Solanascone: a Novel Sesquiterpene Ketone from *Nicotiana tabacum*. *X*-Ray Structure Determination of the Corresponding Oxime

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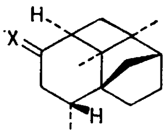
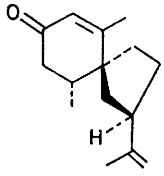
Summary Solanascone (**1**), a new tetracyclic sesquiterpene ketone, has been isolated from *Nicotiana tabacum* cv. Burley; its structure was confirmed by *X*-ray analysis of its corresponding oxime (**2**).

We have previously reported the isolation of (−)-solavetivone (**3**) from air-cured Burley tobacco (*Nicotiana tabacum* cv. Burley).[1] This compound had a vetispirane skeleton and was obtained originally from potato tubers as a major stress metabolite by Coxon *et al.*[2] Further, Anderson *et al.* reported the isolation and stereochemistry of four vetispirane sesquiterpene glucosides from flue-cured Virginia tobacco.[3] We report here the isolation and structure of a new tetracyclic sesquiterpene ketone (**1**) from *N. tabacum* and have given it the trivial name solanascone.



(1) X = O
(2) X = NOH



(3)

Solanascone (**1**), (2*R*, 6*S*, 7*S*)-trimethyltetracyclo$[6.2.1.1^{5,7}.0^{1,6}]$dodecan-4-one, was isolated from 370 kg of air-cured American Burley tobacco leaves[4] by dichloromethane extraction, steam-distillation under reduced pressure, fractionation, and distillation under reduced pressure. Repeated silicic acid column chromatography of the volatile neutral fraction (b.p. 29—96 °C at 0·002 mmHg) followed by preparative gas chromatography gave 30 mg of (**1**) as a mobile oil, $[\alpha]_D^{24}$ + 20·3° (*c* 1·97, $CDCl_3$), *m/e* 218 (M^+, $C_{15}H_{22}O$, 28%), 203 (10), 190 (62), 121 (49), 120 (C_9H_{12}, 100), 105 (37), 91 (31), and 41 (45); ν_{max} 1710 (C=O), 1460, 1426, 1382, and 1300 cm^{-1}; ^{1}H n.m.r. (CCl_4): δ 1·03 (3H, s), 1·11 (3H, d, *J* 7 Hz), 1·31 (3H, s), and 2·43 (2H, m, AB part of an ABX system, J_{AB} 14, J_{AX} 8, J_{BX} 7·3 Hz‡); ^{13}C n.m.r. ($CDCl_3$): δ 219·3 (s), 50·8 (s), 50·1 (s), 49·1 (d), 46·7 (t), 46·2 (s), 44·5 (d), 43·0 (t), 37·3 (d), 34·8 (t), 26·6 (t), 23·7 (t), 20·5 (q), 18·2 (q), and 17·8 (q) p.p.m.

^{1}H and ^{13}C N.m.r., mass, and i.r. spectra indicated that (**1**) was tetracyclic, and contained a six or higher membered saturated ketone, a methylene adjacent to the ketonic function, two methyl groups attached to quaternary carbons, a methyl group attached to a tertiary carbon, and a quaternary carbon bearing no methyl groups. The complete structure and stereochemistry of (**1**) was elucidated by *X*-ray crystallography of its oxime (**2**), m.p. 121—123 °C.

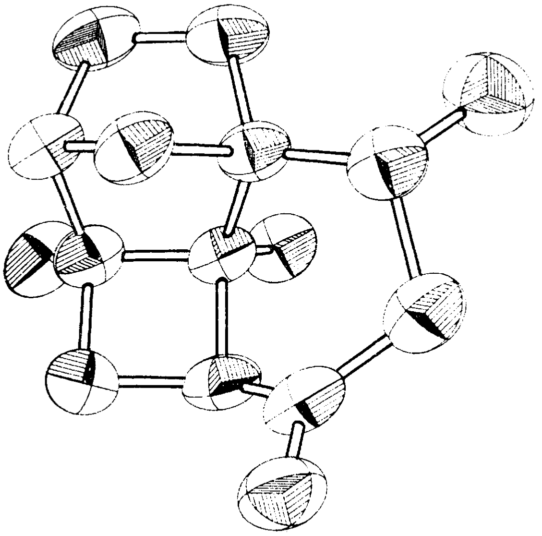


FIGURE. Perspective view of the oxime (**2**) of solanascone. The oxygen and hydrogen atoms have been omitted for the sake of clarity.

Crystal data: $C_{15}H_{23}NO$, tetragonal, space group $P4_12_12$ or $P4_32_12$, $a = b = 7{\cdot}496(3)$, $c = 47{\cdot}936(10)$ Å, $Z = 8$, $D_c = 1{\cdot}151$ g cm^{-3}. Intensity data with 2θ-values up to 140° were collected on a Rigaku four-circle diffractometer using Cu-K_α radiation monochromated with an LiF crystal. 1526 independent structure factors above their estimated standard deviations were selected for the structural study. The structure was solved by the direct method on the basis of 266 *E*-values above 1·30. Close examination of a difference Fourier map and a model revealed that the crystal had a disordered structure which contained equimolecular amounts of the *E*- and *Z*-isomers of (**2**). All hydrogen atoms except hydroxy hydrogen were located in a second difference Fourier map, and full-matrix least-squares refinement was repeated including these hydrogen atoms. The final *R*-value is 7·4%. The molecular framework obtained is shown in the Figure. Thus, the structure of solanascone has been established as (**1**).§

Irradiation of (−)-solavetivone (**3**)[3,5] in methanol produced solanascone (**1**) by a [2 + 2] photocyclization. This

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‡ These values were obtained from the ^{1}H n.m.r. spectrum in the presence of Eu(fod)$_3$.

§ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

result suggests that (**3**) may be a direct precursor of (**1**) and the absolute configuration of (+)-solanascone was shown to be as in the stereostructure (**1**). Further, the octant projection of (+)-solanascone was consistent with this result (positive Cotton effect, $[\phi]_{310}$ + 3367, *c* 0·04, EtOH). The currently accepted scheme for the biogenesis of vetispirane sesquiterpenes involves a migration of a methylene group in a common hypothetical eudesmane-related intermediate (**4**).[6] A possible route for the biogenesis of (+)-solanascone (**1**) is in the Scheme.

Compound (**1**) was also present in the leaves of *N. tabacum* cv. Matsukawa, a Japanese domestic tobacco, and Phillipine cigar tobacco (Manila leaves).

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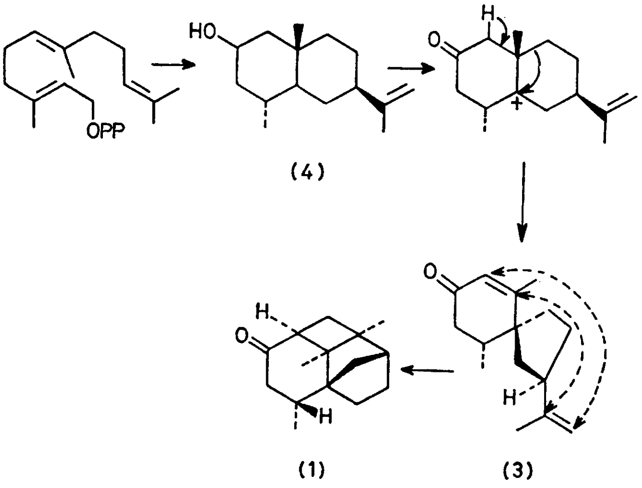

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