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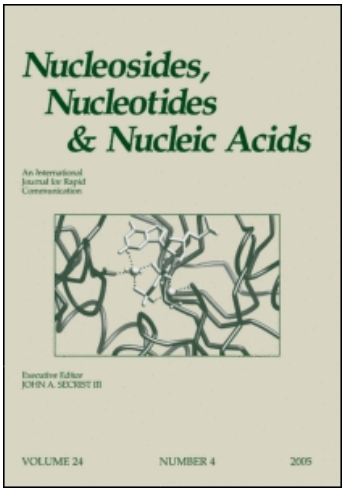

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Arylamidation of Purine Nucleosides by 2-Acetylalkoxy- Aminofluorene - an Intramolecular Approach to the Synthesis of Nucleoside - Carcinogen Adducts

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NUCLEOSIDES & NUCLEOTIDES, 6(1&2), 401-402 (1987)

ARYLAMIDATION OF PURINE NUCLEOSIDES BY 2-ACETYLALKOXY-AMINOFLUORENE - AN INTRAMOLECULAR APPROACH TO THE SYNTHESIS OF "NUCLEOSIDE - CARCINOGEN" ADDUCTS.

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Abstract. Arylamidation of the guanosine ring at position C-8 by the carcinogen N-2-acetylalkoxyaminofluorene was achieved using an intramolecular approach.

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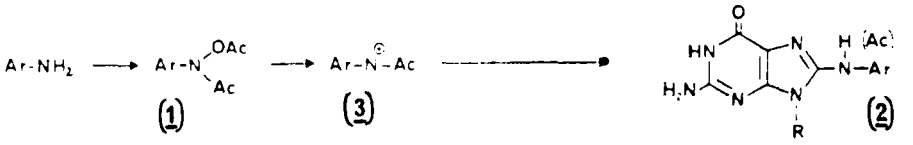
The mode of formation and the identification of the adducts formed in the reaction between chemical carcinogens and DNA is of major importance for the understanding of tumor formation. 2-Aminofluorene is frequently used as a model to study the mode of action of carcinogenic aromatic amines. Tumor initiation is thought to involve reaction between the intercalated metabolite N-2-acetylacetoxyaminofluorene (1) and DNA bases leading as a major product to the C-8 deoxyguanosine adduct (2)[1]. Such adducts are equally formed in very poor yields in the reaction of (1) with the nucleosides. Electrophilic attack of the guanine ring by a nitrenium ion species (3) generated from (1) is thought to be responsible[2] for the formation of (2), although clear mechanistic evidence is still largely missing.



(1) (3) (2)

In order 1/ to study this arylamidation reaction and the role of the complexation on the reaction and 2/ to develop a general preparative route to "nucleoside - carcinogen adducts", we devised an

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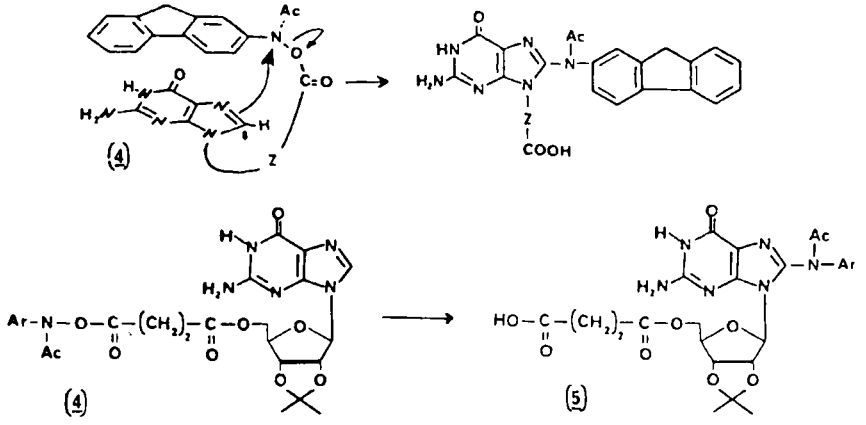
intramolecular approach which mimics both the base-carcinogen ring-ring stacking interaction in DNA[3] and the base-metabolite reaction.

Such models as (4) have been prepared. Intramolecular arylamidation of the guanine ring occurs by warming in different solvents. When the bridge Z incorporates the ribose moiety, the guanosine-carcinogen adduct (5) is thus synthetized.



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