# CONVENIENT SYNTHESIS OF CYCLOHEXA[*a*]PYRROLO[2,1-*b*][3]BENZAZEPINE, A CEPHALOTAXUS ALKALOID ANALOGUE

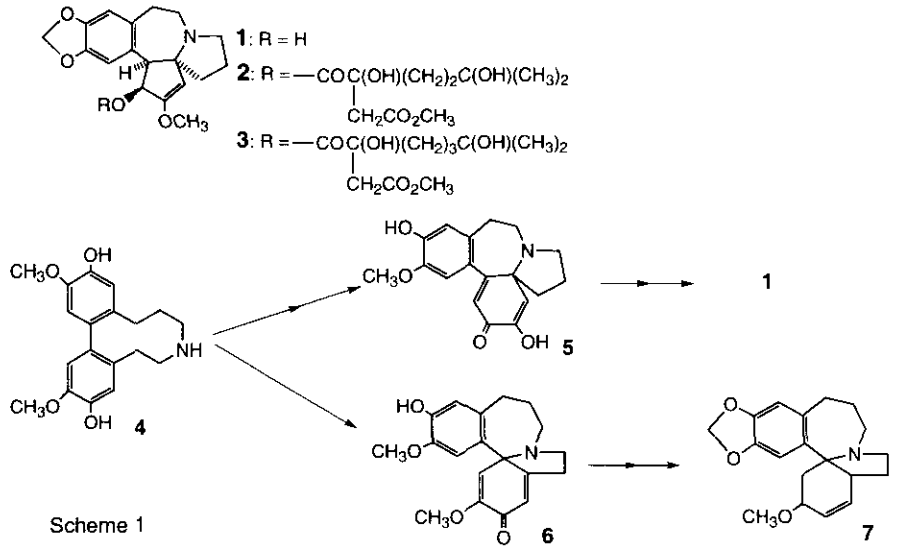
Hitoshi Tanaka,*[a] Mitsunobu Doi,[b] Hiroshi Shimizu,[c] and Hideo Etoh[d]

[a]Faculty of Pharmacy, Meijo University, Yagoto, Tempaku-ku, Nagoya 468-8503, Japan, [b]Osaka University of Pharmaceutical Sciences, 4-20-1, Nasahara, Takatsuki, Osaka, 569-1094, Japan, [c]Gifu Pharmaceutical University, 6-1 Mitahora-higashi 5 chome, Gifu 502-8585, Japan, [d]Faculty of Agriculture, Shizuoka University, Shizuoka 422-8529, Japan

**Abstract** — Irradiation of *N*-(3-hydroxy-4-methoxyphenethyl)-3-(2-iodo-5-methoxyphenyl)propionamide (**11**) in methanol in the presence of sodium hydroxide furnished 3-hydroxy-2,12-dimethoxy-6,7,9,10-tetrahydrodibenz-[*d,f*]azecin-8(5*H*)-one (**14**) which was successfully led to cephalotaxine analogue (**17**) bearing pyrrolo[2,1-*b*][3]benzazepine skeleton by reduction with borane followed by Birch reduction and subsequent acidic treatment. The structure of **17** was established by means of X-Ray crystallography.

We previously reported that bromophenolic amides underwent photochemical cyclization reaction to form easily dibenz[*d,f*]azecine skeleton,[1,2] which was subjected to reduction with borane followed by Birch reduction and subsequent acidic treatment to give homoerythrinan derivative.[2] The dibenz[*d,f*]azecine base (**4**) might be the important intermediate in the biosynthesis of homoerythrinan alkaloids and cephalotaxan alkaloids[3] (Scheme 1) whose estef derivatives, harringtonine (**2**) and homoharringtonine (**3**), have potent antileukemic activity.[4] From view of spectrum of the biological activity and unique structural features, there are many reports on the synthesis of cephalotaxine (**1**)[5] and its analogues, homocephalotaxine[6] and aza-cephalotaxine derivative,[7] whose pivotal skeleton is pyrrolo[2,1-*b*][3]benzazepine. In this paper, we wish to describe a novel route for the synthesis of a cephalotaxine analogue (**17**) having the pyrrolo[2,1-*b*][3]benzazepine skeleton from a dibenz[*d,f*]azecine base (**15**) using Birch reduction followed by acidic treatment.

