

## THE STRUCTURE OF PERUVININ—A PSEUDO-GUAIANOLIDE ISOLATED FROM *AMBROSIA PERUVIANA* WILLD<sup>1</sup>

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(Received in U.S.A. 25 April 1966; accepted for publication 21 June 1966)

**Abstract**—The structure of peruvinin, a constituent of *Ambrosia peruviana* Willd., has been established as a pseudoguaianolide Ia.

IN A recent communication, the isolation of peruvinin (II), pseudoguaianolide, from *Ambrosia peruviana* Willd. was described.<sup>2</sup> The structural proof of a new constituent of *Ambrosia peruviana* Willd., which we propose to name peruvinin, is now reported.

Peruvinin ( $C_{18}H_{30}O_4$ ), m.p. 169–171°,  $[\alpha]_D^{25} - 34^\circ$  was obtained from the mother liquors left after the crystallization of peruvinin (II).<sup>3</sup> Peruvinin (Ia) possesses a hydroxyl group (IR band at  $3500\text{ cm}^{-1}$ ) which could be acetylated under basic conditions. A broad band at  $1742\text{ cm}^{-1}$  in the IR spectrum suggested the presence of two chromophores, a cyclopentanone and a five membered lactone conjugated with an exocyclic methylene group confirmed by the following evidence. The exocyclic methylene group conjugated with the lactone is responsible for the UV max at  $212\text{ m}\mu$  ( $\epsilon$  10500) and for a weak IR band at  $1660\text{ cm}^{-1}$ . Treatment of Ia with an ethereal solution of diazomethane yielded a pyrazoline. Hydrogenation of peruvinin (Ia) gave the dihydroderivative IIIa.

The NMR spectrum<sup>3</sup> of peruvinin (Ia) exhibited a pair of low field doublets (J 2 c/s) at 6.28 and 5.68 ascribed to the exocyclic methylene protons. The multiplicity and the chemical shift of a signal centered at 4.8 which in the NMR spectrum of peruvinin acetate (Ib) is observed as a triplet centered at 4.85 ( $J = 9\text{ c/s}$ ) with smaller doubling ( $J = 3\text{ c/s}$ ) indicates a lactone closure at C-8.<sup>4</sup> The proton on the carbon bearing the hydroxyl group of peruvinin (Ia) appears as a singlet at 4.2 which is shifted downfield (5.27) on acetylation. A doublet ( $J = 7\text{ c/s}$ ) at 1.17 and a singlet at 0.91 exhibited by Ia are ascribed to a secondary and a tertiary methyl group respectively. In the NMR spectrum of dihydroperuvinin (IIIa), the low field doublets of the exocyclic methylene are not observed, a doublet ( $J = 7\text{ c/s}$ ) at 1.17 is assigned to a new methyl group. The IR spectrum of IIIa did not show the weak band at  $1660\text{ cm}^{-1}$

<sup>1</sup> Contribution No. 231 from the Instituto de Química de la Universidad Nacional Autónoma de México.

<sup>2</sup> P. Joseph-Nathan and J. Romo, *Tetrahedron* 22, 1723 (1966).

<sup>3</sup> The NMR spectra were determined by Mr. Eduardo Díaz on a Varian A-60 spectrometer, in  $CDCl_3$  solution using tetramethylsilane as internal standard. All chemical shifts are reported in ppm as  $\delta$  values (c/s/60).

<sup>4</sup> W. Herz, A. Romo de Vivar, J. Romo and N. Viswanathan, *J. Amer. Chem. Soc.* 85, 19 (1963).

associated with the double bond. The vicinal position of the hydroxyl and keto groups was evident after a methanol solution of Ia consumed periodic acid. Further proof of the presence of a ketol group in peruvinin (Ia) was obtained by calcium in liquid ammonia reduction of dihydroperuvinin acetate (IIIb). The product obtained from this reaction apparently was a mixture of the ketone IV and the corresponding alcohol, formed by further reduction of the carbonyl group. Chromium trioxide oxidation of the above mixture afforded the ketolactone IV.<sup>5</sup> It has IR bands at  $1740\text{ cm}^{-1}$  (cyclopentanone) and at  $1762\text{ cm}^{-1}$  ( $\gamma$ -lactone). An alternative procedure for obtaining IV is treatment of dihydroperuvinin mesylate (IIIc) with sodium iodide in acetic acid.

