 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 \( \text{CH}_2=\text{CHCH}_2\text{X} \) (\( \text{X} = \text{OAc}, \text{OC}(\text{O})\text{CH}_2\text{CN}, \text{OPh}, \text{OEt}, \text{OC}(\text{O})\text{OPh}, \text{N}(\text{H})(\text{C}(\text{O})\text{Ph}, \text{N}(\text{Ph})(\text{C}(\text{O})\text{Ph}, \text{N}(\text{H})\text{Boc}, \text{N}(\text{Ph})\text{Boc}, \text{Ph}, \text{CO}_2\text{Bn}, \text{CN}) \), 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 \( \beta,\gamma \)-unsaturated carbonyl derivatives through the formation of a \( \pi \)-allyl palladium intermediate. An accurate study, carried out using allyl acetate as model substrate, allowed to maximize the selectivity in the envisioned 2-CH\(_2\)X substituted succinates. The best catalyst is generated \textit{in situ} by mixing Pd(TFA)\(_2\) (TFA = trifluoroacetate) and the \( N,N' \)-di(anthracen-9-yl)butane-2,3-diimine ligand. \( \text{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 \( \pi \)-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 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. 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. 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.\(^{[5–16]}\) In the last years, more attention has been given to the carbonylation of allylic compounds.\(^{[5–16]}\) In particular, allyl derivatives (\( \text{CH}_2=\text{CHCH}_2\text{X} \), \( \text{X} = \text{leaving group} \)) have been successfully carbonylated to obtain synthetically useful \( \beta,\gamma \)-unsaturated carbonyl compounds (Scheme 1a). So far, versatile methods for the substitutive carbonylation of allyl carbonates,\(^{[6]}\) acetates,\(^{[7]}\) halides,\(^{[7a,b]}\) amines,\(^{[8]}\) ethers,\(^{[7a,10]}\) alcohols,\(^{[7a,b,11]}\) phosphates,\(^{[7,c,12]}\) in the presence of a suitable nucleophile \( \text{NuH} \) (generally an alcohol or an amine), have been developed (Scheme 1a,i). 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 \( \pi \)-allylpalladium complex\(^{[13]}\) (Scheme 1b). Then, the coordination/insertion of CO takes place forming an acyl palladium intermediate, which reacts with \( \text{NuH} \). The subsequent reductive
elimination leads to the expected unsubstituted carbonylated product.\(^\text{[17]}\) Remarkably, in the case of allyl amines,\(^\text{[9,14]}\) allyl chlorides,\(^\text{[7a-15]}\) allyl acetate,\(^\text{[74]}\) allyl ether,\(^\text{[16]}\) and allyl alcohols,\(^\text{[11e]}\) if no external nucleophile is added, the acyl palladium intermediate directly undergoes reductive elimination yielding an unsubstituted 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\(^2\))-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-alkoxycar- bonylated so far. In 1979, Stille and co-workers reported the oxidative bis-methoxycarbonylation of allylic substrates, with retention of the X group into the final succinic product.\(^\text{[88 %],}\)\(^\text{[11e]}\) However, the succinate derivative bearing the acetate group could not be isolated, because, owing to the basic conditions, hydrolysis of the solvent at 70 °C for 21 h, obtaining a good product yield (88%).\(^\text{[15]}\) 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\(_2\))\(^\text{[19]}\) fell within the explosion limits for CO–O\(_2\) mixtures.\(^\text{[20]}\)

