series from the unsaturated cyclic amines the peak of germicidal activity was observed in the cetylpyridinium salts. In the saturated series the peak was observed in cetylmethylpiperidinium bromide.

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[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY OF THE NATIONAL RESEARCH COUNCIL]

The Papilionaceous Alkaloids. I. *Lupinus Macounii*, Rydb.[1]

BY LÉO MARION

Until relatively recently the alkaloids of the leguminous sub-family Papilionaceae had received but little attention. Although in the course of the last fifteen years these alkaloids have formed the subject of several publications, many plants in this group have never been investigated. It is the author's purpose to undertake the study of the alkaloids contained in a number of these plants.

The first plant investigated, which forms the subject of this paper, is *Lupinus Macounii*, Rydb. It was described by Rydberg[2] and the type was collected by John Macoun in the Cypress Hills of Saskatchewan.[3] The plant was made available by Dr. R. H. F. Manske, whose generosity is here gratefully acknowledged.

L. Macounii contains three alkaloids, the major one of which is identical with rhombinine previously isolated from *Thermopsis rhombifolia*.[4] The other two alkaloids appear to be new. One is an oily base ($C_{16}H_{30}O_2N_2$) which differs from rhombinine by containing eight hydrogen atoms more. It is proposed to designate it as hydrorhombinine because it is identical with the product of the catalytic hydrogenation of rhombinine. It was isolated as its perchlorate. The third (alkaloid P1) is crystalline but present in small quantity only. Until the isolation of more of this alkaloid makes it possible to characterize it better, it will be designated by a number.

Experimental

The dried and ground plant material (4900 g.) was extracted in soxhlets with methanol and the solvent largely distilled from the combined extract which was then diluted with water, acidified with hydrochloric acid and kept on the steam-bath overnight. The mixture was cooled, filtered and the insoluble cake warmed again with dilute acid and filtered after cooling. The combined aqueous acid solution was thoroughly extracted with ether, basified with ammonia and repeatedly extracted with chloroform. The basic material recovered from the chloroform extract was dissolved in dilute hydrochloric acid, the solution filtered through charcoal, extracted with ether, basified with ammonia and repeatedly extracted with chloroform. From the combined chloroform extract, after removal of the solvent by distillation, the crude alkaloid was obtained as a thick gum. It was redissolved in dilute hydrochloric acid, the solution thoroughly extracted with ether, basified with ammonia, repeatedly extracted with ether (extract A) and then with chloroform (extract B). The ether extract A was dried over potassium hydroxide pellets and distilled to dryness. The basic residue consisted of a thick oil (9.5 g.) which was fractionated *in vacuo*. Two fractions were obtained: fraction I, b. p. 145–150° (0.3 mm.), a thick, colorless oil, wt. 3.34 g.; fraction II, b. p. 160–170° (0.3 mm.), a thick oil, wt. 2.99 g. and a residue.

Isolation of Rhombinine.—The oily fraction II could not be induced to crystallize. It was dissolved in methanol and the solution made just acid to congo by the cautious addition of 65% perchloric acid. The perchlorate which crystallized immediately was filtered and recrystallized twice from boiling methanol from which it separated as colorless needles melting at 315.[5] Admixture with rhombinine perchlorate failed to depress the melting point. A small quantity of this perchlorate was dissolved in hot water, the solution basified with ammonia, cooled and extracted repeatedly with ether. The combined ether extract was dried over pellets of potassium hydroxide and distilled to dryness on the steam-bath. The residual oil was dissolved in hot methanol and added to a solution of picric acid in methanol. On cooling a picrate separated as an oil which gradually crystallized on standing. After recrystallization from methanol–acetone, it was obtained as pale-yellow leaflets melting at 254° either alone or after admixture with rhombinine picrate.[4]

