and the solvent evaporated. The viscous residue was applied to a Lobar silica gel column, and compound **8b** was eluted with solvent A. After evaporation, viscous **8b** was isolated: 0.84 g (78.5%); TLC (solvent C) R_f 0.38; UV (methanol) λ_{max} 270 nm (ϵ 7200), 301 (8300); ^{1}H NMR ($CDCl_3$) δ 2.53 (s, SCH_3), 3.45 (s, OCH_3), 3.70 (d, H-5', J = 5.0 Hz), 4.0–4.83 (m, H-4',3',2'), 4.17, 4.53, 4.63 (s, 3 benzyl CH_2), 5.62 (s, NCH_2), 6.58 (d, H-1', J = 4.0 Hz), 6.60 (d, H-5, J = 3.5 Hz), 7.15 (d, H-6, J = 3.5 Hz), 6.83–7.40 (m, 15 aromatic H); ^{13}C NMR (Me_2SO-d_6) δ 14.57 (SCH_3), 56.21 (OCH_3), 69.22 (C-5'), 71.30, 71.75, 72.33 (3 CH_2), 73.24 (NCH_2O), 79.33 (C-2'), 80.63 (C-3'), 82.05 (C-4', C-1'), 102.38 (C-5), 102.90 (C-4a), 122.07 (C-6), 127.57, 128.22 (15 aromatic C), 138.06, 137.93, 137.16 (3 aromatic C), 145.72 (C-7a), 157.23 (C-2), 158.14 (C-4).

Anal. Calcd for $C_{35}H_{37}N_3O_6S$: C, 66.97; H, 5.94; N, 6.69; S, 5.11. Found: C, 67.14; H, 5.94; N, 6.60; S, 5.08.

2-(Acetylamino)-3-(methoxymethyl)-7-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)pyrrolo[2,3-*d*]pyrimidine (8c). A mixture of sodium hydride (0.48 g, 16 mmol, 20% in paraffin) and freshly sublimized acetamide (5.0 g) was heated to a clear melt at 100 °C in an oil bath under nitrogen. After the mixture cooled, the nucleoside **8b** (1.0 g, 1.6 mmol) was added to the molten material, and the resulting mixture was heated for another 40 min at 100 °C. The cooled mixture was then carefully neutralized with glacial acetic acid at 0 °C, diluted with water, and extracted with benzene. The organic layer was separated, dried over sodium sulfate, filtered, and evaporated. The remaining residue was dissolved in chloroform and applied to a Lobar silica gel column (solvent B). From the main zone compound **8c** (0.87 g, 86%) was obtained as a colorless syrup after evaporation: TLC (solvent C) R_f 0.38; UV (methanol) λ_{max} 265 nm (ϵ 7700), 295 (8500); ^{1}H NMR ($CDCl_3$) δ 2.37 (s, $NHCOCH_3$), 3.38 (s, OCH_3), 3.68 (d, H-5', J = 5.0 Hz), 3.90–4.67 (m, H-4',3',2'), 4.27, 4.51, 4.60 (s, 3 benzyl CH_2), 5.52 (s, NCH_2O), 6.46 (d, H-1', J = 5.0 Hz), 6.62 (d, H-5, J = 3.5 Hz), 7.21 (d, H-6, J = 3.5 Hz), 6.83–7.45 (m, 15 aromatic H), 8.45 (br s, NHAc); ^{13}C NMR (Me_2SO-d_6) δ 22.99 ($COCH_3$), 56.27 (OCH_3), 69.55 (C-5'), 71.29, 71.75, 72.33 (3 CH_2), 72.33 (OCH_2N), 79.39 (C-2'), 81.33 (C-3'), 82.05 (C-1', C-4'), 103.33 (C-4a), 104.65 (C-5), 124.60 (C-6), 127.57, 128.22 (15 aromatic C), 137.28, 137.93, 138.06 (3 aromatic C), 145.32, 144.73 (C-2, C-7a), 158.33 (C-4), 170.25 (CO).

Anal. Calcd for $C_{36}H_{38}O_7N_4$: C, 67.69; H, 6.00; N, 8.77. Found: C, 67.88; H, 6.04; N, 8.76.

