The mother liquors from the first two recrystallizations (solvent ethyl acetate-hexane) were combined and evaporated. The residue melted at 144° after several recrystallizations from aqueous methanol. A mixed m. p. with acetyltetrahydrohelenalin showed no depression.

Anal. Calcd. for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85. Found: C, 65.98; H, 8.09.

Diacetate of I.—Acetylation of 88 mg. of tetrahydrohelenalin oxide (I) in pyridine yielded 54 mg. of white crystals after dilution of the reaction mixture with water and partial removal of the solvents in an air stream. After recrystallization from water the product melted at 165.5°. The same compound was obtained by acetylation of acetyltetrahydrohelenalin oxide.

Anal. Calcd. for $C_{19}H_{26}O_7$: C, 62.28; H, 7.15. Found: C, 62.06; H, 7.20.

Tetrahydro Derivative of Helenalin Oxide (IV).—The reduction of 405 mg. of helenalin oxide in 50 ml. of absolute ethanol was carried out as usual, but with 230 mg. of palladium-charcoal as catalyst. Slightly more than two moles of hydrogen was taken up. The residue was recrystallized from ethyl acetate and weighed 193 mg. Two further recrystallizations raised the m. p. to 224° when the capillary was immersed at a bath temperature of 210°. Lower-melting products were isolated from the mother liquors. The compound gave an impure 2,4-dinitrophenylhydrazone and was not oxidized by lead tetraacetate.

Anal. Calcd. for $C_{15}H_{22}O_5$: C, 63.81; H, 7.86. Found: C, 64.09; H, 8.00.

The same product was obtained by reduction of helenalin oxide in ethanol using Raney nickel.

Anal. Found: C, 63.96; H, 7.75.

Acetyldihydrohelenalin.—Acetylation of 200 mg. of the above yielded 193 mg. of crude product after dilution with water and partial removal of the solvents. Recrystallization from water afforded white needles, m. p. 166°, which proved to be identical with an authentic sample of acetyldihydrohelenalin, m. p. 166–167°.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.51; H, 7.49.

Isomerization of Helenalin Oxide.—A solution of 374 mg. of helenalin oxide in 40 ml. of acetic acid was reduced with 80 mg. of platinum oxide. The reduction was stopped after three and one-half hours when approximately 2.5 moles of hydrogen had been taken up. The residue obtained on evaporation to dryness *in vacuo* was taken up in 50 ml. of hot ethyl acetate, decolorized and allowed to cool after concentration to 5 ml. The white needles, which weighed 123 mg., were recrystallized several times from ethanol-water. The m. p. was difficult to determine due to decomposition; the highest value was 285-287° (dec.) when the sample was immersed at 282° and the bath was heated up rapidly. The test with potassium iodide–acetic acid was positive. The mother liquors yielded more material of slightly lower melting point.

Anal. Calcd. for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52. Found: C, 64.59; H, 6.62.

The ultraviolet spectrum of this material had bands at 216 mμ (ϵ = 14500) and at 304 mμ (ϵ = 62). Acetylation of 68 mg. in the usual manner yielded 27 mg. of pink solid, purified twice by solution in acetone–water and treatment with charcoal. On removal of the acetone crystals melting at 188–191° were obtained.

Anal. Calcd. for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.81; H, 6.35.

Summary

Additional proof that helenalin is an α,β-unsaturated ketone has been furnished by the preparation of keto-epoxides from helenalin and acetylhelenalin.

Helenalin oxide was converted to a glycol by the action of dilute sulfuric acid. The reduction of helenalin and acetylhelenalin oxide yielded a variety of products depending on the reaction conditions. In some instances, the ketone was reduced to an alcohol with retention of the epoxide group, in others the epoxide was reduced to an alcohol with retention of the ketone group.

URBANA, ILLINOIS RECEIVED FEBRUARY 11, 1949

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Helenalin. III. Reduction and Dehydrogenation

BY ROGER ADAMS AND WERNER HERZ

Catalytic reduction of helenalin is reported to saturate two double bonds, thus leading to the formation of tetrahydrohelenalin.[1,2] Reduction of helenalin under a variety of conditions has now led to the isolation of other reduction products whose reactions, together with those of tetrahydrohelenalin, have been investigated in order to elucidate the structure of the bitter principle.

The low pressure reduction of helenalin was studied using a variety of solvents and catalysts. In each instance tetrahydrohelenalin was obtained, the best yields reaching 60–70%. By stopping the reduction of helenalin after the absorption of one mole of hydrogen, it was possible to isolate in small amounts a dihydrohelenalin, m. p. 224–225°.

