132. A Chemical Study of *Virginia* Tobacco Flavour *(Nicotiana tabacum* L.) II. Isolation and Synthesis of *cis*-2-Isopropenyl-8-methyl-1,2,3,4-tetrahydro-1-naphthalenol and 3-Isopropenyl-5-methyl-1,2-dihydronaphthalene[1])

by **Edouard Demole** and **Paul Enggist**

Firmenich SA, Research Laboratories, 1211 Geneva 8

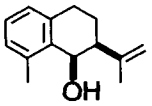
Dedicated to Professor *Edgar Lederer* on the occasion of his 70th birthday

(16.III.78)

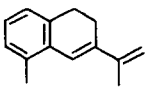
Summary

Gas liquid chromatography allowed isolation of the novel *cis*-2-isopropenyl-8-methyl-1,2,3,4-tetrahydro-1-naphthalenol (**A**) and its dehydration product, 3-isopropenyl-5-methyl-1,2-dihydronaphthalene (**B**), from two small subfractions of *Virginia* tobacco condensate. Both these norsesquiterpenes were identified on spectral grounds and synthesized from 1-methylnaphthalene in a way (9 steps) that also afforded the «non-natural», *trans*-alcohol **A'**. The possible biogenesis of **A** and **B** in tobacco is briefly outlined.

As part of our study of *Virginia* tobacco condensate [1], we have examined the subfractions VN2(f) and -(g) [1] from this material using gas liquid chromatography (GLC.). Among other results, the numerous semi-preparative separations carried out by combining relatively «polar» (Carbowax) and «non-polar» (silicone oil) columns allowed the novel norsesquiterpenes **A** and **B** to be isolated in minute amounts. These compounds represent at least 0.10 and 0.38‰ of the whole starting tobacco condensate, respectively[2]).



A in subfr. VN2(f)



B in subfr. VN2(f) and (g)

The *planar* structure of compound **A** was deduced from the following spectral evidence. A parent ion at *m/e* 202 corresponding to the molecular formula

[1]) First publication of this series: [1].

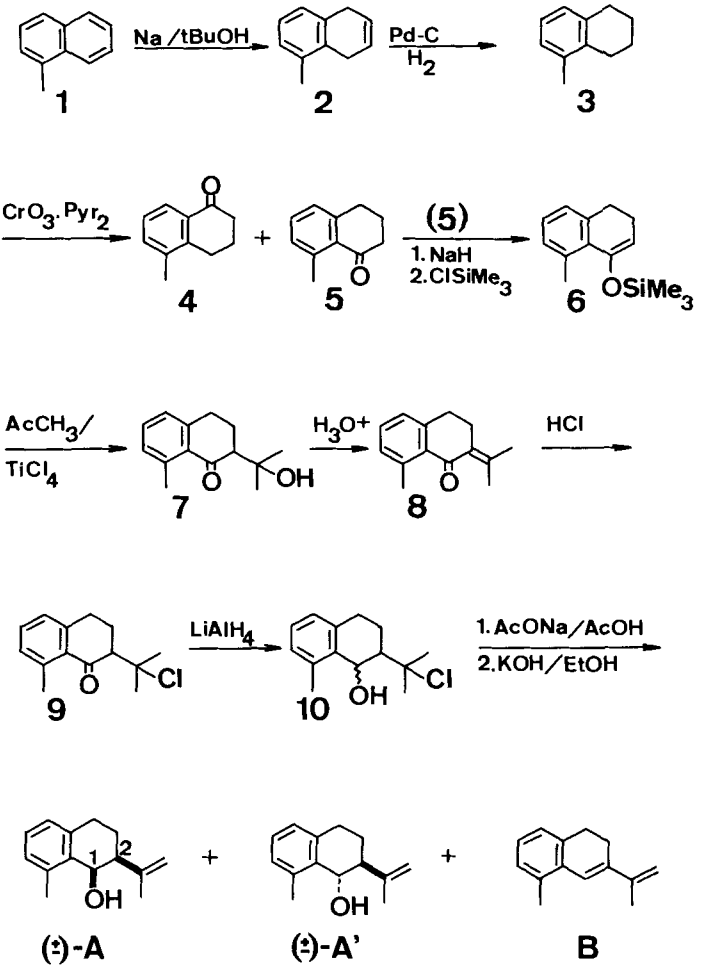
[2]) Compounds **A** and **B** occur also in *Oriental*-type, sun cured tobaccos (*E. Demole* and *P. Enggist*, unpublished results).

