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Studies on the Alkaloids of Papaveraceous Plants. XXX.[1] Conformational Analysis of Some Hydrobenzo[*c*]-phenanthridine-type Alkaloids

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In some hydrobenzo[*c*]phenanthridine-type alkaloids, the preferred conformation of the B and C rings in solution and the orientation of the N-methyl group in solution and in crystalline state were examined using infrared, proton magnetic resonance, and carbon magnetic resonance spectroscopies. The alkaloids, chelidonine (**1**), corynoline (**2**), 6-quasi-axial and quasi-equatorial alkyl-substituted derivatives of **2** (**2a'**—**c'** and **2a**—**c**), and corynolamine (**3**), exist in the conformation with type I-*cis* and B/C-half chair/half chair, 6-quasi-axial alkyl-substituted derivatives of **2**-acetate (**2b'**-Ac and **2a'**-Ac) and **3**-diacetate adopt the conformation with type I-*cis* and B/C-twist half-chair/half chair, and **2**-acetate and its 6-quasi-equatorial alkylsubstituted derivatives (**2a**-Ac and **2b**-Ac) possess the conformation with type I-*cis* and B/C-half chair/twist halfboat. Chelidonine acetate (1-Ac) exists in the conformation with type II-*cis* and B/C-half chair/twist half-chair. (+)-14-Epicorynoline (**4**) and its acetate adopt the conformation with *trans* and B/C-half chair/twist half-chair.

The preferred conformation of the N-methyl group in solution in **1**, **2**, **2a**—**c**, **2a'**—**c'**, **2a**-Ac, **2b**-Ac, and **3** is equatorial and that in **1**-acetate, **2a'**-Ac, **2b'**-Ac, **3**-diacetate, **4**, and **4**-acetate is axial. In **2**-acetate, the position of equilibrium in the N–Me(*ax*)⇄N–Me-(*eq*) shifts to the equatorial side than the axial side.

Orientation of the N-methyl group in a crystalline state is in accord with the preferred conformation in solution.

Keywords——conformational analysis; IR, PMR, and CMR spectroscopies; hydrobenzo[*c*]phenanthridines; corynoline; chelidonine; 14-epicornoline

The preferred conformations for chelidonine (**1**), corynoline (**2**), and their acetates belonging to hydrobenzo[*c*]phenanthridine-type alkaloids were considered by Bersch,[3] Seoane,[4] MacLean,[5] and Naruto.[6] It has been shown that **1** and **2** both exist in type I-*cis* and B/C-half chair/half chair conformation, and their acetates, chelidonine acetate (**1**-Ac) and corynoline acetate (**2**-Ac), in type I-*cis* and B/C-half chair/twist half-chair conformation and in type I-*cis* and B/C-half chair/twist half-boat conformation, respectively. Kametani *et al*,[7] have shown from X-ray analysis that *p*-bromobenzoate of **2** exists in a conformation with type I-*cis*, B/C-half chair/twist half-boat, and equatorial N-methyl group. We undertook X-ray analysis[8a] of (+)-14-epicorynoline (**4**) bromoacetate and indicated that it adopts a *trans*-B/C

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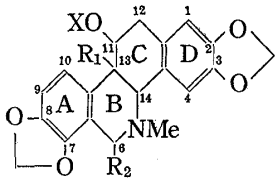
fusion together with B/C-half chair/twist half-chair conformation and an axial N-methyl group.

This paper deals with the results of studies using infrared (IR), proton magnetic resonance (PMR), and carbon magnetic resonance (CMR) spectroscopies on both the preferred confor-

Table I. Hydrobenzo[*c*]phenanthridine-type Alkaloids



	R_1[a]	R_2	X[a]
(+)-Chelidonine (**1**)	H	H	H
(+)-Chelidonine acetate (**1**-Ac)	H	H	Ac
(±)-Corynoline (**2**)	Me	H	H
(±)-Corynoline acetate (**2**-Ac)	Me	H	Ac
(±)-6-eq′-Methylcorynoline (**2a**)	Me	eq′-Me	H
(±)-6-eq′-Methylcorynoline acetate (**2a**-Ac)	Me	eq′-Me	Ac
(±)-6-ax′-Methylcorynoline (**2a′**)	Me	ax′-Me	H
(±)-6-ax′-Methylcorynoline acetate (**2a′**-Ac)	Me	ax′-Me	Ac
(±)-6-eq′-Vinylcorynoline (**2b**)	Me	eq′-$CH{=}CH_2$	H
(±)-6-eq′-Vinylcorynoline acetate (**2b**-Ac)	Me	eq′-$CH{=}CH_2$	Ac
(±)-6-ax′-Vinylcorynoline (**2b′**)	Me	ax′-$CH{=}CH_2$	H
(±)-6-ax′-Vinylcorynoline acetate (**2b′**-Ac)	Me	ax′-$CH{=}CH_2$	Ac
(±)-6-eq′-Acetonylcorynoline (**2c**)	Me	eq′-CH_2COCH_3	H
(±)-6-ax′-Acetonylcorynoline (**2c′**)	Me	ax′-CH_2COCH_3	H
(±)-Corynolamine (**3**)	Me	ax′-CH_2OH	H
(±)-Corynolamine diacetate (**3**-diAc)	Me	ax′-CH_2OAc	Ac
(+)-14-Epicorynoline (**4**)[b]	Me	Me	H
(+)-14-Epicorynoline acetate (**4**-Ac)[b]	Me	Me	Ac

a) The relative orientation of OX and R_1 is *trans*.
b) The junction of B/C ring is *trans*.

