the isolated and synthetic material were identical.

By means of paper chromatography and a specific color test[6] glucose was shown to be formed on treatment of the seed meal extract with myrosinase. This information is interpreted as showing the compound is derived from a glucoside.

The identification of this enzymatically formed isothiocyanate from *L. lasiocarpa* seed adds the homologous 8-carbon compound to the previously identified 5-, 6-, and 7-carbon compounds of similar structure elaborated in nature by Cruciferae. The lower homologs have been identified by Kjaer and co-workers[7-9] as enzymic hydrolysis products of glucosides present in the seeds of *Iberis sempervirens*, *Eruca sativa*, and *Berteroa incana*, respectively. In accordance with the method of naming the parent glucosides followed by these workers, the name glucolesquerellin is suggested for the postulated parent glucoside.

EXPERIMENTAL

Isolation and characterization of N-(6-methylthiohexyl)-thiourea. Four 5-g. samples of finely ground, petroleum ether-extracted seed meal from *Lesquerella lasiocarpa* were treated with myrosinase (for preparation see Wetter[10] and Wrede[11]) in order to hydrolyze the glucoside. To each sample was added 100 ml. of citrate buffer, *p*H 4 (0.20*M* citric acid adjusted to *p*H 4 with saturated sodium hydroxide) and 6 ml. of myrosinase solution in a 500-ml. flask that could be attached to a steam distillation apparatus. The stoppered flask was shaken for 3 hr. at room temperature. Prior to steam distillation 15 ml. of a mixture of ethanol-butanol (1:1) was added. Rapid steam distillation of the volatile isothiocyanate was continued until about 200 ml. was collected in 25 ml. of ice-cooled concd. ammonium hydroxide. The four ammonium hydroxide solutions were combined after standing overnight, concentrated to about 100 ml. on a rotary evaporator at 40°, and filtered. The filtrate was further concentrated to 25 ml. After cooling in the refrigerator for at least 2 hr., the crystalline material was collected on a micro Büchner funnel, dissolved with 4 ml. of absolute ethanol, and refiltered. On adding 8 ml. of water, recrystallization occurred. After cooling again in the refrigerator the material was filtered, air-dried and then dried *in vacuo* at room temperature to constant weight. Yield, 122 mg. Melting point on a micro hot stage, 72–73°.

Anal. Calcd. for $C_8H_{18}N_2S_2$: C, 46.6; H, 8.9; N, 13.6; S, 31.1. Found: C, 46.8; H, 8.8; N, 13.5; S, 31.0.

Comparison with authentic *N*-(6-methylthiohexyl)thiourea gave no depression of mixed melting point. Both compounds gave the same R_{ph} value of 1.19 by ascending chromatography using water-saturated chloroform as the mobile phase. Their X-ray patterns and infrared absorption spectra (2 to 15 μ) were identical. Two crude preparations of the thiourea (m.p. 70–72°) from different accessions gave yields of 99 and 132 mg. from 10 g. of each seed meal.

Evidence for the presence of the parent glucoside. A hot acetone-water (3:1) extract (200 ml.) obtained from 3 g. of oil-free meal was concentrated under vacuum to 10 ml. A portion of the solution was hydrolyzed with the myrosinase-citrate solution as used in Wetter's[10] analytical procedure. The hydrolyzed solution and appropriate controls, including the myrosinase-citrate solution, were examined by paper chromatography using two different solvent systems: (1) Ethyl acetate:pyridine:water (3:1.25:1)[12] and (2) 1-butanol:water:acetic acid (4:3:1). Two different detection reagents were used: (1) Aniline–diphenylamine–phosphoric acid in acetone[12] and (2) glucose oxidase reagent.[6]

Only trace amounts of glucose were detected when the unhydrolyzed solution was chromatogrammed. A significant amount of glucose was detected when a hydrolyzed solution equal to about one fifth of the unhydrolyzed material was chromatogrammed.

Analysis of seed meals. Composition of the seed meal for total volatile isothiocyanate determined by the method of Wetter[10] and calculated as 6-methylthiohexyl isothiocyanate was 1.2%. Seed meals from two different accessions of *L. lasiocarpa* contained about the same amounts of steam-volatile isothiocyanate. No thiooxazolidone was found.

