Phytochemistry, 1981, Vol. 20, pp. 157–160. © Pergamon Press Ltd. Printed in England. 0031–9422/81/0101–0157 $02.00/0

TWO STEROIDAL ALKALOIDS, HAPEPUNINE AND ANRAKORININE, FROM THE MATURE *FRITILLARIA CAMTSCHATCENSIS*

KO KANEKO, UTAKO NAKAOKA, MIKAKO TANAKA, NAOTOSHI YOSHIDA and HIROSHI MITSUHASHI

Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

(*Revised received* 19 *May* 1980)

Key Word Index—*Fritillaria camtschatcensis*; Liliaceae; *N*-methyl-22,26-epiminocholestene; spirosolane.

Abstract—After acid hydrolysis of a glycosidic fraction from the aerial parts of *Fritillaria camtschatcensis*, in addition to solanidine, tomatidenol, and solasodine, two *N*-methyl-22,26-epiminocholestenes, hapepunine and anrakorinine, were isolated and their structures elucidated by physical and chemical methods.

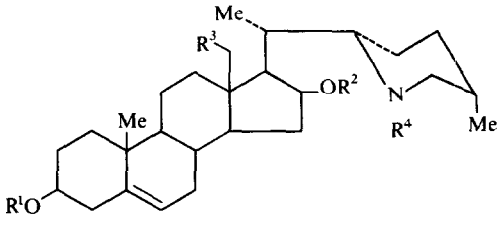
INTRODUCTION

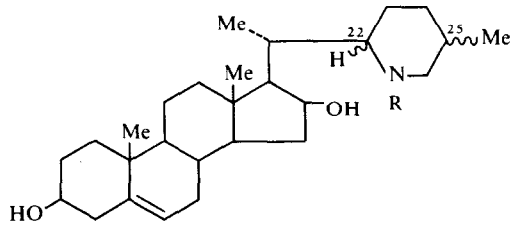
Fritillaria camtschatcensis (L.) Ker. (Japanese name, 'kuroyuri') grows in northern Japan, and is important in the diet of natives in Hokkaido, but no investigation on the chemical constituents of this plant has been reported, except for the isolation of solanidine from its bulb [1]. In our project of biogenetic studies on the C-nor-D-homo steroidal alkaloids, we tried to isolate alkaloids from this plant. Although C-nor-D-homo steroidal alkaloids could not be detected, two new *N*-methyl-22,26-epiminocholestenes, hapepunine (**1a**) [2] and anrakorinine (**2a**), in addition to solanidine, solasodine, and tomatidenol, were isolated from the aerial parts of the mature plant after hydrolysis of a glycosidic fraction. Solasodine and tomatidenol were isolated from this plant for the first time.

RESULTS AND DISCUSSION

Hapepunine (**1a**), $C_{28}H_{47}NO_2$, afforded on acetylation in pyridine a diacetate (**1b**). The ^{1}H NMR spectrum of **1a** displayed three singlets (3H each) at δ 0.96 and 1.02 for the C-18 and C-19 angular methyl groups of a normal ring system with a Δ^5-double bond [3] and at 2.30 for the *N*-methyl group [as well as at δ 1.98 and 2.00 (two acetates) in **1b**], two doublets (3H each, J = 6 Hz) at 1.03 and 1.09 corresponding to two secondary methyl groups at C-21 and C-27, and a signal at 5.36 for a vinyl proton. A multiplet centred at 3.52 was associated with the α-hydrogen at C-3, bearing a hydroxyl group (this signal shifted downfield to 4.56 on acetylation), and another multiplet centred at 4.50 ($W_{\frac{1}{2}}$ = 12 Hz) was associated with the α-hydrogen at C-16 bearing a β-hydroxyl group (this signal shifted downfield to 5.24 on acetylation). The mass spectrum of **1a** revealed ions at *m/e* 429 (M^+) and 112 (base peak). In the light of the ^{1}H NMR and mass spectra of **1a**, it was assumed that the base peak at *m/e* 112 was due to the *N*-methyl-piperidyl side chain moiety produced as a result of a bond fission between C-20 and C-22 of *N*-methyl-22,26-epiminocholestane. This compares with the mass spectrum of teinemine [4] which shows its base peak at *m/e* 98. From these results **1a** was expected to be an *N*-methyl-22,26-epiminocholest-5-ene-3β,16β-diol.

