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Pd-Catalyzed Regioselective Alkoxycarbonylation of 1-Alkenes Using a Lewis Acid [$SnCl_2$ or $Ti(O^iPr)_4$] and a Phosphine

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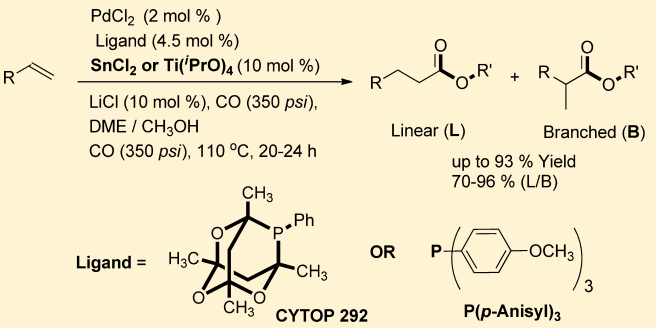
Supporting Information

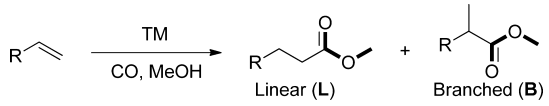
ABSTRACT: The phosphine ligand mediated palladium catalyzed alkoxycarbonylation of alkenes was investigated with the objective of attaining good linear selectivity for the ester. The effect of various parameters such as solvents, additives, palladium precursors, CO pressures, and alkenes of various structural complexities were examined. The results revealed the importance of using a Lewis acid such as $SnCl_2$ or $Ti(O^iPr)_4$ in combination with a monodentate ligand such CYTOP 292 or P(*p*-anisyl)$_3$ to enhance the regioselectivity for the linear isomers in the range of 70−96%.



INTRODUCTION

Transition metal mediated functionalization of olefins in the presence of reagents such as carbon monoxide and methanol constitutes an industrial core technology for the synthesis of linear and branched esters known as alkoxycarbonylation (Scheme 1).[1] The products, particularly alkyl esters, are useful

Scheme 1



reagents for different industrial applications which include the production of solvents, perfumes, flavorings, detergents, and surfactants.[2]

From a sustainability perspective, methoxycarbonylation (alkoxycarbonylation) represents an attractive and practical method for the functionalization of olefins because of the low cost, atom economy, and readily available starting materials.

Although other transition metal complexes, especially those of ruthenium,[3] have recently been employed as catalysts for the reaction, numerous examples in the literature show that palladium catalysts are generally preferred because they offer milder reaction conditions and allow for the use of a broader substrate scope. Even with the use of palladium catalysts, the reaction generally suffers from a few disadvantages which include the following: the need for high temperatures to achieve full conversion; challenges to avoid poor regioselectivity particularly for aliphatic systems; and the need to use traditional Brønsted acids to promote the reaction at the expense of corroding the reaction vessel. Although the need for Brønsted acid promoters is largely supported by evidence that the catalytic mechanism involves stabilization of palladium through the formation of a "Pd−H" species,[4] Lewis acids including salicylborates are increasingly being used to address Brønsted acid related problems and have been shown to be effective for a variety of methoxycarbonylation protocols.[5] However, besides the known promotion effect of Lewis acids for the hydroesterification reaction, research in this area remains fairly limited. On the other hand, the problems associated with low regioselectivity in alkoxycarbonylation have benefited by contributions from researchers who have attempted to address the issue through ligand design. For example, in the palladium-phosphine catalyzed alkoxycarbonylation of styrene, the use of bidentate diphosphine ligands is known to furnish predominantly linear esters although some exceptions[6] have also been found. Monodentate phosphine ligands on the other hand are widely known to give branched esters[7] although Alper and coworkers showed that exceptional selectivity for linear esters of styrene can result using a monodentate phosphine.[5b]

While there are a substantial number of methods to obtain the linear and branched esters from styrene with reasonable selectivity, there are relatively few catalytic methods using aliphatic alkenes (especially higher olefins C_8 and above) to produce long-chain esters with appreciable selectivity.[8] Recently we became interested in exploring the catalytic properties of the cage phosphaadamantane ligand CYTOP 292 (Figure 1) for the transition metal mediated catalysis of carbonylation reactions.[9]

In this paper, our aim is to develop a palladium catalyst system that uses CYTOP 292 (**L1**) and compare it with P(*p*-anisyl)$_3$ (**L2**) in the presence of a Lewis acid, to achieve the

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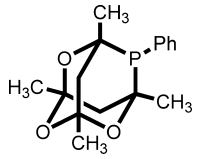


Figure 1. Structure of the cage phosphaadamantane ligand CYTOP 292 (**L1**).

alkoxycarbonylation of olefins, with good regioselectivity for the linear isomers.

