

## LITERATURE

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## A NOVEL WITHANOLIDE FROM *DATURA QUERCIFOLIA*

MUSHTAQ A. QURISHI, ASHOK K. KALLA\* and KANAYA L. DHAR

Regional Research Laboratory, Jammu Tawi-180001, India

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**Key Word Index**—*Datura quercifolia*; Solanaceae; withanolide; daturalactone-4; 5 $\alpha$ -hydroxy-1-oxo-6 $\alpha$ ,7 $\alpha$ ,24 $\alpha$ ,25 $\alpha$ -diepoxy-(22*R*)-with-2-enolide.

### INTRODUCTION

Earlier investigations on this species revealed the presence of three new withanolides [1–3]. In this communication we report the isolation and structural elucidation of another novel withanolide, daturalactone-4, from the fresh leaves of this species.

### RESULTS AND DISCUSSION

Benzene extraction of the fresh leaves followed by chromatographic fractionation gave colourless needle-shaped crystals, mp 282°,  $M^+$  470 analysed for  $C_{28}H_{38}O_6$ . The UV spectrum showed strong absorption at 225 nm ( $\epsilon$  15 500) indicating the presence of an  $\alpha\beta$ -unsaturated ketone and/or an unsaturated lactone chromophore. The IR spectrum exhibited bands at 1690 ( $\alpha\beta$ -unsaturated ketone), 1730 (six-membered ring lactone) and 3440  $cm^{-1}$  (—OH group). Acetylation under mild conditions ( $C_5H_5N/Ac_2O$  at room temperature) was unsuccessful and indicated the tertiary nature of the hydroxyl group. CD (acetonitrile) showed the absence of a positive Cotton effect at 250 nm due to a  $\Delta^{24}$ -enolactone moiety.

$^1H$  NMR (100 MHz,  $CDCl_3$ ) showed signals at  $\delta$  5.83 (1H, *dq*,  $J = 10, 3.1$  Hz, H-2), 6.54 (1H, *dq*,  $J = 10, 4.5, 3$  Hz, H-3), 3.03 (1H, *d*,  $J = 4$  Hz, H-6), 3.3 (1H, *dd*,  $J = 4, 1$  Hz, H-7), 4.5 (1H, *dt*,  $J = 12, 3.5$  Hz, H-22), 0.75 (3H, *s*, H-18), 1.16 (3H, *s*, H-19), 0.92 (3H, *d*,  $J = 7$  Hz, H-21), 1.48 (3H, *s*, H-27) and 1.56 (3H, *s*, H-28). MS of the compound showed small fragment ions due to elimination of water and methyl and a base peak at  $m/e$  125 which was probably obtained by the double fission of ring B. The other fragments which are in conformity with the assigned structure are given in Scheme 1.

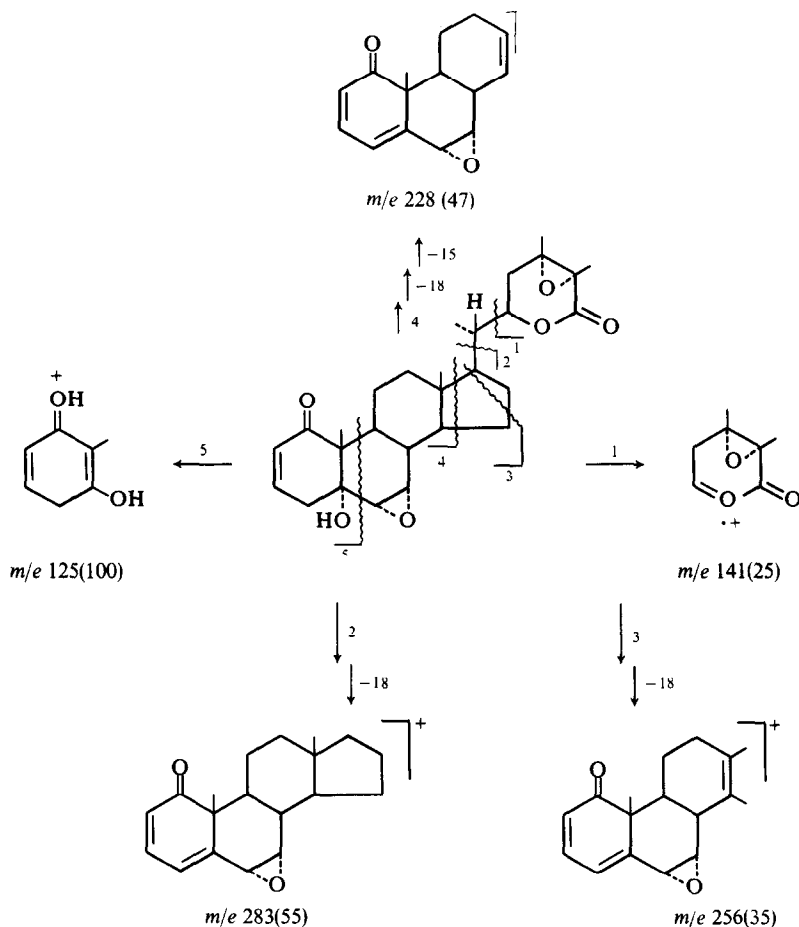
Catalytic hydrogenation proceeded with the absorption of 1 mol of hydrogen to give a dihydro derivative.

mp 269°. The IR spectrum was characterized by a shift of the absorption band at 1690 to 1709  $cm^{-1}$  due to a saturated ketone which reflected the presence of an  $\alpha\beta$ -unsaturated ketone in the daturalactone-4. This was also evident by inspection of its  $^1H$  NMR spectrum which showed two vinylic signals at  $\delta$  5.83 and 6.54. The  $^1H$  NMR spectrum of the hydrogenated product showed the absence of these two signals which confirmed the above assignment.

