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Abstract

Palladium catalysts, generated from Pd(OAc)2 and 2 equiv of *N,N*-dialkylbenzimidazolium iodide, are effective for the alkoxycarbonylation of olefins in high yields (>90%). Alkoxycarbonylation of 1-hexene in dimethylacetamide is achieved within 24 h at 110 °C using 1 mol % catalyst, 1000 psi CO, and ethanol. Reactions can be prepared in air, without the need of an acid additive to produce ethyl 2-methylhexanoate and ethyl heptanoate in approximately a 2:1 ratio.

Disciplines
Chemistry

Palladium Complexes with N-Heterocyclic Carbene Ligands As Catalysts for the Alkoxycarbonylation of Olefins

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ABSTRACT: Palladium catalysts, generated from Pd(OAc)$_2$ and 2 equiv of *N,N*-dialkylbenzimidazolium iodide, are effective for the alkoxycarbonylation of olefins in high yields (>90%). Alkoxycarbonylation of 1-hexene in dimethylacetamide is achieved within 24 h at 110 °C using 1 mol % catalyst, 1000 psi CO, and ethanol. Reactions can be prepared in air, without the need of an acid additive to produce ethyl 2-methylhexanoate and ethyl heptanoate in approximately a 2:1 ratio.
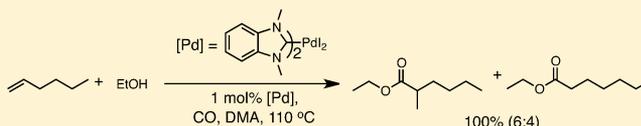
INTRODUCTION

Carbonylation reactions have been used to synthesize a wide variety of valuable polymer and oxygenate material.[1] Interest in Pd-phosphine catalysts for polymerization and alkoxycarbonylation of olefinic materials was piqued in the early 1980s with the discovery that cationic palladium-phosphine complexes could effectively copolymerize α-olefins with CO in the presence of methanol.[2−6] Subsequent studies of ligand influence indicated that bidentate tertiary phosphines favored polymerization (i.e., generation of polyketones), whereas monodentate tertiary phosphines favored single-insertion alkoxycarbonylation products.[3,7−10] While monodentate phosphines, such as triphenylphosphine, provided good yields of methyl propanoate from ethylene, longer chain olefins resulted in poor regioselectivity with mixtures of branched and linear esters.[7,11] Improvements by the research groups of Drent,[12] Pringle,[12,13] Tooze,[14,15] and Cole-Hamilton[16] have led to new Pd ligands (Chart 1) that greatly enhanced the linear selectivity

Chart 1. Chelating Phosphine Ligands for Alkoxycarbonylation of Olefins
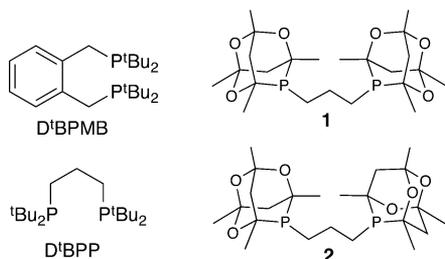
for alkoxycarbonylation. Although these ligands were chelating, the enhanced steric bulk of these phosphines effectively resulted in conversion of terminal and internal C5−C14 olefins to the corresponding linear ester products (eqs 1 and 2).

In seeking to develop more robust carbonylation catalysts, we evaluated palladium N-heterocyclic carbene complexes. Use of NHC ligands avoids the oxygen sensitivity and multistep ligand syntheses that are often associated with the use of
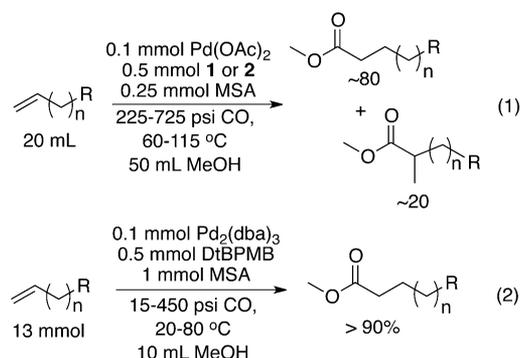
phosphines.[13,17] To date, very few Pd-NHC-catalyzed carbonylation reactions have been reported. Examples are limited to carbonylation of aryl halides, oxidative carbonylation of phenolic and amino compounds, and copolymerization of ethylene with CO.[18−22] Herein, we report our preliminary results for the first known alkoxycarbonylation of olefins using bis(benzimidazolylidene)palladium complexes (**4a−c**). These studies illustrate the systematic differences between NHC and phosphine ligands in alkoxycarbonylation.

