extracted with ethyl acetate; evaporation of the organic extract yielded an oil which crystallized upon addition of methanol to provide 0.01 g (2.5%) of needles, mp 149–151° (lit.[15] mp 151–152°), homogeneous by tlc (R_f 0.95, systems A, B, and D). The mass spectrum (direct probe at 260°, 2.6 kV dynode, 0.5 slit width) exhibited peaks at m/e (rel intensity) 199 (6.3) attributed to $(C_6H_5)_2CHS^+$ and a pattern from 167 (100) down consistent with $(C_6H_5)_2CH^+$. These data are consistent with the structure of benzhydryl disulfide.

Method B.—A solution of 0.323 g (0.0011 mol) of N$^\epsilon$-*t*-butyloxycarbonyl-L-lysylglycine and 0.170 g (0.002 mol) of sodium bicarbonate in 3 ml of water was treated with a solution containing 0.576 g (0.001 mol) of N-carbobenzoxy-S-benzhydryl-L-cysteinylglycine N-hydroxysuccinimide ester in 5 ml of dimethoxyethane. The reaction mixture was stirred for 18 hr at room temperature, diluted with 100 ml of water, and acidified to pH 3 with 1 *N* sulfuric acid. The precipitate was filtered, washed with 50 ml of water, and dried *in vacuo* to yield 0.71 g of crude product. The substance was washed with ethyl acetate and ether and recrystallized from chloroform–hexane to provide 0.62 g (82%) of white solid, mp 134–139°, $[\alpha]^{28}D$ −22.6° (*c* 0.53, DMF).

Anal. Calcd for $C_{39}H_{49}N_5O_9S \cdot 0.5H_2O$: C, 60.60; H, 6.52; N, 9.06; S, 4.15. Found: C, 60.59; H, 6.45; N, 9.07; S, 4.08.

Preparation of *t*-Butyl N-*o*-Nitrophenylsulfenyl-S-benzoyl-L-cysteinylglycinate.—A solution of 5.60 g (0.01 mol) of N-*o*-nitrophenylsulfenyl-S-benzoyl-L-cysteine N,N-dicyclohexylamine salt[16] in 20 ml of chloroform at −10° was treated with 1.30 ml (0.01 mol) of isobutyl chloroformate and stirred at −10° for 10 min. The solution was then treated with 1.68 g (0.01 mol) of *t*-butyl glycinate hydrochloride and 1.01 g (0.01 mol) of N-methylmorpholine in 10 ml of chloroform. The reaction mixture was stirred for 2 hr at 0° and 5 hr at 25°. The solution was evaporated *in vacuo* and the residue was suspended in an ether ethyl acetate mixture. The suspension was filtered and the filtrate was washed with 0.5 *N* sulfuric acid, water, 10% potassium bicarbonate, water, and saturated brine. The dried extract was evaporated *in vacuo* to a yellow oil which was dissolved in chloroform, slurried with 5 g of silica gel, and filtered. The resulting solution was evaporated *in vacuo* to give 4.48 g (91%) of a yellow foam, homogeneous by tlc (system A). An analytical sample was prepared by crystallization from benzene–ether–hexane, mp 81–83°, $[\alpha]^{27}D$ −10.6° (*c* 1.37, $CHCl_3$).

Anal. Calcd for $C_{22}H_{25}N_3O_6S_2$: C, 53.75; H, 5.13; N, 8.55; S, 13.08. Found: C, 53.29; H, 5.15; N, 8.75; S, 13.29.

Preparation of *t*-Butyl N-Carbobenzoxy-S-benzhydryl-L-cysteinylglycyl-N$^\epsilon$-*t*-butyoxycarbonyl-L-lysylglycyl-S-benzoyl-L-cysteinylglycinate (VII).—To a solution of 4.48 g (0.091 mol) of *t*-butyl N-*o*-nitrophenylsulfenyl-S-benzoyl-L-cysteinylglycinate in 300 ml of dry ether was added 18 ml of 2.2 *N* hydrogen chloride in ether. An oil formed after 2 hr at 25°, the supernatant was decanted, and the oil was crystallized from chloroform–ether to give 2.09 g of *t*-butyl S-benzoyl-L-cysteinylglycinate hydrochloride, homogeneous (ninhydrin, iodine vapor) by tlc (system A).