Selective reductive cleavage by a Zn–Cu couple proved a very valuable tool during the structure elucidation of the compound. The epoxide at C-24 and C-25 was reduced by this reaction, leading to the formation of the usual withanolide type of unsaturated lactone ring in the side chain. The epoxide at C-6 and C-7 remained intact but the double bond in ring A was hydrogenated. This was confirmed by  $^1H$  NMR and CD studies on this compound. The product obtained gave colourless crystals, mp 265°,  $M^+$  456 analysed for  $C_{28}H_{40}O_5$ . The IR spectrum exhibited bands at 1710 (saturated ketone), 1725 (six-membered ring lactone) and 3480  $cm^{-1}$  (—OH group). The  $^1H$  NMR (100 MHz,  $CDCl_3$ ) spectrum showed signals at  $\delta$  0.76 (3H, *s*, H-18), 0.99 (3H, *d*,  $J = 7$  Hz, H-21), 1.18 (3H, *s*, H-19), 1.96 (6H, two overlapped singlets, H-27 and H-28), 3.03 (1H, *d*,  $J = 4$  Hz, H-6), 3.2 (1H, *dd*,  $J = 4, 1$  Hz, H-7), 4.38 (1H, *dt*,  $J = 12, 3.5$  Hz, H-22). CD (acetonitrile) of this compound showed a positive Cotton effect at 254 nm ( $\Delta\epsilon = +3.72$ ) confirming the presence of a  $\Delta^{24}$ -enolactone ring moiety.

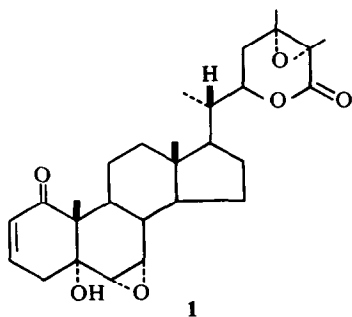
In our earlier communication [5], we showed daturalactone-2 to have 6,7,24,25-epoxides by comparison with the oxidation product of NIC-7. Daturalactone-4 showed the same pattern in the spectral data as daturalactone-2 in so far as the stereochemistry of the epoxides is concerned. This led us to the assignment of the  $\alpha$ -orientation of the epoxides in daturalactone-4. Most of the  $^1H$  NMR spectral signals of the new compound were similar to the corresponding signals of other withanolides [4] and daturalactones [1–3].

\* Present address: Department of Chemistry, Kashmir University, Srinagar-190006, India.



Scheme 1. Probable mass fragmentation pattern of daturalactone-4. Relative intensities of the ions are given in parentheses.

From the above chemical and spectral studies, the compound has been assigned the structure 5 $\alpha$ -hydroxy-1-oxo-6 $\alpha$ ,7 $\alpha$ ,24 $\alpha$ ,25 $\alpha$ -diepoxy-(22*R*)-with-2-enolide (1).



#### EXPERIMENTAL

**Isolation.** Crushed fresh leaves (1 kg) of *D. quercifolia* were extracted with cold C<sub>6</sub>H<sub>6</sub>. On concn, the extract deposited a pale green crystalline substance, which on CC yielded daturalactones-1 and -2 [1, 2], respectively. The mother liquor, on chromatography over Si gel and elution with CHCl<sub>3</sub>-EtOAc (4:1) gave colourless crystalline needles, mp 282°. (Found: C, 71.75; H, 8.05. Calculated for C<sub>28</sub>H<sub>38</sub>O<sub>6</sub>: C, 71.49; H, 8.09%).

**Hydrogenation.** The compound (35 mg) was hydrogenated

(10% Pd/C in EtOAc, H<sub>2</sub> uptake 1 mol). The product, on crystallization from CHCl<sub>3</sub>-EtOAc, gave colourless crystals, mp 269°. (Found: C, 71.25; H, 8.35. Calculated for C<sub>28</sub>H<sub>40</sub>O<sub>6</sub>: C, 71.18; H, 8.47%).

**Reduction.** To a Zn-Cu couple (4 g in EtOH) was added 100 mg of the compound and the reaction mixture was refluxed on a water bath for 24 hr. After the usual work-up, the product was passed through a small Si gel column to yield a crystalline compound, mp 265°. (Found: C, 73.70; H, 8.75. Calculated for C<sub>28</sub>H<sub>40</sub>O<sub>5</sub>: C, 73.68; H, 8.77%).

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