Isolation of Hydrorhombinine.—The oil obtained as fraction I (b. p. 145–150° (0.3 mm.)) was dissolved in a small volume of methanol and the solution neutralized with 65% perchloric acid. A perchlorate separated which after several crystallizations from methanol still melted over a range. It was dissolved in boiling ethyl acetate and the solution on cooling deposited a crop of crystals of rhombinine perchlorate. The mother liquor was evaporated to dryness, the residue stirred with water containing an excess of ammonia and the resulting solution extracted several times with chloroform. The combined extract was evaporated to dryness and the residue distilled *in vacuo*. The bulk distilled at 140° (0.2 mm.) as a thick, colorless oil which was dissolved in methanol and reconverted to perchlorate. The crystalline perchlorate, after several recrystallizations from methanol, consisted of small stout, colorless prisms melting at 213°, $[\alpha]_D$ −40.9° (c = 0.9 in water). Found: C, 50.67, 50.51; H, 8.10, 8.07; N, 7.38, 7.47. Calcd. for $C_{16}H_{30}O_2N_2 \cdot HClO_4$: C, 50.19; H, 8.10; N, 7.32. The base did not yield a crystalline picrate.

Isolation of Alkaloid P1.—The original mother liquor from which impure hydrorhombinine perchlorate had been obtained was diluted with water and heated on the steam-bath until the methanol had evaporated. The residual aqueous liquor was basified with ammonia and thoroughly extracted with ether. The base recovered from the ether was fractionated *in vacuo*. A small forerun distilled at 110° (0.15 mm.) while the bulk was obtained as a colorless oil, b. p. 120–122° (0.1 mm.), which crystallized on standing. It was crystallized twice from a mixture of absolute ether and petroleum ether from which it separated as small, colorless plates which sintered at 123° and melted at 126°. No perchlorate or picrate of this base could be obtained

(1) Published as *Natl. Research Council, Bull.*, No. 1356.

(2) Rydberg, *Bull. Torrey Botan. Club*, **34**, 42 (1907).

(3) It was suggested by Dr. H. A. Senn, botanist, Central Experimental Farm, Ottawa, that the plant may be identical with, or closely related to *Lupinus argenteus*, Pursh.

(4) R. H. F. Manske and L. Marion, *Can. J. Research*, **B21**, 144 (1943).

(5) All melting points given are corrected.

crystalline. Found: C, 72.14, 72.41; H, 8.96, 9.03; N, 11.30, 11.27. Calcd. for $C_{15}H_{22}ON_2$: C, 73.18; H, 8.94; N, 11.39. Insufficient material was available for further purification or characterization.

The mother liquors from fraction II, the undistilled residue and the base obtained from extract B yielded further quantities of rhombinine isolated as perchlorate.

Hydrogenation of Rhombinine.—Rhombinine (0.5 g.), obtained from the perchlorate, was dissolved in water (75 cc.) and hydrogenated in the presence of Raney nickel (*ca.* 0.2 g.) for three hours at 65° and 460 lb. and three hours at 105° and 520 lb. pressure. The content of the bomb was filtered to remove the catalyst, and potassium hydroxide (10 g.) was dissolved in the filtrate which was then repeatedly extracted with chloroform. The base recovered from the combined extract was fractionated *in vacuo*. The bulk (0.3 g.) distilled at 120–130° (0.08 mm.) as a colorless oil which was dissolved in a little methanol and the solution made just acid to congo with 65% perchloric acid. The crystalline perchlorate which separated was recrystallized once from hot methanol from which it separated on cooling as clusters of small, colorless, stout prisms melting at 213° either alone or after admixture with the perchlorate of naturally occurring hydrorhombinine $[\alpha]_D$ −40.3° (*c* = 1.06 in water). Calcd. for $C_{16}H_{30}O_2N_2 \cdot HClO_4$: N, 7.32. Found: N, 7.35.

Summary

1. *Lupinus Macounii*, Rydb., has been shown to contain three alkaloids, the main one of which is identical with rhombinine, previously isolated from *Thermopsis rhombifolia*.

