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Bis-zirconium and bis-hafnium catalysts for the strong activation of carbonyl substrates

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Abstract

(3,3′-Di-*t*-butyl-5,5′-dimethylbenzophenone-2,2′-dioxy)bis(triisopropoxyzirconium) and its hafnium derivative can be successfully utilized in organic synthesis as bimetallic Lewis acid catalysts. The high activation ability of such catalysts toward carbonyls is emphasized using several synthetic examples including the asymmetric allylation in comparison with the corresponding mono-Zr as well as bis-Ti catalysts. © 2000 Elsevier Science Ltd. All rights reserved.

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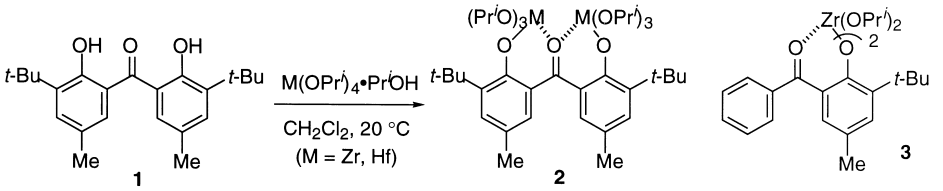
Our recent publication on the simultaneous coordination and double activation phenomena of carbonyl oxygens by bis-titanium reagent as a bidentate Lewis acid catalyst prompted us to examine the chemical reactivity of a homologous series of Ti such as Zr and Hf.[1,2] The requisite bis-Zr catalyst **2** (M = Zr) can be prepared by mixing 3,3′-di-*t*-butyl-2,2′-dihydroxy-5,5′-dimethylbenzophenone (**1**) with $Zr(OPr^i)_4{\cdot}Pr^iOH$ (2 equiv.) (Scheme 1) in a manner similar to that of the corresponding bis-Ti catalyst as described previously.[1] The corresponding mono-Zr catalyst **3** was obtainable by a simple mixing of 3-*t*-butyl-2-hydroxy-5-methylbenzophenone and $Zr(OPr^i)_4{\cdot}Pr^iOH$.[3]



Scheme 1.

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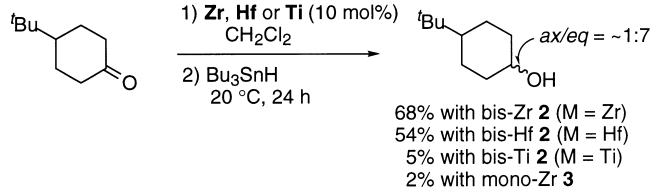
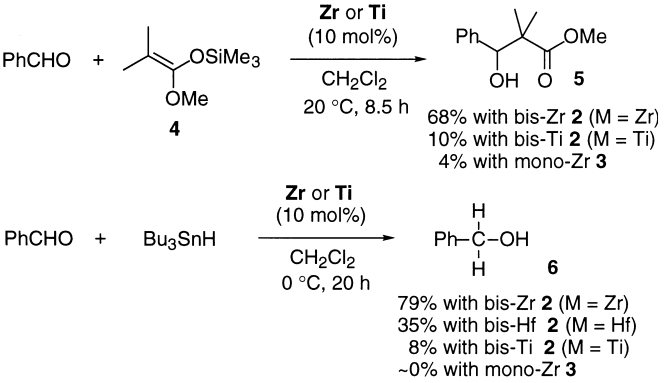
Complexation of 4-*tert*-butylcyclohexanone with the in situ-generated bis-Zr catalyst **2** (M = Zr, 10 mol%) in CH_2Cl_2 and subsequent treatment of Bu_3SnH (1.1 equiv.) at 0°C for 5 min and at 20°C for 24 h afforded 4-*tert*-butylcyclohexanol in 68% yield (Scheme 2). Bis-Hf catalyst **2** (M = Hf) showed to be less reactive in this reduction (54%). In contrast, the corresponding bis-Ti catalyst (10 mol%) dramatically lowered the yield of the alcohol product (5%). Further, reduction of 4-*tert*-butylcyclohexanone with mono-Zr catalyst **3** (10 mol%) under otherwise similar reduction conditions gave 4-*tert*-butylcyclohexanol in only 2% yield. These results clearly demonstrate that the bis-Zr catalyst **2** strongly enhances the reactivity of ketone carbonyl toward hydride transfer via the strong electrophilic activation of carbonyl moiety.



Scheme 2.

