Synthesis and antifungal activity of 6-arylthio-/6-arylamino-4,7-dioxobenzothiazoles

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6-Arylthio-/6-arylamino-4,7-dioxobenzothiazoles were synthesized and tested for in vitro antifungal activity against Candida species and Aspergillus niger. 6-Arylamino-4,7-dioxobenzothiazoles showed, in general, more potent antifungal activity than 6-arylthio-4,7-dioxobenzothiazoles. The 6-arylamino-substituted compounds exhibited the greatest activity. In contrast, 6-arylthio-, 2-/5-methyl- or 5-methoxy-moieties of compounds did not improve their antifungal activity significantly. The results of this study suggest that 6-arylamino-4,7-dioxobenzothiazoles would be potent antifungal agents

[PD1-21] [2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function]

Total synthesis of 1,4-Dideoxy-1,4-Imino-D-Arabinitol(DAB1)

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Naturally occurring sugar mimics with a nitrogen in the ring are classified into five structural classes: polyhydroxylated pyrrolidines, piperidines, indolizidines. pyrrolizidine, and nortropanes. Glycosidase are involved in a wide range of important biological processes, such as intestinal digestion, post-translational processing of glycoproteins and the lysosomal catabolism of glycoconjugate. The realization that alkaloidal sugar mimics might have enormous therapeutic potential in many diseases such as viral infection, cancer and diabetes has led to increasing interest and demand for these compounds. Most of these effects can be shown to result from the direct or indrect inhibition of glycosidases. Since glycosidase inhibitors(azasugars) proved to have the biological activity, we have held considerable interest in the context of the synthesis of nitrogen-containing natural products. In connection with previous work on the regioselective and stereoselective Chlorosulfonyl isocyanate(CSI) reaction with various benzyl ethers, we envisioned the synthesis of 1,4-dideoxy-1,4-imino-D-arabinitol(DAB1) from polybenzyl ethers, which were prepared from commercially available D-arabinose, by means of a regioselective and stereoselective amination of CSI as the key transformation. The efficient synthesis of DAB1 had been achieved in 9 steps in 21% overall yield. This new synthetic strategy involving our regioselective and stereoselective CSI reaction as a key step can be widely applicable to the total synthesis of other alkaloidal sugar mimics.

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Synthesis and Two Electrode Voltage Clamp Assay of PPADS Derivatives as the P2X Antagonists

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P2X receptors are ligand gated cation channels activated by the binding of extracellular adenosine 5'-triphosphate (ATP) and classified into 7 subtype families. $P2X_1$ receptors are abundantly expressed in smooth muscle mediates blood vessel and mediate constriction upon binding of neuronal ATP. The activation of $P2X_3$ receptor by ATP has been known to initiate the pain signaling in the peripheral nervous system, which is involved in chronic inflammatory nociception and neuropathic pain by nerve injury. Therefore, selective antagonists targeting $P2X_1$ and $P2X_3$ receptors can be used as the specific drugs. It has been reported that P2X receptors are effectively blocked by PPADS (Pyridoxal-5'-phosphate-6-azopheny-2',4'–disulfonic acids) analogue. We synthesized derivatives of PPADS containing carboxylic acid side chains instead of phosphates and tested them with TEVC (two electrode voltage clamp) assay system on the Xenopus Oocyte expressed with cloned mouse $P2X_1$ and human $P2X_3$ receptors. The result showed that the carboxylic acid chain is able to replace the phosphate in the skeleton of PPADS with maintaining the potent antagonistic properties on the P2X receptors.