

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 diastereoselectivity in this reaction.

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

### Synthesis of <sup>14</sup>C-Radio Isotope Labeled Quinolone Intermediates

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