

단 신

이온성 액체를 이용한 산화인 기반의 양측 리간드의 합성

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(2008. 1. 21 접수)

Synthesis of IL-Supported Phosphine Oxide-Based Pincer Ligand

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(Received January 21, 2008)

주제어: 이온성 액체, 조역물 화학, 산화인의 양측(협공) 리간드, 합성

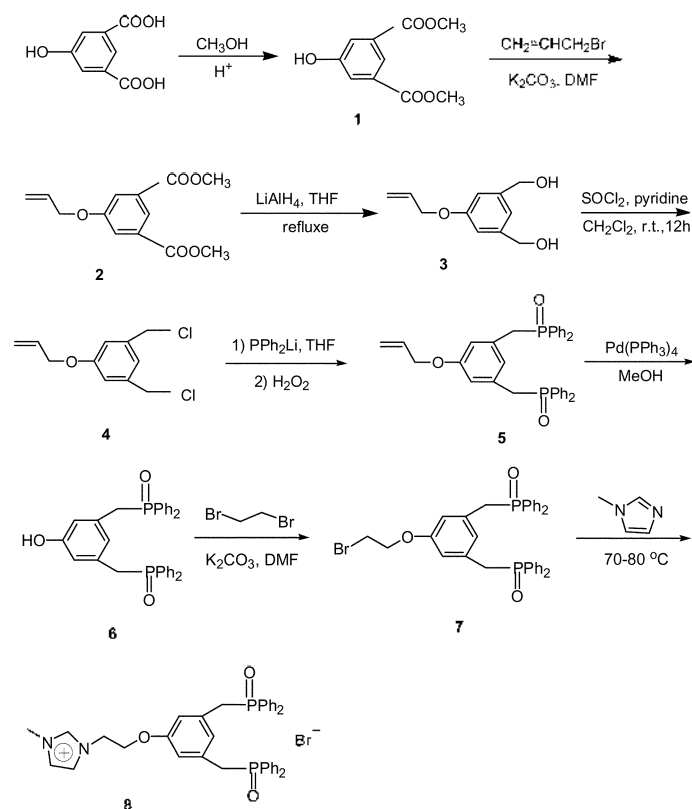
Keywords: Ionic Liquid, Supported Chemistry, Phosphine Oxide-Based Pincer Ligand, Synthesis

Room temperature ionic liquids (RTILs) are a new class of attractive mediums for many homogeneously catalyzed reactions.¹ In many cases, the catalysts can be easily immobilized in ILs, and thus, separated by simple phase-separation and recycled.² However, the problems associated with leaching and/or stability of the transition metal catalysts in ILs still remained to be solved.³ Recently a new interest was to explore these low molecular weight ionic liquids as soluble supports for organic synthesis, and a series of phosphine ligands have been successfully grafted on ionic liquids, such as the 1,4-bisphosphine,⁴ 1-imidazolium phosphines,⁵ phenoxaphosphino-modified ligand and other phosphine ligands.^{7,8} It has been clearly demonstrated that introduction of imidazolium ionic liquid pattern to the catalyst not only avoided catalyst leaching but also increased the stability of catalyst in ionic liquid. However, to the best of our knowledge, no RTIL-bound pincer ligand was reported.

Pincer ligands play an increasing role in coordination chemistry and catalysis, which can tune the reactivity of the metal center by adjusting the nature and the electronic properties of the different pincer ligands. Since Merrifield introduced the use of polymer supports in organic synthesis a variety of

supports have been introduced to graft pincer ligands.⁹ Herein we report the synthesis of IL-supported phosphine oxide-based pincer ligand, a precursor for PCP pincer ligand.

The route for the synthesis of IL-supported phosphine oxide-based pincer ligand is illustrated in *Scheme*. The first step was the esterification of commercially available 5-hydroxyisophthalic acid according to literature procedures.¹⁰ The phenolic group was protected with allyl bromide in 92% yield and subsequently the esters were reduced with LiAlH_4 in THF to the diol **3** in 93% yield.¹¹ The allyl-protected dichloride was then formed using equal amounts of SOCl_2 and pyridine in CH_2Cl_2 stirred for 12 h at room temperature. The phosphine ligand was afforded by treatment of dichloride with PPh_2Li in THF. Due to its sensitivity to air, it was necessary to transfer to the corresponding phosphine oxide in order to facilitate the operation in the next steps. Then subsequent oxidation with H_2O_2 may lead to the synthesis of compound **5** under an air atmosphere. In ^1H NMR spectra, the coupling constant was bigger ($J_{\text{C12, P}} = 10.0$ Hz), and indicated the formation of phosphine oxide, while that of the phosphine ligand was lower.¹² Deprotection of the 5-allyloxy-phosphine oxide ligand with



