

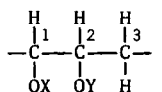
THE STRUCTURE OF ALATOL, A NEW SESQUITERPENE POLYALCOHOL FROM EUONYMUS ALATUS FORMA STRIATUS (THUNB.) MAKINO, AND TRANSFORMATION OF EVONINOL TO ALATOL

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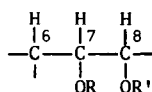
Various sesquiterpene polyalcohols of eudesmane type esterified with aliphatic and aromatic acids have been isolated from Celastraceae family, and their structures elucidated in recent years<sup>1</sup> [e.g., a key representative, evonine (1)<sup>1a</sup>]. In our continuing studies on the constituents of Celastraceae family, we have isolated from Euonymus alatus forma striatus (Thunb.) Makino a new polyester, alatolin, hydrolysis of which afforded a new sesquiterpene hexaol named alatol. In the present paper, the structure of alatol is described, which has been deduced by chemical and spectral means, and unambiguously established by transforming an evoninol derivative (5)<sup>1a</sup> to alatol.

A non-basic fraction from the hexane extract of dried seeds of the plant was chromatographed on silica gel with CHCl<sub>3</sub>, affording the polyester, alatolin C<sub>42</sub>H<sub>44</sub>O<sub>13</sub> (amorphous powder)<sup>7</sup>; ir (CHCl<sub>3</sub>) 1745 (broad), 1595 cm<sup>-1</sup>; mass 756 (M<sup>+</sup>); nmr (Table 1). From the nmr spectrum and the result of the hydrolysis (vide post), alatolin was suggested to contain three acetate and three benzoate ester groups. Further, the presence of the following groups, I, II, and III<sup>2</sup> was indicated by the double resonance (NMR) experiments on alatolin (cf. Table 1).



(X, Y = Acyl)

(I)



(R, R' = Acyl)

(II)



(R = Acyl)

(III)

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Table 1. NMR Spectral Data ( $\delta$  in ppm, 100 MHz, benzene- $d_6$ )

	H-1	H-2	H-3	H-5	H-6	H-7	H-8	H-11
<u>2</u> a)	6.38 d 3.2	6.15 ddd 2.5, 3.2, 3.8	2.34 m	6.77 br.s	2.13 d 3.6	5.92 dd 3.6, 4.0	5.93 d 4.0	4.90, 6.17 AB q 13.0
<u>4</u> b)	5.68 d 3.5	5.65 m	2.23 m	6.80 br.s	2.15 d 2.0	5.63 m	5.59 d 3.8	4.71, 5.43 AB q 13.5

a) Ac  $\times$  3 : 1.45 (3H, s), 1.67 (3H, s), 2.03 (3H, s).

PhCO  $\times$  3 : 6.9 - 8.5 (15H).

Me  $\times$  3 : 1.19 (3H, d, 8.0, H-12), 1.42 (3H, s, H-14), 1.23 (3H, s, H-15).

b) Me  $\times$  3 : 1.11 (3H, d, 7.0, H-12), 1.28 (3H, s, H-14), 1.19 (3H, s, H-15).

