Ternary Electrocatalysts for Oxidizing Ethanol to Carbon Dioxide: Making It Capable of Splitting C-C Bond

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Supporting Information

ARTICLE: Splitting the C-C Bond in the scarb alcohol-to-carbon dioxide electrolysis.- Supporting Information is available for this article, in the on-line version, at http://dx.doi.org/10.1021/jacs.5b01234

Additional experimental details as well as supplementary figures and tables are available in the Supporting Information.

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Groove Binding Mechanism of Ionic Liquids: A Key Factor in Long-Term Stability of DNA in Hydrated Ionic Liquids?

Aneesh Chandran, Debostuti Ghoshdastidar, and Sanjib Senapati

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Figure 1 of 10
Groove Binding Mechanism of Ionic Liquids: Term Stability of DNA in Hydrated Ionic Liquids

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ABSTRACT: Nucleic acid sample storage is of paramount importance in biotechnology and forensic sciences. Very recently, hydrated ionic liquids (ILs) have been identified as ideal media for long-term DNA storage. Hence, understanding the binding characteristics and molecular mechanism of interactions of ILs with DNA is of both practical and fundamental interest. Here, we employ molecular dynamics simulations and spectroscopic experiments to unravel the key factors that stabilize DNA in hydrated ILs. Both simulation and experimental results show that DNA maintains the native B-conformation in ILs. Simulation results further suggest that, apart from the electrostatic association of IL cations with the DNA backbone, groove binding of IL cations through hydrophobic and polar interactions contributes significantly to DNA stability. Circular dichroism spectral measurements and fluorescent dye displacement assay confirm the intrusion of IL molecules into the DNA minor groove. Very interestingly, the IL ions were seen to disrupt the water cage around DNA, including the spine of hydration in the minor groove. This partial dehydration by ILs likely prevents the hydrolytic reactions that denature DNA and helps stabilize DNA for the long term. The detailed understanding of IL–DNA interactions provided here could guide the future development of novel ILs, specific for nucleic acid solutions.

1. INTRODUCTION

DNA, apart from being a natural biological information carrier, utilizes the basic natural principles of anhydrobiosis, is becoming a more attractive alternative to the conventional cold storage of DNA.
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1. INTRODUCTION

DNA, apart from being the fundamental information carrier, has also been recognized as a component in pharmaceutical and forensic realms and in the development of advanced molecular diagnostics. For example, it has been reported that DNA vaccination confers protective immunity against anthrax; however, the practicality of this approach utilizes the basic principles of anhydrous DNA, which is becoming more attractive as an alternative to the conventional cold storage of DNA. Nonetheless, there is a continuous quest to develop suitable media for long-term preservation of DNA.

Ionic liquids (ILs) have found a wide range of applications in various fields, including organic synthesis, extraction/separa-
1. DNA vaccines: ready for prime time?

Kutzler, Michele A.; Weiner, David B.


A review. In the past 16 years, there has been much excitement in the area of DNA vaccine development for a range of medical conditions. The recent licensure of DNA vaccines for veterinary use bodes well for applications in humans, in which progress has been slower. Since the discovery, over a decade and a half ago, that genetically engineered DNA can be delivered in vaccine form and elicit an immune response, there has been much progress in understanding the basic biology of this platform. A large amount of data has been generated in preclinical model systems, and more sustained cellular responses and more consistent antibody responses are being observed in the clinic. Four DNA vaccine products have recently been approved, all in the area of veterinary medicine. These results suggest a productive future for this technology as more optimized constructs, better trial designs and improved platforms are being brought into the clinic.

1. INTRODUCTION

DNA, apart from being a natural biological information carrier, has also been recognized as a key component in pharmaceutical and forensic realms and a crucial material in the development of advanced molecular devices. For example, it has been reported that DNA vaccination confers protective immunity against viral infection. DNA vaccines are rapidly emerging as a potential replacement for traditional vaccine approaches that utilize the basic natural principles of antibody production, becoming a more attractive alternative to the traditional cold storage of DNA. Nonetheless, there is an urgent need to develop suitable methods for long-term preservation of DNA.

