

Research Article

Synthesis of BINOL-thiourea Derivatives

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Introduction

It is well documented that enantiopure R-BINOL-derivatives and thiourea-derivatives belong to privileged compounds which were widely applied in the field of asymmetric synthesis and organocatalysis [1]. Dual hydrogen bonding (DHB) catalyst have been received much attention in the field of enantioselective synthesis [2]. Among the hydrogen-bonding complex, thiourea derivatives have been proved to be one of the most promising scaffolds, and much effort has been dedicated to find alternative motifs [3]. As a result, several scaffolds such as guanidines, squaramides, were identified. On the other hand, Bronsted acid catalyst especially BINOL-derivatives has attracted much Attention [4]. Whereas thiourea and BIONL-derivatives are well known as scaffolds and have been explored successfully as catalysts as well as ligand, however, combining the two units as a whole has scarcely been reported? The synthesis of phosphorylthiourea through the addition nucleophilic reaction of phosphorylthiocyanide and substitute amines was published in 1987 [5,6]. Phorylthioureas have been used as insecticide, herbicide ficigide plant growth regulator and so on [7,8]. Due to our current interests in the synthesis and applications of thiourea as well as R-BINOL-derivatives, we herein report a convenient and efficient protocol for the preparation of chiral organocatalyst I, II and III, which are promising reagents for further and diverse application.

Experimental

General

Melting points were determined in a capillary using a Melt Temp. II apparatus (Aldrich) or STUART SMP 30 and are uncorrected. ¹H NMR spectra were measured on a Bruker Avance III instrument (300MHZ). Chemical shifts (d) are given in ppm and coupling constants J in Hz.

Starting material

All solvents and reagents are commercially available and used as received.

Synthesis of compound B

Procedure: Phosphorus oxychloride (0.1mol) was added with stirring into a solution of (R)-(+)-1,1'-Bi-2-naphthol A (0.1mol) in CH₂Cl₂ (5ml), the reaction mixture was stirred at room temperature for 12 hours, then the formed hydrogen chloride and solvent were evaporated and a white solid was obtained.

Abstract

Herein a convenient synthesis of BINOL-thiourea derivatives I, II and III via the reaction of phosphorylthiocyanide C with amines was described in modest yield.

The compound was used for next step without further purification (Yield: 88%).

Synthesis of compound C

To a solution of 2 (0.12mol) in acetonitrile (20mL), KSCN (0.25mol) was added gradually with stirring, and the mixture was stirred at 65°C for 10 hours, which was filtrated and extracted with dichloromethane (15mL*2), the solvent was evaporated under reduced pressure to give a yellow liquid, which was used for the next step without further purification.

The synthesis of I, II and III

General procedure: To a mixture of 3 (10mmol) in chloroform (30mL), a solution of aniline (10mmol) in chloroform (10mL) was added drop wise with stirring. The mixture was refluxed until reaction completion was detected by thin-layer chromatography. The solvent was evaporated under the reduced pressure, the residue was diluted with ether (10mL) and cooled in ice-water bath, the crude product was crystallized with DMF-H₂O to give the target compound.

Compound I: White solid, mp: 152-154°C, yield: 64%.

¹H-NMR (CDCl₃, 300MHZ): 8.5812 (m, 1H): 8.5525-8.0446 (m, 1H), 7.9772-7.8824 (m, 4H): 7.8139-7.7832 (m, 1H), 7.7232-7.6962 (m, 1H), 7.5431-7.5145 (m, 3H), 7.3224—7.2597 (m, 4H), 6.7526-6.7230 (m, 1H), 6.3390 (s, 1H), 2.5864-2.5562 (m, 1H), 2.3828-2.3453

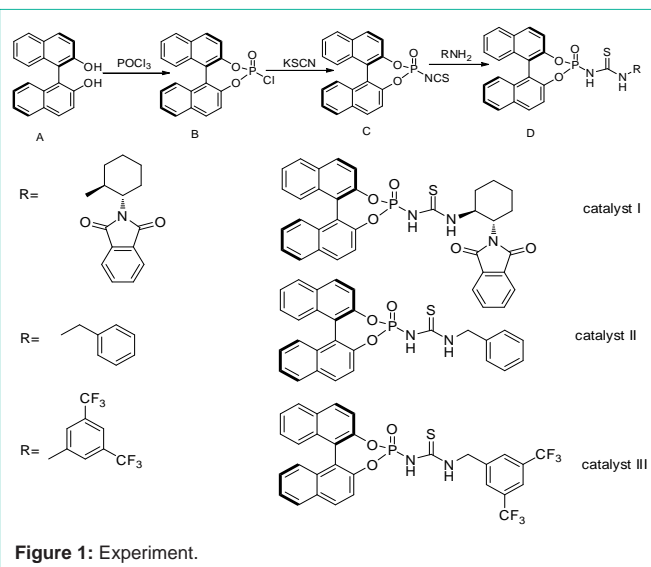


Figure 1: Experiment.

(m, 1H), 1.8722-1.8195 (m, 3H), 1.4284-1.2335 (m, 4H), 0.9577-0.8556 (m, 1H).

HRMS: [M+Na]: 656.1; found: 656.4

Compound II: Yellow solid, mp: 178-181°C, yield: 70%.

¹H-NMR (CDCl₃, 300MHz): 8.5812-8.5525 (m, 1H), 8.6446-8.0152 (s, 1H); 7.9772-7.8824 (m, 4H), 7.8139-7.7842 (m, 1H), 7.7232-7.7135 (m, 2H), 7.5431-7.5145 (m, 3H), 7.3226-7.3121 (m, 4H); 6.7526-6.7230 (d, 1H); 6.3390 (s, 1H); 2.5864-2.5562 (d, 1H); 2.3828-2.3453 (m, 1H); 2.0407 (s, 1H).

HRMS: [M+Na]: 519.4; found: 519.1

Compound III: Yellow solid, mp: 155-156°C, yield: 63%.

¹H-NMR (CDCl₃, 300MHz): 10.9985 (s, 1H), 8.2316 (s, 2H), 8.1535-8.1358 (m, 1H), 8.0182-7.9923 (m, 2H), 7.7506 (s, 1H), 7.6158-7.5335 (m, 4H), 7.4101-7.3632 (m, 4H), 6.8569 (s, 1H).

HRMS: [M+Na]: 641.5; found: 641.1

Results and Discussion

A typical procedure for the synthesis of phosphorylthiocyanide is the treatment of the phosphorus oxychloride with KSCN [9]. Then BINOL-thiourea derivatives were easily achieved through the reaction between phosphorylthiocyanide and amines. Herein, catalyst I, II and III were prepared in this way with moderate yield and their structures were confirmed by ¹HNMR and MS

Conclusion

Herein we have reported that BINOL-derivatives can be prepared conveniently by using phosphorylthiocyanide with amines. And their applications in asymmetric organocatalysis were still under way in our group.

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