Tetrahedron Letters No. 12, pp 1047 - 1050, 1978. Pergamon Press. Printed in Great Britain.

NONACYCLIC AMIDES FROM LICHENS OF THE GENUS XANTHOPARMELIA

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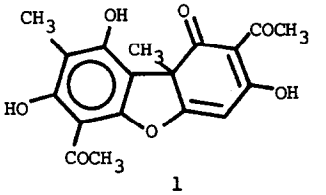
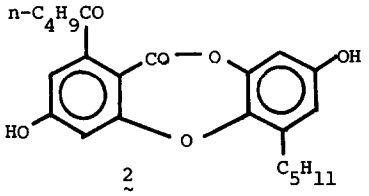
(Received in USA 21 December 1977; received in UK for publication 30 January 1978)

Preparative layer chromatography of the ethereal extracts of a chemical strain of the lichen Xanthoparmelia scabrosa (Tayl.) Hale has led to our isolating four novel nitrogen containing esters[1] in addition to the known metabolites, usnic acid (1) and norlobaridone (2). The multicyclic diol moiety from which natural esters are derived has been termed scabrosin. Hence we describe the new metabolites as scabrosin 4,4'-diacetate (3), m.p. 262°, scabrosin 4-acetate-4'-butyrate (4), m.p. 216.5-217.5°, $[\alpha]_{246}^{25}$ -9600°, scabrosin 4,4'-dibutyrate (5), m.p. 196-7° and scabrosin 4-acetate-4'-hexanoate (6), m.p. 213°.



1



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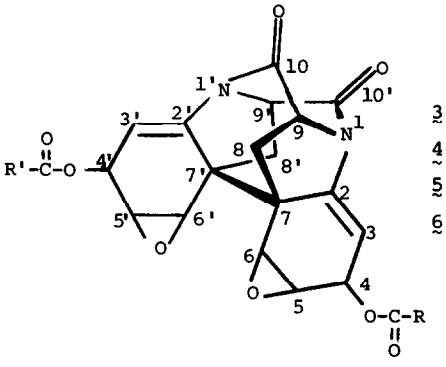
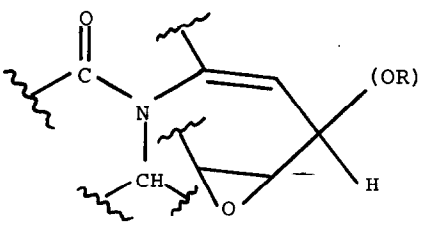


	R	R'
3	CH_3	CH_3
4	CH_3	$n\text{-}C_3H_7$
5	$n\text{-}C_3H_7$	$n\text{-}C_3H_7$
6	CH_3	$n\text{-}C_5H_{11}$

The molecular formula of the scabrosin diesters (3-6) follows from microanalytical data and mass measurements. Infrared absorptions at 1740 and 1710-cm^{-1} indicated the presence of ester carbonyl and non-planar amide functions, but no UV absorption was observed. The alkyl ester side chains were identified from the p.m.r. and ^{13}C n.m.r. spectra and by the facile cleavage of these fragments in the low resolution mass spectra (i.e., peaks at M-60, M-88 and M-116 corresponding to the loss of acetic butyric and hexanoic acids). Alkaline hydrolysis was ineffective and led to the degradation of these compounds.

The multicyclic structure of the esters (3-6) was primarily deduced from evidence provided by the high field (67.89 MHz) ^{13}C n.m.r. spectrum of 4[2] (see Table). The ^{13}C shift assignments were made on the basis of signal intensity and multiplicity, absolute $^{1}J_{^{13}C-^{1}H}$ coupling constants and chemical shift criteria as determined from off-resonance, gated decoupled, nOe suppressed and noise decoupled spectra. The identification of epoxide ring carbons and the nitrogen substituted olefinic group was facilitated by the magnitudes of the $^{1}J_{CH}$ coupling constants[3,4]. Further, the amide carbonyl carbon is characterised by its typical chemical shift (163.38 p.p.m.) as is the nitrogen substituted methine carbon (56.84 p.p.m.). Most significant is the asymmetric nature of 4 (due to the differential substitution) which is indicated by small differences ($\Delta\delta$) in chemical shifts of four pairs of easily distinguishable resonances. The magnitude of $\Delta\delta$ provides a mechanism for locating the asymmetrically substituted carbon atoms in 4. Thus the acetate and butyrate ester side chains are bonded to the methine carbons (65.55 and 65.30 p.p.m.) with the largest $\Delta\delta$ value. Similarly the pair of epoxide carbon resonances (51.48 and 51.44 p.p.m.) and olefinic methine carbons (120.76 and 120.62 p.p.m.) must be located adjacent to the substituent site. The attenuation of the differential substituent effect with distance is demonstrated by the shifts of the quaternary olefinic carbon atoms (138.33 and 138.27 p.p.m.). It is noteworthy that the features of asymmetry in 4 are also exhibited in the highly complex coupled p.m.r. spectrum measured at 270 MHz. In particular, the H3,3' and H5,5' protons show overlapping multiplicities when compared with the corresponding resonances in 3 or 5[5]. With these features in mind and with the remaining two carbon atoms established as quaternary and methylene, the two symmetrical fused $C_9H_7NO_2$ units (excluding the ester side chains) are defined and a partial structure for each unit may be drawn:



