THE PAPILIONACEOUS ALKALOIDS

XV. THE STRUCTURE AND THE PARTIAL SYNTHESIS OF RHOMBIFOLINE[1]

By William F. Cockburn[2] and Léo Marion

ABSTRACT

Rhombifoline is isomeric with thermopsine and anagyrine, and, like both these alkaloids, contains an α-pyridone ring. It can be dealkylated to cytisine, and, on catalytic hydrogenation, yields octahydrodesoxyrhombifoline, which is identical with hexahydrodesoxy-N-(*n*-butyl)-cytisine, the hydrogenation product of N-(*n*-butyl)-cytisine. The results of the hydrogenation thus indicate that the molecule of rhombifoline contains a third double bond, which is shown by its infrared spectrum to be located at a terminal methylene group. Rhombifoline is therefore N-(but-3-enyl)-cytisine, a conclusion which was confirmed by the partial synthesis of the alkaloid from cytisine.

Rhombifoline occurs in *Thermopsis rhombifolia* (Nutt.) Richards along with 3-methoxypyridine, cytisine, N-methylcytisine, *l*-thermopsine, and anagyrine (6). Its formula was originally reported as $C_{15}H_{20}O_2N_2$, but reanalysis of its derivatives now shows that this should be corrected to $C_{15}H_{20}ON_2$, making the alkaloid isomeric with thermopsine and anagyrine. Like the latter, rhombifoline distilled as a thick, almost colorless oil, which failed, however, to give consistent results on repeated analysis. The above formula was derived from numerous analyses of the hydrochloride, perchlorate, picrate, and chloroplatinate. The homogeneity of the base was tested by chromatography, but no separation was achieved. It is apparently susceptible to air oxidation, however, since a sample of the base which has been allowed to stand in air several days darkens in color, and does not readily form a perchlorate.

Although there are two nitrogen atoms in the molecule, rhombifoline behaves as a monoacidic base towards most salt-forming acids; potentiometric titration of the perchlorate with sodium hydroxide solution shows only one inflection in the neutralization curve, giving a pK value of 7, and a molecular weight of 325 for the perchlorate. In addition, the single oxygen atom is neutral, exhibiting neither ketonic nor hydroxylic reactions, which suggests that it is combined with the neutral nitrogen atom in a lactam grouping. This is confirmed by the infrared spectrum of a chloroform solution of the base, which shows a strong carbonyl peak at 1651 cm.$^{-1}$, with smaller peaks at 1565 and 1552 cm.$^{-1}$, which is typical of α-pyridones (7, 1) and no band in the NH and OH region (Fig. 1). The presence of an α-pyridone ring is further confirmed by examination of the infrared spectrum of the product obtained by hydrogenation of the alkaloid with Adams' catalyst in glacial acetic acid, which shows only a carbonyl peak at 1611 cm.$^{-1}$, typical of α-piperidones (7, 1). The fact that rhombifoline gives a red-brown color with aqueous ferric chloride also indicates the presence of such a ring.

[1] *Manuscript received September 28, 1951.*
Contribution from the Division of Chemistry, National Research Council, Ottawa, Canada. Issued as N.R.C. No. 2631.
[2] *National Research Council of Canada Postdoctorate Fellow (1949-1951).*

A preliminary examination of rhombifoline by chemical methods gave little information as to the structure of the remainder of the molecule. With bromine in carbon tetrachloride, a solid perbromide was formed, which gradually evolved bromine on standing, leaving a red gum which could not be purified. No reaction was obtained with acetic anhydride in the presence of either sulphuric acid or pyridine, the alkaloid being recovered unchanged. A similar result was obtained by refluxing with alkaline ferricyanide solution. With neutral permanganate in acetone, however, after an initial period of sluggish

