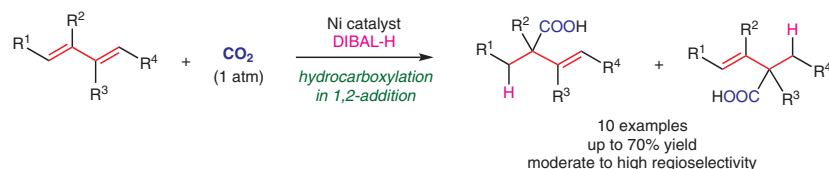


Nickel-Catalyzed Carboxylation of Conjugated Dienes with Carbon Dioxide and DIBAL-H for the Synthesis of β,γ -Unsaturated Carboxylic Acids

Ying Luo
Bun Chan
Tsutomu Fukuda
Gen Onodera
Masanari Kimura*

Graduate School of Engineering, Nagasaki University,
Bunkyo-machi 1-14, Nagasaki 852-8521, Japan
masanari@nagasaki-u.ac.jp

Published as part of the Cluster
Modern Nickel-Catalyzed Reactions



Received: 15.11.2020
Accepted after revision: 14.12.2020
Published online: 14.12.2020
DOI: 10.1055/a-1336-8034; Art ID: st-2020-r0596-c

Abstract Conjugated dienes underwent Ni-catalyst-promoted 1,2-hydrocarboxylation in a 1:1 ratio with carbon dioxide under atmospheric pressure in the presence of diisobutylaluminum hydride (DIBAL-H) to give the corresponding β,γ -unsaturated carboxylic acids, without dimerization or oligomerization of the conjugated diene.

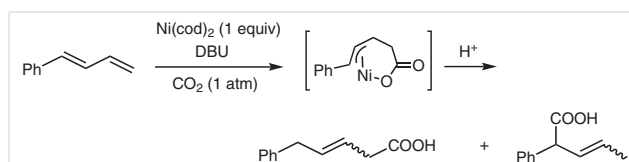
Key words nickel catalysis, carbon dioxide, dienes, hydrocarboxylation, diisobutylaluminum hydride, alkenoic acids

Carbon dioxide is a nontoxic, inexpensive, and abundant resource that can serve as a one-carbon unit in organic synthesis.¹ In this regard, transition-metal-catalyzed coupling reactions of carbon dioxide with various unsaturated hydrocarbons have attracted attention in recent years.²

Among unsaturated hydrocarbons, conjugated dienes form accessible and useful C4 elongation units in organic synthesis.³ The transition-metal-catalyzed CO₂-fixation reaction with conjugated dienes has considerable potential as a practical method for the preparation of unsaturated alcohols⁴ or carboxylic acids.⁵ However, there are formidable challenges in C–C bond construction by this method because some conjugated dienes dimerize easily; for example, in the presence of nickel(0), they can dimerize to produce bis- π -allylnickel complexes.⁶ These bis- π -allylnickel intermediates can often serve as reactive nucleophiles that combine with carbonyl compounds such as aldehydes or ketones.⁷ Furthermore, Ni-catalyzed two-to-one couplings of dienes and carbon dioxide via bis- π -allylnickel species have been reported by several groups as useful methods for producing feedstocks from carbon dioxide.⁸

Despite the problem of dimerization, some examples of one-to-one couplings of conjugated dienes and carbon dioxide have been reported.⁹ For instance, Takimoto and Mori

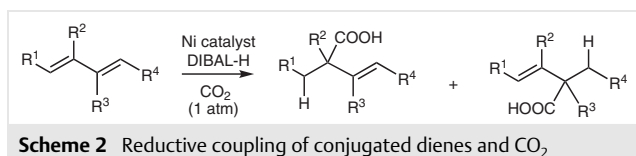
successfully developed a nickel-promoted oxidative cyclization of 1,3-dienes with carbon dioxide followed by hydrolysis of the oxo- π -allylnickel intermediate to produce β,γ -unsaturated carboxylic acids (Scheme 1).¹⁰ In this case, a stoichiometric amount of bis(cycloocta-1,5-diene)nickel [Ni(cod)₂] and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were required to enhance the reductive coupling of carbon dioxide with the conjugated dienes through a 1,4-addition. No catalytic version of a one-to-one coupling reaction of conjugated dienes with carbon dioxide has yet been fully developed, except for a Pd pincer-complex-catalyzed hydrocarboxylation of conjugated dienes with carbon dioxide promoted by triethylaluminum as a hydride source to produce β,γ -unsaturated carboxylic acids.¹¹



