

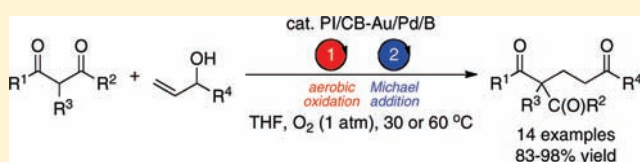
Polymer-Incarcerated Gold–Palladium Nanoclusters with Boron on Carbon: A Mild and Efficient Catalyst for the Sequential Aerobic Oxidation–Michael Addition of 1,3-Dicarbonyl Compounds to Allylic Alcohols

Woo-Jin Yoo, Hiroyuki Miyamura, and Shū Kobayashi*

Department of Chemistry, School of Science and Graduate School of Pharmaceutical Sciences, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

S Supporting Information

ABSTRACT: We have developed a polymer-incarcerated bimetallic Au–Pd nanocluster and boron as a catalyst for the sequential oxidation–addition reaction of 1,3-dicarbonyl compounds with allylic alcohols. The desired tandem reaction products were obtained in good to excellent yields under mild conditions with broad substrate scope. In the course of our studies, we discovered that the excess reducing agent, sodium borohydride, reacts with the polymer backbone to generate an immobilized tetravalent boron catalyst for the Michael reaction. In addition, we found bimetallic Au–Pd nanoclusters to be particularly effective for the aerobic oxidation of allylic alcohols under base- and water-free conditions. The ability to conduct the reaction under relatively neutral and anhydrous conditions proved to be key in maintaining good catalyst activity during recovery and reuse of the catalyst. Structural characterization (STEM, EDS, SEM, and N₂ absorption/desorption isotherm) of the newly prepared PI/CB-Au/Pd/B was performed and compared to PI/CB-Au/Pd. We found that while boron was important for the Michael addition reaction, it was found to alter the structural profile of the polymer–carbon black composite material to negatively affect the allylic oxidation reaction.



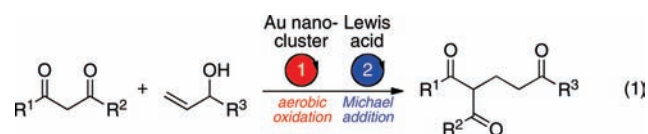
INTRODUCTION

In nature, complex organic molecules are constructed elegantly in confined environments through multistep cascade reactions. In order to mimic the catalytic efficiencies enjoyed by nature, synthetic chemists have shown great interest in the preparation and application of self-assembled nanoreactors for catalysis.¹ In addition, the development of one-pot, multistep homogeneous catalysis has been growing due to the inherent efficiency caused by the elimination of isolation and purification steps of intermediates generated from traditional iterative synthetic methods.²

In our laboratory, we have a long-standing interest in the immobilization of metal catalysts in self-assembled microstructures with the dual purpose of facilitating recovery and reuse and serving as a reactive environment for efficient catalysis.³ Recently, we have reported the synthesis and use of styrene-based polymer-incarcerated (PI) transition metals and Lewis acids as robust and highly active heterogeneous catalysts. As a natural extension of this chemistry, we considered the incarceration of two different metal catalysts that can perform two distinct organic transformations on our polymer support as an efficient heterogeneous catalyst for tandem reactions (Scheme 1).⁴

In particular, we were interested in the incorporation of our recently reported aerobic oxidation reaction catalyzed by Au nanoclusters, and as such we decided to examine the sequential aerobic oxidation–Michael reaction of 1,3-dicarbonyl compounds

with allylic alcohols catalyzed by PI-Au nanocluster/Lewis acid (eq 1).



RESULTS AND DISCUSSION

Discovery of an Immobilized Boron Catalyst for the Michael Reaction. We began our study by examining the compatibility of the mixed PI catalysts for the Michael addition of β -ketoester **1a** to methyl vinyl ketone in DCM at room temperature (Table 1).

As shown in entry 1, we confirmed that Sc(OTf)₃ is an excellent catalyst to provide the desired Michael adduct **3a** in excellent yield. We also confirmed that PI-Au is a poor catalyst for the Michael reaction (entry 2).⁵ However, to our disappointment, we found PI-Au/Sc to be an ineffective catalyst as well (entry 3). We realized that the loss in catalytic activity was due to the deactivation of Sc(OTf)₃ as a Lewis acid during the preparation step caused by the reducing agent required for the Au

Received: November 11, 2010

Published: February 08, 2011

nanocluster formation.⁶ While only a trace amount of the desired Michael adduct **3a** was observed, we believed it was possible to improve the reaction by increasing the concentration of the reaction mixture. As shown in entries 4 and 5, a 10-fold increase in concentration resulted in the formation of **3a** with an excellent yield. With this result in hand, we performed control studies in order to confirm that the Au nanoclusters were responsible for

Scheme 1. Sequential Catalysis in a Confined Environment

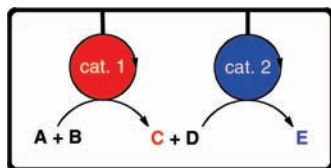


Table 1. Optimization of Reaction Conditions for the Michael Reaction^a

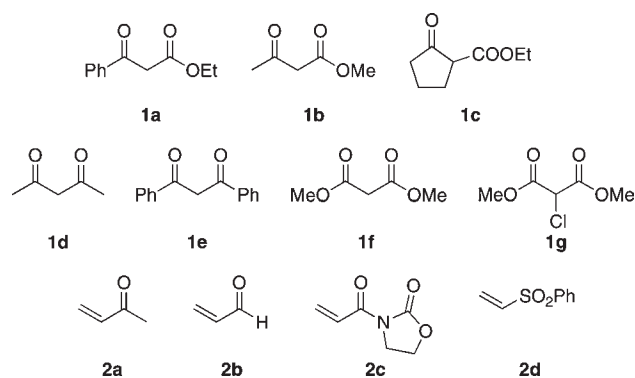
entry	catalyst	yield (%) ^b
1 ^c	Sc(OTf) ₃ (2 mol %)	>95
2 ^c	PI-Au (2 mol %)	<5
3 ^c	PI-Au/Sc (2 mol %)	<5
4	PI-Au/Sc (2 mol %)	>95
5	PI-Au (2 mol %)	>95
6	-	<5
7	cross-linked polymer	<5
8	PI-B (5 mol %)	>95
9	PI-Au (boron-free) (5 mol %)	<5
10	PI/CB-B (5 mol %)	90
11 ^d	PI/CB-B (5 mol %)	>95

^a β -Ketoester **1a** (0.26 mmol), methyl vinyl ketone (0.39 mmol), and catalyst in DCM ($C = 1.0$ M) at room temperature. ^b Yield based on **1a** and determined by ¹H NMR using mesitylene as an internal standard. ^c $C = 0.1$ M. ^d Using toluene or THF as a solvent.

