JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Ruthenium-Catalyzed Redox-Neutral and Single-Step Amide Synthesis from Alcohol and Nitrile with Complete Atom Economy

Byungjoon Kang,[†,‡,§] Zhenqian Fu,[‡,§] and Soon Hyeok Hong*[,†,‡]

[†]Center for Nanoparticle Research, Institute for Basic Science (IBS), Seoul 151-742, Republic of Korea
[‡]Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151-747, Republic of Korea

Supporting Information

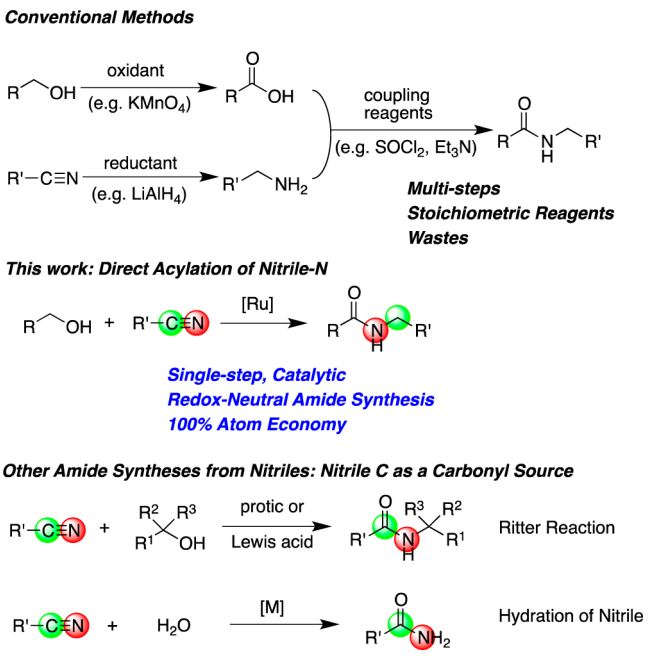
ABSTRACT: A completely atom-economical and redox-neutral catalytic amide synthesis from an alcohol and a nitrile is realized. The amide C−N bond is efficiently formed between the nitrogen atom of nitrile and the α-carbon of alcohol, with the help of an N-heterocyclic carbene-based ruthenium catalyst, without a single by-product. A utility of the reaction was demonstrated by synthesizing ^{13}C or ^{15}N isotope-labeled amides without involvement of any separate reduction and oxidation step.

Atom-economical amide synthesis[1] is one of the top challenges in green organic synthesis and process chemistry as discussed in the round table of global pharmaceutical corporations and the ACS Green Chemistry Institute in 2005.[2] Many approaches such as oxidative amide synthesis directly from alcohols and amines by liberating hydrogen gas as the byproduct have been extensively studied to realize the highly atom-economical and environmentally benign amide synthesis.[3,4]

Catalytic methods to utilize nitriles as primary amine surrogates have been less explored in organic synthesis, although it can offer efficient and versatile synthetic strategies with high atom economy and waste prevention.[5] Recently, Ru-catalyzed selective hydrogenation of nitriles into primary amines, suppressing the formation of side products such as imines and secondary amines, has been reported.[6] Inspired by the recent advances in the selective catalytic nitrile reductions, we envisioned that a completely atom-economical and redox-neutral amide synthesis could be realized through hydrogen transfer from alcohol to nitrile with the subsequent C−N bond formation between the nitrogen of a nitrile and the α-carbon of a primary alcohol without generation of any byproduct (Scheme 1). Herein, we report the first catalytic, single-step, and redox-neutral transformation of alcohols and nitriles into amide with 100% atom economy. To the best of our knowledge, it is the first completely atom-economical amide synthesis. This method also provides a distinctive way of amide syntheses directly from nitriles, compared with other well-known methods using C of nitriles as a carbonyl source as in the Ritter reaction[7] and hydration of nitriles (Scheme 1).[8]

Initially, the reaction between 2-phenylethanol and 3-phenylpropionitrile was chosen as a model reaction to investigate the catalytic conditions to realize the goal (Table 1). We first tried several catalytic systems that have been known as active for the direct amidation between alcohols and amines.

