Research Article
doi.org/10.1002/cctc.202101923

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Combined Effect of Palladium Catalyst and the Alcohol to Promote the Uncommon Bis-Alkoxycarbonylation of Allylic Substrates

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A chemoselective method for the carbonylation of allylic substrates CH_2=$CHCH_2X$ (X = OAc, OC(O)CH_2CN, OPh, OEt, OC(O)OPh, OC(O)O*i*Bu, N(H)C(O)Ph, N(Ph)C(O)Ph, N(H)Boc, N(Ph)Boc, Ph, CO_2Bn, CN), leading to alkyl succinates with preservation of the X group, under Pd(II)-catalyzed oxidative carbonylation conditions, has been developed. Our method shows a completely different inverse chemoselectivity with respect to the "classical" substitutive carbonylation of the allyl compounds, which is known to provide β,γ-unsaturated carbonyl derivatives through the formation of a π-allylpalladium intermediate. An accurate study, carried out using allyl acetate as model substrate, allowed to maximize the selectivity in the envisioned 2-CH_2X substituted succinates. The best catalyst is generated *in situ* by mixing $Pd(TFA)_2$ (TFA = trifluoroacetate) and the *N*,*N*′-di(anthracen-9-yl)butane-2,3-diimine ligand. *p*-Benzoquinone was used as oxidant in presence of benzyl alcohol, which acts as a nucleophile and as a solvent, under 4 bar of CO at 20 °C. A combined effect of the ligand and the nucleophile, rationalized through DFT calculations, has been observed both in promoting the bis-alkoxycarbonylation process and in preventing π-allylpalladium-mediated side reactions, allowing the attainment of succinate derivatives with moderate to good yields.

Introduction

The carbonyl group is omnipresent in a large variety of useful organic compounds, including pharmaceuticals, agrochemicals, specialty polymers, bulk chemicals and natural products. In the last decades, intensive efforts have been devoted to the synthesis of carbonyl-containing compounds, such as ketones, aldehydes, carboxylic acids and their derivatives, in order to find efficient and straightforward pathways to achieve such important molecules. Besides all, carbonylation reactions[1] have gained much attention due to the possibility of directly obtaining the desired carbonylated molecule starting from relatively low cost materials, including carbon monoxide, which is an interesting C1 building block, already widely used in industry.[2] Furthermore, the use of transition metals, in combination with tailor-made ligands, allows to achieve high chemo- and regioselectivities, operating under mild and sustainable conditions.[3] In this context the carbonylation of unsaturated compounds, such as alkenes or alkynes, to obtain mono- or bis- carbonylated products, is one of the most explored processes.[4] In the last years, more attention has been given to the carbonylation of allylic compounds.[5–16] In particular, allyl derivatives (CH_2=$CHCH_2X$, X = leaving group) have been successfully carbonylated to obtain synthetically useful β,γ-unsaturated carbonyl compounds (Scheme 1a). So far, versatile methods for the substitutive carbonylation of allyl carbonates,[6] acetates,[7] halides,[7a,8] amines,[9] ethers,[7a,10] alcohols,[7a,8a,11] phosphates,[7c,g,12] in the presence of a suitable nucleophile NuH (generally an alcohol or an amine), have been developed (Scheme 1a,*ii*). Despite differences in catalysts, substrates and nucleophiles, these reactions usually proceed according to a generally accepted mechanism,[5,13] which starts with the oxidative addition of the allylic substrate to the metal in a low oxidation state, usually palladium(0), to form a π-allylpalladium complex[13b] (Scheme 1b). Then, the coordination/insertion of CO takes place forming an acyl palladium intermediate, which reacts with NuH. The subsequent reductive

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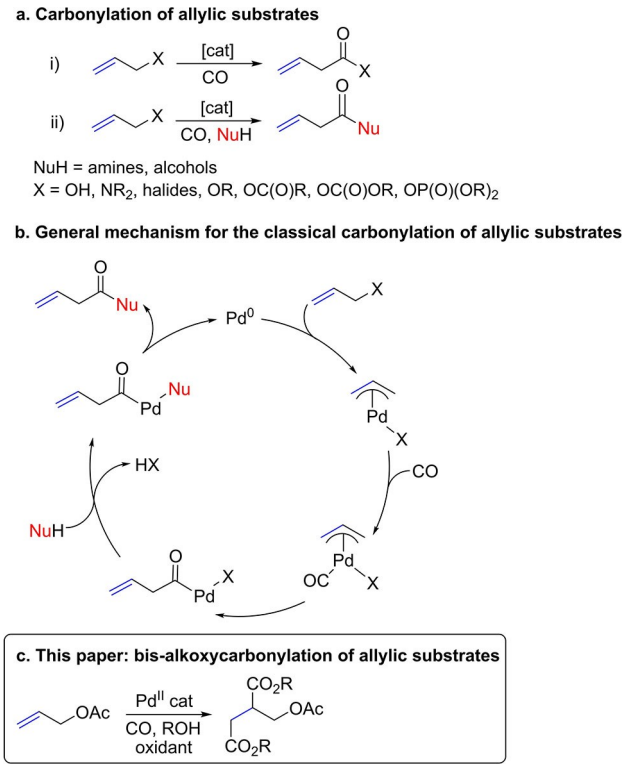
Supporting information for this article is available on the WWW under https://doi.org/10.1002/cctc.202101923



Scheme 1. (a) Classical direct (*i*) or substitutive (*ii*) carbonylation of allyl compounds; (b) generally accepted reaction mechanism; (c) envisioned oxidative bis-alkoxycarbonylation reaction.

elimination leads to the expected unsaturated carbonylated product.[17] Remarkably, in the case of allyl amines,[9,14] allyl chlorides,[7a,15] allyl acetate,[7a] allyl ether[16] and allyl alcohols,[11e] if no external nucleophile is added, the acyl palladium intermediate directly undergoes reductive elimination yielding an unsaturated carbonylated molecule still bearing the X group (direct carbonylation, Scheme 1a,*i*). In any case, in all these processes, regardless the presence of an external nucleophile, CO is formally inserted into the existing C(sp^3)-X polar bond, leaving the C=C olefinic double bond unaltered in the final product.

In contrast to the above-mentioned substitutive and direct carbonylations, the oxidative bis-alkoxycarbonylation of allylic substrates, with retention of the X group into the final succinic product, has been poorly studied. In fact, to the best of our knowledge, only two allyl substrates have been bis-alkoxycarbonylated so far. In 1979, Stille and co-workers reported the oxidative bis-methoxycarbonylation of allyl acetate,[18] however, the succinate derivative bearing the acetate group could not be isolated, because, owing to the basic conditions, hydrolysis of the acetate group took place. Some years later, in 1991, Inomata *et al.* reported the oxidative bis-methoxycarbonylation of the (allyloxy)benzene using $PdCl_2$ and $CuCl/O_2$ in MeOH as the solvent at 70 °C for 21 h, obtaining a good product yield (88%),[19] but no extension of this reactivity to other allylic derivatives was reported, neither in that paper nor successively. Moreover, the employed reaction conditions (1 atm of a 1:1 mixture of CO–O_2)[19] fell within the explosion limits for CO–O_2 mixtures.[20]

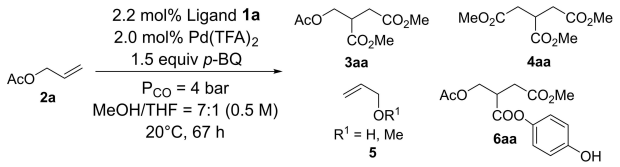
Clearly, an efficient and selective bis-alkoxycarbonylation process of allyl substrates CH_2=$CHCH_2X$ can only be achieved if the formation of the π-allylpalladium intermediate, leading to β,γ-unsaturated carbonyl compounds, is avoided under the reaction conditions. We have recently focused our attention on the bis-alkoxycarbonylation of olefins[21] working under low CO pressure and room temperature.[22] Excellent results have been obtained with terminal[22a] and internal[22b] aromatic and aliphatic alkenes, as well as with acrylic esters and amides,[22c] attaining variously substituted succinic esters in high yields. These molecules find important applications in many industrial fields,[23–26] such as cosmetics,[24] agricultural chemistry[25] and material science.[26] Moreover, succinic acid and its derivatives are important precursors of industrially relevant starting materials[23] and the succinic scaffold is present in a variety of natural products.[27]

Based on our knowledge, we have envisioned the possibility of shifting the widely documented reactivity of allyl compounds CH_2=$CHCH_2X$ in carbonylation reactions, which leads to β,γ-unsaturated carbonyl compounds (Scheme 1a), towards the bis-alkoxycarbonylation process (Scheme 1c). This uncommon reactivity would lead to the synthesis of succinates bearing a CH_2X substituent in 2-position, that are biologically active molecules[28] and useful intermediates for the synthesis of lactones,[29] γ-butyrolactones[30] and lactams,[31] depending on the functional group X. Therefore, we started to study the reactivity of allyl substrates with the aim to develop an efficient and selective bis-alkoxycarbonylation process.

