# STUDIES IN THE SANTONIN SERIES

## Part II.—The Nitration Products of Desmethyldesmotroposantonins

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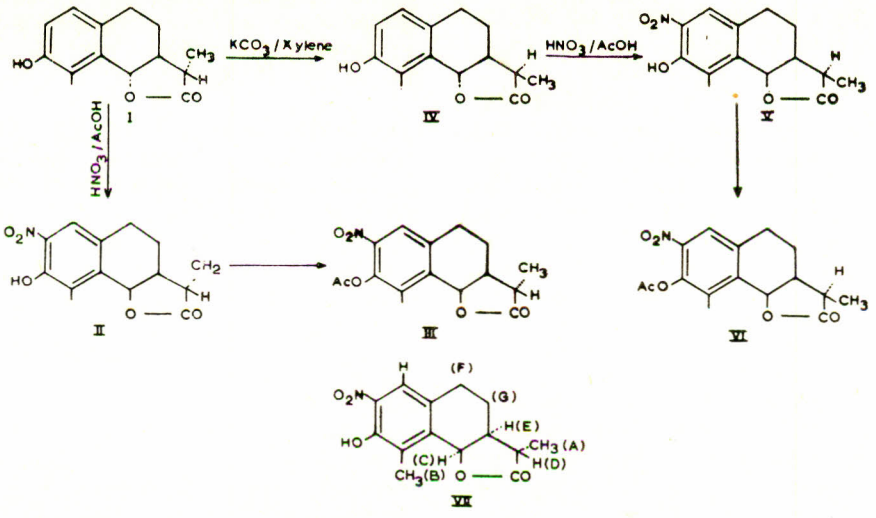
Nitration of 6β(H), 11β(H)-desmethyldesmotrosantonin (1) gave the 2-nitro-6α(H), 11β(H) derivative (II), which on acetylation with $Ac_2O$ and $H_2SO_4$ gave compounds III. The nitro acetate of III was also obtained by acetylation with Py and $Ac_2O$. The 6 β(H),11α(H)-desmethyldesmotroposantonin (IV) obtained by $K_2CO_3$ and xylene isomerisation of II, on nitration, gave 2-nitro-6α(H),11α(H) derivative (V). Nitration thus gave only two isomers.

In the earlier paper,[1] the bromination products of desmethyldesmotroposantonin (I) were described. The present communication describes the nitro derivatives of desmethyldesmotroposantonin and their spectral properties.

For a mononitro derivative one can expect four isomers, possible by the combination of different orientations at assymetric carbons 6 and 11.

Nitration of 6β(H),11β(H)-desmethyldesmotroposantonin (I) by the conventional procedure using acetic acid and nitric acid,[2] led to 2-nitro-6α(H),11β(H)desmethyldesmotroposantonin (II). The nitro group is assigned position 2 in analogy with similar derivatives of desmotroposantonin[2] and the bromo derivatives of desmethyldesmotroposantonin.[1] Acetylation of II with acetic acid and sulphuric acid which is known to alter the stereochemistry at C-6, and with acetic anhydride and pyridine where the reaction proceeds with retention of configuration[3] led to the formation of the same acetylated product (III).

Nitration thus is accompanied by a change of configuration at C-6. The nitro derivative (II), therefore, has 6α(H),11β(H) configuration. This is in accord with an earlier observation by Huang Minlon *et al.* for nitrodesmotroposantonins.[2] The nitro derivative (II) exhibits characteristic NMR spectrum. Various protons as labelled in VII absorb as follows: (1) Lactone methyl (A); doublet (3H) centred at 1.33 ppm ($J$=6 c/s). (2) Aromatic methyl; singlet (3H) at 2.45 ppm. (3) The benzylic methylene (F) and the methine (D) adjacent to lactone methyl, overlapped and appeared as a multiplet (3H) from 2.85 to 3.15 ppm. (4) Protons G and E appeared as multiplets (3H) from 1.8 to 2.25 ppm. The doublet ($J$=9 c/s) due to E was clearly distinguishable on account of its higher intensity and its components indicated some further splitting. (5) The methine proton (C) showed itself as a doublet (1H) centred at 4.96 ppm ($J$=9 c/s). Each component of the doublet showed some further splitting as in the case of E. (6) The aromatic proton appeared as a singlet (1H) at 7.7 ppm while the phenolic proton was observed downfield at 10.8 ppm.



The NMR spectrum of acetylated 2-nitro-6-α(H),11β(H)-desmethyldesmotroposantonin (III) in addition to the usual features indicated acetate methyl as a sharp singlet at 2.48 ppm.

In another experiment compound I was isomerised with anhydrous potassium carbonate in refluxing xylene to get 6β(H),11α(H) derivative (IV). This was nitrated to get the 6α(H),11α-(H) derivative (V), which was acetylated to yield VI. The NMR spectrum of V is similar to that of II. Following the notation as in VII it depicts peaks for A (doublet centred at 1.34 ppm, $J$= 6 c/s); B (singlet at 2.42 ppm); C (doublet centred at 5.29 ppm, $J$=9 c/s); G and E (multiplet from 1.8 to 2.25 ppm); F and D (multiplet around 2.86 ppm) and the aromatic proton a singlet at 7.76 ppm. The slight shift observed in the case of some peaks is due to the change in stereochemistry at C-11.