RESULTS AND DISCUSSION

Simple N-alkyl-substituted benzimidazolium salts and the corresponding palladium catalysts were readily prepared as summarized in Scheme 1. Symmetrically substituted salts **3a−c** were synthesized from benzimidazole and 1° or 2° alkyl halides by heating in CH$_3$CN with base.[23]

Formation of the corresponding benzimidazolylidene complexes was accomplished via adapted procedures by heating Pd(OAc)$_2$ and the salt in a minimal amount of DMSO in air.[24,25]

The general reaction conditions for Pd-phosphine carbonylation of olefins commonly involve (1) the use of alcohol as solvent; (2) the addition of strong Brønsted acids as activating

**Scheme 1. Synthesis of Benzimidazolium Salts 3a−c and Pd-NHC Complexes 4a−c**

3a: R = H, R' = Me
3b: R = H, R' = iPr
3c: R = R' = Me

4a-c

additives; and (3) the use of phosphine steric bulk to control product selectivity. Specifically, alkoxycarbonylation with ligands from Chart 1 was optimized with methanol as the solvent and methane sulfonic acid (MSA), which presumably generates an active hydrido-Pd(II)-phosphine complex.[4,7,15,16,26] However, attempts to carbonylate 1-hexene with **4a** under similar conditions resulted only in catalyst decomposition, via elimination of the NHC ligands from Pd. These results led us to examine systematically the Pd-NHC reaction conditions.

Initially it was assumed that the failure of **4a** to carbonylate hexene under conditions similar to those used for eqs 1 and 2 was due to the strength of MSA and the poor solubility of the catalyst in alcohol. Therefore we employed a milder acid (pyridinium mesylate, PMS) and DMA as a cosolvent (Table

Table 1. Optimization of Alkoxycarbonylation Conditions for Catalyst 4a[a]

entry	PMS (mol %)	EtOH/1-hexene	T (°C)	yield % (b:l)
1	5	1:4	100	32 (2.3)
2	10	1:4	100	44 (2.4)
3	15	1:4	100	58 (2.4)
4	10	1:4	110	80 (1.8)
5	15	1:4	110	88 (2.0)
6	15	1:1	110	22[b] (2.1)
7	15	4:1	110	6 (2.1)[b]

[a]Conditions: 14 mmol of EtOH, 56 mmol of 1-hexene, 1 mol % **4a**, and 5 mL of DMA, 1000 psi CO, 24 h. [b]14 mmol EtOH, 14 mmol 1-hexene. [c]14 mmol of 1-hexene and 56 mmol of EtOH used.

1). Under conditions of excess EtOH to 1-hexene (4:1), a 1 mol % loading of **4a** was moderately active for carbonylation in the presence of 15 mol % PMS and DMA. Moreover, maintaining reagent ratios and increasing the catalyst loading to 5 mol % did not significantly increase the yield of ester product, even with prolonged reaction times. Notable yield increase was seen when the EtOH to hexene ratio was reversed. It was found that **4a** (1 mol %) and PMS (15 mol %) could achieve overall ester product yields of 88% within 24 h at 110

°C and 1000 psi CO with a 4-fold excess of 1-hexene to EtOH (Table 1, entry 5). These reactions could be prepared in air using reagents as received from the supplier without reduction in yield. The transformation of 1-hexene under these conditions resulted in two major products, ethyl 2-methylhexanoate (branched) and ethyl heptanoate (linear) in a 2:1 (b:l) ratio.

