

# Lewis acid-promoted reactions of zirconacyclopentadienes with isocyanates. A one-pot three-component synthesis of multiply-substituted iminocyclopentadienes from one isocyanate and two alkynes†

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Multiply-substituted iminocyclopentadienes were formed from Lewis acid-promoted reactions of zirconacyclopentadienes and isocyanates *via* a one-pot three-component coupling process; the C=O double bond of the RN=C=O moiety in the isocyanate was cleaved, and the isocyanates behaved formally as a one-carbon unit with Lewis acid-dependent and substituent-dependent reactions being realized.

We have recently been interested in Lewis acid-mediated reactions of organometallic compounds with organic substrates,<sup>1,2</sup> since the development of synthetic methods can be expected from a combination of transition metal-mediated C–C bond-forming reactions and Lewis acid-mediated organic transformations.<sup>1–10</sup> This strategy has been proved to be efficient and useful by us,<sup>1,2</sup> Tilley,<sup>3</sup> Negishi<sup>4</sup> and others.<sup>5–10</sup> Zirconacyclopentadienes **1**, which can be easily prepared *in situ* from two alkyne molecules and low valent zirconocene species, are generally inert towards most organic substrates.<sup>11</sup> Interestingly, as we have reported previously, zirconacyclopentadienes **1** could react smoothly with aldehydes to afford cyclopentadiene derivatives when a Lewis acid such as AlX<sub>3</sub> or BF<sub>3</sub> was present in the reaction mixture.<sup>1</sup>

Isocyanates (RN=C=O) are a class of important synthetic intermediates. The site selectivities of these unsymmetrical heterocumulenes toward nucleophiles are of great interest in heteroatom chemistry and controlled synthetic chemistry. As part of our continuous interest in the development of synthetically useful methods by combining transition metal-mediated C–C bond forming reactions with Lewis acid-mediated organic transformations, we investigated the reactions of **1** with unsymmetrical heterocumulenes such as isothiocyanates (RN=C=S) and isocyanates (RN=C=O). Iminocyclopentadiene derivatives composed of three different components were prepared in one pot in excellent yields *via* cleavage of the C=O double bond of the RN=C=O moiety (Scheme 1). Depending on the Lewis acids used and the reaction conditions, different types of products were formed.

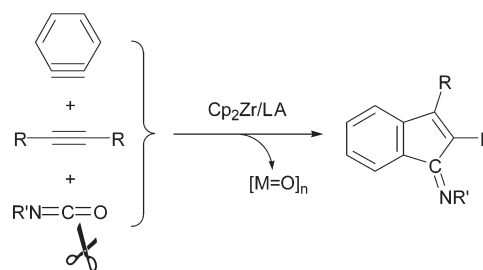
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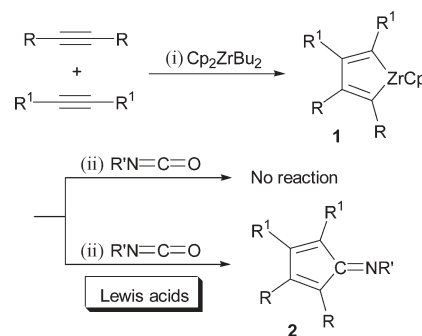
† Electronic Supplementary Information (ESI) available: Experimental details and copies of <sup>1</sup>H and <sup>13</sup>C NMR charts for all new compounds. See <http://dx.doi.org/10.1039/b509142j>

No reaction was observed when zirconacyclopentadienes **1** were treated with isocyanates. As demonstrated in Scheme 2, after addition of BF<sub>3</sub>·Et<sub>2</sub>O, reaction of zirconacyclopentadienes **1** with isocyanates immediately took place to afford cyclopentadienyl imines **2**. Representative examples are given in Table 1.

