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CONCISE SYNTHESIS OF FAGARIDINE AND DECARINE, PHENOLIC BENZO[*c*]PHENANTHRIDINE ALKALOIDS, USING THE PALLADIUM-ASSISTED BIARYL COUPLING REACTION†

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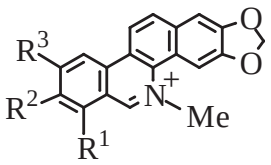
Abstract—Total synthesis of fagaridine (**5**) and decarine (**6**), phenolic benzo[*c*]phenanthridine alkaloids, was accomplished *via* the aryl-aryl coupling reaction of bromo amides protected by an isopropyl group with palladium, followed by reduction with $LiAlH_4$ and treatment with conc. HCl

Palladium-assisted aryl-aryl coupling reactions have been used to synthesize many condensed aromatic compounds.[1] Recently, we reported that intramolecular coupling reactions between aromatic halides and arenes using palladium reagents were a very versatile way to synthesize polycyclic heteroaromatic compounds[2-5] and a novel palladium reagent prepared from $Pd(OAc)_2$, DPPP (1,3-bis(diphenylphosphino)propane), and Bu_3P was very effective for coupling reactions, not only between aryl triflates and arenes, but also between aryl halides and arenes.[6] Moreover, we succeeded in synthesizing the benzo[*c*]phenanthridine alkaloids chelerythrine (**1**),[2,7] nitidine (**2**),[4,7] norchelerythrine (**3**), 3,7,12-methoxydihydrochelerythrine (**4**),[2a,7] and others,[3,6] by taking advantage of the palladium-assisted aryl-aryl coupling reaction. Subsequently, in order to examine the generality of these methods, we designed a plan to synthesize fagaridine (**5**) and decarine (**6**), phenolic benzo[*c*]phenanthridine alkaloids, as shown in Scheme 1. This is the subject of this paper.

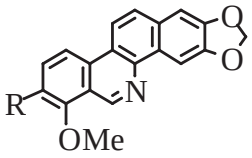
In 1973, Torto *et al.* identified a quaternary phenolic alkaloid, fagaridine, from *Fagara xanthoxyloides*, and proposed its structure.[8] However, Nakanishi and Suzuki revised the structure of fagaridine as **5** after synthesizing it in 1998.[9] A tertiary phenolic alkaloid, decarine (**6**), was isolated from *Zanthoxylum decaryi* by Cave *et al.*[10] and synthesized *via* the benzyne route by Kesser *et al.*[11]

We designed a common retorosynthetic plan for these phenolic alkaloids, as shown in Scheme 1. We postulated that isopropyl or TBDMS group could be used to protect the phenol, because they are stable in the hydride reduction and can be deprotected with hydrochloric acid, two steps that are very useful for

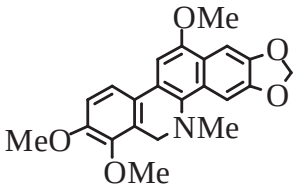
† Dedicated to Professor Yuichi Kanaoka for the celebration of his 75th birthday.



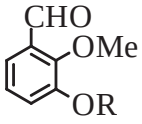
$R^1 = R^2 = OMe, R^3 = H$ chelerythrine (**1**)
$R^1 = H, R^2 = R^3 = OMe$ nitidine (**2**)
$R^1 = OMe, R^2 = OH, R^3 = H$ fagaridine (**5**)



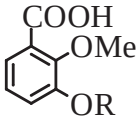
R = OMe norchelerythrine (**3**)
R = OH decarine (**6**)



12-methoxydihydrochelerythrine (**4**)

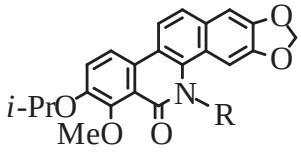


16 : R = H
17 : R = TBDMS
18 : R = Pr-*i*

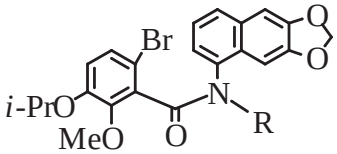


19 : R = TBDMS
20 : R = Pr-*i*

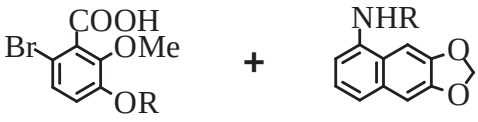
fagaridine (**5**)
or
decarine (**6**)