Results and Discussion

We started our investigation on the bis-alkoxycarbonylation of the allyl substrates CH_2=$CHCH_2X$, using the allyl acetate as olefin benchmark and applying a catalytic system similar to that previously used by us for the carbonylation of acrylic esters and amides.[22c] The catalyst is generated *in situ* by mixing $Pd(TFA)_2$ and the bis(2,6-dimethylphenyl)butane-2,3-diimine ligand **1a**. The reaction proceeds employing *p*-benzoquinone (*p*-BQ) as the oxidant, and methanol as the main solvent and nucleophile, under 4 bar of carbon monoxide at room temperature. Under these reaction conditions, the desired bis-alkoxycarbonylated dimethyl 2-(acetoxymethyl)succinate product **3aa** was formed in 33% yield together with the symmetric trimethyl propane-1,2,3-tricarboxylate **4aa** (37%) and other minor unidentified species (29%) (Table 1, entry 1).[32] Compound **4aa** comes probably from the well-known substitutive carbonylation pathway, which pass through the formation of a π-allylpalladium intermediate to give a β,γ-unsaturated alkoxycarbonylated compound,[5,7] which is then bis-alkoxycarbonylated on the olefinic double bond, under the same reaction conditions. Usually, a catalytic amount of *p*-toluenesulfonic acid (*p*-TSA) improves the bis-alkoxycarbonylation process, as the acid contributes to create a free coordination site on the metal center[33] and accelerates the oxidation of Pd(0) to Pd(II)

Table 1. Screening of the conditions in the bis-methoxycarbonylation of the allyl acetate.



Entry[a]	Conversion [%][b]	Yield [%][b]				Other species [%][b]
		3aa	**4aa**	**5**	**6aa**	
1	100	33	37	0	2	29
2[c]	100	5	0	95	0	0
3[d]	100	57	22	0	4	18
4[d,e]	100	46	25	0	2	28
5[d,f]	91	63	24	0	5	8
6[d,g]	100	30	43	0	2	24
7[d,h]	95	20	55	0	6	19

[a] Reaction performed in autoclave at P_{CO} = 4 bar, with allyl acetate **2a** (2 mmol-scale), $Pd(TFA)_2$ 2 mol%, ligand **1a** 2.2 mol%, using 1.5 equiv. of *p*-BQ, in 7:1 MeOH/THF (0.5 M) as the reaction medium, for 67 h at 20 °C. [b] Determined by ^{1}H NMR analysis of the reaction crude. [c] Reaction performed with 5 mol% of *p*-TSA. [d] Reaction performed with 2 mol% of *p*-TSA. [e] Reaction performed with 3 equiv. of *p*-BQ. [f] Olefin concentration = 0.25 M. [g] Temperature = 55 °C. [h] CO pressure = 1 atm.

promoted by *p*-BQ.[34] Unfortunately, in our conditions, the addition of 5 mol% of *p*-TSA·H_2O (entry 2) resulted in the total conversion of the starting olefin into the corresponding allyl alcohol and its methyl ether (products **5**), which was probably obtained by acid-catalyzed transesterification of **2a** with MeOH. In this case, only traces of **3aa** were detected, likely due to the excessive amount of water in the reaction mixture, deriving from both the monohydrated acid and the etherification of the formed allyl alcohol, which inhibits the catalytic system.[21c]

Gratifyingly, reducing the quantity of *p*-TSA·H_2O to 2 mol% a total different scenario was found, and **3aa** became the major product (57%), over a complete conversion of **2a** (entry 3). Therefore, we proceeded our screening using 2 mol% *p*-TSA·H_2O as acidic additive. Other changes, such as doubling the amount of oxidant (entry 4), decreasing the concentration of the starting alkene (entry 5), rising the temperature to 55 °C (entry 6) and reducing the CO pressure (entry 7) did not lead to a significant improvement in **3aa** yield. Remarkably, the symmetric triester **4aa** became the main product by both increasing the temperature or decreasing the CO pressure (Table 1, entries 6 and 7).

In addition, from a screening on palladium (II) counterions, the following activity scale emerged: TFA > OAc ≫ OTf ≈ Cl, confirming that $Pd(TFA)_2$ is the best palladium salt (see *Supporting Information*, Table S1, page S2).

Regarding the ligand, in our previous studies,[22] we observed that the presence of *ortho*-disubstitution on the aromatic rings of the aryl α-diimine ligands, having a DAB (1,4-diaryl-2,3-diazabutadiene) or a BIAN (bis(aryl)acenaphthenequinonediimine) skeleton, could favor the achievement of high yields and selectivities in bis-alkoxycarbonylation reactions. Thus, the aryl α-diimine ligands depicted in Figure 1 were tested, and the results obtained are shown Table 2.

Changing the ligand **1a** with the BIAN ligand **1b**, compounds **3aa** and **4aa** were obtained in a 1:1 ratio (35% each, entry 2, Table 2). On the other hand, utilizing the ligand **1c**,

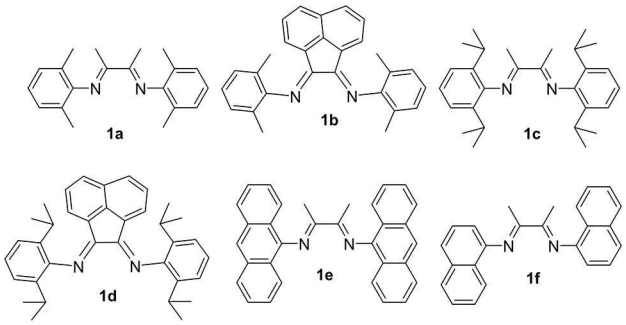


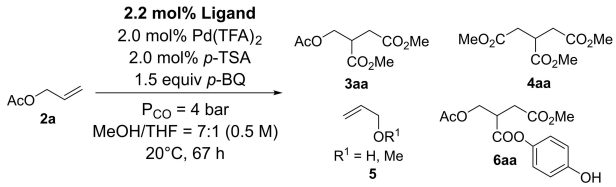
Figure 1. List of aryl α-diimine ligands.

bearing bulky isopropyl groups on the aromatic rings, an olefin conversion of 77% was achieved, but only 16% of **3aa** was formed, together with 13% of **4aa** (entry 3). Interestingly, changing the backbone of **1c** with an acenaphthene moiety (ligand **1d**), still an incomplete conversion was observed but the amount of **3aa** was doubled (entry 4). With the 9-antracenyl α-diimine ligand **1e**, a complete conversion was obtained, with 56% of **3aa** isolated yield (entry 5). This result is similar to that with ligand **1a** (entry 1), however, in this case the distribution of the other products is completely different. Indeed, with **1a** a higher amount of product **4aa** was formed (22%), while with **1e** the amount of **4aa** was significantly lower (7%), being the percentage of the unidentified by-products higher. With the naphthyl ligand **1f**, only 20% of carbonylated product **3aa** was detected, confirming the importance of a double *ortho*-substitution on the aromatic rings of the ligand (entry 6).

From all the results reported so far, it appears that the maximum amount of **3aa** reached is around 50%. We assumed that the formation of by-products could be facilitated by the presence of MeOH, which, owing to its nucleophilicity, can easily promote undesired reactions.

Therefore, other alcohols were tested as nucleophiles and as solvent using the best performing ligands **1a** and **1e** (Table 3).

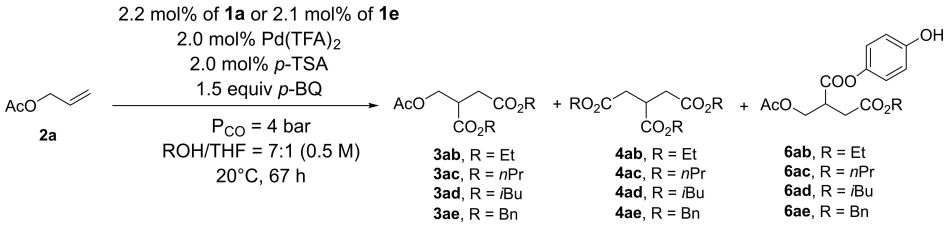
Table 2. Effect of the ligand in the bis-methoxycarbonylation of the allyl acetate.



Entry[a]	Ligand	Conversion [%][b]	Yield [%][b]				Other species [%][b]
			3aa	**4aa**	**5**	**6aa**	
1[c]	**1a**	100	57	22	0	4	18
2	**1b**	85	35	35	20	trace	10
3	**1c**	77	16	13	33	6	31
4	**1d**	84	33	8	13	5	41
5	**1e**	100	57[d]	7	0	4	32
6	**1f**	50	20	18	21	6	35

[a] Reaction performed in autoclave at P_{CO} = 4 bar, with allyl acetate **2a** (2 mmol-scale), $Pd(TFA)_2$ 2 mol%, ligands **1a**–**1f** 2.2 mol%, using 2 mol% of *p*-TSA and 1.5 equiv. of *p*-BQ, in 7:1 MeOH/THF (0.5 M) as the reaction medium, for 67 h at 20 °C. [b] Determined by ^{1}H NMR analysis of the reaction crude. [c] Data from Table 1, entry 3. Reported here for comparison. [d] Isolated yield of **3aa** after column chromatography = 56 %.

Table 3. Effect of the alcohols in the bis-alkoxycarbonylation of the allyl acetate.



Entry[a]	Ligand	ROH	Conversion [%][b]	Yield [%][b]			Other species [%][b]
				3	**4**	**6**	
1[c]	**1a**	EtOH	100	60 (58)	9	8	18
2	**1a**	*n*PrOH	100	56	10	12	22
3[c]	**1a**	*i*BuOH	100	40 (38)	15 (14)	20 (16)	25
4	**1a**	BnOH	100	47	23	7	22
5	**1e**	EtOH	100	65	11	15	8
6	**1e**	*n*PrOH	100	58	13	21	8
7	**1e**	*i*BuOH	100	48	10	28	14
8	**1e**	BnOH	100	80	7	8	6
9[d]	**1e**	BnOH	100	53	17	7	24
10[e]	**1e**	BnOH	>98	43	19	4	34

[a] Reaction performed in autoclave at P_{CO} = 4 bar, with allyl acetate **2a** (2 mmol-scale), $Pd(TFA)_2$ 2 mol%, ligand **1a** 2.2 mol% or ligand **1e** 2.1 mol%, using 2 mol% of *p*-TSA and 1.5 equiv. of *p*-BQ, in 7:1 MeOH/THF (0.5 M) as the reaction medium, for 67 h at 20 °C. [b] Determined by ^{1}H NMR analysis of the reaction crude. [c] Isolated yields after column chromatography are reported in brackets. [d] Olefin concentration = 0.25 M. [e] CO pressure = 1 atm.

