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ISOLATION AND STRUCTURES OF A NEW ALKALOID ALATAMINE AND AN INSECTICIDAL ALKALOID WILFORDINE FROM *EUONYMUS ALATUS* FORMA *STRIATUS* (THUNB.) MAKINO.

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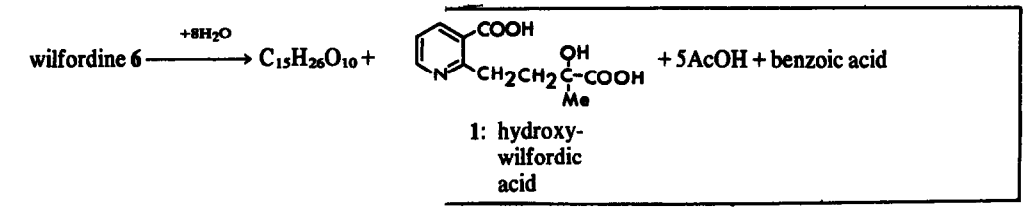
Abstract—A new alkaloid alatamine **5** and an insecticidal alkaloid wilfordine **6** were isolated together with evonine **2**, neo-evonine **3**, and euonymine **4** from *Euonymus alatus* forma *striatus* (Thunb.) Makino (family *Celastraceae*). The structures of alatamine **5** and wilfordine **6** were fully established by chemical and spectroscopic methods. Transformation of alatamine **5** to wilfordine **6** was made.

Although the presence of alkaloids in the family *Celastraceae* has for a long time been known,[1] and isolation[2,3,9] of a few alkaloids and some structural studies[3,10] were made, complete structural elucidation of a number of new and previously known alkaloids[4] and the related new sesquiterpenes[5] has been carried out only in recent years.

As part of our studies on alkaloids[6] and sesquiterpenoids[7] of the *Euonymus* genus in the family *Celastraceae*, we have examined the alkaloidal components of *Euonymus alatus* forma *striatus* (Thunb.) Makino (Japanese name, Komayumi), and isolated a new alkaloid alatamine **5** and an insecticidal alkaloid wilfordine **6** previously obtained from *Tripergium wilfordii* Hook (family *Celastraceae*). Insecticidal activity of *Tripergium wilfordii* Hook has recorded since 1931,[8] and efforts to extract the active component(s) were made by Acree and Haller[9] and by Beroza,[10a,b] resulting in the isolation of wilfordine as one of the insecticidally active alkaloids of this plant. The results of the structural studies of wilfordine by Beroza, which are summarized below, indicate that wilfordine **6** is a C_{15}-decahydroxy compound which is esterified with hydroxywilfordic acid **1**, benzoic acid, and 5 moles of acetic acid.[10a,c] The structure of hydroxywilfordic acid **1** was determined by Beroza.[10e]



1: hydroxy-wilfordic acid

We have determined the structures of alatamine **5** and wilfordine **6**, and the results were reported as a short communication.[6h] The present paper describes the details of our structural studies on these alkaloids **5** and **6**.

ISOLATION AND STRUCTURES

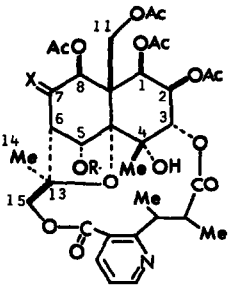
The fruits of *Euonymus alatus* forma *striatus* (Thunb.) Makino were ground in MeOH and the mixture was filtered. The MeOH extract was concentrated to give an aqueous solution, which was shaken with ether repeatedly. The residue obtained on evaporation of the ethereal solution was again dissolved in ether, and the mixture was repeatedly extracted with dil. HCl solution. The aqueous layers were made basic (pH 9) with solid K_2CO_3 and extracted with AcOEt. On removal of AcOEt the crude alkaloidal mixture was obtained, which was chromatographed over silicic acid, affording evonine **2**[4b,6a–f] neoevonine **3**,[6c–f] euonymine **4**,[6c,d,i] alatamine **5**, and wilfordine **6**.[11] The physical and spectral properties of the two alkaloids follow:

Alatamine **5**: $C_{41}H_{45}NO_{18}$; m.p. 185–193°; $[\alpha]_D^{22}+44°$ (*c* 1.08, $CHCl_3$); UV, λ_{max} (EtOH), nm (ϵ) 233 (24,400), 272 (5300); IR ($CHCl_3$) 3540, 3470, 1750 (broad), 1603, 1588, 1576 cm^{-1}; NMR (Table 1); Mass 839 (molecular ion peak).

