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CEMBRANE-DERIVED DITERPENOID HAVING A CARBOTRICYCLIC SKELETON

REIKO UEGAKI, TAKANE FUJIMORI, NASUO UEDA* and AKIO OHNISHI

Central Research Institute, Japan Tobacco Inc., Umegaoka 6–2, Midori-ku, Yokohama 227, Japan; *Department of Chemistry, Faculty of General Education, Tottori University, Tottori 680, Japan

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Key Word Index—*Nicotiana tabacum*; Solanaceae; tobacco; diterpenoid; 18-oxo-3-virgene.

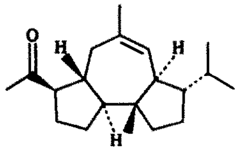
Abstract—A novel carbotricyclic diterpenoid, 18-oxo-3-virgene, has been isolated from the waxy, surface resins of tobacco. Its structure was determined by spectroscopic and chemical transformation methods, and confirmed by X-ray crystallography.

INTRODUCTION

Nicotina tabacum L., produces tobacco-specific diterpenoids, namely cembranoids and labdanoids. Cembranoids are present as components of the cuticular wax secreted from the trichomes of leaves, stalks and flowers in all varieties of tobacco, while labdanoids are found particularly in Oriental tobacco. Up to the present time, 52 cembranoids have been isolated from tobacco [1]. Cembranoids possess a 14-membered carbon ring; the most typical ones are (1*S*, 2*E*, 4*R*, 6*R*, 7*E*, 11*E*)- and (1*S*, 2*E*, 4*S*, 6*R*, 7*E*, 11*E*)-2,7,11-cembratriene-4,6-diols (3). Recently, a carbotricyclic, basmane type diterpenoid, which seems to be derived from cembrane, has been isolated from Greek tobacco [2]. And we have also encountered a cembrane derived diterpenoid having a novel, carbotricyclic skeleton, designated as virgane (2), from the tobacco cultivar Virginia 115. In this paper, we report on the isolation and structure determination of a derivative of virgane, 6-acetyl-13-isopropyl-3,10-dimethyltricyclo [8.3.0.$0^{5,9}$]-tridec-2-ene (1, 18-oxo-3-virgene).

RESULTS AND DISCUSSION

18-Oxo-3-virgene (1) ($[\alpha]_D - 69.1°$), was obtained by prep. GC from *N. tabacum* flowers. Its molecular formula was estimated as $C_{20}H_{32}O$ (HRMS). Its IR, ^1H NMR and ^{13}C NMR spectra indicated the presence of one isopropyl group, one olefinic methyl group, one methyl group attached to a fully substituted carbon atom, one saturated methyl ketone and one double bond. From these results, compound 1 was presumed to have a carbotricyclic skeleton derived from a cembranoid skeleton. The results of the ^1H–^{13}C shift correlation spectrum and spin systems obtained by the measurement of homonuclear correlated experiment (COSY 45) revealed its partial structures (Fig. 1). As the cross peaks in the COSY spectrum due to long range coupling between H-7 and H-10 were recognized, H-7 and H-10 seemed to be orientated syn-diaxial.



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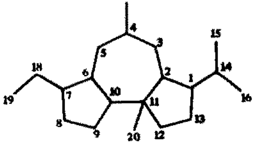

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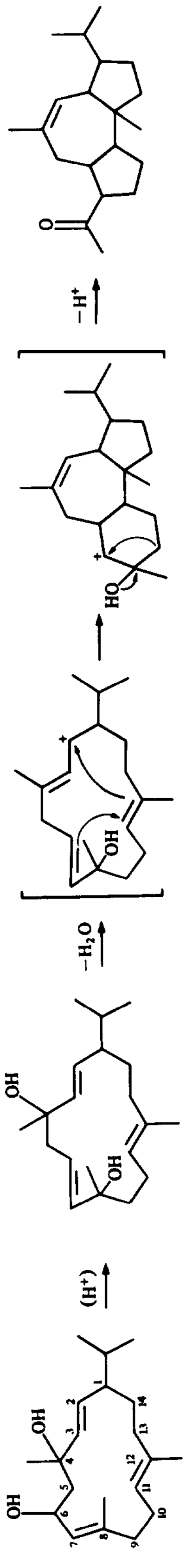
To determine the complete structure and relative stereochemistry, compound 1 (an oily substance) was subjected to X-ray analysis after conversion to its semicarbazone. The crystal data of semicarbazone were as follows: $C_{21}H_{35}N_3O$, monoclinic, space group C2, $a = 17.406$ (7), $b = 7.298$ (1), $c = 17.882$ (7) Å, $Z = 4$, $D_c = 1.07$ g/cm^{-3}. The result visualized by a computer generated drawing (Fig. 2) indicates, that the semicarbazone and 1 are diterpenoid having a carbotricyclic skeleton. Since the stereochemistry of C-1 of all tobacco cembranoids is 1*S*, the absolute configuration of 1 was assumed to be 1*S*, 2*S*, 6*R*, 7*R*, 10*S*, 11*R*. A possible biosynthetic route for the formation of 1 from a typical cembranoid (3) is shown in Scheme 1. The 4,8-diol(4) formed from 3 by an allylic rearrangement reaction would be converted into 1 by dehydration, acid-induced cyclization and a pinacol-type rearrangement reaction.