the catalytic activity. We established that the background reaction (entry 6) and the cross-linked polymer support (entry 7) did not play a significant role for the formation of **3a**. However, when we examined the cross-linked polymer with just the reducing agent (NaBH₄) as a catalyst for the Michael reaction, we were surprised to find that it was just as effective as PI-Au (entry 8).^{7,8} We re-examined the metal content of PI-Au by inductively coupled plasma-atomic emission spectroscopy (ICP) and found significant amounts of boron (1.469 mmol/g). Furthermore, when we prepared PI-Au without boron, we could not observe any catalytic activity for the Michael reaction (entry 9).⁹

Although we prepared (Scheme 2) and demonstrated that PI-B is an active catalyst for the Michael reaction, there were some technical difficulties associated with its synthesis. When NaBH₄ was added to the dissolved polymer solution, over time (within 1 h), the polymer began to cross-link and stirring became near impossible. We overcame this issue by the introduction of carbon black (CB), slight thickening of the composite material was observed, but this did not prevent stirring. The newly prepared polymer-incarcerated boron on carbon black (PI/CB-B) was applied to the Michael reaction, and the desired Michael adduct **3a** was obtained in good yield (entry 10). Further optimization by solvent screening (MeCN, hexane, THF, toluene) revealed that both toluene and THF provides the desired product **3a** in quantitative yields (entry 11).

Chart 1. List of Michael Donors and Acceptors



Scheme 2. Preparation Methods for PI-B and PI/CB-B

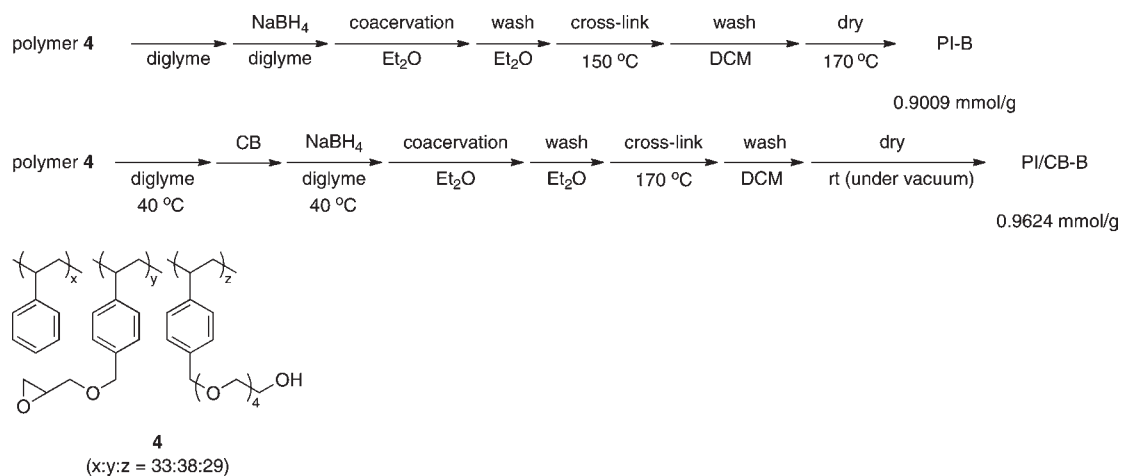


Table 2. Scope of the PI/CB-B-Catalyzed Michael Reaction^a

entry	donor	acceptor	product	yield (%) ^b
1	1a	2a		94
2	1b	2a		95
3	1c	2a		99
4	1d	2a		92
5	1e	2a		93
6	1f	2a		78
7	1g	2a		70
8	1a	2b		71 ^c
9	1a	2c		98 ^d
10	1a	2d		96 ^d

^a 1,3-Dicarbonyl compounds **1a–g** (0.26 mmol), Michael acceptors **2a–d** (0.39 mmol), and PI/CB-B (5.0 mol %) in THF ($C = 1.0$ M) at room temperature. ^b Yield based on **1a–g** and determined by weight of the isolated product. ^c Reaction performed at -20 °C for 12 h. ^d 1.1 equiv of the Michael acceptor used.

With the optimized conditions in hand, we decided to examine the scope of the Michael addition of 1,3-dicarbonyl compounds (**1a–g**) with various electron-deficient alkenes (**2a–d**) (Chart 1) catalyzed by PI/CB-B (Table 2).

Table 3. Recovery and Reuse of PI/CB-B Catalyst^a

run	yield (%) ^b	run	yield (%) ^b
1	>95	6	>95
2	>95	7	>95
3	>95	8	>95
4	>95	9	93
5	>95	10	93

^a β -Ketoester **1a** (1.0 equiv), vinyl ketone **2a** (1.5 equiv), and PI/CB-B (5.0 mol %) in THF ($C = 1.0$ M) at room temperature. ^b Yield based on **1a** and determined by ¹H NMR using mesitylene as an internal standard.

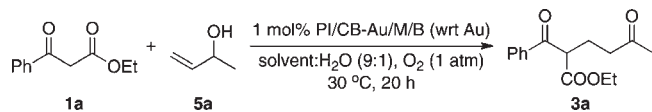
As expected, when β -ketoesters **1a–c** were utilized as nucleophiles, the desired 1,4-addition products were obtained with excellent yields when coupled with **2a** (entries 1–3). Furthermore, 1,3-diketones **1d,e** were found to be good Michael donors (entries 4 and 5). However, when dimethyl malonate (**1f**) was used as a substrate, the yield was slightly diminished. Under the assumption that malonate **1f** was less reactive due to being less acidic than β -ketoesters and 1,3-diketones, we decided to use chlorinated malonate **1g** (entry 7). However, we did not observe the expected improvement in the yield for the reaction. Next, we examined the Michael acceptors. We found that reactive and unstable acrolein (**2b**) was a viable electrophile when utilized at a lower temperature (-20 °C) and furnished the desired product **3h** with a modest yield (entry 8). In cases where nonvolatile Michael acceptors such as oxazolidone **2c** and vinyl sulfone **2d** were used, the amounts required for the electrophile could be reduced and still provide the desired products in excellent yields (entries 9 and 10).

Next, we examined the viability of recycling the PI/CB-B catalyst (Table 3).

