Chem. Pharm. Bull. 28(3) 831—836 (1980)

Constituents of Rhizoma Nupharis. XXVIII.[1] New Syntheses of (±)-7-Epideoxynupharidine, (±)-1-Epi-7-epideoxynupharidine, (±)-Deoxynupharidine, and (±)-1-Epideoxynupharidine

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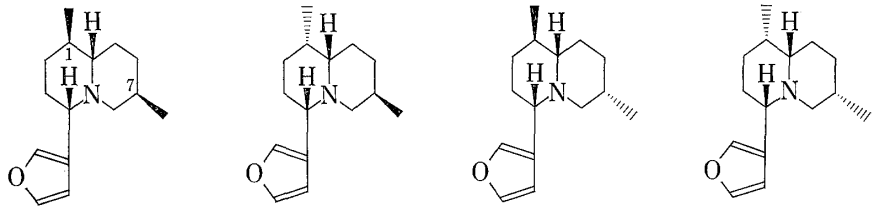
(Received August 17, 1979)

A new stereoselective synthesis of (±)-7-epideoxynupharidine (**1**), the most stable quinolizidine-type Nuphar alkaloid, is described. Condensation of 2-ethyl-5-methylpyridine (**5**) with acetonitrile, followed by ketalization, gave the ketal (**13**), which was hydrogenated to afford the piperidine (**14**). Deketalization of **14** afforded the aminoketone (**15**). Condensation of **15** with 3-furylaldehyde afforded four quinolizidin-2-ones (**8**, **16**, **17**, and **18**) in 14, 45, 1, and 3% yields, respectively. The *cis*-quinolizidines (**16** and **18**) were isomerized to the *trans*-quinolizidines (**8** and **17**, respectively). Wolff–Kishner reduction of **8** afforded (±)-7-epideoxynupharidine (**1**) (45%) and (±)-1-epi-7-epideoxynupharidine (**2**) (15%). Similar reduction of **17** provided (±)-deoxynupharidine (**3**) (33%) and (±)-1-epideoxynupharidine (**4**) (14%).

Keywords——Nuphar alkaloids; quinolizidine; stereoselective synthesis; isomerization *via* amino-enone; Wolff–Kishner reduction; (±)-7-epideoxynupharidine; (±)-1-epi-7-epideoxynupharidine; (±)-deoxynupharidine; (±)-1-epideoxynupharidine

7-Epideoxynupharidine (**1**),[3] an alkaloid from *Nuphar luteum* subsp. *variegatum*, was shown to be the most stable isomer of the quinolizidine-type Nuphar alkaloids. Recently, **1** and its stereoisomers, 1-epi-7-epideoxynupharidine (**2**), deoxynupharidine (**3**), and 1-epideoxynupharidine (**4**) were isolated from scent glands of the Canadian beaver.[4] Unstereoselective synthesis of **1** together with five other stereoisomers had been reported[5] before its isolation.



1 **2** **3** **4**

Chart 1

In the previous paper,[1] we presented a design for a stereoselective synthesis of **1**, as shown in Chart 2, and its validity was demonstrated by a stereoselective synthesis of 1-methyl(*e*)-4-phenyl(*e*)-*trans*-quinolizidin-2-one (**11**) and 7-methyl(*e*)-4-phenyl(*e*)-*trans*-quinolizidin-2-one (**12**), the most stable isomers of their stereoisomers. The present paper is concerned with a

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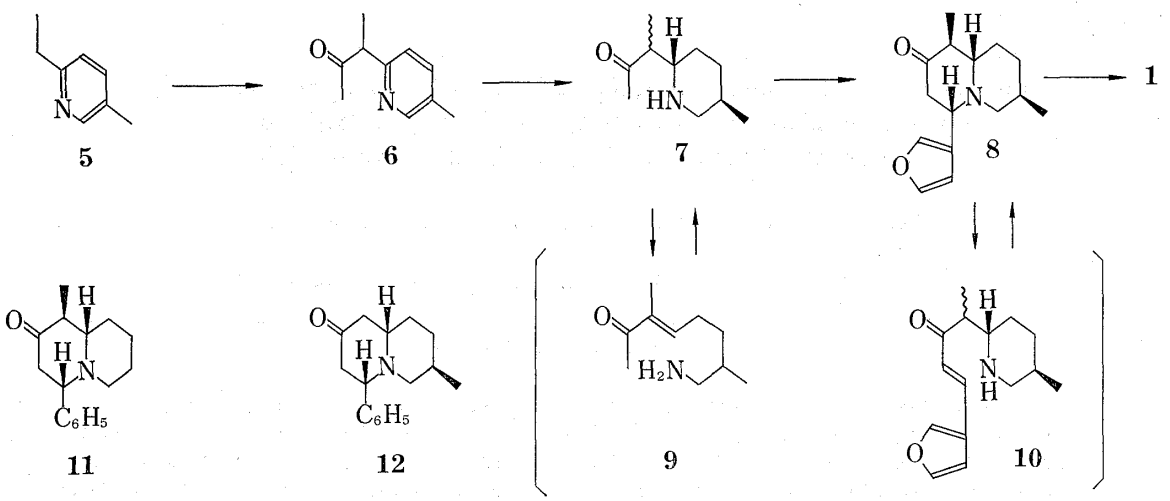

