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THE STRUCTURE OF AILANTHOL, A NEW TRITERPENOID FROM *AILANTHUS MALABARICA* DC†

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Summary: The structure of ailanthol (1), having the triterpene skeleton (20S)-4,4,8β-trimethyl-14,18-cyclo 5α,13α,14α,17α-cholestane, has been assigned by spectral analysis and X-ray crystal structure determination.

Ailanthus malabarica DC. (Simarubaceae) is a large tree found commonly on the west coast of India.[1] Our earlier investigations of the bark and roots had afforded eight β-carboline alkaloids.[2] From the exudate of the trunk bark, Chawla and Sukh Dev reported the isolation of the triterpenoids malabaricol, epoxymalabaricol and malabaricane diol.[3]

In the present communication we wish to report the isolation of a new triterpenoid, *ailanthol* (1), obtained by hexane extraction of the powdered roots at ~ 25°C and fractional crystallization, m.p. 165°; $[\alpha]_D$ -28° ($CHCl_3$, c 0.5); i.r. (nujol) ν_{max} 3580, 3500, 1665 cm^{-1}; u.v. λ_{max} 216 nm (log ε 3.57). The analysis fits the formula $C_{30}H_{46}O_4$ and the mass spectral data (M^+, m/z 470) supported this formulation. A positive Liebermann-Burchard reaction[3a] and a yellow coloration with tetranitromethane indicated that ailanthol is an unsaturated triterpene. An Ehrlich color test with dimethylaminobenzaldehyde-HCl was negative suggesting that it does not contain a furan ring. The ^1H n.m.r. spectrum (360 MHz) indicates a triterpene structure having six methyl groups: δ 0.84 (3H, s, C(4) β-CH_3), 0.89 (3H, s, C(4) α-CH_3), 0.95 (3H, s,-CH_3), 1.05 (3H, s,-CH_3), 1.32, 1.35 (each 3H, 2s, O-C-$(CH_3)_2$) and two hydroxyl groups δ 3.4 (1H, brs, W1/2, 7 Hz, C_3 β-H(OH)), 3.77 (1H, brs, W1/2, 7 Hz, C_7 β-H (OH)). On acetylation with acetic anhydride in pyridine, ailanthol afforded the diacetate (2), $C_{34}H_{50}O_6$, m.p. 215°; δ 4.65 (1H, brs, w1/2 8 Hz, C_3 β-H (OAc), 5.03 (1H, brs, w1/2 8Hz, C_7 β-H (OAc)) Similarly ailanthol afforded a di-p-bromobenzoate (3), indicating the presence of two secondary hydroxyl groups. The remaining two oxygens appeared to be present

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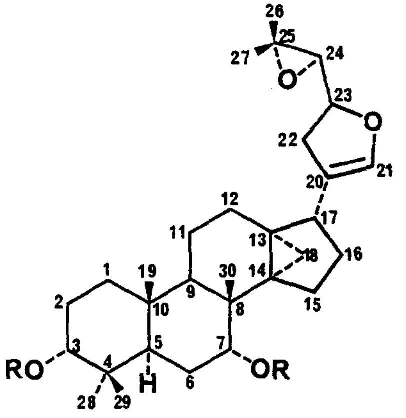
†Dedicated to the memory of Dr. Gopinath Kartha

as ether functions. Ailanthol contains a cyclopropane ring as shown by the cyclopropyl methylene in the ^1H n.m.r. spectrum, δ 0.56, 0.73 (2H, ABq, J = 5Hz); acetate (**2**) 0.46, 0.74 (2H, ABq, J = 5Hz). The presence of a vinyl proton at δ 6.13 and the absence of the same in dihydroailanthol suggestes that ailanthol contains an isolated double bond. Decoupling experiments showed the following relationships between some of the protons in ailanthol (**1**).

Assignment of the proton	Chemical shift δ	Multiplicity	Coupling J,Hz		Decoupling results	
					Irr.	Change
21	6.13	br s	$H_{21},H_{22}a$ $H_{21},H_{22}b$	1.5 1.5		
23	4.32	ddd	H_{23},H_{24} $H_{23},H_{22}a$ $H_{23},H_{22}b$	8 8 10.5		
24	2.94	d	H_{24},H_{23}	8		
22a	2.65-2.8	ddd	$H_{22}a,H_{23}$ $H_{22}a,H_{22}b$ $H_{22}a,H_{21}$	8 8 1.5		
22b	2.3-2.4	ddd	$H_{22}b,H_{23}$ $H_{22}b,H_{22}a$ $H_{22}b,H_{21}$	10.5 8 1.5		

The results above indicate that ailanthol is a pentacyclic triterpenoid with a side chain similar to that found in melianol with unsaturation in the furan moeity.[4] The ^{13}C n.m.r. spectrum of ailanthol exhibits 30 lines of all the carbon atoms of the molecule and off resonance decoupled spectrum shows 7 singlets, 8 doublets, 9 triplets and 6 quartets. Because of the uncertainty of positioning the ether oxygens and the cyclopropane ring in the molecule and the paucity of compound available for detailed chemical studies, we decided to complete the structure by X-ray analysis.

