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# Stereoselective synthesis of the advanced precursor of (+)-myriocin

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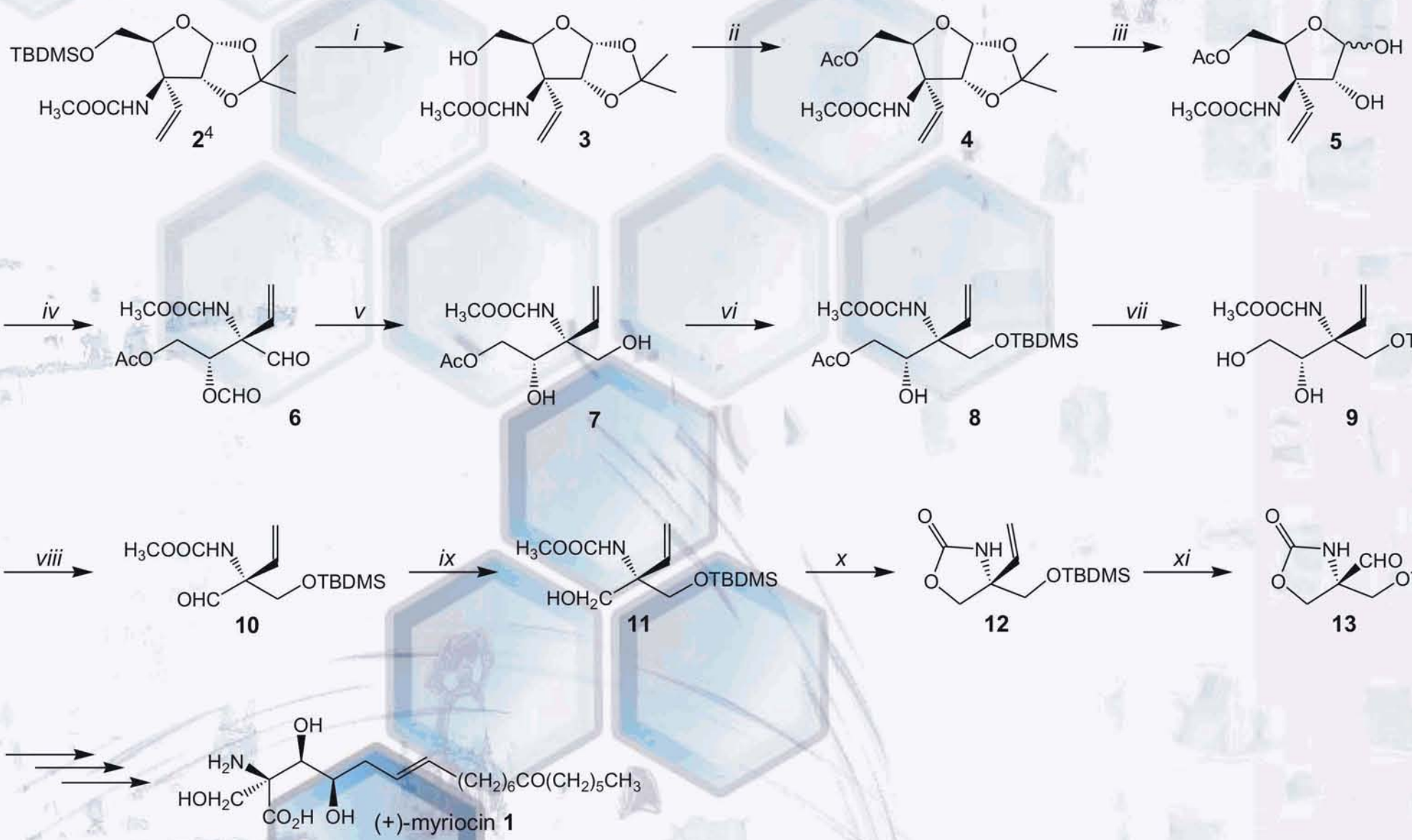
***Abstract:***
*A stereoselective approach toward 2-amino-1,3-propanediol **13** is described. This compound represents the key intermediate in the total stereoselective synthesis of (+)-myriocin **1**, an inhibitor of serine palmitoyltransferase (SPT). Moreover, synthon **13** can be used for synthesis of myriocin analogues. 2-amino-1,3-propanediol moiety is necessary for their biological activity.*

## Introduction:

Myriocin **1** is a sphingosine-like natural product, initially characterized as an antifungal agent. This compound is reported to show the inhibitory activity against T cell proliferation and to be a remarkable immunosuppressive agent with potency equivalent to and 10- to 100-fold higher then those of clinically used FK506 and cyclosporin A, respectively. The second advantage of myriocin **1** is its simple structure. Myriocin **1** has also been converted into several analogues, many of which are currently undergoing clinical testing. Together with the other antifungal agents (sphingofungin E and F) induce apoptosis. This effect is due to their potent inhibitory activities against serine palmitoyltransferase (SPT), as an essential enzyme involved in the first step of sphingolipid biosynthesis.[1,2,3]

## Synthesis:




Reagents and conditions: (i) TBAF, THF (94.5%); (ii) $Ac_2O$, pyridine, DMAP, RT (95%); (iii) TFA/$H_2O$, RT (89%); (iv) $NaIO_4$, MeOH/$H_2O$, RT (93%); (v) $NaBH_4$, MeOH, 0°C (61%); (vi) TBDMSiCl, DMAP, $Et_3N$, DMF, RT (78%); (vii) DIBAH, $CH_2Cl_2$, -20°C (86%); (viii) $NaIO_4$, MeOH/$H_2O$, RT (88%); (ix) $NaBH_4$, MeOH (87.5%); (x) NaH, THF, 0°C (95.5%); (xi) $O_3$, MeOH, -78°C then $Ph_3P$, $CH_2Cl_2$, RT (72%).

## Conclusion:

The advanced precursor **13** for the total stereoselective synthesis of (+)-myriocin **1** was synthesized in 11 steps (16% yield) starting from **2**.

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