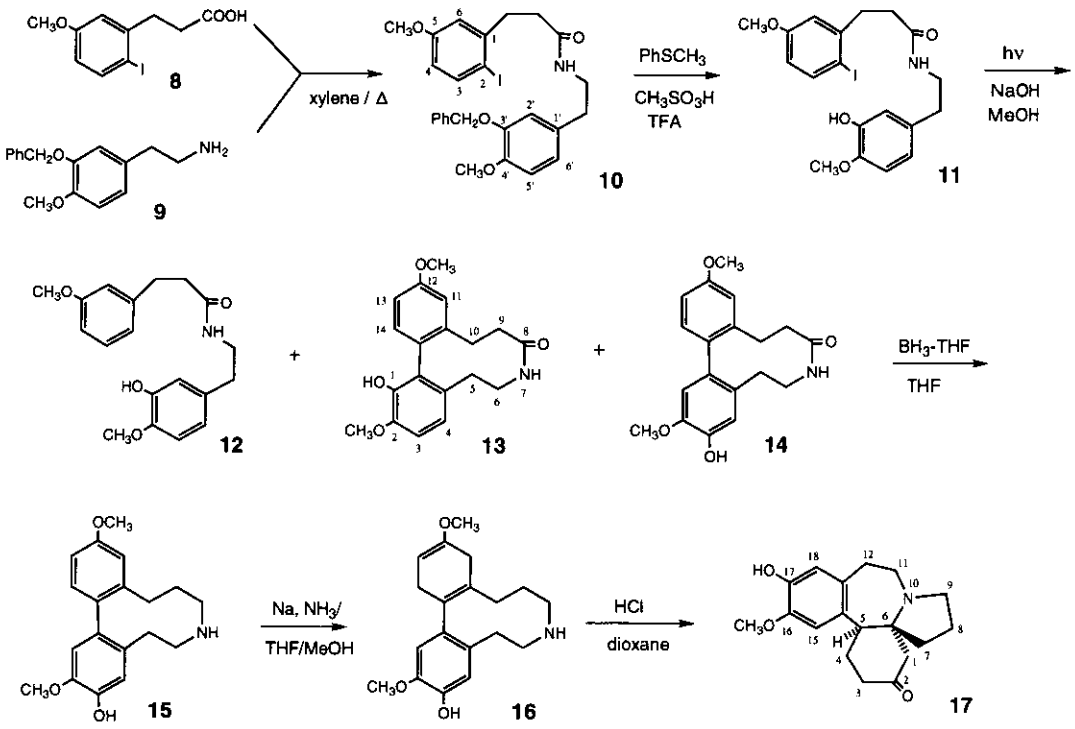
First, the dibenz[*d,f*]azecine base (**15**) was prepared as shown in Scheme 2. The condensation reaction of β-(2-iodo-5-methoxyphenyl)propionic acid (**8**)[8] and 3-benzyloxy-4-methoxyphenethylamine (**9**) in refluxing xylene gave **10** in 73% yield. Treatment of **10** with methanesulfonic acid and thioanisole in