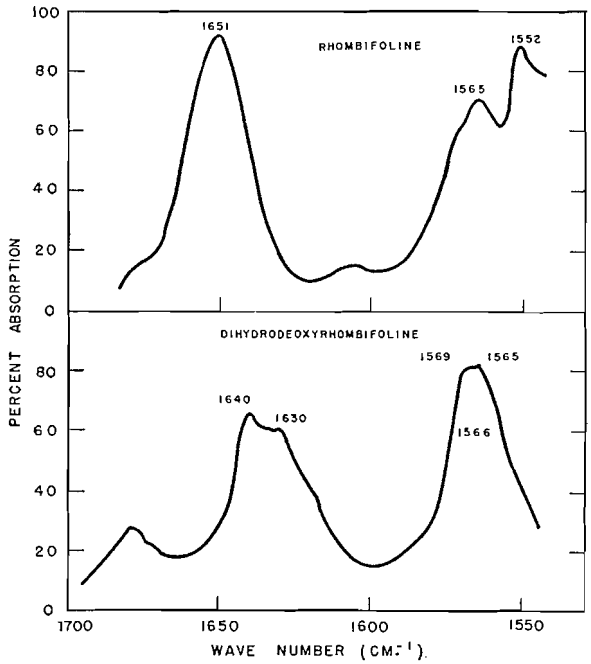


Fig. 1. Infrared spectra of chloroform solutions of the bases, using a calcium fluoride prism. Concentration of rhombifoline 3 mgm. per ml. Concentration of dihydrodesoxyrhombifoline 10 mgm. per ml.

reaction, extensive oxidation took place, and no identifiable products were isolated. Attempts to form a methiodide by heating with methyl iodide in methanol solution in a sealed tube yielded only the hydriodide of the base, while milder methods gave unchanged starting material.

Hydrogenation with Adams' catalyst in 2*N* hydrochloric acid, a method first used by Galinovsky for the conversion of α-pyridone and α-piperidone bases to the fully saturated form (3), gave an uptake of five molecules of hydrogen. The product was a mobile, pale-yellow oil, b.p. 140-145° at 14 mm., which readily formed a monoperchlorate, m.p. 139-140°. Since saturation of the pyridone ring only accounts for four molecules of hydrogen, the presence of a third double bond in the molecule is indicated. This was confirmed by analysis of the reduced base and its perchlorate, which indicated the formula $C_{15}H_{28}N_2$, corresponding to octahydrodesoxyrhombifoline. When the hydro-

genation was carried out in glacial acetic acid, slightly more than three molecules of hydrogen were taken up, corresponding to conversion of the pyridone to a piperidone ring, and saturation of the third double bond. The product could be distilled in two fractions; the first being a mobile oil, b.p. 60-70° at 0.2 mm., which was not analyzed, but showed no carbonyl or hydroxyl band in its infrared spectrum; while the second was a more viscous oil, b.p. 70-100° at 0.2 mm., which failed to give a picrate or perchlorate, and appeared from

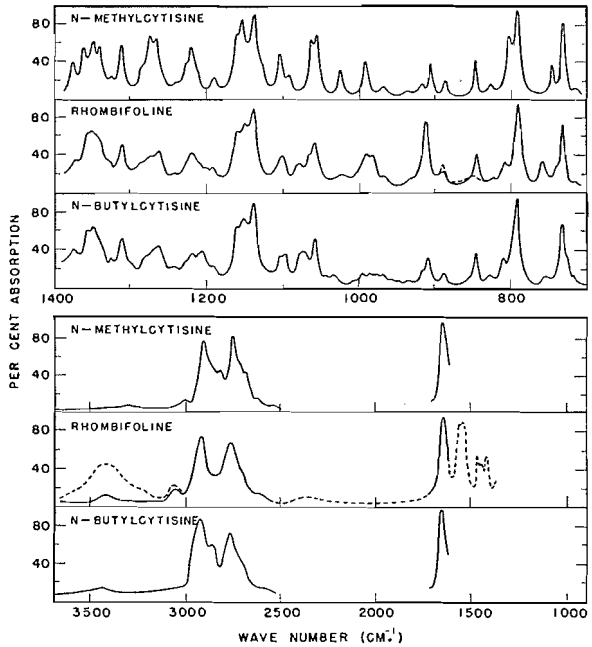


Fig. 2. Infrared spectra of carbon disulphide solutions of the bases, containing 10 mgm. per ml., and using a rock salt prism. The broken line in the spectrum of rhombifoline gives the absorption of a liquid film of the alkaloid.