RESULTS AND DISCUSSION

As shown in Table 1, initial investigations began with the treatment of 1-decene (**2a**) under typical methoxycarbonylation conditions, which usually consists of palladium acetate, a tertiary phosphine, and a weak acid such as *para*-toluenesulfonic acid (PTSA) containing a noncoordinating anion. Using **L1** as the ligand in the presence of $Pd(OAc)_2$, it was observed that a relatively high amount of PTSA·H_2O (20 mol %) was required for the reaction to reach satisfactory conversion (Table 1, entries 1−3). Although these initial results revealed that CYTOP 292 was an active ligand, the linear selectivity obtained in all cases was relatively average with a maximum of 75:25 (L/B). In 2004, Nozaki and Hiyama reported that an acetone−methanol solution containing $PdCl_2$, BINAP ligand, and no protic acid under CO pressure could efficiently catalyze the hydroesterification of styrene with 100% selectivity for the branched ester.[10] When $PdCl_2$ and acetone cosolvent were used under our conditions, quantitative conversion was obtained, but the regioselectivity of 60:40 (L/B) was low (Table 1, entry 4). This acid-free condition was however encouraging because it indicated that the reaction could proceed under Brønsted acid free conditions when **L1** is used as a ligand. This result also prompted us to consider another ketone-based solvent, 2-butanone, which has been shown elsewhere[11] to be an effective cosolvent. Unfortunately, in this case, the results in 2-butanone also gave full conversion, with mediocre linear selectivity as well (Table 1, entry 5). Doping the reaction mixture with varying amounts of LiCl as the additive in cosolvents such as 2-butanone, acetonitrile, and acetone did not improve the selectivity of the reaction irrespective of the solvent employed (Table 1, entries 6−8). However, when 1,2-dimethoxyethane (DME) was used as the cosolvent, the reaction proceeded in higher selectivity 81:19 (L/B).

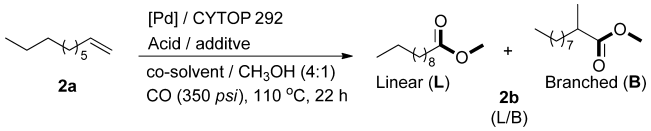
In order to further improve the linear regioselectivity obtained in DME, stannous chloride ($SnCl_2$), a Lewis acid previously shown by Ojima and co-workers[12] to be effective for controlling linear selectivity in palladium catalyzed hydroesterification reactions, was added to the reaction mixture in varying amounts. As shown in Table 2, entries 1 and 2, the linear selectivity steadily increased to 85:15 (L/B) when 5 mol % of $SnCl_2$ was used; the linear selectivity further improved to 90:10 (L/B), when the amount of $SnCl_2$ was increased to 10 mol %. When the solvent was changed to acetone, the linear selectivity was 85% with 10 mol % $SnCl_2$, whereas increasing the amount of $SnCl_2$ to 20 mol % in the same solvent reduced the selectivity to 80:20 (L/B) (Table 2, entries 3 and 4). A similar linear selectivity of 80:20 (L:B) was obtained in

Table 2. Optimization Study with $SnCl_2$[a]

entry	[M] precursor	Lewis Acid/ mol %	cosolvent	Conv. [%][b]/ L:B [%][c]
1	$PdCl_2$	$SnCl_2$/5	DME	100 (85:15)
2	**$PdCl_2$**	**$SnCl_2$/10**	**DME**	**100 (90:10)**
3	$PdCl_2$	$SnCl_2$/10	acetone	100 (85:15)
4	$PdCl_2$	$SnCl_2$/20	acetone	100 (80:20)
6	$PdCl_2$	$SnCl_2$/10	CH_3CN	100 (80:20)
7	$Pd_2(dba)_3$	$SnCl_2$/10	DME	100 (79:21)
8	$Co_2(CO)_8$	$SnCl_2$/10	DME	0
9	$Pd(PhCN)_2Cl_2$	$SnCl_2$/10	DME	75 (77:23)

[a]Reaction conditions: 1-decene (**2a**) (1.0 mmol), metal precursor (2.0 mol %), CYTOP 292 (4.5 mol %), LiCl (10.0 mol %), $SnCl_2$ (10.0 mol %), CO (350 psi), solvent (5.0 mL), 110 °C, 22 h. [b]Percent conversion was determined by ^{1}H NMR spectroscopy based on the amount of alkene consumed. [c]Linear/branched was ratio determined by ^{1}H NMR.