Scheme 1

trifluoroacetic acid according to the procedure of Kiso and coworkers[9] afforded the iodophenolic amide (**11**) in 69% yield. Irradiation of **11** in methanol in the presence of sodium hydroxide with a 100 W high pressure mercury lamp and subsequent chromatographic separation provided three products **12**, **13** and **14** in 7, 1 and 22% yields, respectively. The slower moving product (**14**) was recrystallized from EtOH and showed a molecular ion peak at *m/z* 327 in the MS and the IR spectrum indicated the presence of hydroxyl and amide groups. The $^1$H NMR spectrum revealed two singlet signals at δ 6.54 and 6.86 due to H-1 and H-4 together with ABX type signals (δ 6.80, 6.88 and 7.01). Thus, the structure of this product is clearly represented as formula (**14**) and it indicates that the photochemical coupling reaction occurred at *para* position to hydroxyl group of **11**. The second slower moving product (**13**) had the same molecular formula and functional groups (hydroxyl and amide groups) as those of **14** from the observation of the MS and IR spectrum of **13**. In the $^1$H NMR spectrum, *ortho* coupling signals (δ 6.71 and 6.87) were observed along with ABX type signals (δ 6.55, 6.66 and 6.75). Therefore, this compound was assigned to **13**. The fast moving product (**12**) had the same hydroxyl and amide groups as those of starting material (**11**) by the MS and IR spectrum of **12**. The $^1$H NMR spectrum showed a similar signal pattern to that of **11** except for the aromatic proton regions, in which four proton signals (δ 6.73-6.78 (3H) and 7.20 (1H)) were observed together with the typical ABX pattern signals (δ 6.56, 6.69 and 6.76). The MS of this compound indicated the molecular ion peak at *m/z* 329, which corresponds to the lack of an iodine atom of **11**. Therefore, this compound was assigned to **12**. Reduction of **14** with borane gave the dibenz[*d,f*]azecine (**15**) in good yield.

The dibenz[*d,f*]azecine (**15**) was treated with sodium in liquid ammonia and methanol to afford reduction product (**16**) in 34% yield. In the $^1$H NMR spectrum of **16**, an olefinic proton appeared at δ 4.69. Finally,




Scheme 2

20% hydrochloric acid treatment of **16** in dioxane furnished cyclization product (**17**) in 26% yield. The IR spectrum of **17** showed carbonyl absorption band at 1700 $cm^{-1}$ and in the $^1H$ NMR spectrum, the olefinic proton and methoxyl group signals disappeared and the methine proton signal due to H-5 appeared newly as doublet of doublet at δ 3.44. The structural determination of compound (**17**) was finally carried out by X-Ray analysis(see EXPERIMENTAL). The molecular structure of compound (**17**) is illustrated in Figure 1. Thus, we have achieved a convenient synthesis of cephalotaxine analogue (**17**) *via* Birch reduction of the dibenz[*d,f*]azecine (**15**) followed by acidic treatment.

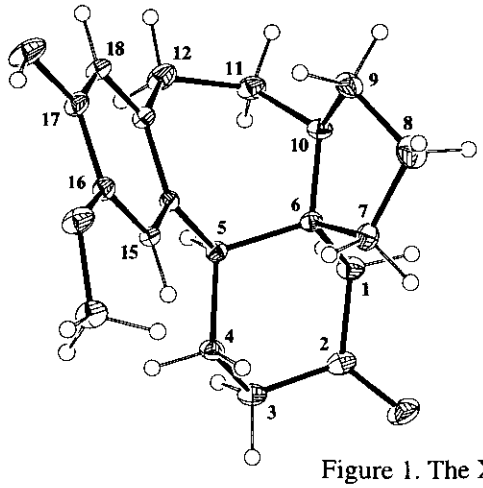



Figure 1. The X-Ray structure of **17**

## EXPERIMENTAL

**General.** The instruments used for this study were as follows: a JASCO IR-810 spectrophotometer (for IR spectra); a JEOL JMS-D 300 spectrometer (for MS and HRMS spectra); a JEOL JNM-A 400 spectrometer (for NMR spectra using tetramethylsilane as an internal standard). Column chromatography was carried out with Merck silica gel 60 (70-230 mesh).

