Crystal Structure of (*dl*)-Corynoloxine

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The crystal structure of the racemic alkaloid (*dl*)-corynoloxine (**1**), 5b,6,7,12b,13,14-hexahydro-5b,13-dimethyl-6,14-epoxy-1,3-dioxolo[4,5-*i*][1,3]dioxolo[4,5]benzo[1,2-*c*]phenanthridine, is reported here. The crystal is orthorhombic, space group *Pbca* with $a = 20.375(3)\text{\AA}$, $b = 41.499(3)\text{\AA}$, $c = 8.139(3)\text{\AA}$, and $Z = 16$. The crystal contains two crystallographically independent molecules. These two molecules take essentially the same conformation.

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(*dl*)-Corynoloxine (**1**) is an hexahydrobenzo[*c*]phenanthridine-type alkaloid uniquely isolated as a racemate from *Corydalis incisa* (Papaveraceae).¹ The structure of **1** (Fig. 1) has been decided by spectroscopic and chemical methods.² (*dl*)-**1** is biosynthesized from (*dl*)-Corynoline (**2**), which is the main alkaloid of *C. incisa*. Previously, we reported on the correlation of the structure and the adhesion inhibitory effect on corynoline (**2**).³

It was found that (*dl*)-**1** showed a comparatively advantageous inhibitory effect for adhesion control between human umbilical vein cultured endothelial cell (HUVEC) and human polymorphonuclear leukocyte (PMNCs).⁴ To understand the cell-adhesion inhibitory effect of **1** for its receptor protein (ICAM-1, etc.), it is important to know the detailed structure of (*dl*)-**1**, and thus it was investigated by X-ray structure analysis.

(*dl*)-**1** was obtained by the oxidation of (*dl*)-**2**. (*dl*)-**2** (100 mg) was dissolved in a mixture of AcOH (5%) and Hg₂(OAc)₂ (210 mg) and stirred at 98°C. After 4 h, the reaction mixture was adjusted to pH 10 with NH₄OH (28%) solution and extracted with ether (2 × 200 ml). The ether layer was dried (K₂CO₃) and evaporated to give (*dl*)-**1** as a yellow-colored oil. The oil was chromatographed on a column of Al₂O₃ (benzene) to give (*dl*)-**1** (49 mg) as needles, mp. 209 – 210°C (ether/MeOH). Single crystals suitable for X-ray structure analysis were obtained by crystallization from a mixed solution of CHCl₃ and MeOH,

which afforded transparent needle crystals. The crystal and structure refinement data are summarized in Table 1. The crystal structure of (*dl*)-**1** is shown in Fig. 2. The structure was determined to be 5b,6,7,12b,13,14-hexahydro-5b,13-dimethyl-6,14-epoxy-1,3-dioxolo[4,5-*i*][1,3]dioxolo[4,5]benzo[1,2-*c*]phenanthridine and supports the chemically estimated structure. The crystal of (*dl*)-**1** contained two crystallographically independent molecules (molecule A, B). Characteristically, two molecules took essentially the same conformation, as is obvious in Fig. 2; only the bending degree of

Fig. 1 Chemical formula of **1** and **2**.

Table 1 Crystal data and experimental data of (*dl*)-**1**

CCDC deposition number: 701087
Chemical formula: C ₂₁ H ₁₉ NO ₅
Formula weight = 365.37
$T = 298\text{ K}$
Crystal system: orthorhombic
Space group: <i>Pbca</i>
$a = 20.375(3)\text{\AA}$
$b = 41.499(3)\text{\AA}$
$c = 8.139(3)\text{\AA}$
$V = 6882(2)\text{\AA}^3$
$Z = 16$
$D_{\text{calc}} = 1.410\text{ g/cm}^3$
$\lambda(\text{Cu } K\alpha) = 0.84\text{ mm}^{-1}$
$F(0\ 0\ 0) = 3072$
Radiation: Cu $K\alpha$ ($\lambda = 1.54180\text{ \AA}$)
No. of reflections collected = 6094
No. of observed reflections = 3378
θ range for data collection: 2.13 to 67.62°
Data/Restraints/Parameters = 3378/0/488
Goodness-of-fit on $F^2 = 1.113$
R indices [$I > 2\sigma(I)$]: $R1 = 0.0695$, $wR2 = 0.1712$
R indices (all data): $R1 = 0.1548$, $wR2 = 0.2034$
$(\Delta\sigma)_{\text{max}} = 0.004$
$(\Delta\rho)_{\text{max}} = 0.318$
$(\Delta\rho)_{\text{min}} = -0.299$
Measurement: Rigaku AFC5R
Program system: WSC/AFC
Structure determination: SHELXS-97
Refinement: full matrix SHELXL-97 ⁶

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Fig. 2 ORTEP structure of two molecules of (*dl*)-corynoxine (**1**), showing 50% probability ellipsoids.

the methylenedioxy unit on the A or D ring was different between both molecules: torsion angle C19–O1–C8–C7 = 2.2(7)° for A, and 14.2(6)° for B; C8–O1–C19–O2 = –3.2(7)° for A and –22.0(6)° for B. The *cis* conformation in the B/C ring joint moiety of the hexahydrobenzo[*c*]phenanthridine skeleton is anticipated to lead to whole conformational flexibility. The B/C ring moiety of (*dl*)-**1** was shown to be of the *anti-cis* type.⁵ As for the C6–C11 ether linkage, the conformation adopted a twist-

half-boat on the B ring and a twist-half-chair on the C ring. The direction of the *N*-methyl group was *axial* with respect to the B ring. This conformation agreed with that from the NMR spectroscopic method. The dihedral angle between two aromatic rings, A and D, was 87.7(2)° for both molecules. The ether bond cross-linking molecular center appears to be relatively less strained, because it forms a stable 6-member ring, and the bond lengths are within the usual value: O5–C6 = 1.418(6)Å for A and 1.424(6)Å for B; O5–C11 = 1.443(6)Å for A and 1.441(6)Å for B. As the structural feature in the crystal (*dl*)-**1**, no crystal solvents and no intermolecular hydrogen bonds were formed. The respective molecules are held by van der Waals forces among the neighboring molecules.

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