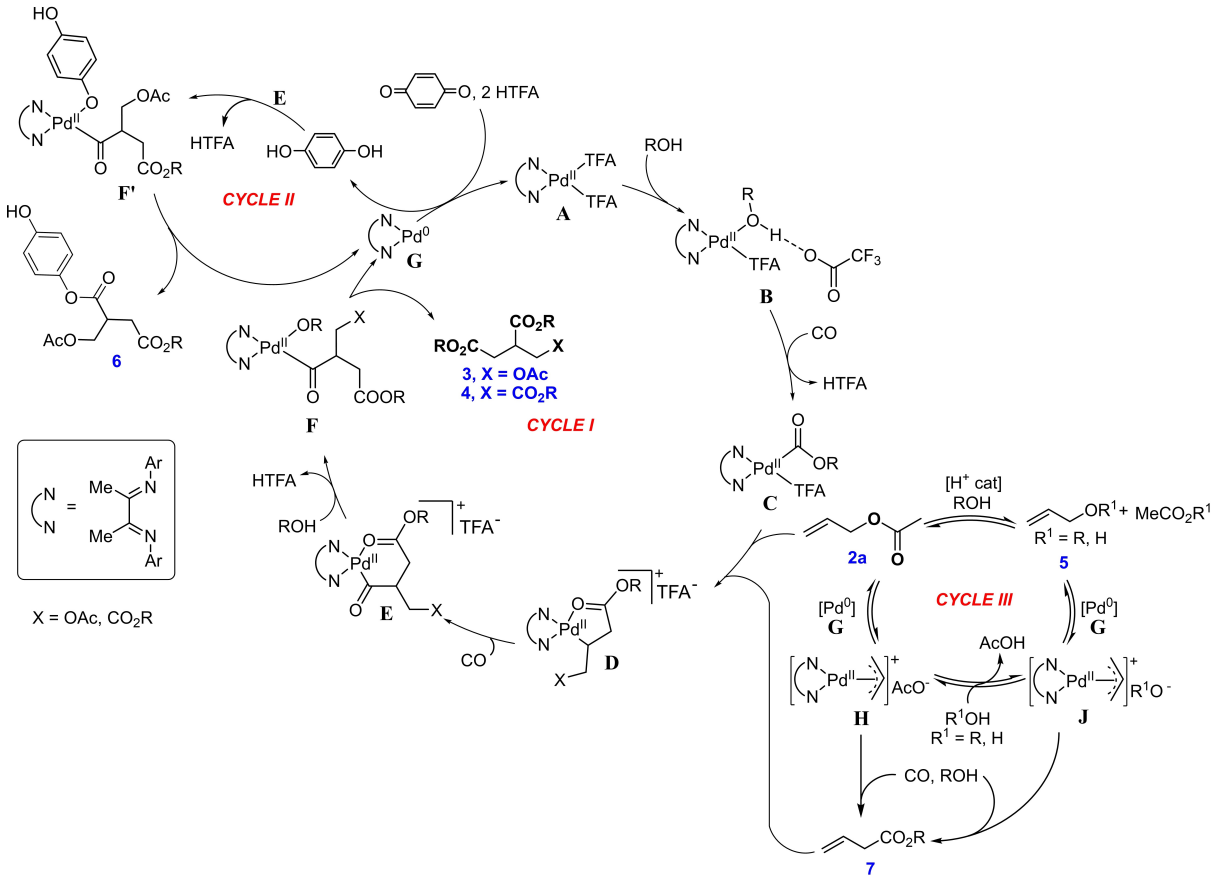
Using EtOH in presence of ligand **1a**, the desired product **3ab** was obtained with 58 % of isolated yield, **4ab** and **6ab** being present in 1:1 ratio and the remaining 20 % consisted of other unidentified minor compounds (Table 3, entry 1). Specifically, product **6ab** derives from the ability of hydroquinone, generated by the reduction of the *p*-benzoquinone, to act as nucleophile. Similar results were observed with *n*-propanol (entry 2), while with isobutanol (entry 3) a slight increase in the quantity of by-products was detected, together with a low isolated yield of **3ad** (38 %). Interestingly, when benzyl alcohol was used, an increase in the amount of **4ae** and a decrease in the amount of **6ae** was noted (entry 4) and the distribution of the products was in line with that found with MeOH (Table 1, entry 3). However, for all the other alcohols, employing ligand **1a**, a general reduction of the symmetric products **4** was highlighted, confirming that the use of MeOH negatively influences the selectivity. Switching to the ligand **1e**, better results were obtained with EtOH, *n*PrOH and *i*BuOH, observing a general reduction of unidentified species together with a slight increase in the desired product **3** (Table 3, entries 5–7). The main by-product was the bis-carbonylated compound **6**, which could be found up to 28 %. Finally, using BnOH in combination with the ligand **1e**, the quantity of the desired product **3ae** rose up to 80 %, with all by-products being limited to 20 % (entry 8). The reduction of both olefin concentration and CO pressure caused a significant drop in **3ae** yield (Table 3, entries 9 and 10).

From Table 3 it is evident that both the ligand and the alcohol play a key role in determining the selectivity of the reaction. In particular, ligand **1e** reduces the formation of **4**

(entry 8 *vs* entry 4 of Table 3 and entry 5 Table 2 *vs* entry 3 Table 1) and of unidentified minor products with alcohols other than MeOH (Table 3, entries 5–8). Moreover, the formation of **6** is considerably reduced in the presence of benzyl alcohol (Table 3 entry 8), suggesting that the steric hindrance of the nucleophile is relevant in this transformation.[22b]

With all this data in hand, in order to explain the performance of the reaction and the distribution of the obtained products, a catalytic cycle is proposed as shown in Scheme 2. The actual catalyst is the Pd(II) square planar complex (N–N)Pd-$(TFA)_2$ **A** that features the bidentate aryl α-diimine ligand and two trifluoroacetate groups.[22b,35] Complex **A** reacts with the alcohol allowing the formation of the intermediate **B**, where the displaced TFA^- anion interacts with the alcohol linked to the palladium through an hydrogen bonding.[36] This facilitates the formation of the alkoxycarbonyl-palladium complex **C**, in which the first molecule of CO is inserted.[37] The subsequent coordination and insertion of allyl acetate **2a** in complex **C** produces the 5-membered palladacycle **D**[38] and a second CO insertion leads to the formation of the 6-membered palladacycle **E**.[39] This latter complex can be in equilibrium with other open-chain species, bearing the TFA or a CO molecule linked to the Pd, in place of the Pd–O bond.[21c,40] Thereafter, a nucleophilic attack of the alcohol on the metal center, again assisted by the trifluoroacetate anion, evolves into the alkoxy/acyl-Pd intermediate **F**. If, on the other hand, hydroquinone acts as a nucleophile on intermediate **E**, the **F′** complex is formed (Scheme 2, cycle II). In both cases, alkoxy/acyl-palladium intermediates **F** and **F′** undergo reductive elimination giving the desired product **3** and by-product **6**, respectively. From Table 3 it appears that the amount of product **6**, deriving from intermediate **F′**, rises as the steric hindrance of the used alcohol increases. The formation of the succinic product in bis-alkoxycarbonylation reactions has been usually associated with an alcoholysis[21c,33,41] of the Pd–CO bond in the intermediate **E** to give the carbonylated product and a Pd-hydride complex. The latter, after reductive elimination, gave a Pd^0 species, which was re-oxidized by the benzoquinone.[34,42] However, in a recent study on an analogous process, we have shown through a theoretical study,[36] that the Pd^0 complex is more likely formed by means of a direct reductive elimination on an alkoxy/acyl-palladium complex of type **F**, hence the formation of a Pd–H complex can be ruled out, at least under our conditions.

As can be seen in Scheme 2, also the symmetric by-product **4** derives from a bis-alkoxycarbonylation reaction. In particular, the oxidative addition of the allyl acetate to Pd^0 gives the π-allylpalladium acetate intermediate **H**[13,43] (Scheme 2, cycle III), which can be monocarbonylated, under the reaction conditions, to form the alkyl 3-butanoate product **7**.[7] The latter can enter Cycle I, accounting for the formation of the trycarboxylate



Scheme 2. Proposed catalytic cycle for the bis-alkoxycarbonylation of allyl acetate **2a** (Cycle I), together with possible envisioned pathways for the formation of the observed by-products (Cycle II and Cycle III). X = OAc when olefin **2a** is inserted; X = CO_2R when olefin **7** is inserted.

product **4**. Moreover, in presence of a large excess of ROH, a ligand exchange on the allylpalladium complex **H** can take place affording intermediate **J**,[13,43] in which the acetate is replaced by an alkoxy group. This intermediate can as well be carbonylated to form again the β,γ-unsaturated carbonyl compound **7**.[10,16] On the other hand, the η^3-allylpalladium complex **J** can also be generated by oxidative addition of the allyl compounds **5** to Pd^0.[10,13] Compounds **5** in turn can be obtained by methanolysis of the allyl acetate **2a**, *via* acid catalysis, or by reductive elimination on complex **J** (Scheme 2, Cycle III). Although **7**, deriving from **2a** or **5**, was not directly detected in the reaction mixture, it has been demonstrated that tricarboxylate products **4** can be generated from carbonyl compounds **7** *(vide infra)*.