$C_{14}H_{18}O$ was obvious in the mass spectrum. In IR. absorption bands due to OH (3500 cm^{-1}) and C=CH_2 (890, 1635, 3080 cm^{-1}) were noted, and a band at 765 cm^{-1} was ascribed to a 1,2,3-trisubstituted benzene ring. The ^{1}H-NMR. spectrum (90 MHz) confirmed the presence of 3 aromatic protons (6.9–7.2 ppm, *m*) and 2 vinylic (methylenic) protons (5.10, *t*, fine coupling, and 4.93, *s*) and the benzylic proton of the secondary alcohol function (4.85, br. *s*, ArC*H*OH). Further signals appeared at 2.7–3.0 (*m*, $ArCH_2$), 2.47 (*s*, $ArCH_3$), 2.25 (*m*, CH), 1.94 (*s*, C=CCH_3), 1.74 (*d*, $J \sim 3$ Hz, OH), and 1.6–2.1 ppm (*m*, CH_2). All these results were highly suggestive of the norsesquiterpene structure **A**.

The correctness of this assumption was confirmed by study of the related hydrocarbon **B**, 3-isopropenyl-5-methyl-1,2-dihydronaphthalene. Although this tobacco constituent was isolated from subfractions VN2(f) and (g), it also resulted from the dehydration of alcohol **A** on aged, probably slightly acidic GLC. columns at $\geq 200°$. The mass spectrum of **B** exhibited the expected parent ion at *m/e* 184 ($C_{14}H_{16}$). In ^{1}H-NMR., there were signals at 7.02 ppm (*s*, 3 H arom.), 6.79 (*s*, ArCH=C), 5.07 and 5.25 (2 *s*, C=CH_2), 2.67 (*sext.* A_2B_2, apparent $J \sim 8$ Hz, with additional, fine coupling, $ArCH_2CH_2C$=C), 2.39 (*s*, $ArCH_3$), 2.10 (*s*, C=CCH_3). These results appeared to be consistent with structure **B**.

At this point some synthetic work settled the relative configuration of natural **A**. 1-Methylnaphthalene (**1**) was converted *via* the dihydro derivative **2** [2] to 5-methyl-1,2,3,4-tetrahydronaphthalene (**3**). The latter was oxidized with dipyridine/CrO_3 complex [3] to afford a separable mixture of both 5- and 8-methyl-3,4-dihydro-1(2*H*)-naphthalenones **4** and **5** ($\sim$ 1.3:1.0) [4]. The trimethylsilyl enol ether **6** from ketone **5** was condensed with acetone in the presence of $TiCl_4$, following *Mukaiyama*'s procedure [5], to yield ketol **7** (61% from **5**). Enone **8**, resulting from the dehydration of **7** under acidic conditions [6], was then treated with gaseous HCl and the intermediate chloroketone **9** reduced to **10** with $LiAlH_4$. Finally, chloroalcohol **10** underwent ready HCl elimination in the presence of acetate anion [7] to give, after alkaline hydrolysis, a mixture (72%) of **A**, **A'**, and hydrocarbon **B** ($\sim$ 1.4:1.0:2.2).