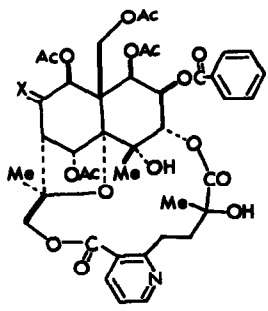
Wilfordine **6**: $C_{43}H_{49}NO_{19}$; m.p. 170–176°; $[\alpha]_D^{22}+5°$ (*c* 5.0, $CHCl_3$); UV λ_{max} (EtOH), nm (ϵ) 232 (22,600), 71 (4400); IR ($CHCl_3$) 3530, 3460, 1745 (broad), 1602, 1585, 1565 cm^{-1}; NMR (Table 1); Mass 883 (molecular ion peak).

Transformation of alatamine **5** *to wilfordine* **6**, *and the structure of the sesquiterpene part of wilfordine* **6**. Comparison of the molecular formulas and the spectral data of alatamine and wilfordine suggests that a keto group in alatamine would exist as a secondary acetoxyl group in wilfordine. This inference was confirmed by transforming alatamine to wilfordine: reduction of alatamine with $NaBH_4$ in DMF followed by acetylation with Ac_2O in pyridine afforded a mixture of two epimers, one of which was identified as wilfordine. Beroza obtained a crystalline C_{15}-compound ($C_{15}H_{26}O_{10}$) by alkaline hydrolysis of wilfordine.[10c] We have confirmed the Beroza's results and obtained the C_{15}-compound more conveniently by reduction of wilfordine with LAH in THF. This C_{15}-compound was proved to be euonyminol **7**, the structure of which was unambiguously established in our laboratory.[6e]

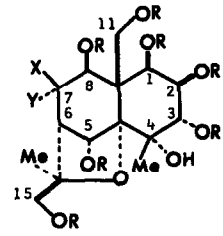
Alatamine **5**. Considering the Beroza's results on



2: R = Ac, X = O (evonine)
3: R = H, X = O (neoevonine)
4: R = Ac, X =  (euonymine)



5: X = O (alatamine)
6: X =  (wilfordine)



7: R = H, X = OH, Y = H
8: R = Ac, X = OAc, Y = H
9: R = Ac, X = H, Y = OAc
10: R = H; X, Y = O

Table 1. NMR spectral data (δ ppm, 60 MHz, $CDCl_3$)

	H-1	H-2	H-3	H-5	H-6	H-8	H-11	H-15
2	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	5.90 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
6	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
11	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
12	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
13	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
20	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
21	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
22	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
25	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
28	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
29	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

* This signal appeared in the region of δ 4.5 - 5.5.

wilfordine **6** (*vide ante*) together with the transformation of alatamine **5** to wilfordine **6**, alatamine was shown to be the C_{15}-polyhydroxy compound ($C_{15}H_{24}O_{10}$) which was esterified with hydroxywilfordic acid **1**, benzoic acid, and four molec of AcOH. The NMR spectrum of alatamine showed the presence of four acetate groups [δ 1.95, 2.10, 2.12, 2.24 (3H each) in $CDCl_3$], and methanolysis of alatamine (MeONa–MeOH) gave one mole each of methyl benzoate and the dimethyl ester of hydroxywilfordic acid **1**, as expected.

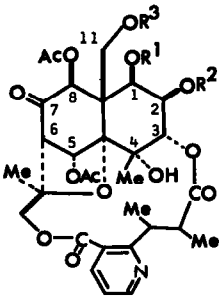
In the NMR spectra (Table 1) the signals due to the C_{15}-part of alatamine **5** was shown to correspond well to those of the sesquiterpene part (evoninol) of evonine **2**, suggesting the sesquiterpene moiety of alatamine **5** to be evoninol **10**. This view was verified by the following findings: (1) alatamine **5** afforded euonyminol octaacetate **8**[6e] and isoeuonyminol octaacetate **9**[6e] in the ratio of 1:2 on reduction with LAH followed by acetylation in the same manner as evonine **2** did;[6e] (2) both alatamine **5** and evonine **2** were transformed to a common evoninol derivative **25** (*vide post*).

In order to establish the positions of the benzoate and hydroxywilfordate groups in the evoninol nucleus **10** of alatamine **5**, experiments included in (A) and (B) were performed.