2,3,4,5-Tetra-substituted-1-zirconacyclopentadienes **1a** (with tetraalkyl substituents) and **1b** (with tetraaryl substituents),<sup>12</sup> and zirconaindene **1c**<sup>13</sup> all reacted with aryl isocyanates in the presence of BF<sub>3</sub>·Et<sub>2</sub>O to afford multiply-substituted iminocyclopentadiene derivatives **2a–f** and indenyl imines **2g–i**, respectively, in good to high isolated yields. This reaction is highly site selective; only the C=O double bond in the RN=C=O moiety is cleaved to form the iminocyclopentadienes. No cleavage of the C=N double bond is observed. Iminocyclopentadiene and indenimine derivatives are all interesting and useful intermediates for synthetic chemistry and organometallic chemistry.<sup>14,15</sup> The reaction reported here provides an alternative practical method for the preparation of such complex compounds, *via* a one-pot three-component procedure. It should be noted that reactions of aliphatic isocyanates with



Scheme 1



Scheme 2

**Table 1** Preparation of multi-substituted iminocyclopentadienes from  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ -mediated reaction of zirconacyclopentadienes with isocyanates<sup>a</sup>

Run	Zirconacyclopentadiene <b>1</b>	Isocyanate Ar group	Product <b>2</b>	Yield of <b>2</b> (%) <sup>b</sup>	
1		3,5-dichlorophenyl		74	
2		2,4-dichlorophenyl		<b>2b</b>	73
3		4-bromophenyl		<b>2c</b>	81
4		4-fluorophenyl		<b>2d</b>	77
5		2-chlorophenyl		<b>2e</b>	75
6		2-chlorophenyl		<b>2f</b>	91
7		2-chlorophenyl		<b>2g</b>	59
8		4-methoxyphenyl		<b>2h</b>	55
9		4-methylphenyl		<b>2i</b>	51

<sup>a</sup> Reaction conditions: 2 equiv. of  $\text{ArNCO}$ , 4 equiv. of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ ; the reaction mixture was stirred firstly at  $0^\circ\text{C}$  for 1 h then at  $80^\circ\text{C}$  for 1 h.<sup>b</sup> Isolated yields.

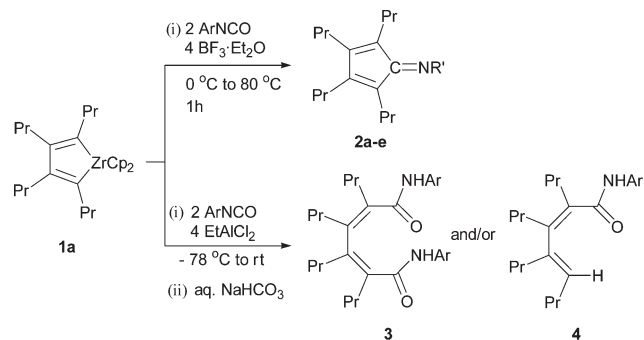
zirconacyclopentadienes and zirconaindenes under the same reaction conditions described above generally gave messy mixtures of products. Messy mixtures of products were also obtained when isothiocyanates, either aryl or aliphatic, were applied under the same reaction conditions.

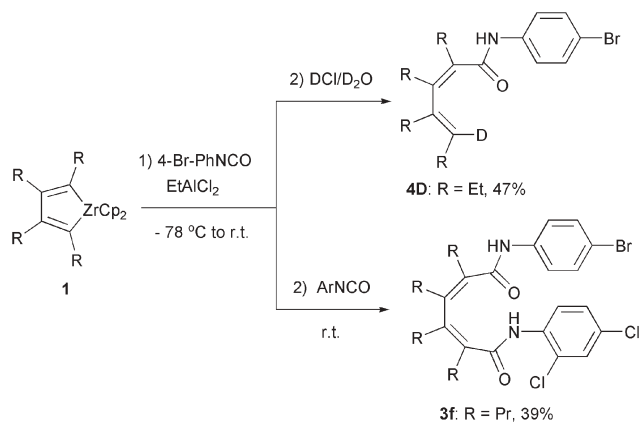
Other Lewis acids generally behaved differently from  $\text{BF}_3$ . For example,  $\text{CsF}$ ,  $\text{InCl}_3$ ,  $\text{CoCl}_2$ ,  $\text{VCl}_3$ ,  $\text{TiCl}_4$  and  $\text{CrCl}_3$  did not promote the above reactions. In the case of  $\text{FeCl}_3$  as the Lewis acid, a messy mixture of reaction products was observed. When  $\text{AlCl}_3$  and  $\text{AlBr}_3$  were used, the zirconacyclopentadienes **1** and isocyanates disappeared, but did not result in formation of isolable products. Very interestingly, when  $\text{EtAlCl}_2$  was used as the Lewis acid, substituent-dependent and Lewis acid-dependent selectivities were observed. Scheme 3 shows a representative example. Results are given in Table 2. Treatment of 2,3,4,5-tetrapropyl-1-zirconacyclopentadiene **1a** with  $\text{ArNCO}$  in the presence of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  afforded their iminocyclopentadiene derivatives in high yields (Table 1). However, on the contrary, different products were obtained only by changing the Lewis acid from  $\text{BF}_3$  to  $\text{EtAlCl}_2$  (Table 2). No iminocyclopentadiene derivatives were obtained when  $\text{EtAlCl}_2$  was used as the Lewis acid. Furthermore, the substituent on the Ar ring played a very important role in

