ORGANIC
LETTERS

XXXX
Vol. XX, No. XX
000–000

Graphene-Supported RuO_2 Nanoparticles for Efficient Aerobic Cross-Dehydrogenative Coupling Reaction in Water

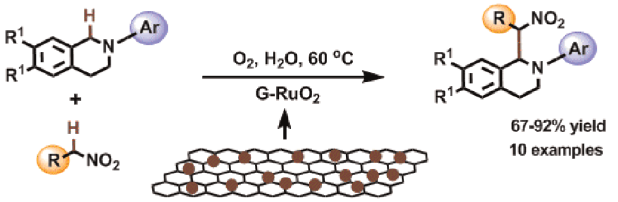
**Qing-Yuan Meng,[†] Qiang Liu,[†,‡] Jian-Ji Zhong,[†] Hui-Hui Zhang,[†] Zhi-Jun Li,[†]
Bin Chen,[†] Chen-Ho Tung,[†] and Li-Zhu Wu*,[†]**

*Key Laboratory of Photochemical Conversion and Optoelectronic Materials, Technical
Institute of Physics and Chemistry, Chinese Academy of Sciences, Beijing 100190,
People's Republic of China, and State Key Laboratory of Applied Organic Chemistry,
College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000,
People's Republic of China, and*

lzwu@mail.ipc.ac.cn

Received October 21, 2012

ABSTRACT



A cross-dehydrogenative coupling (CDC) reaction between tertiary amines and nitroalkanes has been realized under an oxygen atmosphere in water simply by using graphene-supported RuO_2 as the catalyst, which was made from water-soluble graphene with sulfonic groups and $RuCl_3 \cdot nH_2O$ to form $RuO_2 \cdot nH_2O$ nanocomposites in situ. In contrast to $RuCl_3 \cdot nH_2O$ and $RuO_2 \cdot nH_2O$, the graphene-supported RuO_2 nanoparticles exhibited higher activity and stability for the aerobic CDC reaction in water.

Transition-metal-catalyzed activation of C–H bonds for C–C bond formation has always been an important concern of organic chemistry.[1] As exemplified by one of the most successful reaction protocols, cross-dehydrogenative coupling (CDC) reaction that avoids prefunctionalization and defunctionalization has aroused much interest in recent years.[2] With the aid of a sacrificial oxidant, inorganic metal salts[3] and organic oxidants[4] have been successfully employed for such organic transformation.[2–5] Among various oxidants, molecular oxygen[5] is one of the best choices due to

---

[†] Chinese Academy of Sciences.

[‡] Lanzhou University.

(1) (a) Arndtsen, B. A.; Bergman, R. G.; Mobley, T. A.; Peterson, T. H. *Acc. Chem. Res.* **1995**, *28*, 154. (b) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731. (c) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (d) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780.

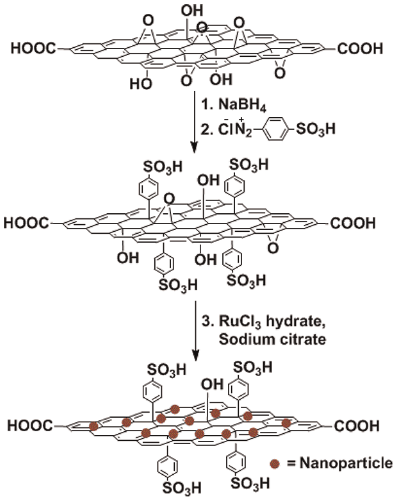
(2) (a) Murahashi, S.-I.; Komiya, N.; Terai, H.; Nakae, T. *J. Am. Chem. Soc.* **2003**, *125*, 15312. (b) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 11810. (c) Zhang, Y.; Li, C.-J. *Angew. Chem., Int. Ed.* **2006**, *45*, 1949. (d) Borduas, N.; Powell, D. A. *J. Org. Chem.* **2008**, *73*, 7822. (e) Deng, G.; Zhao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 6278. (f) Li, C.-J. *Acc. Chem. Res.* **2008**, *42*, 335. (g) Murahashi, S.-I.; Nakae, T.; Terai, H.; Komiya, N. *J. Am. Chem. Soc.* **2008**, *130*, 11005. (h) Jia, Y.-X.; Kündig, E. P. *Angew. Chem., Int. Ed.* **2009**, *48*, 1636. (i) Perry, A.; Taylor, R. J. K. *Chem. Commun.* **2009**, 3249. (j) Condie, A. G.; González-Gómez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464. (k) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (l) Rueping, M.; Vila, C.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C. *Chem. Commun.* **2011**, *47*, 2360. (m) Boess, E.; Schmitz, C.; Klussmann, M. *J. Am. Chem. Soc.* **2012**, *134*, 5317. (n) Liu, Q.; Li, Y.-N.; Zhang, H.-H.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *Chem.—Eur. J.* **2012**, *18*, 620.

