ORGANIC
LETTERS

2005
Vol. 7, No. 14
2889−2892

Recyclable Self-Assembly-Supported Catalytic System for Orthoalkylation

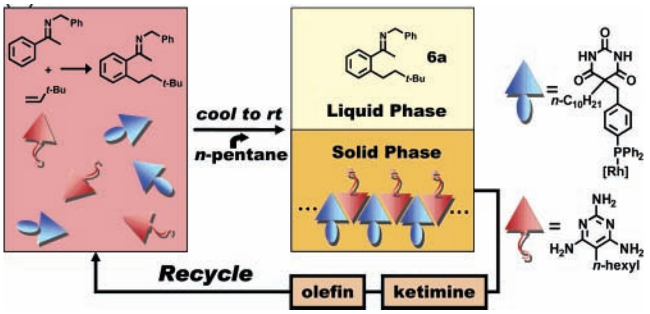
Jong Huem Yoon, Young Jun Park, Jun Hee Lee, Jaeho Yoo, and Chul-Ho Jun*

Department of Chemistry and Center for Bioactive Molecular Hybrid (CBMH),
Yonsei University, Seoul 120-749, Korea

junch@yonsei.ac.kr

Received April 20, 2005

ABSTRACT



A new recyclable supported catalyst system for orthoalkylation was devised using a self-assembly consisting of the barbiturate and 2,4,6-triaminopyrimidine H-bonding motifs. At high temperature, the system is completely homogeneous so as to give an efficient catalytic activity, while it is heterogenized at room temperature to form an insoluble solid phase for the easy recovery of the catalyst after the reaction.

Catalyst immobilization on organic polymers or inorganic solid supports is one of the current interests in synthetic organic chemistry. The resulting catalytic system can make the chemical reaction more convenient, economical, and environmentally benign by virtue of its readiness for separation.[1] However, in certain cases, covalently immobilized catalysts often suffer from low efficiency because of reduced homogeneity during the reaction. Therefore, to obtain a comparable reactivity to the homogeneous system, various attempts using soluble supports, such as hyperbranched polymers,[2] dendrimers,[3] and hybrid materials,[4] or tagging the catalyst noncovalently to the solid or soluble supports[5] have been made. Recently, we developed a hydrogen-bonding solvent system for recycling catalysts in the chelation-assisted hydroacylation.[6] Inspired by that result, we have searched for a novel support system that can remain homogeneous during the reaction and become heterogeneous for separation after the reaction. Here, we present a new self-assembly-supported (SAS) system consisting of a decylbarbiturate-substituted triphenylphosphine (**1**) and a 5-hexyl-2,4,6-

---

(1) (a) Special issue on recoverable catalysts and reagent: *Chem. Rev.* **2002**, *102*, 3215. (b) For review, see: Cornils, B., Herrmann, W. A., Eds. *Applied Homogeneous Catalysis with Organometallic Compounds*; VCH: New York, 1996; Vol. 2, p 575.

(2) (a) Bergbreiter, D. E. *Catal. Today* **1998**, *42*, 389. (b) Bergbreiter, D. E.; Osburn, P. L.; Liu, Y.-S. *J. Am. Chem. Soc.* **1999**, *121*, 9531. (c) Wentworth, P., Jr.; Janda, K. D. *Chem. Commun.* **1999**, 1917. (d) Buchmeiser, M. R.; Wurst, K. *J. Am. Chem. Soc.* **1999**, *121*, 11101. (e) Schlenk, C.; Kleij, A. W.; Frey, H.; van Koten, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3445. (f) Bergbreiter, D. E.; Osburn, P. L.; Wilson, A.; Sink, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 9058. (g) Bergbreiter, D. E.; Osburn, P. L.; Frels, J. D. *J. Am. Chem. Soc.* **2001**, *123*, 11105. (h) Bergbreiter, D. E. *Chem. Rev.* **2002**, *102*, 3345.

(3) Recent review on dendrimers in catalysis: Oosterom, G. E.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1829.

(4) Lindner, E.; Schneller, T.; Auer, F.; Mayer, H. A. *Angew. Chem., Int. Ed.* **1999**, *38*, 2154.

