

formation of an enol ester and was then heated to 110° and maintained at this temperature for 3 h. After cooling, the mixture was poured into ice-cold 4 N hydrochloric acid and extracted repeatedly with chloroform, and the extract was shaken with concentrated aqueous sodium hydrogen carbonate. The aqueous layer was acidified with conc. hydrochloric acid and extracted with chloroform. The dried chloroform extract gave on evaporation the pure 3-acylated tetrionic acid. Only 3-acetyl- and 3-propionyl-tetrionic acid had to be recrystallized from petrol ether.

(R,S)-*Carolic acid*. 5-Methyltetrionic acid (4.38 mmol) was acetylated with 500 mmol of 4-chlorobutyl chloride to give 0.47 g of dark red oil, which solidified when treated with ether. Four recrystallizations from ethyl acetate-light petrol gave 50 mg (5%) of amber coloured crystals, m.p. 112.5–115.2°. Sublimation raised the m.p. to 116–118°. ¹H NMR in CDCl₃: 1.46 d (CH₃), 4.64 q (H), 3.45 t (COCH₃), 2.28 m (CH₂CH₂CH₂), 4.80 t (CH₂O). M_{MS} = 182.05843; M_{calc} = 182.0579 (Lit.⁵ m.p. 117°).

(S)-*Carolic acid*. Acylation of 2 mmol of synthetic (S)-5-methyltetrionic acid⁴ resulted in the isolation of 70 mg (14%) colourless crystals m.p. 130–132° (Lit.⁶ 132°). [α]_D²⁵ = -70.8° (c = 0.49, H₂O) (Lit. val. for the enantiomeric form +84°) ¹H NMR as above.

Attempted synthesis of (R,S)-carolic acid (3). 5-Methyltetrionic acid (4.38 mmol), 5.0 mmol of β-carbomethoxypropionyl chloride and 6.50 mmol of tin(IV) chloride reacted very slowly and did not become homogeneous. On working up about 100 mg of a yellow syrupy reaction product was obtained. On acid hydrolysis and extraction with a small amount of chloroform, the chloroform extract contained only succinic anhydride.

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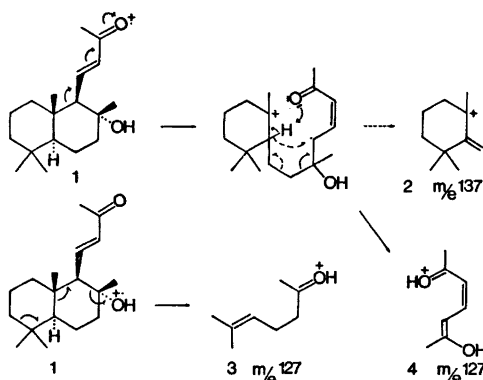
Tobacco Chemistry. 26. Synthesis of 14,15-Bisnor-8-hydroxyabd-11*E*-en-13-one, A New Tobacco Constituent

JOSEPH R. HLUBUCEK, ARNE J. AASEN, SVEN-OLOF ALMQVIST and CURT R. ENZELL*

Research Department, Swedish Tobacco Co., Box 17 007, S-104 62 Stockholm, Sweden

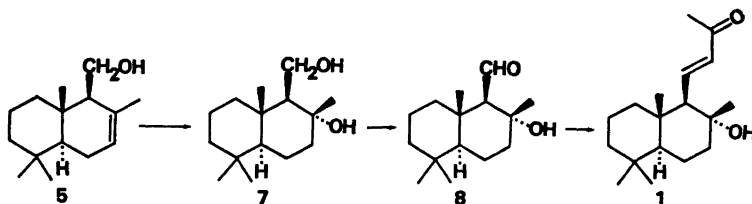
Current research in this laboratory has revealed that tobacco flavour comprises a large number of norisoprenoid constituents.^{1,2} The present report deals with the identification and synthesis of a probable diterpenoid degradation product isolated from a medium-volatile, neutral fraction³ of an extract⁴ of sun-cured Greek *Nicotiana tabacum* L.

The elemental composition of this new tobacco compound, C₁₈H₃₀O₂, was established by high resolution mass spectrometry. The two oxygen atoms were accommodated by a 3*E*-penten-2-oxo-1-ylidene moiety, >CH-CH=CH-CO-CH₃, [978 and 1661 cm⁻¹, 230 nm, δ 2.24 (3H, s), δ 6.16 (1H, d, *J* 16 Hz), δ 6.82 (1H, dd, *J* 10 and 16 Hz)], and a tertiary hydroxyl group (3450 cm⁻¹) attached to a methyl substituted [δ 1.26, (3 H, s)] carbon atom, >C(OH)-CH₃, respectively. Based on this evidence, the presence of three quaternary methyl groups (singlets at δ 0.83, 0.89, 0.99), its electron-impact induced fragmentation pattern being characteristic of labdane-type diterpenoids devoid of oxygen-substituents on ring A (cf. Scheme 1),⁵ and no indication of further double bonds, 14,15-bisnor-8-hydroxyabd-11*E*-en-13-one (*I*)** appeared likely as the structure for this new tobacco compound. This structure, including the stereochemistry inferred in *I*, was confirmed by total synthesis using drimenol⁶ (*5*) as starting material.



