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206. A Chemical Study of *Burley* Tobacco Flavour (*Nicotiana tabacum* L.) VII. Identification and Synthesis of Twelve Irregular Terpenoids Related to Solanone, Including 7,8-Dioxabicyclo[3.2.1]octane and 4,9-Dioxabicyclo[3.3.1]nonane Derivatives[1][2]

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(11. VIII. 75)

Summary. Twelve novel constituents isolated from *Burley* tobacco condensate by semi-preparative GLC. have been identified as (*E*)-3,4-epoxy-5-isopropyl-nonane-2,8-dione (**A**), *exo*-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)methyl ketone (**B**), *exo*-1-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-ethanol (**C**), (*E*)-5-isopropyl-8-hydroxy-8-methyl-non-6-en-2-one (**D**), (*E*)-5-isopropyl-6,7-epoxy-8-hydroxy-8-methyl-nonan-2-one (**E**), *endo*-2-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-propan-2-ol (**F**), 3,3,5-trimethyl-8-isopropyl-4,9-dioxabicyclo[3.3.1]nonan-2-ol (**G**), (*E*)-5-isopropyl-non-3-ene-2,8-diol (**H**), 5-isopropyl-nonane-2,8-diol (**I**), (*E*)-5-isopropyl-8-hydroxy-non-6-en-2-one (**J**), 5-isopropyl-8-hydroxy-nonan-2-one (**K**), and (*E*)-3-isopropyl-6-methyl-hepta-4,6-dien-1-ol (**L**). Compounds **A**–**K** were synthesized from norsolanadione (**2**), and compound **L** from 2-isopropyl-5-oxo-hexanal (**15**). The relative configuration of the bicyclic internal acetals **B**, **C**, **F**, **G** and their δ-keto-epoxide precursors **A** and **E** is discussed. All these *Burley* tobacco flavour components belong to a growing family of metabolites structurally related to solanone (**1**). They are believed to arise from the breakdown of cembrene-type precursors.

The number of solanone-related constituents isolated from tobacco is currently increasing [1]. Twelve further novel representatives (**A-L**) of this class of compounds have now been identified in miscellaneous *Burley* tobacco flavour subfractions. As assumed for solanone (**1**) itself [3], these irregular C_{11-13} terpenoids presumably arise from the ring cleavage and degradation of some cembrene-type precursor(s) (*e.g.* the α- and β-duva-4,8,13-triene-1,3-diols [4]) during the tobacco processing (fermentation, curing, ageing).

According to *Enzell et al.* [5], all the solanone-related tobacco metabolites should logically have the same *S*-configuration as solanone (**1**) [5] [6] at the carbon atom bearing the isopropyl group if they do originate from a common, cembrene-type precursor. This proposal was found to be indeed correct in the cases of (*E*)-4-methyl-7-isopropyl-10-oxo-undec-5-en-4-olide [5a] [1], norsolanadione (**2**) [5b], and (*E*,*E*)-3-methyl-6-isopropyl-9-oxo-deca-2,4-dienoic acid [5c]. Our compounds **A-L** were un-

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[1] For the 6th publication of this series see [1].

[2] Part of this work was the subject matter of a preliminary communication with *D. Berthet* [2][3], and of a paper presented by *E. D.* at the VIth International Congress of Essential Oils (San Francisco, California, Sept. 8–12, 1974).

[3] We thank Mr. *D. Berthet* for the isolation of compounds **A-L**.

fortunately isolated in amounts too small to permit their absolute configuration to be investigated (semi-preparative GLC.)[3]. For instance, only the mass spectra of **C**, **F**, and **G** were available to us.

1. *(E)-3,4-Epoxy-5-isopropyl-nonane-2,8-dione* (**A**). Two stereoisomeric diketo-epoxides **A** were isolated from *Burley* tobacco condensate[4]) subfractions B3-PN-g and -h[5]). Since these substances could be either *E* or *Z* and *threo* or *erythro* isomers, we undertook the following synthesis to determine their configuration (*Scheme 1*). Norsolanadione-monoacetal (**3**) was reduced by lithium aluminium hydride and the resulting hydroxy-acetal **4** epoxidized with *m*-chloroperoxybenzoic acid. Successive manganese dioxide oxidation[6]) and acid hydrolysis of the resulting **5** completed the synthesis, affording diketo-epoxide **A** (overall yield 69%) as a ~1:3 mixture of diastereoisomers that could be separated by GLC. [15% Carbowax, 220°, 2.5 m column; relative R_T = 1.00, 1.05–1.09 (minor, major diastereoisomers)]. The *E-threo* ($\mathbf{A_1}$) and *E-erythro* ($\mathbf{A_2}$) configurations were respectively assigned to the major and minor diastereoisomers, according to the evidence later provided by the NMR. study of the four related stereoisomeric hydroxy-acetals $\mathbf{C_1}$-$\mathbf{C_4}$ (*Section 3*).

Comparison of spectral data (IR., MS., NMR.) indicated that the major synthetic diastereoisomer $\mathbf{A_1}$ was identical with the major natural isomer, and that the same was also true for the two corresponding minor isomers. Thus, diketo-epoxide **A** occurs in tobacco as *E-threo*-($\mathbf{A_1}$) and *E-erythro*-($\mathbf{A_2}$) diastereoisomers, and not as *E*- and *Z*-stereoisomers as formerly indicated [2].

2. *Exo-(1-Methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl) methyl ketone* (**B**) was isolated from *Burley* tobacco condensate[4]) subfractions B2-PN-f[4]) and B3-PN-d[5]). The synthesis of this compound was easily accomplished by acid-catalyzed isomerization of *threo*- and *erythro*-(*E*)-3,4-epoxy-5-isopropyl-nonane-2,8-diones ($\mathbf{A_1}$ and $\mathbf{A_2}$), a stereospecific reaction[7]) that may proceed through the following formal steps in the particular case of the *E-threo*-diastereoisomer $\mathbf{A_1}$ (*Scheme 1*): the protonated oxirane group in **6** would first undergo ring opening *via* the 'modified S_N2 path' [11], producing intermediate **7** (note that the incipient positive charge develops exclusively at the β-position with respect to the destabilizing carbonyl group [11]); pseudo-chair inversion and ~180° rotation about the 3,4 bond would then lead to **8** which finally undergoes cyclization/deprotonation to *endo* keto-acetal **9**. In fact, the latter compound suffers immediate enolization and epimerization to the more stable *exo* isomer $\mathbf{B_1}$, the reaction product (yield 63%). If such an enolization is not allowed, the outcome of the process appears to be the expected *endo* isomer as observed in the **E** → **F** isomerization (*Scheme 2*).

The NMR. spectrum of synthetic keto-acetal **B** revealed no coupling between H–C(5) and H–C(6), thereby establishing the *exo* configuration of the acetyl side-chain (expected dihedral angle ≃ 90°). However, all major NMR. signals were split

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[4]) *Burley* tobacco condensate and subfractions B2-PN-a to -j were obtained and investigated as previously described [7].

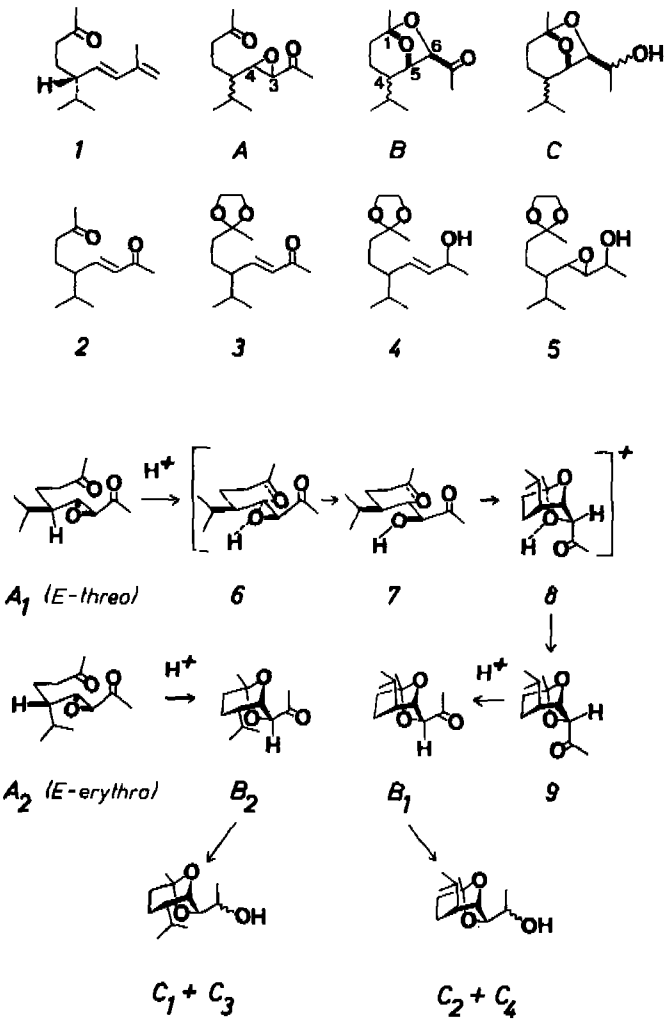
[5]) The preparation and study of subfractions B3-PN-a to -i will be described in a future paper.