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Transformation of Squill Bufadienolides to Pyridone Counterparts

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The bufadienolides are a group of naturally occurring α-pyrones in which the pyrone ring is linked at the 5-position to the 17β-position of a substituted steroid nucleus.[1] One of the reactions characteristic of simpler α- and γ-pyrones embodies their conversion with ammonia, or with amines, to pyridone derivatives.[2] Although the transformation has been considered general, experimental conditions required—at least those employed—have varied widely.[3]

In a study of the behavior of white squill bufa-

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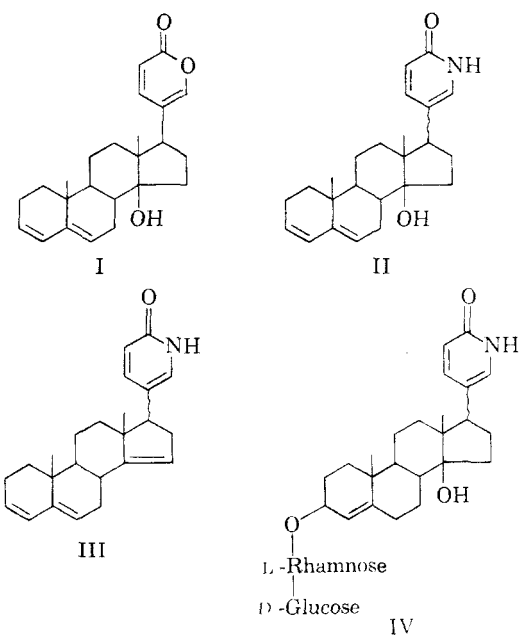
(3) H. S. Mosher in *Heterocyclic Compounds*, edited by R. C. Elderfield, John Wiley and Sons, Inc., New York, Vol. 1 (1950), p. 472.

dienolides with ammonia, scillaridin A (I) was recovered unchanged after treatment with ammonium acetate in refluxing acetic acid, as well as after treatment with anhydrous methanolic ammonia. Aqueous methanolic ammonia in the presence of ammonium chloride at 120°, however, gave 14% of the pyridone II. Under more favorable conditions, four hours of treatment of a dimethylformamide solution of scillaridin A with 6.5 equivalents of ammonium acetate and 1.5 equivalents of acetic acid in a sealed tube at 175° afforded II in 58% yield.

Elimination of the 14β-hydroxyl group of II with thionyl chloride in pyridine at 0° gave III, identical with the pyridone prepared directly from 14-anhydroscillaridin A. The very sparingly soluble pyridones II and III gave a red coloration with ferric chloride and provided infrared spectra with prominent bands at 6.05 and 6.25 μ.

With the ammonium acetate-dimethylformamide procedure, scillaren A, the native 3β-glucorhamnoside from *Scilla maritima*, afforded 36% of the pyridone bioside IV. Proscillaridin A, the 3β-rhamnoside obtained by enzymatic cleavage of scillaren A, gave the corresponding pyridone monoside.

Since epimerization at C17 during pyridone formation is possible,[4] degradation of IV to a



derivative of established configuration was attempted. Potassium permanganate in acetone at 0°, under conditions developed for conversion of scillaren A to the β-etio acid,[5] did not attack the pyridone nucleus. Less cautious oxidation gave no definite product.

An alternative scheme, involving perhydrogenation of III to the piperidone, followed by deamination to a saturated lactone for comparison with the hydrogenation product of 14-anhydroscillaridin A, likewise was not successful. Although sodium nitrite–acetic anhydride–acetic acid nitrosation of the platinum–acetic acid reduction product of III (five equivalents of hydrogen absorbed) gave a crystalline *N*-nitrosolactam, satisfactory conditions for pyrolytic decomposition to the saturated lactone were not found. Consequently, assignment of orientation at C-17 must remain in abeyance.

The sparingly soluble nature of the steroid pyridones imposes limitations on biological work with the compounds. In pharmacological studies at the Sandoz laboratories, the pyridone glucorhamnoside IV, at a concentration of 10^{-6}, exhibited no cardiotonic properties when tested with the isolated guinea pig auricle.

EXPERIMENTAL[6]

14β-Hydroxy-17ξ-(2′-hydroxy-5′-pyridyl)-3,5-androstadiene (pyridone counterpart of scillaridin A) (II). A. A solution of 366 mg. (0.001 mole) of scillaridin A (I), 500 mg. (0.0065 mole) of ammonium acetate and 0.1 ml. (0.0016 mole) of glacial acetic acid in 10 ml. of dimethylformamide, together with a magnetic bar, was sealed under nitrogen in a Pyrex tube and heated with stirring at 170–180° for 4 hr. After the cooled solution had been diluted with 10 ml. of water, the precipitate was collected by filtration, washed with water and with ethanol, and dried to give 212 mg. (58%) of crystalline material. The substance was virtually insoluble in the common organic solvents, precluding measurement of the rotation or determination of the ultraviolet spectrum. For analysis the compound was recrystallized from hot dimethylformamide to give a product which was sublimed at 260° and 0.02 mm.; m.p. 330–345°; infrared spectrum: 6.05, 6.25 μ (pyridone).