A solution of 1.553 g (2.04 mmol) of IIb and 0.283 ml (2.04 mmol) of triethylamine in 15 ml of N,N-dimethylacetamide was treated with 0.25 ml (2.08 mmol) of pivaloyl chloride at −10°. After 10 min, 0.763 g (2.04 mmol) of crude *t*-butyl S-benzoyl-L-cysteinylglycinate hydrochloride and 0.283 ml (2.04 mmol) of triethylamine in 5 ml of N,N-dimethylacetamide was added to the reaction mixture. The solution was stirred at −10° for 1 hr and at 25° for 6.5 hr. The suspension was filtered and washed with ether and ethyl acetate, and the filtrate was added to 400 ml of ether. The supernatant was decanted and the gum was triturated with ether to give 1.91 g of solid. The material was filtered through silica gel G with 2% methanol in chloroform (v/v). The effluent was evaporated *in vacuo* and the solid was recrystallized from hot 95% ethanol–water (40:30, v/v) to give 1.616 g (73%) of VII: mp 174–180°; $[\alpha]^{26}D$ −23.0° (*c* 0.50, DMAc); homogeneous by tlc (system A, E).

Anal. Calcd for $C_{55}H_{69}N_7O_{12}S_2$: C, 60.92; H, 6.41; N, 9.04; S, 5.91. Found: C, 60.91; H, 6.29; N, 9.08; S, 5.98.

Preparation of *t*-Butyl N-Carbobenzoxy-S-benzhydryl-L-cysteinylglycyl-N$^\epsilon$-*t*-butyloxycarbonyl-L-lysylglycyl-L-cysteinylglycinate.—To a cooled solution of 324.5 mg (0.3 mmol) of VII in 300 ml of dry methanol was added 6 ml (0.33 mmol) of an 0.055 *N* solution of sodium methoxide in methanol. The reaction, followed on tlc with system E, required 2.5 hr for completion. The solution was acidified with 0.5 ml of glacial acetic acid, concentrated *in vacuo* to 50 ml, and poured into 700 ml of water. The washed precipitate was dried *in vacuo* to yield 283.8 mg (96.5%) of thiol: mp 185–188°; $[\alpha]^{28}D$ −10.8° (*c* 0.250, DMAc); homogeneous by tlc (system E).

Anal. Calcd for $C_{48}H_{65}N_7O_{11}S_2$: C, 58.82; H, 6.68; N, 10.00; S, 6.54. Found: C, 58.80; H, 6.63; N, 9.86; S, 6.57.

When the methanolysis of VII was carried out in more concentrated solution (0.02 *M* rather than 0.001 *M*), a spot corresponding to II appeared on the tlc of the reaction mixture.

Pyruvate Analyses. A. Saponification Reactions.—The substrate (*ca.* 0.02 mmol) was accurately weighed into a hydrolysis tube and dissolved in sufficient solvent (ethanol or N,N-dimethylformamide) to give the desired substrate concentration. The solution was treated with 1.1 equiv of 1.0 *N* sodium hydroxide solution, and the reaction mixture was left at room temperature for 5 hr. Solvent was then evaporated *in vacuo*, and 1 ml of constant-boiling 6 *N* hydrochloric acid solution was added. The tube was sealed and heated at 110° for 5 hr to liberate, by hydrolysis,[8] pyruvic acid from the dehydroalanine peptide present in the reaction mixture. The contents of the tube were carefully washed into a 5-ml volumetric flask with 1.1 *M* potassium hydrogen phosphate, the pH was brought to 7.5 with 50% sodium hydroxide, and the solution was diluted to volume with phosphate buffer. Aliquots of this solution were then analyzed for pyruvic acid with reduced diphosphopyridine nucleotide and lactic dehydrogenase as previously described.[8]

