Tetrahedron Letters No. 26, pp. 2429-2432, 1971. Pergamon Press. Printed in Great Britain.

BOCCONOLINE : A NEW TYPE DIHYDROBENZO[c]PHENANTHRIDINE ALKALOID POSSESSING A UNIQUE SUBSTITUENT AT C_6 POSITION

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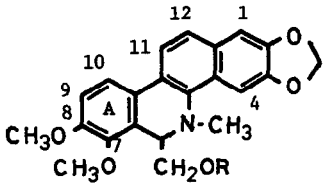
(Received in Japan 22 May 1971; received in UK for publication 25 May 1971)

Benzo[c]phenanthridine alkaloid is one of fairly common constituents of the Papaveraceous and the Rutaceous plants[2)]. In 1962, Tani and Takao[3)] isolated a minor alkaloid, mp 223-224°, tentatively designated as base C, from *Bocconia cordata* Willd. [*Macleaya cordata* (Willd.) R. Br.], Japanese name "Takenigusa or Champa-giku", Papaveraceae, with several other alkaloids. In this communication the authors wish to present the structure establishment of base C, bocconoline (1), which has a unique substituent at C_6 in dihydrobenzo[c]phenanthridine alkaloid group.

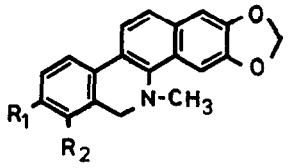
Thin layer chromatography showed that base C was contaminated with a very minute amount of another minor base. Pure bocconoline (1) was obtained by preparative thin layer chromatography as colorless pillars, mp 232-233°. The proposed molecular formula $C_{21}H_{19}O_4N\cdot H_2O$[3)] is revised to $C_{22}H_{21}O_5N$ which is fixed on the basis of analytical and mass spectral data [M^+: m/e 379; M^+-31: m/e 348 (base peak)]. The IR spectrum shows the presence of a hydroxy group by an absorption band at 3470 cm^{-1}. The NMR spectrum ($CDCl_3$, δ) shows an N-methyl 3H singlet at 2.74, two methoxy 3H singlets at 3.92 and 3.95, and a methylenedioxy 2H singlet at 6.03. This functionalization has been expected by the results of Zeisel's methoxy and N-methyl determination and Gaebel's color test as shown in the previous paper[3)]. These evidences lead us to a conclusion that 1 must have an expanded formula, $C_{18}H_9(CH_2O_2)(OCH_3)_2(NCH_3)(OH)$.

The UV spectrum of 1 is rigidly superimposable on that of dihydrochelerythrine (2) but slightly different from that of dihydrosanguinarine (3) as shown in Fig. 1. This fact strongly indicates that 1 and 2 have not only a common conjugated system but also a methylenedioxy and



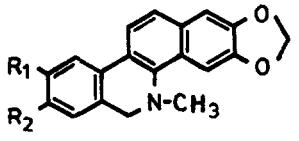
(1) R = H

(8) R = Ac



(2) $R_1 = R_2 = OCH_3$

(3) $R_1 + R_2 = OCH_2O$



(4) $R_1 = R_2 = OCH_3$
dihydronitidine

(5) $R_1 + R_2 = OCH_2O$
dihydroavicine

Fig. 1 Ultraviolet Absorption Spectra (EtOH)

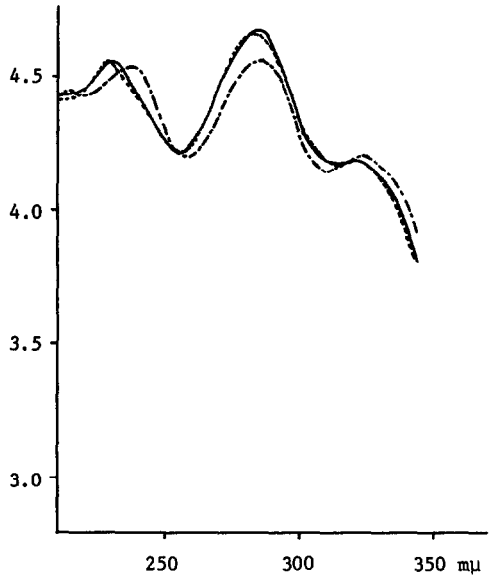
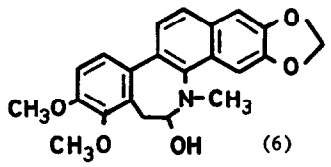
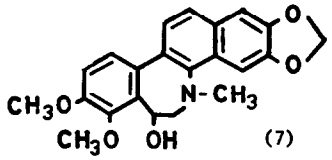
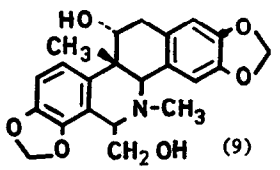


Table 1 NMR Signals of Aromatic Protons ($CDCl_3$, δ)