The ultraviolet absorption spectrum[3] of dihydrohelenalin ($\lambda_{1\ \max} = 227$ mμ, $\epsilon_{1\ \max} = 7200$; $\lambda_{2\ \max} = 314$ mμ, $\epsilon_{2\ \max} = 59$) is very similar to that of helenalin,[2] indicating that catalytic reduction preferentially saturates the unconjugated double bond. This is confirmed by the infrared spectrum[4] from which the bands due to unconjugated C=C are missing, while the bands ascribed to conjugated C=O and C=C are comparable to those in the helenalin spectrum. Chemical evidence is furnished by the failure to obtain formaldehyde on the ozonolysis of dihydrohelenalin, and by the results of C-methyl determinations which yielded 2.20 moles of acetic acid as compared with 0.85 mole from helenalin.

---

(1) Clark, THIS JOURNAL, **58**, 1982 (1936).

(2) Adams and Herz, *ibid*, **71**, 2546 (1949).

(3) Ultraviolet spectra were determined by Mrs. Dorothy C. Brantley on 0.001 *N* solutions in 95% ethanol.

(4) Infrared spectra were determined and interpreted by Mrs. Agatha Roberts Johnson.

Dihydrohelenalin was further characterized by the preparation of an acetyl derivative and a dibromide whose spectrum revealed that the conjugated system had been saturated. Further reduction of dihydrohelenalin led to tetrahydrohelenalin.

The ketone group of tetrahydrohelenalin appears to be singularly resistant to chemical reduction; various modifications of the Clemmensen and Wolff–Kishner reactions were tried without success. Tetrahydrohelenalin also fails to yield a semicarbazone; on the other hand, the ketone group is sufficiently reactive to give an oxime and a 2,4-dinitrophenylhydrazone. While helenalin itself did not react with phenyl isocyanate,[2] tetrahydrohelenalin easily gave a phenylurethan; the hydroxyl group whose presence is therefore demonstrated, has been further characterized by the preparation of a dinitrobenzoate.

Proof that the hydroxyl group in tetrahydrohelenalin is secondary was furnished by the isolation of a compound containing two hydrogen atoms less, when tetrahydrohelenalin was oxidized with chromic acid. Dehydrotetrahydrohelenalin contained a new keto group since the infrared spectrum showed the disappearance of the usual —OH frequency and the presence of a new carbonyl band at 1697 cm.$^{-1}$.[5] This is the normal frequency of a band due to an aliphatic or a six- and seven-membered ring ketone, whereas the unusually high frequency of the original carbonyl band (1737 cm.$^{-1}$ in tetrahydrohelenalin, 1750 cm.$^{-1}$ in dehydrotetrahydrohelenalin) is in a region where cyclopentanones absorb. The difference in frequency makes it likely that the hydroxyl radical which gives rise to the new carbonyl group is not attached to the ring containing the keto group of helenalin.

In spite of the presence of two keto groups, dehydrotetrahydrohelenalin reacts with only one molecule of 2,4-dinitrophenylhydrazine, hydroxylamine or semicarbazide. The spectra of these derivatives suggest that dinitrophenylhydrazine and hydroxylamine combine with the original C=O group in preference to the new, a low-frequency carbonyl band still being in evidence. Semicarbazide, on the other hand, which does not react with tetrahydrohelenalin, appears to attack the new keto group, since the spectrum of the product contains the high, but not the low, carbonyl frequency.

Tetrahydrohelenalin and its oxidation product do not give the iodoform test. Oxidative degradation of tetrahydrohelenalin with potassium permanganate or dichromate has so far given no identifiable products other than oxalic acid. Tetrahydrohelenalin gives a positive Legal and Zimmermann test; it forms a mono-piperonylidene derivative and therefore contains an active methylene group. The possible presence of such a group in helenalin has been discussed previously.[2] It is more likely, however, that the active methylene group has been formed on reduction since all of the available evidence suggests that the substituent on the α-carbon of the α,β-unsaturated ketone system of helenalin is hydrogen.

Bromination of tetrahydrohelenalin furnished a mono- and a dibromo derivative. The former is an α-bromo-substituted ketone, the latter presumably is α,α'-disubstituted. The chromic acid oxidation of bromotetrahydrohelenalin proceeded in the expected manner and gave dehydrobromotetrahydrohelenalin in which the hydroxyl group had been oxidized to a ketone. The infrared spectrum of the corresponding product obtained by oxidation of dibromotetrahydrohelenalin showed that it possessed an analogous structure although the analytical values were not quite satisfactory. Attempts to obtain acyl derivatives of mono- and di-bromotetrahydrohelenalin were not successful and neither they nor their oxidation products gave dinitrophenylhydrazones. Hydrolysis of mono- and di-bromotetrahydrohelenalin, undertaken with a view to obtaining the easily oxidizable α-hydroxyketones, has not yet furnished the desired compounds.

As it seemed desirable to remove as many functional groups as possible by dehydration before undertaking attempts at dehydrogenation, the action of hydrogen on helenalin at elevated temperatures and pressures was investigated. The infrared spectrum of the glassy hexahydrohelenalin obtained in the presence of Raney nickel indicated conversion of the carbonyl to a hydroxyl group. The physical state of the product makes it likely that the reduction has resulted in the formation of diastereoisomers which so far have not been separated. A mono-phenylurethan of one of the forms was isolated from the mixture of phenylurethans obtained by reaction of hexahydrohelenalin with phenyl isocyanate, but attempts to prepare an acetate, benzoate or dinitrobenzoate gave oils or solids melting over a wide temperature range.

