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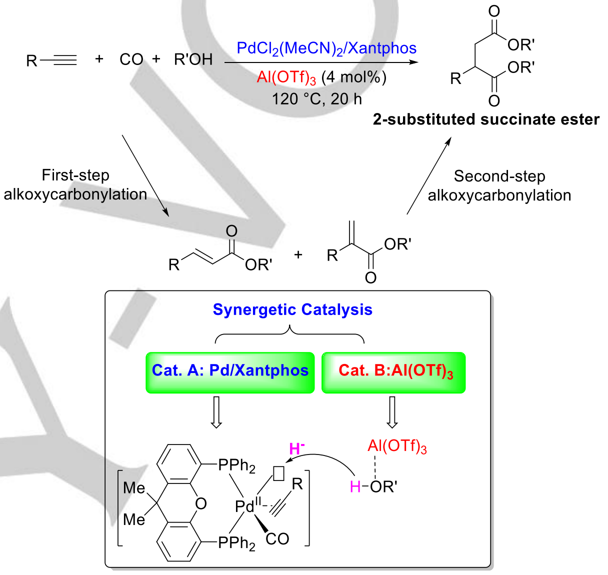
Synergetic catalysis for one-pot bis-alkoxycarbonylation of terminal alkynes over Pd/Xantphos-Al(OTf)₃ bi-functional catalytic system

Wen-Di Guo[a], Lei Liu[a], Shu-Qing Yang[a], Xiao-Chao Chen[a], Yong Lu[a], Giang VO-Thanh[b]* and Ye Liu[a]*

Abstract: Tandem bis-alkoxycarbonylation of alkynes allows for the preparation of 2-substituted succinates from alkynes and nucleophile alcohol via two successive alkoxycarbonylation with advantages of 100% atomic economy and simplified one-pot operation. Herein, the one-pot tandem bis-alkoxycarbonylation of alkynes was accomplished over the bi-functional catalytic system containing Xantphos-modified Pd-complex and Lewis super-acid of $Al(OTf)_3$. It was found that, via the synergetic catalysis, the involved Xantphos-modified Pd-complex was responsible for the activation of CO and the alkynes through coordination to Pd-center while $Al(OTf)_3$ was in charge of the activation of the alcohol to facilitate the formation of $[Pd–H]^+$ active species. The *in situ* high-pressure FT-IR analysis, coupled with $^1H/^{13}C$ NMR spectral characterizations, confirmed that the introduced $Al(OTf)_3$ with intensive oxophilicity (via acid-base pair interaction) was able to activate nucleophilic MeOH to be a reliable proton-donor (*i.e.* hydride-source) to warrant the formation and stability of $[Pd–H]^+$ species upon the oxidation of Pd^0 by H^+ ($Pd^0 + H^+ \rightarrow [Pd^{II}\text{-}H]^+$). Over the developed bi-functional catalytic system, the yields of the target diesters were obtained in the range of 36~86% in this sequence with the wide substrate scope.

Introduction

Succinate esters (and the related derivatives) have been used as extremely important intermediates in organic synthesis and medicinal chemistry for a long time, with widespread applications in materials science,[1] such as for the synthesis of plasticizers, lubricants oils and other high-value chemicals.[2] Typically, succinates (derivatives) are obtained by oxidative alkoxycarbonylation of olefins, but suffering from the disadvantages like high loading of the palladium catalyst, excessive side reactions, and the risky use of dangerous oxidants.[3] In comparison, the strategy based on bis-alkoxycarbonylation of alkynes has attracted great attention due to 100% atomic economy and simplified one-pot operation, which allows for the preparation of succinates from alkynes and alcohol (nucleophile) via two successive alkoxycarbonylation (Scheme 1).[4]



Scheme 1. Bis-alkoxycarbonylation of alkynes over Pd-Xantphos/$Al(OTf)_3$ bi-functional catalytic system in the way of synergetic catalysis.

In 2018, Beller's group achieved the one-pot bi-alkoxycarbonylation of various aromatic and aliphatic alkynes over the catalytic system containing $Pd(acac)_2$, an pyridinyl- tailed ligand and the Bronsted acid of $PTSA{\cdot}H_2O$, which exhibited the good activity as well as the high chemical/regional selectivity.[5] More recently, our group developed a bi-functional ligand containing both tert-phosphino-fragment and Bronsted acid group ($-SO_3H$), which was applied successfully for Pd-catalyzed bis-alkoxycarbonylation of alkynes towards 2-substituted succinates (diesters) in one-pot process.[6] It is evident that this sequence usually requires two indispensable catalytic factors in order to initiate the unfavored second-step alkoxycarbonylation of electron-deficient functional alkenes (α,β-unsaturated esters): the phosphine-modified palladium catalyst and the Bronsted acid as co-catalyst, wherein the Bronsted acid ($MeSO_3H$, p-TsOH, etc.) serves as hydride-source by reacting with Pd(0) to form active and stable $[Pd\text{-}H]^+$ species ($H^+ + Pd^0 \rightarrow [Pd\text{-}H]^+$).[7] However, the presence of Bronsted acid as co-catalyst no matter in the way of mechanical mixing or chemical-bond combination, often results in undesirable alkylation of phosphines (*i.e.* phosphine degradation) and the corrosion to equipment if excess proton-acid is present.[8] Accordingly, the explorations for the alternatives to replace such undesirable Bronsted acids in bis-alkoxycarbonylation are in demand but has never been reported before.

