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THE STRUCTURE OF CHELIRUBINE (BOCCONINE)

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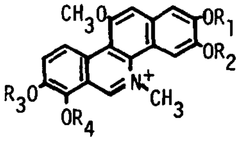
There are several reports[1-3] describing the occurrence of fully aromatized O_5-benzo[c]-phenanthridine alkaloids in the *Papaverous* plants. Among those alkaloids, chelirubine,[1] base B in *Bocconia cordata*,[2] and bocconine[3] were known to have one methoxy and two methylenedioxy groups in their structures. Although these three alkaloids were proved to be identical,[2-4] two different structures (1a[4,5] and 1b[6]) were independently proposed mainly on the basis of their spectral interpretations. In the course of study on bocconoline[7] (2), we (H. I.) established the assignments of NMR signals of various types of benzo[c]phenanthridine alkaloids. According to these assignments, we (H. I.) reinvestigated the reported NMR data of dihydrochelirubine (dihydrobocconine) and found that the structure of chelirubine should be revised to the new structure[8,9] as depicted by the formula (1c). In this communication, we would like to report total synthesis of oxychelirubine (5), therefore establishing the structure of chelirubine as the formula (1c).

We showed that photocyclization[10] of the enamide bearing an ortho-methoxy group takes place regiospecifically at the ortho position occupied by a methoxy group to give a dehydro derivative



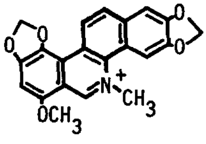
Slavík's formula

(1a): $R_1+R_2=R_3+R_4=CH_2$

(21): $R_1+R_2=CH_2$; $R_3=R_4=CH_3$

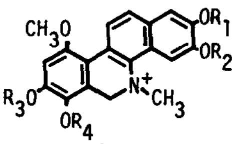
(22): $R_1=R_2=CH_3$; $R_3+R_4=CH_2$

(23): $R_1=R_2=R_3=R_4=CH_3$



Onda's formula

(1b)



Ishii's formula

(1c): $R_1+R_2=R_3+R_4=CH_2$

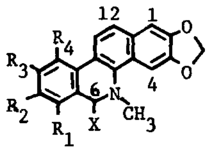
(24): $R_1+R_2=CH_2$; $R_3=R_4=CH_3$

(25): $R_1=R_2=CH_3$; $R_3+R_4=CH_2$

(26): $R_1=R_2=R_3=R_4=CH_3$

Assignments of the Published Data of NMR Signals[6)] due to the Aromatic Protons of Dihydrosanguinarine (3) and Dihydrochelirubine

	Dihydrosanguinarine (3)	Dihydrochelirubine		
		by Slavik's f. (4a)	by Onda's f. (4b)	by Ishii's f. (4c)
C_8 -H			6.59 (s)	
C_9 -H	6.83 (d, J=8 Hz)	7.47 (d, J=9 Hz)		6.59 (s)
C_{10}-H	7.30 (d, J=8 Hz)	8.35 (d, J=9 Hz)		
C_{11}-H	7.69 (d, J=9 Hz)		8.35 (d, J=9 Hz)	8.35 (d, J=9 Hz)
C_{12}-H	7.46 (d, J=9 Hz)	6.59 (s)	7.47 (d, J=9 Hz)	7.47 (d, J=9 Hz)
C_1 -H	7.10 (s)	7.11 (s)		
C_4 -H	7.72 (s)	7.72 (s)		