[6]) This seems to be the first example of manganese dioxide oxidation of a secondary α,β-epoxy-alcohol to the corresponding ketone, a reaction which should offer some generality.

[7]) Similar acid-catalyzed isomerizations of δ,ε-epoxycarbonyl compounds are known, for instance in the manool [8], brevicomin [9], and 1-acetoxy-3,4-epoxy-pentane [10] series.

in the presence of $Eu(fod)_3$[8]), indicating the product to be a ~1:3 mixture of both epimers at C(4). This result, confirmed by GLC. (2 peaks clearly separated on a 50 m capillary column), was not unexpected since the (*E*)-3,4-epoxy-5-isopropyl-nonane-2,8-dione (**A**) used for the synthesis was itself a ~1:3 mixture of diastereoisomers. If isomerization **A** → **B** proceeds stereospecifically, as assumed in *Scheme 1*, *exo/exo* keto-acetal $\mathbf{B_1}$ would indeed be formed from *E-threo* diketo-epoxide $\mathbf{A_1}$ and *endo/exo* keto-acetal $\mathbf{B_2}$ from *E-erythro* diketo-epoxide $\mathbf{A_2}$. The *exo/exo* configuration $\mathbf{B_1}$ could be attributed to the major epimer of **B** owing to the evidence provided by the NMR. study of the four stereoisomeric hydroxy-acetals $\mathbf{C_1}$–$\mathbf{C_4}$ described in the next section (all steric relationships between compounds **A**, **B**, and **C** are depicted in *Scheme 1*).

Scheme 1



All compounds except *1* are racemic.

[8]) We are much indebted to Dr. *B. Willhalm* and to Mr. *W. Thommen* (*Firmenich SA*, Geneva) for having conducted this experiment.

Despite its lack of steric homogeneity at C(4), synthetic *exo*-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl) methyl ketone (**B**) exhibited IR. and mass spectra identical with those of the natural isolate, the NMR. spectrum of which was not available. This suggests natural **B** to be also a mixture of epimers $\mathbf{B_1}$ and $\mathbf{B_2}$, in accordance with the fact that both corresponding diketo-epoxide 'precursors' $\mathbf{A_1}$ and $\mathbf{A_2}$ occur in *Burley* tobacco condensate (*Section 1*)[9]).

3. *Exo-1-(1-Methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-ethanol* (**C**) was isolated from *Burley* tobacco condensate[4]) subfraction B2-PN-i[4]) and synthesized by sodium borohydride reduction of a ~1:3 mixture of keto-acetal epimers $\mathbf{B_2}$ and $\mathbf{B_1}$. This reaction afforded four stereoisomeric hydroxy-acetals $\mathbf{C_1}$-$\mathbf{C_4}$ in a ratio of 2.2:6:1:1.9 [GLC., 5% Carbowax, 180°, 2.5 m column; relative $R_T = 1.00$ ($\mathbf{C_1}$), 1.22 ($\mathbf{C_2}$), 1.33 ($\mathbf{C_3}$), 1.50 ($\mathbf{C_4}$)]. The NMR. data of these stereoisomers are summarized in the *Table*. It is immediately obvious that the signal due to the slowly exchangeable OH proton appears at $\delta = 2.5$ in the case of $\mathbf{C_1}$ and $\mathbf{C_2}$, and at $\delta = 1.8$ for the $\mathbf{C_3}$ and $\mathbf{C_4}$ compounds. This suggests that the *exo*-1-hydroxy-ethyl side-chain has the same configuration (respectively *threo* and *erythro*) in each of these pairs of compounds. Similarly, the fact that the isopropyl methyl-groups give rise to relatively similar

Table. *NMR. spectral characteristics of hydroxy-acetals* $\mathbf{C_1}$–$\mathbf{C_4}$ (90 MHz, δ values, $CDCl_3$)

	$\mathbf{C_1}$	$\mathbf{C_2}$	$\mathbf{C_3}$	$\mathbf{C_4}$
CH_3-C(1)	1.48	1.48	1.42	1.46
CH_3 (isopropyl)	1.00	0.92	0.95	0.92
CH_3 (isopropyl)	1.05	0.92	1.03	0.98
CH_3–C(OH)–	1.19	1.15	1.18	1.21
>CH–O–	~3.7	~3.7	~3.7	~3.7
OH	2.54, *d* (2 Hz)	2.58, *d* (2 Hz)	1.81, *d* (4 Hz)	1.85
H-C(5)	4.30	4.25	4.49	4.49
H-C(6)	3.74	3.75	3.80	3.85

signals in the cases of $\mathbf{C_1} + \mathbf{C_3}$ ($\delta = 0.95$–1.05, 2 *d*, $J = 6.5$–7 Hz) and $\mathbf{C_2} + \mathbf{C_4}$ ($\delta = 0.92$–0.98, *m* or *t*, $J \leqq 5$ Hz) stereoisomers suggests that the isopropyl group has the same configuration (respectively *endo* and *exo*) in each of these alternative pairs of compounds. More reliable evidence for $\mathbf{C_1}$ and $\mathbf{C_2}$ being indeed C(4)-epimers was obtained from their NMR. spectra measured in the presence of $Eu(fod)_3$[8]). In these conditions, the isopropyl methyl protons were relatively more deshielded in isomer $\mathbf{C_1}$, whereas the other protons examined exhibited similar or identical paramagnetic shifts in both compounds (Fig. 1). This led us to assign the *endo/exo* configuration to stereoisomer $\mathbf{C_1}$, since that configuration allows the shortest possible intramolecular distance between the isopropyl group and the OH function.

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[9]) Keto-acetal **B** was also identified in Greek tobacco (private communication from Dr. *A. J. Aasen*, Swedish Tobacco Company), as well as in Turkish tobacco [12].

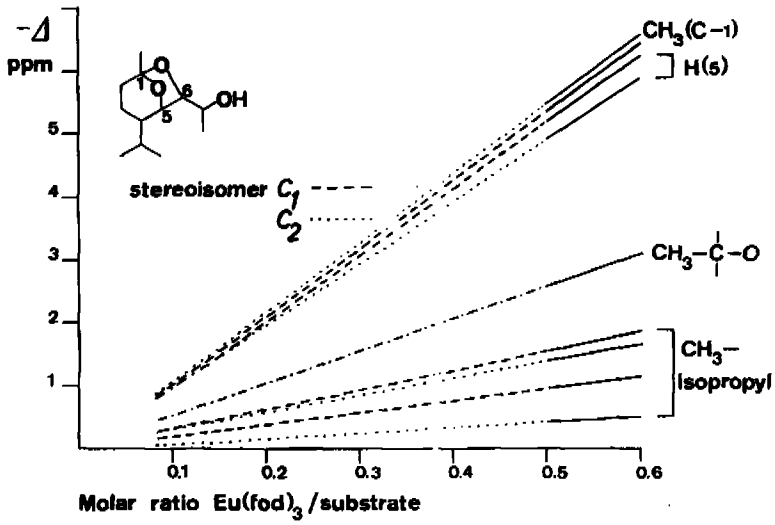


Fig. 1. NMR. lanthanide-induced shifts for hydroxy-acetals C_1 *and* C_2

From all these results it follows that the $C_1 + C_3$ and $C_2 + C_4$ pairs of stereo-isomers should have the respective *endo/exo* and *exo/exo* configurations indicated in *Scheme 1*. Hence, the *exo/exo* configuration B_1 can in turn be assigned to the major stereoisomer of synthetic keto-acetal **B**, and the *E-threo* structure A_1 to the corresponding diastereoisomer of diketo-epoxide **A**.