Although high yields of ester product were obtained, modification of the NHC structure as well as the pyridinium acids was explored for possible improvement of regioselectivity (Table 2). Increasing the steric bulk of the N-bound

Table 2. Effect of Acid and NHC Ligand Structure on Alkoxycarbonylation[a]

entry	[Pd]	acid	yield % (b:l)
1	**4a**	PMS	88 (2.0)
2	**4a**	2-PicMS	94 (1.6)
3	**4a**	4-PicMS	90 (1.8)
4	**4a**	LMS	90 (1.6)
5	**4a**	PTF	83 (1.8)
6	**4b**	PMS	87 (2.0)
7	**4b**	LMS	94 (1.6)
8	**4c**	PMS	84 (1.9)
9	**4a**	MSA	76 (1.8)
10	**4a**	PTSA	85 (1.7)
11	**4a**	Ph₃B	81 (1.7)
12	**4a**	nonanoic acid	91 (1.7)
13	**4a**	ZnCl₂	trace
14	**4a**	**3a**	95 (1.0)
15	Pd(OAc)₂	**3a**	21 (1.1)
16	Pd(OAc)₂	none	trace
17	**4a**	none	100 (1.6)

[a]Conditions: 14 mmol of EtOH, 56 mmol of 1-hexene, 1 mol % **4a**, 15 mol % acid, 5 mL of DMA, 1000 psi CO, 24 h.

substituents of the NHC ligand (**4b**) or increasing the electron donation of the NHC backbone (**4c**) indicated that ligand structure did not have a substantial influence on yield or selectivity. Both **4b** and **4c** maintained similar conversions and selectivity to those observed for **4a**. These results brought into question the nature of the active species and the lability of the NHC ligands during catalysis. Analogous concerns with the lability of the NHC ligand(s) arose for Rh-NHC-catalyzed hydroformylations and Pd-NHC-catalyzed aryl halide carbonylations.[19] In examining this issue with our system, it was found that alkoxycarbonylation did not occur in the absence of NHC ligands. For example, alkoxycarbonylation was ineffective with PMS and Pd reagents such as Pd₂(dba)₃ or Pd(OAc)₂, under similar conditions that gave high conversion with **4a**. However, Pd(OAc)₂ became active for carbonylation (32% yield of products) in the presence of **3a** (15 mol %), producing a nearly 1:1 ratio of branched to linear products. Catalyst **4a** also remained active when PMS was replaced with a similar loading of dimethylbenzimidazolium iodide (**3a**), resulting in a 95% yield of products and an improved linear selectivity (b:l = 1:1).

The presence of Pd was necessary, as salt **3a** alone was inactive for carbonylation in the absence of a palladium source.

Improvement of the linear selectivity by replacing the acid additive PMS with **3a** suggested that altering the acid source might be key to catalytic performance (Table 2). Initially, the influence of the pyridinium acid structure was explored. Neither the presence of a single methyl group on the pyridinium ring (2-picolinium, 2-PicMS; 4-picolinium, 4-PicMS) nor the inclusion of 2,6-methyl groups (lutidinium, LMS) resulted in a significant change in product selectivity. It was also noted that similar yield and selectivity were maintained if the mesylate anion was switched to triflate. Therefore, the range of acids was expanded to include Lewis acids (ZnCl$_2$, Ph$_3$B), nonanoic acid, and sulfonic acids (MSA; *p*-toluene sulfonic acid, PTSA), none of which provided an improvement to selectivity or yield. Surprisingly, reevaluation of the catalytic system revealed that quantitative alkoxycarbonylation could be obtained without any acid additive.

Since the optimized system was not dependent upon acid for catalysis, further evaluation of the importance of the cosolvent was undertaken. Addition of DMA was key to achieving high carbonylation yields. Yields of 8% or less occurred at 110 °C after 3 d in the absence of DMA. However, use of DMA also produced small amounts (<3%) of side products, *N,N*-dimethylheptanamide and *N,N*-dimethyl-2-methylhexanamide, which resulted from addition of DMA to hexene. To eliminate side product formation, other solvents were evaluated. Use of THF or CH$_3$CN as cosolvent resulted in a lower overall yield, but an improvement in linear selectivity and reduction in side products (Table 3).
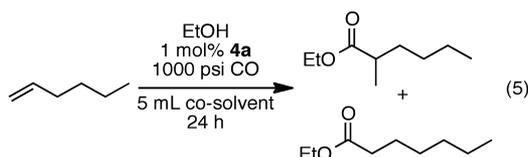
Pd-NHC-catalyzed alkoxycarbonylation of additional olefins generally resulted in quantitative conversion of terminal olefins to ester product (Table 4). It is also important to note that alkoxycarbonylation of internal olefins was dramatically