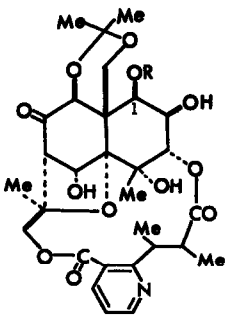
(A) *Concerning the site of the benzoate group in alatamine* **5**. As shown in (B), hydroxywilfordic acid **1** is attached to C-3 and C-15 of the evoninol nucleus **10** in alatamine, the benzoate group in alatamine was expected to occupy one of the possible five positions (C-1, C-2, C-5, C-8, C-11) in the evoninol nucleus. Thus, three monobenzoates **11**, **12**, and **13** were synthesized from evonine **2** as model compounds. The monobenzoate **11** was obtained as follows: pentadesacetyl evonine acetonide **14**[6e] was benzoylated with $(PhCO)_2O$ in pyridine to give **15**, which was subjected to deacetalization followed by acetylation. The position of the benzoate group in **15** was determined by the downfield shift of the NMR signal due to H-1 from δ 4.24 in **14** to δ 5.90 in **15**.

The monobenzoate **12** was synthesized as follows: pentadesacetyl evonine **16**[6e] was acetylated with Ac_2O–AcONa, affording the 2-desacetyl evonine **17**, which on benzoylation with PhCOCl in pyridine yielded **12**. From the NMR spectrum of **17**, OH groups at C-1, C-5, C-8, and C-11 were shown to be acetylated, proving that the position of the benzoate group in **12** is at C-2. The monobenzoate **13** was prepared from pentadesacetyl evonine triacetate **18**:[6e] benzoylation of **18** with $(PhCO)_2O$ in pyridine gave **19**, which on acetylation was led to **13**. In this case again, the site of benzoylation in **19** was detected by the NMR spectral comparison of **18** and **19**.

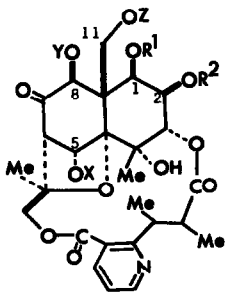
Concerning the chemical shifts of the NMR signals due to H-1, H-2, H-3, and H-11, and due to four acetate methyls (δ 1.95, 2.10, 2.12, 2.24 in alatamine **5**; δ 1.52, 2.05, 2.20, 2.26 in **11**; δ 1.90, 2.10, 2.10, 2.25 in **12**; δ 1.92, 2.06, 2.25, 2.25 in **13**), comparison was made among alatamine **5** and these three benzoates (**11**, **12**, and **13**),



11: R^1 = PhCO, R^2 = R^3 = Ac
12: R^1 = R^3 = Ac, R^2 = PhCO
13: R^1 = R^2 = Ac, R^3 = PhCO



14: R = H
15: R = PhCO



16: R^1 = R^2 = X = Y = Z = H
17: R^1 = X = Y = Z = Ac, R^2 = H
18: R^1 = R^2 = X = Ac, Y = Z = H
19: R^1 = R^2 = X = Ac, Y = H, Z = PhCO

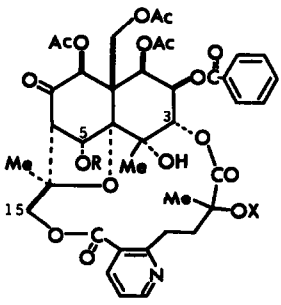
suggesting that the benzoate group would be located at C-2 in alatamine **5**. It should be noted that the chemical shifts of four acetate Me signals of alatamine **5** correspond well to those of **12**, but not to those of **11** and **13**.

(B) *Determination of the sites of the two ester linkages of hydroxywilfordic acid in alatamine* **5**. Acetylation of alatamine **5** with Ac_2O–AcONa gave acetyl alatamine **20**, which on methanolysis (MeONa–MeOH) yielded 5-desacetyl derivative **21** and 5-desacetyl methyl ester **22**. From the NMR spectra of **20**, **21**, and **22** (Table 1) it is evident that deacetylation occurred at C-5 in the reaction, **20**→**21**+**22**. The aromatic carboxyl group of hydroxywilfordic acid **1** could be assigned to be attached to C-15 of the evoninol nucleus in alatamine, if one considers in the NMR spectra the chemical shift (δ 3.89)[6e,f] of the signal of the methyl ester in **22** and the upfield shift of the signal arising from H-15 (Table 1) in the reaction **20**→**22**.

