binding of TATA-binding protein (TBP) and its association with p65. More importantly, TPA-induced activation of ERK1/2 resulted in increased interaction of p65 with TBP. These findings suggest that genistein inhibits COX-2 expression and PGE_2 production in MCF10A cells by indicating the transcriptional initiation complex that involves TBP.

[OC-3] [10/18/2002 (Fri) 16:20 - 16:30 / Hall B]

A new mechanism for unsaturated fatty acid biosynthesis in *Streptococcus pneumoniae*

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The anaerobic pathway for unsaturated fatty acid biosynthesis was established in the 1960s in Escherichia coli. The double bond is introduced into the growing acyl chain by FabA, an enzyme capable of both the dehydration of β-hydroxydecanoyl-[acyl carrier protein] (ACP) to trans-2-decenoyl-ACP, and the isomerization of trans-2 to cis-3-decenoyl-ACP. However, there are a number of anaerobic bacteria whose genomes do not contain a fabA homolog, but these organisms nonetheless produce unsaturated fatty acids. We cloned and biochemically characterized a new enzyme in type II fatty acid synthesis from *Streptococcus pneumoniae* R6 that carries out the isomerization of trans-2-decenoyl-ACP to cis-3-decenoyl-ACP, but is not capable of catalyzing the dehydration of β-hydroxy intermediates. This tetrameric enzyme, designated FabM, has no similarity to FabA, but rather is a member of the hydratase/isomerase superfamily. Thus, the branch point in the biosynthesis of unsaturated fatty acids in S. pneumoniae occurs following the formation of trans-2-decenoyl-ACP, in contrast to *Escherichia coli* where the branch point takes place after the formation of β-hydroxydecanoyl-ACP.

[OD-1] [10/18/2002 (Fri) 11:30 - 11:40 / Hall B]

Novel Asymmetric Synthesis of Unsaturated 1,2-Amino Alcohols

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The synthesis of chiral 1,2-amino alcohols has been an area of intense study in the synthetic and industrial fields, because of their important roles in organic synthesis as fundamental building blocks and their occurrence in a number of natural products, drugs, and chiral auxiliaries or ligands. General methods for the synthesis of these compounds can be divided into two large categories: functional group transformations and the C-C or the C-N bond formations. Of these two methods, the former has been used widely so far, including the reduction of α-amino acids, α-amino ketones or α-hydroxy imines, the nucleophilic substitution of 1,2-diols, epoxides, aziridines, cyclic carbonates or cyclic sulfates, the aminohydroxylation or oxymecuration of olefins and the hydroboration of enamines. The latter involves the addition of an organometallic reagent to the N-protected α-amino aldehydes or to the O-protected α-hydroxy imines and coupling of carbanions with imines. Many of these procedures sometimes have one or more problems, for example, low stereoselectivity, limited applications and the use of heavy metals.
Recently, we have developed the novel synthetic methods for N-protected allylic amines from allyl ethers using chlorosulfonyl isocyante (CSI), we found that the reaction of 1,4-diphenylbut-2-enyl methyl ether with CSI gave only one product, methyl N-(1-benzylcinnamyl)carbamate, due to the steric hindrance of the phenyl ring and the formation of a stable conjugated product.

Herein, we now describe a new synthetic approach to a variety of unsaturated 1,2-amino alcohols by the control of the remote stereocenters by asymmetric induction as an extension of the CSI reactions and how to control the diastererselectivity in this reaction.

[OD-2] [10/18/2002 (Fri) 11:40 - 11:50 / Hall B]

Synthesis of 14C-Radio Isotope Labeled Quinolone Intermediates

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Methods of 14C-radio isotope labeling of quinolone intermediates at four different sites are described. 14C-radio isotope labeled quinolone intermediates can be synthesized from 14C-1-malonic acid, 14C-2-malonic acid, 14C-benzene ring, and 14C-trimethyl orthoformate. The major site of 14C-radio isotope labeled quinolone intermediates is from 14C-2-malonic acid. We want to help customers to choose the best way for synthesis of 14C-radio isotope labeled quinolone derivatives, and give a general comprehension for 14C-radio isotope labeled pharmaceutical compounds.

[OD-3] [10/18/2002 (Fri) 11:50 - 12:00 / Hall B]

Dexamethasone 21-sulfate sodium : A potential colon-specific prodrug of dexamethasone.

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Corticosteroids have been used most frequently for inflammatory bowel disease. They are well absorbed and only a limited fraction of the dose is delivered to the inflammatory site in the colon. To reduce side effects by the systemic absorption, colon-specific delivery is highly desirable. We designed dexamethasone 21-sulfate sodium (DS) as a colon-specific prodrug of dexamethasone (D) expecting that it might be stable and nonabsorbable in the upper intestine and dissociate in the colon by the sulfatase, an enzyme solely found in the colon. DS was prepared in good yield by a simple route. In vitro/in vivo properties were investigated using rats. It was stable on incubation with buffer solutions at pH 1.2 and pH 6.8, the pH representing stomach and small intestine, respectively. Apparent partition coefficient of DS or D in 1-octanol/pH 6.8 phosphate buffer at 37 ℃ was 0.27 or 52.48, respectively. It was stable on incubation with the contents of small intestine (SI), but hydrolyzed over 90% with the cecum contents. After oral administration of D, concentration of D was high in the plasma and very low in the large intestine, which implies high risk of systemic side effects with low therapeutic efficacy. After oral administration of DS, it was not detected from plasma, feces or urine, which indicates that DS is not absorbed from the GI tract and completely dissociates by the time of defecation. Concentration of D, produced from DS by sulfatase, was high in the large intestine and non-detectable in the plasma, which implies high therapeutic efficacy with low risk of systemic side effects. Effect of DS on myeloperoxidase activity (MPO), an indicator for inflammation, was compared with that of D using TNBS-induced colitis rats. MPO activity from DS-treated rats was much lower than that of D-treated rats on an equal dose level after treating with D or DS for 6 days. Macroscopic ulceration was greatly improved with DS-treated group. These results imply that efficacy of DS is much greater than free D. DS has a great potential to develop as a clinically applicable colon-specific prodrug of D.