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SYNTHESES OF AN ALKALOID, (±)-3-DEMETHOXYERYTHRATIDINONE

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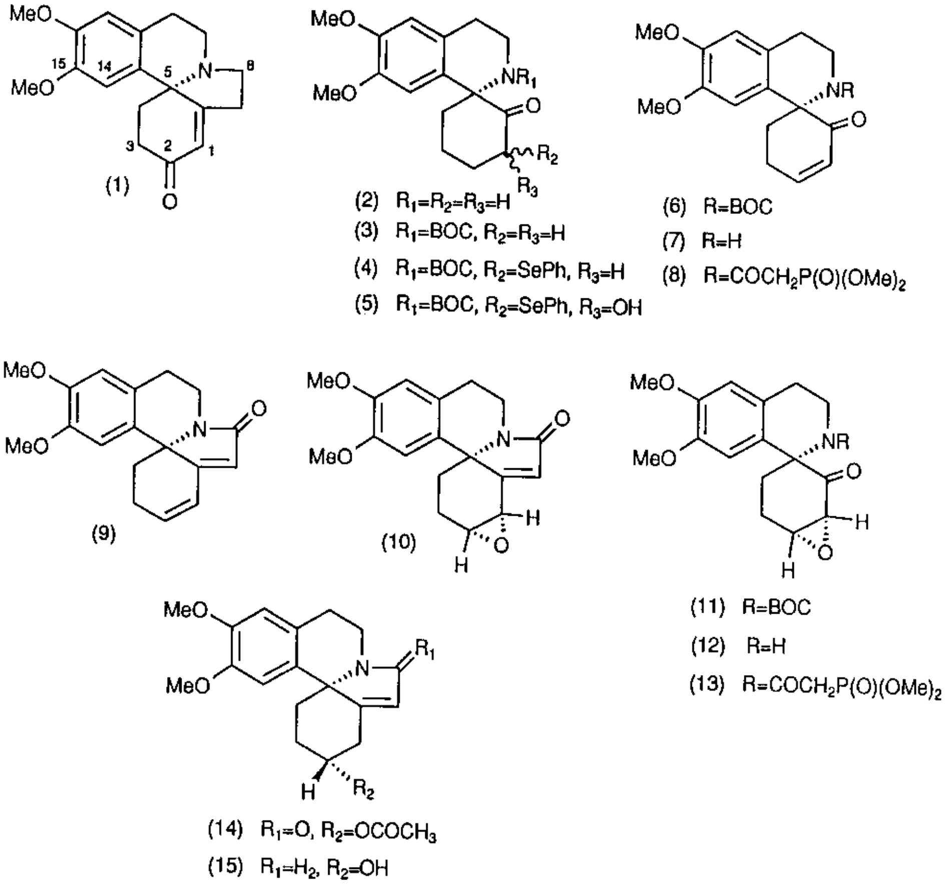
Abstract —— Synthesis of (±)-3-demethoxyerythratidinone, one of the simple erythrina-alkaloids, was accomplished by application of an intramolecular Wittig reaction for constructing α,β-unsaturated five membered lactam as a key step.

Recently, Ikeda and his co-workers$^{1)}$ reported a synthesis of an alkaloid, 3-demethoxyerythratidinone (1)$^{2)}$ by constructing the five membered lactam using trapping reaction of an intermediate of Pummerer's rearrangement. This report prompted us to report our recent work on the synthesis of the alkaloid as a continuing our synthetic work of natural products using the intramolecular Wittig reaction.$^{3)}$