Scheme 1. Redox-Neutral Amide Synthesis Directly from Alcohols and Nitriles



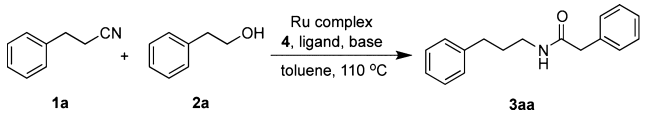
Various Ru(II)- and Ru(III)-chloride precatalysts accompanied with an NHC precursor, 1,3-diisopropylimidazolium bromide (**4**), and a base, however, showed no activity (entries 1−4). It has been suggested that the role of the base is not only to generate the NHC by deprotonation of the imidazolium salt but also to activate a Ru precatalyst from the reaction between the precatalyst and alkoxide formed by deprotonation of an alcohol substrate.[4h−l] Also, a Milstein catalyst gave only 18% product yield (entry 5). Then we found that a $RuH_2(PPh_3)_4$-based catalytic system, reported as active for the synthesis of amides and cyclic imides,[4e,h,9] showed significant activity (entry 6). After screening experiments with other Ru hydride complexes, $RuH_2(CO)(PPh_3)_3$ was identified as an efficient precatalyst for this reaction (entry 7).

With the optimal conditions in hand, substrate scope was investigated. First, different nitriles were tested with 2-phenylethanol (Table 2). Various aliphatic nitriles including acetonitrile afforded the corresponding amides in moderate to

Received: May 10, 2013

   dx.doi.org/10.1021/ja404695t | J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

Table 1. Catalyst Screening[a]

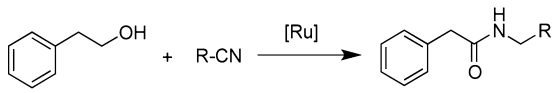


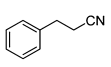
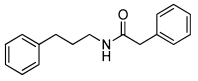
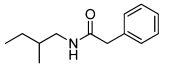
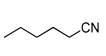
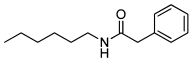
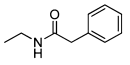
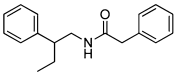
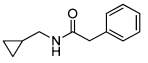
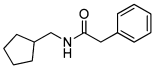
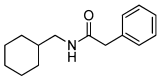
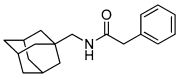
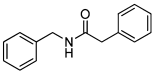
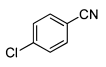
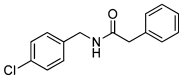
1a 2a 3aa

entry	Ru complex	ligand	base	time (h)	yield (%)[b]
1	$[Ru(benzene)Cl_2]_2$	CH_3CN	NaH	24	0
2	$[Ru(n\text{-cymene})Cl_2]_2$	pyridine	NaH	24	0
3	$Ru(COD)Cl_2$	PCy_3	*t*-BuOK	24	5
4	$RuCl_3$	CH_3CN	NaH	24	0
5[c]	Milstein catalyst[d]			24	18
6	$RuH_2(PPh_3)_4$		NaH	48	82
7	$RuH_2(CO)(PPh_3)_3$		NaH	48	90

[a]Reaction conditions: **1a** (0.5 mmol, 1.0 equiv), **2a** (0.55 mmol, 1.1 equiv), Ru complex (5 mol %), **4** (5 mol %), ligand (5 mol %), base (20 mol %), toluene (0.6 mL), 110 °C. [b]Determined by GC. [c]Without NHC precursor **4**. [d]Milstein catalyst = carbonylhydrido[6-(di-*tert*-butylphosphinomethylene)-2-(*N*,*N*-diethyl aminomethyl)-1,6-dihydropyridine]ruthenium(II).

Table 2. Amide Synthesis from 2-Phenylethanol and Nitriles[a]



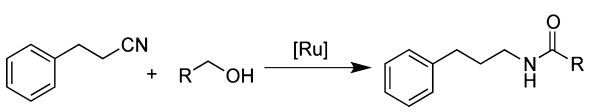
Entry	Nitrile		Product		Yield(%)[b]
1		**1a**		**3aa**	>99
2		**1b**		**3ba**	97
3		**1c**		**3ca**	91
4	CH_3CN	**1d**		**3da**	56
5		**1e**		**3ea**	84
6		**1f**		**3fa**	84
7		**1g**		**3ga**	83
8		**1h**		**3ha**	83
9		**1i**		**3ia**	89
10		**1j**		**3ja**	89
11		**1k**		**3ka**	53