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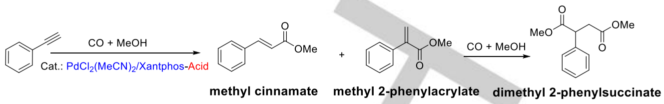
Metal triflates are unique Lewis acids with acidity stronger than $AlCl_3$.[9] The non-coordinating ability of triflate anion (OTf^-) due to the charge delocalization as well as the intensive electron-withdrawing effect of $-CF_3$ group against O-atom and the relatively larger volume confers the corresponding metal cations the Lewis super-acidity.[10] In the literature, metal triflates are powerful Lewis-acid catalysts in organic synthesis in charge of activation of electron-rich O-atom (oxophilicity) in carbonyl group (-CO), hydroxyl (-OH) or epoxy ring.[11] In addition, metal triflates also can serve as the co-catalysts in transition metal catalyzed hydrogenation of carboxylic acids and alkoxycarbonylation of olefins.[8, 12] In comparison to Bronsted acids as the most typical hydride-sources, metal triflates also can interact with proton-donor like H_2O or alcohol (usually as the nucleophilic reactants) to promote the formation of metal-hydride intermediate, with advantages of low-cost, no need of overdosage, less corrosion to equipment, and satisfactory robustness against hydrolysis.[13, 14] Based on the knowledge of metal triflates as Lewis super-acids catalyst to activate alcohols through acid-base pair interaction, herein, we are inspired to combine the metal triflate with the typical phosphine-modified Pd-catalyst, to develop a bi-functional catalytic system with the expected synergetic catalysis for one-pot bis-alkoxycarbonylation of alkynes for the first time (Scheme 1),[15] wherein the phosphine-modified Pd-catalyst is responsible to activate CO and unsaturated C≡C/C=C bond (electrophiles), and simultaneously the metal triflate is to activate alcohol (nucleophile) to supply proton required by Pd(0) to form $[Pd\text{-}H]^+$ active species instead of the use of an auxiliary Bronsted acid. In order to get a clear insight into the role of $Al(OTf)_3$ to induce alcohol (MeOH) as the hydride-source for this tandem bis-alkoxycarbonylation, the *in situ* high-pressure FT-IR analysis was conducted to monitor the formation and stability of active $[Pd–H]^+$ species. Additionally, the isotope labelling experiment was carried out with CD_3OD instead of CH_3OH to determine the source of hydride by FT-IR and ^1H NMR spectroscopic analyses.

Results and Discussion

Firstly, the bis-methoxycarbonylation of phenylacetylene was investigated as a model reaction in the presence of Xantphos modified $PdCl_2(MeCN)_2$ and $Al(OTf)_3$. Based on our interest in using metal triflates as Lewis super-acid in combination with the conventional Pd-catalyst to fulfill synergetic catalysis, the effect of the different Lewis/Bronsted acids on this tandem transformation was compared in Table 1. Under the selected conditions (Pd 1 mol%, P/Pd = 2 molar ratio, CO 1 MPa, MeOH as solvent, 120 °C, 20 h), free of any acid co-catalyst, the target product of dimethyl 2-phenylsuccinate was obtained in 31% yield, along with the abundant mono-carbonylated products of methyl cinnamate ($Sel._{L\text{-}ester}$ of 31%) and methyl 2-phenylacrylate ($Sel._{B\text{-}ester}$ of 38%) (Entry 1), implying the sluggish and inefficient second-step methoxycarbonylation of the α,β-unsaturated esters. The screening of the conventional Lewis acids from $B(OH)_3$, anhydrous $AlCl_3$ and $ScCl_3·6H_2O$ indicated that the addition of 2 mol% $B(OH)_3$ had induced a slight improvement for the selectivity of diester (Entries 2 vs 1) whereas the use of high-valent metal chlorides $AlCl_3$ or $ScCl_3·6H_2O$ with enhanced Lewis acidity was able to appreciably increased the selectivity of the diester up to ~50% (Entries 3 and 4). Highlighted by the obtained results over $AlCl_3$ or $ScCl_3·6H_2O$, the analogues of $Al(OTf)_3$ and $Sc(OTf)_3$, defined as Lewis super-acids,[9] were applied to repeat the reaction. It was found that $Al(OTf)_3$ and $Sc(OTf)_3$ both resulted in the greatly increased yields of target diester (Entries 5 and 6). Especially over $Al(OTf)_3$, 82% yield of dimethyl 2-phenylsuccinate was obtained along with 18% yield of methyl cinnamate and non-detectable methyl 2-phenylacrylate (Entry 5), implying that the branched α,β-unsaturated ester derived from the first-step methoxycarbonylation was more reactive than the linear one towards the second-step carbonylation. The increased amount of $Al(OTf)_3$ could further promote the transformation of the relatively inert linear methyl cinnamate towards the diester (Entries 8 vs 5 and 7). While the equivalent HOTf (2 mol%) as a strong Bronsted acid was applied instead of $Al(OTf)_3$ with the same counter-anion, the diester yield was 5% lower than that over $Al(OTf)_3$ (Entry 9 vs 5). The presence of $PTSA·H_2O$ (2 mol%) led to 75% yield of the target diester accompanied by the linear (Yield 24%) and branched (Yield 1%) mono-esters (Entry 10). When 4 mol% $PTSA·H_2O$ was applied instead of $Al(OTf)_3$, the target diester was obtained in the yield of 80%, which was still lower than that with the presence of the same concentrated $Al(OTf)_3$ (Entries 11 vs 8). Only the further increased concentration of $PTSA·H_2O$ up to 8 mol% led to the competitive yield of 85% for the target diester (Entries 12 vs 8). These results indicated that the low-cost and highly safe $Al(OTf)_3$ was indeed an ideal candidate to replace the irritative proton acid with high risk of corrosion.

Table 1. The effect of Lewis/Bronsted acids on Pd-catalyzed bis-methoxycarbonylation of phenylacetylene with MeOH.[a]

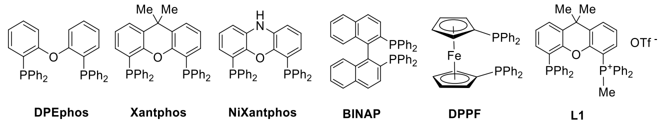


Entry	Acid	Conv. (%)[b]	$Sel._{L\text{-}ester}$ (%)[b]	$Sel._{B\text{-}ester}$ (%)[b]	$Sel._{diester}$ (%)[b]
1	-	100	31	38	31
2	$B(OH)_3$	100	38	23	39
3	$AlCl_3$	100	34	10	56
4	$ScCl_3·6H_2O$	100	31	19	50
5	$Al(OTf)_3$	100	18	0	82
6	$Sc(OTf)_3$	100	20	2	78
7[c]	$Al(OTf)_3$	100	24	0	76
8[d]	$Al(OTf)_3$	100	14	0	86
9	HOTf	100	23	0	77
10	$PTSA·H_2O$	100	24	1	75
11[e]	$PTSA·H_2O$	100	19	1	80
12[f]	$PTSA·H_2O$	100	15	0	85

[a] Standard reaction conditions: $PdCl_2(MeCN)_2$ 0.05 mmol (Pd 1 mol%), Xantphos 0.05 mmol (P/Pd = 2 molar ratio), phenylacetylene 5 mmol, MeOH 3 mL, acid 0.1 mmol (2 mol%), CO 1 MPa, 120 °C, 20 h. [b] Determined by GC. $Sel._{L\text{-}ester}$ represents selectivity to linear methyl cinnamate. $Sel._{B\text{-}ester}$ represents selectivity to branched methyl 2-phenylacrylate. $Sel._{diester}$ represents selectivity to dimethyl 2-phenylsuccinate. [c] $Al(OTf)_3$ 1 mol%. [d] $Al(OTf)_3$ 4 mol%. [e] $PTSA·H_2O$ 4 mol%. [f] $PTSA·H_2O$ 8 mol%.

