Design of Chiral Pyridines as Organocatalysts for Asymmetric Cyclopropanation Reaction

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Pyridine derivatives are widely used as organocatalysts and as ligands in transition metal catalysis. Herein, we report the synthesis of chiral piridines (*S*,*S*)-**7aa'-cc'** and their use in cyclopropanation reaction.

Chiral organocatalysts (*S*,*S*)-**7aa'-cc'** were synthesized by ortho-lithiation of pyridine **5** followed by quenching with aldehydes (*S*)-**6a'-c'**.

To find suitable conditions for pyridine **4a-c** catalyzed cyclopropanation, a range of solvents and bases was screened. It was found that the desired reaction proceeded smoothly without non-catalyzed background cyclopropanation reaction if $K_2HPO_4 \cdot 3H_2O$ or KOAc were used as base in dichloromethane.

When catalysts (*S*,*S*)-**7aa'-cc'** were employed in cyclopropanation reaction, the best enantioselectivities (48.8% ee) were achieved with sterically large substituent R^3 (Piv and Ts).

Further investigation on pyridine derivative **4a-c** structure showed that electron donating groups in para-position accelerated cyclopropanation. Notably, 4-methoxypyridine (**4a**) and N-pyridin-4-ylacetamide (**4b**) showed the best yields (80% and 78%, respectively) whereas 4-dimethylaminopyridine (**4c**) gave only trace amounts of cyclopropane **3**.