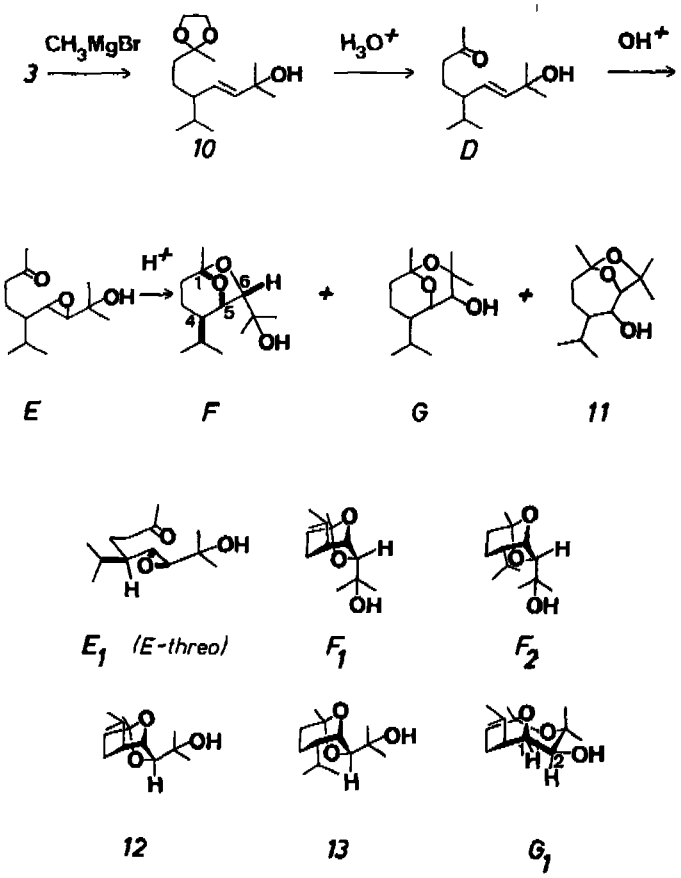
Synthetic hydroxy-acetals C_1 and C_2 exhibited mass spectra identical with that of the natural tobacco isolate, the exact configuration of which could not be investigated due to material shortage.

4. (E)-*5-Isopropyl-8-hydroxy-8-methyl-non-6-en-2-one* (**D**) was isolated from *Burley*-tobacco-condensate[4]) subfractions B2-PN-i[4]) and B3-PN-i[5]). The synthesis of this *solanone hydrate* was carried out according to *Scheme 2*, by allowing norsolanadione-monoacetal **3** to react with methylmagnesium bromide and then subjecting the resulting hydroxy-acetal **10** to acid hydrolysis (yield 80%). Natural and synthetic ketol **D** exhibited identical IR., mass, and NMR. spectra. This fairly unstable compound was easily dehydrated to racemic **1** upon heating in the presence of minute amounts of acids.

5. (E)-*5-Isopropyl-6,7-epoxy-8-hydroxy-8-methyl-nonan-2-one* (**E**), identified in *Burley* tobacco condensate[4]) subfraction B3-PN-i[5]), was synthesized by direct epoxidation of solanone hydrate **D** with *m*-chloroperoxybenzoic acid (yield 79%). GLC. indicated the product thus obtained to consist of a ~1:9 mixture of diastereoisomers [Ucon HB 5100, 170°, 53 m × 0.3 mm capillary column; relative $R_T = 1.00$, 1.01 (major, minor diastereoisomers)]. Despite this steric heterogeneity, no signal splitting was observed when the NMR. spectrum of epoxy-ketol **E** was measured in the presence of $Eu(fod)_3$[8]). We assigned the *E-threo* structure E_1 to the major diastereoisomer, in accordance with the result of the similar epoxidation of hydroxy-acetal **4** (*Section 1* and *Scheme 1*). Synthetic and natural epoxy-ketol **E** exhibited identical IR., mass, and NMR. spectra.

6a. Endo-*2-(1-Methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-propan-2-ol* (**F**) isolated from *Burley* tobacco condensate[4]) subfractions B2-PN-h[4]) and B3-PN-h[5]), was synthesized by acid-catalyzed isomerization of epoxy-ketol **E**. This reaction led to a ~1.9:7.4:1.0 mixture[10]) of hydroxy-acetals **F**, **G**, and **11**[11]) as major products [GLC., 5% Carbowax, 190°, 2.5 m column; relative $R_T = 1.00$ (**F**), 2.03 (**G**), 2.29 (**11**)]. Hydroxy-acetal **F** was separated from the synthetic mixture as a single stereoisomer (GLC., OV 101, 115°, 50 m × 0.3 mm capillary column), in the NMR. spectrum of which H(5) and H(6) appeared as a pair of doublets ($J = 4$ Hz) at $\delta = 4.28$ and 3.80 respectively. This demonstrates the *endo* configuration of the hydroxypropyl side-chain (expected dihedral angle ≃ 20°). The *exo* configuration was considered to be the most probable for the isopropyl group, assuming that the isomerization of epoxy-ketol **E** (mainly as *E-threo* isomer E_1) followed the same stereospecific course as that of A_1 to **9** (*Scheme 1*) and led to F_1. In any event, formation of the alternative, highly crowded *endo/endo* structure F_2 would appear questionable.

Scheme 2



All compounds are racemic.

10) Quite different ratios between compounds **F**, **G**, and **11** can be obtained by altering the experimental procedure.

11) This isomer has not so far been detected in tobacco.

Synthetic and natural hydroxy-acetal **F** exhibited identical mass spectra[12]), which clearly differed from those of either C(4)-epimers of *exo*-2-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-propan-2-ol (**12** and **13**) synthesized below.

6b. *Non-natural* exo-*2-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-propan-2-ols* (**12**) *and* (**13**), needed to make certain the *endo* configuration assigned to natural hydroxy-acetal **F**, were synthesized by allowing methylmagnesium bromide to react with *exo*-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl) methyl ketone (**B**) (as a ~3:1 $\mathbf{B_1}/\mathbf{B_2}$ mixture). This reaction afforded a ~7:3 mixture of epimers **12** and **13** in 90% yield [GLC., 5% Carbowax, 180°, 2.5 m column; relative $R_T = 1.00$ (**13**), 1.25 (**12**)]. Each isomer proved to be homogeneous (GLC. on a capillary column) and was examined by NMR. in the presence of $Eu(fod)_3$[8]). The isopropyl methyl protons exhibited relative paramagnetic shifts quite analogous to those observed in the related pair of hydroxy-acetals $\mathbf{C_1}$ and $\mathbf{C_2}$[13]) described in *Section 3*, and were more deshielded in epimer **13** (Fig. 2). This led us to assign the *endo/exo* configuration to this minor epimer. Incidentally, the *exo/exo* isomer **12** appeared to be thermodynamically preferred since it was selectively formed *via* acid-catalyzed isomerization of a mixture of hydroxy-acetals **G** and **11** under relatively drastic conditions (see experimental part).

The mass spectra of both *exo*-epimers **12** and **13** were clearly different from that of the natural *endo* hydroxy-acetal **F**.

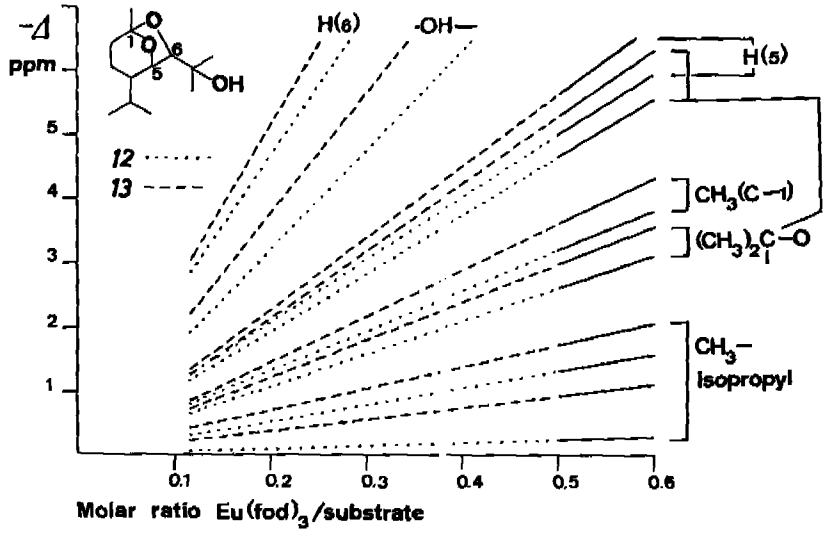


Fig. 2. *NMR. lanthanide-induced shifts for hydroxy-acetals* **12** *and* **13**

[12]) Hydroxy-acetal **F** has also been identified in Turkish tobacco [12].