(5) (a) de Groot, D.; de Waal, B. F. M.; Reek, J. N. H.; Schenning, A. P. H. J.; Kamer, P. C. J.; Meijer, E. W.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2001**, *123*, 8453. (b) Chen, R.; Bronger, R. P. J.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *J. Am. Chem. Soc.* **2004**, *126*, 14557. (c) Yang, J.; Ding, S.; Radosz, M.; Shen, Y. *Macromolecules* **2004**, *37*, 1728. (d) Davies, H. M. L.; Walji, A. M.; Nagashima, T. *J. Am. Chem. Soc.* **2004**, *126*, 4271. (e) van de Coevering, R.; Kuli, M.; Gebbink, R. J. M. K.; van Koten, G. *Chem. Commun.* **2002**, 1636.

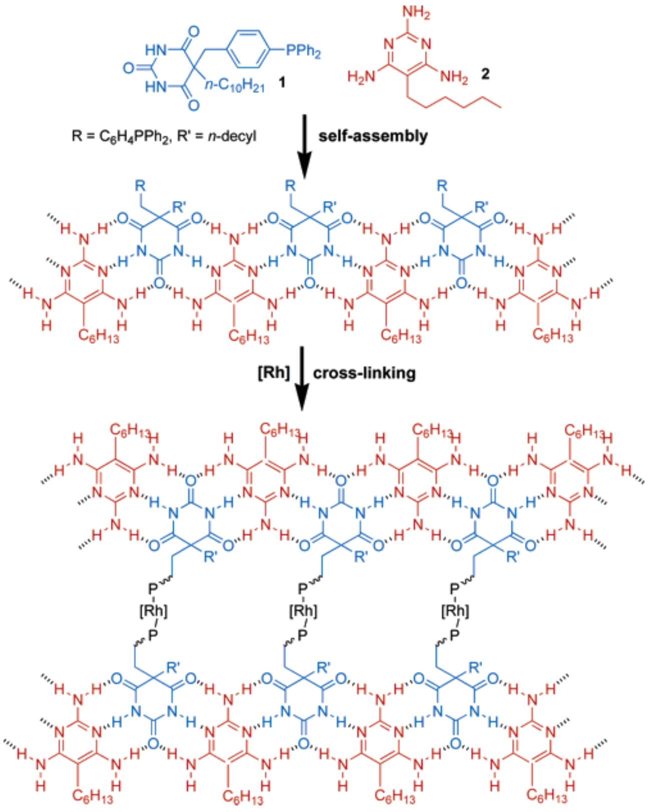
(6) Chang, D.-H.; Lee, D.-Y.; Hong, B.-S.; Choi, J.-H.; Jun, C.-H. *J. Am. Chem. Soc.* **2004**, *126*, 424.

10.1021/ol050865n CCC: $30.25

triaminopyrimidine (**2**) for Rh(I)-catalyzed orthoalkyl and orthoalkenylation,[7] in which a rhodium complex can be immobilized as an insoluble solid after the reaction and thus separated from products for repeated use.

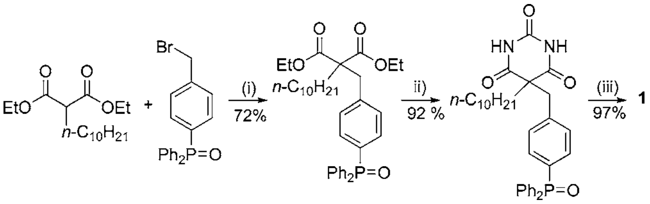
The barbiturate (**BA**) and 2,4,6-triaminopyrimidine (**TP**) motifs are known to form large and stable supramolecular assemblies through six hydrogen bondings per molecule.[8] There may be two possible modes of aggregation, an infinite tape and a discrete rosette-like form. Thus, we anticipated that the introduction of a phosphinyl group on **BA** should lead to supramolecular assemblies (Scheme 1), which can serve dual roles as a catalyst support and a ligand for the transition metals.

Scheme 1. Barbiturate-Substituted Phosphine Ligand (**1**) and Its Possible Interaction with Triaminopyrimidine (**2**)



The ligand **1** was prepared successfully in several steps: a nucleophilic addition of decyl diethylmalonate on the 4-benzylbromide group of triphenylphosphine oxide, followed by barbiturate formation with urea, and subsequent deoxygenation of phosphine oxide (Scheme 2).

