mg. of tetrahydroalstonine (VIII) by the above procedure gave 45 mg. (51%) of amorphous hemiacetal. Wolff-Kishner reduction (by the method used for ajmaliciol) of 90 mg. the latter yielded a gum, which on alumina chromatography and elution with 2% methanol in ether gave 65 mg. (76%) of non-crystalline alcohol, m.p. 80–88°. A solution of 350 mg. of the latter in 7 ml. of acetic anhydride and 6 ml. of pyridine was left standing for three days at room temperature. The mixture was poured onto crushed ice, ammonia added, extracted with chloroform and concentrated. The residual dark gum was chromatographed on alumina giving 85 mg. (21%) of a pale yellow substance on 3:2 benzene–ether elution which was crystallized from methanol to colorless needles, m.p. 220–223°. Sublimation under vacuum and recrystallization from methanol produced crystalline 19-acetoxydihydrocorynantheane (XVI), m.p. 224°; infrared spectrum ($CHCl_3$): N–H, 2.87(m) μ; C=O, 5.80 (s) μ; $[\alpha]D$ −51° (chloroform).

Anal. Calcd. for $C_{21}H_{28}O_2N_2$: C, 74.08; H, 8.29; N, 8.23. Found: C, 73.88; H, 8.37; N, 8.55.

Quaternization Experiments.—A solution of 50 mg. of dihydrocorynantheol (m.p. 185–187°) (XIX) and 85 mg. of *p*-toluenesulfonyl chloride in 1 ml. of pyridine was left standing in the refrigerator for 36 hr. The precipitated, colorless crystals, 33 mg., m.p. 260°, were filtered, suspended in dilute aqueous sodium hydroxide and extracted with chloroform. Evaporation of the solvent yielded 15 mg. of a substance, m.p. 305–310° dec., which on refluxing for half an hour in 0.6 ml. of dimethylformamide and slow cooling produced glistening colorless needles of the salt XX m.p. 315–316° dec., no change in m.p. on recrystallization from dimethylformamide, $[\alpha]D$ −66° (90% methanol).

A solution of 50 mg. of dihydrocinchonamine, 85 mg. of *p*-toluenesulfonyl chloride in 1 ml. of dry pyridine was left standing in the refrigerator for 36 hr. The precipitated crystalline substance, 31 mg., m.p. 318–319° dec. was identified as a quaternary chloride by a positive halogen test, by the absence of characteristic sulfonate ester or salt absorption peaks in the infrared spectrum, and by analysis of a sample, crystallized from chloroform–methanol, m.p. 320–321° dec., whose results fitted best the molecular formula of a quaternary chloride chloroform solvate. The latter was recrystallized from dimethylformamide and dried over P_2O_5 at 2 mm. and 80° for 20 hr.

Anal. Calcd. for $C_{19}H_{25}N_2Cl$: C, 72.02; H, 7.95. Found: C, 72.43; H, 8.01.

Dissolution of 20 mg. of the chloride in 2 ml. of distilled water, addition of 17 mg. of silver *p*-toluenesulfonate, filtration of the precipitated silver chloride, basification of the filtrate with ammonia, extraction with chloroform and evaporation of the solvent gave colorless crystals, which on crystallization from dimethylformamide appeared as long needles of the salt XX, m.p. 313–315° dec., mixed m.p. 315° dec. with above salt XX, identical infrared spectrum (KBr pellet) with that of the above sample, $[\alpha]D$ −69.5° (90% methanol).

AMES, IOWA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE FLORIDA STATE UNIVERSITY]

Constituents of *Helenium* Species. VII. Bitter Principles of *H. pinnatifidum* (Nutt.) Rydb., *H. vernale* Walt., *H. brevifolium* (Nutt.) A. Wood and *H. flexuosum* Raf.[1]

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RECEIVED SEPTEMBER 25, 1958

Several new sesquiterpene lactones have been isolated from three of the plants named in the title. *H. vernale* Walt. yielded the previously known helenalin.

