

HETEROCYCLES, Vol. 76, No. 1, 2008, pp. 381 - 390. © The Japan Institute of Heterocyclic Chemistry  
Received, 17th February, 2008, Accepted, 16th April, 2008, Published online, 21st April, 2008. COM-08-S(N)19

## CHIRAL CATIONIC Pd-PHOSPHINOXAZOLIDINE CATALYSTS FOR A HIGHLY EFFICIENT ASYMMETRIC DIELS-ALDER REACTION IN IONIC LIQUIDS<sup>‡</sup>

Hiroto Nakano,\* Yasuhiro Nishiuchi, Kouichi Takahashi, Reiko Fujita, Koji  
Uwai, and Mitsuhiro Takeshita\*

Tohoku Pharmaceutical University, 4-4-1, Komatsushima, Aoba-ku, Sendai  
981-8558, Japan; E-mail: catanaka@tohoku-pharm.ac.jp

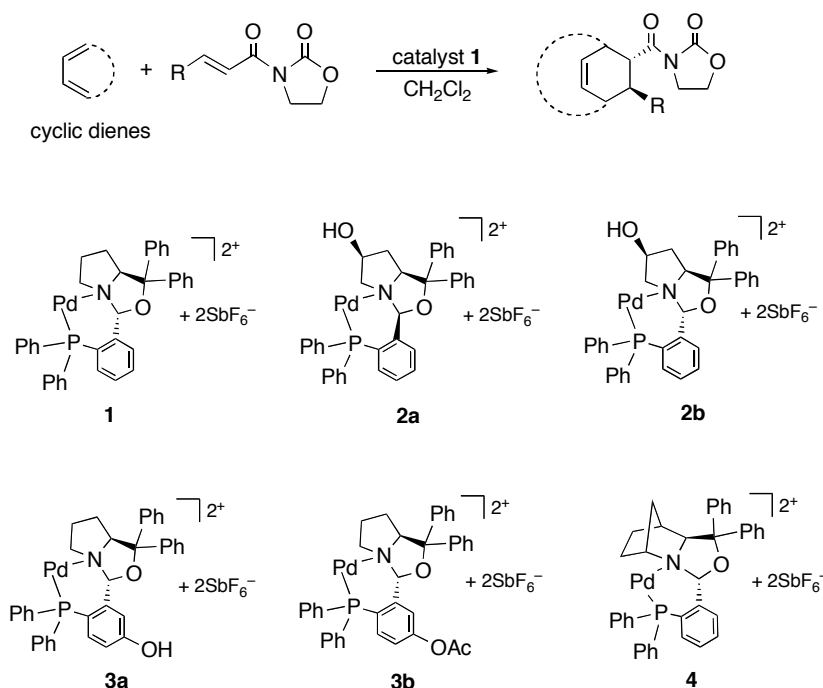
**Abstract** – Chiral cationic palladium-phosphinoxazolidine catalysts in ionic liquid afforded good to excellent enantioselectivity in Diels-Alder reactions. The catalyst was recycled three times in ionic liquid (85-90%, 71-88% ee) or seven times in a mixed ionic liquid/CH<sub>2</sub>Cl<sub>2</sub> (91-94%, 91-94% ee).

## INTRODUCTION

A catalytic asymmetric reaction is one of the most attractive methods of obtaining single enantiomers from a practical point of view. Several efficient chiral ligands and catalysts have been developed and investigated with regard to their use in such reactions.<sup>1</sup> Recently, the recovery and reuse of catalysts has attracted growing interest with the goal of meeting the need for environmentally friendly and cost-effective reaction processes.<sup>2</sup> Many methodologies have been attempted to achieve recovery and reuse; among them is the use of immobilized chiral catalysts on polymers in an asymmetric synthesis.<sup>2</sup> Ionic liquids have attracted extensive interest as excellent alternatives to organic solvents due to their favorable properties such as nonflammability, low toxicity, reusability, and high thermal stability.<sup>3</sup> Additionally, they provide good solubility for a wide range of organic, inorganic, and organometallic compounds.<sup>4</sup> To date, several reactions have been demonstrated in ionic liquids. However, the use of a catalytic asymmetric reaction has not yet been studied extensively. Furthermore, most of the reported studies have found that the efficient chemical yield of the reaction and the enantiomeric excess (ee) obtained in the usual organic solvents are difficult to reproduce in ionic liquid, and that recycling of the catalyst is less satisfactory,<sup>5</sup> except as reported by only a few groups.<sup>6</sup> The Diels-Alder (DA) reaction is one of the most efficient bond-forming reactions used widely in synthetic organic chemistry. This

<sup>‡</sup>Dedicated to Professor Ryoji Noyori on the occasion of his 70<sup>th</sup> birthday.

