tation broths of *Bacillus subtilis*,[9] from cultures of *Aspergillus niger*,[10] and as a product of tryptophane metabolism by *claviceps Paspali*.[11] In general the *o*-dihydric phenolic structure is rare among microbial products.

Experimental

A sample (40 mg.) of the crude yellow amorphous phenolic metabolite was dissolved in a minimum quantity of boiling water. The aqueous solution was acidified with sulfuric acid and the free phenol was extracted with ethyl acetate. The ethyl acetate solution was treated with Darco G-60 activated carbon, filtered, and evaporated. The product was recrystallized twice from hot water. When the amorphous or colorless crystalline phenol was heated on a Kofler hot stage, it began to sublime at 140° and formed beautiful hard cubes, m.p. 204–205° (cor.). A mixture melting point determination with an authentic sample of 2,3-dihydroxybenzoic acid produced no melting point depression.

Anal. Calcd. for $C_7H_6O_4$: C, 54.55; H, 3.92; O, 41.53. Found: C, 54.77; H, 3.94; O, 41.29.

Nuclear magnetic resonance spectra were determined using a Varian A-60 instrument; tetramethylsilane served as an external reference. Solutions were prepared using 10 mg. of the sample and 0.2 ml. of deuterium oxide; sufficient anhydrous potassium carbonate was added so that the sample dissolved. The final solutions were deoxygenated before the spectra were determined.

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Essential Oils and Their Constituents. XXI.[1] Isomerization of α-Humulene Monoxide to β-Humulen-7-ol. A New Sesquiterpene Alcohol

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During a recent study of the volatile components of wild ginger (*Zingiber zerumbet* Smith), the authors observed formation of a sesquiterpene alcohol when the essential oil or *l*-humulene monoxide, one of its constituents, was chromatographed over active alumina.[3] It is the purpose of this Note to present experimental evidence which established its structure.

The infrared spectrum of the compound, $C_{15}H_{24}O$ (shown in Fig. 1), displayed absorptions characteristic of a free hydroxyl group (3390 cm.$^{-1}$), an exocyclic methylene group $>C{=}CH_2$ (895 and 1642 cm.$^{-1}$), a trisubstituted double bond $>C{=}CH-$ (835 cm.$^{-1}$), and a *trans*-symmetrical disubstituted double bond $-CH{=}CH-$ (975 cm.$^{-1}$). In accordance with these structural features of the molecule, 3 moles of hydrogen were consumed during hydrogenation with Adams catalyst. The ultraviolet absorption spectrum of the compound was practically featureless, suggesting absence of conjugated unsaturation.

Column chromatography of the hydrogenated product over neutral grade I alumina followed by gas chromatography of petroleum ether eluates revealed the presence of humulane (II, Fig. 2) as a product of hydrogenolysis, the identity of the hydrocarbon being established by comparison of its retention time on both Reoplex 400 and SAIB, respectively, as well as by comparison of its infrared absorption spectrum with that of an authenticated sample prepared *via* hydrogenation of pure α-humulene (V). Similar examination of diethyl ether eluates showed the presence of two isomeric saturated alcohols (III), emerging after 19.8 and 23.4 min., respectively, from the Reoplex column operated at 200°.

Chromic acid oxidation converted the alcohols to the corresponding saturated ketones (VI) isomeric with regard to the spatial arrangement of the methyl groups at C-4 and C-8 positions. These ketones were resolved by preparative gas chromatography. Their retention times, indicative of the corresponding boiling points of the two compounds, and refractive indices would permit the following tentative configurational assignments: *cis*—retention time of 32.6 min., $n^{25}\mathrm{D}$ 1.4735; and *trans*—retention time of 30.4 min., $n^{25}\mathrm{D}$ 1.4729. Of the two ketones only the *cis* isomer yielded a crystalline semicarbazone (m.p. 190–191°).

Formation of the alcohol during column chromatography of humulene monoxide (IV)[3] suggested an allylic humulane-type skeleton of the molecule. The assumption was confirmed by examination of the reaction product obtained on refluxing the epoxide with pyridinium bromide. Caryophyllene oxide so treated has been reported to yield a mixture of allylic alcohols.[4] Gas chromatographic analysis of the humulene monoxide–pyridinium bromide isomerization product showed that its major component displayed the same retention time as the alcohol obtained *via* either alumina-catalyzed isomerization of α-humulene 7,8-epoxide or column chromatography of oil of wild ginger. The infrared absorption spectra of the three alcohols proved to be identical as well. The course of the chemical reactions is illustrated in Fig. 2 and relevant experimental data are recorded in Table I.