determining the type of products obtained. 2,4-Dichlorophenyl isocyanate (Table 2, run 1) and 2-chlorophenyl isocyanate (Table 2, run 2) afforded 1,6-bisamide derivatives in high isolated yields whilst 4-bromophenyl isocyanate (Table 2, run 3) gave the monoamide product.<sup>16</sup> Other aryl isocyanates such as 4-chloro-, 4-fluoro-, and 4-methyl- isocyanates afforded a mixture of bis- and monoamide derivatives. Such dramatic Lewis acid-dependent and substituent-dependent changes have not been observed in our previous work. Transmetalation of the zirconium species to an aluminium species is assumed to be essential for this reaction. Further investigation is needed to explain this novel selectivity.

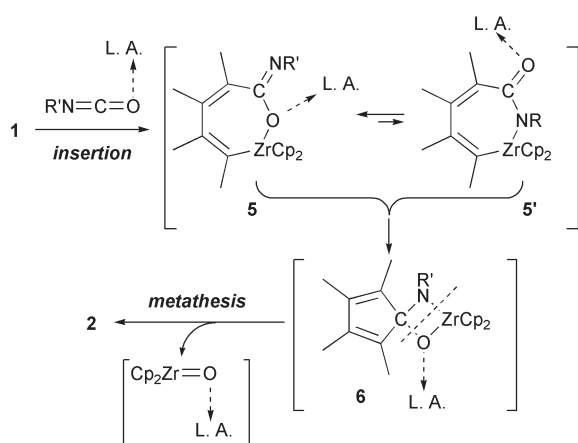
**Table 2**  $\text{EtAlCl}_2$ -mediated substituent-dependent reactions of zirconacyclopentadiene **1d** with isocyanates<sup>a</sup>

Run	Isocyanate	Yield of <b>2</b> (%)	Yield of <b>3</b> (%)	Yield of <b>4</b> (%)
1		0	<b>3a</b> : 89	trace
2		0	<b>3b</b> : 80	0
3		0	0	<b>4a</b> : 54
4		0	<b>3c</b> : 23	<b>4b</b> : 30
5		0	<b>3d</b> : 26	<b>4c</b> : 40
6		0	<b>3e</b> : 34	<b>4d</b> : 21

<sup>a</sup> Isolated yields**Scheme 3**



Scheme 4



Scheme 5

As given in Table 2, 4-bromophenyl isocyanate (run 3) afforded **4a** as the sole product after hydrolysis, which indicates that the intermediate can be further applied. Indeed, as demonstrated in Scheme 4, deuteration of the reaction mixture with DCI/D<sub>2</sub>O afforded the deuterated product **4D** in 47% isolated yield. Addition of 2,4-dichlorophenyl isocyanate to the reaction mixture of **1a** with 4-bromophenyl isocyanate generated the mixed bisamide derivative **3f** in 39% isolated yield.

For the formation of iminocyclopentadienes **2** from the BF<sub>3</sub>-mediated reaction of zirconacyclopentadienes **1** with isocyanates, a proposed reaction mechanism is given in Scheme 5. Metathesis in **6** is assumed to be a key process in the mechanism from **1** to **2**.<sup>17</sup> Detailed investigation to understand the scope, application and reaction mechanisms is in progress.

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