Scheme 2 helps to rationalize the data reported in Tables 1–3. In the presence of the highly nucleophilic MeOH, the yield of **4**, that comes from **7**, is generally higher, suggesting that reactions involved in Cycle III become particularly favored when methanol is used as nucleophile. On the other hand, a reduction in the amount of **4** has been observed with all the other alcohols (Table 3). Furthermore, it is important to note that, regardless of the alcohol considered, the direct bis-alkoxycarbonylation of the allyl acetate **2a**, in the presence of ligand **1e**, is highly preferred, being the sum of the quantities of products **3** and **6** around 80% of the total conversion (Table 3, entries 5–8). This might suggest that ligand **1e** inhibits the formation of the other by-products, speeding up the bis-alkoxycarbonylation process. To prove this, we have performed DFT calculations evaluating the energies associated with the formation of the allyl-palladium intermediate **H** from the Pd^0 complex **G** and olefin **2a**, using both ligand **1a** and **1e** (assuming benzyl alcohol as the solvent). From this study resulted that the Δ_rG° relative to the formation of complex **H** with the ligand **1a** is about 20 kJ/mol lower than that with ligand **1e** (see *Supporting Information*, page S3). Therefore, with **1e**, the Cycle III of Scheme 2 is less favored, thus indirectly promoting the Cycle I and explaining the observed preference for the production of both carbonylated products **3** and **6**.

However, only when benzyl alcohol is used, the amount of **6ae** formed is negligible (Table 3, entry 8). To explain this interesting effect, we focused our attention on the results obtained with the BnOH and the *i*BuOH in presence of the ligand **1e** (Table 3, entries 7 and 8). With benzyl alcohol the ratio **3:6** is 10, while with isobutanol this ratio is 1.7, being the product **6** present in larger amount. Since the same quantity of hydroquinone is always present in the reaction mixture, the lower amount of product **3** observed with *i*BuOH indicates that, with this alcohol, Cycle I is slightly less favored, resulting in an increase of product **6**. Consequently, assuming a 2,1-insertion of the olefin in the intermediate **C**[18,22c] and the fact that the hydroquinone can interact only during the second nucleophilic attack of the alcohol, on intermediate **E**,[22b] the effect of the alcohols have to be found at the level of Cycle I, in particular within the steps from **E** to **G** (Scheme 2). Therefore, additional DFT calculations were performed to determine the energies of the intermediates and transition states from **E** to **G**, utilizing the actual catalyst structure and both benzyl and isobutyl alcohols.

Complex **E** resulted to be the most stable intermediate of the whole catalytic sequence,[36] and its opening is endoergonic for both the alcohols considered. However, since the alcohol is also the solvent, its large excess can shift the equilibrium towards the complex **K**, in which the alcohol, linked to the palladium, is still protonated (Scheme 3).

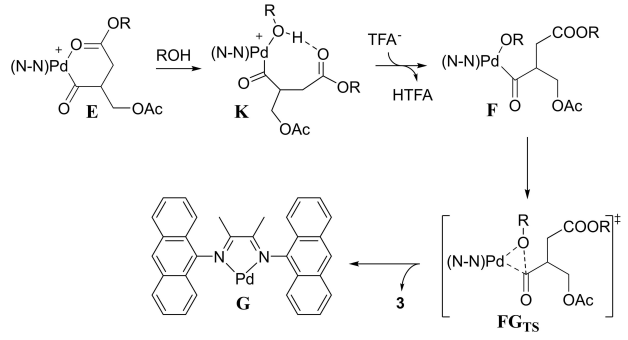
Intermediate **K** features an internal H-bond between ROH and the first inserted CO_2R group for both alcohols considered. The deprotonation of the coordinated alcohol in complex **K** is mediated by the trifluoroacetate anion, as occurred in intermediate **B** (Scheme 2), and it was found barrierless at the computational level adopted in the present work. The resulting alkoxy/acyl-palladium complex **F** evolves giving the expected succinic product **3** and the Pd^0 complex **G**, passing through the transition state $\mathbf{FG_{TS}}$. The structure of the latter allows appreciating the formation of the new C–O bond between the acyl and the alkoxy groups (see *Supporting Information*, Table S2, page S5). Excluding the final reductive elimination, all steps are endoergonic for the two alcohols considered (Figure 2).

In Figure 3 are depicted the structures of complexes **F** calculated for BnOH (left) and *i*BuOH (right), which are oriented in order to appreciate the different dihedral angle (θ) formed by the anthracenyl rings plane and the palladium coordination plane (see *Supporting Information* for details, pages S5–S6).

In the case of isobutanol, the steric hindrance of the *i*Bu group forces the anthracenyl rings in a position almost perpendicular to the Pd coordination plane ($\theta_{1,iBuO} = 78.35°$), resulting in an increase of the energy in complex **F–*i*BuOH** (72.5 kJ/mol). On the other hand, with BnOH, the anthracenyl rings from the same side of the less bulky OBn group, can orient themselves less perpendicularly with respect to the Pd coordination plane ($\theta_{1,BnO} = 68.41°$). This conformation, being less constrained, resulted to be at lower energy (54.2 kJ/mol).

Moreover, since the orientation of anthracenyl rings of the diimine ligand in complex **F–BnOH** is close to that of the transition state relative to the reductive elimination step ($\mathbf{FG_{TS}}$), the energy cost to reach the TS is lower respect to complex **F–*i*BuOH** (30.9 kJ/mol *vs* 37.8 kJ/mol).

Indeed, for BnOH to pass from **F** to $\mathbf{FG_{TS}}$, the sum of the dihedral angles ($\theta_1 + \theta_2$) changes by only 7.6°, while with the



Scheme 3. Computed steps of the catalytic cycle: from **E** to **G**. R = Bn or *i*Bu.

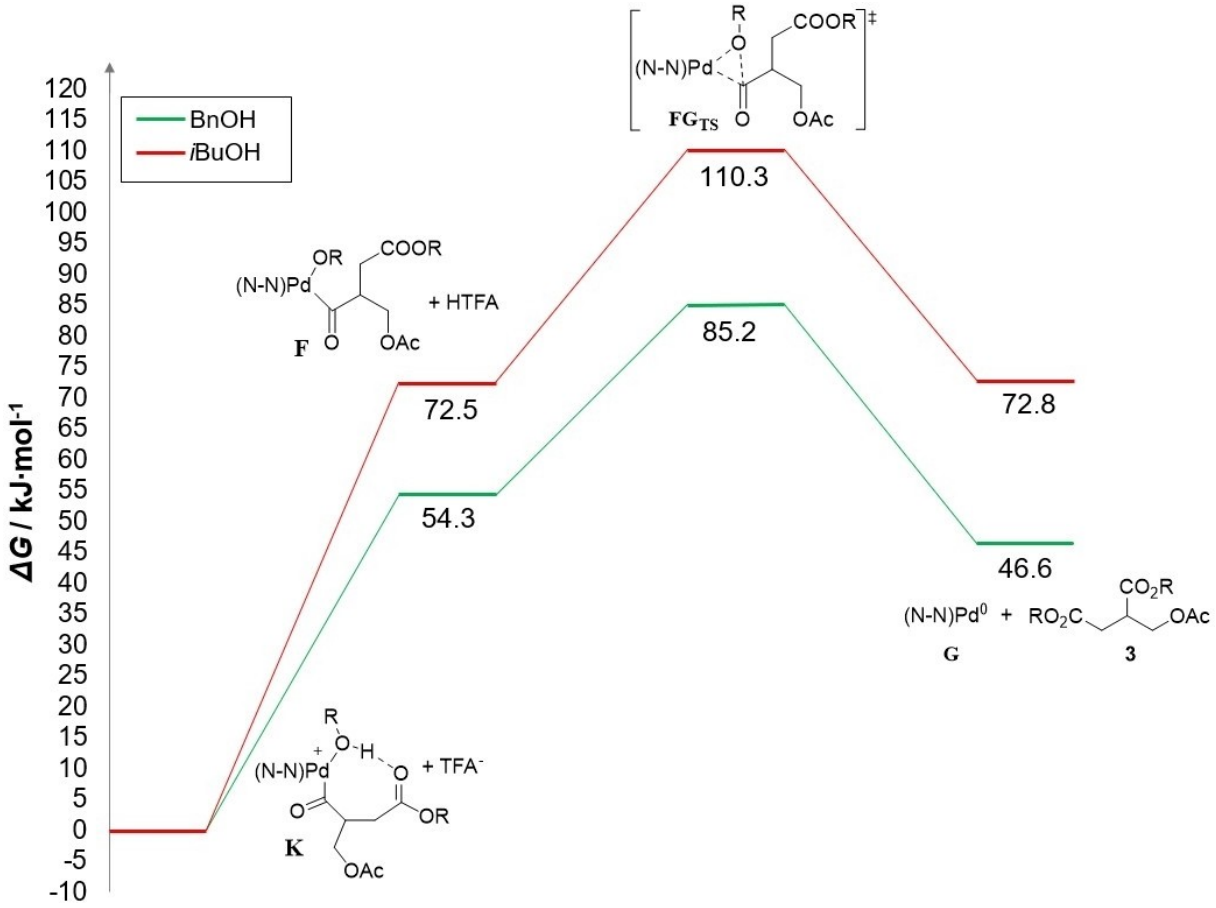


Figure 2. Energy profile (kJ/mol) for the final part of the catalytic cycle (from intermediate **K** to product **3**).

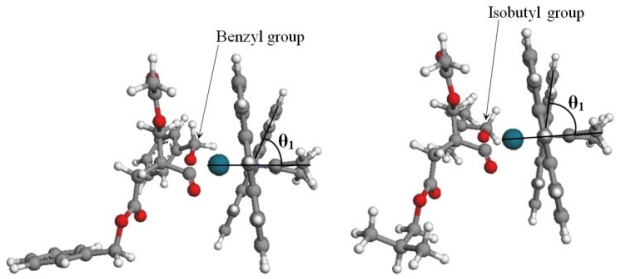


Figure 3. Computed structure of intermediates **F**—**BnOH** (left) and **F**—***i*BuOH** (right). θ_1 = dihedral angle calculated between the N–Pd–N plane and the plane containing the anthracenyl rings that are *trans* respect to the Pd–C bond.