reaction shows excellent “atom” economy,<sup>8</sup> due to a simple cycloaddition using a diene and dienophile. Therefore many research groups have reported an enantioselective version of the reaction that relies on a chiral catalyst.<sup>9</sup> Nevertheless, to the best of our knowledge, only a few examples of asymmetric DA reactions in ionic liquid have been reported, including the use of copper-bisoxazoline,<sup>10</sup> platinum-BINAP,<sup>11</sup> platinum-NUPHOS<sup>11</sup> catalysts, and MacMillan's organocatalyst.<sup>12</sup> Most recently, we have reported that the Pd-POZ **1** catalyzed the DA reaction of cyclic dienes with *N*-acryloyl-1,3-oxazolidin-2-one dienophiles in the imidazole-typed ionic liquid was effective to obtain the DA adducts in excellent chemical yield and enantioselectivities (Scheme 1).<sup>13</sup> We report herein the catalytic asymmetric DA reactions of several cyclic and acyclic dienes with dienophiles using our explored cationic Pd-POZ catalysts **1-4** in several ionic liquids (Scheme 1).

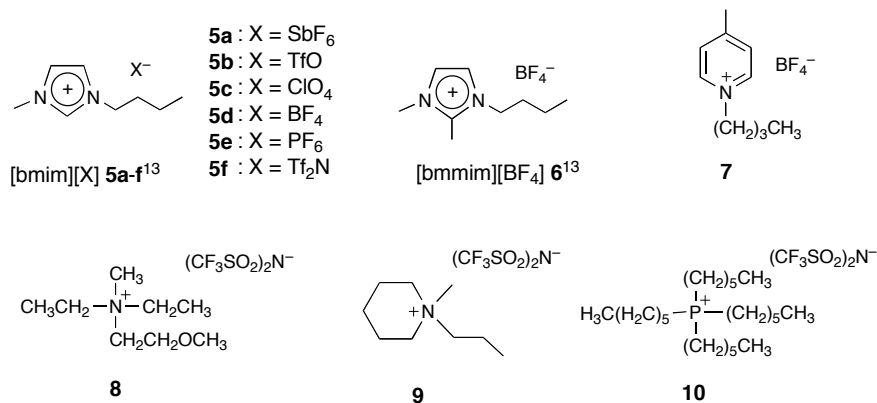


**Scheme 1.** Catalytic asymmetric Diels-Alder reaction using cationic Pd-phosphinooxazolidine catalyst **1-4**

## RESULTS AND DISCUSSION

The DA reaction using the simplest antimotate Pd-POZ catalyst **1** proceeded effectively in [1-butyl-3-methylimidazolium : bmim][BF<sub>4</sub>] **5d** among [bmim][X] **5a-f** and **6** (Table 1, entry 1).<sup>13</sup> We examined the effectiveness of catalyst **1** in four different ionic liquids **7-10** (Figure 1), a pyridinium typed 1-butyl-4-methylpyridinium tetrafluoroborate **7**, a quaternary ammonium type *N,N*-diethyl-*N*-methyl-*N*-(2-methoxyethyl)ammonium bis(trifluoromethanesulfonyl)imide **8**, a cyclic ammonium type *N*-methyl-*N*-propylpiperidinium bis(trifluoromethanesulfonyl)imide **9**, and a phosphonium type

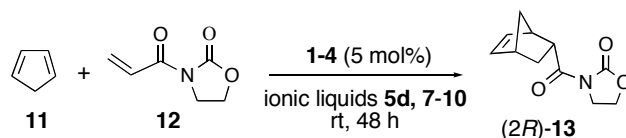
tetrahexyl phosphonium bis(trifluoromethanesulfonyl)imide **10**. The reaction of cyclopentadiene **11** with *N*-acryloyl-1,3-oxazolidin-2-one **12** was carried out in the presence of 5 mol% of catalyst **1** at room temperature for 48 h (Table 1).



**Figure 1.** Ionic liquids **5a-f**, **6-10**.

Ether was used for the separation of DA adduct **13** because ionic liquids **7-10** form a bilayer with ether. The desired **13** was isolated from the ether layer after purification by preparative thin layer chromatography (TLC). Low to Moderate chemical yields (36-61%) and good enantioselectivities (80-84% ee) were obtained in the examined reactions in ionic liquids **7-10** (Table 1, entries 2-5). The results indicate that the combination of catalyst **1** and ionic liquids **7-10** were not more effective than the combination of **1** and ionic liquid **5d**.