7 : R = Me
8 : R = MOM



9 : R = Me
10 : R = H
11 : R = MOM



12 : R = TBDMS
13 : R = Pr-*i*

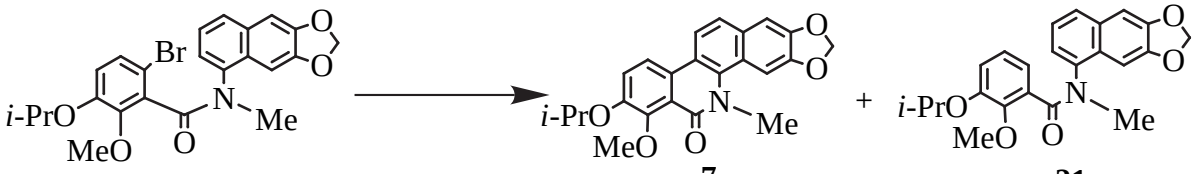
14 : R = Me
15 : R = H

Scheme 1

transforming benzophenanthridone to base, as previously reported.[2,3]

First, the synthesis of bromo-acids (**12**) and (**13**) was investigated. Therefore, **16**[12] was treated with TBDMS chloride and imidazole to afford the silyl ether (**17**), which was oxidized with $NaClO_2$ and 31% H_2O_2 to produce silyl acid (**19**) in 72% total yield. Bromination of **19** with dibromodimethylhydantoin (DBDMH)[13] was unfruitful. By contrast, oxidation of **18**[14] with $NaClO_2$ and 31% H_2O_2 followed by bromination with DBDMH successfully gave bromo acid (**13**) in 71% total yield. Then, bromo amides (**9**) and (**11**), the starting materials for the coupling reaction, were synthesized as follows: **13** was successively treated with oxalyl chloride followed by **14**,[7,15] to afford bromo amide (**9**) in 64% yield. Next, bromo amide (**11**) possessing a MOM group, which was suitable for synthesizing the tertiary bases norchelerythrine (**3**)[3] and triphaeridine,[3] was prepared from **13** and naphthylamine (**15**)[4] *via* methoxymethylation in 59% total yield.

Table 1. Results of coupling reaction of 6-bromo-3-isopropoxy-2-methoxy-*N*-methyl-*N*-(6,7-methylenedioxy-1-naphthyl)benzamide (**9**) in DMF under reflux[a)]

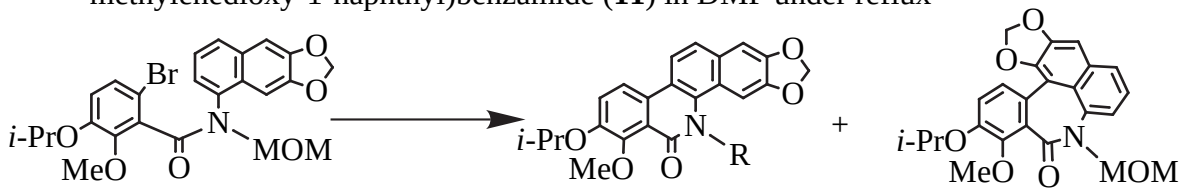


9 **7** **21**

run	$Pd(OAc)_2$	ligand	L/Pd[b)]	base	time (h)	yield(%) **7**	**21**	**9**
1	1.0	DPPP[c)]	1	Ag_2CO_3	1	86	–	10
2	1.0	Ph_3P	2	Ag_2CO_3	4	50	–	26
3	1.0	DPPP	1	Ag_2CO_3	4	84	14	–
4	1.0	(*o*-tol)$_3$P	2	Ag_2CO_3	2	93	–	5
5	0.2	DPPP[c)]	1	K_2CO_3	1	72	11	–
6	0.2	*n*-Bu_3P	3	Ag_2CO_3	4	51	–	39
7	0.2	*n*-Bu_3P	3	K_2CO_3	4	68	6	–
8	0.2	(*o*-tol)$_3$P	2	Ag_2CO_3	4	87	–	13
9	0.2	(*o*-tol)$_3$P	2	K_2CO_3	4	89	7	–

a) All reactions were carried out using 2 equivalents of base.
b) Molar ratio between ligand and $Pd(OAc)_2$.
c) One eqivalent of *n*-Bu_3P was added.
DPPP : 1,3-bis(diphenylphosphino)propane. (*o*-tol)$_3$P : tri-*ortho*-tolylphosphine