Table II. Stereostructure of Hydrobenzo[*c*]phenanthridine-type Alkaloids

	Ring junction and conformations of rings B and C	Orientation of N–Me in solution	in crystal
(+)-**1**			eq
(−)-**2**			eq
(±)-**2**			eq
(±)-**2a**			eq
(±)-**2a′**	*cis*-Type I		—
(±)-**2b**	B/C-half chair/half chair	eq⟵ax	eq
(±)-**2b′**			—
(±)-**2c**			—
(±)-**2c′**			—
(±)-**3**			—
(±)-**2a**-Ac		eq⟵ax	eq
(±)-**2b**-Ac	*cis*-Type I	eq⟵ax	eq
(+)-**2**-Ac	B/C-half chair/twist half-boat		eq
(±)-**2**-Ac		eq⟷ax	eq
(±)-**2a′**-Ac			—
(±)-**2b′**-Ac	*cis*-Type I	ax⟵eq	—
(±)-**3**-diAc	B/C-twist half chair/half chair		—
(+)-**1**-Ac	*cis*-Type II half chair/twist half-chair	ax⟵eq	ax
(+)-**4**	*trans*	ax⟵eq	ax
(+)-**4**-Ac	B/C-half chair/twist half-chair		ax

Table III. PMR Spectra Data on Hydrobenzo[*c*]-

	4	1	9 and 10[c]	6	11[d]	12[d]
1	6.71	6.69	6.78	3.47, d (16) 4.11, d (16)	4.27, d-d (3.0, 2.5)	3.81, t (3.0)
2	6.71	6.69	6.86 6.83	3.49, d (16) 4.04, d (16)	3.99, $\left(w\frac{1}{2}=8\right)$	3.14, d (2.9)
2a	6.73	6.67	6.87 6.88	3.68, q (6.2)	4.05, $\left(w\frac{1}{2}=9\right)$	3.20, d (3.2)
2a′	6.70	6.70	6.84 6.96	4.26, q (6.5)	3.97, $\left(w\frac{1}{2}=8\right)$	3.12, d (2.8)
2b	6.71	6.68	6.87 6.99	3.98, d (7.0)	4.06, $\left(w\frac{1}{2}=9\right)$	3.19, d (3.4)
2b′	6.71	6.64	6.89 7.01	4.55, d (7.0)	3.98, $\left(w\frac{1}{2}=8\right)$	3.13, d (2.8)
2c	6.69	6.68	6.86 6.98	4.33, t (4.0)	3.99, $\left(w\frac{1}{2}=9\right)$	3.18, d (3.4)
2c′	6.70	6.65	6.87 6.98	4.89, d-d (6.5, 3.7)	4.00, $\left(w\frac{1}{2}=9\right)$	3.13, d (3.0)
3	6.79	6.68	6.89 7.01	4.18	3.99, $\left(w\frac{1}{2}=8\right)$	3.09, d (2.8)
1-Ac	7.26	6.46	6.74 7.29	3.50, d (17) 3.77, d (17)	5.38, sf (9.5, 7.0, 3.5)	2.82, d-d (16, 7.0) 2.88, d-d (16, 9.5)
2-Ac	6.92	6.57	6.76 6.98	3.58, d (16) 3.91, d (16)	5.25, d-d (8.0, 7.5)	2.91, d-d (16, 7.5) 2.96, d-d (16, 8.0)
2a-Ac	6.72	6.68	6.76 6.91	3.72, q (6.2)	5.16, t (7.5—8.0)	3.02, d-d (15, 7.5) 3.34, d-d (15, 8.0)
2a′-Ac	7.09	6.56	6.76 6.96	4.12, q (6.5)	5.44, t (5.0)	2.96, d-d (17, 5.0) 3.00, d-d (17, 5.0)
2b-Ac	6.73	6.69	6.76 6.87	3.98, d (7.0)	5.18, t (8.0—7.5)	2.98, d-d (15, 8.0) 3.38, d-d (15, 7.5)
2b′-Ac	7.16	6.56	6.80 6.93	4.60, d (4.5)	5.51, t (4.0)	2.96, d-d (18, 4.0) 3.02, d-d (18, 4.0)
3-diAc	7.0	6.47	6.71 6.89	4.76, d-d (12, 9.0)	5.41, t (4.0—4.5)	2.91, d-d (18, 4.0) 3.01, d-d (18, 4.5)
4	7.24	6.67	6.84 6.93	4.02, d (17) 4.29, d (17)	4.29, d-d (4.5, 1.5)	2.90, d-d (19, 1.5) 3.21, d-d (19, 4.5)
4-Ac	7.30	6.64	6.76 6.83	4.04, d (17) 4.30, d (17)	5.56, d-d (4.5, 1.5)	2.89, d-d (19, 1.5) 3.26, d-d (19, 4.5)

a) Chemical shifts are quoted in ppm units and coupling constants J as Hz in parenthese.
b) All other resonances are singlet except where indicated otherwise; d=doublet, t=triplet, m=multiplet, q=quartet, sf=sevenfold
c) The signals due to H_9 and H_{10} are observed as a AB quartet (J=8.5 Hz) in the compounds except **1**.
d) Approximate coupling constants between H_{11} and H_{12} (ABX type) are obtained by the spin-decoupling experiments ($w\frac{1}{2}$: half
e) W coupling.