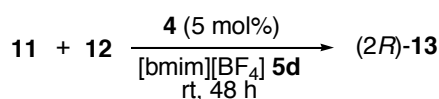
We also tested the DA reactions using other antimonate Pd-POZ catalysts **2a,b**, **3a,b**, and **4** in superior **5d** as a solvent (Table 1). In a previous study, the antimonate catalysts **1a**, **2b**, and **3b** showed superior catalytic activities to give the DA adduct **13** in high chemical yield and excellent enantioselectivity in the range of 10 to 5 mol% at -45--50 °C.<sup>14b</sup> In the present study, the reaction was carried out in the presence of 5 mol% of catalysts **2a,b**, **3a,b**, and **4** in **5d** at room temperature for 48 h. As a result, 2,7-*cis*-7-hydroxy-POZ **2a** and its counterpart 2,7-*trans*-7-hydroxy-POZ **2b** did not show satisfactory catalytic activities for chemical yields and enantioselectivities (**2a**: 43%, 65% ee, **2b**: 54%, 82% ee, entries 6,7). Similarly, Pd-POZ catalyst **3a**, having a hydroxy group on the benzene ring afforded a poor chemical yield, although good ee was observed (39%, 83% ee, entry 8). In contrast, catalyst **3b**, having an acetoxy group on the benzene ring, gave the DA adduct **13** in moderate chemical yield and good ee (70%, 86% ee, entry 9). These results indicate that the hydroxy group might not be effective in this reaction in ionic liquid, though the reason for this phenomenon is unclear. The effectiveness of the ionic liquid was demonstrated by the use of bulkier Pd-POZ catalyst **4** having an isoquinuclidine ring system as a backbone (entry 10). Thus the reaction afforded the DA adduct **13** in higher chemical yield and ee (90%, 88% ee) than those obtained in CH<sub>2</sub>Cl<sub>2</sub> at -50°C (87%, 79% ee).<sup>14b</sup>

**Table 1.** Pd-POZ catalyzed asymmetric DA reactions of cyclopentadiene **11** with dienophile **12** in ionic liquids **5d**, **7-10**

Entry	Catalyst	Ionic Liquid	Yield <sup>a</sup> (%)	<i>Endo/exo</i> <sup>b</sup>	E.e. <sup>c</sup> (%)
1 <sup>d</sup>	<b>1</b>	<b>5d</b> : BF <sub>4</sub>	89	96 : 4	96
2	<b>1</b>	<b>7</b> : BF <sub>4</sub>	36	91 : 9	83
3	<b>1</b>	<b>8</b> : Tf <sub>2</sub> N	45	87 : 13	84
4	<b>1</b>	<b>9</b> : Tf <sub>2</sub> N	56	85 : 15	80
5	<b>1</b>	<b>10</b> : Tf <sub>2</sub> N	61	97 : 3	82
6	<b>2a</b>	<b>5d</b> : BF <sub>4</sub>	43	92 : 8	65
7	<b>2b</b>	<b>5d</b> : BF <sub>4</sub>	54	94 : 6	82
8	<b>3a</b>	<b>5d</b> : BF <sub>4</sub>	39	94 : 6	83
9	<b>3b</b>	<b>5d</b> : BF <sub>4</sub>	70	94 : 6	86
10	<b>4</b>	<b>5d</b> : BF <sub>4</sub>	90	93 : 7	88

a) Isolated yields. b) The *endo/exo* ratio was determined by HPLC.c) The ee of the *endo* isomer was determined by chiral HPLC using a Daicel OD-H column. d) see reference 13.

POZ catalyst **1** was reused 3 times in ionic liquid **5d** and was successfully reused 8 times in a mixed ionic liquid **5d**/CH<sub>2</sub>Cl<sub>2</sub> (2:1) solvent.<sup>13</sup> We also examined the reuse of the effective bulkier catalyst **4** under optimized conditions, as shown in Table 2. After the first run, the same amounts of starting materials were again added to the separated ionic liquid layer. The reaction produced DA adduct **13** in 89% yield and 83% ee in the second run. In the third run, enantioselectivity decreased to 71% ee, although the chemical yield remained constant at 85%. Unfortunately, both the chemical yield and the enantioselectivity decreased to 71% and 60% ee in the fourth run due to the generation of palladium black. Effective recycling was carried out 3 times. This effective frequency of recycling was the same as that of catalyst **1**.<sup>13</sup>

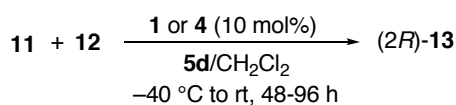
**Table 2.** Reuse of Pd-POZ catalyst **4** in ionic liquid **5d**<sup>a</sup>

Cycle	1	2	3	4
Yield (%) <sup>b</sup>	90	89	85	71
<i>Endo/exo</i> <sup>c</sup>	96 : 4	97 : 3	92 : 8	92 : 8
E.e. (%) <sup>d</sup>	88	83	71	60

a) DA reaction was performed in presence of catalyst **4** (5 mol%) at room temperature for 48 h in **5d**. b) isolated yields.c) The *endo/exo* ratio was determined by HPLC. d) The ee of the *endo* isomer was determined by chiral HPLC using a Daicel OD-H column.

