Cisplatin is important antineoplastic agent, but dose-limiting nephrotoxicity prevents potential efficacy. There is interest in developing new platinum agents that have less toxicity. We have synthesizes a nove platinum (II) coordination complex containing cis-1,2-diaminocyclohexane as a carrier ligand, and glycolic acid as a leaving group. In this study, new platinum (II) complex compound [Pt(II)(cis-DACH)(GA)] was evaluated for cytotoxicity on cancer cell-lines and normal kidney cells. The new platinum complex has demonstrated high efficacy in the cytotoxicity against human ovarian adenocarcinoma cel lines (SKOV-3/NIH OVCAR-3). The cytotoxicity of this compound against rabbit proximal renal tubular cells and human renal cortical tissues was determined by MTT assay , the [3H]-thymidine uptake and glucose consumption test, and found to be quite less than those of cisplatin. Based on these results, this novel platinum compound appear to be a valuable lead compound with high efficacy and low nephrotoxicity.

[PD1-51] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Synthesis and Analgesic-antiinflammatory Activity of Cinmetacin Amides

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Five cinmetacin amides as potential nonsteroidal analgesic and antiinflammatory compounds were prepared and their analgesic-antiinflammatory activity was compared with cinmetacin. Cinmetacin and hydroxysuccinimide were reacted with dicyclohexyl carbodiimide to give cinmetacin active ester (4), which was treated with amines to yield cinmetacin amides (5-9). Compounds (5)and (9) showed stronger analgesic activity than cinmetacin, and compounds (5), (6), (9) showed comparable antiinflammatory activity to cinmetacin.

[PD1-52] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Total synthesis of (+)-Spectaline

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Functionalized piperidines are very important heterocycles because of their presence in numerous alkaloids, pharmaceuticals, and synthetic intermediates.
Recently, we have reported diastereoselective palladium(0)-catalyzed oxazoline formation reation from the acyclic allylic and homoallylic benzamide(Tetrahedron Lett. 1998, 39, 8129, J.Org. Chem. 1999, 64, 9450).
We envisioned that this method could be utilized to set the vicinal amino alcohol stereochemistry of (+)-spectaline. Also, we envisaged that hydrogenolysis of the oxazoline generated amino group, which condensed intramolecularly with the carbonyl group spontaneously to provide piperidine, which was in situ hydrogenated with hydrogen coming from the least hindered surface to provide the piperidine.
The key steps in our strategy are diastereoseletive oxazoline formation reaction catalyzed by Pd(O) and piperidine formation by hydrogenolysis of oxazoline using Pearlman's catalyst.

[PD1-53] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Total Syntheses of Sphingofungin F

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Sphingofungins, compounds consisting of polar polyhydroxyl amino head groups, and long lipid chains, are membrane constituent involved in a number of cellular events including protein binding and transmembrane signaling.
We now report concise synthesis of sphingofungin F. The key steps of our syntheses are diastereoselective alkylation of oxazoline, diastereoselective addition of g-alkoxy allylic stannane, and palladium-catalyzed coupling of vinyl iodide with alkylzinc.

[PD1-54] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Total Synthesis of Myriocin

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Myriocin was first isolated from the fermentation broth of the thermophilic fungi, Myriococcus albomyces and Mycelia sterila as an antifungal principle in 1972. It have a quaternary center, three consecutive chiral centers and trans-olefinic group in polar hydroxyl amino head group.
Herein, we report an enantioselective strategy for the total synthesis of myriocin that features the use of the stereoselective intramolecular cyclization of homoallyl benzamide via p-allylpalladium complex catalyzed by Pd(0).
Our convergent, stereocontrolled synthesis of myriocin was executed via palladium-catalyzed coupling between polar head group and long lipid chain. The polar hydroxyl amino head group was synthesized by using diastereoselective hydroxymethylation of oxazoline and asymmetric allylation.

[PD1-55] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

A Simple Synthesis of Rutaecarpine

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Rutaecarpine is one of the indoloquinazoline alkaloids of the Rutaceous plants such as *Evodia rutaecarpa* which has long been utilized for the treatment of inflammation-related disorders in the traditional oriental medicinal practice. Recent research revealed that such an antiinflammatory activity stemmed from the attribution of rutaecarpine by a quite potent and selective inhibitory activity onto COX-2. Addition to antiinflammatory activity, the vasorelaxing, antiplatelet, and antianoxic activities were reported for rutaecarpine. The derivative, dehydroevodiamine was found to show a potent and promising activity on Alzheimer disease. Such interesting biological activities prompted us to design a simple synthetic route for the synthesis of rutaecarpine. We herein describe a simple 6 step synthesis of rutaecarpine from readily available anthranilic acid *via* 9,10,11,12-tetrahydro-4*H*-pyrido[2,1-*b*]-quinazoline-4,9-dione as a key intermediate.

[PD1-56] [10/19/2001 (Fri) 14:00 - 17:00 / Hall D]

Total Synthesis of (+)-Lauthisan