Scheme

$\text{Pd}(\text{PPh}_3)_4$ and K_2CO_3 in MeOH for 1-3 h yielded the compound **6** as an oily white solid, and the singlet H signal of Ph-OH (δ 9.82) in ^1H NMR was observed. Linker between IL and phosphine oxide-based pincer ligand was employed by reaction with 1,2-dibromoethane and K_2CO_3 in dry DMF. To avoid the reaction between one molecule of 1,2-dibromoethane and two molecules of compound **6**, 10-fold excess of 1,2-dibromoethane were added. In mass spectrum (ESI), the spectra of parent ion (^{79}Br) and isotopic ion (^{81}Br) were observed, which indicated that compound **7** was given successfully. An equimolar mixture of **7** and methyl imidazole was refluxed at 70 °C for 72 h, and the oily white solid was obtained. By analysis of the ^1H NMR spectra of the product, imidazolium-H and Ph-H were found at the same time at δ -10.85-6.46, showing that **7** has been bound to the ionic liquid moiety to give **8**. Compound **8** is an effective proli-

gand for soft and hard transition metal ions, behaving as a tridentate non-bridging donor,¹³ and it will be demonstrated that attachment of PCP-ligand-based catalysts to imidazolium salt not only avoid catalysts leaching but also increase the preferential solubility of the catalysts to IL. The extending research for characteristics of synthesized imidazolium ionic liquid such as coordination ability and activation ability of catalyst to some reactions is on the going. Compounds **7** and **8** were characterized by ^1H NMR, ^{13}C NMR, and their features could be established.

In summary, we have synthesized imidazolium ionic liquids supported phosphine oxide-based pincer ligand. IL phases allow standard analytical methods (NMR, TLC) to monitor reaction progress. This example may offer a useful strategy for preparation of "pincer" ligand. These novel phosphine ligands may be employed as catalyst components in

biphasic ionic liquid systems.

EXPERIMENTAL

General

THF was distilled from sodium-benzophenone ketyl, CH_2Cl_2 was distilled from calcium hydride, and DMF was distilled from and stored over molecular sieves. All other reagents and solvents were obtained from commercial sources and were generally used without further purification. Column chromatography was carried out on silica gel (300-400 mesh). ^1H NMR spectra were recorded at 500 MHz, ^{13}C NMR spectra were recorded at 125 MHz, using TMS as internal standard. Mass spectroscopy data of the product were collected on a MS-ESI instrument.

Synthesis of dimethyl 5-hydroxy-1, 3-benzenedicarboxylate **1**

To a stirred mixture of 5-hydroxyisophthalic acid (9.10 g, 0.05 mol) and methanol in an ice-salt bath was slowly added a catalytic amount of sulfuric acid (3 mL). After addition, the reaction mixture was stirred in an ice-salt bath for 0.5 h, then at room temperature for 1 h, and was refluxed for 5 h. After it was cooled to room temperature, the reaction mixture was neutralized with aqueous sodium carbonate solution and then acidified by concentrated hydrochloric acid. Water was added and the resulting mixture was extracted with dichloromethane to give a white solid. Crude dimethyl 5-hydroxy-1, 3-benzenedicarboxylate **1** was recrystallized from methanol. Yield 10.10 g (84%). ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.25 (s, 1 H, Ph-H), 7.79(s, 2 H, Ph-H), 6.49(s, 1 H), 3.95(s, 6 H, $-\text{OCH}_3$). MS (ESI): m/z 241($[\text{M}+\text{H}]^+$).

Synthesis of dimethyl 5-allyloxy-1,3-benzenedicarboxylate **2**

Dimethyl 5-hydroxy-1,3-benzenedicarboxylate **1** (2.40 g, 0.01 mol) was dissolved in dry DMF (20 mL), and then K_2CO_3 (2.21 g, 0.016 mol) was added, and stirred for 2 h, then allyl bromide (1.20 g, 0.01 mol) was added. The mixture was stirred 9 h at 70 °C after which DMF was evaporated. The crude product was treated with water (100 mL). The reaction

mixture was extracted with dichloromethane (100 mL), and dried over Na_2SO_4 . The organic layer was concentrated, and gave white solid **2**. Yield 2.44 g (92%). ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.24 (s, 1 H, Ph-H), 7.78(s, 2 H, Ph-H), 6.06-6.03(m, 1 H, allyl-H), 5.43-5.39(d, $J=4.5$ Hz, 1 H, allyl-H), 5.30-5.28(d, $J=3.1$ Hz, 1 H, allyl-H), 4.54-4.53(m, 2 H, allyl-H), 3.95(s, 6 H, $-\text{OCH}_3$). MS (ESI): m/z 288($[\text{M}+\text{Na}]^+$).