The dehydration of hexahydrohelenalin, tetrahydrohelenalin or helenalin itself has not met with success. Even as vigorous a procedure as fusion with potassium bisulfate did not effect dehydration. Hexahydrohelenalin was therefore used for dehydrogenation experiments directly. The use of selenium or palladized charcoal at temperatures ranging from 300–360° yielded small amounts of a blue azulene and somewhat larger fractions of colorless hydrocarbons characterized as azulenogenic by application of the Sabetay[6] test. Naphthalenic hydrocarbons were not isolated. The azulene yielded a crystalline trinitro-

---

(5) The appearance of this frequency was also noted in the spectrum of an anomalous product isolated only once during the reduction of helenalin with aluminum isopropoxide[2] and further supports the conclusion that this material represents the product of an intramolecular Oppenauer oxidation.

(6) Sabetay and Sabetay, *Compt. rend.*, **199**, 313 (1934).

benzolate, trotylate and picrate. Analysis of the trinitrobenzolate gave values corresponding to a compound of formula $C_{21}H_{21}N_3O_6$ from which it follows that the azulene has the formula $C_{15}H_{18}$. Such a compound could only have been formed by reduction of the lactone group during dehydrogenation. A similar observation has recently been made by Naves[7] who obtained what is claimed to be a mixture of S- and Se-guiazulene on selenium dehydrogenation of hexahydrocostus lactone. This was accompanied by formation of a dihydrosesquiterpene, whereas the colorless azulenogenic hydrocarbon obtained by us appears to have the formula $C_{15}H_{24}$.

The ultraviolet spectrum of the azulene after regeneration from the picrate is given in Fig. 1.

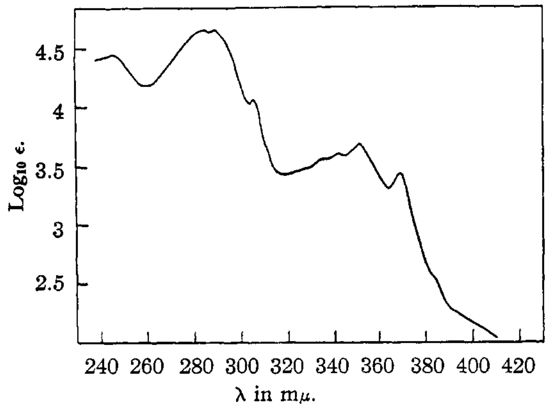
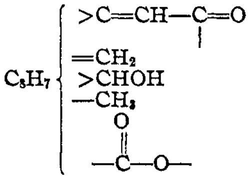


Fig. 1.—Ultraviolet absorption spectrum of azulene from dehydrogenation of hexahydrohelenalin.

The very close resemblance to the spectra of 1,4-dimethylazulene[8] and of S-guiazulene (1,4-dimethyl-7-isopropylazulene)[9] suggests the presence of alkyl groups in at least positions 1 and 4 of the azulene nucleus, while the position and strength of the maxima[10] and the deep blue color[11] would appear to exclude substitution in the 2-position. Unfortunately the visible spectrum which is reported to be much more useful for assignment of structure[10] affords no such clearly-defined bands as the ultraviolet, only broad, faint bands appearing against a background of general absorption. The approximate position of these bands, given in the experimental part, would seem to place our azulene in the group of azulenes designated as class I by Plattner.[11] This again suggests that there is no alkyl group in position 2 of the azulene nucleus.

Absorption measurements were made before and after purification of the azulene through the trinitrobenzolate, trotylate and picrate. While the extinction coefficients increased somewhat, presumably due to removal of non-azulenic impurities, the position and sharpness of the bands were not altered significantly. Nevertheless, the possibility of non-homogeneity exists since the melting points of our derivatives, while sharp, are considerably lower than those of any $C_{15}H_{18}$ azulene previously isolated from natural sources.[12]

The isolation of an azulene by dehydrogenation of hexahydrohelenalin establishes helenalin itself as a sesquiterpene derivative. The smallness of the yield (0.4%) is not surprising in a compound as highly oxygenated as helenalin. Our failure to isolate naphthalenic hydrocarbons would appear to exclude a structure based on two six-membered rings, such as is found in lactones of the santonin type whose dehydrogenation would be expected to furnish predominantly derivatives of naphthalene. Consideration of the partial formula indicated by facts available at this time suggests that helenalin



$$C_5H_7\left\{\begin{array}{l} >C{=}CH{-}\underset{|}{C}{=}O \\ {=}CH_2 \\ >CHOH \\ {-}CH_3 \\ {-}\overset{\overset{O}{\|}}{C}{-}O{-} \end{array}\right.$$

is bicyclic and eliminates the possibility of a tricyclic system containing a cyclopropane ring which is known to give rise to azulenes[13]; a monocyclic structure[14] is excluded for the same reason. In view of the evidence previously adduced in favor of the presence of a cyclopentenone ring[2] it is therefore entirely possible that helenalin possesses a carbon skeleton based on the cyclopentanocycloheptane ring system of azulene itself. It is hoped that degradation studies now under way in this Laboratory will give further information concerning this at present only tentative suggestion.