Chart 2

new synthesis of **1** according to the above synthetic design, as well as syntheses of **2**, **3**, and **4**. A part of this work has been reported in a preliminary communication.[6]

Condensation of 2-ethyl-5-methylpyridine (**5**)[7] with acetonitrile in the presence of phenyllithium, followed by acidic treatment, gave the ketone (**6**) [$\nu_{max}^{CHCl_3}$ cm^{-1}: 1705 (C=O), δ: 1.44 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 2.10 (3H, s, CH_3), 2.33 (3H, s, CH_3), 3.94 (1H, q, J=7 Hz, $C\underline{H}CH_3$)] in 35% yield. Ketalization of **6** with ethylene glycol afforded the ketal (**13**) in 76% yield, and this was hydrogenated over 5% rhodium on alumina in acetic acid to give the piperidine (**14**) [90%, $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (NH)] as a mixture of stereoisomers. The mixture (**14**) was subjected to deketalization without separation into stereoisomers, since its deketalization products were predicted[1] to isomerize mutually *via* the amino-enone (**9**) under deketalization conditions. The previous paper[1] reported that such isomerization was promoted by the use of 10% hydrochloric acid as a deketalization reagent and that this effect was prevented to a considerable extent by the use of 10% acetic acid or *p*-toluenesulfonic acid. Deketalization of **14** with 10% hydrochloric acid provided the aminoketone (**15**) [$\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (NH), 1705 (C=O), *m/e*: 169(M^+)] as a mixture of stereoisomers in 87% yield.

Condensation of the aminoketone (**15**) with 3-furylaldehyde in aqueous methanol in the presence of sodium hydroxide, followed by chromatographic separation, afforded the four stereoisomeric quinolizidin-2-ones (**8**, **16**, **17**, and **18**) in 14, 45, 1, and 3% yields, respectively. Their spectral data are listed in Table I.

The *cis* relationship between C_4–H and C_{10}–H in **8** and **17** was confirmed by the presence of the Bohlmann bands in their IR spectra and C_4–H signals in their NMR spectra. The equatorial methyl group on C_1 in **8** and **17** was suggested by the finding that no epimerization occurred at C_1 on treatment of **8** and **17** with sodium methoxide in methanol. The *trans*-quinolizidines (**8** and **17**) are, therefore, epimeric at C_7. The higher chemical shift and smaller coupling constant of the C_7-methyl signal of **8** in comparison with those of **17** in the NMR spectra indicated that the C_7-methyl group in **8** is equatorial, while that in **17** is axial.[8] The stereochemistry of **8** and **17** was thus established as depicted.

The presence of the *cis*-quinolizidine ring in **16** and **18** was confirmed by the lower chemical shift of C_4–H in their NMR spectra[9] and the absence of a Bohlmann band in their IR spectra. As the *cis*-quinolizidines (**16** and **18**) isomerized to the *trans*-quinolizidines (**8** and **17**) *via* the

