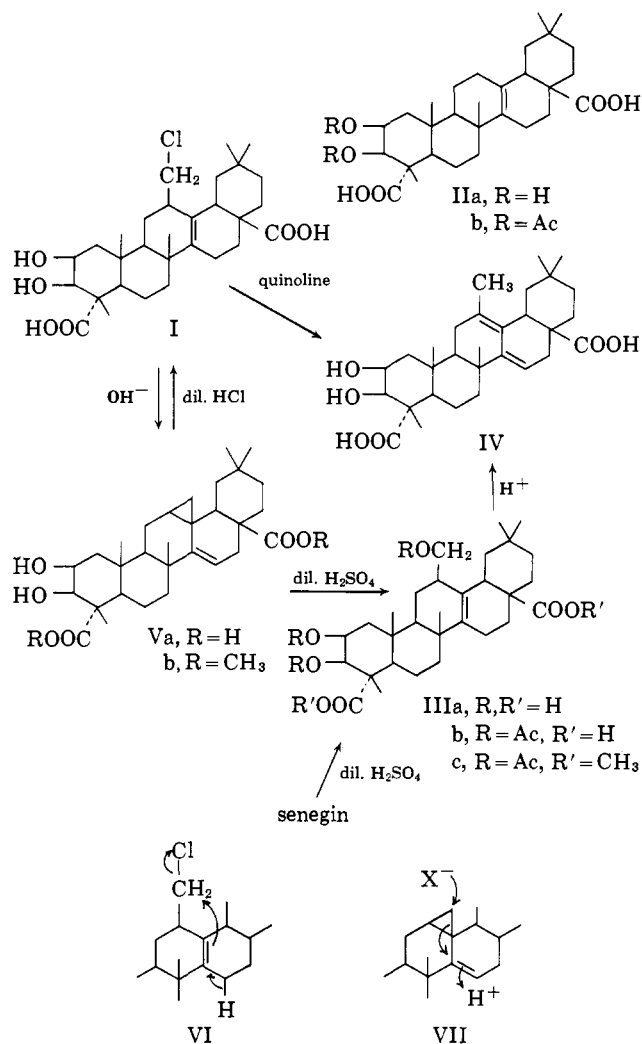


tion from aqueous alcohol gave in 30% yield⁶ a chlorine-free compound, C₃₀H₄₄O₆, designated as *cyclosenegenin*, m.p. 302–305° (with effervescence), [α]_D²² +57.8° (c 0.81, EtOH).

Surprisingly, when the compound was warmed briefly with dilute hydrochloric acid re-introduction of chlorine occurred to give senegenin (I) in almost quantitative yields. Furthermore, when treated with dilute sulfuric acid, it gave the previously described triol IIIa and a small amount of the diene IV. The following spectral data lead to the assignment of structure Va to this compound. The ultraviolet spectrum of Va has no diene absorption but a maximum at 209 mμ (ε 6780, EtOH), consistent with the presence of a conjugated cyclopropane.⁷

The p.m.r. spectra of Va taken in pyridine shows two complex signals at τ 9.94 and 9.47.⁸ The noncrystalline methyl ester Va shows one spot on a thin-layer chromatograph, has also two complex peaks centered at τ 10.11 and 9.61,⁸ besides a broad signal at τ 4.47 for one vinylic proton and others at τ 9.09 (9 H), 8.76 (3 H), and 8.67 (3 H) for five methyl groups and at τ 6.39 (3 H) and 6.30 (3 H) for two methyl esters. Those signals at high field near τ 10.00 are characteristic of a cyclopropane hydrogen.⁹ The infrared spectrum of Vb shows a weak absorption at 3050 cm.⁻¹ with an inflection at 3070 cm.⁻¹.¹⁰ These data can be explained reasonably by assuming a 12,13-methylen-14-ene structure for V, which results from the solvolytic removal of chlorine with the concomitant formation of the cyclopropane ring and abstraction of a hydrogen at C-15¹¹ (see VI).