Scheme 1 Previously reported oxidative coupling of a conjugated diene and CO₂

A site-selective catalytic incorporation of several molecules of carbon dioxide into conjugated dienes was recently developed by Martin and co-workers, who developed a bis(tetrabutylammonium) tetrabromonickelate [NiBr₄(TBA)₂]-catalyzed dicarboxylation of conjugated dienes under atmospheric pressure with carbon dioxide in the presence of Mn as a reductant in DMA as a solvent.¹² In this case, the π -allylnickel species derived by oxidative cyclization of a conjugated diene and carbon dioxide in a 1:1 ratio served as nucleophilic intermediates to capture an additional molecule of carbon dioxide at the γ -position to give adipic acid derivatives.

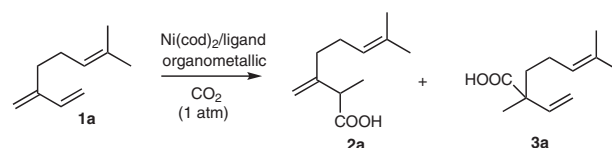
As an alternative CO₂-fixation process for the construction of a carbon framework, we have developed a Ni-catalyzed one-to-one reductive coupling of conjugated dienes with carbon dioxide in the presence of diisobutylaluminum hydride (DIBAL-H) to give β,γ-unsaturated carboxylic acid through a 1,2-addition, without dimerization of the conjugated diene (Scheme 2). The mild reaction conditions permitted the use of a broad range of substrates, and the products were obtained in good yields with moderate to good regioselectivities.



First, by using myrcene as a substrate, we examined the effects of various ligands and organometallic compounds on the desired reaction (Table 1). In the absence of any ligand, DIBAL-H produced a 70% yield of the hydrocarboxylation products **2a** and **3a** in a 5:1 ratio (Table 1, entry 1).¹³ A combination of PPh₃ and the DIBAL-H system gave the one-to-one coupling products a 3:1 mixture of regioisomers **2a** and **3a** in a modest 34% yield (entry 2). In the presence of PCy₃, a complicated mixture was obtained (entry 3). The use of 1,10-phenanthroline (1,10-Phen) and IPr carbene ligands provided the desired products in low yields (entries 4 and 5). We also found that polar solvents such as 1,4-dioxane or diethyl ether led to a worsening of the reaction outcome.¹⁴ It therefore appeared that competitive binding and steric crowding of ligands or polar solvents might prevent coordination of Ni. The use of other hydride sources such as 9-borabicyclo[3.3.1]nonane (9-BBN), Et₃SiH, or triethylaluminum did not provide good results in terms of the formation of the desired products as complex mixtures were obtained (entries 6–8). These results showed that the catalytic activity of the Ni species is affected by the ligand and the organometallic compound, and also demonstrated a significant role for the hydride donor in the reaction. These results indicated that the conditions in entry 1 are the most suitable for this coupling reaction. It appears that a combination of a Ni catalyst and a variety of ligands has a marked effect on the formation of dimers and oligomers from conjugated dienes.

Next, by using this optimal strategy, we examined the reactions of various commercially available conjugated dienes (Table 2). Under similar catalytic conditions to those shown in entry 1 of Table 1, a substrate containing a phenyl group gave the desired product in a moderate yield as a 2:1 mixture of regioisomers (Table 2, entry 2).¹⁴ Notably, substrates containing electron-donating groups, such as 4-methoxybenzyl or benzodioxole gave good yields of the corresponding products with improved regioselectivities (entries 3 and 4). In the case of alkyl substituents at the terminal

Table 1 Ni(0)-Promoted Hydrocarboxylation of Myrcene with CO₂^a

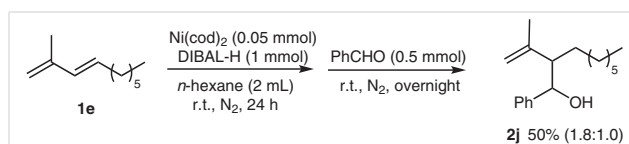


Entry	Ligand (mmol)	Organometallic	Yield (%) (2a/3a)
1	–	DIBAL-H	70 (5:1)
2	PPh ₃ (0.1)	DIBAL-H	34 (1:1)
3	PCy ₃ (0.1)	DIBAL-H	0
4	1,10-Phen (0.05)	DIBAL-H	25 (3:1)
5	IPr (0.05)	DIBAL-H	34 (3:1)
6	–	Et ₃ Al	0
7	–	9-BBN-H	0
8	–	Et ₃ SiH	0

^a Reaction conditions: Ni(cod)₂ (0.05 mmol), myrcene (4 mmol), ligand, organometallic (1 mmol), CO₂ (1 atm), hexane (2 mL), rt.

