Study toward the convergent total synthesis of the aporphine alkaloid PO-3

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INTRODUCTION

Due to the great importance of benzyne as a highly reactive intermediate in organic chemistry, with applications in total syntheses and in preparations of functional materials, we intend to accomplish the convergent total synthesis of the aporphine alkaloid PO-3 (1), a natural dye of green color, employing as key reaction a [4+2] cycloaddition between 1-methylene-1,2,3,4-tetrahydroisoquinoline (3) and the benzyne derivative 7, formed from 2-(trimethylsilyl)aryl triflate (8), under mild reaction conditions.

RESULTS AND DISCUSSION

Attracted by the dye property of the aporphine alkaloid PO-3 (1), we decide to perform the total synthesis of the mentioned natural product of green color, employing a convergent synthetic route. Thus, according to the retrosynthetic analysis, the alkaloid PO-3 (1) can be obtained by functional group transformations from the intermediate 2, which can be produced by the [4+2] cycloaddition reaction between 1-methylene-1,2,3,4-tetrahydroisoquinoline (3) and 2-(trimethylsilyl)aryl triflate (8), followed by a spontaneous dehydrogenation process (Scheme 1).

Scheme 1. Retrosynthetic analysis for the alkaloid PO-3 (1).

Guided by the retrosynthetic analysis outlined in Scheme 1, we started the synthesis to obtain the dye PO-3 (1), by the preparations of 1-methylene-1,2,3,4-tetrahydroisoquinoline (3) (fragment A) and of the silylaryl triflate 8 (fragment B), which were obtained in good yields (Scheme 2).

Scheme 2. Synthetic route for the alkaloid PO-3 (1).

Afterwards, compound 3 was subjected to the [4+2] cycloaddition reaction with the arylene precursor 8, resulting in the highly regioselective formation of the intermediate 12 in 40% yield, which contains the basic structure of the alkaloid PO-3 (1). However, to our surprise, the process of spontaneous dehydrogenation did not occur. After optimizing the reaction which leads to the intermediate 12, we intend to obtain the alkaloid PO-3 (1) by reactions described in the literature (Scheme 2).

CONCLUSION

Fragments A and B were obtained by reactions that presented high yields. Compounds 3 and 8 are going to be used in the optimization of the [4+2] cycloaddition reaction, i.e., the key step for the convergent synthesis of the aporphine alkaloid PO-3 (1).

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REFERENCES