TABLE I

CRITERIA OF IDENTITY FOR SESQUITERPENE ALCOHOL OBTAINED BY THREE DIFFERENT ROUTES

Method of preparation	$n^{25}\mathrm{D}$	$[\alpha]^{25}\mathrm{D}$	Retention time,[a] min.
(1) Column chromatography of oil of wild ginger	1.5135	+25.81°	29.5
(2) Isomerization of *dl*-humulene monoxide over alumina	1.5135	±0.0	29.5
(3) Isomerization of *dl*-humulene monoxide with pyridinium bromide	1.5140	±0.0	29.5

[a] Column, Reoplex 400; temperature 200°.

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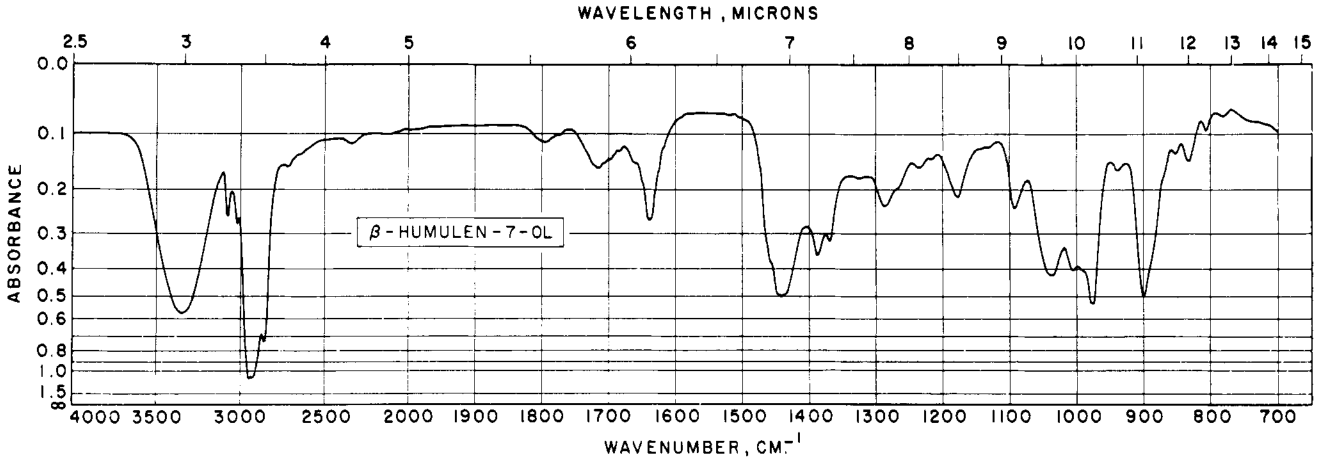

Figure 1.

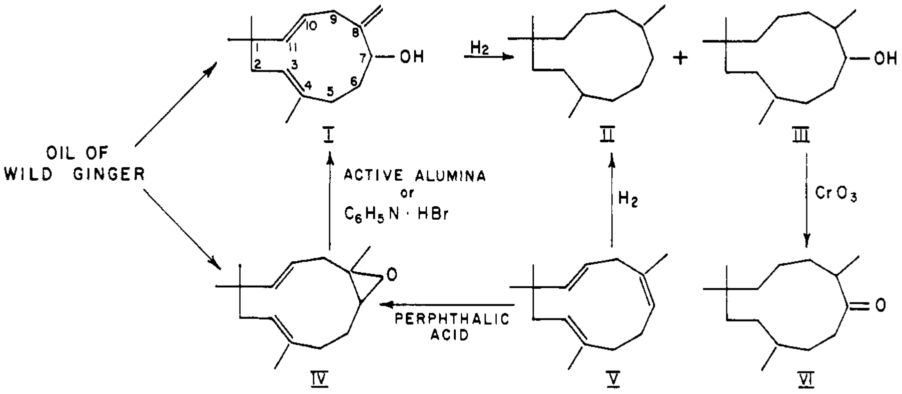

Fig. 2.—Isolation and reactions of β-Humulen-7-ol.

The alcohol isolated from the essential oil, known to contain levorotatory humulene monoxide,[5] was found to be strongly dextrorotatory. Hydrogenation of the compound obtained *via* isomerization of the epoxide with alumina (method 2) or with pyridinium bromide (method 3) yielded mixtures of isomeric β-humulan-7-ols exhibiting both gas chromatographic and infrared absorption characteristics identical with those shown by the hydrogenation product of the alcohol obtained *via* column chromatography of the essential oil (method 1). Chromic acid oxidation of the isomeric saturated alcohols formed by any of the three routes yielded, in turn, mixtures of 7-humulanones (VI) displaying identical properties also.