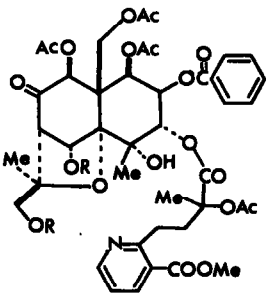
Acetylation of 5-desacetyl methyl ester **22** gave a hexaacetate methyl ester **23**. Catalytic hydrogenation of **23** in the presence of PtO_2 in AcOH afforded a piperidine derivative **24**, which, on intramolecular aminolysis effected by heating in dioxane, was cleaved into an evoninol pentaacetate **25** and a diasteromeric mixture of the δ-lactams **26** [$\nu_{C=O}$(CHCl$_3$) 1735, 1640 cm^{-1}], the former being identical in all respects with the specimen derived from evonine **2** as described later.

Based on the formation of δ-lactams **26** coupled with the finding that the NMR signal of H-3 underwent the upfield shift in the conversion of **22** *via* **23** and **24** to **25** (Table 1), it is clearly indicated that the aliphatic carboxyl group of hydroxywilfordic acid **1** is connected to C-3 of the evoninol nucleus. Therefore, the site of attachment of hydroxywilfordic acid to the evoninol nucleus in alatamine was established. A sequence of reactions (**20**→**22**→**23**→**24**→**25**+**26**) provide a general and unambiguous mean for determining the locations of two ester linkages (macrocyclic bislactone) formed between a sesquiterpene polyol and an unsymmetric dibasic acid, constituents often found in *Celastraceae* alkaloids.

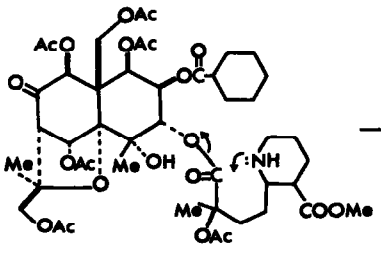
The evoninol derivative **25** discussed above was prepared from evonine **2** as follows. Pentadesacetyl evonine methyl ester **27**[6e] was acelated with Ac_2O–AcONa to give a pentaacetate methyl ester **28**, the structure of which was established by the NMR spectral comparison



20: R = X = Ac
21: R = H, X = Ac



22: R = H
23: R = Ac



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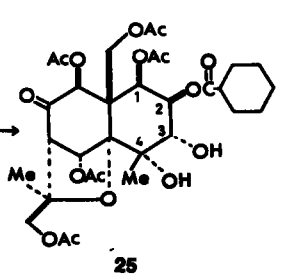
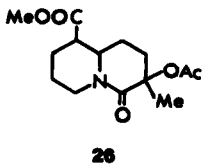


25



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of **27** and **28**: the signal of H-2 was essentially unchanged, whereas those of H-1, H-5, H-8, H-11, and H-15 shifted downfield in the reaction, **27**→**28**. Benzoylation of **28** with PhCOCl in pyridine afforded a benzoate **29** (Table 1). On catalytic hydrogenation (PtO_2–AcOH) the benzoate **29** was split into a stereoisomeric mixture of the γ-lactams **30** [$\nu_{C=O}$($CHCl_3$) 1730, 1670 cm^{-1}] and an evoninol derivative **25**, the latter being found to be identical with the one **25** obtained from alatamine **5**.

Whole structure of alatamine. Formation of the common derivative **25** from alatamine **5** and evonine **2** firmly established not only the sesquiterpene part of alatamine to be evoninol **10**, but also the sites of the benzoate (C-2) and four acetate groupings (C-1, C-5, C-8, C-11) in alatamine. Further, a macrocyclic bislactone in alatamine was proved to be formed between hydroxywilfordic acid **1** and two OH groups at C-3 and C-15 of the evoninol nucleus. Consequently the structure of alatamine was determined as **5**.

Wilfordine **6**. Considering the transformation of alatamine **5** to wilfordine **6** together with the finding that the sesquiterpene part of wilfordine **6** is euonyminol **7** as described above, the structure of wilfordine is represented by **6**.

