[*Chem. Pharm. Bull.*, **45**, 1218-1220 (1997)] [Lab. of Pharm. Chemistry]

N-[2-(1-Azabicyclo[3.3.0]octan-5-yl)ethyl]-2-nitroaniline, A Potent Muscarinic Agonist.

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The muscarinic receptor agonist SK-946, an aniline derivative with a 1-azabicyclo[3.3.0]octyl moiety, was found. SK-946 was attached to the M_1 muscarine receptor with an IC_{50} value of 0.10 μ M, and M_2 with an IC50 value of 83 μ M, and superior to YM796 and SR46559 with regard to affinity and selectivity to the M1 receptor. The ability of SK-946 to improve cognitive function was assessed using passive avoidance tests in pirenzepine-, scopolamine-, cycloheximide- and electric shock-induced mice and rats. These tests suggested that SK-946 was effective for Alzheimer-type dementia. Synthesis of SK-946 was also described.

[*Tetrahedron Lett.*, **38**, 1809-1812 (1997)] [Lab. of Pharm. Chemistry]

Reactions of Alkynylselenonium Salts with Sodium Benzenesulfinate.

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Dimethyl(phenylethynyl)selenonium tetrafluoroborate was prepared by methylation of methyl phenylethynyl selenide with the Meerwein reagent in 62% yield. Diphenyl derivative was synthesized by the reaction of trimethyl(phenylethynyl)silane and diphenyl selenoxide with trifluoromethanesulfonic anhydride in dichloromethane in 87% yield. The reaction of the dimethyl salt with sodium benzenesulfinate in an alcohol yielded a (*Z*)-alkoxyvinylsulfone as the main product although the reaction gave rise to demethylation to some extent to give methyl phenylethynyl selenide. On the reaction of the diphenyl salt, the sulfone and diphenyl selenide were isolated in good yields. The addition-elimination mechanism is most plausible for formation of the (*Z*)-alkoxyvinylsulfone. In contrast, the reactions of alkynylselenonium salts with benzenesulfinic acid in isopropanol afforded (*Z*)-(β-phenylsulfonyl)vinylselenonium salts in high yields.

[*Phosphorus, Sulfur, and Silicon*, **120**, 471-472 (1997)] [Lab. of Pharm. Chemistry]

Reactions of Thiazolo[3,2-*b*]-1,2,4-triazolium *N*-Ylides with Electron-deficient Acetylenes: Novel Benzoyl Migration of Intermediary 1:1-Adducts and Michael Addition to the Acetylenes.

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Reactions of thiazolo[3,2-*b*]-1,2,4-triazolium *N*-methylides with electron-deficient acetylenes gave the thiazole ring-opened products as a mixture of the (*E*)- and (*Z*)-isomers. In contrast, the *N*-phenacylides reacted with dimethyl acetylenedicarboxylate to give the thiobenzoates together with the thiazole ring-opened products. The *N*-ylides would react with the electron-deficient acetylenes in the way of 1,3-dipolar cycloaddition to give spiro-tricyclic intermediates, which gave the thiazole ring-opened products by Michael addition or the thiobenzoates by an intramolecular benzoyl migration. The reaction mechanism is proposed on the basis of the crossover experiments and the reaction of the α-deuterated *N*-phenacylide.

[*Med. Chem. Res.*, **7**, 204-218 (1997)] [Lab. of Pharm. Chemistry]

5-HT_{5A} Serotonin Receptor Binding: a Preliminary Structure-affinity Investigation.

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5-HT_{5A} receptors represent one of the newest populations of the serotonin (5-HT) receptor family, and essentially nothing is known regarding the structure-affinity relationships for 5-HT binding. Beginning with the structure of 5-HT (5-HT: 5-HT_{5A} Ki = 170 nM), minor structural modifications were examined in a stepwise fashion so that the effect of structural alteration could be related back as much as possible to the structure of 5-HT. Subsequently, more dramatic modifications were examined such that a total of about 30 tryptamines and related compounds were investigated. A comparative molecular field analysis (CoMFA) study was performed in order to gain further insight into the nature of the drug-receptor interaction. One of the significant findings of the study is that 1-(1-naphthyl)piperazines bind at 5-HT_{5A} receptors; in particular, 1-(7-hydroxynaphth-1-yl)piperazine (7-OH 1-NP; Ki = 3 nM) was found to bind with >50-fold higher affinity than 5-HT itself.