

# GEORGIA INSTITUTE OF TECHNOLOGY

OFFICE OF RESEARCH ADMINISTRATION

Date: 7 September 1965

## RESEARCH PROJECT INITIATION

Project Title: Sesquiterpenoid Studies

Project No.: B-1555

Project Director: Dr. Leon H. Zalkow

Sponsor: National Institute of Arthritis and Metabolic Diseases, Public Health Service

Agreement Period: From 1 September 1965 until 31 August 1965

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### Grant Administrator

National Institute of Arthritis and  
Metabolic Diseases  
Department of Health, Education and  
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Bethesda, Maryland 20014

### Reports Required

Interim progress - when application  
is made for continuation or renewal  
support (Form FHS-2590)  
Final - upon completion of project

Assigned to: School of Chemistry

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A. Summary Page

Title: SESQUITERPENOID STUDIES

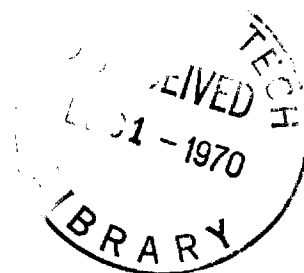
Grant no.: AM-07010 and AM-10099 B-1555

Principal Investigator: Dr. L. H. Zalkow

Sponsoring Institution: Georgia Institute of Technology

Period Covered: January 1, 1963 to December 31, 1965

Date of Preparation: March 14, 1966



Summary:

An investigation of the steam volatile oils of various races of the grass Bothriochloa intermedia has led to the isolation and structure elucidation of three new sesquiterpenes, intermedeol, neointermedeol and epiacorenone. The first two belong to the eudesmane group of sesquiterpenes and intermedeol possesses the unusual antipodal configuration to that usually encountered in higher isoprenoid compounds. Neointermedeol has been synthesized. Epiacorenone belongs to the rare group of spirosesquiterpenes of the acorane group and is epimeric with acorenone presumably at the spiro carbon. Plants of this group appear to have a great facility for synthesizing sesquiterpenes.

## B. Detailed Report

### (1) Description of research accomplished.

The following description of research accomplished includes reprints of two communications: (1) "Constitution of Intermedol", L. H. Zalkow V. B. Zalkow and D. R. Brannon, Chem. and Ind., 38 (1963) and (2) "Constitution and Synthesis of Neo-Intermedeol", V. B. Zalkow, A. M. Shaligram and L. H. Zalkow, Chem. and Ind., 194 (1964); a preprint of a paper to be submitted to Tetrahedron, "The Structure of Epiacorenone. A New Spirosesquiterpene", L. H. Zalkow R. McClure and K. Schorno and finally an addendum briefly summarizing incomplete or inconclusive work in this area. The first communication covers work completed prior to receipt of this grant but the work therein described was continued and additional data was obtained, to be included eventually in a full paper, under this grant.

Slight differences appear in the proposal and in the preprint describing the work on epiacorenone. The preprint describes work accomplished since the proposal was written and contains more conclusive evidence for the structure of epiacorenone.

## Constitution of Intermedeol

By L. H. Zalkow, V. B. Zalkow and D. R. Brannon

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma, U.S.A.

Intermedeol (I), a new sesquiterpene alcohol isomeric with eudesmol but having the rare antipodal absolute configuration has been isolated from the steam volatile oil of the grass *Bothriochloa intermedia*. It crystallised in white needles, m.p. 47–48° (Found C, 81.36; H, 11.82; O, 6.97. Calc. for  $C_{15}H_{26}O$ : C, 81.01; H, 11.79; O, 7.19%),  $[\alpha]_D^{25} + 10.7^\circ$  (c., 0.957 in EtOH),  $\nu_{\text{max}}^{\text{film}}$  3480, 1645, 890, 910  $\text{cm}^{-1}$ , and absorbed one mole of hydrogen in the presence of platinum-on-carbon in acetic acid to give the dihydro-derivative, m.p. 70° (Found C, 79.99; H, 12.40. Calc. for  $C_{15}H_{28}O$ : C, 80.29; H, 12.58%),  $[\alpha]_D^{25} + 29^\circ$  (c., 1.66 in EtOH). Ozonolysis of intermedeol in methylene chloride solution at  $-70^\circ$  followed by aqueous hydrolysis, afforded a 45% yield of formaldehyde (isolated as the dimethone derivative) and a hydroxy-ketone,  $\nu_{\text{max}}^{\text{film}}$  3480, 1710  $\text{cm}^{-1}$ , which gave iodoform with alkaline sodium hypiodite. Dehydrogenation of intermedeol with 10% palladium-on-carbon gave eudalene identified as the molecular complex with *s*-trinitrobenzene and picric acid.

