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Diastereospecific Bis-Alkoxycarbonylation of 1,2-disubstituted Olefins Catalyzed by Aryl α-Diimine Palladium(II) Catalysts

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Abstract. Readily synthesized aryl α-diimine derivatives have been used as efficient ligands for the palladium-catalyzed oxidative bis-alkoxycarbonylation reaction of 1,2-disubstituted olefins. The most active catalyst **A** was formed *in situ* from bis-(2,6-dimethylphenyl)-2,3-dimethyl-1,4-diazabutadiene and $Pd(TFA)_2$ (TFA = trifluoroacetate). This catalytic system was able to selectively convert 1,2-disubstituted olefins into 2,3-disubstituted-succinic diesters with total diastereospecificity, in good yields (up to 97%) with 2 mol% of catalyst loading, under mild reaction conditions (4 bar of CO at 20 °C in presence of *p*-toluenesulfonic acid as additive and *p*-benzoquinone as oxidant). The optimized reaction conditions could be successfully applied to 1,2-disubstituted aromatic, aliphatic, cyclic olefins and to unsaturated fatty acid methyl esters, employing methanol or benzyl alcohol as nucleophiles. The use of the bulky, less reactive isopropyl alcohol has allowed to better understand the mechanisms involved in the catalytic process. The geometry of the carbonylated products can be explained as a consequence of a concerted *syn* addition of the Pd-alkoxycarbonyl moiety to the olefin C=C bond. Catalyst **A** was isolated, characterized and analyzed by single crystal X-ray diffraction analysis.

Keywords: alkenes; aryl α-diimine ligands; palladium; carbonylation; oxidative carbonylation; succinic acid esters

Introduction

Carbonylation reactions are among the most important reactions in organic and organometallic chemistry. They convert inexpensive feedstock such as olefins and carbon monoxide into highly valuable building blocks like aldehydes, esters or lactones.[1] Despite the toxicity, carbon monoxide is one of the preferred C_1 building blocks especially in combination with palladium catalysis. After the pioneering contributions made by Heck and Tsuji,[2] carbonylation reactions are performed in the presence of an oxidant to make the reaction conditions milder.[3] Among carbonylation reactions, the bis-alkoxycarbonylation is one of the most useful, actually an olefin, carbon monoxide and a suitable alcohol are converted into succinic acid derivatives,[4] very important building blocks in organic and medicinal chemistry. In particular the succinic acid moiety is ubiquitous in molecules that act as inhibitors of renin[5] and matrix metalloproteinases.[6] Moreover succinates are employed in various industrial fields, for instance in cosmetics,[7] agricultural chemistry and in material science, where they are largely used as non-phthalate plasticizers[8] and as monomers for polymers and dendrimers.[9]

In literature various types of Pd-catalyzed olefin bis-alkoxycarbonylations have been described using phosphine or nitrogen ligands and molecular oxygen or benzoquinone as oxidant.[3a,f] In particular, stereoselective bis-alkoxycarbonylation reactions have been widely studied,[10] but only very few examples regarding disubstituted olefins have been reported so far,[11] probably due to their lower reactivity compared to α-olefins.[12] Recently, we have reported a novel catalytic system able to promote the alkoxycarbonylation of olefins and

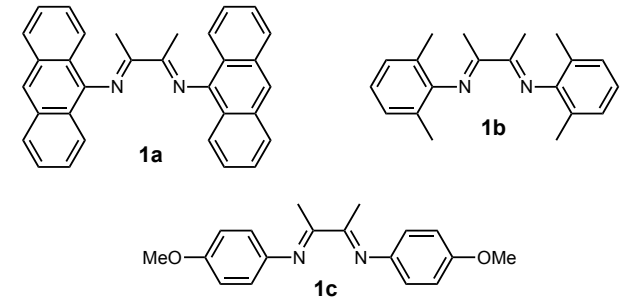
alkynes.[13] The catalytic systems are made of a palladium salt with 1,4-diaryl-2,3-diazabutadiene (Ar_2DABMe_2) or bis(aryl)acenaphthenequinonediimine (diaryl-BIAN) ligands. Analogous Pd(II) catalysts bearing aryl α-diimine ligands were also used by us in the copolymerization of styrenes with CO to yield copolymers with a high degree of tacticity.[14] On the basis of the acquired knowledge[13,14,15] and considering the results obtained on the carbonylation of terminal olefins,[13a] in this paper we have extensively studied the diastereoselective bis-alkoxycarbonylation reaction of 1,2-disubstituted olefins with different alcohols for the synthesis of 2,3-disubstituted succinic acid esters, under mild reaction conditions.