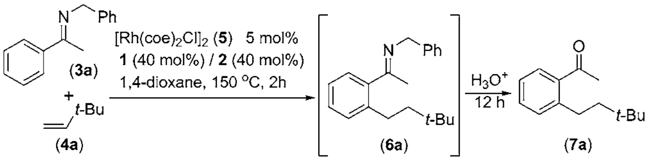
Scheme 2. Synthesis of **1**[a]



[a] Reagents and conditions: (i) NaH, DMF, 60 °C 8 h; (ii) excess urea and NaH, DMF, 100 °C 24 h; (iii) Cl_3SiH, $PhSiH_3$, 60 °C, 4 h.

Using the SAS catalytic system of barbiturate **1** bearing a phosphinyl group and pyrimidine **2** in the presence of 5 mol % of **5** as a catalyst, the orthoalkylation of benzylimine **3a** of acetophenone with *tert*-butylethylene (**4a**) was carried out at 150 °C for 2 h in 1,4-dioxane (Scheme 3).

Scheme 3. Orthoalkylation Using the SAS Catalytic System



During the reaction, the solution was homogeneous because a hydrogen-bonding network cannot be established at the high reaction temperature (Figure 1a,b), but a pale yellow solid precipitate was formed at room temperature upon addition of *n*-pentane after the reaction (Figure 1c).[9]

The formation of the solid precipitate can be attributed to the hydrogen-bonded self-assembly of **1** and **2**, including the Rh(I) metal with phosphorus coordination of **1**, not to a simple solidified mixture. This speculation is clearly supported by comparing preliminary DSC traces between each component and their mixture having the same composition in the catalytic reaction (Figure 2).

The DSC trace of the mixture of **1** and **2** exhibited a new endothermic signal (Figure 2c) without showing the identical endothermic signals of each component (Figure 2a,b).[10] In the case of the Rh(I)-containing mixture of **1**, **2**, and **5**, we could not observe any significant endothermic peak up to 240 °C (Figure 2d). Considering the theoretical coordination number of square planar Rh(I) (CN = 4), the structure of the mixture of **1**, **2**, and **5** might be a highly cross-linked polymeric one in which the hydrogen-bonded linear polymers

---

(7) (a) Jun, C.-H.; Moon, C. W.; Hong, J.-B.; Lim, S.-G.; Chung, K.-Y.; Kim, Y.-H. *Chem.—Eur. J.* **2002**, *8*, 485. (b) Jun, C.-H.; Hong, J.-B.; Kim, Y.-H.; Chung, K.-Y. *Angew. Chem., Int. Ed.* **2000**, *39*, 3440. (c) Lim, S.-G.; Lee, J.-H.; Moon, C. W.; Hong, J.-B.; Jun, C.-H. *Org. Lett.* **2003**, *5*, 2759. (d) Lim, S.-G.; Ahn, J.-A.; Jun, C.-H. *Org. Lett.* **2004**, *6*, 4687.

(8) (a) Lehn, J. M. *Supramolecular Chemistry: Concepts and Perspectives*; Verlag Chemie: Weinheim, Germany, 1995; Chapter 9, p 139. (b) Lehn, J. M.; Mascal, M.; Decian, A.; Fischer, J. *J. Chem. Soc., Chem. Commun.* **1990**, 479.

(9) For selective precipitation of the homogeneous catalyst using PEG support, see: (a) Yao, Q. *Angew. Chem., Int. Ed.* **2000**, *39*, 3896. For autoprecipitation of the catalyst after the reaction, see: (b) Dioumaev, V. K.; Bullock, R. M. *Nature* **2003**, *424*, 530. For the self-supported heterogeneous catalysts, see: (c) Bianchini, C.; Farnetti, E.; Graziani, M.; Kaspar, J.; Vizza, F. *J. Am. Chem. Soc.* **1993**, *115*, 1753. (d) Dorta, R.; Shimon, L.; Milstein, D. *J. Organomet. Chem.* **2004**, *689*, 751. (e) Wang, X.; Ding, K. *J. Am. Chem. Soc.* **2004**, *126*, 10524.