The sesquiterpene lactones tenulin[4] and helenalin[5] have been isolated from a number of *Helenium* species[5a,6] which, except for *H. amarum* (Raf.)[7] and *H. autumnale*, occur in the Southwestern United States. However, there exists a subgenus, or section, *Leptopoda*, whose geographic distribution is limited to the Southeastern United States and which has not been investigated chemically. A revision of this section, which is characterized by the perennial, vernal-flowering habit and the neutral and sterile rays, has been published recently.[8] Because it was hoped that a knowledge of the main constituents might contribute to a greater understanding of the phylogenetic relationships existing in this subgenus we have undertaken its chemical examination. The present paper deals with the isolation of a number of new substances from four of the six species belonging to the section.

Extraction of *H. pinnatifidum* (Nutt.) Rydb.[8] gave in 0.08% yield a crystalline substance of formula $C_{15}H_{18}O_3$. m.p. 164–165°, which we have named pinnatifidin. The ultraviolet spectrum, λ_{max} 237.5 mμ, ϵ_{max} 13550 (in ethanol), indicated the presence of a disubstituted α,β-unsaturated ketone. This was supported by the infrared evidence (band at 1675 cm.$^{-1}$; the position of this band excludes the cyclopentenone chromophore found in helenalin and tenulin). The remaining two oxygen atoms must be ascribed to a γ-lactone group (band at 1770 cm.$^{-1}$) which is probably conjugated with a methylene group as in helenalin (high intensity at 215 mμ,[5b] band at 1.64 μ in the near infrared,[9] strong band at 1630 cm.$^{-1}$ due to the two conjugated double bonds).

H. vernale Walt.[8] which has frequently been confused with *H. pinnatifidum*, furnished as the sole crystallizable component (0.02%) a substance which was identical in all respects with helenalin. Thus these two morphologically very similar species can be differentiated by chemical means.

The crude extract of *H. brevifolium* (Nutt.) A. Wood[8] furnished, after extensive chromatography,

(1) Previous paper, W. Herz and R. B. Mitra, THIS JOURNAL, **80**, 4876 (1958).

(2) Fulbright Travel Scholar, 1957–1958.

(3) Ethyl Corporation Predoctorate fellow, 1957–1958.

(4) (a) D. H. R. Barton and P. DeMayo, *J. Chem. Soc.*, 142 (1956); (b) B. H. Brown, W. Herz and K. Rabindran, THIS JOURNAL, **78**, 4423 (1956).

(5) (a) R. Adams and W. Herz, *ibid.*, **71**, 2546, 2551, 2554 (1949); (b) G. Büchi and D. Rosenthal, *ibid.*, **78**, 3860 (1956).

(6) E. P. Clark, *ibid.*, **58**, 1982 (1936); **61**, 1836 (1939); **62**, 597 (1940).

(7) The correct designation of *H. tenuifolium* Nutt., the most common source of tenulin, appears to be *H. amarum* (Raf.)[8] and will be employed in this and subsequent papers.

(8) H. F. L. Rock, *Rhodora*, **59**, 101, 128, 168, 203 (1957).

(9) W. H. Washburn and M. S. Mahoney, THIS JOURNAL, **80**, 504 (1958). In the absence of a cyclopropane ring this band is characteristic of $=CH_2$. The methylene band usually found near 890 cm.$^{-1}$ is displaced toward higher frequencies when conjugated[10] and is difficult to identify in the sesquiterpenoid lactones which we have encountered.

(10) W. Brügel, *Angew. Chem.*, **68**, 440 (1956).

