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A NOVEL WITHANOLIDE FROM *DATURA QUERCIFOLIA*

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Key Word Index—*Datura quercifolia*; Solanaceae; withanolide; daturalactone-3.

Abstract—A novel withanolide, 5α,12β-dihydroxy-1-oxo-6α,7α-epoxy-(22*R*)-witha-2,24 dienolide was isolated from a benzene extract of fresh leaves of *Datura quercifolia*. The structure was established by chemical and spectroscopic methods.

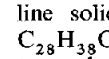
INTRODUCTION

Recently two withanolides have been reported from the fresh leaves of *Datura quercifolia* [1, 2]. In this communication we report the isolation and characterization of another novel withanolide, daturalactone-3, from the fresh leaves of this species.

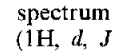
RESULTS AND DISCUSSION

A benzene extract of the fresh leaves of *D. quercifolia* gave on chromatographic fractionation a white crystalline solid, mp 285–86°, M^+ *m/e* 470, analysed for $C_{28}H_{38}O_6$, $[\alpha]_D^{26}$ +73° (*c*, 1.0; $CHCl_3$). The UV spectrum showed a strong absorption at 223 nm (ε 16 700) indicating the presence of an α,β-unsaturated ketone and an unsaturated lactone chromophore. The IR spectrum exhibited principal bands at 1685 (unsaturated ketone), 1710 (unsaturated six-membered lactone) 3450 and 3510 cm^{-1} (two —OH groups). The PMR spectrum (100 MHz, $CDCl_3$) showed signals at δ 5.85 (1H, *d*, *J* = 10 Hz, H-2, showed weak allylic coupling with H-4) 6.60 (1H, *dq*, *J* = 10:4.5:3 Hz, H-3) 3.08 (1H, *d*, *J* = 4 Hz; H-6) 3.35 (1H, *dd*, *J* = 4, 1 Hz; H-7) 3.44 (1H, *dd*, *J* = 10 and 5 Hz, H-12) 4.55 (1H, *m*, H-22) 1.90 (6H, two overlapped *s*, H-27, -28) 1.18 (3H, *s*, H-19) 1.02 (3H, *d*, *J* = 6 Hz, H-21) and 0.85 (3H, *s*, H-18). The MS of the compound showed trivial fragments at *m/e* 452 ($M^+ - 18$), 434 ($M^+ - 2 \times 18$) and other fragments at 416, 328, 263, 198 and 125.

Acetylation under mild condition (Ac_2O–C_5H_5N) at room temp. gave a monoacetate (mp 248°) indicating the tertiary nature of the other hydroxyl group. The IR spectrum exhibited principal bands at 1740 and 1250



(—O—C—Me) in addition to bands at 1710 and 1685 cm^{-1}. The PMR spectrum (60 MHz, $CDCl_3$) showed signals at 5.85 (1H, *d*, *J* = 10 Hz, H-2) 6.60 (1H, *dq*, *J* = 10:4.5:3 Hz; H-3) 3.08 (1H, *d*, *J* = 4 Hz; H-6) 3.35 (1H, *dd*, *J* = 4 and 1 Hz, H-7) 4.85 (1H, *dd*, *J* = 10 and 5 Hz,

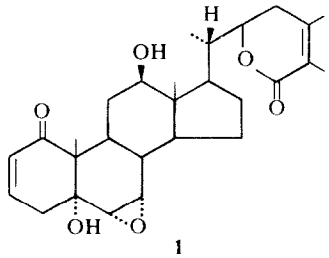


H-12) 4.55 (1H, *m*, H-22) 2.00 (3H, *s*, —O—C—Me) 1.90 (6H, two overlapped *s*, H-27, -28) 1.18 (3H, *s*, H-19) 1.02 (3H, *d*, *J* = 6 Hz, H-21) and 0.85 (3H, *s*, H-18).

Upon catalytic hydrogenation, the compound quickly absorbed one mole of hydrogen to give a dihydro derivative mp 249–50°, λ_{max}^{MeOH} at 227 nm (ε 8000) and a low intensity band between 320 and 260 nm. This showed that only the double bond of the αβ-unsaturated carbonyl chromophore was hydrogenated. This was confirmed by the absence of signals at δ 5.85 and 6.60 (assigned to H-2 and H-3) in the PMR of the parent compound.

