[S1-1] [4/18/2002(Thur) 14:00-14:30/Hall A]

Novel Synthetic Approaches to the Biologically Active Natural Products via Functionalized Oxazoline Compounds

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Sphingosine, compounds consisting of polar polyhydroxy amino head groups and long lipid chains, are membrane constituents involved in a number of cellular events including protein binding (GPI anchor) and transmembrane signaling. A related series of compounds where in the primary alcohol is oxidized to a carboxylic acid such as sphingofungin B or possesses a quaternary center such as sphingosine F (1) were found to inhibit the biosynthesis of sphingolipids due to their activity as serine palmitoyl transferase inhibitors. These compounds are also strikingly similar to myriocin (2), a compound shown to be 10-100 times more potent than cyclosporin A.

Preussin (3), a potent antifungal agent, is a naturally occurring pyrrolidine alkaloid.

Functionalized piperidines (Spectalin, 4) are very important heterocycles because of their presence in numerous alkaloids, pharmaceuticals, and synthetic intermediates.

Azasugars (5,6), which have been called the "sugar-shaped" alkaloids from plants, are reversible, competitive inhibitors of glycosidases. The purpose of these natural products is possibly to inhibit the carbohydrate metabolism and consequently the growth of plant consuming pests. Since selective glycosidase inhibitors have a large number of interesting potential applications including treatment of AIDS, diabetes, and tumor metastasis they have received a considerable attentions.

Pancratistatin (7) exhibits a range of antineoplastic properties, including activity against murine P-5076 ovarian sarcoma and P-388 lymphocytic leukemia. No detailed examination of the molecular basis of this activity has been conducted, but work on structurally related narciclasine has suggested that these compounds could act by distrupting protein biosynthesis in eukaryotic organism.

The difficulties of creating stereochemistries and the noted biological activity of these products led us to develop a general strategy to these series.

In a previous paper, we described a new Pd(0)-catalyzed procedure for the stereoselective formation of a oxazoline ring from an acyclic allylic and homoallylic amide having a benzoyl substituent as an *N*-protecting group. The most significant point of the method is that it is based on the *trans*-oxazoline ring formation in palladium(0)-catalyzed condition.

In this seminar, we will present the total synthesis of sphingofungin F (1), myriocin (2), preussin(3), spectaline (4), and azasugars (deoxy-galacto nojirimycin (5), deoxy-gluonojirimycin (6)) via functionalized oxazoline compounds. Also, we will discuss our synthetic efforts toward *pancratistatin* (7).