ALKALOIDS OF THE LEAVES OF COCCULUS LAURIFOLIUS

THE STRUCTURE OF COCLAFINE

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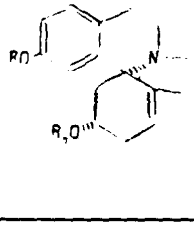
Cocculine, isoboldine, norisoboldine, and a new erythrinan alkaloid, coclafine, for which the structure and absolute configuration of 3S,5R-3,15-dihydroxyerythrin-Δ1(6)-ene have been established, have been isolated from the leaves of Cocculus laurifolius DC.

Cocculus laurifolius (one of the typical alkaloid-bearing plants) grows mainly in India, Japan, and Southern China. In the USSR it has been introduced in the Black Sea littoral, the Crimea, and the Caucasus. The alkaloids of plants of this genus have been fairly well studied, and erythrinan alkaloids are the main ones among them [1-4]. Cocculine (II) and cocculidine (III) have previously been isolated from the leaves of C. laurifolius introduced into Batumi Botanical Garden, and their structures and absolute configurations have been established on the basis of chemical transformations and spectral characteristics [5-8].

We have investigated the leaves of C. laurifolius collected in Kobuletti (Adzhar ASSR). Chloroform extraction yielded 0.72% of alkaloids, from which cocculine [5], isobolding [9], norisoboldine [9], and a new alkaloid with mp 264-266°C (acetone), which we have called coclafine, were isolated.

Coclafine (I) has the composition $C_{16}H_{19}NO_2$, $[\alpha]_D$ +255° (c 0.15; methanol), and is sparingly soluble in ether, benzene, and chloroform and readily soluble in alkalis. The UV spectra of (I) had absorption maxima at 208, 230, and 285 nm (log ε 4.30, 3.71, and 3.41), and the IR spectrum had absorption bands in the 3455 cm^{-1} (OH) and 1585 and 1510 cm^{-1} (aromatic ring) regions. In the mass spectrum of coclafine, together with the peak of the molecular ion (M^+ 257) peaks were observed of ions with m/z 240 $(M-17)^+$, 213 $(M-44)^+$, 212 $(M-45)^+$, 196, and 150, which are characteristic for erythrinan bases [6]. The PMR spectrum of (I) taken in CD_3OD (δ scale) contained the signals of an olefinic proton (5.58 ppm, 1 H, broadened singlet, $W_{1/2}$ = 7 Hz) and of three aromatic protons (6.54 ppm, 1 H, broadened singlet, 6.58 ppm, 1 H, quartet with J_1 = 8.0 Hz and J_2 = 3 Hz, and 6.92 ppm, 1 H, doublet with J = 8 Hz).

A comparison of the spectral characteristics of (I) and cocculine and also the difference in their molecular masses by 14 mass units permitted the assumption that coclafine was erythrin-1(6)-ene with two hydroxy groups [6, 7]. In actual fact, when coclafine was methylated with methyl iodide in the presence of NaH in dry dioxane, di-O-dimethylcoclafine methiodide, identical with cocculidine methiodide [5], (TLC, mixed melting point, IR spectrum), was obtained. Thus, on the basis of the facts given above, it is possible to conclude that coclafine has the structure and absolute configuration of 3S,5R-3,15-dihydroxyerythrin-1(6)-ene (I).



I. $R=R_1=H$
II. $R=H$; $R_1=CH_3$
III. $R=R_1=CH_3$

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EXPERIMENTAL

For thin-layer and column chromatographies we used alumina and KSK silica gel. The system for TLC was benzene—methanol (4:1). IR spectra were taken on a UR-20 spectrometer in KBr, PMR spectra on a JNM-4H-100/100 MHz instrument (δ scale, CD_3OD, HMDS), and mass spectra on a MKh 1310 instrument.

Isolation of the Alkaloids. By the usual chloroform extraction, 5.5 kg of *Cocculus laurifolius* leaves yielded 28.8 g of ether-soluble and 11.2 of chloroform-soluble alkaloids. The total amount of alkaloids was 40 g or 0.72% on the weight of the dry plant. The ether-soluble material was separated into phenolic (8.3 g) and nonphenolic (11.2 g) fractions.

When the phenolic fraction of the ether-soluble alkaloids was treated with acetone, 3.5 g of cocculine separated out. After recrystallization from acetone, mp 215-217°C. The mother liquor after the separation of the cocculine was chromatographed on a column of silica gel. The column was eluted with benzene—methanol (98:2 and 95:5). The benzene—methanol (98:2) eluate yielded isobolding (0.08 g) and norisoboldine (0.03 g). Elution by the same mixture in the ratio of 95:5 gave coclafine (0.05 g) and cocculine (0.5 g).

Coclafine. $C_{16}H_{19}NO_2$ (I), mp 264-266°C (acetone), $[\alpha]_D$ +255° (c 0.15; methanol), R_f 0.33.

Methylation of Coclafine. Sodium hydride (45 mg) was added in small portions to a solution of 26 mg of coclafine in 5 ml of dry dioxane, and the mixture was stirred at 60°C for 1 h. Then 1 ml of methyl iodide was added dropwise to the reaction mixture and it was heated for 3 h. The excess of sodium hydride was separated off, and the filtrate was evaporated. Treatment of the residue with acetone gave a crystalline product with mp 237-238°C, identical with cocculidine methiodide (mixed melting point, TLC, IR spectra).

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