## **Preparation and Catalytic Performance of Novel Dimeric Tetranuclear Zinc Complexes in Hydroamination of Alkenes at Room Temperature**

Mustafa Biyikal, Karolin Löhnwitz, Peter W. Roesky,\*a Siegfried Blechert\*b

<sup>a</sup> Institut f
ür Anorganische Chemie, Universit
ät Karlsruhe, Engesserstr. 15, 76128 Karlsruhe, Germany Fax +49(721)6084854; E-mail: roesky@chemie.uni-karlsruhe.de

<sup>b</sup> Institut für Chemie, Technische Universität Berlin, Strasse des 17. Juni 135, 10623 Berlin, Germany Fax +49(30)31423619; E-mail: blechert@chem.tu-berlin.de

Received 10 August 2008

**Abstract:** The synthesis of two novel dimeric tetranuclear zinc complexes has been described. The application of these complexes in hydroamination of unactivated alkenes showed at room temperature high catalytic activity.

Key words: alkenes, heterocycles, hydroamination, tetranuclear, zinc

The catalytic addition of an organic amine N–H to C=C bonds giving nitrogen-containing molecules is of great interest for academic and industrial research, whereas the hydroamination of alkenes at room temperature remains a significant challenge. Numerous single-side metal catalysts for this transformation have been developed, but their sensitivity towards air and functional groups, their toxicity and their high price limit their use in organic synthesis.<sup>1</sup> Zinc is noted for its mild and unique reactivity in organic synthesis and tolerates numerous functional groups. Nowadays zinc is applied as catalyst or reagent in numerous reactions<sup>2</sup> and also in hydroamination reactions of olefins as ATI- and AT-zinc (ATI = aminotroponiminate; AT = aminotroponate) complexes that we recently reported.<sup>1a,e,h,i,p</sup> These zinc complexes catalyze the

reactions at high temperatures only. Therefore, we were motivated to develop effective zinc catalysts for hydroamination reactions at room temperature.

Herein we report the intramolecular hydroamination of nonactivated alkenes at room temperature by using dimeric tetranuclear zinc complexes, derived from a novel type of phenolic ligand. It is believed that the unique catalytic properties of bimetallic complexes originate from double activation by the two metal centers. The cooperative interaction of the metal centers with the substrate molecule allows enhancing the catalytic activity, which cannot be achieved with monometallic catalysts. In general, the application of bimetallic catalysts in organic synthesis is in contrast to monometallic catalysts rare.<sup>2e,2m-2p,2u-2w,3</sup> In response to this trend we have established two different strategies to synthesize novel well-designed phenolic ligands suitable for two metal centers. We first envisaged the synthesis of *ortho*-aminated salicylaldimine ligand **3** from tropolone via a rearrangement reaction. The mechanistically pathway of ortho-aminated salicylaldimines from brominated tropolones with amines is specified in the literature and has attracted our attention for our objectives.<sup>4</sup> Therefore, we adopted this procedure and synthe-



**Scheme 1** Synthesis of the dimeric tetranuclear zinc complex 4. *Reagents and conditions*: a) *i*-PrNH<sub>2</sub>, hexane, -78 °C to r.t., 20 h, 62%; b) *i*-PrNH<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, -40 °C to 0 °C, 3 h, 93%; c) *i*-PrNH<sub>2</sub>, hexane, -78 °C to r.t., 20 h, 62%; d) ZnEt<sub>2</sub>, hexane, r.t., overnight, 98%.

*SYNLETT* 2008, No. 20, pp 3106–3110 Advanced online publication: 27.11.2008 DOI: 10.1055/s-0028-1087418; Art ID: G24908ST © Georg Thieme Verlag Stuttgart · New York sized the brominated ligand 3 from 1 in one step (Scheme 1).

The first step was a bromination and a subsequent methylation of tropolone to give 1.5 Different strategies were established for the methylation step of tribromotropolone, whereas 1 was obtained in moderate yields. The extensive studies of aryl ethers directed us to the Mitsunobu reactions and we were able to synthesize 1 with diisopropylazodicarboxylate and triphenylphosphine in an excellent yield of 90%.<sup>5b</sup> Compound 1 was then converted in one step into the phenolic ligand 3 in a reasonable yield of 62%.

