

IONIC LIQUID-HAIRPIN DNA CONJUGATES AS STIMULI RESPONSIVE MATERIALS

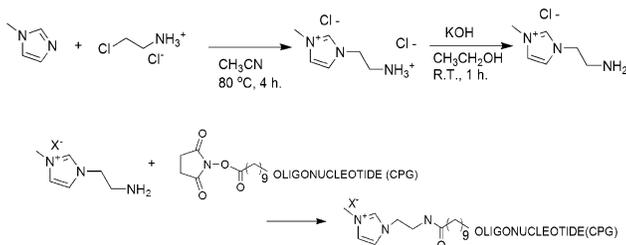
RESULTS

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INTRODUCTION

Stimuli-responsive materials are expected to play a major role in nanoscience by providing dynamic scaffolds that may be used to control energy transfer and signal transduction. In this work we describe our efforts to prepare soft, temperature-responsive, self-assembled nanostructures based on the conjugation of an oligonucleotide with a dialkylimidazolium ionic liquid (IL). This work builds upon our prior work that demonstrated that methyldecylimidazolium ILs can be organized into a variety of self-assembled 1D, 2D and 3D nanostructures[1,2] by making these scaffolds stimuli-responsive and biocompatible. This has been achieved by coupling a self-complementary (or “hairpin”) oligonucleotide sequence to methylaminoethylimidazolium chloride ([MeIMEtNH₂]⁺ [Cl]⁻). The oligonucleotide will impart the ability to undergo reversible conformational changes to the self-assembled material triggered by a variety of stimuli, including temperature and pH. Specifically, increasing temperature is expected to disrupt the base pairing within the oligonucleotide sequence (dehybridization), causing it to increase in molecular length and expanding the self-assembled ionic-liquid-derived physical gel.

EXPERIMENTAL



Scheme 1: Synthesis of imidazolium ionic liquid and coupling to oligonucleotide

The synthesis of the [MeILEtNH₂]⁺ [Cl]⁻ - oligonucleotide hybrid is shown in scheme 1. The synthesis of [MeIMEtNH₂]⁺ [Cl]⁻ was based on previously reported literature methods [3]. In brief, 2-chloroethylammonium chloride was heated with 1-methylimidazole producing a viscous, phase separated material, and the ammonium moiety was neutralized in a reaction with potassium hydroxide. The [MeIMEtNH₂]⁺ [Cl]⁻ was then coupled to the hairpin oligonucleotide (5'-GGATACTT TTGTATCC-3') modified with a C₁₀-NHS ester linker on solid support. The resulting oligonucleotide-IL hybrid was analyzed *via* mass spectrometry, HPLC, differential scanning calorimetry (DSC) and small-angle X-ray scattering (SAXS).

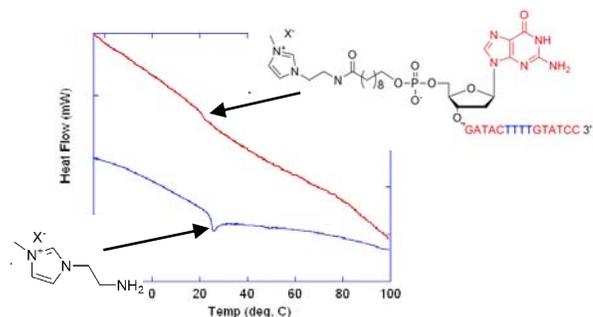


Figure 1: Comparison of differential scanning calorimetry of imidazolium ionic liquid in the presence and absence of hairpin oligonucleotide

Once the oligonucleotide-IL coupling via amide bond formation was shown to be successful, characterization of the material was undertaken. The oligonucleotide-IL conjugate was shown (via DSC) to possess a low melting point. Comparison of the oligonucleotide-IL hybrid material with the unmodified IL revealed both materials to have a melting point approximately 35 °C (figure 1). The minimal difference in the two materials suggests the addition of the DNA moiety does not interfere with the innate characteristics of the IL.

Polarized light microscopy revealed birefringence, indicating formation of a mesoscopic liquid crystalline phase upon addition of water, suggesting the oligonucleotide modified [MeIMEtNH₂]⁺ [Cl]⁻ is capable of self assembly. We are currently investigating the effect of diluting the oligonucleotide -IL hybrid with analogous ionic liquids not modified with oligonucleotide on the self assembly characteristics of the hybrid material through SAXS.

REFERENCES

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- 2 Batra, D., Hay, D.N.T., Firestone, M.A., *Chem. Mater.*, **2007**, *19*, 4423
- 3 Cai, Y., Peng, Y., and Song, G., *Cat. Lett.*, **2006**, *109*, 61

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