(3) (a) Pei, T.; Wang, X.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2003**, *125*, 648. (b) Liu, C.; Wang, X.; Pei, T.; Widenhoefer, R. A. *Chem.—Eur. J.* **2004**, *10*, 6343. (c) Wang, X.; Widenhoefer, R. A. *Chem. Commun.* **2004**, 660. (d) Li, R.; Liang, L.; Lu, W. *Organometallics* **2006**, *25*, 5973. (e) Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 11904. (f) Wang, K.-L.; Lü, M.-Y.; Wang, Q.-M.; Huang, R.-Q. *Tetrahedron* **2008**, *64*, 7504. (g) Martin, C. L.; Overman, L. E.; Rohde, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 7568. (h) Li, J.-J.; Mei, T.-S.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 6452. (i) Cheng, D.; Gallagher, T. *Org. Lett.* **2009**, *11*, 2639. (j) Potavathri, S.; Pereira, K. C.; Gorelsky, S. I.; Pike, A.; LeBris, A. P.; DeBoef, B. *J. Am. Chem. Soc.* **2010**, *132*, 14676. (k) Wei, Y.; Su, W. *J. Am. Chem. Soc.* **2010**, *132*, 16377. (l) Wang, F.; Song, G.; Li, X. *Org. Lett.* **2010**, *12*, 5430. (m) He, C.; Guo, S.; Ke, J.; Hao, J.; Xu, H.; Chen, H.; Lei, A. *J. Am. Chem. Soc.* **2012**, *134*, 5766.

10.1021/ol3028785

it being abundant, clean, and atom-efficient. Although considerable progress has been made, most of the aerobic CDC reactions are carried out in organic solvents. It seems difficult to realize a CDC reaction in water that is safe and environmentally benign. In 2006, Li and Wang reported an efficient "on water"-promoted direct coupling of 1,4-benzoquinones with indole compounds.[6] Later, Li et al. found that copper salts could catalyze the aerobic CDC reaction of tertiary amines with nitroalkanes or dialkyl malonates to proceed efficiently in water.[7] Lipshutz et al. recently employed cationic $[Pd(MeCN)_4](BF_4)_2$ salts as a catalyst to activate aromatic C–H bonds for the Fujiwara–Moritani reaction of anilides in water.[8] Nonetheless, examples on aerobic CDC reactions in water[6–9] that are as stable and efficient as those in organic solvents are quite rare.

Scheme 1. Preparation of the Water-Soluble Nanocomposites



In this contribution, we wish to report an aerobic CDC reaction in water, in which graphene, a two-dimensional sp^2-hybridized carbon network, was incorporated into the transition-metal-catalyzed CDC reaction. It is anticipated that the excellent electronic, mechanical, and thermal properties[10] of graphene would be useful not only to provide a support for the transition metal catalyst but also to improve the performance of the CDC reaction. In order to make the whole system water-soluble, sulfonic groups were used to functionalize graphene in this work. Inspired by the work of Murahashi,[2a] who discovered $RuCl_3$-catalyzed oxidation of tetrahydroisoquinolines by oxygen, we expected that $RuCl_3$ could be successfully anchored on the surface of the water-soluble graphene with sulfonic groups. However, we found that $RuO_2 \cdot nH_2O$ rather than $RuCl_3$ was formed on the surface of the graphene in situ. More importantly, graphene-supported RuO_2 (G-RuO_2) is able to catalyze the CDC reaction between tertiary amine and nitroalkane under an oxygen atmosphere in water. A comparison of the performance revealed that G-RuO_2 nanocomposites are more efficient than $RuCl_3 \cdot nH_2O$ and $RuO_2 \cdot nH_2O$ under the same condition. Moreover, G-RuO_2 catalyst could be recycled simply by filtration.