mation of the B and C rings and that of the N-methyl group in (+)-chelidonine (**1**), (±)-corynoline[8b] (**2**), (±)-corynoline acetate[8c] (**2**-Ac), (±)-corynolamine[8d] (**3**), (+)-14-epicorynoline[8e] (**4**), and (+)-14-epicorynoline acetate[8c] (**4**-Ac) isolated in nature and their derivatives prepared by the chemical method, (+)-chelidonine acetate[8f] (**1**-Ac), (−)-corynoline[8f] (**2**), (+)-corynoline acetate[8f] (**2**-Ac), (±)-6-quasi-equatorial(=eq′)-methylcorynoline[8d] (**2a**), its acetate[8d] (**2a**-Ac), (±)-6-quasi-axial(=ax′)-methylcorynoline[8d] (**2a′**), its acetate[8d] (**2a′**-Ac), (±)-6-eq′-vinylcorynoline (**2b**), its acetate (**2b**-Ac), (±)-6-ax′-vinylcorynoline (**2b′**), its acetate (**2b′**-Ac), (±)-eq′-acetonylcorynoline (**2c**), (±)-6-ax′-acetonylcorynoline (**2c′**), and (±)-corynolamine diacetate[8d] (**3**-diAc) (Table I).

In hydrobenzo[*c*]phenanthridine alkaloids, there are two kinds of types, *trans*-fused type and *cis*-fused type of rings B and C (Fig. 1). In *trans* compounds, the conformational problem concerns the position of equilibrium with respect to nitrogen inversion and distortion of the B and C rings. In *cis* alkaloids the conformations of type I and II by ring inversion should

phenanthridine-type Alkaloids in $CDCl_3$[a,b]

14	N–Me	C_{13}–Me	O–Ac	OCH_2O	Other proton
3.60, d (2.5)	2.29			5.98, m	H_{13}, 3.01, t(2.5)
3.33	2.23	1.13		5.94, m	
3.39, d (2.0)[c]	2.19	1.07		6.0, m	C_6-Me, 1.58, d(6.2)
3.88	2.15	1.11		6.0, m	C_6-Me, 1.40, d(6.5)
3.42, d (2.0)[c]	2.15	1.09		5.98, m	C<u>H</u>=CH_2, 5.72, m CH=C<u>H</u>$_2$, 5.27—5.53, m
3.94	2.17	1.12		5.98, m	CH=C<u>H</u>$_2$, 6.21, sf(17, 10, 7), CH=C<u>H</u>$_2$, 5.29, d–d(17, 2.2), 5.53, d–d(10, 2.2)
3.42, d (2.0)[c]	2.16	1.08		5.96, m	CH_2CO<u>Me</u>, 2.04, C<u>H</u>$_2$COMe, 2.81, d–d (19, 4.0), 3.24, d–d(19, 3.0)
3.76	2.30	1.13		5.98, m	CH_2CO<u>Me</u>, 2.08, C<u>H</u>$_2$COMe, 2.76, d–d (17, 3.7), 3.12, d–d(17, 6.5)
4.29	2.31	1.11		6.0, m	C<u>H</u>$_2$OH, 4.18
4.16, d (5.0)	2.57		2.16	5.92	H_{13}, 3.64, d–d(5.0, 3.5)
3.56	2.49	1.27	1.87	5.94	
3.36	2.21	1.01	1.64	5.98, m	C_6–Me, 1.49, d(6.2)
4.13	2.30	1.26	1.78	5.96	C_6–Me, 1.51, d(6.5)
3.34	2.13	1.01	1.61	5.94, m	CH=CH_2, 5.74, d–d(9.0, 7.0), CH=CH_2, 5.14—5.44, m
4.12	2.24	1.16	1.73	5.96	CH=CH_2, 6.22, sf(18, 10, 4.5), CH=CH_2, 5.01, d–d(18, 2.0), 5.32, d–d(10, 2.0)
4.21	2.27	1.25	1.74 2.11	5.89 5.93	C<u>H</u>$_2$OCOMe, 4.13—4.31, m
4.56	2.51	1.11		5.96 6.01	
4.56	2.51	1.18	1.76	5.99, m	

[b] band width of the multiplet resonance).

be considered and, in each type, there are problems in regard to nitrogen inversion and distortion of the B and C rings (Fig. 1).

Comformation of the B and C rings

The preferred conformation of the B and C rings is summarised in Table II. From PMR spectra (Table III), the J values, $J_{11,12\alpha}$ and $J_{11,12\beta}$ in **1**, **2**, **2a**—**c**, **2a′**—**c′**, **3**, **2a′**-Ac, **2b′**-Ac, **3**-diAc were 2.8—5.0 Hz. This fact suggests that these alkaloids adopt the conformation with type I-*cis* and the ring C in half chair (Fig. 2-A), in which the dihedral angles of H(11)-C(11)-C(12)-H(12α)(or H(12β)) are about 60°, and therefore both $J_{11,12\alpha}$ and $J_{11,12\beta}$ are small.[9] The result for **2** is in agreement with the conclusion indicated by Naruto, *et al.*[6] PMR spectra of **4** and **4**-Ac showed the J values of $J_{11,12\alpha}$=1.5 Hz and $J_{11,12\beta}$=4.5 Hz. In comparison

