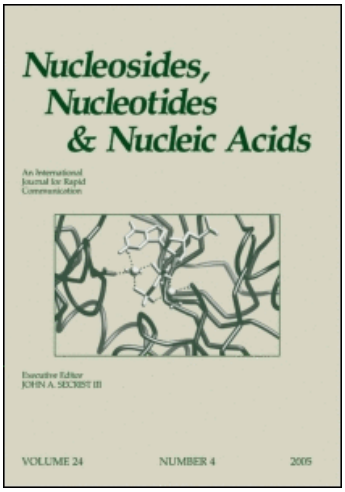

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Comparative Studies of the Electronic Structure of 2-Chloro-2'-Deoxyadenosine Studied by ^{35}CI-NQR Spectroscopy and Quantum Chemical Calculations

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To cite this Article Latosinska, J. N. , Kasprzak, J. , Bojarska, E. and Kazimierczuk, Z.(1999) 'Comparative Studies of the Electronic Structure of 2-Chloro-2'-Deoxyadenosine Studied by ^{35}CI-NQR Spectroscopy and Quantum Chemical Calculations', Nucleosides, Nucleotides and Nucleic Acids, 18: 4, 1075 — 1076
To link to this Article: DOI: 10.1080/15257779908041650
URL: http://dx.doi.org/10.1080/15257779908041650

NUCLEOSIDES & NUCLEOTIDES, 18(4&5), 1075–1076 (1999)

COMPARATIVE STUDIES OF THE ELECTRONIC STRUCTURE OF 2-CHLORO-2'-DEOXYADENOSINE STUDIED BY ^{35}Cl-NQR SPECTROSCOPY AND QUANTUM CHEMICAL CALCULATIONS

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ABSTRACT: Chlorine-35 NQR spectroscopy and quantum chemical calculations have been applied to provide detailed information on the structure and conformation of 2-chloro- 2'-deoxyadenosine and 2-chloroadenosine. The Gaussian package was used and the calculations were performed at the B3LYP level of the theory in the 6-31G* basis set.

2-chloro-2'-deoxyadenosine (2CldAdo, Cladribine) is an antileukemic agent widely used for the treatment of lymphoid malignancies[1-3]. This nucleoside differs from the naturally occurring deoxyadenosine by the chlorine atom substituted at the 2-position of the purine ring. The chemical and physical properties of 2CldAdo aroused great interest because of its promising medical applications. The ^{35}Cl-NQR spectroscopy can be used to provide detailed information on the structure and conformation of biologically active systems. It offers a possibility of determining the quadrupole coupling constants and consequently effective charges, and in this way allows a determination of the electronic structure of molecules.

The studied material were samples of 2CldAdo and 2-chloroadenine (2-ClAde) purchased from the Department of Biophysics, University of Warsaw and used without further purification. The spectra of the compounds studied, taken at 77K, show only one line which means that there are no chemically inequivalent positions of Cl atoms in their elementary cells, which is in a good agreement with the crystallographic data for

2CldAdo[4]. The NQR signals coming from Cl nuclei were very week (S/N=3 after 1000 accumulations). The ^{35}Cl-NQR frequencies are 34.05MHz and 33.99MHz 2CldAdo and 2-ClAde, respectively. The influence of the deoxyribose (N9 position) can be practically neglected, because the NQR frequency shift is very small and equal to 60kHz.

In this paper we present the results of new ab initio calculations at the B3LYP level using -31G* basis set for the NQR spectra of 2CldAdo and 2-ClAde. A comparison between the experimental and the calculated (at B3LYP level of the theory at 6-31G* basis set) NQR frequencies suggests that the dipole moment for 2CldAdo is higher than for 2-ClAde (as it is 5.45D and 4.63D, respectively) and the effective charge on chlorine nuclei is lower for 2CldAdo than for 2-ClAde (it is of -0.010e and -0.001e, respectively). The redistribution of electron density as a result of deoxyribose substitution first of all takes place at the nitrogen atoms; the effective charge on N9 and N7 decreases by 0.223e and 0.023e, respectively, whereas on N2 and N6 - by 0.007e. On the carbon atoms C5 and C6, the charge increases by 0.018e and 0.010e, respectively. The changes on the other atoms are negligibly small, which suggests the electron density transfer of about 0.341e in total, from the atoms of the ring towards deoxyribose.

The usefulness of NQR spectroscopy and quantum chemical calculations for the investigation of redistribution of electron density in 2CldAdo and 2-ClAde was assessed and a comparison of the electron distribution was made.

Acknowledgements

This work was supported by the Committee for Scientific Research (grant No. 4PO5F 027 12) which is gratefully acknowledged.

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