Clearly, an efficient and selective bis-alkoxycarbonylation process of allyl substrates CH\(_2=CHCH\(_2\)X can only be achieved if the formation of the \(\pi\)-allylpalladium intermediate, leading to \(\beta\gamma\)-unsaturated carbonyl compounds, is avoided under the reaction conditions. We have recently focused our attention on the bis-alkoxycarbonylation of olefins\(^\text{[21]}\) working under low CO pressure and room temperature.\(^\text{[28]}\) Excellent results have been obtained with terminal\(^\text{[22a]}\) and internal\(^\text{[22b]}\) aromatic and aliphatic alkenes, as well as with acrylic esters and amides,\(^\text{[22c]}\) attaining variously substituted succinic esters in high yields. These molecules find important applications in many industrial fields,\(^\text{[23-26]}\) such as cosmetics,\(^\text{[24]}\) agricultural chemistry\(^\text{[25]}\) and material science.\(^\text{[26]}\) Moreover, succinic acid and its derivatives are important precursors of industrially relevant starting materials\(^\text{[23]}\) and the succinic scaffold is present in a variety of natural products.\(^\text{[27]}\)

Based on our knowledge, we have envisioned the possibility of shifting the widely documented reactivity of allyl compounds CH\(_2=CHCH\(_2\)X in carbonylation reactions, which leads to \(\beta\gamma\)-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\(_2\)X substituent in 2-position, that are biologically active molecules\(^\text{[28]}\) and useful intermediates for the synthesis of lactones,\(^\text{[29]}\) \(\gamma\)-butyrolactones\(^\text{[30]}\) and lactams,\(^\text{[31]}\) 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\(_2\)X, 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.\(^\text{[32]}\) The catalyst is generated in situ by mixing Pd(TFA)\(_2\), and the bis(2,6-dimethylphenyl)butane-2,3-dimine ligand 1 a. 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 3 aa was formed in 33% yield together with the symmetric trimethyl propane-1,2,3-tricarboxylate 4 aa (37%) and other minor unidentified species (29%) (Table 1, entry 1).\(^\text{[32]}\) Compound 4 aa comes probably from the well-known substitutive carbonylation pathway, which pass through the formation of a \(\pi\)-allylpalladium intermediate to give a \(\beta\gamma\)-unsaturated alkoxycarbonylated compound,\(^\text{[33]}\) 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\(^\text{[33]}\) and accelerates the oxidation of Pd(0) to Pd(II).
promoted by p-BQ. Unfortunately, in our conditions, the addition of 5 mol% of p-TSA-H₂O (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.

Gratifyingly, reducing the quantity of p-TSA-H₂O 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-H₂O 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 > OTf ≈ Ac ≈ BF₄ ≈ 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, 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-diabutadiene) or a BIAN (bis(aryl)acenaphthenequinonediimine) skeleton, could favor the achievement of high yields and selectivities in bisalkoxy-carbonylation 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, 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).
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, nPrOH and iBuOH, 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.

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

| Entry[^][a] | Ligand | ROH | Conversion [%][b] | 3aa | 4aa | 5 | 6aa | Other species [%][b] |
|-------------|--------|-----|------------------|-----|-----|---|-----|-------------------|
| 1[^][c]     | 1a     | EtOH | 100              | 57  | 22  | 0 | 4  | 18                |
| 2           | 1b     | nPrOH| 100              | 35  | 35  | 20 | trace | 10                |
| 3           | 1c     | iBuOH| 100              | 16  | 13  | 33 | 6  | 31                |
| 4           | 1d     | BnOH | 100              | 33  | 8   | 13 | 5   | 41                |
| 5           | 1e     | iBuOH| 100              | 57  | 7   | 0  | 4  | 32                |
| 6           | 1f     | BnOH | 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 1H 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] | 3 | 4 | 6 | Other species [%][b] |
|-------------|--------|-----|------------------|---|---|---|-------------------|
| 1[^][c]     | 1a     | EtOH| 100              | 60 (58) | 9 | 8 | 18                |
| 2           | 1a     | nPrOH| 100             | 56 | 10 | 12 | 22                |
| 3[^][d]     | 1a     | iBuOH| 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     | nPrOH| 100             | 58 | 13 | 21 | 8                 |
| 7           | 1e     | iBuOH| 100             | 48 | 10 | 28 | 14                |
| 8           | 1e     | BnOH | 100             | 80 | 7  | 8  | 6                 |
| 9[^][e]     | 1e     | BnOH | >98             | 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 1H 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.
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. 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. This facilitates the formation of the alkoxycarbonyl-palladium complex C, in which the first molecule of CO is inserted. The subsequent coordination and insertion of allyl acetate 2a in complex C produces the 5-membered palladacycle D and a second CO insertion leads to the formation of the 6-membered palladacycle E. 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. 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 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. However, in a recent study on an analogous process, we have shown through a theoretical study, 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$^0$ 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 4 (Scheme 2, cycle III), which can be monocarbonylated, under the reaction conditions, to form the alkyl 3-butanoylate product 7. The latter can enter Cycle I, accounting for the formation of the trycaboxylate

