

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.), $[\alpha]_D^{25} -0.4^\circ$, $n_D^{25} 1.4988$, 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-Humulanes.—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-Humulane.—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 $\text{C}_{16}\text{H}_{31}\text{N}_3\text{O}$: 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-Humulane only was being generated. The *trans* isomer failed to yield a crystalline semicarbazone under the experimental conditions.

Acknowledgment.—The authors are indebted to Mr. P. B. Kurup, Managing Director, Techno Chemi-

(8) J. Pliřa, M. Horák, V. Herout, and F. Šorm, "Die Terpene. Sammlung der Spektren und Physikalischen Konstanten," Teil I; "Sesquiterpene," Akademie-Verlag, Berlin, 1960.

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

cal Industries, Ltd., Kozhikode, Calicut, India, for a genuine specimen of oil of wild ginger and to Dr. S. C. Bhattacharyya, National Chemical Laboratory, Poona, India, for authenticated samples of α -humulene and *l*-humulene monoxide derived from this oil. They wish to express their appreciation also to Dr. L. T. Capell, Nomenclature Director and Executive Consultant, Chemical Abstract Service, Ohio State University, Columbus, Ohio, for helpful discussions regarding the naming of humulene compounds

1-Methoxy- and 1-Ethoxyazulene¹

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In 1951 Treibs and Stein² 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 $\text{m}\mu$.

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 shift³ when substituted in the 1-position. The related 1-benzoyloxy group is reported to cause a shift of +28 $\text{m}\mu$.^{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 observed⁵ 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 $\text{m}\mu$,⁶ one would expect a greater bathochromic shift for a 1-methoxy group.

Reid and co-workers⁶ 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).

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

(2) W. Treibs and A. Stein, *Ann.*, **572**, 161 (1951).

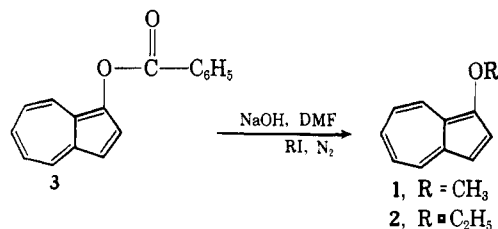
(3) A. G. Anderson, Jr., and B. M. Steckler, *J. Am. Chem. Soc.*, **81**, 4941 (1959), and references therein.

(4) (a) A. G. Anderson, Jr., and G. M.-C. Chang, *J. Org. Chem.*, **23**, 151 (1958); (b) L. L. Replogle, Ph.D. Thesis, University of Washington, 1960.

(5) A. G. Anderson, Jr., and L. L. Replogle, *J. Org. Chem.*, **28**, 2578 (1963).

(6) D. H. Reid, W. H. Stafford, and J. P. Ward, *J. Chem. Soc.*, 1100 (1958).

These ethers are conveniently prepared by the basic cleavage of 1-azulyl benzoate⁴ (**3**) in *N,N*-dimethylformamide (DMF) in the presence of methyl or ethyl iodide (nitrogen atmosphere). 1-Methoxyazulene (**1**) was obtained in 81% yield as a green oil that crystallized when it was cooled and scratched, m.p. 26–28°.



A slightly lower yield (69%) of **1** was obtained when the reaction was carried out without a nitrogen atmosphere. The ethyl ether, **2**, was obtained in good yield (80%) as a green oil that would not crystallize. The spectra of **1** and **2** are nearly identical. As anticipated, their visible spectra show a strong bathochromic shift from that of azulene, with the principal maxima appearing at 684 and 686 $m\mu$ for **1** and **2** respectively.

The n.m.r. spectra of **1** and **2** show the characteristic patterns for a 1-substituted azulene⁷ and for the particular alkoxy group. Thus the spectrum of **1** shows a sharp singlet (relative intensity of three) due to the methoxy group at τ 6.05, while the spectrum of **2** shows the characteristic splitting pattern for an ethyl group with the methylene quartet appearing at τ 5.80, and the methyl triplet at τ 8.53.⁸

The ester **3** is quite susceptible to basic cleavage as shown by the mild conditions, room temperature, and weakly alkaline (*ca.* 0.16 *N*) solution employed. Also an immediate color change was observed when the methanolic sodium hydroxide solution was added to the DMF solution of the ester and alkyl iodide. If methanol was used as the solvent in the preparation of **1**, only small amounts of the product could be isolated, and extensive decomposition occurred. Attempts to isolate the unknown 1-azulol were unsuccessful, and only resinous material was obtained.

The question of the identity of the products isolated by Treibs and Stein² still remains. One might postulate that a rearrangement occurred and they isolated the isomeric 2-methoxyazulene. However, this cannot be so since Nozoe, *et al.*⁹ have prepared 2-methoxyazulene, and its properties do not correspond with those of the "methoxyazulene" reported by the German workers. It seems likely that Treibs and Stein did not have a methoxyazulene at all since the reported properties do not correspond with those of the known 1-methoxy, 2-methoxy, 4-methoxy,⁶ or 5-methoxyazulene,⁶ and a 6-methoxy group is reported¹⁰ to cause a spectral shift of $-43 m\mu$ in the visible spectrum.