Besides of the presence of $Al(OTf)_3$ co-catalyst, the properties of phosphine ligands also played important role in adjusting the performance of Pd-catalyst as demonstrated in Table 2. It has been known that the chelation ability (P-M-P) has critical

Table 2. The effect of phosphine ligands on the performance of $PdCl_2(MeCN)_2$-$Al(OTf)_3$ system for bis-methoxycarbonylation of phenylacetylene with MeOH.[a]



Entry	Ligand	Conv. (%)[b]	Sel.$_{\text{L-ester}}$ (%)[b]	Sel.$_{\text{B-ester}}$ (%)[b]	Sel.$_{\text{diester}}$ (%)[b]
1[c]	DPEphos	100	16	0	64
2	Xantphos	100	18	0	82
3[c]	Nixantphos	100	29	8	55
4[c]	BINAP	100	1	19	31
5[c]	DPPF	100	22	4	47
6[c]	**L1**	100	14	25	1
7[c]	-	90	2	5	0

[a] Standard reaction conditions: $PdCl_2(MeCN)_2$ 0.05 mmol (Pd 1 mol%), Ligand 0.05 mmol (P/Pd = 2 molar ratio), phenylacetylene 5 mmol, MeOH 3 mL, $Al(OTf)_3$ 0.1 mmol (2 mol%), CO 1 MPa, 120 °C, 20 h. [b] Determined by GC. Sel.$_{\text{L-ester}}$ represents selectivity to linear methyl cinnamate. Sel.$_{\text{B-ester}}$ represents selectivity to branched methyl 2-phenylacrylate. Sel.$_{\text{diester}}$ represents selectivity to dimethyl 2-phenylsuccinate. [c] The side-products of acetophenone and the polymers of phenylacetylene were identified by GC-MS.

impact on the stability and catalytic performance of a transition metal complex. As shown in Table 2, a series of diphosphines with typical chelation ability were selected on purpose. It was found that only the rigid and xanthene-skeleton based Xantphos with wide natural bite angle of 111° enabled Pd-$Al(OTf)_3$ system to spur the reaction rate of the second-step methoxycabonylation,[16] giving 82% yield of the target diester (Entry 2). The relative lower yield of the diester (55%) over the similar structured Nixantphos might be attributed to the competitive coordination interference from its incorporated N-atom to Pd-center (Entry 3). As for the diphosphines like DPEphos, BINAP and DPPF, wherein the relative positions of the two phosphino-fragments were not as rigidly fixed as those in Xantphos due to the rotatory σ-bond linking PPh_2-substituted aryl rings, the low yields of dimethyl 2-phenylsuccinate in the range of 31~64% were observed (Entries 1, 4 and 5). When the mono-phosphine of **L1** with the destroyed chelation effect was applied in place of Xantphos, the second-step methoxycarbonylation was completely inhibited (Entry 6). It was also noted that, except for Xantphos, the side-reactions like hydration and polymerization of the alkyne universally happened. Evidently, only Xantphos could guarantee $PdCl_2(MeCN)_2$-$Al(OTf)_3$ system to accomplish the synergetic catalysis for bis-methoxycarbonylation due to its rigid structure with the fixed chelation effect.[17] In addition, we conducted the reaction in the absence of any phosphine ligand. It was found that only the very low yield of the α,β-unsaturated esters (7%) was obtained but along with 90% conversion of phenylacetylene (Entry 7 in Table 2), further suggesting that the presence of the suitable ligand (like Xantphos) played indispensable role in initiating the alkoxycarbonylation against the hydration and polymerization of the alkyne.

The evolving processes of bis-methoxycarbonylation of phenylacetylene over $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ bi-functional system were presented in Figure 1. It was indicated that, the first-step methoxycarbonylation occurred rapidly. Under the applied conditions, the first-step methoxy-carbonylation occurred rapidly. In the initial 30 min, 97% of phenylacetylene converted to the α,β-unsaturated esters along with the products distributions of 72% methyl 2-phenylacrylate (branched) and 23% methyl cinnamate (linear) as well as 5% dimethyl 2-phenylsuccinate (diester). Subsequently, the branched methyl 2-phenylacrylate was continuously converted to the diester until it was depleted completely in 8 h whereas the transformation of the linear mono-ester barely happened. Later on, the remained linear mono-ester sluggishly converted to the same target diester. In 20 h reaction process, only 7% of the formed methyl cinnamate was continuously carbonylated to the diester, implying that the branched methyl 2-phenylacrylate with exposed C=C bond in *gem*-position was indeed more reactive than the double-bond embedded linear one towards the second-step methoxycarbonylation.

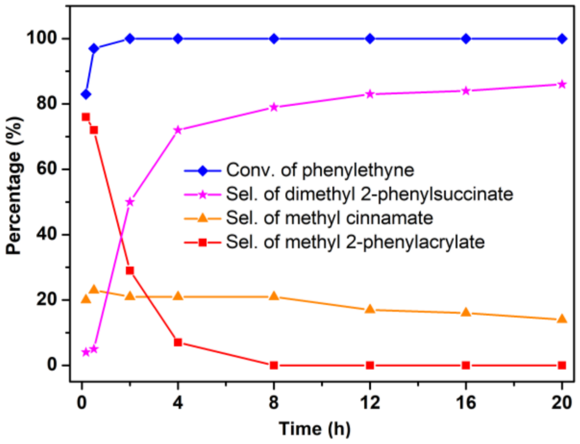


Figure 1. Evolution profiles of the one-pot bis-methoxycarbonylation of phenylacetylene *vs* reaction time catalyzed by $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ bi-functional system (conditions: $PdCl_2(MeCN)_2$ 0.05mmol, Xantphos 0.05 mmol, $Al(OTf)_3$ 0.2 mmol, phenylacetylene 5 mmol, MeOH 3 mL, CO 1 MPa, 120 °C).