4-Amino-3-(methoxymethyl)-7-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)pyrrolo[2,3-*d*]pyrimidine (8d). Compound **8c** (1.0 g, 1.6 mmol) in methanol/concentrated ammonia (50 mL, 10:1) was stirred for 12 h and then evaporated to dryness. The oily residue was applied to a Lobar silica gel column (solvent B) to afford a colorless syrup: 0.94 g (94%); TLC (solvent C) R_f 0.38); UV (methanol) λ_{max} 262 nm (ϵ 12700), 289 (7400); ^{1}H NMR ($CDCl_3$) δ 3.36 (s, OCH_3), 3.66 (d, H-5', J = 5.0 Hz), 4.00–4.30 (m, H-4',3',2'), 4.20, 4.53, 4.60 (s, 3 benzyl CH_2), 5.20 (s, NH_2), 5.45 and 5.57 (NCH_2O, J = 10.5 Hz), 6.43 (d, H-1', J = 5.0 Hz), 6.53 (d, H-5, J = 3.5 Hz), 7.00 (d, H-6, J = 3.5 Hz), 6.92–7.45 (m, 15 aromatic H); ^{13}C NMR (Me_2SO-d_6) δ 55.63 (OCH_3), 70.16 (C-5'), 71.19, 71.55, 72.33 (3 CH_2), 72.33 (OCH_2N), 79.46 (C-3'), 81.27 (C-2'), 81.79 (C-1', C-4'), 98.62 (C-5), 103.50 (C-4a), 121.36 (C-6), 127.51, 128.22 (15 aromatic C), 137.42, 137.97, 138.20 (3 aromatic C), 149.14 (C-7a), 153.03 (C-2), 158.27 (C-4).

Anal. Calcd for $C_{34}H_{36}O_6N_4$: C, 68.44; H, 6.08; N, 9.39. Found: C, 68.29; H, 6.18; N, 9.26.

4-Amino-7-(β-D-arabinofuranosyl)pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-one (2). To a solution of compound **8d** (355 mg, 0.59 mmol) in methylene chloride (30 mL) was added a solution of 1.2 M boron trichloride in methylene chloride (10 mL, 12 mmol) at −78 °C (dry ice–acetone). The mixture was kept for 4 h at the same temperature. It was then treated with methanol–methylene chloride (50 mL, 1:1) and stored at room temperature for another 30 min. The solvent was evaporated, the residue dissolved in ethanol (150 mL) and carefully neutralized with 1 N aqueous sodium hydroxide. Inorganic precipitate was filtered and the solution evaporated. The resultant was dissolved in methanol (50 mL), adsorbed on silica gel (10 g) and the solvent removed in vacuo. The suspension of this silica gel in solvent E was applied to the top of a silica gel column (30 × 2.5 cm). Elution with solvent E yielded a colorless syrup (97 mg, 58.0%) which could be crystallized from ethanol as colorless crystals which decompose at 210 °C; TLC (solvent E) R_f 0.2; UV (methanol) λ_{max} 218 nm (ϵ 19800), 259 (12500), 280 (7800); ^{1}H NMR, see Table II; ^{13}C NMR (Me_2SO-d_6) δ 61.54 (C-5'), 75.95 (C-3',2'), 83.16 (C-1'), 83.76 (C-4'), 99.64 (C-4a), 100.88 (C-5), 119.94 (C-6), 150.71 (C-7a), 152.71 (C-2), 158.78 (C-4).

Anal. Calcd for $C_{11}H_{14}N_4O_5$: C, 46.80; H, 5.00; N, 19.85. Found: C, 46.58; H, 5.28; N, 19.25.

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Registry No. **2**, 79816-01-6; **3**, 7355-55-7; **4**, 29877-76-7; **5**, 70613-79-5; **6**, 72564-99-9; **7**, 72564-98-8; **8a**, 79816-02-7; **8b**, 79816-03-8; **8c**, 79816-04-9; **8d**, 79816-05-0; guanosine, 118-00-3; guanine, 73-40-5.

Syntheses of Isoretronecanol and Lupinine

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Syntheses of (±)-isoretronecanol and (±)-lupinine are described which employ the 1,3-dipolar additions of cyclic nitrones to dihydrofuran and dihydropyran. The reaction proceeded regio- and stereoselectively to afford the adducts, which were converted into the title compounds by two-step processes.