Synthesis of 5-allyloxy-1,3-benzenedimethanol **3**

LiAlH_4 (4.50 g, 0.12 mol) was suspended in dry THF (200 mL) and a solution of diester **2** (16.40 g, 0.06 mol) in THF (100 mL) was slowly added. The mixture was refluxed for 12 h after which THF was evaporated. The resulting paste was dissolved in dichloromethane (100 mL) and cooled to 0 °C and 2 M HCl (100 mL) was slowly added, after which the layers were separated. Extraction of the aqueous layer with dichloromethane (3 \times 100 mL) and drying of the combined organic layers gave, after removal of the solvent, **3** as a white solid. Yield 11.20 g (93%). ^1H NMR (500 MHz, CDCl_3 , TMS): δ 6.91 (s, 1 H, Ph-H), 6.84 (s, 2 H, Ph-H), 6.05-6.02 (m, 1 H, allyl-H), 5.42-5.38 (d, $J=5.0$ Hz, 1 H, allyl-H), 5.29-5.27 (d, $J=3.3$ Hz, 1 H, allyl-H), 4.63 (s, 4 H, $-\text{CH}_2-$), 4.54-4.53 (m, 2 H, allyl-H), 1.95 (s, 2 H, $-\text{OH}$). MS (ESI): m/z 195 ($[\text{M}+\text{H}]^+$).

Synthesis of *O*-Allyloxy-3,5-bis(chloromethyl)benzene **4**

A suspension of **3** (1.94 g, 0.01 mol) in 50 mL of dichloromethane was prepared. Pyridine (2.20 mL, 0.03 mmol) was added and the resulting mixture was cooled to 0 °C. Then, thionyl chloride (2.5 mL, 0.03 mmol) was added dropwise to the mixture, resulting in the eventual dissolution of the starting material. The ensuing homogeneous solution was stirred at room temperature for 18 h. After the reaction, the organic phase was washed with water (3 \times 30 mL), 1 N HCl (2 \times 10 mL), and brine (2 \times 10 mL) and then dried over MgSO_4 . The solvent was removed under reduced pressure and the isolated yellowish solid was dried under vacuum, yielding 2.29 g (88%) of the dichloride: ^1H NMR (500 MHz, CDCl_3 , TMS): δ 6.98 (s, 1 H, Ph-H), 6.89(s, 2 H, Ph-H), 6.03-6.02(m, 1 H, allyl-H), 5.43-5.39(q, $J=$

6.7 Hz, 1 H, allyl-H), 5.30-5.28(q, $J=3.3$ Hz, 1 H, allyl-H), 4.54-4.53(m, 2 H, allyl-H), 4.52(s, 4 H, $-\text{CH}_2-$). MS (ESI): m/z 261 ($[\text{M}+\text{H}]^+$, ^{35}Cl), 263 ($[\text{M}+\text{H}]^+$, ^{37}Cl).

Synthesis of phosphine oxide ligand 5

Dropwise addition of allyl-protected 1,3-bis(chloromethyl)-benzene(2.61 g, 0.01 mol) in THF to a solution of PPh_2Li (0.022 mol) in THF/hexane (prepared *in situ* by dropwise addition of PPh_2H in THF to a solution of BuLi in hexanes at -40°C) afforded a pale yellow solution, which was stirred overnight. The volatiles were removed, and the oily white solid was dissolved hot EtOH (100 mL), and then added H_2O_2 (3 mL). The mixture was refluxed overnight after which EtOH was evaporated. The residue was purified by extraction into dichloromethane (100 mL) to give an oily material. The crude product was purified by flash column chromatography ($\text{CH}_2\text{Cl}_2/\text{EtOAc}/\text{MeOH}$), and gave the oily white solid 5. Yield 4.43 g (75%). ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.67-7.63 (m, 8 H, Ph-H), 7.50-7.40 (m, 12 H, Ph-H), 6.64 (s, 1 H, Ph-H), 6.49 (s, 2 H, Ph-H), 5.91-5.83 (m, 1 H, allyl-H), 5.26-5.22 (q, $J=6.3$ Hz, 1 H, allyl-H), 5.17-5.15 (q, $J=3.3$ Hz, 1 H, allyl-H), 4.22-4.21 (d, $J=5.0$ Hz, 2 H, allyl-H), 3.52-3.50 (d, $J=10.0$ Hz, 4 H, $-\text{CH}_2-$). MS (ESI): m/z 614 ($[\text{M}+\text{Na}]^+$).