Experimental[15]

Tetrahydrohelenalin.—To 3 g. of helenalin dissolved in 100 ml. of pure ethyl acetate was added one-half of one teaspoon of Raney nickel. The mixture was shaken in an atmosphere of hydrogen until absorption had stopped. The solutions resulting from three such reductions were combined and evaporated to dryness in a vacuum. The residue was taken up in 100 ml. of *n*-butyl ether and enough *n*-butanol to effect complete solution when boiling, the solution decolorized with charcoal if necessary and allowed to cool. The yield of tetrahydrohelenalin was 6.2 g., m. p. 172-175°. This was sufficiently pure for further work. Further recrystallizations raised the m. p. to 176°, in agreement with the value reported by Clark.

---

(7) Naves, *Helv. Chim. Acta*, **31**, 1172 (1948).

(8) Plattner and Lemay, *ibid.*, **23**, 897 (1940).

(9) Susz, Pfau and Plattner, *ibid.*, **20**, 469 (1937).

(10) Plattner and Heilbronner, *ibid.*, **31**, 804 (1948).

(11) Plattner, *ibid.*, **24**, 283E (1941).

(12) The literature appears to record only one instance in which a compound with as many or more oxygen atoms has been dehydrogenated to an azulene. Schechter and Haller, THIS JOURNAL, **62**, 3507 (1940), obtained an azulene of formula $C_{11}H_{14}$ on zinc dust distillation of pyrethrosin, $C_{17}H_{22}O_5$. Palladium-charcoal dehydrogenation of pyrethrosin is also reported to yield an azulene, but no details have been published.

(13) Arnold, *Chemie*, **56**, 7 (1943); Harper, *Ann Repts. Chem. Soc.*, **44**, 143 (1947).

(14) The sesquiterpene alcohol elemol appears to be the only monocyclic compound giving an azulene on dehydrogenation. Its identity with vetivazulene has recently been demonstrated; Ruzicka and Haagen-Smit, *Helv. Chim. Acta*, **19**, 858 (1931); Sörensen and Hougen, *Acta Chem. Scand.*, **2**, 447 (1948).

(15) Analyses by Mrs. Jane Wood, Miss Emily Davis and Miss Theta Spoor; C-methyl determinations by Mr. Howard C. Clark.

The mother liquors contained a considerable amount of lower-melting solids. Similar yields of tetrahydrohelenalin were obtained when the reduction was carried out in ethanol with platinum oxide, palladium-charcoal and nickel, and in ethyl acetate or acetic acid using platinum oxide or palladium-charcoal.

3,5-Dinitrobenzoyltetrahydrohelenalin.—The yield of crude ester by reaction of 0.2 g. of tetrahydrohelenalin and 0.18 g. of the acid chloride in pyridine was 0.27 g. After several recrystallizations from benzene–petroleum ether the white crystals melted at 243° (dec.).

Anal. Calcd. for $C_{22}H_{24}N_2O_9$: C, 57.39; H, 5.25. Found: C, 57.24; H, 5.23.

Phenylurethan of Tetrahydrohelenalin.—A mixture of 0.2 g. of tetrahydrohelenalin, 0.1 g. of phenyl isocyanate and 2 ml. of benzene was refluxed for one hour. The material obtained on dilution with petroleum ether (b. p. 30–60°) was extracted with two 10-ml. portions of carbon tetrachloride. Evaporation of the extracts yielded unreacted tetrahydrohelenalin. The undissolved material (0.16 g.) was recrystallized from benzene–petroleum ether and melted at 249–250° (dec.).

Anal. Calcd. for $C_{22}H_{27}NO_5$: C, 68.54; H, 7.06. Found: C, 69.32; H, 7.04.

Formyltetrahydrohelenalin.—In an attempt to dehydrate tetrahydrohelenalin, 420 mg. was refluxed with 4 ml. of formic acid for four hours. After partial removal of the solvent at reduced pressure the residue was cooled and diluted with water. The product, after several recrystallizations from benzene–petroleum ether, melted at 137–138°.

Anal. Calcd. for $C_{16}H_{22}O_5$: C, 65.29; H, 7.54. Found: C, 65.24; H, 7.46.

Tetrahydrohelenalin 2,4-Dinitrophenylhydrazone.—On bringing together 100 mg. of tetrahydrohelenalin and 80 mg. of the hydrazine in the usual fashion[16] no crystals separated on cooling. The solution was allowed to evaporate in air; the orange residue was stirred with ethanol-water, filtered and washed with a little ethanol. Recrystallization from ethanol gave orange needles melting at 248° (dec.) when immersed at 242°.