The two isomers II and V depict similar UV spectra $\lambda_{max}^{MeOH}$ =280 mμ, log ε=3.9. The lactone absorption was masked by a low wavelength band due to *o*-nitrophenol chromophore.

Less drastic methods of nitration such as nitration via nitrosation[4] and by metal salt method[5] were also tried with a view to retaining the configuration at C-6 but were found to be unsuccessful.

## Experimental

All m.ps are uncorrected. The IR spectra were recorded by Leitz spectrometer. The UV spectra were run on Beckman-DB spectrophotometer. NMR spectra were recorded on Varians NMR-EPR model DP. 60 and A-60 with TMS as internal standard. The purity of all compounds was checked by TLC.

2-*Nitro*-6α(*H*) 11β(*H*)-*desmethyldesmotroposantonin* (*II*).—A suspension of 1 g of 6β(H), 11β(H)-desmethyldesmotroposantonin (I), in glacial acetic acid (10 ml), was cooled to 7°C. A solution of 10% nitric acid in glacial acid (4 ml) was added dropwise to the stirred suspension of I in 80 min at 10°C. After addition was complete, the mixture was stirred for an additional 15 min at the same temperature. The mixture was poured into ice–cold water, the precipitate was filtered, washed with water and air-dried. Recrystallisation of the crude nitro product from alcohol gave 600 mg of pure 2-nitro-6α(H), 11β(H)-desmethyldesmotroposantonin as yellow needles m.p. 154–155°C. IR $\lambda_{max}^{Nujol}$ 1767 cm$^{-1}$ (lactone) 1560, 1350 cm$^{-1}$ ($NO_2$).

Found: C, 60.78; H, 5.45; N, 5.08. Calc for $C_{14}H_{15}O_5N$: C, 60.64; H, 5.45; N, 5.05%.

2-*Nitro*-6α(*H*), 11β(*H*)-*desmethyldesmotrosantonin acetate* (*III*).—(a) A solution of 250 mg of II in a mixture of 2 ml acetic anhydride and 2 ml pyridine was allowed to stand overnight at room temperature and then poured with stirring into a mixture of the ice–cold water. The precipitate was filtered, washed with water and air-dried. Recrystallisation of the solid from methanol gave 175 mg 2-nitro-6α(H), 11β(H)-desmethyldesmotroposantonin acetate, m.p. 158–159°C. IR $\lambda_{max}^{Nujol}$ 1760 cm$^{-1}$ (lactone) 1355 cm$^{-1}$ ($NO_2$).

(b) To a solution of 250 mg compound II in 4 ml acetic anhydride, was added a drop of concentrated sulphuric acid and the mixture was heated on a water bath for 15 min. The reaction mixture was poured into ice–cold water. The precipitate was filtered, washed with water and air-dried. Recrystallisation of the crude solid from methanol gave 180 mg fine needles m.p. 158–159°C, which was undepressed on admixture with the acetate prepared by method (a) as above. IR spectra of both the acetates were also identical. IR $\lambda_{max}^{Nujol}$ 1765 cm$^{-1}$ (lactone), 1355 cm$^{-1}$ ($NO_2$). Found: C, 60.40; H, 5.50; N, 4.37. Calc for $C_{16}H_{17}O_6N$: C, 60.18; H, 5.37; N, 4.39%.

6β(*H*), 11α(H)-*desmethyldesmotroposantonin* (*IV*).—1.0 g 6β(H),11β(H)-desmethyldesmotroposantonin (I), 1.0 g anhydrous potassium carbonate, and 25 ml xylene were refluxed for 24 hr. The xylene was removed under reduced pressure. The residue was washed with water and extracted with ethyl acetate. The ethyl acetate was distilled off. The residue was extracted with acetone, decolorised with charcoal, recrystallisation from acetone gave 200 mg compound IV, m.p. 232°C. Found: C, 72.43; H, 6.84. Calc for $C_{14}H_{16}O_3$: C, 72.39: H, 6.94%.

2-*Nitro*-6α(*H*), 11α(*H*)-*desmethyldesmotroposantonin* (*V*).—Nitration of 6β(H), 11α(H)-desmethyldesmotroposantonin (IV) by the method given above gave compound V. Recrystallisation of crude solid from alcohol gave yellow needles, m.p. 189–191°C which was depressed on admixture with III. IR $\lambda_{max}^{Nujol}$ 1768 cm$^{-1}$ (lactone), 1565, 1355 cm$^{-1}$ ($NO_2$). (Found: C, 60.60; H, 5.27; N, 4.81. Calc for $C_{14}H_{15}O_5N$:C, 60.64: H, 5.45; N, 5.05%.

2-*Nitro*-6α(*H*), 11α(*H*)-*desmethyldesmotroposantonin acetate* (*VI*).—(a) Acetylation of compound V with acetic anhydride in pyridine and recrystallisation from alcohol gave the acetate,

m.p. 184–185°C, mixed m.p. with III showed depression.

(b) Acetylation of V with acetic anhydride and concentrated sulphuric acid gave compound VI, which on recrystallisation from alcohol gave a compound of m.p. 184–185°; mixed m.p. with the acetate prepared by method (a) showed no depression. IR spectra of both the acetates were identical.

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