The reaction from Va to I or IIIa involves non-Markovnikov cleavage of the cyclopropane ring caused by the protonation on the double bond as shown in VII.¹² These results suggest that cyclosenegenin (Va) may be the primary sapogenin which gives rise to senegenin on treatment with alcoholic HCl. Also the



(6) The mother liquors contain a crystalline mixture, whose ultraviolet spectrum shows a composite of the diene (IV) (λ_{\max} 249 mμ) and Va (λ_{\max} 209 mμ, *vide infra*). An approximate calculation from the relative intensities gives a ratio of about 1:2 (IV:Va).

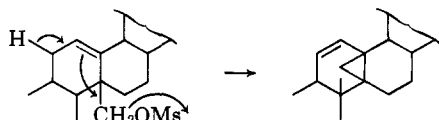
(7) 3α,5-Cyclo-Δ⁶-cholestene absorbs at λ_{\max} 207.5 mμ [R. A. Micheli and T. H. Applewhite, *J. Org. Chem.*, **27**, 245 (1962)], and many other vinylcyclopropanes are reported to have maxima around 210 mμ with extinction between 5300 and 12,000. Cf. A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," The Macmillan Co., New York, N. Y., 1964, p. 49, and also O. L. Chapman, G. W. Borden, R. W. King, and B. Winkler, *J. Am. Chem. Soc.*, **86**, 2660 (1964).

(8) The measurement was done with and without tetramethylsilane as an internal standard.

(9) There are many examples. Among them, 20-methylamino-12β,18-cyclopregnan-3β-ol was reported to have two complex peaks at τ 10.08 and 9.67 by V. Georgian, J. F. Kerwin, M. E. Wolff, and F. F. Owings [*J. Am. Chem. Soc.*, **84**, 3954 (1962)], and 4α,5-methylenecholestane a complex peak at τ 10.00 by K. Kocsis, P. G. Ferrini, D. Arigoni, and O. Jeger [*Helv. Chim. Acta*, **43**, 2178 (1960)].

(10) A. R. H. Cole [*J. Chem. Soc.*, 3807, 3810 (1954)] reported 3042–3058 cm.⁻¹ for the cyclopropane C–H stretching, *e.g.*, i-cholestane shows a peak at 3050 cm.⁻¹.

(11) A similar reaction was utilized in the synthesis of phyllanthol [A. Zürcher, O. Jeger, and L. Ruzicka, *Helv. Chim. Acta*, **37**, 2145 (1954)].



The *i*-steroid rearrangement is also an analogous case, but here the attack of hydroxyl ion, instead of proton abstraction, usually takes place.

(12) Cyclopropanes usually open according to Markovnikov's rule [D. H. R. Barton, J. E. Page, and E. W. Warnhoff, *J. Chem. Soc.*, 2715 (1954)], but with a conjugated cyclopropane protonation takes place first on the double bond, which leads to non-Markovnikov opening [cf. V. Georgian, J. F. Kerwin, M. E. Wolff, and F. F. Owings, *ref. 9*].

interconversion of I and Va explains the contradictory reports concerning the recovery of senegenin when boiled with alkali.¹³

Acknowledgment. This work was supported in part by Grant GM 10966 from the National Institutes of Health, U. S. Public Health Service.

(13) Although Jacobs and Isler reported that senegenin was not recovered after consumption of three equivalents of alkali,³ in some unpublished experiments in our laboratory it was recovered.