![Scheme 2](image-url)
product 4. Moreover, in presence of a large excess of ROH, a ligand exchange on the allyl/palladium complex H can take place affording intermediate J,[10,16] in which the acetate is replaced by an alkoxy group. This intermediate can as well be carboxylated to form again the β,γ-unsaturated carboxyl compound 7.[10,16] On the other hand, the η²-allylpalladium complex J can also be generated by oxidative addition of the allyl compounds 5 to Pd⁰.[16,13] 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 carboxyl 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 Pd⁰ complex G and olefin 2a, using both ligand 1a and 1e (assuming benzyl alcohol as the solvent). From this study resulted that the ΔG° 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 carboxylated 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 BrOH and the iBuOH 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 iBuOH 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[18,22] and the fact that the hydroquinone can interact only during the second nucleophilic attack of the alcohol, on intermediate E,[22] 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,[19,20] and its opening is endoergic 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 CO₂R 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 Pd⁰ complex G, passing through the transition state FGTS. 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 endoergic for the two alcohols considered (Figure 2).

In Figure 3 are depicted the structures of complexes F calculated for BrOH (left) and iBuOH (right), which are oriented in order to appreciate the different dihedral angle (i) 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 sterical hindrance of the iBu group forces the anthracenyl rings in a position almost perpendicular to the Pd coordination plane (θiBrOH = 78.35°), resulting in an increase of the energy in complex F–iBuOH (72.5 kJ/mol). On the other hand, with BrOH, 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 (θiOBn = 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–BrOH is close to that of the transition state relative to the reductive elimination step (FGTS), the energy cost to reach the TS is lower respect to complex F–iBuOH (30.9 kJ/mol vs 37.8 kJ/mol).

Indeed, for BrOH to pass from F to FGTS, the sum of the dihedral angles (i, +j) changes by only 7.6°, while with the
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-G complex G is supposed to occur with BnOH, while with iBuOH this final step is more endoergonic, allowing the hydroquinone to react forming a higher amount of 6 (Table 3, entry 7). With EtOH and nPrOH 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 nPr 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-alkoxycarbylated 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<sup>a</sup> | Olefin 2 | ROH     | Product 3          | Yield [%]<sup>b</sup> |
|------------------|---------|---------|---------------------|-----------------------|
| 1                | OAc     | BnOH    | 3ae CO₂Bn OAc       | 82                    |
| 2                | CN      | BnOH    | 3b CO₂Bn OCN        | 52                    |
| 3                | Ph      | BnOH    | 3c CO₂Bn OP       | 86                    |
| 4                | Et      | BnOH    | 3d CO₂Bn OEt       | 82                    |
| 5                | Ph      | BnOH    | 3e CO₂Bn OPh       | 56 (91)<sup>e</sup>   |
| 6                | OBu     | BnOH    | 3f CO₂Bn OOBu      | 58 (93)<sup>e</sup>   |
| 7                | Ph      | BnOH    | 3g CO₂Bn NPh       | 80 (83)<sup>e</sup>   |
| 8                | Ph      | BnOH    | 3h CO₂Bn NHBoc     | 56 (88)<sup>e</sup>   |
| 9                | NHBoc   | BnOH    | 3i NHBoc           | 63                    |
| 10               | Ph      | BnOH    | 3j NHBoc           | 76                    |
| 11               | OAc     | BnOH    | 3k CO₂Bn OAc       | 76                    |
| 12<sup>c,d</sup> | Ph      | MeOH    | 3l CO₂Me CO₂Ph     | 98                    |
| 13<sup>c,d</sup> | CO₂Bn   | MeOH    | 3m CO₂Me CO₂Bn     | 87                    |
| 14<sup>c,d</sup> | CH      | MeOH    | 3n CO₂Me CO₂CN     | 50 (55)<sup>e</sup>   |
| 15<sup>c,d</sup> | OPh     | MeOH    | 3c CO₂Me OPh       | 74                    |