[13]) Fig. 2 suggests that complexation of epimers **12** and **13** by $Eu(fod)_3$ took place on both the acetal group and the relatively hindered OH function. This not unexpected behaviour [13] does not appear to upset the relative paramagnetic shifts exhibited by the isopropyl group in these compounds.

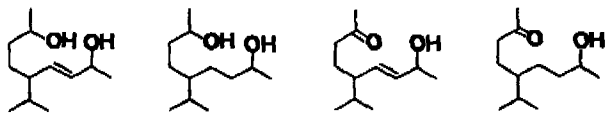
7. *3,3,5-Trimethyl-8-isopropyl-4,9-dioxabicyclo[3.3.1]nonan-2-ol* (**G**), isolated from *Burley* tobacco condensate[4]) subfraction B3-PN-h[5]), was obtained together with isomers **F** and **11** as described in *Section 6a*. Synthetic **G** melted at 67° and proved to be a single stereoisomer (GLC., OV 101, 115°, 50 m × 0.3 mm capillary column), the most probable configuration of which should be G_1 (*exo* OH), assuming that this compound resulted from kinetically-controlled isomerization of E_1 or F_1 without steric inversion at C(2). The chair/boat conformation shown appears to fit our NMR. data best ($J_{1,2} = 3$ Hz, corresponding to an expected dihedral angle of ~125°).

Synthetic and natural hydroxy-acetal **G** presented identical mass spectra.

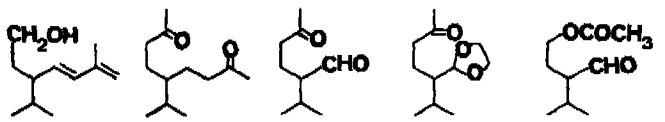
8. (E)-*5-Isopropyl-non-3-ene-2,8-diol* (**H**) was isolated from *Burley* tobacco condensate[4]) subfraction B3-PN-i[5]) and synthesized by lithium aluminium hydride reduction of norsolanadione (**2**) (yield 60% after purification by chromatography). Natural and synthetic diol **H** exhibited identical IR., mass, and NMR. spectra.

9. *5-Isopropyl-nonane-2,8-diol* (**I**), identified in subfraction B3-PN-i[5]) was synthesized by catalytically hydrogenating norsolanadione (**2**) to 5-isopropylnonane-2,8-dione (**14**), and reducing the latter by lithium aluminium hydride (overall yield 79%). Natural and synthetic diol **I** exhibited identical IR. and mass spectra.

10. (E)-*5-Isopropyl-8-hydroxy-non-6-en-2-one* (**J**) was isolated from subfraction B3-PN-i[5]) and synthesized by lithium aluminium hydride reduction of norsolanadione-monoacetal **3** followed by acid hydrolysis (yield 96%). Natural and synthetic ketol **J** exhibited identical IR., mass, and NMR. spectra.



H *I* *J* *K*



L *14* *15* *16* *17*

11. *5-Isopropyl-8-hydroxy-nonan-2-one* (**K**) occurred in subfraction B3-PN-i[5]) and was prepared by lithium aluminium hydride reduction of the monoethylene acetal of 5-isopropylnonane-2,8-dione (**14**) followed by acid hydrolysis (yield 34% after purification by chromatography). Natural and synthetic ketol **K** had identical IR. and mass spectra.

12. (E)-*3-Isopropyl-6-methyl-hepta-4,6-dien-1-ol* (**L**) was isolated from *Burley* tobacco condensate[4]) subfractions B2-PN-f, -g, -h[4]), and B3-PN-f, -g[5]). Dienol **L** was synthesized *via* successive *Baeyer-Villiger* oxidation and acid hydrolysis of 2-isopropyl-5-oxo-hexanal monoacetal **16**, *Wittig* reaction of the resulting acetoxy-aldehyde **17** with $Ph_3P{=}CH{-}C(CH_3){=}CH_2$, and alkaline saponification. The overall

yield was low (~15%), because the acetal group in **16** was partly oxidized to an ester during the *Baeyer-Villiger* reaction [14]. Natural and synthetic dienol **L** exhibited identical IR., mass, and NMR. spectra.

Experimental Part

The spectra were obtained with the instruments already described [15] (the mass spectra were measured at 70 eV, inlet temperature 150°; the NMR. spectra were measured in $CDCl_3$ unless otherwise stated). The GLC. separations were performed on gas chromatographs *Aerograph*, Model 1820–3 (*Varian Aerograph AG*), and *Carlo Erba*, Model 2301 AC. All liquid/solid chromatographic separations were carried out using 0.05–0.2 mm silica gel for column chromatography (*Merck AG*). The melting points are not corrected.

1. *2-Isopropyl-5-oxo-hexanal* (**15**). Methyl vinyl ketone (5.0 g, 71.5 mmol, in 10 ml anhydrous ether) was added over 45 min at –2° to a stirred solution of 1-pyrrolidino-3-methyl-1-butene [16] (9.0 g, 65 mmol) in anhydrous ether (50 ml) (nitrogen atmosphere). The reaction mixture was set aside for 24 h at 20°. Water (1.95 ml) was added with stirring, followed by sufficient 6N HCl (about 11.2 ml) to adjust the pH of the solution between 5 and 6 [17]. After 1 h additional stirring at 20° under N_2, the mixture was extracted twice with ether and the organic layers washed successively with 1% hydrochloric acid (1×, quickly), 5% sodium hydrogencarbonate (1×), and brine. Usual work up and rapid distillation afforded 6.6 g (65%) of *2-isopropyl-5-oxo-hexanal* (**15**), b.p. 47–49°/0.001 Torr; $d_4^{20} = 0.940$; $n_D^{20} = 1.4401$. – IR. (neat, bands with decreasing intensities): 1715, 1360, 2900, 2730 cm^{-1}. – MS.: *m/e* 43 (base peak), 58, 138 (*M*-18), no discernible parent ion. – NMR. (CCl_4): 0.96 (6H, *d*, $J = 6$); 2.07 (3H, *s*); 1.5–2.6 (6H, *m*); 9.55 (1H, *d*, $J \simeq 2$).

$C_9H_{16}O_2$ (156.22) Calc. C 69.19 H 10.32% Found C 69.46 H 10.12%

2. *Norsolanadione* (**2**). A mixture of 2-isopropyl-5-oxo-hexanal (**15**) (10.1 g, 64.7 mmol), triphenylphosphine-acetylmethylidene [18] (22.2 g, 69.7 mmol) and anhydrous benzene (75 ml) was refluxed for 4 days under nitrogen. The solvent was removed in vacuum, the residue taken up in about 200 ml of light petroleum, and the precipitated triphenylphosphine oxide removed by filtration. The solution was evaporated to dryness and the residue distilled (0.001 Torr): Fr. 1, b.p. 50–70°, 1 g; Fr. 2, b.p. 70–84°, 10.9 g. GLC. indicated Fr. 2 to be 94% pure *norsolanadione* (**2**) (yield 80%). After a further distillation, **2** had b.p. 74°/0.001 Torr; $d_4^{20} = 0.940$; $n_D^{20} = 1.4704$. – IR. (neat): 1675, 1710, 1250, 1360, 1620, 1160, 985 cm^{-1}. – MS.: 43 (base peak), 97, 178 (*M*-18), no discernible parent ion. – NMR. (CCl_4): 0.89 (3H, *d*, $J = 6.5$); 0.93 (3H, *d*, $J = 6.5$); 2.04 (3H, *s*); 2.17 (3H, *s*); 2.36 (2H, *t*, $J = 7$); 1.4–2.6 (4H, *m*); 5.90 (1H, *d*, $J = 16$); 6.52 (1H, *d*×*d*, $J = 16$, $J' = 8$). GLC. indicated the product to be homogeneous (Ucon HB 5100, 160°, 50 m × 0.3 mm capillary column).