These data prove that the sesquiterpene alcohol possesses structure I and that it is formed by catalytic isomerization of α-humulene monoxide during chromatography of the essential oil of *Zingiber zerumbet* Smith on an alumina column.

Experimental

Apparatus and gas chromatographic procedures were previously described.[6]

Properties of Sesquiterpene Alcohol.—The compound, prepared by column chromatography of oil of wild ginger,[1] displayed the following properties: $n^{25}\text{D}$ 1.5135, $\alpha^{25}\text{D}$ +25.81° (1% solution in chloroform), and retention time of 29.5 min. (Reoplex 400 at 200°).

Anal. Calcd. for $C_{15}H_{24}O$: C, 81.75; H, 10.97. Found: C, 81.21[7]; H, 11.29.[7]

Hydrogenation of Sesquiterpene Alcohol to Humulane and β-Humulan-7-ols.—A sample of the alcohol (355.5 mg.) was dissolved in glacial acetic acid and, following addition of 25 mg. of Adams catalyst, reduced with hydrogen at 25° and 765-mm. pressure. Hydrogen uptake of 99 ml. was equivalent to 2.9 double bonds. The reaction product (310.5 mg.), isolated in the usual manner, was chromatographed over 6 g. of neutral, grade I alumina.

Fraction 1, petroleum ether eluate (11.5 mg.), was subjected to gas chromatographic analysis through a 20% SAIB column operated at 170°. Its major component, emerging after 14.0 min. (shoulder at ascending portion of gas chromatographic peak), was isolated by preparative g.l.c. over a 10% silicone nitrile column operated at 145°. Retention time was 17.2 min.; infrared absorption spectrum was identical with that of pure humulane examined similarly.

Fraction 2, diethyl ether eluate (270 mg.), was found to be a mixture of two saturated alcohols, emerging after 19.8 (33%) and 23.4 min. (67%) (Reoplex 400 at 200°).

Oxidation of Saturated Alcohols to Ketones.—The mixture of saturated alcohols (261 mg.) was dissolved in 3.8 ml. of pyridine and added to a solution of 230 mg. of chromium trioxide in 2.3 ml. of pyridine. After standing at room temperature for 48 hr., it was diluted with distilled water and extracted with ether, the combined extracts being washed repeatedly with dilute sulfuric acid and distilled water. The ethereal solution was dried over sodium sulfate and the solvent was evaporated; the yield was 221 mg.

Gas chromatographic analysis (Reoplex 400 at 170°) showed that the product was largely composed of two saturated ketones (VI) emerging after 30.4 (30%, $n^{25}\text{D}$ 1.4729) and 32.6 min. (70%, $n^{25}\text{D}$ 1.4735). Their infrared spectra displayed intense carbonyl stretching vibration at 1704 cm.$^{-1}$, characteristic of medium-

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(6) I. C. Nigam and L. Levi, *Can. J. Chem.*, **40**, 2083 (1962).

(7) Microanalyses were performed by Drs. G. Weiler and F. B. Strauss, Oxford, England.

sized saturated cyclic ketones, and resembled closely throughout all other regions indicating the similarity of gross structures.

Hydrogenation of α-Humulene to Humulane.—α-Humulene (87 mg.), b.p. 97–98 (3 mm.), $[\alpha]^{25}\mathrm{D}$ $-0.4°$, $n^{25}\mathrm{D}$ 1.4988, was hydrogenated at atmospheric pressure and room temperature in glacial acetic acid by means of Adams catalyst. Hydrogen uptake was 99.1%, theoretical; product yield was 73 mg. Gas chromatographic examination of the isolate (SAIB 20%, temperature 170°) showed that its major constituent emerged after 14.0 min. (shoulder at ascending portion of gas chromatographic peak). Following isolation by preparative g.l.c. (silicone nitrile 10%, temperature 145°), its infrared absorption spectrum was determined. Characteristic bands were observed at 1372, 1360, 1305, 1287, 1251, 1233, 1147, 1105, 1064, 1012, 970, 943, 908, 895, 820, 785, 765, 743, and 725 cm.$^{-1}$.

Preparation of Humulene Monoxide.—α-Humulene (506 mg.) was allowed to react with perphthalic acid (451 mg.) in ether solution at 5° for 72 hr. Conventional processing of the reaction mixture yielded 533 mg. of crude product from which a pure specimen of humulene monoxide (421 mg.) was obtained by column chromatography over neutral, grade III alumina (12 g.). Its infrared absorption spectrum was identical with that published previously.[5,8]

Isomerization of Humulene Monoxide to β-Humulen-7-ol. A. Cleavage of Epoxide Ring by Active Alumina.—α-Humulene monoxide (120 mg.), dissolved in 1 ml. of petroleum ether, was transferred to a column of neutral, grade I alumina (6 g.) and eluted with ether. The first 2 ml. of eluate containing unchanged epoxide only was discarded, and the sesquiterpene alcohol (105 mg.) was recovered from 25 ml. of eluate collected subsequently. No isomerization was observed when the epoxide was chromatographed over grade II alumina.