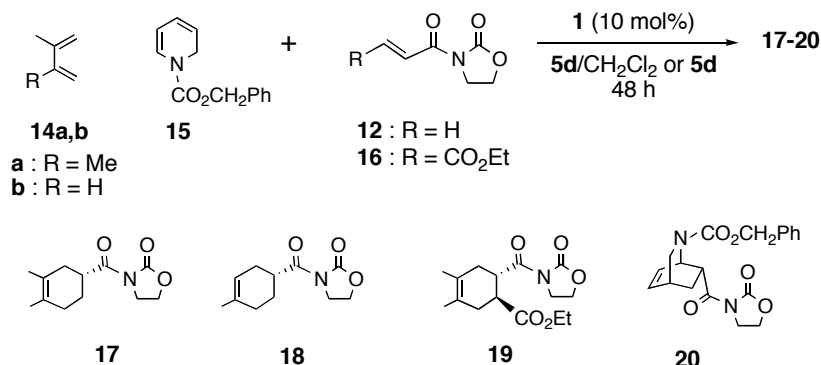
We next tried to reuse catalyst **4** in a mixed **5d**/CH<sub>2</sub>Cl<sub>2</sub> solvent. In the case of the reaction using catalyst **1**, a 1:2 ratio of mixed **5d**/CH<sub>2</sub>Cl<sub>2</sub> was effective.<sup>13</sup> The reactions using **4** were examined in both 1:1 and 1:2 ratios of mixed **5d**/CH<sub>2</sub>Cl<sub>2</sub>. This attempt had the possibility of preventing the generation of Pd-black and making it possible to carry out the reaction at low temperature because of the high viscosity of the ionic liquid. The results are summarized in Table 3. First, the reaction using catalyst **1** in **5d**/CH<sub>2</sub>Cl<sub>2</sub> (1:1) was examined. After the first run, CH<sub>2</sub>Cl<sub>2</sub> was removed under reduced pressure. [bmim][BF<sub>4</sub>] **5d** formed a bilayer with the ether, and the desired DA adduct **13** was isolated from the ether layer after purification by preparative TLC. Consistent with our expectations, the reaction afforded DA adduct **13** in 97% yield and with 96% ee (entry 1). CH<sub>2</sub>Cl<sub>2</sub> solvent and the same amounts of starting materials were again added to the separated ionic liquid layer. Fairly good chemical yield and excellent ee (99%, 97% ee, entry 2) were also obtained in the second run. The catalyst was successfully recycled 5 times without any significant decrease in the excellent ee (95-97% ee, entries 1-5, cycle 1-5), although the chemical yield decreased to 90%. And both chemical yield and ee decreased to 85% and 85% ee in the sixth run (entry 6). Effective recycling was carried out 5 times. Next, the reaction using catalyst **4** was examined in a 1:1 ratio of **5d**/CH<sub>2</sub>Cl<sub>2</sub>. As a result, the catalyst was successfully recycled 5 times without any significant decrease in the fairly good chemical yield and ee (90-93%, 90-93% ee, entries 7-11, cycle 1-5). However, both chemical yield and ee decreased to 80% and 83% ee in sixth run (entry 12). Effective recycling was carried out 5 times. Furthermore, the reuse of catalyst **4** in a 1:2 ratio of **5d**/CH<sub>2</sub>Cl<sub>2</sub> was examined. This attempt also brought about an increase in the fairly good chemical yield and enantioselectivity (94%, 93% ee, entry 13) in the first run. Fairly good chemical yield and ee (93%, 93% ee) were also obtained in the second run (entry 14). The catalyst was successfully recycled 7 times without any significant decrease in the good chemical yield and ee (91-94%, 91-94% ee, entries 13-19, cycles 1-7). Unfortunately, the chemical yields and enantioselectivities decreased sequentially in the eighth and ninth runs (eighth run: 88%, 87% ee, ninth run: 75%, 79% ee, entries 20,21). In addition, the reaction afforded only a moderate chemical yield and ee in the tenth run (60%, 70% ee, entry 22). The effective number of recycling time was 7.

