ERYTHLAURINE AND ERYTHRAMIDE, TWO NEW ERYTHRINAN ALKALOIDS POSSESSING A DIRECTLY ATTACHED C_1-UNIT TO THE AROMATIC RING

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Abstract ——— Two new erythrinan alkaloids named erythlaurine and erythramide were isolated from the leaves of Cocculus laurifolius DC. (Menispermaceae) and their structures were elucidated by chemical and spectral studies as (1) and (2), respectively.

Many erythrinan alkaloids have been isolated from the leaves of Cocculus laurifolius DC. (Menispermaceae).[1,2] We have already reported the isolation and structure elucidation of erythroculine, having a directly attached C_1-unit to the aromatic ring at C_{15} position, from the same plant.[2] In continuation of our investigation of the alkaloid constituents of this plant, we isolated two new erythrinan alkaloids named erythlaurine (1) and erythramide (2).

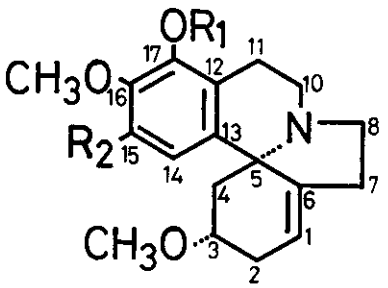
In this communication, we wish to report the structure elucidation of these alkaloids.

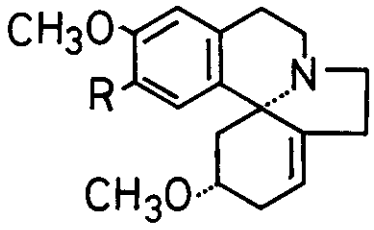
Erythlaurine (1), oil, $C_{20}H_{25}NO_5$, $[\alpha]_D$+232° (EtOH); IR ($CHCl_3$, cm^{-1}): 3500, 1710; NMR ($CDCl_3$, δ): 3.30 (3H, s., OCH_3), 3.91, 3.93 (each 3H, s., OCH_3, $COOCH_3$), 5.63 (1H, m., olefinic-H), 7.18 (1H, s., aromatic-H). These data suggested the presence of two methoxy groups, one methoxycarbonyl group, one phenolic hydroxy group, one trisubstituted double bond, and one pentasubstituted aromatic ring in

(1). Treatment of (1) with diazomethane afforded O-methylerythlaurine (3) as a colorless oil; IR ($CHCl_3$, cm^{-1}): 1710; NMR ($CDCl_3$, δ): 3.29, 3.88 (each 3H, s., OCH_3), 3.90 (6H, s., OCH_3, $COOCH_3$), 5.63 (1H, m., olefinic-H), 7.28 (1H, s., aromatic-H).

Lack of any signal due to NH or an N-methyl group in the IR and NMR spectra of (1) and (3) led us to conclude that (1) must be a tetracyclic alkaloid. The skeletal structure of (1) was presumed from its mass spectrum. The base peak at m/e 273 (M-58) arises from a retro Diels-Alder type fragmentation of the cyclohexene ring with an aliphatic methoxy group and this peak is a characteristic one for aromatic erythrinan alkaloids of alkenoid-type.[3] On the basis of these data, the structure of erythlaurine was assigned to (1) except for the relative position of hydroxyl, methoxycarbonyl and methoxyl groups on the aromatic ring. The relative positions of these functional groups were defined by the INDOR experiments. Thus, the signal due to nuclear Overhauser effect (ca. 15%) was observed between C_3-proton (δ 3.90) and the aromatic proton (δ 7.56).[4] This result indicates that these two protons exist spacially close enough to permit observation of NOE and examination of the Dreiding model led us to conclude that the aromatic proton is located at C_{14} and C_3-proton is β, respectively. Reduction of (1) with $LiAlH_4$ gave the alcohol (4). In the NMR spectrum of (4), the aromatic proton signal resonates at δ 6.65 which is 0.53 ppm upfield compared with that of (1). This result shows that a methoxycarbonyl group is located at C_{15} vicinal to the C_{14} aromatic proton. Furthermore, the absence of hydrogen bond in IR and NMR spectra of (1) suggests that the hydroxy and the methoxycarbonyl groups are not located ortho to each other. Consequently, erythlaurine can be represented by the relative stereostructure of (1).

Erythramide (2), colorless cubes, $C_{19}H_{24}N_2O_3$, mp 87-89°, $[\alpha]_D$+262° (EtOH); IR ($CHCl_3$, cm^{-1}): 3500, 3350, 1660; NMR (acetone-d_6, δ): 4.87, 3.99 (each 3H, s., OCH_3), 5.58 (1H, m., olefinic-H), 6.93, 7.91 (each 1H, s., aromatic-H); MS m/e: 328 (M^+), 270 (base peak, M-58). These data suggest that erythramide has the erythrinan skeleton, possessing two methoxy groups, one trisubstituted double bond and a carbamoyl group. Reduction of (2) with $LiAlH_4$, followed by treatment with Ac_2O-pyridine gave the acetate (5). The NMR spectrum of (5) shows the signals at δ 1.97 (3H, s., $COCH_3$), 4.37 (2H, d., J=6.0 Hz, -CO-NH-CH_2-) and 5.93 (1H, m., -CO-NH-CH_2-). From the above results, the presence of carbamoyl group on the aromatic ring was concluded.





(1) R_1=H, R_2=$COOCH_3$

(2) R=$CONH_2$

(3) R_1=CH_3, R_2=$COOCH_3$

(5) R=$CH_2NHCOCH_3$

(4) R_1=H, R_2=CH_2OH

(6) R=$COOCH_3$

Hydrolysis of (2) with dil. HCl followed by treatment with diazomethane gave erythroculine (6), which was proved to be identical with an authentic specimen by IR, NMR and mass spectra and TLC comparisons. On the basis of these results, the absolute stereostructure of erythramide was assigned unequivocally to (2). Erythramide (2) is the first example of the erythrinan alkaloids having a carbamoyl group on the aromatic ring.[5,6] Among many erythrinan alkaloids isolated from Cocculus species,[1,2,7] the presence of a directly attached C_1-unit to the aromatic ring was found only in erythroculine (6)[2] so far, and erythlaurine and erythramide are the second and the third examples of this type of alkaloids.

References and Footnotes

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4) INDOR experiments were performed on a Hitachi R 22 spectrometer (90 MHz) in C_6D_6: M. Ju-ichi, Y. Ando, A. Satoh, J. Kunitomo, T. Shingu, and H. Furukawa, Chem. Pharm. Bull., 1978, 26, 563.

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6) It is possible, though improbable, that the carbamoyl group in erythramide (2) was derived from the methoxycarbonyl group in erythroculine (6) as an artifact in extraction process. Although erythramide (2) was detected on treatment of erythroculine (6) with NH_4OH for 2 days, it was verified that erythramide was not obtained on treatment of erythroculine with the extraction condition from the plant source.

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