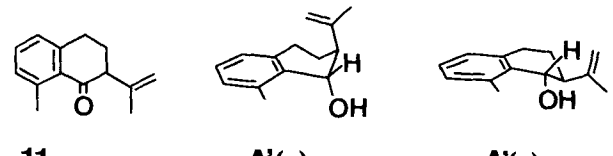
Whereas compounds **A** and **B** were found to be identical (IR., MS., ^{1}H-NMR.) with their natural counterparts, **A** and **A'** were shown to be epimers by oxidation to the same ketone **11**. An NMR. study of the H–C(1)/H–C(2) coupling ($J_{1,2}$) in these epimers sufficed to demonstrate their configurations. In **A**, the signal due to H–C(1) overlapped with that of one methylenic proton at 4.85 ppm but was shifted to 5.90 ppm as a clearly separated, broad singlet after addition of an incremental amount of Eu(fod)$_3$. Since the width at half-height ($W_{1/2}$) of this singlet decreased from 6 Hz to 3.5 Hz upon decoupling the OH proton (appearing at 4.20 ppm as a doublet, $J = 3$ Hz), $J_{1,2}$ was estimated to be 2–3 Hz, a value agreeing well with the *cis* configuration of **A**. In the *trans* epimer **A'**, similarly examined by ^{1}H-NMR./Eu(fod)$_3$, H–C(1) gave rise to a pseudotriplet at 6.70 ppm, $J = 5$ Hz, collapsing to a doublet, $J = 4.7$ Hz, by irradiation of the OH proton at 8.40 ppm. This somewhat small coupling constant suggested that **A'** exists substantially as pseudodiaxial conformer **A'**(a) in which $J_{1,2}$ (eq-eq) should be only about 2 Hz. Clearly, the alternative pseudodiequatorial con-



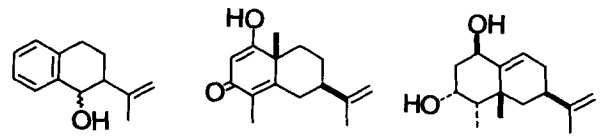
former A'(e) with expected $J_{1,2}$ (ax-ax) ~ 8 Hz is destabilized to some extent by a non-bonded interaction occurring between the CH_3–C(8) and the OH groups. In this respect, it is interesting to note that $J_{1,2} = 8.5$ Hz in the related *trans* stereoisomer of alcohol **12** that lacks such an $A^{(1,3)}$ strain (see exper. part).

These results demonstrated our novel tobacco constituent to be *cis*-2-isopropenyl-8-methyl-1,2,3,4-tetrahydro-1-naphthalenol (**A**), whose absolute configuration should be (1*R*,2*S*) since the isopropenyl group is normally β-oriented in eudesmane-type sesquiterpenes[3]). This norsesquiterpene might in principle have been formed by oxidation and loss (as CO_2) of the angular methyl group from a suitably functionalized eudesmane- or eremophilane-type «precursor» [8], completed by ring A aromatization and benzylic hydroxylation reactions. Potential

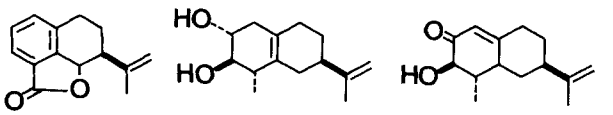
[3]) Determination of optical rotation was not possible owing to material shortage.



11 A'(a) A'(e)



12 13 14



15 16 17

precursors of **A** in tobacco could thus be 1-keto-*a*-cyperone (**13**) [9], the *phytoalexin* capsidiol (**14**) [10], or analogous compounds. Other examples of naturally occurring norsesquiterpenes structurally related to **A** but not isolated from *Nicotiana tabacum* are platyphyllid (**15**) [11], rishitin (**16**) [12], and glutinosone (**17**) [13].

The ready dehydration of **A** mentioned earlier raises the possibility that hydrocarbon **B** is an artifact in aged tobacco.

We thank Miss *M. Hagmann* and Mr. *T. Lander* for efficient technical assistance.

Experimental Part

The spectra were obtained with the instruments already described [14] (the mass spectra were determined at 70 eV, inlet temperature 150°; the ^{1}H-NMR. spectra were measured in $CDCl_3$). The GLC. separations were performed on gas chromatographs *Aerograph*, Models 1820-3 or 2720-3 *(Varian Aerograph AG)*, and *Carlo Erba*, Model 2301 AC. All liquid-solid chromatographic separations were carried out on 0.05–0.2 mm silica gel for column chromatography *(Merck AG)*.

