evaluated in vitro. The key intermediate 2β-formyl penam ester was obtained by multistep synthesis starting from 6-amino penicillanic acid. The wittig reaction of 2β-formyl penam ester with various phosphonium ylide containing double bond resulted in conjugated double bond at 2 position. The β-lactamase inhibitory activity of the prepared compounds was determined by microiodometric assay using the β-lactamase type I, III, IV, and E.coli TEM.

[PD1-14] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis of Pyridine, Thiophene and Furane-containing Compounds and their Antitumor Activities

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Terpyridine has been extensively studied as a ligand in a wide range of metal complexes and DNA binding agents. In our research program for the discovery and development of novel antitumor agents, a series of terpyridine derivatives containing pyridine, thiophene and furane moiety were synthesized and their cytotoxicity against several human solid tumor cell lines were evaluated. Selective cytotoxicity were also investigated. Some of the terpyridine derivatives showed high antitumor cytotoxicity with GI_{50} values in the range of 10^{-5} - 10^{-7} μg/ml while the GI_{50} value of Doxorubycin was larger than 10^{-3} μg/ml. The structure-activity relationships of these new antitumor agents would be further discussed.

[PD1-15] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

SYNTHESIS AND HIV-1 INTEGRASE INHIBITORY ACTIVITIES OF CAFFEOYLGLUCOSIDES

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Human immunodeficiency virus type 1 (HIV-1) is the probable causative agent of acquired immune deficiency syndrome (AIDS). The recent understanding of life cycle of this virus has afforded targets for anti-HIV-1 therapy, one of which is HIV-1 Integrase (IN). HIV-1 integrase is an enzyme that mediates the integration of HIV-1 DNA into a host chromosome and is essential to replication of the virus. This enzyme inhibitor is therefore thought to be a suitable drug for chemotherpeutic agent. In an effort to identify new structural leads for anti-HIV-1 agent, caffeoylglucosides were synthesized from methyl D-glucosides and their anti-HIV-1 activities were tested. Among them, a few of dicaffeoylglucosides showed HIV-1 integrase inhibitory activity as potent as chicoric acid.

[PD1-16] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis of Thienopyrimidines as Potential NMDA Receptor Antagonists

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2-substituted quinoline derivatives, represented by L-695902 and L-701324, are one of the most important class of compounds for NMDA glycine binding site antagonists. The characteristic feature

of this calss of compounds is that they exhibit improved pharmacological profiles due to their blood brain barrier(BBB) permeability, when compared to other calss of compounds. It is also known that thiophen ring can be utilized as isostere for the benzene ring.
So we modified the quinolone structure by substituting thiophene for the benzene ring of L-701324 to give several thienopyrimidine compounds. The synthesis of the thienopyrimidines starting from readily available material and their brief biological activities will be presented

[PD1-17] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Practical large scale synthesis to introduce t-butyl group as a non-polar moiety of D-serine

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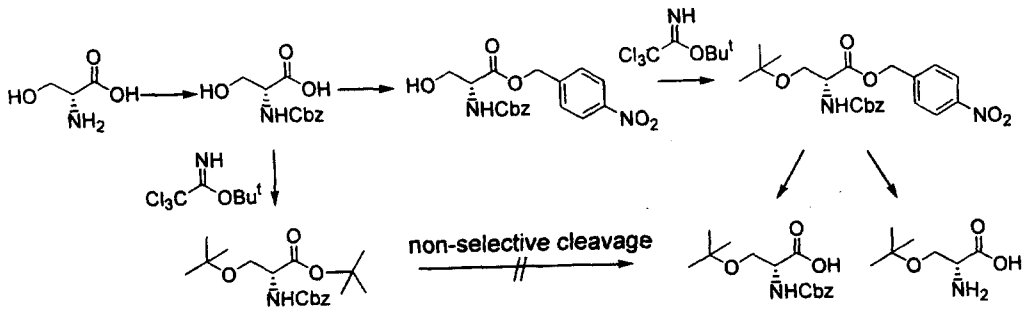
Synthetic peptides has been increasingly widely recognized as potential pharmaceutical agents. Therefore, there are growing demands for amino acid derivatives used as building blocks in peptide synthesis. Especially, the side-chain protection of polyfunctional amino acids such as SER, THR, TYR is not easy. Although these derivatives are commercially available, they are expensive and not supplied sometimes.
Here we describe practical large scale synthesis of tert-butyl introduced D-serine which is, for example, one of building blocks of zoladex, peptide drug(pyro-gly-his-trp-ser-tyr-D-ser(But)-Leu-Arg-Pro-Azgly-NH2 acetate).



[PD1-18] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis and properties of dextran-nalidixic acid ester as a colon-specific prodrug of nalidixic acid

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Dextran-nalidixic acid ester with varied degree of substitution (DS) was synthesized as a colon-specific prodrug of nalidixic acid (NA). Solubility in water (mg/ml) of dextran-nalidixic acid ester (dextran-NA) with DS (mg NA/100 mg dextran-NA) of 7, 19, or 32 was 57.57 (equivalent to 4.00 mg NA/ml), 0.53 (equivalent to 0.10 mg NA/ml), or 0.03 (equivalent to 0.01 mg NA/ml), respectively, and that for NA was 0.03 at 25℃. To assure the chemical stability of dextran-NA at conditions similar to stomach and small intestine, dextran-NA was placed in a solution of pH 1.2 hydrochloric acid buffer or pH 6.8 phosphate buffer and incubated at 37℃ and no NA was detected during the 6 hours of incubation period, which indicated that dextran-NA might be chemically stable during the