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Structure of Piericidin A

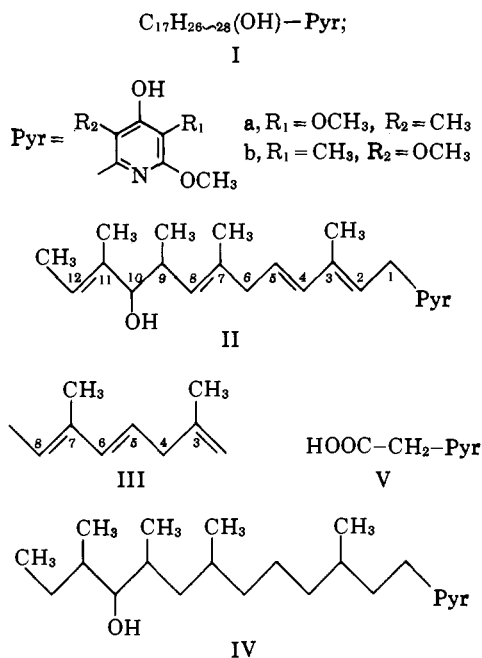
Sir:

Piericidin A (PA) is a new insecticidal metabolite of *Streptomyces mobaraensis* and its isolation,¹ physiological activity, functional groups,² and partial structure³ Ia or Ib have been presented in previous papers. We wish now to report evidence which allows the assign-

(1) S. Tamura, N. Takahashi, S. Miyamoto, R. Mori, S. Suzuki, and J. Nagatsu, *Agr. Biol. Chem.* (Tokyo), **27**, 576 (1963).

(2) N. Takahashi, A. Suzuki, S. Miyamoto, R. Mori, and S. Tamura, *ibid.*, **27**, 583 (1963).

(3) N. Takahashi, A. Suzuki, and S. Tamura, *ibid.*, **27**, 798 (1963).



ment of structure IIa to PA, $C_{25}H_{37}NO_4$,⁴ and IVa to octahydropiericidin A (HPA), $C_{25}H_{45}NO_4$.

The n.m.r.⁵ spectrum of HPA shows that its side chain contains a secondary hydroxyl (1 H, m, δ 3.00; shifts to δ 4.60 on acetylation) and five methyl groups (15 H, δ 0.8–1.2). Nitric acid oxidation of HPA gives 2-methylbutyric acid, suggesting the presence of partial structure $CH_3CH_2CH(CH_3)CH(OH)-$. This was also confirmed by the following series of reactions: the C_{18} -keto acid,³ derived from HPA diacetate through ozonolysis, hydrolysis, and chromium trioxide oxidation, was treated with trifluoroacetic acid to give a mixture of two isomeric ester acids, $C_{18}H_{34}O_4$. On hydrolysis, this mixture gave 2-methylbutyric acid together with a C_{13} -hydroxy acid VII, $C_{13}H_{26}O_3$, and a C_{14} -dicarboxylic acid VIII, $C_{14}H_{26}O_4$. Oxidation of VII with chromium trioxide afforded a C_{13} -keto acid IX, $C_{13}H_{24}O_3$, containing a methyl keto group, which was further oxidized to a C_{12} -dicarboxylic acid X, $C_{12}H_{22}O_4$, with sodium hypobromite. Treatment of IX with trifluoroacetic acid followed by hydrolysis and chromium trioxide oxidation gave a C_{11} -dicarboxylic acid XI, $C_{11}H_{20}O_4$. Comparison of the n.m.r. spectrum of XI ester (two 3 H, d, δ 1.09 and 0.86) with that of X ester (6 H, t, δ 0.9–0.8) in the methyl region reveals the presence of a methyl group (3 H, d, δ 1.09) at an α -position to a carboxyl group in XI. α -Bromination of the acyl chloride of VIII in thionyl chloride, followed by hydrolysis and chromium trioxide oxidation, yielded a C_{14} - α -oxo- α' -hydroxydicarboxylic acid XII, $C_{14}H_{24}O_6$. The n.m.r. spectrum of XII ester shows an octet of AB protons of ABX type⁶ in δ 3.0–2.2 ($J_{AB} = 16$,⁷ $J_{AX} = 6$, and $J_{BX} = 7$ c.p.s.) due to the methylene in the system $-CH(CH_3)CH_2COCOOCH_3$. This indicates the presence of a methyl group in the γ -position to the

(4) One of the two possible formulas proposed previously, $C_{25}H_{37}NO_4$ is compatible with the degradative evidence described in this paper.