$C_{12}H_{20}O_2$ (196.29) Calc. C 73.43 H 10.27% Found C 73.67 H 10.32%

3. (E)-*5-Isopropyl-8-ethylenedioxy-non-3-en-2-one* (**3**). Regio-selective monoacetalization of norsolanadione (**2**) was carried out as formerly described [1], yielding 74% of 95% pure **3**.

4. (E)-*5-Isopropyl-8-hydroxy-non-6-en-2-one* (**J**). Norsolanadione-monoacetal **3** (4.50 g, 95% pure, 17.8 mmol, in 50 ml anhydrous ether) was added over 50 min at 20° (water cooling) to a slurry of lithium aluminium hydride (0.455 g, 12 mmol) in anhydrous ether (30 ml). After 4 h further stirring, sufficient moist ether was added to destroy excess hydride and the mixture was quenched with ammonium chloride solution. Usual work up afforded 4.5 g of an oil that was hydrolyzed by overnight stirring at 20° with ether (50 ml) and 5% sulfuric acid (50 ml) under nitrogen. The resulting product was chromatographed on silica gel (100 g) using EtOAc/benzene 5:95 as initial eluent. *Ketol* **J** (3.4 g, 96%) was eluted with EtOAc/benzene 2:3 and had b.p. 80°/0.001 Torr; $d_4^{20} = 0.926$; $n_D^{20} = 1.4608$. – IR. (neat): 1710, 1360, 975, 3450 cm^{-1}. – MS. (*m/e* (% relative abundance)): 43 (100), 55 (11), 71 (20), 79 (9), 95 (15), 107 (11), 122 (7), 137 (5), 180 (1) (*M*-18), no discernible parent ion. – NMR.: 0.85 (3H, *d*, $J = 6.5$); 0.90 (3H, *d*, $J = 6.5$); 1.29 (3H *d*, $J = 6.5$); 1.0–2.0 (5H, *m*); 2.13 (3H, *s*); 2.40 (2H, *t*, $J = 7$); 4.30 (1H, *m*); 5.45 (2H, *m*).

$C_{12}H_{22}O_3$ (198:30) Calc. C 72.68 H 11.18% Found C 72.89 H 11.34%

5. (E)-*3,4-Epoxy-5-isopropyl-nonane-2,8-dione* (**A**). Norsolanadione-monoacetal **3** (10.2 g, 95% pure, 40 mmol, in 125 ml anhydrous ether) was reduced by lithium aluminium hydride (1.14 g, 30 mmol, in 75 ml anhydrous ether) as described above, except that the final acid hydrolysis was omitted. There was thus obtained about 10 g of crude hydroxy-acetal **4**, a sample of which had, after GLC. purification (5% silicone oil, 200°, 2.5 m column), IR. (CCl_4): 1050, 1365, 965, 3450 cm^{-1}. – MS.: 43, 73, 87 (base peak), 227 (*M*-15), no discernible parent ion. – NMR. (CCl_4): 0.90 (6H, *m*); 1.20 (3H, *d*, J = 6); 1.20 (3H, *s*); 1.0-2.3 (7H, *m*); 3.80 (4H, *s*); 3.9–4.5 (1H, *m*); 5.35 (2H, *m*). Crude hydroxy-acetal **4** (10 g, ~ 40 mmol) was added to a solution of *m*-chloroperoxybenzoic acid (20.4 g, 85% pure, 100 mmol) in chloroform (380 ml). The mixture was set aside for 24 h at 20°, the solvent removed in vacuum, the residue taken up in light petroleum, and the filtered solution washed with 5% sodium carbonate and brine. Usual work up afforded 11.2 g of crude (*E*)-3,4-epoxy-5-isopropyl-8-ethylenedioxy-nonan-2-ol (**5**). This product was stirred for 2 days at 20° with manganese dioxide[6][14] (112 g, previously activated for 20 h at 120°) in toluene (980 ml) under nitrogen. The mixture was filtered, evaporated to dryness, the residue was taken up in dioxan (100 ml), 25 ml of 3% sulfuric acid were added, and the solution was abandoned overnight at 20°. It was then diluted with water (400 ml), saturated with sodium chloride, and extracted twice with ether. After washing the organic layers with brine, usual work up afforded ~ 7 g of a crude product which was chromatographed on silica gel (140 g). Relatively unpolar impurities were eluted first (with ether/light petroleum 1:9 to 1:4), followed by 5.92 g (69%) of (*E*)-*3,4-epoxy-5-isopropyl-nonane-2,8-dione* (**A**) (with ether/light petroleum 1:1). This compound had b.p. 90°/0.001 Torr; d_4^{20} = 1.010; n_D^{20} = 1.4594. – IR. (CCl_4): 1700, 1355, 1240, 1160, 1410, 860 cm^{-1}. – MS.: 43 (100), 55 (11), 71 (5), 85 (18.5), 97 (4.5), 109 (4), 123 (3.5), 151 (<1), 169 (*M*-43) (<1), no discernible parent ion. – NMR.: 0.95 (3H, *d*, J = 7); 0.97 (3H, *d*, J = 7); 1.0–2.0 (4H, *m*); 2.09 (3H, *s*); 2.18 (3H, *s*); 2.65 (2H, *t*, J = 7.5); 2.85 (1H, *d* × *d*, J = 8.5, J' ≃ 2); 3.20 (1H, *d*, J ≃ 2).

$C_{12}H_{20}O_3$ (212.28) Calc. C 67.89 H 9.50% Found C 68.10 H 9.73%

Diketo-epoxide **A** was a ~ 1:3 mixture of diastereoisomers $\mathbf{A_2}$ and $\mathbf{A_1}$, as evidenced by GLC. (OV 101, 125°, 50 m × 0.3 mm capillary column) and by NMR.: both CH_3CO- signals at δ = 2.09 and 2.18 were split in the presence of Eu(fod)$_3$[8]. These isomers could be separated by preparative GLC. using the conditions indicated in the theoretical part (*section 1*).

Threo-(E)-*3,4-epoxy-5-isopropyl-nonane-2,8-dione* ($\mathbf{A_1}$). IR. (neat): 1700, 1355, 1240, 1160, 1410, 860 cm^{-1}. – MS.: 43 (100), 55 (11), 71 (5), 85 (19), 97 (4.5), 109 (5), 123 (6), 151 (2), 169 (1.5), no discernible parent ion. – NMR.: 0.94 (3H, *d*, J = 7); 0.97 (3H, *d*, J = 7); 1.3–2.0 (4H, *m*); 2.08 (3H, *s*); 2.17 (3H, *s*); 2.63 (2H, *t*, J = 7.5); 2.84 (1H, *d* × *d*, J = 8, J' ≃ 2); 3.17 (1H, *d*, J ≃ 2).

Erythro-(E)-*3,4-epoxy-5-isopropyl-nonane-2,8-dione* ($\mathbf{A_2}$). IR. (neat): 1700, 1355, 1240, 1160, 1410, 865 cm^{-1}. – MS.: 43 (100), 55 (12), 71 (6), 85 (13), 97 (8), 109 (6), 123 (4.5), 151 (1.5), 169 (6), no discernible parent ion. – NMR.: 1.00 (6H, *d*, J = 7); 1.3–2.0 (4H, *m*); 2.08 (3H, *s*); 2.17 (3H, *s*); 2.48 (2H, *t*, J = 7.5); 2.92 (1H, *d* × *d*, J = 8, J' ≃ 2); 3.16 (1H, *d*, J ≃ 2).

