A Calorimetric Investigation of the B to Z Transition in a Model DNA Oligonucleotide

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The importance in understanding the B to Z transition in DNA has led our group to study the thermodynamics involved in the transition. The NaCl induced B to Z transition of the poly(dC-dG), first reported by Pohl and Jovin, was found to be independent of temperature over the range of 30-50 C [1]. The van't Hoff analysis indicated that, under their conditions, the enthalpy of the B to Z transition was near zero. On the contrary, Chaires and Sturtevant [2] reported a reversible thermally-driven conversion of the polymer upon raising the temperature from 18 to 50 C and determined an enthalpy of 0.61 $\pm$ 0.07 kcal/mol base pair by differential scanning calorimetry for the B to Z transition of poly(5mdC-dG). Our research entails observing conformational changes and their thermodynamic parameters associated with two self-complementary model eight-base pair DNA oligomers, known as Z8A and Z8M. Both double-stranded DNA oligomers are studied under different concentrations of cobalt (III) hexamine chloride and NaCl in order to observe any conformational differences. Isothermal titration calorimetry (ITC) allows a direct and sensitive determination of the transition enthalpy, and provides a significant advantage over methods based on the indirect van't Hoff analysis. Circular Dichroism and UV/Vis spectroscopies allow us to determine the conformational traits at different conditions. Both duplexes assume right-handed conformations under conditions of "low salt" while only Z8M undergoes the B to Z conformational transition under "high salt" conditions. The titration of Z8M with NaCl is more endothermic than that of Z8A while the titration ob Z8A with cobalt hexamine is more exothermic than that of Z8M. We attribute the difference to the enthalpy of the transition. The information obtained allows us to depict an accurate thermodynamic cycle associated with the B to Z transition and the Z to B transition by independent methods. The influence of temperature and the presence of an osmolyte on the transition enthalpy were also investigated. The results of these studies will be reported and discussed.

[1] Pohl, F. M., Jovin, T. M. *J. Mol. Biol.,* **67**, 375-396 (1972).
[2] Chaires, J. B., Sturtevant, J. M., *Proc. Natl. Acad. Sci. USA,* **83**, 5479-5483 (1986).