We found that PI/CB-B could be recovered and reused up to 7 times without noticeable loss of activity. Furthermore, pretreatment of PI/CB-B was not necessary in order to reactivate the catalyst. However, we found it was necessary to purify **2a** and remove the hydroquinone stabilizer prior to use in order to achieve good recyclability.¹⁰

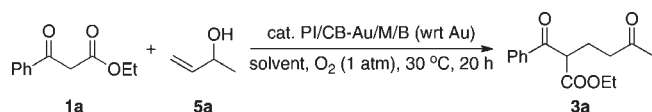
Sequential Aerobic Oxidation–Michael Addition of 1,3-Dicarbonyl Compounds to Allylic Alcohols. With our serendipitous discovery of an immobilized boron catalyst from the excess NaBH_4 required for the reduction of metal nanoclusters, we decided to examine the viability of the sequential aerobic oxidation–Michael addition of 1,3-dicarbonyl compounds to allylic alcohols (Table 4). We decided to utilize bimetallic nanoclusters on a polymer-carbon black (PI/CB-Au/M/B, M = second metal) composite material as catalysts since we anticipate these heterogeneous catalysts to facilitate the desired sequential reaction under base-free¹¹ conditions in relatively high concentrations.¹² The preparation of the PI/CB-Au/M/B composite materials followed our previously reported synthesis of PI/CB-Au/Pd with the minor exception of removing the aqueous washing sequence in order to retain the boron required for the Michael reaction.¹³

On the basis of our previous studies with aerobic oxidation of alcohols using bimetallic nanoclusters, we initially examined PI/CB-Au/Pt/B as a catalyst in the absence (entry 1) and presence

Table 4. Optimization of Reaction Conditions for the Sequential Aerobic Oxidation of β -Ketoester **1a to Allylic Alcohol **5a**^a**

entry	M	metal source	solvent	yield (%) ^b
1 ^c	Pt	Na ₂ PtCl ₆	DCM	N.R.
2	Pt	Na ₂ PtCl ₆	DCM	65
3	Pt	Na ₂ PtCl ₆	BTF	59
4	Pt	Na ₂ PtCl ₆	MeCN	54
5	Pt	Na ₂ PtCl ₆	THF	69
6	Ru	[RuCl ₂ (<i>p</i> -cymene)] ₂	THF	70
7	Pd	Pd(OAc) ₂	THF	>95
8	Cu	Cu(OAc) ₂	THF	12
9	Ni	(PPh ₃) ₂ NiCl ₂	THF	22
10	Co	CoCl ₂	THF	7
11	Rh	[RhCl(COD)] ₂	THF	22
12	Fe	FeCl ₂	THF	8
13 ^d	Pt	Na ₂ PtCl ₆	THF	>95
14 ^d	Ru	[RuCl ₂ (<i>p</i> -cymene)] ₂	THF	>95
15 ^e	—	—	THF	25
16 ^f	Pd	Pd(OAc) ₂	THF	48

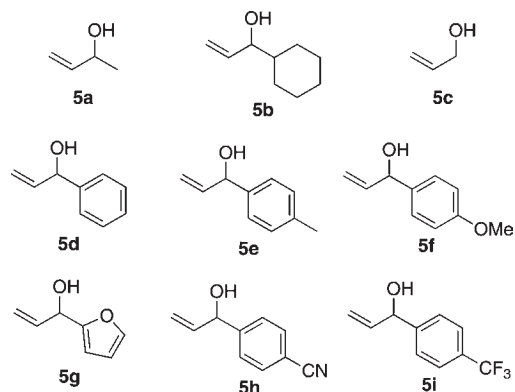
^a β -Ketoester **1a** (0.50 mmol), allylic alcohol **5a** (0.75 mmol), and PI/CB-Au/M/B (1:1 Au:M, 1 mol % wrt Au) in solvent:H₂O (C = 1.0 M) at 30 °C in O₂ (1 atm). ^bYield based on **1a** and determined by ¹H NMR using mesitylene as an internal standard. ^cIn the absence of H₂O. ^dUsing 1.5 mol % of PI/CB-Au/M/B. ^eUsing 2.0 mol % of PI/CB-Au/B. ^fUsing 2.0 mol % of PI/CB-Pd/B.

Table 5. Recovery and Reuse Studies of PI/CB Bimetallic Catalysts^{a,b}

run	1.5 mol % PI/CB-Au/Ru/B		1 mol % PI/CB-Au/Pd/B	
	THF:H ₂ O (9:1) (%)	THF (%)	THF:H ₂ O (9:1) (%)	THF ^d (%)
1	>95	<5	>95	>95
2	66	—	78	>95
3	29	—	64	>95
4	—	—	—	91
5	—	—	—	93
6	—	—	—	88

^a β -Ketoester **1a** (0.50 mmol) and allylic alcohol **5a** (0.75 mmol) in solvent (C = 1.0 M) at 30 °C in O₂ (1 atm). ^bYield based on **1a** and determined by ¹H NMR using mesitylene as an internal standard. ^cAverage metal leaching determined by ICP analysis of the reaction filtrate (Au, N.D.; Pd, 3%; B, 8%). ^dAverage metal leaching determined by ICP analysis of the reaction filtrate (Au, N.D.; Pd, 0.8%; B, 0.2%).

of water (entry 2) to learn that water is a critical component to provide **3a** with a modest yield. Screening of solvents revealed that THF provides a slight improvement in yield (entries 2–5).

Chart 2. Allylic Alcohols **5a–i**

Next, we examined a variety of different metals and found that Pd (entry 7) provides the desired Michael adduct **3a** in excellent yield. We also found that the yield of **3a** could be improved when the catalyst loading is slightly increased for bimetallic nanoclusters containing Pt and Ru (entries 13 and 14). As a control, we examined the tandem reaction with PI/CB-Au/B (entry 15) and PI/CB-Pd/B (entry 16) to clearly show the beneficial effect of utilizing a bimetallic system.

Next, we examined the viability of recycling the PI/CB-Au/M/B catalysts (Table 5).

We found that in both cases with PI/CB-Au/Ru/B and PI/CB-Au/Pd/B, the catalytic activity was diminished after each subsequent recovery and reuse. Examination by ICP analysis of the resulting filtrate of the reaction mixture revealed significant leaching of both boron and palladium. Although we believed that water was responsible for the metal leaching, our previous results suggested that water plays an important role in the aerobic oxidation of the allylic alcohol. However, to our delight, we found that PI/CB-Au/Pd/B could catalyze the sequential aerobic oxidation–Michael addition reaction in the absence of added water. The recovered Au–Pd bimetallic nanoclusters were shown to catalyze the desired tandem reaction with excellent yields without noticeable loss of the desired Michael adduct **3a** up to the third run.

With the optimized reaction in hand, we examined the scope of the PI/CB-Au/Pd/B catalyzed sequential aerobic oxidation–Michael addition of 1,3-dicarbonyl compounds **1a–f** with allylic alcohols **5a–i** (Chart 2) (Table 6).

As expected, when β -ketoesters **1a–c** were utilized as nucleophiles, the desired 1,4-addition products were obtained in excellent yields with allylic alcohol **5a** (entries 1–3). Furthermore, 1,3-diketones **1d,e** were found to be good Michael donors (entries 4 and 5). When dimethyl malonate (**1f**) was used as a substrate, higher reaction temperature and slight excess of **5a** was required in order to obtain a high yield of **3f** (entry 6). Next, we examined allylic alcohols **5b–i** (entries 7–14). We found that the reaction temperature must be slightly increased in order to fully convert some of the allylic alcohols to the corresponding α,β -unsaturated ketones required for the Michael reaction with β -ketoester **1a**. Fortunately, we did not observe any significant decomposition or isomerization of these substrates at elevated temperatures and were able to decrease the equivalence required for these relatively nonvolatile Michael acceptors without sacrificing the excellent yields enjoyed for the sequential aerobic oxidation–Michael addition reaction.