Anal. Calcd. for $C_{24}H_{31}NO_2$ (365.50): C, 78.86; H, 8.55; N, 3.84. Found: C, 78.99; H, 8.54; N, 3.81.

B. A solution of 73 mg. (0.0002 mole) of scillaridin A and 5 mg. (0.0001 mole) of ammonium chloride in 5 ml. of 90% aqueous methanol was saturated with ammonia at 25°, sealed in a Pyrex tube, and heated at 120° for 3 hr. The solution was concentrated under reduced pressure to give a residue which was dissolved in a mixture of chloroform and methanol. Addition of ether afforded 12 mg. (14%) of crystalline product; m.p. 300–310°; infrared spectrum: identical with that from the product prepared according to procedure A.

17ξ-(2′-Hydroxy-5′-pyridyl)-3,5-14-androstatriene (pyridone counterpart of 14-anhydroscillaridin A) (III). A. To a magnetically stirred suspension of 365 mg. (0.001 mole) of 14β-hydroxy-17ξ-(2′-hydroxy-5′-pyridyl)-3,5-androstadiene (II) in 170 ml. of anhydrous pyridine at 0° was added 1.7 ml. of thionyl chloride. The flask was closed with a calcium chloride tube. After 45 min. at 0°, followed by 45

(4) *Cf.* the transformation of uzarigenin to 17α-uzarigenin in good yield through heating with sodium *p*-toluenesulfonate in dimethylformamide: A. Kuritzkes, J. Von Euw, and T. Reichstein, *Helv. Chim. Acta.*, **42**, 1502 (1959). The reaction appears to be a general method for conversion of 17β- to 17α-cardenolides: J. H. Russel, O. Schindler, and T. Reichstein, *Helv. Chim. Acta.*, **43**, 167 (1960).

(5) A. von Wartburg, *Helv. Chim. Acta*, **43**, 686 (1960).

(6) Melting points were observed on a calibrated micro hot stage. Microanalyses were performed by Dr. S. M. Nagy, Massachusetts Institute of Technology, Cambridge, Mass. Infrared spectra were recorded with a Perkin-Elmer spectrophotometer, model 137. Only those functional bands of significance in interpretation are mentioned.

min. at 25°, the mixture was concentrated under reduced pressure to one-third its volume and was diluted with 30 g. of ice. The precipitate was collected by filtration, washed with water, and dried to give 386 mg. Recrystallization from chloroform-ether gave 318 mg. (91%); m.p. 262–275°. After decolorization with Norite in chloroform-methanol, followed by several recrystallizations from chloroform-ether, the analytical sample melted at 267–282°; $[\alpha]_D$ −154° (chloroform); infrared spectrum: 6.05, 6.25 μ (pyridone).

Anal. Calcd. for $C_{24}H_{29}NO$ (347.48): C, 82.95; H, 8.41; N, 4.04. Found: C, 82.70; H, 8.26; N, 3.94.

B. A solution of 35 mg. (0.0001 mole) of 14-anhydroscillaridin A,[7] 100 mg. (0.0013 mole) of ammonium acetate and 0.01 ml. (0.00016 mole) of glacial acetic acid in 3 ml. of dimethylformamide was sealed in a Pyrex tube and heated at 150° for 3 hr. After the solution had been diluted with 6 ml. of water, the amorphous precipitate was collected by filtration, washed with water, and dried to give 23 mg. Recrystallization from methanol-ether, after decolorization with Norite, gave 4 mg. of crystalline material; m.p. 260–275°; mixed melting point with the product prepared according to procedure A, 260–275°; infrared spectrum: identical with that of the product prepared according to procedure A.

*3β,14β-Dihydroxy-17ξ-(2′-hydroxy-5′-pyridyl)-4-androstene 3β-*D*-gluco-*L*-rhamnoside (pyridone counterpart of scillaren A)* (IV). A solution of 346 mg. (0.0005 mole) of scillaren A, 650 mg. (0.0084 mole) of ammonium acetate, and 0.1 ml. (0.0016 mole) of glacial acetic acid in 8 ml. of dimethylformamide, together with a magnetic bar, was sealed under nitrogen in a Pyrex tube and heated with stirring for 4 hr. at 180°. The solution was concentrated nearly to dryness under diminished pressure to give a residue which was washed with 5 ml. of ether and with 10 ml. of acetone. A solution of the solid in 40 ml. of chloroform-ethanol (2:1) was washed with water and was dried over anhydrous sodium sulfate. The filtrate from the desiccant was concentrated under reduced pressure to give 320 mg. of amorphous residue. Recrystallization from methanol-acetone gave 125 mg. (36%); m.p. 250–267°. Several recrystallizations from methanol-acetone afforded fine rosettes of needles; the analytical sample was dried 4 hr. at 100° and 0.02 mm.; m.p. 283–284°; infrared spectrum: 6.05, 6.25 μ (pyridone).