In order to confirm the configurations at C-22 and C-25 of **1a**, tomatidenol (25*S*) and solasodine (25*R*) were reduced with lithium aluminium hydride–aluminium chloride following the methods of Sato [5] and Schreiber [6]. Four products were obtained and proved to be isomeric in the configurations at C-22 and C-25 of





1a $R^1 = R^2 = R^3 = H, R^4 = Me$
1b $R^1 = R^2 = Ac, R^3 = H, R^4 = Me$
2a $R^1 = R^2 = H, R^3 = OH, R^4 = Me$
2b $R^1 = R^2 = Ac, R^3 = OAc, R^4 = Me$
2c $R^1 = Ac, R^2 = H, R^3 = OAc, R^4 = Me$

3 R = H, 22*S*:25*S*
4 R = H, 22*R*:25*S*
5 R = H, 22*S*:25*R*
6 R = H, 22*R*:25*R*
7 R = Me, 22*R*:25*S*
8 R = Me, 22*R*:25*R*

dihydrospirosolane; (22*S*,25*S*)- and (22*R*,25*S*)-dihydrotomatidenol (**3** and **4**) and (22*S*,25*R*)- and (22*R*,25*R*)-dihydrosolasodine (**5** and **6**), but the minute amount of **5** isolated prevented further study. Compounds **3**, **4** and **6** were methylated with methyl iodide and potassium hydroxide leading to (22*S*,25*S*)- and (22*R*,25*S*)-*N*-methyldihydrotomatidenol (**1a** and **7**) and (22*S*,25*R*)-*N*-methyldihydrosolasodine (**8**) respectively. Each isomer showed a different R_f value on Si gel TLC: R_f 0.14 for **7**, 0.32 for **1a**, 0.43 for **8**, and 0.32 for the natural product (**1a**) (solvent system, cyclohexane–EtOAc–MeOH, 2:2:1). The R_f value and physical constants of **1a** agreed completely with those of the natural product, and the melting point of **1a** was not depressed by admixture with the natural product. From these results, **1a** was identified as (22*S*,25*S*)-*N*-methyl-22,26-epiminocholest-5-ene-3β,16β-diol.

Anrakorinine (**2a**), named after the Ainu name for the original plant 'Anrakor', $C_{28}H_{47}NO_3$, afforded on acetylation in pyridine an amorphous triacetate (**2b**): ^{1}H NMR δ 2.03 (6H, *s*, –2OAc) and 2.09 (3H, *s*, –OAc). The ^{1}H NMR spectrum of **2a** exhibited a singlet at δ 1.02 (3H, *s*), indicative of a C-19 angular methyl group of a normal steroidal ring system with a Δ^5-double bond, two doublets at 1.06 (6H, *d*, J = 8 Hz), corresponding to two secondary methyl groups at C-21 and C-27, a singlet at 2.28 (3H) for an *N*-methyl group, a multiplet centred at 3.48 (1H) for a 3α-H (this signal shifted downfield to δ 4.62 on acetylation), a multiplet centred at 4.62 (1H, $W_{1/2}$ = 12 Hz) for a 16α-H (this signal shifted downfield to δ 5.38 on acetylation), and a multiplet centred at 5.32 (1H) for an olefinic proton by direct comparison of the ^{1}H NMR spectrum of **1a**. The mass spectrum of **2a** revealed species at *m/e* 445 (M^+), 414 ($M^+ - 31$), and 112 (base peak). From these spectral data, the basic structure of **2a** was concluded to be *N*-methyl-22,26-epiminocholestene with a 16β-hydroxyl group.

In the ^{1}H NMR spectrum of **2a**, an AB quartet at δ 3.62 and 3.88 (1H each, J = 12 Hz each) was associated with two protons at C-18 (bearing a hydroxyl group). The presence of a fragment ion at *m/e* 414 corresponding to $M^+ - CH_2OH$, in the mass spectrum of **2a**, and the lack of a tertiary methyl group in its ^{1}H NMR spectrum supported the presence of a hydroxyl methyl group at C-18 in **2a**.

To determine the absolute configuration of **2a**, it was converted to **1a** by treatment of a solution of **2a** in pyridine with excess of tosyl chloride under non-aqueous conditions, and the resulting monotosylate was reduced with lithium aluminium hydride. The reduction product, **1a**, was crystallized from acetone. The physical constants of **1a** agreed well with those of the natural product, and the melting point of **1a** was not depressed by admixture with the natural product. From this synthetic proof, **2a** was identified as (22*S*,25*S*)-*N*-methyl-22,26-epiminocholest-5-ene-3β,16β,18-triol.