The hydroxyl function of intermedeol was esterified only under forcing conditions (acetic anhydride at  $140^\circ$ ) but was readily eliminated to give an unstable diene,  $\nu_{\text{max}}^{\text{film}}$  1650, 890  $\text{cm}^{-1}$ . Dehydration of dihydro-intermedeol with phosphorous oxychloride in pyridine

spectrum (0.15 mm. cell), and N.M.R. spectrum with a sample of selinane prepared from  $\beta$ -eudesmol by the following sequence: hydrogenation, dehydration, and finally hydrogenation. However the two selinanes were antipodal ( $[\alpha]_D^{25} + 12.5^\circ$  from eudesmol and  $[\alpha]_D^{25} - 10.5^\circ$  from intermedeol). The two selinanes must be conformationally identical in order to give identical N.M.R. and infrared spectra. A *trans* ring fusion and equatorial isopropenyl group can therefore be assigned to intermedeol, since these structural assignments are well established in the case of eudesmol.<sup>1</sup> The hydroxyl group at C(4) is assigned the equatorial configuration by analogy with the dehydration studies of Barton *et al.*<sup>2</sup>

Šorm and co-workers<sup>3</sup> have previously reported the structure of the *optically inactive* juniper camphor (IV). Dihydrointermedeol and dihydro-juniper camphor were found to differ in their infrared and N.M.R. spectra. Contrary to the conclusion of Šorm *et al.*, it appears more likely that juniper camphor contains an axial hydroxyl group. On dehydration of dihydro-juniper camphor these workers obtained an olefin mixture containing only 33% of the isomer possessing a methylene group. In contrast, dehydration of dihydro-intermedeol gave a mixture of olefins containing 70% of the *exo* methylene isomer. Dehydration of such an equatorial hydroxyl group is expected to give predominantly the *exo* methylene isomer.<sup>2</sup> Since dihydro-juniper camphor has also been converted into selinane,<sup>3</sup> it must differ from dihydro-intermedeol in the conformation of the hydroxyl group at C(4).

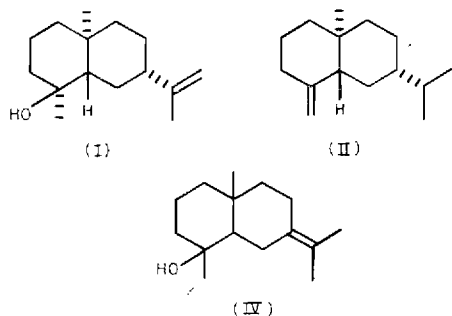
Of the large number of selinane type sesquiterpenes found in nature only two others, laevojunenol<sup>4</sup> and maaliol<sup>5</sup> have thus far been found to have the antipodal stereochemistry at C(5) and C(10) found in intermedeol.

We thank Dr. J. R. Harlan and Mr. R. M. Ahring of the Agronomy Department, Oklahoma State University, for generously supplying us with plant material; and Academician F. Šorm for providing us with a sample of dihydro-juniper camphor and we thank Fritzsche Brothers, Inc. for a sample of  $\beta$ -eudesmol.

Received August 13, 1962

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- 1 Cocker, W. & McMurry, T. B. H., *Tetrahedron*, 1960, **8**, 181
- 2 Barton, D. H. R., Campos-Neves, A. Da S. & Cookson, R. C., *J. chem. Soc.*, 1956, 3500
- 3 Motl, O., Herout, V. & Šorm, F., *Coll. Czech. Chem. Commun.*, 1958, **23**, 1293
- 4 Bhattacharyya, S. C., Rao, A. S. & Shaligram, A. M., *Chem. & Ind.*, 1960, 469
- 5 Buchi, G., Schach, M., Wittenau, V. & White, D. M., *J. Amer. chem. Soc.*, 1959, **81**, 1968



gave a mixture of liquid olefins (Found C, 87.32; H, 12.59. Calc. for  $C_{15}H_{26}$ : C, 87.30; H, 12.70%),  $\nu_{\text{max}}^{\text{film}}$  890  $\text{cm}^{-1}$ , whose gas chromatograms indicated a minimum of 70% of the isomer (II) containing an *exo* methylene group. Treatment of compound (II) with osmium tetroxide followed by lead tetraacetate gave a saturated liquid ketone (III) (Found C, 80.57; H, 11.31. Calc. for  $C_{14}H_{24}O$ : C, 80.71; H, 11.61%),  $[\alpha]_D^{25} - 75.7^\circ$  (c., 1.08, in EtOH), semicarbazone, m.p. 197–198°. Ozonolysis of (II) gave, in addition to (III), formaldehyde, isolated as the dimethone derivative.

