Constitution of Four Novel Methyl Steroid Relatives (Ring-D Aromatic) from the Insect Repellent Plant *Nicandra physaloides*; *X*-Ray Analysis of Nic-10†

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Summary *Nicandra physaloides* (Solanaceae) contains four new methyl steroid, relatives (**1**)—(**4**), all containing an aromatic ring D; the constitution of the first is demonstrated by crystallographic analysis using direct methods.

Recently[1] we reported the molecular structures of two new methyl steroid constituents from *Nicandra physaloides* (Solanaceae); extractives of the latter show insect-repellent activity.[2] We now describe the constitution of four further methyl steroid relatives from this plant, all possessing an aromatic ring D, a feature unique in natural steroids. The key structural information was provided by *X*-ray analysis of Nic-10, m.p. 207°, $C_{21}H_{22}O_4$,‡ crystallising in the space group $P2_12_12_1$ with $a = 6{\cdot}45$, $b = 9{\cdot}59$, $c = 27{\cdot}84$ and $Z = 4$. Intensity data were collected with Cu-K_α radiation using an automatic four-circle diffractometer. The structure was solved by direct methods using the Multan[3] procedure and refinement has proceeded to a current R index 12·7%, using 1610 observed data. The constitution was shown to be as in (**1**), an oxidised methyl steroid, with rings A–C the same as those in Nic-3.[1] Ring D is aromatic, and presumably contains, at a higher oxidation level, the

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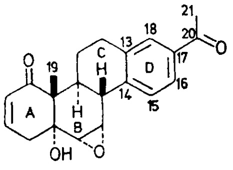
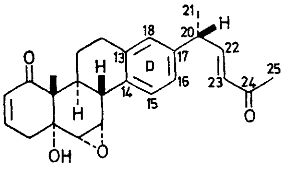
† See footnote in ref. 1 for use of the 'Nic' terminology.

‡ All molecular formulae based on accurate mass measurements.

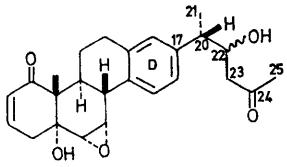
carbon otherwise found as the C-18 angular methyl; the side chain acetyl is thus displaced from the position vicinal to the C–D ring junction.



(1)



(2)



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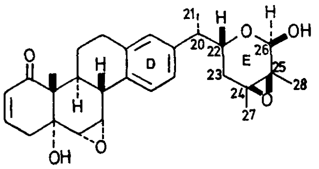

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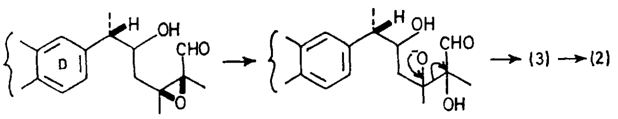

(5) (6)

Three more terpenoids with ring D aromatic were separated; Nic-12, m.p. 175°, $C_{25}H_{28}O_4$; Nic-17, m.p. 86°, $C_{25}H_{30}O_5$; and Nic-1, m.p. 138°, $C_{28}H_{34}O_6$. Spectroscopic comparison strongly indicates that these share a common ring A—D pattern with Nic-10, differing only in the attachment to C-17. All showed aromatic n.m.r. signals§ [τ 2·35—2·45 (d, 15-H), 2·70—2·95 (d, $J_{15,16}$ 7—8 Hz, 16-H), and 2·85—3·05 (s, 18-H)], with the signals for 16-H and 18-H at higher field than in Nic-10 [τ 2·28 (d, 15-H), 2·07 (d, 16-H), and 2·24 (s, 18-H)], and a secondary methyl (τ 8·55—8·65, d, J 7 Hz) replacing the Nic-10 arylmethyl ketone resonance τ (7·30 s). All four compounds displayed λ_{max} 212—219 nm (enone), but only Nic-10 showed an aryl ketone chromophore, λ_{max} 256 (ϵ 18,530) nm.

Nic-12 is assigned structure (**2**); the side chain is characterised by τ 2·94 (dd, $J_{20,22}$ 7, $J_{22,23}$ 16 Hz, 22-H), 3·75 (d, 23-H), and 7·79 (3H, s, 25-H), and ν_{max}¶ 1665 cm^{-1} (C=O). Two enone chromophores overlap at λ_{max} 219 (ϵ 26,520) nm. Nic-17 (**3**) is closely related to Nic-12 but contains a secondary as well as a tertiary hydroxy-group [ν_{max} 3490 and 3450 cm^{-1}; τ 5·43 (m, 22-H)], a saturated methyl ketone group [ν_{max} 1698 cm^{-1}; τ 7·86 (s)], and only one unsaturated ketone chromophore, λ_{max} 216 (14,480) nm. The side chain attachment of Nic-1 is the same as that in Nic-3 and Nic-7,[1] and was recognised by spectroscopic comparison; it incorporates an epoxylactol ring E. Salient n.m.r. features are τ 5·52 (1H, m, 22-H), 8·70 and 8·79 (CH_3-27 and 28) τ $[(CD_3)_2SO]$ 5·14 (1H, d, J 7 Hz, 26-H), and 3·97 (1H, d, J 7 Hz, OH).

In Nature, Nic-1 (**4**) may precede Nic-17 in a biogenetic sequence; thus, if the 24,25-epoxy-function in Nic-1 [shown in the δ-hydroxyaldehyde form (**5**)] is opened, *e.g.* hydrolysed to diol (**6**), retro-aldol cleavage can proceed as shown in (**6**), giving rise to Nic-17 and an aldehyde. Dehydration affords Nic-12, and further oxidative degradation may lead to Nic-10.

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§ All n.m.r. data collected at 100 MHz in C_5D_5N unless otherwise stated.

¶ All i.r. measurements in KBr.

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[2] G. Fraenkel, J. Nayar, O. Nalbandov, and R. T. Yamamoto, *Intern. Congr. Entomol. Verl.*, 11th, Vienna, 1960, III, p. 122; O. Nalbandov, R. T. Yamamoto, and G. Fraenkel, *J. Agric. Food Chem.*, 1964, **12**, 55; F. v. Gizycki and G. Kotitschke, *Arch. Pharm.*, 1951, **284**, 129.

[3] G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.