The Stereochemistry of Deoxynupharidine: The Absolute Configuration of Deoxynupharidine[1]

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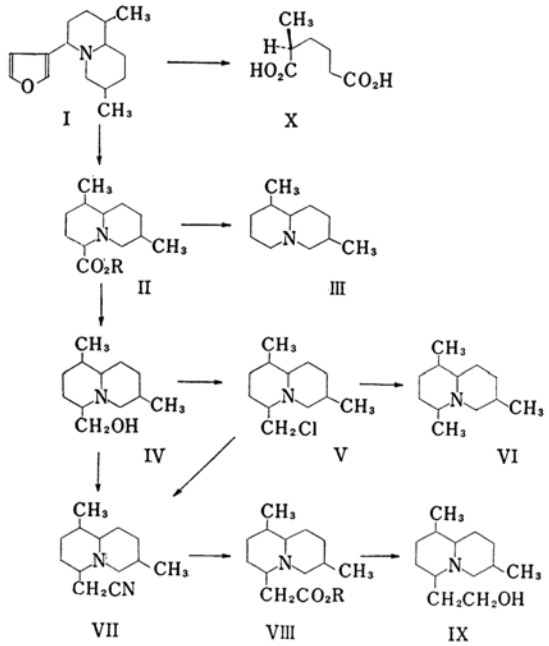
In 1956, Kotake, Kusumoto and Ohara[2] assigned structure I to deoxynupharidine, an alkaloid isolated from the roots of the water lily *Nuphar japonicum*, DC., and a compound that seemed to have the same structure was synthesized[3]. Though the infrared spectrum of synthetic deoxynupharidine could almost be superimposed on that of the natural product, a slight difference was found in the fingerprint region. Since the 2-[5-methyl-pyridyl-(2)]-5-[furyl-(3)]-pentane obtained by the dehydrogenation of the synthetic sample had an infrared spectrum identical with that obtained from natural deoxynupharidine by the same procedure, the synthetic deoxynupharidine was probably a mixture of diastereomers. In this paper the determination of the absolute configuration of deoxynupharidine by means of a conformational analysis using the NMR spectrum is reported on.

1,7-Dimethylquinolizidine (III) (defuryldeoxynupharidine) was obtained by the sodalime distillation of nupharidinic acid hydrochloride, which was obtained by the oxidation of deoxynupharidine. On the other hand, the methyl ester of II was reduced with lithium aluminum hydride to alcohol IV, which was converted with thionyl chloride to chloro compound V, and V was then reduced with palladium on charcoal to 1, 4, 7-trimethylquinolizidine (VI), which has a 4-methyl group in place of the β-furyl group of deoxynupharidine. Nitrile VII, obtained from chloro compound V by treatment with sodium cyanide, was hydrolized and esterified to VIII. Methyl ester VIII was reduced with lithium aluminum hydride to 1, 7-dimethyl-4-hydroxyethylquinolizidine (IX). In this compound IX, an equatorial hydroxyethyl group would make intramolecular hydrogen bonding between the hydroxyl and nitrogen possible. Actually, the absorption band of the hydroxyl group of IX in the infrared region appeared at 3260 cm^{-1} (in carbon tetrachloride), and a dipole moment of 2.63 D was found[4]. These results suggested that compound IX had an equatorial hydroxyethyl group.



Recently, the determination of the conformation of methylquinolizidine by means of the NMR spectrum has been reported on briefly[5]. Independently, we have prepared 1-, 3- and 4-methylquinolizidines with a definite conformation, and their NMR spectra have been compared in order to determine the configuration of deoxynupharidine with those of di- and trimethylquinolizidines, III and IV.

The preparation of the diastereomer of 1-methylquinolizidine was as follows: diethyl 2-[pyridyl-(2)]-allylmalonate[6] (XI) gave diethyl

1) A part of this work was presented to the 5th Meeting on Natural Organic Compounds of the Chemical Society of Japan at Sendai on October 12, 1961.

2) M. Kotake, S. Kusumoto and T. Ohara, *Ann.*, **606**, 148 (1957).

3) M. Kotake, I. Kawasaki, T. Okamoto, S. Kusumoto and T. Kaneko, ibid., **636**, 158 (1960).

4) J. Ratusky, A. Reiser and F. Sorm, *Collection Czechoslov. Chem. Communs.*, **20**, 798 (1955).