Table 1. Screening Reaction Conditions[a]



entry	[Pd]/(2.0 mol %)	CYTOP 292 [x mol %]	acid/[x mol %]	additive/[x mol %]	cosolvent	Conv. [%][b]/L:B [%][c]
1	$Pd(OAc)_2$	4.5	PTSA·H_2O/10	–	–	77 (75:25)
2	$Pd(OAc)_2$	10	PTSA·H_2O/20	–	–	100 (68:32)
3	$PdCl_2$	10	PTSA·H_2O/20	–	–	96 (70:30)
4	$PdCl_2$	4.5	–	–	acetone	100 (60:40)
5	$PdCl_2$	4.5	–	–	2-butanone	100 (63:37)
6	$PdCl_2$	4.5	–	LiCl/10	2-butanone	100 (70:30)
7	$PdCl_2$	4.5	–	LiCl/50	2-butanone	100 (72:28)
8	$PdCl_2$	4.5	–	LiCl/100	2-butanone	100 (69:31)
9	$PdCl_2$	4.5	–	LiCl/10	CH_3CN	100 (67:33)
10	$PdCl_2$	4.5	–	LiCl/10	acetone	100 (74:26)
11	$PdCl_2$	4.5	–	LiCl/10	DME	100 (81:19)

[a]Reaction conditions: 1-decene (**2a**) (1.0 mmol), $PdCl_2$ or $Pd(OAc)_2$ (2.0 mol %), CYTOP 292 (4.5 mol %), acid (10.0 mol %), LiCl (10−100 mol %), CO (350 psi), solvent (5.0 mL), 110 °C, 22 h. [b]Percent conversion was determined by ^{1}H NMR spectroscopy based on the amount of alkene consumed. [c]Linear/branched ratio was determined by ^{1}H NMR.

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acetonitrile (CH_3CN) in the presence of 10 mol % of $SnCl_2$ (Table 2, entry 6).

Using the best solvent (DME) and an optimal amount of $SnCl_2$ (10 mol %), other metal precursors such as $Pd_2(dba)_3$, $Co_2(CO)_8$, and $Pd(PhCN)_2Cl_2$ were evaluated (Table 2, entries 7−9). While full conversion was achieved with $Pd_2(dba)_3$ with a selectivity of 79:21 (L/B), $Pd(PhCN)_2Cl_2$ on the other hand was less efficient, resulting in 75% conversion and a lower selectivity for L/B (75:25) esters. Cobalt carbonyl was ineffective under these reaction conditions (Table 2, entry 9).

With the most optimal reaction conditions in hand (Table 2, entry 2), we compared the catalytic activity of some common ligands to that of CYTOP 292 by screening the reaction conditions using the phosphines listed in Table 3.

Table 3. Screening Reaction Conditions with Other Phosphine Ligands[a]

entry	ligand	Conv. [%][b]	L:B [%][c]
1	PPh_3	–	–
2	dppb	–	–
3	dppm	–	–
4	$PCy_3{\cdot}HBF_4$	100	80:20
5	P(*p*-MeO-Ph)$_3$ (**L2**)	100	93:7
6	P(*m*-MeO-Ph)$_3$	99	88:12
7	P(*p*-Me-Ph)$_3$	99	84:16
8	P(*m*-Me-Ph)$_3$	100	87:13
9	P(*o*-Me-Ph)$_3$	100	74:26

[a]Reaction conditions: 1-decene (**2a**) (1.0 mmol), $PdCl_2$ (2.0 mol %), Ligand (4.5 mol %), LiCl (10.0 mol %), $SnCl_2$ (10.0 mol %), CO (350 psi), DME/MeOH (4:1, 5.0 mL), 110 °C, 22 h. [b]Percent conversion was determined by ^{1}H NMR spectroscopy based on the amount of alkene consumed. [c]Linear/branched ratio determined by ^{1}H NMR.