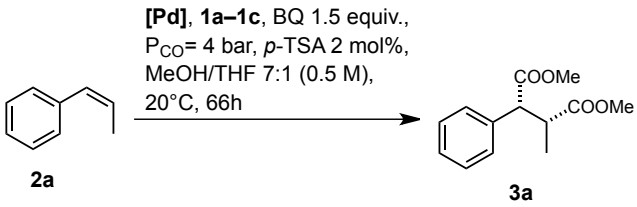
Results and Discussion

As a disubstituted olefin benchmark, *cis*-β-methylstyrene was used to optimize the reaction conditions. Taking into account the conditions previously employed in the case of terminal olefins,[13a] a further optimization study on the ligands and palladium sources in the oxidative bis-alkoxycarbonylation reaction was performed. In the initial experiment, the *in situ* formed complex $Pd(TFA)_2$/**1a**, in 0.5 mol% of catalyst loading, was used with *p*-benzoquinone as oxidizing agent, *p*-toluenesulfonic acid (*p*-TSA) as additive, in 7:1 MeOH/THF (0.5 M) as reaction medium, at 4 bar of pressure of CO and room temperature, converting only 50% of *cis*-β-methylstyrene (Table 1, entry 1). By switching the ligand to the more straightforward synthesized ligand **1b**, the same result was obtained in terms of conversion (50%, entry 2). Lowering the concentration of the catalyst $Pd(TFA)_2$/**1b** a detrimental effect on the conversion has been detected (table 1, entries 3 and 4). On the other hand, by using ligand **1c** no conversion was observed, confirming the necessity for an *ortho*-disubstituted diaryl α-diimine ligand (table 1, entry 5).[13]
Besides ligands, other palladium sources were tested in order to improve the efficiency of the process. However, neither $Pd(OAc)_2$ nor $(PhCN)_2PdCl_2$/2AgOTf were active enough to raise the conversion of the carbonylation reaction (Table 1, entries 6 and 7). Complete substrate conversion was instead observed when increasing the catalyst loading up to 2 mol% with both ligands **1a** and **1b** (entries 8 and 9). Due to its easier synthesis, the ligand of choice for the next experiments was **1b** (see Experimental Section). Thus, the combination of $Pd(TFA)_2$/**1b** (2 mol%) with benzoquinone as the oxidizing agent, *p*-TSA (2 mol%) as the acidic additive and 7:1 MeOH/THF (0.5 M) solution as reaction medium allowed obtaining the *syn*-2,3-disubstituted succinic acid methyl ester **3a** with total diastereospecificity under particularly mild reaction conditions, such as room temperature 20 °C and 4 bar of CO (Table 1, entry 9).

With optimized experimental reaction conditions in hand, we then proceeded to evaluate the scope of the reaction.

Table 1. Optimization of bis-methoxycarbonylation reaction of *cis*-β-methylstyrene **2a**.





Entry[a]	[Pd]	Ligands 1a–1c	Conversion (%)[b]
1	$Pd(TFA)_2$ 0.5 mol%	**1a** 0.55 mol%	50
2	$Pd(TFA)_2$ 0.5 mol%	**1b** 0.55 mol%	50
3	$Pd(TFA)_2$ 0.1 mol%	**1b** 0.11 mol%	21
4	$Pd(TFA)_2$ 0.01 mol%	**1b** 0.011 mol%	<5
5	$Pd(TFA)_2$ 0.5 mol%	**1c** 0.55 mol%	<5
6	$Pd(OAc)_2$ 0.5 mol%	**1b** 0.55 mol%	25
7[c]	$(PhCN)_2PdCl_2$ 0.5 mol%	**1b** 0.55 mol%	35
8	$Pd(TFA)_2$ 2 mol%	**1a** 2.2 mol%	≥98
9	$Pd(TFA)_2$ 2 mol%	**1b** 2.2 mol%	≥98

[a] Reaction performed in autoclave at P_{CO} = 4 bar, with *cis*-β-methylstyrene **2a** (2 mmol-scale), palladium salts [Pd] (0.01 - 2 mol%), ligands **1a–c** (0.011 - 2.2 mol%), 2 mol% of *p*-TSA and 1.5 equiv. of BQ, in 7:1 MeOH/THF (0.5M) as the reaction medium, for 66 h. [b] Determined by direct ^{1}H NMR analysis on a sample of the reaction mixture. [c] Reaction performed by using 1.2 mol% of AgOTf instead of *p*-TSA.