It has been widely accepted that $[Pd–H]^+$ species is a real active catalyst for bis-alkoxycarbonylation of alkynes.[6] And any factor able to improve the formation and stability of such $[Pd–H]^+$ species will speed up the reaction. As for Bronsted acids such as HOTf, $MeSO_3H$, etc, they could serve as hydride-sources upon oxidizing Pd(0) to afford palladium hydride ($H^+ + Pd^0 \rightarrow [Pd\text{-}H]^+$). In contrast, while the Lewis super-acid of $Al(OTf)_3$ is applied instead, proton-donor can serve as the efficient hydride-source to generate $[Pd\text{-}H]^+$ species. In order to get a deeper insight into the role of $Al(OTf)_3$ in improving the generation and stabilization of $[Pd–H]^+$ species, the *in situ* high-pressure FT-TR analysis was carried out over $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ and $PdCl_2(MeCN)_2$/Xantphos systems in parallel. As illustrated in Figure 2, the characteristic peaks at 2177 and 2117 cm^{-1} assigned to gaseous CO vibrations (*i.e.* symmetric stretching vibration mode and the anti-symmetric stretching vibration mode of free CO molecule) were clearly observed in each case. Over $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ bi-functional system (Figure 2-A), a weak peak at 1944 cm^{-1}, which was attributed to the active

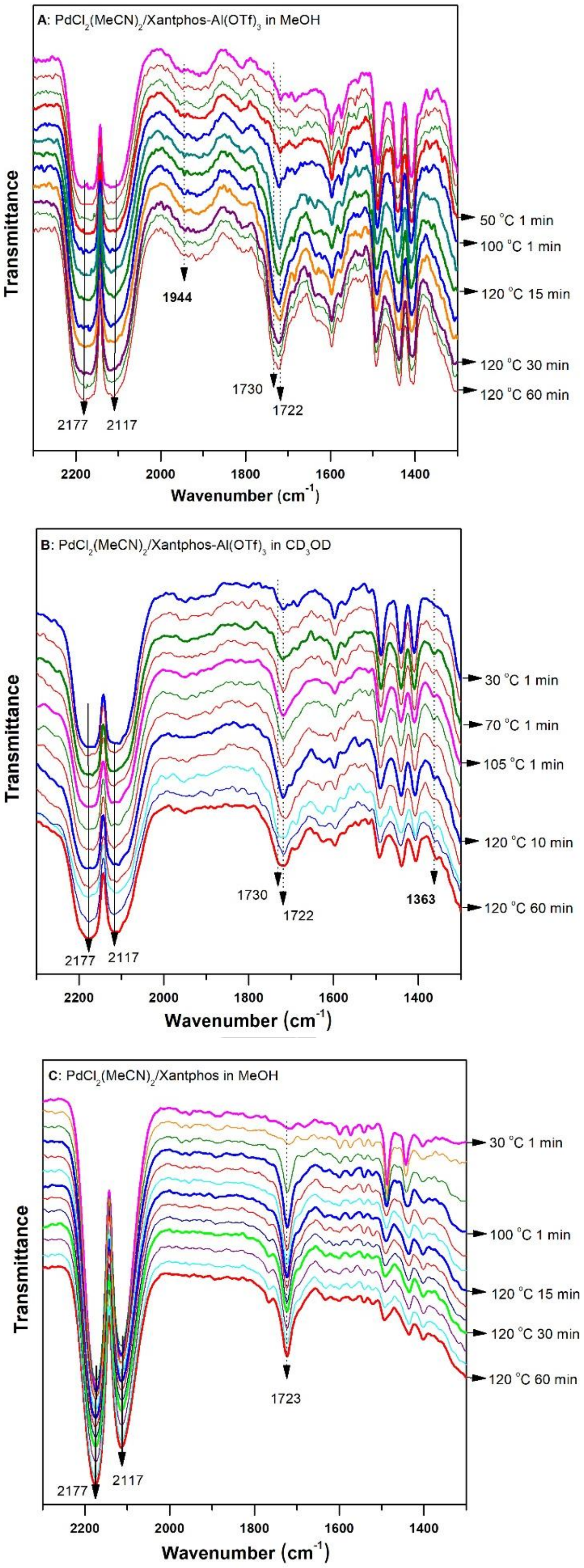


Figure 2. The *in situ* high-pressure FT-IR spectra obtained from 30 to 120 °C after mixing phenylacetylene, CH_3OH or CD_3OD, $PdCl_2(MeCN)_2$, Xantphos and $Al(OTf)_3$ (if required) in 1 MPa CO (**A**: phenylacetylene, $PdCl_2(MeCN)_2$, Xantphos and $Al(OTf)_3$ were mixed in CH_3OH; **B**: phenylacetylene, $PdCl_2(MeCN)_2$, Xantphos and $Al(OTf)_3$ were mixed in CD_3OD; **C**: phenylacetylene, $PdCl_2(MeCN)_2$ and Xantphos were mixed in CH_3OH).

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$[Pd\text{-}H]^+$ species,[6] was observed initially while the temperature was increased to 50 ºC. As the temperature further increasing from 50 to 120 ºC, this absorption peak gradually grew and then reached the maximum intensity at 120 ºC. Concurrently the carbonyl vibration at 1730 cm^{-1} assigned to the target product of dimethyl 2-phenylsuccinate (the standard FT-IR spectrum was given in S. Figure 2 of SI) was observed with steadily increased intensity, accompanied by the universal co-existence of α,β-unsaturated esters (methyl 2-phenylacrylate and methyl cinnamate, ν 1722 cm^{-1}) (the standard FT-IR spectra were given in S. Figure 3 and S. Figure 4 of SI). To further confirmed the adsorption band at ca. 1944 cm^{-1} as observed in Figure 2-A was truly ascribed to the stabilized $[Pd–H]^+$ species and CH_3OH was the hydride-source, CD_3OD was used instead of CH_3OH in the evolving processes of $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ under same conditions (Figure 2-B). Since the vibration frequency is inversely proportional to the square root of the mass, the vibration frequency of Pd-D bond is theoretically expected to redshift to ca. ~ 1370 cm^{-1} when D replaces H in $[Pd\text{-}H]^+$ species ($\nu_{Pd\text{-}H}$ 1944 cm^{-1}).[18] As observed in Figure 2-B, the absorption bands of $[Pd\text{-}H]^+$ species at 1944 cm^{-1} completely disappeared whereas the evolving vibrations at 1363 cm^{-1} were observed concurrently. The latter was consistent to the theoretical vibration frequency of Pd-D bond ($\nu_{Pd\text{-}D}$ ~1370 cm^{-1}). The simultaneous absence of the peaks of 1944 cm^{-1} and the concurrent presence of 1363 cm^{-1} (Figure 2-B, $\nu_{Pd\text{-}D}$) with the involvement of CD_3OD supportively verified that the observed vibration at 1944 cm^{-1} was indeed attributed to the formation of $[Pd–H]^+$ species and that methanol truly participated its formation as a hydride-donor. In comparison, as for $PdCl_2(MeCN)_2$/Xantphos system without the involvement of $Al(OTf)_3$ (Figure 2-C), the continuous derivation of the $[Pd–H]^+$ species with characteristic peak at 1944 cm^{-1} was barely observed during the overall monitoring process, indicating the transient $[Pd–H]^+$ species in the Xantphos-$PdCl_2(MeCN)_2$ system was barely detectable by the FT-IR spectroscopic technique. Meanwhile, only methyl 2-phenylacrylate and methyl cinnamate derived from the first-step methoxycarbonylation of phenylacetylene was found with carbonyl characteristic vibration at ca. 1723 cm^{-1}. The obtained observations from *in situ* high-pressure FT-IR analysis revealed the following facts: (1) The stability of the generated $[Pd\text{-}H]^+$ species, the active catalytic species of the bis-methoxycarbonylation, could be facilitated by the presence of $Al(OTf)_3$ as the co-catalyst (Figure 1 vs Figure 3); (2) Only the stabilized active $[Pd–H]^+$ species promoted by $Al(OTf)_3$, whose longevity was long enough to be captured by the routine FT-IR spectroscopic technique, could inherently guarantee the success of second-step methoxycarbonylation (of the electron-deficient α, β-unsaturated esters) to afford the target diester; (3) Methanol upon activation by $Al(OTf)_3$ through Lewis acid-base pair interaction could serve as an ideal hydride-source for the formation of $[Pd–H]^+$ species (Figure 1 and Figure 2). Knowingly, the non-coordinating ability of OTf^- confers $Al(OTf)_3$ the Lewis super-acidity.[10] The synergetic activation of MeOH by $Al(OTf)_3$ upon Lewis-acid pair interaction makes MeOH be an available hydride-source.[12, 19]