5) T. M. Moynehan, K. Schofield, R. A. Y. Jones and A. R. Katritzky, *Proc. Chem. Soc.*, **1961**, 218. In the course of the preparation of the manuscript of this contribution, we discovered Moynehan's communication.

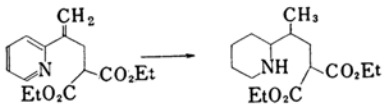
6) F. Bohlmann. N. Ottawa and R. Keller, *Ann.*, **587**, 162 (1954); E. E. Tamelen and F. S. Baran, *J. Am. Chem. Soc.*, **80**, 4659 (1958).

2-[piperidyl-(2)]-propylmalonate (XII) by hydrogenation at an ordinary pressure and temperature over a platinum catalyst. This diester, XII, afforded 1-methyl-4-ketoquinolizidine (XIII) through successive hydrolysis, esterification and cyclization. The hydride reduction of XIII gave an epimeric mixture of 1-methylquinolizidine (XIV), which was separated into two racemates by chromatography on alumina; the picrates were formed, m. p. 185~188 and 162~164°C. On the other hand, synthetic 1-lupinine has been separated, by chromatography on alumina[7], to *dl*- and *epi*-isomers, which were converted into 1-methylquinolizidine by Karrer's method[8]. The isomer from *dl*-lupinine formed a picrate which melted at 180~181°C, while the isomer obtained from the *epi*-isomer melted at 160~161°C. From these results, it is suggested that the higher melting picrate has the axial methyl group, while the other has the equatorial methyl group.

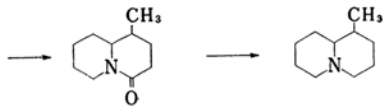
3-Methylquinolizidine (XVIII) was prepared from diethyl 2-[pyridyl-(2)]-ethyl methylmalonate (XV)[9] through XVI and XVII by the same manner as that used in the preparation of 1-methylquinolizidine, which was separated on an alumina chromatogram into two isomers. The corresponding picrates melted at 151~152 and at 183~185°C. Moreover, synthetic 3-lupinine was separated into *dl*- and *epi*-forms by the same manner as that used for 1-lupinine. The reduction of 3-*dl*-lupinine afforded an isomer, its picrate melted at 151~152°C, and 3-*epi*-lupinine gave a higher melting picrate, m. p. 177~178°C. Thus, we have suggested that the isomer of the lower melting picrate has the axial methyl group and the other has the equatorial methyl group.

The diastereomers of 4-methylquinolizidine have been obtained previously[10,11], and Boekelheide[12] has suggested that the methyl group of the higher melting picrate can be assigned to the equatorial group. We obtained 4-methylquinolizidine by the catalytic hydrogenation of 1-[pyridyl-(2)]-4-pentanone with simultaneous cyclization, and the two racemates which were separated by chromatography on alumina formed picrates; m. p. 193~196 and 187~190°C.

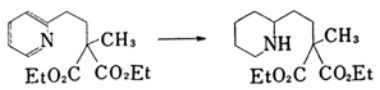
The NMR spectra of methylquinolizidines in a benzene solution (Figs. 1—6) showed that in the 1- and 3-methyl compounds the peak for an axial methyl group is at a lower field than that for the corresponding equatorial methyl group, but that for the 4-methylquinolizidine, in which the methyl group seemed to be equatorial, the peak is at a lower field than that of the axial isomer[5].



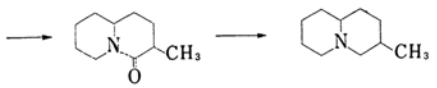
XI XII



XIII XIV

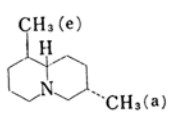


XV XVI

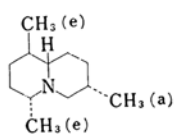


XVII XVIII

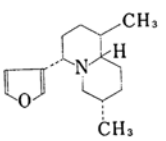
A doublet of 350~354 c. p. s. and another doublet of 327~333 c. p. s., present in the spectrum of 1, 7-dimethylquinolizidine (III), were assigned to 1-equatorial and 3-axial methyl groups respectively. A doublet of 337~344 c. p. s. in the spectrum of 1, 4, 7-trimethylquinolizidine (VI) was assigned to a 4-equatorial methyl group, since the intensity of the peak at 337 c. p. s. was twice that of the peak at 354.