1. *5-Methyl-1,2,3,4-tetrahydronaphthalene* (**3**). A solution of 5-methyl-1,4-dihydronaphthalene (**2**) [2] (35 g) in 300 ml anhydrous ethanol was hydrogenated at 20°/730 Torr in the presence of 5% Pd/C (3 g) until H_2 uptake ceased (~ 1 h). The combined products (105 g) from 3 hydrogenation batches were distilled through a Teflon spinning band column *(Nester/Faust)*, yielding a first fraction of 55 g of > 98% pure **3**, b.p. 94–97°/10 Torr (GLC., 15% Carbowax, 230°, 2.5 m column); $d_4^{20} = 0.964$; $n_D^{20} = 1.5452$. – IR. (neat, bands with decreasing intensities): 765, 1465, 3050, 705, 1090, 1590 cm^{-1}. – ^{1}H-NMR. (δ, ppm): 1.5–2.1 (*m*, 4 H); 2.2 (*s*, 3 H); 2.4–3.1 (*m*, 4 H); 6.97 (*s*, 3 H). – MS. (*m/e* (% relative abundance)): 146 (M^+, 79), 131 (100), 118 (73), 105 (37), 91 (20).

$C_{11}H_{14}$ (146.22) Calc. C 90.35 H 9.65% Found C 90.52 H 9.39%

2. *5- and 8-Methyl-3,4-dihydro-1(2H)-naphthalenones* (**4**) and (**5**) [4]. CrO_3 (103 g, 1.03 mol) was quickly added at 0° and under N_2 to a stirred solution of anhydrous pyridine (163 g, 2.06 mol) in 1000 ml of anhydrous CH_2Cl_2 [3]. After further stirring for 5 min at 10° and 10 min at 18°, **3** (10 g, 68.4 mmol, in 50 ml of CH_2Cl_2) was added at once. The mixture was then stirred for 15 h at 20°, when the liquid phase was separated from precipitated tars and concentrated to dryness at 25°/10 Torr. The residue taken up in ether was washed with 5% HCl-solution (2×) and brine (3×). Usual work-up gave 9.8 g of a crude product that was distilled (0.001 Torr): Fr. 1, b.p. 45–55°, 2.36 g; Fr. 2, b.p. 55–74°, 5.00 g. These fractions had the following composition (GLC., 15% Carbowax, 230°, 2.5 m column): Fr. 1, **1** (11.8%), **3** (76.4%), **5** (11.8%); Fr. 2, **1** (2.9%), **3** (11.2%), **4** (52.1%), **5** (33.8%) [relative $R_T = 1.0$ (**3**), 1.6 (**1**), 2.9 (**5**), 4.7 (**4**)]. Thus oxidation of **3** with dipyridine/CrO_3 complex gave a total yield of 41.6% (54.5% based on recovered **3**) of ketones **4** and **5**, formed in a ratio of ~1.3:1.0. The above Fr. 2 was chromatographed on silica gel (200 g) using light petroleum (b.p. 50–70°)/ether mixtures. This allowed the successive elution of hydrocarbons **1** and **3** (with 1–15% ether), ketone **5** (with 15–18% ether), and ketone **4** (with > 18% ether). Both ketones were finally distilled.

5-Methyl-3,4-dihydro-1(2*H*)-naphthalenone (**4**): b.p. 70°/0.001 Torr; m.p. (uncorrected) 48–49°. – IR. (neat): 1680, 1280, 1595, 1325, 1465, 900, 1110. – ^{1}H-NMR.: 1.8–2.4 (*m*, 2 H); 2.30 (*s*, 3 H); 2.65 (*t*, $J = 6$ Hz, 2 H); 2.87 (*t*, $J = 6$ Hz, 2 H); 7.0–7.5 (*m*, 2 H); 7.95 (*d*×*d*, $J = 7.5$, $J' \sim 1.5$ Hz, 1H). – MS.: 160 (M^+, 83), 132 (100), 104 (58), 78 (15).