In order to further confirm that MeOH rather than water served as the original hydride-source upon activation by $Al(OTf)_3$, a set of control experiments labelled by CH_3OH and CD_3OD were carried out respectively under non-aqueous condition. As shown in Table 3, when the absolutely anhydrous reactants of phenylacetylene and methanol were applied to repeat the reaction over $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ system, there was nearly no change for the yield of the diester in comparison to the result obtained with phenylacetylene and methanol containing trace of water (Entries 2 vs 1), which ruled out the possibility of water as the potential hydride-source. In addition, it was found that the use of CD_3OD instead of CH_3OH corresponded to the comparable yield of the target diester (74%) (Entries 3 vs 2). The ^1H NMR spectra of the non-deuterated diester and deuterated diester (Figure 3) also showed that in the deuterated diester, the peak area of D_a and D_b reduced nearly unobservable, which implied that H_a and H_b in non-deuterated diester came from methanol rather than other H-donors like H_2O in this bis-methoxycarbonylation. These control experiments were the supportive evidences that $Al(OTf)_3$ really behaved as an independent catalyst to polarize MeOH (due to its oxophilicity) to release proton ($H^+ + Pd^0 \rightarrow [Pd^{II}\text{-}H]^+$), which was similar to the observations in $Al(OTf)_3$-catalyzed cyclization of alkenols or the ring opening reactions of epoxides].[11, 20]

Table 3. The control experiments for bis-methoxycarbonylation using CH_3OH and CD_3OD.[a]

Entry	Alcohol	Conv. (%)[b]	Sel.$_{L\text{-}ester}$ (%)[b]	Sel.$_{B\text{-}ester}$ (%)[b]	Sel.$_{diester}$ (%)[b]
1	MeOH	100	18	0	82
2[c]	MeOH	100	20	0	80
3[d]	CD_3OD	100	26	0	74

[a] Standard reaction conditions: $PdCl_2(MeCN)_2$ 0.05 mmol (Pd 1 mol%), Xantphos 0.05 mmol (P/Pd = 2 molar ratio), phenylacetylene 5 mmol, MeOH 3 mL, $Al(OTf)_3$ 0.1 mmol (2 mol%), CO 1 MPa, 120 ºC, 20 h. [b] Determined by GC. Sel.$_{L\text{-}ester}$ represents selectivity to linear methyl cinnamate. Sel.$_{B\text{-}ester}$ represents selectivity to branched methyl 2-phenylacrylate. Sel.$_{diester}$ represents selectivity to dimethyl 2-phenylsuccinate. [c] Phenylacetylene was dried by anhydrous sodium sulfate, methanol was dried by 3A molecular sieves. [d] Phenylacetylene was dried by anhydrous sodium sulfate.

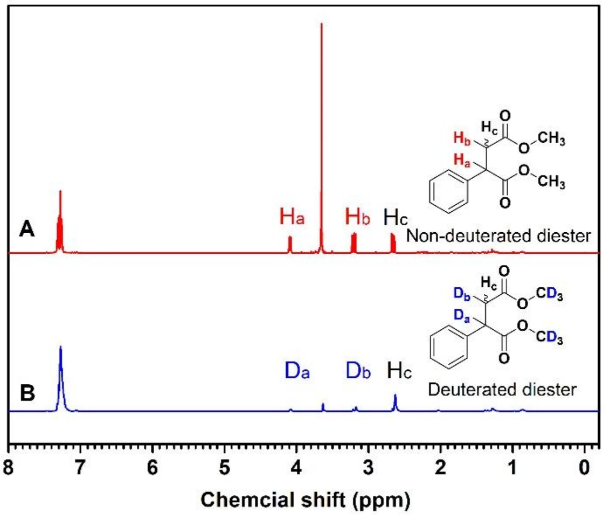

Figure 3. The ^1H NMR spectra of the non-deuterated diester (**A**) and deuterated diester (**B**).

In addition, the activation of MeOH by $Al(OTf)_3$, the Lewis super-acid, was clearly demonstrated in $^1H/^{13}C$ NMR spectra (Figure 4). It was indicated that, in the mixture of MeOH and $Al(OTf)_3$, the signal of methyl's proton low-field shifted by 0.31 ppm along with the complete disappearance of the signal of hydroxyl's proton, in comparison to that of MeOH itself. Likewise, the signal of methyl's carbon also low-field shifted by 2.87 ppm compared to the pure MeOH. Reasonably, $Al(OTf)_3$ as a Lewis super-acid, its oxophilicity to the electron-rich O-atom of MeOH resulted in the decreased electron-density around H-/C-atom, leading to the lower field signals as observed herein. On the other hand, the intensive acid-base pair interaction between $Al(OTf)_3$ and O-atom in MeOH dramatically weakened the hydroxy's O-H bond, leading to the transient H↔D exchange as the result of the unobservable H-signal in ^1H NMR spectra of the mixture. Additionally, the hygroscopicity of $Al(OTf)_3$ completely eliminated free H_2O impurity in the mixture, accounting for the disappeared H_2O-signal simultaneously.

