the ratios of dehydration have been determined.

2. Dehydration tends to take place in such a manner that the double bond formed enters the ring when this is possible.

3. It is noted that a proton is lost from the cyclohexane ring more readily than from a methyl, ethyl or isopropyl group.

WILMINGTON, DELAWARE RECEIVED OCTOBER 28, 1939

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

Lupine Studies. XV.[1] The Alkaloids of *Lupinus sericeus* Pursh

BY JAMES FITTON COUCH

The silky lupine, *Lupinus sericeus*, occurs in the plains and canyons of the pinyon and yellow pine belts from Saskatchewan to South Dakota, Wyoming, Oregon, and Washington.[2]

A collection made by the late A. B. Clawson has been examined and found to contain two alkaloids, spathulatine previously isolated[3] and a new alkaloid now named nonalupine, $C_{15}H_{24}ON_2$, isomeric with lupanine and differing from it in important respects.

The discovery of spathulatine in another lupine presented an opportunity for a revision of the chemistry of the alkaloid, particularly in the light of new developments in our knowledge of the lupine alkaloids since spathulatine was first described. The formula then assigned to the alkaloid on the basis of analyses of the base and the mercuric iodide compound as well as the molecular weight determination is $C_{33}H_{64}O_5N_4$. This formula cannot easily be harmonized with the series of sparteine derivatives now known. The molecular weight is more than twice that of lupanine but is supported by the high melting point reported, 227° (uncor.). Moreover, the large content of hydrogen precludes a combination of structures with a sparteine skeleton and requires a largely aliphatic structure with not more than two 6-membered rings.

Analyses of both the anhydrous and the hydrated alkaloid for carbon, hydrogen, and nitrogen gave figures that agree with the previously assigned formula. The newly prepared compound with potassium iodide which is analogous to the mercuric iodide compound previously described also furnishes analytical evidence consistent with the previously assigned formula. In this study no evidence has been obtained to indicate that the formula requires revision.

The behavior of spathulatine suggests the presence of amine-oxide groups, possibly adjacent to a carbonyl group, for three of the nitrogen atoms, the function of the fourth being undetermined. This view is supported by the slight basicity of spathulatine and the inability to prepare crystalline salts with the usual acids and by its sparing solubility in acetone and ether. The formation of a compound with three molecules of potassium iodide also supports this view since compounds with one molecule of potassium iodide to each amine-oxide group are readily formed. When treated with sulfur dioxide spathulatine is converted into an unidentified base probably as a result of reduction of the amine-oxide groups.

When boiled with hydrochloric acid spathulatine is converted into an isomer of spartyrine, $C_{15}H_{24}N_2$, which is positive to the modified Grant's test.[4] This behavior indicates the probability of hydrolysis with subsequent ring closure to form the sparteine skeleton. This relates spathulatine to the other lupine alkaloids.

The other alkaloid in the plant, nonalupine, is of interest because of its non-basic character. When a solution of nonalupine and camphor-sulfonic acid is evaporated to dryness the free alkaloid may be dissolved out of the residue by ether. No salts with mineral acids have been obtained. This behavior is difficult to explain. Since the alkaloid contains two nitrogen atoms and but one oxygen atom it cannot have lost its basicity because of amine-oxide formation or because of ad-

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(1) Paper XIV, THIS JOURNAL, **61**, 3327 (1939).

(2) W. W. Eggleston in I. Tidestrom, "Flora of Utah and Nevada," *Contr. U. S. Nat. Herbarium*, **25**, 297 (1925).

(3) J. F. Couch, THIS JOURNAL, **46**, 2507 (1924). The alkaloid was isolated from a lupine collected by the writer and identified by W. W. Eggleston as *L. spathulatus* Rydb. whence the name spathulatine given to the new base. Since that time there has arisen a difference in opinion among botanists as to the proper name of the species used, I. Tidestrom (personal communication) referring it to *L. marianus* Rydb. and being confirmed by C. P. Smith. Eggleston considered *marianus* a synonym of *spathulatus* and recombined the species. Material of a species identified by C. P. Smith as *L. spathulatus* collected near Puffer's Lake, Utah, has been examined and found free from spathulatine. The alkaloid has, it appears, been misnamed since, unless there is a reversal of botanical opinion, it does not occur in *L. spathulatus*.

(4) J. F. Couch, *Am. J. Pharm.*, **97**, 36 (1925).

jacent carbonyl groups. The possibility of an oxygen bridge between the nitrogen atoms involves assumptions of structure which are unacceptable. The alkaloid is unaffected by warming with sulfur dioxide in water. It reduces potassium permanganate in neutral solution forming a crystalline compound containing two atoms of oxygen more than the parent substance. This compound which may be an amine-oxide is also unaffected by hot sulfur dioxide in water.

These alkaloids differ from octalupine found in *L. sericeus* var. *flexuosus*[5] which is considered by botanists to be only a variety of *L. sericeus*. It appears that the dissimilarities between the two forms extend to the physiological processes and are deeper than mere varietal differences.