$C_{11}H_{12}O$ (160.21) Calc. C 82.46 H 7.55% Found C 82.25 H 7.26%

8-Methyl-3,4-dihydro-1(2*H*)-naphthalenone (**5**): b.p. 63°/0.001 Torr; $d_4^{20} = 1.074$; $n_D^{20} = 1.5670$. – IR. (neat): 1680, 1595, 1465, 1265, 1215, 770. 780. – ^{1}H-NMR.: 1.8–2.3 (*m*, 2 H); 2.5–2.8 (*t* in part obscured, 2 H); 2.63 (*s*, 3 H); 2.95 (*t*, $J = 5.5$ Hz, 2 H); 6.9–7.5 (*m*, 3 H). – MS.: 160 (M^+, 67), 132 (100), 104 (39), 78 (10).

$C_{11}H_{12}O$ (160.21) Calc. C 82.46 H 7.55% Found C 82.87 H 7.28%

3. *2-(1-Methyl-1-hydroxyethyl)-8-methyl-3,4-dihydro-1(2H)-naphthalenone* (**7**). A well-stirred mixture of ketone **5** (3.82 g, 23.8 mmol) and sodium hydride (1.53 g of 55–60% dispersion in oil, 36.6 mmol) in glyme (40 ml, distilled over $LiAlH_4$) was refluxed for 4 h under N_2 and allowed to cool [15]. Triethylamine (5 ml, 35 mmol, distilled over $LiAlH_4$) and trimethylchlorosilane (4.5 ml, 35 mmol) were then successively added [15]. After 1 h further stirring at 20°, the mixture was diluted with pentane (150 ml), filtered, and the filtrate concentrated to dryness in vacuum. The residue was treated once again with pentane (100 ml) to remove further insoluble material and distilled to give **6**: b.p. 65°/0.001 Torr, 5.0 g (90%). – IR. (neat): 1250, 840, 880, 1630, 765, 1185. – ^{1}H-NMR.: 0.25 (*s*, 9 H); 1.9–2.4 (*m*, 2 H); 2.4–2.9 (*m*, 2 H); 2.48 (*s*, 3 H); 5.17 (*t*, $J = 5$ Hz, 1 H); 6.87 (narrow *m*, 3 H).

Enol ether **6** (5.0 g, 21.5 mmol, in 75 ml of CH_2Cl_2) was added dropwise over 15 min at 3° to a stirred solution of $TiCl_4$ (2.70 ml, 24.6 mmol) and anhydrous acetone (1.75 ml, 23.8 mmol) in 160 ml of CH_2Cl_2 [5]. After 2 h further stirring at 20°, the reaction mixture was quenched with water (250 ml). The aqueous layer was extracted with ether (2×) and the combined organic layers were washed with 5% $NaHCO_3$ (2×). Usual work-up afforded 4.3 g of an oil that was chromatographed on silica gel (90 g) with light petroleum (b.p. 50–70°)/ether 1:1. Unreacted ketone **5** (1.03 g) was first eluted (with 160 ml of solvent), followed by ketol **7** (3.19 g, 68%) (with 270 ml of solvent). The latter compound had IR. (neat): 1660, 1470, 1595, 1220, 1390, 960, 780, 3500. – ^{1}H-NMR.: 1.22 (*s*, 3 H); 1.27 (*s*, 3 H); 1.5–2.5 (*m*, 2 H); 2.57 (*s*, 3 H); 2.5–3.1 (*m*, 3 H); 5.0 (*s*, OH); 6.8–7.4 (*m*, 3 H).

4. *2-Isopropylidene-8-methyl-3,4-dihydro-1(2H)-naphthalenone* (**8**). A solution of ketol 7 (3.19 g, 14.6 mmol) in 90% acetic acid (60 ml) was stirred for 24 h at 70° and under N_2 [6]. After 22 h of further stirring at 90° to complete the reaction, the mixture was concentrated to dryness at 80°/10 Torr and the residual oil distilled, yielding **8**, b.p. 86°/0.001 Torr, 2.60 g (89%). – IR. (neat): 1660, 1590, 1465, 1220, 1295, 780. – ^{1}H-NMR.: 1.87 (*s*, 3 H); 2.20 (*s*, 3 H); 2.60 (*s*, 3 H); 2.76 (narrow *m*, 4 H); 6.8–7.4 (*m*, 3 H). – MS.: 200 (M^+, 21), 160 (68), 132 (100), 104 (46), 103 (16).

