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Review Article

Research on Phase Transfer Catalytic Reactions and their Application in Drug Synthesis

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Abstract

Our recent work was reviewed herein and our future work was also planned herein. Herein our achievements in the investigation on the phase transfer catalytic reactions were reported, and our future plan on the phase transfer catalytic reactions were also reported.

Keywords: Phase transfer catalysis; Asymmetric phase transfer catalysis; Drug synthesis; Synthesis of chiral drugs

Introduction

Phase transfer catalysis is of great importance in organic synthesis of drug synthesis [1]. The study of phase transfer catalytic reaction and their application in drug synthesis was focused by our group. Herein our work on the phase transfer catalytic reactions was reviewed.

A number of new phase transfer catalytic reactions were investigated and were applied in drug synthesis. For example, the Darzens reaction between aldehydes and chloroacenitrile (Figure 1) was accomplished and then applied in the synthesis of diltiazem. Similarly the Darzen reactions between aldehyde and t-butyl chloroacetate was performed and then applied in the synthesis of diltiazem (Figure 1) by our research group [2a, 2b].

Also, the phase transfer catalytic reactions were applied in the synthesis of drug intermediate of vernakalant, which was more convenient and more easily handled than the traditional routine [3] (Figure 2).

Further, the phase transfer catalytic reactions were also applied in the synthesis of firocoxib and etoricoxib (Figure 3), which was now in preparation of patent.

Based on the study above, we also turned our attention to asymmetric phase transfer catalytic reactions; several new chiral phase transfer catalysts were designed and synthesized in our study. For example, the cyclic chiral phase transfer catalysts were designed and synthesized by treating cinchona with 2-bromo-1-(4-(trifluoromethyl) phenyl) ethan-1-one(catalyst 1-4), and the new catalysts were applied in the asymmetric alkylation and asymmetric sulfenylation of glycine derivative with moderate to high enantioselectivity (Figure 4) [4, 5].

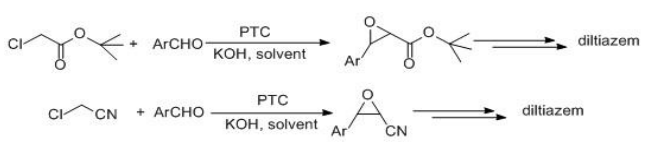

Figure 1: Phase transfer catalytic Darzens reaction.

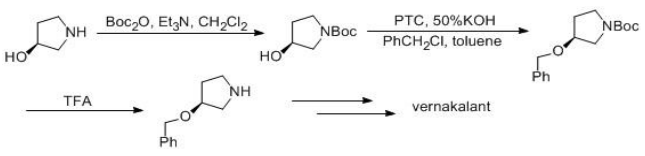

Figure 2: Synthesis of vernakalant.

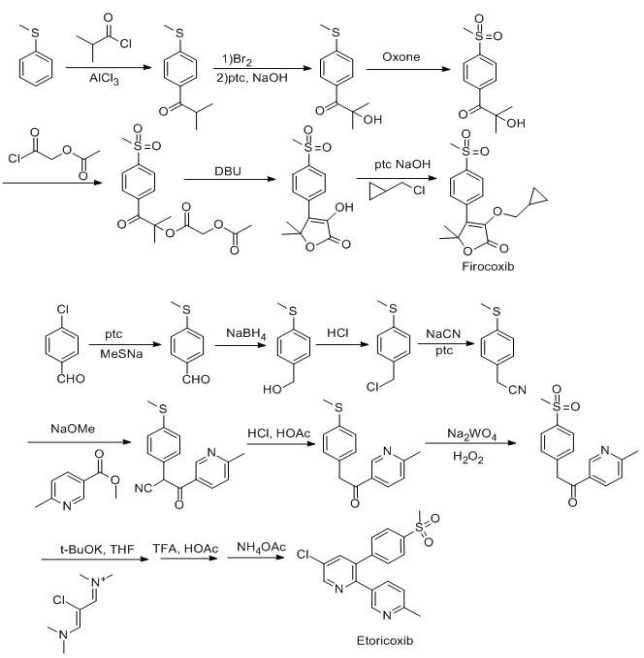

Figure 3: Synthesis of firocoxib and etoricoxib.