Table 6. Scope of the PI/CB-Au/Pd/B-Catalyzed One-Pot Sequential Reaction^a

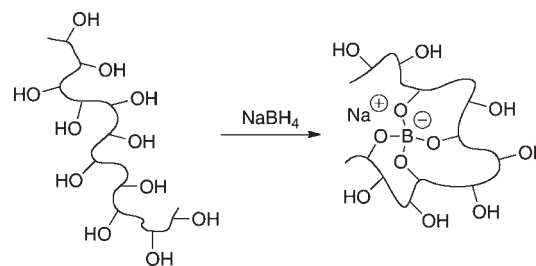
entry	donor	alcohol	product	yield (%) ^b	entry	donor	alcohol	product	yield (%) ^b
1	1a	5a		95	8	1a	5c		83
2	1b	5a		98	9 ^{c,e}	1a	5d		95
3	1c	5a		97	10 ^{c,e}	1a	5e		94
4	1d	5a		82	11 ^e	1a	5f		89
5	1e	5a		86	12 ^{c,e}	1a	5g		93
6 ^{c,d}	1f	5a		88	13 ^{c,e}	1a	5h		98
7 ^{c,e}	1a	5b		87	14 ^{c,e}	1a	5i		98

^a 1,3-Dicarbonyl **1a–f** (0.50 mmol), allylic alcohol **5a,c** (0.75 mmol), and PI/CB-Au/Pd/B (1:1 Au:Pd, 1 mol % wrt Au) in THF ($C = 1.0\text{ M}$) at $30\text{ }^\circ\text{C}$ in O_2 (1 atm). ^b Yield based on **1a–f** and determined by weight of the isolated products **3a–f**, **3h**, **3k–q**. ^c $60\text{ }^\circ\text{C}$. ^d 2.0 equiv of **5a**. ^e 1.1 equiv of allylic alcohol **5b,d–i**.

Structural Characterization of PI Catalysts. With the unexpected immobilization of boron and its use as a catalyst for the Michael reaction, we wanted to understand the nature of the boron immobilization process. From our previous efforts in developing highly active immobilized metal catalysts, the immobilization process is believed to occur through the encapsulation of the metal species via nonbonding interaction between the π -electrons of the aromatic rings of the polystyrene backbone and the vacant orbitals of the metal species.^{3b} However, in the case of boron, we believe that the boron immobilization occurs through the formation of a tetravalent boron complex through the esterification of NaBH_4 with the alcohol functional groups present on the polymer backbone (Scheme 3).

This hypothesis is quite reasonable since Echavarren¹⁴ and Sundararajan¹⁵ both reported the preparation of tetraalkoxyborates from NaBH_4 and alcohols and these anionic species were shown to be excellent catalysts for the Michael reaction. Evidence to support the existence of the tetravalent boron species was found through ^{11}B CP-MAS (cross-polarization magic angle spinning) NMR spectrum of PI/CB-B. While a mixture of broad boron peaks were observed, the major peak of the spectrum was at 0.46 ppm, which is indicative of a tetravalent alkoxy boron species.¹⁶

Scheme 3. Immobilization of Boron



In addition, we conducted scanning transmission electron microscopy (STEM) and energy dispersive spectroscopy (EDS) analyses to characterize and understand the newly prepared bifunctional composite catalyst (Figure 1).

From the EDS line analysis, a single Gaussian distribution of X-rays of Au and Pd across the nanoparticle ($3.6 \pm 1.3\text{ nm}$) was obtained and is indicative of the random arrangement of Au and Pd atoms within a Au/Pd alloy. EDS analysis also revealed a higher ratio of Au:Pd ($\sim 1.3:1$ to $2.5:1$ of Au:Pd, Figure S-3, Supporting Information) within the metal nanoclusters while

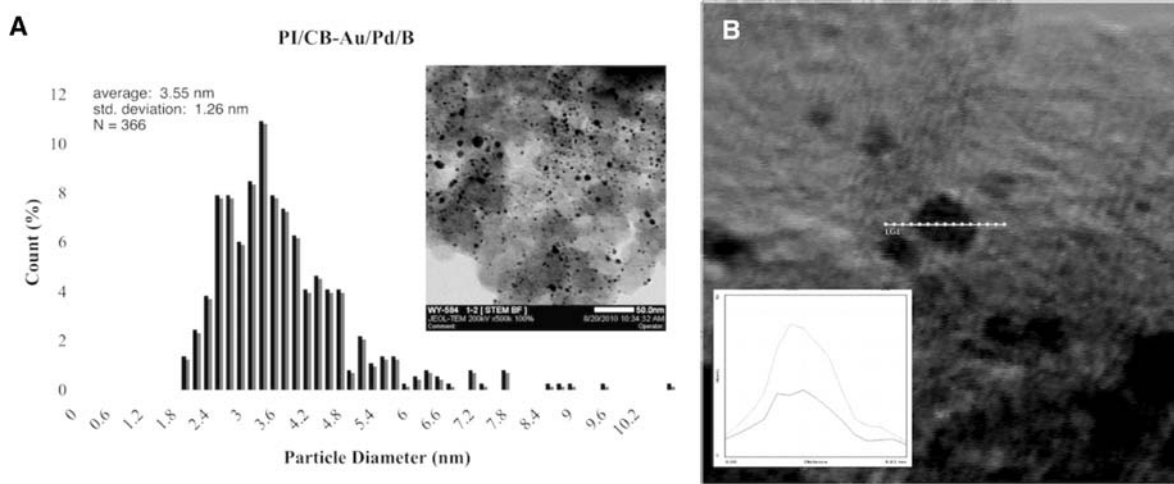


Figure 1. STEM and EDS analysis of PI/CB-Au/Pd/B: (A) Typical STEM image and size distribution of PI/CB-Au/Pd/B; (B) EDS line analysis of a cluster of PI/CB-Au/Pd/B (red = Au, green = Pd).

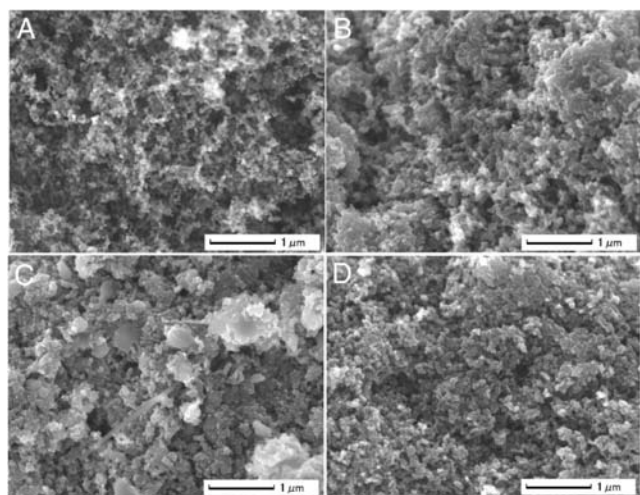


Figure 2. Typical SEM image of (A) CB; (B) CB + polymer 4; (C) PI/CB-Au/Pd/B; (D) PI/CB-Au/Pd.