The structure of peruvinin (Ia) was fully elucidated by correlation with cumanin (V) a pseudoguaianolide isolated from *Ambrosia cumanensis* H.B.K.<sup>6</sup> Hydrogenation of cumanin acetone<sup>6</sup> afforded in good yield dihydrocumanin acetone (VI). Acid hydrolysis of VI furnished dihydrocumanin (VIIa) previously described.<sup>6,7</sup>

Treatment of an acetic acid solution of dihydrocumanin dimesylate (VIIb) with sodium iodide yielded the lactone VIII. The NMR spectrum of VIII indicates that its vinyl protons appear to be involved in an ABX system since two pairs of quadruplets are observed, centered at  $5.70$  ( $J_{AB} = 7\text{ c/s}$ ) ( $J_{AX} = 2.5\text{ c/s}$ ) and at  $5.40$  ( $J_{BX} = 1.5\text{ c/s}$ ). Chemical evidence for the double bond was provided by the formation of an epoxide IX.

Hydrogenation of the lactone VIII yielded the saturated derivative X identical with a product obtained by desulfurization of the cycloethylene mercaptol of desoxy-dihydroperuvinin (IV). Therefore peruvinin (Ia) is a pseudoguaianolide with its lactone group closed at C-8.

The relative position of the ketol group in the five membered ring was elucidated when sodium borohydride reduction of peruvinin acetate (Ib)<sup>8</sup> afforded dihydrocumanin (VIIa).<sup>6</sup> Furthermore, desulfurization of the cycloethylene mercaptol of dihydroperuvinin acetate (IIIb) furnished the acetate (XI). This product upon acid hydrolysis followed by chromium trioxide oxidation gave the ketone XII of known structure and stereochemistry.<sup>2</sup> The evidence cited above demonstrates that peruvinin possesses the structure Ia with the same stereochemistry of its asymmetric centers as cumanin (VI).

The *trans* ring junction of peruvinin (Ia) is in accord with the strong negative Cotton effects exhibited by the ORD curves of Ia and Ib. Those are of the same type shown by the 16-keto steroids (androstan- $3\beta$ -ol-16-one and the 3,20-bisketal of 16-ketoprogesterone).<sup>9</sup>

Treatment of dihydroperuvinin mesylate (IIIc) with  $\gamma$ -collidine gave a cyclopentenone (XIII) (IR band at  $1695\text{ cm}^{-1}$ ) characterized as its red 2,4-dinitrophenyl hydrazone ( $\lambda_{\text{max}}$   $386\text{ m}\mu$ ;  $\epsilon$  26334). The NMR spectrum of the cyclopentenone XIII exhibited a singlet (1 H) at  $5.94$  corresponding to a vinyl proton, in its derived

<sup>5</sup> C. Djerassi and D. Herbst, *J. Org. Chem.* **26**, 4675 (1961).

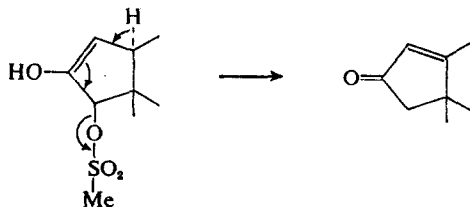
<sup>6</sup> J. Romo, P. Joseph-Nathan and G. Siade, *Tetrahedron* **22**, 1499 (1966).

<sup>7</sup> Hydrogenation of cumanin (V) gave a mixture of dihydrocumanin and isocumanin (Ref. 6). From the hydrogenation of cumanin acetone only dihydrocumanin acetone was isolated.