To specify the transformation we prepared the aminotropone 2 from 1 via a basic substitution reaction with isopropylamine in a very high yield of 93%. The subsequent treatment of 2 with an excess of isopropylamine led to the phenolic ligand 3 via the rearrangement reaction in a yield of 62%. From 3, we obtained the dimeric tetranuclear zinc complex 4 (Figure 1) by treatment with diethylzinc in excellent yields of 98% after recrystallization from hexane–toluene.

In order to examine the influence of bromine on catalytic activity of the dimeric tetranuclear zinc complex **4** we decided to generate the bromine-free dimeric tetranuclear zinc complex **9**.



Scheme 2 Synthesis of the dimeric tetranuclear zinc complex 9. *Reagents and conditions*: a) NaH, chloromethylethylether, THF, 0 °C to r.t., 3 h, quant.; b) *i*-PrNH<sub>2</sub>, MS 4 Å, toluene, r.t., 1 h; c) KOt-Bu, BINAP, Pd(OAc)<sub>2</sub>, 50 °C, overnight; d) HCl [6 M], 5 h, r.t., 20%; e) *i*-PrNH<sub>2</sub>, MS 4 Å, CH<sub>2</sub>Cl<sub>2</sub>, r.t., 0.5 h, 96%; f) ZnEt<sub>2</sub>, hexane, r.t., overnight, 84%.

The synthesis of **9** started from commercially available aldehyde **5**, which was protected with chloromethylethylether in quantitative yield without the need of purification (Scheme 2). For the next step, it was necessary to condense isopropylamine with the protected salicylaldehyde **6** in the presence of molecular sieves. Afterwards it was possible to perform the Buchwald–Hartwig reaction. Due to the low boiling point of isopropylamine the reaction was performed at 50 °C in a sealed tube. The crude product was then deprotected with HCl–MeOH and **7** was obtained in three steps in 20% yield. The condensation of the aldehyde **7** with isopropylamine then afforded the phenolic ligand **8** in 96% yield. The dimeric tetranuclear zinc complex **9** (Figure 2) was obtained in 84% yield under the same conditions as for the zinc complex **4**.



Figure 1 Perspective solid-state structure of 4 showing the atomlabeling scheme, omitting hydrogen atoms

These new metal complexes 4 and 9 were characterized by standard analytical/spectroscopic techniques, and the solid-state structures of some selected compounds were established by single crystal X-ray diffraction.<sup>6</sup> Both compounds are dimeric in the solid state. Four-membered metallacycles (Zn1-N1-Zn3-N3) are formed in which the two anilido nitrogen atoms bridge the zinc atoms. The Zn-N bond distances are for compound 4 Zn1-N1 2.078(5) Å, Zn1-N3 2.136(4) Å, Zn3-N1 2.118(4) Å, and Zn3–N3 2.081(4) Å and for compound 9 Zn1–N1 2.016(5), Zn1-N3 2.191(5), Zn3-N1 2.221(5), and Zn3-N3 2.013(5). As a result of the distorted tetrahedal arrangment of the Zn and the N atoms the four-membered metallacycles have a butterfly structure. As a result of the dimerization the two benzene rings are arranged almost parallel to each other. In both structures the remaining two zinc atoms (Zn2 and Zn4) are located at the opposite side of the dimer. In each part of the dimer two zinc ethyl fragments are coordinated to the ligand framework. The zinc



Figure 2 Perspective solid-state structure of 9 showing the atomlabeling scheme, omitting hydrogen atoms

Synlett 2008, No. 20, 3106-3110 © Thieme Stuttgart · New York

atom (Zn1 and Zn3) which are part of the four-membered metallacycles are coordinated onto the phenolate oxygen atoms (O1 and O2) and the anilido oxygen atoms (N1 and N3), whereas the other zinc atoms (Zn2 and Zn4) are also coordinated to the phenolate oxygen atoms and to the imine nitrogen atoms (N2 and N4). As a result of the different coordination sphere the coordination number of Zn1 and Zn3 is four, whereas Zn2 and Zn4 are only threefold coordinated. In solution a dynamic monomer–dimer equilibrium is observed for compounds **4** and **9**. Whereas in the <sup>13</sup>C NMR spectra only one set of signals is observed, broad peaks, which cannot clearly be assigned, are seen in the <sup>1</sup>H NMR spectra of compounds **4** and **9**. Variable temperature experiments at elevated temperatures resulted in a sharpening of the lines but still broad signals are seen.

