Experimental Part

Reduction of Pentaacetyl-keto-sorbose.—Five grams of powdered pentaacetyl-keto-sorbose, prepared according to the procedure of Schlubach and Vorwerk,[3] and 0.2 g. of platinum catalyst[8] were suspended in 300 cc. of absolute ether and shaken with hydrogen under four atmospheres' absolute pressure for two and one-half hours. During this time all of the pentaacetate dissolved and the material in solution was devoid of action toward boiling Fehling's solution. The ether solution was filtered free of platinum and evaporated to a sirup *in vacuo*. The residue was dissolved in 40 cc. of acetic anhydride containing 0.5 g. of fused zinc chloride, and the solution was kept at 50° for one and one-half hours. After cooling, this was stirred for one hour with an equal volume of cold water and poured into an excess of saturated sodium bicarbonate solution, whereupon the acetylated alcohols separated as a white powder. The whole was extracted several times with chloroform, the extracts united, dried with calcium chloride, filtered, and evaporated *in vacuo* to a semicrystalline mass. This was dissolved in 300 cc. of boiling ether. On cooling to room temperature, 1.9 g. of large hexagonal plates separated. Concentration of the solution brought the total yield of pure hexaacetyl-*l*-iditol[9] to 3.1 g.; m. p. 121.5° and specific rotation −25.5°. The mother liquor was evaporated *in vacuo* to a sticky mass. This was taken up in *ca.* 10 cc. of hot alcohol and placed in the ice box where 1.9 g. of hexaacetyl-*d*-sorbitol[4] separated. After one recrystallization from alcohol the substance showed the correct m. p. of 99° and specific rotation 10°.

Acetylation of Tetraacetylsorbose.—Two grams of sorbose tetraacetate was dissolved in 10 cc. of distilled acetic anhydride containing 0.1 g. of fused zinc chloride, and the mixture was kept at 50° for one hour. After cooling, the solution was stirred with 10 cc. of cold water for one and one-half hours and poured into an excess of saturated sodium bicarbonate solution. The whole was extracted three times with chloroform, the extracts combined, dried with calcium chloride, filtered, and evaporated to dryness *in vacuo*. The residue was dissolved in a little hot alcohol and placed in the ice box. The solution deposited 1.5 g. of crystalline material which was identified as pentaacetyl-keto-sorbose by its melting point and mixed melting point.

In another experiment, 0.5 g. of tetraacetylsorbose was dissolved in 10 cc. of acetic anhydride containing 0.1 g. of fused zinc chloride and left at room temperature for one day. On working up the mixture as above, 0.3 g. of pentaacetyl-keto-sorbose was obtained.

Summary

l-Sorbose pentaacetate is a derivative of the open chain sorbose since, on reduction and subsequent acetylation, crystalline hexaacetyl-*d*-sorbitol and hexaacetyl-*l*-iditol are obtained.

Pentaacetyl-keto-sorbose may be prepared by the acetylation of tetraacetylsorbose with acetic anhydride and fused zinc chloride.

Observations, reported in the literature, concerning certain properties of tetraacetylsorbose cannot be confirmed.

PRINCETON, N. J.

RECEIVED JUNE 7, 1937

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(8) Adams, Vorhees and Shriner, "Organic Syntheses," John Wiley and Sons, Inc., New York, 1928, Vol. VIII, p. 92.

(9) Bertrand, *Bull. soc. chim.*, [3] **33**, 1073 (1906).

[CONTRIBUTION FROM THE PATHOLOGICAL DIVISION, BUREAU OF ANIMAL INDUSTRY]

Lupine Studies. XII. The Alkaloids of *Lupinus laxus* Rydb.

BY JAMES FITTON COUCH

Lupinus laxus was originally reported from Wyoming and Montana by Rydberg[1] as a new species closely related to *L. laxiflorus*. The material used in the present study was collected at Fish Lake in south central Utah in 1932 and 1934. The first lot was identified by C. P. Smith as *L. laxus* who, however, named specimens of the second collection *L. leucopsis* var. ined. An inquiry addressed to Doctor Smith whether these two names are considered synonymous has remained unanswered. We, therefore, are using the published name in preference to the second identification.

Chemical examination has revealed the presence of four alkaloids in this plant, sparteine, *d*-lupanine, trilupine and a base isomeric but not identical with hydroxylupanine isolated from *L. polyphyllus* by Bergh.[2] The fourth base melts at nearly the same temperature as anhydrous hydroxylupanine but differs in that it does not crystallize with water as does Bergh's alkaloid and the optical rotation is twice as large. The quantity obtained from the plant was too small to permit a thorough investigation and the substance is only provisionally accepted as a new alkaloid pending further study.

