CHEMISTRY LETTERS, pp. 1081-1084, 1975. Published by the Chemical Society of Japan

STRUCTURES OF CORYNOXIDINE AND EPICORYNOXIDINE, NEW ALKALOIDS FROM CORYDALIS KOIDZUMIANA

Chiaki TANI, Naotaka NAGAKURA, and Shin HATTORI

Kobe Women's College of Pharmacy

Higashinada-ku, Kobe 658

Norio MASAKI

Faculty of Pharmaceutical Sciences, Kyoto University,

Sakyo-ku, Kyoto 606

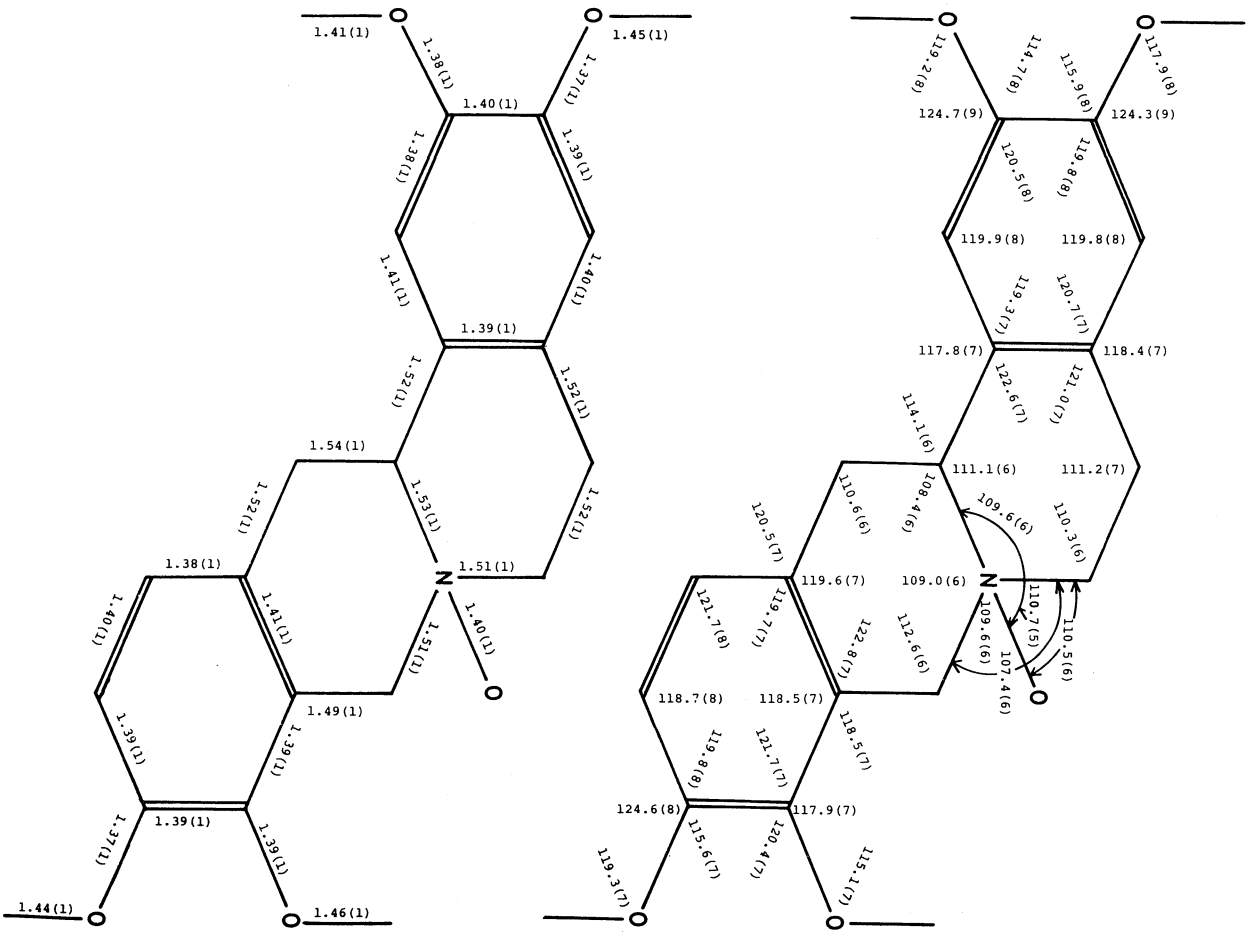
The structures of corynoxidine(I) and epicorynoxidine(II) were determined by X-ray and chemical studies. Both alkaloids are N-oxides of l-tetrahydropalmatine and different only in the B/C ring juncture.