the analytical figures to be a mixture.[3] The latter compound showed a band in its infrared spectrum at 1611 cm.$^{-1}$, corresponding to an α-piperidone, but it could not be purified further. In a repeat run, however, the products were separated by chromatography, the main fraction being obtained as a yellow oil which analyzed for $C_{15}H_{26}ON_2$. On further hydrogenation in 2*N* hydrochloric acid, this oily product took up another two molecules of hydrogen, yielding a colorless, mobile oil, which, however, was apparently different from octahydrodesoxyrhombifoline. The perchlorate melted diffusely at 175-190°, and yielded analytical figures indicating that it was not homogeneous.

Much more valuable information was obtained from the infrared spectrum in the "fingerprint" region. As can be seen from Fig. 2, a comparison of the spectra of rhombifoline and N-methylcytisine shows that a large proportion

[3]*Leonard and Marion report a similar result with dehydrolupanine (MA), which gave a mixture of α-isolupanine and α-isosparteine on hydrogenation with Adams' catalyst in glacial acetic acid, owing to partial reduction of the carbonyl group (5).*

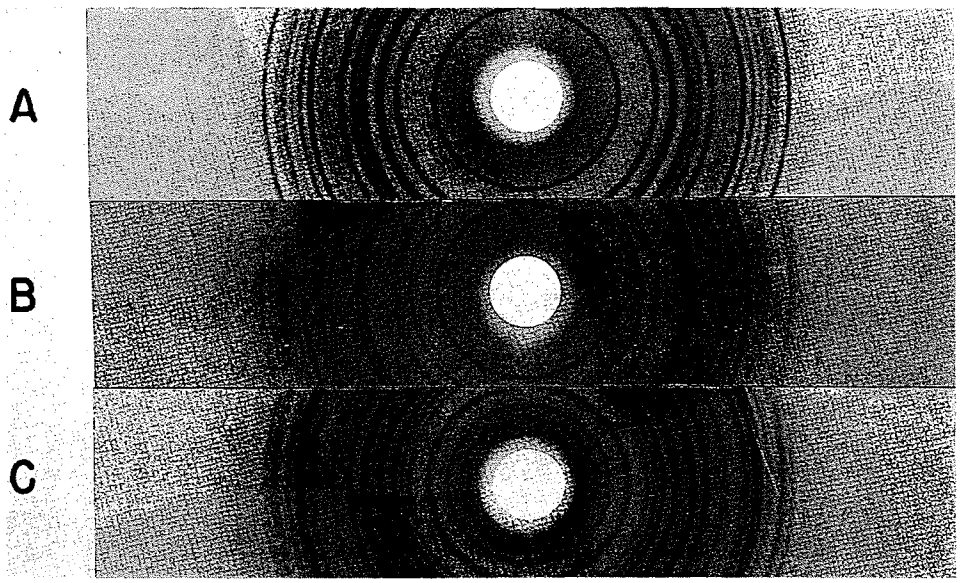


Fig. 3. X-ray powder photographs taken on a Philips camera of 114.59 mm. diameter using a Co target with Fe filter. *A*: cytisine perchlorate. *B*: Rhombifoline perchlorate. *C*: N-methylcytisine perchlorate.

of the peaks in one can be matched with corresponding peaks in the other, differing more or less in shape and intensity, but of approximately the same wave lengths. This similarity in spectra, which is even more pronounced than was noted for anagyrine and thermopsine (1), suggests a possible structural relationship, the most obvious being that of N-alkylcytisines. It was found that N-methylcytisine can be demethylated to cytisine in 50-60% yield by heating the hydriodide in the presence of ammonium iodide, under the conditions of the Herzig-Meyer N-methyl determination. Under the same conditions, rhombifoline gave a 45% yield of cytisine, proving either that it is an N-alkylcytisine, or that it is a mixture containing a large proportion of N-methylcytisine or cytisine itself. The latter possibility is ruled out by a comparison of the X-ray powder photographs of the perchlorates of cytisine, N-methylcytisine, and rhombifoline (Fig. 3). The three patterns are quite distinct, and preclude the possibility of rhombifoline containing either of the other two in anything but the most minute traces. Anagyrine, which has no free alkyl group, was recovered unchanged when submitted to the same treatment. Hence rhombifoline consists of cytisine with an N-alkyl group containing four carbon atoms and one double bond, and can be written $C_{11}H_{13}ON_2.C_4H_7$.