The synthetic route to the nanocomposites is shown in Scheme 1. Graphite oxide was prepared by a modified Hummers' method from graphite powder[11] and used as the starting material. Under the reduction by $NaBH_4$, the majority of the oxygen functional groups on the graphite oxide was removed, and sulfonation of the preliminarily reduced graphene by aryl diazonium salt of sulfanilic acid[12] afforded water-soluble graphene. After addition of $RuCl_3 \cdot nH_2O$ into the aqueous solution of the sulfonated graphene, sodium citrate aqueous solution was further added dropwise to reduce the graphene under heat for 10 h. Then centrifugation was carried out to obtain the nanocomposite.

Transmission electron microscopy (TEM) equipped with energy-dispersive spectroscopy (EDS) and X-ray photoelectron spectroscopy (XPS) were used to study the chemical nature of the catalyst. As shown in Figure 1a,b, the reduced graphene oxide sheets are slightly wrinkled and folded on the ultrathin carbon membrane. The nanoparticles were about 2 nm in size and well-dispersed on the surface of the transparent carbon sheet. Almost no particle was found to scatter out of the surface of graphene, indicating the strong interaction between the graphene and the particles. The EDS images confirmed the existence of S and Ru elements in the nanocomposite (Figure 1c). The nature of nanoparticles on the surface of graphene was further investigated by XPS measurements. Note that the binding energies of Ru $3p_{3/2}$ and $3p_{1/2}$ at 463.4 and 486.3 eV (Figure 1d), respectively, are consistent with the character of

---

(4) (a) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586. (b) Yadav, J. S.; Reddy, B. V. S.; Swamy, T. *Tetrahedron Lett.* **2003**, *44*, 9121. (c) Jean, A.; Cantat, J.; Berard, D.; Bouchu, D.; Canesi, S. *Org. Lett.* **2007**, *9*, 2553. (d) Borduas, N.; Powell, D. A. *J. Org. Chem.* **2008**, *73*, 7822. (e) Song, C.-X.; Cai, G.-X.; Farrell, T. R.; Jiang, Z.-P.; Li, H.; Gan, L.-B.; Shi, Z.-J. *Chem. Commun.* **2009**, 6002. (f) Hull, K. L.; Sanford, M. S. *J. Am. Chem. Soc.* **2009**, *131*, 9651. (g) de Haro, T.; Nevado, C. *J. Am. Chem. Soc.* **2010**, *132*, 1512. (h) Kumar, G. S.; Maheswari, C. U.; Kumar, R. A.; Kantam, M. L.; Reddy, K. R. *Angew. Chem., Int. Ed.* **2011**, *50*, 11748. (i) Wang, P.; Rao, H.; Hua, R.; Li, C.-J. *Org. Lett.* **2012**, *14*, 902.

(5) (a) Baran, P. S.; Corey, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 7904. (b) Hatamoto, Y.; Sakaguchi, S.; Ishii, Y. *Org. Lett.* **2004**, *6*, 4623. (c) Dwight, T. A.; Rue, N. R.; Charyk, D.; Josselyn, R.; DeBoef, B. *Org. Lett.* **2007**, *9*, 3137. (d) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072. (e) Yin, W.; He, C.; Chen, M.; Zhang, H.; Lei, A. *Org. Lett.* **2009**, *11*, 709. (f) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460. (g) Matsuyama, N.; Kitahara, M.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2010**, *12*, 2358. (h) Zhang, B.; Xiang, S.-K.; Zhang, L. H.; Cui, Y.; Jiao, N. *Org. Lett.* **2011**, *13*, 5212. (i) Zhang, C.; Zong, X.; Zhang, L.; Jiao, N. *Org. Lett.* **2012**, *14*, 3280. (j) Shi, Z.-Z.; Zhang, C.; Tang, C.-H.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3381.

(6) Zhang, H.-B.; Liu, L.; Chen, Y.-J.; Wang, D.; Li, C.-J. *Eur. J. Org. Chem.* **2006**, 869.

(7) Basle, O.; Li, C.-J. *Green Chem.* **2007**, *9*, 1047.