Anal. Calcd. for $C_{36}H_{53}NO_{12}$ (691.83): C, 62.53; H, 7.72; N, 2.03. Found: C, 62.74; H, 7.88; N, 2.10.

A solution of 230 mg. (0.0003 mole) of IV and 3 ml. of acetic anhydride in 3 ml. of anhydrous pyridine was kept at 0° for 72 hr. The mixture was concentrated under reduced pressure to give a residue which was dissolved in chloroform. The solution was washed with 2*N* aqueous hydrochloric acid, with 2*N* aqueous sodium carbonate, and with water and was dried over anhydrous sodium sulfate. The filtrate from the desiccant was concentrated under reduced pressure. Recrystallization of the residue (323 mg.) from methanol-ether gave 233 mg., m.p. 170–175°. A chloroform solution of this material was filtered through silica gel. The residue from vacuum evaporation of the solvent was recrystallized from methanol to afford 127 mg. (45%) of very fine needles of the hexaacetyl derivative of IV; m.p. 239–242°/270–280°; infrared spectrum: 5.80 (acetoxy), 6.05, 6.25 μ (pyridone).

*3β,14β,-Dihydroxy-17ξ-(2′-hydroxy-5′-pyridyl)-4-androstene 3β-*L*-rhamnoside (pyridone counterpart of proscillaridin* A). A solution of 106 mg. (0.0002 mole) of proscillaridin A, 300 mg. (0.004 mole) of ammonium acetate and 0.1 ml. (0.0016 mole) of glacial acetic acid in 1 ml. of dimethylformamide was sealed in a Pyrex tube and heated for 3 hr. at 160°. The mixture was concentrated under reduced pressure to give a residue which was washed with ether and with acetone. A solution of the solid in chloroform-ethanol (2:1) was washed with water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure. Recrystallization of the residue from methanol-ether gave 46 mg. (43%) of brown crystalline material; m.p. 283–286°. A methanolic solution of this product was decolorized with Norite. Two recrystallizations from methanol-acetone gave 19 mg. of triangular plates with convex sides; m.p. 289–292°; infrared spectrum: 6.05, 6.25 μ (pyridone).

Anal. Calcd. for $C_{30}H_{43}NO_7$ (529.65): N, 2.64. Found: N, 2.61.

N-Nitrosolactam of hydrogenation product of 17ξ-(2′-hydroxy-5′-pyridyl)-3,5,14-androstatriene. A solution of 315 mg. (0.001 mole) of 17ξ-(2′-hydroxy-5′-pyridyl)-3,5,14-androstatriene (III) and 1 drop of concd. hydrochloric acid in 70 ml. of glacial acetic acid was shaken with hydrogen in the presence of 60 mg. of platinum oxide for 15 hr. at 26°. A total of 140.6 ml. of hydrogen was taken up (theory for five double bonds plus catalyst: 125 ml.). After the catalyst had been removed by filtration, the solution was concentrated under diminished pressure to give a residue which was diluted with chloroform. The chloroform solution was washed with 2*N* aqueous sodium carbonate and with water and was dried over anhydrous sodium sulfate. Vacuum concentration of the filtrate from the desiccant gave 360 mg. of amorphous material which was crystallized from chloroform-ether to afford 269 mg. (82%) of crystalline product; m.p. 200–260°.

To a solution of 218 mg. (0.00067 mole) of this material and 0.8 ml. of glacial acetic acid in 5 ml. of acetic anhydride at 10–15° was added (in small portions during 4 hr.) 800 mg. of sodium nitrite.[8] After addition of 25 ml. of ice water, the mixture was extracted with ether. The organic phase was washed with water and was dried over anhydrous sodium sulfate. Concentration of the filtrate from the desiccant gave a residue which was crystallized from ether-petroleum ether (b.p. 30–60°) to afford 61 mg. (25%) of yellow crystalline product; m.p. 160–170°; infrared spectrum: 5.80 μ.[9]

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(9) *Cf.* the infrared spectrum of *N*-nitroso-2-piperidone (yellow crystals, m.p. 40–45°): prominent band at 5.80 μ.

Preparation of Trimethylsilyl-Substituted Dihydric Phenols and Trimethylsilylbenzoquinone

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It was recently shown that trimethylsilyl-substituted aryloxytrimethylsilanes can be converted to the corresponding phenols without loss of trimethylsilyl groups from the ring by dissolving the