The results showed that triphenylphosphine (PPh_3), 1,4-bis(diphenylphosphino)butane (dppb), and 1,4-(diphenylphosphino)methane (dppm) were less effective under these reaction conditions whereas tricyclohexylphosphine tetrafluoroborate ($PCy_3{\cdot}HBF_4$) provided full conversion but with poor mass recovery and the regioselectivity was 80:20 (L/B) (Table 3, entries 1−4). The most efficient ligand with comparable catalytic properties to CYTOP 292 was tris(4-methoxyphenyl)-phosphine [P(*p*-anisyl)$_3$] (**L2**) which gave 100% conversion and an excellent regioselectivity of 93:7 (L/B); it is noteworthy that changing the position of MeO- or introducing a Me- group in different positions resulted in a decrease in the selectivity. (Table 3, entries 6−9). At this stage, it was gratifying to find that a simple phosphine such as [P(*p*-anisyl)$_3$] could also catalyze this transformation in good yield and *n*-selectivity. However, based on our wish to explore the catalytic effectiveness of the phosphaadamantane ligand CYTOP 292 (**L1**) for alkoxycarbonylation, we used **L1** and the optimum conditions described in Table 2, entry 2.

As shown in Table 4, entries 1−5, a variety of olefins ranging from C_8 to C_{14} were tested using **L1** and **L2** ligands, affording aliphatic esters in good yields, and in good to excellent regioselectivity respectivity, for the linear product. Functional groups such as esters can be tolerated in this reaction. Similar results were obtained using allyl substrates (Table 4, entries 6−8) which were equally effective under these reaction conditions except that some double bond isomerization was detected with allylbenzene substrates (entries 7 and 8). The reaction also proceeded well with an olefin bearing a ketone functionality (Table 4, entry 9). However, in this case, not only was there a reduction in selectivity to 70:30 (L/B), isomerization of the double bond and a lower yield were also observed. When these reactions were conducted using the **L2** ligand, the selectivity and yields were better in all cases. The observed difference in reactivity of the substrates may be due to the starting alkene possibly having a chelating effect if it coordinates in a bidentate manner to the $PdCl_2$ precursor, thus altering the approach of the ligand or hindering the coordination potential of the ligand to the metal center.

Although the substrate tolerance for the alkenes used was good (Table 4), a major shortcoming is the use of a toxic cocatalyst (Lewis acid) such as $SnCl_2$. Therefore, developing an alternative protocol which does not employ a toxic additive, but however still furnishes acceptable yields and selectivity, could be beneficial.

To achieve this goal, we employed the reaction conditions used for the substrate scope in Table 4 and replaced $SnCl_2$ with various Lewis acids. As shown in Table 5, good conversion was achieved in all cases except with Al(O*t*-Bu)$_3$ [only 18% product yield]. However, in most cases, the reaction selectivity decreased (Table 5, entries 1−5). Boron, copper, and indium Lewis acids were efficient in promoting the reaction to full conversion even when the palladium precursor was changed from $PdCl_2$ to $Pd(OAc)_2$; but the regioselectivity in these cases remained quite low (Table 5, entries 6, 8−14).

Gratifyingly, use of Ti(O^{i}Pr)$_4$ furnished both excellent conversion and 88% linear selectivity (entry 7). It is noteworthy that a lower catalyst loading gave only 15% conversion and it is possible to recover the starting material (entry 15). Similarly, use of Pd/C as the catalyst gave no reaction (entry 16). These results encouraged us to explore other reaction conditions (e.g., solvent effects) with Ti(O^{i}Pr)$_4$ as the Lewis acid additive, as shown in Table 6.

The results in Table 6 show that good conversions were achieved in all solvent combinations. Results using CH_2Cl_2/MeOH (4:1 or 1:4) as the solvent were promising in terms of linear selectivity (i.e., > 80%), but were not superior to the result obtained using DME/MeOH. Consequently, we decided to run the reactions in DME/MeOH, in order to test the reactivity of other phosphine ligands.

No product was obtained when other PPh_3, dppb, or $PCy_3{\cdot}HBF_4$ were used as phosphines for the methoxycarbonylation reaction in the presence of Ti(O^{i}Pr)$_4$ as a Lewis acid, whereas P(*p*-anisyl)$_3$ gave 98% conversion but the regioselectivity was 76:24 (L:B). These findings demonstrated that the Ti(O^{i}Pr)$_4$ conditions are likely more compatible with the cage phospha-adamantane ligand.

To evaluate the optimal reaction conditions developed with Ti(O^{i}Pr)$_4$ in the presence of CYTOP 292 (**L1**), a substrate study was conducted as shown in Scheme 2. The results in Table 2 indicate that a long chain alkyl olefin favored reaction, giving the corresponding esters in quite good yields. An olefin bearing an ester functional group afforded the highest yield and selectivity, while allylbenzene and allylcyclohexene gave moderate yields with a good selectivity of up to 86:14 (L/B), in contrast, the selectivity changed using an aryl olefin, styrene, as the substrate, 27:73 (L/B) (Scheme 2). The results obtained from this Ti(O^{i}Pr)$_4$-mediated protocol closely resemble those obtained with the $SnCl_2$-mediated protocol, hence providing a relatively nontoxic pathway for the functionalization of olefins.

