Enantioselective Heck desymmetrization toward heteroatomic chiral centers

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Abstract

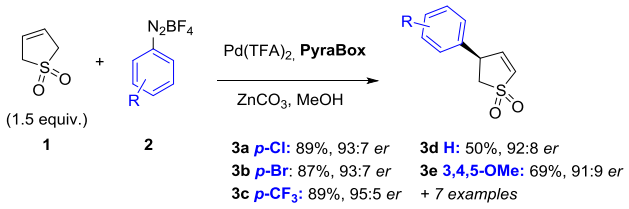
An efficient enantioselective Heck arylation of symmetrical sulfoxides has been developed leading to interesting chiral building blocks bearing a stereogenic center at the sulfur atom.

Introduction

Enantioselective desymmetrizations have emerged as efficient tools to the assembly richly decorated chiral building blocks.[1] Recent work of our group demonstrated the Heck-Matsuda as an excellent alternative to realize such transformations under open-flask and mild conditions, in the absence of complex and sensitive phosphine ligands.[2] Herein, we report our first efforts to extend this strategy to the synthesis of chiral heterocyclic building blocks bearing two stereogenic centers, being one of them at the heteroatom.

Results and Discussion

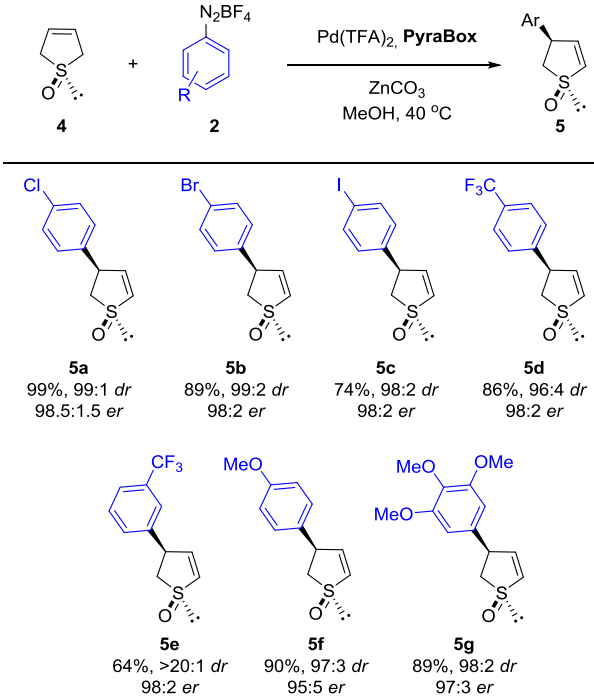
At the outset of our research we studied the arylation of cheap and readily available butadiene sulfone **1**. Using our newly developed PyraBox[3] (2,5-bis((*S*)-4-(*tert*-butyl)-4,5-dihydrooxazol-2-yl)pyrazine) ligand we were able to access a number of arylated sulfones **3** in good yields and enantiomeric ratios (Scheme 1).



Scheme 1. Arylation of butadiene sulfone **1**

Next, we turned our attention to the arylation of cyclic symmetric sulfoxide **4** in an attempt to generate two stereocenters in the same reaction step, including one at the sulfur atom. Using the same conditions depicted above to sulfone **1**, the arylations proceeded smoothly to afford chiral sulfoxides in excellent yields, diastereo- and enantioselectivities.

Table 1. Synthesis of chiral sulfoxides **5**



Conclusions

In summary, a straightforward route toward functionalized cyclic chiral sulfoxides was developed using an enantioselective Heck desymmetrization under mild and open-flask conditions. Further studies are underway in our laboratory.

Ackowledgement

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