EXPERIMENTAL

M.ps were uncorrected. UV spectra were measured on a Perkin-Elmer Model 202 spectrophotometer. IR spectra were recorded with JASCO Model IRS and JASCO DS-402G instruments. NMR spectra were obtained using a JNMC-60H instrument: chemical shifts (δ) are reported in ppm downfield from internal TMS: signals arising from the sesquiterpene part are cited. Low resolution mass spectra were determined on a Hitachi RMU-6C mass spectrometer equipped with a direct inlet system. High resolution mass spectra were recorded on a JEOLCO GMS-01SG mass spectrometer. Optical rotations were measured on an Oyo-denki Model MP-1 spectropolarimeter. For tlc and plc silica gel GF_{254}, PF_{254} and alumina GF_{254}, PF_{254}-Type T (E. Merck, A. G., Germany) were used. For column chromatography silicic acid (100 Mesh, Mallinckrodt, U.S.A., and Silica Gel 60, No. 7734, E. Merck, A. G., Germany) were used. Organic solns were washed with sat NaCl aq, dried over Na_2SO_4, and evaporated by vacuum rotary evaporator.

Isolation of alatamine **5** *and wilfordine* **6**. The seeds (*ca* 28 Kg) of *Euonymus alatus* forma *striatus* (Thunb.) Makino collected in October at Mt. Ibuki (Shiga Prefecture) were ground mechanically in MeOH (15 l.). The mixture was filtered with suction. The concentrated soln of the filtrate (*ca* 3 l.) was extracted with five 3–1 portions of ether. The residue obtained on evaporation of the combined ethereal soln was again dissolved in ether (5 l.). The ethereal soln was extracted with five 1–1 portions of 2.5% HCl. The combined aqueous extracts were made basic (pH 9) with solid K_2CO_3, giving ppts. The mixture was extracted with AcOEt five times (5 × 1 l.). The combined AcOEt soln was dried and evaporated to afford an oily alkaloidal mixture (9.4 g). The mixture was chromatographed on silicic acid (300 g). The column was eluted with solvents of increasing polarity, 200 ml fractions being collected [$CHCl_3$ and MeOH–$CHCl_3$ (percentages of MeOH: 0.5, 1, 2, 3 and 5%)]. The following alkaloids were obtained, which are listed in the order of elution: evonine **2** (1.3 g), euonymine **4** (240 mg), neoevonine **3** (60 mg), alatamine **5**, and wilfordine **6**. Alatamine **5** was recrystallized from MeOH to give pure **5** (600 mg). Pure wilfordine **6** (1.2 g) was obtained by recrystallization from EtOH. Physical and spectral data of **5** and **6** are listed in the text. **5** (Found: C, 58.61; H, 5.28; N, 1.67. $C_{41}H_{45}NO_{18}$ requires: C, 58.64; H, 5.40; N, 1.67%). **6** (Found: C, 58.53; H, 5.61; N, 1.52. $C_{43}H_{49}NO_{19}$ requires: C, 58.44; H, 5.55; N, 1.59%).

Transformation of alatamine **5** *to wilfordine* **6**. To a soln of **5** (18 mg) in DMF (1 ml) was added $NaBH_4$ (4 mg). The mixture was stirred at 25° for 2.5 hr, added with AcOH (0.05 ml), and extracted with AcOEt. The AcOEt extract was dried and concentrated. A soln of the residue in Ac_2O (0.5 ml) and pyridine (0.5 ml) was stirred at room temp. overnight and concentrated. A soln of the mixture in AcOEt was washed with sat $NaHCO_3$ aq, dried, and concentrated. The mixture was separated by plc (silica gel) with benzene–AcOEt to give **6** (1.7 mg), m.p. 170–176° after recrystallization from EtOH.

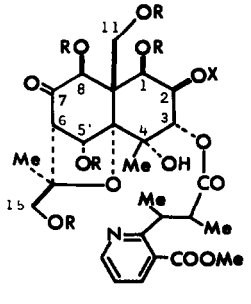
Reduction of wilfordine **6** *with LAH*: *Euonyminol* **7**. A soln of **6** (15 mg) in THF (2 ml) was added with stirring to a soln of LAH (10 mg) in THF (5 ml) under ice-bath cooling. The mixture was stirred at room temp. for 12 hr and diluted with AcOEt to give ppts. These were filtered off, washed with THF (10 ml), and dissolved in AcOH–H_2O (1:1). The soln was passed through a column of ion-exchange resin Amberlite IR-120 (H form). Evaporation of the eluate yielded a colorless residue, recrystallization of which from EtOH afforded pure **7** (6 mg) m.p. 250° (dec). Identification was made by m.m.p. and IR spectral comparison with the authentic specimen.[6a]