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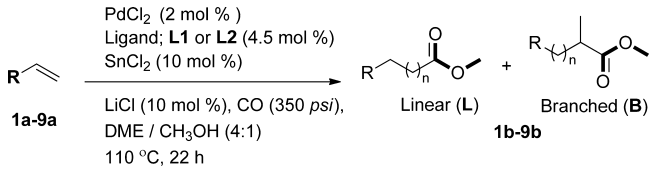
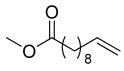
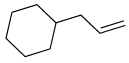
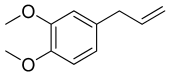
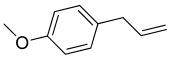
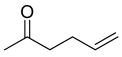
Table 4. Substrate Scope with Optimized Reaction Conditions[a]



Entry	1-alkene	Ligand	Product	Yield [%][b] / (L/B ratio)[c]
1	1-dodecene	L1	1b	83 (85:15)
		L2		93 (93:7)
2	1-decene	L1	2b	70 (90:10)
		L2		91 (93:7)
3	1-octene	L1	3b	75 (86:14)
		L2		91 (96:4)
4	1-tetradecene	L1	4b	85 (90:10)
		L2		89 (96:4)
5		L1	5b	86 (91:9)
		L2		90 (94:6)
6		L1	6b	70 (80:20)
		L2		86 (91:9)
7		L1	7b	72 (85:15)[d]
		L2		85 (95:5)
8		L1	8b	70 (85:15)[d]
		L2		83 (93:7)[d]
9		L1	9b	60 (70:30)
		L2		81 (93:7)

[a]Reaction conditions: 1-alkene (1.0 mmol), $PdCl_2$ (2.0 mol %), ligand (4.5 mol %), **L1** = CYTOP 292, **L2** = P(*p*-anisyl)$_3$, LiCl (10.0 mol %), $SnCl_2$ (10.0 mol %), CO (350 psi), DME/MeOH (4:1, 5.0 mL), 110 °C, 22 h. [b]Yield after flash column chromatography on silica gel. [c]Linear/branched ratio was determined by ^{1}H NMR. [d]Some isomerization of the double bond was observed.

To find out if the Ti(O^iPr)$_4$-mediated protocol is amendable to other alcohols, we evaluated the reaction in the presence of ethanol, propanol, isopropanol, *tert*-butanol, and phenol (Scheme 3). As expected, reasonably good yields and selectivity (>81%) resulted using ethanol, propanol, and isopropanol as the alcohol. The reaction was unsuccessful with *tert*-butanol perhaps due to an unproductive pathway which involves the possible formation of a 3° carbocation resulting from the coordination of Ti(O^iPr)$_4$ to the oxygen atom of *tert*-butanol making it a good leaving group. It was equally interesting to observe that phenyl esters can be obtained with this protocol using a weakly nucleophilic alcohol such as phenol.

In conclusion, we have developed a new general protocol for the alkoxycarbonylation of 1-alkenes using a palladium based catalyst system mediated by either the cage phospha-adamantane CYTOP 292 or P(*p*-anisyl)$_3$ with the aid of Lewis acids such as $SnCl_2$ or Ti(O^iPr)$_4$. The protocol does not require a Brønsted acid and tolerates a variety of substrates, affording esters in quite good to excellent yields and selectivity. We believe this Lewis acid promoted protocol is a useful addition to the methodology of Brønsted acid free hydroesterification/alkoxycarbonylation processes.

EXPERIMENTAL SECTION

General Procedure for the Methoxycarbonylation Reaction. Into a glass liner were added $PdCl_2$ (3.5 mg, 0.02 mmol, 2.0 mol %), Ligand (16.1 mg, 0.045 mmol, 4.5 mol %), $SnCl_2$ (19.3 mg, 0.1 mmol, 10 mol %) or Ti(O^iPr)$_4$ (30 μL, 0.1 mmol, 10 mol %), and LiCl (4.28 mg, 0.1 mmol, 10 mol %). The autoclave (45 mL) was flushed with argon, followed by the addition of the solvent combination (DME/MeOH, ratio: 4:1, 5 mL) and the olefin (1.0 mmol). The glass liner was placed into a stainless steel autoclave, flushed three times with carbon monoxide, and pressurized to 350 psi. The autoclave was then placed in an oil bath preset to 110 °C and stirred with a magnetic bar for at least 22 h. After this time, the autoclave was removed from the oil bath and cooled to room temperature prior to the release of excess carbon monoxide. The products were isolated from the reaction mixture by solvent evaporation and further purified by column chromatography on silica gel, using hexane/ethyl acetate as the eluent.