Alkaloids containing the nitrogen atom in bridgehead position of two rings, indolizidine, pyrrolizidine, and quinolizidine alkaloids, have a wide and varied distribution in the nature.[1] Some of these alkaloids demonstrate a broad range of pharmacological activities[2] and have generated substantial synthetic interest.[3] This report deals

(1) (a) J. D. Hunt and A. McKillop in "Rodd's Chemistry of Carbon Compounds", Vol. IVB, S. Coffey, Ed., Elsevier, Amsterdam, 1978, p 37; (b) H. C. S. Wood and R. Wrigglesworth, *ibid.*, Vol. IVH, p 285.

(2) (a) F. L. Warren in "The Alkaloids-Chemistry and Physiology", Vol. XII, R. H. F. Manske, Ed., Academic Press, New York, 1970, p 319; (b) D. H. G. Croat in "The Alkaloids", Vol. 6, The Chemical Society, London, 1976, p 84.

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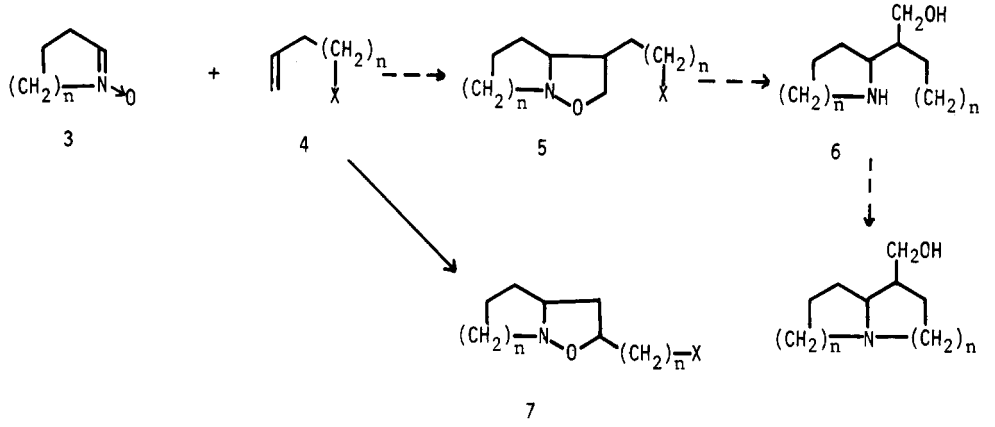
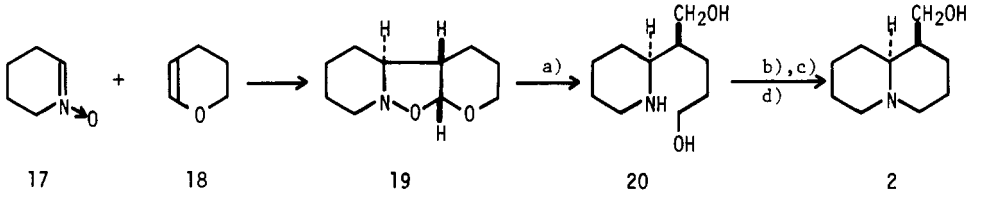
Scheme I



Scheme II

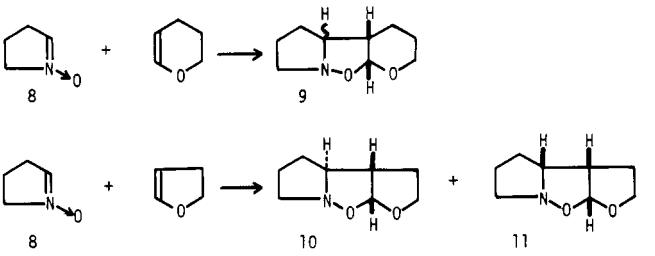


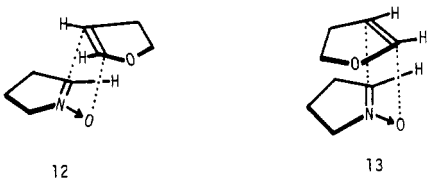
(a) $LiAlH_4$, (b) Et_2N-$SiMe_3$, (c) Me_3SiI, (d) $Bz{\cdot}Me_3NF$

with new stereoselective syntheses of isoretronecanol (1)[4] and lupinine (2).

