

A CHEMICAL INVESTIGATION OF SOME FLORIDA VOLATILE OILS.\*<sup>1</sup>BY P. A. FOOTE<sup>2</sup> AND A. W. MATTHEWS.<sup>3</sup>

Early in the Fall of 1936 B. W. Calvert, a farmer near Orlando, sent to the School of Pharmacy of the University of Florida samples of several volatile oils, four of which are herewith reported upon. Specimens of the plants were also received and were identified by Erdman West, botanist at the Experiment Station. The oils were submitted to Fritzsche Brothers, Inc., of New York, who examined them for commercial possibilities. Their report was negative. However, it seemed advisable as a matter of scientific interest, to report on the properties of these oils. The small quantities at hand prevented a thorough investigation; nevertheless the facts as observed will no doubt be of interest to future workers. The oils were produced by steam distillation. All samples were kept in well-stoppered containers, protected from light for two years. Standard methods of examination were usually used. At times the use of dry ice and of semi-micro methods were of great advantage in making and separating derivatives.

## OIL OF PYCNOTHYMUS RIGIDUS (BART.) FAM. LAMIACEÆ.

This small shrub is common in southern Florida (1). The literature failed to reveal any previous work on this oil. The 20-cc. sample was greenish yellow in color and possessed a strong mint-like odor and taste. The following constants were found:

$d_{15}^{20}$  0.9323;  $\alpha_D$  -4.14°;  $n_D^{20}$  1.4681; A. V. 1.75; E. V. 135.51; E. V. after acetylation 272.17; boiling range 160-220° C., with the greater portion distilling over at 214-215° C. Tests for nitrogen, sulfur, phenols and aldehydes were negative.

*Alcohols*.—A 3.5-cc. portion of the oil (from a 5-cc. sample), which boiled between 207-220° C.,  $n_D^{20}$  1.4668, failed to yield a crystalline phenylurethane or a hydrogen phthalate ester that could be crystallized. Its odor and properties were indicative of thujyl alcohol but lack of material hindered definite proof. Assuming a composition of  $C_{10}H_{18}O$ , the ester values, before and after acetylation, calculate out to the equivalent of 47.02% free alcohol and 47.23% acetate.

*Ketones*.—A 3.5-cc. sample of the original oil yielded a sodium bisulfite addition product, which required forty-eight hours for separation. After filtration and washing it was regenerated by treatment with sodium carbonate and steam distillation. It possessed an odor similar to pulegone and gave an oxime, m. p. 115-117° C., very close to that reported for this ketone. Further purification might have raised the melting point but the quantity was too small.

## OIL OF SOLIDAGO RIGIDA LINNÉ, FAM. COMPOSITÆ.

According to Small (1) this herb is found in swampy woodlands and thickets and is fairly widely distributed in North America. Several oils of the genus *Solidago* have been reported in the literature, including those of *S. rugosa* (3), (4); *S. canadensis* (5), (6); *S. nemoralis* (7), (8); and *S. odora* (4), which was official in the United States Pharmacopœia from 1820 to 1870. The oil of *S. rigida* seems to have escaped previous attention. Among the constituents which have been found in these oils are  $\alpha$ -pinene, phellandrene, dipentene, limonene, borneol, bornyl acetate and methylchavicol.

The 26-cc. sample was almost water-white in appearance and both odor and taste were somewhat reminiscent of oil of pine. The following constants were found:  $d_{15}^{20}$  0.8500;  $\alpha_D$  +38.15°;  $n_D^{20}$  1.4798; A. V. 0.39; E. V. 8.68; E. V. after acetylation 160.15. The main bulk of the oil distilled over at 165° C., less than 0.5 cc. of higher boiling material remaining from a 3-cc. sample. Tests for nitrogen, sulfur, phenols, aldehydes and ketones were negative.

\* Presented before the Scientific Section, A. PH. A., Atlanta meeting, 1939.

<sup>1</sup> Abstract of a portion of a thesis to be submitted to the Graduate Council of the University of Florida in partial fulfilment of the requirement for the degree of Doctor of Philosophy.

