ORCADEME
ORganoCAtalyzed DEsymmetrization of *MEso* compounds - JCJC 2010

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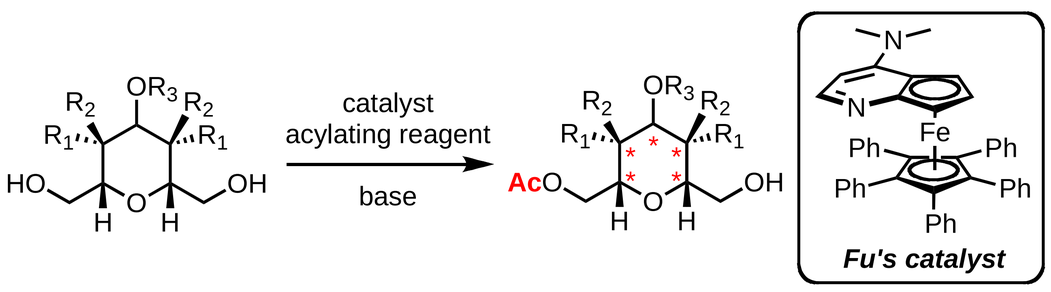
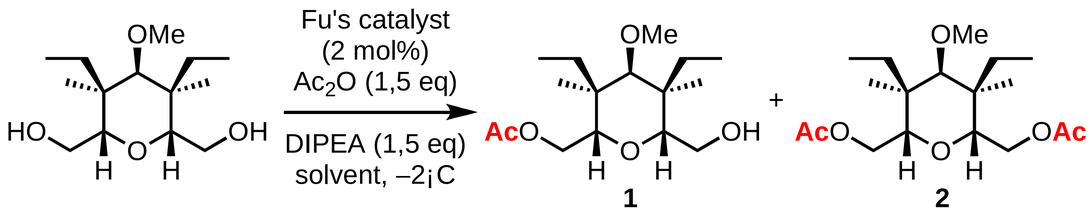
Introduction and Objectives

Studies on organocatalyzed enantioselective desymmetrization of diols have shown that organocatalysts such as 4-dialkylaminopyridine derivatives (Fu), diamines (Oriyama and Kündig), and heterocycles (Birman and Vedejs) are highly efficient. However, to our knowledge only one example involving *meso* primary alcohols desymmetrization has been described. In connection with our previous works on tetrahydropyran (THP) heterocycles we have developed a non-enzymatic desymmetrization of diols bearing a THP ring using Fu's DMAP with a planar chirality.



Optimization and Kinetic Study

Solvent screening led to improvement of enantiomeric excess. Interestingly, halogenated solvents present the advantage to produce mainly monoacetate with moderated to good conversion and enantioselectivity.

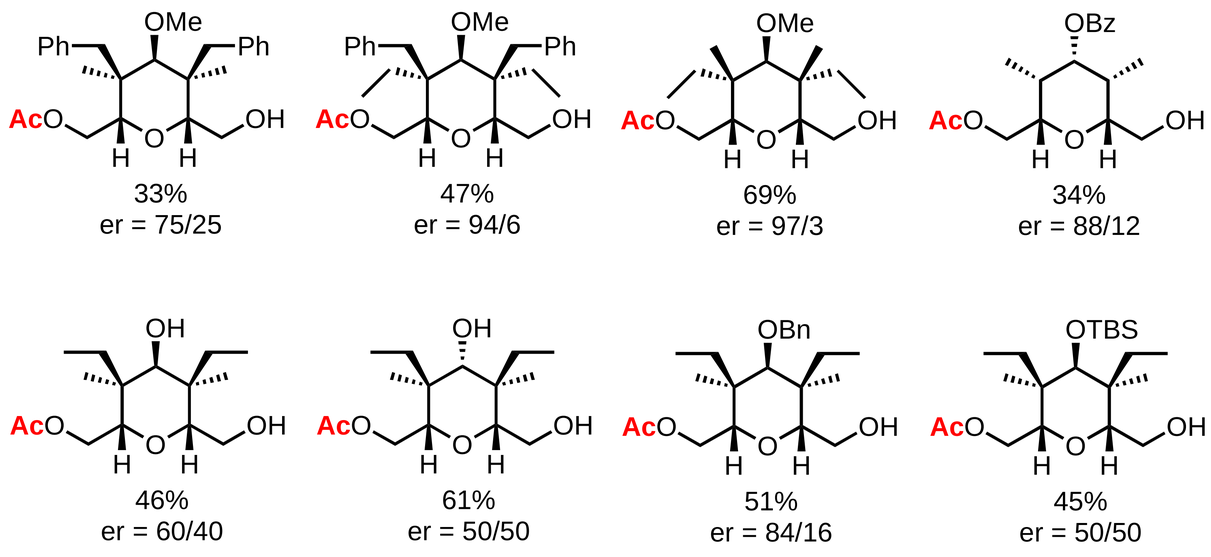


Solvent	Conversion	1	2	er
t-AmOH	96	72	24	94 : 6
$CHCl_3$	98	93	5	78 : 22
C_6F_6	7	7	0	95 : 5
$C_6F_6/CHCl_3$ (1/1)	65	65	0	90 : 10

Kinetic study brought to light the fact that the reaction was a combination of a desymmetrization step (formation of **1**) and a kinetic resolution step (formation of **2**).