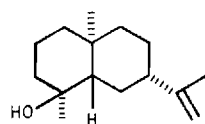
Hydrogenation of compound (II) over 5% platinum-on-carbon in acetic acid solution gave a saturated hydrocarbon identical in refractive index, infrared

## Constitution and Synthesis of Neo-Intermedeol<sup>1</sup>

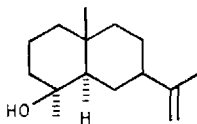
By V. B. Zalkow, A. M. Shaligram and L. H. Zalkow

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma, U.S.A.

During the course of an investigation of several races of grasses of the species *Bothriochloa intermedia* two new sesquiterpenic alcohols of the selinane type have been isolated. One of these, intermedeol (I), was recently described;<sup>2</sup> it was isolated from races of *Bothriochloa intermedia*, indigenous to India, and found to possess an absolute configuration at C(5) and C(10) antipodal to that usually encountered in higher isoprenoid compounds. We now report the structure and synthesis of neo-intermedeol (II), C<sub>15</sub>H<sub>26</sub>O, found in the steam volatile oil of races of this species endemic to Malaya and East Africa.



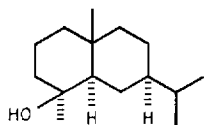
(I)



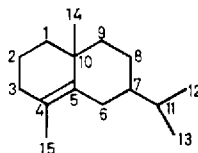
(II)

Neo-Intermedeol was isolated from the oil as a colourless liquid, by chromatography on alumina, b.p. 85-87° (0.5 mm.),  $[\alpha]_D^{25} +7.5^\circ$  (c., 2.635 in EtOH),  $\nu_{\text{max}}^{\text{film}}$  3500, 1640, and 890 cm.<sup>-1</sup>. Its nuclear magnetic resonance (N.M.R.) spectrum (reported as dimensionless "chemical shift" units relative to tetramethylsilane  $\delta=0$ ) showed sharp singlets at  $\delta$ 1.02 C(10) methyl),  $\delta$ 1.12 (C(4) methyl) and  $\delta$ 1.72 (isopropenyl methyl) integrating for three protons each and a broad signal which integrated for two protons at  $\delta$ 4.62 (olefinic protons). On dehydrogenation with 10% palladium-on-carbon, eudalene, identified as the molecular complex with *s*-trinitrobenzene, and picric acid, was obtained in good yield.

In the presence of platinum-on-carbon in acetic acid, neo-intermedeol absorbed one mole of hydrogen to give the dihydroderivative (III), C<sub>15</sub>H<sub>28</sub>O, which could be readily dehydrated with potassium hydrogen sulphate or phosphorus oxychloride in pyridine to give almost exclusively (according to its gas chromatograms) the tetrasubstituted olefin, (IV);



(III)

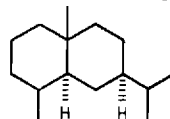


(IV)

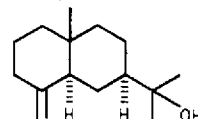
this olefin had no bands in its infrared spectrum characteristic of carbon-carbon double bonds but absorbed one mole of hydrogen in the presence of platinum-on-carbon in acetic acid to give a mixture of selinanes.

When dihydro-neo-intermedeol was heated under reflux in acetic anhydride and pyridine,<sup>3</sup> an acetate, C<sub>17</sub>H<sub>30</sub>O<sub>2</sub>,  $\nu_{\text{max}}^{\text{film}}$  1730, 1250 cm.<sup>-1</sup> was obtained in 70% yield. Pyrolysis of the acetate at 375° yielded a mixture of the C(3) and C(4)[C-(15)] olefins,  $\nu_{\text{max}}^{\text{film}}$  1640,

890, 800 cm.<sup>-1</sup>, which on hydrogenation over platinum-on-carbon in acetic acid gave selinane (V),  $[\alpha]_D^{30} +10.3^\circ$ , identical in its infrared spectrum and gas chromatogram with a sample of selinane,  $[\alpha]_D^{30} +12.5^\circ$ , prepared from  $\beta$ -eudesmol, (VI)



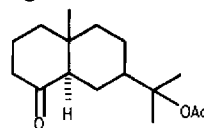
(V)



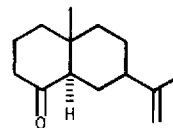
(VI)

whose absolute configuration is well established.<sup>4</sup> The absolute configuration of neo-intermedeol at C(5), C(10) and C(7) is therefore identical to that in  $\beta$ -eudesmol and antipodal at these centres to intermedeol. The axial hydroxyl group at C(4) was assigned on the basis of the mode of dehydration of (III).