Deprotection reaction of 5 to prepare compound 6

To a stirred solution of allyl-protected compound 5 (5.91 g, 0.01 mol) in MeOH (100 mL) was added catalytic amounts of $\text{Pd}(\text{PPh}_3)_4$ (0.05-1.00 mol%) under a nitrogen atmosphere. The slightly yellow solution was stirred for 5 min, and K_2CO_3 (5.52 g, 0.04 mol) was added. The action was monitored by TLC. The reaction was completed in 1-3 h. The reaction mixture was concentrated in vacuo, and the residue was treated with 2 M HCl. The aqueous solution was extracted with dichloromethane. The organic layer was washed with brine, dried over Na_2SO_4 , and concentrated in vacuo. The crude product was purified by flash column chromatography (hexanes/EtOAc), and gave the oily white solid 6. Yield 5.01 g (91%). ^1H NMR (500 MHz, CDCl_3 , TMS): δ 9.82 (s, 1 H, Ph-OH), 7.69-7.60 (m, 8 H, Ph-H), 7.47-7.37 (m, 12 H, Ph-H), 6.74 (s, 1 H, Ph-H), 6.44 (s, 2

H, Ph-H), 3.46-3.44 (d, $J=13.0$ Hz, 4 H, $-\text{CH}_2-$). MS (ESI): m/z 552 ($[\text{M}+\text{H}]^+$).

Synthesis of compound 7

Compound 6 (5.51 g, 0.01 mol) was dissolved in dry DMF (20 mL), and then K_2CO_3 (2.21 g, 0.016 mol) was added. 1,2-Dibromoethane (18.8 g, 0.1 mol) was added to the mixture. The mixture was stirred 9 h at 50°C after which DMF was evaporated. The crude product was treated with water (100 mL). The reaction mixture was extracted with dichloromethane (100 mL) and dried over Na_2SO_4 . The organic layer was concentrated, and obtained the oily white solid 7. Yield 5.40 g (82%). ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.69-7.60 (m, 8 H, Ph-H), 7.47-7.37 (m, 12 H, Ph-H), 6.74 (s, 1 H, Ph-H), 6.44 (s, 2 H, Ph-H), 4.54-4.52(t, $J=3.8$ Hz, 2 H, $-\text{CH}_2-$), 3.61-3.49 (t, $J=4.2$ Hz, 2 H, $-\text{CH}_2-$), 3.44-3.42 (d, $J=13.5$ Hz, 4 H, $-\text{CH}_2-$). ^{13}C NMR (125 MHz, CDCl_3): δ 150.6, 138.2, 135.0, 131.5, 129.6, 128.6, 121.5, 111.9, 76.1, 43.2, 39.8. MS (ESI): m/z 658 ($[\text{M}+\text{H}]^+$, ^{79}Br), 661 ($[\text{M}+\text{H}]^+$, ^{81}Br).

Compound 7 bonded on IL to prepare compound 8

Equimolar amounts of 1-methylimidazole (0.82 g, 0.01 mol) with 7 (6.57 g, 0.01 mol) was refluxed at 70°C for 72 h. The resulting crude product was washed with ethyl acetate and dried under vacuum, and compound 8 was obtained. Yield 6.89 g (93%). ^1H NMR (500 MHz, CDCl_3 , TMS): δ 10.85 (s, 1 H, imidazolium-H), 8.32 (s, 1 H, imidazolium-H), 7.65 (s, 1 H, imidazolium-H), 7.71-7.68 (m, 8 H, Ph-H), 7.49-7.39 (m, 12 H, Ph-H), 6.76 (s, 1 H, Ph-H), 6.46 (s, 2 H, Ph-H), 4.53 (s, 3 H, $-\text{CH}_3$), 4.52-4.50 (t, $J=3.8$ Hz, 2 H, $-\text{CH}_2-$), 3.63-3.50 (t, $J=4.2$ Hz, 2 H, $-\text{CH}_2-$), 3.46-3.44 (d, $J=14.0$ Hz, 4 H, $-\text{CH}_2-$). ^{13}C NMR (125 MHz, CDCl_3): δ 158.6, 138.8, 135.3, 134.5, 131.0, 130.0, 129.7, 129.3, 128.6, 128.2, 127.9, 120.2, 112.1, 70.1, 35.0, 25.8. MS (ESI): m/z 661($[\text{M}]^+$).

Acknowledgments. I thank the financial support provided by the Scientific Research Fund of Shandong Provincial Education Department (No. J07WC02) and Natural Science Foundation of Dezhou University (No. 07RC001).

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