiary hydroxyl and a secondary methyl group, its structure must then be **3**.

That this formula is indeed correct was shown by double-irradiation experiments with ivaxillarin which established the presence of partial structure F and hence **3**. The signal assigned to H_a (doublet at 4.35 ppm) was found to collapse to a sharp singlet upon irradiation 50 cps upfield at the center of the signal assigned to H_b. Conversely this signal (broadened doublet at 3.51 ppm) collapsed to a broadened singlet upon irradiation 50 cps downfield.

That the appearance of the H_b signal could be partially attributed to allylic coupling with H_c and H_d was confirmed by irradiating at the H_b frequency and observing the collapse of the H_c and H_d doublets to singlets. Vicinal coupling between H_b and H_e was verified by irradiating at 1.45 ppm (cyclopropyl methinyl) which sharpened the doublet of H_b. Irradiation at 1.45 ppm also caused simplification of the cyclopropane methylene (H_f) signal at 0.58 ppm; conversely, irradiation at 0.58 ppm resulted in collapse of H_e to a doublet (J = 2 cps). Hence coupling exists between H_b and H_e and between H_e and H_f which completes the structure proof. H_4 was verified as being in the complex multiplet (intensity four protons—H_1, H_2, and H_4 centered at 2.50 ppm) because irradiation at 82 cps downfield from the methyl doublet at 1.21 ppm caused perturbation of the doublet but effected no other changes.

Although the double-irradiation experiments provided irrefutable proof for the formulation of ivaxillarin as **3**, chemical evidence could be adduced as well. Reduction of **5b** with lithium aluminum hydride followed by dehydrogenation resulted in the formation of guaiazulene which established the distribution of groups on the perhydroazulene skeleton.

Scheme I



1 2 3 4 5a, R=H b, R=Ac 6 7 8 9

Axivalin, the compound of intermediate polarity isolated from *I. axillaris* ssp. *robustior*, had the formula $C_{17}H_{22}O_5$, mp 138–140°, $[\alpha]^{27}D$ −132.4° (*c* 0.37, $CHCl_3$), λ_{max} 209 mμ (ε 9300), and exhibited infrared bands at 3450 (OH), 1770 (γ-lactone) and 1730 cm^{-1} (acetate). The nmr spectrum possessed features reminiscent of those of ivaxillarin. Two pairs of doublets at 6.25 and 5.79 (J = 1 cps) were charactristic of the exocyclic methylene group conjugated with the lactone, a doublet at 4.17 (J = 6 cps) suggestive of H_6, and a broadened doublet (J = 6 cps) at 3.43 ppm apparently due to H_7. A methyl doublet at 1.09 ppm was partially superimposed on a methyl singlet and a two-proton cyclopropane methylene signal was centered at 0.5 ppm. An additional feature was an acetate singlet at 2.1 which

was undoubtedly associated with a multiplet at 5.26 ppm (proton on carbon carrying the acetate function).

The supposition that axivalin might be the acetyl derivative (**9**) of a diol resulting from reduction of the cyclopentanone function of ivaxillarin could be verified in a very simple fashion. Catalytic hydrogenation of axivalin produced a substance which was identical in all respects with acetyltetrahydroivaxillarin (**5b**).

Experimental Section[13]

Extraction of *Iva axillaris* Pursh. ssp. *robustior*. A.—Ground, whole herb (565 g) from a collection arranged by Dr. P. T. Tueller near Reno, Nev., in late Aug 1964, was extracted with chloroform and worked up in the usual manner.[3] The crude gum (30 g) was taken up in benzene and chromatogaphed over 225 g of silicic acid (Mallinckrodt 100 mesh), 500 ml fractions being collected. Fractions 1–3 (benzene) and 4–12 (benzene–chloroform, 3:1) gave gums. Fractions 13–18 (benzene–chloroform, 2:1) gave a semisolid material which was rechromatographed over 40 g of silicic acid. The residue from the benzene–chloroform (2:1) eluates of the rechromatography was recrystallized from petroleum ether (bp 30–60°) to yield axivalin: 55 mg; mp 138–140°; λ_{max} 209 mμ (ε 9300); $[\alpha]^{27}D$ −132.4° (*c* 0.37); infrared bands at 3450, 1770, 1730, and 1665 cm^{-1}.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.66; H, 7.19; O, 26.14. Found: C, 66.24; H, 7.36; O, 26.13.