ICP analysis of the PI/CB-Au/Pd/B determined the Au:Pd ratio to be essentially 1:1. These results suggest that Pd exists in the metal nanoclusters and is also dispersed throughout the polymer/CB composite material.

In addition, the scanning electron microscopy (SEM) image of PI/CB-Au/Pd/B was obtained and significant differences in the structural morphologies of the composite material with and without boron were revealed (Figure 2).

From the SEM image of CB, relatively uniform spheres (≈ 45 nm) were observed and the polymer–CB composite material also possessed similar structural profile with slightly larger spheres (≈ 55 nm). The increase observed size of the microspheres is most likely due to the polymer absorbed on the surface of the carbon black particles. Surprisingly, the SEM image of PI/CB-Au/Pd/B revealed dramatic structural changes with uneven and large (>100 nm) spheres. These large spheres may represent clustered polymer–CBs held together by cross-linked borate ester bonds. Indeed, when PI/CB-Au/Pd/B was washed thoroughly with H_2O and THF

(to wash away the boron), the small, uniformed spheres were restored. We believed that this difference in the structure between PI/CB-Au/Pd/B and PI/CB-Au/Pd should affect its physical properties such as surface area. This hypothesis was confirmed by the N_2 adsorption/desorption analysis of the PI/CB catalysts (Figure 3).

On the basis of the adsorption/desorption isotherm, the Brunauer–Emmett–Teller (BET) surface area was calculated to be $19.1 \text{ m}^2/\text{g}$ for PI/CB-Au/Pd/B and $56.4 \text{ m}^2/\text{g}$ for PI/CB-Au/Pd.¹⁷ Examination of the isotherms also revealed these PI/CB catalysts to be essentially macroporous since the hysteresis loops were only noticeable at relatively high pressures and that the adsorption isotherms increased sharply near the saturation vapor pressures.¹⁸

Comparison Studies. We performed some control studies to understand our catalyst system and to demonstrate advantages of performing the tandem aerobic oxidation–Michael addition reaction with the bifunctional PI/CB-Au/Pd/B. We first examined the Michael addition reaction between β -ketoester **1a** and methyl vinyl ketone (MVK) (Table 7).

From the data shown in Table 7, the order of reactivity of PI/CB-M catalysts for the Michael reaction is PI/CB-B $>$ PI/CB-Au $>$ PI/CB-Pd $>$ PI/CB-Au/Pd. Although there exists the possibility that the metal nanoparticles may interact with the boron species to alter its reactivity, we believe this trend simply reflects the amount of tetravalent boron that exists in the various PI/CB-M catalysts. Since 1 equiv of $NaBH_4$ is required for the reduction of M(I) to M(0), PI/CB-Au/Pd/B should possess the least amount of the active tetravalent boron Michael addition catalysts.

Next, we performed comparison studies between our composite bifunctional PI/CB-Au/Pd/B catalyst and a mixed catalyst system composed of PI/CB-Au/Pd and PI/CB-B to see if an advantage in the rate of reaction is gained from the bifunctional catalysts (Table 8).¹⁹

As shown in Table 8, the aerobic oxidation–Michael reaction was slightly faster when the mixed catalyst system was employed. One possible explanation for this result is the decrease in the rate of the allylic oxidation using PI/CB-Au/Pd/B due to the reduced surface area of the polymer–CB

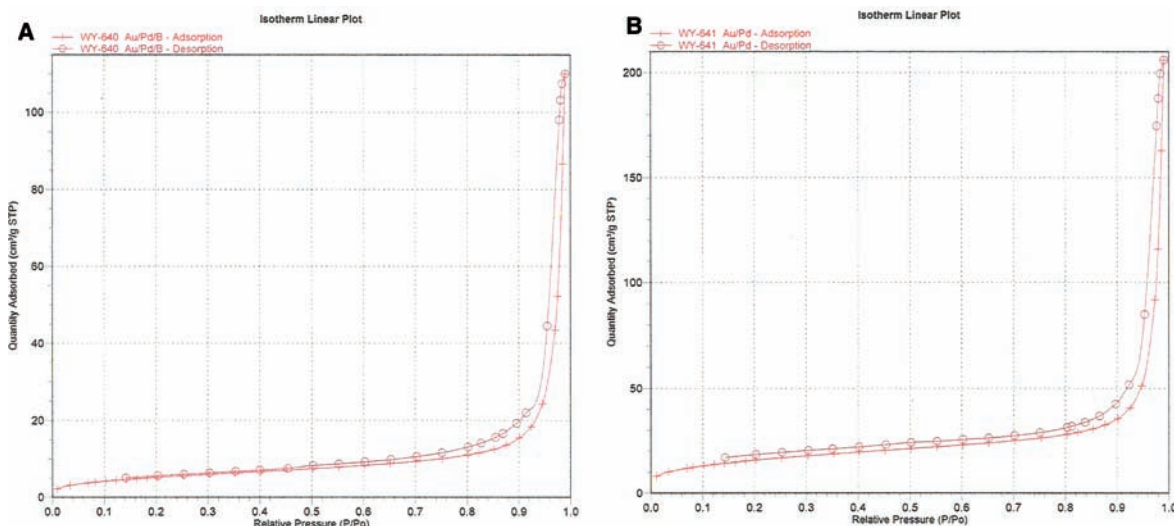
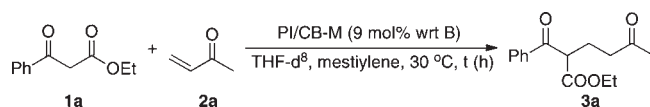


Figure 3. Nitrogen adsorption/desorption isotherm of (A) PI/CB-Au/Pd/B; (B) PI/CB-Au/Pd (+ = adsorption, O = desorption).

Table 7. Comparison of Various PI/CB-M Catalysts for the Michael Reaction^a



entry	t (h)	PI/CB-M yield 3a (%) ^b			
		Au/Pd/B ^c	Pd/B ^d	Au/B ^e	B ^f
1	0.5	40	60	76	>95
2	1.5	73	93	>95	>95

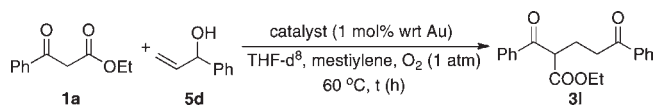
^a β -Ketoester **1a** (0.50 mmol), alkene **2a** (0.75 mmol), and mesitylene (0.17 mmol) in THF-*d*₈ (C = 1.0 M) at 30 °C. ^bYield based on **1a** and determined by ¹H NMR using mesitylene as an internal standard. ^cMetal loading of PI/CB-Au/Pd/B: 0.1962 mmol/g Au, 0.1847 mmol/g Pd, 1.778 mmol/g B. ^dMetal loading of PI/CB-Pd/B: 0.1783 mmol/g Pd, 2.467 mmol/g B. ^eMetal loading of PI/CB-Au/B: 0.2041 mmol/g Au, 2.371 mmol/g B. ^fMetal loading of PI/CB-B: 2.173 mmol/g B.

composite material. Indeed, when the allylic oxidation of **5d** was examined with PI/CB-Au/Pd/B and PI/CB-Au/Pd, we observed an increase in the rate of the oxidation reaction with the boron-free catalyst (Table 9).