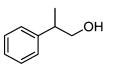
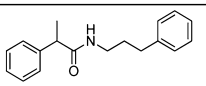
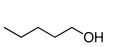
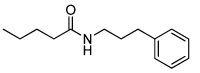
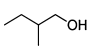
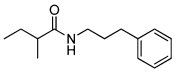
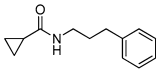
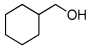
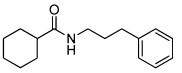
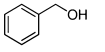
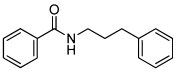
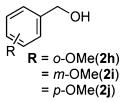
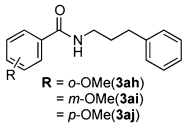
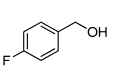
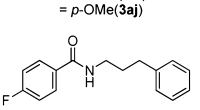
[a]Reaction conditions: nitrile (0.5 mmol, 1.0 equiv), **2a** (0.55 mmol, 1.1 equiv), $RuH_2(CO)(PPh_3)_3$ (10 mol %), NHC precursor **4** (10 mol %), NaH (20 mol %), toluene (0.6 mL), 110 °C, 48 h. [b]Isolated yield.

excellent yields (entries 1−4). Acetonitrile afforded a moderate yield of **3da** presumably due to its low boiling point. Secondary cyanides showed good activity for the reaction (entries 5−8). In the case of cyclopropanecarbonitrile (**1f**), no ring opening with C−C bond cleavage was observed, affording the desired amide (**3fa**) in 84% yield (entry 6). To our delight, even a sterically bulky tertiary cyanide worked well for the amidation (entry 9). Benzonitrile was also transformed to the corresponding amide in a good yield (entry 10). Aryl chloride exhibited reduced activity (entry 11). Aryl bromide, alkyl halides, and esters were not tolerant in the reaction, presumably due to the basic reaction conditions with the involvement of hydrogen transfer.

Next, the reactions between 3-phenylpropionitrile and various alcohols were investigated (Table 3). A range of aliphatic alcohols generated the corresponding amides in moderate to excellent yields (entries 1−5). In the case of substituted benzyl alcohols, electron-donating methoxy-group-substituted benzyl alcohols gave good yields regardless of the substituted positions (entry 7). An electron-withdrawing fluoride-substituted benzyl alcohol **2k** exhibited reduced activity

Table 3. Amide Synthesis from 3-Phenylpropionitrile and Alcohols[a]



Entry	Alcohol		Product		Yield(%)[b]
1		**2b**		**3ab**	82
2		**2c**		**3ac**	80
3		**2d**		**3ad**	62
4		**2e**		**3ae**	79
5		**2f**		**3af**	56
6		**2g**		**3ag**	81
7	 R = *o*-OMe(**2h**) = *m*-OMe(**2i**) = *p*-OMe(**2j**)	**2h** **2i** **2j**	 R = *o*-OMe(**3ah**) = *m*-OMe(**3ai**) = *p*-OMe(**3aj**)	**3ah** **3ai** **3aj**	80 82 81
8		**2k**		**3ak**	53
9		**2l**		**3al**	76
10		**2m**		**3am**	73

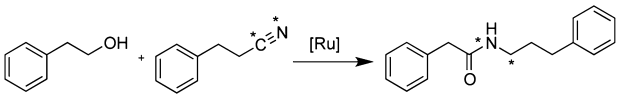
[a]Reaction conditions: **2a** (0.5 mmol, 1.0 equiv), alcohol (0.55 mmol, 1.1 equiv), $RuH_2(CO)(PPh_3)_3$ (10 mol %), NHC precursor **4** (10 mol %), NaH (20 mol %), toluene (0.6 mL), 110 °C, 48 h. [b]Isolated yield.

dx.doi.org/10.1021/ja404695t | J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

(entry 8). Furan ring (entry 9) or tertiary amine group (entry 10) were tolerant to the catalytic conditions.

Encouraged by the results, we applied newly developed methodology into synthesizing specific isotope-labeled amides. A site-specific labeled amide is used as an important tool for a spectroscopy-based protein-structure-defining process[10] and metabolic pathway tracking.[11] By using our method, specific labeled amide was easily synthesized within two steps from alkyl halide and labeled potassium cyanide. First, simple S_N2 reaction between 2-bromoethylbenzene and three commercially available isotope-labeled potassium cyanide ($K^{13}CN$, $KC^{15}N$, and $K^{13}C^{15}N$) afforded the corresponding isotope-substituted 3-phenylpropionitriles. Then they were reacted with 2-phenylethanol to make the labeled amides in good yields with complete incorporation of isotopes (Scheme 2).

