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Synthesis of a New Chiral Organocatalysts and its Application in Asymmetric Morita-Baylis-Hillman Reaction

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Introduction

The Morita–Baylis–Hillman (MBH) reaction was an organocatalyzed chemical transformation that provided effective and atom economical carbon–carbon bond-forming reactions [1-5]. Formally, this reaction promoted condensation between α-position of an electron-deficient alkene and the sp^2 carbon atom of an aldehyde catalyzed by nucleophilic bases such as DABCO [5]. With highly functionalized MBH adducts and their derivatives, structurally complex and diverse molecules (such as acaterin, asmarines A and B, borrelidin, PPAPs and so many natural products [4,6]) could be easily achieved. Hence, the development of the MBH reaction has attracted considerable interest in recent years. However, several disadvantages such as poor conversions, low reaction rates, low enantioselectivity and the lack of definite mechanism also limited the applicability of the MBH reactions [2,4,6,7]. Therefore, it is important to investigate new catalytic system to solve known problems.

Results and Discussion

For the asymmetric MBH reaction, thiourea derivatives were widely used {7-12]. Besides, cyclohexanediamine and proline were both important chiral frameworks. Therefore, we combined these two structural units and synthesized a new catalyst C (Figure 1, Table 1).

In comparison to DABCO, there was no product when the reaction was carried out with DMAP as base. Meanwhile, the yield with DBU as base was much lower though DBU played an important role in the MBH reaction [13].

For further optimization, the effect of the solvents on the reaction was also investigated (Table 2).

Obviously, for this reaction, the presence of solvent exerted a tremendous influence.

Therefore, in order to get superior yields, DABCO should be used as the base while DCM should be chosen as the solvent.

According to the best condition we got above, many other reactions had been tested. Besides, optical rotation also had tested, and from Table 3, we could see that the selectivity of the catalyst was not satisfying. Thus further work should be done to improve the

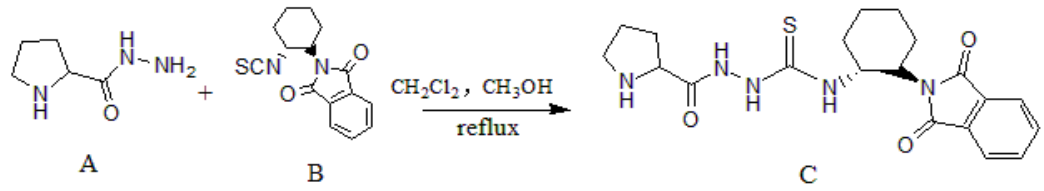
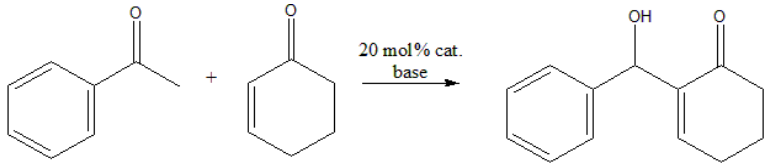


Figure 1: Synthesis of catalyst.



entry	Base	yield
1	DMAP	/
2	DBU	33.7%
3	DABCO	85.3%

Table 1: Optimization of the Base in the Reaction of 2-Cyclohexen-1-one with benzaldehyde.

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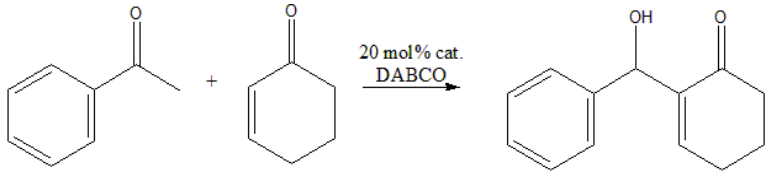
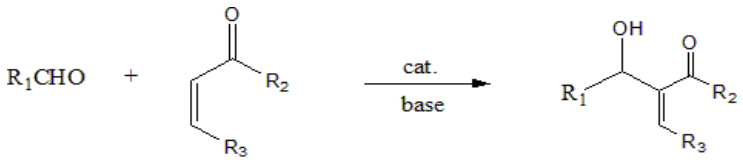


entry	solvent	yield
1	/	69.1%
2	DCM	85.3%

Table 2: Solvent Effects on the MBH Reaction of 2-Cyclohexen-1-one with benzaldehyde.



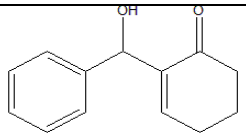
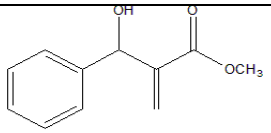
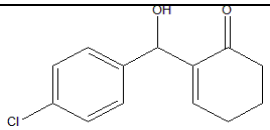
entry	product	yield	optical rotation
1	 J1	85.3%	-1.3°
2	 J2	82.3%	-1.5°
3	 J3	83.2%	+0.3°

Table 3: MBH Reaction of Enones and Acrylates with Aldehydes Catalyzed by C.

enantioselectivity of the reaction.

Experimental

Materials and measurements

All reagents and solvents were chemically pure (CP) grade or analytical reagent (AR) and were used as received unless otherwise indicated general. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker AV 500 spectrometer at 303k from sample solution in $CDCl_3$. Mass spectra were measured on a Waters Q-TOF micro spectrometer.

Synthesis of C [14-16]

In a flask, A (0.1508g) and B (0.076g) was dissolved in DCM (10mL) and CH_3OH (1ml). The mixture was refluxed overnight. After concentrated, the residue was subjected to flash column chromatography (silica gel thin layer chromatography; mineral ether: ethyl acetate 2:1) to give dark yellow powder. Yield: 0.1463g (25.67%).

1H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 2H), 7.65 (s, 2H), 4.04 (s, 1H), 3.40 (s, 1H), 3.26 (s, 1H), 2.60 (dd, 2H), 1.99 (d, 3H), 1.93 (s, 2H), 1.84 (s, 2H), 1.79 (s, 2H), 1.49 (dd, 2H), 1.39 – 1.12 (m, 4H).

13C NMR (75 MHz, $CDCl_3$) δ 182.07 (s), 136.18 (s), 134.71 (s), 126.19 (s), 79.62 (s), 65.75 (s), 58.70 (s), 58.34 (s), 57.72 (d, J = 15.3 Hz), 54.28 (s), 35.89 (s), 31.89 (s), 30.96 (s), 28.38 (s), 27.12 (s), 26.68 (s).

General procedure for the synthesis of J1-3 [12]

The reaction was carried out with 1 equiv of aldehyde and 4 equiv of enone or acrylate in the presence of 20mol% catalyst and base at 10°C for 72h. After concentrated, the residue was subjected to flash column chromatography to get product.

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