(10) (a) Bauer, T.; Thomann, R.; Mülhaupt, R. *Macromolecules* **1998**, *31*, 7651. (b) Fuchs, K.; Bauer, T.; Thomann, R.; Wang, C.; Friedrich, C.; Mülhaupt, R. *Macromolecules* **1999**, *32*, 8404.

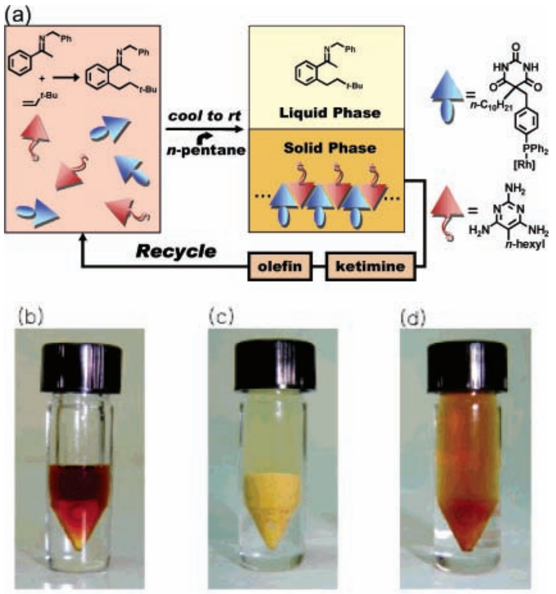


Figure 1. (a) Schematic illustration of the catalyst recycle. (b) Homogeneous phases consisting of **1**, **2**, **3**, **4**, **5**, and 1,4-dioxane after heating (150 °C). (c) Precipitation of hydrogen-bonding supramolecular solid from Figure 1b upon addition of *n*-pentane after cooling to room temperature. (d) Nonprecipitating mixture in the absence of **2** under the same conditions as that of Figure 1c.

of **1** and **2** were bridged by the coordination of the phosphorus atom of **1** to the Rh(I) center, as in Scheme 1. Therefore, it is also noteworthy that **2** has turned out to be an essential component to form the insoluble hydrogen-bonding assembly in pentane. Without **2**, no precipitation occurs even with addition of pentane (Figure 1d).

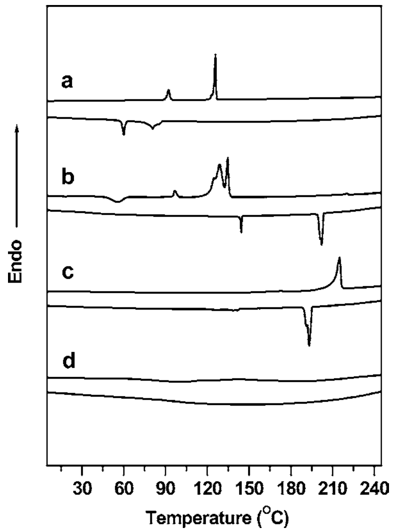
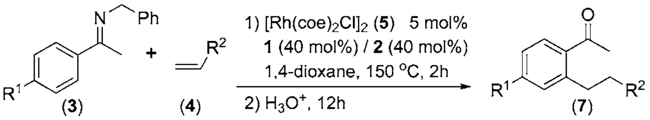


Figure 2. DSC traces of (a) **1**, (b) **2**, (c) equimolar mixture of **1** and **2**, and (d) 8:8:1 mixture of **1**, **2**, and **5** during the first heating scans and first cooling scans (rate = 10 °C/min) showing all different DSC signals.