In order to ascertain whether the N-alkyl group is a straight or branched chain, N-*n*-butylcytisine was synthesized by refluxing equimolecular amounts of cytisine and *n*-butyl bromide in acetone in the presence of potassium carbonate. The product was a yellow oil which analyzed as $C_{15}H_{22}ON_2$, and gave a perchlorate m.p. 246-8°. The melting point was depressed to 237-9° by admixture with rhombifoline perchlorate. Hydrogenation with Adams' catalyst in 2 *N* hydrochloric acid gave hexahydrodesoxy-N-*n*-butylcytisine, which was converted directly to the monoperchlorate, m.p. 139-140°. This melting point was not depressed by admixture with octahydrodesoxyrhombifoline monoperchlorate, and the two compounds are identical. Rhombifoline is therefore an N-*n*-butenylcytisine, and it only remained to discover the position of the double bond.[4]

Below is a table, based on various sources (2, 8, 9, 10) of the probable position of the principal infrared absorption bands used to distinguish between different types of ethylenic double bond.

TABLE I

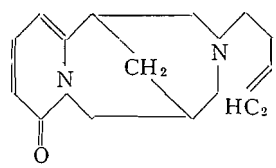
PROBABLE POSITIONS OF THE PRINCIPAL ABSORPTION BANDS ASSOCIATED WITH DIFFERENT TYPES OF ETHYLENIC BOND

$R.CH = CH_2$	R.CH = CH.R	$R_2C = CH_2$	R_2C = CH.R
910 and 990 $cm.^{-1}$	965 (*trans*)	890	810–840
1640	1670	1640	1670
3000–3100 and 2900–3000	2950–3050	3040–3120 (3080) and 2910–3040	2950–3050

[4]*The nonreactivity of this double bond towards permanganate and bromine is difficult to explain, but may be connected with the comparatively large size of the molecule.*

The carbon–carbon stretching absorption at 1640-1670 cm.$^{-1}$ shown by ethylenic double bonds is relatively weak, and would be obscured by the strong carbonyl band at 1651 cm.$^{-1}$, and an attempt was made to remove this group by reduction with lithium aluminum hydride. The spectrum of the product showed, in addition to the conjugated double bonds at 1569 and 1565 cm.$^{-1}$, a double peak at 1630-1640 cm.$^{-1}$, which may be due to a terminal methylene group (Fig. 1).[5] The analysis of this dihydrodesoxyrhombifoline was unsatisfactory, however, and more definite evidence was sought. This was found in a comparison of the infrared spectra in the "fingerprint" region (650 to 1500 cm.$^{-1}$) of rhombifoline and N-*n*-butylcytisine (Fig. 2). It can be seen that the two are very similar, except for additional bands in rhombifoline at 759, 911, 982, 990, and 3060 cm.$^{-1}$. The band at 759 cm.$^{-1}$ has often been found to occur in the spectra of other lupine alkaloids, and may or may not be present in the spectra of different samples of the same compound. It is possibly due to contamination with extracting solvent, such as chloroform, and may be discounted, while that at 990 cm.$^{-1}$ is also present in the spectrum of N-methylcytisine, and may therefore be due to a skeletal vibration. Hence the significant bands are those at 911, 982, and 3060 cm.$^{-1}$. Reference to the table above shows that these frequencies are normally given by a terminal methylene group.