Ionic liquids (ILs) have found applications in various fields, including recent drug delivery systems. ILs are highly viscous, weakly polar, and strongly ionic media that are immiscible with water and most solvents. They are unique in their ability to stabilize DNA structures and enhance the delivery of nucleic acids.
1. INTRODUCTION

DNA, apart from being a natural biological information carrier, has also been recognized as a key component in pharmaceutical and forensic realms and a crucial material in the development of advanced molecular devices. For example, it has been reported that DNA vaccination confers protective immunity against specific infectious diseases. Ionic liquids (ILs) utilize the basic natural principles of anhydriosis, is becoming a more attractive alternative to the conventional cold storage of DNA. Nonetheless, there is a continuous quest to develop suitable media for long-term preservation of DNA.

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1. INTRODUCTION

DNA, apart from being a natural biological information carrier, utilizes the basic natural properties of DNA, becoming a more attractive agent for cold storage of DNA. Nonetheless...
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1. INTRODUCTION

DNA, apart from being a natural biological information carrier, has also been recognized as a key component in pharmaceutical and forensic realms and a crucial material in the development of advanced molecular devices. For example, it has been reported that DNA vaccination confers protective immunity against certain diseases. ILs, with their ability to utilize the basic natural principles of anhydrotroisolation, is becoming a more attractive alternative to the conventional cold storage of DNA. Nonetheless, there is a continuous quest to develop suitable media for long-term preservation of DNA.

Ionic liquids (ILs) have found a wide range of applications in various fields, including organic synthesis, extraction/separation, and act as potential media for storage of nucleic acids. However, despite the potential of ILs, limited information exists on the molecular mechanism of IL-DNA interactions. We have previously reported the importance of ILs as a suitable storage media for DNA. Here, we report the mechanism of IL-DNA interactions at a molecular level using various computational and experimental tools.
Figure 1. (a) Radial distribution functions (RDFs) of IL ions in different DNA regions. Color scheme: cation—phosphate, brown; cation—major groove, magenta; cation—minor groove, blue; anion—phosphate, green; anion—major groove, red; anion—minor groove, black. The following sites were considered for calculating the RDFs: center-of-mass (COM) of the imidazolium ring for the cation, Cl− for the anion, P for the phosphate group, electron negative sites N3 and O2 of cationic carbon atoms (either C2 or C3 and C4) pointing toward the bases. In this orientation, the C–H of the imidazolium ring forms hydrogen bonds with the acceptor groups in the nucleotides. However, the geometries of these hydrogen bonds were found to depart significantly from linearity since, in most cases, these interactions involved three sites. For example, a three-centered bifurcated H-bond was seen to be prevalent between C–H and the pair of adenine N3 and thymine O2 or between C–H and the pair of adenine N3 and cytosine O2. Some of these three-centered hydrogen bonds formed a bridge between the bases and ribose sugars of the two opposite DNA strands through the electrostatic sites in bases and O4′ atom in riboses. Three-centered hydrogen bonds were also observed for the bases and riboses of the same strand (Figure S4c, Supporting Information). Such an intrusion of [BMIM]⁺ cations into the DNA minor groove and their mode of interactions resemble the binding of known DNA minor groove binders DAPI, netropsin, distamycin, etc. Table S2 (Supporting Information) lists the occurrences (%) of these hydrogen bonds. As the table indicates, the IL cations spend more time with adenine and cytosine with average occurrences of H-bonds of > 60%. Such a preferential H-bonding was also noted for many known minor groove binders. The presence of the bulky −NH₂ group makes guanine the least accessible H-bond partner. Owing to the perpendicular orientation of [BMIM]⁺ cations with respect to the groove bases, cationic carbon atoms on the opposite face of the imidazolium ring (i.e., C3 and C4 when C2 is hydrogen bond to bases and vice versa) are exposed to the bulk and form H-bonds with water. The proximity and parallel facing of the alkane groups of [BMIM]⁺ cations to the ribose sugar rings imply the possible existence of weak CH⋯π interactions as well.

