

A SYNTHESIS OF 15,16-DIMETHOXYERYTHRIN-6-EN-8-ONE

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Abstract — A synthesis of 15,16-dimethoxyerythrin-6-en-8-one was accomplished using an intramolecular Wadsworth-Emmons reaction for constructing five-membered lactam, indicating a convenient method to the synthesis of the erythrinan skeleton.

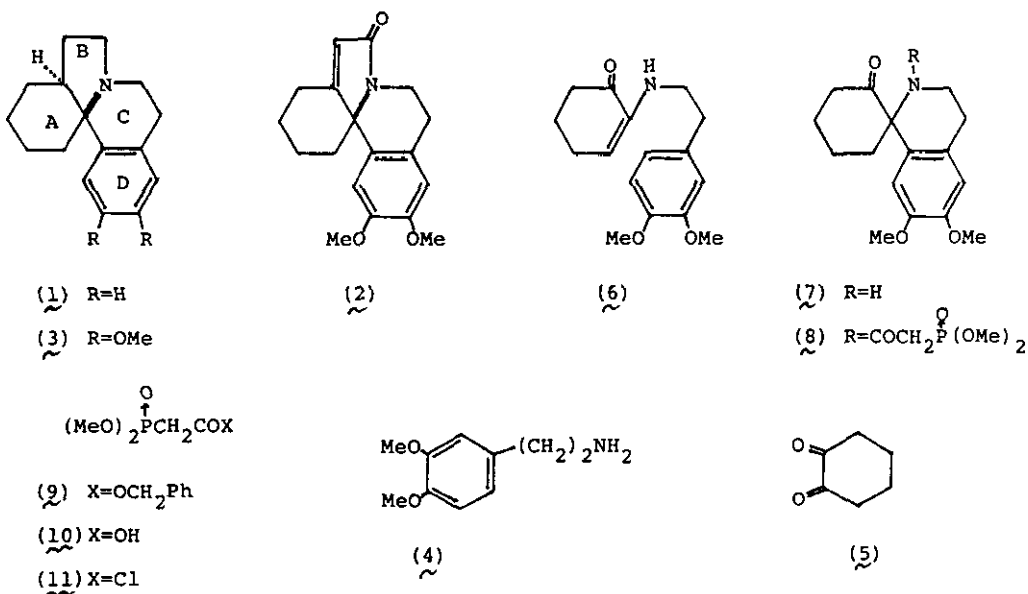
There have been several reports indicating the synthesis of the erythrinan skeleton (1) and erythrina-alkaloids.¹ The most of the syntheses consist of construction reaction of C-ring using a Pictet-Spengler type cyclization reaction as the final bond formation to accomplish the synthesis. On the other hand, Sugasawa and Yoshikawa² synthesized the skeleton by constructing B-ring in direction from nitrogen to A-ring as the final bond formation reaction. Tamura and his co-workers³ also synthesized the skeleton by constructing B-ring in the same direction followed by C-ring formation in one pot. We here describe a synthesis of the erythrinan compound (2) as a continuation of synthetic work of five-membered ring by the intramolecular Wadsworth-Emmons reaction.⁴

Condensation of homoveratrylamine (4) and 1,2-cyclohexanedione (5) in ethanol at room temperature for 3 days gave the enamino-ketone (6) in 80% yield.[†] Treatment of 6 with trifluoroacetic acid (TFA) at 70°C overnight gave the spiro-amine (7) in 85% yield, the latter of which was directly obtained from the condensation reaction of 4 and 5 in TFA, though the yield was decreased (40%). The spiro-amine (7) has been synthesized by Sugasawa and Yoshikawa² by a condensation reaction of the same starting material in the presence of phosphoric acid in less than 10% yield. Treatment of 7 with 1-(dimethylphosphono)acetyl chloride (11) in methylene chloride in the presence of equimolar amount of pyridine at room temperature for 1 h gave the phosphonate (8), mp 152-153°C, in 95% yield. The acetyl chloride (11) was prepared as follows. Thus hydrogenation of benzyl 1-(dimethylphosphono)acetate (9) with palladium-carbon as a catalyst in

ethanol gave 1-(dimethylphosphono)acetic acid (10) in 90% yield. Treatment of 10 with oxalyl chloride in benzene at 25°C overnight followed by removal of the excess reagent and solvent in a similar manner to the preparation of 1-(diethylphosphono)acetyl chloride⁵ gave the acid chloride (11).

The intramolecular Wadsworth-Emmons reaction of the phosphonate (8) was carried out in two phases with benzene and aqueous 10% potassium hydroxide at room temperature for 1 h to furnish the erythrinan (2) in 95% yield. The erythrinan (2) was also obtained in one pot operation in 93% yield: the acylation of the spiro-amine (7) with the chloride (11) in the same manner as above and treatment of the whole with aqueous 10% potassium hydroxide with efficient stirring successively. The ¹H-N.M.R. spectrum of the erythrinan (2) obtained was identical with that supplied by Professor Tamura (Osaka University).¹¹ Since the erythrinan (2) has been converted to the dimethoxyerythrinan (3), the synthesis provided a short-step method for synthesis of erythrinan compound and showed an example of usefulness of the intramolecular Wadsworth-Emmons reaction for construction of five membered lactam.

Chart



¹¹ All the new compounds had IR and ¹H-N.M.R. spectra consistent with the proposed structures.

¹¹¹ We thank Professor Y. Tamura for his generous supply of ¹H-N.M.R. spectrum of the compound (2).

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