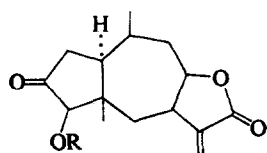
<sup>8</sup> It has already been shown that sodium borohydride reduction of the exocyclic methylene group in lactones closed at C-8 gave a C-11  $\beta$ -methyl group. R. A. Lucas, S. Rovinski, R. J. Kiesel, L. Dorfman and H. B. MacPhillamy, *J. Org. Chem.* **29**, 1549 (1964).

<sup>9</sup> C. Djerassi, R. Riniker and B. Riniker, *J. Amer. Chem. Soc.* **78**, 6362 (1956).

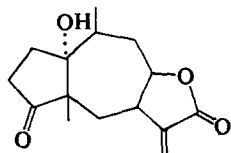
2,4-dinitrophenylhydrazone the same singlet is observed at 6.23. This result may be rationalized as follows:



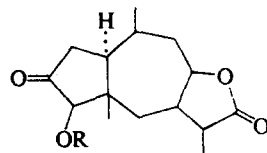
Several C-11 epimers of the products described above were prepared. Treatment of 11-epidihydrocumanin (XIVa)<sup>8</sup> with methane sulfonylchloride afforded the dimesyate (XIVb). Elimination of the mesyloxy groups in XIVb with sodium iodide yielded the olefin XV. The patterns of the NMR signals displayed by the vinyl protons of XV were practically identical to those of VIII. Epoxidation of XV furnished the derivative XVI. Dehydration of 11-epidihydrocumanin<sup>8</sup> (XIVa) with potassium bisulfate gave the ketone XVII. It had IR bands at  $1760\text{ cm}^{-1}$  ( $\gamma$ -lactone and at  $1735\text{ cm}^{-1}$  (cyclopentanone). Alkaline treatment of desoxydihydroperuvinin (IV) afforded XVIII.



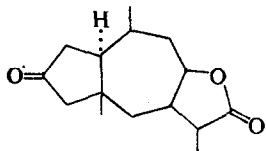
I a, R = H  
b, R = Ac



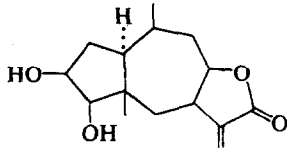
II



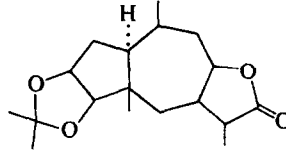
III a, R = H  
b, R = Ac  
c, R = MeSO<sub>2</sub>



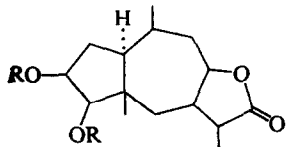
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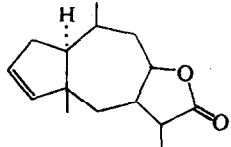
V



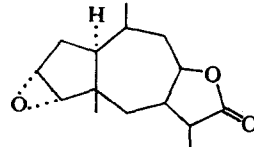
VI



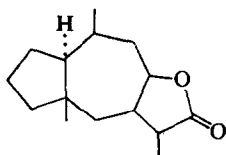
VII a, R = H  
b, R = MeSO<sub>2</sub>



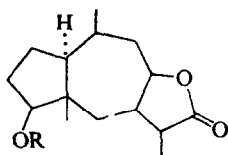
VIII



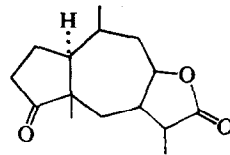
IX



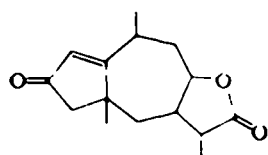
X



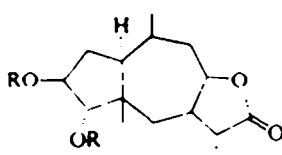
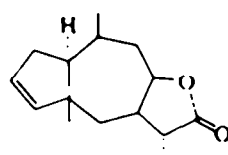
XI



