Toward Total Synthesis of Asteropusazole A.

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Introduction

Biologically active carbazole alkaloids have been extensively studied over the past century and among the reported ways of synthesizing this scaffold, the easiest one is probably the construction of the central pyrrole ring via diarylamines or *ortho*-nitrogen substituted biphenyls.[1] Indolo[3,2-*a*]carbazoles, received less attention and only a few molecules with this framework have been reported to date (Figure 1).[2,3] The nonlinear scaffold shows antimicrobial and potential neurological activities.[4] Recently, a total synthesis of Asteropusazole A (**1**) has been achieved using a benzannulation of indole through rearrangement of *t*-butylperoxyde.[5] Herein we describe our efforts to the total synthesis of indolo[3,2-*a*]carbazole **1**.

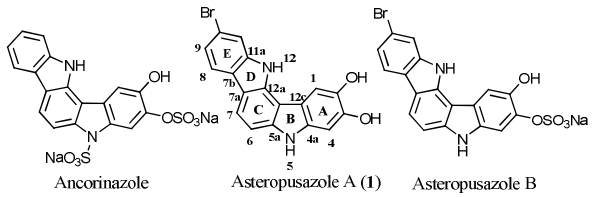

Figure 1. Natural indolo[3,2-*a*]carbazoles reported to date.

Results and Discussion

The retrosynthetic analysis for compound **1** is shown in Figure 2.

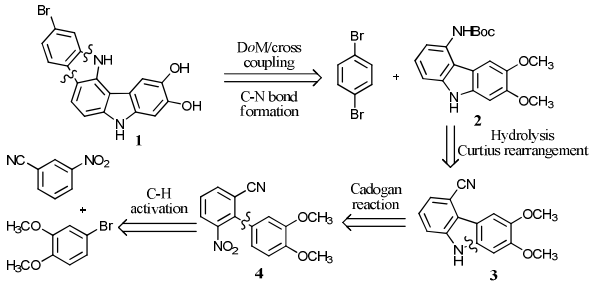

Figure 2. Retrosynthetic analysis of natural product **1**.

The synthesis commenced with the construction of carbazole **3** from commercially available nitrile **5** and bromide **6** via a Pd-catalyzed C-H activation coupling followed by a Cadogan reaction. After hydrolysis of the nitrile in **3**, the carboxylic acid **7** underwent a Curtius rearrangement, affording compound **2** in reasonable yields (Figure 3).

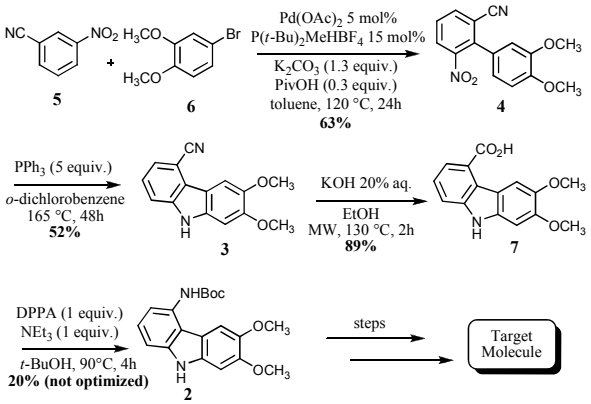

Figure 3. Synthesis of intermediates **4**, **3** and **2**.

Next, intermediate **2** will undergo a D*o*M/Borylation/Suzuki coupling strategy followed by a Pd-catalyzed *N*-tosy-directed C-N bond formation reaction. Compound **1** will be achieved after global deprotection using BBr_3.

Conclusion

We have developed so far an efficient strategy to construction of intermediate **2**. Further steps to the natural product total synthesis are under study in our laboratory.

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