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(-)-α-narcotine(1R,9S) is one of the major bases in Papaver somniferum L., the sourse plant for opium, while (-)-β-narcotine(1R,9R) is a synthetic phthalideisoquinoline alkaloid. Although some advanced methods for the preparation of α-narcotine have been developed using modified Bischler-Napieralski cyclization, the facile synthesis of β-narcotine has not further been attempted, supposingly because of its no clinical efficacy contrary to α-narcotine having an antitussive effect. We could conveniently prepare β-narcotine using cotarnine as a starting material. Direct condensation of cotarnine and iodomeconine prepared by aromatic iodination using thallium trifluoroacetate/ KI and by the successive reduction of resulting iodo-β-narcotine with aluminum amalgam. Its structure including a stereochemistry was confirmed by instrumental analyses. This synthetic alkaloid was degraded with ethyl chloroformate at room temperature to afford the chloro-carbamate as a crystalline intermediate, which was unexpectedly converted into the carbinol by exchange of Cl with OH of water contained in the solvents and the ethoxy-carbamate, probably because of ethanol added to chloroform as a solvent stabilizer during the purification by column chromatography.

[PD1-31] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Acyclic Vanilloid Receptor Antagonist Based on Capsazepine

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Capsaicin, the pungent component of chili pepper, opens a novel cation selective ion channel in the plasma membrane of peripheral sensory neurons. Capsaicin channel agonists induce pain upon topical application in the early stage, which is followed by a period of desensitization. Although the agonists have been studied as a analgesics, their initial irritancy became sever side effect. So competitive antagonists have been pursued as a novel pharmacological agent for analgesics, rather than agonists. Since the introduction of the first competitive antagonist, capsazepine by forming 7-membered rigid ring system, the more potent antagonist has not been reported yet. As part of our program to find a new scaffold for a competitive antagonist against the capsaicin receptor, we modified capsazepine by opening the 7-membered rigid ring system, which has a virtually similar orthogonal conformation. In this communication, we report the synthesis of N,N,N-trisubstituted acyclic thiourea derivatives and their biological activities.

[PD1-32] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Cleavage of Benzyl and p-Methoxybenzyl Ethers Using Chlorosulfonyl Isocyanate Reaction

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Deprotection of the benzyl group has been widely used in multi-step organic synthesis with a variety of reaction conditions, including catalytic hydrogenolysis, Lewis acids such as $FeCl_3$ or $MgBr_2$ and lithium naphthalenide. However, these procedures sometimes can be problematic with multifunctional substrates, such as unsaturated bonds during hydrogenolysis, an acid-labile moiety in $FeCl_3$, and a easily reducible functional group in lithium naphthalenide.

Also, there are various methods for selectively removing of the p-methoxybenzyl group which include Lewis acid-catalyzed cleavage (TMSCl-$SnCl_2$-anisole, Me_2BBr, BF_3OEt_2-$NaCNBH_3$, $AlCl_3$-EtSH, $CeCl_3$-NaI), oxidation (2,3-dichloro-5,6-dicyanobenzoquinone, ceric ammonium nitrate), trifluoroacetic acid, and clay-supported ammonium nitrate-irradiation. Many of these procedures sometimes have one or more problems, for example, use of a heavy metal, a side reaction, low yield, or the cost of the reagent. Especially, DDQ is inclined to overoxidize allylic p-methoxybenzyl ether to an unsaturated ketone.

These facts prompt us to find a milder and more widely applicable method for deprotection of benzyl and p-