$$C_6H_5NHCOCCl_3 + OH^- \xrightarrow{\text{C-C bond fission}} C_6H_5NHCOO^- + CHCl_3 \quad (1)$$

$$C_6H_5NHCOCCl_3 + OH^- \xrightarrow{\text{C-N bond fission}} C_6H_5NH_2 + CCl_3COO^- \quad (2)$$

$$C_6H_5NHCOO^- + H^+ \longrightarrow C_6H_5NH_2 + CO_2 \quad (3)$$

$$C_6H_5NH_2 + CHCl_3 + 3OH^- \longrightarrow C_6H_5NC + 3Cl^- + 3H_2O \quad (4)$$

The amount of phenylcarbamate ion and of aniline formed were determined on separate aliquot of the reaction mixture by the method of Christenson.[3] The rate of the decomposition of the anilide (in 10% aqueous dioxane containing 0.01 to 1.0 M sodium hydroxide at 50°) followed by measuring the decrease in absorption at 248 mμ was faster than that of the formation of aniline. The concentration of phenylcarbamate ion attained a maximum during the reaction (Fig. 1). This may indicate the occurrence of reaction 1 and can explain reaction 3 and 4. Really the mixture of chloroform and phenylcarbamate ion produced from phenylisocyanate in aqueous solution gave phenylisocyanide.

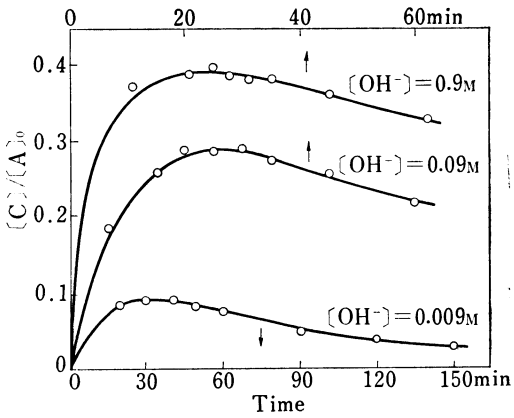

Fig. 1. Change in Concentration of Phenylcarbamate Ion during the Hydrolysis of Trichloroacetanilide

[C] represents the conentration of phenylcarbamate ion and $[A]_0$ represents the initial concentration of trichloroacetanilide used.

In order to obtain the ratio of C-C bond fission to C-N bond fission, which can be derived from the respective rate constant of reaction 1 and 2, and to confirm the reaction process more definitely, further kinetic study is in progress.

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3) I. Christenson, *Acta Chem. Scand.*, **18**, 904 (1964).

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Structure of Erybidine, a New Alkaloid from *Erythrina xbidwilli* LINDL.

In a previous communication,[1] we reported the structure determination of a new Erythrina alkaloid, erythrinine (I), which was isolated from the leaves of *Erythrina xbidwilli* LINDL.[2] (Leguminosae). Further, we explored the alkaloid constituents of the same plant material

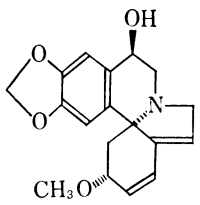
1) K. Ito, H. Furukawa, and H. Tanaka, *Chem. Commun.*, **1970**, 1076.
2) We revised the assignment of the plant material which we described as *Erythrina indica* LAM. in the previous paper.[1]

and isolated another new alkaloid to which we proposed the name "erybidine." Now, the structure elucidation of erybidine (II) is presented.

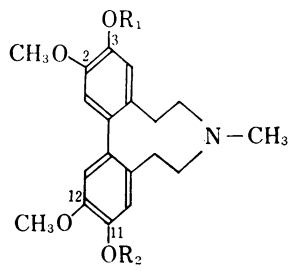
Erybidine (II) was obtained as colorless needles, mp 178—180°, $[\alpha]_D \pm 0°$ (EtOH); $C_{20}H_{25}O_4N$ (high mass spectrum: Calcd. 343.1783, *obs.* 343.1782). The ultraviolet (UV) spectrum of erybidine had two maximum absorptions at 216 nm (log ε 4.50) and 284 nm (log ε 3.92), supporting the presence of a biphenyl moiety. The nuclear magnetic resonance (NMR) spectrum[3] showed three methoxyl groups at 6.08 τ (3H) and 6.13 τ (6H), a N-methyl group at 7.68 τ (3H), and four aromatic protons at 3.22—3.33 τ. The infrared (IR) ($CHCl_3$) band at 3500 cm^{-1} indicated the presence of the hydroxyl group.