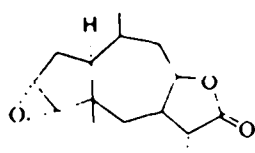
XII



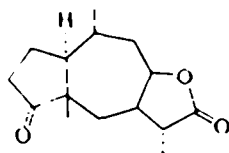
XIII

XIV a, R = H  
b, R = MeSO<sub>2</sub>

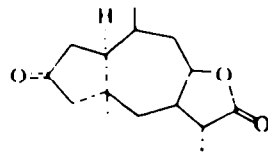
XV



XVI



XVII



XVIII

EXPERIMENTAL<sup>10</sup>

*Isolation of peruvinin (Ia).* This product was isolated from the mother liquors of Peruvín (II).<sup>9</sup> Repeated crystallizations from acetone-ether afforded prisms (3.5 g), m.p. 169-171°,  $[\alpha]_D + 34^\circ$ ;  $\lambda_{max}$  212 m $\mu$ ;  $\epsilon$  10500; IR bands at 3500 (OH group), at 1742 (broad, cyclopentanone and  $\gamma$ -lactone) and at 1660 cm<sup>-1</sup> (C=C double bond); rotatory dispersion (in dioxan):  $[\alpha]_{400} - 210^\circ$ ,  $[\alpha]_{300} - 532^\circ$ ,  $[\alpha]_{250} - 2542^\circ$ ,  $[\alpha]_{200} - 3005^\circ$ ,  $[\alpha]_{180} - 2526^\circ$ . (Found: C, 68.52; H, 7.35; O, 24.26. Calc. for C<sub>15</sub>H<sub>20</sub>O<sub>4</sub>: C, 68.16; H, 7.63; O, 24.21%.)

*Peruvinin acetate (Ib).* Acetylation of Ia with Ac<sub>2</sub>O and pyridine for 1 hr on the steam bath furnished Ib, m.p. 220° (prisms from acetone-hexane):  $[\alpha]_D - 37^\circ$ ;  $\lambda_{max}$  212 m $\mu$ ;  $\epsilon$  10000; IR bands 1750 (broad, acetate, cyclopentanone and  $\gamma$ -lactone) and at 1655 cm<sup>-1</sup> (C=C double bond). Rotatory dispersion (in dioxan):  $[\alpha]_{400} - 191^\circ$ ,  $[\alpha]_{300} - 466^\circ$ ,  $[\alpha]_{250} - 1685^\circ$ ,  $[\alpha]_{200} - 2325^\circ$ ,  $[\alpha]_{180} - 2167^\circ$ . (Found: C, 66.46; H, 7.24; O, 26.16. Calc. for C<sub>17</sub>H<sub>22</sub>O<sub>5</sub>: C, 66.65; H, 7.24; O, 26.11%.)

*Pyrazoline of peruvinin.* A soln of Ia (100 mg) in MeOH (5 ml) was treated with an ethereal soln of diazomethane and left overnight at 4°. The excess diazomethane was decomposed with AcOH, the soln evaporated to dryness and the residue crystallized from ether-hexane. This yielded prisms (55 mg) m.p. 145° (dec);  $\lambda_{max}$  322 m $\mu$ ;  $\epsilon$  195. (Found: C, 62.54; H, 7.10; N, 9.16. Calc. for C<sub>16</sub>H<sub>20</sub>O<sub>4</sub>N<sub>2</sub>: C, 62.72; H, 7.24; N, 9.14%.)

*HIO<sub>4</sub> oxidation of peruvinin (Ia).* A soln of Ia (200 mg) in MeOH (6 ml) was treated with an aq soln of HIO<sub>4</sub> (200 mg) and left overnight. The soln was diluted with water and extracted with AcOEt. The organic layer was washed with NaHCO<sub>3</sub> aq and water, dried and evaporated to dryness. The gummy residue resisted crystallization. IR bands at 1760 ( $\gamma$ -lactone), at 1730 (six membered lactone) and at 1660 cm<sup>-1</sup> (C=C double bond).

