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THE STRUCTURES OF WILFORDINE AND A NEW ALKALOID ALATAMINE, OBTAINED FROM *EUONYMUS ALATUS* FORMA *STRIATUS* (THUNB.) MAKINO

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The structures of complex alkaloids of *Celastraceae* family have recently been elucidated (e.g., evonine).[1,2,3] In our continuing studies on alkaloidal components of *Celastraceae* family we have isolated several alkaloids from *Euonymus alatus* forma *striatus* (thunb.) Makino (Japanese name, Komayumi) evonine **1**,[2,3] euonymine,[2] wilfordine **5**,[4] and a new alkaloid alatamine **6**,[5] mp 185-193° (MeOH), $C_{41}H_{45}NO_{18}$, $[\alpha]_D^{22°}$ + 44° (c 1.08 $CHCl_3$), UV (EtOH) 233 (ε 24,400), 272 nm (5,300), IR ($CHCl_3$) 3540, 1750 (broad), 1603, 1588, 1576 cm^{-1}, mass 839 (M^+), NMR (Table).

I. Relationship of wilfordine **5** and alatamine **6**

Wilfordine **5** was first isolated in 1950, and some structural studies were performed by Acree and Haller,[6] and Beroza,[7,8] which are summarized below.

$$C_{43}H_{49}NO_{19} \xrightarrow{8\ H_2O} C_{15}H_{26}O_{10} + \underset{(5\ \text{moles})}{\text{AcOH}} + \text{benzoic acid} + \text{hydroxywilfordic acid } \mathbf{16}$$

In the present work, correlation of wilfordine **5** and alatamine **6** was achieved: reduction of **6** ($NaBH_4$/DMF) followed by acetylation (Ac_2O/pyridine) afforded wilfordine **5** and its C-7 epimer.

II. Structure of alatamine **6**

Based on the result described in Section I, alatamine was shown to be the C_{15}-polyhydroxy compound ($C_{15}H_{24}O_{10}$) whose hydroxy groups form seven ester linkages with benzoic acid, hydroxy wilfordic acid **16**,[8] and four moles of acetic acid. The NMR spectrum of alatamine confirmed the presence of four acetate groups (δ 1.95, 2.10, 2.12, 2.24, 3H each), and methanolysis of **6** with NaOMe-MeOH afforded one mole each of methyl benzoate and dimethyl hydroxywilfordate **17**,[9] as expected. The C_{15}-component ($C_{15}H_{24}O_{10}$) of alatamine **6** was deduced to be the same one (evoninol **14**[2e]) that exists in evonine **1**, considering the molecular formulas and the NMR spectra (cf. Table). This view was verified by transforming the both alkaloids (**1**, **6**) into the common derivative 15 (vide post)

In order to establish the positions of benzoate and hydroxywilfordate groups in the C_{15}-component of alatamine 6, the following experiments (i, ii, iii) were performed

i) The close examination of the NMR spectra of alatamine 6 and evonine 1 (cf Table) indicated that the benzoate group was located on one of the possible four positions, C-1, C-2, C-8, and C-11 in evoninol 14 Thus three monobenzoates[9] 2, 3, 4 were synthesized from evonine 1 as model compounds [10] Regarding the chemical shifts of four methines (H-1, H-2, H-3, and H-11) (Table) and four acetate methyls,[11] comparison was made among alatamine 6 and these three benzoates (2, 3, 4), suggesting the position of the benzoate group to be at C-2

ii) The derivative 9[2] of evonine 1 was acetylated (Ac_2O-NaOAc, 45°) giving a mixture of the acetates, the separation of which afforded a pentaacetate 10[9] [11%, amorphous powder, $C_{37}H_{47}NO_{18}$, mass 793 (M^+), NMR (Table)] Benzoylation of 10 (PhCOCl-pyridine) gave a benzoate 11[9] [amorphous powder, $C_{44}H_{51}NO_{19}$, mass 897 (M^+), NMR (Table)], which on catalytic hydrogenation (PtO_2/AcOH) afforded an evoninol derivative 15[12] [amorphous powder, $C_{32}H_{44}O_{16}$, mass 611 (M^+-73), NMR (Table)] and a stereoisomeric mixture of the γ-lactam 18[2e] [liquid, $C_{12}H_{19}NO_3$, mass 225 (M^+)]

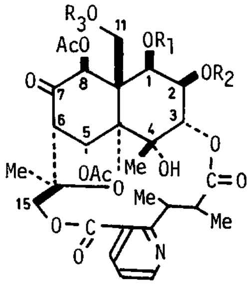
Table NMR Spectral Data (δ in ppm, 60 MHz, $CDCl_3$)