Methyl Tridecanoate (1b).[13] Light yellow oil, 205.3 mg, 93% yield, L/B = 93:07. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 3.62 (s, 3H), 2.26 (t, *J* = 7.2 Hz, 2H), 1.65−1.54 (m, 2H), 1.25−1.22 (m, 18H), 0.84 (t, *J* = 6.8 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 174.2, 51.3, 34.0, 31.9, 29.63, 29.62, 29.4, 29.3, 29.2, 29.1, 24.9, 22.7, 22.5, 14.0.

Methyl Undecanoate (2b).[5b] Light yellow oil, 178.1 mg, 91% yield, L/B = 93:07. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 3.63 (s, 3H), 2.27 (t, *J* = 7.6 Hz, 2H), 1.64−1.50 (m, 2H), 1.25−1.23 (m, 14H), 0.84 (t, *J* = 6.8 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 174.3, 51.3, 34.1, 31.8, 29.5, 29.4, 29.29, 29.25, 29.1, 24.9, 22.6, 14.0.

Methyl Nonanoate (3b).[14] Light yellow oil, 154.9 mg, 91% yield, L/B = 96:04. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 3.62 (s, 3H), 2.26 (t, *J* = 7.6 Hz, 2H), 1.54−1.50 (m, 2H), 1.25−1.23 (m, 10H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 174.3, 51.3, 34.0, 31.7, 29.2, 29.14, 29.10, 24.9, 22.6, 14.0.

Methyl Pentadecanoate (4b).[5b] Colorless oil, 217.8 mg, 89% yield, L/B = 96:04. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 3.61 (s, 3H), 2.25 (t, *J* = 7.6 Hz, 2H), 1.59−1.55 (m, 2H), 1.23−1.21 (m, 22H), 0.83 (t, *J* = 6.8 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ

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Table 5. Screening Various Lewis Acid Additives[a]

Entry	Lewis Acid	Conversion[%][b]	L:B [%][c]
1	$B(O^tBu)_3$	100	75:25
2	$Al(O^tBu)_3$	18	87:13
3	$CeCl_3.H_2O$	96	79:21
4	$CeCl_3$	100	77:23
5	$Ce(SO_4)_2$	100	65:35
6		98	72:28
7	**$Ti(O^iPr)_4$**	**100**	**88:12**
8	$B(OH)_2$	100	65:35
9	$CuCl_2$	95	73:27
10	$InBr_3$	100	64:36
11[d]	$B(OH)_2$	100	66:34
12[d]	$CuCl_2$	100	60:40
13[d]	$InBr_3$	100	69:31
14	$InCl_3$	100	76:24
15[e]	$Ti(O^iPr)_4$	15	-
16[f]	$Ti(O^iPr)_4$	0	-

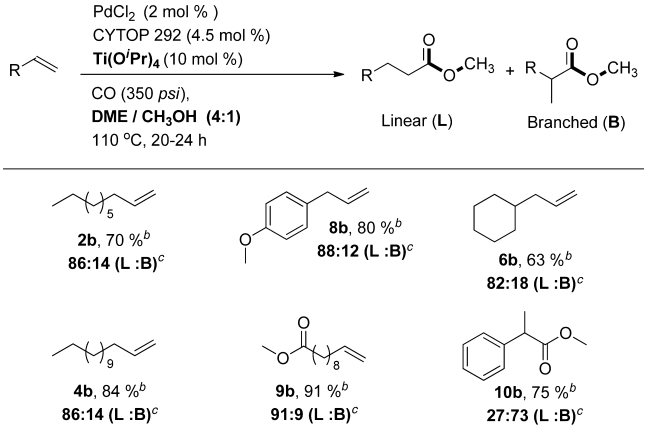
[a]Reaction conditions: 1-decene (**2a**) (1.0 mmol), $PdCl_2$ (2.0 mol %), CYTOP 292 (4.5 mol %), LiCl (10.0 mol %), $SnCl_2$ (10.0 mol %), CO (350 psi), DME/MeOH (4:1, 5.0 mL), 110 °C, 22 h. [b]Percent conversion was determined by ^{1}HNMR spectroscopy based on the amount of alkene consumed. [c]Linear/branched ratio was determined by ^{1}HNMR. [d]$Pd(OAc)_2$ was used instead of $PdCl_2$. [e]$PdCl_2$ (0.5 mol %). [f]Pd/C.