The precatalysts **4** and **9** were tested in the hydroamination reactions of nonactivated olefins bearing different functional groups. The reactions were carried out at room temperature in  $C_6D_6$  with a precatalyst loading of 2.5 mol% and 5.0 mol% of commercially available [PhNMe<sub>2</sub>H][B( $C_6F_5$ )<sub>4</sub>] as cocatalyst. The precatalysts **4** and **9** are catalytic inactive in the case of exclusion of the cocatalyst. The two equivalents of cocatalyst were used to remove the ethyl groups from the bimetallic zinc complexes to liberate coordination sites and to form more reactive cationic zinc complexes.

However, the challenge of the NMR-scaled reactions was to homogenize the in situ formed catalysts in  $C_6D_6$  that generated an insoluble ionic phase at room temperature in most of the cases. Ultrasonic techniques failed and therefore the NMR tubes were kept in horizontal position to enlarge the surface area and to enhance the transfer of the substrates into the ionic phase. This method allowed us to convert (1-allyl-cyclohexylmethyl)-benzyl-amine with the precatalyst 4 in 4.5 hours quantitatively (entry 2). The same reaction took 6 hours for a conversion of 99% in the vertically held NMR tube. An explicit result was observed in the conversion of (2,2-diphenyl-pent-4-enyl)-furan-2ylmethyl-amine with the precatalyst 4. The reaction took only 23 hours for a quantitative conversion with enlarged surface area of the ionic phase, whereas with a small surface area 56 hours were needed for a conversion of 98% (entry 6).

The cocatalyst [PhNMe<sub>2</sub>H][B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub>] itself showed in hydroamination reactions a very minor activity only. In the case of benzyl-(2,2-dimethyl-pent-4-enyl)-amine with a cocatalyst loading of 5.0 mol% only traces of product were observed after 30 hours at room temperature. At 80 °C only 14% conversion of the substrate was achieved during 1 hour. The addition of precatalyst **4** accelerated the reaction resulting in complete conversion in 30 minutes at 80 °C (entry 4).

In all hydroamination reactions the precatalyst **4** showed a higher catalytic activity than the precatalyst **9**. All substrates were converted in 99% or quantitatively within the time stated. Isolated yields are given in Table 1. The results in entries 1–3 showed in the case of both zinc complexes that the ring-closure reactions with sterically demanding gem-substituted substrates occur faster according to the Thorpe–Ingold effect.<sup>7</sup> By using precatalyst 9 the reaction took 5–8 hours longer for the conversion of these substrates than with precatalyst 4 (entries 1–3). It was also possible to reduce the reaction times by heating. In the case of benzyl-(2,2-dimethyl-pent-4-enyl)-amine the reaction time could be reduced from 30 hours at room temperature to 30 minutes at 80 °C with the precatalyst 4 and to 1 hour with the precatalyst 9 quantitatively (entry 4). Furan- and thiophene-substituted substrates decreased the catalytic activity of both precatalysts at room temperature (entry 5 and 6). However, a tremendous acceleration of the reaction was observed at 80 °C, whereas both catalysts converted (2,2-diphenyl-pent-4-enyl)-furan-2-ylmethyl-amine in 20 minutes to 1-furan-2-ylmethyl-2-

methyl-4,4-diphenyl-pyrrolidine (entry 7). The substrates shown in entries 8 and 9 could be converted within a short time and in high yield. In both cases the brominated precatalyst 4 catalyzed the reactions 2 hours faster than the precatalyst 9. The cyclization of norbornene substrates took place exclusively at the terminal double bond. With the precatalyst 4 the thiophene-substituted norbornene derivative was cyclized in 38 hours quantitatively at room temperature. The same reaction with the precatalyst 9 took 30 hours longer for a conversion of 99% under the same conditions (entry 10). At 80 °C the reaction time could be reduced to 1.5 hours in both cases (entry 11). The same effect was observed for the tosylated substrate (entries 12 and 13). In these cases the reaction time could be reduced from 69 hours at room temperature to 50 minutes at 80 °C with the precatalyst 4, and to 1 hour with the precatalyst **9**.

