[Med. Chem. Res., **6**, 593-602 (1996)] [Lab. of Pharm. Chemistry]

4-(6-Fluorobenzisoxazol-3-yl)piperidine, a Risperidone Metabolite with Serotonergic Activity of Potential Clinical Significance.

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Because of 6-FBIP [4-(6-fluorobenzisoxazol-3-yl)piperidine] has been identified as a metabolite of risperidone, and due to its structural resemblance to certain serotonin agonist, it was of interest that this metabolite was studied to have any 5-HT_2 activity of its own. 6-FBIP (5-HT_{2A} Ki = 49 nM) bound with only 16-fold lower affinity than risperidone. In tests of functional activity (inositol phosphate production, stimulus generalization in DOM-trained rats), however, 6-FBIP behaved as a 5-HT_2 antagonist. It is concluded that 6-FBIP would likely act as a 5-HT_2 antagonist if it was produced to any significant extent upon metabolism of risperidone.

[Tetrahedron, **52**, 9971-9978 (1996)] [Lab. of Medicinal Chemistry]

Stable Thioaldehydes: Synthesis, Structure Assignment, and Stability of 6-Amino-5-thioformyluracils.

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6-Amino-5-thioformyluracils were synthesized starting from 6-amino-1,3-disubstituted uracils in 23-98% yields. Although reasonable double-bond character of the C=S bond of the thioaldehydes was evidenced by means of spectral data and especially x-ray crystal analysis, the length of C=S bond of the thioaldehydes is longer than that of the kinetically stabilized thioaldehydes due to the mesomeric effect of the 6-amino group. These thioaldehydes can be good starting materials for fused pyrimidine synthesis by the use of condensation reactions with various active methylene compounds or acid amides in analogy with 6-amino-5-formyluracils.

[Jpn. J. Hosp. Pharm., **22**, 547-555 (1996)] [Lab. of Medicinal Chemistry]

Photo-stability of Cefotaxime in Aqueous Vitamin Solutions

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Although cephem derivatives are stable in aqueous solution without vitamins during 4 hours of sun light irradiation at room temperature, addition of flavin adenine dinucleotide or pyridoxal phosphate thereto causes the photo-degradation of cefotaxime (CTX) and in addition, the residual rate of CTX in the solution also decreased to less than 70%. Similarly, the residual rate of CTX in a solution of benzophenon, a triplet photosensitizer, also rapidly decreased during sun light irradiation. Sun light irradiation also decreased the residual rates of other cephalosporins with an oxyimino group at position 7 under the same conditions. The main degradation product was identified as an anti-isomer of CTX. These above described findings thus suggest that FAD and PAL-P may act as photosensitizers in the sun light-induced degradation of cephalosporins.