

## EXPERIMENTAL

All melting points were taken in open capillaries and are uncorrected.

**Determination of the Number of Oxygen Atoms Needed for a Known Weight of the Organic Substance (10).**—The organic substance (0.2 Gm.) was added to a known volume of perbenzoic acid in chloroform with known normality. The mixture was left for 6 hr. in a dark place with occasional shaking. Five milliliters of 10% KI solution as well as 2 drops of concentrated H<sub>2</sub>SO<sub>4</sub> were added to the mixture. The liberated iodine was then titrated against sodium thiosulfate (0.1 N).

**With N-Methylpyrrole (I)**—The determination showed two oxygen atoms to be involved in the reaction.

**N-Methyl Succinimide (II)**—*N*-Methylpyrrole (2.0 Gm.) was added to 190 ml. 0.54 N perbenzoic acid in chloroform. The reaction mixture was left in a dark place for 12 hr. Then it was neutralized by sodium bicarbonate solution. The chloroform layer was then isolated, washed with water several times, dried over calcium chloride, and finally evaporated.

Two and one half grams of *N*-methylsuccinimide was left. Yield 92%. Crystallization from acetone as white needles gave m.p. 67–68°. [Lit. m.p. 66° (11).]

*Anal.*—Calcd. for C<sub>5</sub>H<sub>7</sub>NO<sub>2</sub>: C, 53.09; H, 6.29; N, 12.30; O, 28.31. Found: C, 53.00; H, 6.18; N, 12.30; O, 28.30.

**With N-Methyl-3-pyrroline (III)**—The determination showed that one oxygen atom was involved with each mole of the compound.

**N-Methyl- $\alpha$ -pyrrolidone (IV)**—*N*-Methyl-3-pyrroline (2.0 Gm.) was added to 120 ml. of perbenzoic acid in chloroform 0.4 N (one oxygen atom). The whole mixture was left for 3 hr. in a dark place at room temperature, then neutralized by sodium bicarbonate solution. The chloroform layer was then isolated, washed with water, dried over calcium chloride, and evaporated.

A 1.9-Gm. (79.1%) quantity of *N*-methyl- $\alpha$ -pyrrolidone was collected as a colorless oil, b.p. 201°/740 mm. [Lit. 202°/760 mm. (12).]

*Anal.*—Calcd. for C<sub>5</sub>H<sub>9</sub>NO.HCl: C, 44.40; H, 7.40; N, 10.36; O, 11.84. Found: C, 44.38; H, 6.99; N, 10.30; O, 11.81.

**With N-Methylindoline (V)**—The determination showed one oxygen atom was consumed in the reaction.

***o*-Dimethylaminobenzaldehyde (VI)**—*N*-Methylindoline (2.0 Gm.) was added to 104 ml. 0.29 N perbenzoic acid in chloroform (one oxygen atom). The reaction mixture was left at room temperature in a dark place for 24 hr. with occasional shaking, then neutralized by solution of sodium bicarbonate. The chloroform layer was then separated, washed with water several times, dried over calcium chloride, and finally evaporated.

A 1.8-Gm. (81%) quantity of *o*-dimethylaminobenzaldehyde was collected at 141/30 mm. as yellow oil. [Lit. 142°/30 mm. (13).]

*Anal.*—Calcd. for C<sub>9</sub>H<sub>13</sub>N<sub>2</sub>O: C, 60.10; H, 6.66; N, 15.55. Found: C, 59.87; H, 6.29; N, 15.49.

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Isolation of Matricin from *Artemisia caruthii*

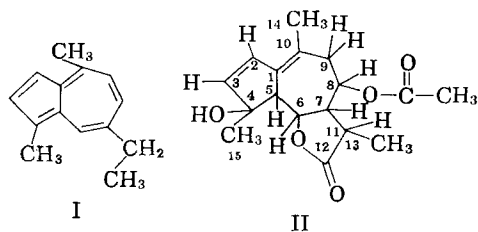
By JEFFREY C. SPITZER and CORNELIUS STEELINK

The sesquiterpene lactone, matricin, has been isolated from *Artemisia caruthii* and is shown to be the precursor of chamazulene, previously reported in the steam distillate of this species.