*Dihydroperuvinin (IIIa).* A soln of Ia (500 mg) in AcOEt (80 ml) was hydrogenated with Pd-C (80 ml) until the uptake of H ceased. The soln was filtered, evaporated to dryness and the solid residue crystallized from acetone-ether. This yielded prisms (410 mg) m.p. 210-212°,  $[\alpha]_D - 64^\circ$ ;  $\lambda_{max}$  290-296 m $\mu$ ;  $\epsilon$  70; IR bands at 3660 (OH group) and at 1765 cm<sup>-1</sup> (broad, cyclopentanone and  $\gamma$ -lactone). (Found: C, 67.67; H, 8.12; O, 23.86. Calc. for C<sub>16</sub>H<sub>22</sub>O<sub>5</sub>: C, 67.64; H, 8.33; O, 24.03%.)

*Dihydroperuvinin acetate (IIIb).* Acetylation of IIIa with Ac<sub>2</sub>O and pyridine for 1 hr on the steam bath or Pd-C catalyzed hydrogenation of Ib in AcOEt afforded IIIb, m.p. 205-206° (needles from acetone-hexane),  $[\alpha]_D - 66^\circ$ ;  $\lambda_{max}$  286-292 m $\mu$ ;  $\epsilon$  65; broad IR bands at 1765 cm<sup>-1</sup> (acetyl group, cyclopentanone and  $\gamma$ -lactone). (Found: C, 66.57; H, 7.49; O, 26.08. Calc. for C<sub>17</sub>H<sub>24</sub>O<sub>6</sub>: C, 66.21; H, 7.84; O, 25.95%.)

<sup>10</sup> M.P.s are uncorrected. IR spectra and rotations were run CHCl<sub>3</sub>, UV spectra in 95% EtOH. The alumina used in the chromatograms was Alcoa, F-20 (washed with AcOEt). Analyses Dr. Franz Pascher, Bonn, Germany. We are grateful to Syntex, S.A., for the determination of the rotations.

**Ca in liquid  $\text{NH}_3$  reduction of IIIb.** To a soln of Ca (1.2 g) in liquid  $\text{NH}_3$  (200 ml) at  $-70^\circ$  with mechanical stirring was added a soln of IIIb (600 mg) in THF (18 ml). The mixture was stirred for 30 min, treated with 10 ml MeOH and left at room temp until elimination of  $\text{NH}_3$ . The residue was diluted with water, acidified with dil HCl and extracted with AcOEt. The organic layer was washed with water, dried and evaporated to dryness. The gummy residue was dissolved in acetone (10 ml) and oxidized with 8N  $\text{CrO}_3$  at  $5^\circ$ , diluted with water and extracted with AcOEt. The organic solution was washed with water, dried and evaporated to dryness. Crystallization of the residue from acetone-hexane yielded IV as prisms (125 mg), m.p.  $183-188^\circ$ . The analytical sample showed m.p.  $190^\circ$ ;  $[\alpha]_D^{25} -84^\circ$ ; IR bands at  $1762$  ( $\gamma$ -lactone) and at  $1740\text{ cm}^{-1}$  (cyclopentanone); (Found: C, 71.85; H, 8.77; O, 19.22. Calc. for  $\text{C}_{18}\text{H}_{22}\text{O}_5$ : C, 71.79; H, 8.86; O, 19.35%.)

**NaI treatment of IIIc.** A soln of IIIc (150 mg) in AcOH (10 ml) was treated with NaI (200 mg) and heated under reflux for 2 hr, diluted with water and extracted with AcOEt. The organic layer was washed with water, 5% NaOH aq, dried and evaporated to dryness. Crystallization of the residue from acetone-hexane yielded prisms m.p.  $183-187^\circ$ . Identified by the standard methods with IV, obtained by Ca in liquid  $\text{NH}_3$  reduction of IIIa.

