INVESTIGATION OF AN ORIGINAL STRATEGY FOR THE SYNTHESIS OF KINGIANINS

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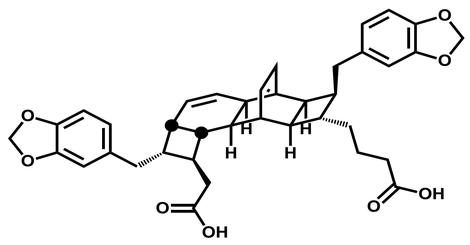
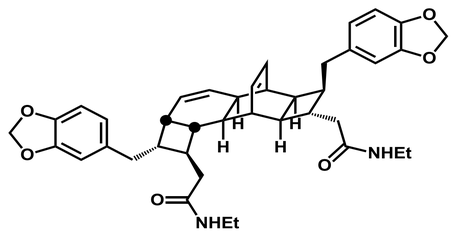
INTRODUCTION

The kingianins are a family of inhibitors of the antiapoptotic protein Bcl-xL, isolated from the bark of *Endiandra kingiana*.[1] In this subject, we propose a solution to the problems of regioselectivity in the key step – a Diels-Alder reaction: use an enone (a dienophile) and a diene to replace the use of two dienes in the syntheses of Parker[2] and Sherburn[3].