The synthesis of neo-intermedeol was accomplished as follows: ozonolysis of (VI) in ethyl acetate gave the previously reported keto-alcohol<sup>5</sup> which was converted into the keto-acetate (VII),  $[\alpha]_D^{25} +26.1^\circ$ ,  $n_D^{25}$  1.4850,  $\nu_{\text{max}}^{\text{film}}$  1725, 1710, 1380, 1250, 1140, 1020 cm.<sup>-1</sup>. Pyrolysis of (VII) at 400°C. gave the unsaturated ketone, (VIII)  $\nu_{\text{max}}^{\text{film}}$  1706, 1640, 890 cm.<sup>-1</sup>, which on treatment with methylmagnesium iodide gave, after chromatography on alumina, a product ( $[\alpha]_D^{25} +7.04^\circ$ ) identical in all respects with naturally occurring neo-intermedeol.



(VII)



(VIII)

Satisfactory carbon and hydrogen analyses were obtained for all compounds. We gratefully acknowledge support of this work by the National Institutes of Health (NIH-AM-07010), and thank Dr. J. R. Harlan and Mr. R. M. Ahring of the Agronomy Department, Oklahoma State University, for generously supplying us with plant material. We thank Fritzsche Brothers, Inc. for samples of  $\beta$ -eudesmol.

Received October 7, 1963

### References

- 1 Terpenes IX. For Terpenes VIII, see "Oxidation of the Fumaric Acid-Methyl Abietate Diels-Alder Adduct with Alkaline Permanganate," Zalkow, L. H. & Brannon, D. R., *J. org. Chem.*, in press
- 2 Zalkow, L. H., Zalkow, V. B. & Brannon, D. R., *Chem. & Ind.*, 1963, 38
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- 4 Cocker, W. & McMurry, T. B. H., *Tetrahedron*, 1960, **8**, 181
- 5 Simonsen, Sir John, "The Terpenes," Vol. 3, 1952, p. 147, (Cambridge: University Press)

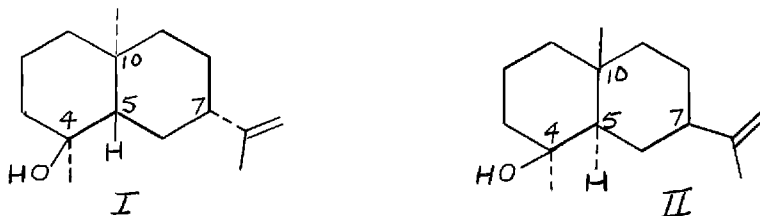
The Structure of Epiacorenone. A New Spirosesquiterpene<sup>1</sup>

L. H. Zalkow, R. McClure and K. Schorno

School of Chemistry,  
Georgia Institute of Technology and Oklahoma State University

Abstract - The new  $\alpha,\beta$ -unsaturated sesquiterpenoid ketone, epiacorenone (IIIa), has been isolated from the steam volatile oil of a hybrid of the grass Bothriochloa intermedia. Epiacorenone has been degraded to the same dicarboxylic acid previously obtained from acorenone. On the basis of this evidence together with other degradative work and NMR and mass spectral studies, structure IIIa has been assigned to this new sesquiterpene.

During the course of an investigation on the steam-volatile oil of a race of the grass Bothriochloa intermedia indigenous to India, a new sesquiterpene, intermedeol, was isolated and its structure and absolute configuration were determined and found to be as depicted in I<sup>2</sup>. Thus this

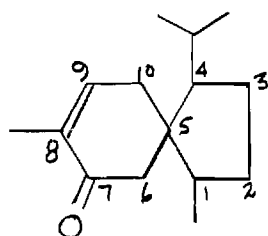


terpene has an absolute configuration at C-5 and C-10 antipodal to that usually encountered in higher isoprenoid compounds. Further investigation of the steam-volatile oil of a race of B. intermedia indigenous to Malaya provided a second new sesquiterpene, neointermedeol, which has been shown to possess the structure and absolute configuration depicted in II<sup>3</sup>. Intermedeol and neointermedeol were shown to belong to the eudesmane (selinane) group of sesquiterpenes by their ready conversion into eudalene in good yield. The absolute configurations of I and II at all centers except C-4 were established by their conversion to enantiomeric selinanes, while the configuration at C-4 in each case was determined from the conformational assignments of the hydroxyl groups based on modes of dehydration. The enantiomeric selinanes were found to give identical IR (thick film), NMR and mass spectra<sup>4</sup>, and the selinane from II was identical in all respects, including optical rotation ( $[\alpha]_D$ ), with selinane prepared from eudesmol. Finally neointermedeol was synthesized from  $\beta$ -eudesmol, which in turn has been recently totally synthesized.<sup>5</sup>