Table 3. Effect of Cosolvent on Alkoxycarbonylation with Catalyst 4a[a]

entry	acid	EtOH/1-hexene	solvent	yield % (b:l)
1	PMS	1:4	DMF	trace
2	PMS	1:4	CH$_3$CN	78 (1.4)
3	none	1:4	CH$_3$CN	59 (1.4)
4	PMS	1:4	THF	27 (1.0)
5	none	1:4	THF	30 (1.1)
6	PMS	1:4	–	3 (1.0)[b]
7	none	1:4	–	8 (1.1)[b]
8	PMS	1:4	DMA	89 (1.8)
9	none	1:4	DMA	100 (1.6)
10	PMS	4:1	DMA	6 (2.1)[c]
11	MSA	4:1	DMA	7 (1.8)[c]
12	none	4:1	DMA	10 (1.8)[c]

[a]Conditions: 14 mmol of EtOH, 56 mmol of 1-hexene, 1 mol % **4a**, 15 mol % acid, 5 mL of DMA, 1000 psi CO, 24 h. [b]Reaction ran in the absence of DMA for 72 h. [c]14 mmol of 1-hexene and 56 mmol of EtOH used.

Table 4. Alkoxycarbonylation of Various Olefins with Catalyst 4a[a]

entry	substrate	acid	yield % (b:l)
1	1-pentene	PMS	85 (1.8)
2	1-pentene		99 (1.6)
3	1-octene		100 (1.6)
4	cyclohexene	PMS	16
5	cyclohexene		83
6	ethyl 4-pentenoate		100 (2.1)
7	styrene	PMS	27 (2.2)[b]
8	ethyl acrylate	PMS	31[b]

[a]Conditions: 14 mmol of EtOH, 56 mmol of olefin, 1 mol % **4a**, 15 mol % PMS, 5 mL of DMA, 1000 psi CO, 24 h. [b]Large amount of polymer product was detected.

improved over systems that included an acid additive such as PMS. When using compounds containing a vinylic functionality (e.g., styrene and ethyl acrylate), a large amount of polymeric material was formed.

SUMMARY

We have shown that Pd benzimidazolylidene complexes are robust and high-yielding alkoxycarbonylation catalysts in the absence of acid additives. While many reports indicate analogies between phosphines and NHC ligands, it is evident from our preliminary work that Pd-NHC alkoxycarbonylation systems are quite disparate from those of Pd-phosphines. The nature of the active Pd intermediates remains unclear, but there is strong evidence that the NHC is vital to reactivity. Future studies will focus on identifying catalytic intermediates in hopes of better understanding the systematic and mechanistic differences between Pd-NHC and Pd-phosphine complexes as well as developing the scope and applicability of these catalysts in a variety of carbonylation reactions.

EXPERIMENTAL SECTION

General Considerations. All reagents and solvents were of reagent grade or higher and were used as received. 4,5-Dimethylbenzimidazole[27] and 1,3-diisopropylbenzimidazolium bromide[23] were synthesized following previously reported procedures. Benzimidazolium salts (**3a–c**) and the corresponding catalysts (**4a–c**) were synthesized without rigorous exclusion of air and water. The carbonylation reactions were prepared in open air prior to sealing and pressurizing the reactor. Routine NMR spectra were recorded on a Varian VXR-400 spectrometer. Gas chromatography was performed on an HP-6890 instrument fitted with a HP-5 capillary column (30 m length, 0.25 mm internal diameter, 0.25 μm film thickness).

Synthesis and Characterization of Benzimidazolium Salts 3a and 3c. As adapted from published reports,[23] a flask was charged with CH$_3$CN (10 mL), benzimidazole (8.5 mmol), and K$_2$CO$_3$ (1.18g, 8.5 mmol). MeI (4.0 equiv, 2.1 mL, 33.7 mmol) was added, and the reaction was heated at reflux for 18 h. After reaction completion, all volatiles were removed in vacuo. The residue was washed with CH$_2$Cl$_2$, and the filtrates were collected. CH$_2$Cl$_2$ was removed in vacuo, resulting in a sticky residue. Removal of the remaining benzimidazole and isolation of a solid product were achieved by sonicating the residue with EtOAc (3 × 5 mL), decanting after each sonication step. The solid was then filtered, and washed with EtOAc. The white powder was dried under vacuum for at least 24 h before use. Yield: 85−91%. NMR analysis for **3a** matched published values.[28] 1,3,4,5-Tetramethylbenzimidazolium iodide (**3c**): ^{1}H NMR (400 MHz, CDCl$_3$) δ 10.92 (s, 1H, NC*H*N), 7.43 (s, 2H, Aryl-H), 4.20 (s, 6H, NCH$_3$), 4.29 (s, 6H, aryl-CH$_3$).