Anal. Calcd. for $C_{21}H_{26}N_4O_7$: C, 56.49; H, 5.87. Found: C, 56.59; H, 6.04.

Tetrahydrohelenalin Oxime.[17]—To a solution of 250 mg. of hydroxylamine hydrochloride in 1 ml. of water and 2.5 ml. of *N* sodium hydroxide solution was added 200 mg. of tetrahydrohelenalin; introduction of 2 ml. of ethanol was necessary to dissolve the solid. After refluxing for two hours, the white material which separated on removal of ethanol was recrystallized twice from ethanol. The yield was 188 mg. of product, m. p. 185–187°.

Anal. Calcd. for $C_{15}H_{23}NO_4$: C, 64.02; H, 8.24; N, 4.98. Found: C, 64.25; H, 8.42; N, 5.18.

Piperonylidene Derivative of Tetrahydrohelenalin.—A solution of 100 mg. of tetrahydrohelenalin and 62 mg. of piperonal in 2 ml. of absolute ethanol was treated with ethanolic hydrogen chloride. After eighteen hours the yellow crystals weighing 89 mg. which had separated from the deep purple solution, were filtered and washed with a little ethanol. They were remarkably insoluble in all common organic solvents and, after recrystallization from methyl cellosolve, melted at 257–258°.

Anal. Calcd. for $C_{23}H_{26}O_6$: C, 69.33; H, 6.58. Found: C, 69.04; H, 6.74.

Reaction of tetrahydrohelenalin with two equivalents of piperonal also gave the monopiperonylidene derivative.

Anisylidene Derivative of Tetrahydrohelenalin.—Reaction of anisaldehyde with 100 mg. of tetrahydrohelenalin in the same manner gave 137 mg. of light-yellow crystals which after recrystallization from methyl cellosolve–ethanol melted at 224°.

Anal. Calcd. for $C_{23}H_{28}O_5$: C, 71.85; H, 7.34. Found: C, 71.94; H, 7.56.

Dehydrotetrahydrohelenalin.—A solution of 200 mg. of chromic anhydride in 1 ml. of acetic acid and 0.4 ml. of water was added slowly to a solution of 200 mg. of tetrahydrohelenalin in 4 ml. of acetic acid. The mixture was warmed on the steam-bath after every addition until the color had changed. Dilution with water gave 128 mg. of slightly-colored crystals which were washed thoroughly with water and recrystallized from ethanol–water. The shiny white plates did not reduce Tollens reagent or Fehling solution and melted at 213–214°.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.11; H, 7.75.

This compound was also obtained in very low yield by the oxidation of hexahydrohelenalin with chromic oxide. The ultraviolet spectrum contained the expected carbonyl absorption at 293 mμ (ϵ_{max} = 98) and a new band at 218 mμ (ϵ = 1700). Bands in the double bond region of the infrared spectrum included absorptions at 1782 (lactone), 1750 (old keto) and 1697 $cm.^{-1}$ (new keto group); the —OH frequency was absent.

Dehydrotetrahydrohelenalin Dinitrophenylhydrazone.—From 105 mg. of the ketone and 80 mg. of 2,4-dinitrophenylhydrazine, 147 mg. of crude product was obtained. The golden-yellow crystals, after recrystallization from ethanol, melted at 246–247° (dec.).

Anal. Calcd. for $C_{21}H_{24}N_4O_7$: C, 56.74; H, 5.44. Found: C, 57.15; H, 5.49.

Dehydrotetrahydrohelenalin Semicarbazone.—A solution of 100 mg. of the diketone, 200 mg. of semicarbazide hydrochloride and 300 mg. of sodium acetate in 4 ml. of 50% ethanol was refluxed for two hours. Removal of the ethanol caused separation of 98 mg. of white solid which was recrystallized by dissolving in a large volume of hot ethanol, diluting with water, concentrating and cooling. The white prisms became yellow above 240° and decomposed at 247–248°. The carbon content was somewhat low even after prolonged drying, possibly due to the presence of a small amount of disemicarbazone.

Anal. Calcd. for $C_{17}H_{26}N_6O_4$: C, 59.80; H, 7.21; N, 13.08. Found: C, 58.99; H, 7.42; N, 13.23.

The oxime, prepared by refluxing the diketone with hydroxylamine hydrochloride in pyridine-ethanol did not melt sharply; analysis indicated the possibility of a mixture of mono- and dioxime.

Bromotetrahydrohelenalin.—A solution of 510 mg. of bromine in 10 ml. of chloroform was added to 200 mg. of tetrahydrohelenalin dissolved in 1 ml. of chloroform until the color was permanent. A little warming was required to continue the reaction after the addition of the first few drops. The viscous residue obtained on evaporation of the solvent solidified on triturating with petroleum ether (b. p. 30–60°) and weighed 265 mg. After several recrystallizations from benzene, the silky white needles melted at 185.5°.