Scheme 1.

**Nomenclature according to J. W. Rowe, Oct., 1968; personal communication.



Scheme 2.

Drimenol (5) was converted to the diol 7 via the epoxide 6 as described elsewhere.⁷ The diol 7 was oxidised employing Collins' reagent,⁸ to the hydroxyaldehyde 8 which in turn was subjected to base-catalysed aldol condensation with acetone followed by *in situ* dehydration furnishing 14,15-bisnor-8-hydroxyabd-11E-en-13-one (1, Scheme 2), identical in all respects to the natural product. Very recently it has been reported that 1 could be obtained by oxidative degradation of the diterpenoid abienol.⁹ 14,15-Bisnor-8-hydroxyabd-11E-en-13-one (1) has been isolated previously from the resin of *Abies sibirica* and the published¹⁰ data are in agreement with ours except that 1 isolated by the Russian workers was reported to be optically inactive.

Experimental. NMR, IR, UV, and mass spectra were recorded on Varian XL-100, Digilab FTS-14, Beckmann DB-2A, and LKB 9000 (70 eV) instruments, respectively. Rotations were measured on a Perkin-Elmer 141 instrument, and accurate mass determinations were carried out at the Laboratory for Mass Spectrometry, Karolinska Institutet, Stockholm.

14, 15-Bisnor-8-hydroxyabd-11E-en-13-one (1, 40 mg) was isolated from a medium-volatile, neutral fraction³ of an extract⁴ of sun-cured Greek *Nicotiana tabacum*. L. leaves, employing liquid chromatography on silica gel. The fractionation of this medium-volatile material will be described elsewhere.³ M.p. 126–127° (lit.¹⁰ 126°); MS: *m/e* 278 (M^+ , 7), 43 (100), 109 (56), 260 (33), 41 (32), 95 (27), 81 (26), 69 (26), 137 (25), 245 (25); accurate mass determination: $C_{16}H_{20}O_2$, found 278.2250, calc. 278.2246; $C_8H_{11}O_2$, found 127.0764, calc. 127.0759; $C_8H_{15}O$, found 127.1123, calc. 127.1123; δ ($CDCl_3$): 0.83 (3 H, s), 0.89 (3 H, s), 0.99 (3 H, s), 1.26 (3 H, s), 2.24 (3 H, s), 6.16 (1 H, d, *J* 16 Hz), 6.82 (1 H, dd, *J* 10 and 16 Hz); ν_{max} (KBr): 3450 (broad), 3026 (w), 1661 (s), 1633 (shoulder), 1268 (m), 1123 (m), 1084 (m), 986 (m), 978 (m), 970 (shoulder); λ_{max} (EtOH): 230 nm (ϵ 9300); $[\alpha]_D^{20}$ 15.8° (*c* 0.43, $CHCl_3$).

8-Hydroxydriman-11-al (8). 8,11-Dihydroxydrimane (7, 17 mg)⁷ was added to a suspension of anhydrous CrO_3 -pyridine complex (Collins' reagent,⁸ 100 mg) in methylene chloride (2 ml). The dark mixture was stirred for 75 min at

room temperature, diluted with ether and filtered through celite. The concentrated filtrate was applied in chloroform solution to a silica gel column (2 g) packed in 10% ether/pentane. Elution with 50% ether/pentane gave crystalline hydroxyaldehyde 8 (12 mg). δ ($CDCl_3$) 0.85 (3 H, s), 0.91 (3 H, s), 1.14 (3 H, s), 1.40 (3 H, s), 3.3 (1 H, broad s), 10.02 (1 H, d, *J* 2 Hz); ν_{max} (KBr): 3400 (broad), 2740 (w), 1710 (s); $[\alpha]_D^{20}$ 66.2° (*c* 0.58, $CHCl_3$).

Synthetic 14,15-bisnor-8-hydroxyabd-11E-en-13-one (1). 10% aqueous KOH solution (0.5 ml) was added to a solution of the hydroxyaldehyde 8 (7 mg) in acetone (3 ml) and the mixture heated under reflux for 7 h. The cooled reaction mixture was concentrated *in vacuo*, diluted with ether, washed well with water and dried (Na_2SO_4). The residue obtained after evaporation of the solvent was chromatographed on silica gel (2 g) to yield crystalline 1 (4 mg), indistinguishable from 1 isolated from tobacco.

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