EXPERIMENTAL

General procedures. IR: film: ^{13}C NMR: 25 MHz, $CDCl_3$, TMS as int. standard; ^1H NMR and 2D NMR: 500 MHz, $CDCl_3$, TMS as int. standard.

Extraction and isolation. The flowers of *Nicotiana tabacum* cv. Virginia 115 (63 kg), collected in June 1982 at Tottori City, were steam distilled. The steam-distillate was extracted with Et_2O and the Et_2O extract evapd to dryness to give 9.5 g of volatiles. The volatiles were washed with 5% Na_2CO_3 soln and 5% H_2SO_4 soln to obtain the neutral fraction. The neutral fraction (5.5 g) was applied on a column of silica gel which was eluted with a gradient from *n*-hexane to Et_2O. All the fractions were measured by capillary GC/MS chromatography (Carbowax 20 M fused silica, 0.31 mm × 25 m). The 10% Et_2O fraction contained 1, which was isolated from the fraction in 5.2 mg yield by prep. GC (Carbowax 20 M, 5% on Chromosorb W(AW-DMCS) 60–80 mesh, 2.6 mm × 1 m).



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4

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Scheme 1.

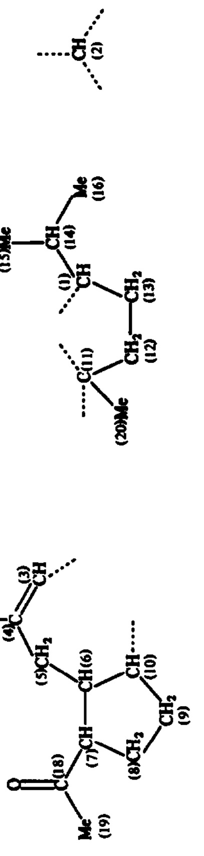

Fig. 1.

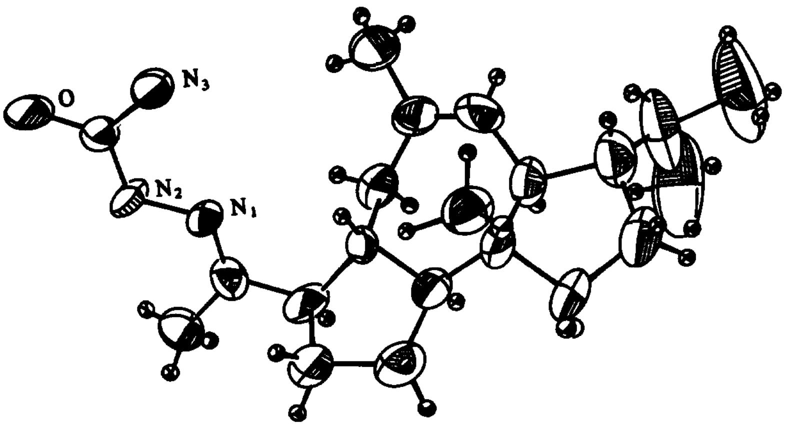

Fig. 2.

18-*Oxo-3-virgene* (1). $C_{20}H_{32}O$ [found: 288.2414, calcd: 288.2451]; $[\alpha]_D -69.1°$; MS *m/z* (rel. int): 288(10) $[C_{20}H_{32}O]^+$, 273 (4), 245 (28), 123 (100), 107 (26), 91 (20), 81 (23), 43 (61), 41 (25); IR: ν_{max}^{film} cm^{-1} 1710, 1460, 1435, 1380, 1365, 1350, 1165; ^{1}H NMR ($CDCl_3$): δ0.68 (3H, *s*, H-20), 0.82 (3H, *d*, *J* = 6.6 Hz)/0.87 (3 H, *d*, *J* = 6.85 Hz) (H-15/H-16), 1.72 (3 H, *br s*, H-17), 1.93 (1 H, *d*, *J* = 12 Hz, H-5 β), 1.95 (1 H, *br s*, H-2), 2.09 (1 H, *br t*, *J* = 12 Hz, H-5 α), 2.14 (3 H, *s*, H-19), 2.48 (1 H, *dt*, *J* = 10.5, 7.6 Hz, H-7), 5.23 (1 H, *br s*, H-3); ^{13}C NMR ($CDCl_3$): δ 50.0 (C-1), 52.7 (C-2), 129.5 (C-3), 135.9 (C-4), 38.0 (C-5), 39.3 (C-6), 58.3 (C-7), 25.8 (C-8), 27.0 (C-9), 62.3 (C-10), 45.8 (C-11), 40.3 (C-12), 24.6 (C-13), 31.5 (C-14), 18.8/21.9 (C-15/C-16), 25.8 (C-17), 211.6 (C-18), 29.0 (C-19), 14.2 (C-20).

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