Based on both the present results and our previous study, catalysts **1** and **4** are effective in ionic liquid. In particular, catalyst **1** appears to be the most effective for obtaining good chemical yield, enantioselectivity, and recycling time. To expand the utility of this system, we examined the DA reactions of several dienes (**14a,b**, **15**) with oxazolidin-2-one dienophiles (**12**, **16**) in a superior combination of **5d** and CH<sub>2</sub>Cl<sub>2</sub> as a mixed solvent using superior antimonate catalyst **1**. The results are summarized in Table 4. In our previous study, the reactions of cyclic dienes such as cyclopentadiene or cyclohexadiene with *N*-acryloyl-

**Table 3.** Reuse of Pd-POZ catalyst **1** or **4** in ionic liquid **5d**/CH<sub>2</sub>Cl<sub>2</sub><sup>a</sup>

Entry	Catalyst	<b>5d</b> / CH <sub>2</sub> Cl <sub>2</sub>	Cycle	Time (h)	Yield (%) <sup>b</sup>	Endo/ exo <sup>c</sup>	E.e. (%) <sup>d</sup>	Entry	Catalyst	<b>5d</b> / CH <sub>2</sub> Cl <sub>2</sub>	Cycle	Time (h)	Yield (%) <sup>b</sup>	Endo/ exo <sup>c</sup>	E.e. (%) <sup>d</sup>
1	<b>1</b>	1/1	1	48	97	97:3	96	12	<b>4</b>	1/1	6	72	80	95:5	83
2	<b>1</b>	1/1	2	48	99	98:2	97	13	<b>4</b>	1/2	1	48	94	98:2	93
3	<b>1</b>	1/1	3	48	97	98:2	95	14	<b>4</b>	1/2	2	48	93	96:4	93
4	<b>1</b>	1/1	4	48	96	97:3	96	15	<b>4</b>	1/2	3	48	94	97:3	94
5	<b>1</b>	1/1	5	72	90	97:3	95	16	<b>4</b>	1/2	4	48	92	98:2	91
6	<b>1</b>	1/1	6	72	85	95:5	85	17	<b>4</b>	1/2	5	72	93	96:4	92
7	<b>4</b>	1/1	1	48	93	95:5	92	18	<b>4</b>	1/2	6	72	91	97:3	92
8	<b>4</b>	1/1	2	48	91	96:4	93	19	<b>4</b>	1/2	7	72	91	95:5	93
9	<b>4</b>	1/1	3	48	93	96:4	90	20	<b>4</b>	1/2	8	72	88	96:4	87
10	<b>4</b>	1/1	4	48	90	95:5	92	21	<b>4</b>	1/2	9	96	75	97:3	79
11	<b>4</b>	1/1	5	72	91	97:3	91	22	<b>4</b>	1/2	10	96	60	96:4	70

a) DA reaction was performed in presence of catalyst **1** or **4** (10 mol%) at  $-40^\circ\text{C}$  to room temperature for 48-96 h in **5d**/CH<sub>2</sub>Cl<sub>2</sub>. b) Isolated yields. c) The *endo/exo* ratio was determined by HPLC. d) The ee of the *endo* isomer was determined by chiral HPLC using a Daicel OD-H column.

**Table 4.** Pd-POZ **1** catalyzed asymmetric DA reaction of dienes **14a,b**, **15** with dienophiles **12**, **16** in **5d**/CH<sub>2</sub>Cl<sub>2</sub><sup>a</sup> or **5d**

Entry	Diene / Dienophile	Solvent	Product	Temp. ( $^\circ\text{C}$ )	Time (h)	Yield <sup>b</sup> (%)	Endo / exo <sup>c</sup>	E.e. <sup>d</sup> (%)
1	<b>14a</b> / <b>12</b>	<b>5d</b> /CH <sub>2</sub> Cl <sub>2</sub>	<b>17</b>	-40 to rt	48	70	---	60
2 <sup>e</sup>	<b>14a</b> / <b>12</b>	CH <sub>2</sub> Cl <sub>2</sub>	<b>17</b>	-45	48	88	---	51
3	<b>14b</b> / <b>12</b>	<b>5d</b> /CH <sub>2</sub> Cl <sub>2</sub>	<b>18</b>	-40 to rt	48	82	---	60
4 <sup>e</sup>	<b>14b</b> / <b>12</b>	CH <sub>2</sub> Cl <sub>2</sub>	<b>18</b>	-45	48	70	---	50
5	<b>14a</b> / <b>16</b>	<b>5d</b> /CH <sub>2</sub> Cl <sub>2</sub>	<b>19</b>	-40 to rt	48	71	---	78 <sup>f</sup>
6 <sup>e</sup>	<b>14a</b> / <b>16</b>	CH <sub>2</sub> Cl <sub>2</sub>	<b>19</b>	-45	72	56	---	82
7	<b>15</b> / <b>12</b>	<b>5d</b>	<b>20</b>	rt	48	71	<i>endo</i>	86

a) DA reaction was performed in **5d**/CH<sub>2</sub>Cl<sub>2</sub>=1/2. b) Isolated yields. c) The *endo/exo* ratio was determined by HPLC or <sup>1</sup>H NMR. d) The ee of the *endo* isomer was determined by chiral HPLC using a Daicel D-H column or AD-H column. e) See reference 14b. f) The ee was determined by comparison with known optical rotation after iodolactonization.