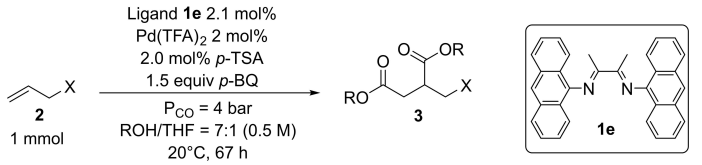
*i*BuOH this rearrangement is 17.5° (see *Supporting Information*, Table S4, page S6).

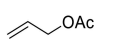
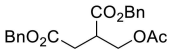
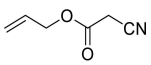
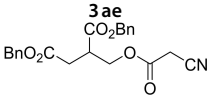
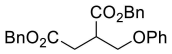
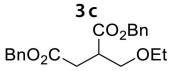
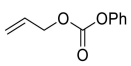
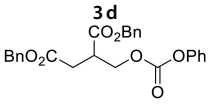
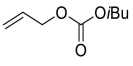
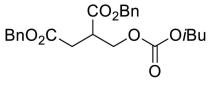
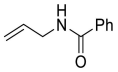
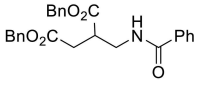
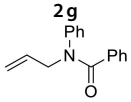
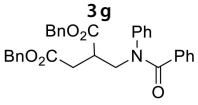
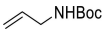
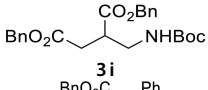
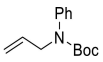
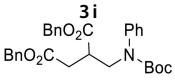
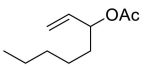
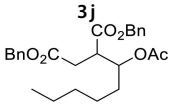
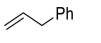
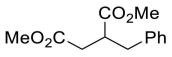
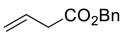
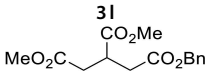
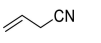
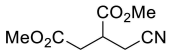
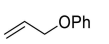
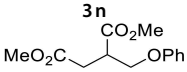
For all these reasons, utilizing BnOH the last part of the reaction is favored by 25.1 kJ/mol respect to isobutanol (Figure 2). No major differences between all the other investigated intermediates with the two alcohols were highlighted.

Therefore, an easier formation of the product **3** and the Pd^0 complex **G** is supposed to occur with BnOH, while with *i*BuOH this final step is more endoergonic, allowing the hydroquinone to react forming a higher amount of **6** (Table 3, entry 7). With EtOH and *n*PrOH a similar behavior to that observed with isobutanol can be foreseen, although the quantity of **6** is lower (Table 3, entries 5 and 6), probably because Et and *n*Pr are less bulky substituents and therefore smaller effects on the orientation of the anthracenyl rings can be expected.

Summarizing, ligand **1e** strongly favors the direct bis-alkoxycarbonylation reaction of **2a**, to form both **3** and **6**, hindering the formation of the π-allylpalladium intermediate. Moreover, **1e** in combination with BnOH reduces the amount of by-product **6** thanks to the easy formation of complex **F** and to its subsequent easy reductive elimination, which is due to a more favorable orientation of the anthracenyl rings. All these combined effects result in an increase in the amount of the desired bis-alkoxycarbonylated product **3** (Table 3, entry 8). We then applied the optimized conditions to different classes of allylic compounds (Table 4). The succinic product **3ae**, derived from the allyl acetate **2a**, was isolated with a yield of 82% (Table 4, entry 1). To the best of our knowledge, this is the first example of bis-alkoxycarbonylation of an allyl acetate to the corresponding succinic derivative, having the acetate group retained at the end of the reaction. Starting from the allyl 2-cyanoacetate **2b**, the result was less satisfactory, probably due to partial inactivation of the catalyst caused by the coordinating

Table 4. Scope of the bis-alkoxycarbonylation of allyl compounds.



Entry[a]	Olefin **2**	ROH	Product **3**	Yield [%][b]
1	 **2a**	BnOH	 **3ae**	82
2	 **2b**	BnOH	 **3b**	52
3	 **2c**	BnOH	 **3c**	86
4	 **2d**	BnOH	 **3d**	82
5	 **2e**	BnOH	 **3e**	56 (91)[e]
6	 **2f**	BnOH	 **3f**	58 (93)[e]
7	 **2g**	BnOH	 **3g**	80 (83)[e]
8	 **2h**	BnOH	 **3h**	82
9	 **2i**	BnOH	 **3i**	56 (88)[e]
10	 **2j**	BnOH	 **3j**	63
11	 **2k**	BnOH	 **3k**	76
12[c,d]	 **2l**	MeOH	 **3l**	98
13[c,d]	 **2m**	MeOH	 **3m**	87
14[c,d]	 **2n**	MeOH	 **3n**	50 (55)[e]
15[c,d]	 **2c**	MeOH	 **3ca**	74

[a] Reaction performed in autoclave at P_{CO} = 4 bar, with olefins **2a**–**2n** (1 mmol-scale), $Pd(TFA)_2$ 2 mol%, ligand **1e** 2.1 mol%, using 2 mol% of *p*-TSA and 1.5 equiv. of *p*-BQ, in 7:1 BnOH/THF (0.5 M) as the reaction medium, for 67 h at 20 °C. [b] Isolated yield after column chromatography. [c] 2 mmol of starting olefin were utilized. [d] MeOH was used as alcohol and **1a** as ligand. [e] The conversion, when incomplete, is reported in brackets.

CN group (entry 2).[22c,36,44] It is worth to mention that when the same reaction is performed with ligand **1a** in the presence of MeOH, no trace of the expected bis-methoxycarbonylated compound was detected. Other than allyl esters, also allyl ethers could be efficiently utilized as substrates, in fact the bis-alkoxycarbonylation of the (allyloxy)benzene **2c** (entry 3) and 3-ethoxyprop-1-ene **2d** (entry 4) gave the desired products **3c** and **3d** with 86% and 82% isolated yields, respectively.

Remarkably, the process could be successfully applied also to allyl carbonates. Indeed, allyl carbonates are usually synthesized specifically to facilitate the formation of the η^3-allylpalladium intermediate,[5] making the use of these substrates very difficult to achieve our goal. Therefore, the feasibility of the bis-alkoxycarbonylation of allyl carbonates clearly demonstrates the efficiency of our catalytic system, being able to provide products **3e** (entry 5) and **3f** (entry 6) in satisfactory yields.

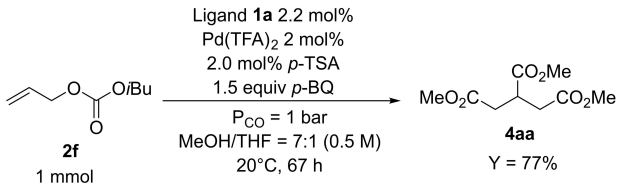
Although allyl thioesters and allyl sulfides were not reactive under our reaction conditions (see *Supporting Information*, Table S5, page S58), the developed method proved to be efficient even using allyl amides as substrates. In fact, the succinic products **3g** and **3h** were isolated in 80% and 82% yields respectively (entries 7 and 8). Gratifyingly, also the *N*-Boc protected allyl amines **2i** and **2j** have been carbonylated, obtaining products **3i** and **3j** with satisfactory yield (entries 9 and 10).

Notably, up to now, the bis-alkoxycarbonylation of allyl carbonates, allyl amides and protected allylic amines have never been reported. A C1 alkyl substitution on allyl acetate does not affect the reactivity and the product **3k** has been achieved with 76% yield (entry 11). Hence, as various functional groups are tolerated, the reaction proved to be quite general.[45]

We also tested allyl compounds $CH_2{=}CHCH_2X$ where X is an electron-withdrawing group, such as $-CO_2Bn$ or $-CN$, and the simple allylbenzene. These substrates are less prone to undergo oxidative addition on Pd^0 to form a π-allylpalladium intermediate unless a C–H activation of the $CH_2(sp^3)$ is involved. Therefore, for these carbonylation reactions we have safely used MeOH as nucleophile together with the easily synthesizable ligand **1a**. We successfully realized the bis-methoxycarbonylation of the allylbenzene **2l**[46] (Table 4, entry 12) and of the benzyl 3-butenoate **2m** (entry 13), achieving excellent yields and complete selectivity of the corresponding products **3l** and **3m**. In particular, the bis-alkoxycarbonylation of **2m** opened the possibility to successfully bis-alkoxycarbonylate β,γ-unsaturated carbonyl compounds, under our reaction conditions. This result confirms that the formation of the symmetric by-product **4** actually passes through intermediate **7**, supporting the proposed catalytic cycle (see Scheme 2). Surprisingly, product **3n** can be obtained in synthetically useful yield, despite the presence of the CN group (entry 14).[22c,36,44]

Even though a slightly better result was reached with BnOH (Table 4, entry 3), a good product yield was obtained with the allyl ether **2c** also using MeOH as solvent and **1a** as ligand (entry 15). This may indicate that allyl ethers are not so prone to form allyl palladium intermediates.

Finally, since the symmetric triester **4aa** could be interesting from a synthetic point of view,[47] on the base of the results described so far, we have identified a catalytic system to selectively obtain this compound. Specifically, we carried out a reaction, employing the best conditions to promote the formation of a π-allylpalladium intermediate, that foresees the use of i) the allyl carbonate **2f** as substrate, ii) MeOH as solvent and iii) **1a** as ligand, under 1 bar of CO pressure,[48] obtaining the desired symmetric triester **4aa** in 77% isolated yield (Scheme 4).



