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# EVONINE, AN ALKALOID OBTAINED FROM EUONYMUS SIEBOLDIANA BLUME. II.

## THE STRUCTURE OF EVONINE

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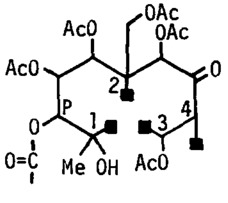
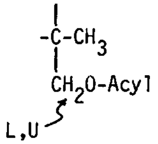
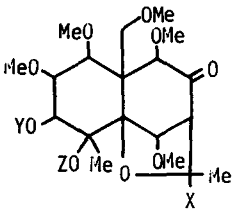
In the previous paper[1] we reported the partial structure (A) of the sesquiterpene part of evonine, $C_{36}H_{43}NO_{17}$, an alkaloid isolated from Euonymus Sieboldiana Blume.
In this paper the whole structure of evonine is presented.



(A)



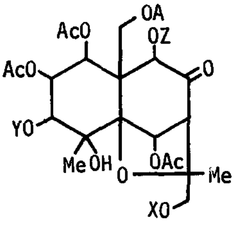
(B)



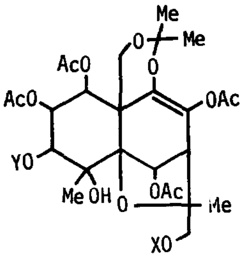
1: X=CH$_2$O-Acyl; Y=Acyl; Z=H
2: X=CH$_2$OH; Y=Z=H
3: X=CH$_2$OH; Y,Z=isopropylidene
4: X=CHO; Y,Z=isopropylidene

Methanolysis of pentamethyl ether 1[1] (MeONa-MeOH, room temperature, 10 hr) gave dimethyl evoninate 22[1,2] and a pentamethyl ether triol 2 [mp 116-121°; $C_{20}H_{34}O_{10}$; mass 402 ($M^+$-32)].[3] The acetonide 3 [mp 195-200°; $C_{23}H_{38}O_{10}$; mass 459 ($M^+$-15)] of 2 was obtained by treatment with 2,2-dimethoxypropane - camphor sulfonic acid (50°, 3 hr), which was oxidized with $CrO_3$-pyridine (room temperature, 12 hr), affording an aldehyde 4 [mp 150-154° ; $C_{23}H_{36}O_{10}$; NMR $CDCl_3$, $\delta$ 9.80 (s, CHO): mass 457 ($M^+$-15)].[4] Since the nuclear magnetic double resonance experiment revealed the presence of a long range coupling ($J = \sim 1$ Hz) between a tertiary methyl and the hydroxymethyl discussed above, a structural unit (B) was proved to be present in evonine.

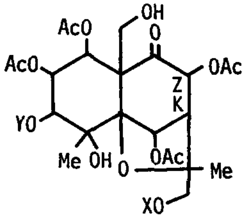
An acetonide triacetate 5[1] could further be acetylated with $Ac_2O$ - AcONa - pyridine (85-90°, 40 hr), giving an acetonide tetraacetate 6 (amorphous powder). For removal of the isopropylidene group, 6 was treated with aqueous AcOH (1:1) (room temperature, 12 hr) to afford a tetraacetate 7 [mp 196-198°; $C_{34}H_{41}NO_{16}$; mass 569 ($M^+$-150)]. In the NMR spectrum of 7 two protons, $H_Z$ and $H_K$ appeared as a doublet at 5.83 ($J$ = 3 Hz) and 2.63 ($J$ = 3 Hz),



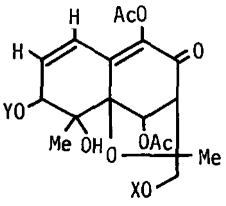
5 : X,Y= OC-(Ev)-CO ;[5] A,Z= >CMe$_2$
11: X=H; Y= OC-(Ev)-COOMe; A=Z=H
12: X=H; Y= OC-(Ev)-COOMe; A,Z=>CMe$_2$