These results also demonstrate the synthetic utility of performing the tandem allylic oxidation–Michael addition reaction since the α,β -unsaturated ketone **2e** quickly reacts to form the Michael adduct **3l** instead of undergoing side reactions. In fact, while monitoring the sequential oxidation–Michael reaction shown in Table 8, the expected intermediate, α,β -unsaturated ketone **2e**, was not detected by ¹H NMR. Interestingly, by comparing the results from Tables 8 and 9, we observe a decrease in the rate of the allylic oxidation reaction in the presence of β -ketoester **1a**. This may suggest that coordinating ligands can affect the rate of the oxidation reaction catalyzed by the bimetallic nanoclusters.

Finally, we examined the sequential reaction using air (under balloon pressure) as the terminal oxidant and found that the

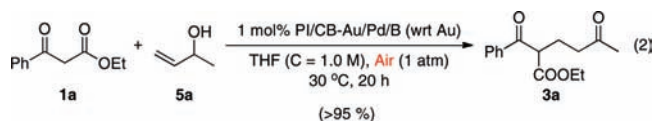
Table 8. Comparison between Bifunctional Composite Catalyst and Mixed Catalyst System for the Sequential Oxidation–Michael Reaction^a



entry	t (h)	yield 3l (%) ^b	
		PI/CB-Au/Pd/B ^c	PI/CB-Au/Pd + PI/CB-B ^d
1	0.5	N.D.	N.D.
2	1.5	<5	6
3	4	13	18
4	8	35	49
5	22	>95	>95

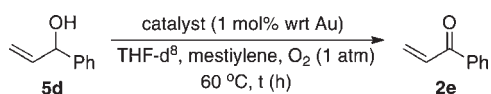
^a β -Ketoester **1a** (0.50 mmol), allylic alcohol **5d** (0.56 mmol), and mesitylene (0.17 mmol) in THF-*d*₈ (C = 1.0 M) at 60 °C in O₂ (1 atm). ^bYield based on **1a** and determined by ¹H NMR using mesitylene as an internal standard. ^cCatalyst loading of PI/CB-Au/Pd/B: 1.0 mol % Au, 1.2 mol % Pd, 16.2 mol % B. ^dCatalyst loading of PI/CB-Au/Pd + PI/CB-B: 1.0 mol % Au, 1.1 mol % Pd, 13.2 mol % B.

reaction occurred smoothly under our optimized reaction conditions (eq 2).



CONCLUSION

In summary, we have developed a novel sequential aerobic oxidation–Michael addition reaction of 1,3-dicarbonyl compounds to allylic alcohols using a Au–Pd bimetallic nanocluster with boron immobilized on a polymer–CB composite material. The PI/CB-Au/Pd/B nanoclusters proved to be an excellent catalyst that delivered the desired Michael adducts in good to

Table 9. Comparison between PI/CB-Au/Pd/B and PI/B-Au/Pd for the Allylic Oxidation of 5d^a

entry	<i>t</i> (h)	PI/CB-Au/Pd/B ^c		PI/CB-Au/Pd ^d	
		yield 2e (%) ^b	conv (%) ^b	yield 2e (%) ^b	conv (%) ^b
1	0.5	N.D.	15	<5	25
2	1.5	<5	20	14	44
3	4	13	33	26	64
4	8	25	60	46	91
5	22	59	>95	48	>95

^a Allylic alcohol **5d** (0.50 mmol), and mesitylene (0.17 mmol) in THF-*d*₈ (C = 0.86 M) at 60 °C in O₂ (1 atm). ^b Yield and conversion is based on **5d** and determined by ¹H NMR using mesitylene as an internal standard. ^c Catalyst loading of PI/CB-Au/Pd/B: 1.0 mol % Au, 1.2 mol % Pd, 16.2 mol % B. ^d Catalyst loading of PI/CB-Au/Pd: 1.0 mol % Au, 1.1 mol % Pd.

excellent yields under mild conditions. We have uncovered the dual role that NaBH₄ plays as both the reducing agent required for the generation of the bimetallic nanoclusters and as a catalyst precursor for the Michael reaction. In addition, the Au–Pd bimetallic nanoclusters were shown to be a remarkably effective catalyst that was able to oxidize allylic alcohols without addition of water as a cosolvent under neutral conditions. By eliminating the water cosolvent, the leaching of boron was minimized to maintain good catalyst activity during the recovery and reuse cycles. Finally, we demonstrate the structural changes of the polymer–CB composite material caused by boron and its negative effects on the catalytic activity for the allylic oxidation reaction.

EXPERIMENTAL SECTION

General Information. Standard column chromatography was performed on 70–230 mesh silica gel (obtained from Merck) using flash column chromatography techniques.²⁰ IR spectra were measured on a JASCO FT/IR-610 spectrometer. Melting points were obtained using a Büchi Melting Point B-545 and were not corrected. ¹H and ¹³C NMR spectra were recorded on a JEOL ECX-500 in CDCl₃. Chemical shifts were reported in parts per million (ppm) from tetramethylsilane using the solvent resonance as the internal standard (chloroform: δ 7.26 ppm) for ¹H NMR and (deuteriochloroform: δ 77.0 ppm) for ¹³C NMR. ¹¹B CP-MAS NMR spectrum was recorded on a JEOL/JNM ECA-500 spectrometer with a 4 mm MAS probe at spectral frequency 160.47 MHz. The boron spectrum was referenced to H₃BO₃ as a standard. High resolution mass spectrometry was carried out using a JEOL JMS-T100TD (DART). The content of all metals in the final material was determined by ICP analysis using a Shimadzu ICPS-7510 equipment: 10–20 mg of the final material was heated in a mixture of sulfuric acid and nitric acid at 200 °C for 2 h. After cooling at room temperature, aqua regia (HCl:HNO₃ = 1:3 v/v) was added and the samples were diluted to 50 mL with distilled water. STEM images and EDS analyses were obtained using a JEOL JEM-2100F instrument operated at 200 kV. All TEM specimens were prepared by placing a drop of a suspension of the sample in methanol on carbon-coated copper grids and allowed to dry in air without staining. SEM images were obtained using a JEOL JSM-6700F instrument operated at 5.0 KV. Nitrogen adsorption

measurements at 77 K were performed on a ASAP 2010 volumetric adsorption analyzer surface area and porosity analyzer equipped with pressure transducers covering the 1, 10, and 1000 Torr ranges (Micromeritics Instrument Corp.). The instrument was equipped with a turbo vacuum pump capable of reducing the pressure to below 10^{−7} Torr. The initial pressure at the start of any run was below 10^{−5} Torr.