The isolation, from this species, of trilupine which was first found in *L. barbiger*[3] is of interest in that it is here associated with *d*-lupanine of which it is the diamino oxide while no *d*-lupanine could be detected in *L. barbiger*. It was found

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(1) P. A. Rydberg, *Bul. Torr. Club*, 258, 1903.

(2) G. F. Bergh, *Arch. Pharm.*, **242**, 416–440 (1904).

(3) J. F. Couch, THIS JOURNAL, **58**, 1926 (1936).

Fraction	B. p., °C.	*P*, mm.	Wt., g.	n^{25}_{D}	$(a)^{22.5}_{D}$ in alcohol	
A	to 175	4	25.3	1.5316	29.36	Limpid chrome-yellow oil of burnt wool odor and greenish fluorescence
B	175–205	3	28	1.5440	70.99	Thick yellow oil of burnt wool odor and greenish fluorescence
C	205–220	3	37.1	1.5454	83.06	Viscous orange oil of burnt wool odor and greenish fluorescence
D	220–245	3	17.6			Viscous orange oil that solidified in the receiver
E	Residue		26.5			Dark red tar

possible to separate the three alkaloids by selective precipitation from acetone solution; sparteine could be removed as the disulfate, *d*-lupanine as the dihydrochloride and trilupine could be recovered from the residual solution.

Experimental

Material.—Two lots of plants collected at different times by A. B. Clawson at Fish Lake, Utah, were examined separately. The first was collected on August 14, 1932, and consisted of the entire above-ground parts of the plant in flower. The second was collected on July 12 and August 9, 1934, and consisted of similar plants in all stages of maturity. No qualitatively significant differences were found between the two lots. The second lot contained 12.66% moisture.

Extraction of the Alkaloids.—The dried plants were ground to a coarse powder, extracted with alcohol and the alkaloids recovered from the alcoholic extract by the process already described.[4] Of lot 1, 18.73 kg. yielded 411 g. or 2.19%, and 23.37 kg. of lot 2 yielded 774 g. or 2.93% of crude alkaloids.

Fractionation of the Alkaloids.—The crude alkaloids yielded nothing to petroleum ether; 385 g. was then dissolved in 100 cc. of alcohol and 4 volumes of ether was added which precipitated a sirup. The solution was poured off and the sirup was exhaustively extracted with ether. The solvent was distilled from the combined extracts and the residue was then thoroughly extracted with ether. On distilling the solvent and removing the last traces of ether by warming the residue under a vacuum of 12 mm., there remained 268.6 g. of a brownish alkaline sirup (n^{25}_{D} 1.5485) from which nothing could be made to crystallize. This was Fraction AA.

The portions of the original crude alkaloidal mixture that were insoluble in ether were mixed with 50 cc. of alcohol and treated with 300 cc. of ethyl acetate. The solution was decanted and the undissolved residue was extracted with ethyl acetate. The mixed solutions were freed from solvent by distillation and left 64 g. of brownish alkaline sirup (n^{26}_{D} 1.5292). This was Fraction AB.

The undissolved residue when freed of solvent weighed 27 g. and consisted for the greater part of amorphous resinous substances. This was Fraction AC.

Fractionation of the Ether-Soluble Alkaloids.—The sirup referred to as Fraction AA and similar fractions obtained from other lots of crude alkaloid were submitted to fractional distillation under reduced pressure. Since a sharp separation cannot be effected by this means, the distillates were collected at arbitrarily chosen temperatures. A typical distillation yielded the following results. To 137 g. of ether-soluble alkaloids freed of solvent by warming under 12 mm. pressure was added 10 g. of ground glass and the mixture was distilled.

Above 220° there was much decomposition. All of the distillates gave positive tests with the modified Grant procedure.[5]

Similar fractions obtained from other lots were refractionated and the various fractions recombined and refractionated but all the products were fluid mixtures of two or three alkaloids and yielded no crystalline material on standing.

