[PC3-8] [10/20/2000 (Fri) 15:30 - 16:30 / [Hall B]]

Characterization of Immortalized Hepatic Stellate Cell Line

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PURPOSE: Hepatic stellate cells (HSCs) are now known to play central roles in hepatic fibrosis, but primary HSCs isolation is time-consuming, yield are modest, and they have a limited lifespan in vitro. To overcome these defects, we developed and characterized an immortalized hepatic stellate cell line. METHODS: Immortalized hepatic stellate cell line was established by transformation with simian virus 40. We investigated their growth, expression of TGF-beta, collagen type I (COL-I) and smooth muscle alpha actin (alpha-SMA) and NF-kappa B induction using electrophoretic mobility shift assay. RESULTS: Morphology of immortalized HSCs was not changed. The growth of immortalized HSCs was dependent on serum concentration, which showed apoptosis in 36 hours in serum-free condition. The immortalzed HSCs expressed high level of COL-I and alpha-SMA and expressed COL-I and TGF-beta mRNAs. Some drugs such as curcumin and pentoxifylline inhibited the production of COL-I and NF-kappaB induction. NF-kappa B was induced in the nucleus when the immortalized HSC was stimulated by serum, TNF-alpha and IL-1 beta but not PDGF-BB, TGF-beta and IFN-gamma. CONCLUSIONS: We suggest that the immortalized HSCs could be useful tool to study hepatic fibrosis.

[PD1-1] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Study on the Stability of Carbocation by CSI reaction with Ethers

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Of all reaction intermediates, the carbocation holds a paramount position as the first to be extensively studied and perhaps the most widely understood and harnessed in organic synthesis. Thus, the stability of carbocations have been studied by many chemists. The methods for the study can be divided into two large categories: the determination of accurate values for the heats of formation of carbocations in the gas phase, and the study of correlation between relative solvolysis rate constants in solvent and the competition constant in the present of nucleophile. Already, we developed synthetic method for N-protected allylic amines from allyl ethers using chlorosulfonyl isocyanate(CSI) via the stable allylic carbocation.
In this presentation, we will report the stability order of carbocations by the simple CSI reaction which we developed with various allyl ethers and benzyl ethers.
As one of our results, the reaction of p-methoxycinnanyl p-methoxybenzyl ether with CSI afforded p-methoxybenzyl N-(p-methoxycinnamyl)carbamate and p-methoxycinnamyl N-(p-methoxybenzyl)carbamate in a 4 : 1 ratio, on the other hand, cinnamyl p-methoxybenzyl ether afforded only cinnamyl N-(p-methoxybenzyl)carbamate. This result show us stability order of carbocation: p-methoxycinnamyl > p-methoxybenzyl > cinnamyl carbocation.

[PD1-2] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Inhibitory Effect of 2-Hydroxychalcones on Rat Lens Aldose Reductase and Rat Platelet Aggregation

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Inhibitory effects of synthetic 2-hydroxychalcone derivatives on rat lens aldose reductase(RLAR) and on platelet aggregation were investigated for the prevention or the treatment of chronic diabetic complications.
5-chloro-4,2-dihydroxychalcone and 5-chloro-3,2-dihydroxychalcone exhibited a potent inhibitory effects on rat platelet aggregation induced by ADP(IC_{50}=0.10 and 0.06 mg/ml, respectively.) and collagen(IC_{50}=44 and 16 μg/ml, respectively.) but showed relatively weak inhibitory activities on RLAR. 2,4,2,4-Tetrahydroxychalcone, 3,4,2,4-tetrahydroxychacone, 5-chloro-2,4,2-trihydroxychalcone and 5-chloro-3,4,2-trihydroxychalcone possessing o-dihydroxy or m-dihydroxy moiety exhibited relatively potent inhibitory activities in both systems.

[PD1-3] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Stereoslective trans-oxazoline formation via Pd(0)-catalyzed cyclization of isopropenyl acetate.

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Palladium(0)-catalyzed intramolecular cyclization of benzamide via p-allylpalladium complex is useful tool for the synthesis of highly functionalized compounds. Ongoing program for the formal total synthesis of (+)-lactacystin, which is remarkably selective and potent inhibitor of the 20S proteasome, we applied the newly developed Pd(0)-catalyzed cyclization reaction to the highly stereoselective synthesis of trans-oxazoline, which is key intermediate of (+)-lactacystin. The requisite cyclization precursor, isopropenyl acetate, was straightforwardly prepared from the L-serine by a seven-step sequences (overall 61%).

[PD1-4] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and In vitro evaluation indandione-2-carboxamides.

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6-(2-Dimethylaminoethylamino)-3-hydroxyindeno[2,1-c]quinoline-7-one (TAS-103) is a dual topoisomerase I and II inhibitor with preclinical efficacy in a broad spectrum of tumors and in multidrug-resistant tumor cell lines. It is currently in Phase I clinical trials in the U.S. It could be useful as a lead compound for development of new drugs.
In this study, we presented the synthesis and cytotoxicity of indandione-2-carboxamides. These were designed as an open form of tetracyclic TAS-103. The cytotoxicities of TAS-103 analogs against various tumor cell lines were worse than that of Doxorubicin and Mitomycin-C. The compounds containing methyl substituents were more potent than other compounds in this result

[PD1-5] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis and Structure Activity Relationships of a series of 7-acylamino-3-(isoxazolylmethylthio)-3-cephem exhibiting activity against MRSA.

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