In conclusion, we have reported different strategies for the synthesis of two novel multidentate phenolic ligands and their corresponding zinc complexes and showed their high catalytic activity in intramolecular hydroamination reactions of unactivated olefins at room temperature and at 80 °C. The catalytic activity of our novel dimeric tetranuclear zinc complexes was compared to our previously reported ATI-zinc complexes and showed a significant higher catalytic activity.<sup>1a,e,i</sup> Especially the brominated zinc complex 4 showed a higher catalytic activity at room temperature than the zinc complex 9. This is ascribed to the electron-poor arene ring system caused by the bromine substitution, which increases the Lewis acidity of the zinc complex. These results prompted us to focus on mechanistic investigations and the enhancement of the reactivity and selectivity of new brominated multimetallic zinc complexes.

Entry	Substrate		4		9	Product
		Time (h)	Yield (%)	Time (h)	Yield (%)	
1	Ph Ph H	3	99	8	99	H NTs
2		4.5	93	11	91	
3 4	, H	30 0.5 <sup>b</sup>	80 88	38 1 <sup>b</sup>	77 83	
5	Ph Ph H S	6	96	6	93	Ph N Ph
6 7	Ph Ph H O	23 0.33 <sup>b</sup>	94 97	77 0.33 <sup>b</sup>	93 98	Ph N
8	H C	9	88	11	82	
9	H	7	92	9	93	
10 11	H_S_	38 1.5 <sup>b</sup>	99 91	68 1.5 <sup>b</sup>	94 89	S N
12 13	H N N N N N Ts	69 0.83 <sup>b</sup>	97 96	79 1 <sup>b</sup>	94 96	Ts N
						$\mathbb{N}$

 Table 1
 Results of the Hydroamination Reactions Catalyzed with the Precatalysts 4 and 9<sup>a</sup>

<sup>a</sup> *Reagents and conditions:* substrate (0.43 mmol), catalyst (2.5 mol%), [PhNMe<sub>2</sub>H][B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub>] (5.0 mol%), C<sub>6</sub>D<sub>6</sub>, r.t.; NMR tubes were kept in horizontal position; conversions are determined by <sup>1</sup>H NMR; all conversions are 99–100%; isolated yield of >95% purity. <sup>b</sup> The reaction was performed at 80 °C.

**Supporting Information** for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

## Acknowledgment

The authors acknowledge support from the Cluster of Excellence 'Unifying Concepts in Catalysis' coordinated by the Technische Universität Berlin and funded by the Deutsche Forschungsgemeinschaft.

## **References and Notes**

 (a) Dochnahl, M. *PhD Thesis*; Technische Universität Berlin: Germany, **2007**. (b) Horrillo-Martínez, P.; Hultzsch, K. C.; Gil, A.; Branchadell, V. *Eur. J. Org. Chem.* 2007, 3311. (c) Datta, S.; Roesky, P. W.; Blechert, S. *Organometallics* 2007, 26, 4392. (d) Wood, M. C.; Leitch, D. C.; Yeung, C. S.; Kozak, J. A.; Schafer, L. L. *Angew. Chem.* 2007, 119, 358. (e) Dochnahl, M.; Löhnwitz, K.; Pissarek, J.-W.; Biyikal, M.; Schulz, S. R.; Schön, S.; Meyer, N.; Roesky, P. W.; Blechert, S. *Chem. Eur. J.* 2007, 13, 6654. (f) Zhang, Z.; Bender, C. F.; Widenhoefer, R. A. *Org. Lett.* 2007, 9, 2887. (g) Yu, X.; Marks, T. J. *Organometallics* 2007, 26, 365. (h) Meyer, N.; Löhnwitz, K.; Zulys, A.; Roesky, P. W.; Dochnahl, M.; Blechert, S. *Organometallics* 2006, 25, 3730. (i) Dochnahl, M.; Pissarek, J.-W.; Blechert, S.; Löhnwitz, K.; Roesky, P. W. *Chem. Commun.* 2006, 3405. (j) Michael, F. E.; Cochran, B. M. J. Am. Chem. Soc. 2006, 128, 4246. (k) Bender,