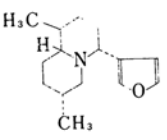
III′



VI′



Ia



Ib

The relative configurations of these compounds can thus be shown as III′ and VI′,

7) J. Ratusky and F. Sorm, *Collection Czechoslov. Chem. Communs.*, **19**, 340 (1954).
8) P. Karrer and A. Vogt, *Helv. Chim. Acta*, **13**, 1073 (1930).
9) V. Boekelheide and S. Rothchild, *J. Am. Chem. Soc.*, **71**, 879 (1949).
10) N. J. Leonard, A. S. Hay, R. W. Fulmer and V. W. Gash, ibid., **77**, 439 (1955).
11) R. Lukes and F. Sorm, *Colleation Czechoslov. Chem. Communs.*, **12**, 356 (1947).
12) V. Boekelheide and J. M. Ross, *J. Am. Chem. Soc.*, **77**, 5691 (1955).

and the absolute configuration of deoxynupharidine, as either Ia or Ib. Since the configuration of (−)-α-methyladipic acid (X), obtained from the Hofmann degradation of deoxynupharidine, was found to have an s(−)-configuration[13], we came to the conclusion that the formula Ib shows the absolute configuration of deoxynupharidine.

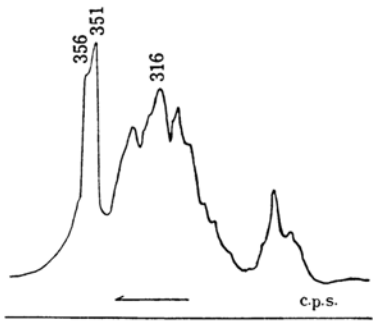


Fig. 1. NMR spectrum of 1(e)-Methylquinolizidine [picrate; m. p. 162~164°C].

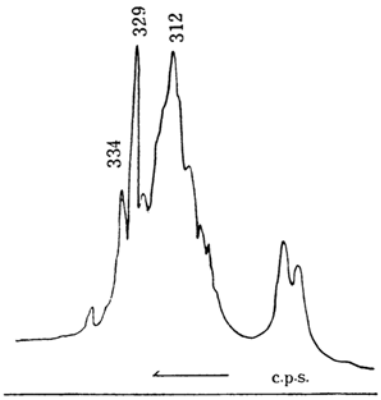


Fig. 2. NMR spectrum of 1(a)-Methylquinolizidine [picrate; m. p. 185~188°C].

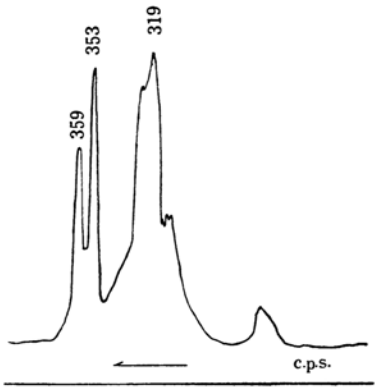


Fig. 3. NMR spectrum of 3(e)-Methylquinolizidine [picrate; m. p. 183~185°C].

13) T. Kaneko, K. Wakabayashi and H. Katsura, This Bulletin, 35, 1149 (1962).

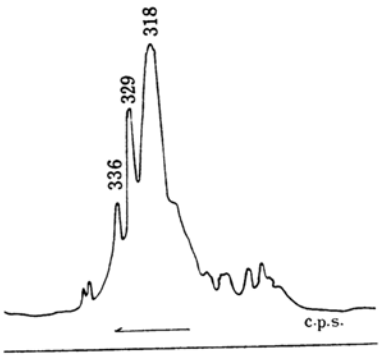


Fig. 4. NMR spectrum 3(a)-Methylquinolizidine [picrate; m. p. 151~153°C].

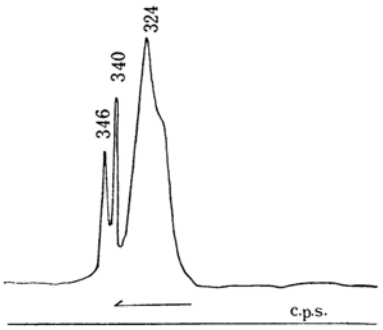


Fig. 5. NMR spectrum of 4(e)-Methylquinolizidine [picrate; m. p. 193~196°C].

