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ISOLATION AND STRUCTURE OF 13,18-DEHYDROEXCELSIN, A QUASSINOID, AND GLAUCARUBOL FROM *AILANTHUS EXCELSA*

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Key Word Index—*Ailanthus excelsa*; Simaroubaceae; 13,18-dehydroexcelsin; glaucarubol; quassinoid.

Abstract—A new quassinoid, 13,18-dehydroexcelsin and glaucarubol have been isolated from the bark of *Ailanthus excelsa*.

Previous studies on *Ailanthus excelsa* have resulted in the isolation of sitosterol, 2,6-dimethoxybenzoquinone and malanthin from the bark [1], vitexin from the leaves [2], glaucarubin [3] and excelsin [4] from the bark, and ailanthinone, glaucarubinone and mixture of glaucarubol 15-isovalerate and 13,18-dehydroglaucarubol 15-isovalerate and alkaloids from root bark [5, 6].

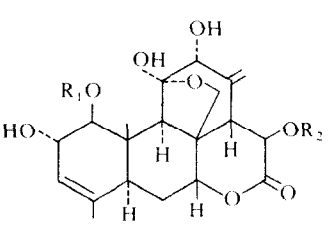
Investigations of the physiological properties of quassinoids have highlighted the antileukemic activity of several of them [7, 8] and has culminated in the selection of bruceantin for clinical trials [9] by the U.S. National Cancer Institute. These facts prompted this investigation which resulted in the isolation of 13,18-dehydroexcelsin and glaucarubol from the alcoholic extract of the defatted bark and the assignment of structure **1a** to the former.

The appearance of the typical lactone resonance at δ 4.69 in the ^{1}H NMR spectrum, dual maxima in the IR spectrum in the carbonyl region (1750, 1730 cm^{-1}), and fragments in the MS at *m/e* 57 (C_4H_9), 85 (C_5H_9O), 376 ($C_{20}H_{24}O_7$) and 377 ($C_{20}H_{25}O_7$) suggested **1a** to be a C_{20} quassinoid esterified with a C-5 acid. The existence of a hemiketal linkage in ring C [10] (4.1, 1H, *d*, J = 10 Hz; 3.85, 1H, *d*, J = 10 Hz), and the location of the ester function of C-15 (6.2, 1H, *d*, J = 12 Hz) in **1a** were also inferred from the ^{1}H NMR data. Lack of conjugation was indicated by the UV spectrum (λ_{max} 205 nm) and the appearance of signals corresponding to a vinyl methyl and a vinyl proton at δ 1.56 and 5.71 respectively in the ^{1}H NMR spectrum suggested the formulation of ring A as in **1a**. Further confirmation for this was provided by the formation of a methyl ether (**1b**), mp 298–300°, on treatment of **1a** with diazomethane [11]. A ^{1}H NMR signal at 3.82 (3H) and fragmentation ions in the MS at *m/e* 492 (M^+), 265, 247 and 149 were entirely compatible with the structure proposed for **1b**.

Spectral features of **1a** further suggested the presence of an exocyclic methylene function in **1a** (IR, 890 cm^{-1}; ^{1}H NMR: δ 5.32 and 5.2, 1H each, *d*, J = 2 Hz) and its location at C-13 (^{1}H NMR: δ 4.56, 1H, *s*; MS *m/e* 232 and 248) [12].

Compound **1a** was saponified to give **1c**, mp 265–266°, which showed the presence of only two methyl functions at δ 1.56 (C-4) and 1.63 (C-10) in its ^{1}H NMR spectrum. The C-15 proton appeared at 5.2 (1H, *d*, J = 10 Hz) which was coupled to the C-14 proton appearing at 2.93. The exocyclic methylene appeared as a pair of doublets at 5.4 and 5.45 (J = 2 Hz) and the olefinic proton was at 5.73. The two non-equivalent protons of the hemiketal function (CH_2—O—C—) appeared at 3.7 and 4.1 as an AB quartet (J = 8 Hz). In addition, the following protons were evident: H-1 (3.9, *d*, J = 7 Hz), H-2 (4.55, *m*), H-7 (4.55, *t*), H-12 (4.6, *s*), H-9 (3.35, *s*), H-5 and H-6 appearing at 2.56 and between 2 and 2.06, respectively. The ^{1}H NMR spectrum in which total assignment was possible, taken in conjunction with the MS in which the M^+ appeared at *m/e* 394 and the prominent fragments were at the expected values of *m/e* 376, 361, 348, 332, 135 and 122, conclusively demonstrated it to have the structure **1c**. The presence of signals in the ^{1}H NMR spectrum of **1a** corresponding to two additional methyls, appearing at 0.93 (*d*, J = 7 Hz) and 1.13 (*t*, J = 7 Hz) validated the structure proposed for 13,18-dehydroexcelsin.