Table 2. Results of coupling reaction of 6-bromo-3-isopropoxy-2-methoxy-*N*-methoxymethyl-*N*-(6,7-methylenedioxy-1-naphthyl)benzamide (**11**) in DMF under reflux[a)]



11 **8** : R = MOM **22** : R = H **23**

run	$Pd(OAc)_2$	ligand	L/Pd[b)]	base	time (h)	yield(%) **8**	**22**	**23**	**11**
1	1.0	DPPP[c)]	1	Ag_2CO_3	5	58	18	18	–
2	1.0	DPPP[c)]	1	K_2CO_3	8	50	15	26	–
3	1.0	*n*-Bu_3P	3	K_2CO_3	5	58	13	22	–
4	1.0	(*o*-tol)$_3$P	2	Ag_2CO_3	5	91	3	6	–
5	0.2	DPPP[c)]	1	K_2CO_3	5	22	13	–	65
6	0.2	*n*-Bu_3P	3	K_2CO_3	5	31	6	–	41
7	0.2	(*o*-tol)$_3$P	2	Ag_2CO_3	5	33	–	–	57
8	0.2	(*o*-tol)$_3$P	2	K_2CO_3	5	55	16	12	–

a) All reactions were carried out using 2 equivalents of base.
b) Molar ratio between ligand and $Pd(OAc)_2$.
c) One eqivalent of *n*-Bu_3P was added.

The results of the biaryl coupling reaction of bromo-amides (**9**) and (**11**) using the palladium reagent are summarized in Tables 1 and 2, respectively. The coupling reactions proceeded in a good yield, especially when using equimolar $Pd(OAc)_2$, (*o*-tol)$_3$P, and Ag_2CO_3 (See run 4 in Tables 1 and 2). The structure of benzazepinone (**23**) was elucidated from ^{1}H-NMR spectral data, in which **23** showed only one singlet signal due to an aromatic proton in addition to the signals due to other aromatic protons[16] (see EXPERIMENTAL). The reduction of coupling products (**9**) and (**11**) with $LiAlH_4$ followed by treatment with conc. HCl gave fagaridine (**5**) and decarine (**6**), respectively. The spectral data for each synthetic sample were in good agreement with those of the corresponding authentic sample.

EXPERIMENTAL

Melting points were measured on a micro melting point hot-stage apparatus (Yanagimoto) and are uncorrected. IR spectra were recorded on a JASCO A-102 or JASCO FT/IR 350 spectrophotometer and ^{1}H-NMR spectra in deuteriochloroform on a Hitachi R-1500 (60 MHz) or a Varian VXR-200 (200 MHz) or -500 (500 MHz) spectrometer unless otherwise stated. NMR spectral data are reported in parts per million downfield from tetramethylsilane as an internal standard (δ 0.0) and coupling constants are given in Hertz. MS spectra were obtained on a VG-70SE spectrometer. Column chromatography was carried out on Wako gel C-200. All experiments were carried out in an argon atmosphere and the extract was washed with brine, dried over anhydrous $MgSO_4$, then filtered, and the filtrate was evaporated to dryness under reduced pressure, unless otherwise noted. $Pd(OAc)_2$ was treated with boiling benzene and the mixture was filtered while hot. The hot filrate was then concentrated to dryness to give purified $Pd(OAc)_2$.

3-[(*tert*-Butyldimethylsilyl)oxy]-2-methoxybenzaldehyde (17)

A solution of **16** (1.00 g, 6.57 mmol), TBDMS chloride (1.19 g, 7.89 mmol) and imidazole (1.34 g, 19.7 mmol) in dry DMF (15 mL) was stirred at 50˚C for 1 h. The reaction mixture was diluted with water and extracted with AcOEt. The residue dissolved in $CHCl_3$ was subjected to column chromatography on silica gel. Elution with hexane : AcOEt (30 : 1) gave **17** (1.65 g, 95%) as an oil. IR ($CHCl_3$) cm^{-1}: 1687 (C=O). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 0.21 (6H, s), 1.03 (9H, s), 3.93 (3H, s), 7.01－7.14 (2H, m), 7.44 (1H, dd, *J*=7.2, 2.4 Hz),10.39 (1H, s). FAB-MS *m/z*: 265.1281 (Calcd for $C_{14}H_{21}O_3BrSi$: 265.1259).