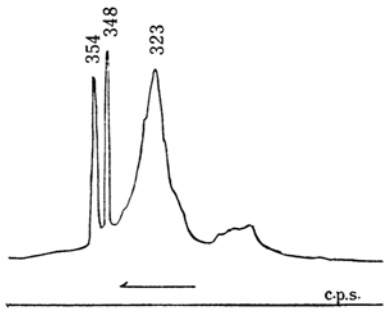


Fig. 6. NMR spectrum of 4(a)-Methylquinolizidine [picrate; m. p. 181~190°C].

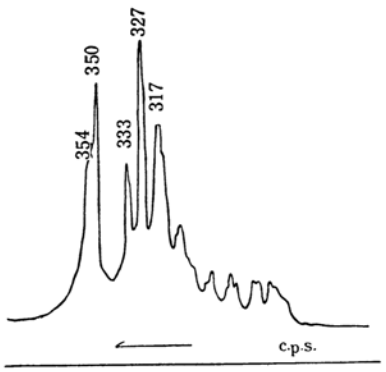


Fig. 7. NMR spectrum of 1, 7-dimethylquinolizidine (III).

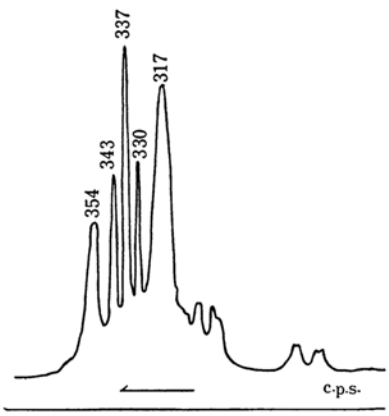


Fig. 8. NMR spectrum of 1, 4, 7-trimethylquinolizidine (VI).

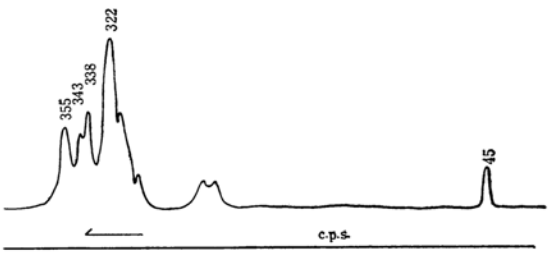


Fig. 9. NMR spectrum of deoxynupharidine (I).

Experimental

The NMR spectra were measured in a benzene solution at 56.4 Mc/sec. using a Varian Associates 4300 C instrument and the c.p.s. value was calculated from benzene.

Dehydrogenation of Synthetic Deoxynupharidine.—A mixture of 500 mg. of synthetic deoxynupharidine and 100 mg. of palladium black was heated at 280~290°C for 1 hr. After filtration of the catalyst, 250 mg. of pale yellow oil, b.p. 87~90°C/0.02 mmHg, was obtained.

The infrared spectrum of this oil was identical with that of 2-[5-methyl-pyridyl-(2)]-5-[furyl-(3)]-pentane derived from natural deoxynupharidine.

Nupharidinic Acid (II).—Hydrochloride: $[\alpha]_D$ −40.3° (*c* 1.18, ethanol), $[\alpha]_D$ −68.05° (*c* 1.44, water), $[\alpha]_D$ −75.16° (*c* 3.02, 6 N hydrochloric acid). (Found: C, 58.31; H, 9.02; N, 5.66. Calcd. for $C_{12}H_{21}O_2N \cdot HCl$: C, 58.16; H, 8.95; N, 5.65%).

Methyl ester; b. p. 87~90°C/1 mmHg, $[\alpha]_D$ −76.15° (*c* 2.78, ethanol).