**Dihydrocumanin acetoneide (VI).** The acetoneide of cumenin<sup>6</sup> (1 g) was dissolved in AcOEt (90 ml) and hydrogenated with Pd-C (100 mg) until the uptake of H ceased. Crystallization of acetone-hexane yielded prisms (920 mg), m.p.  $151-154^\circ$ ;  $[\alpha]_D^{25} +120^\circ$ ; IR band at  $1760\text{ cm}^{-1}$  ( $\gamma$ -lactone). (Found: C, 69.94; H, 8.94; O, 20.61. Calc. for  $\text{C}_{18}\text{H}_{22}\text{O}_4$ : C, 70.10; H, 9.15; O, 20.75%.)

**Dihydrocumanin (VIIa).** A soln of VI (800 mg) in MeOH (12 ml) was treated with 5 ml of 20% HCl and heated under reflux for 15 min. It showed m.p.  $177-179^\circ$ . Identified by the standard methods with a sample obtained by hydrogenation of cumenin.<sup>6</sup>

**Dihydrocumanin dimesylate (VIIb).** This was prepared according to the method described for cumenin dimesylate.<sup>6</sup> Crystallization from acetone-hexane afforded prisms m.p.  $202-204^\circ$ ,  $[\alpha]_D^{25} +51^\circ$ . (Found: C, 48.34; H, 6.81; O, 30.06; S, 14.82. Calc. for  $\text{C}_{18}\text{H}_{20}\text{O}_5\text{S}_2$ : C, 48.11; H, 6.65; O, 30.16; S, 15.08%.)

**11-Epidihydrocumanin dimesylate (XIVb).** Prepared by treatment of XIVa with  $\text{MeSO}_3\text{Cl}$  and pyridine. Prisms from acetone-hexane m.p.  $209^\circ$ ,  $[\alpha]_D^{25} +84^\circ$ . (Found: C, 48.06; H, 6.56; O, 29.93; S, 15.04. Calc. for  $\text{C}_{17}\text{H}_{18}\text{O}_5\text{S}_2$ : C, 48.11; H, 6.65; O, 30.16; S, 15.08%.)

**Treatment of dihydrocumanin dimesylate (VIIb) with NaI.** A soln of VIIb (400 mg) and NaI (800 mg) in AcOH (15 ml) was heated under reflux for 1.5 hr, diluted with water and extracted with AcOEt. The organic layer was washed with water, 5% NaOH aq, dried and evaporated to dryness. The residue crystallized from hexane yielding 50 mg of recovered mesylate (VIIb), m.p.  $196-198^\circ$ , the mother liquors were chromatographed on alumina (10 g). The crystalline fractions eluted with hexane were combined and recrystallized from hexane. This yielded VIII (110 mg), m.p.  $88^\circ$ ,  $[\alpha]_D^{25} +54^\circ$ ; IR band at  $1765\text{ cm}^{-1}$  ( $\gamma$ -lactone). (Found: C, 76.89; H, 9.34; O, 13.93. Calc. for  $\text{C}_{18}\text{H}_{20}\text{O}_5$ : C, 76.88; H, 9.47; O, 13.65%.)

**m-Chloroperbenzoic acid epoxidation of the lactone (VIII).** A cold soln of VIII (200 mg) in  $\text{CH}_2\text{Cl}_2$  (15 ml) was treated with m-chloroperbenzoic acid (180 mg), heated under reflux for 1 hr, washed with  $\text{NaHCO}_3$  aq and evaporated to dryness. Crystallization from ether-hexane furnished IX as prisms (140 mg), m.p.  $155-157^\circ$ ;  $[\alpha]_D^{25} +54^\circ$ ; IR band at  $1765\text{ cm}^{-1}$  ( $\gamma$ -lactone). (Found: C, 71.71; H, 8.77; O, 19.12. Calc. for  $\text{C}_{18}\text{H}_{20}\text{O}_5$ : C, 71.79; H, 8.86; O, 19.35%.)