2. The second alkaloid, hydrorhombinine, is identical with the product of the catalytic hydrogenation of rhombinine.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

The Acylation and Carbethoxylation of Nitriles in the Presence of Sodium Amide[1]

BY ROBERT LEVINE[2] AND CHARLES R. HAUSER

In the presence of the amide ion, nitriles having α-hydrogen may undergo two different types of reaction. One involves the addition of the amide ion to the nitrile group to form the amidine (as an anion), while the other consists in the removal of the α-hydrogen of the nitrile to form the nitrile anion, which is the reactive intermediate in carbon-carbon condensations such as the acylation, alkylation or self-condensation of nitriles. These two courses of reaction may be represented, thus

$$RCH_2C{\equiv}N + Na^+NH_2^- \longrightarrow \begin{cases} RCH_2C{=}N^-Na^+ \text{ or } RCH{=}C{=}NH \\ \quad\quad NH_2 \qquad\qquad\quad HN^-Na^+ \\ (RCHCN)^-Na^+ + NH_3 \end{cases}$$

Phenylacetonitrile forms the nitrile anion apparently exclusively but acetonitrile and especially higher aliphatic nitriles may form the amidine in addition to the nitrile anion.[3] However, even diethylacetonitrile, in which the α-hydrogen is relatively unreactive, appears to be converted to the nitrile anion since, under certain conditions, it may be alkylated with allyl chloride to form diethylallylacetonitrile[4]; in the absence of the alkyl halide, the corresponding amidine is obtained in good yield.[4]

In the present investigation the anions of phenylacetonitrile and acetonitrile, prepared by means of sodium amide in ether suspension, have been acylated with ordinary esters to form β-keto nitriles and carbethoxylated with diethyl carbonate to form α-cyano esters. The products and yields are listed in Table I. These reactions may be illustrated with phenylacetonitrile, thus

$$RCO_2C_2H_5 + (C_6H_5CHCN)^-Na^+ \longrightarrow RCOCH(C_6H_5)CN$$

$$C_2H_5OCO_2C_2H_5 + (C_6H_5CHCN)^-Na^+ \longrightarrow C_6H_5CH(CN)CO_2C_2H_5$$

It can be seen from Table I that the yields are good with phenylacetonitrile and fairly good with acetonitrile.[5] As in the acylation[6] or carbethoxylation[7] of ketones the presence of excess sodium amide improves the yield (based on the nitrile). An attempt to carbethoxylate caprylonitrile has failed. Apparently, the corresponding amidine was formed, since caprylamide, a hydrolysis product,[3] was obtained from the aqueous acid solution.

Earlier workers have reported the carbethoxylation,[8] acetylation[9] and propionylation[9] of phenylacetonitrile in the presence of a slight excess of sodium amide. We confirmed their yield for the carbethoxylation but were able to approach their high yield of 70% for acetylation only when we used an extra equivalent of sodium amide. We were able even with this extra equivalent to obtain only a 60% yield instead of their 75% yield for the propionylation.

Sodium amide appears to be as good as or superior to sodium ethoxide for the acylation or carbethoxylation of phenylacetonitrile or acetonitrile, although only the latter base (or sodium) has been satisfactory with higher aliphatic ni-

(1) Paper XXXIV on "Condensations"; paper XXXIII, THIS JOURNAL, **68**, 672 (1946)

(2) Present address: Mathieson Alkali Works, Niagara Falls, New York.

(3) See especially Bergstrom and Fernelius, *Chem. Rev.*, **12**, 136–138 (1933); Shriner and Neumann, *ibid.*, **35**, 359 (1944).

(4) Ziegler and Ohlinger, *Ann.*, **495**, 84 (1932).

(5) Propionyl acetonitrile, from ethyl propionate and acetonitrile, has been alcoholyzed to ethyl propionylacetate in 60% yield by the method described previously for other β-keto nitriles (ref. 12, 13, 14). It was hoped that these reactions would furnish a satisfactory method for the preparation of this β-keto ester but the over-all yield from acetonitrile has been only 24%.

(6) Adams and Hauser, THIS JOURNAL, **66**, 1220 (1944).

(7) Levine and Hauser, *ibid.*, **66**, 1768 (1944).

(8) Nelson and Cretcher, *ibid.*, **50**, 2758 (1928).

(9) Bodroux, *Bull. soc. chim.*, [4] **7**, 848 (1910).