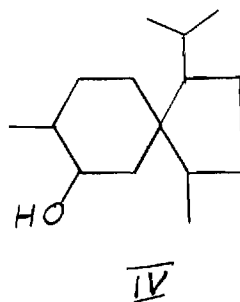
The steam-volatile oil of a hybrid grass prepared from two parent races of B. intermedia<sup>6</sup> has now been found to contain as the major component, a third new sesquiterpene, epiacorenone. The molecular formula  $C_{15}H_{24}O$  could be assigned to this compound on the basis of its and its derivatives elemental analyses and its molecular weight (mass spec). The presence of an  $\alpha,\beta$ -unsaturated ketone grouping

was indicated by the u. v. ( $\lambda_{\text{max}}^{\text{EtOH}}$  240m $\mu$ , log E 4.08), I. R. ( $\nu$  1675 cm $^{-1}$  and n. m. r. ( $\beta$ -vinylic proton,  $\delta$  6.75) spectra and by the formation of a red 2,4-dinitrophenylhydrazone. Hydrogenation gave dihydroepiacorenone, which contained a six-membered ring keto group ( $\nu$  1725 cm $^{-1}$ , yellow DNP). The NMR spectrum of epiacorenone showed that the carbonyl group was flanked by a methylene group uncoupled to any other protons, by the presence of an AB quartet centered at  $\delta$  2.34, J=16cps. Two protons also appeared to be adjacent to the double bond (broad multiplet centered  $\sim \delta$  2.16) which were shown to be coupled to the  $\beta$ -vinylic proton by decoupling experiments. In addition, the NMR spectrum of epiacorenone showed that methyl group was attached to the double bond  $\alpha$  to the carbonyl group ( $\delta$  1.70) and three secondary methyl groups were present in the molecule ( $\delta$  0.78, 0.87, 0.95, J=cps).

By application of the isoprene rule together with the above data structure III is suggested for epiacorenone. Preliminary support for



IIIa epiacorenone  
IIIb acorenone



such a structure was found in the observation that under conditions where I and II gave excellent yields of eudalene, epiacorenone gave only traces of an unidentified aromatic product. However, structure III has already been assigned to the sesquiterpene acoronenone isolated by Sorm et al.<sup>7</sup> from sweet-flag oil. A comparison of the physical



properties of acorenone (IIb) and epiacorenone (IIIa, homogenous by g.l.c.) as shown in Table I suggests that the two compounds are similar. However, epiacorenone readily gave a 2,4-dinitrophenyl-hydrazone (m.p. 151-152°),

Table I

	$n_D^{20}$	$d$	$[\alpha]_D$ (neat)
acorenone <sup>7</sup>	1.5039	0.9599(20°)	-22.3(20°)
epiacorenone	1.5039	0.9664(25°)	-13°(25°)

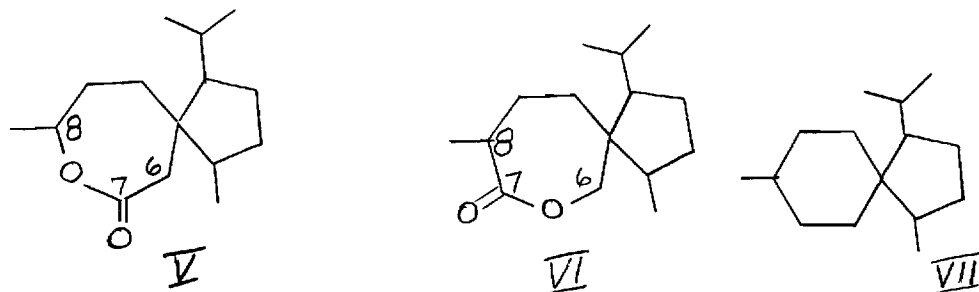
whereas acorenone, is reported not to yield such a derivative. An authentic sample of acorenone was not available for comparison purposes, but its published infrared spectrum<sup>8</sup> was identical to that of epiacorenone in the regions 5.5-7.5 $\mu$  and 10.5-15 $\mu$  with slight differences appearing in the region 7.5-10.5 $\mu$ . Epiacorenone showed a positive Cotton effect in its optical rotatory dispersion curve.