Previously, many alkaloids have been isolated by the usual procedure including alumina column chromatography from Corydalis koidzumiana Ohwi collected in Taiwan at the flowering stage.[1-3]

From the same species before the flowering stage have been obtained through a similar extraction method two new alkaloids, corynoxidine(I), mp 183.5-184° (decomp., acetone); $[\alpha]_D$ -57°; UV λ_{max}^{EtOH} nm(log ε): 208.5(4.56), 229(4.16), 281.5(3.67); NMR[4] δ: 3.83(3H, s, OMe), 3.85(6H, s, 2xOMe), 3.86 (3H, s, OMe), 4.51 and 4.66(2H, ABq, J_{AB}=16 Hz), 6.67(2H, s), 6.85 and 6.97(2H, ABq, J_{AB}=8.5 Hz); mass m/e: 371(M^+), 353, 338,294, 164, 149 and epicorynoxidine(II), mp 193-195° (decomp., acetone); $[\alpha]_D$ -2°; UV λ_{max}^{EtOH} nm(log ε): 208(4.71), 230(4.16), 282(3.70); NMR δ: 3.82(3H, s,OMe), 3.83(9H, s, 3xOMe), 4.68 and 4.84(2H, ABq, J_{AB}=16.5 Hz), 6.63(1H, s), 6.69(1H, s), 6.85(2H, s); mass m/e: 371 (M^+), 353, 338, 294, 190, 164, 149, which were assumed to be tetrahydroprotoberberine alkaloids from their spectral data.[5]

As tetrahydropalmatine was obtained upon catalytic reduction of corynoxidine(I), this base must be of the tetrahydropalmatine structure containing an extra "oxygen function".

In order to elucidate the configuration and conformation of those molecules the crystal structure determination of corynoxidine(I) was undertaken. Crystal data are : formula unit $C_{21}H_{25}O_5N\cdot H_2O$; space group $P2_12_12_1$; four formula units per cell with dimensions a=24.961(4), b=12.828(3), c=6.042(2) Å; D_x=1.35 g/cm^3. A total of 1974 independent reflections(h0l-h9l, hk0-hk4) were


1.41(1)
1.38(1)
1.45(1)
1.37(1)
1.40(1)
1.38(1)
1.39(1)
1.41(1)
1.40(1)
1.39(1)
1.53(1)
1.52(1)
1.54(1)
1.53(1)
1.52(1)
1.38(1)
1.51(1)
1.40(1)
1.41(1)
1.51(1)
1.40(1)
1.49(1)
1.39(1)
1.39(1)
1.37(1)
1.39(1)
1.44(1)
1.46(1)
124.7(9)
124.3(9)
119.9(8)
119.8(8)
117.8(7)
118.4(7)
114.1(6)
111.1(6)
111.2(7)
120.5(7)
119.6(7)
109.0(6)
118.7(8)
118.5(7)
124.6(8)
117.9(7)
109.6(6)
110.3(6)
107.4(6)

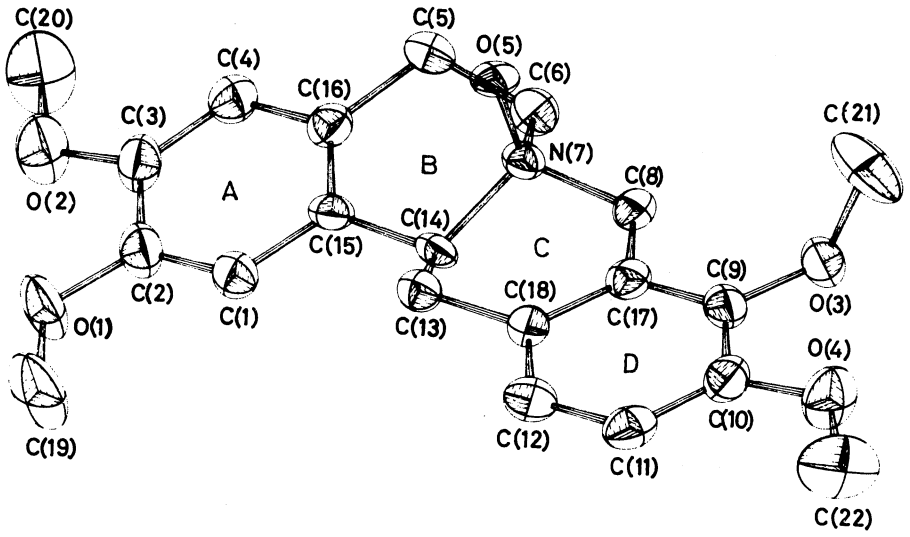

C(20)
C(5)
O(5)
C(4)
C(6)
C(16)
C(3)
C(21)
N(7)
B
C(8)
O(2)
A
C(14)
C(15)
C
C(9)
C(2)
C(18)
O(3)
O(1)
C(1)
C(13)
C(17)
O(4)
D
C(10)
C(12)
C(11)
C(19)
C(22)

Fig. 1

visually estimated from equi-inclination Weissenberg photographs by Ni-filtered Cu Kα radiation.