The most critical clue to the incorporation of the remaining carbon atoms lies in the fully coupled ^{13}C spectrum. Thus the doublet, triplet, doublet pattern of the methylene group must arise from magnetic non-equivalence of the methylene protons and long range coupling with an adjacent methine proton ($^{1}J_{CH}$ 137, 134 and $^{2}J_{CH}$ 4.8 Hz). The methine carbon of choice is that bound to the nitrogen atom since both epoxide methines exhibit relatively sharp but overlapped couplings. Confirmation of this bonding arrangement is obtained from the p.m.r. spectrum which exhibits a typical AB pattern for the methylene protons (δ2.81 and 3.71 p.p.m. J_{AB} 16.4 Hz), the lower field part of which is differentiated from the higher field part by a vicinal coupling of approximately 1.2 Hz to the adjacent methine proton. A rigid structure (meeting the implied Karplus relationships) is thus indicated. The unique carbon skeleton incorporating all these features is that shown in (3-6).

We postulate that the proposed carbon skeleton may arise bio-synthetically from the intermolecular condensation of two tyrosine molecules to form a diketopiperazine with subsequent intermolecular oxidative coupling and cyclisation. Additional structural, stereochemical and synthetic work is in progress.

References and Notes

1. These metabolites have also been detected (but not structurally identified) in other Parmelia sp., C.F. Culberson, W.L. Culberson and T.L. Esslinger, Bryologist, 80, 125 (1977); and Xanthoparmelia sp. (present authors).
2. Determined using a Bruker HFX-270 spectrometer as described in A.J. Jones, J.A. Elix and U. Engkaninan, Aust. J. Chem., 29, 1947 (1976).
3. L.M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry" (Pergamon Press: New York, 1972), p.347; E.R. Malinowski and N.J. Hobeker, J. Amer. Chem. Soc., 83, 4479 (1961).
4. L.A. Paquette and M.J. Carmody, J. Amer. Chem. Soc., 98, 8975 (1976).

5. The complexity of couplings in the ^1H spectrum of 3 determined at 270 MHz precludes first order analysis. Chemical shift assignments are H3,3' 5.90, H4,4' 5.69, H5,5' 4.34, H6,6' 3.63, H8,8' 2.81 and 3.71 and H9,9' 4.44 p.p.m. A full iterative spectral analysis is in progress.

Table

^{13}C Chemical Shifts[a] of Scabrosin 4-acetate-4'-butyrate (4)

δ (p.p.m.)	Intensity	C-Type	$^1J_{CH}$ value (Hz)	Assignment	Δδ
173.45	1	butyrate carbonyl			
170.78	1	acetate carbonyl			
163.38	2	amide carbonyl		10,10'	
138.33	1	olefinic qC		2,2'	0.06
138.27	1				
120.76	1	olefinic methine	162	3,3'	0.14
120.62	1				
76.64	2	qC		7,7'	
65.55	1	CH hetero-atom substituted	146.3	4,4'	0.25
65.20	1				
56.84	2	CH hetero-atom substituted	146.3	9,9'	
55.48	2	CH epoxide	185	6,6'	
51.48	1	CH epoxide	181	5,5'	0.04
51.44	1				
37.36	2	CH_2 (asymmetric)	137,134	8,8'	
36.21	1	CH_2 butyrate	129.6		
20.83	1	CH_3 acetate	129.6		
18.91	1	CH_2 butyrate	129.6		
13.74	1	CH_3 butyrate	129.6		

[a]Determined for a 0.1M solution in dichloromethane-d_2 with TMS as an internal standard.