(5) Chemical shifts are expressed in δ -values (p.p.m.) from tetramethylsilane as internal standard.

(6) L. M. Jackman, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 102.

(7) T. Takahashi, *Tetrahedron Letters*, 565 (1964).

carboxyl group in XII. Thus structures of XI, X, VIII, XII, and VII should be 2,6-dimethylnonanedioic, 3,7-dimethyldecanedioic, 2,4,8-trimethylundecanedioic, 2-hydroxy-2,4,8-trimethyl-10-oxoundecanedioic, and 10-hydroxy-4,8-dimethylundecanoic acids, respectively. Mass spectra of IX, X, and XI esters gave the following fragmentation patterns as deduced from their structures: 242 (M^+), 211 ($M - 31$), and 185 ($M - 57 = \text{acetone}$) in IX ester; 227 ($M - 31$) and 112 (β -methyl)⁸ in X ester; 213 ($M - 31$) and 88 (α -methyl)⁹ in XI ester. Finally the ester of X was synthesized from 2,6-dimethylheptanedioic acid¹⁰ by an unambiguous route. This synthetic sample was identical with the C_{12} -diester from the natural source in all respects (infrared, n.m.r., and mass spectra). Thus the positions of all substituents (five methyls and a secondary hydroxyl group) in the side chain of HPA have been assigned definitely.

Consideration of the n.m.r. spectrum of PA and its ozonolysis reaction indicates that the following groups exist in its side chain: $>CH-CH_3$ (3 H, d, δ 0.78); four double bonds (one conjugated diene,¹¹ λ_{max} 239 $m\mu$ ($\log \epsilon$ 4.6)) substituted with four methyl groups (12 H, δ 1.8–1.5) and five hydrogens (5 H, δ 6.2–5.0); $CH_3CH=C<$ (evolution of acetaldehyde on ozonolysis); $=CHCH_2C(CH_3)=$ (2 H, d, δ 2.73); $=CHCH_2Pyr$ (yield of acid II⁸ on ozonolysis, 2 H, d, δ 3.30); $=C-(CH(OH)CH(CH_3)-)$ (1 H, d, δ 3.53; shifts to δ 4.90 on acetylation).

Further investigation of the ozonolysis products of PA diacetate resulted in the isolation of a new acid, acid III (XIII), $C_8H_{12}O_5$, m.p. 98°, different from acids I and II.³ Since XIII contains an acetoxy, a methyl keto, and a carboxyl group, it must have originated from a structural part which is located between two double bonds and contains an acetylated secondary hydroxyl group. On the basis of the HPA structure and the n.m.r. spectrum of XIII (3 H, d, δ 1.30; 6 H, s, δ 2.23; 1 H, m, δ 3.5–3.1; 1 H, d, δ 5.22), XIII must be 3-acetoxy-2-methyl-4-oxopentanoic acid. Only two side chain structures of II and III accommodate all these data. Spin decoupling study¹² of PA not only afforded a rigorous proof to the structure II or III but also revealed precise chemical shifts of "hidden" protons in the olefinic region (H-2, δ 5.30; H-5, 5.48; H-6, 5.95; H-8, 5.12; H-12, 5.35) and methinyl proton (H-9, δ 2.66). The signal of the H-8 (δ 5.12) observed at the highest field of five olefinic protons indicates that it belongs to the isolated double bond,¹³ not the conjugated diene. Although all attempts to differentiate chemically between II and III have been unsuccessful, this n.m.r. evidence shows that II is more probable than III.

The diacetyl evolved on ozonolysis of PA cannot originate from the side chain of II. This is explainable only by decarboxylation of an intermediate, 3,4-dioxo-

(8) F. W. McLafferty, "Mass Spectrometry of Organic Ions," Academic Press Inc., New York, N. Y., 1963, p. 449.

