Mechanistic Studies for the Cyclization of 
t-Amine Substituted Anilines and Their Utilization to the 
Synthesis of Pyrrolo[1,2-a]benzimidazoquinone Derivatives

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ABSTRACT. A few t-amine substituted anilines and amidines were synthesized and cyclized to pyrrolo[1,2-a]benzimidazole by heating in various solvents having different polarity. Subsequent nitration of cyclized compound followed by reduction and oxidation of resulting amine afforded quinone such as 7 in 14% yield. The formation of imidazole moiety by thermal cyclization was independent on the solvent polarity. The regiochemistry for the nitration of 4 was unambiguously determined by chemical transformation.

INTRODUCTION

Previous works in this laboratory have shown that pyrrolo[1,2-a]benzimidazoquinone derivatives can be synthesized by cyclization of t-amine substituted aniline derivatives. The importance of the synthesis and studies of the quinone bearing heterocycles were well documented in conjuction with the design of bioreductive alkylating agents. The reductive alkylating agents are usually quinones functionalized with leaving groups so as to permit quinone methide formation upon reduction followed by elimination of leaving group. Since tumor cell generally possesses a low reduction potential which could stabilize electron rich hydroquinone, it has been great interests toward reductive alkylating quinones as selective antitumor agents. So it is worthwhile to synthesize and study the characteristics of quinone bearing heterocyclic compounds.

In these juncture, we report a synthesis of pyrrolo[1,2-a]benzimidazole-5,8-diones and their reduced analogues as a precursor of reductive alkylating quinones. Also a mechanistic studies for the formation of imidazole moiety by cyclization of t-amine substituted aniline are presented.

Only a few pyrrolo[1,2-a]benzimidazoles have been synthesized and studied previously. In spite of the fact that such compounds participate in the reductive alkylaion in various biological system, there were not much focuses regarding the