Anal. Calcd. for $C_{15}H_{21}O_4Br_2$: C, 52.18; H, 6.13. Found: C, 52.42; H, 5.98.

The ultraviolet spectrum had a single peak at 317 mμ (ϵ = 105). The greater intensity and the shift toward longer wave length is typical of an α-halogen substituted ketone.[18]

Bromodehydrotetrahydrohelenalin.—Oxidation of 200 mg. of the bromoketone with 100 mg. of chromic anhydride gave 143 mg. of crude product. On recrystallization from benzene the shiny white prisms melted at 175.5°. The infrared spectrum showed disappearance of the —OH frequency and a new ketone band at 1700 $cm.^{-1}$.

Anal. Calcd. for $C_{15}H_{19}O_4Br$: C, 52.49; H, 5.58. Found: C, 52.40; H, 5.75.

---

[16] Shriner and Fuson, "The Systematic Identification of Organic Compounds," 2nd ed., 1940, p. 143.

[17] This experiment was carried out by B. F. Aycock and A. E. Senear.

[18] Herold, *Z. physik. Chem.*, **B18**, 265 (1932); Lowry and Lishmund, *J. Chem. Soc.*, 1313 (1935); Barr, Heilbron, Jones and Spring, *ibid.*, 334 (1938).

Dibromotetrahydrohelenalin.—The procedure followed was identical to that in the preparation of the monobromo derivative. Addition of bromine to 2 g. of tetrahydrohelenalin was continued until the solution was light red; the equivalent of almost two moles of bromine was required. The solvent was removed in an air stream and the residual solid, weighing 3.2 g., was triturated with petroleum ether (b. p. 30–60°), filtered and washed with petroleum ether. On recrystallization from 60 ml. of boiling benzene, 1.7 g. of fairly pure bromotetrahydrohelenalin, m. p. 175–178°, separated. The filtrate was concentrated and allowed to cool; the precipitate weighed 0.7 g. The mother liquors yielded an additional 0.45 g. of lower purity. Recrystallization of the first fraction from 10 ml. of benzene gave small white needles which melted at 203° when immersed at 200°.

Anal. Calcd. for $C_{15}H_{20}O_4Br_2$: C, 42.47; H, 4.75. Found: C, 42.73; H, 5.02.

The ultraviolet spectrum (λ_{max} = 316 mμ, ϵ_{max} = 86) was similar to that of the monobromo derivative. Oxidation of 213 mg. of dibromotetrahydrohelenalin with chromic anhydride yielded 196 mg. of product, which, after recrystallization from ethanol, melted at 187° (dec.). The carbon and hydrogen values obtained by analysis of two separate preparations were consistently high.

Anal. Calcd. for $C_{15}H_{18}O_4Br_2$: C, 42.68; H, 4.30. Found: C, 43.49, 43.53; H, 4.69, 4.73.

Dihydrohelenalin.—A solution of 524 mg. of helenalin in 30 ml. of purified ethyl acetate was shaken with 30 mg. of prereduced platinum oxide until a quantity of hydrogen equivalent to one mole had been absorbed. Since part of the product had separated, the solution was warmed, filtered, concentrated to 10 ml. and chilled. The weight of crude dihydrohelenalin was 264 mg. An additional 87 mg. was obtained by concentration of the filtrate to 5 ml. Recrystallization from 10 ml. of ethyl acetate gave pure crystals, m. p. 224–225°. The mother liquors yielded lower-melting solids which were utilized in the preparation of tetrahydrohelenalin.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.13; H, 7.63. Found: C, 68.43; H, 7.88; C-methyl, 2.20 moles.

The double bond region of the infrared spectrum contained bands at 1748 (lactone), 1716 (conjugated C=O) and 1578 cm.$^{-1}$ (conjugated C=C). Further reduction of dihydrohelenalin gave tetrahydrohelenalin. Ozonolysis of 1 g. of crude dihydrohelenalin, m. p. 216–223°, was carried out in the manner previously described.[2] Treatment of the distillate with a saturated solution of methone in water precipitated 9 mg. (0.8%) of the methone derivative of formaldehyde, possibly due to the presence of a small amount of unreduced helenalin. No neutral fraction was obtained; the acid fraction was a non-crystallizable gum.

Acetyldihydrohelenalin.—The acetylation of 200 mg. of dihydrohelenalin in the usual manner yielded 219 mg. of white solid after partial removal of the solvents. The product, after recrystallization from water, melted at 167°.

Anal. Calcd. for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.56; H, 7.41.

Dibromodihydrohelenalin.—Bromination of 100 mg. of dihydrohelenalin in acetic acid yielded 23 mg. of product. It was recrystallized repeatedly from ethanol-water. Extensive foaming and decomposition interfered with the exact determination of the melting point which was in the neighborhood of 110°. The infrared spectrum contained no band corresponding to conjugated C=C; the ketone frequency was at 1748 cm.$^{-1}$.