<sup>2</sup> Professor of Pharmacy, University of Florida.

<sup>3</sup> Associate Professor of Pharmacy, University of Alberta.

*Alcohols.*—The above-mentioned higher boiling-point residue gave a phenylurethane, m. p. 136–140° C., which was not available in sufficient quantity for recrystallization. This was believed to be bornyl phenylurethane, m. p. 138–139° C. (2). The odor of the oil was also suggestive of borneol. However, the low density and boiling range do not support a high borneol content and, since an ester value after acetylation of 160.15 was observed, the presence in the oil of some other alcohol in addition to borneol is suggested.

*Terpene Fraction.*—The 2.5-cc. fraction boiling at, or below, 165° C.,  $n_{D}^{20}$  1.4820, gave a nitrosochloride somewhat resembling  $\alpha$ -pinene nitrosochloride in appearance but the presence of other terpenes or substances hindered crystallization of a characteristic nitrol piperidine. Thus positive identification was not established. The refractive index of this fraction was considerably higher than would be given by  $\alpha$ -pinene alone.

#### OIL OF ERIGERON CANADENSIS LINNÉ, COMPOSITÆ.

This plant, sometimes known as fleabane, horseweed or butterweed, has a wide distribution and is often found growing in mint fields. Upon distillation the fresh herb yields 0.33% to 0.66% of oil (2). Procter (9) attributes the introduction of erigeron oil into medical practice to the "eclectic" physicians. Various investigators in this country and in Germany and Russia have reported on the constants of this oil and their results show wide variation. Wallach (10) identified limonene as one of the constituents and Meissner (11) confirmed the presence of this substance in samples of oil from two different sources. Hunkel (12) established the presence of terpineol in a fraction boiling 205–206° C.

The 28-cc. sample of this oil was a light amber color and, at the time of examination, showed distinct evidence of resinification. The odor appeared to combine the characteristics of dill and lemon and the taste suggested caraway. The following constants were found:  $d_{15}^{20}$  0.8642;  $\alpha_D$  +71.70°;  $n_{D}^{20}$  1.4809; A. V. 1.94; E. V. 17.12; E. V. after acetylation 75.05 (method of V. Boulez (13)). All these with the exception of the ester value are within the reported limits for erigeron oil, the reported ester values ranging from 39.09 to 70.9. With a 5-cc. sample, less than 1 cc. distilled over at about 145° C., while about 3 cc. passed over in the region of 170° C., leaving a dark-brown residue of higher boiling material. Tests for nitrogen, sulfur and phenols were negative.

*Aldehydes.*—A positive aldehyde reaction was obtained both with Tollen's and Schiff's reagents and when tested by the method of Rodionow and Korolew (14). At least one investigator (11) has called attention to the likely presence of an aldehyde in oil of erigeron but no record could be found of the successful separation and identification of same. It is believed that the amount of aldehyde present in this case was very small and no addition product with bisulfite was separated. With semicarbazide a trace of a crystalline residue was obtained, which after one recrystallization was observed to melt at 149–152.5° C. (Fisher-Johns melting point apparatus). An odor suggestive of citral was noted in the saponification residues of this oil and it has been stated (2) that mixtures of the semicarbazones of citral *a* and citral *b* may show melting points between 139° and 170° C.

*Alcohols.*—Since terpineol had been reported (12) as a constituent of oil of erigeron, the ester value after acetylation was determined both by the classical method and by the method of V. Boulez (13), which is claimed to be superior to the former when tertiary alcohols are present. The Boulez method gave a significantly higher result, 75.05 as compared to 45.15 by the usual method. This former value is found to be equivalent to 16.82% terpineol and the observed ester value of 17.12% to 5.94% terpineol acetate. The high boiling-point residue (approximately 1 cc.) was not sufficiently pure to yield a crystalline terpineol nitrosochloride by the method of Wallach (10).