Reduction of alatamine **5** *with LAH*: *Euonyminol octaacetate* **8** *and isoeuonyminol octaacetate* **9**. A soln of **5** (60 mg) in THF (2 ml) was added to a soln of LAH (50 mg) in THF (5 ml). The mixture was stirred at room temp. for 12 hr and diluted with AcOEt. The ppts were filtered off with suction and washed with THF (10 ml). A soln of the $p_{r,t}s$ in AcOH–H_2O (1:1) was passed through a column of ion-exchange resin Amberlite IR-120 (H form), the resin being further eluted with H_2O (100 ml). A solid (25 mg) obtained on evaporation of the eluate was dissolved in Ac_2O (1.5 ml)-pyridine (2 ml), and the soln was stirred at 60° for 12 hr. Evaporation of the mixture gave a residue, which was separated by plc (silica gel) with n-hexane–AcOEt, yielding 12 mg of **8** and 15 mg of **9**. Identification of **8** and **9** with authentic specimens was made by m.m.p. and the IR spectral comparison.

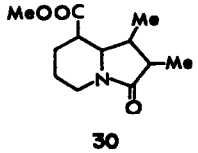
Pentadesacetyl evonine acetonide benzoate **15**. A soln of **14**[6a] (98 mg) and $(PhCO)_2O$ (50 mg) in pyridine (2 ml) was kept at 60° for 12 hr and concentrated. A residue was purified by plc (silica gel) with benzene–AcOEt. Recrystallization from MeOH afforded **15** (110 mg), m.p. 211–213°; IR ($CHCl_3$) 3450, 1725 (broad), 1605, 1585, 1575 cm^{-1}; NMR (60 MHz, $CDCl_3$) 5.90 (1H, d, J = 3.0, H-1), 4.13 (1H, dd, J = 3.0, 2.8, H-2). 4.87 (1H, d, J = 2.8, H-3), 5.25 (1H, d, J = 1.0, H-5), 3.12 (1H, d, J = 1.0, H-6), 4.55 (1H, s, H-8), 3.76 and 6.01 (2H, ABq, J = 13.0, H-15); Mass 695 (M^+). (Found: C, 62.23; H, 5.95; N, 1.97. $C_{36}H_{41}NO_{13}$ requires: C, 62.16; H, 5.90; N, 2.01%).

Monobenzoate **11**. A soln of **15** (90 mg) in 5 ml of AcOH–H_2O (1:1) was stirred at 80° for 4 hr under N_2 and concentrated. A residue was acetylated with Ac_2O (2 ml)–pyridine (2 ml) at room temp. for 12 hr. Evaporation of the mixture gave a residue, which was purified by plc (silica gel) with benzene–AcOEt. Recrystallization from EtOH afforded **11** (54 mg), m.p. 183–186°; IR ($CHCl_3$) 3450, 1755 (broad), 1605, 1585, 1575 cm^{-1}; NMR (Table 1); Mass 823 (M^+). (Found: C, 59.91; H, 5.45; N, 1.79. $C_{41}H_{45}NO_{17}$ requires: C, 59.78; H, 5.47; N, 1.70%).

2-Desacetyl evonine **17**. A mixture of **16**[6a] (200 mg) and AcONa (70 mg) in Ac_2O (4 ml) was stirred at 45° for 12 hr, diluted with



27: R = H, X = H
28: R = Ac, X = H
29: R = Ac, X = PhCO



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MeOH (3 ml), and concentrated. The residue was separated by plc first by silica gel and subsequently by alumina with benzene–AcOEt, affording **2** (118 mg) and **17** (36 mg; amorphous powder). IR ($CHCl_3$) 3460, 1755 (broad), 1590, 1575 cm^{-1}; NMR (60 MHz, $CDCl_3$) 5.57 (1H, d, J = 3.5, H-1), 4.07 (1H, dd, J = 3.5, 3.0, H-2), 4.81 (1H, d, J = 3.0, H-3), 6.75 (1H, d, J = 1.0, H-5), 3.05 (1H, d, J = 1.0, H-6), 5.57 (1H, s, H-8), 1.65 (3H, d, J = 1.0, H-12), 1.57 (3H, s, H-14), 3.75 and 6.03 (2H, ABq, J = 11.0, H-15); Mass 719. (Found: C, 56.90; H, 5.68; N, 1.99. $C_{34}H_{41}NO_{16}$ requires: C, 56.74; H, 5.74; N, 1.95%).

