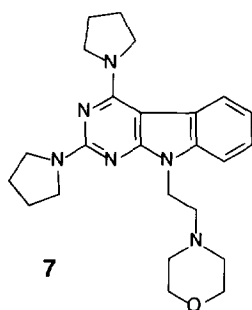


## 2,4-Diaminopyrrolo-[2,3-*d*]pyrimidines

The administration of reactive oxygen inhibitors and scavengers may have applications in the treatment of a wide range of disease states where pathological conditions result in elevated levels of reactive oxygen species. Bundy, G.L. and coworkers [*J. Med. Chem.* (1995) 38, 4161–4163] have reported the synthesis of a range of novel 2,4-diaminopyrrolo-[2,3-*d*]pyrimidines with antioxidant, neuroprotective and antiasthma activity.

Following extensive studies of pharmacology, toxicity and bioavailability, compound **7** has been selected for clinical evaluation in the treatment of asthma and several chronic neurodegenerative disorders.

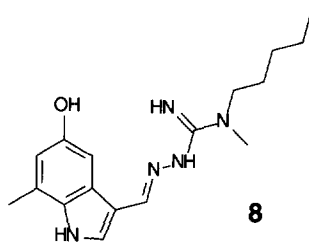


## Selective 5-HT<sub>4</sub> receptor antagonists

Of the 5-HT receptor subtypes, the 5-HT<sub>4</sub> receptor has attracted particular interest because it appears to have

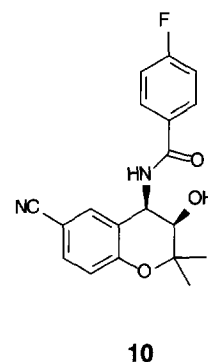
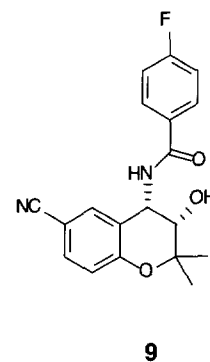
several roles both peripherally and centrally. For example, the 5-HT<sub>4</sub> receptor has been implicated in several cardiac conditions and may be involved in the liberation of corticotropin releasing factor (CRF). The use of 5-HT<sub>4</sub> receptor antagonists as pharmacological probes has been limited by their poor receptor selectivity and/or duration of action *in vivo*. Buchheit, K-H. and coworkers [*Bioorg. Med. Chem. Lett.* (1995) 5, 2495–2500] report the design and pharmacological evaluation of a new class of indolecarbrazimidamide antagonists.

Compound **8** was found to be a potent competitive antagonist of 5-HT<sub>4</sub> receptor-mediated effects in the guinea pig ileum with only moderate affinity for the 5-HT<sub>2C</sub> receptors and weak affinity for the other 5-HT subtypes.



## Stereochemical modulation of pharmacological activity

The importance of stereochemistry in determining the pharmacological activity of a compound was illustrated in a recent study by Brown, T.H. and

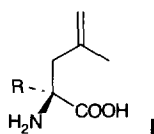


coworkers [*Bioorg. Med. Chem. Lett.* (1995) 5, 2563–2566]. The study demonstrated that the stereochemistry at C(4) of a series of 4-fluorobenzoylamino benzopyrans dictated the pharmacological activity of the compound.

The compounds with (*S*) stereochemistry **9** showed anticonvulsant activity whereas those of the (*R*) configuration **10** were found to lack the anticonvulsant activity but were found to be effective antihypertensive agents.

## $\alpha$ -Alkylated $\gamma,\delta$ -unsaturated amino acids

Kazmaier, U. and Maire, S. [*J. Chem. Soc., Chem. Commun.* (1995) 19, 1991–1992] describe synthesis of a range of  $\alpha$ -alkylated  $\gamma,\delta$ -unsaturated amino acids **I** using a highly diastereoselective Claisen rearrangement of chelated N-protected amino acid allylic esters.

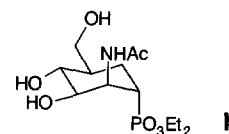


Optimal results were obtained using zinc chloride as the chelating metal salt. The authors demonstrated that the methodology could be applied to functionalized amino acids as well as amino acids with simple aliphatic or amino acid side chains.

## N-Acetyl- $\alpha$ -D-mannosamine 1-phosphate analogues

Analogues of N-acetyl- $\alpha$ -D-mannosamine 1-phosphate are important synthetic targets because this molecule is an intermediate in the biosynthesis of N-acetylneuraminic acid. Cipolla, L. and co-

workers have described the first synthesis of a phosphono analogue **II** [*J. Chem. Soc., Chem. Commun.* (1995) 19, 1993–1994].



## Synthesis of pyrrolo [2,3-*d*]pyrimidines

The synthesis of pyrrolo[2,3-*d*]pyrimidines is used in the preparation of folate