1, 7-Dimethylquinolizidine (III).—A mixture of 3.7 g. of II-HCl salt and 10 g. of soda lime was distilled. The distillate was dissolved in dilute hydrochloric acid and extracted with ether, and the aqueous layer was made basic with potassium carbonate and extracted with ether. The basic ether extracts were washed with water and dried over sodium sulfate, and the solvent was distilled off. The residue was distilled at 65°C/15 mmHg; yield 1.0 g. (40%) (Found: C, 79.16; H, 12.36. Calcd. for $C_{11}H_{21}N$: C, 78.97; H, 12.65%), $[\alpha]_D$ −34.28° (*c* 2.45, ethanol). The picrate crystallized from ethanol as orange yellow prisms, m. p. 124~125°C (Found: C, 51.66; H, 6.05; N, 14.09. Calcd. for $C_{17}H_{24}O_7N_4$: C, 51.51; H, 6.10; N, 14.14%). The picrolonate from ethanol was in the form of yellow needles, m. p. 200~204°C (Found: C, 58.71; H, 6.92; N, 16.03. Calcd. for $C_{22}H_{29}O_5N_5$: C, 58.95; H, 6.77; N, 16.23%).

Alcohol (IV).—A solution of 12.3 g. of methyl ester of II in 30 ml. of absolute ether was added, drop by drop, to a solution of 2 g. of lithium aluminum hydride in 100 ml. of ether, After being heated under reflux for 3 hr. the reaction mixture was decomposed with the required amount of water and the precipitated hydroxide was extracted with boiling ether, the extracts evaporated and the residue distilled. The product was a colorless oil, b. p. 119~122°C/3.5 mmHg; yield 9.6 g. (90%) (Found: C, 72.76; H, 11.69; N, 6.93. Calcd. for $C_{12}H_{23}ON$: C, 73.04; H, 11.75; N, 7.10%). $[\alpha]_D$ −37.10° (*c* 2.57, ethanol). The infrared absorption band in carbon tetrachloride was at 3460 cm^{-1} (OH). The hydrochloride, prepared in an ethereal solution with dry hydrogen chloride and recrystallized from acetone-ethanol, was colorless and cubic; m. p. 195~196°C (Found: C, 61.41; H, 10.27; N, 5.88. Calcd. for $C_{12}H_{23}ON \cdot HCl$: C, 61.65; H, 10.35; N, 5.99%). The methiodide recrystallized from acetone-ethanol as colorless prisms; m. p. 173~174°C (Found: C, 46.17; H, 7.65; N, 4.39. Calcd. for $C_{12}H_{23}ON \cdot CH_3I$: C, 46.02; H, 7.72; N, 4.13%).

Chloride (V).—To a solution of 7.6 g. of IV in 200 ml. of ether was added 30 ml. of thionyl chloride, and the mixture was refluxed for 2 hr. The reaction mixture was evaporated in vacuo and added to a small amount of ice. The solution was carefully made basic with potassium carbonate and extracted with ether, and the solvent was removed and residue distilled at 93~95°C/1 mmHg; yield 7.1 g. (86%). $[\alpha]_D$ −69.4° (*c* 4.27, ethanol) (Found: C, 67.18; H, 10.40; N, 6.26. Calcd. for $C_{12}H_{22}NCl$: C, 66.80; H, 10.28; N, 6.49%).

1, 4, 7-Trimethylquinolizidine (VI).—A solution of 1.1 g. of V in 20 ml. of ethanol was shaken with hydrogen at atmospheric pressure in the presence of 500 mg. of 5% palladium charcoal. After 7 hr., the catalyst was filtered off and the solvent evaporated. Distillation of the residue in vacuo gave trimethylquinolizidine; b. p. 74~78°C/15 mmHg, yield 0.7 g. (76%). $[\alpha]_D$ −47.8° (*c* 2.56, ethanol) (Found: C, 78.96; H, 12.76. Calcd. for $C_{12}H_{23}N$: C, 79.49; H, 12.79%). It was volatile. The picrolonate recrystallized from ethanol as yellow needles, m. p. 180~184°C (Found: C, 59.17; H, 7.13; N, 15.57. Calcd. for $C_{22}H_{31}O_5N_5$: C, 59.31; H, 7.01; N, 15.72%). The methiodide recrystallized from acetone as colorless needles, m. p. 189~191°C (Found: C, 48.21; H, 8.13; N, 4.17. Calcd. for $C_{12}H_{23}N \cdot CH_3I$: C, 48.30; H, 8.11; N, 4.33%).