5. *2-(2-Chloroisopropyl)-8-methyl-1,2,3,4-tetrahydro-1-naphthalenol* (**10**). An excess of HCl gas mixed with N_2 was introduced over 2 h and at 0°/−5° into a stirred solution of ketone **8** (2.60 g, 13 mmol) in anhydrous ether (25 ml). The mixture was concentrated to dryness at 40°/10 Torr, giving 2.99 g (97%) of crude **9** as an oil that solidified below 0°. – ^{1}H-NMR.: 1.75 (*s*, 3 H); 1.84 (*s*, 3 H); 2.54 (*s*, 3 H); 2.0–3.15 (*m*, 5 H); 6.9–7.4 (*m*, 3 H).

Crude chloroketone **9** (2.95 g, 12.4 mmol) in 30 ml of anhydrous ether was added over 25 min at −2°/−8° to a stirred suspension of $LiAlH_4$ (0.48 g, 12.6 mmol) in 15 ml of the same solvent. The mixture was further stirred for 1 h at 0° and 1 h at 25°, when 3.0 ml of acetic acid was added over 3 min at 0°, followed by 10 ml of water. Usual work-up (ethereal extraction, washings with 5% $NaHCO_3$ and water) afforded 2.90 g (98%) of crude chloroalcohol **10**. – IR. (neat): 1120, 770, 1470, 1375, 1390, 800, 940, 3500, 3600. – ^{1}H-NMR.: 1.75 (*s*, 3 H); 1.82 (*s*, 3 H); 1.5–2.2 (*m*, 4 H); 2.43 (*s*, 3 H); 2.6–3.1 (*m*, 2 H); 5.15 (narrow *m*, 1 H); 6.75–7.25 (narrow *m*, 3 H).

6. cis- *and* trans-*2-Isopropenyl-8-methyl-1,2,3,4-tetrahydro-1-naphthalenols* **A** *and* **A'**, *3-isopropenyl-5-methyl-1,2-dihydronaphthalene* (**B**). Crude chloroalcohol **10** (2.90 g, 12.1 mmol) was added to a solution of anhydrous sodium acetate (3.5 g, 42.5 mmol) in acetic acid (29 ml) [7]. The mixture was stirred for 7.5 h at 80° under N_2, allowed to cool, concentrated to about 1/3 of its volume at 40°/10 Torr, diluted with water, and extracted twice with ether (5% $NaHCO_3$ and water washings). Usual work-up afforded 2.38 g of a product (containing some chloroalkyl acetate), that was refluxed for 30 min under N_2 in 22.7 ml of N ethanolic KOH. The alkaline solution was concentrated to about half its volume in vacuum, diluted with water, and extracted twice with ether (water washings). Usual work-up gave 2.08 g of an oil that was chromatographed on silica gel (44 g) with 5% ether in light petroleum (b.p. 50–70°). Pure hydrocarbon **B** (821 mg, 36.8%) was first eluted, followed by pure *cis*-alcohol **A** (512 mg, 20.9%). Further elution with 15% ether in light petroleum gave a third fraction consisting of *trans*-alcohol **A'** (365 mg, 14.9%). The separation process was best monitored by thin-layer chromatography (TLC.) since **A** and **A'** can undergo partial dehydration under the GLC. conditions. Each compound was finally distilled (over a small amount of K_2CO_3 in the case of **A** and **A'**).

3-Isopropenyl-5-methyl-1,2-dihydronaphthalene (**B**): b.p. 68°/0.001 Torr; $d_4^{20} = 0.981$; $n_D^{20} = 1.6126$. – GLC. (15% Carbowax, 240°, 2.5 m column) and TLC. (silica gel, ether/light petroleum 1:1) indicated this compound to be homogeneous. – IR. (neat): 875, 760, 780, 1470, 1440, 1375, 1605, 3100. – ^{1}H-NMR.: see theoretical part. – MS.: 184 (M^+, 100), 169 (66), 155 (22), 143 (43), 129 (49), 115 (15).