**_N_-(3-Benzyloxy-4-methoxyphenethyl)-3-(2-iodo-5-methoxyphenyl)propionamide (10)**

A mixture of **8**[8] (8.8 g, 28.77 mmol) and **9** (7.4 g, 28.79 mmol) in xylene (200 mL) was refluxed for 3 h. The mixture was evaporated to dryness and the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed in turn with 5% HCl, 5% NaOH and $H_2O$, dried over $Na_2SO_4$, and then evaporated. The crude solid was recrystallized from EtOH to give colorless prisms (**10**)(11.4 g, 73%), mp 150 °C. IR (KBr) $\nu_{max}$ $cm^{-1}$: 3300 (NH), 1640 (CO), 1590. $^1H$ NMR ($CDCl_3$): δ 2.34 (2H, *t*, *J*=7.4 Hz, C$\underline{H}_2$$CH_2CO$), 2.65 (2H, *t*, *J*=6.7 Hz, C$\underline{H}_2$$CH_2NH$), 2.97 (2H, *t*, *J*=7.4 Hz, $CH_2$C$\underline{H}_2$CO), 3.41 (2H, *q*, *J*=6.7 Hz, $CH_2$C$\underline{H}_2$NH), 3.75, 3.87 (6H, 2 x *s*, 2 x $OCH_3$), 5.13 (2H, *s*, OC$\underline{H}_2$Ph), 5.33 (1H, *br s*, NH), 6.51 (1H, *dd*, *J*=3.0, 8.7 Hz, H-4), 6.66 (1H, *dd*, *J*=2.0, 8.1 Hz, H-6'), 6.70 (1H, *d*, *J*=2.0 Hz, H-2'), 6.82 (1H, *d*, *J*=8.1 Hz, H-5'), 6.83 (1H, *d*, *J*=3.0 Hz, H-6), 7.28-7.53 (5H, *m*, 5 x arom. H), 7.64 (1H, *d*, *J*=8.7 Hz, H-3). MS *m/z*: 545 $[M]^+$, 418, 328, 306, 268, 247, 240. *Anal.* Calcd for $C_{26}H_{28}NO_4I$: C, 57.26; H, 5.17; N, 2.57. Found: C, 57.16; H, 5.12; N, 2.44.

**_N_-(3-Hydroxy-4-methoxyphenethyl)-3-(2-iodo-5-methoxyphenyl)propionamide (11)**

A mixture of **10** (8 g, 14.68 mmol), $PhSCH_3$ (4.3 mL, 36.63 mmol) and $CH_3SO_3H$ (2 mL, 30.82 mmol) in TFA (14 mL) was stirred under a nitrogen atmosphere at 0 °C for 2 h. The reaction mixture was poured into ice water and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with $H_2O$, dried over $Na_2SO_4$, and evaporated. The crude solid was recrystallized from benzene to give colorless needles (**11**)(4.6 g, 69%), mp 122 °C. IR ($CHCl_3$) $\nu_{max}$ $cm^{-1}$: 3550 (OH), 3450 (NH), 1670 (CO), 1595. $^1H$ NMR ($CDCl_3$): δ 2.38 (2H, *t*, *J*=7.4 Hz, C$\underline{H}_2$$CH_2CO$), 2.66 (2H, *t*, *J*=6.7 Hz, C$\underline{H}_2$$CH_2NH$), 2.99 (2H, *t*, *J*=7.4 Hz, $CH_2$C$\underline{H}_2$CO), 3.46 (2H, *q*, *J*=6.7 Hz, $CH_2$C$\underline{H}_2$NH), 3.76, 3.87 (6H, 2 x *s*, 2 x $OCH_3$), 5.41 (1H, *br s*, NH or OH), 5.65 (1H, *br s*, OH or NH), 6.51 (1H, *dd*, *J*=3.0, 8.7 Hz, H-4), 6.59 (1H, *dd*, *J*=2.0, 8.1 Hz, H-6'), 6.72 (1H, *d*, *J*=2.0 Hz, H-2'), 6.77 (1H, *d*, *J*=8.1 Hz, H-5'), 6.83 (1H, *d*, *J*=3.0 Hz, H-6), 7.64 (1H, *d*, *J*=8.7 Hz, H-3). MS *m/z*: 455 $[M]^+$, 328, 306, 289, 247. *Anal.* Calcd for $C_{19}H_{22}NO_4I$: C, 50.12; H, 4.87; N, 3.08. Found: C, 50.02; H, 4.85; N, 3.06.