<sup>a</sup>Reaction performed in autoclave at P<sub>CO2</sub> = 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. <sup>b</sup>Isolated yield after column chromatography. <sup>c</sup>2 mmol of starting olefin were utilized. <sup>d</sup>MeOH was used as alcohol and 1a as ligand. <sup>e</sup>The conversion, when incomplete, is reported in brackets.
CN group (entry 2). 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^1-allylpalladium intermediate,[35] 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 are 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 allyl 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=CHCH₂X where X is an electron-withdrawing group, such as −CO₂Bn or −CN, and the simple allylbenzene. These substrates are less prone to undergo oxidative addition on Pd⁰ to form a η⁵-allylpalladium intermediate unless a C−H activation of the CH₂(sp³) 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 allyl carbonate 2f (Table 4, entry 12) and of the benzyl 3-butenolate 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 (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,[46] 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 the α-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).

**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 CH₂=CHCH₂X (X=OAc, OC(O)CH₂CN, OPh, OEt, OC(O)OPh, OC(O)OBU, N(H)C(O)Ph, N(Ph)C(O)Ph, N(H)Boc, N(Ph)Boc, Ph, CO₂Bn, 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-dimine 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 monocabonylation (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^1-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-alkoxy-carbonylation of allyl amides, N-Boc protected allyl amines and allyl carbonates which are known to easily form the undesired α-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. All reactions were carried out under nitrogen atmosphere with dry chemicals were purchased from Merck Sigma-Aldrich and used without further purification. Olefins were purchased from Flurochem, Pd(PhCN)₂Cl₂ was purchased by Flurochem, and was filtered off a plug of silica gel, and used without further purification. Olefins were filtered off a plug of neutral Al₂O₃, and used without further purification. Olefins were synthesized according to literature procedure, but using 2 mmol of the starting olefin, the compound has been isolated by flash column chromatography on silica gel (when BnOH is employed as alcohol, more than one column could be necessary to isolate the whole product pure).

**Computational Details**: All DFT calculations have been performed using the ORCA 4.2.1 suite of quantum chemistry programs. The Becke-Perdew 13 functional, Geometries were optimized in vacuum using the Becke-Perdew 13 functional, and the def2-TZVP basis. 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-QZVPPP basis[22] and the M06 functional[18] with the inclusion of solvation effects through the SMD model[24] and of dispersion interactions[19]. 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-QZVP single point electronic energy.

**Typical Procedure for the Bis-alkoxy-carbonylation of Allyl Compounds**: In a nitrogen flushed Schlenk tube, equipped with a magnetic stirring bar, the respective olefins 2a–2m (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-H₂O (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 CH₂Cl₂:Et₂O 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).