Fractions 19–20 (benzene–chloroform, 2:1) and 21–28 (benzene–chloroform, 1:1) gave gums. Fractions 29–33 (benzene–chloroform, 1:2) solidified on trituration with ether. The solid was rechromatographed over 40 g of silicic acid. The residue from the benzene–chloroform (2:1) eluates of the rechromatography was recrystallized from benzene–petroleum ether: yield of ivaxillin, 150 mg; mp 173–176°; $[\alpha]^{27}D$ −117.4° (*c* 0.86 CH_3OH); infrared band at 1780 cm^{-1} (γ-lactone); nmr signals at 4.34 tc (lactone hydrogen), 3.0–2.5 (complex series of bands four protons), 1.40 and 1.29 (two methyl singlets or two superimposed methyl doublets), and 1.24 d ppm (6.5, methyl doublet), no change on addition of D_2O. The material was recovered on attempted acetylation and hydrogenation. Treatment with BF_3 resulted in the formation of gums which exhibited additional infrared bands at 3500 and 1725 cm^{-1}. On the basis of these results we suggest that ivaxillin is a diepoxyguaianolide, but the material on hand was insufficient for further studies.

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33; O. 24.03. Found: C, 68.16; H, 8.44; O, 23.59.

Fractions 34 and 35 (chloroform) gave gums. Fractions 36–40 (chloroform) gave a residue which solidified on trituration with ether. Recrystallization from benzene and then from ethyl acetate–benzene yielded 0.7 g of ivaxillarin: mp 186–188°; λ_{max} 207 mμ (ε 10,050); infrared bands at 3680, 3500, 1775, 1750, and 1665 cm^{-1}; $[\alpha]^{27}D$ −240.8° (*c* 0.72, CH_3OH).

Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.68; H, 6.76; O, 24.40. Found: C, 68.60; H, 6.76; O, 24.57.

The pyrazoline was prepared by allowing 40 mg of ivaxillarin in 10 ml of tetrahydrofuran to stand with 10 ml of ethereal diazomethane for 2 days at 5°. Evaporation furnished a solid which was recrystallized several times from chloroform–petroleum ether, mp 152° dec with frothing at 138°.

Anal. Calcd for $C_{16}H_{20}N_2O_4$: C, 63.14; H, 6.62; N, 9.21. Found: C, 63.60; H, 6.78; N, 8.71.

Fractions 41–42 (chloroform–methanol, 99:1), 43–44 (chloroform–methanol, 49:1), and 45–46 (chloroform–methanol, 97:3) gave gums which could not be induced to crystallize. Fractions 47–48 (chloroform–methanol, 19:1) gave a residue which solidified on trituration with ether. Recrystallization from ethyl acetate yielded 0.5 g of microcephalin, mp 204–208°, melting point undepressed on admixture of an authentic sample, infrared spectra superimposable. Elution with more polar solvents did not give solid material.