1 2

Retrosynthetic analysis of these alkaloids indicated that one possible means of assembling the molecular framework would involve 1,3-dipolar addition of a cyclic nitrone to an ω-haloalkene as shown in Scheme I. However, accumulated[5] data about the regioselectivity of 1,3-dipolar addition of nitrones indicated that the reaction of 3 and 4 would afford an unfavorable isomeric adduct 7 rather than 5. Thus, Tufariello and Tette,[3g] in their synthetic studies of isoretronecanol, chose a symmetrical olefin, diethyl fumarate, as the dipolarophile to the nitrone 3, and they converted the adduct into pyrrolizidine derivatives. The unfavorable orientation of the vinyl compound 4 to the nitrone 3 was expected to be reversed by displacement of a terminal ethylenic hydrogen atom in 4 with a heteroatom, but the regioselectivity of the 1,3-dipolar addition of nitrones to heteroatom-substituted ethylenes was not well documented.[6] The authors examined first the reaction of 1-pyrroline 1-oxide (8) and dihydropyran. The





12 13

reaction of the nitrone 8 with dihydropyran occurred on brief heating in benzene solution to give a single adduct (9). The NMR spectrum of the adduct revealed a doublet at δ 5.06 (J = 4 Hz) due to an acetal proton, showing that the reaction proceeded regiospecifically to afford a product having the structure 9. This finding encouraged further exploration of this approach. Under the same conditions, dihydrofuran reacted with nitrone 8 more smoothly than

(3) (a) N. J. Leonard and T. Saba, *J. Org. Chem.*, **34**, 1066 (1969); (b) S. Brandange and C. Lundin, *Acta Chem. Scand.*, **25**, 2447 (1971); (c) M. Viscontini and H. Gillhofschaufelberger, *Helv. Chim. Acta*, **54**, 449 (1971); (d) M. Viscontini and H. Buzek, *ibid.*, **55**, 670 (1972); (e) M. T. Pizzorno and S. M. Albonico, *J. Org. Chem.*, **39**, 731 (1974); (f) J. W. Lown and T. Itoh, *Can. J. Chem.*, **53**, 960 (1975); (g) J. J. Tufariello and J. P. Tette, *J. Org. Chem.*, **40**, 3866 (1975); (h) R. V. Stevens, Y. Luh, and J.-T. Sheu, *Tetrahedron Lett.*, 3799 (1976); (i) R. F. Borch and B. C. Ho, *J. Org. Chem.*, **42**, 1225 (1977); (j) S. Danishefsky, R. McKee, and R. K. Singh, *J. Am. Chem. Soc.*, **99**, 4783 (1977); (k) H. W. Pinnick and Y.-H. Chang, *J. Org. Chem.*, **43**, 4662 (1978); (l) H. W. Pinnick and Y.-H. Chanq, *Tetrahedron Lett.*, 837 (1979); (m) D. J. Robins and S. Sakdarat, *J. Chem. Soc., Chem. Commun.*, 1181 (1979); (n) F. M. Schell, R. N. Ganguly, K. S. Percell, and J. E. Parker, *Tetrahedron Lett.*, 4925 (1975); (o) A. S. Howard, G. C. Gerrans, and J. P. Michael, *J. Org. Chem.*, **45**, 1713 (1980); (p) G. A. Kraus and K. Neuenschwander, *Tetrahedron Lett.*, 3841 (1980); (q) J. M. Muchowski and P. Nelson, *ibid.*, 4585 (1980); (r) W. Flitsch and P. Wernsmann, *ibid.*, 719 (1981).

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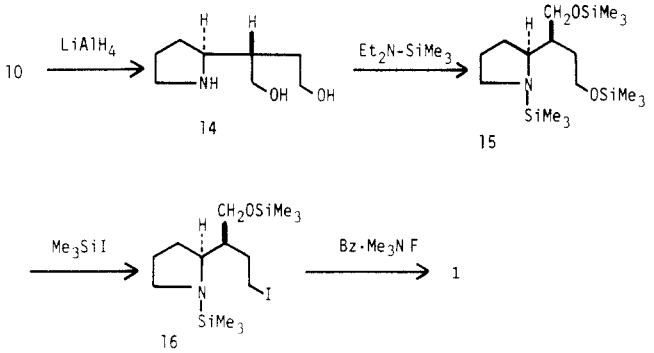
(5) D. St. C. Black, R. F. Crozier, and V. C. Davis, *Synthesis*, 205 (1975).