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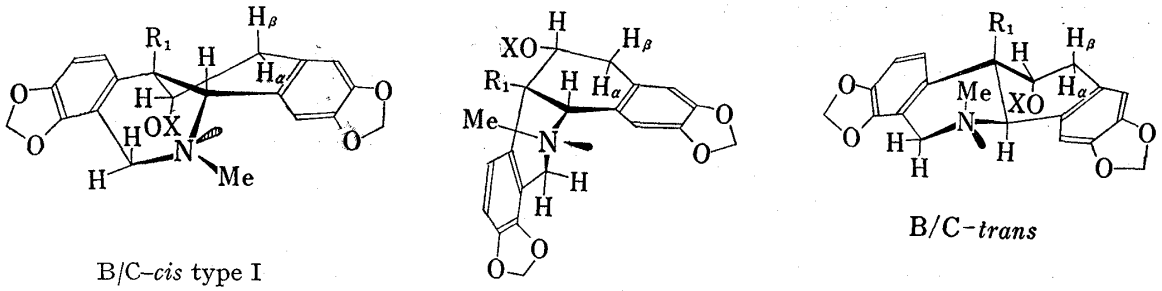

Fig. 1. Conformations of Hydrobenzo[*c*]phenanthridine-type Alkaloids

with above values, an increase of *ca.* 1.1 Hz in $J_{11,12\beta}$ and a decrease of *ca.* 1.9 Hz in $J_{11,12\alpha}$ are observed. These observations are consistent with the conformational conversion of the half chair into the twist half-chair in the C ring (Fig. 2 A→B), because the change in J values may be caused by the variation[9] of dihedral angles. Both $J_{11,12\alpha}$ and $J_{11,12\beta}$ take values between 7.5 and 8.0 Hz in 2-Ac, **2a**-Ac, and **2b**-Ac. These values correspond to the dihedral angles[9] of H(11)-C(11)-C(12)-H(12α) (or H(12β)) showing that the ring C is a twist half-boat (Fig. 2-C). The result for 2-Ac agreed with the conclusion indicated by Naruto, *et al.*[6] PMR spectra of **1**-Ac showed the J values of $J_{11,12\beta}$=7.0, $J_{11,12\alpha}$=9.5, and $J_{11,13}$=3.5 Hz, which suggested the conformation to be type II-*cis* (Fig. 1) and the twist half-chair in the ring C (Fig. 2-C). This assumption is supported by the CMR spectral analysis described below.

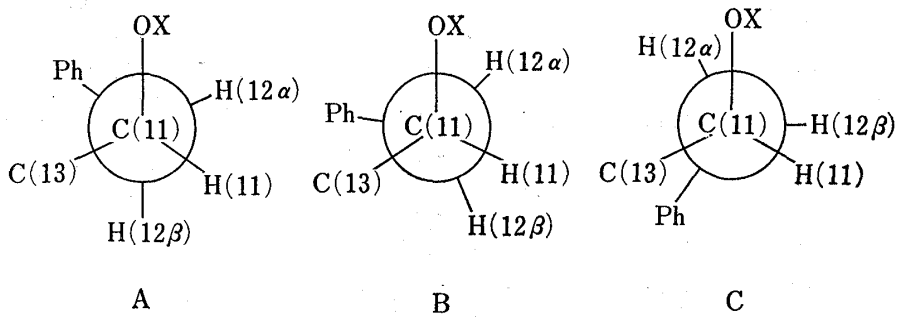

Fig. 2. Conformations of Ring C

In the CMR spectra (Table IV) of **2** and 2-Ac, the signal assigned to C(1) in 2-Ac appeared at a higher field and, the signal assigned to C(10) in 2-Ac at a lower field than that in **2**. The high field shift of C(1) and the low field shift of C(10) might arise from increase in the steric compression between C(12)-H and C(1)-H in the former and decrease in that between C(10)-H and C(11)-H in the latter, which are conceivable as being due to the distortion of the ring C. As can be seen from Table IV, the signals due to C(1) appeared at a higher field in the order of (**2**, **2a**—**c**, **2a**′—**c**′, **3**, **2a**′-Ac, **2b**′-Ac, 3-diAc)→(**4**, **4**-Ac)→(2-Ac, **2a**-Ac, **2b**-Ac) and those due to C(10) at a lower field in the order of (**2**, **2a**—**c**, **2a**′—**c**′, **3**, **2a**′-Ac, **2b**′-Ac, 3-diAc)→(2-Ac, **2a**-Ac, **2b**-Ac). These orders might correspond to that of the increase in the distortion of the ring C. By comparison of the CMR spectra of **1** and **1**-Ac, the signals due to C(6), C(12), and C(13) in **1**-Ac appeared at a higher field than those in **1**. These observations are interpreted by the model consideration that the model of type II has three gauche interactions which are not present in the model of type I. Therefore, the conformation with type II can be assigned to **1**-Ac. However, the presence of a small proportion of type I conformation could not be excluded. These results are in good agreement with the PMR evidences for the conformation of the ring C.