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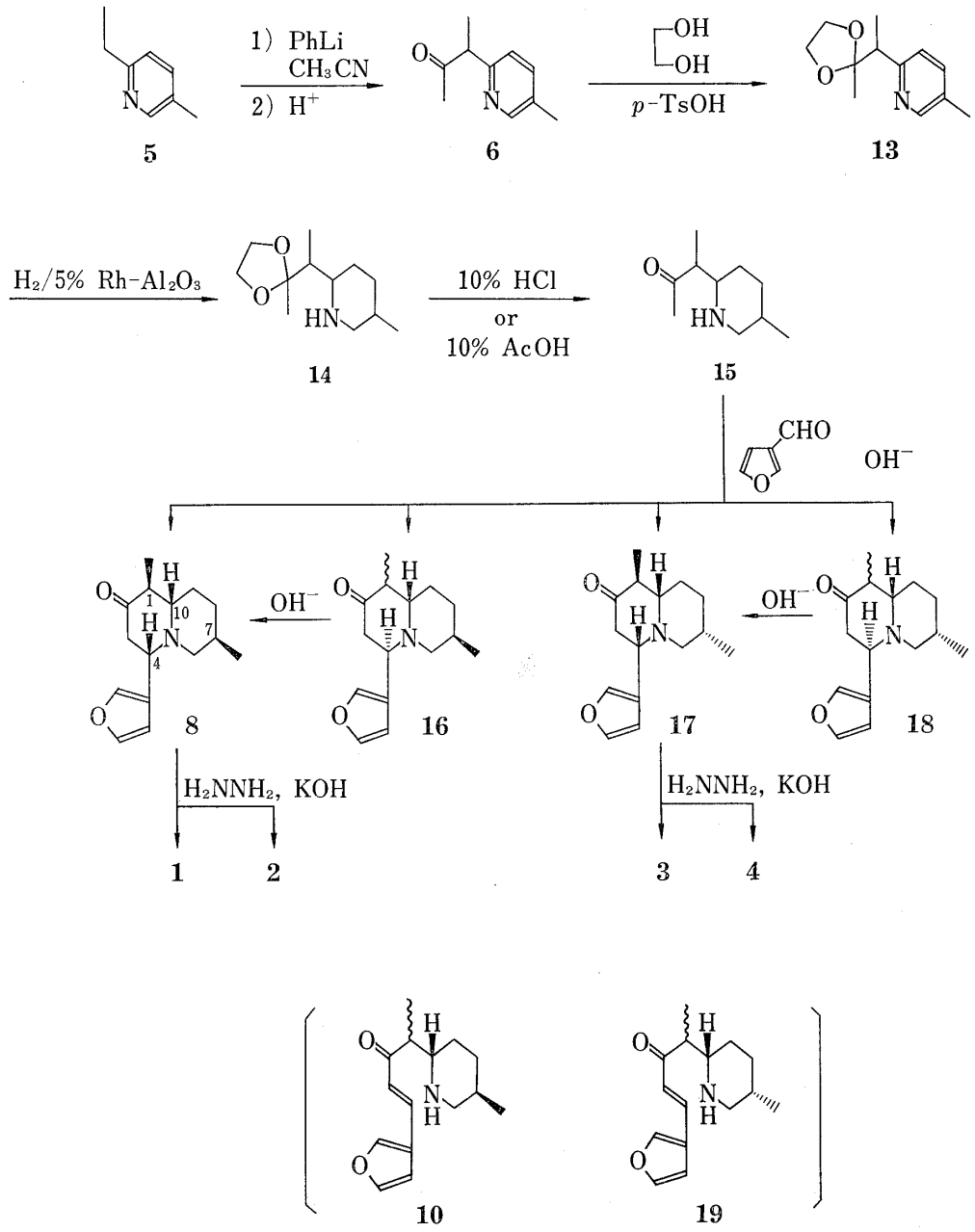

5 6 13 14 15 8 16 17 18 1 2 3 4 10 19

Chart 3

TABLE I. Spectral Data for 4-Furylquinolizidin-2-ones (**8**, **16**, **17**, and **18**) and Nuphar Alkaloids (**1**, **2**, **3**, and **4**)

Compd.	IR cm^{-1}: Bohlmann band	IR cm^{-1}: Carbonyl	NMR δ: C_1-methyl	NMR δ: C_7-methyl	NMR δ: C_4–H
8	2790, 2770	1712	1.05 (d, J=6.5)	0.77 (d, J=6)	3.31 (d-d, J=12; 3)
16	—	1708	1.10 (d, J=6.5)	0.86 (d, J=5.5)	4.24 (d-d, J=7; 2)
17	2790, 2765	1710	1.03 (d, J=7.5)	1.03 (d, J=7.5)	3.52 (d-d, J=11.5; 3.5)
18	—	1700	1.03 (d, J=6.5)	0.96 (d, J=6)	4.20 (br-d, J=6)
1	2790, 2770	—	0.90 (d, J=6)	0.72 (d, J=6.5)	
2	2790, 2765	—	1.07 (d, J=6.5)	0.73 (d, J=6.5)	
3	2780, 2750	—	0.86 (d, J=5.5)	0.98 (d, J=7)	
4	2790, 2760	—	1.08 (d, J=7)	0.98 (d, J=7)	

