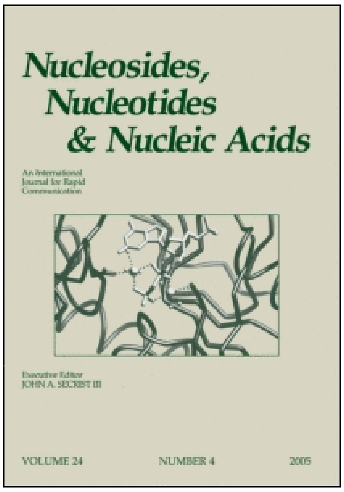

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Intermolecular Association of Deoxycytidylyl-(3',5')deoxy-guanosine and Thymidylyl-(3',5')-deoxyadenosine in Dimethylsulfoxide

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To cite this Article Barbarella, Giovanna , Tondelli, Luisa and Tugnoli, Vitaliano(1991) 'Intermolecular Association of Deoxycytidylyl-(3',5')deoxy-guanosine and Thymidylyl-(3',5')-deoxyadenosine in Dimethylsulfoxide', Nucleosides, Nucleotides and Nucleic Acids, 10: 1, 593 — 594

To link to this Article: DOI: 10.1080/07328319108046541

URL: http://dx.doi.org/10.1080/07328319108046541

NUCLEOSIDES & NUCLEOTIDES, 10(1-3), 593-594 (1991)

INTERMOLECULAR ASSOCIATION OF DEOXYCYTIDYLYL-(3',5')DEOXYGUANOSINE AND THYMIDYLYL-(3',5')-DEOXYADENOSINE IN DIMETHYLSULFOXIDE

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We have recently shown by nitrogen-15 and carbon-13 NMR in dimethylsulfoxide that, contrary to expectations, in the homodimer d(ApA) protonation of the phosphate group is competitive with protonation of the N1 nitrogen of adenine *(1)*.

In this communication we are presenting a multinuclear NMR study aimed to establish whether in the heterodimer d(TpA) the same competition exists and if this has any consequence on the capability of d(TpA) to self-associate according Watson and Crick. For comparison, a similar investigation was carried out on the other self-complementary heterodimer, d(CpG), for which we have already shown *(2)* that the relative basicities of N3(C), N7(G) and of the phosphate group are those expected on the basis of the pK values of the corresponding nucleosides and phosphate diester.

Carbon-13 and Nitrogen-15 chemical shift variations of d(TpA) upon addition of increasing amounts of CF3COOH in dimethylsulfoxide, show unambiguously that $pK_{N1(A)}$ (DMSO) $\sim$ pK_{PO4^-} (DMSO).

DMSO is a solvent with no exchangeable protons, in which stacking interactions are negligible and where hydrogen bondings between complementary bases may be monitored by proton NMR *(3)*. Thus, we measured the chemical shift variations of the amino and imino protons of d(CpG)and d(TpA) in this solvent in the concentration range 10^{-1}-10^{-4} M. We found that there are large downfield shifts of the amino and imino protons of d(CpG) as the concentration increases and that there is a linear dependence of the chemical shifts of the same protons on concentration. This behaviour indicates the formation of a one-to-one self-complementary Watson & Crick d(CpG)-d(CpG) complex *(3)*. By contrast, only minor chemical shift variations of the amino and imino protons of d(TpA) were found in the same concentration range, indicating that there is very small, if any formation of a one-to-one Watson & Crick self-associated complex. The relevant chemical shift variations of the amino and imino protons of d(CpG) and d(TpA) are reported in the following table:

Concentration dependence of the chemical shifts[a] of the amino and imino protons of d(CpG) and d(TpA) in DMSO

	d(CpG)			*d(TpA)*	
	NH(G)	NH2(G)	NH2(C)	NH2(A)	NH(T)
10^{-1} M	3394.6	2062.3	2222.6	2189.0	3401.5
10^{-4} M	3185.4	1970.7	2138.4	2170.1	3385.2

a) In Hz, at 300 MHz (Bruker CXP-300) with respect to TMS

We also found that, while in the 10^{-4} M solution of d(TpA) the hydroxyl protons of the ribose moieties, namely OH-3' and OH-5', are separately observed, progressive increase of concentration leads to the progressive broadening of the same protons, which are no more apparent in the spectrum of the 10^{-1} M solution. This phenomenon - which does not occur in d(CpG) in the same concentration range - is due to the hydrogen bonding of the hydroxyl protons to the phosphate group.

We conclude that, whereas in d(CpG) the strong basicity of N3(C) is the driving force for the formation of a one-to-one Watson & Crick self-complementary complex, in d(TpA) the lack of a similar strongly basic site leads to the predominance of other modes of intermolecular association, involving the hydroxyl protons and the phosphate group.

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