Compounds **1a** and **2a** are the first *N*-methyl-22,26-epiminocholestane-16β-ols isolated from natural sources. In this plant, tomatidenol accumulated in the aerial parts at budding and then gradually decreased during plant development. During plant growth, the content of **1a** was almost constant, but **2a** gradually accumulated and its content reached about three times that of tomatidenol, as shown in Table 1. Because **1a** and **2a** were contained in the bulb as a trace alkaloid at every stage of growth, it appears that **1a** and **2a** are synthesized from tomatidenol in the aerial parts by biological degradation, not from the precursor of spirosolane biosynthesis.

Table 1. Seasonal variation on steroidal alkaloids in *F. camtschatcensis*.

	Harvested at		
	January	May	June
Tomatidenol content (%)	7.5	3.3	0.3
Hapepunine (**1a**) content (%)	2.6	2.4	0.8
1a: Tomatidenol	0.35:1	0.73:1	2.67:1
Anrakorinine (**2a**) content (%)	1.0	2.2	1.0
2a: Tomatidenol	0.13:1	0.67:1	3.33:1

Although cevanine alkaloids could not be detected in budding, growing, or resting plants, it appears that *F. camtschatcensis* is closely related to the *Fritillaria* genus, because **1a** was also isolated from the mature *F. verticillata* in our recent work [7].

EXPERIMENTAL

Plant material. The aerial parts of the mature plant of *Fritillaria camtschatcensis* (L.) Ker. were harvested in the districts along the sea of Okhotsk, Hokkaido, at the end of June (after flowering). The powdered aerial parts of the plant (4.5 kg) were extracted with hexane to remove the free neutral fraction and free alkaloids, then extracted with ammoniacal $CHCl_3$–MeOH (6:4), and 408.8 g of glycoside fraction was obtained.

Separation of alkaloids. The glycoside (408.8 g) was hydrolysed with 1 N methanolic HCl for 6 hr and the hydrolysate was extracted with Et_2O after being made alkaline with NaOH. The Et_2O phase was extracted with 5% aq. tartaric acid, and the aq. sol extracted with $CHCl_3$ after being made alkaline with NaOH. The $CHCl_3$ extract (7.1 g) was crystallized from Me_2CO and gave 3 g of crystals of solanidine. The residue (4 g) was purified by CC on Al_2O_3, and eluted consecutively with Et_2O–C_6H_6 (1:9), Et_2O–C_6H_6 (1:4), $CHCl_3$, MeOH–$CHCl_3$ (1:9), and MeOH (Table 2).

Solanidine. Needles from Me_2CO, 4.65 g, mp 204–209.5°; MS *m/e*: 397 (M^+), 396 ($M^+ - 1$), 382 ($M^+ - Me$), 204, 150 (base peak); IR ν_{max}^{Nujol} cm^{-1}: 3300, 1060. The mp was not depressed on admixture with authentic solanidine.

Tomatidenol. Fractions III and IV from CC on Al_2O_3 were purified by Si gel TLC (cyclohexane–EtOAc–MeOH, 2:2:1), and the substance with R_f 0.87 was crystallized from Me_2CO (21 mg); mp 233–235°; $[\alpha]_D$ – 38.6° (*c* 0.07, $CHCl_3$); MS *m/e*: 413 (M^+), 138, 125, 114 (base peak), 113; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 1040, 975, 960, 890, 865; ^{1}H NMR ($CDCl_3$): δ 0.84 (3H, *d*, J = 6 Hz, 27-Me), 0.97 (3H, *d*, J = 6 Hz, 21-Me), 1.04 (3H, *s*, 19-Me), 2.74 (2H, *d*, J = 7 Hz, 26-H_2), 3.52 (1H, *m*, 3α-H), 4.16 (1H, *m*, 16α-H), 5.34 (1H, *m*, 6-H); mmp 232–242° (authentic tomatidenol, mp 236–242°).

