Evaluation of novel one-electron reduction with metal in DNA

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ABSTRACT

Indium(0) is known to work as a good one-electron reductant with a small first ionization potential. Additionally, this metal is very stable in aqueous media. Therefore, indium has a bright prospect of developing a new method for the site-selective reduction of biopolymers. In this paper, the reduction of 5-halouracils with indium in aqueous solution is reported. We prepared four halouracils, i.e., 5-fluorouracil, 5-chlorouracil, 5-bromouracil, and 5-iodouracil, and evaluated their reduction with indium in water. Incubation of 5-bromouracil and 5-iodouracil with sonication in the presence of indium efficiently caused dehalogenation to uracil. Natural nucleobases (G, A, C, T and U) were not damaged by indium under the same reaction condition.

INTRODUCTION

Radical generation is one of the significant events in organisms because radical damages to biomolecules can be etiopathogenesis or carcinogenesis.¹,² The control of radical generation is expected to contribute to the further understanding of the radical behavior on biomolecules and to make possible to site-selectively incorporate functional molecules into biomolecules.

Homolysis caused by light irradiation in the presence of photosensitizers is well known as the manner of the effective radical generation on biomolecules. Hydrogen abstraction by oxygen or superoxide is also one of naturally occurring radical-generating reactions. However, several reagents and stimulations are simultaneously required for the radical generation, and it is not easy to regulate reaction sites or reactivities for suppressing side reactions.

Indium(0) has the approximately same first ionization potential as alkaline or alkaline earth metals (Table 1), and acts as an effective electron donor. It is noteworthy that indium metal shows high stability in an aqueous solution and efficiently provides one electron to electron acceptors. Several significant radical reactions with indium in an aqueous phase, such as Barbier-like allylation, dehalogenation, and reduction of disulfide, have been reported earlier.³,⁴ Therefore, this unique metal would be effective and useful for the site-selective reduction of biomolecules.

<p>| Table 1. First ionization potentials of several metals. |</p>
<table>
<thead>
<tr>
<th>Metals</th>
<th>In</th>
<th>Na</th>
<th>Li</th>
<th>Sn</th>
<th>Mg</th>
<th>Zn</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. P. (eV)</td>
<td>5.79</td>
<td>5.12</td>
<td>5.39</td>
<td>7.43</td>
<td>7.65</td>
<td>9.39</td>
</tr>
</tbody>
</table>

Scheme 1

Herein, we report the reduction of 5-halouracils with indium. We investigated the reaction efficiencies of 5-halouracils by incubation with sonication in the presence of indium metal in water. Indium showed high reactivity to 5-bromouracil and 5-iodouracil, which were converted efficiently into uracil.

RESULTS AND DISCUSSION

We prepared four 5-halouracils, i.e. fluorouracil, chlorouracil, bromouracil, and iodouracil, for investigation of their reactivity in the presence of indium(0) in aqueous solutions (Scheme 1). Indium powder was added to a solution of halouracil in water, and the resulting suspension was incubated with sonication at room temperature. Consumption of halouracil was monitored with HPLC (Figure 1). Consumption of 5-fluorouracil and 5-chlorouracil was negligible in 24 h, showing that they have very low reactivity for indium metal. In contrast, 5-bromouracil was consumed in the presence of indium metal (t1/2 = 7.5 h). In HPLC profile, a new peak appeared with decrease in the peak of 5-bromouracil. The new product was collected and analyzed with ESI mass spectroscopy. The product was identified as a uracil base, showing that dehalogenation via one-electron reduction occurred in the reaction mixture. Additionally, 5-iodouracil was more rapidly converted into uracil (t1/2 = 4.5 h). On the other hand, we did not observe any consumption of five natural nucleobases, i.e. guanine, adenine, cytosine, thymine, and uracil under the same reaction condition. Therefore, one-electron reduction with indium metal occurs only for artificially brominated or iodinated uracil. These results
suggest that the site-selective radical generation on DNA without any degradation of other natural DNA bases would be possible using indium reduction of 5-halouracils.

CONCLUSION

In conclusion, indium(0) acted as an efficient reductant for halouracils in aqueous media. 5-Bromouracil and 5-iodouracil were effectively converted into uracil via one-electron reduction by indium powder. In addition, indium was not reactive for natural nucleobases. The reduction with indium metal in aqueous media can be a powerful tool for further understanding of radical behaviors in biomolecules.

REFERENCES