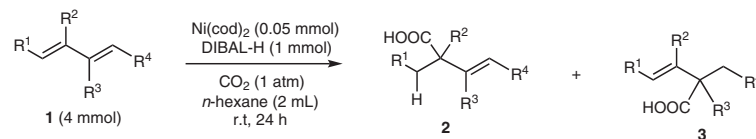
position of the conjugated diene, single isomers were obtained in good yields (entries 5–8). In addition, cyclohexa-1,3-diene gave a single isomer (entry 9). However, when 1,4-dimethylbuta-1,3-diene was used, the corresponding carboxylic acid was almost undetectable and a highly intractable mixture was formed (entry 10). Therefore, the catalytic process is subtly affected by structural variations in the substrate.

To verify the reactivity of conjugated dienes, we investigated the reaction in the presence of benzaldehyde as an electrophile instead of carbon dioxide, under a nitrogen atmosphere. The reaction of (*E*)-2-methyldeca-1,3-diene (**1e**) with benzaldehyde in the presence of Ni(cod)₂ catalyst and DIBAL-H gave the corresponding homoallylic alcohol **2j** in 50% yield as a mixture of diastereoisomers (Scheme 3). This result suggests that the formation of the homoallylic alcohol under the present conditions proceeds through the electrophilic attack of the aldehyde at the γ-position of an allylic anion species, such as a σ-allylaluminum intermediate.¹⁵



Scheme 3 Ni(0)-catalyzed three-component coupling reaction of a conjugated diene, DIBAL-H, and benzaldehyde

Although it is premature to rationalize the reaction mechanism, a plausible catalytic cycle is presented in Scheme 4, based on our experimental results. We propose that the reaction commences with the oxidative addition of

Table 2 Ni(0)-Catalyzed Hydrocarboxylation of Conjugated Dienes with DIBAL-H and Carbon Dioxide^a

Entry	R ¹	R ²	R ³	R ⁴	Products	Yield (%) (ratio 2/3)
1	H	H	1,1-dimethylbut-1-enyl	H	2a + 3a	70 (5:1)
2 ^b	Ph	H	H	H	2b + 3b	40 (2:1)
3 ^b	4-MeOC ₆ H ₄	H	H	H	2c + 3c	58 (13:1)
4 ^b	1,3-benzodioxole	H	H	H	2d + 3d	48 (6:1)
5	hexyl	H	Me	H	2e	52
6	octyl	H	H	H	2f	50
7	Ph(CH ₂) ₂	H	H	H	2g	51
8	Cy	H	H	H	2h	67
9	cyclohexa-1,3-dienyl				2i	46
10	Me	H	H	Me		–

^a Reaction conditions: Ni(cod)₂ (0.05 mmol), conjugated diene (4.0 mmol), DIBAL-H (1 mmol), CO₂ (1 atm), hexane (2 mL), rt, 24 h.

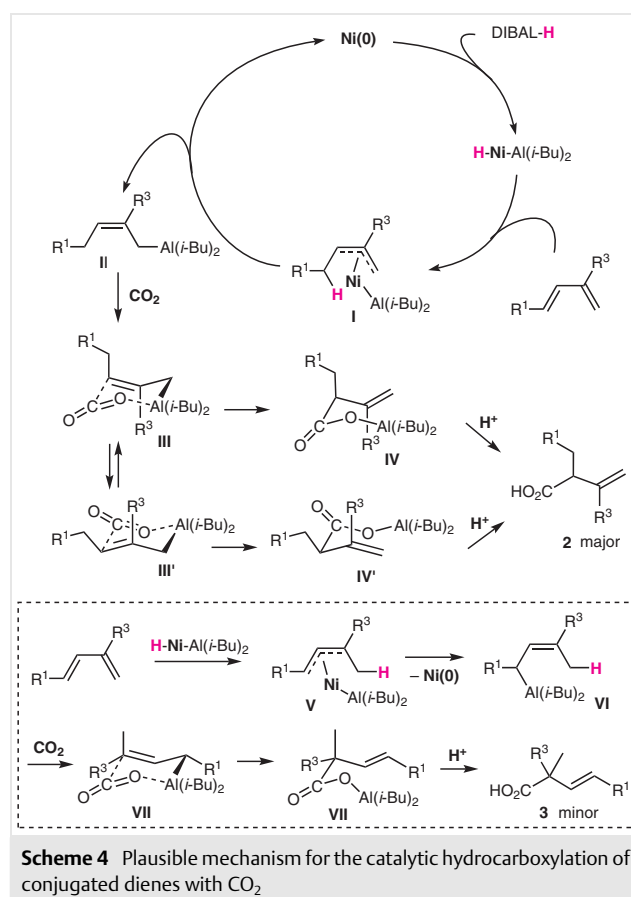
^b A small amount of the 1,4-addition product was also formed; for detailed spectral data, see the Supporting Information.