B. Methanolysis Reactions.—The substrate (*ca.* 0.01 mmol) was accurately weighed into a hydrolysis tube and dissolved in sufficient solvent (methanol, N,N-dimethylacetamide, or a mixture of both) to give the desired substrate concentration. One equivalent of 0.074 *N* sodium methoxide in methanol was then added, and the reaction mixture was allowed to stand at room temperature for 5 hr. The reaction mixture was then treated as described above. In all saponification and methanolysis reactions, the presence of unreacted starting material was observed by tlc (system A).

Registry No.—Ia, 22423-71-8; Ib, 22423-72-9; VII, 22423-77-4; N-carbobenzoxy-S-benzhydryl-L-cysteine N-hydroxysuccinimide ester, 22423-73-0; N-carbobenzoxy-S-benzhydryl-L-cysteinylglycine, 22423-74-1; ethyl N-carbobenzoxy-N$^\epsilon$-*t*-butyloxycarbonyl-L-lysylglycinate, 21869-27-2; *t*-butyl N-*o*-nitrophenylsulfenyl-S-benzoyl-L-cysteinylglycinate, 22423-76-3; *t*-butyl N-carbobenzoxy-S-benzhydryl-L-cysteinylglycyl-N$^\epsilon$-*t*-butyloxycarbonyl-L-lysylglycyl-L-cysteinylglycinate, 22423-78-5.

(15) A. Schonberg, E. Singer, E. Frese, and K. Praefcke, *Chem. Ber.*, **98**, 3311 (1965).

(16) L. Zervas, D. Borovas, and E. Gazis, *J. Amer. Chem. Soc.*, **85**, 3660 (1963).

Synthesis of Lamprolobine

ERNEST WENKERT AND A. ROBERT JEFFCOAT[1]

Department of Chemistry, Indiana University, Bloomington, Indiana 47401

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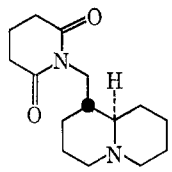
The two-step reaction sequence of partial hydrogenation of 1-alkyl-3-acylpyridinium salts and acid-catalyzed cyclization of the resultant 1-alkyl-3-acyl-2-piperideines has formed the basis of general synthesis of quinolizidines[2] and alkaloids based on this ring system.[3] Heretofore only methyl nicotinate, nicotin-

(1) Public Health Service Predoctoral Fellow, 1966–1969.

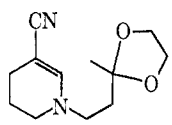
(2) E. Wenkert, K. G. Dave, and R. V. Stevens, *J. Amer. Chem. Soc.*, **90**, 6177 (1968), and references cited therein.

(3) E. Wenkert, *Accounts Chem. Res.*, **1**, 78 (1968).

aldehyde, and β-acetylpyridine have served as starting materials. Nicotinonitrile, in the form of its N_a-methyl derivative, has been shown to be susceptible to partial reduction,[4] but has not been tested in the second step of the aforementioned reaction sequence. Since it appeared to be an ideal starting compound for the construction of dinitrogenous natural bases, an investigation of the synthesis of such a product—lamprolobine (**1**), the major alkaloidal constituent of the leaves of *Lamprolobium fructicosum* Benth.[5]—from nicotinonitrile was undertaken.

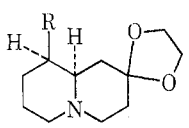


1

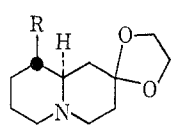


2

Alkylation of nicotinonitrile with 4-bromo-2-butanone ethylene ketal[6] and hydrogenation of the salt yielded the 2-piperideine **2**, whose treatment with *p*-toluenesulfonic acid in benzene solution afforded the pair of isomeric cyanoquinolizidone ketals **3a** and **4a**. Their reduction with lithium aluminum hydride gave the labile, liquid diamines **3b** and **4b**, which were characterized as phthalimides **3c** and **4c**, respectively.