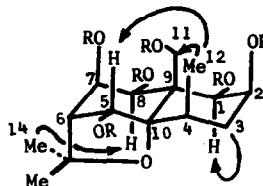
On alkaline hydrolysis (5% NaOH, 45°, 12 hr) alatolin afforded a new sesquiterpene hexaol, alatol (3)<sup>7</sup> C<sub>15</sub>H<sub>26</sub>O<sub>7</sub> [amorphous powder; ir (KBr) 3360 cm<sup>-1</sup> (strong), no C=O bands; mass 318 (M<sup>+</sup>); nmr (CD<sub>3</sub>OD)  $\delta$  1.32 (3H, s), 1.43 (3H, d, J = 6.3 Hz), 1.49 (3H, s), 4.02 (1H, m), 4.21 (1H, d, J = 3.2 Hz), 5.03 (1H, br.s)] and benzoic acid. Acetylation (Ac<sub>2</sub>O - Py, 50°, 13 hr) of alatol (3) provided the hexaacetate (4)<sup>7,8</sup> C<sub>27</sub>H<sub>28</sub>O<sub>13</sub> [mp 205 - 207°, nmr (Table 1)], which has no hydroxyl group (ir spectrum), indicating that alatol is a tricyclic compound containing one ether ring. The nmr spectrum of the hexaacetate (4) revealed the presence of three methyl groups [ $\delta$  1.11 (3H, d, J = 7.0 Hz), 1.19 (3H, s), 1.28 (3H, s)] in addition to six acetate methyls. These structural data of alatol and the hexaacetate (4) in conjunction with the partial structures, I, II, and III suggested the structure of alatol to be 3,<sup>3</sup> assuming that alatol is an eudesmane type sesquiterpene.

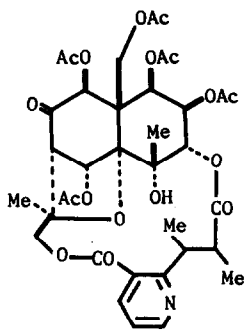
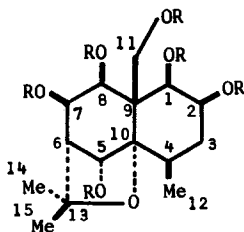
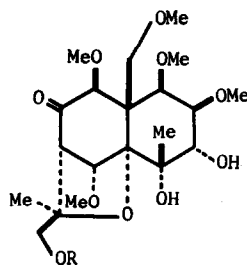
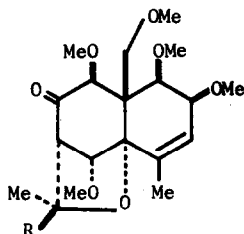
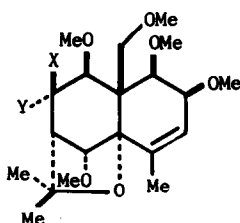
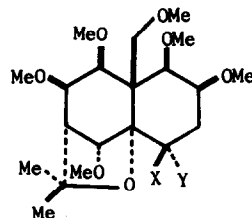
Stereochemistry at C-1, C-4, C-5, C-8, C-9, and C-10 of alatol (3) was deduced by the NOE experiments on alatolin (2) and the hexaacetate (4), the results of which are summarized in Table 2. Further, the coupling constants (J<sub>1,2</sub> = 3.2 Hz, J<sub>7,8</sub> = 4.0 Hz) in the nmr spectrum of alatolin indicated the *cis* relationship between H-1 and H-2, and between H-7 and H-8, respectively. Therefore, the stereostructure of alatol is represented by 3.

Unambiguous proof of the structure of alatol (3) was secured by the transformation of the evoninol derivative (5)<sup>1a</sup> into alatol (3). Evoninol pentamethyl ether (5) was converted (Ph<sub>3</sub>CCl - Py, reflux, 14 hr) to the trityl ether (6)<sup>7,8</sup> (mp 213 - 214°), which on treatment

Table 2. NOE (100 MHz, benzene- $d_6$ )

Compound	Irradiate	Observe	Percentage of enhancement
<u>2</u>	H-3	H-1	14
	H-14	H-8	28
<u>4</u>	H-12	H-11	17
	H-12	H-5	10



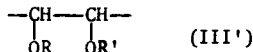
1 (evonine)2 : R = Ac × 3, PhCO × 3 (alatalin)3 : R = H (alatalol)4 : R = Ac5 : R = H6 : R = CPh<sub>3</sub>7 : R = CH<sub>2</sub>OCPH<sub>3</sub>8 : R = CHO9 : R = CH(S)<sub>2</sub>10 : R = Me11a : X = OMe, Y = H11b : X = H, Y = OMe12a : X = Me, Y = H12b : X = H, Y = Me