(6) Addition of a nitrone to an enamine has been reported by O. Tsuge, M. Tashiro, and Y. Nishihara, *Tetrahedron Lett.*, 3769 (1967).

dihydropyran to afford two adducts, in 92% and 3% yields, which were separated by chromatography. The structure **10** for the major product and **11** for the minor product including the stereochemistry were assigned from the spectral properties and the reaction mechanism. It has been reported that 1,3-dipolar cycloadditions of a conjugated nitrone, *C*-phenyl-*N*-methylnitrone, to conjugated alkenes such as styrene and alkyl acrylate afford mainly endo adduct because of secondary orbital interactions in the transition state.[7] However, unconjugated alkenes are known to give exclusively exo addition product owing to disfavored steric interaction of the rest of molecule in the endo mode of addition. Thus, unconjugated nitrone **8** and dihydrofuran would react through an exo-oriented transition state **12** rather than an endo transition state **13** to afford an adduct having the stereostructure **10**. This was finally confirmed by converting it into isoretronecanol.

The major adduct **10** was reduced with lithium aluminum hydride to afford an amino diol, **14**, in quantitative yield. Many efforts to cyclize the amino diol directly to the pyrrolizidine ring by using reagents such as thionyl chloride[8] or hydrobromic acid only resulted in formation of a trace amount of isoretronecanol (**1**). But the amino diol **14** was converted into the alkaloid in a modest yield by using the following new method. The amino and hydroxyl groups of the amino diol **14** were thoroughly silylated by being heated with diethylsilazan. After the excess reagent was removed, the trisilylated **15** was treated with



1 equiv of trimethylsilyl iodide[11] in chloroform. This iodide was anticipated to attack mainly at sterically less hindered carbon-4 of **15** leading to an iodide **16**. Without the isolation of the reaction product, mixture was further treated with benzyltrimethylammonium fluoride at room temperature and then at 50 °C to afford isoretronecanol in 59% yield. Addition of potassium hydroxide solution to the iodide **16** also afforded the alkaloid **1** in 45% yield. The synthetic compound showed the same spectral properties as those of an authentic sample.[9]

Lupinine,[12] a quinolizidine alkaloid isolated from yellow lupin seeds, was synthesized by the same method as isoretronecanol. The cycloaddition reaction of a 1-piperine 1-oxide **17** with dihydropyran (Scheme II) occured upon heating in a benzene solution to afford a single adduct **19** in 18% yield. The low yield in this reaction was considered due to the low reactivity of dihydropyran and the instability of the nitrone **17**. The yield was slightly improved to 32% by using ethanol as a solvent. Tricyclic adduct **19** was converted into lupinine via **20** by using exactly the same method as for isoretronecanol. The IR and NMR spectra of the synthetic compound were identical with those of an authentic sample.

These syntheses of indolizidine and quinolizidine alkaloids suggest that the 1,3-cycloaddition reaction of cyclic nitrones and cyclic enol ether should serve as a useful method for the synthesis of more complex alkaloids with a nitrogen atom at bridgehead position.

Experimental Section

Melting points were determined on a Yamato capillary melting point apparatus. Infrared (IR) spectra were recorded on a Hitachi 215 grating spectrophotometer. Proton magnetic resonance (^{1}H NMR) spectra were measured on either a Hitachi H-60 or JEOL JNM-MH-100 instrument with chemical shifts given in parts per million (δ) downfield from tetramethylsilane as an internal standard. Mass spectra were obtained on a Hitachi RMU-6H instrument. Elemental analyses were performed by the University of Tsukuba-Chemical Analysis Center. GLC data were obtained with a Shimazu GC-3F gas chromatograph using nitrogen at flow rate of 43 mL/min. The column used was a 1.7 m × 3 mmi.d. glass column packed with 5% OV-1.