TABLE IV. Carbon-13 Data on Hydrobenzo[*c*]phenanthridine-type Alkaloids in $CDCl_3$ (in ppm from TMS)[a)]

	C(13)-CH_3	12	13	N-CH_3	6	14	11	OCH_2O	1	9	4	10
1		39.7	42.1	42.4	53.9	62.9	72.4	101.1 101.4	107.4	109.6	111.9	120.4
2	23.5	36.8	40.8	43.2	54.4	69.8	76.1	101.0 101.4	107.7	109.4	112.8	118.7
2a	24.1	37.4	41.2	39.7	58.5	68.8	75.3	100.8 101.0	107.7	109.4	112.9	119.1
2a′	23.3	36.6	40.3	39.2	54.8	60.5	75.7	101.0 101.2	107.8	109.4	112.5	118.9
2b	24.2	37.3	41.1	40.0	67.0	68.4	75.3	100.9×2	107.9	109.3	112.8	118.9
2b′	23.3	36.5	40.3	39.6	61.7	62.4	76.4	101.0 101.4	108.2	109.4	112.7	118.9
2c	24.0	37.2	40.1	40.8	57.0	69.0	75.4	101.0×2	107.8	109.5	112.8	119.2
2c′	23.7	36.4	40.2	39.3	55.0	61.8	76.0	101.1 101.4	108.1	109.4	112.3	119.0
3	24.0	36.2	*c*)	40.0	61.5[b)]	61.8[b)]	75.7	101.0 101.4	108.3	109.2	112.4	119.1
1-Ac		31.3	33.1	41.6	45.4	62.0	72.7	100.9×2	108.2	108.2	106.4	121.5
2-Ac	27.8	32.9	42.5	43.7	49.5	70.1	75.6	100.8 101.0	106.3	109.5	108.4	120.4
2a-Ac	27.1	33.7	43.6	41.1	56.6	70.8	75.0	100.9×2	106.2	108.9	110.9	120.1
2a′-Ac	23.9	29.6	39.0	39.7	53.3	61.3	73.8	100.9 101.3	108.2	109.4	106.6	119.1
2b-Ac	26.8	34.0	44.2	40.8	64.9	70.6	75.2	100.9×2	106.5	108.9	110.9	120.2
2b′-Ac	29.1	31.8	38.0	38.9	60.2[b)]	60.5[b)]	72.9	100.8 101.1	108.1	109.4	107.3	118.7
3-diAc	29.4	31.9	37.6	39.5	57.7[b)]	59.9[b)]	73.2	100.9 101.2	108.1	109.7	107.9	119.1
4	23.9	33.7	39.4	38.1	52.1	58.3	74.1	100.7 101.3	107.3	108.8	106.8	117.6
4-Ac	24.2	32.4	37.8	38.2	51.9	59.0	74.9	100.9 101.2	107.0	108.6	107.0	117.9

	6a	1a	4a	10a	7	2, 3, and 8			$\underline{C}OCH_3$	$\underline{C}OCH_3$	Other carbon	
1	117.1	125.8	128.9	131.4	143.1	145.3	145.6	148.2				
2	116.9	125.3	128.0	136.2	142.9	145.2	145.4	148.2				
2a	122.7	126.9	128.2	136.0	143.3	145.4	145.7	148.1			C(6)-CH_3	19.6
2a′	123.3	125.5	127.9	135.8	142.9	145.3	145.5	148.0			C(6)-CH_3	10.6
2b	119.6	126.3	128.1	136.3	143.8	145.3	145.8	148.1			$CH=CH_2$	137.0 119.6
2b′	119.3	125.3	128.3	136.2	143.6	145.5	145.5	148.0			$CH=CH_2$	131.5 120.9
2c	122.1	126.3	128.0	136.2	142.9	145.4	145.6	*c*)	*c*)	29.8	$\underline{C}H_2COCH_3$	50.5
2c′	121.9	125.0	128.2	135.8	142.7	145.4	145.7	148.1	206.2	30.2	$\underline{C}H_2COCH_3$	43.2
3	118.4	125.8	127.8	137.2	143.2	145.2	145.7	148.0			CH_2OH	61.0
1-Ac	117.3	126.6	127.6	129.5	144.1	145.3	146.6	147.0	175.4	21.4		
2-Ac	117.6	127.6	130.1	133.1	143.0	144.7	146.1	146.8	162.8	20.8		
2a-Ac	123.7	127.9	132.3	133.2	143.1	145.4	145.8	146.9	170.6	21.0[b)]	C(6)-CH_3	19.7[b)]
2a′-Ac	122.7	126.4	129.3	133.5	144.0	144.9	146.6	146.6	170.4	21.0[b)]	C(6)-CH_3	18.5[b)]
2b-Ac	120.2	128.1	132.0	133.1	143.7	145.6	145.8	147.1	170.6	20.9	$CH=CH_2$	138.1 116.8
2b′-Ac	117.8	126.0	128.8	134.4	144.6	145.0	146.8	146.8	170.4	21.2	$CH=CH_2$	138.6 117.3
3-diAc	116.4	126.0	126.0	128.3	135.0	144.7	146.9	146.9	170.4 171.0	21.1 21.1	$\underline{C}H_2OCOCH_3$	63.0
4	117.6	126.9	129.5	135.5	145.3	145.3	146.2	146.5				
4-Ac	116.5	126.3	129.5	135.5	144.7	144.9	146.4	146.8	170.5	21.2		

a) Assignments were made from off-resonance experiments and by comparing with the spectra of various alkaloids.
b) Assignment may be interchanged. *c*) No assignment.

The B ring might adopt the half-chair conformation in these compounds except **2a'**-Ac, **2b'**-Ac, and 3-diAc because of a negligible difference in the chemical shift of C(7) between the alkaloids (**2**, **2a**, and **2b**) and their acetates (**2**-Ac, **2a**-Ac, and **2b**-Ac).

Conformation of N-Methyl Group in Solution

The X-ray analysis of (+)-**4**-bromoacetate[8a] established that it adopts the axial N-methyl group in crystalline state. Spectral data of each of alkaloid in solution suggested that the preferred conformation of the N-methyl group is also axial in solution.