Synlett 2008, No. 20, 3106-3110 © Thieme Stuttgart · New York

C. F.; Widenhoefer, R. A. Org. Lett. 2006, 8, 5303. (1) Komeyama, K.; Morimoto, T.; Takaki, K. Angew. Chem. 2006, 45, 2938. (m) Zhang, J.; Yang, C.-G.; He, C. J. Am. Chem. Soc. 2006, 128, 1798. (n) Meyer, N.; Zulys, A.; Roesky, P. W. Organometallics 2006, 25, 4179. (o) Riegert, D.; Collin, J.; Meddour, A.; Schulz, E.; Trifonov, A. J. Org. Chem. 2006, 71, 2514. (p) Zulys, A.; Dochnahl, M.; Hollmann, D.; Löhnwitz, K.; Herrmann, J.-S.; Roesky, P. W.; Blechert, S. Angew. Chem. 2005, 44, 7794. (q) Karshtedt, D.; Bell, A. T.; Tilley, T. D. J. Am. Chem. Soc. 2005, 127, 12640. (r) Kim, J. Y.; Livinghouse, T. Org. Lett. 2005, 7, 1737. (s) Bexrud, J. A.; Beard, J. D.; Leitch, D. C.; Schafer, L. L. Org. Lett. 2005, 7, 1959. (t) Kim, J. Y.; Livinghouse, T. Org. Lett. 2005, 7, 4391. (u) Crimmin, M. R.; Casely, I. J.; Hill, M. S. J. Am. Chem. Soc. 2005, 127, 2042. (v) Lauterwasser, F.; Hayes, P. G.; Bräse, S.; Piers, W. E.; Schafer, L. L. Organometallics 2004, 23, 2234. (w) Gribkov, D. V.; Hultzsch, K. C. Angew. Chem. 2004, 43, 5542. (x) Ryu, J.-S.; Marks, T. J.; McDonald, F. E. J. Org. Chem. 2004, 69, 1038. (y) Hong, S.; Marks, T. J. Acc. Chem. Res. 2004, 37, 673. (z) Hong, S.; Kawaoka, A. M.; Marks, T. J. J. Am. Chem. Soc. 2003, 125, 15878.

(2) (a) Luo, G.; Chen, L.; Civiello, R.; Dubowchik, G. M. Tetrahedron Lett. 2008, 49, 296. (b) Gong, H.; Sinisi, R.; Gagné, M. R. J. Am. Chem. Soc. 2007, 129, 1908. (c) Melzig, L.; Gavryushin, A.; Knochel, P. Org. Lett. 2007, 9, 5529. (d) Huang, Z.; Negishi, E. J. Am. Chem. Soc. 2007, 129, 14788. (e) Pilz, M. F.; Limberg, C.; Lazarov, B. B.; Hultzsch, K. C.; Ziemer, B. Organometallics 2007, 26, 3668. (f) Paradowska, J.; Stodulski, M.; Mlynarski, J. Adv. Synth. Catal. 2007, 349, 1041. (g) Yan, G.; Wu, Y.; Lin, W.; Zhang, X. Tetrahedron: Asymmetry 2007, 18, 2643. (h) Tanyeli, C.; Odaba•, S.; Erdem, M.; Çakir, E.; Keskin, E. Tetrahedron: Asymmetry 2007, 18, 2349. (i) El-Shehawy, A. A. Tetrahedron 2007, 63, 5490. (j) Du, H.; Long, J.; Shi, Y. Org. Lett. 2006, 8, 2827. (k) Jankowska, J.; Mlynarski, J. J. Org. Chem. 2006, 71, 1317. (l) Bok, T.; Yun, H.; Lee, B. Y. Inorg. Chem. 2006, 45, 4228. (m) Xiao, Y.; Wang, Z.; Ding, K. Chem. Eur. J. 2005, 11, 3668. (n) Lee, B. Y.; Kwon, H. Y.; Lee, S. Y.; Na, S. J.; Han, S.; Yun, H.; Lee, H.; Park, Y.-W. J. Am. Chem. Soc. 2005, 127, 3031. (o) Trost, B. M.; Shin, S.; Sclafani, J. A. J. Am. Chem. Soc. 2005, 127, 8602. (p) Fernandez-Lopez, R.; Kofoed, J.; Machuqueiro, M.; Darbre, T. Eur. J. Org. Chem. 2005, 5268. (q) Cozzi, P. G.; Rudolph, J.; Bolm, C.; Norrby, P.; Tomasini, C. J. Org. Chem. 2005, 70, 5733. (r) Aggarwal, V. K.; Fang, G. Y.; Meek, G. Org. Lett. 2003, 5, 4417. (s) Ross, N. A.; Bartsch, R. A. J. Org. Chem. 2003,