Synthesis and Characterization of Benzimidazolium Salt 3b. After dissolving 1,3-diisopropylbenzimidazolium bromide (1.0 g, 3.5

mmol) in acetone (5 mL), NaI (0.6 g, 4.0 mmol) was added. A white precipitate immediately formed, and the solution was filtered through Celite, washing with small portions of acetone. The filtrate was collected and dried in vacuo. The resulting residue was washed with dichloromethane, filtering again through Celite, and the filtrate was dried in vacuo. Removal of the remaining benzimidazole and isolation of a solid product were achieved by sonicating the residue with EtOAc (3 × 5 mL), decanting after each sonication step. The solid was then filtered, and washed with EtOAc. The white powder was dried under vacuum for at least 24 h before use. Yield: 89%. NMR analysis for **3b** matched published values.[25]

Adapted General Synthesis of Catalysts 4a and 4c (ref 24). In a 20 mL flask, both Pd(OAc)$_2$ (0.5 g, 2.2 mmol) and the appropriate benzimidazolium salt (2.1 equiv, 4.7 mmol) were dissolved in a minimal amount of DMSO (5 mL). The reaction was stirred with gentle heating (30−60 °C) for 6 h. During this time the dark red-brown solution lightened to orange. The DMSO solution was filtered and washed with small amounts of DMSO, to separate any Pd black from the solution. To the DMSO filtrate was added 50 mL of H$_2$O to precipitate the product. The solid was collected via filtration, washed with water (3 × 50 mL), and dried under suction for 5 m. The resulting orange solid was subsequently washed with several small portions of ether and hexanes, until the filtrates were clear. The solid was dried in vacuo for at least 24 h before use. Products **4a** and **4c** were mixtures of *cis-* and *trans-*isomers, with the *trans-*isomer prevalent. The isomer mixtures were used as the carbonylation catalysts.

cis- and *trans-***4c**: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.15 (s, 2H, Ar-H), 7.09 (s, 2H, Ar-H), 4.19 (s, 6H, NCH$_3$), 4.17 (2, 6H, NCH$_3$), 2.40 (s, 6H, Ar-CH$_3$), 2.35 (s, 6H, Ar-CH$_3$).

Adapted Synthesis of Catalyst 4b (ref 25). In a 20 mL flask, both Pd(OAc)$_2$ (0.5 g, 2.2 mmol) and **3b** (1.3 g, 4.6 mmol) were dissolved in a minimal amount of DMSO (5 mL). The reaction was stirred at 80 °C for 12 h, then at 100 °C until the reaction lightened to yellow-orange. To the DMSO filtrate was added 50 mL of H$_2$O to precipitate the product. The solid was collected via filtration, washed with water (3 × 50 mL), and dried under suction for 5 min. The resulting orange solid was subsequently washed with several small portions of ether and hexanes, until the filtrates were clear. The solid was then washed with CH$_2$Cl$_2$, collecting the filtrate. All volatiles were removed in vacuo, and the solid was dried in vacuo for at least 24 h before use. A minor amount of *cis-***4b** was present (<5%), and excess **3b** prevented Pd-dimer formation.

General High-Pressure Reactions. To a high-pressure bomb, catalyst (0.14 mmol), acid (2.13 mmol), cosolvent (5.0 mL), olefin (55.8 mmol), and EtOH (0.83 mL, 14.2 mmol) were added in that order. The reactor was sealed and pressurized with CO to 1000 psi. The reaction was heated with stirring at the indicated temperature and pressure for the noted duration. After reaction completion, the reactor was cooled to 25 °C and depressurized. To the reaction solution were added 30 mL of hexane and 100 μL of decane, which was subsequently washed with saturated NaHCO$_3$ (3 × 5 mL) and saturated NaCl (3 × 5 mL). The resulting organic layer was evaluated via GC to determine product yields.