Experimental Part

Material Used.—The plant material used was collected by A. B. Clawson in the neighborhood of Meeker, Colo., on August 24, 1934, and was identified by C. P. Smith. The plant was air-dried and shipped to Washington, D. C., for examination. It then contained 11.36% of moisture.

Isolation of the Alkaloids.—The finely ground plant (5.55 kg.) was extracted with alcohol and the alkaloids were recovered by the process previously described.[6] The yield of crude alkaloids freed of solvent was 181 g. or 3.68% of the moisture-free plant. The sirupy mass was dissolved in acetone plus 10% of alcohol, filtered from a little resin, and the solvent was distilled off. The residue solidified to a mass of prismatic crystals embedded in a thick brownish sirup. The mass was negative to the modified Grant's test for sparteine.[7] It was only slightly soluble in ether.

Isolation of Spathulatine.—The alkaloidal mixture was treated with cold acetone which dissolved the sirup, leaving most of the crystals undissolved. These were recrystallized several times from hot acetone plus a little norit and then melted constantly at 233–234°.[8] Mixture with spathulatine from *Lupinus marianus* caused no change in the melting point. A sample was dried at 110° to constant weight.

Anal. Calcd. for $C_{33}H_{64}O_5N_4$: C, 66.39; H, 10.82; N, 9.39. Found: C, 66.11, 66.65; H, 11.14, 10.64; N, 9.54, 9.48. Undried sample: calcd. for $C_{33}H_{64}O_5N_4 \cdot 4^1/_2H_2O$: C, 58.45; H, 10.85; H_2O, 11.96. Found: C, 58.65; H, 10.91, averages of 6 analyses; H_2O, 12.01.

The picrate forms yellow needles, quite soluble in water and melting at 182–184°. A methiodide was obtained in scanty yield as diamond-shaped crystals melting at 250–252°. It did not depress the melting point of authentic spathulatine methiodide. Spathulatine decomposed when an attempt was made to distill it under reduced pressure.

Spathulatine Potassium Iodide.—Spathulatine (3 g.) in 5 cc. of water was mixed with 2.1 g. of potassium iodide in 2 cc. of water. There was an immediate precipitation of small crystals in good yield. These were recrystallized from hot water as large prisms of m. p. 260–261°. A test portion was moistened with sulfuric acid and ashed. It evolved iodine vapor and left a residue of potassium sulfate.

Anal. Calcd. for base·3KI: I, 34.81. Found: I, 34.85, 34.82.

Spathulatine and Sulfur Dioxide.—A stream of sulfur dioxide was passed through a solution of 2 g. of spathulatine in 10 cc. of water for two days. The product was alkalized with sodium hydroxide and the milky precipitate extracted with chloroform which on evaporation left a brownish oil from which nothing crystalline could be isolated. It has not yet been identified but it has been shown not to contain spathulatine.

Spathulatine and Hydrochloric Acid.—Spathulatine (3 g.) and 10 cc. of concd. hydrochloric acid and 25 cc. of water was maintained at the boiling point for six hours until fumes of hydrogen chloride were given off. The mixture turned dark brown. On cooling nothing crystallized. The mixture was alkalized with sodium hydroxide and extracted with chloroform. The chloroform extract was a yellow oil which was strongly positive to the modified Grant's test. It formed a crystalline perchlorate of m. p. 216–217°. When mixed with *d*-lupanine perchlorate (m. p. 214–216°) the mixture melted at 194–207° like a mixture.

Anal. Calcd. for $C_{15}H_{24}N_2HClO_4$: C, 53.98; H, 7.5; N, 8.42. Found: C, 54.15, 53.85; H, 7.51, 7.80; N, 8.61, 8.34.[9] The base was very slightly levorotatory.

The new base gave a precipitate with mercuric chloride like that given by sparteine and formed a picrate which was recrystallized from hot water, m. p. 214–216°. Mixed with spartyrine picrate (m. p. 206–207°) the mixture melted at 192–202°.

Isolation of a New Lupine Alkaloid, Nonalupine.—The acetone solution containing the sirup dissolved from the original alkaloidal residue was allowed to evaporate. It solidified to a mass of crystals. It was dissolved in hot acetone and filtered from the crystals that formed on cooling. The solution was evaporated and the brownish crystalline residue was recrystallized several times from methyl isobutyl ketone plus a little norit as colorless leaflets of m. p. 91.5–92.5°, b. p. 260–270° (18 mm.). Mixed with 16-keto sparteine (m. p. 85–86°) the mixture melted from 80 to 97°. Dried to constant weight at 110° the substance softened at 219° and was completely melted at 235°. On recrystallizing from water the substance took up solvent and then melted at 90–91°, regenerating the original hydrated base.

Anal. Calcd. for $C_{15}H_{24}ON_2 \cdot 2H_2O$: C, 63.34; H. 9.97; N, 9.85; H_2O, 12.68. Found: C, 63.11, 63.23; H, 9.39, 9.88; N, 9.71, 9.68; H_2O, 12.51.[9] In alcohol, $[\alpha]^{25}_D$ $-21.3°$, $c = 5.15$, $l = 1$, $a = 2.19°$.