three crystalline fractions, each in less than 0.01% yield, which we have named brevilin A, B and C in the order of increasing m.p. Brevilin A, m.p. 116–117°, $C_{15-16}H_{18-20}O_4$,[11] and brevilin B, m.p. 186–187°, $C_{17}H_{22}O_5$, were obtained from the less polar fractions of the chromatogram. Their ultraviolet spectra had identical maxima at 219 and 319 mμ. The asymmetrical character of the high intensity band (skewed toward longer wave lengths with a faint shoulder near 240 mμ) indicated that they were composites of two chromophores, an α,β-unsaturated ketone band also responsible for the low-intensity long wave length band and a conjugated lactone. The infrared spectrum of brevilin A had bands at 1770 (lactone), 1720 (double intensity, composite of cyclopentenone and other carbonyl), 1650 (strong, C=C conjugated with lactone) and 1586 cm.$^{-1}$ (double bond of cyclopentenone). Brevilin B, on the other hand, exhibited bands at 1755 (double intensity, lactone and acetoxy), 1708 and 1590 cm.$^{-1}$ (cyclopentenone). Brevilin C, the most strongly adsorbed material, $C_{15}H_{18-20}O_4$, m.p. 245–246°, had a hydroxyl group (rel. weak band centered at 3450 cm.$^{-1}$), γ-lactone (1760 cm.$^{-1}$) and what appeared to be the usual cyclopentenone chromophore (strong band at 1700, weaker band at 1585 cm.$^{-1}$). However, the ultraviolet spectrum in ethanol indicated the presence of a normal ketone function (λ_{max} 283 mμ, ϵ_{max} 239) coupled with an α,β-unsaturated lactone responsible for a high intensity band at 214 mμ (ε 8160).

Chromatography of the crude extract of *H. flexuosum* Raf.[8] furnished, in 0.06% yield, a new substance, flexuosin, $C_{15}H_{18}O_4$, m.p. 221°. The infrared spectrum had bands at 3400 (OH), 1760 (γ-lactone), 1697 and 1610 (probably cyclopentenone) and 1640 cm.$^{-1}$ (rel. strong, possibly C=C conjugated with lactone). The presence of an α,β-unsaturated ketone was confirmed by the ultraviolet spectrum, λ_{max} 237 mμ (shoulder near 228 mμ), ϵ_{max} 13900 (shoulder 11500).

Work on the structure of several of these substances is now in progress.

Acknowledgment.—This investigation was supported by grants from the National Science Foundation, Eli Lilly and Co., and the Research Corporation, to whom we express our thanks. We are greatly indebted to Dr. Robert K. Godfrey of our Department of Botany and his associates Paul Redfearn, William D. Reese and Robert Kral for help with the collection and identification of the plants and to Dr. Howard F. L. Rock of the Department of Botany, University of Tennessee, for valuable suggestions.

Experimental[12]

Pinnatifidin.—Air-dried *H. pinnatifidum*, collected in the vicinity of St. Marks, Florida, in May, 1956, weight 17 oz., was crushed (whole plant) and extracted in a large Soxhlet extractor with 2 l. of chloroform for a period of two days. The solvent was removed, the residue was dissolved in 120 ml. of ethanol and diluted with 200 ml. of water. The solution was acidified by adding 1 ml. of acetic acid, a concentrated solution of 5 g. of lead acetate was added and the mixture was allowed to stand overnight. The clear supernatant solution was filtered and the filtrate concentrated to about 100 ml. at reduced pressure. The concentrate was extracted thoroughly with chloroform, the chloroform extract was dried and evaporated to dryness *in vacuo*. Since the gummy residue could not be induced to crystallize, it was dissolved in benzene and chromatographed over 8 g. of alumina. Elution with benzene and evaporation of solvent gave after a small amount of oil, 0.50 g. of crystalline material, m.p. 145-150°. Later fractions, using benzene–ether as eluent, did not crystallize.

The solid product on recrystallization from benzene–ligroin (b.p. 65–110°) furnished colorless needles, wt. 0.40 g., m.p. 164–165°, $[\alpha]_D$ + 302.2° (95% ethanol, *c* 0.752). The Zimmermann test was negative.

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.52; H, 7.64. Found: C, 73.14; H, 7.37.

Helenalin.—Extraction of 17 oz. of dried whole plant of *H. vernale*, collected in the vicinity of Sopchoppy, Florida, May, 1956, gave 1.1 g. of a dark brown oil. A solution of the material in benzene was chromatographed over 15 g. of alumina; the benzene eluate (6 fractions of 10 ml. each) gave an oil which could not be induced to crystallize cleanly. Subsequent elution with ether–petroleum ether (1:1, 4 fractions) gave 0.10 g. of crystalline solid. Recrystallization from benzene–petroleum ether furnished colorless sternutatory crystals, m.p. 166–167°, no depression on admixture of an authentic sample of helenalin furnished by Prof. George Büchi of the Massachusetts Institute of Technology. The infrared spectrum coincided with that of the authentic sample and the rotation was similar, $[\alpha]_D$ −105° (95% ethanol, *c* 0.815).