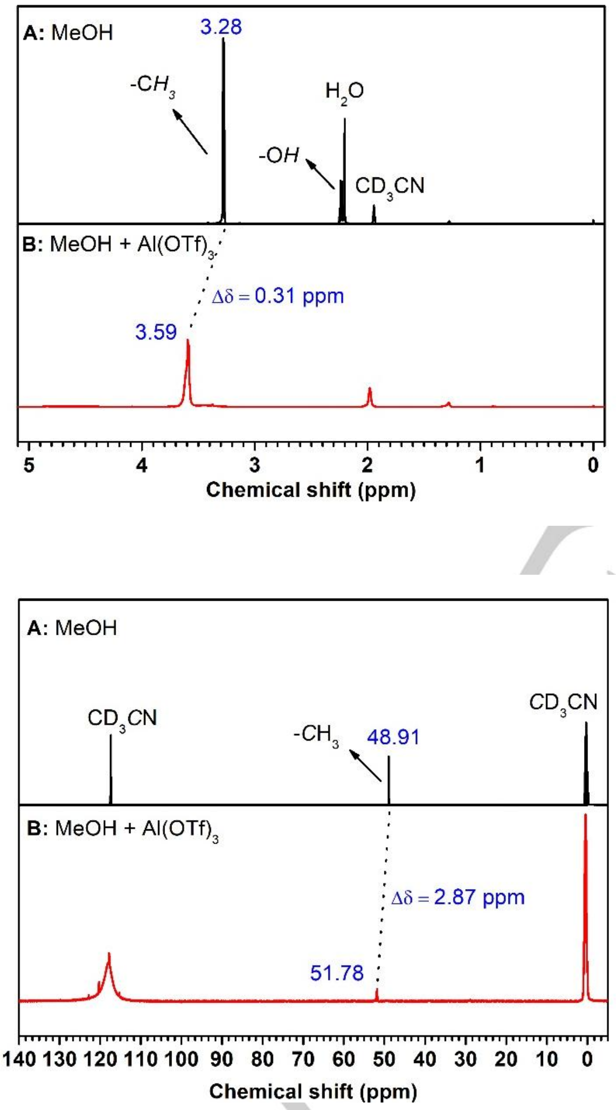

Figure 4. The $^1H/^{13}C$ NMR spectra: (**A**) MeOH (0.1 mmol) in CD_3CN (0.5 mL); (**B**) The mixture of MeOH and $Al(OTf)_3$ (MeOH 0.1 mmol, $Al(OTf)_3$ 0.2 mmol) in CD_3CN (0.5 mL).

On the basis of the above discussion, coupled with the *in situ* high-pressure FT-IR analysis (Figure 2) and the $^1H/^{13}C$ NMR spectral characterizations (Figure 3 and Figure 4), the catalytic mechanism of the bis-alkoxycarbonylation of terminal alkynes over the bi-functional catalytic system of $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ was proposed in Scheme 2. Firstly, Pd^{II} was reduced to Pd^0 in the presence of CO. Subsequently, the O-H bond of MeOH was weakened to facilitate the proton-release upon the activation by $Al(OTf)_3$. The released proton then interacted with Pd^0 to formed Pd-H species **A**.[7] The addition of Pd-H species **A** to C≡C bond in the concertedly Pd-coordinated alkyne intermediate **B** afforded (β-vinyl) palladium intermediate **C** and intermediate **C'**. The insertion of CO (activated by Pd-center) to Pd-C bond in **C** and **C'** afforded the acyl-palladium complex intermediates (**D** and **D'**). The later proceeded alcoholysis with alcohol (R'OH) to give the α,β-unsaturated esters (B-ester and L-ester), accompanied by the regeneration of Pd-H species **A**. Due to the stabilized η^3-Pd configuration of **C** as well as the steric hindrance between R-group and $-PPh_2$ of bulky Xantphos in **C'**, the formation of the branched **C** as well as **D** was more favorable than that of **C'** and **D'**, leading to the predominant generation of the branched α,β-unsaturated ester in the first-step alkoxycarbonylation. In the second-step alkoxycarbonylation, the transformation rate of the α,β-unsaturated esters decreased dramatically due to the electron-deficient nature of the C=C bond neighboured to C=O group. Specifically, the branched α,β-unsaturated ester with the exposed terminal C=C double bond in *gem*-position was preferentially add to Pd-H species **A** again to afford the alkyl-palladium intermediate complex **E**. The subsequent insertion of another CO to **E** afforded the acyl-palladium intermediate of **F**, which led to the production of the bis-carbonylated product of the diester.

The scope of the reaction was explored with various alkyne derivatives and alcohols under the optimal reaction conditions. As shown in Table 4, a variety of terminal alkynes were all smoothly transformed into the corresponding diesters in moderate to good yields (36-86%). It was worth noting that the presence of the substituents such as alkyl, tertiary-butyl, fluoro, chloro and bromo at the *para*-position of phenylacetylene barely had influence on the yields of the target products (Entries 2-6, 67-85%). Additionally, the phenylacetylene derivatives with *meta*-substituents were also successfully applied to repeat the reaction, affording the corresponding diesters with the yields of 79%–86% (Entries 7-9). Comparatively, the steric effect of the substituents at *ortho*-position obviously influenced the yield of product. Take an example of 2-ethynyltoluene, the target diester was obtained with the lower yield of 45% (Entry 10). Furthermore, the reactions proceeded smoothly when a variety of alcohols were used as the nucleophiles. When the linear alcohol like EtOH or *n*-BuOH was applied to repeat the reaction, the target diester was obtained with the good yield (Entry 11, 75%; Entry 13, 77%). When *i*-PrOH was applied, the reaction rate was decreased obviously, leading to 52% yield of the diester (Entry 12). Evidently, the increased steric hindrance effect of the applied alcohol (like *i*-PrOH) could greatly deaccelerate the alcoholysis of intermediate **D** and **F** (Scheme 2), accounting for the relatively lower yield of the target diester. When the linear aliphatic alkyne (1-hexyne or 1-octyne) was applied as the substrate to repeat the reaction, the target diester was obtained only in a moderate yield (Entry 14, 36%; Entry 15, 43%), along with many isomerized diesters due to the side-reaction of the double-bond shift in the course of the first-step methoxycarbonylation. When the internal alkynes (such as 2-heptyne or 5-decyne) was applied to repeat the reaction over Pd/Xantphos-$Al(OTf)_3$ bi-functional catalytic system, only the mono-alkoxycarbonylation was performed. It was found that 91%