Scheme 2. Selective Isotope Labeling[a]

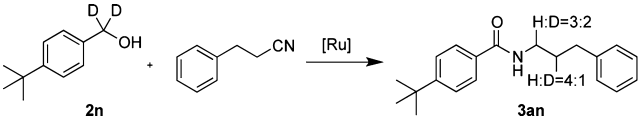


3la, 88% (>99% of ^{13}C)
3ma, 94% (>98% of ^{15}N)
3na, 96% (>99% of ^{13}C and ^{15}N)

[a]Reaction conditions: nitrile (0.5 mmol), 2-phenylethanol (0.55 mmol), $RuH_2(CO)(PPh_3)_3$ (10 mol %), NHC precursor **4** (10 mol %), NaH (20 mol %) in toluene (0.6 mL), 110 °C, 48 h.

To gain insight on the mechanism, several experiments were performed. First, to investigate overall hydrogen transfer during the catalysis, the reaction between 4-*tert*-butylbenzylalcohol-1,1-d_2 (**2n**) and 3-phenylpropionitrile was monitored with ^2D NMR spectroscopy (Scheme 3). Deuteration at α-CH_2 of the

Scheme 3. Deuterium Labeling Study[a]



[a]Reaction conditions: 3-phenylpropionitrile (0.5 mmol), 2-phenylethanol (0.55 mmol), $RuH_2(CO)(PPh_3)_3$ (5 mol %), NHC precursor **4** (5 mol %), NaH (20 mol %), benzene-d_6 (10 μL) in toluene (0.6 mL), 110 °C, 48 h.

nitrogen of the amide, originated from nitrile carbon, was observed during the reaction, while the deuterium peak of alcohol diminished. This result is concrete evidence that hydrogen generated from oxidation of alcohol is used for reduction of nitrile. In addition, deuteration at the acidic C2 carbon of 3-phenylpropionitrile, resulting in deuteration at β-CH_2 of the nitrogen of the amide, presumably mediated by sodium hydride, was observed.

To investigate real catalytic species, the reaction between 2-phenylethanol and 3-phenylpropionitrile in benzene-d_6 was monitored with ^1H and ^{31}P NMR spectroscopy. Two sets of new Ru hydride complexes, in addition to $RuH_2(CO)(PPh_3)_3$ precatalyst, were observed (Figure S2). One is identified as $RuH_2(CO)(PPh_3)_2(I^iPr)$ (I^iPr = 1,2-diisopropylimidazol-2-ylidene) complex reported by Whittlesey and Williams.[12] Independently synthesized $RuH_2(CO)(PPh_3)_2(I^iPr)$ was active for the reaction between **1a** and **2a**, generating the amide **3aa** in 90% GC yield with 5 mol % catalyst loading. The other hydride complex could be bis-NHC complex, $RuH_2(CO)(PPh_3)(I^iPr)_2$, because its chemical shifts and coupling constants of hydrides are almost identical with the reported complex $RuH_2(CO)(PPh_3)(ICy)_2$ (ICy = 1,2-dicyclohexylimidazol-2-ylidene).[13,14] As previously proposed,[4i,l] an NHC-bound ruthenium dihydride complex is considered a major catalytic species in this process.

Interestingly, we could observe an unusual doublet peak around δ = 10.2 ppm with a large coupling constant of 23 Hz by ^1H NMR spectroscopy during the experiment. To confirm its identity, another reaction of benzonitrile and 0.5 equiv of the precatalyst mixture was performed at 90 °C in benzene-d_6 in a sealed NMR tube. Two sets of doublets appeared with almost identical coupling constant of ~23 Hz (Figure 1A). Based on

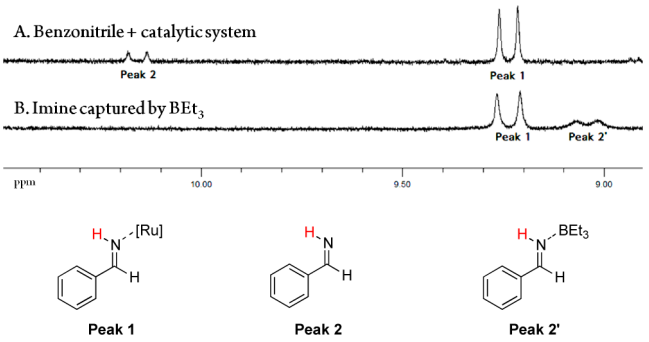


Figure 1. Observation of benzaldimine intermediates by ^1H NMR spectroscopy.