THE COMMON SAGE brush *Artemisia caruthii* Wood, var. *Wrightii* (A. Gray), yields a blue oil upon steam distillation or upon simple brewing as a "folk" tea. The oil has been identified (1) as chamazulene (I). Because of the occasional use of the plant as a folk medicine by the Indians of Northern Arizona, and because of the wide distribution of sesquiterpene lactones in the *Artemisia* species, the authors were prompted to investigate

the sesquiterpene lactone precursors of chamazulene (pro-chamazulenogens) in this species.

The isolation and characterization of matricin (II) in *A. caruthii* is reported. This compound exists in low concentrations in the plant, and is readily converted to chamazulene (I) by simple



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steam distillation or by heating in the presence of

dilute mineral acid. Matricin is concentrated in the bitter leaves of the plant and exhibits its maximum concentration during July. By September, it is almost undetectable in the plant. It has been previously found only in *Matricaria chamomilla* (2); this is the first report of its occurrence in the *Artemisia* species.

#### EXPERIMENTAL

Dried ground leaves of *A. caruthii* (collected from the Graham Mountain region of Arizona at elevations above 6000 ft.) were soaked in chloroform overnight. The green slurry was filtered, evaporated to dryness, and taken up in 100 ml. of 95% ethanol. The addition of 300 ml. of water precipitated a tar. The supernatant liquid was filtered through a mat of diatomaceous earth<sup>1</sup> and activated carbon.<sup>2</sup> The filtrate was then shaken with chloroform, and the chloroform layer concentrated to a gum (yield, 1.1%). Preparative thin-layer chromatography (1 mm. thick Silica Gel G; solvent: 90:1 chloroform-methanol) proved to be the most efficient method for separating the pro-chamazulenogen from other lactonic materials. Methanol elution of the band at  $R_f$  0.22 from a number of TLC plates yielded enough tan colored material for characterization.

The following physical constants were entirely consistent with structure II and with a sample of authentic matricin,<sup>3</sup> m.p. 152–156°.  $[\alpha]_D^{20} -122^\circ$  (CHCl<sub>3</sub>);  $\lambda_{max}$ . 242 m $\mu$  ( $\epsilon$ , 11,200);  $\nu$ , 3600 cm.<sup>-1</sup> (OH), 1780 cm.<sup>-1</sup> ( $\gamma$ -lactone), 1747 cm.<sup>-1</sup> (acetoxy). The NMR assignments are shown in Table I. Although the evidence is not unequivocal, one would deduce from the NMR data that 5, 6, and 7 protons are all *trans*.

In addition to the above evidence, co-chromatography of the pro-chamazulenogen and authentic matricin in four different solvent systems showed no differences. Matricin polymerizes readily on exposure to light or upon moderate heating; this creates some problems in handling.

Since the original interest in the plant was motivated by reports of its use as a folk medicine,

TABLE I—NMR ASSIGNMENTS

p.p.m. <sup>a</sup>	Multi- plicity	Assignment	No. Protons
1.36	2	C-13 }	6
1.43	1	C-14 }	
1.90	1	C-15 }	
2.14	1	OAc }	
2.0–3.3	...	C-5,7,9,11, —OH	11 or 12
4.12	3	C-6	
4.9	...	C-8	1
5.94	2	C-3	1
6.33	2	C-2	1

<sup>a</sup> Relative to tetramethylsilane.

the authors submitted certain fractions for physiological analysis. The chloroform extract (matricin-rich) exhibited minor depressant activity with cats.<sup>4</sup> Chamazulene, whose precursor is matricin, showed some antispasmodic activity. It also produced urination and emesis in cats, when given intraperitoneally.

#### CONCLUSION

The labile sesquiterpene matricin (II) has been found to be the precursor of the blue oil, chamazulene (I), in *A. caruthii*. This is the first report of the occurrence of matricin (II) in an *Artemisia* species; the taxonomic implication of this type of lactone in plants is discussed elsewhere (3). The activity of I as an emetic is interesting. The Navajo and Hopi Indians use *A. caruthii* as an emetic in cleansing ceremonies (4). Although chamazulene (I) does not exist in the plant as such, it can be obtained from matricin (II) by the simple steam distillation or tea-brewing process. The conversion of II to I is not only a remarkable example of dehydration and dehydrogenation, but is also the basis of an effective folk medicine.

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<sup>1</sup> Marketed as Celite by the Johns-Manville Corp., New York, N. Y.

<sup>2</sup> Marketed as Nuchar by Braun Chemical Co.

<sup>3</sup> The authors are indebted to Professor Z. Cekan, Czechoslovak Academy of Science, for this sample of matricin.

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