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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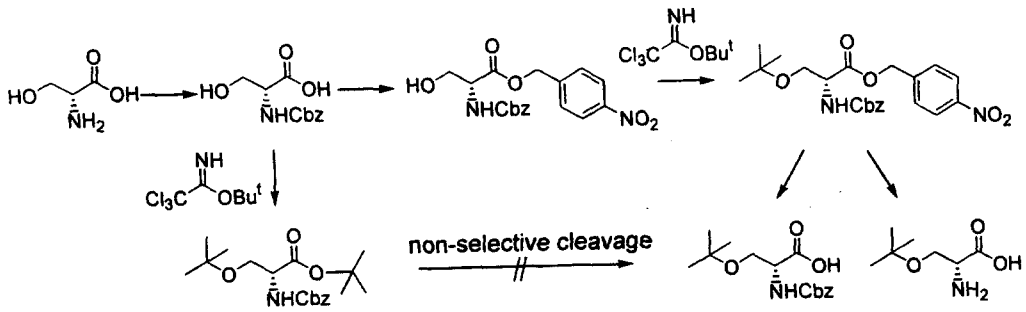
Synthetic peptides has been increasingly widely recognized as potential pharmaceutical agents. Therefore, there are growing demands for amino acid derivatives used as building blocks in peptide synthesis. Especially, the side-chain protection of polyfunctional amino acids such as SER, THR, TYR is not 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

transit through the gastrointestinal tract. Degree of depolymerization (%) by dextranase determined by DNS method at 37℃ for dextran-NA with DS of 7, 19, or 32 was 81, 68, or 8, respectively, in 8 hrs and that for dextran was 91. When dextran-NA (equivalent to 50 ?g of NA) with DS of 7 or 17 was incubated with cecal contents (100 mg) of rats at 37℃, the extent of NA released in 24 hrs was 41% or 32% of the dose, respectively. NA was not liberated from the incubation of dextran-NA with the homogenate of tissue and contents of the small intestine.

[PD1-19] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis of Affinity column-packing Materials for Seeking Binding Protein Related to Costunolide

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Costunolide, which is known as chemopreventive drug, is a sesquiterpene lactone compound isolated from Magnolia sieboldii and has antitumor and anti-inflammatory activities. It is expected to be farnesyl transferase inhibitor and anti-inflammatory activities, because the structure of costunolide is similar to farnesyl moiety Costunolide is one of macrocyclic compounds and their derivatives have already been synthesized from santonin as a starting material by Corey and followed by Grieco and Nishizawa presented total synthesis from santonin through Cope rearrangement.
The aim of this research is to develop new and easy method. Costunolide has farnesyl moiety in its structure. We can synthesize costunolide resin by attaching it with resin using a linker. Once synthesized, product, derivatives, and all of its intermediates go through Affinity Column-packing material. Anti-inflammatory Protein will come out late since it binds with Protein resulting in longer retention time. However, unbounded ones will come out fast. For now, we are trying to synthesize various derivatives. After attaching resins on these derivatives, we will put them through Affinity Column-packing and search for prospective anti-inflammatory proteins.

[PD1-20] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis of Some Cyclopropyl Nucleosides as Potential Antiviral Agents

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Some novel cyclopropyl nucleosides possessing additional methyl spacer between the base and the ring were synthesized as potential antiviral agents. The important intermediate, cyclopropyl compound was synthesized from feist's acid, via esterfication, reduction, the partial protection by using TBDPS chloride and activated by tosylation. The condensation of cyclopropyl intermediate with bases in the presence of potassium carbonate and a crown compound and its deprotection by using tetrabuthylammonium fluoride gave the final cyclopropyl nucleosides.

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

Synthesis of Affinity column-packing Materials for Seeking Binding Protein Related to Costunolide

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