Nitrile (VII).—A solution of 3.4 g. of chloride V in 40 ml. of ethanol was added, drop by drop, to a boiling solution of 2.4 g. of sodium cyanide in 36 ml. of ethanol and 12 ml. of water. After being heated under reflux for 8 hr., the reaction mixture was evaporated in vacuo. The residue was

extracted several times with boiling chloroform, and the combined extracts were evaporated to an oil, which was distilled, b. p. 96~99°C/1 mmHg, yield 2.5 g. (76%). The infrared absorption spectrum was at 2280 cm^{-1} (CN). $[\alpha]_D$ −78.1° (*c* 3.52, ethanol) (Found: C, 75.75; H, 10.81. Calcd. for $C_{13}H_{22}N_2$: C, 75.67; H, 10.75%).

Methyl Ester (VIII R=CH_3).—A solution of 10.0 g. of nitrile VII in 100 ml. of concentrated hydrochloric acid was heated for 2 hr. and evaporated to dryness. The residue was dissolved in 100 ml. of methanol and saturated with hydrogen chloride. After standing overnight at room temperature, the solvent was removed in vacuo. Water was added to the residue, and the solution was made basic with potassium carbonate; it was then extracted with ether and the extract dried. On distillation there was obtained 10.3 g. (89%), b. p. 105~108°C/1.5 mmHg, $[\alpha]_D$ −30.2° (*c* 4.97, ethanol) (Found: C, 70.59; H, 10.76; N, 6.21. Calcd. for $C_{14}H_{15}O_2N$: C, 70.25; H, 10.53; N, 5.85%).

1,7-Dimethyl-4-hydroxyethylquinolizidine (IX).—A solution of 4.0 g. of methyl ester VIII in 10 ml. of absolute ether was added to a solution of 1 g. of lithium aluminum hydride in 60 ml. of ether. The reaction mixture was refluxed for 2 hr., decomposed with the required amount of water, and the precipitate extracted several times with boiling ether. The extracts were evaporated, and the residue distilled. The product was obtained as an oil (b.p. 122~124°C/1.5 mmHg, yield 3.1 g. (88.5%)), which solidified and which was recrystallized from acetone as colorless needles, m. p. 84~85°C. The infrared absorption band of the hydroxyl group was at 3140 cm^{-1} (Nujol) and 3260 cm^{-1} (carbon tetrachloride). $[\alpha]_D$ −18.8° (*c* 1.06, ethanol) (Found: C, 73.67; H, 11.83; N, 6.39. Calcd. for $C_{13}H_{25}ON$: C, 73.88; H, 11.92; N, 6.63%).

The dipole moment was determined in a benzene solution. The dielectric constants were measured at 25°C with a measuring condenser of 300 p*F* and a liquid condenser of 30 p*F*. The density was determined at 25°C in a Lipkin's Pyknometer. The refraction of compound IX was calculated from the atomic refraction. The results were evaluated according to the procedure of Halverstadt and Kumler[14] and are summarized below:

ω	ε^{25}	d^{25}
0.0000	2.2724	0.8729
0.0048	2.2938	0.8736
0.0088	2.3035	0.8738
0.0115	2.3165	0.8742
0.0165	2.3343	0.8747
0.0205	2.3476	0.8751
0.0288	2.3787	0.8759
0.0311	2.3852	0.8760

R_D=63.30, P=207.1, μ=2.63

α-Methyladipic Acid (X).—$[\alpha]_D$ −12.0° (*c* 3.00, ethanol).

1-Methyl-4-ketoquinolizidine (XIII).—A solution of diethyl 2-[pyridyl-(2)]-allylmalonate (XI) in a glacial acetic acid was hydrogenated over platinum oxide at room temperature and atmosphere. After filtration of the catalyst, the solvent was removed in vacuo and concentrated hydrochloric acid was added and then refluxed for 6 hr. The solution was evaporated to dryness. Absolute ethanol was then added to the residue, and the solution was saturated with hydrogen chloride and left to stand overnight. The solution was concentrated and neutralized with potassium carbonate. After extraction with ether, the ethereal solution dried over sodium sulfate. The solvent was then distilled off, and the residue, on heating to 180~200°C, began to distill at 102~105°C/1 mmHg with an overall yield of 60%.