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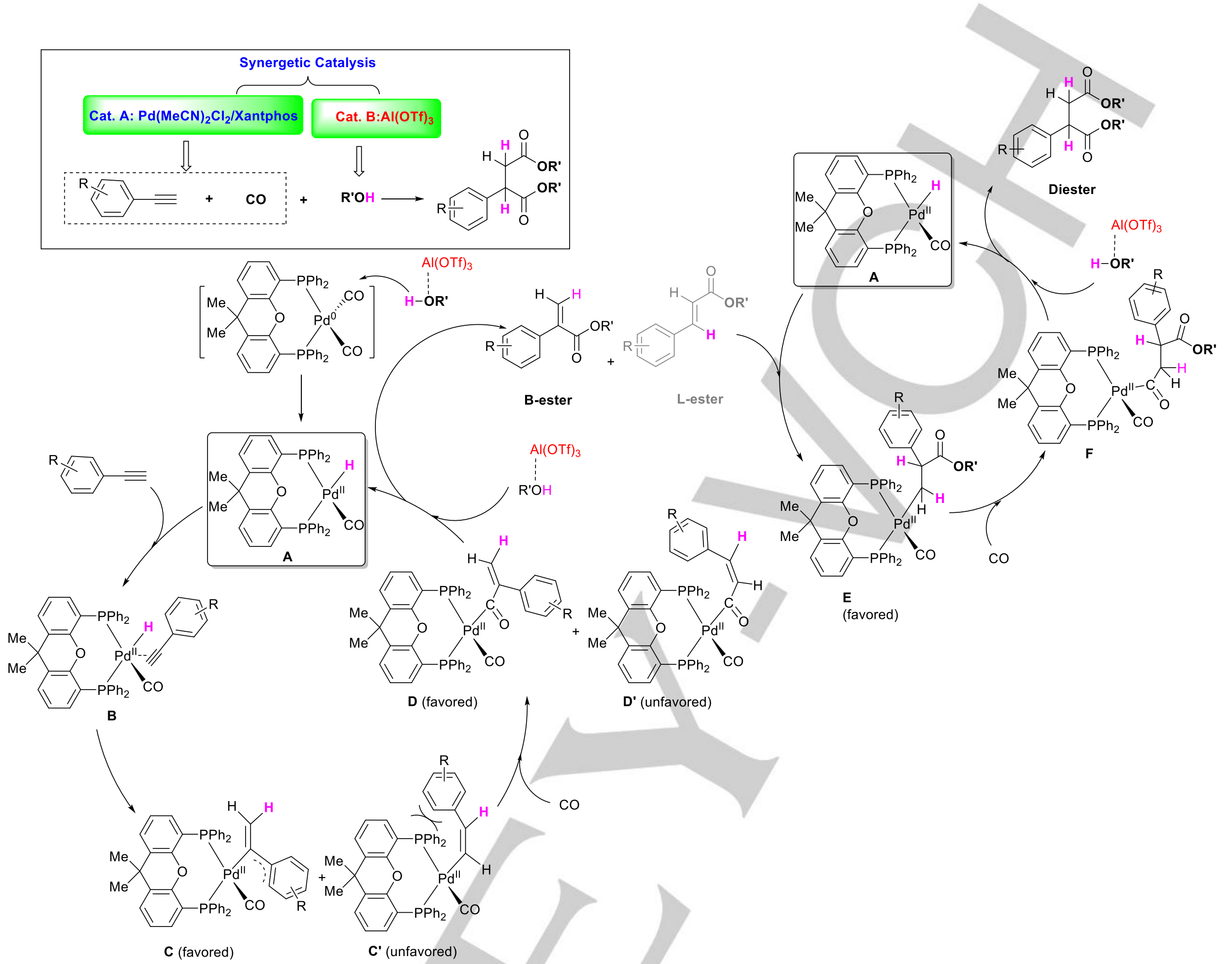
of 2-heptyne and 74 % of 5-decyne were transformed into the corresponding mono-carbonylated products respectively (Entries 16 and 17).



Scheme 2. The proposed synergetic catalytic mechanism over bi-functional catalytic system of $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ for bis-alkoxycarbonylation of alkynes.

Conclusions

The one-pot tandem bis-alkoxycarbonylation of terminal alkynes to the target 2-substituted succinates was achieved with the yields ranged from 36% to 86%. The synergetic catalysis of the bi-functional catalytic system containing the Xantphos-modified Pd-complex and the Lewis super-acid of $Al(OTf)_3$ accounted for the high efficiency of this sequence, wherein the involved transition metal catalyst [$PdCl_2(MeCN)_2$/Xantphos] was responsible for the activation of CO and the alkynes while $Al(OTf)_3$ corresponded to the activation of the alcohol to serve as the hydride-source. It was found that the diphosphine ligand of Xantphos with rigid skeleton and fixed chelation ability could improve the performance of Pd-catalyst dramatically. In this bis-alkoxycarbonylation, the first-step reaction of the alkynes towards the α,β-unsaturated esters occurred rapidly with the branched ones as the major products whereas the second-step alkoxycarbonylation performed sluggishly. Comparatively, the branched α,β-unsaturated esters with the exposed C=C bond in *gem*-position transformed to the diester more effectively than the corresponding linear one. The *in situ* high-pressure FT-IR analysis and $^1H/^{13}C$ NMR spectral characterizations confirmed that the introduced $Al(OTf)_3$ was able to activate nucleophilic MeOH via acid-base pair interaction to be a reliable proton-donor (or hydride-source) to warrant the formation and stability of $[Pd–H]^+$ active species.

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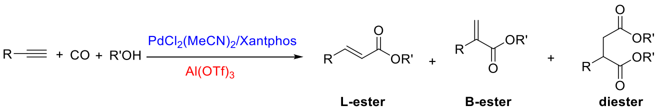
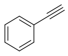
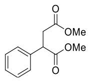
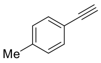
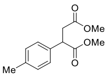
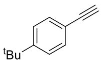
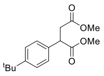
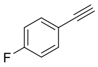
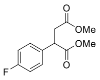
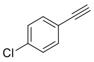
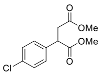
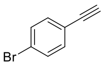
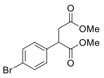
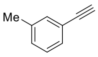
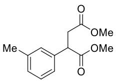
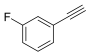
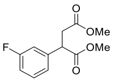
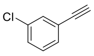
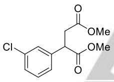
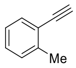
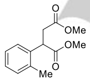
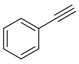
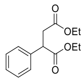
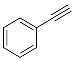
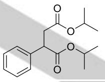
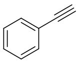
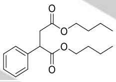
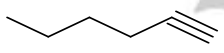
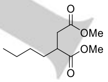
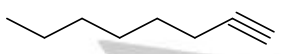
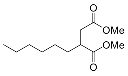
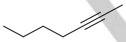
Table 4. The generality of $PdCl_2(MeCN)_2$/Xantphos-$Al(OTf)_3$ bi-functional system for bis-alkoxycarbonylation of terminal alkynes.[a]