amino-enones (**10** and **19**) in 60 and 50% yields, respectively, on treatment with aqueous sodium hydroxide in methanol, the stereochemistry of the C_7-methyl group in **16** and **18** was suggested to be as depicted. However, the stereochemistry of the C_1-methyl group in **16** and **18** remained undetermined.

Thus, the condensation of **15** with 3-furylaldehyde followed by isomerization gave the most stable *trans*-quinolizidine (**8**) stereoselectively.

On the other hand, deketalization of **14** with 10% acetic acid gave another stereoisomeric mixture of the aminoketone (**15**) in 88% yield. Similar condensation of this mixture with 3-furylaldehyde afforded the four stereoisomeric quinolizidines (**8**, **16**, **17**, and **18**) in 18.6, 21, 8.5, and 6% yields, respectively.

Wolff–Kishner reduction of the quinolizidin-2-one (**8**) afforded (±)-7-epideoxynupharidine (**1**) and (±)-1-epi-7-epideoxynupharidine (**2**) in 45 and 15% yields, respectively. The higher chemical shift of the C_1-methyl signal of **1** in comparison with that of **2** in their NMR spectra (Table I) indicated that the C_1-methyl group in **1** is equatorial, while that in **2** is axial.[8]

Similar reduction of the quinolizidin-2-one (**17**) afforded (±)-deoxynupharidine (**3**) and (±)-1-epideoxynupharidine (**4**) in 33 and 14% yields, respectively. The chemical shifts (Table I) of the C_1-methyl signals of **3** and **4** established the stereochemistry at C_1.

The four synthetic alkaloids, (±)-7-epideoxynupharidine (**1**), (±)-1-epi-7-epideoxynupharidine (**2**), (±)-deoxynupharidine (**3**), and (±)-1-epideoxynupharidine (**4**) were found to be identical with the corresponding natural alkaloids on the basis of IR, NMR, and mass spectral comparison and thin-layer chromatographic behavior.

The synthesis of the four Nuphar alkaloids (**1**, **2**, **3**, and **4**) was thus completed. This stereocontrolled synthesis provides a new and general synthetic method for the quinolizidine-type Nuphar alkaloids.

Experimental[10]

3-(5-Methyl-2-pyridyl)butan-2-one (**6**)——Bromobenzene (38 g) was added dropwise to a stirred suspension of lithium (3.2 g) in dry ether (200 ml) for 1 hr under an N_2 atmosphere with cooling in an ice bath. The reaction mixture was stirred for 1 hr at room temperature. 2-Ethyl-5-methylpyridine (**5**) (16.66 g) was added dropwise to the reaction mixture with cooling in an ice bath, and the reaction mixture was then refluxed gently for 30 min. Acetonitrile (5.0 g) was added dropwise to the reaction mixture with cooling in an ice bath and stirring was continued for 3 hr at room temperature. The reaction mixture was acidified to pH 1 with 4 N H_2SO_4 with cooling, then stirred for 2 hr at room temperature. The ethereal layer was separated. The aqueous layer was washed with ether, then made alkaline with K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with water, dried, and concentrated *in vacuo*. The residue was distilled to give **6** (7.8 g, 35%) as a yellow oil, bp 125—128°/17 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1705 (C=O). NMR δ: 1.44 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 2.10 (3H, s, CH_3), 2.33 (3H, s, CH_3), 3.94 (1H, q, J=7 Hz, $C\underline{H}CH_3$).

Picrate: yellow needles, mp 123—124° (EtOH). *Anal.* Calcd for $C_{16}H_{16}N_4O_8$: C, 48.98; H, 4.11; N, 14.28. Found: C, 49.06; H, 3.91; N, 14.26.