Jones' reagent failed to oxidize the compound both at 0° and room temp., but oxidation with Sarett's reagent was successful. The oxidation product after crystallization yielded a solid mp 275° (lit. [3] mp 267–69°). The IR spectrum exhibited principal bands at 1685 (αβ-unsaturated ketone), 1710 (unsaturated six-membered ring lactone), 1700 (saturated six-membered ring ketone) and 3450 cm^{-1} (—OH group). The PMR spectrum (60 MHz, $CDCl_3$) showed signals at δ 5.85 (1H, *d*, *J* = 10 Hz, H-2) 6.60 (1H, *dq*, *J* = 10:4.5:3 Hz, H-3) 3.08 (1H, *d*, *J* = 4 Hz, H-6) 3.40 (1H, *dd*, *J* = 4 and 1 Hz, H-7) 4.55 (1H, *m*, H-22) 1.90 (6H, two overlapped *s*, H-27, -28) 1.26 (3H, *s*, H-19) 1.12 (3H, *s*, H-18) and 0.95 (3H, *d*, *J* = 7 Hz, H-21). This shows that the C-18 methyl protons have moved downfield to δ 1.1, while the C-21 methyl protons move upfield to δ 0.95. The only position which can simultaneously affect C-18 and C-21 methyl protons is C-12. Therefore, the secondary hydroxyl group was located at C-12. This is true of daturalactone-1* also. It is well established that the rate of oxidation of axial alcohols is more rapid than the corresponding equatorial alcohols [4–6]. This is true of daturalactone-1* where the C-12 hydroxyl, being axial, gets rapidly oxidized by Jones' reagent, and in the PMR spectrum H-12 appears as a singlet. However, daturalactone-3 is inert to Jones' reagent and in the PMR spectrum H-12 appears as a double doublet at δ 3.44. The upfield shift, its complexity and its inertness to Jones' oxidation clearly indicates the C-12 hydroxyl to be β. CD (acetonitrile) was run to determine the sterochemistry at C-22 [7, 8].

* Previously reported daturalactone-1 and 12-oxo withanolide 2 are here designated as daturalactone-1 and -2, respectively.



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The compound showed a positive Cotton effect at 253.5 nm ($\Delta\varepsilon$ + 3.75) which confirmed the configuration at C-22 to be *R*. Most of the PMR signals of our compound were similar to the corresponding signals of withanolides [9]. From the above data the compound was assigned the structure 5α,12β,dihydroxy-1-oxo-6α,7α-epoxy-(22*R*)-witha-2,24-dienolide (**1**).

EXPERIMENTAL

Isolation. Crushed fresh leaves (1 kg) of *D. quercifolia* were extracted with cold C_6H_6. The extract on concn deposited a pale green crystalline substance which on CC yielded daturalactone-1 and -2*. The mother liquor on chromatography over Si gel and elution with $CHCl_3$–EtOAc (3:2) gave a white crystalline solid, mp 285–86°. (Found: C, 70.85; H, 8.01. Calculated for $C_{28}H_{38}O_6$: C, 71.5; H, 8.08%).

Acetylation. 30 mg of the compound was acetylated (Ac_2O–C_5H_5N) at room temp. After the usual procedure, the product crystallized from $CHCl_3$–EtOAc to give a white crystalline solid, mp 248°. (Found: C, 70.20; H, 7.66. Calculated for $C_{30}H_{40}O_7$: C, 70.31; H, 7.81%).

Hydrogenation. 35 mg of the compound were hydrogenated (H_2 uptake 1 mol) over 5% Pd/C in EtOAc. The product on crystallization from $CHCl_3$–EtOAc gave white crystalline needles, mp 249–50°. (Found: C, 71.10; H, 8.35. Calculated for $C_{28}H_{40}O_6$: C, 71.18; 8.47%).

Oxidation. To a freshly stirred slurry of CrO_3–C_5H_5N complex (Sarett's reagent) was added the compound (60 mg, in C_5H_5N) slowly for 1.5 hr. After the usual procedure the product crystallized from $CHCl_3$–EtOAc to give white crystalline solid, mp 275°. (Found: C, 71.66; H, 8.44. Calculated for $C_{28}H_{36}O_6$: C, 71.79; H, 8.54%).

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