Scheme 4. Bis-methoxycarbonylation of the allyl carbonate **2f**.

Conclusion

In conclusion, an efficient and versatile method for the one-pot synthesis of 2-substituted succinates **3**, through Pd(II)-catalyzed oxidative bis-alkoxycarbonylation of allyl compounds $CH_2{=}CHCH_2X$ (X=OAc, $OC(O)CH_2CN$, OPh, OEt, OC(O)OPh, OC(O)O*i*Bu, N(H)C(O)Ph, N(Ph)C(O)Ph, N(H)Boc, N(Ph)Boc, Ph, CO_2Bn, CN) with preservation of the X group, has been developed.

In particular, using $Pd(TFA)_2$ as palladium source, *N*,*N*′-di(anthracen-9-yl)butane-2,3-diimine **1e** as ligand, and *p*-benzoquinone as oxidant, in the presence of benzyl alcohol as nucleophile and as the solvent, a good chemoselective process toward the formation of benzyl succinates has been achieved under mild conditions. The possible competitive and well-established substitutive monocarbonylation (leading to β,γ-unsaturated carbonyl compounds through the formation of a π-allyl complex) was effectively prevented. Remarkably, the present methodology allows the selective activation of the olefinic double bond while preserving the functional group (X) of the allyl substrate, including the easily removable acetate and carbonate groups.

The observed experimental data were rationalized through a proposed catalytic cycle, corroborated by the identification and characterization of the most important products involved in the process, together with DFT calculations, which allowed understanding the reasons underlying this unusual kind of reactivity for allylic substrates.

From this study it emerges that the ligand **1e** disfavors the formation of the η^3-allylpalladium intermediate, boosting the bis-alkoxycarbonylation pathway. In addition, when BnOH is used together with ligand **1e**, the energies associated to the formation of the alkoxy/acyl-palladium complex **F** and to the final reductive elimination step, are lower, promoting the formation of the succinic product **3**. According to our calculations, this effect is justified by a more favorable orientation of the anthracenyl rings of the ligand.

The reaction was successfully applied to different classes of allyl compounds obtaining the expected succinates with moderate to good yields. Notably, the first examples of bis-alkoxycarbonylation of allyl amides, *N*-Boc protected allyl amines and allyl carbonates which are known to easily form the undesired π-allylpalladium intermediate, have been reported, further increasing the versatility of our developed method.

Experimental Section

All reactions were carried out under nitrogen atmosphere with dry solvents under anhydrous conditions, in a stainless steel autoclave, by using Schlenk technique. Reactions were monitored by ^{1}H NMR taking a direct sample of the crude mixture. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker Avance 400 spectrometer (^{1}H: 400 MHz, ^{13}C: 101 MHz), using $CDCl_3$ as solvent. Chemical shifts are reported in the δ scale relative to residual $CHCl_3$ (7.26 ppm) for ^{1}H NMR and to the central line of $CDCl_3$ (77.16 ppm) for ^{13}C NMR. ^{13}C NMR were recorded with ^{1}H broadband decoupling. The following abbreviations were used to explain the multiplicities: s = singlet, br = broad, d = doublet, t = triplet, q = quartet, p = pentet, dd = doublet of doublets, dt = doublet of triplets, app dq = apparent as doublet of quartets, m = multiplet. Coupling constants (*J*) are reported in Hertz (Hz). ESI-MS spectra were recorded on Waters Micromass ZQ 4000, using electrospray ionization techniques, with samples dissolved in MeOH. Carbon monoxide (Cp grade 99.99%) was supplied by Air Liquide. Caution: carbon monoxide is a toxic gas with potentially lethal action, therefore adequate precautions must be observed. The *p*-benzoquinone was purchased by Alfa Aesar and was filtered off a plug of silica gel washing with CH_2Cl_2, obtaining a yellow solid after drying the solution under vacuum. Pure compounds were isolated through flash column chromatography on silica gel 60 (40–60 μm, 230–400 mesh). Olefins **2a**, **2b**, **2l**, **2n** were purchased from Merck Sigma-Aldrich. Olefins **2c** and **2d** were purchased from Fluorochem. The olefin **2k** was purchased from TCI. The purchased olefins were filtered off a plug of neutral Al_2O_3 and used without further purification. Olefins **2e**–**2j** were synthesized as reported in the *Supporting Information* (pages S55–S57). The olefin **2m** was synthesized according to literature procedure.[49] Anhydrous THF was distilled from sodium-benzophenone and methanol was distilled from $Mg(OMe)_2$. Ethanol, *n*-propanol, isobutanol and benzyl alcohol were dried over molecular sieves (Alfa Aesar, 4 Å, 1–2 mm, beads). $Pd(TFA)_2$ was purchased by Flurochem, $Pd(PhCN)_2Cl_2$ and $Pd(OAc)_2$ were purchased from Merck Sigma-Aldrich. All other chemicals were purchased from Merck Sigma-Aldrich and used without further purification. The ligands **1a**–**1d** and **1f** were synthesized according to literature procedures,[41a] while the ligand **1e** was synthesized according to a procedure developed by our group.[35] All solid reagents were weighted in an analytical balance without excluding moist and air.

Computational Details: All DFT calculations have been performed using the ORCA 4.2.1 suite of quantum chemistry programs.[50] Geometries were optimized in vacuum using the Becke-Perdew functional[51] and the def2-TZVP basis.[52] Vibrational frequencies were then calculated at the optimized geometries to check the stability of the stationary points and to evaluate the vibrational contribution to free energies at 298 K. Final single point energy calculations at the previously optimized geometries were performed with the large def2-QZVPP basis[52] and the M06 functional,[53] with the inclusion of solvation effects through the SMD model[54] and of dispersion interactions.[55] The final energy of each structure, used to evaluate the relative free energies of the various products and intermediates, was built by summing the difference between the def2-TZVP electronic and free energies to the def2-QZVPP single point electronic energy.

Typical Procedure for the Bis-alkoxycarbonylation of Allyl Compounds: In a nitrogen flushed Schlenk tube, equipped with a magnetic stirring bar, the respective olefins **2a**–**2n** (1 mmol) and the alcohol ROH (1.75 mL) were added in sequence. The mixture was left under stirring for 10 min. In another nitrogen flushed Schlenk tube, equipped with a magnetic stirring bar, the $Pd(TFA)_2$ (6.6 mg, 0.02 mmol) and THF (0.25 mL) were added in sequence. After the mixture turned in a red/brown color (20 min), the ligand **1e** (9.2 mg, 0.021 mmol) was added. The mixture was left under stirring for 15 min, turning in a dark orange-brown color with a precipitate. The olefin solution and the formed catalyst were injected in sequence in a nitrogen flushed autoclave, equipped with a magnetic stirring bar, containing *p*-benzoquinone (162.3 mg, 1.5 mmol) and *p*-TSA·H_2O (3.8 mg, 0.02 mmol). After 5 min of stirring, the autoclave was flushed three times with CO and pressurized with 4 bar of carbon monoxide. The reaction was vigorously stirred at room temperature (20 °C) for 67 h. The autoclave was vented off, flushed with nitrogen and the crude was dried under reduced pressure and filtered off a plug of silica gel, washing with CH_2Cl_2/Et_2O 1:1. The solution was dried up in vacuum and the product was eventually obtained after column chromatography on silica gel (when BnOH is employed as alcohol, more than one column could be necessary to isolate the whole product pure).

Dimethyl 2-(acetoxymethyl)succinate (3aa) Following the general procedure, but using 2 mmol of the starting olefin, the compound **3aa** has been isolated by flash column chromatography on silica gel (petroleum ether/Et_2O = 80:20) together with 10% of **4aa** (**3aa** : **4aa** = 9:1, see *Supporting Information*, page S59), obtaining a colorless oil; overall yield: 63% (275 mg). R_f = 0.25 (petroleum ether/EtOAc = 8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.31 (dd, *J* = 11.2, 5.5 Hz, 1H), 4.27 (dd, *J* = 11.2, 5.7 Hz, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 3.18 (app dq, *J* = 8.1, 5.7 Hz, 1H), 2.81 (dd, *J* = 17.0, 8.2 Hz, 1H), 2.54 (dd, *J* = 17.0, 5.8 Hz, 1H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 171.9, 170.7, 63.8, 52.4, 52.1, 40.9, 32.8, 20.8. ESI-MS: m/z = 219 $[M+H]^+$.

Diethyl 2-(acetoxymethyl)succinate (3ab): Following the general procedure, but using the ligand **1a** and 2 mmol of the starting olefin, the compound **3ab** has been purified by flash column chromatography on silica gel (petroleum ether/Et_2O 85:15 to 80:20), obtaining a pale yellow oil; yield: 58% (285.7 mg). R_f = 0.17 (petroleum ether/Et_2O = 80:20). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.30 (d, *J* = 5.7 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.15 (d, *J* = 7.1 Hz, 2H), 3.17 (app dq, *J* = 8.2, 5.7 Hz, 1H), 2.80 (dd, *J* = 16.8, 8.2 Hz, 1H), 2.53 (dd, *J* = 16.8, 5.8 Hz, 1H), 2.04 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 171.4, 170.7, 63.9, 61.3, 61.0, 41.1, 33.1, 20.9, 14.3, 14.3. ESI-MS: m/z = 247 $[M+H]^+$.

