Structural analysis of the complex of a distamycin analogue with the Dickerson dodecamer $^{13}$C labeled at 5'-carbons using NMR spectroscopy

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ABSTRACT

Structural analysis of the complex of a distamycin analogue (Tallimustine) with the Dickerson dodecamer d(C*G*C*G*A*ATT*C*G*C*G) {N*: [5'-$^{13}$C]nucleotide} was performed by NMR spectroscopy and the results will be described in detail.

INTRODUCTION

Studies of the complexes of distamycin analogue with a variety of oligonucleotide have led feasible to design synthetic ligands which specifically recognize DNA sequence.

The $^1$H-NMR spectroscopic study of the complex of distamycin with the Dickerson dodecamer has been reported by Wemmer et al. Distamycin is an oligopeptide antibiotic that inhibits binding of RNA polymerase by binding to the minor groove of A-T rich initiation sites.

The complexes formed between such a drug including its analogues and various DNA oligomers have been used as model systems for the investigation of sequence-specific recognition and have thus been the subject of structural studies by NMR.

However, structural information on surrounded by H5' protons in a complex of these drug with DNA has not been obtained, because of the difficulty of the assignment for H5' proton signals. We have overcome this problem by NMR analysis of a complex of [5'-$^{13}$C]-d(C*G*C*G*A*ATT*C*G*C*G)$_2$ with distamycin analogue.

RESULTS

Development of the efficient methodology for the synthesis of ribonucleosides and 2'-deoxyribonucleosides site-specifically labeled with $^{13}$C at their 5'-positions from D-ribose prompted us to prepare the Dickerson dodecamer, d(C*G*C*G*A*ATT*C*G*C*G)$_2$ {N*: [5'-$^{13}$C]nucleotide}(1), and to conduct the structural analysis of 1 by NMR spectroscopy. The analysis provided us with the correlation between C5'(i)-C6H(i-1) or -C8H(i), the sequential NOEs of C5'(i)-C1'H(i-1), C5'(i)-C2'H(i-1), and C5'(i)-C2H(i-1), and unambiguous assignment of all the signals of C6H, C8H, C1'H, C2'H, C2'H, C3'H, C5', C5''H, and C4'H for the seven residues involved therein.
Based on these results, the spectroscopic analysis of the complex of 1 with distamycin analogue, \(N\)-desformyl-\(N\)-(4-(\(N\),\(N\)-bis-(2-chloroethyl)amino)-benzoyl)distamycin hydrochloride (Tallimustine) (2) (Figure 1) was conducted to elucidate the stereochemistry in the vicinity of each 5'-\(^{13}\)C involved therein.

![Figure 1](https://example.com/figure1.png)

Figure 1. \(N\)-desformyl-\(N\)-(4-(\(N\),\(N\)-bis-(2-chloroethyl)amino)benzoyl)distamycin hydrochloride (Tallimustine) (2)

Information obtained from our studies should aid in the investigation of sequence-specific DNA-protein or -drug recognition processes.

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**REFERENCES**