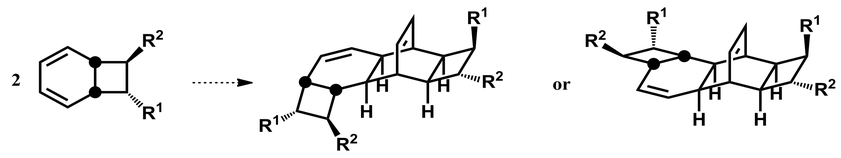


kingianine G
the most active compound of kingianins

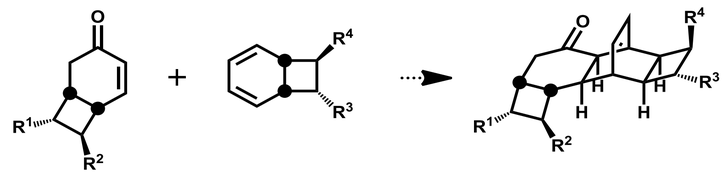


kingianin A
the major compound of kingianins

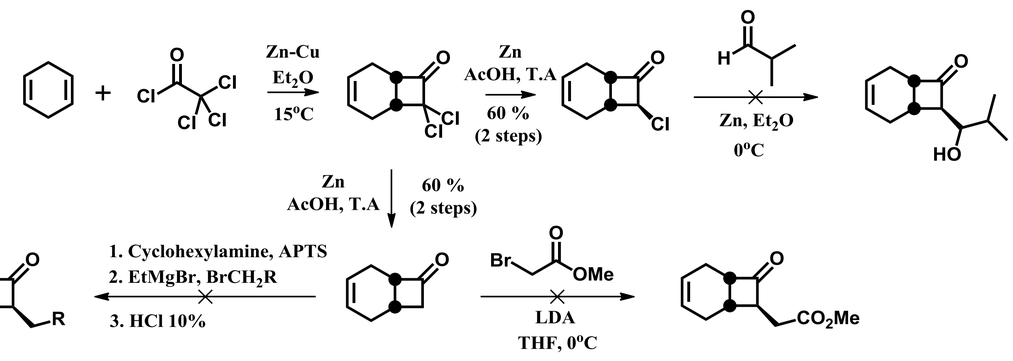
PROBLEM OF SELECTIVITY



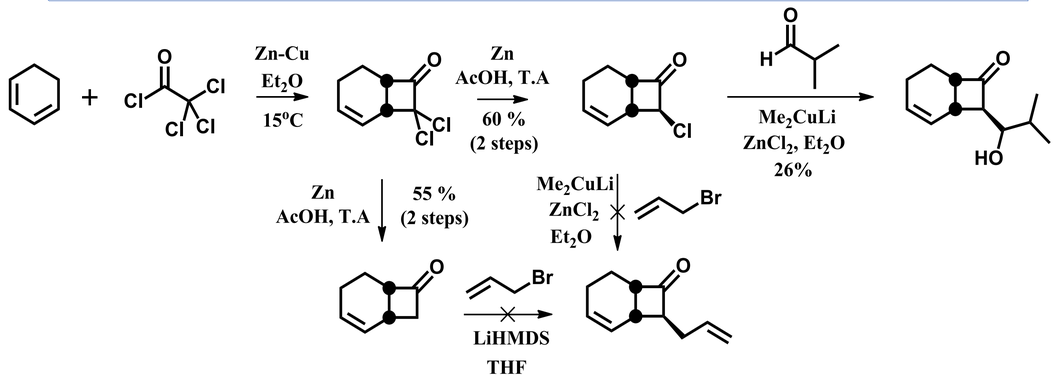
STRATEGY



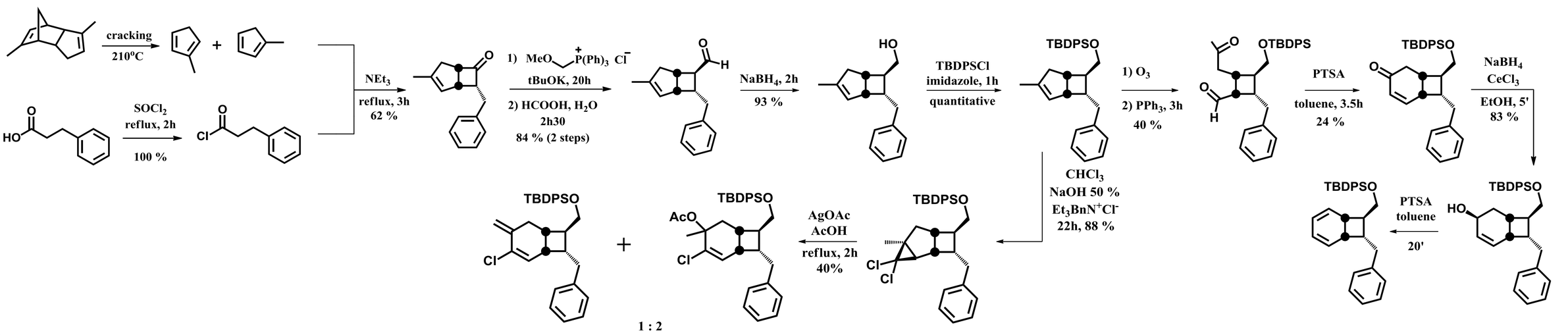
PATHWAY 1



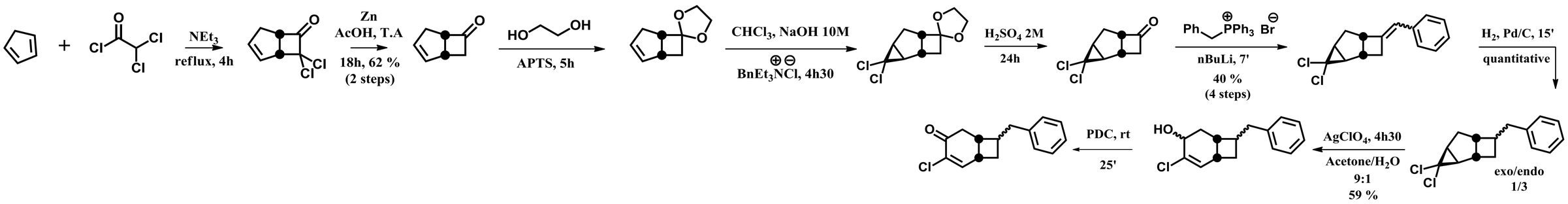
PATHWAY 2



PATHWAY 3



PATHWAY 4



CONCLUSION

Our first results with respect to the multi-step preparation of the enone key intermediate, from simple starting materials, are presented. They open a new route for the synthesis of a series of simplified analogues of the natural products.

REFERENCES

[1] A. Leverrier, M. E. Tran Huu Dau, P. Retailleau, K. Awang, F. Gueritte, M. Litaudon, *Org. Lett.*, **2010**, *12*, 3638-3641.

[2] Hee Nam Lim, Kathlyn A. Parker, *Org. Lett.*, **2013**, *15*(2), 398-401.

[3] Samuel L. Drew, Andrew L. Lawrence, Michael S. Sherburn, *Angew. Chem. Int. Ed.*, **2013**, *52*, 4221-4224.