Brevilin A, B and C.—*H. brevifolium* was collected in the spring of 1957 near De Funiak Springs, Florida. The whole in plant, wt. 20 oz., was extracted in the usual manner, yield 4.5 g. of a crude resin which was dissolved in benzene and chromatographed over 30 g. of alumina. The first eight fractions (25 ml. of benzene) did not crystallize. Fractions 9–11 (benzene, 95% ethanol, 1:1) yielded 45 mg. of brevilin C, m.p. 237–238°, on recrystallization from ethanol. Fractions 5 and 6 also gave 45 mg. of brevilin C when recrystallized from benzene–petroleum ether.

After removal of brevilin C from fractions 5 and 6, the residue from the mother liquors was combined with fractions 1–4. Crystallization from benzene–ligroin (b.p. 60–90°) gave 65 mg. of brevilin B, contaminated with some brevilin C.

After separation of brevilin B the oily residue obtained from the mother liquors was dissolved in benzene–petroleum ether (88–12) and chromatographed over 30 g. of alumina. All material was retained on the column (150 ml. of eluate), but benzene–petroleum ether (19:1, two fractions of 35 ml. each) eluted an oil which was stirred repeatedly with petroleum ether. The petroleum ether solutions were combined and allowed to evaporate slowly; during this process fine needles of brevilin A, m.p. 113–118°, wt. 35 mg., separated. Recrystallization of brevilin A by dissolving in excess of boiling petroleum ether and allowing it to evaporate furnished fine needles, m.p. 116–117°, λ_{max} 219 and 320 mμ, ϵ_{max} 14150.

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Calcd. for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found: C, 69.23; H, 7.39.

The crude brevilin B isolated as described above was digested with 80 ml. of petroleum ether to remove any brevilin A. The residue, wt. 50 mg., melted at 185–187°. Two recrystallizations from benzene–petroleum ether gave the analytical specimen; m.p. 186–187°, λ_{max} 219 and 320 mμ, ϵ_{max} 7750.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.67; H, 7.22.

Brevilin C was recrystallized twice from ethanol, m.p. 245–246°; λ_{max} 214, 283 mμ, ϵ_{max} 8160, 239.

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Calcd. for $C_{16}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.31; H, 7.24.

(11) The analysis of this substance checked best for $C_{16}H_{20}O_4$. On the basis of its infrared spectrum, it is tempting to formulate it as a formyl derivative of a substance isomeric with isohelenalin.[5b] The small amounts of material available prevented reanalysis.

(12) M.p.'s are uncorrected. Analyses by Drs. Weiler and Strauss, Oxford, England. Ultraviolet spectra were run in 95% ethanol on a Beckman model DK1 recording spectrophotometer. Infrared spectra were determined in chloroform solution on a Perkin–Elmer model 21 recording spectrometer.

Flexuosin.—*H. flexuosum* was collected near Tallahassee in June, 1956. The air-dried whole plant, wt. 12 oz., on extraction in the usual manner, yielded 11 g. of gummy material which could not be induced to crystallize. Chromatography over 40 g. of alumina (eluate benzene) gave 7 g. of viscous material; the more polar fractions were highly colored and discarded. The fractions eluted with benzene were rechromatographed over freshly-ignited alumina. Benzene eluted 5 g. of non-crystalline gum; ethanol eluted partially crystalline material which on crystallization from ethanol furnished 0.24 g. of colorless crystals, m.p. 221°, $[\alpha]_D$ −90° (95% ethanol, *c* 0.50).

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.68; H, 6.92. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.18; H, 6.74.