Overall, the results from Figures 1 and S3 and S4 (Supporting Information) indicate that, irrespective of the concentration of our model IL in solution, a certain fraction of IL cations always enter the DNA minor groove. The finding was further strengthened by simulating two different sequences of the DNA dodecamer (S'−d(GCAAACGTTTGC),S) and S'−d(GCGCGCGCGCGC),S) with [BMIM]Cl solutions.
Figure 1. (a) Radial distribution functions (RDFs) of IL ions in different DNA regions. Color schemes: cation—phosphate, brown; cation—major groove, magenta; cation—minor groove, blue; anion—phosphate, green; anion—major groove, red; anion—minor groove, black. The following sites were considered for calculating the RDFs: center-of-mass (COM) of the imidazolium ring for the cation, C1' for the anion, P for the phosphate group, electronegative sites N3 and O2, cationic carbon atoms (either C2 or C3 and C4) pointing toward the bases. In this orientation, the C—H of the imidazolium ring forms hydrogen bonds with the acceptor groups in the nucleotides. However, the geometries of these hydrogen bonds were found to depart significantly from linearity since, in most cases, these interactions involved three sites. For example, a three-centered bifurcated H-bond was seen to be prevalent between C—H and the pair of adenine N3 and thymine O2 or between C—H and the pair of adenine N3 and cytosine O2. Some of these three-centered hydrogen bonds formed a bridge between the bases and ribose sugars of the two opposite DNA strands through the electronegative sites in bases and O4' atom in riboses. Three-centered hydrogen bonds were also observed for the bases and riboses of the same strand (Figure S4c, Supporting Information). Such an intrusion of [BMIM]⁺ cations into the DNA minor groove and their mode of interactions resemble the binding of known DNA minor groove binders, e.g., distamycin, etc. Table S2 (Supporting Information) indicates the IL cations spend more time with a preference of guanine with average occurrences (%) of these hydrogen bonds. The presence of the bulky—ND4 group makes guanine the least accessible H-bond partner, owing to the perpendicular orientation of [BMIM]⁺ cations with respect to the groove bases, cationic carbon atom on the opposite face of the imidazolium ring (i.e., C3 and C4 when C2 is hydrogen bonded to bases and vice versa) are exposed to the bulk and form H-bonds with water. The proximity and parallel facing of the alkane groups of [BMIM]⁺ cations to the ribose sugar rings imply the possible existence of weak CH···π interactions as well.

Overall, the results from Figures 1 and S3 and S4 (Supporting Information) indicate that, irrespective of the concentration of our model IL in solution, a certain fraction of IL cations always enter the DNA minor groove. The finding was further strengthened by simulating two different sequences of the DNA dodecamer (5' d(GCAAAAGTTCG)₂ 3') and 5' d(GCAAAAGTTCG)₂ 3'.
Figure 1. (a) Radial distribution functions (RDFs) of IL ions in different DNA regions. Color scheme: cation—phosphate, brown; cation—major groove, magenta; cation—minor groove, blue; anion—phosphate, green; anion—major groove, red; anion—minor groove, black. The following sites were considered for calculating the RDFs: center-of-mass (COM) of the imidazolium ring for the cation, Cl− for the anion, P for the phosphate group, electron-dense sites N3 and O2 of cationic carbon atoms (either C2 or C3 and C4) pointing toward the bases. In this orientation, the C−H of the imidazolium ring forms hydrogen bonds with the acceptor groups in the nucleotides. However, the geometries of these hydrogen bonds were found to depart significantly from linearity since, in most cases, these interactions involved three sites. For example, a three-centered bifurcated H-bond was seen to be prevalent between C−H and the pair of adenine N3 and thymine O2 or between C−H and the pair of adenine N3 and cytosine O2. Some of these three-centered hydrogen bonds formed a bridge between the bases and ribose sugars of the two opposite DNA strands through the electronegative sites in bases and O4′ atom in riboses. Three-centered hydrogen bonds were also observed for the bases and riboses of the same strand (Figure S4c, Supporting Information). Such an intrusion of [BMIIM] cations into the DNA minor groove and their mode of interactions resemble the binding of known DNA minor groove binders DAPI, netropsin, distamycin, etc.34,35 Table S2 (Supporting Information) lists the occurrences (%) of these hydrogen bonds. As the table indicates, the IL cations spend more time with adenine and cytosine with average occurrences of H-bonds of >60%. Such a preferential H-bonding was also noted for many known minor groove binders.39 The presence of the bulky −NH2 group makes guanine the least accessible H-bond partner. Owing to the perpendicular orientation of [BMIIM] cations with respect to the groove bases, cationic carbon atoms on the opposite face of the imidazolium ring (i.e., C3 and C4 when C2 is hydrogen bonded to bases and vice versa) are exposed to the bulk and form H-bonds with water. The proximity and parallel facing of the alkane groups of [BMIIM] cations to the ribose sugar rings imply the possible existence of weak CH⋯π interactions as well.