(9) K. Biemann, "Mass Spectrometry: Organic Chemical Applications," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 258.

(10) P. Karrer, F. Benz, R. Morf, H. Raundnitz, M. Stoll, and T. Takahashi, *Helv. Chim. Acta*, 15, 1399 (1932).

(11) In contradiction to the earlier proposal, isolation of acid III excludes the presence of two conjugated dienes in PA.

(12) J. D. Baldeschwieler and E. W. Randall, *Chem. Rev.*, 63, 81 (1963).

(13) (a) ref. 6, p. 61; (b) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance" McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 285

pentanoic acid, derived from decomposition of the pyridine ring of a type along with fission of the C-2 double bond in the side chain.

The presence of this novel polysubstituted pyridine ring was further confirmed by comparison of the ultraviolet spectra of HPA and acid II with that of a new model compound, 4-hydroxy-6-hydroxymethyl-2,3-dimethoxypyridine, synthesized from 2-bromo-6-hydroxymethyl-4-oxo-3-methoxy-(4H)-pyran.¹⁴ Shifts of ultraviolet spectra in neutral, acidic, and basic solutions of these compounds were superimposable. Thus structures IIa and IVa are assigned to PA and HPA, respectively.

(14) (a) T. Yabuta, *J. Chem. Soc.*, **125**, 575 (1924); (b) I. Ichimoto, K. Miyagawa, and C. Tatsumi, *Bull. Univ. Osaka Pref.*, **B15**, 61 (1964).

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Photooxidative Cyclization of Quercetin Pentamethyl Ether

Sir:

Although flavone and quercetin pentamethyl ether (I) have been used as a photosensitizer¹ and ultraviolet absorption filter,² respectively, their irradiation products have not been reported. We have found that whereas intense, short wave length ultraviolet radiation causes extensive degradation and polymerization of I, less energetic treatment (350 m μ) induces a novel and important type of ring closure.

A methanolic solution (2.7 $\times 10^{-3}$ M) of I, freed from oxygen and under pure dry nitrogen, was irradiated in a Pyrex flask set in a photochemical reactor³ for 40 hr., using low pressure mercury lamps at 350 m μ . Light yellow crystals (II) were isolated as the major product in 31% yield.⁴

Compound II is a monomer, C₂₀H₁₈O₇, m.p. 209–210°. *Anal.* Calcd. for C₁₈H₈O₈(OCH₃)₄: C, 64.86; H, 4.90; OCH₃, 33.5. Found: C, 64.6; H, 5.04; OCH₃, 33.1. Ultraviolet maxima appeared at 375, 261, and 243 m μ ; infrared showed a broad peak at 1610–1640 cm⁻¹. The parent compound, I, showed maxima at 339, 264, and 249 m μ and absorption bands in the infrared at 1610 and 1630 cm⁻¹. The n.m.r. spectrum of II gave five singlets at τ 2.90, 3.41, 4.90, 6.03, and 6.14, integrated for 1, 1, 2, 3, and 9 protons, respectively, and two one-proton doublets ($J = 2.5$ c.p.s.) at τ 3.55 and 3.80.

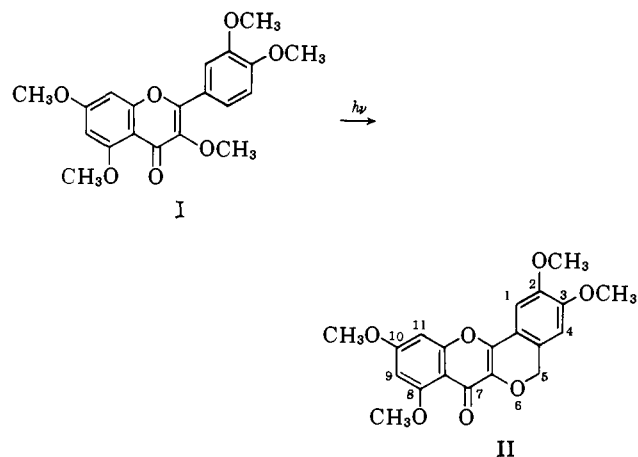
The physical data are in agreement with compound II being 2,3,8-10-tetramethoxy-7-oxo[2]benzopyrano[4,3-b][1]benzopyran, and the reaction occurring as shown.

