METABOLISM LINKED SYNTHESES OF FLUORINATED ANTI-TUMOUR DRUG THE FLUORINE - DEUTERIUM GAMBIT

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Metabolism studies of the known anti-tumour agents 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (C C N u), 4-[4-bis(2-chloroethyl) amino phenyl] butyric acid (chloroambucil) and [2-bis(2 chloroethyl) amino] tetrahydro-2 H-1, 3, 2 oxazaphosphorine-2-oxide (cyclophosphamide) and their polydeuterio derivatives have led to an understanding of their mode of action, deactivation and ultimate excretion.

In an attempt to modify or halt these processes, with the object of improving drug design and potency we have synthesised analogues of these drugs with fluorinated substituents in strategic positions within the molecules as indicated by metabolism data.

The synthesis of each set of derivatives will be described with emphasis on the overcoming of problems of isomer distribution.

Biological test results will be presented.