Anal. Calcd. for $C_{15}H_{20}O_4Br_2$: C, 42.47; H, 4.75. Found: C, 42.38; H, 4.81.

Hexahydrohelenalin.—A solution of 3 g. of helenalin in 20 ml. of ethanol was reduced with Raney nickel at 100° and 1500 lb. pressure. The hydrogen uptake corresponded to approximately three moles. The material obtained on removal of the solvent at reduced pressure was triturated with petroleum ether (b. p. 30–60°) and became glassy on being kept in a vacuum desiccator. For purification a small amount was placed in a vacuum sublimation apparatus heated in an oil-bath. The product distilled at a bath temperature above 175° (0.1 mm.). It could also be prepared by the high-pressure reduction of tetrahydrohelenalin.

Anal. Calcd. for $C_{15}H_{24}O_4$: C, 67.15; H, 9.02. Found: C, 67.10; H, 9.02.

Reduction of helenalin in ethanol with copper chromite yielded hexahydrohelenalin, but when the reduction was carried out in dioxane at 250° and 4000 p. s. i. the viscous product no longer contained a lactone group. Analysis suggested the formula $C_{14}H_{26}O_2$, indicating partial hydrogenolysis. It could not be dehydrated by fusion with potassium acid sulfate. Selenium dehydrogenation at 330–360° did not yield hydrocarbons, but a mixture of oxygenated compounds.

Attempted reduction of hexahydrohelenalin with phosphorus, potassium iodide and phosphoric acid by the method of Miescher and Billeter[19] yielded an oily acid. It could not be purified by distillation or conversion to crystalline derivatives. Treatment with diazomethane gave a small yield of a methyl ester of formula $C_{15}H_{22}O_2$ or $C_{16}H_{24}O_2$. The neutral fraction consisted in part of a hydrocarbon of formula $C_{15}H_{24}$ and traces of a blue azulene.

Phenylurethan of Hexahydrohelenalin.—A solution of 270 mg. of hexahydrohelenalin in 3 ml. of benzene was refluxed for two hours with 0.2 ml. of phenyl isocyanate. On cooling and diluting with petroleum ether (b. p. 30–60°), a white viscous precipitate appeared. It solidified on rubbing, was washed with petroleum ether and extracted with three 8-ml. portions of hot carbon tetrachloride. The insoluble material weighing 53 mg. was extracted with two 10-ml. portions of hot benzene. Dilution of the benzene extract with petroleum ether precipitated white crystals which decomposed at 248–250°. Lack of material prevented further purification. The analysis showed the presence of a monophenylurethan; the infrared spectrum revealed that a second hydroxyl group had not reacted.

Anal. Calcd. for $C_{22}H_{29}O_5N$: C, 68.21; H, 7.54; N, 3.62. Found: C, 68.07; H, 7.77; N, 3.94.

Concentration of the carbon tetrachloride extracts yielded 132 mg. of white solid, m. p. 79–95°. The spectrum suggested that this was a mixture of phenylurethans.

Dehydrogenation of Hexahydrohelenalin.—Hexahydrohelenalin, prepared by catalytic reduction of 25 g. of helenalin, was heated with 12 g. of 10% palladium charcoal at a bath temperature of 310–320° for twenty hours and at 360° for two hours. The mixture refluxed briskly and the formation of a blue color was noted. The dark-green ether extract was filtered, dried, concentrated on the steam-bath and distilled in a vacuum until the distillate no longer showed a blue color. Two fractions were collected, fraction A, approximately 1 ml., boiling at 60–90° (0.02 mm.), fraction B, much more viscous and containing the major portion of the azulene, boiling at 105–135° (0.06 mm.). The high-boiling residue was considerable and consisted primarily of undehydrogenated hexahydrohelenalin.

Each fraction was taken up in petroleum ether and the azulene was extracted with 85% phosphoric acid in the usual way.[20] The weight of crude azulene was 0.33 g. Half of this was distilled in a vacuum; 45 mg. of a deep-blue viscous liquid was obtained, b. p. 120–140° (0.2 mm.). A solution of 7.3 mg. of this material in 10 ml. of 95% ethanol was used for absorption measurements. The remainder was converted to the trinitrobenzolate[20] After three recrystallizations from ethanol, 24 mg. of fine violet-black needles, m. p. 132–133°, was obtained.

Anal. Calcd. for $C_{21}H_{21}N_3O_6$: C, 61.34; H, 5.14; N, 10.21. Found: C, 61.44; H, 5.32; N, 10.39; C-methyl, 2.18 moles.

The mother liquors were combined, concentrated to

---

[19] Miescher and Billeter, *Helv. Chim. Acta*, **22**, 601 (1939).