(8) Nishikata, T.; Lipshutz, B. H. *Org. Lett.* **2010**, *12*, 1972.

(9) Alagiri, K.; Kumara, G. S. R.; Prabhu, K. R. *Chem. Commun.* **2011**, *47*, 11787.

(10) (a) Geim, A. K.; Novoselov, K. S. *Nat. Mater.* **2007**, *6*, 183. (b) Wan, X.; Huang, Y.; Chen, Y. *Acc. Chem. Res.* **2012**, *45*, 598.

(11) (a) Kovtyukhova, N. I.; Ollivier, P. J.; Martin, B. R.; Mallouk, T. E.; Chizhik, S. A.; Buzaneva, E. V.; Gorchinskiy, A. D. *Chem. Mater.* **1999**, *11*, 771. (b) Zhang, H.-H.; Liu, Q.; Feng, K.; Chen, B.; Tung, C.-H.; Wu, L.-Z. *Langmuir* **2012**, *28*, 8224.

(12) Si, Y.; Samulski, E. T. *Nano Lett.* **2008**, *8*, 1679.

hydrous RuO_2 (also written as RuO_xH_y).[13] The absence of $RuCl_3 \cdot nH_2O$ might be a result of hydrolysis during reaction under an alkaline environment.[14] The alkaline environment is related to sodium citrate, which could act as a capping reagent to interact with the surface of sulfonic-group-functionalized graphene.[15] As a result, the real catalytic center on the graphene is RuO_2 rather than $RuCl_3$. The prepared nanocomposition is stable and soluble in water without the need for any polymeric or surfactant stabilizers.

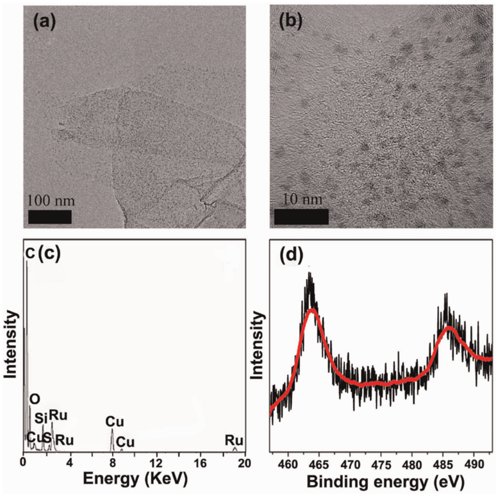
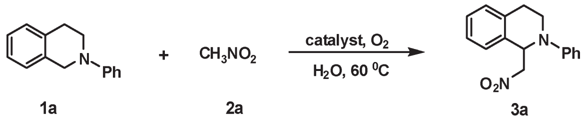


Figure 1. (a,b) TEM images of the G-RuO_2 at different magnifications; (c) typical EDS spectrum of G-RuO_2; (d) Ru $3p_{3/2}$ and $3p_{1/2}$ XPS spectrum of G-RuO_2 composites.

Our preliminary studies focused on the CDC reation of *N*-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**) and nitromethane (**2a**) in water. Typically, an aqueous solution of G-RuO_2 (2 mol %) containing **1a** and **2a** (3.0 equiv) was heated at 60 °C in an oxygen atmosphere for 16 h. It was a pleasure to see that 78% yield of cross-coupling product was obtained (Table 1, entry 1). In contrast, either $RuCl_3 \cdot nH_2O$ or $RuO_2 \cdot nH_2O$ gave lower yields under the same condition (Table 1, entries 2 and 3). The water-soluble graphene G-RuO_2 is indeed important for the reaction performance. Control experiments showed that G-RuO_2 catalyst and oxygen are all essential for the CDC reaction in water. Replacement of oxygen by air caused a significant drop in the reaction yield (Table 1, entry 4). Furthermore, the absence of any of G-RuO_2 and oxygen led to no product formation (Table 1, entries 5 and 6).

Time course of the yield for coupling production in the reaction was also investigated (Figure 2). Both $RuCl_3 \cdot nH_2O$ and $RuO_2 \cdot nH_2O$ were found to lose their catalytic activity in water within 5 h. However, when G-RuO_2 was used to catalyze the reaction, the yield of **3a** was increased in 24 h and the CDC reaction product was obtained in a yield of 89%. Clearly, the catalytic activity of G-RuO_2 nanocomposite is much better than that of $RuCl_3 \cdot nH_2O$ and $RuO_2 \cdot nH_2O$ for the reaction.