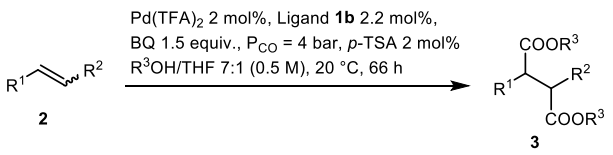
Several 1,2-disubstituted aromatic, aliphatic and cyclic olefins were used together with different alcohols as nucleophiles (Table 2). In general, moderate to excellent results were achieved in the bis-alkoxycarbonylation of internal olefins. 2,3-Disubstituted aromatic and aliphatic methyl succinates **3a, 3d**, **3g**, **3j**, **3m** (Table 2, entries 1, 4, 7,

10, 13) and benzyl esters **3b**, **3e**, **3h**, **3k**, **3n** (entries 2, 5, 8, 11, 14) were obtained with excellent isolated yields, up to 97%, and a total diastereospecificity.

In particular, all reactions performed with the optimized reaction conditions and methanol or benzyl alcohol as nucleophiles, gave complete conversion of the starting olefins, and near quantitative isolated yields of the corresponding products even with the cyclic olefin **2c** (Table 2, entries 7–8). Interestingly 1,2-dialkyl substituted olefins (**2d**, **2e**) gave similar results to those obtained with the aromatic ones and, at the best of our knowledge, this is the first time that the bis-alkoxycarbonylation was successfully applied to such alkenes (entries 10–11, 13–14).

With less nucleophilic isopropyl alcohol, less satisfactory results were attained. In particular, although the aromatic β-methylstyrenes **2a** and **2b** were fully converted, only 40% and 50% isolated yields of the corresponding succinic esters **3c** and **3f** were achieved (Table 2 entries 3 and 6).

Table 2. Scope of the bis-alkoxycarbonylation of aromatic and aliphatic 1,2-disubstituted olefins **2a–2e**.



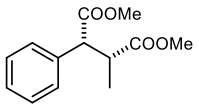
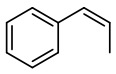
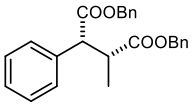
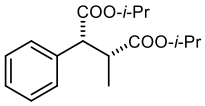
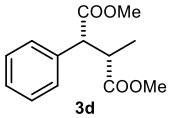
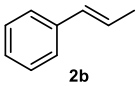
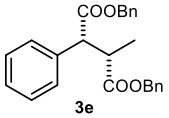
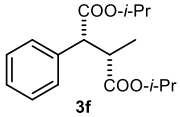
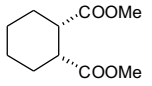
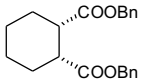
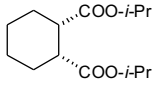
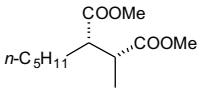
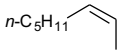
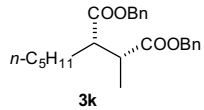
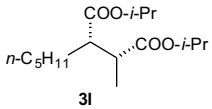
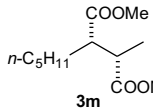
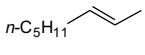
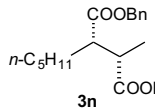
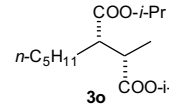
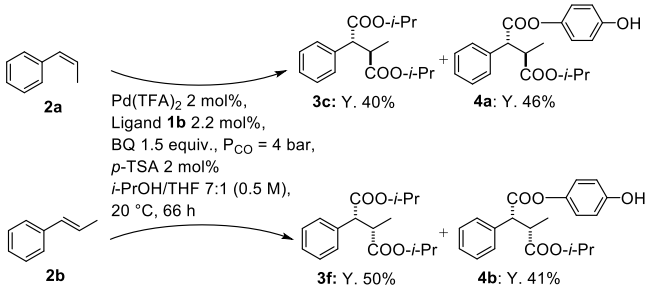
Entry[a]	2	R^3OH	3	Yield [%][b]
1		CH_3OH	 **3a**	87
2	 **2a**	BnOH	 **3b**	92
3		*i*-PrOH	 **3c**	40
4		CH_3OH	 **3d**	93
5	 **2b**	BnOH	 **3e**	90
6		*i*-PrOH	 **3f**	50