Methylation of erybidine with diazomethane afforded monomethyl ether (III), mp 139—140°, *m/e* 357 (M^+). In the NMR spectrum of O-methylerybidine (III), four methoxyls appeared at 6.08 τ (6H) and 6.14 τ (6H) as two singlets, and four aromatic protons were also observed as two singlets at 3.27 τ (2H) and 3.31 τ (2H). Treatment of O-methylerybidine (III) with methyl iodide, followed by the Hofmann degradation afforded a methine base (V). In the NMR spectrum of this methine (V), the typical ABX pattern newly appeared at 4.97 τ (1H, doublet-doublet, J=10.0, 1.5 Hz), 4.48 τ (1H, doublet-doublet, J=1.5, 17.5 Hz) and 3.57 τ (1H, doublet-doublet, J=10.0, 17.5 Hz), in addition to four methoxyls (6.16, 6.12, 6.06, 6.04 τ) and two N-methyl protons (7.91 τ (6H)), suggesting the intervention of two ethylene groups between the nitrogen atom and aromatic rings of O-methylerybidine (III).

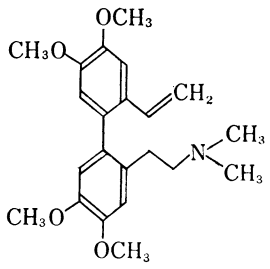
From these data mentioned above, we assumed the 2,3,11,12-tetra-substituted dibenz-(*d*,*f*)azonine structure for erybidine.



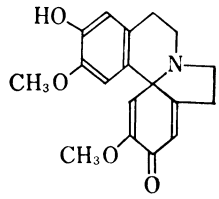
I



II : R_1 = H, R_2 = CH_3
III : R_1, R_2 = CH_3
IV : R_1, R_2 = H



V



VI

Chemical proof of the skeletal structure of erybidine was obtained by the synthesis of III from erysodienone (VI) according to the method previously reported by D.H.R. Barton, *et al.*[4] Treatment of erysodienone (VI)[5] with $CrCl_2$ in aquous HCl, followed by the N-methyl-

3) All NMR spectra were measured in $CDCl_3$ with tetramethylsilane (TMS) as internal standard.
4) D.H.R. Barton, R.B. Boar, and D.A. Widdowson, *J. Chem. Soc.* (*C*), **1970**, 1208.

ation with formalin and $NaBH_4$ gave a product (IV), mp 220—222° (decomp.). O-Methylation of IV with diazomethane resulted in the compound III, mp 139—141°, which was proved to be completely idenfical with O-methylerybidine by mixed mp and comparisons of IR ($CHCl_3$) and NMR spectra.

The position of a hydroxyl group in the molecule of erybidine was defined by the comparison of NMR spectra of compounds III, IV and erybidine.

The methoxyl signals of compound III showed at 6.08 τ and 6.14 τ as two six-proton singlets, and in the compound IV, lacking 3,11-methoxyls, only one six-proton singlet at 6.15 τ was observed. Then, it is deduced that the signal at 6.08 τ is attributable to 3- and/or 11-methoxyls and that at 6.14—6.15 τ to 2- and/or 12-methoxyls, respectively. We suggested, by comparison with these assignments, that in the NMR spectrum of erybidine, three-proton singlet at 6.08 τ would be due to 3- or 11-methoxyl, and six-proton singlet at 6.13 τ is to 2- and 12-methoxyl groups, and hence the hydroxyl group must be attached to 3-(or 11-)position of dibenz(*d,f*)azonine moiety.

On the basis of these evidences, the structure of erybidine should be assigned to the formula II.

From the view point of biosynthesis, it is interest that we isolated the dibenz(*d,f*)azonine type base which was postulated as one of the intermediates of Erythrina alkaloids biosynthesis,[6] in addition to some erythrinan type bases.

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5) This compound was supplied generously by Dr. D.A. Widdowson.
6) D.H.R. Barton, R. James, G.W. Kirby, D.W. Turner, and D.A. Widdowson, *J. Chem. Soc.* (*C*), **1968**, 1529.

[Chem. Pharm. Bull. 19(7)1511—1513(1971)]

UDC 547.779.09 : 615.276.076.9

Metabolism of Benzydamine Hydrochloride

Benzydamine hydrochloride (BZY) is a non-steroid anti-inflammatory agent. It has been reported that about 50% of the administered drug in men and about 30% in rats were excreted in the urines,[1] but the conclusive information concerning its metabolites are not available. We studied the metabolic pathway of BZY by means of its strong fluorescence and identified some metabolites.

BZY was administered orally at a dose of 200 mg/kg to rabbits and the 24 hr urine adjusted pH 5 was extracted with $CHCl_3$. About 20% of fluorescence excreted in the urine was extracted into this fraction. After concentrating and dissolving the residue into a small amount of $CHCl_3$, thin-layer chromatography (TLC) was carried out on Silica gel HF_{254} (0.25 mm) developing by a solvent system of benzene: $CHCl_3$: MeOH: EtOH: conc. NH_4OH (15: 15:10:5:0.5). At least four spots were visualized with Dragendorff reagent (*Rf*=0.13, 0.25, 0.40, 0.80). A spot of *Rf* 0.80 was indistinguishable with authentic BZY. The main spot,

1) B. Catanese, A. Grasso, and B. Silvestrini, *Arzneim.-Forsch.* (*Drug Res.*), **16**, 1354 (1966).