



Sugar-based Catalyst for the Highly Diastereoselective Desymmetrization of dbas

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INTRODUCTION

Carbohydrates as catalysts have been explored by several research groups due to structural diversity and their chirality. Particularly in the field of organocatalysis they appear as alternative in the synthesis of different catalysts with different backbones.¹ Recently, we described a diastereoselective Michael addition between enones and azlactones by using (+/-)-CSA as a catalyst.² In this diastereoselective version only unfunctionalized dibenzylidene acetone (dba) was described. Thus, in this communication we show our results on a Brønsted acid catalyzed stereoselective desymmetrization of dbas.

RESULTS AND DISCUSSION

Our studies began with the preparation of the new catalysts **1** and **2**, which can be easily prepared in five steps from D-galactose.

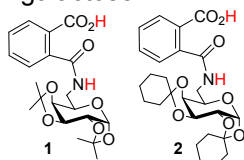
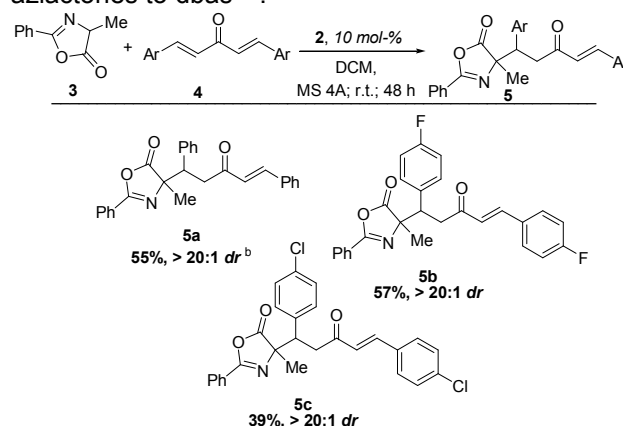


Figure 1. Designed organocatalysts based on sugar.

To our satisfaction using 10 mol% of both **1** or **2** catalyzes the reaction between azlactone **3** and dba **4**, providing the Michael adduct **5a** in moderate yield, however, excellent diastereoselectivity was achieved, > 20:1 dr (Table 1). By using the catalyst **1** the corresponding product was isolated in only 35 % yield.

At this point we start the evaluation of substrates. For the first time functionalization on the dba structure was well tolerated. Desymmetrization of symmetrical dbas containing chlorine or fluorine gave the corresponding Michael-type products in good yields and perfect control of both regio- and stereochemistry. Unfortunately, no enantiomeric excess was observed.

Table 1. Diastereoselective Michael-type addition of azlactones to dbas ^[a].



*[a] Reactions were carried out using 0.2 mmol of **3**, 0.02 mmol of **2** (10 mol%), and 0.21 mmol of **4** in DCM (0.2 M in azlactone). [b] Determined by ¹H NMR analysis of the crude reaction mixture.

CONCLUSION

In summary, a Brønsted acid catalyzed regio- and diastereoselective desymmetrization of dbas in presence of azlactones is presented. A new σ C-C bond and two stereogenic centers are created, one of them a quaternary center. Besides, for the first time, the diastereoselective desymmetrization of functionalized dbas catalyzed by a Brønsted acid is reported. Studies on the design of new catalysts, substrate scope as well as mechanistical investigations are ongoing and will be reported in due course.

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REFERENCES

- ¹ Ávila, E. P.; Amarante, G. W. *ChemCatChem* **2012**, 4, 1713.
- ² Ávila, E. P.; De Mello, A. C.; Diniz, R.; Amarante, G. W. *Eur. J. Org. Chem.* **2013**, 10, 1881.