Final confirmation of the structure assigned was obtained by a partial synthesis of the molecule. But-3-enol was prepared by the action of allyl magnesium bromide on trioxymethylene, and converted to but-3-enyl bromide with phosphorus tribromide in the presence of pyridine (4). The bromide was then refluxed in acetone with an equimolecular amount of cytisine in the presence of anhydrous potassium carbonate for 65 hr. The product was freed from unchanged cytisine by acetylation, and distilled as a thick yellow oil, which, on account of the behavior of natural rhombifoline, was converted directly to the picrate, perchlorate, and hydrochloride. These salts were found to have almost the same decomposition melting points as those of the corresponding salts of the natural alkaloid, and admixture caused no depression. Final proof of identity was obtained by comparison of the infrared spectra of the free bases, and X-ray powder photographs of the perchlorates, which were in both cases identical. Rhombifoline is thus N-(but-3-enyl)-cytisine, and is represented by the formula below



The close relationship of this alkaloid to thermopsine and anagyrine is obvious, and suggests that all three may stem from a common precursor.

[5]*The small band at 1680 cm.$^{-1}$ was found to increase at the expense of the 1569–1565 cm.$^{-1}$ band after the compound had been exposed to air for several hours, and may be due to an oxidation product.*

EXPERIMENTAL

All melting points are corrected, unless otherwise stated. In every case, the capillary tube was inserted in the bath or block about 15° below the melting point, with a heating rate of 3-5° per minute.

All spectra were taken on a Perkin-Elmer Model 12*c* Spectrometer, with a 1 mm. cell.

Rhombifoline

The alkaloid was obtained from *Thermopsis rhombifolia* by hot methanol extraction, and fractional vacuum distillation of the purified bases, and purified by recrystallization of the perchlorate from water until the melting point was constant at 243-245° (6). The free base distilled as a thick yellowish oil b.p. 120° at 0.2 mm. (air-bath temperature), $[\alpha]_D^{25}$–232.4° (*c*, 2.130 in ethanol), which could be reconverted to the same perchlorate. The analysis results were inconsistent, however, and varied between the values calculated for $C_{15}H_{20}ON_2$ and $C_{15}H_{22}O_2N_2$. That this was due to partial hydration is supported by the fact that the infrared spectrum of a liquid film of the base showed a pronounced band at 3410 cm.$^{-1}$, possibly corresponding to a bonded OH (Fig. 2). This band is in the NH region also, however, and may indicate slight dealkylation on distillation, which would also account for the poor analysis figures. Consistent results were obtained with the following salts:

Hydrochloride.—A methanolic solution of the alkaloid was made just acid to Congo red by the addition of concentrated hydrochloric acid, evaporated to dryness in vacuum, and the residue recrystallized from methanol–acetone. It was obtained as nacreous white platelets, m.p. 256-258° (dec.). Calcd. for $C_{15}H_{20}ON_2.HCl$: C, 64.15; H. 7.54; N, 9.98. Found: C, 64.44, 64.32; H, 7.37, 7.53; N, 9.69%. This salt could be sublimed unchanged at 120° at 10^{-4}mm. Found: C, 64.30, 64.48; H, 7.50, 7.69%.

Perchlorate.—This was obtained by the standard procedure as colorless flat spears from water, m.p. 243-245° (dec.). Calcd. for $C_{15}H_{20}ON_2.HClO_4$: C, 52.24; H, 6.14; N, 8.13. Found: C, 52.51, 52.48, 52.49; H. 5.72, 5.99, 5.84; N, 8.03, 8.22%.

Picrate.—Formed by mixing equimolecular amounts of rhombifoline and picric acid in methanol, and recrystallization from acetone–methanol. Obtained as flat, efflorescent needles, m.p. 226° (dec.) which were dried at 60° in high vacuum for analysis. Calcd. for $C_{15}H_{20}ON_2.C_6H_3O_7N_3$: C, 53.27; H, 4.89; N, 14.79. Found: C, 53.04, 53.22; H, 4.80, 4.71; N, 14.89%.

Chloroplatinate.—Crystallized in red needles from acidified aqueous methanol, m.p. 268°. Calcd. for $C_{15}H_{20}ON_2.H_2PtCl_6$: C, 27.53; H, 3.39; Pt. 29.84. Found: C, 26.16; H, 3.52; Pt, 29.33%.

The hydriodide and hydrobromide had unsharp melting points, and appeared from the analysis figures to be variable in constitution between the mono- and di-salts.