Overall, the results from Figures 1 and S3 and S4 (Supporting Information) indicate that, irrespective of the concentration of our model IL in solution, a certain fraction of IL cations always enter the DNA minor groove. The finding was further strengthened by simulating two different sequences of the DNA dodecamer (5′−d(GCCACCGTTGCG)−3′ and 5′−d(GCCACCGTTGCG)−3′).
Figure 1. (a) Radial distribution functions (RDFs) of IL ions in different DNA regions. Color scheme: cation—phosphate, brown; cation—major groove, magenta; cation—minor groove, blue; anion—phosphate, green; anion—major groove, red; anion—minor groove, black. The following sites were considered for calculating the RDFs: center-of-mass (COM) of the imidazole ring for the cation, C1’ for the anion, P for the phosphate group, electronegative sites N3 and O2 for the minor groove, and electronegative sites N7, O6, and O4 for the major groove.
cationic carbon atoms (either C2 or C3 and C4) pointing toward the bases. In this orientation, the C−H of the imidazolium ring forms hydrogen bonds with the acceptor groups in the nucleotides. However, the geometries of these hydrogen bonds were found to depart significantly from linearity since, in most cases, these interactions involved three sites. For example, a three-centered bifurcated H-bond was seen to be prevalent between C−H and the pair of adenine N3 and thymine O2 or between C−H and the pair of adenine N3 and cytosine O2. Some of these three-centered hydrogen bonds formed a bridge between the bases and ribose sugars of the two opposite DNA strands through the electronegative sites in bases and O4′ atom in riboses. Three-centered hydrogen bonds were also observed for the bases and ribose of the same strand (Figure S4c, Supporting Information). Such an intrusion of [BMIM]⁺ cations into the DNA major groove and their mode of interactions resemble the binding of known DNA minor groove binders DAPI, metoprolol, distamycin, etc.³¹,³² Table S2 (Supporting Information) lists the occurrences (%) of these hydrogen bonds. As the table indicates, the IL cations spend more time with adenine and cytosine with average occurrences of H-bonds of >60%. Such a preferential H-bonding was also noted for many known minor groove binders.³¹ The presence of the bulky −NH₂ group makes the [BMIM]⁺ cations a possible H-bond partner. Only C2 carbon atoms of [BMIM]⁺ cations are in contact with cationic carbon atoms on the opposite face of the imidazolium ring (i.e., C3 and C4 when C2 is hydrogen bonded to bases and vice versa) are exposed to the bulk and form H-bonds with water. The proximity and parallel facing of the alkane groups of [BMIM]⁺ cations to the ribose sugar rings imply the possible existence of weak CH−π interactions as well.

Overall, the results from Figures 1 and S4 and Table S2 (Supporting Information) indicate that, regardless of the concentration of our model IL in solution, a considerable...
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