Reagents. Unless stated otherwise, commercial reagents were used as received with the exception of NaBH₄, which was recrystallized from diglyme according to the literature.²¹ The carbon black source used in this study was ketjen black EC 300J purchased from Lion Corporation. Allylic alcohols **2b**, **2d**–**i** were prepared according to the literature.²²

Preparation of PI/CB-B. To a solution of copolymer **4** (0.1563 g) in diglyme (3.9 mL) at 40 °C was added ketjen black (0.1573 g). After stirring the heterogeneous solution for 15 min, a solution of NaBH₄ (17.7 mg, 0.469 mmol) in diglyme (1.6 mL) was added dropwise. After the heterogeneous solution was stirred for 4 h at 40 °C, diethyl ether (40 mL) was added dropwise. The boron-containing polymer-coated carbon black was washed several times with diethyl ether and dried at room temperature. Next, the recovered solid powder was heated at 170 °C for 4 h without solvent. After being cooled to room temperature, the cross-linked polymer-coated carbon black was washed several times with DCM, filtered, ground with a mortar and pestle, and dried under vacuum to provide the desired black powder (PI/CB-B, 0.3312 g, B loading: 0.9624 mmol/g).

Typical Procedure for the PI/CB-B-Catalyzed Michael Addition of 1,3-Dicarbonyl Compounds to Electron-Deficient Olefins. To a screw-cap glass vial were added PI/CB-B (0.0261 g, 0.0251 mmol, 5 mol %), β-ketoester **1a** (87.0 μL, 0.502 mmol), and vinyl ketone **2a** (61.0 μL, 0.754 mmol). The mixture was dissolved in THF (0.5 mL) and stirred for 20 h at room temperature. Then the reaction mixture was filtered and washed with DCM, and the resulting filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (EtOAc:hexane = 1:4) to provide **3a** (0.1239 g, 0.472 mmol, 94%) as a clear colorless oil.

Ethyl 2-Benzoyl-5-oxohexanoate (3a) (Table 2, entry 1). *R*_f 0.22 (EtOAc:hexane = 1:4); ¹H NMR (CDCl₃, 500 MHz) δ 8.00–7.91 (m, 2H), 7.53–7.50 (m, 1H), 7.43–7.40 (m, 2H), 4.37 (dd, *J* = 6.3, 6.2 Hz, 1H), 4.10–4.04 (m, 2H), 2.58–2.47 (m, 2H), 2.21–2.10 (m, 2H), 2.06 (s, 3H), 1.09 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 207.8, 195.2, 169.7, 135.8, 133.6, 128.7, 128.6, 61.3, 52.5, 40.4, 29.9, 22.6, 13.9. This is a known compound, and the spectral data are identical to those reported in literature.²³

Preparation of PI/CB-Au/Pd/B. To a solution of **4** (0.1448 g) in diglyme (9.6 mL) was added ketjen black (0.1458 g). The resulting suspension was cooled to 0 °C, and then a solution of NaBH₄ (46.0 mg, 1.21 mmol) in diglyme (2.2 mL) was added dropwise. The reaction mixture was stirred for approximately 15 min, and then a solution of PPh₃AuCl (40.2 mg, 0.0811 mmol) and Pd(OAc)₂ (18.2 mg, 0.0811 mmol) in diglyme (5.8 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature and was stirred for 4 h. Diethyl ether (80 mL) was added dropwise, and then the suspension was filtered and washed with excess diethyl ether. The isolated polymer-coated carbon black was allowed to dry, gently ground with a mortar and pestle, and then heated at 170 °C for 4 h. The polymer-incarcerated catalyst was then resuspended in DCM, filtered, washed with excess DCM, and allowed to dry to provide PI/CB-Au/Pd/B (0.4035 g, Au loading: 0.2007 mmol/g, Pd loading: 0.2183 mmol/g, B loading: 2.456 mmol/g).

Typical Procedure for the PI/CB-Au/Pd/B-Catalyzed Sequential Aerobic Oxidation–Michael Addition of 1,3-Dicarbonyl Compounds to Allylic Alcohols. In a screw-cap glass vial was added PI/CB-Au/Pd/B (0.0250 g, 5.02 μmol, 1 mol % with respect to Au), β-ketoester **1a** (87.0 μL, 0.502 mmol), and allylic alcohol **5d** (73.0 μL, 0.555 mmol) and dissolved in THF (0.5 mL). The reaction mixture was allowed to stir for 20 h at 60 °C under a balloon of oxygen gas. Then the reaction mixture was filtered and washed with DCM, and

the resulting filtrate was concentrated under reduced pressure. The crude product was purified by column chromatography (EtOAc:hexane = 1:4) to provide **3l** (0.1544 g, 0.476 mmol, 95%) as a clear colorless oil.

Ethyl 2-Benzoyl-5-oxo-5-phenylpentanoate (3l) (Table 6, entry 9). R_f 0.36 (EtOAc:hexane = 1:4); IR (neat, NaCl): 3064 (m), 2981 (s), 2937 (s), 1974 (w), 1913 (w), 1734 (s), 1686 (s), 1596 (m), 1448 (s), 1221 (s), 974 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 8.07 (d, $J = 7.9$ Hz, 2H), 7.95 (d, $J = 7.4$ Hz, 2H), 7.59–7.53 (m, 2H), 7.50–7.43 (m, 4H), 4.57 (dd, $J = 7.9$, 6.2 Hz, 1H), 4.19–4.10 (m, 2H), 3.22–3.16 (m, 1H), 3.12–3.06 (m, 1H), 2.49–2.36 (m, 2H), 1.15 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 199.2, 195.3, 169.8, 136.6, 135.9, 133.6, 133.1, 128.71, 128.70, 128.6, 128.0, 61.4, 52.8, 35.6, 23.2, 13.9; ESI-HRMS (m/z) calcd for $\text{C}_{20}\text{H}_{20}\text{O}_4$ [(M + H) $^+$]: 325.14398, found: 325.14334.

■ ASSOCIATED CONTENT

S Supporting Information. Detailed experimental procedures and characterization of all new compounds. This material is free of charge via the Internet at <http://pubs.acs.org>.

■ AUTHOR INFORMATION

Corresponding Author

shu_kobayashi@chem.s.u-tokyo.ac.jp

■ ACKNOWLEDGMENT

This work was partially supported by a Grant-in-Aid for Scientific Research from the Japan Society of the Promotion of Science (JSPS), ERATO (JST), NEDO, and GCOE. W.-J.Y. thanks JSPS for the JSPS Postdoctoral Fellowship for Foreign Researchers. We also thank Mr. Noriaki Kuramitsu (The University of Tokyo) for STEM, EDS, and SEM analyses, and Mr. Tomoyoshi Higashi, Mr. Yoshikuni Okumura, and Mr. Tetsuo Nakajo (SDK) for N_2 adsorption/desorption analysis.