Table 6. Optimizing Reaction Conditions with $Ti(O^iPr)_4$ in the Presence Other Solvents[a]

entry	solvent	Conv. [%][b]	L:B [%][c]
1	THF/MeOH (4:1)	100	76:24
2	EtOAc/MeOH (4:1)	100	75:25
3	toluene/MeOH (4:1)	100	78:22
4	CH_2Cl_2/MeOH (4:1)	100	86:14
5	CH_2Cl_2/MeOH (1:4)	93	80:20

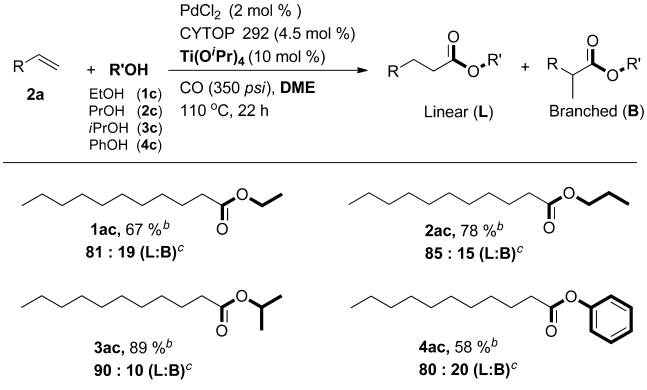
[a]Reaction conditions: 1-decene (**2a**) (1.0 mmol), $PdCl_2$ (2.0 mol %), CYTOP 292 (4.5 mol %), LiCl (10.0 mol %), $Ti(O^iPr)_4$ (10.0 mol %), CO (350 psi), Solvent (5.0 mL), 110 °C, 22 h. [b]Percent conversion determined by ^{1}HNMR spectroscopy based on the amount of alkene consumed. [c]Linear/branched ratio determined by ^{1}HNMR.

Scheme 2[a]



[a]Reaction conditions: 1-alkene (1.0 mmol), $PdCl_2$ (2.0 mol %), CYTOP 292 (4.5 mol %), LiCl (10.0 mol %), $Ti(O^iPr)_4$ (10.0 mol %), CO (350 psi), DME/MeOH (4:1, 5.0 mL), 110 °C, 22 h. [b]Yield after flash column chromatography on silica gel. [c]Linear/branched was ratio determined by ^{1}H NMR.

Scheme 3[a]



[a]Reaction conditions: 1-alkene (1.0 mmol), $PdCl_2$ (2.0 mol %), CYTOP 292 (4.5 mol %), LiCl (10.0 mol %), $Ti(O^iPr)_4$ (10.0 mol %), CO (350 psi), DME/ROH (**1**−**4c**) (4:1, 5.0 mL), 110 °C, 22 h. [b]Yield after flash column chromatography on silica gel. [c]Linear/branched ratio determined by ^{1}HNMR.

ppm): 174.1, 51.3, 34.0, 31.9, 29.67, 29.65, 29.63, 29.5, 29.47, 29.44, 29.3, 29.2, 29.1, 24.9, 22.6, 14.0.

Dimethyl Decane-1,10-dioate (5b).[15] Colorless solid, 208.2 mg, 91% yield, L/B = 96:4. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 3.61 (s, 6H), 2.25 (t, J = 7.5 Hz, 4H), 1.58−1.53 (m, 4H), 1.23 (br, 8H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 174.2, 51.4, 34.0, 29.3, 29.1, 29.0, 24.9.

Methyl 4-Cyclohexylbutanoate (6b).[16] Yellow oil, 156.5 mg, 86% yield, L/B = 91:09. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 3.62 (s, 3H), 2.24 (t, J = 7.6 Hz, 2H), 1.76−1.48 (m, 7H), 1.17−1.13 (m, 6H), 0.93−0.69 (m, 2H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 174.2, 51.5, 37.3, 36.9, 34.3, 33.2, 26.6, 26.3, 22.3.