**Hydrogenation of the lactone (VIII).** A soln of VIII (60 mg) in AcOEt (20 ml) was hydrogenated with PtO<sub>2</sub> (20 mg) until the absorption of H ceased. Crystallization from hexane yielded X as plates (45 mg), m.p.  $102^\circ$ ,  $[\alpha]_D^{25} +40^\circ$ ; IR band at  $1765\text{ cm}^{-1}$  ( $\gamma$ -lactone). (Found: C, 76.13; H, 10.21; O, 13.70. Calc. for  $\text{C}_{18}\text{H}_{22}\text{O}_5$ : C, 76.22; H, 10.24; O, 13.54%.)

**Preparation of the lactone X from the ketone IV.** A mixture of IV (100 mg), ethanedithiol (0.3 ml) and  $\text{BF}_3$ -etherate (4 ml) was left at room temp for 3 hr poured into ice-water and extracted with AcOEt. The organic layer was washed with 5% NaOH aq, water, dried and evaporated to dryness. The residue dissolved in EtOH (50 ml) was treated with Raney Ni (2 g), heated under reflux for 14 hr, filtered and evaporated to dryness. Crystallization of the residue from hexane yielded plates (25 mg), m.p.  $105^\circ$ . It showed no depression in m.p. on admixture with the product obtained by hydrogenation of VIII and the IR spectra were superimposable.

**$\text{NaBH}_4$  reduction of peruvinin acetate (Ib).** A soln of Ib (1.5 g) in MeOH (50 ml) was treated with  $\text{NaBH}_4$  (1.5 g) and left at room temp for 5 hr. The soln was concentrated to a small volume, diluted with water, acidified with dil HCl and extracted with  $\text{CH}_2\text{Cl}_2$ . The organic layer was washed with water,

dried and evaporated to dryness. The residue was chromatographed on alumina (30 g). The crystalline fractions were combined and recrystallized from acetone-ether, yielding needles m.p. 178–179°. (Found: C, 66.93; H, 9.10; O, 24.05. Calc. for  $C_{11}H_{10}O_4$ : C, 67.13; H, 9.01; O, 23.86%.) Identified by the standard methods with dihydrocumanin (VIIa).<sup>9</sup>

**3-Desoxodihydroperuvinin acetate (XI).** A soln of IIIb (735 mg) in AcOH (6 ml) was treated with ethanedithiol (2 ml) and  $BF_3$ -etherate (2 ml), left overnight at room temp, poured in ice-water and extracted with AcOEt. The organic layer was washed with 5% NaOH aq. water, dried and evaporated. A soln of the mercaptol (500 mg) in EtOH (200 ml) was treated with Raney Ni (5 g) and heated under reflux for 16 hr. The soln was filtered, evaporated to dryness and the residue chromatographed on alumina (12 g). The crystalline fractions eluted with hexane were combined and recrystallized from hexane-pentane. This yielded plates (150 mg) m.p. 123°;  $[\alpha]_D^{+50}$ : IR bands at 1760 ( $\gamma$ -lactone) and at 1725  $cm^{-1}$  (acetyl group). (Found: C, 69.57; H, 8.81; O, 21.59. Calc. for  $C_{11}H_{10}O_4$ : C, 69.36; H, 8.90; O, 21.74%.)

**Dihydroperuvinin mesylate (IIIc).** An ice cold soln of IIIa in pyridine (8 ml) was treated with  $MeSO_3Cl$  (2 ml), left for 10 hr at room temp, poured into ice-water and extracted with AcOEt. The organic soln was washed with dil HCl,  $NaHCO_3$  aq. water, evaporated to dryness and the residue crystallized from acetone-ether. This yielded needles (380 mg), m.p. 204–205°;  $[\alpha]_D^{+49}$ . (Found: C, 55.59; H, 7.22; O, 27.95; S, 9.31. Calc. for  $C_{11}H_{10}O_6S$ : C, 55.80; H, 7.03; O, 27.87; S, 9.29%.)