Potentiometric Titration

An aqueous solution of 50 mgm. rhombifoline perchlorate was titrated at 20°

against 0.100 *N* sodium hydroxide solution, using a Beckmann pH meter. The single end point gave a value of pK 7 for the base, and a molecular weight of 325 for the perchlorate.

Chromatography of Rhombifoline

A freshly distilled sample of the alkaloid was chromatographed on alumina of activity I, but came through in a homogeneous band with a solvent containing equal parts by weight of chloroform and ether. This band was quantitatively converted to pure rhombifoline picrate, m.p. 226°.

Hydrogenation

(1) *Octahydrodesoxyrhombifoline*

Rhombifoline hydrochloride (278.8 mgm.) was shaken under hydrogen with 150 mgm. Adams' catalyst in 10 ml. 2 *N* hydrochloric acid. Absorption of hydrogen was slow, 10 hr. being required for completion of the reaction. The uptake corresponded to 113 ml. of hydrogen at N.T.P., while the theoretical amount for five moles is 112 ml. The solution was filtered from catalyst, alkalized with sodium hydroxide, and the free base extracted with methylene chloride. The extract was dried with potassium carbonate, the solvent removed on the steam bath, and the residue distilled in vacuum, being obtained as a mobile, light yellow oil, b.p. 140-145° at 14 mm. Calcd. for $C_{15}H_{28}N_2$: C, 76.20; H, 11.93. Found: C, 76.85; H, 11.99%. The base was converted to the perchlorate, which crystallized from methanol–ether in small colorless prisms, which melted at 139-140° without decomposition, and recrystallized on cooling. Calcd. for $C_{15}H_{28}N_2.HClO_4$: C, 53.48; H, 8.68; N, 8.32. Found: C, 53.91, 53.74; H, 8.67, 8.65; N, 8.15%.

(2) *Hexahydrorhombifoline*

Freshly distilled rhombifoline (105 mgm.) was dissolved in 20 ml. of glacial acetic acid, 100 mgm. Adams' catalyst added, and the mixture shaken under hydrogen. The solution rapidly took up 32 ml. of hydrogen (at N.T.P.) then continued to absorb gas at a much slower rate, possibly indicating slow reduction of the carbonyl group. The theoretical amount of hydrogen for three moles is 29 ml. at N.T.P. The product was freed from acetic acid in vacuum, and distilled in two fractions. The first fraction, b.p. 60-70° at 0.2 mm., was a mobile oil, which was not analyzed, but which showed no indication of CO or OH in the infrared spectrum. The second, b.p. 70-100° at 0.2 mm., was a thicker oil, the analysis of which was intermediate between the values for $C_{15}H_{26}N_2$ and $C_{15}H_{26}ON_2$. The infrared spectrum was taken in chloroform solution, using a calcium fluoride prism, and exhibited a strong band at 1611 $cm.^{-1}$ corresponding to an α-piperidone. This compound failed to give a picrate or perchlorate.

In a second run, employing 380 mgm. of free base, and the same conditions as above, the main product was purified by chromatography, being obtained as a thick yellow oil, b.p. 110-120° at 0.05 mm. Calcd. for $C_{15}H_{26}ON_2$: C, 71.94; H, 10.47. Found: C, 71.70; H, 10.47%. This compound was further hydrogenated in 2 *N* hydrochloric acid with Adams' catalyst, when it was found to take up a further two molecules of hydrogen. The product was a mobile oil,

resembling octahydrodesoxyrhombifoline in general appearance, and odor. When converted to the perchlorate, however, it was not seeded by the monoperchlorate of the latter, and when finally obtained crystalline from methanol–ethylacetate, melted diffusely at 175-190°. It was not homogeneous as shown by the analytical figures which were intermediate between those required by a monoperchlorate and those of a diperchlorate of a base $C_{15}H_{28}N_2$. Found: C, 44.46, 44.78; H, 7.69, 7.19%. The reason for this discrepancy is not known.