The structure was solved by the direct method with the program MULTAN[6] and refined by the block-diagonal least-squares method assuming anisotropic thermal factors for C, O and N atoms.

The thirteen hydrogen atoms attached to the four rings were located using a difference Fourier map and included in the final structure factor calculation, where the R-value was reduced to 0.093.

The bond lengths and angles and the perspective view of the molecule are shown in Fig.1.

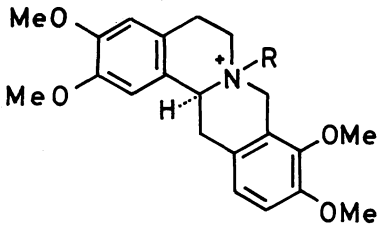
The result of this analysis showed that corynoxidine(I) is a N-oxide of l-tetrahydropalmatine with a trans B/C ring juncture.

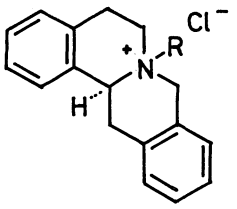
Table I Carbon-13 Chemical Shifts(δ_C)

		I	II	Δ_1^a	III[7]	IV[7]	Δ_2^a	
C	5	25.1	25.7	-0.6	24.7	24.4	0.3	t[b]
C	6	65.4	58.7	6.7	62.6	53.3	9.3	t
C	8	67.8	66.0	1.8	66.7	64.9	1.8	t
C	13	30.4	36.3	-5.9	30.3	35.4	-5.1	t
C	14	68.9	71.7	-2.8	67.7	67.3	0.4	d

a) Δ_1; $\delta_{C(I)} - \delta_{C(II)}$ Δ_2; $\delta_{C(III)} - \delta_{C(IV)}$

b) t(triplet) and d(doublet) indicate patterns of off-resonance decoupling.





I : R = → O⁻ III : R = — Me

II : R = ⇢ O⁻ IV : R = ···· Me

dl-Corynoxidine and dl-epicorynoxidine were obtained by perbenzoic acid oxidation of dl-tetrahydropalmatine. As shown in Table I, in the C-13 NMR spectra[4] the relationships between the chemical shifts of the B and C ring carbons in I and II are similar to those between the β form(III) and α form(IV) of N-methyltetrahydroprotoberberinium chloride.[7]

As the B/C ring juncture of the α and β forms have cis and trans conformations respectively, we conclude that epicorynoxidine(II) is a N-oxide of l-tetrahydropalmatine with a cis B/C ring juncture.

When a chloroform solution of tetrahydropalmatine was exposed to air, only palmatine chloride was obtained suggesting that both I and II are natural compounds and are not artifacts of the isolation procedure.

These are the first examples of naturally occurring tetrahydroprotoberberine N-oxides, which would provide a intriguing material for considering the biogenesis of tetrahydroprotoberberine alkaloids.

Acknowlegement We are grateful to Dr. Z. Taira, Faculty of Pharmaceutical Sciences, Kyoto University, for his helpful discussions.

REFERENCES

1) C. Tani, N. Nagakura, and S. Hattori, Tetrahedron Lett., 1973, 803.

2) C. Tani, N. Nagakura, S. Hattori, and M.T. Kao, Yakugaku Zasshi, 94, 844(1974).

3) C. Tani, N. Nagakura, and S. Hattori, Chem. Pharm. Bull.(Tokyo), 23, 313(1975).

4) Proton and C-13 NMR spectra were taken with TMS as an internal standard on a Varian HA-100 spectrometer(100 MHz) in $CDCl_3$ and a NEVA NV-21 spectrometer(22.6 MHz) in CD_3OD, respectively.

5) A.W. Sangster, and K.L. Stuart, Chem. Rev., 65, 69(1965).

6) G. Germain, P. Main, and M.M. Woolfson, Acta Crystallogr., A27, 368(1971).

7) N. Takao, K. Iwasa, M. Kamigauchi, and M. Sugiura, The Abstract Papers of the 95th Annual Meeting of Pharmaceutical Society of Japan, Nishinomiya, II, 219(1975).

(Received August 11, 1975)