TALLAHASSEE, FLA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, TEMPLE UNIVERSITY]

The Reaction of Triphenylphosphine with Some Aromatic Amine Oxides[1]

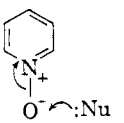
BY EDGAR HOWARD, JR., AND WILLIAM F. OLSZEWSKI

RECEIVED AUGUST 11, 1958

A new method is presented for the deoxygenation of pyridine-N-oxides by the use of triphenylphosphine. The yields of the corresponding pyridine and triphenylphosphine oxide are good. The reaction between 4-nitropyridine-N-oxide and triphenylphosphine gave triphenylphosphine oxide as the only product which could be isolated; a kinetic study showed this reaction to be first order with respect to each of the reactants.

Pyridine-N-oxide has received considerable attention recently as an intermediate in the synthesis of pyridine derivatives.[2,3] Substitution reactions in the pyridine ring are much more difficult than in the benzene ring owing to electronic effects exerted by the hetero nitrogen atom. If, however, pyridine is converted to the N-oxide, the over-all distribution of electrons is modified. The effect is an increased concentration of electrons at the 2- and 4-positions, facilitating electrophilic substitution in these positions.

Deoxygenation of pyridine-N-oxides may be accomplished by a variety of methods. A nucleophilic reagent (Nu) may attack the oxygen atom of pyridine-N-oxide as[3]



Electron donors such as phosphorus trichloride can supply an electron pair to the oxygen atom and cause deoxygenation. The most common laboratory method for accomplishing the deoxygenation consists in refluxing a chloroform solution of the N-oxide with phosphorus trichloride.

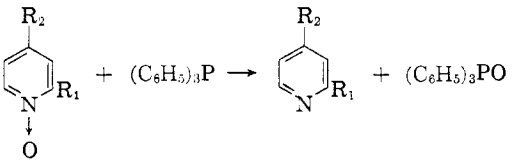
Our search for a reagent of wider applicability has led to the use of triphenylphosphine as the deoxygenating agent. Although triphenylphosphine is substantially stable in air, it is attacked by a wide variety of oxygen-containing compounds with the formation of triphenylphosphine oxide. This property of triphenylphosphine, and of phosphines in general, has been utilized in the removal of oxygen atoms of several substrate molecules.[4]

It has been reported[4] that aliphatic amine oxides, such as trimethylamine oxide, react quantitatively with tertiary phosphines in boiling glacial acetic acid to form the corresponding amine and phosphine oxide. The same authors reported that, in

$$(CH_3)_3N \longrightarrow O + PR_3 \longrightarrow (CH_3)_3N + OPR_3$$

contrast, the N-oxides of pyridine and quinoline were found to be quite stable toward both triphenylphosphine and triethylphosphine. It was observed that the ease of removal of the oxygen from amine oxides often decreases with the dipole moment of the amine oxide, *e.g.*, trimethylamine oxide 5.04 D., pyridine-N-oxide 4.24 D.

In our investigation it was discovered that triphenylphosphine will cause deoxygenation of a variety of aromatic amine oxides at high temperatures



I, $R_1 = R_2 = H$
II, $R_1 = CH_3$, $R_2 = H$
III, $R_1 = H$, $R_2 = CH_3$
IV, $R_1 = H$, $R_2 = OCH_3$

Quinoline-N-oxide is also smoothly deoxygenated by triphenylphosphine.

The optimum method for performing this reaction is to heat the reactants in the absence of a solvent. At temperatures considerably above 200° the amine distils from the reaction mixture in good yield in most cases. Triphenylphosphine oxide was isolated from the residue by recrystallization from a water–methanol solvent pair. In the reactions of 4-methoxypyridine-N-oxide and quinoline-N-oxide the products were isolated by column chromatography. The only solvent found suitable for the reaction was triethylene glycol; however, there is no apparent advantage derived from its use. Observations of the reaction of triphenylphosphine with several amine oxides are summarized in Table I.

Considerable difficulty was encountered in the reaction of triphenylphosphine with 4-nitropyridine-N-oxide. Upon heating the reactants in the absence of a solvent a vigorous exothermic reaction

(1) From a thesis submitted by William F. Olszewski in partial fulfillment of the requirements for the M.A. degree, Temple University, June, 1958.

(2) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).

(3) A. R. Katritzky, *Quart. Revs. (London)*, **10**, 395 (1956).

(4) L. Horner and H. Hoffmann, *Angew. Chem.*, **68**, 480 (1956).