Monobenzoate **12**. A soln of **17** (36 mg) and PhCOCl (0.05 ml) in pyridine (1.5 ml) was stirred at 45° for 36 hr and concentrated. A $CHCl_3$ soln of the residue was washed with sat $NaHCO_3$ aq, dried and concentrated. The residual mixture was separated twice by plc (silica gel) with benzene–AcOEt to give **17** (18 mg) and **12** (15 mg), the latter being recrystallized from MeOH. **12** (11 mg), m.p. 170–178°; IR ($CHCl_3$) 3450, 1750 (broad), 1605, 1585, 1575 cm^{-1}; NMR (Table 1); Mass 823 (M^+). (Found: C, 60.11; H, 5.58; N, 1.63. $C_{41}H_{45}NO_{17}$ requires: C, 59.78; H, 5.47; N, 1.70%).

Pentadesacetyl evonine triacetate benzoate **19**. A soln of **18**[6c] (50 mg) and $(PhCO)_2O$ (20 mg) in pyridine (1 ml) was kept at 50° for 12 hr and concentrated. A $CHCl_3$ soln of the residue was washed with sat $NaHCO_3$ aq, dried, and concentrated. The residue was purified by plc (silica gel) with benzene–AcOEt, affording **19** (46 mg, amorphous powder). IR ($CHCl_3$) 3440, 1755, 1735, 1605, 1590, 1575 cm^{-1}; NMR (60 MHz, $CDCl_3$) 5.92 (1H, d, J = 3.5, H-1), 5.25 (1H, dd, J = 3.5, 3.0, H-2), 4.85 (1H, d, J = 3.0, H-3), 6.68 (1H, d, J = 1.0, H-5), 3.26 (1H, d, J = 1.0, H-6), 4.61 (1H, s, H-8), 4.66 and 4.97 (2H, ABq, J = 12.5, H-11), 1.65 (3H, s, H-12), 1.56 (3H, s, H-14), 3.75 and 6.04 (2H, ABq, J = 11.0, H-15); Mass 781 (M^+). (Found: C, 60.23; H, 5.78; N, 1.54. $C_{39}H_{43}NO_{16}$ requires: C, 59.92; H, 5.51; N, 1.66%).

Monobenzoate **13**. A soln of **19** (40 mg) in Ac_2O (2 ml)-pyridine (2 ml) was kept at room temp. for 12 hr and concentrated. Recrystallization of the residue from EtOH gave **13** (30 mg), m.p. 176–184°; IR ($CHCl_3$) 3520, 1760, 1730, 1605, 1590, 1580 cm^{-1}; NMR (Table 1); Mass 823 (M^+). (Found: C, 59.73; H, 5.62; N, 1.64. $C_{41}H_{45}NO_{17}$ requires: C, 59.78; H, 5.47; N, 1.70%).

Acetyl alatamine **20**. A mixture of **5** (120 mg) and AcONa (50 mg) in Ac_2O (2.5 ml) was stirred at 60° for 18 hr and concentrated. A $CHCl_3$ soln of the mixture was washed with sat $NaHCO_3$ aq, dried, and concentrated. Recrystallization of the residue from EtOH gave **20** (118 mg), m.p. 183–189°; IR ($CHCl_3$) 3450, 1745 (broad), 1600, 1585, 1573 cm^{-1}; NMR (Table 1); Mass 881 (M^+). (Found: C, 58.15; H, 5.22; N, 1.52. $C_{43}H_{47}NO_{19}$ requires: C, 58.47; H, 5.37; N, 1.59%).

Methanolysis of acetyl alatamine **20**: *5-Desacetyl derivative* **21** *and 5-desacetyl methyl ester* **22**. To a soln of **20** (100 mg) in MeOH (8 ml) was added a soln (0.05 ml) of 0.75% NaOMe in MeOH under N_2. The soln was stirred at 0° for 30 min, added to AcOH (0.1 ml), and concentrated. The residual mixture was separated by plc (silica gel) with benzene–AcOEt, giving crystalline **21** (40 mg) and amorphous **22** (44 mg). Recrystallization of the former from MeOH–H_2O afforded pure **21** (35 mg), m.p. 179–184°; IR ($CHCl_3$) 3380, 1760, 1738, 1598, 1585, 1573 cm^{-1}; NMR (Table 1); Mass 839 (M^+). (Found: C, 58.78; H, 5.30; N, 1.73. $C_{41}H_{45}NO_{18}$ requires: C, 58.64; H, 5.40; N, 1.67%). **22**; IR ($CHCl_3$) 3450, 1760, 1740, 1600, 1588, 1575 cm^{-1}; NMR (Table 1); Mass 871 (M^+). [High resolution mass spectrum. Found: 871.2917 (M^+). $C_{42}H_{49}NO_{19}$ requires: 871.2898].