Treatment of the spiro-amine (2)$^{3b)}$ with di-t-butyldicarbonate in chloroform under reflux for two days gave the BOC compound (3)$^{\#}$ in 75% yield, which was subjected to the dehydrogenation reaction. Thus, treatment of (3) with LDA followed by phenylselenenyl chloride in THF under argon atmosphere gave the seleno-compound (4) in 83% yield, while insufficient replacement of air by argon resulted in a mixture of (4) and the hydroxyl compound (5) in low yield. Oxidation of (4) with sodium periodate in ethanol furnished the conjugated ketone (6) in good yield. Removal of BOC-group with TFA in methylene chloride gave the amine (7) which was acylated with dimethyl phosphonoacetyl chloride in methylene chloride in the presence of pyridine to afford the phosphonate (8) in 77% yield. Intramolecular Wittig reaction of (8) with aqueous potassium hydroxide and benzene (two layers) under efficient stirring at room temperature gave smoothly the erythrinan (9) in 75% yield. Confirmation of the structure of (9) was provided from its ^{1}H-nmr spectrum exhibiting the signals at δ 6.83 (1H, d, J=10Hz), 6.32 (1H, m), and 5.89 (1H, s).

Oxidation of (9) with mCPBA in methylene chloride gave an epoxide (10) in low yield. On the other hand, oxidation of the ketone (6) with hydrogen peroxide and aqueous sodium hydroxide in methanol gave the epoxide (11) in good yield. After deprotection of BOC group, the amine (12) was acylated with the phosphonoacetyl chloride to give the the phosphonate (13) which was submitted to the intramolecular Wittig reaction under the same conditions mentioned above, affording the lactam (10) in 75% yield. Confirmation of the configuration of the oxide ring to have cis relationship with C-N bond was provided at this stage from an NOE experiment between C_1-H and C_{14}-H (erythrinan numbering). Reduction of (10) with zinc in acetic acid and acetic anhydride gave the acetate (14) and the erythrinan (9) in 67% and 26% yield, respectively. Alkaline hydrolysis of the former with lithium carbonate in methanol gave (9) in good yield as a result of dehydration of a vinylogous aldol system in (14). Eventually, we found that treatment of (14) with aluminium hydride (prepared from lithium aluminum hydride

Chart



(1)

(2) $R_1=R_2=R_3=H$

(3) $R_1=BOC, R_2=R_3=H$

(4) $R_1=BOC, R_2=SePh, R_3=H$

(5) $R_1=BOC, R_2=SePh, R_3=OH$

(6) R=BOC

(7) R=H

(8) $R=COCH_2P(O)(OMe)_2$

(9)

(10)

(11) R=BOC

(12) R=H

(13) $R=COCH_2P(O)(OMe)_2$

(14) $R_1=O, R_2=OCOCH_3$

(15) $R_1=H_2, R_2=OH$

and aluminium chloride in THF and ether) furnished the hydroxy amine (15) in 60% yield. Swern oxidation[5] of (15) gave (±)-3-demethoxyerythratidinone (1) in 45% yield. Accomplishment of the synthesis of the alkaloid (though a racemic modification) was confirmed by comparison of the ^{1}H-nmr. spectrum of the synthetic product with that of the authentic sample[4] kindly supplied by Professor Y. Tsuda (Kanazawa University).

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REFERENCES AND NOTE

1. H. Ishibashi, T. Sato, M. Takahashi, M. Hayashi, and M. Ikeda, Heterocycles, 1988, 27, 2787.
2. D.H.R. Barton, A.A.L. Gunatilaka, R.M. Letcher, A.M.F.T. Lodo, and D.A. Widdowson, J. Chem. Soc.,Perkin Trans. 1, 1973, 874.
3. a) H. Irie, S. Takeda, A. Yamamura, Y. Mizuno, H. Tomimasu, K. Ashizawa, and T. Taga, Chem. Pharm. Bull., 1984, 32, 2886, b) Y. Zhang, S. Takeda, T. Kitagawa, and H. Irie, Heterocycles, 1986, 24, 2151.
4. Y. Tsuda, A. Nakai, K. Ito, F. Suzuki, and M. Haruna, Heterocycles, 1984, 22, 1817.
5. A.J. Mancuso, D.S. Brownfain, and D. Swern, J. Org. Chem., 1979, 23, 4148.

\# All the compounds cited in this report showed satisfactory elemental analysis and spectroscopic properties.

This paper is dedicated to Professor Haruaki Yajima on this occasion of his retirement from Kyoto University in March 1989.

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