

**Tobacco Chemistry. 32. The Absolute Configuration of Norsolanadione, (5*S*)-5-Isopropyl-3*E*-nonen-2,8-dione, a Nor-thunberganoid of *Nicotiana tabacum* L.**

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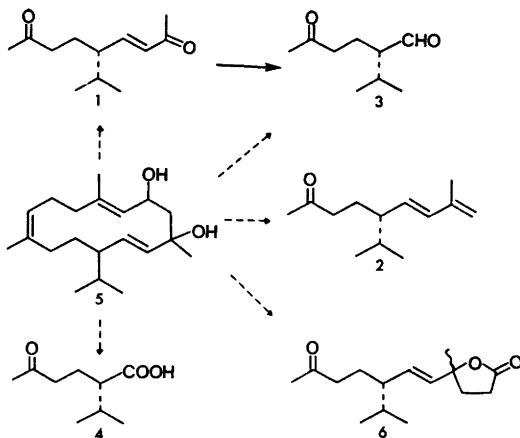
Synthetic, racemic norsolanadione, ( $\pm$ )-5-isopropyl-3*E*-nonen-2,8-dione (*1*), was first described in 1965 as an air oxidation product of synthetic solanone, ( $\pm$ )-2-methyl-5-isopropyl-1,3*E*-nonadien-8-one (*2*), by Johnson and Nicholson who had isolated the dextrorotatory form of the latter from aged Burley tobacco.<sup>1</sup> The absolute configuration of solanone was later established\*\* as *S* by Fukuzumi *et al.*<sup>2</sup> by correlation with (2*S*)-2-isopropyl-5-oxohexanoic acid (*4*). In 1971 norsolanadione (*1*) was identified by Shigematsu *et al.*<sup>3</sup> as a component of tobacco smoke, and it was subsequently also found to be a constituent of Burley,<sup>4,5</sup> Turkish<sup>6</sup> and Greek tobacco leaves.<sup>7</sup>

Since norsolanadione (*1*), solanone (*2*) and other structurally related tobacco constituents can be viewed as degradation products of thunbergane diterpenoids,<sup>8</sup> determination of remaining chiral centres offers a possibility of checking the assumed interrelationships. The absolute configuration of norsolanadione (*1*) was elucidated by converting it and solanone (*2*), both isolated from Greek tobacco,<sup>9</sup> to a common degradation product, (2*S*)-5-oxo-2-isopropylhexanal (*3*), by ozonolysis and reductive work-up. In view of their identical absolute configurations and since solanone decomposes to norsolanadione when subjected to air oxidation,<sup>1</sup> and the  $\beta$ -4,8,13-duvatrien-1,3-diol (*5*),<sup>10</sup> commonly encountered in tobacco, is known to yield solanone on irradiation,<sup>11</sup> it seems plausible that norsolanadione (*1*) is formed by a similar pathway in the tobacco plant.

The absolute configurations\*\*\* of the eleven thunbergane diterpenoids encountered in tobacco are presently unknown,<sup>12</sup> although it is probable that cembrene, detected in tobacco only under the influence of enzyme-blocking agents,<sup>13</sup> possesses the same absolute configuration, *S*, as cembrene [(1*S*)-2*E*,4*Z*,7*E*,11*E*-thunbergatetraene] isolated from pine-trees of the subgenus *Haploxyton*.<sup>14,15</sup> Since it has been demonstrated<sup>13</sup> that <sup>14</sup>C-labelled cembrene enzy-

\*\* The *R/S*-convention was erroneously applied in the original paper<sup>2</sup> by attributing the *R*-configuration to solanone.

\*\*\* Note added in proof: By ozonolytic degradation we have recently established that the tobacco thunberganoids possess the 1*S*-configuration.



