Phytochemistry, 1980, Vol. 19, pp. 1499–1501. Pergamon Press Ltd. Printed in England.

3S,24S,25-TRIHYDROXYTIRUCALL-7-ENE FROM *AILANTHUS EXCELSA*

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(*Received* 14 *September* 1979)

Key Word Index—*Ailanthus excelsa*; Simaroubaceae; 3S,24S,25-trihydroxytirucall-7-ene; triterpene triol.

Abstract—A new triterpene has been isolated from the root bark of *Ailanthus excelsa* (Simaroubaceae) and identified as 3S,24S,25-trihydroxytirucall-7-ene.

INTRODUCTION

The quassinoids are a group of complex, highly oxygenated, degraded triterpenes occurring only in the family Simaroubaceae (for a review see [1]). They are currently of interest because certain members display interesting anticancer activity [2–6]. Biosynthetically, the skeleton is believed to be derived from a tirucall-7-ene derivative by way of an apo-euphol rearrangement [7, 8], during the course of which the C-14 methyl group migrates back to C-8. Relatively few tirucall-7-ene derivatives have been obtained from Simaroubaceous plants [9–11] and we report here an additional new member of this series.

RESULTS AND DISCUSSION

During the isolation of canthin-6-one-type alkaloids [12] and anticancer quassinoids [3] from the root bark of *Ailanthus excelsa* Roxb. (Simaroubaceae), we obtained a new triterpene alcohol to which we have assigned the structure 3S,24S,25-trihydroxytirucall-7-ene (**1**).

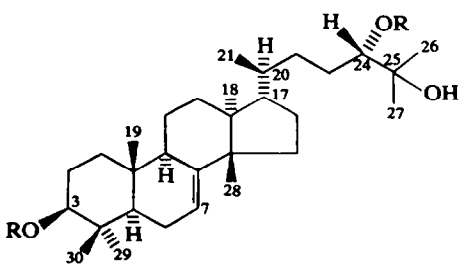
The isolate, mp 174–176°, possessed a molecular formula $C_{30}H_{52}O_3$ (by MS) and its ^{1}H NMR spectrum indicated the presence of seven tertiary methyl groups, one secondary methyl group, two multiplets for oxymethine protons and one olefinic proton. These signals were regarded as being characteristic of the euphane–tirucallane system having a double bond and a 3-hydroxy group [13, 14]. However, a doublet for the C-26 and C-27 methyl groups was absent and was replaced by two methyl singlets shifted downfield to δ 1.16 and 1.26. From these data an oxygen function was deduced to be at C-25, with a further substituent at C-24 accounting for the asymmetry of the tertiary methyl groups [15].

Acetylation afforded a diacetate derivative **2**, in which two methine signals had each shifted downfield by about δ 1.3. Biogenetically, one acetylatable hydroxy group could be placed at C-3 and from the $W_{1/2}$ (19 Hz) of the C-3 proton, the hydroxy group had a β configuration.

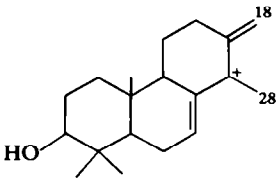
A characteristic ion present in the MS of the parent compound appeared at *m/e* 273 (**3**), which could be rationalized in terms of loss of the side-chain with C-15, C-16 and C-17 ($C_{11}H_{23}O_2$) through internal H transfer from C-18 [10]. An abundant ion at *m/e* 255 in the spectrum of the diacetate may be assigned the structure **4** by analogy.

Confirmation that C-24 was substituted by a hydroxy group was obtained when periodic acid oxidation of **1** afforded a hydroxy aldehyde **5** (M^+ 400). It remained, therefore, to place the double bond and determine the stereochemistry at C-20 and C-24.

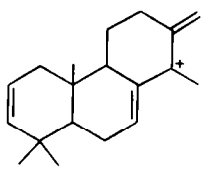
One feature of the ^{1}H NMR spectrum was that, except for the methyl groups at C-25, no methyl groups appeared more downfield than δ 0.97 in either the alcohol or the diacetate, nor upfield of 0.7. Such data would indicate that the compound was a member of the Δ^7-euphane or Δ^7-tirucallane series of compounds (differing C-20 stereochemistry) [13, 14, 16]. A distinction between these skeleta was made from the optical rotation of **1**, which had $[\alpha]_D - 37.2°$ indicating it to belong to the tirucallane rather than euphane series [14]. A strong ion at $M^+ - 15$ (loss of C-14 Me, $m^* = 430.5$) also supports the assignment of a double bond to C-7 rather than C-9(11) since an allylic cation results from this process.



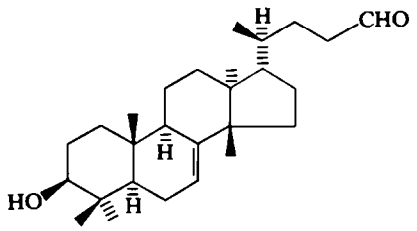
1 R = H
2 R = Ac



3 *m/e* 273



4 *m/e* 255



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The stereochemistry at C-24 was deduced by the lanthanthide complex method of Nakanishi [17–19]. Complexation [4:1 ratio, substrate:Eu(dpm)$_3$] of **1** in EtOH-free, dry $CHCl_3$ gave a CD spectrum showing $\Delta\varepsilon + 4.5$ at 314 nm indicating the C-24 hydroxy group to have the *S* configuration. The isolate is therefore represented by the complete structure 3*S*,24*S*,25-trihydroxytirucall-7-ene (**1**). It was inactive in the P-388 lymphocytic leukemia and Eagles carcinoma of the nasopharynx test systems *in vitro* [20].