6. Exo-(*1-Methyl-4-isopropyl-7,8-dioxabicyclo*[3.2.1]*oct-6-yl*) *methyl ketone* (**B**). (*E*)-3,4-Epoxy-5-isopropyl-nonane-2,8-dione (**A**) (as ~ 1:3 mixture of $\mathbf{A_2}$ and $\mathbf{A_1}$) (0.50 g, 2.35 mmol), in toluene (10 ml), was stirred at 80–90° with *p*-toluenesulfonic acid (20 mg) under nitrogen. After 4 h, a second portion of 20 mg of *p*-toluenesulfonic acid was added and the stirring at 80–90° resumed for further 3 h. Usual work up (ethereal extraction, 5% sodium hydrogencarbonate washings) and distillation afforded 0.315 g (63%) of 95% pure *keto-acetal* **B**. Redistilled, this compound had b.p. 65°/0.001 Torr; d_4^{20} = 1.032; n_D^{20} = 1.4608. – IR. (CCl_4): 1700, 1375, 1345, 1025, 1190, 840, 1165, 1220 cm^{-1}. – MS.: 43 (100), 55 (12), 71 (8.5), 81 (13), 99 (20), 109 (9), 127 (5), 141 (4), 169 (38), very weak parent ion at *m/e* 212. – NMR.: 1.00 (6H, *m*); 1.57 (3H, *s*); 1.2–2.0 (6H, *m*); 2.25 (3H, *s*); 4.25 (1H, *s*); 4.55 (1H, narrow *m*).

$C_{12}H_{20}O_3$ (212.28) Calc. C 67.89 H 9.50% Found C 67.70 H 9.62%

GLC. (OV 101, 115°, 50 m × 0.3 mm capillary column) indicated that keto-acetal **B** was a ~ 1:3 mixture of epimers $\mathbf{B_2}$ and $\mathbf{B_1}$ [relative R_T = 1.00 ($\mathbf{B_1}$), 1.01 ($\mathbf{B_2}$)], a result that was confirmed by measuring its NMR. spectrum in the presence of Eu(fod)$_3$[8].

[14] *Merck AG.*

7.Exo-*1-(1-Methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-ethanol* (**C**). Sodium borohydride (10 mg, 0.26 mmol) was added to a solution of keto-acetal **B** (100 mg, 0.47 mmol, as a ~ 1:3 mixture of $\mathbf{B_2}$ and $\mathbf{B_1}$) in methanol (3 ml). After 3 h at 20°, the solvent was removed and the residue taken up in 10% hydrochloric acid. Usual work up (ethereal extraction, 5% sodium hydrogencarbonate washings) afforded a nearly quantitative yield of a 2.2:6:1:1.9 mixture of *stereoisomeric hydroxy-acetals* $\mathbf{C_1}$-$\mathbf{C_4}$. These isomers were separated by GLC. as indicated in the theoretical part (*section 3*).

Hydroxy-acetal $\mathbf{C_1}$. MS.: 43 (100), 55 (13.5), 69 (8.5), 82 (17.5), 99 (15.5), 111 (13.5), 129 (32), 169 (35), 171 (13.5), no discernible parent ion. NMR.: 1.00 (3H, *d*, J = 7); 1.05 (3H, *d*, J = 7); 1.19 (3H, *d*, J = 6); 1.48 (3H, *s*); 1.35–2.20 (6H, *m*); 2.54 (1H, *d*, $J \simeq 2$, OH); 3.74 (2H, *m*); 4.30 (1H, broad *s*).

Hydroxy-acetal $\mathbf{C_2}$. MS.: 43 (100), 55 (14), 69 (11), 82 (22), 99 (17.5), 111 (16.5), 129 (33), 169 (34.5), 171 (13.5), no discernible parent ion. – NMR.: 0.92 (6H, narrow *m*); 1.15 (3H, *d*, J = 7); 1.48 (3H, *s*); 1.3–2.0 (6H, *m*); 2.58 (1H, *d*, $J \simeq 2$, OH); 3.75 (2H, *m*); 4.25 (1H, broad *s*).

Hydroxy-acetal $\mathbf{C_3}$. M.p. 45°; NMR.: 0.98 (6H, pseudo *t*, J = 6.5 Hz); 1.18 (3H, *d*, J = 6); 1.42 (3H, *s*); 1.81 (1H, *d*, J = 4, OH); 1.3–2.2 (6H, *m*); 3.80 (2H, *m*); 4.49 (1H, broad *s*).

Hydroxy-acetal $\mathbf{C_4}$. M.p. 102–103°; NMR.: 0.96 (6H, pseudo *t*, J = 5); 1.21 (3H, *d*, J = 6.5); 1.46 (3H, *s*); 1.1–2.0 (6H, *m*); 1.85 (1H, *s*, OH); 3.85 (2H, *m*); 4.49 (1H, broad *s*).

8. (E)-*5-Isopropyl-8-hydroxy-8-methyl-non-6-en-2-one* (**D**). Norsolanadione-monoacetal **3** (4.55 g, 95% pure, 18 mmol) in anhydrous ether (20 ml) was added at 20° to a stirred solution of methylmagnesium bromide (40 mmol, in 60 ml anhydrous ether). After 1 h refluxing, the mixture was set aside overnight at 20°, quenched with chilled, saturated ammonium chloride solution, and worked up as usual. The resulting product was taken up in 40 ml of dioxan/3% sulfuric acid 2:1, the solution was stirred overnight at 20° under nitrogen, saturated with sodium chloride, and extracted with ether. This afforded 4.3 g of crude **D** that was chromatographed on silica gel (85 g), using ether/light petroleum 1:4 as starting eluent. *Ketol* **D** was eluted with pure ether after miscellaneous impurities. This acid-sensitive substance was cautiously distilled over a small amount of solid sodium carbonate: b.p. 85°/0.001 Torr, 3.06 g (80%). A sample further purified by GLC. (5% silicone oil, 200°, 2.5 m column) had d_4^{20} = 0.917; n_D^{20} = 1.4600. – IR. (CCl_4): 1700, 1355, 965, 1150, 1450, 3450, 1220 cm^{-1}. – MS.: 43 (100), 55 (8), 69 (15), 81 (7.5), 93 (34), 109 (13.5), 121 (22), 136 (17), 151 (2), 194 (6.5), no discernible parent ion. – NMR. (CCl_4): 0.83 (3H, *d*, J = 6); 0.88 (3H, *d*, J = 6); 1.22 (6H, *s*); 1.3–2.0 (4H, *m*); 2.03 (3H, *s*); 2.30 (2H, *t*, J = 6.5); 2.53 (1H, *s*, OH); 5.40 (2H, *m*).

$C_{13}H_{24}O_2$ (212.33) Calc. C 73.53 H 11.39% Found C 73.28 H 11.26%

9. (E)-*5-Isopropyl-6,7-epoxy-8-hydroxy-8-methyl-nonan-2-one* (**E**). A mixture of ketol **D** (2.96 g, 13.9 mmol) and *m*-chloroperoxybenzoic acid (3.4 g, 85% pure, 16.7 mmol) in chloroform (90 ml) was allowed to stand for 3 days at 20°. After solvent removal in vacuum, the product was taken up in light petroleum, the solution was filtered and washed successively with 5% sodium carbonate (2×) and brine (3×). The crude product (3 g) resulting from the usual work up was chromatographed on silica gel (60 g) using ether/light petroleum 1:4 as starting eluent. *Epoxy-ketol* **E**, eluted with pure ether, represented 2.51 g (79%), b.p. 100°/0.001 Torr. A sample further purified by GLC. (5% silicone oil, 200°, 2.5 m column) had d_4^{20} = 0.990; n_D^{20} = 1.4572. – IR. (neat): 1705, 1360, 1160, 3500, 905 cm^{-1}. – MS.: 43 (100), 59 (30), 69 (18.5), 81 (20), 97 (23), 112 (18), 123 (2.5), 139 (3), 169 (< 1), no discernible parent ion. – NMR.: 0.95 (6H, *d*, J = 7); 1.25 (3H, *s*); 1.29 (3H, *s*); 1.4–2.0 (5H, *m*); 2.15 (3H, *s*); 2.62 (2H, *t*, J = 8), 2.67 (1H, *d*, $J \simeq 2$); 2.82 (1H, *d*×*d*, J = 9, $J' \simeq 2$).

$C_{13}H_{24}O_3$ (228.33) Calc. C 68.38 H 10.59% Found C 68.41 H 10.57%

GLC. indicated epoxy-ketol **E** to be a ~ 1:9 mixture of diastereoisomers (see theoretical part, *section 5*).