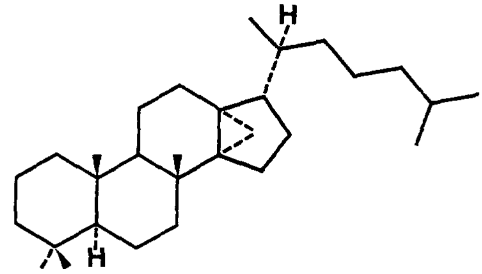
Crystals of 3,7-diacetylailanthol (**2**) obtained by slow crystallization from methanol are orthorhombic with space group $P2_12_12_1$, a= 7.493(1), b= 17.496(1), c= 24.006(4)Å and z= 4. Intensity data were collected on a CAD-4 automated diffractometer with CuKα radiation to a Bragg angle of 77°, ω-2θ scans and integrated counts. There were 3207 independent reflections measured, of which 1735 with $I>2\sigma(I)$ were considered observed. The structure was solved by direct methods using MULTAN[5] programs and refined by block diagonal least squares to an R value of 0.05 for 40 non-hydrogens anisotropic and 50 hydrogens isotropic.



1 R = H

2 R = $COCH_3$

3 R = p-COC_6H_4Br



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An ORTEP drawing of the molecule is shown in Figure 1. The structure consists of four fused-rings as in a steroid nucleus with a substituted five-membered ring at C(17). It has acetyl groups at C(3) and C(7), methyl groups at C(8) and C(10), a cyclopropane ring at C(13)-C(14) and an epoxide at C(24)-C(25), all in the α-position except for the methyls. The bond distances* in the four fused-rings range from 1.487(6) to 1.562(6)Å with C(9)-C(10) and C(9)-C(11) being the longest and C(12)-C(13) the shortest. C(20)-C(21) in the dihydrofuran ring is 1.305Å, indicating double bond character. Other than these, bond distances are in the range of reported values.[6]

More than ten years have elapsed since the first report of the isolation of compounds belonging to the new triterpene skeleton (20S)-4,4,8β-trimethyl-14,18-cyclo-5α,13α,14α,17α-cholestane (**4**). These triterpenoids were isolated from the heartwood of *Guarea glabra* (Meliaceae)[7], and this is the second example of a plant of the family Simarubiacae which has elaborated this unusual triterpene skeleton. A number of interesting bitter principles with the carbon framework of tirucallanes or apotirucallanes and an oxidized side chain have recently been reported from the plant family Cneoraceae, many of which have a cyclopropane ring at the same position.[8]

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*Bond distances and angles, fractional coordinates and thermal papameters and list of structure factors are deposited with the Cambridge Crystallographic Data Centre.

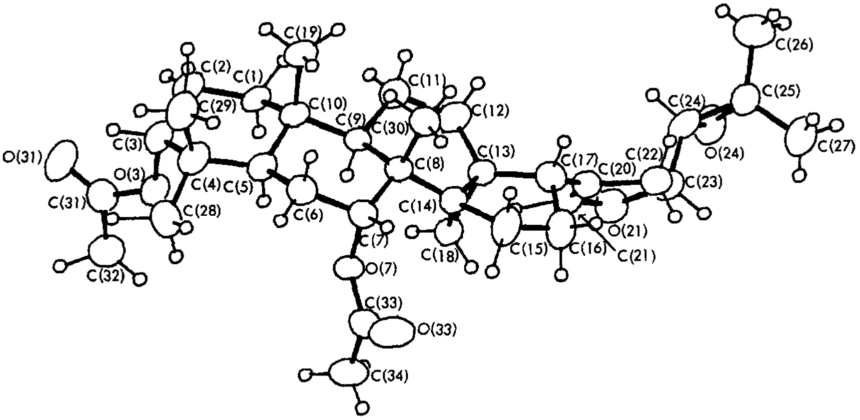

Figure 1. ORTEP drawing of 3,7- diacetylailanthol

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