Reaction of 1-Pyrroline 1-Oxide (8) with 2,3-Dihydropyran. A solution of 1-pyrroline 1-oxide,[10] prepared from 613 mg (7.0 mmol) of *N*-hydroxypyrrolidine, and 1.27 g (15.1 mmol) of 2,3-dihydropyran in 2.4 mL of dry benzene was placed in a sealed tube under an argon atmosphere and heated in refluxing xylene for 2 h. The excess 2,3-dihydropyran and the solvent were removed under reduced pressure, giving 709 mg of crude oil. The oil was purified by flash chromatography to afford 300 mg (18%) of 1-aza-2,4-dioxatricyclo[7.3.0.0^{3,8}]dodecane (**9**) in a pure state. An analytical sample was further purified by short-path distillation at 80–85 °C (0.06 mm): IR ($CHCl_3$) 2940, 2860, 1445, 1105, 1095, 1075, 1050, 990, 900 cm^{-1}; NMR (CCl_4, 60 MHz) δ 1.32–2.2 (9 H, m), 2.7–4.0 (5 H, m), 5.06 (1 H, d, J = 4 Hz); mass spectrum, m/e 169.1089 (M^+, calcd for $C_9H_{15}O_2N$, 169.1102).

Preparation of 1-Aza-2,4-dioxatricyclo[6.3.0.0^{3,7}]undecane (10). A solution of 1-pyrroline 1-oxide (**8**), prepared from 2 g (23 mmol) of *N*-hydroxypyrrolidine, and 2.92 g (42 mmol) of 2,3-dihydrofuran in 8.6 mL of benzene was placed in three glass tubes, which were sealed under argon atmosphere and heated in refluxing xylene for 1 h. The excess 2,3-dihydrofuran and the solvent were removed under reduced pressure to give 3.64 g of crude adducts which contained two compounds. These compounds were separated by silica gel column chromatography. Elution with chloroform gave 3.3 g (92%) of the major oil and 109 mg (3%) of the minor one, which were further purified by distillation for elemental analyses.

Major oil **10**: bp 86.0–87.5 °C (4 mm); IR ($CHCl_3$) 2960, 2870, 1440, 1365, 1075, 1030, 995, 995, 920, cm^{-1}; ^{1}H NMR (CCl_4) δ 1.2–2.4 (6 H, m), 2.5–3.5 (4 H, m), 3.5–4.2 (2 H, m), 5.50 (1 H, d, J = 5 Hz); mass spectrum, m/e 155 (M^+), 138, 110, 96, 86 (base), 70.

Anal. Calcd for $C_8H_{13}O_2N$: C, 61.91; H, 8.44; N, 9.02. Found: C, 61.57; H, 8.41; N, 9.00.

Minor oil **11**: bp 62 °C (bath temperature, 0.007 mm); IR ($CHCl_3$) 2960, 2890, 1450, 1370, 1125, 1075, 1050, 995, 950 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.3–2.3 (6 H, m), 2.5–4.1 (6 H, m), 5.52 (1 h, d, J = 5 Hz); mass spectrum, m/e 155 (M^+), 138, 110, 96, 86 (base), 70.

2-(1,4-Dihydroxybut-2-yl)pyrrolidine (14). To a solution of 2.92 g (1.88 mmol) of the major adduct **10** in 200 mL of dry tetrahydrofuran, was added 2.52 g (66.3 mmol) of lithium aluminum hydride. The mixture was heated at reflux temperature with stirring under an argon gas atmosphere. After 40 h, the reaction mixture was successively treated with 2.5 mL of water, 2.5 mL of 15% sodium hydroxide solution, and 7.5 mL of water with cooling by ice–water. The precipitate was filtered off and

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(8) I. Ninomiya, T. Naito, and T. Kiguchi, *J. Chem. Soc., Chem. Commun.*, 1669 (1970).
(9) All the chemical shifts of the synthetic compound has been slightly different from the values reported by Pinnick and Chang,[3k] but the published values were found to be uncalibrated with respect to the reference tetramethylsilane on comparison with the spectrum provided from Professor Pinnick.
(10) S. R. Sandler and W. Karo, "Organic Functional Group Preparation", Vol. III, Academic Press, New York, 1972.
(11) M. E. Jung and P. L. Ornstein, *Tetrahedron Lett.*, 2659 (1977).
(12) G. Baumert, *Chem. Ber.*, **14**, 1321 (1881); **15**, 634 (1882); P. Karrer, F. Canal, and K. Zohner, *Helv. Chim. Acta*, 11, 1062 (1928).