Isolation of Sparteine as Sulfate.—A fraction (123 g.) distilling at 150–175° at 5 mm., of n^{29}_{D} 1.5262, $(a)^{30}_{D}$ -2.60 in substance, and d^{25}_{4} 0.9871, was dissolved in 500 cc. of acetone and the solution was treated dropwise with an excess of freshly prepared alcoholic solution of sulfuric acid. Crystallization started within a few minutes and after cooling there was an abundant crop of crystals which was filtered by suction and washed with a mixture of alcohol (25%) and acetone (75%). The yield was 178 g., leaving unaccounted for 23.6 g. of alkaloid. Dried in a desiccator it darkened at 210° and melted at 264.5–265.5°.[6]

Anal. Calcd. for $B \cdot 2H_2SO_4$: SO_4, 44.63. Found: unheated salt, SO_4, 44.82; salt dried at 110° and slightly discolored, 45.18, 45.31.

Free Sparteine.—The sulfate (10 g.) dissolved in water was alkalized with sodium hydroxide and the oily precipitate was extracted with ether. On removing the solvent the base remained as a light yellow oil of n^{25}_{D} 1.5260 and $(a)^{25}_{D}$ $-16.3°$ (0.7107 g. in alcohol). It was positive to the modified Grant and Jorissen[7] tests.

Sparteine Methiodide.—The free base (3 g). mixed with methyl iodide (3 cc.) began to deposit crystals in half an hour. Recrystallized from alcohol–acetone and dried they melted at 237–238° and did not depress the melting point of authentic sparteine methiodide.

Anal. Calcd. for $B \cdot CH_3I$; I, 33.75. Found: I, 33.62, 33.58.

Sparteine Perchlorate.—The base dissolved in dilute perchloric acid deposited no crystals. A solution of sodium acetate was added and crystals of sparteine perchlorate were formed immediately. These were recrystallized from boiling water and dried. They melted at 170.5–172.5° and solidified quickly on cooling. Mixed with perchlorate prepared from authentic sparteine there was no depression of the melting point.

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(4) J. F. Couch, THIS JOURNAL, **56**, 2434 (1934).

(5) J. F. Couch, *Am. J. Pharm.*, **97**, 38 (1925).

(6) Melting points are corrected unless otherwise stated.

(7) Jorissen, *Ann. chim. anal.*, **16**, 412 (1911).

Sparteine hydrobromide prepared from this base melted at 194–195°.

Anal. Calcd. for $B \cdot 2HBr \cdot H_2O$: Br, 38.63. Found: Br, 38.68, 38.75.

The picrate and zinc chloride melted at 207.5 and 325°, respectively, and did not depress the melting point of the corresponding salts from authentic sparteine. The mercuric chloride recrystallized from hot 10% hydrochloric acid melted at 200° sharply.

Isolation of *d*-Lupanine as Dihydrochloride.—A fraction (92.8 g.) distilling at 200–250° at 6 mm. and of $n^{25}\mathrm{D}$ 1.5465 was dissolved in 250 cc. of acetone and 2 moles of hydrochloric acid in 75 cc. of alcohol was added. On cooling, crystals formed which were recrystallized from a mixture of alcohol (25%) and acetone (75%) and dried. They melted at 162–163° and did not depress the melting point of authentic salt. Heated at 115° they lost weight equivalent to 1 mol each of water and hydrochloric acid and the resulting monohydrochloride melted at 269–271° and did not depress the melting point of authentic salt.

Anal. Calcd. for $B \cdot 2HCl \cdot H_2O$: Cl_2, 20.95; 1 HCl and 1 H_2O, 16.06; Cl_1, 10.47; N, 8.25. Found: Cl_2, 20.84, 20.86; "moisture" 15.97; Cl_1, 10.51; N, 8.29. In water $(\alpha)^{27}\mathrm{D}$ 58.2, $l = 1$, $c = 7.8640$, $a = 4.57°$.

Free *d*-Lupanine.—Fifteen grams of the dihydrochloride in 30 cc. of water was alkalized with sodium hydroxide and the precipitated oil was extracted with ether. On evaporating the solvent the base remained as a light yellow oil, $n^{25}\mathrm{D}$ 1.5448.

Anal. Calcd. for $C_{15}H_{24}ON_2$: N, 11.28. Found: N, 11.36. In alcohol, $(\alpha)^{29}\mathrm{D}$ 80.12, $l = 1$, $c = 6.882$, $a = 5.51°$.

***d*-Lupanine Monohydrochloride.**—The residue obtained by heating the dihydrochloride to constant weight was recrystallized from alcohol as prisms melting at 129–130°, not depressing the melting point of authentic salt.