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Notes
The authors declare no competing financial interest.
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REFERENCES

(1) *Modern Carbonylation Methods*; Kollár, L., Ed.; Wiley: Weinheim, 2008.
(2) Belov, G. P.; Novikova, E. V. *Russ. Chem. Rev.* **2004**, *73*, 267−291.
(3) Drent, E.; Budzelaar, P. H. M. *Chem. Rev.* **1996**, *96*, 663−681.
(4) Cavinato, G.; Toniolo, L.; Vavasori, A. In *Catalytic Carbonylation Reactions*; Beller, M., Ed.; Springer, 2006; pp 125−164.
(5) Bianchini, C.; Meli, A. *Coord. Chem. Rev.* **2002**, *225*, 35−66.
(6) Mul, W. P.; Oosterbeek, H.; Beitel, G. A.; Kramer, G. J.; Drent, E. *Angew. Chem., Int. Ed.* **2000**, *39*, 1848−1851.
(7) Robertson, R. A. M.; Cole-Hamilton, D. J. *Coord. Chem. Rev.* **2002**, *225*, 67−90.
(8) Bianchini, C.; Meli, A.; Oberhauser, W. *Dalton Trans.* **2003**, 2627−2635.
(9) Zuidema, E.; Bo, C.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2007**, *129*, 3989−4000.
(10) Van Leeuwen, P. W. N. M.; Zuideveld, M. A.; Swennenhuis, B. H. G.; Freixa, Z.; Kamer, P. C. J.; Goubitz, K.; Fraanje, J.; Lutz, M.; Spek, A. L. *J. Am. Chem. Soc.* **2003**, *125*, 5523−5539.
(11) Drent, E.; Van Broekhoven, J. A. M.; Doyle, M. J. *J. Organomet. Chem.* **1991**, *417*, 235−251.
(12) Pugh, R. I.; Drent, E.; Pringle, P. G. *Chem. Commun.* **2001**, 1476−1477.
(13) Gee, V.; Orpen, A. G.; Phetmung, H.; Pringle, P. G.; Pugh, R. I. *Chem. Commun.* **1999**, 901−902.
(14) Clegg, W.; Eastham, G. R.; Elsegood, M. R. J.; Tooze, R. P.; Wang, X. L.; Whiston, K. *Chem. Commun.* **1999**, 1877−1878.
(15) Eastham, G. R.; Heaton, B. T.; Iggo, J. A.; Tooze, R. P.; Whyman, R.; Zacchini, S. *Chem. Commun.* **2000**, 609−610.
(16) Jimenez-Rodriguez, C.; Foster, D. F.; Eastham, G. R.; Cole-Hamilton, D. J. *Chem. Commun.* **2004**, 1720−1721.
(17) Yamamoto, Y.; Koizumi, T.; Katagiri, K.; Furuya, Y.; Danjo, H.; Imamoto, T.; Yamaguchi, K. *Org. Lett.* **2006**, *8*, 6103−6106.
(18) Veige, A. S. *Polyhedron* **2008**, *27*, 3177−3189.
(19) Jeletic, M.; Veige, A. In *N-Heterocyclic Carbenes in Transition Metal Catalysis and Organocatalysis*; Cazin, C. S. J., Ed.; Springer: Dordrecht, 2010; pp 217−235.
(20) McGuinness, D. *Dalton Trans.* **2009**, *35*, 6915−6923.
(21) Subramanium, S. S.; Slaughter, L. M. *Dalton Trans.* **2009**, *35*, 6930.
(22) Xue, L.; Shi, L.; Han, Y.; Xia, C.; Huynh, H. V.; Li, F. *Dalton Trans.* **2011**, *40*, 7632−7638.
(23) Huynh, H. V.; Han, Y.; Ho, J. H. H.; Tan, G. K. *Organometallics* **2006**, *25*, 3267−3274.
(24) Huynh, H. V.; Ho, J. H. H.; Neo, T. C.; Koh, L. L. *J. Organomet. Chem.* **2005**, *690*, 3854−3860.
(25) Han, Y.; Huynh, H. V.; Koh, L. L. *J. Organomet. Chem.* **2007**, *692*, 3606−3613.
(26) Clegg, W.; Eastham, G. R.; Elsegood, M. R. J.; Heaton, B. T.; Iggo, J. A.; Tooze, R. P.; Whyman, R.; Zacchini, S. *J. Chem. Soc., Dalton Trans.* **2002**, 3300−3308.
(27) Wagner, E. C.; Millet, W. H. *Org. Synth.* **1943**, *2*, 65.
(28) Katritzky, A. R.; Jishkariani, D.; Sakhuja, R.; Hall, C. D.; Steel, P. J. *J. Org. Chem.* **2011**, *76*, 4082−4087.