1,3-oxazolidin-2-one dienophiles afforded good to excellent chemical yield and ee.<sup>13</sup> We tried the reaction using acyclic dienes in ionic liquid. When 2,3-dimethyl-1,3-butadiene **14a** or isoprene **14b** were used as acyclic dienes, the ee of the corresponding DA adducts increased compared with the results obtained under the usual conditions<sup>14b</sup> (entries 1-4). Moreover, the reaction of **14a** with dienophile **16** afforded the DA adduct **19** in good chemical yield and ee (entry 5). In this reaction, only the chemical yield increased compared with the results obtained under the usual conditions.<sup>14b</sup> The isoquinuclidine type DA adduct from 1,2-dihydropyridines are useful synthetic intermediates for oseltamivir (Tamiflu),<sup>15</sup> ibogain,<sup>16</sup> and so on. The reaction of **15** with **12** was also carried out only with the use of **5d** as a solvent. As a result, the corresponding DA adduct **20** was obtained in good chemical yield and ee (71%, 86% ee, entry 7), although the results are not superior to those in the case of 1-phenoxy-carbonyl-1,2-dihydropyridine.<sup>13</sup>

In conclusion, we have developed an efficient asymmetric DA reactions using cationic Pd-POZ catalysts in ionic liquids. Under the conditions using ionic liquid, the catalyst was easily recycled and showed good asymmetric catalytic activity. The combination of antimonate catalyst **4** and ionic liquid **5d** was the effective for affording a good chemical yield and enantioselectivity. Furthermore, the use of the mixed **5d** and CH<sub>2</sub>Cl<sub>2</sub> as a solvent brought about an increase in the chemical yield, enantioselectivity, and recycling times. Using the mixed **5d**/CH<sub>2</sub>Cl<sub>2</sub> (1:2), catalyst **4** was successfully reused 7 times without any significant decrease in chemical yield (91-94%) and enantioselectivity (91-94% ee). Moreover, this system was also effective in the DA reaction for deriving synthetically useful intermediates using **15** as a diene. The asymmetric DA reactions using our Pd-POZ catalyst in ionic liquid have been shown to be practical from both economical and environmental perspectives. Further studies to examine the scope and limitations of our Pd-POZ catalyst in the asymmetric DA reaction in ionic liquids are now in progress.

## EXPERIMENTAL

IR spectra was measured with a PERKIN ELMER 1725X spectrophotometer. <sup>1</sup>H-NMR spectra was recorded on a JEOL JNM-GSX 400 spectrometer with TMS as an internal standard. MS were taken on a Hitachi RMG-6MG and a JEOL-JNM-DX 303 spectrometers. Optical rotations was measured with a JASCO-DIP-370 digital polarimeter. All reactions were carried out under argon in oven-dried glassware with magnetic stirring. Ionic liquid **5d** was purchased from Tokyo kasei. Ionic liquids **7** and **10** were purchased from Fluka. Ionic liquids **8** and **9** were purchased from Kanto Chemical. Commercial grade solvents and reagents were used without further purification with the following exceptions: Dichloromethane was distilled from calcium hydride. Cyclopentadiene was distilled by cracking dicyclopentadiene over calcium hydride.

**General procedure for the asymmetric DA reactions using cationic catalysts **1**, **2a,b**, **3a,b**, and **4** in ionic liquids **5d**, **7-10**.** PdCl<sub>2</sub>-POZ complexes<sup>14b</sup> (0.018 mmol) and AgSbF<sub>6</sub> (0.053 mmol) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL), and the mixture was stirred for 1 h at rt under Ar to produce a yellow solution with a white AgCl precipitate, respectively. The mixture was filtered in air through filter paper, and evaporated. To the resulting cationic catalysts **1**, **2a,b**, **3a,b**, **4** were added ionic liquids **5d**, **7-10** (0.5 mL) and a solution of dienophile **12** (50 mg, 0.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL). After the mixture was stirred for a few minutes, CH<sub>2</sub>Cl<sub>2</sub> was removed under reduced pressure and diene **11** (0.12 mL, 1.77 mmol) was added. The reaction mixture was stirred at room temperature under Ar. After 48 h, the reaction mixture was quenched with saturated aqueous NaHCO<sub>3</sub> solution and extracted twice with Et<sub>2</sub>O. The combined organic layer was washed with brine, dried with anhydrous MgSO<sub>4</sub>, and concentrated. The crude product was purified by preparative TLC on silica gel (1:1 hexane:AcOEt) to give the DA adduct **13**. HPLC analysis (Daicel Chiralcel OD-H) indicated the *endo/exo* ratio and the enantiomeric excess of the product (Tables 1).<sup>14b</sup>