**Anhydrodihydroperuvinin (XIII).** The mesylate IIIc (350 mg) in  $\gamma$ -collidine (6 ml) was heated under reflux for 7 hr, diluted then with ether, washed with dil HCl, dried, evaporated to dryness and the gummy residue dissolved in hexane was chromatographed on alumina (6 g). The purified product (80 mg) resisted crystallization. It had IR bands at 1770  $cm^{-1}$  ( $\gamma$ -lactone) and at 1695 and 1610  $cm^{-1}$  (cyclopentenone).

The 2,4-dinitrophenylhydrazones showed m.p. 240° (red prisms from MeOH-ether),  $\lambda_{max}$  (chf) 386  $m\mu$ ;  $\epsilon$  26334. (Found: C, 58.71; H, 5.67; O, 22.64; N, 12.87. Calc. for  $C_{11}H_{10}O_6N_4$ : C, 58.87; H, 5.65; O, 22.41; N, 13.08%.)

**Treatment of epidihydrocumanin dimesylate (XIVb) with NaI.** The mesylate XIVb (350 mg) was treated as described for the prep of VIII. The olefin XV did not crystallize; IR band at 1760  $cm^{-1}$  ( $\gamma$ -lactone). (Found: C, 76.59; H, 9.33; O, 13.75. Calc. for  $C_{11}H_{10}O_3$ : C, 76.88; H, 9.47; O, 13.65%.)

**Treatment of XV with *m*-chloroperbenzoic acid.** The epoxide XVI was prepared according to the procedure employed for IX. Crystallization from hexane yielded material m.p. 104–106°.  $[\alpha]_D^{+77}$ : IR band at 1770  $cm^{-1}$  ( $\gamma$ -lactone). (Found: C, 71.99; H, 8.73; O, 18.88. Calc. for  $C_{11}H_{10}O_3$ : C, 71.79; H, 8.86; O, 19.35%.)

**Dehydration of epidihydrocumanin (XIVa) with  $KHSO_4$ .** An intimate mixture of XIVa (400 mg) and  $KHSO_4$  (2 g) was heated under high vacuum (0.5 mm) until no more sublimate was collected. Crystallization of XVII from acetone-hexane yielded prisms (90 mg), m.p. 118°;  $[\alpha]_D^{+156}$ ;  $\lambda_{max}$  286–292  $m\mu$ ;  $\epsilon$ , 60. IR bands at 1760 ( $\gamma$ -lactone) and at 1735  $cm^{-1}$  (cyclopentanone). (Found: C, 71.69; H, 8.84; O, 19.35. Calc. for  $C_{11}H_{10}O_3$ : C, 71.79; H, 8.86; O, 19.35%.)

**Alkaline treatment of the ketone IV.** A soln of IV (80 mg) in MeOH (6 ml) was mixed with  $KHCO_3$  (100 mg) in water (2 ml), the mixture was heated under reflux for 1 hr, diluted with water and evaporated to dryness. Crystallization of the residue from ether-hexane yielded XVIII as prisms (25 mg) m.p. 117–120°;  $[\alpha]_D^{+55}$ ;  $\lambda_{max}$  286–292  $m\mu$ ;  $\epsilon$ , 60; IR bands at 1760  $cm^{-1}$  ( $\gamma$ -lactone) and at 1740  $cm^{-1}$  (cyclopentanone). (Found: C, 71.89; H, 8.81; O, 19.34. Calc. for  $C_{11}H_{10}O_3$ : C, 71.79; H, 8.86; O, 19.35%.)

**Formation of the ketone XII from the acetate XI.** A soln of XI (300 mg) in MeOH (20 ml) was treated with 5 ml 20% HCl, heated under reflux for 3 hr, concentrated to half its volume, diluted with water and extracted with AcOEt. The organic solution was washed with water and evaporated to dryness. The residue dissolved in acetone (10 ml) was oxidized with 8N  $CrO_3$ , diluted with water, extracted with AcOEt, washed with water dried and evaporated to dryness. Crystallization of the residue from acetone-hexane yielded plates (70 mg), m.p. 146–147°.  $[\alpha]_D^{+128}$ . Identified by the standard methods with the product of the same structure obtained from cumenin (V).<sup>9</sup>