washed with ether. The combined organic layer was concentrated under reduced pressure to afford the amino diol **14** in quantitative yield: 3.07 g; IR (liquid film) 3320, 2930, 2860, 1410, 1050 cm^{-1}; ^1H NMR($CDCl_3$) δ 1.2–2.1 (6 H, m), 2.8–3.4 (4 H, m), 3.5–3.9 (4 H, m), 4.57 (3 H, s); mass spectrum, m/e 160 ($M^+ + 1$), 112, 98, 84, 70 (base).

This compound was difficult to distill, and therefor it was converted into its triacetate by treatment with acetic anhydride in pyridine. The triacetate was purified by silica gel column chromatography and distillation for elemental analysis.

Anal. Calcd for $C_{14}H_{23}O_5N$: C, 58.93; H, 8.12; N, 4.90. Found: C, 58.65; H, 8.12; N, 5.17.

Preparation of *dl*-Isoretronecanol (1). A mixture of 1.1 g (7 mmol) of the amino diol **14** and 5.53 g (38.1 mmol) of *N*-(trimethylsilyl)diethylamine was heated at 145 °C with continuous removal of diethylamine by distillation. After 3 h, excess reagent was removed under reduced pressure. The residue was dissolved in 10 mL of dry chloroform and treated with 1.4 g (7 mmol) of trimethylsily iodide. The mixture was stirred at 50 °C under an argon atmosphere. After 12.5 h, 15 mL of 23% potassium hydroxide solution was added into the reaction mixturea at 0 °C. The mixture was stirred for 1 h at room temperature under an argon atmosphere, and the product was extracted with ether. The solvent was removed under reduced pressure to give 1.24 g of the crude trimethylsilyl ether of *dl*-isoretroncanol, which was distilled under reduced pressure [Kugelrohr; bath temperature 82–89 °C (2mm)] to give 875 mg (59%) of the ether in a pure state. This trimethylsilyl ether was hydrolized with water to afford 443 mg (45%) of isoretronecanol, which was converted into the picrate. After three recrystallizations, its melting point rose to 188.5–189.0 °C (corrected value 190.8–191.3 °C, lit.[3a] mp 189.5–190 °C). The pure free *dl*-isoretronecanol was liberated from the picrate by treatment with potassium hydroxide: IR (liquid film) 3380, 2950, 2880, 1460, 1110, 1080, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2–2.1 (6 H, m), 2.2–3.4 (6 H, m), 3.60 (2 H, d, J = 7 Hz), 5.58 (1 H, br s); mass spectrum, m/e 141 (M^+), 124, 110, 83 (base).

Benzyltrimethylammonium Fluoride Treatment of the Disilyl Iodide 16. After treatment of the tris(trimethylsilyl) ether of the amino diol **14** (105.7 mg, 0.66 mmol) with trimethylsilyl iodide as stated above, 115.8 mg (0.69 mmol) of benzyltrimethylammonium fluoride in 5 mL of tetrahydrofuran was added to the reaction mixture which was stirred for 2 h at room temperature and 30 min at 50 °C. Filtration and removal of solvent afforded 54.7 mg (59%) of crude isoretronecanol; picrate, mp 184.0–185.0 °C (mmp 185.0–187.5 °C).

1-Piperine 1-Oxide (17). To a solution of 1.8 g (17.8 mmol) of *N*-hydroxypiperidine in 50 mL of dry chloroform was added 10 g of yellow mercuric oxide in one portion. The reaction was exothermic, and the mixture changed to gray. After the mixture was stirred for 2 h under an argon atmosphere at room temperature, another 2 g of yellow mercuric oxide was added to the reaction mixture, and the whole was stirred for additional 2 h. The inorganic precipitate was filtered off, and the filtrate was concentrated under reduced pressure to afford 2.1 g of crude oil, which was purified by flash chromatography to give 1.7 g (97%) of 1-piperine 1-oxide (**17**): ^1H NMR ($CDCl_3$) δ 1.3–2.2 (4 H, m), 2.2–2.7 (2 H, m), 3.5–4.0 (2 H, m), 7.22 (1 H, m).