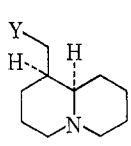
3



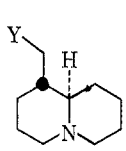
4

a, R = CN
b, R = CH_2NH_2
c, R = $CH_2N(CO)_2C_6H_4$

Hydrolysis of the ketals **3b** and **4b** with aqueous acid and Wolff–Kishner reduction of the resultant ketones produced diamines **5b**[7] and **6b**, respectively, whose stereochemistry was determined in the following manner. *dl*-Lupinine (**5a**)[2] and *dl*-epilupinine (**6a**)[2]



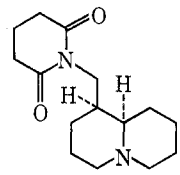
5



6

a, Y = OH
b, Y = NH_2
c, Y = Br
d, Y = $N(CO)_2C_6H_4$

were converted into bromides[8–10] **5c** and **6c**, respectively. Interaction of the bromides with potassium phthalimide[11] led to the crystalline imides **5d** and **6d**, respectively, the latter of which proved identical with the product of phthalation of **6b**. Furthermore, interaction of bromide **5c** with sodium glutarimide yielded isolamprolobine (**7**), identical with the imide derived from amine **5b** and glutaric anhydride.



7

Treatment of the amine **6b** with glutaric anhydride led to *dl*-lamprolobine (**1**), spectrally identical with the natural alkaloid.[5]

(4) E. Wenkert, K. G. Dave, F. Haglid, R. G. Lewis, T. Oishi, R. V. Stevens, and M. Terashima, *J. Org. Chem.*, **33**, 747 (1968).
(5) N. K. Hart, S. R. Johns, and J. A. Lamberton, *Aust. J. Chem.*, **21**, 1619 (1968).
(6) L. Williman and H. Schinz, *Helv. Chim. Acta*, **32**, 2151 (1949).
(7) F. Bohlmann, D. Schumann, U. Friese, and E. Poetsch, *Chem. Ber.*, **99**, 3358 (1966).
(8) G. R. Clemo and J. Rudinger, *J. Chem. Soc.*, 2714 (1951).
(9) F. Bohlmann, E. Winterfeldt, and U. Friese, *Chem. Ber.*, **96**, 2251 (1963).
(10) G. Fodor, *J. Amer. Chem. Soc.*, **88**, 1040 (1966).
(11) *Cf.* S. Okuda, H. Katoaka, and S. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **13**, 491 (1965).

Experimental Section

Melting points were determined on a Reichert micro hot stage and are uncorrected. Infrared spectra were recorded on Perkin-Elmer 137 and 621 spectrophotometers. Unless otherwise stated, proton magnetic resonance spectra of deuteriochloroform solutions containing tetramethylsilane as internal standard were determined on Varian A-60 and HA-100 spectrometers.

1-(3-Ketobutyl)-3-cyanopyridinium Bromide Ethylene Ketal.—A mixture of 6.24 g of nicotinonitrile and 12.4 g of 4-bromo-2-butanone ethylene ketal[6] was stirred at 60°. When, after 2 days, the mixture had set into a paste, 25 ml of ether was added and the solid was filtered and washed with ether. The filtrate and washings were combined, the solvent was evaporated, and the residue was left standing for 24 hr. Filtration of the resultant precipitate, washing as before, and combination with the previous solid yielded 17.0 g of salt which was sufficiently pure to be used in the next reaction. Its crystallization from a mixture of methanol and acetone ethylene ketal gave pure pyridinium salt: mp 151–153° dec; ir (KBr) 4.50 (w, C≡N) and 6.13 μ (m, C=C); pmr (dideuteriomethyl sulfoxide) δ 1.35 (s, 3, methyl), 2.4–2.6 (m, 2, methylene), 3.87 (s, 4, oxymethylenes), 4.81 (t, 2, J = 7.0 cps, aminomethylene), and 8.2–9.7 (m, 4, pyridine H).