3-[(*tert*-Butyldimethylsilyl)oxy]-2-methoxybenzoic acid (19)

To a stirred mixture of **17** (1.00 g, 3.75 mmol), sodium phosphate monobasic dihydrate (146 mg, 0.94 mmol), and 31% hydrogen peroxide (0.63 mL, 5.63 mmol) in MeCN (30 mL) and water (1 mL) was added a solution of sodium chlorite (80%; 636 mg, 5.63 mmol) in water (1 mL) and then the whole was stirred at 10˚C for 2 h. After the decomposition of excess hydrogen peroxide with aqueous 10% sodium sulfite solution, the mixture was poured into water and acidified to pH 3 with 10% HCl, and then extracted with AcOEt. The crystalline residue was recrystallized from hexane-ether to provide **19** (805 mg, 76 %) as colorless needles, mp 109－110˚C. IR (KBr) cm^{-1}: 2929 (OH), 1675 (C=O). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 0.22 (6H, s), 1.02 (9H, s), 4.03 (3H, s), 7.06－7.16 (2H, m), 7.73 (1H, dd, *J*=3.6, 2.5 Hz), 11.50 (1H,

br). *Anal*. Calcd for $C_{14}H_{22}O_4Si$: C, 59.54; H, 7.85. Found: C, 59.41; H, 7.55.

3-Isopropoxy-2-methoxybenzoic acid (20)

To a stirred mixture of **18** (500 mg, 2.57 mmol), sodium phosphate monobasic dihydrate (100 mg, 0.64 mmol), and 31% hydrogen peroxide (0.42 mL, 3.86 mmol) in MeCN (15 mL) and water (0.5 mL) was added a solution of sodium chlorite (80%; 436 mg, 3.86 mmol) in water (1 mL) and then the whole was stirred at 10˚C for 8 h. After the decomposition of excess hydrogen peroxide with aqueous 10% sodium sulfite solution, the mixture was poured into water and acidified with 10 % HCl and then, extracted with AcOEt. The crystalline residue was recrystallized from hexane to provide **20** (483 mg, 89 %) as colorless needles, mp 78—79.5°C. IR (KBr) cm^{-1}: 2980 (OH), 1660 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.41 (6H, d, *J*=6.1 Hz), 4.10 (3H, s), 4.61 (1H, septet, *J*=6.1 Hz), 7.14—7.19 (2H, m), 7.71 (1H, dd, *J*=7.0, 6.0 Hz), 11.49 (1H, br). *Anal*. Calcd for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71. Found: C, 62.96; H, 6.74.

6-Bromo-3-isopropoxy-2-methoxybenzoic acid (13)

Acid (**20**) (2.00 g, 9.52 mmol) was dissolved in a 0.7*N* NaOH solution (15 mL, 10.5 mmol) and the solution was cooled to 0°C. After dibromodimethylhydantoin (1.50 g, 5.24 mmol) was added in portions over 5 min and the solution was allowed to warm to rt and stirred for 40 min. The reaction was quenched by the addition of sodium sulfite and filtered. The filtrate was acidified to pH 2 with conc. HCl under rapid stirring and the whole was extracted with ether. The residue was recrystallized from benzene-hexane to afford **13** (2.21 g, 80%) as colorless needles, mp 108.5—110°C. IR (KBr) cm^{-1}: 2980 (OH), 1700 (C=O). ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 1.35 (6H, d, *J*=6.1 Hz), 3.93 (3H, s), 4.56 (1H, septet, *J*=6.1 Hz), 6.85 (1H, d, *J*=8.6 Hz), 7.26 (1H, d, *J*=8.6 Hz). *Anal*. Calcd for $C_8H_{13}O_4Br$: C, 45.70; H, 4.53. Found: C, 45.87; H, 4.80.

6-Bromo-3-isopropoxy-2-methoxy-*N*-methyl-*N*-(6,7-methylenedioxy-1-naphthyl)-benzamide (9)