DIBAL-H to Ni(0) metal to form a (*i*-Bu)₂Al–Ni–H species; this is followed by hydronickeleation across the conjugated dienes to produce a π-allylnickel complex.¹⁶ Subsequently, the least-hindered σ-allylaluminum species **II** might be formed by reductive elimination of the π-allylnickel intermediate **I** to regenerate the nickel(0) catalyst. Carbon dioxide then attacks at the γ-position of the allylaluminum intermediate **II** via a six-membered-ring transition state **III** or **III'**, predominantly producing the desired β,γ-unsaturated carboxylic acid **2**.¹⁷ The alternative σ-allylaluminum complex **VI** obtained through the unfavorable hydronickeleation of (*i*-Bu)₂Al–Ni–H toward the conjugated diene results in the formation of carboxylic acid **3** as a minor regioisomer.

In conclusion, we have developed a Ni-catalyzed one-to-one reductive coupling of conjugated dienes with carbon dioxide in the presence of DIBAL-H in the presence of carbon dioxide at atmospheric pressure. The process proceeds via an allylaluminum intermediate to produce a β,γ-unsaturated carboxylic acid. The mild reaction conditions (room temperature and atmospheric pressure) permit good yields and high regioselectivities without oligomerization or polymerization of the conjugated diene.

Funding Information

This work was supported by a Grant-in-Aid for Scientific Research (B) (JP18H01981) from JSPS and partly by a Grant-in-Aid for Scientific Research on Innovative Areas, 'Precise Formation of a Catalyst Having a Specified Field for Use in Extremely Difficult Substrate Conversion Reactions' (18H04266) from MEXT. This work was also carried out as



part of the research program on Artificial Photosynthesis at Osaka City University.

Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/a-1336-8034>.