3-(5-Methyl-2-pyridyl)butan-2-one Ethylene Acetal (**13**)——A mixture of the ketone (**6**) (8.98 g), ethylene glycol (9.5 g), and *p*-toluenesulfonic acid monohydrate (15.25 g) in benzene (90 ml) was refluxed for 10 hr with stirring in a flask equipped with a Dean–Stark water separator. Water was added to the cooled reaction mixture and the benzene layer was separated. The aqueous layer was made alkaline with K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried, and concentrated *in vacuo*. The residue was distilled to give **13** (8.65 g, 76%) as a colorless oil, bp 138—139°/17 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1150, 1055 (C–O). NMR δ: 1.21 (3H, s, CH_3), 1.32 (3H, d, J=7 Hz, $CHC\underline{H}_3$), 2.23 (3H, s, CH_3), 3.17 (1H, q, J=7 Hz, $C\underline{H}CH_3$), 3.86 (4H, m, OCH_2CH_2O).

10) All melting points were measured with a Yanagimoto micro melting point apparatus. Melting points and boiling points are uncorrected. Alumina (Brockmann grade II—III, Merck) was used for column chromatography, and alumina (GF_{254}, type 60/E, Merck) and silica gel (GF_{254}, type 60, Merck) for thin-layer chromatography (TLC). Extracts were dried over anhyd. Na_2SO_4. IR spectra were measured with an IR-G spectrophotometer (Japan Spectroscopic Co.), NMR spectra in $CDCl_3$ with a PS-100 machine (Japan Electron Optics Lab. Co.), using tetramethylsilane as an internal standard, mass spectra with JMS-01SG mass spectrometer (Japan Electron Optics Lab. Co.), and gas chromatography with a GC-4BPF gas chromatograph (Shimadzu Co.), employing an OV-17 column (column temp. 190°).

Picrate: yellow needles, mp 127—128° (EtOH). *Anal.* Calcd for $C_{18}H_{20}N_4O_9$: C, 49.54; H, 4.62; N, 12.84. Found: C, 49.45; H, 4.64; N, 12.64.

3-(5-Methyl-2-piperidyl)butan-2-one Ethylene Acetal (14)——A solution of the ketal (**13**) (3.00 g) in acetic acid (15 ml) was hydrogenated over 5% Rh–Al_2O_3 (1.0 g) at room temperature under atmospheric pressure until no more hydrogen was absorbed, then the catalyst was filtered off. The filtrate was concentrated *in vacuo*. The residue was made alkaline with aq. K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with brine, dried, and concentrated *in vacuo*. The residue was distilled to give **14** (2.78 g, 90%) as a colorless oil, bp 135—138°/17 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (NH), 1120, 1045 (C–O). MS *m/e*: 213 (M^+).

3-(5-Methyl-2-piperidyl)butan-2-one (15)——1) A solution of the ketal (**14**) (616 mg) in 10% HCl (10 ml) was heated at 85° for 6 hr with stirring. After cooling, the reaction solution was made alkaline with 20% NaOH and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried, and concentrated *in vacuo*. The residue was distilled to give **15** (425 mg, 87%) as a pale yellow oil, bp 115—117°/17 mmHg (under an N_2 atmosphere). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (NH), 1705 (C=O). MS *m/e*: 169 (M^+).

2) A solution of **14** (1.173 g) and *p*-toluenesulfonic acid monohydrate (1.334 g) in acetone (75 ml) was refluxed for 16 hr with stirring, then acetone was evaporated off *in vacuo*. The residue was treated by the procedure described in 1) to give **15** (685 mg, 77%) as a pale yellow oil, bp 115—118°/17 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (NH), 1705 (C=O).

3) A solution of **14** (1.27 g) in 10% AcOH (100 ml) was heated at 95° for 17 hr with stirring. The reaction solution was treated by the procedure described in 1) to give **15** (0.89 g, 88%) as a pale yellow oil, bp 115—118°/17 mmHg. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3320 (NH), 1705 (C=O).

1,7-Dimethyl-4-(3-furyl)quinolizidin-2-ones (8, 16, 17, and 18)——1) A solution of the aminoketone **15** (obtained by deketalization of **14** with 10% HCl) (2.74 g), 3-furylaldehyde (1.51 g) and 5% aq. NaOH (15 ml) in MeOH (55 ml) was heated at 70—75° for 7 hr with stirring under an N_2 atmosphere. After cooling, the reaction mixture was acidified with 10% HCl and MeOH was evaporated off *in vacuo*. The residue was washed with ether, made alkaline with K_2CO_3, and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried, and concentrated *in vacuo*. The residue was chromatographed on alumina using benzene as an eluent. The first fraction gave **18** (120 mg, 3%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700 (C=O). NMR δ: 0.96 (3H, d, J=6 Hz, C_7–CH_3), 1.03 (3H, d, J=6.5 Hz, C_1–CH_3), 4.20 (1H, br-d, J=6 Hz, C_4–H). MS *m/e*: 247 (M^+), 98 (base peak), 94.