	H-1	H-2	H-3	H-5	H-6	H-8	H-11	H-15
1	5 71 d 3 2	5 29 dd 3 2, 3 2	4 78 d 3 2	6 72 d 1 0	3 04 d 1 0	5 57 s	4 58, 4 82 AB q 13 0	3 78, 6 04 AB q 13 0
5	5 77 d 3 0	*	5 08 d 2 8	6 85 d 1 0	2 40 dd 4 5, 1 0	*	4 21, 5 50 AB q 13 0	3 77, 5 82 AB q 13 0
6	5 90 d 3 5	5 46 dd 3 5, 3 0	5 18 d 3 0	6 82 d 1 0	3 10 d 1 0	5 65 s	4 85 s	3 80, 5 94 AB q 12 0
15	5 81 d 3 2	5 50 dd 3 2, 3 0	3 60 d 3 0	6 62 d 1 0	3 08 d 1 0	5 60 s	4 43, 4 86 AB q 13 0	4 37, 4 60 AB q 12 0
2	6 07 d 3 5	5 42 dd 3 5, 3 0	4 90 d 3 0	6 76 d 1 0	3 07 d 1 0	5 68 s	4 70, 5 12 AB q 13 0	3 79, 6 10 AB q 12 0
3	5 85 d 3 2	5 57 dd 3 2, 3 0	4 95 d 3 0	6 82 d 1 0	3 07 d 1 0	5 63 s	4 70, 5 00 AB q 13 0	3 75, 6 07 AB q 12 0
4	5 78 d 3 2	5 35 dd 3 2, 3 0	4 75 d 3 0	6 70 d 1 0	3 19 d 1 0	5 64 s	4 99 s	3 76, 6 05 AB q 12 0
10	5 64 d 3 2	3 99 dd 3 2, 3 0	4 78 d 3 0	6 56 d 1 0	3 13 d 1 0	5 62 s	*	4 00, 4 38 AB q 12 0
11	5 89 d 3 2	5 45 dd 3 2, 2 8	4 94 d 2 8	6 56 d 1 0	3 13 d 1 0	5 64 s	4 76 s	3 85, 4 23 AB q 12 0
7	5 88 d 3 5	5 45 dd 3 5, 3 0	5 30 d 3 0	6 78 d 1 0	3 12 d 1 0	5 73 s	4 86 s	4 17, 5 72 AB q 12 0
8	5 84 d 3 5	5 46 dd 3 5, 2 8	5 17 d 2 8	5 36 d 1 0	3 17 d 1 0	5 66 s	4 65, 5 02 AB q 13 0	4 03, 5 86 AB q 12 0
12	6 01 d 3 2	5 52 dd 3 2, 3 0	5 30 d 3 0	5 30 d 1 0	3 15 d 1 0	5 73 s	4 67, 5 03 AB q 13 0	3 61, 4 15 AB q 12 0

* This signal appeared in the region of δ 4 5 - 5 5

iii) Acetylation of alatamine 6 (Ac$_2$O-NaOAc, 60°) afforded acetyl alatamine 7[5] [mp 183-189°, $C_{43}H_{47}NO_{19}$, mass 881 (M^+), NMR (Table)] Methanolysis of 7 with NaOMe-MeOH gave a desacetyl derivative 8[9] [amorphous powder, $C_{41}H_{45}NO_{18}$, mass 839 (M^+), NMR (Table)] and a methyl ester 12[9] [amorphous powder, $C_{42}H_{49}NO_{19}$, mass 871 (M^+), NMR (Table)] The NMR spectra of the two compounds 8 and 12 (cf Table) clearly indicated that one of the ester linkages of hydroxywilfordic acid was attached to C-15 Acetylation of 12 (Ac$_2$O-pyridine) gave a hexa-acetate 13[9] [amorphous powder, $C_{46}H_{53}NO_{21}$, mass 955 (M^+)], which on catalytic hydrogenation (PtO$_2$/AcOH) yielded an amorphous piperidine derivative The piperidine derivative was heated in dioxane, giving a stereoisomeric mixture of the δ-lactam 19[9] [liquid, $C_{14}H_{21}NO_5$, mass 283 (M^+)] and the evoninol derivative 15, the latter being identical in all respects with the specimen prepared from evonine 1 as described in ii)

Formation of the common derivative 15 from alatamine 6 and evonine 1 firmly established