B. Cleavage of Epoxide by Pyridinium Bromide.—α-Humulene monoxide (271 mg.) was refluxed for 1 hr. with pyridinium bromide (510 mg.) in 10 ml. of pyridine. Following removal of solvent under reduced pressure the residual oil was diluted with ether. Unreacted pyridinium bromide was filtered off, the filtrate was concentrated in a gentle stream of nitrogen, and the recovered product (262 mg.) was chromatographed over 13 g. of neutral, grade II alumina. Elution with petroleum ether removed unchanged epoxide while elution with diethyl ether permitted recovery of the sesquiterpene alcohol (155 mg.).

Gas chromatographic and infrared analyses proved that the same product was obtained by either method and that the compound formed was, moreover, also identical with that isolated by column chromatography from oil of wild ginger.

Conversion of Sesquiterpene Alcohol to Isomeric 7-Humulanones.—The alcohol obtained by each of the three methods described was hydrogenated with Adams catalyst in glacial acetic acid solution; product yields were 94–96%; retention time of main component generated was 23.4 min.

Each of the three saturated alcohols was in turn oxidized with chromium trioxide in accordance with the procedure reported. Conventional processing of each of the three reaction mixtures led to recovery of 80–88% of product whose two major constituents were separated by gas chromatography. Retention times of these constituents (Reoplex 400 at 170°) were, in each case, 30.4 and 32.6 min., respectively.

Preparation of Semicarbazone of *cis*-7-Humulanone.—The mixture of isomeric humulanones (160 mg.) obtained from a sample of β-humulen-7-ol, isolated in turn *via* column chromatography of oil of wild ginger, was reacted with semicarbazide hydrochloride (80 mg.) in pyridine and the reaction product was fractionally recrystallized from acetone. This product had m.p. 190–191°.

Anal. Calcd. for $C_{16}H_{31}N_3O$: N, 14.93. Found: N, 14.93.[9]

The derivative was decomposed with oxalic acid (4 ml. of 5% aqueous solution). Gas chromatographic examination of the reaction product confirmed its purity. *cis*-7-Humulanone only was being generated. The *trans* isomer failed to yield a crystalline semicarbazone under the experimental conditions.

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[9] Microanalyses were performed by Dr. K. W. Zimmermann, Commonwealth Scientific and Industrial Research Organization, University of Melbourne, Victoria, Australia.

1-Methoxy- and 1-Ethoxyazulene[1]

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In 1951 Treibs and Stein[2] claimed the preparation of 1-methoxy- (**1**) and 1-ethoxyazulene (**2**). Their synthetic method involved the ring expansion of the corresponding 1-alkoxyindane with ethyl diazoacetate, followed by hydrolysis, decarboxylation, and dehydrogenation to the 1-alkoxyazulene. After a rather complicated purification procedure they reportedly isolated the 1-azulyl ethers as crystalline solids in the form of blue needles, and reported melting points of 72° for **1** and 81° for **2**. No yield data were given. They also reported that both **1** and **2** had virtually the same visible spectrum as azulene itself, with the principal absorption maximum for each occurring at 581 mμ.

The visible spectra reported by Treibs and Stein for **1** and **2** are quite surprising and, in consideration of the spectra of similar compounds, rather unlikely. One would expect a good electron-donating group such as an alkoxy group to effect a bathochromic shift[3] when substituted in the 1-position. The related 1-benzoyloxy group is reported to cause a shift of +28 mμ.[4b] The alkoxy group which can release electrons better by resonance would be expected to cause an even greater bathochromic shift. Further, it has been observed[5] that the visible spectral shift caused by a given group in the 5-position is in the same direction, but generally of lesser magnitude, than the shift caused by the same group in the 1-position. Since the shift due to a 5-methoxy group is +35 mμ,[6] one would expect a greater bathochromic shift for a 1-methoxy group.

Reid and co-workers[6] attempted to reproduce the work of Treibs and Stein, but were unsuccessful. They obtained only unsubstituted azulene from their experiments.

We wish to describe the synthesis and characterization of 1-methoxyazulene (**1**) and 1-ethoxyazulene (**2**).

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[1] Supported in part by a grant (GP-250) from the National Science Foundation.

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