STRATEGIC REACTIONS IN THE SYNTHESIS OF ERGOLINE GROUP OF ALKALOIDS USING ENAMIDE PHOTOCYCLIZATION.

Toshiko Kiguchi, Chiyomi Hashimoto, Takeaki Naito, and Ichiya Ninomiya*
Kobe Women's College of Pharmacy, 4-19-1, Motoyamakita-machi, Higashi-nada-ku, Kobe 658, Japan

According to the strategy of synthesizing all members of one group of alkaloids by one methodology, we have applied reductive photocyclization of N-furoylenamines to the synthesis of ergoline group of alkaloids. Here we discuss the synthetic methodology that we have tackled, thus paved a way to total synthesis of alkaloids.

(I) Stereoselective Synthesis of C/D-trans-Lactam (2) as the Starting Compound.

Reductive photocyclization of the enamide, N-furoylenamine (1), in C_6H_6-MeOH (1:1) afforded the desired C/D-trans-lactam (2) in 76 % yield stereoselectively.

(II) Stereoselective Synthesis of the Key Intermediates (3,4,5)

By establishing the effective ring opening of a dihydrofuran ring of the photocyclized lactam (2), three useful compounds, cis- and trans-1,3-diols (3 and 5), and trans-hydroxyaldehyde (4), which have high potentiality as the synthetic precursors, were prepared in good yields respectively.

(III) Regioselective Introduction of a Double Bond into the Ergoline Skeleton.

(Regioselective Synthesis of 8- and 9-Ergolenes)

Dehydration of a 9α-hydroxy group in the synthetic intermediates, cis- and trans-1,3-diols (3 and 5), under various conditions, was investigated and as a result the regioselective introduction of a double bond into either 8- or 9-position was established.

(IV) Dehydrogenation of Indolines into Indoles.

By using the tricyclic ketone (6) as a model, a synthetic method of preparing indole nucleus from indolines by dehydrogenation with various reagents, such as MnO_2, t-BuOCl-Me_2S-Et_3N, and $(PhSeO)_2O$, was investigated for its application to total synthesis of ergot alkaloids.