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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-

methoxybenzyl group.
Since we have developed the novel synthetic methods for N-protected allylic amines from allyl ether using chlorosulfonyl isocyanate (CSI) and investigated its mechanism, we have found a novel technique for comparing directly the stability of carbocations in the solution phase and have established the stability order of the various carbocations under our reaction conditions.
Herein, we now report the extension of CSI under new reaction condition for the cleavage of various benzyl and p-methoxybenzyl protecting groups of alcohols and phenols in the presence of other functional groups

[PD1-33] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Diaralkylthiourea Derivatives as a Novel Vanilloid Receptor Antagonist

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A series of diaralkylthiourea derivatives was prepared and tested for its antagonistic activity against vanilloid receptor. In this study we explored the possibility of selected compound type (I) with tetrahydronaphthyl group as rigid pendant moiety. Our premise for antagonistic activity of molecules was modeled on the capsazepine, the first antagonist for vanilloid receptor. These compounds (I) showed less potent antagonistic activity than that of capsazepine, but they were devoid of agonistic activity. Low activities were perceived to be originating from their limited degree of freedom in rigid pendant moiety, therefore it was necessary to change the structure of compound (I) to get increased activity . In order to improve their flexibility, tetrahydronaphthyl group of compound (I) was transformed into substituted benzyl or phenethyl group. The calcium uptake antagonistic IC_{50} values of compound type (II) were 0.1 ~ 1 μM which is comparable to that of capsazepine. Discussion on their structure activity relationships was also described.

[PD1-34] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

The Versatile Conversion of Acyclic Amides to a-Alkylated Amines

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The reaction of N-acyliminium ion with a variety of nucleophiles is one of the powerful method to introduce various substituents at the a-carbon of an amine. Particularly this type of inter and intramolecular C-C bond formation can be effectively applied to the synthesis of the bioactive natural or unnatural compounds as well as many bioactive peptidomimetics. Accordingly, much attention has been devoted to the practical and efficient methods for the generation of acyliminium ion precursors though there are many important aspects in the reaction involving N-acyliminium ions.
The use of a-alkoxy carbamates and amides as precursors for N-acyliminium ions is well reviewed, and these versatile systems arise from the partial reduction of cyclic imides, addition of amides or carbamates to aldehydes, or oxidation of the hydrocarbon under electrochemical or transition metal-mediated conditions. Among them, partial reduction of the carbonyl in imides or acylamides has been considered as the best procedure in terms of the reaction efficiency and the substrate diversity. However, this method has a limitation that it can be applicable only to the cyclic systems, and so few are reported for the acyclic ones.
We have been continuously interested in the functionalization of cyclic and acyclic amide carbonyl with regards to the syntheses of natural alkaloids. Herein we report a novel and general method for the preparation of the stable N,O-acetal TMS ethers, the excellent precursors of linear acyliminium ions, and also describe their reactivities and reaction scopes.

[PD1-35] [10/17/2002 (Thr) 09:30 - 12:30 / Hall C]

Antifungal activities of 2-arylthio-,2-arylthio-5-methoxy-, 2,3-bisarylthio-juglones and 2,3-