Anal. Calcd for $C_{12}H_{15}O_2N_2Br$: C, 48.17; H, 5.06; N, 9.36. Found: C, 48.33; H, 5.29; N, 9.62.

1-(3-Ketobutyl)-1,4,5,6-tetrahydronicotinonitrile Ethylene Ketal (2).—A mixture of 10.0 g of the above salt, 1.0 g of 10% palladium on charcoal, and 10 ml of triethylamine in 50 ml of methanol was hydrogenated at room temperature under a pressure of 40 psi for 12 hr. It was filtered and the filtrate was evaporated. The residue from the filtrate was extracted with ether and the extract was evaporated. An ether solution of the residue was passed through a short alumina (activity IV) column and evaporated. Chromatography of the residual oil, 4.70 g, on silica yielded liquid **2**: ir (neat) 4.62 (m, C≡N) and 6.18 μ (m, C=C); pmr δ 1.27 (s, 3, methyl), 3.92 (s, 4, oxymethylenes), and 6.79 (s, 1, olefinic H).

Anal. Calcd for $C_{12}H_{18}O_2N_2$: C, 64.84; H, 8.16; N, 12.60. Found: C, 65.01; H, 8.38; N, 12.60.

9-Cyano-2-quinolizidone Ethylene Ketals 3a and 4a.—A solution of 7.4 g of **2** in 200 ml of dry benzene was added over a 30-min period to a solution of 8.0 g of *p*-toluenesulfonic acid (from which water had been removed by azeotropic distillation from benzene) in 200 ml of dry benzene and the mixture was refluxed under nitrogen for 8 hr. The cooled solution was poured onto a suspension of an excess of sodium bicarbonate in 1 l. of methylene chloride, stirred for some time, and filtered. The filtrate was evaporated and the residue was extracted with ether. The extract was dried over sodium sulfate and evaporated. Silica chromatography of the residual oil, 3.9 g, and elution with 24:1 chloroform–methanol yielded three sets of fractions whose thin layer chromatography revealed the first to contain one isomer, the second a mixture, and the third the second isomer of the desired product. Rechromatography of the second group of fractions, 1.0 g, on silica separated them into the two isomers. Distillation of the first fractions yielded 1.1 g of a crystalline solid whose crystallization from ether–hexane or sublimation gave colorless crystals of **3a**: mp 78–79.5°; ir (KBr) 4.45 μ (w, C≡N); pmr δ 3.96 (s, 4, oxymethylenes).

Anal. Calcd for $C_{12}H_{18}O_2N_2$: C, 64.84; H, 8.16; N, 12.60. Found: C, 64.59; H, 8.29; N, 12.37.

Distillation of the last fractions yielded 1.2 g of a solid whose crystallization from ether–hexane or sublimation afforded colorless crystals of **4a**: mp 71–72.5°; ir (KBr) 4.45 μ (w, C≡N); pmr δ 3.96 (s, 4, oxymethylenes).

Anal. Calcd for $C_{12}H_{18}O_2N_2$: C, 64.84; H, 8.16; N, 12.60. Found: C, 64.82; H, 8.02; N, 12.77.