Table 1. Screening of Reaction Conditions for Aerobic CDC Reaction of **1a** and **2a** Catalyzed by G-RuO_2 in Water[a]



entry	catalyst	solvent	gas (1 atm)	yield (%)[b]
1	G-RuO_2[c]	H_2O	O_2	78
2	$RuCl_3 \cdot nH_2O$	H_2O	O_2	43
3	$RuO_2 \cdot nH_2O$	H_2O	O_2	54
4	G-RuO_2[c]	H_2O	air	36
5	no	H_2O	O_2	0
6	G-RuO_2[c]	H_2O	N_2	0

[a] *N*-phenyl-1,2,3,4-tetrahydroisoquinoline (0.1 mmol), nitromethane (0.3 mmol), and 0.002 mmol of catalyst (the amount of ruthenium) were stirred in 0.6 mL of water under the corresponding gas for 16 h. [b] Isolated yield based on *N*-phenyl-1,2,3,4-tetrahydroisoquinoline. [c] Sonicated in water for 20 min before utilization.

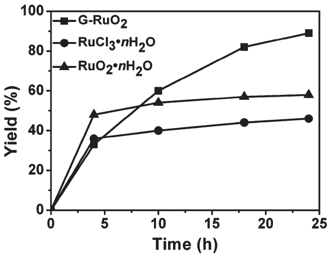


Figure 2. Comparison of $RuCl_3 \cdot nH_2O$, $RuO_2 \cdot nH_2O$, and G-RuO_2 with reaction time.

As tabulated in Table 2, the scope of the CDC reaction between tetrahydroisoquinoline derivatives and nitroalkanes was studied. Using G-RuO_2 as catalyst, the reactions proceeded and the desired coupling products were obtained in good to excellent yields. In the case of tetrahydroisoquinoline derivatives with a methoxy group either at the 4-position of *N*-phenyl (Table 2, entry 5) or at the 5,6-position of isoquinoline (Table 2, entry 6), the yields were obviously decreased. This is possibly due to the steric and electronic effect of the methoxy group. Additionally, the reaction system works well when less reactive nitroethane (Table 2, entries 7−9) or nitropropane (Table 2, entry 10) was used as an electrophilic reagent.

To evaluate the catalytic stability of G-RuO_2, we recycled the catalyst, and the result is shown in Figure 3. Although the yield was decreased from 89 to 64% after five runs, the catalytic activity was still superior to $RuCl_3 \cdot nH_2O$ (Table 1, entry 2). From TEM and fluorescence

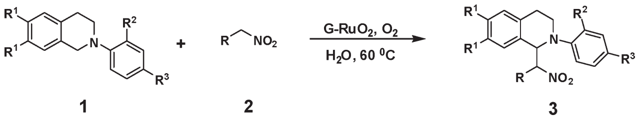
---

(13) Rolison, D. R.; Hagans, P. L.; Swider, K. E.; Long, J. W. *Langmuir* **1999**, *15*, 774.

(14) Zheng, J. P.; Cygan, P. J.; Jow, T. R. *J. Electrochem. Soc.* **1995**, *142*, 2699.

(15) Zhang, Z.; Chen, H.; Xing, C.; Guo, M.; Xu, F.; Wang, X.; Gruber, H.; Zhang, B.; Tang, J. *Nano Res.* **2011**, *4*, 599.

Table 2. G-RuO_2-Catalyzed Aerobic CDC Reactions between *N*-Phenyltetrahydroisoquinoline Derivatives and Nitroalkane in Water[a]



entry	R	R^1	R^2	R^3	product	yield (%)[b]
1	H	H	H	H	**3a**	89
2	H	H	H	Me	**3b**	88
3	H	H	H	F	**3c**	88
4	H	H	H	OMe	**3d**	90
5	H	H	OMe	H	**3e**	72
6	H	OMe	H	H	**3f**	67
7	Me	H	H	H	**3g**	87[c]
8	Me	H	H	Me	**3h**	91[d]
9	Me	H	H	Br	**3i**	92[d]
10	C_2H_5	H	H	H	**3j**	91[d]

[a] *N*-phenyltetrahydroisoquinoline derivatives (0.1 mmol), nitroalkane (0.3 mmol), G-RuO_2 (2.5 mg, sonicated in 0.6 mL of water for 20 min before use), under O_2 (1 atm) at 60 °C for 24 h. [b] Isolated yield. [c] Ratios of the two diastereoisomers were 3:2. [d] Ratios of the two diastereoisomers were 2:1.