(6): $R_1=R_4=R_5=X=H$; $R_2=R_3=OCH_3$

(7): $R_1=R_4=R_5=X=H$; $R_2+R_3=OCH_2O$

(2) : $R_1=R_2=OCH_3$; $R_3=R_4=R_5=H$; $X=CH_2OH$

(3) : $R_1+R_2=OCH_2O$; $R_3=R_4=R_5=X=H$

(4a): $R_1+R_2=OCH_2O$; $R_3=R_4=X=H$; $R_5=OCH_3$

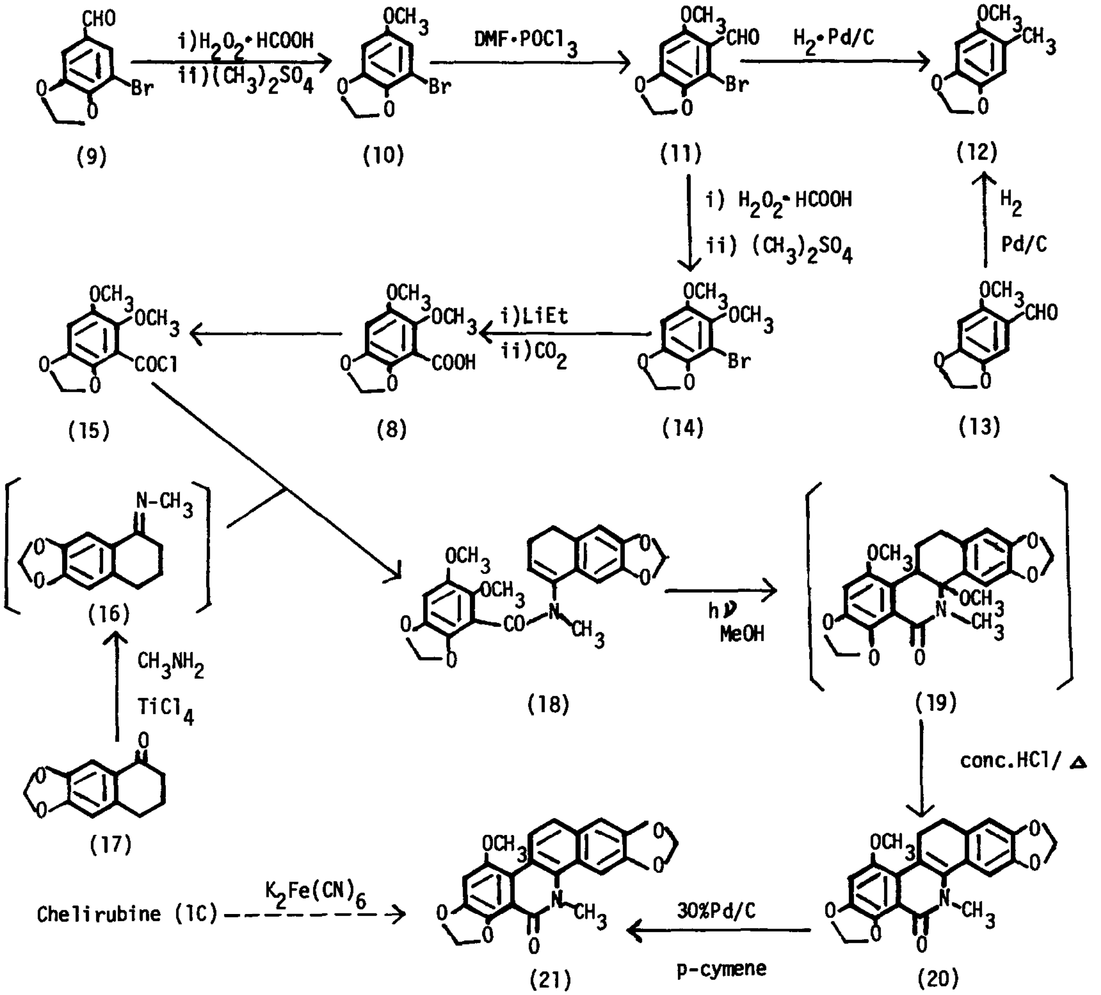
(4b): $R_1=OCH_3$; $R_2=R_5=X=H$; $R_3+R_4=OCH_2O$

(4c): $R_1+R_2=OCH_2O$; $R_3=R_5=X=H$; $R_4=OCH_3$

(I. N.) as exemplified by a convenient preparation[11)] of some benzo[c]phenanthridine alkaloids, dihydronitidine (6) and dihydroavicine (7). For the application of this method to the synthesis of oxychelirubine (5), 2,3-dimethoxy-5,6-methylenedioxybenzoic acid (8) was prepared.

Treatment of 5-bromopiperonal[12)] (9) with 35 % H_2O_2 and HCOOH followed by methylation gave 5-methoxy-2,3-methylenedioxybromobenzene (10), $C_8H_7O_3Br^{**}$; mp 49-51°, in 72.2 % yield. Vilsmeier reaction of (10) with DMF and $POCl_3$ afforded an aldehyde (11), $C_9H_7O_4Br$; mp 208-209°, in 91.5 % yield. The position of the aldehyde group of (11) was established by the fact that hydrogenation of (11) on Pd/C gave 2-methoxy-4,5-methylenedioxytoluene (12), $C_9H_{10}O_3$; mp 49-50°, which was also derived from 6-methoxypiperonal[13)] (13) by the same procedure. Baeyer-Villiger reaction of (11) with 35 % H_2O_2 and HCOOH followed by methylation furnished 2,3-dimethoxy-5,6-methylenedioxybromobenzene (14), $C_9H_9O_4Br$; mp 78-79°, in 71.4 % yield. Carboxylation of (14) with LiEt and dry ice gave 2,3-dimethoxy-5,6-methylenedioxybenzoic acid (8), $C_{10}H_{10}O_6$; mp 186-188°, in 93.2 % yield. Treatment of (8) with $SOCl_2$ gave the corresponding acid chloride (15), $C_{10}H_9O_5Cl$; mp 66-68°, quantitatively.

The imine (16) prepared from 6,7-methylenedioxy-1-tetralone[11)] (17) and CH_3NH_2 was acylated



with (15) to give the enamide (18), $C_{22}H_{21}O_7N$; mp 120-123°, in 76.3 % yield. Irradiation of a solution of (18) in MeOH with a low pressure mercury lamp for 5.5 hr afforded a labile photocyclized product[10)] (19), which was refluxed in the presence of a small amount of conc HCl to give the dehydrolactam (20), $C_{21}H_{17}O_6N$; mp 253-256°, [NMR ($CDCl_3$) δ: 2.60 (2H, t, J=8.0 Hz, C_{12}-H), 3.10 (2H, t, J=8.0 Hz, C_{11}-H), 3.61 (3H, s, NCH_3), 3.80 (3H, s, OCH_3), 5.92 and 6.12 (2H, s, OCH_2O x 2), 6.72 (1H, s, aromatic H), 6.78 (2H, s, aromatic Hs)], in 38.2 % yield. Dehydrogenation of (20) with 30 % Pd/C in p-cymene gave a fully aromatized lactam (21), mp 307-308°, in 70.4 % yield, which was identified with an authentic sample of oxychelirubine (oxybocconine), mp 307-309° (lit[6)] mp 295-296°), by direct comparison. This indicates that chelirubine (bocconine) should be depicted by Ishii's formula (1c).

Finally, in connection with our studies, we (H. I.) would like to make a proposal of the revised structures (24), (25), and (26) for chelirutine, sanguirubine, and sanguiltine, which were claimed to be shown by the formulae (21), (22), and (23) by Slavík in 1968, respectively. In order to establish the structures of these alkaloids, their total syntheses are now under progress.

References and Footnotes

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** The compound gave satisfactory elemental analysis for the formula given.

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