THE STRUCTURE AND STEREOCHEMISTRY OF LANTANILIC ACID, THE β , β -DIMETHYLACRYLOYL ESTER OF LANTANINILIC ACID, ISOLATED FROM LANTANA CAMARA

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Abstract—The structure of lantanilic acid, a new triterpene isolated from the leaves of Lantana camara, has been determined as the β , β -dimethylacryloyl ester of lantaninilic acid.

INTRODUCTION

The isolation of two new triterpene acids, lantanolic acid [1,2] and lantic acid [3,4] besides 3-keto ursolic acid from the leaves of *Lantana camara* has been reported earlier from this laboratory. The present paper reports the structure of another new triterpene acid called lantanilic acid $(1a)^*$ from the petrol extract of the same plant.

RESULTS AND DISCUSSION

Lantanilic acid (1a) C35H52O6, mp 277-279° (dec.), $[\alpha]D + 176^{\circ}$ (Py) formed a methyl ester (1b), $C_{36}H_{54}O_6$, mp 183–85°, $[\alpha]_{\rm D}^{26\circ}$ + 173.5° (Py) on treatment with ethereal diazomethane. The uv spectrum of both (1a) and (1b) showed absorption maxima at 218 nm (log ϵ 4.24) indicating the presence of β , β -dimethyl acryloyl moiety [5]. The MS of methyl lantanilate did not show the molecular ion peak at m/e 582 but showed a peak at m/e 482 for the $(M-100)^+$ ion arising by loss of a molecule of β , β -dimethyl acrylic acid. There was also a peak at m/e 83 for the ion (Me)₂C=CH-C = O⁺. The retro Diels-Alder fragmentation of the molecule led to the ion a $(m/e \ 260)$. Saponification of lantanilic acid (1a) with ethanolic caustic potash (5%) yielded β , β -dimethyl acrylic acid and a new triterpene acid called lantaninilic acid (1c), $C_{30}H_{46}O_5$, mp 293–296° (dec.), $[\alpha]_D^{31\circ} + 155^\circ$ (EtOH) which formed a methyl ester (1d), C₃₁H₄₈O₅, mp 227–229°, $[\alpha]_{D}^{29°} + 151.9°$ (CHCl₃) on treatment with ethereal diazomethane. The UV spectrum of methyl lantaninilate (1d) showed absorption maximum at 206 nm (log ϵ 3.8) for a trisubstituted double bond. The IR spectrum of (1d) showed bands at 3450, 3250 (OH) and 1727 cm^{-1} (COOMe). The MS of methyl lantaninilate (1d) did not show the molecular ion peak at m/e 500 but showed a peak at m/e 482 for the ion $(M-H_2O)^+$. The MS fragmentation pattern of methyl lantaninilate (peaks at m/e 260, (a) 201, 482, 299, and 239) showed a close similarity with that of methyl lantanolate [2], (m/e 262, 203, 484, 301 and 241), the difference of two mass units being due to the loss of a molecule of water from the ring E of (1d). Methyl lantaninilate formed a ketal (1e), $C_{32}H_{50}O_5$ (M⁺ 514) mp 284–287°, on refluxing with methanolic sulphuric acid which on treatment with dilute hydrochloric acid in tetrahydrofuran gave back methyl lantaninilate (cf. methyl lantanolate, ref [2]).

Methyl lantaninilate (1d) on potassium borohydride reduction yielded two epimeric products. The major constituent called triol A (2a) was isolated in a pure state, $C_{31}H_{50}O_5$, mp 216–218°. The minor product (not isolated in a pure state) is presumed to be the 3α -axial isomer as it moved faster on TLC [6] (cf. methyl lantanolate, ref 2). The NMR spectrum of triol A showed a singlet at δ 4.01 for the two protons of the



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hydroxymethylene group (-C<u>H</u>₂OH) at C-10, a triplet at 3.86 (1H, J = 3 Hz) for the 22 α -H and a multiplet (1H) at 3.2 for the 3 α -H. The low coupling constant (J = 3 Hz) of the signal at 3.86 clearly suggested that the secondary hydroxyl group at C-22 must be β -axial.

On heating with acetic anhydride and pyridine on a steam bath for 24 hr, triol A yielded a triacetate, (2b), $C_{37}H_{56}O_8$, mp 234–236°. The NMR spectrum of (2b) showed a singlet at δ 4.46 for the two protons α - to the primary acetoxy group (-CH₂-O-CO-CH₃), a triplet at 4.99 (1H. J = 3 Hz) for the 22 α -H and a multiplet at 4.54 for the 3 α -H.

Oxidation of the ketal (1e) with $Cr\Theta_3$ -pyridine complex yielded a keto compound (3), $C_{32}H_{48}O_5$, mp 241-243°, which as expected, did not respond to Zimmermann's test [7] for a 3-keto group. On saponification with ethanolic caustic potash (10%), (3) gave a norcompound (4), $C_{31}H_{48}O_3$, mp 235-237°, indicating the presence of a hydroxyl group at the β -position to the carboxyl group in lantaninilic acid.