The co-occurrence of **1a** and glaucarubol helped to define the ring junctions of the former. β-Equatorial and α-equatorial configurations of the hydroxyls on C-1 and C-2 respectively are apparent from the ^{1}H NMR spectrum of **1a** in which the C-2 proton splits the C-1 proton by a value of 5 Hz. Similarly, the C-14 and C-15 hydrogens should be *trans* (J = 12 Hz) and as a consequence the ester appendage on C-15 was equatorial [10]. Compound **1a** on acetylation formed an acetate, which from the ^{1}H NMR spectral evidence can be formulated as a mixture, though homogeneous on TLC. The signal ascribable to the C-12 proton in the acetate appeared at 5.26 and the extent of



1a R_1 = H, R_2 = COCHMe CH_2Me
1b R_1 = Me, R_2 = COCHMe CH_2Me
1c R_1 = R_2 = H

deshielding caused on acetylation ($\Delta H = 1.34$, $= 5.26 - 4.6$) defined the hydroxyl on C-12 as α, as in the acetate it lies in the deshielding zone of both the neighbouring carbonyl and methylene functions. Deshielding of the proton on C-12 caused by acetylation of ailanthone [13], on the other hand, is considerably less ($\Delta H = 0.93$). This leads to the stereochemistry shown in **1a** for 13,18-dehydroexcelsin.

The identity of glaucarubol, mp 285°, was confirmed by comparison with an authentic specimen [3].

EXPERIMENTAL

General. The solvent system used for TLC was 10% MeOH in $CHCl_3$ and spots were revealed by spraying with an alcoholic soln of phosphomolybdic acid. The plant material was collected from the University campus. Mps are uncorr.

Extractions. Dried bark of *Ailanthus excelsa* (5 kg) was exhaustively extracted with petrol (60–80°) and then repeatedly extracted with EtOH. The EtOH extract on concn deposited a dark gummy solid (25 g) which was chromatographed (A) on a column of Si gel using $CHCl_3$ containing increasing quantities of MeOH as eluant.

13,18-*Dehydroexcelsin* (**1a**). Fractions eluted with $CHCl_3$–MeOH (98:2) were combined (50 ml each) and the solvent evapd to yield a solid which was homogeneous on TLC (400 mg). It was crystallized from EtOAc–MeOH, 258–60°. UV λ_{max}^{EtOH} nm: 205; IR ν_{max}^{nujol} cm^{-1}: 3480, 3420, 1750, 1730 and 890. ^1H NMR (C_5D_5N): δ 0.93 (3H, *t*, $J = 7$ Hz, CH_2—Me), 1.13 (3H, *d*, 2′-Me), 1.62 (3H, *s*, 10-Me), 1.56 (3H, *s*, 4-Me), 3.08 (1H, *d*, $J = 12$ Hz, H-14), 3.34 (1H, *s*, H-9), 3.85, 4.1 (each 1H, *d*, $J = 10$ Hz, $-CH_2-O$), 4.69, (1H, *br. t*, H-7), 6.20 (1H, *d*, $J = 12$ Hz, H-15), 5.71 (1H, *br. s*, H-3), 5.2, 5.32 (each 1H, *d*, $J = 2$ Hz, $=CH_2$), 3.9 (1H, *d*, $J = 5$ Hz, H-1). 4.56 (1H, *s*, H-12) and 4.5 (1H, *br. m*, H-2). MS *m/e* (rel. int.): 478.2194 (M^+, 7.7), 460 (22.5), 378 (20.8), 361 (80.4), 376 (91.4), 360 (73.3), 377 (22.0), 332 (27.2), 314 (20.0), 229 (20.5), 248 (5.9), 232 (35.6), 231 (100.0), 233 (63.0), 217 (14.0), 135 (79.82), 122 (75.7), 85, 101 and 57.

Compound **1b**. **1a** (50 mg) was dissolved in MeOH (10 ml) and treated with an excess of ethereal soln of CH_2N_2. The soln was left overnight in an ice chest and then evapd, dissolved in MeOH and again treated with an ethereal soln of CH_2N_2. Evapn of the soln deposited a colourless solid, which was chromatographed on a column of Si gel eluted with $CHCl_3$. The crystalline solid eluted was crystallized from MeOH, mp 298–300°. ^1H NMR (C_5D_5N): δ 1.0 (3H, *t*, $J = 7$ Hz, CH_2—Me), 1.21 (3H, *d*, 2′-Me), 1.55 (3H, *s*, 10-Me), 4.55 (1H, *t*, H-7), 1.35 (3H, *s*, 4-Me), 3.82 (3H, *s*, 1-OMe), 4.1, 3.5 (each 1H, *d*, $J = 10$ Hz, $-CH_2-O-$), 6.20 (1H, *d*, $J = 12$ Hz). MS *m/e*: 492 (M^+), 476, 462, 461, 444, 391, 360, 265, 247, 231, 149, 135, 85 and 57.

Compound **1c**. **1a** (150 mg) was dissolved in N NaOH soln (5 ml) and left at room temp. for 5 hr. The soln was neutralized by addition of dilute HCl and the excess acid neutralized by NH_4OH. Solvent was evapd under red. pres. and the solid chromatographed on a column of Si gel. Elution with $CHCl_3$–MeOH (97:3) gave a solid which was crystallized from MeOH, mp 265–266°. MS *m/e*: 394 (M^+), 376, 361, 348, 332, 135 and 122.

Glaucarubol. Elution of the column (A) with $CHCl_3$–MeOH (95:5) yielded a solid which was crystallized from MeOH–EtOAc, mp 285°.

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