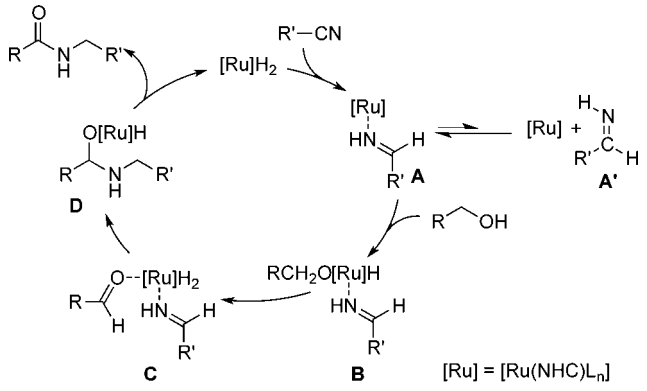
the recent reports on the synthesis and characterization of N-unsubstituted imine, either free[15] or Ru-bound,[6h] one doublet peak at 10.2 ppm was identified as the N−H proton from *trans*-benzaldimine. The other peak at 9.2 ppm was assigned as its ruthenium coordinated form. It was further confirmed by two experimental results. First, when alcohol was added to the in situ generated imine system and stirred at 90 °C for a while, two peaks disappeared with concurrent generation of the corresponding amide. Second, when triethylborane was added to the solution, the reported immediate coordination of BEt_3 to *trans*-benzaldimine was observed,[15] while the other peak remains intact, which suggested that the other species is a Ru-bound imine complex (Figure 1). Although we confirmed the involvement of imine intermediates, neither free aldehyde nor amine was detected during the reaction (Figure S5).

Based on the experimental observations, an innersphere mechanism is proposed (Scheme 4). At the initiation stage, nitrile is hydrogenated to *trans*-imine, generating a Ru-imine complex **A**. We think that steric hindrance from the Ru complex induces the *trans* selectivity of N-unsubstituted imine, as in the reported case of BEt_3-coordination-derived *cis* to *trans* isomerization of benzaldimine.[15] After oxidative addition of alcohol to the Ru complex, dehydrogenation of alcohol to aldehyde occurs, followed by addition of imine to acyl carbon[16] and further reduction. Finally, one more dehydrogenation reaction of the resulting hemiaminal intermediate **D** gives the corresponding amide with regeneration of dihydrido ruthenium species.

In summary, a completely atom-economical catalytic amide synthesis from an alcohol and a nitrile is achieved by an NHC-based Ru hydride catalyst. The reaction is an overall redox-neutral process involving hydrogen transfer from alcohol to nitrile. Facile syntheses of isotope-labeled amides were

dx.doi.org/10.1021/ja404695t | J. Am. Chem. Soc. XXXX, XXX, XXX−XXX

Scheme 4. Proposed Catalytic Cycle



demonstrated. This atom-economical, redox-neutral, and operatively simple method will provide a more environmentally benign method for the fundamental amide bond formation.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedure and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

soonhong@snu.ac.kr

Author Contributions

[§]These authors contributed equally.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (2012004077), and the Research Center Program of IBS (Institute for Basic Science) in Korea. We thank Prof. Y.K. Chung and Dr. S. Muthaiah for helpful discussions. We also thank the Korean Basic Science Institute (Daegu) for mass analysis. This paper is dedicated to Professor Young Keun Chung on the occasion of his 60th birthday.

■ REFERENCES

(1) (a) Humphrey, J. M.; Chamberlin, A. R. *Chem. Rev.* **1997**, *97*, 2243. (b) Han, S. Y.; Kim, Y. A. *Tetrahedron* **2004**, *60*, 2447. (c) Montalbetti, C.; Falque, V. *Tetrahedron* **2005**, *61*, 10827. (d) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337. (e) Valeur, E.; Bradley, M. *Chem. Soc. Rev.* **2009**, *38*, 606. (f) Pattabiraman, V. R.; Bode, J. W. *Nature* **2011**, *480*, 471.