Diisobutyl 2-(acetoxymethyl)succinate (3ad): Following the general procedure, but using ligand **1a** and 2 mmol of the starting olefin, the compound **3ad** has been purified by flash column chromatography on silica gel (petroleum ether/Et_2O = 90:10), obtaining a pale yellow oil; yield: 38% (229.8 mg). R_f = 0.34 (CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (dd, *J* = 11.2, 5.7 Hz, 1H), 4.30 (dd, *J* = 11.2, 5.5 Hz, 1H), 3.93 (dd, *J* = 10.6, 6.7 Hz, 1H), 3.89 (dd, *J* = 9.8, 6.6 Hz, 3H), 3.21 (app dq, *J* = 8.2, 5.6 Hz, 1H), 2.84 (dd, *J* = 16.9, 8.2 Hz, 1H), 2.55 (dd, *J* = 16.9, 5.7 Hz, 1H), 2.04 (s, 3H), 1.99–1.87 (m, 2H), 0.93 (d, *J* = 6.7 Hz, 6H), 0.92 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.9, 171.5, 170.7, 71.4, 71.2, 64.1, 41.1, 33.1, 27.83, 27.82, 20.9, 19.19, 19.18, 19.14, 19.12. ESI-MS: m/z = 303 $[M+H]^+$.

Triisobutyl propane-1,2,3-tricarboxylate (4ad): Following the general procedure, but using ligand **1a** and 2 mmol of the starting

olefin, the compound **4ad** has been purified by flash column chromatography on silica gel (petroleum ether/Et_2O = 90:10), obtaining a colorless oil; yield: 14% (96.4 mg). R_f = 0.5 (CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.88 (d, J = 6.5, 2H), 3.87 (d, J = 6.6, 4H), 3.29 (p, J = 6.6 Hz, 1H), 2.80 (dd, J = 16.7, 6.9 Hz, 2H), 2.63 (dd, J = 16.7, 6.4 Hz, 2H), 1.98–1.86 (m, 3H), 0.92 (d, J = 6.7 Hz, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 171.6, 71.4, 71.1, 37.7, 35.5, 27.8 (2 C), 19.20, 19.18. ESI-MS: m/z = 345 $[M+H]^+$.

1-(4-hydroxyphenyl) 4-isobutyl 2-(acetoxymethyl)succinate (6ad): Following the general procedure, but using ligand **1a** and 2 mmol of the starting olefin, the compound **6ad** has been purified by flash column chromatography on silica gel (CH_2Cl_2/Et_2O 97:3 to 95:5), obtaining a white solid; yield: 16% (108.3 mg). R_f = 0.59 (CH_2Cl_2/Et_2O = 80:20). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94–6.88 (m, 2H), 6.79–6.73 (m, 2H), 4.89 (br s, 1H), 4.49 (dd, J = 11.2, 5.5 Hz, 1H), 4.41 (dd, J = 11.2, 5.6 Hz, 1H), 3.91 (d, J = 6.6 Hz, 2H), 3.40 (app dq, J = 8.9, 5.5 Hz, 1H), 2.94 (dd, J = 17.0, 8.6 Hz, 1H), 2.67 (dd, J = 17.0, 5.4 Hz, 1H), 2.09 (s, 3H), 2.00–1.87 (m, 1H), 0.93 (d, J = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 171.1, 170.8, 153.6, 144.3, 122.5, 116.1, 71.3, 63.8, 41.3, 33.1, 27.8, 20.9, 19.21, 19.20. ESI-MS: m/z = 337 $[M-H]^-$.

Dibenzyl 2-(acetoxymethyl)succinate (3ae): Following the general procedure the compound **3ae** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc 98:2 to 80:20), obtaining a colorless oil; yield: 82% (303.7 mg). R_f = 0.32 (CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.29 (m, 10H), 5.17 (d, J = 12.3 Hz, 1H), 5.12 (d, J = 10.1 Hz, 1H), 5.09 (d, J = 10.1 Hz, 1H), 5.08 (d, J = 12.2 Hz, 1H), 4.34 (dd, J = 11.1, 5.6 Hz, 1H), 4.29 (dd, J = 11.1, 5.4 Hz, 1H), 3.26 (app dq, J = 8.4, 5.6 Hz, 1H), 2.90 (dd, J = 17.0, 8.4 Hz, 1H), 2.60 (dd, J = 17.0, 5.7 Hz, 1H), 1.96 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 171.2, 170.7, 135.69, 135.66, 128.72, 128.69, 128.49, 128.47, 128.42, 128.36, 67.1, 66.9, 63.8, 41.0, 33.1, 20.7. ESI-MS: m/z = 371 $[M+H]^+$.

Dibenzyl 2-((2-cyanoacetoxy)methyl)succinate (3b): Following the general procedure the compound **3b** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc 80:20 to 70:30), obtaining a pale yellow oil; yield: 52% (205.6 mg). R_f = 0.42 (petroleum ether/EtOAc = 75:35). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (m, 10H), 5.18 (d, J = 12.1 Hz, 1H), 5.13 (d, J = 14.3 Hz, 1H), 5.09 (d, J = 12.2 Hz, 2H), 4.48 (dd, J = 11.1, 5.5 Hz, 1H), 4.43 (dd, J = 11.1, 5.7 Hz, 1H), 3.33–3.26 (m, 1H), 3.24 (d, J = 19.2 Hz, 1H), 3.19 (d, J = 19.2 Hz, 1H), 2.91 (dd, J = 17.0, 7.5 Hz, 1H), 2.62 (dd, J = 17.0, 6.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 170.9, 162.6, 135.6, 135.5, 128.82, 128.77, 128.71, 128.67, 128.6, 128.5, 112.6, 67.4, 67.0, 65.9, 40.7, 32.9, 24.4. ESI-MS: m/z = 396 $[M+H]^+$.

Dibenzyl 2-(phenoxymethyl)succinate (3c): Following the general procedure the compound **3c** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc 95:5 to 93:7), obtaining a colorless oil; yield: 86% (347.8 mg). R_f = 0.88 (CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.22 (m, 12H), 6.99–6.93 (m, 1H), 6.87–6.82 (m, 2H), 5.18 (d, J = 12.4 Hz, 1H), 5.12 (d, J = 12.6 Hz, 2H), 5.09 (d, J = 12.3 Hz, 1H), 4.25 (dd, J = 9.2, 5.9 Hz, 1H), 4.21 (dd, J = 9.2, 4.8 Hz, 1H), 3.44–3.37 (m, 1H), 3.03 (dd, J = 17.0, 7.9 Hz, 1H), 2.80 (dd, J = 17.0, 5.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 171.6, 158.5, 135.81, 135.77, 129.6, 128.70, 128.67, 128.42, 128.37, 128.36, 128.2, 121.4, 114.8, 67.5, 67.0, 66.8, 41.9, 33.1. ESI-MS: m/z = 405 $[M+H]^+$.

Dibenzyl 2-(ethoxymethyl)succinate (3d): Following the general procedure the compound **3d** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 90:10), obtaining a pale yellow oil; yield: 82% (292.3 mg). R_f = 0.64 (petroleum ether/EtOAc = 90:10). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 10H), 5.17 (d, J = 12.4 Hz, 1H), 5.11 (d, J = 12.4 Hz, 1H), 5.09 (d, J = 12.4 Hz, 1H), 5.07 (d, J = 12.4 Hz, 1H), 3.65 (dd, J = 8.4, 4.4 Hz, 1H), 3.62 (dd, J = 8.4, 5.2 Hz, 1H), 3.46–3.39 (m, 2H), 3.23–3.15 (m, 1H), 2.88 (dd, J = 16.8, 8.4 Hz, 1H), 2.66 (dd, J = 16.8, 5.6 Hz, 1H), 1.12 (t, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 171.9, 136.02, 135.97, 128.7, 128.64, 128.37, 128.35, 128.3, 128.2, 70.2, 66.7 (2 C), 66.6, 42.3, 33.3, 15.1. ESI-MS: m/z = 357 $[M+H]^+$.

Dibenzyl 2-(((phenoxycarbonyl)oxy)methyl)succinate (3e): Following the general procedure the compound **3e** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 90:10), obtaining a colorless oil; yield: 56% (251.1 mg). R_f = 0.47 (petroleum ether/EtOAc = 80:20) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (m, 12H), 7.26–7.22 (m, 1H), 7.14–7.10 (m, 2H), 5.18 (d, J = 12.3 Hz, 1H), 5.14 (d, J = 12.4 Hz, 1H), 5.13 (d, J = 12.4 Hz, 1H), 5.09 (d, J = 12.3 Hz, 1H), 4.52 (d, J = 5.6 Hz, 2H), 3.37 (app dq, J = 7.7, 5.7 Hz, 1H), 2.97 (dd, J = 17.0, 7.8 Hz, 1H), 2.72 (dd, J = 17.0, 6.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.2, 171.1, 153.4, 151.1, 135.7, 135.5, 129.6, 128.8 (2 C), 128.52 (2 C), 128.46, 128.4, 126.3, 121.1, 67.6, 67.3, 67.0, 41.1, 32.9. ESI-MS: m/z = 449 $[M+H]^+$.

Dibenzyl 2-(((isobutoxycarbonyl)oxy)methyl)succinate (3f): Following the general procedure the compound **3f** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc 95:5 to 90:10), obtaining a pale yellow oil; yield: 58% (248.5 mg). R_f = 0.70 (CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.27 (m, 10H), 5.15 (d, J = 12.4 Hz, 1H), 5.11 (d, J = 12.7 Hz, 2H), 5.08 (d, J = 12.3 Hz, 1H), 4.42 (dd, J = 10.9, 5.5 Hz, 1H), 4.38 (dd, J = 10.9, 5.9 Hz, 1H), 3.88 (d, J = 6.7 Hz, 2H), 3.30 (app dq, J = 8.0, 5.7 Hz, 1H), 2.91 (dd, J = 17.0, 8.1 Hz, 1H), 2.67 (dd, J = 17.0, 5.7 Hz, 1H), 2.00–1.89 (m, 1H), 0.93 (d, J = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.4, 171.1, 155.1, 135.7, 135.6, 128.72, 128.70, 128.48, 128.45, 128.42, 128.3, 74.5, 67.2, 66.87, 66.85, 41.2, 32.9, 27.9, 19.0. ESI-MS: m/z = 429 $[M+H]^+$.