	(1)	(2)	(3)	(4)	(5)	(8)
C_1-H	7.11(s)	7.10(s)	7.06(s)	7.11(s)	7.09(s)	7.15(s)
C_4-H	7.65(s)	7.68(s)	7.65(s)	7.67(s)	7.64(s)	7.72(s)
C_7-H	***	***	***	6.80(s)	6.75(s)	***
C_9-H	6.96(d,J=8.8)	6.94(d,J=8.4)	6.80(d,J=8.6)	***	***	7.02(d,J=8.8)
C_{10}-H	7.54(d,J=8.8)	7.50(d,J=8.4)	7.26(d,J=8.6)	7.31(s)	7.27(s)	7.61(d,J=8.8)
C_{11}-H	7.70(d,J=8.6)	7.70(d,J=8.6)	7.65(d,J=8.6)	7.71(d,J=8.4)	7.62(d,J=8.8)	7.76(d,J=8.6)
C_{12}-H	7.49(d,J=8.6)	7.46(d,J=8.6)	7.43(d,J=8.6)	7.49(d,J=8.4)	7.46(d,J=8.8)	7.51(d,J=8.6)


(6)


(7)


(9)

two methoxy groups at the exactly same positions of the skeleton. This consideration is supported by a survey of signals due to aromatic protons of some dihydrobenzo[c]phenanthridine alkaloids. Recently, MacLean *et al*[4] and Onda *et al*[5] independently reported the assignment of these signals to each aromatic proton and we recognize the propriety of their assignments by comparison of the signals of dihydrochelerythrine type alkaloids with those of dihydroavicine type alkaloids having the oxygen functions at different positions of the ring A [dihydronitidine[6] (4) and dihydroavicine[7] (5)]. We can safely assign all signals of 1 in the aromatic proton region to each aromatic proton as dihydrochelerythrine type alkaloid (Table 1). Moreover, the NMR spectrum ($CDCl_3$ + D_2O, δ) of 1 shows the ABX type signals at 3.09 (1H, triplet, J=10.5 Hz), 3.47 (1H, quartet, J_1=10.5 Hz and J_2=5.0 Hz) and 4.65 (1H, quartet, J_1=10.5 Hz and J_2=5.0 Hz), which were confirmed by spin decoupling experiments. Consideration of all observation mentioned so far leaves only three possible formulae, (1), (6) and (7) for bocconoline.

Treatment of 1 with acetic anhydride in pyridine at room temperature gave acetyl bocconoline (8), mp 188.5-189.5°, $C_{24}H_{23}O_6N$, mass spectrum [M^+: m/e 421; M^+-73: m/e 348 (base peak)], whose IR spectrum shows acetoxy bands at 1739 cm^{-1} and 1249 cm^{-1} but no hydroxy absorption. In the NMR spectrum ($CDCl_3$, δ), it shows four 3H singlets [1.98 (OAc); 2.67 (NCH_3); 3.93 and 3.97 (OCH_3)], a 2H singlet [6.07 (CH_2O_2)] and the aromatic proton signals (see Table 1). Furthermore, it shows a 1H quartet at 4.83 (J_1=8.0 Hz and J_2=6.4 Hz) and 2H signals between 3.88-4.01. Unfortunately, due to overlap with two methoxy signals, these 2H signals are observed as shoulders at 4.01 and 3.88, but the double resonance technique provided the enough supports for the presence of an XX' portion of the AXX' system in this region. That is, irradiation at 4.83 results in disappearence of two shoulders into two methoxy signals. On the other hand, irradiation at 3.97 results in the change of the quartet into a 1H sharp singlet. These experiments show that 1 should have a primary hydroxy group in its molecule, because acetylation of a hydroxy group of 1 causes the signals of two protons to shift to downfield. This partial structure requirement can only be fulfilled up by supposing the structure (1), not others for bocconoline. In addition, MacLean *et al*[4] confirmed the loss of a substituent at C_6 is a characteristic initial step of 6-substituted dihydrobenzo[c]phenanthridine alkaloids in the

mass spectrum as reported by Slavík *et al*[8]. And, those authors also proposed a fragmentation pathway of dihydrochelerythrine derivatives from the base peak at m/e 348 which gave ions at m/e 333, 318, 304, 303, 290, 275, 260, 247 and 232. Mass spectra of 1 and 8 show all of these characteristic features. Consequently, the structure of bocconoline can be depicted by the formula (1).

Independently, Takao *et al*[1] established the structure of corynolamine (9) which was isolated from *Corydalis incisa* (Thunb.) Per., Papaveraceae. This alkaloid also has a hydroxymethyl group at C_6 of a hexahydrobenzo[c]phenanthridine nucleus. Several 6-acetonyl dihydrobenzo[c]phenanthridine alkaloids were reported, but the natural occurrences of them were seriously discussed in many papers[4]. Now, it is very important that the isolation of 1 and 9 from plants demonstrates the possibility of the biogenetical introduction of the carbon unit at C_6, because a hydroxymethyl group could not be insserted into a nucleus during isolation works.

The chemical interconversion of chelerythrine into bocconoline is undertaken.

Reference

1) This communication forms part XVIII of the series "Takao, Studies on the Alkaloids of Papaveraceous Plants". The preceding report, Part XVII, N. Takao and K. Iwasa, Abstracts of Papers, the 20th Annual Meeting of Kinki Branch, Pharmaceutical Society of Japan, Kobe, Nov., 1970, p. 23.

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