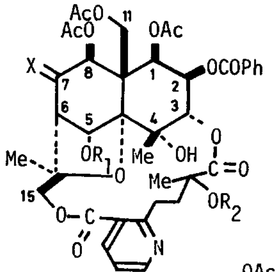


1 $R_1=R_2=R_3$=Ac evonine

2 R_1=PhCO, $R_2=R_3$=Ac

3 $R_1=R_3$=Ac, R_2=PhCO

4 $R_1=R_2$=Ac, R_3=PhCO

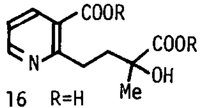


5 R_1=Ac, R_2=H, X=$<^{\mathrm{OAc}}_{\mathrm{H}}$ wilfordine

6 R_1=Ac, R_2=H, X=O alatamine

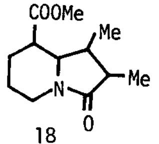
7 R_1=Ac, R_2=Ac, X=O

8 R_1=H, R_2=Ac, X=O



16 R=H

17 R=Me



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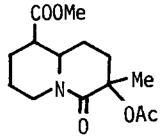

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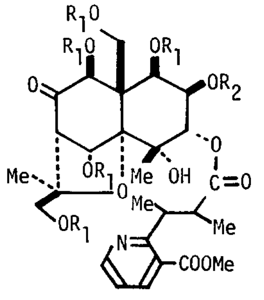
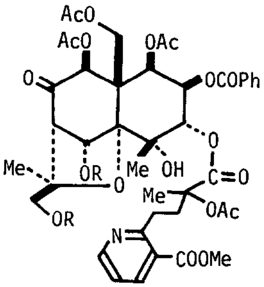


9 R_1=H, R_2=H

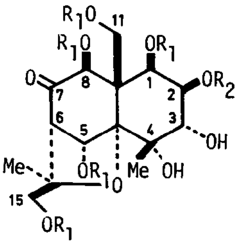
10 R_1=Ac, R_2=H

11 R_1=Ac, R_2=PhCO



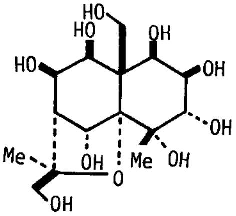
12 R=H

13 R=Ac



14 R_1=H, R_2=H

15 R_1=Ac, R_2=CO



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not only that the C_{15}-component of alatamine 6 was evoninol 14, the component of evonine 1 but also the positions of benzoate (C-2) and four acetate groups (C-1, C-5, C-8, C-11) in alatamine The chemical shift (δ 3 60) of H-3 in 15 (cf δ 5 30 of H-3 in 12) indicated unambiguously that one of the ester linkages of hydroxywilfordic acid was attached to C-3 Further the formation of the stereoisomeric mixture of δ-lactam 19 revealed that the aliphatic carboxyl group of hydroxywilfordic acid was attached to C-3 of evoninol 14 as depicted in 6 Thus the whole structure of alatamine was determined, which is represented by 6

III The structure of wilfordine 5

As described in Section I, correlation was achieved between alatamine 6 and wilfordine 5 In order to establish the stereochemistry at C-7 wilfordine 5 was reduced with $LiAlH_4$ in THF to afford euonyminol 20,[2] the stereochemistry of which was previously established [2] Therefore the structure of wilfordine was determined as 5

Acknowledgement Financial support from the Ministry of Education is deeply appreciated

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3) M Pailer, W Streicher, and J Leitich, Monatsh Chem , 102, 1873 (1971)
4) The identity of our alkaloid with wilfordine was proved by mixed melting points and spectral comparison (solution IR and mass) We express our sincere thanks to Dr M Beroza (USDA, Beltsville, Maryland, U S A) for providing us with wilfordine
5) Elemental analysis for this compound was in accord with theory
6) F Acree, Jr , and H L Haller, J Amer Chem Soc , 72, 1608 (1950)
7) M Beroza, ibid , 73, 3656 (1951), 75, 44 (1953)
8) M Beroza, J Org Chem , 28, 3562 (1963)
9) Elemental composition of this compound was verified by high-resolution mass spectral determination on the molecular ion
10) Monobenzoate 2 was prepared from pentadesacetyl evonine acetonide[2] by the sequence of the following reactions i) $(PhCO)_2O$/Py, ii) $AcOH$-H_2O, iii) Ac_2O/Py Monobenzoate 3 was synthesized from pentadesacetyl evonine[2] by acetylation (Ac_2O-NaOAc) and subsequent benzoylation (PhCOCl/Py) Monobenzoate 4 was prepared from pentadesacetyl evonine triacetate[2] by benzoylation [$(PhCO)_2O$/Py] followed by acetylation (Ac_2O/Py)
11) Signals due to four acetate methyls appeared as follows δ 1 95, 2 10, 2 13, 2 24 in alatamine 6, δ 1 52, 2 05, 2 20, 2 26 in 2, δ 1 90, 2 10, 2 10, 2 25 in 3, δ 1 92, 2 06, 2 25, 2 25 in 4
12) The molecular formula ($C_{32}H_{44}O_{16}$) of this amorphous compound lacking the M^+ peak in the mass spectrum was deduced by the NMR spectral analysis and by considering the molecular formulas of 11 and 18