1-Methylquinolizidine (XIV) and its Chromatogram.—A solution of XIII (15.2 g.) in 100 ml. of absolute ether was added, drop by drop, to a solution of lithium aluminum hydride (3.5 g.) in ether (200 ml.), and the mixture was refluxed for 3 hr., and then decomposed with the required amount of water. The precipitated hydroxides were extracted several times with boiling ether, and the solvent was then distilled off. The residue, on distillation under reduced pressure, yielded 10 g. (72%) of a colorless oil, b. p. 76~78°C/11 mmHg. This product (5.6 g.) was dissolved in petroleum ether and chromatographed on alumina (75 g.).

Fraction	Eluent	Volume ml.	Weight g.
1	Petroleum ether	200	2.5
2,3	Petroleum ether	400	1.1
4	Petroleum ether : benzene (1 : 1)	200	0.6

The picrate from fraction-1 was in the form of yellow plates, m. p. 185~188°C (Found: C, 50.46; H, 5.73; N, 14.62. Calcd. for $C_{16}H_{22}O_7N_4$: C, 50.26; H, 5.80; N, 14.65%). The picrate from fraction-2, 3 melted at 167~175°C. The picrate from fraction-4 was in the form of yellow needles, m. p. 162~164°C (Found: C, 50.46; H, 5.86; N, 14.56%). The picrate from mother liquids of fraction-1 melted at 163~165°C; that of fraction-2, 3 at 164~166°C, and that of fraction-4 at 175~177°C.

1-Methylquinolizidine from 1-Lupinine.—Synthetic 1-lupinine (18.6 g.) was dissolved in petroleum ether and chromatographed on alumina (100 g.).

Fraction	Eluent	Volume ml.	Weight g.	Residue
1	Petroleum ether	300	6.80	B.p. 100~103°C/2.2 mmHg
2	Petroleum ether	120	3.00	M.p. 73~80°C
3	Ether	200	5.50	M.p. 81°C
4	Ether	250	1.80	M.p. 81°C
5	Ether	280	7.50	M.p. 76~80°C
6	Methanol	190	1.20	

To 1-*dl*-lupinine (fraction-1; 5.5 g.) was added, drop by drop, thionyl chloride (8 g.) under ice cooling. The mixture was kept at 50°C for 10 min. and evaporated in vacuo. Ice was added to the residue, and the mixture was made basic with sodium carbonate and then extracted with ether.

14) I. F. Halverstadt and W. D. Kumler, *J. Am. Chem. Soc.*, **64**, 2988 (1942).

The ether extract was dried, and the solvent was removed. On distillation, there was obtained a colorless oil, b. p. 105~107°C/9 mmHg, yield 4.3 g.

A solution of 4.3 g. of the above chloride in 50 ml. of absolute alcohol at the reflux temperature was treated with 4 g. of sodium, added in small pieces. After completion of the addition, the reaction mixture was heated under gentle reflux for 4 hr. The excess sodium was then decomposed by the addition of ethanol and water. The mixture was acidified with 6 N hydrochloric acid and was concentrated to remove the ethanol in vacuo. The residue was then made basic with sodium carbonate and extracted with ether. The ether extract was dried, and the ether was removed. The residual oil was distilled at 81°C/15 mmHg, yield 2.2 g. The picrate was prepared in and recrystallized from ethanol, m. p. 180~181°C (Found: C, 50.07; H, 5.82; N, 14.40%).

Following the procedure given above for 1-*dl*-lupinine, 1-*epi*-lupinine (fraction-3,4; m. p. 81°C, 3.8 g.) was reduced to 1-*epi*-lupinane (b. p. 72~75°C/12 mmHg, 1.3 g.). The picrate melted at 160~161°C (Found: C, 50.26; H, 6.04; N, 14.26%).

Diethyl 2-[Pyridyl-(2)]-ethyl Methylmalonate (XV).—B. p. 132~135°C/1 mmHg.

3-Methylquinolizidine (XVIII) from XV.—Following the procedure given above for the preparation of 1-methylquinolizidine, the product (9.2 g.) was dissolved in petroleum ether and chromatographed on alumina (100 g.).

Fraction	Eluent	Volume ml.	Weight g.
1-3	Petroleum ether	600	7.5
4-9	Petroleum ether	1200	0.5
10	Ether	200	0.7

The picrate from fraction 1-3 was in the form of yellow plates, m. p. 150~153°C, (Found: C, 50.13; H, 5.90; N, 15.08%). The picrate from fraction 4-9 appeared as yellow needles, m. p. 183~185°C. The picrate from fraction 10 was also in the form of yellow needles, m. p. 183~185°C (Found: C, 50.09; H, 5.80; N, 14.79%).