Hexaacetate methyl ester **23**. A soln of **22** (30 mg) in Ac_2O (1.5 ml) and pyridine (1.5 ml) was stirred at room temp. for 12 hr and concentrated. Purification of the product by plc (silica gel) with benzene–AcOEt gave amorphous **23** (33 mg); IR ($CHCl_3$) 3550, 1750 (broad), 1600, 1588, 1575 cm^{-1}; Mass 955 (M^+). [High resolution mass spectrum. Found: 955.3136 (M^+). $C_{46}H_{53}NO_{21}$ requires: 955.3110].

Formation of evoninol pentaacetate **25** *and δ-lactams* **26**. A soln of **23** (22 mg) in AcOH (3 ml) in the presence of PtO_2 (4 mg) was stirred in the atmosphere of H_2 at room temp. for 12 hr. After removal of the catalyst by filtration, the filtrate was concentrated, giving a piperidine derivative **24**, which was dissolved in dioxane (4 ml) and heated at 100° for 12 hr. On removal of solvent there remained a resinous mixture, which was chromatographed on silicic acid with benzene–AcOEt, affording amorphous **25** (10 mg) and *δ*-lactams **26** (6 mg). **25**: IR ($CHCl_3$) 3520, 1750 cm^{-1}; NMR (Table 1); Mass 611 [$M^+ - 73$ (CH_2OAc)]. [High resolution mass spectrum. Found: 611.2359 ($M^+ - 73$). $C_{29}H_{39}O_{14}$ requires: 611.2339]. **26** (four stereoisomers, two of which being the major ones according to the NMR spectral analysis): IR ($CHCl_3$) 1735, 1640 cm^{-1}; Mass 283 (M^+). [High resolution mass spectrum. Found: 283.1401 (M^+). $C_{14}H_{21}NO_5$ requires: 283.1419].

Pentaacetate methyl ester **28**. A mixture of **27**[6a] (300 mg) and AcONa (100 mg) in Ac_2O (10 ml) was stirred at 45° for 12 hr, diluted with MeOH (5 ml), and concentrated. The residue was purified twice by plc (silica gel and alumina) with benzene–AcOEt, affording the starting **27** (186 mg) and amorphous **28** (48 mg); IR ($CHCl_3$) 3460, 1750 (Broad), 1590, 1575 cm^{-1}; NMR (Table 1); Mass 793 (M^+).

Benzoate **29**. A soln of **28** (40 mg) and PhCOCl (0.05 ml) in pyridine (2 ml) was stirred at 45° for 48 hr and concentrated. A $CHCl_3$ soln of the residue was washed with sat $NaHCO_3$ aq, dried, and concentrated. The product was purified by plc (silica gel) twice with benzene–AcOEt, affording amorphous **29** (18 mg); IR ($CHCl_3$) 3400, 1750, 1603, 1590, 1575 cm^{-1}; NMR (Table 1); Mass 897 (M^+). [High resolution mass spectrum. Found: 897.3041 (M^+). $C_{46}H_{51}NO_{19}$ requires: 897.3055].

Formation of evoninol pentaacetate **25** *and γ-lactams* **30**. A soln of **29** (15 mg) in AcOH (2.5 ml) in the presence of PtO_2 (4 mg) was stirred in the atmosphere of H_2 at room temp. for 12 hr. The catalyst was removed by filtration, and the filtrate was concentrated. The mixture was separated by plc (silica gel) with benzene–AcOEt, affording **25** (6 mg) and *γ*-lactams **30** (3.5 mg). **30** (three stereoisomers according to the NMR spectral analysis); IR ($CHCl_3$) 1738, 1675 cm^{-1}; Mass 225 (M^+). [High resolution mass spectrum. Found: 225.1345 (M^+). $C_{12}H_{19}NO_3$ requires: 225.1364].

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