**Irradiation of 11 (Formation of 12, 13 and 14)**

A mixture of **11** (800 mg, 1.76 mmol) and NaOH (650 mg, 16.25 mmol) in MeOH (250 mL) was irradiated with a 100 W high pressure mercury lamp at rt for 2 h under a nitrogen atmosphere. The same procedure was run eleven times and then the reaction mixture was combined. After the whole mixture was evaporated, the residue was acidified with 5% HCl and extracted with $CHCl_3$. The $CHCl_3$ extract was

washed with $H_2O$, dried over $Na_2SO_4$, and evaporated to give a brown oil. The oil was chromatographed on a silica gel column and eluted with a mixture of $CHCl_3$ and acetone (5:1). The starting material (**11**)(414 mg) was first eluted. Then the second (**12**)(452.7 mg, 7% based on consumed starting material), the third (**13**)(63.9 mg, 1%), and the fourth substance (**14**)(1.3 g, 22%) were in turn eluted.

**12**: A crude solid was recrystallized from EtOH to give colorless prisms, mp 114 °C. TLC (silica gel/$CHCl_3$-acetone (5:1), R*f*=0.38). IR ($CHCl_3$) $\nu_{max}$ $cm^{-1}$: 3550 (OH), 3450 (NH), 1660 (CO), 1600. $^1H$ NMR ($CDCl_3$): δ 2.41 (2H, *t*, *J*=7.4 Hz, $C\underline{H}_2CH_2CO$), 2.64 (2H, *t*, *J*=6.7 Hz, $C\underline{H}_2CH_2NH$), 2.93 (2H, *t*, *J*=7.4 Hz, $CH_2C\underline{H}_2CO$), 3.44 (2H, *q*, *J*=6.7 Hz, $CH_2C\underline{H}_2NH$), 3.79, 3.87 (6H, 2 x *s*, 2 x $OCH_3$), 5.31 (1H, *br s*, NH or OH), 5.62 (1H, *s*, OH or NH), 6.56 (1H, *dd*, *J*=2.0, 8.1 Hz, H-6'), 6.69 (1H, *d*, *J*=2.0 Hz, H-2'), 6.76 (1H, *d*, *J*=8.1 Hz, H-5'), 6.73-6.78 (3H, *m*, 3 x arom. H), 7.20 (1H, *m*, arom. H). MS *m/z*: 329 $[M]^+$, 293, 281, 255, 243, 231, 219, 205. HRMS calcd for $C_{19}H_{23}NO_4$: 329.1626. Found: 329.1616.

**13**: A crude solid was recrystallized from benzene to give colorless prisms, mp 224 °C. TLC (silica gel/$CHCl_3$-acetone (5:1), R*f*=0.30). IR ($CHCl_3$) $\nu_{max}$ $cm^{-1}$: 3550 (OH), 3450 (NH), 1665 (CO), 1605. $^1H$ NMR (benzene-$d_6$)[10]: δ 3.18, 3.36 (6H, 2 x *s*, 2 x $OCH_3$), 3.78 (1H, *br s*, NH or OH), 5.60 (1H, *s*, OH or NH), 6.55 (1H, *d*, *J*=8.4 Hz, H-14), 6.66 (1H, *dd*, *J*=3.0, 8.4 Hz, H-13), 6.71 (1H, *d*, *J*=8.4 Hz, H-4 or H-3), 6.75 (1H, *d*, *J*=3.0 Hz, H-11), 6.87 (1H, *d*, *J*=8.4 Hz, H-3 or H-4). MS *m/z*: 327 $[M]^+$, 282, 268, 265, 255, 253, 239, 223. HRMS calcd for $C_{19}H_{21}NO_4$: 327.1469. Found: 327.1460.