From considerations of the Bohlmann band and the N-methyl band in IR spectra, chemical shift of C(4)-H in PMR spectra, and the chemical shift of C(4) in CMR spectra, orientation of the N-methyl group was presumed and its result is given in Table II.

We[10] have previously used the Bohlmann bands for the assignment of the B/C ring juncture of some tetrahydroprotoberines. This method was applied to the assignment of the orientation of the N-methyl group in hydrobenzo[*c*]phenanthridines. From the magnitude of the apparent molecular absorptivity[10] of the band in 2700—2800 cm^{-1} region, the hydrobenzo[*c*]phenanthridines were divided into the three groups; group I (**1**, **2**, **2a**, **2b**, **2a**-Ac, **2b**-Ac), group II (**2**-Ac), and group III (**2a'**, **2b'**, **3**, **1**-Ac, **2a'**-Ac, **2b'**-Ac, 3-diAc, **4**, **4**-Ac) (Table V). The alkaloids of group I showed a band with a large intensity. This band is regarded as

Table V. IR Spectral Data on Hydrobenzo[*c*]phenanthridine-type Alkaloids (in $CHCl_3$)

	N–Me band		Bohlmann band	
	ν_{CH}	ε ($mol^{-1}\cdot l\cdot cm^{-1}$)	ν_{CH}	ε ($mol^{-1}\cdot l\cdot cm^{-1}$)
1	2825	59.2	2790	136.9
2	2830	64.0	2785	145.2
2a			2790	123.6
2a'	2810	77.9	2780	47.8
2b			2795	134.8
2b'	2810	63.8	2780	47.8
3	2810	59.3	2780	46.3
1-Ac	2800	39.0	2775	43.8
2-Ac			2775	101.8
2a-Ac			2775	130.9
2a'-Ac	2800	37.9	2775	40.3
2b-Ac			2775	136.0
2b'-Ac	2805	33.8	2775	37.7
3-diAc	2810	30.0	2775	27.0
4	2805	32.0	2780	30.1
4-Ac	2805	30.7	2780	28.6

the Bohlmann band owing to the existence of two quasi-axial hydrogens on C(6) and C(14). Accordingly, in group I alkalotds, the N-methyl group exists predominantly in equatorial conformation. The alkaloids of group III showed a band with a small intensity. In **4** and **4**-Ac, the intensities of their bands in solution and in crystalline state are approximately the same and similar, respectively, to those of the corresponding bands in **4**-bromoacetate, which possess an axial N-methyl group, both in solution and in crystalline state. This fact suggests that the N-methyl groups of **4** and **4**-Ac in solution exist in axial conformation as in crystalline state. In **2a'**, **2b'**, **3**, **2a'**-Ac, **2b'**-Ac, and 3-diAc the large decrease in the intensity of the band compared with group I alkaloids is due to the fact that C(6)-H bond is not *trans* and diaxial to the lone electron pair on the nitrogen because of the substitution of the axial hydrogen at C(6). The orientation of the N-methyl group in these alkaloids could not be established from

10) N. Takao and K. Iwasa, *Chem. Pharm. Bull.* (Tokyo), **24**, 3185 (1976).

the intensity of the band. However, from the examination of IR spectra of the corresponding 6-oxo compounds,[11] the weak band in 2800—2830 cm^{-1} region might be assinged to the N-methyl group. Intensity of the N-methyl band in **1** and **2**, having an equatorial N-methyl conformation, was larger than that in **4** and **4**-Ac, possessing an axial N-methyl conformation, In other words, the axial and equatorial conformation of the N-methyl group can be differentiated by the magnitude of the intensity of the N-methyl band. The intensity of the N-methyl band in **2a′**, **2b′**, and **3** was close to that in **1** and **2**. This suggests that the N-methyl groups in these alkaloids exist mainly in the equatorial conformation. The intensity of the N-methyl band in **2a′**-Ac, **2b′**-Ac, and **3**-diAc was comparable to those in **4** and **4**-Ac. This implies that the N-methyl groups in these alkaloids exist largely in the axial conformation. In **1**-Ac, the intensity of the band in the Bohlmann band region was weak and that of the N-methyl band was close to those in **4** and **4**-Ac. Therefore, it was assumed that the N-methyl group was largely axial in **1**-Ac. In the group II alkaloid, **2**-Ac, intensity of the Bohlmann band at 2775 cm^{-1} was closer to the values in group I alkaloids than those of the group III alkaloids. This shows that the position of equilibrium in the N-Me(*ax*)⇄N-Me(*eq*) shifts to the *eq* conformation than *ax* conformation.[12]

In **4** and **4**-Ac, in which the N-methyl group adopts the axial conformation. the signals of C(4)-H appeared at a lower field than those of C(1)-H. C(4)-H might be deshielded by the lone-pair electrons nitrogen as reported for quinolizidine derivatives.[13] The C(4)-proton should therefore shift to a lower field according to the increase in the proportion of the equatorial orientation of the lone electron pair on nitrogen. In PMR spectra (Table III), the C(4)-H shifted to a lower field in the order of (**1**, **2a**—**c**, **2a′**—**c′**, **3**, **2a**-Ac, **2b**-Ac)→(2-Ac)→(3-diAc)→(**2a′**-Ac, **2b′**-Ac)→(**1**-Ac, **4**, **4**-Ac). This order agrees with that of the increase in the proportion of the axial N-methyl conformation. This result is in good agreement with the IR evidences for the preferred conformation of the N-methyl group.