(2) Constable, D. J. C.; Dunn, P. J.; Hayler, J. D.; Humphrey, G. R.; Leazer, J. J. L.; Linderman, R. J.; Lorenz, K.; Manley, J.; Pearlman, B. A.; Wells, A.; Zaks, A.; Zhang, T. Y. *Green Chem.* **2007**, *9*, 411.

(3) For reviews, see: (a) Dobereiner, G. E.; Crabtree, R. H. *Chem. Rev.* **2010**, *110*, 681. (b) Allen, C. L.; Williams, J. M. J. *Chem. Soc. Rev.* **2011**, *40*, 3405. (c) Chen, C.; Hong, S. H. *Org. Biomol. Chem.* **2011**, *9*, 20.

(4) For representative examples, see: (a) Gunanathan, C.; Ben-David, Y.; Milstein, D. *Science* **2007**, *317*, 790. (b) Nordstrøm, L. U.; Vogt, H.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 17672. (c) Shimizu, K.; Ohshima, K.; Satsuma, A. *Chem.—Eur. J.* **2009**, *15*, 9977. (d) Zweifel, T.; Naubron, J. V.; Grützmacher, H. *Angew. Chem., Int. Ed.* **2009**, *48*, 559. (e) Zhang, J.; Senthilkumar, M.; Ghosh, S. C.; Hong, S. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 6391. (f) Schley, N. D.; Dobereiner, G. E.; Crabtree, R. H. *Organometallics* **2011**, *30*, 4174. (g) Nova, A.; Balcells, D.; Schley, N. D.; Dobereiner, G. E.; Crabtree, R. H.; Eisenstein, O. *Organometallics* **2010**, *29*, 6548. (h) Muthaiah, S.; Ghosh, S. C.; Jee, J. E.; Chen, C.; Zhang, J.; Hong, S. H. *J. Org. Chem.* **2010**, *75*, 3002. (i) Zhang, Y.; Chen, C.; Ghosh, S. C.; Li, Y.; Hong, S. H. *Organometallics* **2010**, *29*, 1374. (j) Ghosh, S. C.; Hong, S. H. *Eur. J. Org. Chem.* **2010**, 4266. (k) Chen, C.; Zhang, Y.; Hong, S. H. *J. Org. Chem.* **2011**, *76*, 10005. (l) Makarov, I. S.; Fristrup, P.; Madsen, R. *Chem.—Eur. J.* **2012**, *18*, 15683.

(5) (a) Cui, X. J.; Zhang, Y.; Shi, F.; Deng, Y. Q. *Chem.—Eur. J.* **2011**, *17*, 2587. (b) Ikawa, T.; Fujita, Y.; Mizusaki, T.; Betsuin, S.; Takamatsu, H.; Maegawa, T.; Monguchi, Y.; Sajiki, H. *Org. Biomol. Chem.* **2012**, *10*, 293. (c) Srimani, D.; Feller, M.; Ben-David, Y.; Milstein, D. *Chem. Commum.* **2012**, *48*, 11853. (d) Werkmeister, S.; Bornschein, C.; Junge, K.; Beller, M. *Eur. J. Org. Chem.* **2013**, 3671.

(6) (a) Takemoto, S.; Kawamura, H.; Yamada, Y.; Okada, T.; Ono, A.; Yoshikawa, E.; Mizobe, Y.; Hidai, M. *Organometallics* **2002**, *21*, 3897. (b) Enthaler, S.; Addis, D.; Junge, K.; Erre, G.; Beller, M. *Chem.—Eur. J.* **2008**, *14*, 9491. (c) Enthaler, S.; Junge, K.; Addis, D.; Erre, G.; Beller, M. *ChemSusChem* **2008**, *1*, 1006. (d) Addis, D.; Enthaler, S.; Junge, K.; Wendt, B.; Beller, M. *Tetrahedron Lett.* **2009**, *50*, 3654. (e) Das, S.; Zhou, S.; Addis, D.; Enthaler, S.; Junge, K.; Beller, M. *Top. Catal.* **2010**, *53*, 979. (f) Gunanathan, C.; Hölscher, M.; Leitner, W. *Eur. J. Inorg. Chem.* **2011**, 3381. (g) Li, T.; Bergner, I.; Haque, F. N.; Iuliis, M. Z. D.; Song, D.; Morris, R. H. *Organometallics* **2007**, *26*, 5940. (h) Reguillo, R.; Grellier, M.; Vautravers, N.; Vendier, L.; Sabo-Etienne, S. *J. Am. Chem. Soc.* **2010**, *132*, 7854. (i) Miao, X. W.; Bidange, J.; Dixneuf, P. H.; Fischmeister, C.; Bruneau, C.; Dubois, J. L.; Couturier, J. L. *ChemCatChem* **2012**, *4*, 1911. (j) Werkmeister, S.; Bornschein, C.; Junge, K.; Beller, M. *Chem.—Eur. J.* **2013**, *19*, 4437.