**14**: A crude solid was recrystallized from EtOH to give colorless prisms, mp 228 °C. TLC (silica gel/$CHCl_3$-acetone (5:1), R*f*=0.14). IR ($CHCl_3$) $\nu_{max}$ $cm^{-1}$: 3550 (OH), 3450 (NH), 1670 (CO), 1610. $^1H$ NMR ($CDCl_3$): δ 3.81, 3.85 (6H, 2 x *s*, 2 x $OCH_3$), 4.51 (1H, *br s*, NH or OH), 5.58 (1H, *br s*, OH or NH), 6.54 (1H, *s*, H-1 or H-4), 6.80 (1H, *dd*, *J*=3.0, 8.4 Hz, H-13), 6.86 (1H, *s*, H-4 or H-1), 6.88 (1H, *d*, *J*=3.0 Hz, H-11), 7.01 (1H, *d*, *J*=8.4 Hz, H-14). MS *m/z*: 327 $[M]^+$, 268, 255, 239, 237, 227, 225, 223, 211, 209. *Anal.* Calcd for $C_{19}H_{21}NO_4 \cdot 1/2H_2O$: C, 67.84; H, 6.59; N, 4.16. Found: C, 67.69; H, 6.25; N, 4.20.

**3-Hydroxy-2,12-dimethoxy-5,6,7,8,9,10-hexahydrodibenz[*d,f*]azecine (15)**

$BH_3$-THF complex (1 M solution)(8 mL) was added dropwise to a stirred solution of **14** (233 mg, 0.71 mmol) in anhydrous THF (15 mL) at 0 °C under a nitrogen atmosphere. The mixture was continued to stir at rt overnight and then the excess $BH_3$ was decomposed by addition of EtOH. The reaction mixture was evaporated to give a brown oil that was heated with a mixture of MeOH (1 mL) and conc. HCl (1 mL) at 60 °C for 30 min. After the acidic solution was evaporated to dryness, the residue was made alkaline with 5% $NH_4OH$ and extracted with $CHCl_3$. The $CHCl_3$ extract was washed with $H_2O$, dried over $Na_2SO_4$, and evaporated to give a crude solid. The solid was recrystallized from EtOH to afford colorless prisms (**15**)(192 mg, 86%), mp 227 °C. IR ($CHCl_3$) $\nu_{max}$ $cm^{-1}$: 3550 (OH), 1605. $^1H$ NMR ($CDCl_3$): δ 3.78, 3.84 (6H, 2 x *s*, 2 x $OCH_3$), 6.52 (1H, *s*, H-1 or H-4), 6.71 (1H, *s*, H-4 or H-1), 6.77 (1H, *dd*, *J*=3.0, 8.4 Hz, H-13), 6.81 (1H, *d*, *J*=3.0 Hz, H-11), 6.99 (1H, *d*, *J*=8.4 Hz, H-14). MS *m/z*: 313 $[M]^+$, 298, 281, 255.

HRMS calcd for $C_{19}H_{23}NO_3$: 313.1677. Found: 313.1670.

**3-Hydroxy-2,12-dimethoxy-5,6,7,8,9,10,11,14-octahydrodibenz[*d,f*]azecine (16)**

Sodium (3 g, 130 matom) was added to a stirred mixture of **15** (182 mg, 0.58 mmol), anhydrous MeOH (8 mL), anhydrous THF (9 mL), and liquid ammonia (40 mL) at –70 °C over a period of 2h. After cautious addition of MeOH, $H_2O$ and $NH_4Cl$, the ammonia was allowed to evaporate off and the reaction mixture was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with $H_2O$, dried over $Na_2SO_4$, and evaporated to afford a crude solid. The solid was recrystallized from MeOH to give colorless needles (**16**)(63 mg, 34%), mp 229 °C. IR ($CHCl_3$) $\nu_{max}$ $cm^{-1}$: 3550 (OH), 1510. $^1H$ NMR ($CDCl_3$): δ 3.60, 3.83 (6H, 2 x *s*, 2 x $OCH_3$), 4.69 (1H, *br s*, H-13), 6.47 (1H, *s*, H-1 or H-4), 6.70 (1H, *s*, H-4 or H-1). MS *m/z*: 315 $[M]^+$, 300, 284, 258, 243, 239, 231, 227, 225, 211. HRMS calcd for $C_{19}H_{25}NO_3$: 315.1833. Found: 315.1838.