**Reuse of cationic catalyst **4** in [bmim][BF<sub>4</sub>] **5d** for the asymmetric DA reaction.** The cationic catalyst **4** was prepared according to the above procedure. To a solution of **4** (0.018 mmol) in [bmim][BF<sub>4</sub>] **5d** (0.5 mL) was added dienophile **12** (50 mg, 0.35 mmol) and diene **11** (0.12 mL, 1.77 mmol). The reaction mixture was stirred at rt for 48 h. After the reaction, the mixture was washed with Et<sub>2</sub>O (1.0 mL×10). The resulting ionic liquid was dried under reduced pressure for 2 h and charged with dienophile **12** (50 mg, 0.35 mmol) and diene **11** (0.12 mL, 1.77 mmol), and the next cycle was then begun. The combined Et<sub>2</sub>O layer was purified according to the above procedure, giving the DA adduct **7** (Table 2). Spectral data matched literature values.<sup>13,14b</sup>

**General procedure for reuse of cationic catalyst **4** in [bmim][BF<sub>4</sub>] **5d**/CH<sub>2</sub>Cl<sub>2</sub>.** The cationic catalyst **4** was prepared according to the above procedure. To a solution of **4** (0.036 mmol) in [bmim][BF<sub>4</sub>] **5d** (0.5 mL) was added a solution of dienophile **12** (50 mg, 0.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 or 1.0 mL). After the mixture was cooled to -40°C, diene **11** (0.12 mL, 1.77 mmol) was added. The reaction mixture was stirred at -40°C for 6 h, and the temperature was subsequently raised to rt. After the reaction, CH<sub>2</sub>Cl<sub>2</sub> was removed under reduced pressure and the ionic liquid was washed with Et<sub>2</sub>O (1.0 mL ×10). The resulting ionic liquid was dried under reduced pressure for 2 h and charged with a solution of dienophile **12** (50 mg, 0.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL). The mixture was cooled to -40°C, and diene **11** was added (0.12 mL, 1.77 mmol); the next cycle was then begun. The combined Et<sub>2</sub>O layer was purified according to the above procedure, giving the DA adduct **13** (Table 13). Spectral data matched literature values.<sup>14b</sup>



**General procedure for the asymmetric DA reactions of dienes 14a,b, 15 with dienophiles 12, 16, 17 using cationic catalyst 1 in [bmim][BF<sub>4</sub>] 5d/CH<sub>2</sub>Cl<sub>2</sub> or 5d.** The cationic catalyst **1** was prepared according to the above procedure. To a solution of **1** (0.036 mmol) in [bmim][BF<sub>4</sub>] **5d** (0.5 mL) was added a solution of dienophiles **12**, **16**, **17** (50 mg, 0.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL). The cases of the reaction of **14a,b** with **12**, **16**, **17**: after the mixture was cooled to -40°C, dienes **14a,b** (1.77 mmol) were added. The reaction mixture was stirred at -40°C for 6 h, and the reaction temperature was subsequently raised to rt. After the reaction, CH<sub>2</sub>Cl<sub>2</sub> was removed under reduced pressure, and the ionic liquid was washed with Et<sub>2</sub>O (1.0 mL×10). The combined Et<sub>2</sub>O layer was purified according to the above procedure, giving the DA adduct **18-21** (Table 4). Spectral data matched literature values.<sup>13,14b</sup> The case of the reaction of **15** with **12**: to the resulting cationic catalyst, ionic liquids **5d** (0.5 mL) and a solution of dienophile **12** (50 mg, 0.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) was added. After the mixture was stirred for a few minutes, CH<sub>2</sub>Cl<sub>2</sub> was removed under reduced pressure and diene **15** (1.77 mmol) was added. The reaction mixture was stirred at rt under Ar. After 48 h, the reaction mixture was quenched with saturated aqueous NaHCO<sub>3</sub> solution and extracted twice with Et<sub>2</sub>O. The combined organic layer was washed with brine, dried with anhydrous MgSO<sub>4</sub>, and concentrated. The crude product was purified by preparative TLC on silica gel (1:1 hexane:AcOEt) to give the DA adduct **21**. HPLC analysis (Daicel Chiralcel OD-H) indicated the *endo/exo* ratio and the enantiomeric excess of the product (Tables 1).<sup>13, 14d</sup>