Thus, a homogeneous catalysis could be achieved during the reaction, and the reaction mixture would be separated into two phases (liquid/solid) by adding *n*-pentane after the reaction. In this SAS system, it was found that rhodium complex stayed mainly in the solid phase of the SAS system (estimated from ICP−MS: 0.024, 0.009, and 0.012% leaching of Rh over three cycles), while almost all of the orthoalkylated imine product **6a** stayed in solution phase (see below). Therefore, the catalysts could be separated from imine for recycling after the reaction by centrifuge or filtration as in usual solid-supported catalytic reactions. Indeed, other ketimine (**3**) and olefins (**4**) were applied to the reaction to give the corresponding ketones in good yields for the repeated uses of catalyst (Table 1).[11]

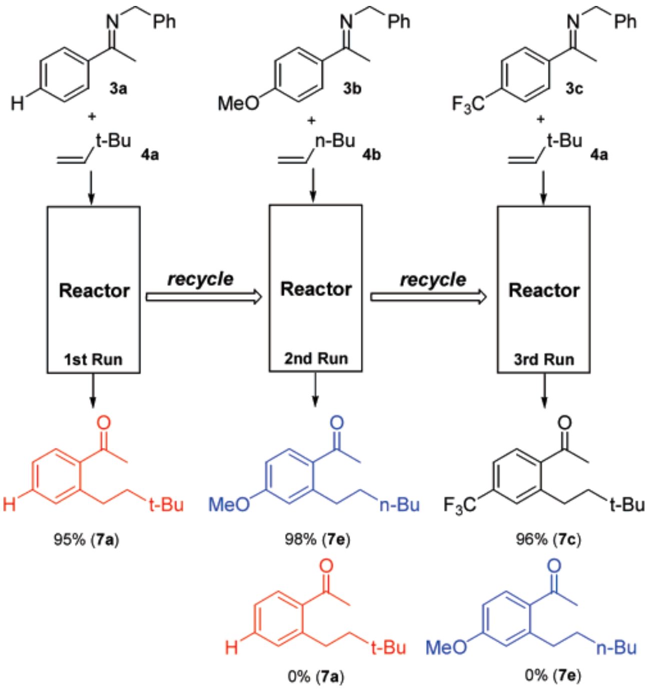
Table 1. Recycle of the Catalyst for Orthoalkylation of **3** with **4**[a]



entry	R^1 (**3**)	R^2 (**4**)	ketone (**7**)	isolated yield of product (%)							
				1	2	3	4	5	6	7	8
1	H (**3a**)	*t*-Bu (**4a**)	**7a**	87	91	94	97	95	92	89	86
2	MeO (**3b**)	**4a**	**7b**	85	90	89	85	88	87	84	87
3	CF_3 (**3c**)	**4a**	**7c**	92	95	94	97	93	93	89	91
4	**3a**	*n*-Bu (**4b**)	**7d**	68	73	77	76	76	74	79	75

[a] A quantity of 0.216 mmol **3** and 3 equiv of **4** were used; coe = cyclooctene.

Scheme 4. Orthoalkylation with Different Substrates Showing the Complete Separation of the Product in Each Run



To examine whether ketimine (**7**) was completely separated from the solid phase, the reactions were performed using different substrates in every run, and it was found that any trace amount of ketimine in the previous run did not remain in the solid phase of the next run, as shown in Scheme 4.

The first reaction was carried out using **3a** and **4a** to give **7a** in a 95% isolated yield. The separated SAS solid was used for the next reaction of **3b** and **4b** to afford **7e** in a 98% yield without detecting any of **7a**. At the third run using **3c** and **4a**, a 96% yield of **7c** was exclusively obtained as in the second run.

In conclusion, a new recyclable supported catalyst system for orthoalkylation was devised using a hydrogen-bonding self-assembly motif consisting of **1** and **2**. During the reaction at high temperature, the system is completely homogeneous so as to give an efficient catalytic activity, while it is heterogenized at room temperature to form an insoluble solid phase for the easy recovery of the catalyst after the reaction. This approach exhibited retention of the catalytic activity for repeated uses. We are currently investigating the exact nature of our system and the application of this protocol to other catalytic reactions.

Acknowledgment. This work was supported by the National Research Laboratory (NRL) (2000-N-NL-01-C-271) Program administered by Ministry of Science and Technology and CBMH. We thank Ho-Joong Kim and Prof. Myungsoo Lee (Yonsei University) for their kind DSC measurements.

Supporting Information Available: Experimental details and the characterization of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL050865N

---

(11) Alkyne, such as a *tert*-butylacetylene (**4c**), was also an applicable substrate, and the reaction was recycled 10 times in an average of 95% yield of a mixture of mono- (**7f**) and dialkenylated products (**7f′**). See Supporting Information for details.