Chamazulene from *Artemesia caruthii*

Sir:

In a recent survey of terpene-bearing plants of the Sonoran desert, it was reported (1) that the steam distillate of common sagebrush (*Artemesia caruthii* Wood var. *wrightii* A. Gray) contained a blue oil. Because of the widespread interest (2*a*, 2*b*) in the azulenes of the Compositae family, and in particular the Artemesia species, we undertook to identify the blue component of this oil. It has now been characterized as chamazulene (1,4-dimethyl-7-ethylazulene).

Stems, leaves, and flowers of *A. caruthii* were collected in August 1961 at elevations above 6000 ft. in the Graham Mountains of Arizona. The wet plant material was steam distilled; the blue distillate was taken up in petroleum ether and extracted into 85% phosphoric acid. The concentrated acid solution was diluted with water, regenerating the blue oil, which was then partitioned into petroleum ether again. After being dried over magnesium sulfate, the petroleum ether solution was evaporated to dryness under vacuum. A viscous blue oil remained; from 1.0 Kg. of wet plant material, 0.50 Gm. of azulenic compound was obtained.

After further purification by chromatography over alumina, the oil was converted to a trinitrobenzene addition compound; m.p. 130.5–131.0°, uncor. [Lit. (3), 132° for chamazulene TNB compound].

Anal.—Calcd. for $C_{14}H_{16}.C_6H_3(NO_2)_3$: C, 60.45; H, 4.82. Found: C, 60.35; H, 4.77.

The ultraviolet, visible, and infrared spectra were identical to the reported values (4) for chamazulene. As might be expected, these spectra were almost superimposable on those of an authentic sample of guaiazulene (1,4-dimethyl-7-isopropylazulene) measured in this laboratory. However, the critical data for the guaiazulene TNB compound [m.p. 151–152° (4); anal. calcd.: C, 61.31; H, 5.15] clearly differentiate it from the chamazulene compound.

Only a few plant species yield chamazulene on simple steam distillation. One of these is *Artemesia absynthium* (5). The precursors of this blue oil have been shown to be a group of closely-related sesquiterpene lactones (5). Because of the recent scientific interest in these sesquiterpene compounds, as well as local interest in the medicine and taxonomy of the Artemesia species in southwestern United States, we are now engaged in isolating and characterizing the lactones of *A. caruthii*.

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Screening Antifatigue Agents by Radiorespirometry

Sir:

Over the past 5 years a number of publications have appeared on the use of the potassium and magnesium salts of aspartic acid in the treatment of human fatigue (1–3). To measure the effect of various agents on fatigue in animals, the rat swim test has been found useful (4). Ideally, the mechanisms whereby these substances modify the energy-yielding processes in fatigue should be studied in the exercising animal. However, the many technical difficulties this would present led us to develop instead the following assay based on the utilization of glucose, a primary source of energy, during recovery from fatigue.

Male white rats, weighing 280 to 350 Gm. were burdened with lead amounting to 3% of their body weight and permitted to swim in tanks containing 18 inches of water at 28° until no longer able to surface.

Prior treatment consisted of 30 mg. per Kg. oral doses, beginning with a single dose 2 days before the experiment, two doses on the day before, and one or two on the day of the experiment, depending on whether the animal was to be used in the morning or afternoon, respectively. The last dose was given immediately before the animal was placed in the tank. Upon removal