Dihydroepiacorenone ( $[\alpha]_D^{25} + 13^\circ$ , neat)\* was prepared from epiacorenone as previously described<sup>7</sup> for the preparation of dihydroacorenone ( $[\alpha]_D^{20} - 10.6^\circ$  neat). The mass spectra of dihydroepiacorenone and dihydroacorenone<sup>9</sup> showed the same peaks but markedly different intensities<sup>10</sup>; the parent peak in the spectrum of dihydroepiacorenone appeared at m/e 41, whereas in dihydroacorenone it appeared at m/e 138. Both spectra gave molecular ion peaks at m/e 222. A comparison of the dihydro derivatives by g.l.c. showed that each was a different mixture; thus under the same conditions (6'x3/4" 3% Ucon polar column at 126°) dihydroacorenone was shown to be a 72:28 mixture of two compounds with retention times of 13.5 and 15.9 min. respectively, whereas dihydroepiacorenone was a 78:22 mixture with retention times of 14.9 and 16.4 min respectively.

\*On another occasion a rotation of  $[\alpha]_D^{26} + 8.8^\circ$  was obtained for dihydroepiacorenone prepared from a different batch of oil.

On reduction in the presence of Pt-Cor with lithium aluminum hydride, epiacorenone gave, after chromatography on alumina, a single (g.l.c.) pure alcohol ( $C_{15}H_{28}O$ ), IV, in good yield, which on Jones oxidation<sup>11</sup> gave the same dihydroepiacorenone mixture as previously mentioned.

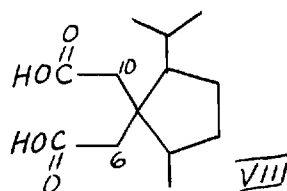
When dihydroepiacorenone was subjected to the Baeyer-Villiger reaction, and the crude product chromatographed on alumina, a mixture of two lactones was obtained in the ratio of 4:1 (g.l.c.). This mixture could not be further separated by repeated chromatography but the major component was isolated in a pure form (m.p. 88.5-89°) by sublimation at reduced pressure. Structure V is assigned to the major lactone. Elemental analysis and mass spectral analysis (MW 238)



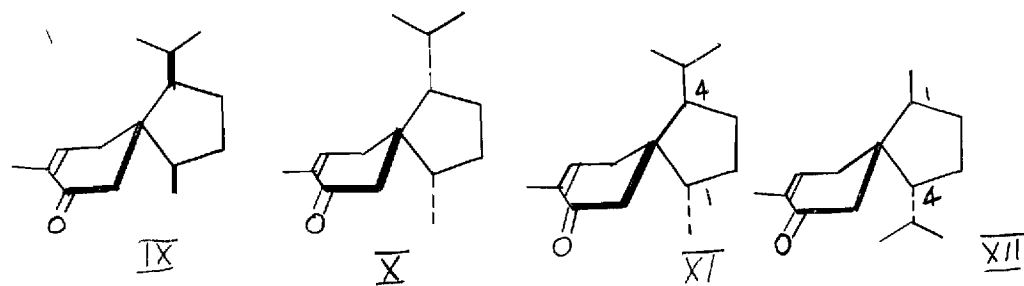
showed that V had the molecular formula  $C_{15}H_{26}O_2$  and the IR spectrum showed the lactone carbonyl band at  $1700\text{cm}^{-1}$ . The NMR spectrum of this lactone supported structure V; thus, the methyl group at C-8 was shifted downfield (doublet,  $J=6.0$  cps, centered at  $\delta 1.3$ ) compared to that in dihydroepiacorenone ( $\delta 0.90, 0.98$  or  $1.00$ ). A broad multiplet integrating for one proton was centered at  $\delta 4.5$  and can be assigned to the C-8 proton of V. If structure VI corresponded to the major lactone, then the low field signal should integrate for two protons and appear as an AB quartet. It is interesting to notice that in the NMR spectrum of V there is a greater difference in the chemical shifts of the two C-6 protons than in the major component of the dihydroepiacorenone mixture.

Thus in the latter case the low field C-6 proton appeared at  $\delta$  2.46 ( $J=14\text{cps}$ ), whereas in V the low field C-6 proton appeared at  $\delta$  3.29 ( $J=13\text{cps}$ ). The high field C-6 proton in each case appeared at  $\sim\delta$  2.05. The minor lactone product obtained in the Baeyer-Villiger reaction undoubtedly possesses structure VI, but it was not possible to isolate it completely free of V in order to verify the structural assignment. Originally we had planned to further degrade lactone V by reduction with lithium aluminum hydride followed by oxidation with chromic acid to yield the dicarboxylic acid. The reduction gave a mixture of products and the oxidation of this mixture did not lead to a clean product. Sorm et al.<sup>7</sup> have reported the conversion of acorenone to the saturated hydrocarbon acorane, VII, and have described its physical properties and recorded its infrared spectrum<sup>12</sup>. We therefore were interested in determining whether epiacorenone gave the same saturated hydrocarbon. First, the previously described alcohol IV was dehydrated with phosphorous oxychloride in pyridine to give a mixture of two olefins (g.l.c.) which was hydrogenated to give an equal mixture of two hydrocarbons. Second, dehydroepiacorenone was transformed into its ethylenedithiol which was reduced with lithium and ethylamine (Raney Nickel gave inconclusive results) to give the same mixture of saturated hydrocarbons described above. The infrared spectrum (thick film) of this mixture of saturated hydrocarbons was very similar to that of acorane<sup>12</sup> but differed in the region 8 to  $9.8\mu$ . Thus, this evidence again suggested a close similarity between acorenone and epiacorenone but more positive evidence was desired in support of structure IIIa. This was obtained as follows.