Dealkylation

An aqueous solution containing 206 mgm. of rhombifoline perchlorate was made alkaline with sodium hydroxide, and the free base extracted with methylene chloride. The extract was dried with potassium carbonate, and the solvent removed in vacuum. The base (145 mgm.) was placed in a 25 ml. round-bottomed flask along with 350 mgm. phenol as solvent, and heated on the steam bath to give a homogeneous melt. After cooling, 3 ml. of freshly distilled constant-boiling hydriodic acid was added, followed by 750 mgm. of ammonium iodide and five drops of 5% gold chloride solution. A strong stream of nitrogen was passed through the flask, and the temperature slowly raised to 150° and held there for 30 min. to drive off excess hydriodic acid and phenol. The temperature was then raised to 225°, and held there for five minutes, to decompose the hydriodide. After cooling, the solid residue was thoroughly triturated with hot dilute hydrochloric acid, and the acid solution filtered. The cooled solution was extracted with ether, alkalized with sodium hydroxide, and extracted again with methylene chloride. This second extract was dried with potassium carbonate, the solvent removed on the steam bath, and the residual oil distilled at 130-140° at 0.1 mm. The distillate consisted of 51 mgm. of colorless needles, m.p. 150-154°. (45% of the theoretical yield of cytisine). This was treated with an equimolecular amount of picric acid in methanol, and the picrate recrystallized from water in feathery aggregates, m.p. 286-7°. Admixture with an authentic sample of cytisine picrate caused no depression in melting point. Calcd. for $C_{11}H_{14}ON_2.C_6H_3O_7N_3$: C, 48.70; H, 4.08. Found: C, 48.75, 48.93; H, 4.22, 4.36%. The free base was liberated and sublimed, m.p. 154-6°. Admixture with authentic cytisine caused no depression. Calcd. for $C_{11}H_{14}ON_2$: C, 69.44; H, 7.42; N, 14.73. Found: C, 69.40, 69.69; H, 7.36, 7.18; N, 15.00%.

The dealkylation of N-methylcytisine and the attempted dealkylation of anagyrine were carried out under identical conditions. N-methylcytisine yielded up to 60% of cytisine, while anagyrine was recovered almost quantitatively.

N-n-butylcytisine

A solution containing 1.130 gm. of cytisine in 25 ml. acetone was stirred with 1.5 gm. of potassium carbonate under nitrogen, and 0.627 ml. (0.815 gm.) of *n*-butyl bromide added from a burette in 0.1 ml. portions every 15 min. After addition was completed, the mixture was refluxed for 20 hr. The solution was filtered, concentrated to an oil under vacuum, and 1 ml. of acetic anhydride added, followed by a few drops of pyridine. The solution was heated on the

steam bath for 15 min. to acetylate any unchanged cytisine, the mixture poured into dilute hydrochloric acid and extracted thoroughly with ether. The aqueous solution was then alkalized with sodium hydroxide, and extracted with methylene chloride. The extract was dried with potassium carbonate, the solvent removed in vacuum and the residue distilled at 140-150° at 0.2 mm. as a thick, pale yellow oil. Calcd. for $C_{15}H_{22}ON_2$: C, 73.13; H, 9.00. Found, C, 74.33, 74.13; H, 9.26, 9.46%. The perchlorate was formed in the normal way, and crystallized from methanol, m.p. 246-8°. Calcd. for $C_{15}H_{22}ON_2.HClO_4$: C, 51.93; H, 6.69; N, 8.08. Found: C, 51.98, 52.19; H, 6.50, 6.36; N, 7.97%.

Hexahydrodesoxy-N-n-butylcytisine

Freshly distilled N-*n*-butylcytisine (149 mgm.) was hydrogenated in 2*N* hydrochloric acid with Adams' catalyst. The hydrogen uptake was 55.0 ml. at N.T.P., while the theoretical volume for four molecules is 53.7 ml. at N.T.P. The solution was filtered, alkalized, and extracted with methylene chloride, and the extract dried with potassium carbonate and concentrated to an oil in vacuum. The oil was dissolved in methanol, and the solution brought to pH 7 with concentrated perchloric acid diluted with three times its own volume of methanol; the solution was concentrated on the hot plate, and seeded with octahydrodesoxyrhombifoline perchlorate. Slow crystallization ensued, and the product could be recrystallized from methanol in small prisms, m.p. 139-140°. No depression in melting point occurred on admixture with octahydrodesoxyrhombifoline perchlorate. Calcd. for $C_{15}H_{28}N_2.HClO_4$: C, 53.48; H, 8.68; N, 8.32. Found: C, 53.46, 53.60; H, 8.40, 8.64; N, 8.37%. The picrate, methiodide, and dinitrodiphenate could not be crystallized.

