(aromatic), 3.8–4.2 (*O*-methyl or methylene), and 3.5–3.8 (*N*-methylene) p.p.m. with proper multiplicities.

3-(2-Aminoethyl)-5-methoxy-1,3-dimethylindole (Compound Ib)—A solution of 3-(2-aminoethyl)-5-methoxy-1,3-dimethyl-2-indolinone (5.5 g., 0.03 mole) in tetrahydrofuran (30 ml.) was added slowly to a suspension of lithium borohydride (0.04 mole) in tetrahydrofuran (25 ml.). The reaction mixture was refluxed with stirring overnight and then cooled to room temperature. A mixture of methanol–water (10:1) was added slowly to the mixture until effervescence ceased. The tetrahydrofuran was removed under reduced pressure, and the residue was extracted with ether. The ether extract was dried over magnesium sulfate and the ether evaporated. The crude oil was distilled to give the compound whose data are summarized in Table II.

SUMMARY

Sixteen 5-alkoxy-3-alkylamino-1,3-dimethyl-2-indolinones and indolines were prepared. These compounds were characterized with IR and NMR spectroscopy. Pharmacological testing is in progress.

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Comptonia asplenifolia: Low Boiling Components

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Abstract □ Room temperature, low pressure vacuum distillation of 920 g. of the fresh leaves from *Comptonia asplenifolia* Ait. typically yielded 3 mg. of methyl acetate, 1 mg. of ethyl acetate, 2 mg. of diisopropyl acetaldehyde acetal, and 5 mg. of cineol. Methyl acetate, ethyl acetate, and diisopropyl acetaldehyde acetal were not previously reported as components of the essential oil and are important contributors to the odor factors of the plant.

Keyphrases □ *Comptonia asplenifolia* Ait.—isolation and identification of low boiling components □ GLC—identification of low boiling components of *Comptonia asplenifolia*

Comptonia asplenifolia Ait.[1] was first investigated phytochemically by Braun (1) and later by de Nicola and Lynn (2). Using distillation techniques, these workers isolated 0.02–0.5% by weight of an oil from fresh or semidried leaves. Only cineol was identified. Other compounds such as lactones, terpenes, esters, and alcohols were suggested to be present. In a more recent study using GLC, this essential oil was shown to contain at least 32 identifiable terpenoids including cineol (3). This work utilized a cohobation still, which allowed isolation of high boiling components but precluded observation of volatile compounds and those that were heat or water sensitive. It was, therefore, of interest to isolate such low boiling components. Compounds determined would add to the chemotaxonomic information about *C. asplenifolia*[2].

Using a sequence of room temperature, low pressure vacuum distillation, ether extraction, and temperature-programmed GLC, small amounts of methyl acetate, ethyl acetate, diisopropyl acetaldehyde acetal, and cineol were isolated. The previously undetected methyl acetate and ethyl acetate are common, expected odor contributors. Diisopropyl acetaldehyde acetal, which was isolated in amounts comparable to about half that of the previously noted cineol (2, 3), appears to be another important odor contributor. This is the first report of this substance being isolated from natural

[1] This plant, a sweet-scented shrub common to the eastern United States, is alternatively designated *Myrica asplenifolia* Endl. or *Comptonia peregrina* L. Coult. and is colloquially named sweet fern. Identification of the plant material used in this study was made by Dr. Fred Barkley of Northeastern University, and a voucher specimen (Clagett and Dubinsky–1) has been deposited with Dr. Barkley, Curator, Husky Herbarium, Northeastern University, Boston, MA 02115

[2] *Comptonia asplenifolia* has been used for many years as a remedy for high blood pressure and as a sickroom air freshener by residents of Appalachia. Its essential oil is patented for use as a perfume fixative (4). The chemotaxonomic information may be useful for chemosystematic evaluations (3).

material. Its presence is somewhat surprising when it is considered that its acid-catalyzed hydrolytic lability[3] is about 13 times greater than that of acetal itself (6).

A preliminary phytochemical survey (by referenced methods) of an alcohol extract from the dried leaves remaining after water and volatile oils were removed indicated little or no sterol (7), alkaloid (8), or saponin matter (9). Tannins (10) and flavonoids (11) were suggested[4]. Separations and identifications of these components are being pursued in these laboratories[5].

EXPERIMENTAL[6]

GLC—Temperature-programmed and isothermal column GLC analyses were performed with a chromatograph[7] equipped with a thermal conductance detector block. All temperature-programmed runs were made at a 10°/min. temperature increase between 60° and the indicated temperature limit. All GLC analyses utilized an injector port temperature of 250° and a detector block temperature of 300°. The columns utilized were: Column 1, 25% Dow 710 silicone oil on 60–80-mesh Chromosorb P, acid washed [2.1-m. (7-ft.) × 0.63-cm. (0.25-in.) o.d. copper tubing]; Column 2, 20% Carbowax 20M on 60–80-mesh Chromosorb P, acid washed [3.04-m. (10-ft.) × 0.63-cm. (0.25-in.) o.d. stainless steel tubing]; Column 3, 13% Apiazon L grease on 60–80-mesh Chromosorb P, acid washed [1.8-m. (6-ft.) × 0.63-cm. (0.25-in.) o.d. copper tubing]; and Column 4, 4% SE-30 methyl silicone oil on 60–80-mesh Chromosorb P, acid washed [2.7-m. (9-ft.) × 0.63-cm. (0.25-in.) o.d. copper tubing]. Collections of GLC-purified material for comparison IR measurements were made using dry ice–acetone-cooled U-tubes.

