

[*Med. Chem. Res.*, **8**, 333-338 (1998)]

[Lab. of Pharm. Chemistry]

**Aryloxyethylamines as h5-HT<sub>1D</sub> Serotonin Receptor Ligands.**

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Although the  $\beta$ -adrenergic antagonist propranolol binds at rodent 5-HT<sub>1B</sub> serotonin receptors, it displays low affinity ( $K_i > 10,000$  nM) for its species homologue 5-HT<sub>1DB</sub> (*i.e.*, h5-HT<sub>1B</sub>) receptors. The structure of propranolol was systematically modified in an attempt to enhance its affinity for the latter population of receptors. Removal of the alkyl hydroxyl group, shortening of the *O*-alkyl chain from three to two methylene groups, and variation of the terminal amine substituent resulted in compounds, such as *N*-monomethyl-2-(1-naphthoxy)ethylamine ( $K_i = 26$  nM), that displayed significantly higher h5-HT<sub>1B</sub> affinity than propranolol. The compound was shown to bind equally well at human 5-HT<sub>1D $\alpha$</sub>  (h5-HT<sub>1D</sub>) receptors ( $K_i = 34$  nM) and was further demonstrated to possess h5-HT<sub>1B</sub> agonist character in an adenylate cyclase assay. (2,3-Disubstituted)phenoxyethylamines were also prepared and characterized for h5-HT receptors activities. Aryloxyethylamines appeared to represent a novel class of 5-HT<sub>1D</sub> receptor agonists.

[*Phosphorus, Sulfur, and Silicon*, **138**, 497-500 (1998)]

[Lab. of Pharm. Chemistry]

**Synthesis of Phenylethynyl dibenzoselenophenium Salt and Its Reactions with Nucleophiles**

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5-Phenylethynyl dibenzoselenophenium triflate was prepared from dibenzoselenophene 5-oxide and phenyltrimethylsilylacetylene in the presence of triflic anhydride. The FAB mass spectrum exhibited an ( $M^+ + 1$ ) peak at  $m/z$  483, and the X-ray crystallographic data showed that two C-Se bonds occupied equatorial positions, and the acetylenic bond and the triflate take an apical array with a bond angle of 172.1°. Namely, the selenonium salt had a distorted trigonal bipyramid structure. Reactions of the selenonium salt with sodium benzenesulfinate in an alcohol gave *Z*-alkoxyvinylsulfone and dibenzoselenophene in moderate yields, whereas the selenonium salt did not react with benzenesulfonic acid.

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[Lab. of Medicinal Chemistry]

**Facile Method for the Preparation of 7-Methyl-8-oxoguanosines as an Immunomodulator.**Yukio KITADE, Naohiro SAITO, Atushi KOZAKI, Kazumasa TAKAHASHI,  
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Reaction of 9-(2,3,5-tri-*O*-acetyl- $\beta$ -D-ribofuranosyl)-7-methylguaninium iodide with hydrogen peroxide in acetic acid gave the corresponding 7-methyl-8-oxoguanosine derivative in good yield. Deprotection of the 7-methyl-8-oxoguanosine derivative easily gave 7-methyl-8-oxoguanosine, which is well-known as an immunomodulator. Substitution of acetyl group at the  $N^2$ -position of guanine ring accelerated the oxidation reaction of 7-methylguaninium iodide.

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[Lab. of Medicinal Chemistry]

**Synthesis of 5-Arylthiouridines via Electrophilic Substitution of 5-Bromouridines with Diaryl Disulfides.**

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Novel synthetic method of 5-arylthiouridine derivatives is described. Treatment of 5-bromo-2',3'-*O*-isopropylideneuridine with diaryl disulfides in the presence of sodium hydride at ambient temperature gave the 5-arylthiouridines in moderate yields. The present method is devised by virtue of a combination of efficient participation of the 5'-hydroxy group onto the uracil ring and the electrophilic nature of diaryl disulfide, which was applied to the synthesis of 5-arylthio-1- $\beta$ -D-arabinofuranosyluracil.