Nonalupine Gold Chloride.—The gold chloride double salt was recrystallized from hot water as small yellow needles, m. p. 177.5–178° decompn. It decomposed when heated to 110°.

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[5] J. F. Couch, THIS JOURNAL, **61**, 1523 (1939).

[6] J. F. Couch. *ibid.*, **56**, 2434 (1934).

[7] J. F. Couch, *Am. J. Pharm.*, **97**, 36 (1925).

[8] Melting points are corrected.

[9] The analyses were made by the Arlington Laboratories, Vera A. Conard, Director.

Anal. Calcd. for base·$2HAuCl_4·5H_2O$: Au, 38.72. Found: Au, 38.71.

Nonalupine picrate recrystallized from 50% alcohol melted at 185–186°.

Oxidation of Nonalupine.—Nonalupine (5 g.) in 600 cc. of water was treated with a saturated solution of potassium permanganate in the cold until the pink color persisted for twenty-four hours. The filtrate was extracted with chloroform, which took out an oil (2.5 g.) that slowly crystallized. Recrystallized from a mixture of chloroform and petroleum ether the substance formed long flat crystals, m. p. 168.5–170.5°. On drying in the oven it slowly volatilized, losing 28% of its weight in fifteen days at 110°. A further crop (2 g.) of the substance was obtained by extracting the precipitated manganese dioxide with alcohol.

Anal. Calcd. for $C_{15}H_{24}O_3N_2$: C, 64.24; H, 8.63; N, 9.99. Found: C, 63.99, 64.18; H, 8.45, 8.58; N, 9.84, 9.94.

The substance was recovered unchanged after warming with sulfur dioxide in water. It is readily soluble in water and the solution is neutral to test papers.

Oxynonalupine Gold Chloride.—This compound is quite soluble in water. On slow evaporation it forms small yellow needles, m. p. 238–239°. Analysis indicated a partial reduction of the base on combination with gold chloride.

Anal. Calcd. for $C_{16}H_{24}O_2N_2·HAuCl_4$: Au, 32.61. For $C_{16}H_{22}O_2N_2·HAuCl_4$: Au, 32.72. Found: Au, 32.82.

Summary

Lupinus sericeus Pursh. collected in Colorado contained when dried 3.68% of alkaloids consisting of spathulatine, previously described, and nonalupine, a new lupine alkaloid. A reinvestigation of the chemistry of spathulatine has confirmed the empirical formula previously assigned to this base. Nonalupine is not basic enough to form salts with strong acids.

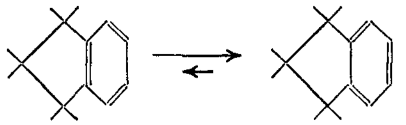
WASHINGTON, D. C. RECEIVED JANUARY 4, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

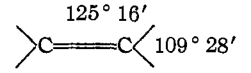
Aromatic Stabilized Double Bonds. Mills–Nixon Problem

BY RICHARD T. ARNOLD AND ROBERT L. EVANS

The fundamental stereochemical problem proposed by Mills and Nixon[1] can be summarized by the equilibrium



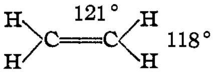
The assumptions in this interesting and clever proposal are: (a) that the structure of the olefinic double bond is represented by



and (b) that there exists a simple relation between bond types and bond angles.

Many experimental and theoretical approaches have been made toward a solution,[2,3,4] but the evidence submitted is most contradictory and leaves the problem completely unsolved. Objections have been raised to practically all of the experimental evidence thus far produced.[5]

The structure of ethylene recently has been determined, apparently with some degree of accuracy, and gives the following picture:[6,7]



Pauling and Brockway[8] have shown however that the angles in tetramethylethylene are nearly tetrahedral. These models, if true, question the validity of a simple correlation between bond angles and bond types. The foremost use of this assumption lies at the basis of the Sidgwick–Springall experiments. The structural work just completed on formaldehyde again raises a serious objection to this correlation.[9]

The wave mechanical treatment of the Mills–Nixon problem leads to the conclusion that substitution reactions (with high activation energies) cannot be used to locate stabilized aromatic double bonds. That this conclusion is in accordance with the experimental evidence is shown by the following

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[1] Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).

[2] Sidgwick and Springall, *J. Chem. Soc.*, 1532 (1936).

[3] McLeish and Campbell, *ibid.*, 1103 (1937).

[4] Sutton and Pauling, *Trans. Faraday Soc.*, **31**, 939 (1935).

[5] Brockway and Taylor, *Brit. Ann. Reports*, **34**, 219 (1937).

[6] H. W. Thompson, *Trans. Faraday Soc.*, **35**, 697 (1939).

[7] Private communication from Professor Verner Schomaker of the California Institute of Technology.

[8] Pauling and Brockway, THIS JOURNAL, **59**, 1223 (1937).

[9] Stevenson, LuValle and Schomaker, *ibid.*, **61**, 2508 (1939).