Phthalimides 3c and 4c.—A solution of 500 mg of **3a** in 50 ml of dry ether was added over a 1-hr period to a stirring solution of 500 mg of lithium aluminum hydride in 50 ml of ether at room temperature and the mixture was stirred for 3 hr. Sodium sulfate decahydrate was added and the mixture was shaken and filtered. The salts were washed with methylene chloride and the combined filtrate and washings were evaporated. The residual liquid amine **3b**, 440 mg, had to be used for further reactions immediately, since it formed readily a carbon dioxide addition product. A solution of 45 mg of **3b** and 50 mg of phthalic anhydride in 3 ml of chloroform was refluxed for 30 min and then evaporated. The residue was heated at 220° (0.001 Torr) and sublimed in a fractional sublimator. Crystallization of the product, 50 mg, from ether–hexane yielded colorless crystals of **3c**: mp 166–168°; ir (KBr) 5.67 (m, C=O), 5.87 (s, C=O), and 6.20 μ (w, C=C).

Anal. Calcd for $C_{20}H_{24}O_4N_2$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.20; H, 6.64; N, 7.68.

The identical procedure was applied to **4a**. Crystallization of its imide from ether–hexane gave crystals of **4c**: mp 137–138°; ir (KBr) 5.65 (w, C=O), 5.86 (s, C=O), and 6.18 μ (w, C=C).

Anal. Calcd for $C_{20}H_{24}O_4N_2$: C, 67.40; H, 6.79; N, 7.86. Found: C, 67.67; H, 6.59; N, 7.82.

Diamines 5b and 6b and Their Derivatives.—A solution of 1.5 g of diamino ketal **4b** in 10 ml of 50% sulfuric acid was kept at room temperature for 18 hr. The solution was cooled, made alkaline with 5 *N* potassium hydroxide, and extracted exhaustively with methylene chloride. The extract was dried and concentrated to a 10-ml volume. Ethylene glycol, 25 ml, was added and the remaining methylene chloride was removed by distillation. Potassium hydroxide, 4.0 g, and 10 ml of 98% hydrazine were added and the mixture was heated at 190° for *ca.* 3 hr and subsequently refluxed under nitrogen for 12 hr. It was then cooled, acidified with 6 *N* hydrochloric acid, and evaporated under vacuum. The residue was dissolved in a minimum amount of 1 *N* potassium hydroxide and the alkaline solution was extracted with methylene chloride. The extract was dried and evaporated. Distillation of the residue gave 135 mg of **6b**, which had to be used immediately in the next reactions in view of its ready air oxidation and formation of a carbon dioxide adduct.

A solution of 50 mg of **6b** and 50 mg of phthalic anhydride in 1 ml of chloroform was refluxed in a sublimation tube for 30 min. It was evaporated and the tube was heated at 250° (0.005 Torr) in a fractional sublimator. Collection of a band of crystals gave 10 mg of solid whose crystallization from ether–hexane yielded colorless crystals of **6d**: mp 128–129°; mmp (with **6d** below) 127–128.5°; mmp (with **5d** below) 108–117°; ir (KBr) 5.66 (m, C=O), 5.85 (s, C=O), and 6.20 μ (w, C=C).

Anal. Calcd for $C_{18}H_{22}O_2N_2$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.63; H, 7.53; N, 9.37.

The preparation of the 1-bromomethylquinolizidines **5c** and **6c** followed the procedure for the conversion of lupinine (**5a**) into optically active **5c**.[8] Epilupinine (**6a**), 330 mg, gave 410 mg of **6c**.

A solution of 100 mg of **5c** and 100 mg of potassium phthalimide in 4 ml of dry dimethylformamide was heated at 130° for 4 hr.[11] The mixture was cooled and evaporated. The residue was extracted with methylene chloride and chromatographed on 3 g of alumina (activity II). Elution with 50:1 ether–methanol gave 65 mg of a solid whose crystallization from ether–hexane yielded crystals of **5d**: mp 135–136°; ir (KBr) 5.66 (m, C=O), 5.87 (s, C=O), and 6.19 μ (w, C=C).

Anal. Calcd for $C_{18}H_{22}O_2N_2$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.21; H, 7.62; N, 9.27.

A similar reaction with 40 mg of **6c** and 40 mg of potassium phthalimide gave 29 mg of **6d**: mp 127.5–129°; ir (KBr) identical with that of **6d** above.