[20] Plattner and Pfau, *ibid.*, **19**, 858 (1936).

small volume and diluted with cyclohexane. The azulene was liberated by chromatographic adsorption on alumina and eluted with cyclohexane. The trotylate, prepared from the eluate, was recrystallized twice from ethanol. The violet-black needles melted at 58–59°. The azulene was again liberated by chromatographic adsorption; the picrate, black needles, melted at 96–98°. The amount of this derivative was not sufficient to permit recrystallization.

The ultraviolet spectrum of 5.6 mg. of the azulene in 5 ml. of *n*-pentane, after regeneration from the picrate and its mother liquors, is reproduced in Fig. 1. The extinction coefficients were larger and the bands somewhat sharper than in the spectrum taken before conversion to the trinitrobenzolate, thus indicating slightly greater purity. The only significant difference was the appearance of a new band at 740 mμ which had not been observed previously. Other faint bands in the visible spectrum (not shown) occurred at 700–710, 665–670, 605–615 and 560 mμ. Maxima and extinction coefficients in the ultraviolet range are tabulated.

mμ	log ε	mμ	log ε
245	4.44	338	3.57
285	4.67	342	3.61
289	4.64	351	3.68
306	4.04	369	3.43

The non-azulenic portion of fraction A weighed 0.64 g. and gave a deep-blue color on treatment with a dilute solution of bromine in chloroform.[6] Distillation at 70–80° (0.5 mm.) gave a colorless liquid which had the analysis of a sesquiterpene. It did not yield a picrate or trinitrobenzolate.

Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. *Found*: C, 87.99; H, 12.00.

The non-azulenic portion of fraction B weighed 1.27 g. and gave a deep purple color on treatment with a dilute solution of bromine in chloroform. Vacuum distillation did not yield fractions boiling within a small temperature range.

Summary

The catalytic reduction of helenalin has been studied. Two new products, dihydrohelenalin and hexahydrohelenalin, have been obtained in addition to the previously known tetrahydrohelenalin. Dihydrohelenalin retains the α,β-unsaturated ketone system of helenalin. Hexahydrohelenalin is completely saturated and contains a hydroxyl in place of the ketone group. The reactions of these compounds have been studied.

The hydroxyl group of helenalin has been shown to be secondary.

Dehydrogenation of hexahydrohelenalin with palladized charcoal yields a blue azulene of formula $C_{15}H_{18}$. Spectroscopic evidence suggests the presence of alkyl substituents in at least positions 1 and 4 of the azulene nucleus. The bearing of these results on the structure of helenalin is discussed.

URBANA, ILLINOIS RECEIVED FEBRUARY 11, 1949

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

On the Stereochemistry of Yohimbine[1]

BY BERNHARD WITKOP

In the present paper, a method is shown by which yohimbine (I) can be degraded to an optically active N-methyl-*trans*-decahydroisoquinoline. The identification of this base with synthetic resolved material subsequently establishes the stereochemical relationship of carbon atoms 15 and 20 in yohimbine.

By treatment of yohimbic acid (II) with thallous oxide, a base, $C_{19}H_{24}N_2$, has been obtained,[2] for which the name desoxyyohimbol and the tentative structure (III) was proposed. It has now been found that this compound gives strong positive Hopkins–Cole and Ehrlich reactions, as well as chromoisomeric picrates (yellow → red). Thus ring C has been opened between carbon atoms 2 and 3. Since "desoxyyohimbol" is accordingly tetracyclic, one double bond must be present. And, in fact, "desoxyyohimbol" is readily hydrogenated to a dihydro derivative, $C_{19}H_{26}N_2$ (V). It is likely that this double bond arises directly from the dehydration of the secondary alcohol function of yohimbine (*cf.* apoyohimbine), and the double bond may be placed provisionally in the 5,6-positions of the hydrogenated isoquinoline nucleus (IV). The inappropriate name "desoxyyohimbol" should be corrected to *chano*desoxyyohimbol.

Confirmation of the formulas (IV) and (V) is obtained through the Hofmann degradation which, in case of the latter, leads to an N-methyldecahydroisoquinoline (yield 79%) isolated as the picrate, m. p. 234–237°. On admixture with synthetic N-methyl-*trans*-decahydroisoquinoline picrate (m. p. 234–237°), obtained from the mixture of *cis*- and *trans*-decahydroisoquinolines by selective dehydrogenation with palladium,[3] no depression was observed. Although these observations offer strong evidence for the *trans* configuration of I, the proof is only conclusive if VI is optically active showing that the configuration of 15,20-atoms was not altered during the degradative process. This was indeed found to be the case. The hydrochloride of VI in alcoholic solution exhibited a small but distinct dextrorotation (1.4°), proving that none of the three degradative operations, *viz.*, distillation with thallous oxide

---

(1) Presented in part before the Division of Organic Chemistry of the American Chemical Society at the Chicago meeting, April, 1948.

(2) Witkop, *Ann.*, **554**, 83 (1943).

(3) Witkop, THIS JOURNAL, **70**, 2617 (1948).