**17-Hydroxy-16-methoxy-8,9,11,12-tetrahydro-7*H*-cyclohexa[*a*]pyrrolo[2,1-*b*][3]benzazepin-2-one (17)**

A stirred mixture of **16** (45 mg, 0.14 mmol) in dioxane (10 mL) and 20% HCl (0.5 mL) was heated at 60 °C for 20 min. After cooling, the reaction mixture was poured into ice water. The whole mixture was made alkaline with 5% $NH_4OH$ and extract with AcOEt. The AcOEt extract was washed with $H_2O$, dried over $Na_2SO_4$, and evaporated to give a crude solid. The solid was recrystallized from MeOH to afford colorless prisms (**17**)(11.1 mg, 26%), mp 90 °C. IR ($CHCl_3$) $\nu_{max}$ $cm^{-1}$: 3550 (OH), 1700 (CO), 1600. $^1H$ NMR ($CDCl_3$): δ 1.39 (1H, *m*, H-8β), 1.43 (1H, *m*, H-7β), 1.51-1.62 (2H, *m*, H-7α and H-8α), 1.91 (1H, *m*, H-4β), 2.14 (1H, *m*, H-4α), 2.24 (1H, *d*, *J*=13.7 Hz, H-1β), 2.38 (1H, *m*, H-9α), 2.46 (1H, *ddd*, *J*=5.9, 12.9, 14.4 Hz, H-3α), 2.53 (1H, *ddd*, *J*=2.7, 5.9, 14.4 Hz, H-3β), 2.70 (1H, *d*, *J*=13.7 Hz, H-1α), 2.72 (1H, *m*, H-9β), 2.86 (1H, *ddd*, *J*=5.1, 10.0, 15.1 Hz, H-12β), 3.10 (1H, *ddd*, *J*=4.4, 10.0, 14.7 Hz, H-11α), 3.25 (1H, *ddd*, *J*=4.4, 9.8, 15.1 Hz, H-12α), 3.38 (1H, *ddd*, *J*=5.1, 9.8, 14.7 Hz, H-11β), 3.44 (1H, *dd*, *J*=3.2, 12.5 Hz, H-5), 3.88 (3H, *s*, $OCH_3$), 5.46 (1H, *br s*, OH), 6.57 (1H, *s*, H-15), 6.74 (1H, *s*, H-18). These signals were assigned by the NOE experiment. MS *m/z*: 301 $[M]^+$, 286, 283, 281, 258, 244, 231, 216. HRMS calcd for $C_{18}H_{23}NO_3$: 301.1677. Found: 301.1690.

**X-Ray Diffraction Study of 17.**

The 2737 reflections were measured on Rigaku RU200/AFC5R up to $\theta_{max}$=62.1° by 2θ–ω scan method. Crystal data --- formula: $C_{18}H_{23}NO_3 \cdot CH_3OH$, *M*r=330.4, *F*(000)=648, μ(Cu Kα)=0.630 $mm^{-1}$, crystal system: monoclinic, space group:$P2_1/c$, *a*=8.486(3) Å, *b*=20.361(9) Å, *c*=10.735(3) Å, β=111.46(2)°, *V*=1726.3(11) $Å^3$, *Z*=4. The structure was solved by *Crystan G* and was refined by *SHELXL*-93. The non-hydrogen atoms were refined with anisotropic temperature factors and the hydrogen atoms were calculated at geometrically ideal positions. In the difference Fourier map, two peaks were found and were separated *ca.* 1.4 Å to each other. These peaks were located at the distance of 2.726 Å from the hydroxyl