A new type of chiral phase transfer catalysts was designed and synthesized by treating cinchona with 1, 4-dibromobut-2-ene(catalyst 5-8), and they were also applied in the asymmetric alkylation of glycine derivative with moderate to excellent enantioselectivity (Figure 5) [6].

The new type of chiral phase transfer catalysts were further applied in other asymmetric reactions, such as asymmetric Darzens reaction, with moderate to high diastereos electivity and moderate enantioselectivity, which also was applied in the synthesis of diltiazem (Figure 6) [7].

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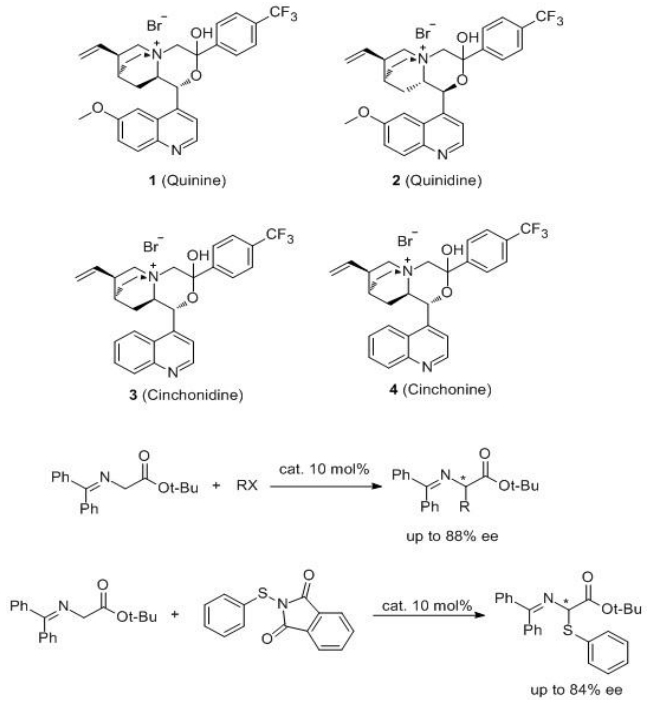

Figure 4: synthesis of the new chiral phase transfer catalysts and their application in asymmetric alkylation and sulfenylation of glycine derivative.

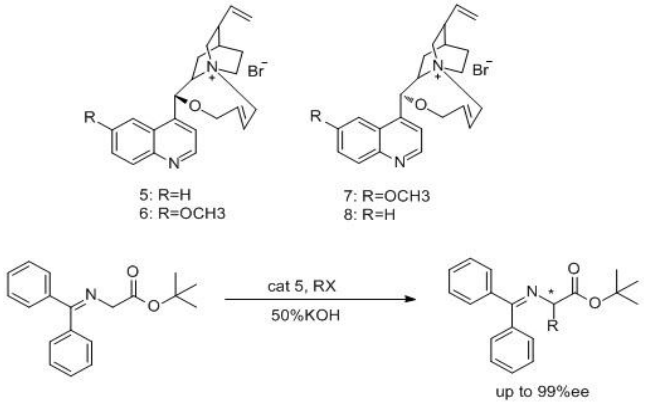

Figure 5: Synthesis of new chiral phase transfer catalysts and their application in asymmetric alkylation of glycine derivative.

In continuation of our study on the phase transfer catalysis, we will try to find some new type of phase transfer catalytic reactions and try to apply them in the drug synthesis. In another aspect, we will also try to design some new type of chiral phase transfer catalysts and apply them in the classical and new type of phase transfer catalytic reactions, and we will also try to apply them in the synthesis of chiral drug or chiral drug intermediates.

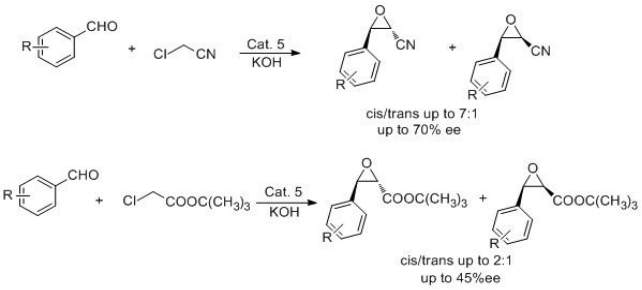

Figure 6: Application of new chiral phase transfer catalysts in asymmetric Darzens reaction.

Acknowledgement

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