Entry	Substrate	Alcohol	Product of diester	Yield of diester (%)
1		MeOH		86[b]
2		MeOH		80[b]
3		MeOH		79[b]
4		MeOH		85[b]
5		MeOH		78[b]
6		MeOH		67[b]
7		MeOH		81[b]
8		MeOH		86[b]
9		MeOH		79[b]
10		MeOH		45[b]
11		EtOH		75[c]
12		*i*-PrOH		52[c]
13		*n*-BuOH		77[c]
14		MeOH		36[c]
15		MeOH		43[c]
16[d]		MeOH	-	-
17[e]		MeOH	-	-

[a] Standard reaction conditions: $PdCl_2(MeCN)_2$ 0.05 mmol (Pd 1 mol%), Xantphos 0.05 mmol (P/Pd = 2 molar ratio), alkyne 5 mmol, alcohol 3 mL, $Al(OTf)_3$ 0.2 mmol (4 mol%), CO 1 MPa, 120 °C, 20 h. [b] The isolated yield ($^1H/^{13}C$ NMR spectra of the isolated products were given in SI). [c] GC yield. [d] 91% of 2-heptyne was transformed into the corresponding mono-carbonylated products. [e] 74 % of 5-decyne was transformed into the corresponding mono-carbonylated products.

Experimental Section

Reagent and analysis

The chemical reagents were purchased from Shanghai Aladdin Chemical Reagent Co., Ltd, Shanghai Macklin Biochemical Co., Ltd and Bide Pharmatech Ltd., which were used as received. Gas chromatography (GC) was performed on a SHIMADZU-2014 equipped with a DM-Wax capillary column (30 m × 0.25 mm × 0.25 μm). GC-mass spectrometry (GC-MS) was recorded on an Agilent 6890 instrument equipped with an Agilent 5973 mass selective detector. The *in situ* high-pressure FT-IR spectra were recorded on a Nicolet NEXUS 670 spectrometer. The $^1H/^{13}C$ NMR spectra were recorded with a Bruker Avance 500 spectrometer.

Synthesis of L1

L1 was synthesized according to the procedures reported by our group before.[21]

General procedures for the one-pot tandem bis-alkoxycarbonylation of alkynes

In a typical experiment, $PdCl_2(MeCN)_2$ (0.05 mmol), Xantphos (0.05 mmol, or other ligand) and $Al(OTf)_3$ (0.1 mmol) were mixed with phenylacetylene (5 mmol, or the other alkyne) and methanol (or the other alcohol, 3 mL). The mixture was added in a 50 mL sealed Teflon-lined stainless-steel autoclave, which was purged twice with CO (0.3 MPa) and then pressurized with CO to 1 MPa. Then, the reaction mixture was stirred vigorously at the appointed temperature for some time. Upon completion, the autoclave was cooled down to room temperature and slowly degassed. The reaction solution was analyzed by GC to determine the conversions (n-dodecane as the internal standard) and the selectivities (normalization method), and the products were further identified by GC-mass and $^1H/^{13}C$ NMR spectra.

In situ high-pressure FT-IR spectral characterization

The *in situ* high-pressure FT-IR spectra were recorded on a Nicolet NEXUS 670 spectrometer. The spectral resolution was about 4 cm^{-1}. A mixture containing 0.025 mmol of Xantphos with 0.025 mmol of $PdCl_2(MeCN)_2$, 0.025 mmol of $Al(OTf)_3$ (if required) and 0.1 mL of phenylacetylene in methanol was fixed in the specially designed high-pressure IR cell, in which cylindric CaF_2 was used as the sealing sheets. Then, 1 MPa CO was charged into the sealed cell. The real time monitoring was performed under the different temperatures. The mixture compositions including $PdCl_2(MeCN)_2$, Xantphos, phenylacetylene, CO and $Al(OTf)_3$ (if required) were completely the same as those for the real reaction in Table 1, except for the much higher concentration of $PdCl_2(MeCN)_2$ and the ligand required for FT-IR spectral detection.

Acknowledgements

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Keywords: Bis-alkoxycarbonylation • Synergetic catalysis • Aluminium triflate • Lewis super-acid • Bi-functional catalysts

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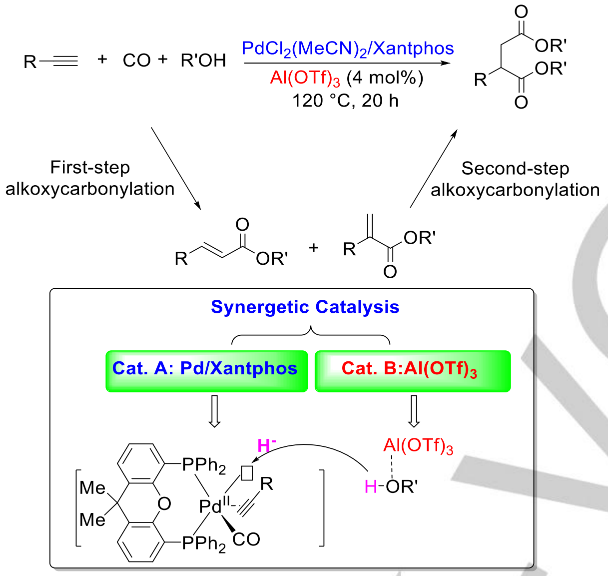
FULL PAPER

The one-pot tandem bis-alkoxycarbonylation of alkynes was accomplished over the bi-functional catalytic system containing Xantphos-modified Pd-complex and Lewis super-acid of Al(OTf)$_3$. Via the synergetic catalysis, the involved Xantphos-modified Pd-complex was responsible for the activation of CO and the alkynes through coordination to Pd-center while Al(OTf)$_3$ was in charge of the activation of the alcohol to facilitate the formation of [Pd–H]$^+$ active species.



*Wen-Di Guo, Lei Liu, Shu-Qing Yang, Dong-Liang Wang, Xiao-Chao Chen, Yong Lu and Ye Liu**

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Synergetic catalysis for one-pot bis-alkoxycarbonylation of terminal alkynes over Pd/Xantphos-Al(OTf)$_3$ bi-functional catalytic system