10a. Endo-*2-(1-Methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-propan-2-ol* (**F**). A mixture of epoxy-ketol **E** (25 mg), anhydrous toluene (0.5 ml) and *p*-toluenesulfonic acid (0.5 mg) was heated at 80° for 2 h under nitrogen. After stirring with some solid sodium hydrogencarbonate, the

solution was filtered and evaporated to dryness. GLC. (5% Carbowax, 190°, 2.5 m column) indicated that the resulting product was a mixture of three major constituents, each of which gave a single peak upon re-injection on a capillary column (OV 101, 115°, 50 m × 0.3 mm). *Hydroxy-acetal* **F** had the shorter R_T (see theoretical part, *section 6a*) and was collected: IR. (CCl_4): 1030, 855, 1380, 1165, 1250, 1465, 3500 cm^{-1}. – MS.: 43 (100), 59 (51), 71 (13.5), 82 (30), 97 (52.5), 112 (8), 125 (6), 140 (31.5), 169 (32), no discernible parent ion. – NMR.: 1.00 (6H, *d*, J = 6.5); 1.23 (3H, *s*); 1.37 (3H, *s*); 1.46 (3H, *s*); 1.3–2.3 (6H, *m*); 2.13 (1H, *s*, OH); 3.80 (1H, *d*, J = 4); 4.28 (1H, br. *d*, J = 4).

10b. Exo-*2-(1-Methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-propan-2-ols* (**12** and **13**). Methylmagnesium bromide (4.5 mmol, in 10 ml anhydrous ether) was added to a stirred solution of keto-acetal **B** (0.85 g, 4 mmol, as a ~ 1:3 mixture of B_2 and B_1) in anhydrous ether (5 ml) at 20°. After 1 h refluxing, the reaction mixture was quenched with chilled, saturated ammonium chloride solution, extracted with ether, and the product distilled: b.p. 70°/0.001 Torr, 0.82 g (90%). GLC. indicated that it consisted of a ~ 7:3 mixture of epimers **12** and **13** (see theoretical part, *section 6b*).

Hydroxy-acetal **12**. – IR. (neat): 1020, 1380, 1170, 855, 1200, 1140, 3500 cm^{-1}. – MS.: 43 (100), 59 (31.5), 71 (10), 82 (17), 97 (18), 112 (14), 125 (13.5), 143 (18), 169 (43), 185 (1.5), no discernible parent ion. – NMR.: 0.95 (6H, pseudo *t*, J = 5); 1.19 (6H, *s*); 1.47 (3H, *s*); 1.1–2.0 (6H, *m*); 2.10 (1H, *s*, OH); 3.82 (1H, *s*); 4.38 (1H, br. *s*).

Hydroxy-acetal **13**. – IR. (neat): 1380, 1020, 845, 1240, 1160, 1460, 3475 cm^{-1}. – MS.: 43 (100), 59 (36), 71 (11.5), 82 (17), 97 (19), 112 (13), 125 (17.5), 143 (21), 169 (45), 185 (3), no discernible parent ion. – NMR.: 1.01 (6H, pseudo *t*, J = 6; 1.20 (6H, *s*); 1.45 (3H, *s*); 1.3–2.2 (6H, *m*); 2.06 (1H, *s*, OH); 3.80 (1H, *s*); 4.44 (1H, br. *s*).

11. *3,3,5-Trimethyl-8-isopropyl-4,9-dioxabicyclo[3.3.1]nonan-2-ol* (**G**). This compound was obtained together with isomers **F** and **11** by acid-catalyzed isomerization of epoxy-ketol **E** (see theoretical part, *section 6a*). M.p. 67°. – IR. (neat): 1025, 1180, 1155, 1375, 965, 3475 cm^{-1}. – MS.: 43 (100), 55 (14), 70 (21), 81 (32.5), 97 (15.5), 112 (57), 127 (12), 170 (11), 185 (< 1), no discernible parent ion. – NMR.: 0.97 (6H, pseudo *t*, J = 6); 1.28 (3H, *s*); 1.36 (3H, *s*); 1.47 (3H, *s*); 1.1–1.9 (6H, *m*); 2.05 (1H, *d*, J = 8, OH); 3.56 (1H, *d* × *d*, J = 8, J' = 3); 4.05 (1H, br. *s*).

$C_{13}H_{24}O_3$ (228.33) Calc. C 68.38 H 10.52% Found C 68.43 H 10.72%

12. *3-Isopropyl-6-methyl-7,9-dioxabicyclo[4.2.1]nonan-2-ol* (**11**). This non-natural hydroxy-acetal was obtained together with the natural isomers **F** and **G** by acid-catalyzed isomerization of epoxy-ketol **E** (see above and theoretical part, *section 6a*).

Hydroxy-acetal **11**. – IR. (CCl_4): 1210, 1370, 1160, 1020, 975, 1060, 3475 cm^{-1}. – MS.: 43 (100), 55 (13), 72 (42), 83 (34), 101 (38), 143 (21), 186 (6.5), no discernible parent ion. – NMR.: 0.82 (3H, *d*, J = 7); 0.95 (3H, *d*, J = 7); 1.38 (6H, *s*); 1.47 (3H, *s*); 1.1–1.9 (6H, *m*); 2.12 (1H, *m*); 3.72 (1H, pseudo *t*, J = 8.5); 4.10 (1H, *s*). Structure **11** was confirmed by decoupling experiments.

13. *Acid-catalyzed isomerization of hydroxy-acetals* **G** *and* **11**. A 3:2 mixture of hydroxy-acetals **G** and **11** (120 mg) was heated for 48 h at 80° in 1 ml toluene containing 10 mg of *p*-toluenesulfonic acid and 40 mg of water (nitrogen atmosphere). After neutralization with solid sodium hydrogencarbonate, solvent removal and distillation under 0.001 Torr, there was obtained 87 mg (72.5%) of a product consisting of 77% of starting hydroxy-acetals **G** and **11** in a practically unchanged ratio, and of 23% of *exo*-2-(1-methyl-4-isopropyl-7,8-dioxabicyclo[3.2.1]oct-6-yl)-propan-2-ol (**12**) [identification by NMR. and GLC. (5% Carbowax, 200°, 2.5 m column)].

14. (E)-*5-Isopropyl-non-3-ene-2,8-diol* (**H**). Norsolanadione (**2**) (19.6 g, 100 mmol, in 80 ml anhydrous tetrahydrofuran) was added at 20° to a stirred suspension of lithium aluminium hydride (2.85 g, 75 mmol) in anhydrous ether (160 ml). After further addition of 80 ml of anhydrous tetrahydrofuran, the mixture was stirred for 2 h at 20°, poured into an excess of ammonium chloride solution, and subjected to usual work up. The crude product was distilled (b.p. 50–101°/0.001 Torr, 18.8 g) and chromatographed on silica gel (360 g) using ether/light petroleum 4:1 as starting eluent. *Diol* **H** (12 g, 60%) was eluted with pure ether: b.p. 102°/0.001 Torr; $d_4^{20} = 0.927$; $n_D^{20} = 1.4645$. IR. (neat): 3360, 1365, 1060, 970, 1120, 1455 cm^{-1}. – MS.: 43 (100), 55 (35), 69 (29), 71 (33), 81

(24), 95 (14), 109 (12), 139 (10), no discernible parent ion. – NMR. (CCl_4): 0.85 (6H, *m*); 1.13 (6H, pseudo *t*, J = 6); 1.0–2.0 (6H, *m*); 3.50 (3H, *m*); 4.15 (1H, *m*); 5.33 (2H, *m*).

$C_{13}H_{24}O_2$ (200.32) Calc. C 71.95 H 12.08% Found C 72.03 H 12.01%

15. *5-Isopropyl-nonane-2,8-diol* (I). Norsolanadione (**2**) (1.96 g, 10 mmol, in 20 ml ethyl acetate) was hydrogenated at 20° under atmospheric pressure in the presence of 196 mg of Pd/C (10%). As soon as the hydrogen uptake reached 0.99 equivalent (~ 30 min), the product was isolated, distilled (b.p. 80°/0.001 Torr, 1.77 g), and chromatographed on silica gel (36 g). Pure 5-isopropyl-nonane-2,8-dione (**14**) was eluted with benzene/ethyl acetate 95:5: d_4^{20} = 0.929; n_D^{20} = 1.4501. – NMR. (CCl_4): 0.85 (6H, *d*, J = 6.5); 1.0–1.9 (6H, *m*); 2.05 (6H, *s*); 2.36 (4H, *t*, J = 7.5).

