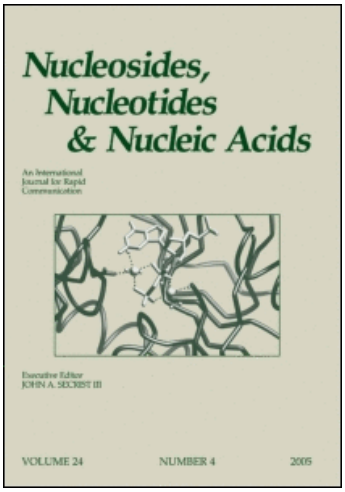

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Unexpected Transposition of a Deoxyguanosine Derivative

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UNEXPECTED TRANSPOSITION OF A DEOXYGUANOSINE DERIVATIVE

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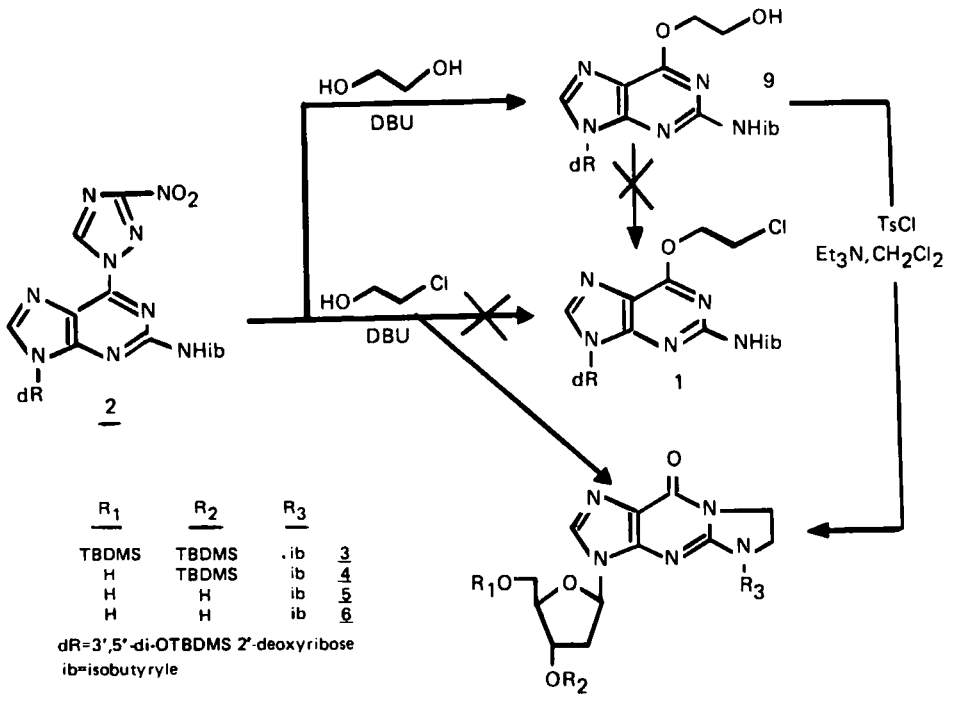
Abstract. The synthesis of a tricyclic deoxynucleoside by reaction of β-substituted ethanols with an activated deoxyguanosine is described. Its formation is rationnalised by an O^6-N^1-transposition.

During the course of our studies on crosslinked dinucleosides[1-2] we wished to prepare O^6-(2-chloroethyl)-deoxyguanosine (1) which is one of the principal promutagenic structures[3] involved in DNA crosslink formation. In principle the compound should be available through direct condensation of the activated deoxyguanosine derivative **2**[2] and chloroethanol, using DBU as strong base.

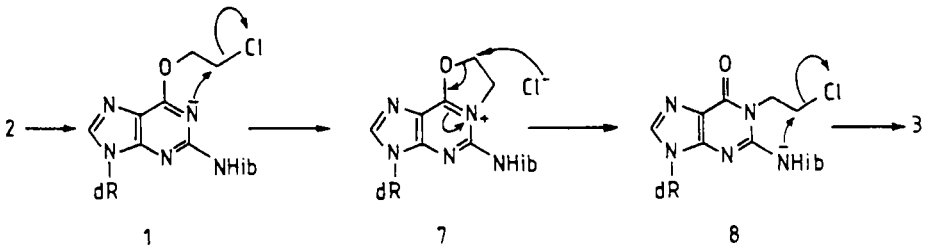
The reaction of 2 (Scheme I) with chloroethanol (3 equ.) in presence of DBU (2.7 equ.) in acetonitrile gave a disilylated nucleoside 3 (70% yield) which on deblocking yielded a new deoxynucleosidic compound 6. This compound was shown to be 3-(2-deoxy-β-D-*erythro*-pentofuranosyl)-5,6,7,9-tetrahydro-9-oxoimidazo [1,2-a]purine. The mass spectrometric data (FAB^+) gave MH^+ = 294, BH^+ = 178.

The problable mechanism of formation of 3 is depicted in Scheme II. Reaction of chloroethanol with the activated deoxyguanosine 2 would be expected to give O^6-(2-chloroethyl) derivative 1 which could rearrange through the postulated[4] oxazolidinium intermediate 7 to the N^1-(2-chloroethyl) derivative 8. Subsequent chlorine displacement by nucleophilic attack of the N^2 atom of deoxyguanosine would afford the protected $1,N^2$-ethanodeoxyguanosine 3. All attempts to isolate any of the postulated intermediates were unsuccessful.

It thus appears that under the conditions described above the O^6-(2-chloroethyl)deoxyguanosine derivative cannot be isolated by direct substitution of suitably activated deoxyguanosine with chloroethanol.



SCHEME 1



SCHEME 2

The presence of a good leaving group (*i.e.* Cl, OTs) on the substituted O^6-ethyl chain gives rise, through transposition, to the corresponding tricyclic nucleoside 6.

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