**Diethyl 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/Et₂O = 80:20) together with 10% of 4aa (3aa : 4aa = 9:1, see Supporting Information, page S59), obtaining a colorless oil; overall yield: 69% (275 mg). R = 0.25 (petroleum ether/ EtOAc = 8:2). 1H NMR (400 MHz, CDCl₃) 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). 13C NMR (101 MHz, CDCl₃) δ 172.3, 171.9, 170.6, 53.2, 51.4, 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/Et₂O = 85:15 to 80:20), obtaining a pale yellow oil; yield: 58% (285.7 mg). R = 0.17 (petroleum ether/Et₂O = 80:20). 1H NMR (400 MHz, CDCl₃) δ 4.30 (d, J = 5.7 Hz, 1H), 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), 3H), 63.9, 61.3, 61.0, 41.1, 33.1, 20.9, 14.3, 14.3. ESI-MS: m/z = 247 [M + H⁺].

**Disobutyl 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/Et₂O = 90:10), obtaining a pale yellow oil; yield: 38% (229.8 mg). R = 0.34 (CH₂Cl₂). 1H NMR (400 MHz, CDCl₃) δ 4.34 (d, 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, 1H), 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). 13C NMR (101 MHz, CDCl₃) 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, 12.19. 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/EtOAc = 90:10), obtaining a colorless oil; yield: 14% (96.4 mg). Rg = 0.5 (CHCl3).

1H NMR (400 MHz, CDCl3) 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).

13C NMR (101 MHz, CDCl3) δ 173.3, 171.6, 71.4, 71.1, 37.7, 35.5, 27.8 (2C), 19.20, 19.18. ESI-MS: m/z = 345 [M + H]+.

Dibenzyl 2-((phenoxycarboxyloxy)ethyl)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). Rg = 0.47 (petroleum ether/EtOAc = 80:20).

1H NMR (400 MHz, CDCl3) δ 8.45–8.37 (m, 7H), 7.82–7.74 (m, 2H), 7.42–7.35 (m, 5H), 6.54 (d, J = 11.3 Hz, 1H), 4.48–4.37 (m, 4H), 2.99–2.87 (m, 1H), 1.92–1.82 (m, 1H), 0.70 (CH3), 0.32 (CH2).

ESI-MS: m/z = 575 [M + H]+.

Dibenzyl 2-((((phenoxycarbonyl)amino)methyl)succinate (3i): Following the general procedure the compound 3i has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 90:5 to 95:10), obtaining a pale yellow oil; yield: 58% (248.5 mg). Rg = 0.70 (CHCl3).

1H NMR (400 MHz, CDCl3) δ 7.45–7.32 (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), 1.92 (dd, J = 17.0, 8.1 Hz, 1H), 1.87 (dd, J = 17.0, 8.1 Hz, 1H), 0.94 (d, J = 6.7 Hz, 6H).

13C NMR (101 MHz, CDCl3) δ 171.4, 171.1, 170.8, 153.6, 144.3, 122.5, 111.6, 71.3, 63.8, 41.3, 33.1, 27.8, 20.9, 19.21, 19.20. ESI-MS: m/z = 377 [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 98:2 to 80:20), obtaining a colorless oil; yield: 82% (303.7 mg). Rg = 0.32 (CHCl3).

1H NMR (400 MHz, CDCl3) 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).

13C NMR (101 MHz, CDCl3) 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-[(tert-butoxycarbonyl)phenyl]amino)methylsuccinate (3k): Following the general procedure the compound 3k 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). 1H NMR (400 MHz, CDCl₃) \( \delta \) 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). 13C NMR (101 MHz, CDCl₃) \( \delta \) 172.7, 171.3, 154.8, 142.0, 135.8, 135.7, 129.0, 128.7, 128.4 (2C), 128.3 (2C), 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]⁺.