Solasodine. Fraction IV from CC on Al_2O_3 was purified by Si gel TLC (cyclohexane–EtOAc–MeOH, 2:2:1) and the substance with R_f 0.81 was crystallized from Me_2CO to give plate crystals (8.5 mg), mp 201–203.5°, $[\alpha]_D$ – 114.7° (*c* 0.11, $CHCl_3$); MS *m/e*: 413 (M^+), 138, 125, 114 (base peak), 113; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 1045, 975, 965, 895, 870; ^{1}H NMR ($CDCl_3$): δ 0.80 (3H, *d*, J = 6 Hz, 27-Me), 0.83 (3H, *s*, 18-Me), 0.96 (3H, *d*, J = 8 Hz, 21-Me), 1.04 (3H, *s*, 19-Me), 2.66 (2H, *d*, J = 5 Hz, 26-H_2), 3.52 (1H,

Table 2. Separation of *F. camschatcensis* alkaloids

Solvent system	Fraction No.	Weight (mg)	
Et_2O–C_6H_6 (1:9)	I	50	
	II	1650	Solanidine
	III	250	Solanidine, tomatidenol
	IV	200	Tomatidenol, solasodine Hapepunine (**1a**)
Et_2O–C_6H_6 (1:4)	V	50	
$CHCl_3$	VI	423	Anrakorinine (**2a**)
	VII	53	
	VIII	312	Unknown alkaloid
MeOH–$CHCl_3$ (1:9)	IX		
MeOH			

m, 3α-H), 4.30 (1H, *m*, 16α-H), 5.36 (1H, *m*, 6-H); mmp 197.5–203.5 (authentic solasodine mp 197–202).

Hapepunine (**1a**). Fraction IV from CC on Al_2O_3 was purified by Si gel TLC (cyclohexane–EtOAc–MeOH, 2:2:1), and the substance with R_f 0.32 was crystallized from Me_2CO to give needles (27 mg), mp 196.5–197.5 ; $[\alpha]_D$ – 72.6 (*c* 0.23, $CHCl_3$); MS *m/e*: 429 (M^+), 423 (M^+ – 1), 154, 113, 112 (base peak), 110; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620, 3500–3200 (br.), 1045; ^1H NMR ($CDCl_3$): δ 0.96 (3H, *s*, 19-Me), 1.03 (3H, *d*, *J* = 6 Hz, 21- or 27-Me), 1.09 (3H, *d*, *J* = 6 Hz, 21- or 27-Me), 2.30 (3H, *s*, N-Me), 3.52 (1H, *m*, 3α-H), 4.50 (1H, *m*, 16α-H), 5.36 (1H, *m*, 6-H). (Calc. for $C_{28}H_{47}NO_2$: C, 78.27; H, 11.03; N, 3.26. Found: C, 78.18; H, 11.07; N, 3.38%).

Hapepunine diacetate (**1b**). Hapepunine (22.2 mg) was acetylated in the usual manner to give 13.5 mg of **1b**, mp 207–212°; MS *m/e*: 513 (M^+), 453 (M^+ – MeCOOH), 393 (M^+ – MeCOOH), 113, 112 (base peak), 110, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720, 1250; ^1H NMR ($CDCl_3$): δ 0.84 (3H, *s*, 18-Me), 1.00 (3H, *s*, 19-Me), 1.02 (3H, *d*, *J* = 6 Hz, 21- or 27-Me), 1.09 (3H, *d*, *J* = 6 Hz, 21- or 27-Me), 1.98 (3H, *s*, –OAc), 2.00 (3H, *s*, –OAc), 2.18 (3H, *s*, N-Me), 4.56 (1H, *m*, 3α-H), 5.24 (1H, *m*, 16α-H), 5.32 (1H, *m*, 6-H).