(7) (a) Plaut, H.; Ritter, J. J. *J. Am. Chem. Soc.* **1951**, *73*, 4076. (b) Ritter, J. J.; Kalish, J. *J. Am. Chem. Soc.* **1948**, *70*, 4048. (c) Bishop, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, UK, 1991; p 261.

(8) (a) Cobley, C. J.; van den Heuvel, M.; Abbadi, A.; de Vries, J. G. *Tetrahedron Lett.* **2000**, *41*, 2467. (b) Murahashi, S.; Naota, T.; Saito, E. *J. Am. Chem. Soc.* **1986**, *108*, 7846. (c) Allen, C. L.; Lapkin, A. A.; Williams, J. M. J. *Tetrahedron Lett.* **2009**, *50*, 4262. (d) Davulcu, S.; Allen, C. L.; Milne, K.; Williams, J. M. J. *ChemCatChem* **2013**, *5*, 435.

(9) Fu, Z. Q.; Lee, J.; Kang, B.; Hong, S. H. *Org. Lett.* **2012**, *14*, 6028.

(10) (a) Senn, H.; Otting, G.; Wüthrich, K. *J. Am. Chem. Soc.* **1987**, *109*, 1090. (b) Clore, G. M.; Gronenborn, A. M. *Science* **1991**, *252*, 1390. (c) Clore, G. M.; Gronenborn, A. M. *Prog. Biophys. Mol. Biol.* **1994**, *62*, 153. (d) Clore, G. M.; Gronenborn, A. M. *Curr. Opin. Chem. Biol.* **1998**, *2*, 564. (e) Brauner, J. W.; Dugan, C.; Mendelsohn, R. *J. Am. Chem. Soc.* **2000**, *122*, 677.

(11) (a) Baillie, T. A. *Pharmacol. Rev.* **1981**, *33*, 81. (b) Baillie, T. A.; Rettenmeier, A. W. *J. Clin. Pharmacol.* **1986**, *26*, 481. (c) Kelly, N. M.; Sutherland, A.; Willis, C. L. *Nat. Prod. Rep.* **1997**, *14*, 205. (d) Mutlib, A. E. *Chem. Res. Toxicol.* **2008**, *21*, 1672. (e) Madhan, B.; Xiao, J. X.; Thiagarajan, G.; Baum, J.; Brodsky, B. *J. Am. Chem. Soc.* **2008**, *130*, 13520.

(12) Burling, S.; Paine, B. M.; Nama, D.; Brown, V. S.; Mahon, M. F.; Prior, T. J.; Pregosin, P. S.; Whittlesey, M. K.; Williams, J. M. J. *J. Am. Chem. Soc.* **2007**, *129*, 1987.

(13) Burling, S.; Kociok-Köhn, G.; Mahon, M. F.; Whittlesey, M. K.; Williams, J. M. J. *Organometallics* **2005**, *24*, 5868.

(14) Full characterization of the hydride complexes and their catalytic activity study are currently in progress. See Supporting Information for spectral support for the complex $RuH_2(CO)(PPh_3)(I^iPr)_2$.

(15) Lee, J. H.; Gupta, S.; Jeong, W.; Rhee, Y. H.; Park, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 10851.

(16) (a) Dghaym, R. D.; Yaccato, K. J.; Arndtsen, B. A. *Organometallics* **1998**, *17*, 4. (b) Kacker, S.; Kim, J. S.; Sen, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 1251. (c) Campbell, J. B.; Dedinas, R. F.; Trumbower-Walsh, S. *Synlett* **2010**, 3008.