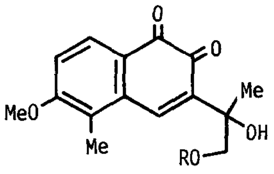
6 : X,Y= OC-(Ev)-CO
13: X=Ac; Y= OC-(Ev)-COOMe



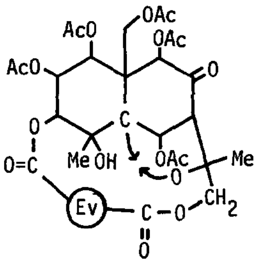
7 : X,Y= OC-(Ev)-CO
14: X=Ac; Y= OC-(Ev)-COOMe



8 : X,Y= OC-(Ev)-CO
15: X=Ac; Y= OC-(Ev)-COOMe



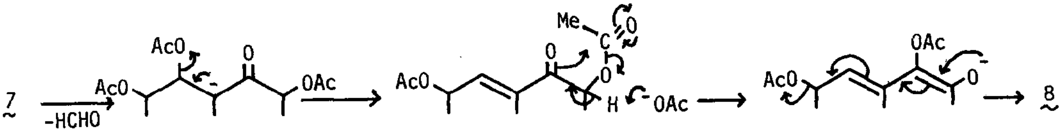
9 : R= OC-(Ev)-COOH
10: R= OC-(Ev)-COOMe
16: R=Ac



(C)

respectively, indicating that the transposition between the carbonyl and the hydroxyl of the α-ketol grouping in 5 took place to give 7.

The derivative 7 was treated with NaOAc-MeOH (refluxing temperature, 25 min), affording a dienone 8 [mp 156-158°; $C_{29}H_{31}NO_{11}$; mass 569 ($M^+$)], the structure of which was established by spectral data.[6] During the reaction (7⟶8) formaldehyde and two moles of AcOH were lost and this finding is rationalized as shown below.

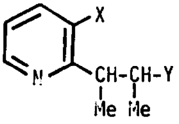


On further treatment of the dienone 8 with NaOAc-MeOH (refluxing temperature, 20 hr) an orange-red amorphous compound 9 was obtained, which was esterified with MeOH-HCl, affording the methyl ester 10 [amorphous powder; $C_{27}H_{29}NO_8$; mass 495 ($M^+$), 497 ($M^+$+ 2)], which was deduced to be a 1,2-naphthoquinone derivative by spectral data.

An attempt was made to obtain a crystalline quinone derivative as follows.
Methanolysis of evonine with NaOMe-MeOH (30°, 12 hr) afforded pentadesacetyl evonine methyl ester 11 (amorphous powder), which formed an acetonide ester 12 [amorphous powder; $C_{30}H_{41}NO_{13}$; mass 623 ($M^+$)]. In 12 one of the diester linkages of evoninic acid underwent methanolysis: a signal due to a methyl ester appeared at δ 3.93 ppm and it was shown that while no significant shift of a doublet of $H_P$ was observed, a doublet of $H_U$ shifted to a higher field in the NMR spectrum [see formulas (A) and (B)]. By applying a series of reactions used in transformation of 5 to 9, orange-red crystals [mp 146-147.5°; $C_{17}H_{18}O_6$; mass 318 ($M^+$), 320 ($M^+$+2), ratio of intensity 1:4] were obtained from 12 through the following intermediates: 13 (amorphous powder), 14 (amorphous powder), and 15 [amorphous powder; $C_{32}H_{37}NO_{13}$; mass 643 ($M^+$)].
From the NMR spectrum of the orange-red crystals [δ ($CDCl_3$) 8.03 (1H, s), 7.97 (1H, d, J = 8.3 Hz), 6.85 (1H, d, J = 8.3 Hz), 4.44 (2H, s), 3.95 (3H, s), 2.37 (3H, s), 2.05 (3H, s), and 1.56 (3H, s)], the presence of the following groups was indicated: three aromatic protons (two vicinal ones and an isolated one), $CH_2OAc$, a tertiary methyl, an aromatic methyl, and a methoxyl.[7] The UV spectrum of this compound [$\lambda_{max}^{EtOH}$ 218 (ε 17,000), 244 (ε 12,000), 280 (ε 16,000), 405 nm (ε 6,700)] was quite similar to that of mansonone D,[8] a 1,2-naphthoquinone derivative. This compound showed a strong $M^+$+2 peak in the mass spectrum, which is a well-known feature of 1,2-naphthoquinones.[9]