In CMR spectra (Table IV), the signal of C(4) in **4** appeared at a higher field than that in **2**. C(4) may be shielded by the electronic effect of the lone electron pair on nitrogen on the aromatic ring. The signals of C (4) shifted to a higher field in the order of (**1**, **2**, **2a**—**c**, **2a′**—**c′**, **3**)→(**2a**-Ac, **2b**-Ac)→(2-Ac)→(3-diAc)→(**2a′**-Ac, **2b′**-Ac, **1**-Ac, **4**, **4**-Ac). This order corresponds to that of the increase in the proportion of the axial N-methyl conformation. This result is consistent with the

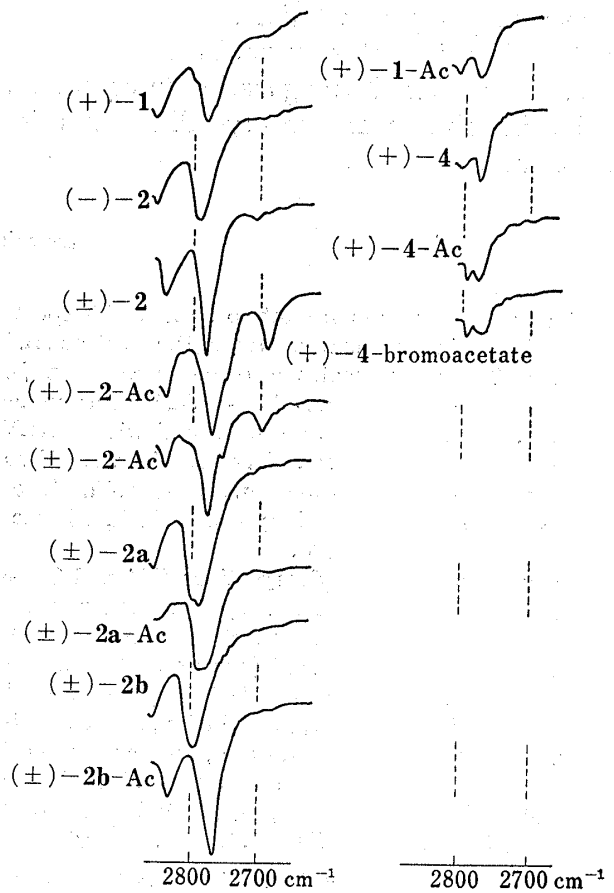

Fig. 3. IR Spectra (in KBr) of Hydrobenzo[*c*]-phenanthridine-type Alkaloids in 2600—2850 cm^{-1} Region

11) I. Ninomiya, T. Naito, T. Kiguchi, and T. Mori, *J. Chem. Soc., Perkin I*, **1973**, 1696.
12) This result for **2**-Ac was confirmed by the low temperature CMR spectrum, which will be discussed in a subsequent paper.
13) N. Takao, *Chem. Pharm. Bull.* (Tokyo), **19**, 247, 259 (1971).

IRand PMR evidences for the preferred conformation of the N-methyl group. In conclusion, the position of the equilibrium should be shifted to the equatorial side largely in **1**, **2**, **2a**—**c**, **2a′**—**c′**, **3**, **2a**-Ac, and **2b**-Ac, to the axial side mostly in **1**-Ac, **2a′**- Ac, **2b′**-Ac, **3**-diAc, **4**, and **4**-Ac. Moreover, in **2**-Ac, it should be shifted to the axial side compared to that of the former and to the equatorial side compared to that of the latter (Table II).

Thus, hydrobenzo[*c*]phenanthridine-type alkaloids might exist largely in such a conformation that the steric interactions are mostly avoided nitrogen inversion, ring distortion, and/or ring inversion because of flexible molecules in solution.

Configuration of N-Methyl Group in Crystalline State

We reported[10] that in the tetrahydroprotoberines, the Bohlmann bands in crystalline state are similar to those in solution. This examination was made to find the relationship between solution and crystalline state of configuration of the N-methyl group in hydrobenzo-[*c*]phenanthridines. Orientation of the N-methyl group in crystalline state was obtained by examination of the Bohlmann band and is summarised in Table II. A prominent Bohlmann band was observed (Fig. 3) in (+)-**1**, (−)-**2**, (±)-**2**, (+)-**2**-Ac, (±)-**2**-Ac, (±)-**2a**, (±)-**2b**, (±)-**2a**-Ac, and (±)-**2b**-Ac. Hence, in these alkaloids, the N-methyl group exists in the equatorial configuration. In (+)-**1**-Ac, (+)-**4**, and (+)-**4**-Ac, intensity of the band in the Bohlmann band region was close to that in (+)-**4**-bromoacetate.[8a] In these alkaloids, therefore, the N-methyl group may exist in the axial configuration. Thus, the alkaloids, in which the preferred conformation of the N-methyl group is axial or equatorial in solution, would adopt the same preferred configuration in crystalline state. The relationship between the configuration in solution and in crystalline state is similar to that observed for tetrahydroprotoberberines.[10]

Experimental

The melting points are not corrected. IR spectra were recorded with a Hitachi EPI-G2 spectrometer. The methods of the measurement and the treatment of the data were the same as that reported in our previous paper.[10] The mass spectra were measured on a JEOL-OIS instrument. PMR spectra were determined with a Varian A-60D and a NEVA-NV-21 spectrometers in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard. CMR spectra were measured with a NEVA-NV-21 spectrometer at 22.6 MHz in 8 mm tube at ordinary probe temperature. The samples were dissolved in $CDCl_3$ containing TMS as an internal reference (δ_c, 0), and concentrations were *ca.* 0.1—1 mol/l. The measurement conditions in the Fourier transform mode were: spectral width, 5000 Hz; pulse width, 15 μsec (flipping angles of *ca.* 20°); aquisition time, 0.4 sec; number of data points, 4096.