$C_{14}H_{16}$ (184.27) Calc. C 91.25 H 8.75% Found C 91.27 H 8.53%

cis-2-Isopropenyl-8-methyl-1,2,3,4-tetrahydro-1-naphthalenol (**A**): b.p. 94°/0.001 Torr (thick oil crystallizing slowly at −15°); $d_4^{20} = 1.058$; $n_D^{20} = 1.5548$. – GLC. (OV-101, 130°, 50 m × 0.3 mm capillary column) and TLC. (as above) indicated this compound to be homogeneous. – IR. (neat): 765, 1060, 890, 3500, 1635, 1585, 3080. – ^{1}H-NMR.: see theoretical part. – MS.: 202 (M^+, 17), 184 (28), 171 (21), 144 (50), 134 (78), 133 (100), 115 (11), 105 (26), 69 (25).

$C_{14}H_{18}O$ (202.28) Calc. C 83.12 H 8.97% Found C 83.35 H 8.91%

trans-2-Isopropenyl-8-methyl-1,2,3,4-tetrahydro-1-naphthalenol (**A'**): b.p. 97°/0.001 Torr; m.p. (uncorrected) 50–51°. – GLC. (capillary column, same conditions as above) indicated this compound to be homogeneous. – IR. (neat): 765, 890, 1000, 3350, 1640, 1590, 3100. – ^{1}H-NMR.: 1.83 (*s*, 3 H); 1.5–2.2 (*m*, 3 H); 2.49 (*s*, 3 H); 2.6 (*m*, 1 H); 2.75 (*t*, $J = 6.5$ Hz, 2 H); 4.50 (*s*, 1 H); 4.75–5.00 (*m*, 2 H); 6.85–7.20 (*m*, 3 H). – MS.: 202 (M^+, 17), 184 (49), 169 (33), 144 (63), 134 (78), 133 (100), 129 (36), 105 (28), 69 (20).

7. *2-Isopropenyl-8-methyl-3,4-dihydro-1(2H)-naphthalenone* (**11**). CrO_3 (0.3 g, 3.0 mmol) was quickly added at 0° and under N_2 to a stirred solution of anhydrous pyridine (0.5 g, 6.3 mmol) in CH_2Cl_2 (10 ml) [3] [16]. After further stirring for 5 min at 0° and 10 min at 20°, alcohol **A** (98 mg, 0.48 mmol, in 0.8 ml of CH_2Cl_2) was introduced into the mixture and the stirring continued for 1 h at 20°. The liquid phase was separated from precipitated tars, the solvent removed in vacuum at 20°, and the residue taken up in ether. The ethereal solution was filtered, washed with 10% HCl (2×), 5% $NaHCO_3$ (1×), and worked up as usual, giving 91 mg (93%) of crude

2-isopropenyl-8-methyl-3,4-dihydro-1(2*H*)-naphthalenone (**11**). – IR. (neat): 1680, 1590, 1465, 1210, 775, 1435, 890. – ^{1}H-NMR.: 1.80 (*d*, $J\sim1$ Hz, 3 H); 1.95–2.50 (*m*, 2 H); 2.63 (*s*, 3 H); 2.85–3.40 (*m*, 3 H); 4.78 (*s*, 1 H); 4.97 (narrow *m*, 1 H); 6.90–7.40 (*m*, 3 H).

Identical oxidation of 75 mg (0.37 mmol) of *trans*-alcohol **A'** also afforded ketone **11** (98%).

