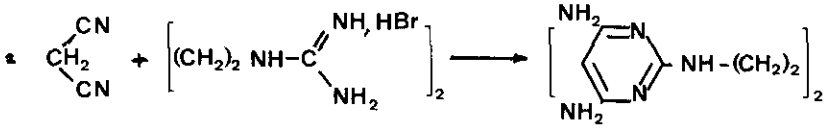
SYNTHESIS OF PYRIMIDINE "ANALOGS" OF NATURAL POLYAMINES

G. MENICHI, J. NACIRI, K. TAKAGI, M.HUBERT-HABART.
Institut Curie, Laboratoire Curie, 11 rue Pierre-et-Marie-Curie
75231 Paris Cedex 05.

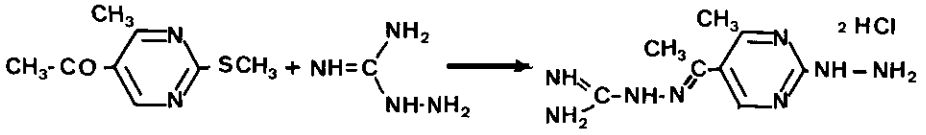
Chemical structures related to natural polyamines (putrescine, spermidine, spermine), have exibited antitumoral activity (e.g.: Me-GAG, DDUG).

Among compounds prepared so far in view of testing their activities as analogs of polyamines and antitumoral drugs none integrated a pyrimidine ring in their structure. We therefore devised several routes of access to pyrimidines substituted in such a way that they could be mistaken by cells for natural polyamines :

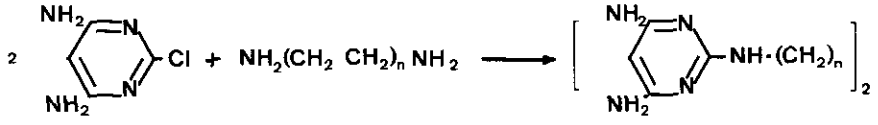
1°) Synthesis of polymethylene-bis-guanidines and condensation on: malononitrile, β-dicarbonylated structures or suitably oxygenated heterocycles.



2°) Reaction of aminoguanidine with 5-acetyl-2-amino-4-methyl-2-methylthio pyrimidine and 5-acetyl-4-methyl-2-methylthio pyrimidine.



3°) Substitution of 4,6-diamino-2-methylthio pyrimidine or 4,6-diamino-2-chloro pyrimidine with different types of amines.



Some unexpected chemical reactions will be interpreted.