B.—Extraction of 1160 g of above-ground material collected by Mr. Gerald Dickerson in late Aug 1964 on Montgomery Pass, Mineral Co., Nev., in the usual manner furnished 67 g of gum which was chromatographed over 275 g of silicic acid. Fractions 1–4 (benzene) yielded nothing, fractions 5–10 (benzene–chloroform, 3:1) gave a gum, and fractions 11–18 (benzene–chloroform, 2:1) gave a semisolid material which was rechromatographed over 60 g of silicic acid. Elution with hexane, hexane–benzene (3:1), and hexane–benzene (2:1) gave oils and gums. Fractions eluted with hexane–benzene (1:1) gave a solid material which was recrystallized from ether–hexane and then melted at 130–133°, identical in mixture melting point and infrared and nmr spectrum with anhydroivaxillarin (*vide infra*). Hexane–benzene (1:2) gave a gum; hexane–benzene (1:3) furnished a solid which was recrystallized from benzene–hexane and then ether–hexane, mp 138–140°, 0.35 g, identical with axivalin. Elution with benzene gave a gum. The material eluted with benzene–chloroform (2:1) solidified on trituration. Recrystallization from benzene–hexane furnished 0.18 g of ivaxillin.

Fractions 19–22 (benzene–chloroform, 1:1) of the original chromatogram gave gums. Fractions 23–27 (benzene–chloroform, 1:2), 28–31 (benzene–chloroform, 1:3), and 32–38 (chloroform) solidified on trituration with ether. Two recrystallizations form ethyl acetate–benzene and one from methanol–benzene furnished 1.2 g of ivaxillarin, mp 186–188°. Fractions 39–45 (chloroform), 46–51 (chloroform–methanol, 99:1), and 52–60 (chloroform–methanol, 39:1) gave gums. Fractions 61–64 (chloroform–methanol, 39:1) gave a gum which was dissolved in chloroform containing a little methanol. When the solution was allowed to evaporate at room temperature, the material solidified. Recrystallization from acetonitrile gave the flavone axillarin which has been described elsewhere.[2]

Dihydroivaxillarin (**4**).—A solution of 100 mg of **3** in 60 ml of ethanol was hydrogenated with 50 mg of palladium on calcium carbonate at 30 psi for 3 hr. The catalyst was filtered, the solvent evaporated, and the residue was chromatographed over 10 g of silicic acid. Elution with chloroform and recrystallization of the product from benzene yielded 65 mg of **4**: mp 183–186°; $[\alpha]^{28}D$ −178.5° (*c* 0.79); infrared bands at 3500 (OH), 1745 (cyclopentanone), and 1775 cm^{-1} (γ-lactone).

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63; O, 24.21. Found: C, 67.95; H, 7.61; P.24.73.

Tetrahydroivaxillarin (**5a**).—A solution of 100 mg of **3** in 60 ml of acetic acid was hydrogenated with 100 mg of platinum oxide at 30 psi for 48 hr. The catalyst was filtered, the solvent was removed, and the residue was chromatographed over 15 g of silicic acid. Elution with chloroform and recrystallization of the product from methanol–benzene–petroleum ether (bp 65–100°) gave 50 mg of **5a**: mp 206–208°; $[\alpha]^{28}D$ −50° (*c* 0.26); infrared bands at 3500 (LH), 3675 (OH), and 1780 cm^{-1} (γ-lactone).

Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33; O, 24.03. Found: C, 67.32; H, 8.20; O, 24.66.

Acetyltetrahydroivaxillarin (**5b**).—A mixture of 100 mg of **5a**, 2 ml of acetic anhydride, and 1.5 ml of pyridine was allowed to stand at room temperature for 12 hr. The usual work-up resulted in an oily residue which was chromatographed over 5 g of silicic acid. Elution with chloroform–benzene (1:1) and recrystallization of the product from chloroform–hexane yielded the acetyl derivative **5b**: 90 mg; mp 139–141°; infrared bands at 3700 (OH), 1730 (acetate), and 1780 cm^{-1} (γ-lactone).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85; O, 25.94. Found: C, 66.21; H, 8.26; O, 25.83.