Dibenzy 2-(1-aceoxyethyl)succinate (3k): Following the general procedure the compound 3k 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). 1H NMR (400 MHz, CDCl₃) \( \delta \) 7.35–7.29 (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). 13C NMR (101 MHz, CDCl₃) \( \delta \) 172.2, 171.8, 170.4, 135.3, 125.7, 128.7, 128.6, 128.5 (2C), 128.4, 73.2, 67.6, 66.5, 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-tricarboxylic acid (3m): Following the general procedure, but using ligand 1a and 2 mmol of the starting olefin, the compound 3m has been purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 90:10 to 80:20), obtaining a pale yellow oil; yield: 87% (512.1 mg). \( R_f = 0.13 \) (petroleum ether/CH₂Cl₂ = 20:80). 1H NMR (400 MHz, CDCl₃) \( \delta \) 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). 13C NMR (101 MHz, CDCl₃) \( \delta \) 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-tricarboxylic acid (4aa): Following the general procedure, but using ligand 1a and 10 mmol of the starting olefin, the product 4aa, selectively obtained from olefin 2f (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). 1H NMR (400 MHz, CDCl₃) \( \delta \) 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). 13C NMR (101 MHz, CDCl₃) \( \delta \) 173.7, 171.9, 52.4, 52.0, 37.4, 35.2. ESI-MS: m/z = 219 [M + H]⁺.

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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.

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For selected articles on the bis-alkoxycarbonylation of olefins, see:

- [30] A. K. Morison, S. C. Stevens, *Biofuels Bioprod. Biorefin.* 2008, 2, 505.
- [31] K. Y. Hwang, T. Y. Jei, K. S. Kochhar, H. Li, A.-L. Hou, L. Kang in *Handbook of Cosmeceutical Excipients and their Safeties*, Elsevier, 2014.
- [32] M. Yoshida, H. Hoshi, *Agric. Biol. Chem.* 1971, 35, 201; b) S. Tajima, I. Kimura, H. Sasahara, *Agric. Biol. Chem.* 1986, 50, 1009.
- [33] For use as plasticsitizer, see: a) A. Stuart, M. M. McCallum, D. Fan, D. J. LeCaptain, C. Y. Lee, D. K. Mohanty, *Polym. Bull. 2010*, 65, 589; b) H. C. Erythropel, P. Dod, R. Leask, M. Maric, D. G. Cooper, *Chemosphere* 2013, 91, 358; c) A. Stuart, D. J. LeCaptain, C. Y. Lee, D. K. Mohanty, *Eur. Polym. J.* 2013, 49, 2785; d) R. Jamarani, H. C. Erythropel, D. Burkart, J. A. Nicell, R. L. Leask, M. Maric, *Processes* 2017, 5, 43. For use as monomers in polymers/dendrimers, see: a) M. Carah, M. W. Grinstaff, *Macromolecules* 2001, 34, 7648; b) M. A. Carah, M. W. Grinstaff, *Macromolecules* 2006, 39, 2427; g) I. Hevus, Z. Pik, *Macromol. Symp.* 2004, 253, 103; h) Y. Jiang, A. J. J. Woortman, G. O. R. A. van Ekenstein, K. Loos, *Biomol. Eng.* 2013, 3, 461; i) J. Xu, B.-H. Guo, *Biotechnol. J.* 2010, 5, 1149.
- [34] Inoguchi, T. Morimoto, K. Achiwa, *J. Organomet. Chem.* 1989, 370; c) K. Yoshikawa, K. Inoguchi, T. Morimoto, K. Achiwa, *Heterocycles* 1990, 31, 1413; c) Y. Ito, T. Kajimo, H. Harada, F. Matsuda, S. Terashima, *Tetrahedron Lett.* 1990, 31, 2731; d) H. Jendralla, *Tetrahedron Lett.* 1991, 32, 3671; e) B. Kammermeier, G. Beck, W. Holla, J. Baciowski, N. Patients, H. Jendralla, *J. Eur. Org. Chem.* 1996, 2, 307; f) M. Whittaker, C. D. Fordy, P. Brown, A. J. H. Gearing, *Chem. Rev. 1999*, 99, 2735; g) M. P. Sibi, H. Hasegawa, *Org. Lett.* 2002, 4, 3347; h) H. Quiroz-Florentio, A. Garcia, E. Burgueño-Tapia, J. Tamariz, *Nat. Prod. Res.* 2009, 23, 1355; i) B. Fabre, A. Ramos, B. de Pascual-Terés, *J. Med. Chem.* 2014, 57, 10205; j) E. Vandenbergbroucke, C. Libert, *Nat. Rev. Drug Discovery* 2014, 13, 904; k) G. X. Fan, D.-J. Zhi, H. Ren, Z.-Y. Yu, Y.-H. Liu, Z.-X. Zhang, D.-Q. Fei, *Nat. Prod. Res.* 2016, 11, 4697.
- [35] A. S. Torii, H. Okumoto, M. Sadakane, A. K. M. A. Ha, H. Tanaka, *Tetrahedron Lett.* 1993, 34, 6553; b) H. Tanaka, A. K. M. A. Ha, M. Sadakane, H. Okumoto, S. Torii, J. Org. Chem. 1994, 59, 3040; c) Z. Zhou, H. Alper, *Angew. Chem. Int. Ed.* 1994, 61, 1256; d) Y. Ito, M. Fujii, Y. Kubota, S. Murahashi, *Tetrahedron Lett.* 1997, 38, 8227.
- [36] T. Yamamoto, O. Saito, A. Yamamoto, *J. Am. Chem. Soc.* 1981, 103, 5600; b) T. Yamamoto, M. Akimoto, O. Saito, A. Yamamoto, *Organometallics* 1986, 5, 1559; f) C. Ozawa, T.-I. Son, K. Osakada, A. Yamamoto, *J. Organomet. Chem.* 1989, 396, 1067; d) T. van Haeren, H. Oevering, P. C. J. Kamer, K. Gobius, J. Fraanje, P. W. N. M. van Leeuwen, G. P. F. van Strijdonck, *J. Organomet. Chem.* 2004, 698, 3800; e) A. Bottoni, G. P. Mischeo, M. A. Carvalj, J. J. Novoa, *J. Organomet. Chem.* 2006, 691, 4948.
- [37] S. Toda, M. Miyamoto, H. Kinoshita, K. Inomata, *Bull. Chem. Soc. Jpn.* 1991, 64, 3600.
- [38] The flammability range for CO|CH₂|CH₂|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|OH|
Takeuchi, Y. Ukaji, K. Inomata, Bull. Chem. Soc. Jpn. 2001, 74, 955 and ref. [21d].
[47] a) R. B. Wetzel, G. L. Kenyon, J. Am. Chem. Soc. 1974, 96, 5189; b) M. T. Shipchandler, C. A. Peters, C. D. Hurd, J. Chem. Soc. Perkin Trans. 1 1975, 1400; c) R. M. Patel, N. P. Argade, Synthesis 2010, 1188.
[48] The same reaction carried out at 4 bar of CO gives a 50% yield of 4aa, together with 23% of the direct bis-methoxycarbonylated product.
[49] D. Drikermann, V. Kerndl, H. Görls, I. Vilotijevic, Synlett 2020, 31, 1158.
[50] a) F. Neese, “The ORCA program system”, Wiley Interdiscip. Rev.: Comput. Mol. Sci. 2012, 2, 73; b) F. Neese, “Software update: The ORCA program system, version4.0”, Wiley Interdiscip. Rev.: Comput.Mol.Sci. 2018, 8, e1327.
[51] a) J. P. Perdew, Phys. Rev. B 1986, 33, 8822; b) A. D. Becke, Phys. Rev. A 1988, 38, 3098.
[52] F. Weigend, R. Ahlrichs, Phys. Chem. Chem. Phys. 2005, 7, 3297.
[53] Y. Zhao, D. G. Truhlar, Theor. Chem. Acc. 2008, 120, 215.
[54] A. V. Marenich, C. J. Cramer, D. G. Truhlar, J. Phys. Chem. B 2009, 113, 6378.
[55] S. Grimme, J. Antony, S. Ehrlich, H. Krieg, J. Chem. Phys. 2010, 132, 154104.