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## (5'R)- and (5'S)-5',8-cyclo-2'-deoxyguanosine lesions

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Diffusible hydroxyl radicals (HO•) are known to react with DNA either by hydrogen abstraction from the 2-deoxyribose units or by addition to the base moieties. The majority of HO• attacks occur at the base moieties. However, there is growing evidence that the oxidation of 2-deoxyribose in DNA plays a critical role in the genetic toxicology of oxidative stress and inflammation.

About the half of HO• attacks toward the sugar unit of DNA occurs at H5' with the formation of C5' radical, that gives an intramolecular attack to the C8 position of the purine base, generating a unique cyclic base-sugar adduct (purine 5',8-cyclo-2'-deoxynucleosides). These tandem-type lesions are observed among the DNA modifications [1,2].

Inspired by the mode of formation of these lesions, the diastereomeric forms (5'R and 5'S) of 5',8-cyclo-2'-deoxyguanosine have been synthesized and fully characterized, as well as their corresponding phosphoramidates. This approach facilitates the quantitative determination of such lesions in biological samples as biomarker of free radical damage and is propedeutic for preparation of modified oligonucleotides for biochemical/biophysical studies related to specific diseases and impairment of enzymatic repair.

Different oligonucleotides models which can occur in double strand and G-quadruplex structures are used to test the reactivity of hydroxyl radicals towards the sugar backbone of DNA. In this context, radiation-induced transformations have been considered in depth for the characterization of reaction intermediates by pulse radiolysis and the products formation by gamma-radiolysis.

[1] Chatgililoglu C, Ferreri C, Terzidis MA, Chem. Soc. Rev. 2011, 40, 1368–1382.

[2] Belmadoui N, Boussicault F, Guerra M, Ravanat JL, Chatgililoglu C, Cadet J, Org. Biomol. Chem. 2010, 8, 3211–3219.

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