with ethyl orthoformate in the presence of benzoic acid<sup>4</sup> (160°, 13 hr) afforded the olefin (7)<sup>7,8</sup> (mp 190 - 193°). After removal of the trityl group in 7 (80% AcOH, 80°, 2 hr) the resulting primary hydroxyl group was oxidized (CrO<sub>3</sub> - Py, 20°, 13 hr), affording the aldehyde (8)<sup>7,8</sup> (mp 110 - 112°). Selective monothioacetalization of the aldehyde group in 8 was effected (HSCH<sub>2</sub>CH<sub>2</sub>SH - BF<sub>3</sub>·OEt<sub>2</sub> - CH<sub>2</sub>Cl<sub>2</sub>, 0°, 3 hr), giving the thioacetal (9)<sup>7,8</sup> which on desulfurization [Raney Ni (W-2) - EtOH, reflux, 2 hr] was led to the compound (10)<sup>7,8</sup> (amorphous powder). Reduction of 10 with LiAlH<sub>4</sub> (DME, 25°, 11 hr) and subsequent methylation (MeI - NaH - DMF, 50°, 10 hr) yielded a mixture<sup>5</sup> of two diastereomeric hexamethyl ethers, (11a) and (11b) (ratio, 1:2), which was separated by preparative tlc (silica gel; benzene - EtOAc, 6:5) to give 11a<sup>7,8</sup> (amorphous powder). Catalytic hydrogenation of 11a (5% Pd-C, EtOH, 20°, 12 hr) afforded a mixture<sup>6</sup> of the two diastereomers, (12a) and (12b) (ratio, 3:2). Separation of the mixture by preparative tlc (silica gel; benzene - EtOAc, 1:3) gave 12a<sup>7,8</sup> (amorphous powder), which was treated with BCl<sub>3</sub> (CH<sub>2</sub>Cl<sub>2</sub>, 20°, 14 hr), affording a hexaol identical with alatalol by spectral and chromatographic comparison.

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2. Although the alternative structure (III') was conceivable for this signal ( $\delta$  4.90, 6.17, AB q, J = 13.0 Hz), the part structure (III) was assigned, because the signal due to the CH<sub>2</sub>OR group (C-11) in the eudesmane type polyalcohols so far known<sup>1</sup> appeared usually as an AB quartet as described above.



3. There are three possibilities, C-11, C-14, and C-15 as to the location of the primary hydroxyl group. Considering the close similarity of the signal pattern of CH<sub>2</sub>OR ( $\delta$  4.90, 6.12, AB q, J = 13.0 Hz) in alatolin and that of the C-11 methylene bearing the primary hydroxyl in some known compounds [e.g.,  $\delta$  4.50, 5.13 (AB q, J = 13.5 Hz) in euonymine;<sup>1b</sup>  $\delta$  4.21, 5.50 (AB q, J = 13.0 Hz) in wilfordine<sup>1g</sup>], the primary hydroxyl group was deduced to be at C-11.
4. J. S. Josan and F. W. Eastwood, Aust. J. Chem., 21, 2013 (1968).
5. Reduction of the C-7 keto group in evonine (1) and the related compounds with LiAlH<sub>4</sub> invariably affords a mixture of two diastereomeric alcohols at C-7 in the ratio of 2:1, the minor diastereomer being the one with C-7 $\beta$  hydroxyl (axial OH).<sup>1a,1c</sup> By analogy with those previous findings, the structure (11a) was assigned to the minor product. This assignment was confirmed by transforming 11a to alatol, whose stereochemistry at C-7 was established by nmr spectral data (cf. text).
6. Although inspection of the molecular models suggested the preferential formation of the diastereomer (12a), the stereoselectivity of hydrogenation of 11a was low. The structure (12a) was assigned to the major one, and the validity of this assignment was secured by converting this isomer to alatol, in which stereochemistry at C-4 was determined by NOE experiments (cf. text).
7. Satisfactory microanalyses or high resolution mass spectral data were obtained.
8. Structure assignments are based on ir, nmr, and mass spectral data.