(1) G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O. Corvan, R. C. Counsell, V. Vogt, and C. Dalton, *J. Am. Chem. Soc.*, **86**, 3197 (1964).

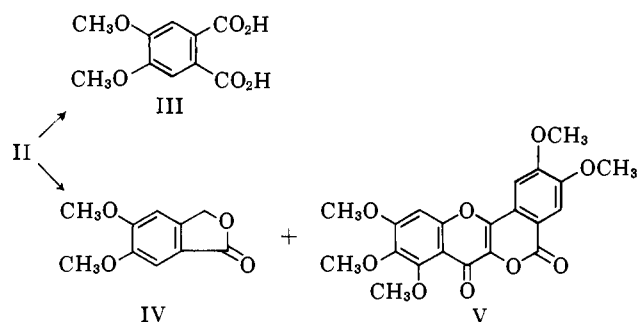
(2) H. Ikeda and K. Toba, *J. Soc. Sci. Phot. Japan*, **18**, 110 (1956).

(3) Available from New England Ultraviolet Co., Middletown, Conn. Reference to a company or product name does not imply approval or recommendation of the product by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

(4) A minor product (16% yield) isomeric with quercetin pentamethyl ether has been isolated. The structure of this compound is under investigation.



The n.m.r. absorption bands at τ 6.03 and 6.14 belong to the four methoxyl groups and the τ 3.55 and 3.80 (doublets, $J = 2.5$ c.p.s.) peaks are attributed to the two *meta* protons at positions 9 and 11, respectively. Since the τ 2.90 and 3.41 peaks are singlets they are assigned to the *para* protons at positions 1 and 4, respectively. The proton at position 1 would be expected to absorb at lower field because of the deshielding effect of its *ortho* α,β -unsaturated substituent. The two-proton singlet at τ 4.90 is reasonably assigned to the benzylic protons.



The structure of II was further supported by chemical evidence. Treatment with magnesium and hydrochloric acid gave a deep red solution typical of flavones.⁵ Oxidation of photoproduct II in basic potassium permanganate solution gave *m*-hemipinic acid (III) which dehydrated during sublimation to its anhydride (m.p. 176–178°). Mild potassium permanganate oxidation of II in acetone yielded a mixture of *m*-meconin (IV, m.p. 155–157°) and the lactone V (m.p. 322–324°). The authenticity of *m*-meconin (IV) and the anhydride of III was demonstrated by comparison with synthetic samples.⁶ The structure of lactone V was determined by elemental analysis (*Anal.* Calcd. for C₂₀H₁₆O₈: C, 62.5; H, 4.20; OCH₃, 32.6. Found: C, 62.6; H, 4.25; OCH₃, 32.2) and infrared and ultraviolet spectroscopic data (ν_{KBr} 1730 cm⁻¹; $\lambda_{\text{max}}^{\text{MeOH}}$ 362, 348, 270, and 262 m μ). The absorption of benzylic protons originally observed at τ 4.90 in the n.m.r. spectrum of photoproduct II is absent in lactone V.

It is interesting to note that, although various photooxidative condensations between aromatic nuclei have been reported,⁷ this is the first example of photooxidative

(5) J. Shinoda, *J. Pharm. Soc. Japan*, **48**, 214 (1928).

(6) G. A. Edwards, W. H. Perkin, Jr., and F. W. Stoye, *J. Chem. Soc.*, 195 (1925).

(7) (a) P. de Mayo, R. A. Raphael, E. C. Taylor, and H. Wynberg, *Advan. Org. Chem.*, **2**, 367 (1960); (b) A. Schönberg, "Präparative Or-