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SYNTHESIS AND ANTIRETROVIRAL ACTIVITY OF FLUORINATED BENZODIAZEPONES: ANALOGUES OF NEVIRAPINE. *R. GUEDJ; *P.B. BOYODE; *A. FARESE; *M-A. FORESTIER; *A.I. AYI; *R. CONDOM; **M.SINET; ***J-N. COLIN and ***R. CHALLAND (* Université de Nice Sophia-Antipolis, Fac. Sc. Lab. Chim. Bio-Organique B.P. 71-F 06108 NICE Cedex 2 FRANCE. ** INSERM U13 Ancien Hôpital Claude Bernard, 190, Bd McDonald 75019 Paris FRANCE. *** The WELLCOME Research Laboratorises, Langlay Court, South Eden Park Road, BECKENHAM, KENT BR3 3BS, U.K.)

In the view to study the antiviral activity and the influence of the modification of the Nevirapine molecule by fluorination, we synthetized trifluoromethyle derivatives. The importance of non-nucleoside analogues in the antiviral chemotherapy retains great attention for chemical and biological researches because, acting as non -competitive inhibitors of HIV-1's RT enzyme, they can be used in combination with the nucleoside analogues. The reaction between, 3-amino-2-chloro-4-trifluoromethylpyridine which is obtained from the reduction of the corresponding azido derivative, and 2-chloronicotinoyl chloride led to a carboxyamide intermediate. This product reacted with different primary aliphatic amines to give the titled compounds in overall good yields. So far, we obtained their antiretroviral activity on MT4 cells infected by HIV-1 virus. A total synthetic method to obtain these molecules was described, then the measured antiviral properties permited us to discuss the structure-activity relationship.

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gp120 of HIV-1 Induces Apoptosis in Rat Cortical Cell Cultures: Prevention by Memantine

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Introduction: In addition to lymphocytes, other cells like human astrocytes and neuronal cell lines are infected by HIV-1 in vitro. However, primary neurons are very rarely, if at all infected by HIV-1. **Results:** After incubation of rat cortical cell cultures with HIV-1 coat protein gp120 for 12 h, cells showed fragmentation of DNA at internucleosomal linkers, the characteristic feature of apoptosis. In a quantitative approach it was determined that the percentage of DNA fragmentation increased from 7%, in the absence of gp120, to 62% following incubation with 24 ng/ml of gp120. Simultaneously, the percentage of viable cells decreased from 94% to 33%. Memantine (1-amino-3,5-dimethyladamantane) as well as the NMDA antagonist MK-801 prevented the effects of gp120 at micromolar concentrations. In human cultured astrocytes, gp120 was ineffective with respect to DNA fragmentation and cell toxicity. **Discussion:** From these data we conclude that the gp120-induced apoptosis may contribute to the neurological complications frequently associated with the immunodeficiency syndrome. The cytoprotective effect of memantine in cortical cell cultures may qualify the drug for the treatment of AIDS-related dementia.