*Terpene Fractions.*—A crystalline nitrol piperidene, m. p. 92–93° C. was obtained from the 3-cc. portion which distilled over at 170–175° C. The melting point of  $\alpha$ -limonene nitrolpiperidine is given as 94° C. (2). The small fraction of lower boiling range may have been a mixture of limonene with some lower boiling terpene, since no characteristic piperidine base could be crystallized.

#### OIL OF HETEROTHECA SUBAXILLIARIS (LAM.), FAM. CARDUACEÆ.

This small herb inhabits pinelands, sand-dunes and waste places, various provinces Fla. to Tex., Ariz., Kans. and Del. (1). No reference could be found to previous investigation of the volatile oil from this source.

The 4-cc. sample possessed a yellow color and a strong pine-like odor. The following constants were found:  $d_{15}^{20}$  0.8877;  $n_p^{20}$  1.4931; A. V. 0.48; E. V. 26.13; E. V. after acetylation 160.91; boiling point (micro-method) about 200° C. Tests for nitrogen and sulfur were negative.

The odor and the approximate boiling point (200° C.) were suggestive of borneol. Calculating ester values obtained in terms of  $C_{10}H_{18}O$ , 9.15% combined and 42.28% free alcohol were found.

#### SUMMARY.

The physical and chemical constants of the following volatile oils have been reported on: Oil of *Pycnothymus rigidus*, Oil of *Solidago rigida*, Oil of *Erigeron canadensis*, Oil of *Heterotheca subaxillaris*. As far as quantities permitted, the principal constituents have been identified.

#### REFERENCES.

- (1) Small, J. K., Manual of the Southeastern Flora, New York (1933).
- (2) Gildemeister u. Hoffmann, Die Aetherischen Oele, III Aufl., Bd. 1., Miltitz (1928).
- (3) Oberhauser, W. P., *Am. J. Pharm.*, 65, 122 (1893).
- (4) Miller, E. R., and Moseley, J. M., *J. Am. Chem. Soc.*, 37, 1285 (1915).
- (5) Report of Schimmel & Co., page 57 (April 1894).
- (6) *Ibid.*, page 46 (April 1897).
- (7) *Ibid.*, page 63 (April–May 1906).
- (8) Miller, E. R., and Eskew, M. H., *J. Am. Chem. Soc.*, 36, 2538 (1914).
- (9) Procter, Wm., Jr., *Am. J. Pharm.*, 26, 502 (1854).
- (10) Wallach, O., *Liebig's Ann. Chem.*, 227, 292 (1885).
- (11) Meissner, F. W., *Am. J. Pharm.*, 65, 420 (1893).
- (12) Kremers, E., *Pharm. Rundsch. (N. Y.)*, 13, 137 (1895).
- (13) Boulez, V., *Bull. soc. chim. (iv)*, 1, 117 (1907)..
- (14) Rodionow, W. M., and Korolew, A. J., *Z. angew. Chem.*, Vol. 47 (1927); through *Quart. J. Pharm. Pharmacol.*, 3, 78 (1930).

#### CHEMOTHERAPEUTIC STUDIES IN THE AZOBENZENE SULFON-CHLORAMIDE SERIES. II. META AND PARA DERIVATIVES.\*<sup>1</sup>

BY SEYMOUR STERN AND ABRAHAM TAUB.<sup>2</sup>

In 1916 Dakin and co-workers (1), (2) investigated the mode of action of the alkali hypochlorites and concluded that their antiseptic action was due to their interaction with proteins and other amino compounds, resulting in the formation of substances containing chlorine linked to nitrogen. In their attempts to find related substances having greater practical utility, they investigated many compounds containing the chloramine group,  $=N-Cl$ . Their studies indicated that all substances containing this group showed some germicidal activity, that slight changes in this activity resulted from nuclear substitution of aromatic chloramines by halogen,

\* Presented before the Scientific Section, A. PH. A., Atlanta meeting, 1939.

<sup>1</sup> Abstracted in part from the dissertation submitted by Dr. Stern to the Graduate Faculty of Columbia University, College of Pharmacy, in partial fulfilment of the requirements for the degree of Doctor of Pharmacy.

<sup>2</sup> Associate Professor of Pharmaceutical Chemistry, Columbia University.