References and Notes

- (1) (a) Aresta, M.; Dibenedetto, A. *Dalton Trans.* **2007**, 2975. (b) Zhang, L.; Hou, Z. *Chem. Sci.* **2013**, *4*, 3395. (c) *Green Carbon Dioxide: Advances in CO₂ Utilization*; Centi, G.; Perathoner, S., Ed.; Wiley: Hoboken, **2014**. (d) Liu, Q.; Wu, L.; Jackstell, R.; Beller, M. *Nat. Commun.* **2015**, *6*, 5933.
- (2) For recent catalytic coupling reactions of carbon dioxide with unsaturated hydrocarbon compounds, see: (a) Ostapowicz, T. G.; Schmitz, M.; Krystof, M.; Klankermayer, J.; Leitner, W. *Angew. Chem. Int. Ed.* **2013**, *52*, 12119. (b) Zhang, L.; Hou, Z. In *New and Future Developments in Catalysis: Activation of Carbon Dioxide*; Suib, S. L., Ed.; Elsevier: Amsterdam, **2013**, Chap. 9, 253. (c) Wu, L.; Liu, Q.; Fleischer, I.; Jackstell, R.; Beller, M. *Nat. Commun.* **2014**, *5*, 3091. (d) Gaydou, M.; Moragas, T.; Juliá-Hernández, F.; Martin, R. *J. Am. Chem. Soc.* **2017**, *139*, 12161. (e) Zhang, L.; Hou, Z. *Curr. Opin. Green Sustainable Chem.* **2017**, *3*, 17. (f) Kuge, K.; Luo, Y.; Fujita, Y.; Mori, Y.; Onodera, G.; Kimura, M. *Org. Lett.* **2017**, *19*, 854. (g) Ye, J.-H.; Miao, M.; Huang, H.; Yan, S.-S.; Yin, Z.-B.; Zhou, W.-J.; Yu, D.-G. *Angew. Chem. Int. Ed.* **2017**, *56*, 15416. (h) Yan, S.-S.; Fu, Q.; Liao, L.-L.; Sun, G.-Q.; Ye, J.-H.; Gong, L.; Bo-Xue, Y.-Z.; Yu, D.-G. *Coord. Chem. Rev.* **2018**, *374*, 439.
- (3) (a) Sato, Y.; Takimoto, M.; Hayashi, K.; Katsuhara, T.; Takagi, K.; Mori, M. *J. Am. Chem. Soc.* **1994**, *116*, 9771. (b) Takimoto, M.; Hiraga, Y.; Sato, Y.; Mori, M. *Tetrahedron Lett.* **1998**, *39*, 4543. (c) Löber, O.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4366. (d) Shibata, K.; Kimura, M.; Kojima, K.; Tanaka, S.; Tamaru, Y. *J. Organomet. Chem.* **2001**, *624*, 348. (e) Kimura, M.; Ezoe, A.; Tanaka, S.; Tamaru, Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 3600. (f) Sato, Y.; Saito, N.; Mori, M. *J. Org. Chem.* **2002**, *67*, 9310. (g) Ezoe, A.; Kimura, M.; Inoue, T.; Mori, M.; Tamaru, Y. *Angew. Chem. Int. Ed.* **2002**, *41*, 2784. (h) Parker, S. E.; Börgel, J.; Ritter, T. *J. Am. Chem. Soc.* **2014**, *136*, 4857. (i) Maza, R. J.; Davenport, E.; Miralles, N.; Carbó, J. J.; Fernández, E. *Org. Lett.* **2019**, *21*, 2251.
- (4) (a) Gui, Y.-Y.; Hu, N.-F.; Chen, X.-W.; Liao, L.-L.; Ju, T.; Ye, J.-H.; Zhang, Z.; Li, J.; Yu, D.-G. *J. Am. Chem. Soc.* **2017**, *139*, 17011. (b) Mori, Y.; Shigeno, C.; Luo, Y.; Chan, B.; Onodera, G.; Kimura, M. *Synlett* **2018**, 29, 742.
- (5) (a) Tenaglia, A.; Brun, P.; Waegell, B. *J. Organomet. Chem.* **1985**, *285*, 343. (b) Hoberg, H.; Gross, S.; Milchereit, A. *Angew. Chem. Int. Ed.* **1987**, *26*, 571.
- (6) (a) Jolly, P. W.; Wilke, G. *The Organic Chemistry of Nickel*; Academic Press: New York, **1974**. (b) Keim, W. *Angew. Chem. Int. Ed.* **1990**, *29*, 235. (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49. (d) Kimura, M.; Tamaru, Y. In *Modern Organonickel Chemistry*; Tamaru, Y., Ed.; Wiley-VCH: Weinheim, **2005**, Chap. 5, 137.
- (7) (a) Kimura, M.; Matsuo, S.; Shibata, K.; Tamaru, Y. *Angew. Chem. Int. Ed.* **1999**, *38*, 3386. (b) Kimura, M.; Kojima, K.; Inoue, T.; Tamaru, Y. *Synthesis* **2004**, 3089. (c) Takimoto, M.; Kajima, Y.; Sato, Y.; Mori, M. *J. Org. Chem.* **2005**, *70*, 8605. (d) Kimura, M.; Ezoe, A.; Mori, M.; Tamaru, Y. *J. Am. Chem. Soc.* **2005**, *127*, 201. (e) Kojima, K.; Kimura, M.; Tamaru, Y. *Chem. Commun.* **2005**, 4717. (f) Kimura, M.; Ezoe, A.; Mori, M.; Iwata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **2006**, *128*, 8559.