■ REFERENCES

- (1) (a) Vriezema, D. M.; Aragonès, M. C.; Elemans, J. A. A. W.; Cornelissen, J. J. L. M.; Rowan, A. E.; Nolte, R. J. M. *Chem. Rev.* **2005**, *105*, 1445. (b) Koblenz, T. S.; Wassenaar, J.; Reek, J. N. H. *Chem. Soc. Rev.* **2008**, *37*, 247.
- (2) (a) Lee, J. M.; Na, Y.; Han, H.; Chang, S. *Chem. Soc. Rev.* **2004**, *33*, 302. (b) Wasilke, J.-C.; Obrey, S. J.; Baker, R. T.; Bazan, G. C. *Chem. Rev.* **2005**, *105*, 1001. (c) Chapman, C. J.; Frost, C. G. *Synthesis* **2007**, *1*. (d) Shindoh, N.; Takemoto, Y.; Takasu, K. *Chem.—Eur. J.* **2009**, *15*, 12168. (e) Zhou, J. *Chem. Asian J.* **2010**, *5*, 422.
- (3) (a) Kobayashi, S.; Manabe, K. *Acc. Chem. Res.* **2002**, *35*, 209. (b) Akiyama, A.; Kobayashi, S. *Chem. Rev.* **2009**, *109*, 594.
- (4) The incorporation of multiple metal catalysts on a single polymer support is quite rare. See: Pittman, C. U., Jr.; Smith, L. R. *J. Am. Chem. Soc.* **1975**, *97*, 1749.
- (5) Gold nanoclusters have been previously suggested to possess Lewis acidic properties under aerobic conditions. See: Kamiya, I.; Tsunoyama, H.; Tsukuda, T.; Sakurai, H. *Chem. Lett.* **2007**, *36*, 646.
- (6) The addition of $\text{Sc}(\text{OTf})_3$ to a solution of NaBH_4 in diglyme resulted in the evolution of a gas.
- (7) The use of immobilized boron as a catalyst is relatively uncommon. For examples, see: (a) Itsuno, S.; Kamahori, K.; Watanabe, K.; Koizumi, T.; Ito, K. *Tetrahedron: Asymmetry* **1994**, *5*, 523. (b) Kamahori, K.; Ito, K.; Itsuno, S. *J. Org. Chem.* **1996**, *61*, 8321. (c) Smith, K.; El-Hiti, G. A.; Hou, D.; DeBoos, G. A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2807. (d) Roesler, R.; Har, B. J. N.; Piers, W. E. *Organometallics* **2002**, *21*, 4300. (e) Itsuno, S.; Arima, S.; Haraguchi, N. *Tetrahedron* **2005**, *61*, 12074. (f) Lakouraj, M. M.; Mokhtary, M. *Monatsh. Chem.* **2009**, *140*, 53.

(8) NaBH_4 is a common reducing agent used for the formation of nanoclusters from metal salts. However, to the best of our knowledge, the possibility of boron remaining and acting as a catalyst has yet been explored.

(9) Boron-free PI-Au was prepared by the microencapsulation of pre-prepared PPh_3 -stabilized Au nanoclusters with the styrene-based polymer, followed by thermally induced cross-linking. Alternatively, boron-free PI-Au can be prepared by stirring the boron-containing immobilized Au catalyst in a THF/ H_2O solution overnight, followed by filtration and drying. For the preparation of PPh_3 -stabilized Au nanoclusters, see: Shichibu, Y.; Negishi, Y.; Tsukuda, T.; Teranishi, T. *J. Am. Chem. Soc.* **2005**, *127*, 13464.

(10) We found that mixing hydroquinone with $\text{NaB}(\text{OMe})_4$ in DCM results in an unidentified blue solid.

(11) The Michael reaction between β -ketoester **1a** and methyl vinyl ketone with 3 equiv of K_2CO_3 in DCM ($C = 1.0$ M) provided 53% of the Michael adduct **3a** along with undesired side products. From our previous studies, we have found that PI bimetallic Au-M nanoclusters can facilitate the oxidation of alcohols under base-free conditions. See: Miyamura, H.; Matsubara, R.; Kobayashi, S. *Chem. Commun.* **2008**, 2031.

(12) From our previous studies, relatively low levels of Au nanoclusters could be loaded on the polymer support (0.07–0.08 mmol/g of Au) to ensure small cluster size and high catalytic activity. We have found that a polymer–carbon black composite material facilitates high Au loading (0.25 mmol/g of Au) while maintaining small cluster size and high catalytic activity. See: Lucchesi, C.; Inasaki, T.; Miyamura, H.; Matsubara, R.; Kobayashi, S. *Adv. Synth. Catal.* **2008**, *350*, 1996.

(13) Kaizuka, K.; Miyamura, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2010**, *132*, 15096.

(14) (a) Gómez-Bengoia, E.; Cuerva, J. M.; Mateo, C.; Echavarren, A. M. *J. Am. Chem. Soc.* **1996**, *118*, 8553. (b) Campana, A. G.; Fuentes, N.; Gómez-Bengoia, E.; Mateo, C.; Oltra, J. E.; Echavarren, A. M.; Cuerva, J. M. *J. Org. Chem.* **2007**, *72*, 8127.

(15) Abraham, S.; Sundararajan, G. *Tetrahedron* **2006**, *62*, 1474.

(16) It is most likely that the tetravalent boron is only the resting state for the true catalyst for the Michael reaction. $\text{NaB}(\text{OMe})_4$ is in equilibrium with $\text{B}(\text{OMe})_3$ and NaOH and may act as a bifunctional acid–base catalyst. For further discussion of the catalytic activity of $\text{NaB}(\text{OMe})_4$, see ref 14b.

(17) Brunauer, S.; Emmett, P. H.; Teller, E. *J. Am. Chem. Soc.* **1938**, *60*, 309.

(18) Kruk, M.; Li, Z.; Jaroniec, M. *Langmuir* **1999**, *15*, 1435.

(19) Rate enhancement has been observed for a cascade reaction catalyzed by two or more enzymes co-immobilized on the surface of silica nanoparticles. See: Pescador, P.; Katakis, I.; Toca-Herrera, J. L.; Donath, E. *Langmuir* **2008**, *24*, 14108.

(20) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(21) Brown, H. C.; Mead, E. J.; Rao, B. C. S. *J. Am. Chem. Soc.* **1955**, *77*, 6209.

(22) Briot, A.; Baehr, C.; Brouillard, R.; Wagner, A.; Mioskowski, C. *J. Org. Chem.* **2004**, *69*, 1374.

(23) Takeuchi, M.; Akiyama, R.; Kobayashi, S. *J. Am. Chem. Soc.* **2005**, *127*, 13096.

■ NOTE ADDED AFTER ASAP PUBLICATION

After this paper was published ASAP February 8, 2011, the description of the preparation of PI/CB-B was modified in the Experimental Section. The corrected version was published February 11, 2011.