EXPERIMENTAL

Mps were determined by means of a Kofler hot plate and are uncorr. ^{1}H NMR spectra were recorded in $CDCl_3$ soln at 60 MHz. TMS was used as an int. standard and chemical shifts are reported in δ units. CC was carried out on Si gel PF-254.

Preliminary processing. Details concerning the collection, identification and preliminary fractionation of the root bark of *Ailanthus excelsa* (Simaroubaceae) have been described previously [3].

3*S*,24*S*,25-*Trihydroxytirucall-7-ene* (**1**). After the isolation of the non-polar canthinones [12] by chromatography of the $CHCl_3$-soluble fraction, continued elution with $CHCl_3$ afforded **1** from MeOH displaying the following physical and spectral properties, mp 174–176°; $[\alpha]_D^{24} - 37.2°$ (*c* 1.0, $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3460, 2975, 2930, 1625, 1380, 1370, and 840; ^{1}H NMR ($CDCl_3$): δ 0.75 (3H, *s*, 19-H$_3$), 0.82 (3H, *s*, 18-H$_3$), 0.86 (3H, *s*, 30-H$_3$), 0.92 (3H, *d*, $J = 6.8$ Hz, 21-H$_3$), 0.97 (6H, *s*, 28-H$_3$, 29-H$_3$), 1.16 (3H, *s*, 26-H$_3$), 1.21 (3H, *s*, 27-H$_3$), 3.24 (1H, *m*, 3α-H), 3.36 (1H, *m*, 24α-H), and 5.26 (1H, *m*, 7-H); MS *m/e* (rel. int.): 460 (M^+, 31.6), 445 ($M^+ - Me$, 23.5), 427 ($M^+ - Me - H_2O$, 100), 409 ($M^+ - Me - H_2O - H_2O$, 100), 391 (9.6), 385 (8.1), 367 (7.4), 315 (6.6), 297 (6.6), 287 (7.3), 273 (12.5), 259 (6.6), 189 (17.6), 187 (19.7), 159 (20.6), 145 (16.2), 135 (29.4), 133 (28.7), 121 (27.2), 119 (30.1), 109 (27.9), 107 (32.3) and 105 (27.2). Mass measurement, obs.: 460.3939, calc. for $C_{30}H_{52}O_3$, 460.3903.

Acetylation of **1**. The triterpene **1** (5 mg) was suspended in Ac_2O–Py (1 ml, 1:1) at room temp. overnight. Dilution with H_2O and extraction with EtOAc yielded a crystalline diacetate **2** from MeOH, mp 148–151°; ^{1}H NMR ($CDCl_3$): δ0.77 (3H, *s*, 18-H$_3$), 0.80, (3H, *s*, 18-H$_3$), 0.85 (3H, *s*, 30-H$_3$), 0.91 (3H, *d*, $J = 6.8$ Hz, 21-H$_3$), 0.93 (3H, *s*, 29-H$_3$), 0.96 (3H, *s*, 28-H$_3$), 1.20 (6H, *s*, 26-H$_3$, 27-H$_3$), 2.04 (3H, *s*, OAc), 2.10 (3H, *s*, OAc), 4.51 (1H, *s*, 3α-H), 4.67 (1H, *s*, 24α-H) and 5.24 (1H, *s*, 7-H); MS *m/e* (rel. int.): 544 (M^+, 70.2), 529 ($M^+ - CH_3$, 57.5), 511 ($M^+ - Me - H_2O$, 93.6), 484 ($M^+ - HOAc$, 11.2), 469 ($M^+ - Me - HOAc$, 100), 451 ($M^+ - Me - H_2O - HOAc$, 45.7), 409 ($M^+ - Me - HOAc - HOAc$, 76.6), 391 ($M^+ - Me - HOAc - HOAc - H_2O$, 17), 369 (13.3), 315 (8.5), 309 (12.2), 297 (13.3), 284 (17.6), 255 (19.2), 189 (26.6), 187 (25.0), 175 (24.5), 159 (23.4), 145 (18.6), 135 (37.2), 133 (28.2), 121 (28.7), 119 (30.8), and 109 (39.4).

Oxidation of **1**. To a soln of **1** (8 mg) in THF (3 ml) was added H_5IO_6 (5 mg) and after 1 hr at room temp. the mixture was diluted with H_2O and extracted with EtOAc. The crude aldehyde was purified by PLC on Si gel ($CHCl_3$–MeOH, 98:2); MS *m/e* (rel. int.): 400 (M^+, 40.0), 385 ($M^+ - Me$, 100), 367 ($M^+ - Me - H_2O$, 50.3), 349 ($M^+ - Me - H_2O - H_2O$, 6.9), 273 (4.6), 260 (7.4), 245 (8.6), 227 (10.3), 215 (7.4), 189 (8.6), 187 (11.4), 175 (16.6), 173 (12.0), 161 (17.7), 159 (14.3), 145 (15.3), 135 (29.7), 133 (23.4), 131 (12.6), 121 (13.1), 119 (29.7), 107 (30.3) and 105 (33.7).

Acknowledgements—This work was carried out under contract CM-67090 with the Division of Cancer Treatment, Drug Research and Development Program of the National Cancer Institute, Department of Health, Education and Welfare, Bethesda, Md. The authors would like to thank the Economic Botany Laboratory, BARC-East, U.S.D.A., Beltsville, Md., funded by the NCI, for the provision and identification of the plant material. A herbarium sample is deposited at the Herbarium of the National Arboretum, A.R.S., U.S.D.A., Washington, D.C. The authors would also like to thank Dr. M. C. Wani, Research Triangle Institute, for the MS of **1** and Dr. V. Madison, Department of Medicinal Chemistry for the use of a JASCO CD spectrometer.

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