- (8) (a) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2002**, *124*, 10008. (b) Mori, Y.; Mori, T.; Onodera, G.; Kimura, M. *Synthesis* **2014**, 46, 2287.
- (9) (a) Hoberg, H.; Jenni, K. *J. Organomet. Chem.* **1987**, *322*, 193. (b) Gao, Y.; Iijima, S.; Urabe, H.; Sato, F. *Inorg. Chim. Acta* **1994**, *222*, 145.
- (10) Takimoto, M.; Mori, M. *J. Am. Chem. Soc.* **2001**, *123*, 2895.
- (11) Takaya, J.; Sasano, K.; Iwasawa, N. *Org. Lett.* **2011**, *13*, 1698.
- (12) Tortajada, A.; Ninokata, R.; Martin, R. *J. Am. Chem. Soc.* **2018**, *140*, 2050.
- (13) **2,7-Dimethyl-3-methyloct-6-enoic Acid (2a) and 2,6-Dimethyl-2-vinylhept-5-enoic acid (3a): Typical Procedure (Table 1, Entry 1)**
An oven-dried flask charged with Ni(cod)₂ (13.7 mg, 0.05 mmol) was subjected to three cycles of evacuation and filling with CO₂. Anhyd hexane (2 mL), myrcene (540 mg, 4.0 mmol), and a 19% solution of DIBAL-H in hexane (1 mL, 1 mmol) were added under a constant flow of CO₂. The mixture was stirred at rt for 24 h, then 2 M aq NaOH was added and the mixture was diluted with H₂O and extracted with EtOAc (×3). The aqueous phases were then neutralized with 2 M aq HCl and extracted with EtOAc (×3). The combined organic phases were washed with brine, dried (MgSO₄), filtered, and concentrated under reduced pressure. The residual oil was placed in a Kugelrohr (30 Torr, 90 °C) to remove the isovaleric acid byproduct. A 5:1 mixture of **2a** and **3a** was obtained in the last bulb as a yellow liquid; yield: 0.13 g (70%).
2a
¹H NMR (400 MHz, benzene-*d*₆): δ = 5.09–5.15 (m, 1 H), 4.99 (s, 1 H), 4.88 (s, 1 H), 3.01 (q, *J* = 7.0 Hz, 1 H), 2.12 (m, 4 H), 1.03 (s, 3 H), 1.51 (s, 3 H), 1.15 (d, *J* = 6.8 Hz, 3 H). ¹³C NMR (100 MHz, CDCl₃): δ = 181.14, 147.45, 131.94, 123.67, 111.46, 45.57, 34.64, 26.30, 25.64, 17.66, 16.05.
3a
IR (neat): 3100, 2860, 2638, 1711, 1645, 1454, 1414, 1286, 1231, 1092, 901, 833 cm⁻¹. ¹H NMR (400 MHz, benzene-*d*₆): δ = 6.04 (dd, *J* = 17.6, 10.8 Hz, 1 H), 5.09–5.15 (m, 1 H), 5.02 (d, *J* = 17.6 Hz, 1 H), 4.98 (d, *J* = 10.8 Hz, 1 H), 2.00 (q, *J* = 8.2 Hz, 2 H), 1.76–1.83 (m, 1 H), 1.60–1.67 (m, 1 H), 1.63 (s, 3 H), 1.51 (s, 3 H), 1.23 (s, 3 H). ¹³C (100 MHz, CDCl₃): δ = 182.64, 140.94, 132.09, 123.62, 114.09, 48.33, 38.95, 25.60, 23.26, 20.16, 17.55. MS (EI): *m/z* (%) = 182.1310 (28) [M⁺], 167 (4), 137..
- (14) For the effects of solvents, see the Supporting Information.
- (15) Shen, Z.-L.; Peng, Z.; Yang, C.-M.; Helberg, J.; Mayer, P.; Marek, I.; Knochel, P. *Org. Lett.* **2014**, *16*, 956.
- (16) (a) Ely, R. J.; Morken, J. P. *J. Am. Chem. Soc.* **2010**, *132*, 2534. (b) Gao, F.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10961. (c) Eisch, J. J.; Sexsmith, S. R.; Fichter, K. C. *J. Organomet. Chem.* **1997**, *527*, 301. (d) Eisch, J. J.; Ma, X.; Singh, M.; Wilke, G. *J. Organomet. Chem.* **1990**, *382*, 273.
- (17) (a) Duong, H. A.; Huleatt, P. B.; Tan, Q.-W.; Shuying, E. L. *Org. Lett.* **2013**, *15*, 4034. (b) Wu, J.; Hazari, N. *Chem. Commun.* **2011**, 47, 1069. (c) Johnson, M. T.; Johansson, R.; Kondrashov, M. V.; Steyl, G.; Ahlquist, M. S. G.; Roodt, A.; Wendt, O. F. *Organometallics* **2010**, *29*, 3521. (d) Takaya, J.; Iwasawa, N. *J. Am. Chem. Soc.* **2008**, *130*, 15254.