Following the procedure previously reported<sup>7</sup> for the conversion of acorenone to the dicarboxylic acid VIII, epiacorenone was



ozonized to give a dicarboxylic acid ( $C_{13}H_{22}O_4$ ) of m.p. 144-146° (reported<sup>7</sup> for VIII, m.p. 145-147°) which on treatment with diazomethane gave a dimethyl ester (M.W. 270 by mass spec.) whose IR spectrum was identical with the spectrum of the dimethyl ester of VIII kindly supplied by Dr. V. Herout. Unfortunately, an authentic sample of VIII or its dimethyl ester, prepared from acorenone, is no longer available for comparison purposes. The NMR spectra of VIII and its dimethyl ester, prepared from epiacorenone, supported the assigned structures, thus in each case the C-6 and C-10 protons gave low field two-proton singlets ( $\delta$ 2.37 and  $\delta$ 2.93 for acid,  $\delta$  2.22 and  $\delta$ 2.78 for ester). When the ozonide obtained from epiacorenone (not isolated) was hydrolyzed in alkaline 30% hydrogen peroxide rather than plain water, a six-membered anhydride ( $\nu$ 1820, 1760 $cm^{-1}$ ) was obtained which on treatment with methanolic diazomethane gave the same dimethyl ester described above. Thus there seems to be little doubt that the structure of epiacorenone is as depicted in IIIa and that epiacorenone and acorenone have the same relative configuration at C-1 and C-4 and differ at C-5. The absolute configuration of acorenone is not known at this time<sup>13</sup> and therefore acorenone and epi-acorenone must be represented by IX and X or visa versa or by XI and XII, or visa versa.



Since the closely related acorane sesquiterpene acorone has been shown by x-ray analysis<sup>14</sup> to have the absolute configuration at C-1 and C-4 as depicted in XI and XII it is presumed that these structures represent epiacorenone and acorenone.

Work is presently underway in our laboratory to determine the absolute configuration of epiacorenone and therefore acorenone also and synthetic approaches to these sesquiterpenes are being investigated.

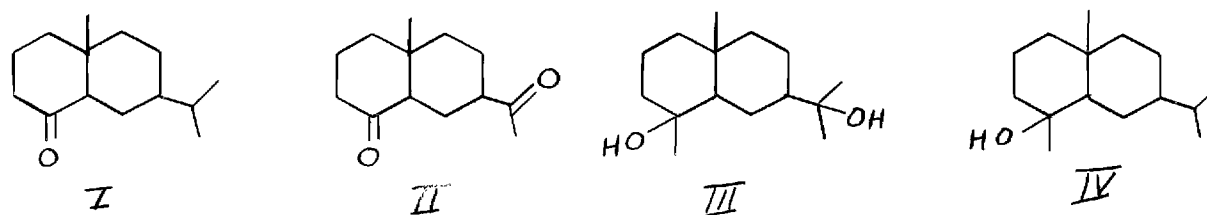
The experimental details upon which the above discussion is based are not included in this report but can be supplied if requested.

- <sup>1</sup> Terpenes XX. This work was generously supported by USPHS-NIH grants AM 07010 and AM 10099.
- <sup>2</sup> L. H. Zalkow and D. R. Brannon, Chem. Ind. (London), 38 (1963).
- <sup>3</sup> V. B. Zalkow, A. M. Shaligram and L. H. Zalkow, Chem. Ind. (London), 194 (1964).
- <sup>4</sup> Unpublished work of V. B. Zalkow
- <sup>5</sup> R. P. Houghton, D. C. Humber and A. R. Pinder, Tetrahedron Letters, 353 (1966).
- <sup>6</sup> All of the grasses utilized in our studies were grown in Stillwater, Oklahoma and kindly provided by Professor Jack Harlan of the Agronomy Department, Oklahoma State University.
- <sup>7</sup> J. Vrkoc, V. Herout and F. Sorm, Coll. Czech. Chem. Comm., 26, 3183 (1961).
- <sup>8</sup> M. Horak, O. Motl, J. Pliva and F. Sorm, "Die Terpene", Teil II, Akademie-Verlag, Berlin, 1963.
- <sup>9</sup> Kindly supplied by Dr. V. Herout, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science.
- <sup>10</sup> The mass spectra were supplied by Professor Carl Djerassi, Stanford University or Professor C. C. Sweeley, University of Pittsburgh.
- <sup>11</sup> K. Bowden, I. M. Heilbron, E.R.H. Jones and B.C.L. Weedon, J. Chem. Soc., 39 (1946).
- <sup>12</sup> J. Pliva, M. Horak, V. Herout and F. Sorm, "Die Terpene", Teil I, Akademie-Verlag, Berlin, 1960.
- <sup>13</sup> Private Communication from Dr. V. Herout
- <sup>14</sup> C. E. McEachan, A. T. McPhail and G. A. Sim, Chem. Comm. 276 (1965).