68, 360. (t) Moore, D. R.; Cheng, M.; Lobkovsky, E. B.; Coates, G. W. J. Am. Chem. Soc. 2003, 125, 11911.
(u) Nakano, K.; Nozaki, K.; Hiyama, T. J. Am. Chem. Soc. 2003, 125, 5501. (v) Trost, B. M.; Silcoff, E. R.; Ito, H. Org. Lett. 2001, 3, 2497. (w) Durant, A.; Delplancke, J. L.; Libert, V.; Reisse, J. Eur. J. Org. Chem. 1999, 2845.
(x) Bieber, L. W.; Malvestiti, I.; Storch, E. C. J. Org. Chem. 1997, 62, 906. (y) Yeh, S.-M.; Huang, L.-H.; Luh, T.-Y. J. Org. Chem. 1996, 61, 3906. (z) Chou, T.; Tseng, H.-J. Tetrahedron Lett. 1995, 36, 7105.

- (3) Shibasaki, M.; Yamamoto, Y. In *Multimetallic Catalysts in Organic Synthesis*; Wiley-VCH: Weinheim, **2004**.
- (4) Nozoe, T.; Okai, H.; Wakabayashi, H.; Ishikawa, S. Bull. Chem. Soc. Jpn. 1989, 62, 2307.
- (5) (a) Crous, R.; Datt, M.; Foster, D.; Bennie, L.; Steencamp, C.; Huyser, J.; Kirsten, L.; Steyl, G.; Roodt, A. *Dalton Trans.* 2005, 1108. (b) Houte, H.; Valnot, J.-Y.; Piettre, S. R. *Tetrahedron Lett.* 2002, *43*, 9217. (c) Piettre, S. R.; Ganzhorn, A.; Hoflack, J.; Islam, K.; Hornsperger, J. M. *J. Am. Chem. Soc.* 1997, *119*, 3201. (d) Nozoe, T.; Takase, K.; Yasunami, M. *Bull. Chem. Soc. Jpn.* 1971, *44*, 2218. (e) Nozoe, T.; Ryu, S.; Toda, T. *Bull. Chem. Soc. Jpn.* 1968, *41*, 2978. (f) Doering, W. von E.; Knox, L. H. *J. Am. Chem. Soc.* 1952, *74*, 5683.
- - $C_{34}H_{56}N_4O_2Zn_4$  (814.31): Oxford Diffraction Xcalibur S Sapphire, space group  $P6_1$  (No. 169) with a = 11.21070 (10) Å, c = 50.8375 (12) Å, at 150 K, Z = 6, V = 5533.25 (15) Å<sup>3</sup>,  $\rho = 1.466$  g cm<sup>-3</sup>,  $2c_{max} = 50^{\circ}$ , 41505 reflections collected, 6515 unique reflections ( $R_{int} = 0.0898$ ). The structure was solved by Patterson methods (SHELXS-97 and SHELXL-97) and refined by full-matrix least-square techniques with  $I > 2\sigma(I)$  to  $R_1 = 0.0605$  and  $wR_2 = 0.0812$ . Positional parameters, hydrogen-atom parameters, thermal parameters, bond lengths and angles have been deposited as Supporting Information; CCDC-689633 (4) and 689634 (9).

<sup>(7)</sup> Kirby, A. J. Adv. Phys. Org. Chem. 1980, 17, 183.

Copyright of Synlett is the property of Georg Thieme Verlag Stuttgart and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.