Dihydrodesoxyrhombifoline

Rhombifoline perchlorate (692 mgm.) was decomposed with sodium hydroxide, the free base (488 mgm.) extracted with methylene chloride and the extract concentrated to an oil, but not distilled. The oil was dissolved in anhydrous ether, and excess lithium aluminum hydride in ether added. The solution was refluxed under nitrogen for 20 hr., and the excess reagent decomposed by the cautious addition of methanol and water. The solution was filtered from aluminum hydroxide, extracted with ether, and the extract dried with sodium sulphate and concentrated to an oil in vacuum. The oil was distilled as rapidly as possible at 100° at 0.2 mm., being obtained as a yellow oil which darkened in air. Calcd. for $C_{15}H_{22}N_2$: C, 78.21; H, 9.63. Found: C, 79.74; 79.60; H, 9.71, 9.68%. Addition of two molecules of picric acid in ether gave a flocculent orange picrate, which rapidly turned into a reddish tarry oil.

Synthetic Rhombifoline

This reaction was carried out as described for N-*n*-butylcytisine, using but-3-enyl bromide, prepared according to the method described by Juvala (4). From 1.196 gm. of cytisine, was obtained 0.950 gm. of an almost colorless oil, b.p. 120° at 0.2 mm. This was directly converted into the following salts.

Perchlorate: Colorless flat needles, m.p. 243° (dec.). Mixture with rhombifoline perchlorate melted at 243°. Calcd. for $C_{15}H_{20}ON_2.HClO_4$: C, 52.24; H, 6.14; N, 8.13. Found: C, 52.85, 52.73; H, 6.26, 6.00; N, 7.93%.

Picrate: Efflorescent flat needles, m.p. 227°. Mixture with rhombifoline picrate melted at 226°. Calcd. for $C_{15}H_{20}ON_2.C_6H_3O_7N_3$: C, 53.27; H, 4.89; N, 14.79. Found: C, 53.38, 53.10; H, 5.00, 5.01; N, 13.67%.

Hydrochloride: Nacreous plates, m.p. 258°. Mixture with rhombifoline hydrochloride melted at 258°. Calcd. for $C_{15}H_{20}ON_2.HCl$: C, 64.15; H. 7.54; N, 9.98. Found: C, 63.60, 63.43; H, 8.26, 8.16; N, 10.39%.

The free base was liberated and redistilled, and the optical rotation measured. $[\alpha]_D^{27}$ −235.8° (*c*, 6.70 in ethanol).

ACKNOWLEDGMENT

We express our gratitude to Dr. W. H. Barnes and Mrs. H. Sheppard who prepared the X-ray powder photographs; also to Dr. R. N. Jones and Mr. R. Lauzon for the infrared absorption spectra.

REFERENCES

1. COCKBURN, W. F. and MARION, L. Can. J. Chem. 29: 13. 1951.
2. COLTHUP, N. B. J. Optical Soc. Am. 40: 397. 1950.
3. GALINOVSKY, F. and STERN, E. Ber. 77: 132. 1944.
4. JUVALA, A. Ber. 63: 1989. 1930.
5. LEONARD, N. J. and MARION, L. Can. J. Chem. 29: 355. 1951.
6. MANSKE, R. H. and MARION, L. Can. J. Research, B, 21: 144. 1943.
7. MARION, L., RAMSAY, D. A., and JONES, R. N. J. Am. Chem. Soc. 73: 305. 1951.
8. RASMUSSEN, R. S. and BRATTAIN, R. R. J. Chem. Phys. 15: 120. 1947.
9. THOMSON, H. W. and TORKINGTON, P. Proc. Roy. Soc. (London), A, 184: 3. 1945.
10. THOMSON, H. W. and WIFFEN, D. H. J. Chem. Soc. 1412. 1948.