A few drops of dry DMF and oxalyl chloride (444 mg, 3.5 mmol) were added to a solution of **13** (500 mg, 1.73 mmol) in dry CH_2Cl_2 (5 mL) under ice-cooling and the mixture was stirred for 2 h. Then, the reaction mixture was concentrated to dryness under reduced pressure. To this residue was added a solution of **14** (348 mg, 1.73 mmol) in dry CH_2Cl_2 (5 mL) and dry NEt_3 (0.26 mL, 1.90 mmol) and the whole was stirred for 3 h at rt. The reaction mixture was concentrated to dryness and diluted with $CHCl_3$, then washed with 10% HCl, aqueous 5% NaOH solution and brine. The residue dissolved in $CHCl_3$ was subjected to column chromatography on silica gel. Elution with hexane : AcOEt (5 : 1) gave **9** (520 mg, 64%) as colorless prisms, mp 148—149°C (from AcOEt-hexane). IR (KBr) cm^{-1}: 1660 (C=O). ^{1}H-NMR (200 MHz, $CDCl_3$, rotamers) δ: 1.21—1.56 (6H, m), 3.16—4.03 (6H, m), 4.56—4.70 (1H, m), 6.04—6.06 (2H, m), 6.60—7.70 (7H, m). *Anal*. Calcd for $C_{23}H_{22}NO_5Br$: C, 58.49; H, 4.70; N, 2.97. Found: C, 58.40; H, 4.84; N, 2.93.

6-Bromo-3-isopropoxy-2-methoxy-*N*-(6,7-methylenedioxy-1-naphthyl)benzamide (10)

A few drops of dry DMF and oxalyl chloride (444 mg, 3.5 mmol)) were added to a solution of **13** (500 mg,

1.73 mmol) in dry CH_2Cl_2 (5 mL) and the stirred mixture was refluxed for 1 h. Then, the mixture was concentrated to dryness under reduced pressure. To this residue was added a solution of **15** (324 mg, 1.73 mmol) in dry CH_2Cl_2 (5 mL) and dry NEt_3 (0.27 mL, 1.90 mmol) and the whole was stirred for 5 h at rt. The reaction mixture was concentrated to dryness and diluted with $CHCl_3$, then washed with 10% HCl, aqueous 5% NaOH solution and brine. The residue was dissolved in $CHCl_3$ and the solution was subjected to column chromatography on silica gel. Elution with hexane : AcOEt (1 : 1) gave **10** (621 mg, 78%) as colorless needles, mp 193—195℃ (from ether). IR (KBr) cm^{-1}: 1655 (C=O). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.40 (6H, d, *J*=6.0 Hz), 3.97 (3H, s), 4.60 (1H, septet, *J*=6.0 Hz), 6.04 (2H, s), 6.60—7.70 (7H, m). *Anal.* Calcd for $C_{22}H_{20}NO_5Br$: C, 57.66; H, 4.40; N, 3.06. Found: C, 57.82; H, 4.31; N, 3.16.

6-Bromo-3-isopropoxy-2-methoxy-*N*-methoxymethyl-*N*-(6, 7-methylenedioxy-1-naphthyl)benzamide (11)

A suspension of **10** (500 mg, 1.73 mmol) and NaH (380 mg, 63% dispersion in mineral oil, 6.3 mmol) in dry DMF (20 mL) was stirred for 30 min at rt and then chloromethyl methyl ether (0.25 mL, 3.27 mmol) was added to the reaction mixture. After stirring for 2 h at rt, the reaction mixture was diluted with ether and washed with brine. The residue dissolved in $CHCl_3$ was subjected to column chromatography on silica gel. Elution with hexane : AcOEt (4 : 1) gave **11** (826 mg, 75%) as colorless prisms, mp 142—143℃ (from AcOEt-hexane). IR (KBr) cm^{-1}: 1662 (C=O). ^{1}H-NMR (200 MHz, $CDCl_3$, rotamers) δ: 1.21—1.45 (6H, m), 3.16—4.09 (6H, m), 4.38—4.98 (3H, m), 5.81—6.05 (2H, m), 6.48—7.70 (7H, m). *Anal.* Calcd for $C_{24}H_{24}NO_6Br$: C, 57.38; H, 4.82; N, 2.79. Found: C, 57.50; H, 4.94; N, 2.64.

General procedure for the biaryl coupling reaction of amide (9) by the Pd reagent

The reaction of amide (**9**) (0.3 mmol) in dry DMF (8 mL) was carried out using $Pd(OAc)_2$ and phosphines in a molar ratio of 1 : 1 and 2 mol equivalents of base under reflux and under the reaction conditions indicated in Table 1. The reaction mixture was diluted with ether and the precipitate was removed by filtration. The filtrate was washed with brine. The residue was dissolved in $CHCl_3$ and subjected to column chromatography on silica gel. Elution with hexane : AcOEt (4 : 1) gave the starting material (**9**) and successive elution with the same solvent gave the debromo amide (**21**) and phenanthridone (**7**).