Among fifteen carbons of the sesquiterpene component the partial structures (A) and (B) account for fourteen ones; the remaining one is a quaternary carbon, which is evidently bonded to carbons, C-1, C-2, and C-3 and not to C-4 in (A), considering the formation of a 1,2-naphthoquinone derivative. The three carbon unit (B) is therefore attached to C-4 of (A). On the basis of this consideration the structure of the orange-red crystals is established as 16.
Among ten oxygens in the sesquiterpene part nine ones were well characterized, and the remaining one was deduced to be ethereal.[1] A tertiary hydroxyl present in the 1,2-naphthoquinone 16 must be due to the ethereal oxygen of 14, indicating the partial structure (C), which, by making a bond between two atoms bearing an arrow mark, is led to the complete structure of the sesquiterpene part.

The remaining problem to be settled is the one regarding two ester linkages formed between evoninic acid and the sesquiterpene group. During the reaction of forming the 1,2-naphthoquinone (15 ⟶ 16) evoninic acid monomethyl ester (D) was formed, the structure of



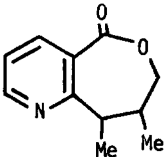
17: X=COOMe; Y=COOH

18: X=COOH; Y=COOMe

19: X=Y=$CH_2OH$

20: X=COOMe; Y=$CH_2OH$

22: X=Y=COOMe



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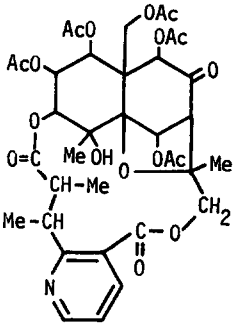

23

which is either 17 or 18. The diol 19[2] obtained by $LiAlH_4$ reduction of evonine was oxidized with $MnO_2$ in benzene (refluxing temperature, 5 hr), affording a lactone 21 [liquid; $C_{11}H_{13}NO_2$; mass 191 ($M^+$)], which was converted to a hydroxy ester 20 by treatment with NaOMe-MeOH (room temperature, 12 hr). Oxidation of 20 with $CrO_3$-pyridine (50°, 12 hr) gave 17, which was found to be identical with the one (D) obtained in the reaction 15 ⟶ 16.

The entire structure of evonine was thus determined, which is represented by 23.

## REFERENCES AND FOOTNOTES

1) H. Wada, Y. Shizuri, K. Yamada, and Y. Hirata, Tetrahedron Letters, this issue.

2) M. Pailer and R. Libiseller, Monatsh. Chem., **93**, 403, 511 (1962).

3) Satisfactory analytical results were obtained for all crystalline compounds. The molecular formulas of amorphous compounds were established by high-resolution mass spectrometry.

4) It should be noted that methylene protons of the hydroxymethyl group showed a typical AX-type pattern [a broad doublet (J = 11.7 Hz) at 6.04 and a doublet (J = 11.7 Hz) at 3.76].

5) For convenience evoninic acid[2] is represented by HOOC-Ⓔⓥ-COOH.

6) UV(EtOH) 225 (ε 8,000), 287 nm (ε 15,000); IR($CHCl_3$) 1775(shoulder), 1740(broad), 1700, 1623 $cm^{-1}$; NMR(δ, $CDCl_3$) 5.13 (d, J=5.3 Hz), 6.35 (dd, J=5.3, 9.8 Hz), 6.58 (d, J=9.8 Hz).

7) The origin of the methoxy group in 16 is methanol employed as solvent, since an ethoxy group was present in the product obtained in the reaction using ethanol as solvent.

8) G. B. Marini Bettolo, C. G. Casinovi, and C. Galeffi, Tetrahedron Letters, 4857 (1965).

9) R. W. A. Oliver and R. M. Rashman, J. Chem. Soc. (B), 1141 (1968).