Picrate: yellow cubes, mp 185—186.5° (AcOEt–ether). *Anal.* Calcd for $C_{21}H_{24}N_4O_9$: C, 52.94; H, 5.08; N, 11.76. Found: C, 53.16; H, 4.99; N, 11.76.

The second fraction gave **17** (40 mg, 1%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2790, 2765 (Bohlmann bands), 1710 (C=O). NMR δ: 1.03 (6H, d, J=7.5 Hz, C_1– and C_7–CH_3), 3.52 (1H, d-d, J=11.5; 3.5 Hz, C_4–H). MS *m/e*: 247 (M^+), 98 (base peak), 94.

Picrate: yellow needles, mp 93—95° (EtOH). *Anal.* Calcd for $C_{21}H_{24}N_4O_9$: C, 52.94; H, 5.08; N, 11.76. Found: C, 52.75; H, 5.23; N, 11.91.

The third fraction gave **8** (560 mg, 14%) as colorless crystals, which were recrystallized from *n*-hexane to afford colorless plates, mp 76.5—77°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2790, 2770 (Bohlmann bands), 1712 (C=O). NMR δ: 0.77 (3H, d, J=6 Hz, C_7–CH_3), 1.05 (3H, d, J=6.5 Hz, C_1–CH_3), 3.31 (1H, d-d, J=12; 3 Hz, C_4–H). MS *m/e*: 247 (M^+), 98 (base peak), 94. *Anal.* Calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.78; H, 8.94; N, 5.68.

The fourth fraction gave **16** (1.801 g, 45%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1708 (C=O). NMR δ: 0.86 (3H, d, J=5.5 Hz, C_7–CH_3), 1.10 (3H, d, J=6.5 Hz, C_1–CH_3), 4.24 (1H, d-d, J=7; 2 Hz, C_4–H). MS *m/e*: 247 (M^+), 98 (base peak), 94.

Picrate: yellow needles, mp 179—180° (EtOH). *Anal.* Calcd for $C_{21}H_{24}N_4O_9$: C, 52.94; H, 5.08; N, 11.76. Found: C, 53.21; H, 4.98; N, 11.62.

2) A solution of the aminoketone **15** (obtained by deketalization of **14** with 10% AcOH) (1.779 g), 3-furylaldehyde (1.48 g) and 5% aq. NaOH (12 ml) in MeOH (40 ml) was stirred at room temperature for 10 hr under an N_2 atmosphere, then heated at 80° for 5 hr with stirring. The reaction mixture was treated by the procedure described in 1) to afford **8** (483 mg, 18.6%), **16** (546 mg, 21%), **17** (218 mg, 8.5%), and **18** (153 mg, 6%), which were identical with the corresponding specimens obtained in 1) by IR, NMR, and TLC.

Isomerization of 16 to 8——A solution of **16** (55.1 mg) and 5% aq. NaOH (5 ml) in MeOH (15 ml) was refluxed for 12 hr. The reaction solution was acidified with 10% HCl and MeOH was evaporated off *in vacuo*. The residue was made alkaline with K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried, and concentrated *in vacuo*. The residue was subjected to preparative TLC (SiO_2, AcOEt) to afford **8** (33 mg, 60%) and **16** (18 mg, 32%), which were identical with authentic specimens by IR, NMR, and TLC.

Isomerization of 18 to 17——A solution of **18** (7.1 mg) and 5% aq. NaOH (1 ml) in MeOH (5 ml) was refluxed for 8 hr. The reaction solution was treated by the procedure described for the preparation of **8** from **16** to give a residue (5.3 mg, 75%), which was found to be a mixture of **17** and **18** in a 1 : 1 ratio by gas chromatography.

Reaction of 17 with Sodium Methoxide——A solution of **17** (12.1 mg) and NaOMe (5 mg) in anhyd. MeOH (3.5 ml) was refluxed for 16 hr, and MeOH was evaporated off *in vacuo*. The residue was diluted with water and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried, and concentrated *in vacuo*. The residue (10 mg, 82%) was identical with **17** (TLC and gas chromatography).

