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AMAROLIDE, ISOLATION FROM CASTELA NICHOLSONI HOOK AND REVISION OF ITS STRUCTURE (1)

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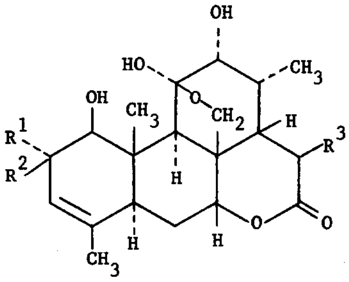
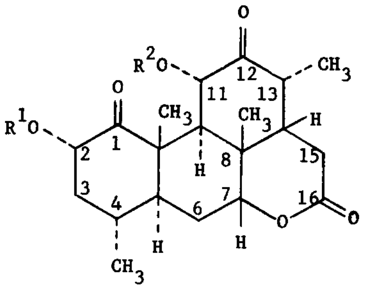
Castela nicholsoni Hook, a shrub growing in the Southern United States and in Mexico, contains several bitter principles characteristic of the simaroubaceous plants. Besides chaparrin (I) (2), the major constituent, glaucarubolone (II) (3), glaucarubol (III) (4) and glaucarubol-15-isovalerate (IV) (4) have been identified.

In the course of further investigation of the lipophilic material (chloroform extract) of this plant we have isolated amarolide, $C_{20}H_{28}O_6$, m.p. 260° (VI), first isolated by Casinovi et al. (5) from Ailanthus glandulosa. Although the melting points of the diacetates prepared from the compounds isolated from A. glandulosa and from C. nicholsoni were at first different (269-270° (from alcohol) and 237° (from acetone) respectively) their 60 Mc n.m.r. spectra (in $CDCl_3$) were identical. After recrystallization from alcohol the lower melting diacetate showed m.p. 260-262° undepressed when mixed with the higher melting diacetate. Two different melting points have also been reported for glaucarubol pentaacetate (6). Amarolide gives no purple color with concentrated sulphuric acid, a reaction characteristic of many related compounds having an allylic hydroxy group in ring A. The earlier direct interrelation of amarolide with quassin (IX) (7) established its carbon skeleton (5). New 100 Mc n.m.r. spectra of amarolide and of amarolide diacetate (VI) showed that the structures proposed by one of us (5) have to be revised to V and

VI, respectively. In particular, in amarolide diacetate the proton at C-9 appears as a doublet at 2.98 ppm (J = 13 cps) and the proton at C-11 as a doublet at 5.30 ppm (J = 13 cps). Double resonance experiments clearly established the AX character of these signals excluding the earlier proposed 11-oxo-12β-acetoxy structure (5). The large coupling constant is only consistent with a <u>trans</u>-diaxial position of the protons at C-9 and C-11; the 11-acetoxy group therefore occupies the equatorial α-position.





I R^1 = OH; R^2 = R^3 = H

II R^1, R^2 = O; R^3 = OH

III R^1 = R^3 = OH; R^2 = H

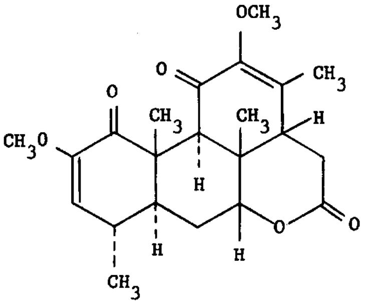
IV R^1 = OH; R^2 = H; R^3 = $OCOCH_2CH(CH_3)_2$

V R^1 = R^2 = H

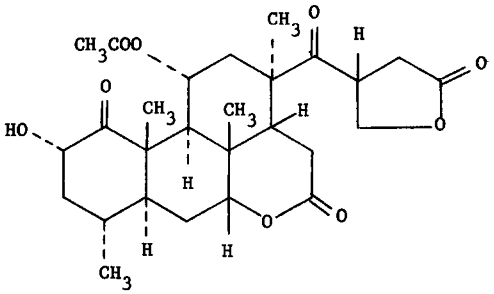
VI R^1 = R^2 = $COCH_3$

VII R^1 = H; R^2 = $COCH_3$

VIII R^1 = $COCH_3$; R^2 = H



IX



X

The poor solubility of amarolide in any solvent suitable for n.m.r. spectra made it difficult to get a spectrum of high quality, but running the spectrum at 50° in $CDCl_3$ (without TMS) made it possible to recognize the proton at C-9 at 2.62 ppm (doublet, J = 12.5 cps) proving that no isomerization had occurred while preparing the diacetate. Amarolide monoacetate, m.p. 264-265° isolated from A. glandulosa (5) has now to be assigned structure VII. The alternate monoacetate (VIII) m.p. 225°, was obtained as a by-product from the acetylation of amarolide with acetic anhydride. Amarolide and amarolide monoacetate (VII) have also been isolated as minor components from Ailanthus altissima (8). The revised structure of amarolide 11-acetate (VII) shows its close relationship to simarolide (X) (9), so far the only bitter principle of the simaroubaceae with a C_{25} carbon skeleton. These two compounds differ only (including stereochemistry) in the presence or absence of the 12-keto group and the 13-side chain. It is probable that this relationship has biogenetic significance. Furthermore it may be noted that all known simaroubaceous bitter principles except simarolide have an oxygen function at C-12.

Table. NMR Signals of Amarolide and of its Derivatives*

	Amarolide (V)	Amarolide diacetate (VI)	Amarolide 11-acetate (VII)	Amarolide 2-acetate (VIII)
$CHCH_3$	0.93,d (J = 6)	0.98,d (J = 5.5)	0.93,d (J = 6)	0.96,d (J = 5)
$CHCH_3$	1.08,d (J = 7)	1.04,d (J = 6.5)	1.07,d (J = 6.5)	1.06,d (J = 6)
CH_3	1.47,s	1.39,s	1.34,s	1.50,s
CH_3	1.50,s	1.54,s	1.57,s	1.55,s
7-H	4.29,t (J = 3)	4.30,t (J = 3)	4.32,t (J = 3)	4.29,t, br
11-H	ca. 4.4,m	5.30,d (J = 13)	5.29,d (J = 13)	ca. 4.35,m
2-H	4.76,q (J_1 = 8; J_2 = 12)	5.55,q (J_1 = 7; J_2 = 12)	4.70,q (J_1 = 7.5; J_2 = 11.5)	5.75,q (J_1 = 7; J_2 = 11)
9-H	2.62,d (J = 12.5)	2.98,d (J = 13)	3.01,d (J = 13)	
CH_3COO	--	2.08,s (6H)	2.04,s	2.05,s

*Varian HA-100 and A-60D in $CDCl_3$, TMS as internal standard (except in amarolide, see text), δ-values. Coupling constants (in parentheses) in cps. s = singlet; d = doublet; t = triplet; m = multiplet; br = broad signal.

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