Diamine **5b**, 1.4 g, was prepared from **3b**, 90 mg, by the procedure outlined above for the conversion of **4b** into **6b**. A solution of 35 mg of diamine **5b** and 35 mg of glutaric anhydride in 4 ml of chloroform was kept at room temperature for 2 hr. Evaporation of the solution and high vacuum distillation (bath temperature 250°) of the residue yielded 10 mg of liquid isolamprolobine (**7**): ir (CCl_4) 5.78 (m, C=O) and 5.95 μ (s, C=O).

A suspension of 232 mg of bromide **5c** and 135 mg of sodium glutarimide in 4 ml of dimethylformamide was refluxed for 2 hr. The mixture was cooled and filtered and the filtrate was evaporated. The residue was chromatographed on alumina (activity IV). Distillation of the 50:1 ether–methanol eluates yielded 40 mg of liquid **7** whose ir and pmr spectra and thin layer chromatographic behavior were identical with those of **7** above.

Lamprolobine (1).—The above procedure of conversion of **5b** into **7** was applied to 100 mg of **6b** and 100 mg of glutaric anhydride. It led to 30 mg of liquid *dl*-lamprolobine (1), ir (CCl_4) 5.78 (m, C=O) and 5.95 μ (s, C=O), identical in all respects with the spectrum of natural lamprolobine (1). Crystallization of its picrate from methanol gave yellow plates, mp 190–192°.

Anal. Calcd for $C_{21}H_{27}O_9N_5$: C, 51.11; H, 5.51; N, 14.19. Found: C, 51.45; H, 5.80; N, 14.12.

Registry No.—**1**, 22142-02-5; **2**, 22423-62-7; **3a**, 22423-63-8; **3c**, 22423-64-9; **4a**, 22423-65-0; **4c**, 22423-67-2; **5d**, 10248-22-3; **6d**, 22423-69-4; **1** picrate, 22142-03-6; 1-(3-ketobutyl)-3-cyanopyridinium bromide ethylene ketal, 22423-66-1.

Acknowledgments.—The authors are indebted to Dr. J. A. Lamberton for a gift of a sample of natural lamprolobine and to the U. S. Department of Health, Education and Welfare (Grant GM-11571) for partial support of this work.

The Stereochemistry of (−)-Deoxynupharidine.[1] The Synthesis of (−)-(*R*)-α-Methyladipic Acid

CHUN FOOK WONG, EGMONT AUER, AND ROBERT T. LALONDE

Department of Chemistry,
State University College of Forestry at Syracuse University,
Syracuse, New York 13210

Received May 22, 1969

A recent publication[2] dealing with the synthesis of (+)-(*S*)-α-methyladipic acid has prompted us to disclose our synthesis of (−)-(*R*)-α-methyladipic acid, a synthesis carried out in an attempt to clarify the absolute configuration of (−)-deoxynupharidine and related Nuphar alkaloids.[3] Also reported here are nuclear magnetic resonance results which support the relative configuration of deoxynupharidine proposed earlier.

Originally, the absolute configuration of (−)-deoxynupharidine (1) was proposed on the basis that the (−)-α-methyladipic acid obtained on degradation (Scheme I) possessed the *S* configuration.[4] The configurational assignment of this acid was made on the basis of its synthesis from (−)-α-methyl-γ-butyrolactone, which in turn was correlated with (−)-(*S*)-methylsuccinic acid.[5] However, Turner[6] questioned

(1) Support of this work by the U. S. Department of Interior, Federal Water Pollution Control Administration and the McIntire–Stennis Cooperative Forestry Research Program of the U. S. Department of Agriculture is gratefully acknowledged.

(2) I. Kawasaki and T. Kaneko, *Bull. Chem. Soc. Jap.*, **41**, 1482 (1968).

(3) These include nupharidine, Δ^8-dehydrodeoxynupharidine, nupharamine, anhydronupharamine, nuphamine, and castoramine.

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