(±)-7-Epideoxynupharidine (1) and (±)-1-Epi-7-epideoxynupharidine (2)——A solution of the quinolizidin-2-one (**8**) (199 mg), hydrazine hydrate (6 ml) and powdered KOH (0.4 g) in diethylene glycol (8 ml) was heated at 120—130° for 2 hr with stirring. The reaction temperature was then raised to 200° over 40 min, and during that time the excess hydrazine was distilled off. The reaction mixture was further heated at 200° for 3 hr. After cooling, the reaction mixture was combined with the distillate, and the resulting mixture was diluted with a small amount of water, then extracted with ether. The ethereal extract was washed with water, dried, and concentrated *in vacuo*. The residue was chromatographed on alumina using benzene as an eluent. The first fraction gave **2** (29 mg, 15%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2790, 2765 (Bohlmann bands). NMR δ: 0.73 (3H, d, J=6.5 Hz, C_7–CH_3), 1.07 (3H, d, J=6.5 Hz, C_1–CH_3). MS *m/e*: 233 (M^+), 98 (base peak).

Picrate: yellow plates, mp 180—182.5° (AcOEt–ether). *Anal.* Calcd for $C_{21}H_{26}N_4O_8$: C, 54.54; H, 5.67; N, 12.12. Found: C, 54.64; H, 5.74; N, 11.89.

The second fraction gave **1** (85 mg, 45%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2790, 2770 (Bohlmann bands). NMR δ: 0.72 (3H, d, J=6.5 Hz, C_7–CH_3), 0.90 (3H, d, J=6 Hz, C_1–CH_3), MS *m/e*: 233 (M^+), 98 (base peak).

Picrate: yellow plates, mp 188—189° (AcOEt). *Anal.* Calcd for $C_{21}H_{26}N_4O_8$: C, 54.54; H, 5.67; N, 12.12. Found: C, 54.68; H, 5.60; N, 12.14.

The products **1** and **2** were identical with natural (−)-7-epideoxynupharidine and (−)-1-epi-7-epideoxynupharidine, respectively, on the basis of IR, NMR, and mass spectra and TLC behavior.

(±)-Deoxynupharidine (3) and (±)-1-Epideoxynupharidine (4)——A solution of the quinolizidin-2-one (**17**) (248 mg), hydrazine hydrate (8 ml) and powdered KOH (0.5 g) in diethylene glycol (10 ml) was treated by the procedure described for **1** and **2** to give a residue, which was chromatographed on alumina using *n*-hexane containing 1—5% ether as an eluent. The first fraction gave **4** (32 mg, 14%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2790, 2760 (Bohlmann bands). NMR δ: 0.98 (3H, d, J=7 Hz, C_7–CH_3), 1.08 (3H, d, J=7 Hz, C_1–CH_3). MS *m/e*: 233 (M^+), 98 (base peak).

Picrate: brownish-yellow prisms, mp 148.5—150° (EtOH). *Anal.* Calcd for $C_{21}H_{26}N_4O_8$: C, 54.54; H, 5.67; N, 12.12. Found: C, 54.66; H, 5.66; N, 11.97.

The second fraction gave **3** (76 mg, 33%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2780, 2750 (Bohlmann bands). NMR δ: 0.86 (3H, d, J=5.5 Hz, C_1–CH_3), 0.98 (3H, d, J=7 Hz, C_7–CH_3). MS *m/e*: 233 (M^+), 98 (base peak).

Picrate: yellow needles, mp 169—170° (EtOH). *Anal.* Calcd for $C_{21}H_{26}N_4O_8$: C, 54.54; H, 5.67; N, 12.12. Found: C, 54.40; H, 5.60; N, 12.07.

The products **3** and **4** were identical with natural (−)-deoxynupharidine and (−)-1-epideoxynupharidine, respectively, on the basis of IR, NMR, and mass spectra and TLC behavior.

Acknowledgement The authors are grateful to Dr. B. Maurer, Firmenich & Co. Ltd., Switzerland, for providing the IR, NMR, and mass spectra of (−)-1-epi-7-epideoxynupharidine and (−)-1-epideoxynupharidine, and to Mr. Y. Itatani, Misses Y. Arano, and K. Ohata of this Faculty for elemental analyses, NMR, and mass spectral measurements. Financial support from the Ministry of Education, Science, and Culture of Japan in the form of a Grant-in-Aid for Scientific Research is also gratefully acknowledged.