Methyl 4-(3,4-Dimethoxyphenyl)butanoate (7b).[17] Yellow oil, 195.2 mg, 85% yield, L/B = 95:05. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 6.75 (d, J = 8.7 HZ, 1H), 6.67 (d, J = 6.3 Hz, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 3.63 (s, 3H), 2.56 (t, J = 7.6 Hz, 2H), 2.29 (t, J = 7.5 Hz, 2H), 1.94−1.86 (m, 2H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 173.9, 148.8, 147.3, 134.0, 120.3, 111.7, 111.2, 55.9, 55.8, 51.4, 34.7, 33.3, 26.2.

Methyl 4-(4-Methoxyphenyl)butanoate (8b).[5b] Light yellow oil, 166.4 mg, 83% yield, L/B = 93:07. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 7.07 (d, J = 8.7 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H), 3.64 (s, 3H), 2.62−2.52 (m, 2H), 2.30 (t, J = 7.5 Hz, 2H), 1.97−1.85 (m, 2H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 174.0, 157.9, 133.4, 129.9, 129.3, 113.8, 113.7, 52.2, 51.4, 34.2, 33.3, 26.7.

Methyl 6-Oxoheptanoato (9b).[18] Yellow oil, 124.8 mg, 81% yield, L/B = 93:07. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 3.51 (d, J = 1.5 Hz, 3H), 2.31 (t, J = 6.3 Hz, 2H), 2.18 (t, J = 6.9 Hz, 2H), 1.99 (m, 3H), 1.52−1.38 (m, 4H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 208.2, 173.6, 51.3, 43.0, 33.6, 29.7, 24.2, 23.0.

Methyl 2-Phenylpropanoate (10b).[5b] Colorless oil, 122.4 mg, 75% yield, L/B = 27:73. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 7.25−7.36 (m, 5H), 3.74 (q, J = 7.2 Hz, 1H), 3.65 (s, 3H), 1.51 (d, J = 7.2 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 175.1, 140.6, 128.6, 127.5, 127.1, 52.0, 45.4, 18.6.

Ethyl Undecanoate (1ac).[16] Light yellow oil, 139.2 mg, 67% yield, L/B = 81:19. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 4.08 (q, J = 7.1 Hz, 2H), 2.24 (t, J = 7.6 Hz, 2H), 1.81−1.45 (m, 2H), 1.37−1.12 (m, 17 H), 0.83 (t, J = 6.8 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz,

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$CDCl_3$, δ ppm): 173.8, 60.0, 34.3, 31.8, 29.5, 29.4, 29.28, 29.24, 29.1, 24.9, 22.6, 14.2, 14.0.

Propyl Undecanoate (2ac). Light yellow oil, 173.4 mg, 78% yield, L/B = 85:15. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 4.00 (t, J = 6.7 Hz, 2H), 2.26 (t, J = 7.5 Hz, 2H), 1.77−1.43 (m, 4H), 1.32−1.18 (m, 14 H), 0.91 (t, J = 7.4 Hz, 3H), 0.83 (t, J = 6.8 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 173.9, 65.7, 34.3, 31.8, 29.5, 29.4, 29.29, 29.26, 29.1, 25.0, 22.6, 22.0, 14.0, 10.3.

Isopropyl Undecanoate (3ac). Yellow oil, 198.5 mg, 89% yield, L/B = 90:10. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 4.97 (m, 1H), 2.22 (t, J = 7.5 Hz, 2H), 1.59−1.54 (m, 2H), 1.33−1.10 (m, 20H), 6.84 (t, J = 6.8 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 173.4, 67.7, 34.7, 31.8, 29.5, 29.4, 29.29, 29.26, 29.1, 25.0, 22.6, 21.8, 14.0.

Phenyl Undecanoate (4ac). Light yellow oil, 149.4 mg, 68% yield, L/B = 80:20. **^{1}H NMR** (400 MHz, $CDCl_3$, δ ppm): 7.36 (t, J = 8.0 Hz, 2H), 7.20 (t, J = 7.4 Hz, 1H), 7.06 (dd, J = 8.5 Hz, 1.0 Hz, 2 H), 2.54 (t, J = 7.5 Hz, 2H), 1.78−1.70 (m, 2H), 1.32−1.17 (m, 14H), 0.87 (t, J = 6.8 Hz, 3H). **^{13}C{^{1}H}-NMR** (400 MHz, $CDCl_3$, δ ppm): 172.3, 150.8, 129.3, 125.7, 121.5, 34.4, 31.9, 29.5, 29.4, 29.3, 29.2, 29.1, 24.9, 22.6, 14.1.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C spectra and spectral data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00851.

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Notes

The authors declare no competing financial interest.

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