Anal. Calcd. for $B \cdot HCl \cdot 2H_2O$: H_2O, 11.07; Cl, 11.38. Found: H_2O, 11.21, 11.14; Cl, 11.11, 11.03. In water, $(\alpha)^{25}\mathrm{D}$ 55.21°, $l = 1$, $c = 2.038$, $a = 1.15°$.

d-Lupanine *d*-camphorsulfonate prepared from the base and the calcd. quantity of acid in acetone solution melted at 113–115° and did not depress the melting point of authentic salt.

Anal. Calcd. for $B \cdot C_{10}H_{16}SO_4 \cdot 2H_2O$: H_2O, 6.96; S, 6.19. Found: H_2O, 6.97; S, 6.24.

***d*-Lupanine Di-*d*-camphorsulfonate.**—A distillate (10 g.), later found to contain both sparteine and lupanine, was dissolved in 25 cc. of acetone and mixed with 10 g. of *d*-camphorsulfonic acid in 25 cc. of acetone. It deposited an abundant crop of crystals. This proved to be a mixture from which two salts could be obtained by fractional crystallization from acetone. The less soluble compound was found to be *d*-lupanine mono-*d*-camphorsulfonate; the more soluble salt was a new compound, *d*-lupanine di-*d*-camphorsulfonate. After recrystallization from acetone and drying it melted at 245–246.5°. Both camphorsulfonates are very soluble in chloroform.

Anal. Calcd. for $B \cdot 2C_{10}H_{16}SO_4$: S, 8.98. Found: S, 9.03.

***d*-Lupanine Hydriodide.**—This salt was prepared by adding potassium iodide either to the camphorsulfonate or to the monohydrochloride. It melted at 189° and did not depress the melting point of authentic salt. When dried it yielded 33.70% of iodine (calcd. for $B \cdot HI$: I, 33.74%). The picrate, gold chloride and perchlorate melted at 185, 205–206 and 211–212°, respectively.

Isolation of Trilupine.—The acetone mother liquors from which *d*-lupanine dihydrochloride had been crystallized were alkalized with solid sodium hydroxide and filtered from the precipitated salt. On removing the solvent from the filtrate a brown sirup was left which soon solidified to a mass of prisms. These were recrystallized several times from ethyl acetate, decolorized with norit and dried. The melting point was 128–129° and when mixed with trilupine from *Lupinus barbiger* the melting point was not depressed. The anhydrous base melted at 256–257°. The same alkaloid was recovered from the acetone extract of fraction D (see below).

Anal. Calcd. for $B \cdot 2H_2O$: H_2O, 11.38. Found: H_2O, 11.35, 11.57. In water $(\alpha)^{25}\mathrm{D}$ 62.64, $l = 1$, $c = 3.322$, $a = 1.73$.

The gold chloride, methiodide and picrate melted at 198.5–199.5, 129, and 180–183°, respectively.

Isolation of an Alkaloid Isomeric with Hydroxylupanine.—Fraction D of the original vacuum fractionation was dissolved out of the receiver with hot acetone. The solvent was removed and the cold residue was treated with cold acetone which dissolved out an alkaloid subsequently found to be trilupine. The undissolved residue amounted to half a gram of white crystals. These were recrystallized from hot acetone and dried in a desiccator, when they melted at 170–172° (uncorr.) and proved to be water free. A water solution allowed to evaporate in a desiccator yielded crystals that melted at 176–177° (uncorr.) and were also water free. This substance yields figures for carbon, hydrogen, and nitrogen consistent with the composition of hydroxylupanine but inconsistent in melting point, water content and optical activity with those reported for that base. It is provisionally regarded as a new substance pending further study when more material is available.

Anal. Calcd. for $C_{15}H_{24}O_2N_2$: C, 68.18; H, 9.16; N, 10.60. Found: C, 68.19; H, 9.65; N, 10.69. In water $(\alpha)^{31}\mathrm{D}$ 133.2, $l = 1$, $c = 1.432$, $a = 3.81$.

Fraction AB.—The alkaloid mixture extracted by ethyl acetate upon examination was found to contain a small amount of *d*-lupanine, much trilupine, and possibly a small amount of the hydroxylupanine-like base.

Fraction AC.—This residue consisted for the greater part of resinous matter and contained only a trace of alkaloid.

Summary

Lupinus laxus Rydb. when dried yields 2 to 3% of alkaloids which consist of sparteine, *d*-lupanine, and trilupine with a minute quantity of a fourth alkaloid isomeric with hydroxylupanine.

WASHINGTON, D. C. RECEIVED JUNE 7, 1937