Addition Reaction of 1-Piperine 1-Oxide (17) with 2,3-Dihydropyran. A solution of 1-piperine 1-oxide (**17**) prepared by oxidizing of 1.4 g (140 mmol) of *N*-hydroxypiperidine and 2.1 g (250 mmol) of 2,3-dihydropyran in 4.5 mL of benzene was divided into three glass tubes. These tubes were heated at three different temperatures, 110, 140, and 190 °C, respectively. After 10 h, the excess reagent was removed under reduced pressure to afford a crude oil, which was purified by flash chromatography to give pure tricyclic adduct **19**. The yield was slightly increased by decreasing the temperature: 3% at 190 °C, 10% at 140 °C, and 12% at 110 °C. The yield of the addition reation was improved by changing the solvent from benzene (18%) to ethanol (32%); other solvents, dimethyl sulfoxide (22%), pyridine (19%), and dihydropyrane (14%), showed almost the same yield.

An analytical sample of **19** was obtained by short-path distillation at 90 °C (0.15 mm): IR ($CHCl_3$) 2950, 1440, 1060, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) 1.2–2.5 (12 H, m), 2.5–3.1 (2 H, m), 3.1–4.2 (2 H, m), 5.22 (1 H, d, J = 4.5 Hz).

Amino Diol 20. To a solution of 2.8 g (15.3mmol) of tricyclic adduct **19** in 100 mL of dry tetrahydrofuran was added 3.1 g (81.8 mmol) of lithium aluminum hydride. The mixture was refluxed with stirring under an argon atmoshpere. After 40 h, the reaction mixture was cooled to −78 °C and treated with 3 mL of water, 3 mL of 15% sodium hydroxide solution, and 9 mL of water. The white precipitate was filtered off, and the filtrate was concentrated under reduced pressure to afford 2.2 g (76.9%) of amino diol **20**: IR ($CHCl_3$) 3350, 2940, 1440, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2–2.0 (1 H, m), 2.5–3.3 (3 H, m), 3.4–4.0 (4 H, m), 3.83 (3 H, s).

This compound was difficult to distill, and it was converted into its acetate and purified by chromatography followed by short-path distillation for elemental analysis: IR (film) 2950, 1730, 1640, 1425, 1360, 1240, 1030, 990 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65 (11 H, br), 2.1 (9 H, br s), 3.6–3.7 (2 H, m), 3.9–4.2 (4 H, m).

Anal. Calcd for $C_{16}H_{27}O_5N$: C, 58.93; H, 8.12; N, 4.90. Found: C, 58.65; H, 8.12; N, 5.17.

***dl*-Lupinine (2).** Amino diol **20** (255 mg, 1.36 mmol), dried by azeotropic distillation with benzene, was heated with 1 g (6.9 mmol) of *N*-(trimethylsilyl)diethylamine at 145 °C for 3 h. After complete removal of the excess reagent under reduced pressure, the silylated amino diol was dissolved in 1 mL of dry carbon tetrachloride. To the solution was added 0.28 g (1.4 mmol) of trimethylsilyl iodide, and the mixture was heated at 80 °C for 12 h under a nitrogen atmosphere. Gas chromatography of the reaction mixture showed the presence of the unreacted silylamino diol. Then, another trimethylsilyl iodide (0.28 g) was added to the reaction mixture, and the solution was heated at 50 °C for 24 h. The reaction mixture was treated with 20% potassium hydroxide solution and extracted with ether. The extract was washed with brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to give 252 mg of a crude oil, which was purified by aluminum oxide (activity II–III) column chromatography to afford 57 mg (25% yield from amino diol **20**) of **2** in a pure state: mp 57.5–58.5 °C; IR ($CHCl_3$) 3200, 2930, 1460, 1435, 1345, 1140, 1120, 1105, 1100, 1080, 1045, 1010, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.2–2.3 (15 H, m), 2.7–2.9 (1 H, m), 3.69 (1 H, dd, J = 11, 1 Hz), 4.11 (1 H, dd, J = 11, 5 Hz), 4.7 (1 H, br s); mass spectrum, m/e 169 (M^+), 152 (base). The synthetic alkaloid was completely identical with authentic sample in spectral properties.

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