$C_{13}H_{22}O_2$ (198.30) Calc. C 72.68 H 11.18% Found C 72.59 H 11.26%

5-Isopropyl-nonane-2,8-dione (**14**) (2.5 g, 12.6 mmol, in 10 ml anhydrous ether) was added at 20° to a stirred suspension of lithium aluminium hydride (0.57 g, 15 mmol) in 20 ml of ether/tetrahydrofuran 1:1. After usual work up, there was obtained 2.3 g (90%) of *5-isopropyl-nonane-2,8-diol* (I): b.p. ~ 120°/0.001 Torr; d_4^{20} = 0.938; n_D^{20} = 1.4631. – IR. (neat): 3360, 1460, 1370, 1120, 1065, 935 cm^{-1}. – MS.: 43 (96), 45 (98), 55 (100), 69 (93), 81 (66), 85 (70), 95 (26), 109 (19), 123 (19), 141 (13), 151 (6), no discernible parent ion. – NMR. (CCl_4): 0.85 (6H, *d*, J = 6.5); 1.13 (6H, *d*, J = 6); 1.0–2.0 (10H, *m*); 3.3–4.4 (4H, *m*).

$C_{13}H_{26}O_2$ (202.33) Calc. C 71.23 H 12.95% Found C 71.14 H 12.94%

16. *5-Isopropyl-8-hydroxy-nonan-2-one* (K). A mixture of 5-isopropylnonane-2,8-dione (**14**) (1.74 g, 8.7 mmol), ethyleneglycol (0.545 g, 8.7 mmol), and *p*-toluenesulfonic acid (20 mg) was refluxed for 1½ h in benzene (20 ml) (*Dean & Stark* separator). Neutralization followed by usual work up gave 2.2 g of a mixture containing the mono(ethylene-acetal) of **14** as major component. This crude product was successively reduced with lithium aluminium hydride (175 mg, 4.6 mmol) in ether at 20° (20 h), and hydrolyzed overnight at 20° in dioxan (20 ml) and 5% sulfuric acid (6 ml). The resulting product was chromatographed on silica gel (40 g), using benzene/ethyl acetate 95:5 as starting eluent. Recovered diketone **14** (490 mg) was first eluted with benzene/ethyl acetate 9:1, followed by *5-isopropyl-8-hydroxy-nonan-2-one* (K) (600 mg, 34%) with a 4:1 mixture of the same solvents. Ketol K had b.p. ~ 90°/0.001 Torr; d_4^{20} = 0.936; n_D^{20} = 1.4589. – IR. (neat): 1705, 1360, 3450, 1460 cm^{-1}. – MS.: 43 (100), 55 (28), 69 (34), 71 (27), 81 (20), 95 (13), 109 (10), 125 (7), 143 (6), no discernible parent ion. – NMR.: 0.85 (6H, *d*, J = 7); 1.20 (3H, *d*, J = 6.5); 1.0–1.8 (9H, *m*); 2.15 (3H, *s*); 2.44 (2H, *t*, J = 8); 3.75 (1H, *m*).

$C_{13}H_{24}O_2$ (200.32) Calc. C 71.95 H 12.08% Found C 72.08 H 12.31%

17. (E)-*3-Isopropyl-6-methyl-hepta-4,6-dien-1-ol* (L). A mixture of 2-isopropyl-5-oxo-hexanal (**15**) (23.4 g, 0.15 mol, prepared as indicated in *section 1* above), ethylene-glycol (15.4 g, 0.24 mol), and *p*-toluenesulfonic acid (150 mg) in benzene (150 ml) was refluxed for 30 min (*Dean & Stark* separator). The product obtained after neutralization and usual work up was distilled under 0.001 Torr: Fr. 1, b.p. ≤ 60°, 0.5 g; Fr. 2, b.p. 60–61°, 21.2 g; Fr. 3, b.p. 65°, 5.9 g; Fr. 4, b.p. 65–75°, 2.5 g. Fraction 2 represented 70% pure monoacetal **16** (containing unreacted keto-aldehyde **15** and its diacetal). A sample of monoacetal **16** purified by GLC. (5% Carbowax, 190°, 2.5 m column) had IR. (neat): 1710, 1120, 1360 cm^{-1}. – MS.: base peak *m/e* 73, weak parent peak *m/e* 200. – NMR. (CCl_4): 0.90 (3H, *d*, J = 6.5); 0.95 (3H, *d*, J = 6.5); 1.2–1.8 (4H, *m*); 2.03 (3H, *s*); 2.46 (2H, *t*, J = 6.5); 3.80 (4H, *m*); 4.65 (1H, *d*, J = 4.5).

A solution of monoacetal **16** (21.2 g, 84 mmol, containing ~ 20% of corresponding diacetal) and *m*-chloroperoxybenzoic acid (52 g, 256 mmol, 85% pure) in chloroform (1 l) was set aside for 12 days at 20° in the dark. The mixture was evaporated to dryness in vacuum, the residue taken up in light petroleum, the precipitate removed by filtration, and the solution washed with 5% sodium carbonate (3×) and water (2×). The crude product thus obtained (18 g) was hydrolyzed for 24 h at 20° in dioxan (100 ml) containing 5% sulfuric acid (40 ml), isolated by ethereal extraction of the solution saturated with sodium chloride, and distilled: b.p. 50–65°/0.001 Torr, 6.5 g. GLC. (15% silicone oil, 200°, 2.5 m column) indicated the product to be 53% pure acetoxy-aldehyde **17** (yield 24%), containing starting keto-aldehyde **15** as major impurity. A sample of **17** purified by GLC. had IR. (neat): 1740, 1720, 1240, 1370, 1035, 2730 cm^{-1}. – MS.: base peak *m/e*

43, *M*-86 at *m/e* 86, no parent peak. – NMR. (CCl_4): 0.95 (3H, *d*, J = 6.5); 0.99 (3H, *d*, J = 6.5); 1.93 (3H, *s*); 1.3–2.4 (4H, *m*); 3.96 (2H, *t*, J = 6); 9.57 (1H, *d*, J = 1.5).

A 14% solution of *n*-butyl-lithium in hexane (5.5 g, 12 mmol) was added over 45 min at +6/+10° to a stirred slurry of triphenylmethallylphosphonium chloride (4.65 g, 13 mmol) [19] in anhydrous ether (40 ml) under nitrogen. The reaction mixture was further stirred for 4 h at 20° and cooled to −70°, when a solution of acetoxy-aldehyde **17** (1.72 g, 5.3 mmol, 53% pure) in anhydrous ether (5 ml) was added over 5 min at this temperature. After 3 h further stirring at −50°, the mixture was kept overnight at 20°, poured into water, and subjected to usual work up. The resulting crude product was then refluxed for 1 h in 50 ml of 1 N ethanolic potassium hydroxide, isolated again by ethereal extraction (1.5 g), and chromatographed on silica gel (30 g). Some solanone (**1**, racemic) was eluted first with benzene, followed by (E)-*3-isopropyl-6-methyl-hepta-4,6-dien-1-ol* (**L**) (579 mg, 65%, ~ 95% pure) with benzene/ethyl acetate 4:1. Dienol **L** had b.p. ~ 60°/0.001 Torr; d_4^{20} = 0.883; n_D^{20} = 1.4805. – IR. (neat): 960, 870, 3340, 1040, 1360, 1375, 1455, 1600, 3090, 1630 cm^{-1}. – UV.: λmax = 230 nm (ε = 24200, EtOH). – MS.: 41 (56), 55 (39), 67 (35), 79 (65), 81 (100), 91 (69), 107 (78.5), 123 (18), 135 (7), 153 (4), 168 (25). – NMR. (CCl_4): 0.85 (3H, *d*, J = 6); 0.89 (3H, *d*, J = 6); 1.81 (3H, *s*); 1.2–2.4 (4H, *m*); 3.47 (2H, *t*, J = 6.5); 3.80 (1H, *s*, OH); 4.81 (2H, *s*); 5.33 (1H, *d* × *d*, J = 16, J' = 8); 6.05 (1H, *d*, J = 16).

$C_{11}H_{20}O$ (168.28) Calc. C 78.51 H 11.98% Found C 78.73 H 12.05%

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