

[Chem. Pharm. Bull., 46, 42-52 (1998)]

[Lab. of Pharm. Chemistry]

**Synthesis and Structure-activity Relationship of 3-Substituted Benzamide, Benzo[*b*]furan-7-carboxamide, 2,3-Dihydrobenzo[*b*]furan-7-carboxamide, and Indole-5-carboxamide Derivatives as Selective Serotonin 5-HT<sub>4</sub> Receptor Agonists.**

Takuji KAKIGAMI, Toshinao USUI, Katsura TSUKAMOTO and Tadashi KATAOKA\*

The title compounds were prepared and evaluated for serotonin 5-HT<sub>4</sub> agonistic activity in *in vitro* tests. Construction of the benzo[*b*]furan skeleton and 2,3-dihydrobenzo[*b*]furan skeleton caused a significant enhancement of the activity. 4-Amino-*N*-[2-(1-azabicyclo[3.3.0]octan-5-yl)ethyl]-5-chloro-2-methylbenzo[*b*]furan-7-carboxamide hemifumarate was as potent as cispride, and was free from dopamine D<sub>1</sub>, D<sub>2</sub>, serotonin 5-HT<sub>1</sub>, 5-HT<sub>2</sub> and muscarine M<sub>1</sub>, M<sub>2</sub> receptor binding activity in the *in vitro* tests.

[Chem. Pharm. Bull., 46, 148-150 (1998)]

[Lab. of Pharm. Chemistry]

**Chemical Behavior of 2'-Vinyl-2*H*-benzothiazine-2-spirocyclopropan-3(4*H*)-ones in Acidic Media.**

Tadashi KATAOKA,\* Tetsuo IWAMA, Harutoshi MATSUMOTO, Hirohito KONDO, Yoshihide NAKAMURA and Hiroshi SHIMIZU

Reactions of 2'-vinyl-2*H*-benzothiazine-2-spirocyclopropan-3(4*H*)-ones with several proton acids were examined. Reactions of 2'-vinyl-2*H*-benzothiazine-2-spirocyclopropan-3(4*H*)-ones with HCl and HBr predominantly gave (*Z*)-allyl halide derivatives. In the cases of HClO<sub>4</sub> and HBF<sub>4</sub>, 4,4a,5,6-tetrahydro-5-oxo-1*H*-thiopyrano[1,2-*a*]-1,4-benzothiazinium salts were isolated in good yields. Allyl halide derivatives were also obtained by treatment of the 1*H*-thiopyrano[1,2-*a*]-1,4-benzothiazinium salts with HCl and HBr.

[Chem. Pharm. Bull., 46, 151-153 (1998)]

[Lab. of Pharm. Chemistry]

**Conformational Effects on Photochemical Thiylation of 2'-Vinyl-2*H*-benzothiazine-2-spirocyclopropan-3(4*H*)-ones.**

Tadashi KATAOKA,\* Tetsuo IWAMA and Harutoshi MATSUMOTO

Photochemical thiylation of 2'-vinyl-2*H*-benzothiazine-2-spirocyclopropan-3(4*H*)-ones was examined to form allyl sulfides. Although the reactions proceeded with complete regioselectivity because of the high stabilizing ability of the capto-dative substituents, geometrical selectivity of the olefinic moiety was dependent on the substituents on the cyclopropane ring. The conformation of 2'-vinyl-2*H*-benzothiazine-2-spirocyclopropan-3(4*H*)-ones probably plays an important role in the addition step of the thiyl radical to the double bond.

[Chem. Pharm. Bull., 46, 757-766 (1998)]

[Lab. of Pharm. Chemistry]

**Stereospecific C-N Bond Cleavage of 4-Silylated 1,2-Thiazetidines 1,1-Dioxides with EtAlCl<sub>2</sub> or AlCl<sub>3</sub>: Formation of (*E*)-Vinylsulfonamides.**

Tetsuo IWAMA, Atsuko TAKAGI and Tadashi KATAOKA\*

Monosilylation of  $\beta$ -sultams gave (3*R*\*, 4*S*\*)-4-monosilyl- $\beta$ -sultams stereoselectively. Disilylated  $\beta$ -sultams were obtained in high yields by the use of trimethylsilyl chloride as a silylating reagent. Treatment of 4-monosilyl- $\beta$ -sultams with EtAlCl<sub>2</sub> caused stereospecific C-N bond cleavage owing to  $\beta$ -cation stabilization of the silicon group to provide (*E*)-vinylsulfonamides. (*E*)- $\alpha$ -Silylstyrylsulfonamides were obtained in the reactions of 4,4-disilyl- $\beta$ -sultams with EtAlCl<sub>2</sub>. Reactions of 4-silyl- $\beta$ -sultams with AlCl<sub>3</sub> afforded *N*-dealkylated (*E*)-vinylsulfonamides in good yields. An allyl alcohol was obtained from a reaction of an (*E*)- $\alpha$ -silylstyrylsulfonamide and benzaldehyde in the presence of TBAF and BF<sub>3</sub>•Et<sub>2</sub>O.