A direct approach towards the preparation of intermediates to the synthesis of Amaryllidaceae alkaloids from Morita-Baylis-Hillman adducts

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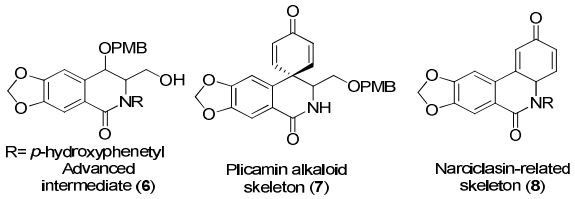
INTRODUCTION

Plants from the Amaryllidaceae family are famous due to its pharmacological relevance.[1] Many of these alkaloids have potent biological activities. The highly sophisticated substitution pattern of the carbon skeleton of these alkaloids, associated with their relevant biological and pharmacological significance, induced the interest of the organic synthesis community The goal of this work is the total synthesis of plicamine skeleton (**7**) and Narciclasin skeleton (**8**) (Figure 1) from Morita-Baylis-Hillman (MBH) adducts.

Figure 1. Carbon skeleton of Amaryllidaceae alkaloids



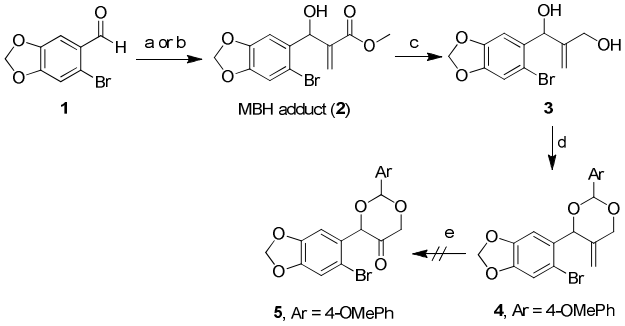
RESULTS AND DISCUSSION

Our approach begins with MBH adduct **2** which was obtained from aldehyde **1** in 53% and in 78% with ionic liquid (1-butyl-3-methylimidazolium bromide ([bmim]Br). [2] Adduct **2** was therefore reduced to **3** in the presence of DIBAL-H[2] to afford allylic diol **3** in 44% yield. The treatment of diol **3** with *p*-methoxy benzaldehyde gave the corresponding ketal **4** in 70% yield, after purification by neutral alumina column chromatography.[3] Unfortunately attempts to ozonolyse the double bond of **4** failed.[4] To circumvent this issue we increase the reaction time but we were able to isolate only overoxidation products (Scheme 1). Because of this result, we change the synthetic sequence. Then, an ozonolysis reaction was carried out directly on allylic diol **3** to afford keto-diol **9** in 70% yield (Scheme 2).

Compound **9** will be used for further chemical transformations. Thus, the hydroxyl groups will be protected as the corresponding 1,3-dioxanyl.

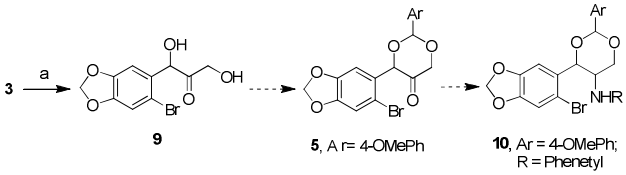
The carbonyl group of **9** will be used as substrate for a reductive amination reaction with benzyl- or phenethylamine to obtain **10**, which in turn will be used toward the synthesis of **6** (Scheme 2).

Scheme1.



Reagents and conditions: a) Methyl acrilate, DABCO, r.t., 38 days, 53% or b) Methyl acrilate, DABCO, [bmim]Br, r.t., 5 days, 78%. c) DIBAL-H (2.0 eq.), CH_2Cl_2, -78 °C, 1 h, 44%. d) *p*-anisaldehyde, CSA, 25 °C, 13h, 70% e) O_3, $MeOH/CH_2Cl_2$ (1 : 4), -72 °C; 10 eq. $S(CH_3)_2$, -72 °C, 3hr.

Scheme 2.



Reagents and conditions: a) O_3, $MeOH/CH_2Cl_2$ (1 : 4), -72 °C; 10 eq. $S(CH_3)_2$, -72 °C, 3h, 70%.

CONCLUSION

The synthesis of **5** is described in 3 steps from MBH adduct **2**. This intermediate should allow the access to an advanced compound to be used in the synthesis of Amaryllidaceae alkaloids.

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