oxygen (position 17) of compound (**17**) and were considered as a solvent molecule (methanol). In the final cycle of the refinement, the *R* and *wR* values were converged to 0.0676 and 0.1715 for 2386 reflections with over $2\sigma(I)$, respectively. The other parameters are as follows. No. of parameters=226, goodness of fit=1.138, $(\Delta/\sigma)_{max} < 0.001$, $(\Delta\rho)_{max}$=0.654 eÅ$^{-3}$, $(\Delta\rho)_{max}$ =-0.411 eÅ$^{-3}$.

## ACKNOWLEDGMENT

We wish to thank Professor Itsuo Mori at Osaka University of Pharmaceutical Sciences for the valuable help.

## REFERENCES AND NOTES

1. H. Tanaka, Y. Takamura, K. Ito, K. Ohira, and M. Shibata, *Chem. Pharm. Bull.*, 1984, **32**, 2063.
2. H. Tanaka, Y. Takamura, M. Shibata, and K. Ito, *Chem. Pharm. Bull.*, 1986, **34**, 24.
3. Y. Tsuda and T. Sano, *The Alkaloids*, Vol. 48, ed. by G. A. Cordell, Academic press, 1996, p. 249.
4. a) L. Huang and Z. Xue, *The Alkaloids*, Vol. 23, ed. by A. Brossi, Academic press, 1984, p. 157; b) J. -Y. Zhou, D. -L. Chen, Z.-S. Shen, and H. P. Koeffler, *Cancer Res.*, 1990, **50**, 2031.
5. Total synthesis of cephalotaxine: a) S. M. Weinreb and J. Auerbach, *J. Am. Chem. Soc.*, 1975, **97**, 2503; b) M. F. Semmelhack, B. P. Chong, R. D. Stauffer, T. D. Rogerson, A. Chong, and L. D. Jones, *J. Am. Chem. Soc.*, 1975, **97**, 2507; c) S. Yasuda, T. Yamada, and M. Hanaoka, *Tetrahedron Lett.*, 1986, **27**, 2023; d) M. E. Kuehne, W. G. Bornmann, W. H. Parsons, T. D. Spitzer, J. F. Blount, and J. Zubieta, *J. Org. Chem.*, 1988, **53**, 3439; e) T. P. Burkholder and P. L. Fuchs, *J. Am. Chem. Soc.*, 1990, **112**, 9601; f) M. Ikeda, M. Okano, K. Kosaka, M. Kido, and H. Ishibashi, *Chem. Pharm. Bull.*, 1993, **41**, 276; g) N. Isono and M. Mori, *J. Org. Chem.*, 1995, **60**, 115; h) X. Lin, R. W. Kavash, and P. S. Mariano, *J. Org. Chem.*, 1996, **61**, 7335; i) L. F. Tietze and H. Schirok, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1124; j) T. Nagasaka, H. Sato, and S.-I. Saeki, *Tetrahedron: Asymmetry*, 1997, **8**, 191.
6. M. Okano, N. Nishimura, K. Maruyama, K. Kosaka, H. Ishibashi, and M. Ikeda, *Chem. Pharm. Bull.*, 1991, **39**, 3163.
7. M. Nyerges, I. Bitter, I. Kadas, G. Toth, and L. Toke, *Tetrahedron*, 1995, **51**, 11489.
8. D. Papa, E. Schwenk, and E. Klingsberg, *J. Am. Chem. Soc.*, 1950, **72**, 2623.
9. Y. Kiso, H. Isawa, K. Kitagawa, and T. Akita, *Chem. Pharm. Bull.*, 1978, **26**, 2562.
10. Although aromatic proton signals of **13** in $CDCl_3$ were overlapped, all of those signals in benzene-$d_6$ were clearly separated.

Received, 27th May, 1999