3-Methylquinolizidine from 3-Lupinine.—Synthetic 3-lupinine (38 g.) was dissolved in petroleum ether and chromatographed on alumina (400 g.).

Fraction	Eluent	Volume ml.	Weight g.	Residue
1—5	Petroleum ether	1300	0.9	M.p. 49~52°C
6	Petroleum ether	300	3.2	M.p. 56~58°C
7	Ether	300	2.1	M.p. 55~57°C
8	Ether	300	1.5	M.p. 51~53°C
9	Ether	400	1.7	M.p. 50~52°C
10	Ether	300	0.8	M.p. 48~51°C
11—16	Ether	2500	3.3	Oil
17	Methanol	500	24.3	Oil

Following the procedure given above for the preparation of 1-lupinane from 1-lupinine, 3-*dl*- and 3-*epi*-lupinine were converted to 3-*dl*- and 3-*epi*-lupinane. 3-Methylquinolizidine (1.6 g., b. p. 71~72°C/15 mmHg) was obtained from 1.5 g. of 3-*dl*-lupinine (m. p. 57~58°C, fraction-6, 7). The picrate was prepared in and recrystallized from ethanol, m. p. 151~152°C, in the form of yellow plates (Found: C, 49.83; H, 5.86; N, 14.74%).

On distillation of the oil (fraction-17), there were obtained 3 fractions: b. p. ~118°C/5 mmHg, 1.0 g; b. p. 118~123°C/5 mmHg, 17.9 g.; b. p. 123~125°C/5 mmHg, 4.9 g.

The product (10 g., b. p. 118~123°C/5 mmHg) was chromatographed on alumina (100 g.).

Fraction	Eluent	Volume ml.	Weight g.	Residue
18	Petroleum ether : Ether	200	1.5	Oil
19	Ether	200	1.4	Oil
20	Ether	160	0.6	Oil
21	Ether	200	1.0	Oil
22	Ether	230	0.9	Oil
23	Ether	200	0.8	Oil
24	Ether	40	0.5	Oil
25	Ethanol	270	3.4	Oil

Two and half grams of fractions 19, 20 and 21 was converted into 3-lupinane b. p. 77~79°C/15 mmHg, 1.1 g.; the picrate melted at 144~151°C and at 163~165°C (trace). The product (4.9 g., b. p. 123~125°C/5 mmHg) was chromatographed on alumina (100 g.).

Fraction	Eluent	Volume ml.	Weight g.	Residue
26	Petroleum ether : Ether	300	0.3	Oil
27	Ether	450	0.3	Oil
28	Ether	380	0.4	Oil
29	Ether	300	0.2	Oil
30	Ethanol	250	3.8	Oil

Nine tenths grams of fractions 27, 28 and 29 was converted into 3-lupinane, b. p. 79~81°C/17 mmHg, 0.6 g. The picrate was in the form of yellow needles, m. p. 177~178°C (Found: C, 50.32; H, 5.74; N, 14.99%).

4-Methylquinolizidine.—The hydrogenation of 1-[pyridyl-(2)]-pentan-4-one was carried out at an ordinary temperature and pressure over a platinium catalyst. 4-Methylquinolizidine was taken up in the usual manner and distilled at 17 mmHg, 81~86°C; yield 74%. The product (9.1 g.) was dissolved in petroleum ether and chromatographed on alumina (100 g.).

Fraction	Eluent	Volume ml.	Weight g.	M. p. of picrate
1—2	Petroleum ether	200	8.2	190~196°C
3	Petroleum ether	100	1.2	193~196°C
4—6	Petroleum ether	300	0.8	193~196°C
7	Ether	100	0.6	189~193°C
8	Ether	100	0.5	187~192°C

The picrate from fraction-3 was recrystallized three times from ethanol; it appeared as yellow prisms,

m. p. 193~196°C (Found: C, 50.07; H, 5.88; N, 14.56%). The picrate from fraction 8 was recrystallized three times from ethanol, appearing as small yellow plates, m. p. 187~190°C (Found: C, 50.51; H, 5.82; N, 14.50%).

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