Dibenzyl 2-(benzamidomethyl)succinate (3g): Following the general procedure the compound **3g** has been purified by flash column chromatography on silica gel (CH_2Cl_2/Et_2O 99:1 to 95:5), obtaining a pale yellow oil; yield: 80% (346.5 mg). R_f = 0.26 (CH_2Cl_2/Et_2O = 95:5). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.3 Hz, 2H), 7.51–7.46 (m, 1H), 7.41–7.28 (m, 12H), 6.64 (s, 1H), 5.17 (d, J = 12.1 Hz, 1H), 5.10 (d, J = 12.2 Hz, 1H), 5.09 (d, J = 12.4 Hz, 1H), 5.05 (d, J = 12.3 Hz, 1H), 3.82–3.69 (m, 2H), 3.26–3.18 (m, 1H), 2.83 (dd, J = 16.9, 7.2 Hz, 1H), 2.74 (dd, J = 16.9, 5.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.3, 171.4, 167.5, 135.7, 135.6, 134.2, 131.7, 128.8, 128.7 (2 C), 128.6, 128.53, 128.48, 128.46, 127.0, 67.2, 66.9, 41.5, 40.6, 34.3. ESI-MS: m/z = 432 $[M+H]^+$.

Dibenzyl 2-((*N*-phenylbenzamido)methyl)succinate (3h): Following the general procedure the compound **3h** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 80:20), obtaining a white solid; yield: 82% (417.2 mg). R_f = 0.14 (petroleum ether/EtOAc = 80:20). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.25 (m, 10H), 7.23–7.08 (m, 8H), 7.02 (d, J = 7.7 Hz, 2H), 5.08 (d, J = 12.3 Hz, 1H), 5.03 (d, J = 12.3 Hz, 1H), 5.02 (d, J = 12.3 Hz, 1H), 4.95 (d, J = 12.3 Hz, 1H), 4.37 (dd, J = 13.7, 7.7 Hz, 1H), 4.17 (dd, J = 13.7, 6.2 Hz, 1H), 3.38–3.27 (m, 1H), 2.92 (dd, J = 17.1, 9.2 Hz, 1H), 2.69 (dd, J = 17.0, 4.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 171.3, 171.0, 143.0, 135.8, 135.7 (2 C), 129.8, 129.3, 128.8, 128.7, 128.6, 128.39 (2 C), 128.37, 128.3, 127.9, 127.8, 127.0, 67.0, 66.7, 51.1, 40.5, 34.2. ESI-MS: m/z = 508 $[M+H]^+$.

Dibenzyl 2-(((*tert*-butoxycarbonyl)amino)methyl)succinate (3i): Following the general procedure the compound **3i** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 84:16), obtaining a colorless oil; yield: 56% (239.4 mg). R_f = 0.56 (petroleum ether/EtOAc = 69:31). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.28 (m, 10H), 5.13 (d, J = 12.3 Hz, 1H), 5.09 (d, J = 12.3 Hz, 1H), 5.08 (d, J = 12.3 Hz, 1H), 5.05 (d, J = 12.3 Hz, 1H),

4.82 (br s, 1H), 3.42 (dd, J=6.4, 6.4 Hz, 2H), 3.14–3.06 (m, 1H), 2.78 (dd, J=16.8, 7.8 Hz, 1H), 2.63 (dd, J=16.8, 5.8 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.2, 171.4, 156.0, 135.8, 135.7, 128.74, 128.70, 128.5, 128.4 (2 C), 128.3, 79.7, 67.0, 66.8, 42.0, 41.5, 33.9, 28.5. ESI-MS: m/z=428 $[M+H]^+$.

Dibenzyl 2-(((*tert*-butoxycarbonyl)(phenyl)amino)methyl)succinate (3 j): Following the general procedure the compound **3 j** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc=84:16), obtaining a pale yellow oil; yield: 63% (317.3 mg). R_f=0.50 (petroleum ether/EtOAc=84:16). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.12 (m, 15H), 5.06 (d, J=12.3 Hz, 1H), 5.02 (d, J=12.3 Hz, 1H), 4.97 (d, J=12.4 Hz, 1H), 4.88 (d, J=12.4 Hz, 1H), 4.07 (dd, J=14.2, 6.9 Hz, 1H), 3.92 (dd, J=14.2, 6.9 Hz, 1H), 3.22–3.14 (m, 1H), 2.82 (dd, J=17.0, 9.1 Hz, 1H), 2.61 (dd, J=17.0, 4.8 Hz, 1H), 1.39 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 171.3, 154.8, 142.0, 135.8, 135.7, 129.0, 128.7, 128.6, 128.4 (2 C), 128.3 (2 C), 127.4, 126.6, 80.9, 66.9, 66.7, 50.8, 41.1, 33.7, 28.4. ESI-MS: m/z=504 $[M+H]^+$.

Dibenzyl 2-(1-acetoxyhexyl)succinate (3 k): Following the general procedure the compound **3 k** has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc=80:20), obtaining a colorless oil; yield: 76% (334.9 mg). R_f=0.48 (petroleum ether/EtOAc=80:20). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.29 (m, 10H), 5.26–5.20 (m, 1H), 5.12 (d, J=12.3 Hz, 1H), 5.11 (d, J=12.2 Hz, 1H), 5.06 (d, J=12.3 Hz, 1H), 5.05 (d, J=12.2 Hz, 1H), 3.16 (dt, J=10.5, 4.0 Hz, 1H), 2.90 (dd, J=17.0, 10.6 Hz, 1H), 2.54 (dd, J=17.0, 3.9 Hz, 1H), 1.93 (s, 3H), 1.61–1.50 (m, 1H), 1.49–1.40 (m, 1H), 1.32–1.16 (m, 6H), 0.85 (t, J=6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 171.8, 170.4, 135.80, 135.75, 128.71, 128.66, 128.6, 128.5 (2 C), 128.4, 73.2, 67.2, 66.8, 45.1, 32.2, 31.5, 31.4, 25.2, 22.6, 20.9, 14.1. ESI-MS: m/z=441 $[M+H]^+$.

1-benzyl 2,3-dimethyl propane-1,2,3-tricarboxylate (3 m): Following the general procedure, but using ligand **1 a** and 2 mmol of the starting olefin, the compound **3 m** has been purified by flash column chromatography on silica gel (petroleum ether/Et_2O 90:10 to 80:20), obtaining a pale yellow oil; yield: 87% (512.1 mg). R_f= 0.13 (petroleum ether/CH_2Cl_2=20:80). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.29 (m, 5H), 5.12 (s, 2H), 3.67 (s, 3H), 3.65 (s, 3H), 3.29 (p, J= 6.7 Hz, 1H), 2.82 (dd, J=16.8, 7.0 Hz, 1H), 2.77 (dd, J=16.8, 6.9 Hz, 1H), 2.65 (dd, J=16.8, 6.4 Hz, 1H), 2.60 (dd, J=16.8, 6.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.6, 171.9, 171.2, 135.7, 128.7, 128.43, 128.39, 66.7, 52.3, 52.0, 37.4, 35.4, 35.2. ESI-MS: m/z=295 $[M+H]^+$.

Trimethyl propane-1,2,3-tricarboxylate (4 aa): Following the general procedure, but using ligand **1 a** and P_{CO}=1 bar, the product **4 aa**, selectively obtained from olefin **2 f** (Scheme 4), has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc 80:20 to 70:30), obtaining a colorless oil; yield: 77% (168 mg). R_f=0.25 (petroleum ether/EtOAc=8:2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.69 (s, 3H), 3.67 (s, 6H), 3.25 (p, J=6.7 Hz, 1H), 2.76 (dd, J=16.8, 6.8 Hz, 2H), 2.59 (dd, J=16.8, 6.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.7, 171.9, 52.4, 52.0, 37.4, 35.2. ESI-MS: m/z= 219 $[M+H]^+$.

Acknowledgements

This work was supported by University of Bologna and University of Urbino "Carlo Bo". We are grateful to the Department of Biomolecular Sciences of the University of Urbino for providing NMR instrumentation. D.O., C.C., and R.T. thank UNI.RIMINI S.p.A. for funding. Open Access Funding provided by Università degli Studi di Bologna within the CRUI-CARE Agreement.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: allylic compounds · carbonylation · ligand effects · density functional calculations · palladium

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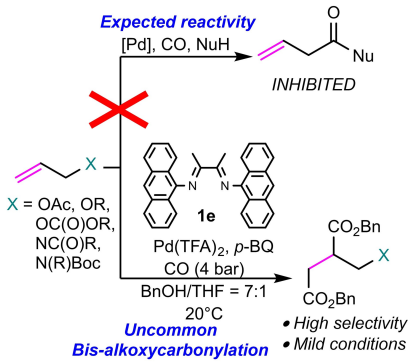
Manuscript received: December 17, 2021
Revised manuscript received: January 17, 2022
Version of record online: ■■, ■■■

RESEARCH ARTICLE

Easy, unexpected access to useful 2-substituted succinates was achieved starting from various allyl derivatives, including allyl carbonates, under mild conditions. The selectivity of this Pd-catalyzed oxidative Bis-Alkoxycarbonylation is governed by the combined effect of the ligand (anthryl α-diimine) and the nucleophile (benzyl alcohol). Mechanistic insights, based on DFT calculations, were proposed.



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Combined Effect of Palladium Catalyst and the Alcohol to Promote the Uncommon Bis-Alkoxycarbonylation of Allylic Substrates