*Scheme 1.* The absolute configuration of norsolanadione (*1*), established by conversion to (2*S*)-5-oxo-2-isopropylhexanal (*3*), and of other tobacco constituents assumed to be derived from diterpenoids of the thunbergane-type, *e.g.* *5*.

matically is converted to duvatrienols in the tobacco plant, and that all tobacco compounds of known chirality and assumed to be derived from thunbergane diterpenoids, possess the *S*-configuration — *i.e.* (2*S*)-2-isopropyl-5-oxohexanoic acid (*4*), (7*S*)-10-oxo-4 $\xi$ -methyl-7-isopropyl-5*E*-undecen-4-olide (*6*),<sup>16</sup> solanone (*2*),<sup>2</sup> and norsolanadione (*1*) — it is reasonable to postulate that all known tobacco thunberganoids possess *S*-configuration.†

*Experimental.* NMR, IR, and mass spectra were recorded on Varian XL-100, Digilab FTS-14, and LKB 9000 instruments, respectively. Rotations were measured on a Perkin-Elmer 141 instrument. Norsolanadione (*1*) was isolated from fraction B7<sup>9</sup> by preparative gas chromatography performed on a 3 m  $\times$  3.2 mm glass column packed with 5% Carbowax 20 M on Chromosorb G.

*Norsolanadione. (1).* MS: 196 ( $M^+$ , 1), 43 (100), 97 (54), 95 (40), 41 (24), 93 (18), 126 (18), 55 (17), 111 (15), 135 (14), 120 (14), 121 (14), 123 (13);  $\delta$ (CDCl<sub>3</sub>): 0.88 (3 H, d, *J* 6.5 Hz), 0.93 (3 H, d, *J* 6.5 Hz), 2.12 (3 H, s), 2.26 (3 H, s), *ca.* 2.37 (2 H, distorted t, *J ca.* 7 Hz), 6.03 (1 H, d, *J* 16 Hz), 6.56 (1 H, dd, *J* 9 and 16 Hz); lit.<sup>1</sup>  $\delta$ (CCl<sub>4</sub>): 0.92 (6 H, 'two superimposed doublets'), 2.04 (3 H, s), 2.15 (3 H, s), 2.35 (2 H, t), AB-part of an ABX-system 'centred at  $\delta$  6.25 (*J* 8 and 16 Hz);  $\nu_{\max}$ (film): 2960 (s), 2931 (m), 2876 (m), 1717 (s), 1676 (s), 1626 (w), 1367 (s), 1258 (s), 1168 (m), 989 (m); lit.<sup>1</sup>  $\nu_{\max}$ : 1715, 1675, 1624, 990;  $[\alpha]^{20}$   $-2.2^\circ$  (589 nm),  $-2.2^\circ$  (578),  $-2.2^\circ$

† In all these compounds the units linked to the asymmetric centre, C(1), are the same, *i.e.* —H, —CH<sub>2</sub>—, —CH=CH—, and —CH(CH<sub>3</sub>)<sub>2</sub>.<sup>17,18</sup>

(546),  $-0.3^\circ$  (436), (c 0.67,  $\text{CHCl}_3$ ).

**Ozonolysis of norsolanadione.** Norsolanadione (1, 30 mg) dissolved in  $\text{CH}_2\text{Cl}_2$  (15 ml) and pyridine (0.1 ml) was treated with excess ozone at  $-65^\circ\text{C}$ . Zinc powder (500 mg) and acetic acid (2 ml) were added and the mixture stirred 35 min during which the temperature was slowly raised to  $20^\circ\text{C}$ . The solution was decanted, the reaction vessel with its residue was washed with  $\text{CH}_2\text{Cl}_2$ , and the combined solutions washed four times with water. Removal of the solvent left a slightly yellow oil which was chromatographed on silica gel furnishing pure (2*S*)-5-oxo-2-isopropylhexanal (3, 10 mg). NMR, IR, and mass spectra were indistinguishable from those of (2*S*)-5-oxo-2-isopropylhexanal (3) prepared previously by ozonolysis of solanone.  $[\alpha]_{\text{D}}^{20} + 47.8^\circ$  (589 nm),  $+ 50.7^\circ$  (578),  $+ 61.4^\circ$  (546),  $+ 146.6^\circ$  (436),  $+ 400.8^\circ$  (365), (c 0.73,  $\text{CHCl}_3$ ); lit.<sup>16</sup>  $[\alpha]_{\text{D}}^{20} + 43.7^\circ$  (589 nm),  $+ 45.9^\circ$  (578),  $+ 55.6^\circ$  (546),  $+ 133.3^\circ$  (436),  $+ 364.8^\circ$  (365) (c 0.54,  $\text{CHCl}_3$ ).