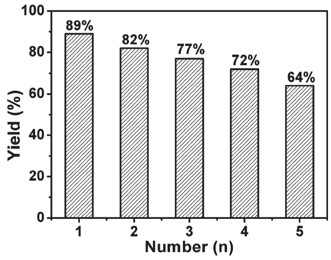
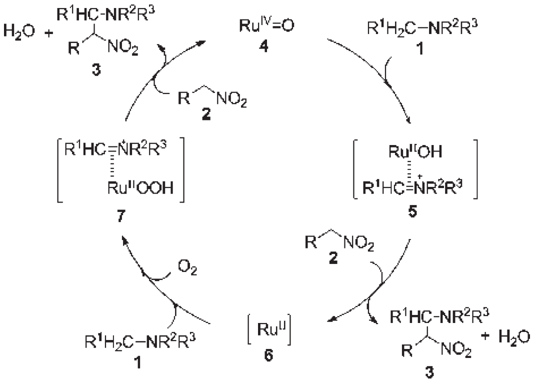


Figure 3. Reaction yield of CDC reaction using the recycled G-RuO_2 catalyst.

microscopic images, we inferred that the decreased catalytic activity of G-RuO_2 is a result of leaching of $RuO_2 \cdot nH_2O$ nanoparticles from the surface of graphene, while that of $RuO_2 \cdot nH_2O$ is the aggregation after reaction (Figures S1 and S2, Supporting Information).

Scheme 2. Proposed Mechanism



On the basis of the above observation, we tentatively proposed the reaction mechanism shown in Scheme 2. The high-valent $RuO_2 \cdot nH_2O$ **4** on the surface of water-soluble graphene could coordinate to tertiary amine to generate the iminium ion $Ru^{II}OH$ **5** by abstracting an electron and one hydrogen atom directly from the amine.[2a,g,16] The intermediate **5** would be trapped by nitroalkane to afford coupling product **3**, reduced Ru species **6**, and water. In the presence of O_2, the low-valent Ru species **6** is able to further react with the other amine, leading to the formation of iminium ion $Ru^{II}OOH$ **7**. Subsequently, nucleophilic attack of iminium **7** with nitroalkane gave the desired product **3**, RuO_2 **4**, and water to complete the catalytic cycle. The better performance of G-RuO_2 over $RuO_2 \cdot nH_2O$ implies that the electronic conductivity of graphene[10] may accelerate the electron transfer to the catalytic species, like $Ru^{IV}{=}O$ and Ru^{II}, which might further suppress the aggregation of the nanoparticles on the surface of graphene during the reaction.

In summary, the nanocomposite G-RuO_2 has been made in situ from sulfonic-group-functionalized graphene and $RuCl_3$ hydrate. The well-dispersed G-RuO_2 has been demonstrated to be a robust catalyst for the CDC reaction between *N*-phenyl-1,2,3,4-tetrahydroisoquinoline derivatives and nitroalkanes in water under an oxygen atmosphere. The higher efficiency of G-RuO_2 than either $RuCl_3 \cdot nH_2O$ or $RuO_2 \cdot nH_2O$ highlights the potential application of transition-metal-functionalized graphene in green and sustainable chemistry. Research is currently underway to functionalize graphene with other metal nanoparticles, especially cheap metals, and to apply these composites in organic transformation.

Acknowledgment. Financial support from the Ministry of Science and Technology of China (2009CB220008, 2013CB834505, and 2013CB834800), the National Natural Science Foundation of China (21090343, 21172102, and 91027041), and the Chinese Academy of Sciences is gratefully acknowledged.

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

---

(16) Murahashi, S.; Naota, T.; Kuwabara, T.; Saito, T.; Kumobayashi, H.; Akutagawa, S. *J. Am. Chem. Soc.* **1990**, *112*, 7820.

The authors declare no competing financial interest.