(22S,25S)- *and* (22R,25S)-22,26-*epiminocholest*-5-*ene*-3β,16β-*diol* (**3** *and* **4**). A soln of tomatidenol (105 mg) in 20 ml THF–Et_2O (1:1) was added dropwise with stirring to the reducing reagent at 0° during 30 min. The reducing reagent was prepared as follows: A soln of $AlCl_3$ (1.4 g) in 15 ml of dry Et_2O was added to a suspension of $LiAlH_4$ (0.4 g) with 15 ml of Et_2O at 0 . After 1 hr of stirring at 0°, the mixture was refluxed for 2 hr. The excess reagent was decomposed by the cautious addition of THF–H_2O (2:1). A satd soln of sodium potassium tartarate and then 8% NaOH were added to the mixture and the aq. layer was extracted with Et_2O. The combined organic phases were washed, dried and evapd to dryness. The residue was purified by TLC (hexane–Et_2NH–EtOH, 9:0.75:0.75) on Si gel. The resulting alkaloid silicates (R_f 0.50 and 0.38) were converted into their hydrochlorides, and liberation of the free bases with NaOH and crystallization from Me_2CO yielded **3** as needles (46 mg) and **4** as prisms (18.0 mg), respectively: Compound **3**: mp 168–171 /187.5–189.5 , (reported [5], 167.5–168.5 /188–191); $[\alpha]_D$ – 73.4 (*c* 0.27, $CHCl_3$), (reported [5], $[\alpha]_D$ – 70.9°); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 3200, 1050; ^1H NMR ($CDCl_3$): δ 0.93 (3H, *s*, 18-Me), 0.97 (3H, *d*, *J* = 7 Hz, 21- or 27-Me), 1.02 (3H, *s*, 19-Me), 1.07 (3H, *d*, *J* = 7 Hz, 21- or 27-Me), 3.48 (1H, *m*, 3α-H), 4.47 (1H, *m*, 16α-H), 5.33 (1H, *m*, 6-H). Compound **4**: mp 218–221.5 (reported [5], mp 222.5–225); $[\alpha]_D$ – 27.7 (*c* 0.20, MeOH), (reported [5], $[\alpha]_D$ – 27.1); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3200, 1045; ^1H NMR ($CDCl_3$): δ 0.81 (3H, *d*, *J* = 6 Hz, 21- or 27-Me), 0.93 (3H, *s*, 18-Me), 0.97 (3H, *d*, *J* = 8 Hz, 21- or 27-Me), 1.01 (3H, *s*, 19-Me), 3.48 (1H, *m*, 3α-H), 4.34 (1H, *m*, 16α-H), 5.33 (1H, *m*, 6-H).

(22S,25R)- *and* (22R,25R)-22,26-*epiminocholest*-5-*ene*-3β,16β-*diol* (**5** *and* **6**). Compounds **5** and **6** were prepared by the method used to prepare **3** and **4**, and 23.3 mg of **6** was obtained from 194 mg of solasodine: mp 258–263.5 (reported [6], 257–262); ^1H NMR ($CDCl_3$): δ 0.78 (3H, *d*, *J* = 6 Hz, 21- or 27-Me), 0.88 (3H, *s*, 18-Me), 0.98 (3H, *s*, 19-Me), 1.02 (3H, *d*, *J* = 8 Hz, 21- or 27-Me), 3.50 (1H, *m*, 3α-H), 4.40 (1H, *m*, 16α-H), 5.32 (1H, *m*, 6-H). Compound **5** was detected only on TLC, the amount of **5** was too small for measurement of physical constants and further studies.

(22S,25S)-N-*Methyl*-22,26-*epiminocholest*-5-*ene*-3β,16β-diol (**1a**). A soln of **3** (44.4 mg) in 1 ml MeOH was added to MeI (28.0 mg) and KOH (140 mg) and the mixture was stirred at 40 . After the reaction, the ppt. (KI) formed was collected by filtration and washed with MeOH. The filtrate and washings were combined and evapd to dryness. The residue was purified by TLC (cyclohexane–EtOAc–MeOH, 2:2:1) on Si gel and crystallized from Me_2CO to **1a** as needles (37.9 mg), mp 197.5–198.5 ; $[\alpha]_D$ – 69.6 (*c* 0.12, $CHCl_3$); MS *m/e*: 429 (M^+), 428 (M^+ – 1), 154, 113, 112 (base peak), 110; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620, 3500–3200, 1045; ^1H NMR ($CDCl_3$): δ 0.94 (3H, *s*, 18-Me), 1.02 (3H, *s*, 19-Me), 1.03 (3H, *d*, *J* = 7 Hz, 21- or 27-Me), 1.09 (3H, *d*, *J* = 7 Hz, 21- or 27-Me), 2.27 (3H, *s*, N-Me), 3.50 (1H, *m*, 3α-H), 4.47 (1H, *m*, 16α-H), 5.35 (1H, *m*, 6-H).

(22R,25S)-N-*Methyl*-22,26-*epiminocholest*-5-*ene*-3β,16β-*diol* (**7**) *and* (22R,25R)-N-*methyl*-22,26-*epiminocholest*-5-*ene*-3β,16β-*diol* (**8**). Compounds **7** and **8** were prepared by the method used to prepare **1a**. Compound **7** was obtained as an amorphous solid (4.0 mg) from 8.5 mg of **4**: $[\alpha]_D$ – 36.8° (*c* 0.13, MeOH) and 10.7 mg of **8** was obtained from 23.3 mg of **6**: mp 260–264°.