Preparation of 6-Vinylcorynolines (2b′ and 2b)——Corynoloxine chloride[13] (1.07 g) suspended in dry tetrahydrofuran was added to $CH_2=CHMgI$ prepared from Mg (0.72 g), MeI (0.1 ml), and $CH_2=CHBr$ (5 ml) in dry tetrahydrofuran. The reaction mixture was stirred for 1 hr. After the addition of H_2O, the solution was evaporated under reduced pressure. A small amount of 5% HCl and H_2O were added to the residue. The resulting precipitate was collected by filtration, dissolved in a small amount of MeOH. MeOH solution was basified with 10% NH_4OH solution, and extracted with ether. The ether layer was washed with H_2O saturated with NaCl solution, dried, and evaporated to give a crystalline residue (770 mg), which was chromatographed over silica gel and recrystallized from $CHCl_3$–MeOH to give 300 mg of colorless prisms (**2b**), 205—206°; MS *m/e*: 393 (M^+), 375, 366; IR ν_{max}^{Nujol} cm^{-1}: 3100 (OH), 2795 (Bohlmann band); PMR ($CDCl_3$): 5.27—5.53 (2H, m, $CH=C\underline{H}_2$), 5.72 (1H, m, $C\underline{H}=CH_2$); and 280 mg of colorless prisms (**2b′**), mp 165—166°; MS *m/e*: 393 (M^+), 375, 366; IR ν_{max}^{Nujol} cm^{-1}: 3160 (OH); PMR ($CDCl_3$): 5.29 [1H, d–d (J=17, 2.2), $^{H}\!>\!C=C<^{\underline{H}}_{H}$], 5.53 [1H, d–d ($J$=10, 2.2), $^{H}\!>\!C=C<^{\underline{H}}_{H}$], 6.21 [1H, sevenfold ($J$=17, 10, 7), $C\underline{H}=CH_2$]. **2b′** and **2b** were acetylated with Ac_2O to afford O-acetates; **2b′**-Ac, mp 119—120° (MeOH); MS *m/e*: 435 (M^+), 408, 375; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1725 (C=O); PMR ($CDCl_3$); 1.73 (3H, s, $COCH_3$); and **2b**-Ac, mp 132—133° (MeOH); MS *m/e*: 435 (M^+), 408, 375; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2775 (Bohlmann band), 1720 (C=O); PMR ($CDCl_3$): 1.61 (3H, s, $COCH_3$).

Preparation of 6-Acetonylcorynolines (2c′ and 2c)——A solution of 15% NaOH (8 ml) was added to a solution of corynoloxine chloride (250 mg) in H_2O–$(CH_3)_2CO$ (1: 1) (8 ml) and the mixture was heated for 15 hr under stirring. The solution was concentrated, diluted with H_2O, and extracted with ether. The ether layer was dried and evaporated. The residue was chromatographed over silica gel to give 35 mg of

colorless prisms (**2c**′), mp 202—203° (MeOH–ether), 5 mg of colorless prisms (**2c**), mp 200.5—201.5° (MeOH–$CHCl_3$), and 90 mg of colorless needles (corynoloxine), mp 209—210° (MeOH–$CHCl_3$). **2c**′: *Anal.* Calcd. for $C_{24}H_{25}NO_6$: C, 68.07; H, 5.95. Found: C, 68.22; H, 6.13. MS *m/e*: 423 (M^+), 366 ($M^+-CH_2COCH_3$). UV λ_{max}^{MeOH} nm (log ε): 288 (3.20), 237 (3.30). IR ν_{max}^{Nujol} cm^{-1}: 3160 (OH), 1712 (C=O). PMR ($CDCl_3$): 2.80 (3H, s, $COCH_3$), 2.76 [1H, d–d (J=17, 3.7), $C\underline{H}_2COCH_3$], 3.12 [1H, d–d (J=17, 6.5), $C\underline{H}_2COCH_3$], **2c**: *Anal.* Calcd. for $C_{24}H_{25}NO_6$: C, 68.07; H, 5.95; N, 3.31. Found: C, 67.64; H, 5.88; N, 3.35. IR ν_{max}^{Nujol} cm^{-1}: 3150 (OH), 2780 (Bohlmann band), 1708 (C=O); PMR ($CDCl_3$): 2.04 (3H, s, $COCH_3$), 2.81 [1H, d–d (J=19, 4), $C\underline{H}_2COCH_3$], 3.24 [1H, d–d (J=19, 4), $C\underline{H}_2COCH_3$].

Optically active alkaloids, (+)-**1**, (+)-**4**, and (+)-**4**-Ac, and (±)-**2**, (±)-**3**, and (±)-**2**-Ac are natural products. The alkaloids, **1**-Ac and 3-diAc, were obtained by acetylation of **1** and **3** with Ac_2O and pyridine. The optically active alkaloids, (−)-**2** and (+)-**2**-Ac, were obtained by the resolution of (±)-**2** and (±)-**2**-Ac.[8f] The preparation of **2a**, **2a**′, **2a**-Ac, and **2a**′-Ac[8d] will be described elsewhere.