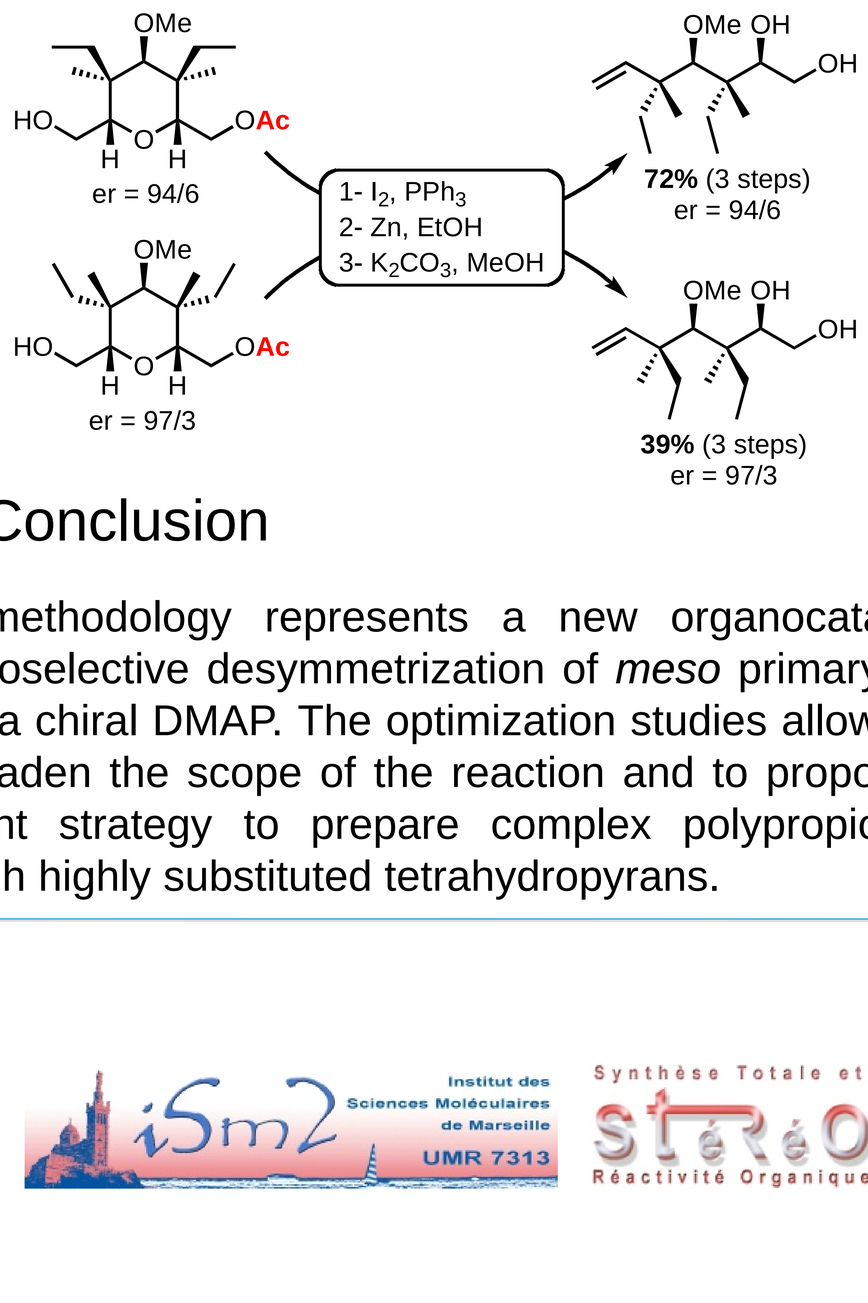
Scope and Limitation

Examination of the scope of the reaction, performed under optimized conditions in *t*-AmOH, revealed a great dependance on the substitution.



Post-functionalizations

A short sequence offered an access to complex highly functionalized polypropionate building blocks bearing quaternary centers.



Conclusion

Our methodology represents a new organocatalyzed enantioselective desymmetrization of *meso* primary diols using a chiral DMAP. The optimization studies allowed us to broaden the scope of the reaction and to propose an efficient strategy to prepare complex polypropionates through highly substituted tetrahydropyrans.

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