## REFERENCES

1. (a) 'Comprehensive Asymmetric Catalysis,' Vol. I-III, ed. by E. N. Jacobsen, A. Pfaltz, and H. Yamamoto, Springer, Berlin, 1999. (b) 'Catalytic Asymmetric Synthesis,' ed. by J. Ojima, Wiley-VCH, New York, 2000.
2. (a) 'Chiral Catalyst Immobilization and Recycling,' ed. by D. E. DeVos, I. F. J. Vankelecom, and P. A. Jacobs, Wiley-VCH, Weinheim, 2000. (b) Q.-H. Fan, Y.-M. Li, and A. S. C. Chan, *Chem. Rev.*, 2002, **102**, 3385. (c) S. Braese, F. Lauterwasser, and R. E. Ziegert, *Adv. Synth. Catal.*, 2003, **345**, 869.
3. (a) 'Ionic Liquids-Industrial Applications for Green Chemistry,' ed. by R. D. Roger and K. R. Seddon, ACS Symposium Series 818, American Chemical Society, 2002. (b) 'Ionic Liquids in Synthesis,' ed. by P. Wasserscheid and T. Welton, Wiley-VCH, Weinheim, 2003. (c) 'Electrochemical Aspect of Ionic Liquids,' ed. by H. Ohno, John Wiley and Sons, New York, 2005.
4. (a) T. Welton, *Chem. Rev.*, 1999, **99**, 2071. (b) P. Wasserscheid and W. Keim, *Angew. Chem. Int. Ed.*, 2000, **39**, 3772. (c) R. Sheldon, *Chem. Commun.*, 2001, 2399.
5. C. Baudequin, J. Baudoux, J. Levillain, D. Cahard, A.-C. Gaumont, and J.-C. Plaquevent, *Tetrahedron: Asymmetry*, 2003, **14**, 3081.
6. (a) Y. Hamashima, H. Takano, D. Hotta, and M. Sodeoka, *Org. Lett.*, 2003, **5**, 3225. (b) N. S. Chwdari,

- D. B. Ramachary, and C. F. Barbas III, *Synlett*, 2003, 1906. (c) I. Kawasaki, K. Tsunoda, T. Tsuji, T. Yamaguchi, H. Shibuta, N. Uchida, M. Yamashita, and S. Ohta, *Chem. Commun.*, 2005, 2134.
7. (a) 'Lewis Acids in Organic Synthesis,' ed. by H. Yamamoto, Wiley-VCH, Weinheim, 2000. (b) 'Cycloaddition Reactions in Organic Synthesis,' ed. by S. Kobayashi and K. A. Jørgensen, Wiley-VCH, Weinheim, 2001.
8. (a) B. M. Trost, *Science*, 1991, **254**, 1474. (b) B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 259.
9. (a) E. J. Corey and A. Guzman-Perez, *Angew. Chem. Int. Ed.*, 1998, **37**, 388. (b) K. Ishihara, H. Kurihara, M. Matsumoto, and H. Yamamoto, *J. Am. Chem. Soc.*, 1998, **120**, 6920. (c) A. K. Ghosh, P. Mathivanan, and J. Cappiello, *Tetrahedron: Asymmetry*, 1998, **9**, 1. (d) K. A. Jørgensen, M. Johannsen, S. Yao, H. Audrain, and J. Thorhauge, *Acc. Chem. Res.*, 1999, **32**, 605. (e) J. S. Johnson and D. A. Evans, *Acc. Chem. Res.*, 2000, **33**, 325.
10. I. Meraczk and T. Oh, *Tetrahedron Lett.*, 2003, **44**, 6465.
11. S. Doherty, P. Goodrich, C. Hardacre, H.-K. Luo, D. W. Rooney, K. R. Seddon, and P. Styring, *Green Chem.*, 2004, **6**, 63.
12. J. K. Park, P. Sreekanth, and B. M. Kim, *Adv. Synth. Catal.*, 2004, **346**, 49.
13. The preliminary results were partially reported, see: K. Takahashi, H. Nakano, and R. Fujita, *Chem. Commun.*, 2007, 263.
14. (a) H. Nakano, Y. Okuyama, Y. Suzuki, R. Fujita, and C. Kabuto, *Chem. Commun.*, 2002, 1146. (b) H. Nakano, K. Takahashi, Y. Okuyama, C. Senoo, N. Tsugawa, Y. Suzuki, R. Fujita, K. Sasaki, and C. Kabuto, *C. J. Org. Chem.*, 2004, **69**, 7092. (c) H. Nakano, N. Tsugawa, and R. Fujita, *Tetrahedron Lett.*, 2005, **46**, 5677. (d) H. Nakano, N. Tsugawa, and R. Fujita, *Tetrahedron*, 2006, **62**, 10879. (e) H. Nakano, Y. Okuyama, K. Takahashi, R. Fujita, and C. Kabuto, *J. Synth. Org. Chem. Jpn.*, 2007, **65**, 1191.
15. N. Satoh, T. Akiba, S. Yokoshima, and T. Fukuyama, *Angew. Chem. Int. Ed.*, 2007, **46**, 5734.
16. N. Takenaka, Y. Huang, and V. H. Rawal, *Tetrahedron*, 2002, **58**, 8299.