8-Isopropoxy-7-methoxy-*N*-methyl-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5*H*)-one (7) : colorless needles, mp 170—171℃ (from benzene). IR (KBr) cm^{-1}: 1660 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.40 (1H, d, *J*=6.0 Hz, $CH(C\underline{H}_3)_2$), 3.90 (3H, s, NCH_3), 4.07 (3H, s, OCH_3), 4.66 (1H, septet, *J*=6.0 Hz, $C\underline{H}(CH_3)_2$), 6.09 (2H, s, OCH_2O), 7.15 (1H, s, Ar-H), 7.38 (1H, d, *J*=8.8 Hz, Ar-H), 7.52 (1H, d, *J*=8.8 Hz, Ar-H), 7.53 (1H, s, Ar-H), 7.94 (1H, d, *J*=8.8 Hz, Ar-H), 7.98 (1H, d, *J*=8.8 Hz, Ar-H). *Anal*. Calcd for $C_{23}H_{21}NO_5$: C, 70.58; H, 5.41; N, 3.58. Found: C, 70.70; H, 5.59; N, 3.69.

3-Isopropoxy-2-methoxy-*N*-methyl-*N*-(6,7-methylenedioxy-1-naphthyl)benzamide (21) : colorless needles, mp 167—168℃ (from benzene-hexane). IR (KBr) cm^{-1}: 1652 (C=O). ^{1}H-NMR (60 MHz, $CDCl_3$, rotamers) δ: 1.13—1.48 (6H, m), 3.22-4.06 (6H, m), 4.25—4.70 (1H, m), 6.06 (2H, s), 6.46—

7.51 (8H, m). *Anal.* Calcd for $C_{23}H_{23}NO_5$: C, 70.21; H, 5.89; N, 3.56. Found: C, 70.48; H, 5.67; N, 3.43.

General procedure for the biaryl coupling reaction of amide (11) by the Pd reagent

The reaction of amide (**11**) (0.3 mmol) in dry DMF (8 mL) was carried out using $Pd(OAc)_2$ and phosphines in a molar ratio of 1 : 1, and 2 mol equivalents of base under reflux and under the reaction conditions indicated in Table 2. The reaction mixture was diluted with ether and the precipitate was removed by filtration. The filtrate was washed with brine. The residue was dissolved in $CHCl_3$ and subjected to column chromatography on silica gel. Elution with hexane : AcOEt (4 : 1) gave azepinone (**23**) and successive elution with the same solvent gave the N-methylphenanthridone (**8**) and then NH-phenanthridone (**22**).

8-Isopropoxy-7-methoxy-*N*-methoxymethyl-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5*H*)-one (8) : colorless needles, mp 169—170℃ (from ether). IR (KBr) cm^{-1}: 1664 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.40 (6H, d, *J*=6.1 Hz), 3.88 (3H, s), 4.06 (3H, s), 4.65 (1H, septet, *J*=6.1 Hz), 5.36 (2H, s), 6.09 (2H, s), 7.14 (1H, s), 7.38 (1H, s), 7.38 (1H, d, *J*=9.0 Hz), 7.52 (1H, d, *J*=9.0 Hz), 7.93 (1H, d, *J*=9.0 Hz), 7.97 (1H, d, *J*=9.0 Hz) 8.02 (1H, s). FAB-MS *m/z*: 442 $(M+1)^+$. *Anal.* Calcd for $C_{24}H_{23}NO_6$: C, 68.40; H, 5.50; N, 3.32. Found: C, 68.52; H, 5.63; N, 3.12.

8-Isopropoxy-7-methoxy-2,3-methylenedioxybenzo[*c*]phenanthridin-6(5*H*)-one (22) : colorless prisms, mp ＞300℃ (from ether). IR (KBr) cm^{-1}: 1647 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.42 (6H, d, *J*=6.5 Hz), 4.07 (3H, s), 4.69 (1H, septet, *J*=6.5 Hz), 6.13 (2H, s), 7.18 (1H, s), 7.45 (1H, d, *J*=9.0 Hz), 7.50 (1H, d, *J*=9.0 Hz), 7.81 (1H, s), 8.02 (1H, d, *J*=9.0 Hz), 8.05 (1H, d, *J*=9.0 Hz), 10.15 (1H, br s). *Anal.* Calcd for $C_{22}H_{19}NO_4 \cdot H_2O$: C, 69.65; H, 5.58; N, 3.69. Found: C, 69.51; H, 5.30; N, 3.68.