The ketal (1e) on treatment with POCl₃ in pyridine gave the dehydro compound (5), $C_{32}H_{48}O_4$, mp 221-223°, which on hydrogenation gave the ketal of methyl lantanolate [2]. Refluxing of the above ketal with hydrochloric acid in tetrahydrofuran yielded methyl lantanolate [2]. This proved the structure of lantaninilic acid except for the position of the secondary hydroxyl group.

Methyl lantaninilate (1d) on heating with pyridine and acetic anhydride for one hour yielded a mixture of a diacetate (6), $C_{35}H_{52}O_7$, mp 156–158° and a monoacetate (1f) $C_{33}H_{50}O_6$, mp 233–235°. The latter on further heating with acetic anhydride and pyridine for 30 hr yielded the diacetate (6). Acetylation of methyl lantaninilate with acetic anhydride and pyridine at 0° yielded a mixture of the monoacetate (1f) and unreacted methyl lantaninilate.

The MS of the diacetate did not show the molecular ion peak at m/e 584 but there was a peak at m/e 524 for the ion (M-MeCOOH)⁺. There were also peaks at m/e 464 and m/e 451 for the ions (M-2MeCOOH)⁺ and (M-MeCOOH-CH₂OCOMe)⁺ respectively. The loss of 73 mass units (CH₂O·COMe) in the latter indicated the presence of a primary acetoxy group in the diacetate (cf. aescigenin pentaacetate [8] and erythrodiol diacetate [9]). The MS of the monoacetate (1f) showed a weak molecular ion peak at m/e 542. The NMR spectrum (CDCl₃, 60 MHz) of the monoacetate was in conformity with the structure (**1f**) for the monoacetate. There were two pairs of doublets centred at δ 4.26 (J = 9 Hz) and 3.9 (J = 9 Hz) for the two non-equivalent methylene protons ($-CH_2-O-C-O-$) of the hemiketal system. The signals at 4.26 (J = 2.5 Hz) and 3.9 (J = 1 Hz) were both split due to long range coupling with one of the C-1 protons (cf. the NMR spectrum of methyl lantanolate [2]). The triplet centred at 4.95 (1H, J = 3.5 Hz) was due to the 22 α -H. The low coupling constant (3.5 Hz) indicated an axial (β) orientation of the secondary hydroxyl group at C-22. A signal at 4.41 (1H. *t*) was due to the C-12 vinyl proton.

The NMR spectrum of methyl lantaninilate is very similar to that of methyl lantanolate, excepting a triplet at δ 3.91 which is due to the 22 α -carbinyl proton which is absent in methyl lantanolate. Barua *et al.* [10] have reported that the 16 β -H (>C<u>H</u>-O-CO-Me) of diacetyl methyl echinocystate gave rise to a signal at 5.69 which is much further down field than the signal observed at 4.95 due to the proton attached to the carbon bearing the secondary acetoxyl group (>C<u>H</u>-O-COMe) in the monoacetate (**1f**). This indicated that the secondary hydroxyl group in lantaninilic acid is located not at C-16 but at C-22.

On the basis of the above observations lantaninilic acid may be represented as **1c**.

Lantanilic acid has been shown previously to be the β , β -dimethyl acryloyl derivative of lantaninilic acid (1c). The NMR spectrum (CDCl₃, 60 MHz) of lantanilic acid was highly informative. It showed two pairs of doublets centred at δ 4.22 (1H, J = 9Hz) and 3.89 (1H, J = 9 Hz) for the two non-equivalent methylene protons (-CH₂-O-C-O-) of the hemiketal system. The signals at 4.22 were further split (J = 2.5 Hz) and the others at 3.89 were also split (J = 1 Hz) due to long range coupling with one of the C-1 protons. In this region there was a close similarity in the NMR spectrum of lantanilic acid with that of methyl lantaninilate. The triplet centred at 3.91 due to the 22α -H found in the NMR spectrum of methyl lantaninilate was, as expected, absent in the NMR spectrum of lantanilic acid but instead was shifted to 5.01 (1H, t, J = 3 Hz; >C<u>H</u>-O-CO-CH=C(Me)₂ due to esterification of the C-22 hydroxyl group. This indicated that the β , β -dimethylacryloyloxy moiety in lantanilic acid is located at C-22. The NMR spectrum of lantanilic acid in the high field region showed five sharp singlets at δ 0.77 (3H), 0.88 (3H), 0.95 (3H), 1.01 (6H) and 1.14 (3H) corresponding to six tertiary methyl groups. The signal at 5.56 (*m*, 1H) was due to the vinyl proton of the β , β -dimethyl acryloyloxy moiety -O-CO-CH=C(Me)₂. The signals for the two β -methyl groups -O-CO-CH=C(CH)₂ appeared, as expected [11,12] at 1.83 (3H, *d*, J = 0.5 Hz) and 2.12 (3H, *d*, J = 0.5 Hz) respectively.

Thus the spectral and other data presented above indicated the structure of lantanilic acid to be **1a**.

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