A similar difference of reactivity among bis-Zr **2** (M = Zr) and the corresponding bis-Hf and bis-Ti catalysts **2** (M = Hf, Ti) is observed in the aldol reaction and reduction of aldehydes. Thus, reaction of benzaldehyde with ketene silyl acetal **4** or Bu_3SnH (1.1 equiv. each) in the presence of catalytic bis-Zr **2** (M = Zr, 10 mol%) proceeded smoothly to furnish the corresponding aldol **5** or alcohol **6** in 68–79% yields, respectively, though its Ti counterpart gave only 8–10% yields of the products under similar conditions (Scheme 3).

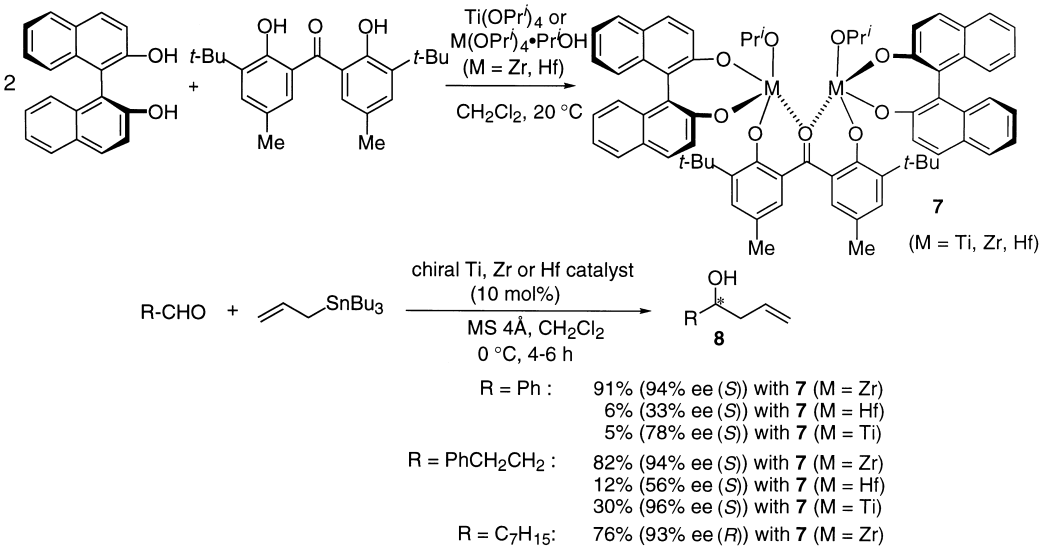


Scheme 3.

The activation phenomena of carbonyl moiety by bis-Zr catalyst **2** (M = Zr) was obtained by ^{13}C NMR spectroscopy using DMF as a carbonyl substrate. Thus, the 75 MHz ^{13}C NMR measurement of the 1:1 $Zr(OPr^i)_4$:DMF complex and the 1:1 mono-Zr **3**:DMF complex in $CDCl_3$ at 20°C showed that the original signal of DMF carbonyl at δ 162.42 shifted slightly to δ 162.87 and 162.64, respectively. These results imply the feeble Lewis acidity of $Zr(OPr^i)_4$ and mono-Zr **3**. In contrast, 1:1 bis-Zr **2** (M = Zr):DMF chelation complex under similar conditions undergoes a

further downfield shift for the DMF carbonyl (δ 163.30), implying the strong electrophilic activation of the DMF carbonyl.

The present approach is applicable to the enantioselective allylation of aldehydes with chiral bis-Zr or bis-Hf catalyst of type **7**,[4–6] which is conveniently prepared by mixing (*S*)-binaphthol (2 equiv.) with $M(OPr^i)_4{\cdot}Pr^iOH$ (2 equiv. M = Zr, Hf) in CH_2Cl_2 at 20°C for 1 h, and subsequent treatment with 3,3′-di-*t*-butyl-2,2′-dihydroxy-5,5′-dimethylbenzophenone (**1**) (1 equiv.) at 20°C for 2 h (Scheme 4). Thus, treatment of benzaldehyde with allyltributyltin (1.1 equiv.) in CH_2Cl_2 under the influence of catalytic bis-Zr **7** (M = Zr, 10 mol%) at 0°C for 5 h gave homoallylic alcohol **8** with high chemical yield and enantioselectivity (91% yield with 94% ee), while replacement of bis-Zr **7** (M = Zr) by bis-Hf **7** (M = Hf) under the otherwise identical reaction conditions dramatically lowered both reactivity and selectivity in the asymmetric allylation (6% yield, 33% ee).[7] Notably, use of chiral Ti catalyst **7** (M = Ti) also showed the unsatisfactory result particularly in reactivity (only 5% yield with 78% ee). A similar tendency is observed in the asymmetric allylation of hydrocinnamaldehyde.



Scheme 4.

Acknowledgements

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