8. *2-Isopropenyl-1,2,3,4-tetrahydro-1-naphthalenol* (**12**). This compound was prepared in the same way as alcohols **A** and **A'**, except that 3,4-dihydro-1(2*H*)-naphthalenone (*a*-tetralone) was substituted for ketone **5** in the reaction sequence **5**→**6**→**7**→**8**→**9**→**10**→products. Alcohol **12** thus obtained with an overall yield of about 15% and distilled over a small amount of K_2CO_3 had b.p. 85°/0.001 Torr; $d_4^{20}=1.059$; $n_D^{20}=1.5572$. – GLC. (Ucon HB 5100, 140°, 20 m×0.3 mm column) indicated **12** to be a mixture of stereoisomers in a ratio of about 2:3 (relative $R_T=1.00/1.03$). Contrary to the case of homologues **A** and **A'**, these stereoisomers could not be easily separated by preparative liquid chromatography on silica gel. – IR. (neat): 740, 890, 775, 1455, 1040, 1490, 1380, 3450, 1640, 3100. – ^{1}H-NMR. (spectrum corresponding to a mixture of *cis* and *trans* stereoisomers in a ratio of ~2:3): 1.7–2.0 (*m*, including 2 major *s* at 1.82 and 1.92 due to CH_3–C=C in *trans* and *cis* stereoisomers, respectively, total 5 H); 2.14 (*d*, $J=4$ Hz, OH); 2.2–2.6 (*m*, 1 H); 2.7–3.0 (*m*, 2 H); 4.5–5.1 (*m*, 3 H); 6.9–7.7 (*m*, 4 H). The configurations were demonstrated by direct ^{1}H-NMR./Eu(fod)$_3$ study of the mixture. With 4 incremental amounts of Eu(fod)$_3$, H–C(1) in the major stereoisomer gave rise to a $d\times d$ ($J=8.5$, $J'=4$ Hz, 0.6 H) at 7.15, collapsing to a *d* ($J=8.5$ Hz) upon irradiation of the OH proton near 11.3. On the other hand, H–C(1) in the minor stereoisomer appeared as a broad *s* ($W_{1/2}$ 6.5 Hz, OH not decoupled, 0.4 H) at 8.10. Since expected $J_{1,2}$(ax-ax)>$J_{1,2}$(ax-eq), the *trans*-configuration was assigned to the major stereoisomer of **12**. – MS.: 188 (M^+, 12), 170 (27), 157 (20), 130 (40), 120 (100), 119 (90), 91 (33), 69 (24).

REFERENCES

[1] *E. Demole & P. Enggist,* Helv. *59*, 1938 (1976).
[2] *V.L. Hansley,* U.S. Patent 2473997 (1949); *W. Hückel & E. Vevera,* Chem. Ber. *89*, 2105 (1956); *W. Hückel & C.-M. Jennewein,* Chem. Ber. *95*, 350 (1962).
[3] *D.S. Fullerton & Chi-Ming Chen,* Synth. Commun. *6*, 217 (1976).
[4] *J.W. Burnham, W.P. Duncan, E.J. Eisenbraun, G.W. Keen & M.C. Hamming,* J. org. Chemistry *39*, 1416 (1974).
[5] *T. Mukaiyama, K. Banno & K. Narasaka,* J. Amer. chem. Soc. *96*, 7503 (1974).
[6] *F.L. Malanco & L.A. Maldonado,* Synth. Commun. *6*, 515 (1976).
[7] *A. van der Gen, L.M. van der Linde, J.G. Witteveen & H. Boelens,* Rec. Trav. chim. Pays-Bas *90*, 1045 (1971); *D. Caine & J.T. Gupton,* J. org. Chemistry *39*, 2654 (1974).
[8] *A. Stoessl, J.B. Stothers & E.W.B. Ward,* Phytochemistry *15*, 855 (1976).
[9] *D.L. Roberts,* Phytochemistry *11*, 2077 (1972).
[10] *J.A. Bailey, R.S. Burden & G.G. Vincent,* Phytochemistry *14*, 597 (1975).
[11] *F. Bohlmann, K.-H. Knoll, C. Zdero, P. Kumar Mahanta, M. Grenz, A. Suwita, D. Ehlers, Ngo Le Van, Wolf-Rainer Abraham & Arvind Anant Natu,* Phytochemistry *16*, 965 (1977).
[12] *T. Masamune, A. Murai, M. Takasugi, A. Matsunaga, N. Katsui, N. Sato & K. Tomiyama,* Bull. chem. Soc. Japan *50*, 1201 (1977).
[13] *R.S. Burden, J.A. Bailey & G.G. Vincent,* Phytochemistry *14*, 221 (1975).
[14] *E. Demole, C. Demole & D. Berthet,* Helv. *56*, 265 (1973).
[15] *G. Stork & P.F. Hudrlik,* J. Amer. chem. Soc. *90*, 4462 (1968).
[16] *R. Ratcliffe & R. Rodehorst,* J. org. Chemistry *35*, 4000 (1970).