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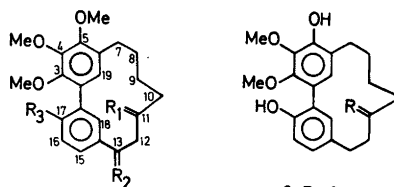
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## Porson, a New [7,0]-Metacyclophane from *Myrica gale* L.

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We have continued<sup>1</sup> our studies of the phenolic constituents of *Myrica gale* L. From an ethyl acetate extract of the stems we have isolated after partition between methanol/water and petroleum ether and repeated column and thin layer chromatography a crystalline phenolic ketone, porson (1) [m.p.  $186-187^\circ\text{C}$ ,  $\nu_{\text{max}}(\text{CHCl}_3)$   $1713\text{ cm}^{-1}$ ,  $\lambda_{\text{max}}(\text{MeOH})$  248 (11 200), 293 (6300) nm, calc. for  $\text{C}_{22}\text{H}_{20}\text{O}_6$  386.1728 as found]. Porson was recognized as a [7,0]-metacyclophane by comparison of its spectroscopic data with two related compounds, myricanone (2) and myricanol (3) previously isolated from *Myrica nagi*.<sup>2</sup>



- |   |                          |                           |                         |
|---|--------------------------|---------------------------|-------------------------|
| 1 | $\text{R}_1=\text{O}$    | $\text{R}_2=\text{H,OH}$  | $\text{R}_3=\text{OH}$  |
| 4 | $\text{R}_1=\text{O}$    | $\text{R}_2=\text{H,OAc}$ | $\text{R}_3=\text{OAc}$ |
| 5 | $\text{R}_1=\text{O}$    | $\text{R}_2=\text{O}$     | $\text{R}_3=\text{OH}$  |
| 6 | $\text{R}_1=\text{H,OH}$ | $\text{R}_2=\text{O}$     | $\text{R}_3=\text{OH}$  |

- |   |                        |
|---|------------------------|
| 2 | $\text{R}=\text{O}$    |
| 3 | $\text{R}=\text{H,OH}$ |

The most prominent features of the NMR spectrum of 1 are the presence of resonances due to three methoxy groups ( $\delta$  3.83, 3.91 and 3.95) and the signals of four aromatic protons [ $\delta$  6.46 (s, H-19), ABX pattern: 6.65 ( $J \approx 2$  Hz, H-18), 6.88 ( $J \approx 8$  Hz, H-16), 7.02 ( $J \approx 2$  and 8 Hz, H-15)]. Two hydroxy resonances are also visible; one phenolic ( $\delta$  7.82) and one due to a secondary aliphatic hydroxy group ( $\delta \sim 3$ ), the carbonyl proton being located at  $\delta$  4.35 as a doublet of doublets ( $J = 2$  and 6 Hz). The relative low field resonance of this proton is indicative of its position at C-13, close to the aromatic nucleus. Irradiation at  $\delta$  4.35 collapses a multiplet at  $\delta$  2.95 and *vice versa* thus indicating the resonance position of the C-12 methylene group. In the same region of the spectrum ( $\delta$  2.5–3.0) is also located the resonances of four more protons, probably 2H-7 and 2H-10. Moreover, the resonance position of the H-12