Reduction of 3 with Sodium Borohydride.—A solution of 100 mg of ivaxillarin in 15 ml of tetrahydrofuran was treated with sodium borohydride (150 mg) and left overnight at room temperature. A few drops of dilute acetic acid was then added and the solvent was removed under reduced pressure. The residue was taken up in chloroform, and the solution was washed with sodium bicarbonate solution, then with water and dried (Na_2SO_4). The residue obtained on removal of the solvent was chromatographed over 12 g of silicic acid. Elution with chloroform and crystallization of the product from benzene yielded 35 mg of white feathery solid, mp 204–206°, identical in infrared spectrum, melting point, and mixture melting point with tetrahydroivaxillarin **5a**.

Anhydroivaxillarin (**6**).—A solution of 100 mg of **3** in pyridine (2 ml) was cooled to 0°, treated with methanesulfonyl chloride (250 mg), and left to stand at 25° for 48 hr. The mixture was poured into ice–water and extracted with ether. The ether extract was washed with sodium becarbonate solution, water, dilute hydrochloric acid, and then water, and dried (Na_2SO_4). The residue obtained by the removal of ether was chromatographed over 10 g of silicic acid. Elution with 1:1 chloroform–benzene

(13) Melting points are uncorrected. Infrared spectra were run in chloroform; ultraviolet spectra were run in 95% ethanol; rotations were in chloroform unless otherwise specified. Analyses were performed by Dr. F. Pascher, Bonn, Germany.

yielded 35 mg of white solid, mp 120–125°. Repeated recrystallizations from petroleum ether (bp 65–100°) raised the melting point to 133–135°; λ_{max} 234 mμ (ε 16,500); infrared bands at 1770 (γ-lactone), 1705 (cyclopentenone), and 1644 cm^{-1} (double bonds).

Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60; O, 19.65. Found: C, 73.58; H, 7.06; O, 19.68.

Chromium Trioxide Oxidation of Ivaxillarin.—A solution of 100 mg of **3** in 4 ml of pyridine was added at 0° to a stirred solution of 1 g of chromium trioxide in 10 ml of pyridine and left overnight at room temperature. The mixture was poured into ice and extracted thoroughly with ether. The ether extract was was washed with sodium bicarbonate solution, water, dilute hydrochloric acid, and then water, and dried. The residue obtained by the removal of the solvent was chromatographed over silicic acid (8 g). The residue obtained from the chloroform–benzene (1:1) eluate was recrystallized from petroleum ether (bp 65–100°) to yield a white solid, mp 130–133°, identical in all respects with anhydroivaxillarin (**6**). Elution with chloroform and recrystallization of the product from methanol–benzene yielded 60 mg of unchanged ivaxillarin.

Anhydrodihydroivaxillarin (7).—A solution of 80 mg of **4** in 1.5 ml of pyridine was treated at 0° with 0.3 ml of methanesulfonyl chloride and left at room temperature for 24 hr. The mixture was poured into ice–water and worked up and the product was chromatographed over 10 g of silicic acid. The residue obtained from the chloroform–benzene (1:1) eluates was recrystallized once from chloroform–hexane and again from chloroform–ether as white needles: 35 mg; mp 209–211°; λ_{max} 236 mμ (ε 16,900), infrared bands at 1780 (lactone), 1705 (cyclopentenone), and 1665 cm^{-1} (double bond).

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37; O, 19.49. Found: C, 73.20; H, 6.97; O, 19.54.

Reduction of Anhydroivaxillarin.—A solution of 100 mg of **6** in 50 ml of ethanol and 0.5 ml of acetic acid was hydrogenated with 100 mg of platinum oxide at 30 psi for 8 hr. The residue obtained by the removal of the solvent from the filtered solution was dissolved in sodium bicarbonate solution, the aqueous solution was extracted with chloroform, and the chloroform extract was rejected. The bicarbonate solution was acidified with hydrochloric acid and again extracted with chloroform. The residue (65 mg) obtained on evaporation of the solvent was chromatographed over 15 g of silicic acid. Elution with benzene–ether (2:1) and recrystallization of the product from ether–petroleum ether (bp 60–100°) yielded acid **8**: mp 142–144°, $[\alpha]^{25}D$ −91.5° (*c* 0.9), infrared bands at 1745 (cyclopentanone) and 1710 cm^{-1} (COOH).

Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86; O, 19.17. Found: C, 72.49; H, 8.60; O, 19.23.

Reduction of Axivalin.—A solution of 80 mg of axivalin (**9**) in 50 ml of ethanol was hydrogenated with 50 mg of 5% palladized charcoal at 30 psi for 3 hr. The catalyst was filtered, the solvent was removed from the filtrate, and the residue was chromatographed over 6 g of siliicic acid. The residue obtained from the benzene–chloroform (2:1) eluates was recrystallized from chloroform–hexane to yield **5b**: 55 mg, mp 140–142°, identical in nmr, infrared, tlc, and melting point with an authentic sample of acetyltetrahydroivaxillarin.

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85; O, 25.94. Found: C, 65.84; H, 8.0; O, 25.85.

Dehydrogenation of Acetyltetrahydroivaxillarin (5b).—To a stirred slurry of lithium aluminum hydride (1 g) in 50 ml of tetrahydrofuran was added dropwise a solution of 250 mg of **5b** in 50 ml of tetrahydrofuran. The mixture was refluxed for 7 hr and cooled, the excess reagent was decomposed with ethyl acetate, and water was added to decompose the complex. The organic layer was dried (Na_2SO_4) and the solvent was removed. The residue was suspended in 15 ml of Nujol and dehydrogenated with 1 g of 10% palladium on charcoal at 340° for 15 min. The acid extract was diluted with water and the aqueous solution was extracted thoroughly with hexane. The azulene obtained by the removal of solvent was chromatographed over 50 g of acid-washed Merck alumina and eluted with hexane. The blue azulene (approximately 20 mg) had a visible spectrum identical with that of guaiazulene, melting point of trinitrobenzene complex 148–150°, mixture melting point of trinitrobenzene complex with guaiazulene undepressed.

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Phosphonic Acids and Esters. XVII. Formation, Aromatization, and Reduction of Diels–Alder Adducts of Vinyl- and Chlorovinylphosphonates[1]

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Diethyl vinylphosphonate has been shown to undergo Diels–Alder reactions in acceptable yields with butadiene, 1,3-pentadiene, isoprene, 2,3-dimethylbutadiene, 1-methoxybutadiene, cyclopentadiene, and hexachlorocyclopentadiene. Mixtures of positional isomers are formed in reactions with 1,3-pentadiene and isoprene; reaction with 1-methoxybutadiene is apparently directionally specific. The adducts from butadiene, 1,3-pentadiene, isoprene, and 1-methoxybutadiene can be aromatized to the corresponding arylphosphonates by the use of nitrobenzene in the presence of a palladium catalyst. Similarly, adducts are formed by the reactions of diethyl α-chlorovinylphosphonate with butadiene, diethyl *trans*-β-chlorovinylphosphonate with butadiene and cyclopentadiene, and diethyl *cis*-β-chlorovinylphosphonate with cyclopentadiene. Mixtures of *endo* and *exo* isomers are obtained in reactions leading to the formation of norbornenylphosphonates.

The literature contains only a limited number of references to the utilization of phosphorus-containing dienes and dienophiles in the Diels–Alder reaction. The readily available diethyl vinylphosphonate[2,3] (**1**) has been reported to form adducts (**2**) with butadiene,[4] 2,4-hexadiene,[5] 1,3-pentadiene,[5] cyclopentadiene,[6] and hexachlorocyclopentadiene[7] in acceptable yields although the adducts were not fully characterized in all cases. On the basis of comparative studies, the dienophilic reactivity of **1** was reported to be less than that of α,β-unsaturated carbonyl compounds and nitriles.[5] To the best of our knowledge, the aromatization of **2** to the corresponding arylphosphonates (**3**)

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