10-Isopropoxy-9-methoxy-7-methoxymethyl-1,2-methylenedioxynaphtho[1,8-*cd*][2]-benzazepin-8(7*H*)-one (23) : colorless prisms, mp 153—154℃ (from ether). IR (KBr) cm^{-1}: 1660 (C=O). ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.36 (6H, d, *J*=6.0 Hz), 3.48 (3H, s), 4.04 (3H, s), 4.57 (1H, septet, *J*=6.0 Hz), 6.11 (2H, br), 6.93 (1H, d, *J*=9.0 Hz), 6.97 (1H, s), 7.25 (1H, dt, *J*=7.8, 7.6 Hz), 7.34 (1H, d, *J*=9.0 Hz), 7.37 (1H, dd, *J*=7.8, 1.2 Hz), 7.57 (1H, dd, *J*=7.6, 1.2 Hz). *Anal.* Calcd for $C_{24}H_{23}NO_6$: C, 68.40; H, 5.50; N, 3.32. Found: C, 68.20; H, 5.74; N,3.21.

Fagaridine (5)

$LiAlH_4$ (8.7 mg, 0.23 mmol) was added to a solution of **7** (30 mg, 0.077 mmol) in anhyd THF (2 mL) and the mixture was stirred for 30 min at rt . Excess hydride was decomposed with wet ether and the organic layer was decanted. The residue dissolved in concd HCl (3 mL) was refluxed for 4 h. The mixture was concentrated to dryness under reduced pressure. The residue was recrystallized from MeOH-ether to give fagaridine (**5**, 26.9 mg, 86%) as brown needles, mp 229—231℃ (lit.,[9a] 231—233℃). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 4.16 (3H, s, C_7-OCH_3), 4.99 (3H, s, C_5-NCH_3), 6.35 (2H, s, OCH_2O), 7.89 (1H, s, C_1-H), 8.15 (1H, d, *J*=9.0 Hz, C_9-H), 8.31 (1H, d, *J*=9.0 Hz, C_{12}-H), 8.34 (1H, s, C_4-H), 8.73 (1H, d, *J*=9.0 Hz, C_{10}-H), 8.77 (1H, d, *J*=9.0 Hz, C_{11}-H), 10.04 (1H, s, C_6-H), 11.31 (1H, s, C_8-OH). FAB-MS *m/z*: 334 $(M)^+$. *Anal*. Calcd for $C_{20}H_{16}NO_4Cl \cdot 2H_2O$: C, 59.19; H, 4.97; N, 3.45. Found: C, 59.05; H, 5.04;

N, 3.28.

Spectral data of synthetic sample were identical with those of authentic sample kindly provided with Dr. T. Nakanishi, Nippon Kayaku Company.

Decarine (6)

$LiAlH_4$ (27 mg, 0.71 mmol) was added to a solution of **8** (100 mg, 0.237 mmol) in anhyd THF (5 mL) and the mixture was stirred for 30 min at rt . Excess hydride was decomposed with wet ether and the organic layer was decanted. The residue dissolved in conc. HCl (5 mL) was refluxed for 4 h. The mixture was concentrated to dryness under reduced pressure. The residue was recrystallized from MeOH-$CHCl_3$ to give decarine (**6**, 64 mg, 84%) as brown needles, mp 243—244.5℃ (lit.,[10] 243℃). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 4.01 (3H, s, C_7-OCH_3), 6.20 (2H, s, OCH_2O), 7.50 (1H, s, C_1-H), 7.57 (1H, d, *J*=9.0 Hz, C_9-H), 7.95 (1H, d, *J*=9.0 Hz, C_{12}-H), 8.46 (1H, d, *J*=9.0 Hz, C_{10}-H), 8.50 (1H, d, *J*=9.0 Hz, C_{11}-H), 8.53 (1H, s, C_4-H), 9.57 (1H, s, C_6-H), 10.09 (1H, s, C_8-OH). FAB-MS *m/z*: 320 $(M+1)^+$. *Anal.* Calcd for $C_{19}H_{13}NO_4 \cdot 0.25\ H_2O$: C, 70.47; H, 4.20; N, 4.33. Found: C, 70.22; H, 4.42; N, 4.12.

This sample was identified with the authentic sample of decarine provided with Professor T. Ishikawa, Graduate School of Pharmaceutical Sciences, Chiba University.

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