Experimental¹¹

1-Methoxyazulene (1).—To a stirred solution containing 50 mg. (0.20 mmole) of 1-azulyl benzoate,⁴ 10 ml. of *N,N*-dimethylformamide, and 1.0 ml. of methyl iodide was added 1.0 ml. of a 1.9 *N* methanolic sodium hydroxide solution (nitrogen atmosphere).

(7) A. G. Anderson, Jr., and L. L. Replogle, unpublished data.

(8) *Cf.* Experimental for a more complete analysis.

(9) T. Nozoe, S. Seto, and S. Matsumura, *Bull. Chem. Soc. Japan*, **35**, 1990 (1962).

(10) K. Hafner and H. Kaiser, *Ann.*, **618**, 140 (1958).

Upon addition of the base, the solution changed from blue to bluish green in color. The reaction mixture was stirred at room temperature for 5 hr., and ether was added. The blue-green ethereal solution was washed with several portions of water, then with saturated salt solution, and dried over sodium sulfate. Removal of solvent left a green oil which was chromatographed over acid-washed alumina (Merck). The large, blue band was eluted with a 3:1 petroleum ether–dichloromethane mixture. Dichloromethane eluted a faint purple band, and ether eluted a small yellow band. Removal of solvent from the blue eluate left 25.5 mg. (81%) of a green oil that crystallized when cooled and scratched, m.p. 26–28°. A cyclohexane solution showed λ_{max} in $m\mu$ in the ultraviolet ($\log \epsilon$) at 236 (4.15), 285 (4.71), 341 (3.46), 350 (3.54), 358 (3.76), 367 (3.48), 376 (3.79), and in the visible (ϵ) with a shoulder at 632 (249), 661 (291), 684 (317), 725 (274), 815 (117), and 863 (104).

The n.m.r. spectrum of a carbon tetrachloride solution of **1** showed a pair of doublets ($J \approx 9$ c.p.s.) of unit intensity at τ 1.89 and 2.12 which were assigned to the 4- and 8-protons. Two other doublets ($J \approx 3.5$ c.p.s.) were observed at τ 2.76 and 2.99 and were assigned to the 2- and 3-protons, respectively. The methoxyl group resonance appeared as a sharp singlet of three times unit intensity at τ 6.05. The rest of the spectrum, including the integrated intensities, was consistent with a 1-substituted azulene.⁷

Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{O}$: C, 83.51; H, 6.38. Found: C, 83.53; H, 6.32.

1-Ethoxyazulene (2).—A 1.9 *N* methanolic sodium hydroxide solution (1 ml.) was added dropwise, over a period of 20 min., to a stirred solution containing 50 mg. (0.20 mmole) of 1-azulyl benzoate,⁴ 1.0 ml. of ethyl iodide, and 10 ml. of *N,N*-dimethylformamide (nitrogen atmosphere). The bluish green reaction mixture was stirred for another 50 min. and then poured into water. The aqueous mixture was extracted with petroleum ether, and the green organic phase was washed well with water and dried over sodium sulfate. Removal of solvent left a green oil which was chromatographed over acid-washed alumina (Merck). The large blue band was eluted with dichloromethane. The residue from the blue eluate was rechromatographed, and the single blue band eluted with a 3:1 petroleum ether–dichloromethane mixture. Removal of solvent from the blue eluate left 27.5 mg. (80%) of a green oil that would not crystallize when cooled and scratched. A cyclohexane solution showed λ_{max} in $m\mu$ in the ultraviolet ($\log \epsilon$) at 236 (4.16), 286 (4.72), 343 (3.47), 351 (3.55), 359 (3.75), 368 (3.49), and 378 (3.77), and in the visible (ϵ) with a shoulder at 637 (254), 662 (293), 686 (319), 725 (272), 765 (258), 814 (116), and 867 (97).

The n.m.r. spectrum of **2** showed the same aromatic proton spectrum as **1**, and the characteristic splitting pattern of an ethyl group with the quartet at τ 5.80 and a triplet at τ 8.53, due to the methylene protons and methyl protons, respectively.

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}$: C, 83.68; H, 7.03. Found: C, 83.97; H, 7.14.

(11) The melting point was taken on a Fisher-Johns apparatus and is uncorrected. Ultraviolet and visible absorption spectra were taken on a Cary Model 14 spectrophotometer. N.m.r. spectra were determined on carbon tetrachloride solutions, containing internal tetramethylsilane as a marker, using a Varian A-60. Microanalyses were performed by Dr. A. Bernhardt, Max Planck Institute, Mulheim, Germany.

The Rate-Determining Step for the Reaction of Acridine N-Oxide with Acetic Anhydride^{1a}

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In a recent paper from this laboratory, it was shown that the rearrangement of acridine N-oxide with excess acetic anhydride to form acridone proceeded *via* an

(1) (a) Rearrangement of Aromatic N-Oxides. III. (b) Based on the Honors Thesis of C. G. Carson, III, 1964.