Anrakorinine (**2a**). Fraction VI from CC on Al_2O_3 was purified by CC on Si gel eluted with EtOAc–cyclohexane–MeOH (1:1:1). The eluate of 140–1500 ml gave **2a** as needles from Me_2CO (68.2 mg), mp 248–251°; $[\alpha]_D$ – 50.4° (*c* 0.79, $CHCl_3$); MS *m/e*: 445 (M^+), 414 (M^+ – 31), 154, 113, 112 (base peak); IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3700–3500, 1040; ^1H NMR ($CDCl_3$): δ 1.02 (3H, *s*, 19-Me), 1.06 (6H, *d*, *J* = 8 Hz, 21- and 27-Me), 2.28 (3H, *s*, N-Me), 3.48 (1H, *m*, 3α-H), 3.62, 3.88 (each 1H, AB*q*, *J* = 12 Hz, 18-H_2), 4.62 (1H, *m*, 16α-H), 5.32 (1H, *m*, 6-H). (Calc. for $C_{28}H_{47}NO_3$: C, 75.46; H, 10.63; N, 3.14. Found: C, 75.27; H, 10.63; N, 3.19%).

Anrakorinine triacetate (**2b**) *and diacetate* (**2c**). Compound **2a** was acetylated in the usual manner to give **2b** (16 mg) and **2c**

(13 mg). Compound **2b**: amorphous; ^{1}H NMR ($CDCl_3$): δ 1.02 (3H, *s*, 19-Me), 1.07 (3H, *d*, J = 7 Hz, 21- or 27-Me), 1.25 (3H, *d*, J = 6 Hz, 21- or 27-Me), 2.03 (6H, *s*, -2OAc), 2.09 (3H, *s*, -OAc), 2.26 (3H, *s*, N-Me), 4.50 (2H, *br. s*, 18-H_2), 4.62 (1H, *m*, 3α-H), 5.36 (1H, *m*, 6-H), 5.38 (1H, *m*, 16α-H); Compound **2c**: amorphous; MS *m/e*: 529 (M^+), 528, 514 (M^+ − Me), 486 (M^+ − 1 − acetyl), 456 (M^+ − CH_2OCOMe), 154, 113, 112 (base peak); ^{1}H NMR ($CDCl_3$): δ 1.03 (3H, *s*, 19-Me), 1.10 (3H, *d*, J = 7 Hz, 21- or 27-Me), 1.14 (3H, *d*, J = 7 Hz, 21- or 27-Me), 2.03 (3H, *s*, -OAc), 2.06 (3H, *s*, -OAc), 2.34 (3H, *s*, N-Me), 4.32 (2H, *br. s*, 18-H_2), 4.54 (1H, *m*, 16α-H), 4.56 (1H, *m*, 3α-H), 5.36 (1H, *m*, 6-H).

Reduction of anrakorinine (**2a**). A soln of **2a** (24.8 mg) in 1 ml of pyridine was added to excess of tosyl chloride on an ice bath. After new spots were detected in the upper region of **2a** on TLC, the mixture was poured into a cold soln of satd $NaHCO_3$. The aq. phase was extracted with $CHCl_3$, a soln of the oily residue from the $CHCl_3$ extract in 6 ml THF was reduced with $LiAlH_4$ (50 mg) on an ice bath, and then the mixture was refluxed. Excess reagent was decomposed by cautious addition of THF–H_2O (2:1), and the soln made alkaline. After removal of THF, the aq. layer was extracted with $CHCl_3$. The $CHCl_3$ extract was purified by TLC (hexane–Et_2NH–EtOH, 9:0.75:0.75) on Si gel, yielding 1 mg of **1a**, mp 194.5–200°.

REFERENCES

1. Mitsuhashi, H., Nagai, U. and Endo, T. (1969) *Chem. Pharm. Bull. (Tokyo)* **17**, 2370.
2. Kaneko, K., Nakaoka, U., Tanaka, M., Yoshida N. and Mitsuhashi, H. (1978) *Tetrahedron Letters* 2099.
3. Budzikiewicz, H. (1964) *Tetrahedron* **20**, 2267.
4. Kaneko, K., Tanaka, M. W. and Mitsuhashi, H. (1977) *Phytochemistry* **16**, 1247.
5. Sato, Y. and Ikekawa, N. (1961) *J. Org. Chem.* **26**, 1945.
6. Schreiber, K. and Rönsch, H. (1965) *J. Org. Chem.* **21**, 645.
7. Kaneko, K., Tanaka, M., Haruki, K., Naruse, N. and Mitsuhashi, H. (1979) *Tetrahedron Letters* 3737.