## Addendum

A gas chromatographic study of a large number of races of the grass B. intermedia showed them to be relatively rich in sesquiterpenes but failed to provide information useful at this time in chemical taxonomy. Further work is required in this area.

An attempt was made to interrelate the well-known sesquiterpene eudesmol and intermedeol via the monoketone I and the diketone II.



Inconclusive results were obtained and this work must be repeated. Likewise an attempt was made to convert intermedeol into a diol III, identical with the naturally occurring selinan-4,7-diol (cryptomeridiol)<sup>1-3</sup> which we obtained as previously described from eudesmol. Again, preliminary results are inconclusive and this work must be repeated. We have also compared dihydrointermedeol and dihydroneointermedeol with an authentic sample<sup>4</sup> of dihydrojuniper camphor<sup>5</sup> and find that none of these are identical. While all three of these substances are supposedly based on structure IV, intermedeol and neointermedeol have been shown<sup>6</sup> to be trans decalin derivatives whereas juniper camphor has been reported to be a cis decalin derivative<sup>7</sup>. However, the later conclusion is unwarranted and is based on the report<sup>8</sup> that in 5-methyl-decalin derivatives the C-5 methyl groups are more highly shielded in the trans isomer than in the cis isomer. We have shown that the C-4 substituents must be considered (ignored in reference 7) and in a number of examples of known trans fused sesquiterpene derivatives possessing a decalin ring system the C-5 methyl groups appear at

lower field than that reported<sup>7</sup> for juniper camphor.

Recently Takeda<sup>9</sup> informed us that a new sesquiterpene alcohol isolated from Oplopanax japonicus had been modified to yield a substance identical with our dihydroneointermedeol.

Attempts to synthesize intermedeol from  $\alpha$ -cyperone and  $\beta$ -eudesmol have not been successful but work along these lines will continue.



- <sup>1</sup> L. Dolejs and V. Herout, Coll. Czech. Chem. Comm., 26, 2047 (1961)
- <sup>2</sup> H. Erdtman and B. R. Thomas, Acta Chem. Scand., 12, 59 (1958).
- <sup>3</sup> M. Sumimoto et al., Chem. and Ind., 780 (1963).
- <sup>4</sup> Kindly supplied by Dr. V. Herout.
- <sup>5</sup> O. Motl, V. Herout and F. Sorm, Coll. Czech. Chem. Comm., 23, 1293 (1958).
- <sup>6</sup> See enclosed reprints.
- <sup>7</sup> K. R. Varma, T. C. Jain and S. C. Bhattacharyya, Tetrahedron, 18, 979 (1962).
- <sup>8</sup> J. I. Musher, J. Am. Chem. Soc., 83, 1146 (1961).
- <sup>9</sup> Dr. K. Takeda, Shionogi Research Laboratory, Osaka, Japan.

B. Detailed Report

(2) List of publications

"Constitution of Intermedeol", L. H. Zalkow, V. B. Zalkow and D. R. Brannon, Chem. and Ind., 38 (1965).

"Constitution and Synthesis of Neointermedeol", V. B. Zalkow, A. M. Shaligram and L. H. Zalkow, Chem. and Ind., 194 (1964).

"The Structure of Epiacorenone. A New Spirosesquiterpene", L. H. Zalkow, R. McClure and K. Schorno, in preparation.

(3) Staffing

Dr. V. B. Zalkow, research associate, Jan. 1, 1963 - Feb. 1, 1965, full time.

Mr. K. Schorno, graduate student, June, 1963 - Aug. 31, 1965, 10% academic year, full-time summers.

Mr. R. McClure, research assistant, Sept. 1, 1965- to present, 50% time.

Dr. L. H. Zalkow, principal investigator, Jan. 1, 1963 - to present, 15% time.