Isolation of Low Boiling Fractions—Fresh *C. asplenifolia* leaves were packed in a 60 × 15-cm. i.d. cylindrical iron vessel. This was connected in turn to a dry ice-cooled 100 × 5-cm. i.d. tubular trap and 25-l./min. vacuum pump. The evacuated iron vessel was maintained at room temperature (approximately 25°) while the pump developed a pressure of 5–10 mm. Hg. Volatiles were frozen out in the trap over a 6-day period. At the end of this time the trap was warmed and the water–oil melt was collected. This mixture was extracted with ether. The ether solution was treated with anhydrous sodium bicarbonate. Ether solvent was removed using a rotary evaporator. In a typical experiment, fresh leaves (920 g.) yielded water (590 g.) and oil (0.12 g., 0.13% of fresh leaf weight). Analysis of the oil by temperature-programmed GLC (Column 1, limit 240°) indicated methyl acetate (0.003 g.), ethyl acetate (0.001 g.), and diisopropyl acetaldehyde acetal (0.002 g.) as the sole components eluted below 125°. At 150°, cineol (0.005 g.) was eluted among other higher boiling components. Positive identification of methyl acetate, ethyl acetate, and diisopropyl acetaldehyde acetal was made by comparing their IR spectra (GLC-collected samples) and programmed retention times (Column 1 and Column 2, limit 240°) with those of authentic samples[8]. Cineol was similarly identified by comparison of its IR spectra and retention times (programmed Column 1, limit 240°, and isothermal Column 3, 150°) with an authentic sample.

Synthesis of Diisopropyl Acetaldehyde Acetal—Diisopropyl acetaldehyde acetal was synthesized by a method analogous to that used for the preparation of the acetal (15). Freshly distilled acetaldehyde (44 g., 1 mole) was added to a mixture of isopropanol (116 g., 1.9 moles) and anhydrous calcium chloride (22 g., 0.2 mole). The vessel was stoppered, shaken, and allowed to stand at room temperature for 24 hr. The solution was decanted onto 0.3-cm. (0.125-in.) activated molecular sieves[9] and dried for an additional 24 hr. The molecular sieves were removed, and anhydrous ether (100 ml.) followed by sodium metal pellets (23 g., 1 mole) was added. After hydrogen evolution ceased, the solution was distilled and the 82–115° boiling fraction was collected. Redistillation yielded a fraction of boiling range 122–124°; yield 42.6 g. (34%); IR (CCl_4): 1390, 1334, 1140, 1085, and 1002 $cm.^{-1}$; NMR (CCl_4): 8.79 d, 8.88 d, 8.91 d (15), 6.16 broad h (2), and 5.29 q (1).

Anal.—Calc. for $C_8H_{16}O_2$: C, 65.71; H, 12.41. Found: C, 65.77; H, 12.20.

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[3] This hydrolytic lability, which results in acetaldehyde formation, probably explains the irritating nature of its concentrated vapors. In this study the ethereal solution obtained after ether extraction, when treated with 2,4-dinitrophenylhydrazine reagent (5), yielded a derivative which was shown to be identical with that of acetaldehyde by melting point (148–150°) and undepressed mixed melting point. Diisopropyl acetaldehyde acetal, when treated similarly, yielded a derivative identical with that of acetaldehyde and that from the natural oil, as shown by melting point and undepressed mixed melting point.

[4] The authors thank Dr. Robert Raffauf for these survey analyses.

[5] Column chromatography of the alcoholic extract, using Dupont nylon 6 on Celite solid phase (12), yielded at least 20 flavonoid substances. Preliminary paper chromatography/color tests indicated the presence of chalcones, isoflavones, flavonols, flavanonols, flavones, and flavanones (12–14).

[6] Fresh *C. asplenifolia* leaves were harvested in the vicinity of Boston, Mass. IR spectrophotometric determinations were made with a Perkin-Elmer model 21 instrument. Samples were dissolved in spectral grade carbon tetrachloride. NMR spectra were obtained using a Varian model T-60 spectrometer. Samples were dissolved in spectral grade carbon tetrachloride, with 1% tetramethylsilane as the internal reference. Melting points were taken using a Thomas-Hoover apparatus, and melting points and boiling points are uncorrected. Carbon–hydrogen analyses were performed by Galbraith Laboratories. Anhydrous calcium chloride, sodium bicarbonate, sodium, isopropanol, methyl acetate, and ethyl acetate were of reagent grade. Technical grade cineol was purchased from Aldrich Chemical Co.

[7] F&M Scientific Corp., model 500.

[8] The synthesis of diisopropyl acetaldehyde acetal was accomplished with complete analytical and spectral data, because all previous syntheses lacked rigorous structure determinations.

[9] Linde Type 5A.