Table 2. (Continued)

Entry[a]	2	R^3OH	3	Yield [%][b]
7		CH_3OH	 **3g**	85
8	 **2c**	BnOH	 **3h**	80
9		*i*-PrOH	 **3i**	43[c] (49)
10		CH_3OH	 **3j**	92
11	 **2d**	BnOH	 **3k**	89
12		*i*-PrOH	 **3l**	42[c] (43)
13		CH_3OH	 **3m**	96
14	 **2e**	BnOH	 **3n**	97
15		*i*-PrOH	 **3o**	65[c] (46)

[a] Reactions performed in autoclave at P_{CO} of 4 bar, with olefins **2a–2e** (2 mmol-scale), 2 mol% of $Pd(TFA)_2$, 2.2 mol% of **1b**, 2 mol% of *p*-TSA and 1.5 equiv. of BQ, in 7:1 R^3OH/THF (0.5M) as the reaction medium, for 66 h. [b] Isolated yields after column chromatography. [c] Conversion of the 1,2-disubstituted olefins and, in parenthesis, isolated yields of the converted products are reported.

In both cases, together with **3c** and **3f**, the respective by-products **4a** and **4b** were formed, deriving from the ability of hydroquinone (generated by reduction of benzoquinone under the reaction conditions) to act as a nucleophile, thus competing with the isopropanol (Scheme 1).

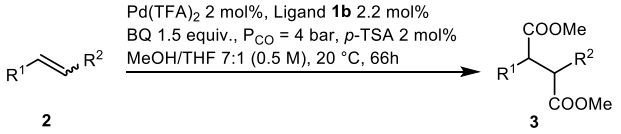


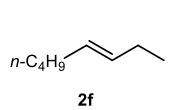
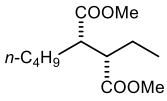
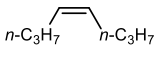
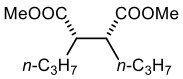
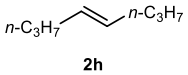
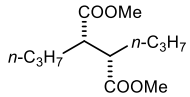
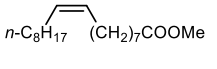
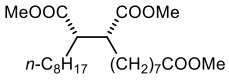
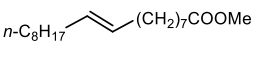
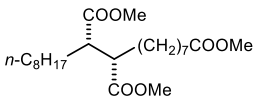
Scheme 1. Formation of by-products **4a** and **4b**

By-products **4a** and **4b** have been isolated (**4a** Y. = 46 %, **4b** Y. = 41 %)[16] and fully characterized.
To identify the structures of compounds **4a** and **b**, in addition to ^{1}H and ^{13}C NMR spectra (Figure S8 and Figure S11), it was necessary to perform HMBC experiments that allowed us to find out that, in both cases, the isopropoxy carbonyl group is bound to the CH bearing the methyl (Figure S9). This carbon-bond connectivity was also confirmed by XRD analysis of single crystals of **4b** obtained upon slow diffusion of *n*-hexane into a dichloromethane solution of the compound (Figure S10 and Table S4). Although compounds **4a**, **4b** represent the by-products of the carbonylation reactions of olefins **2a** and **2b** with *i*-PrOH, they can be regarded as interesting products as they contain two different ester moieties that may have a diverse reactivity in further reactions. Moreover, the identification of structure of compounds **4a** and **4b** provided further details on the catalytic cycle of the bis-alkoxycarbonylation process (*vide infra*). The carbonylation reactions of aliphatic 1,2-disubstituted olefins **2c**, **2d** and **2e** with isopropyl alcohol did not give analogous results compared with the aromatic olefins. Although esters **3i**, **3l** and **3o** were isolated stereospecifically, conversions and yields were less satisfactory, even after further reaction optimization (Table 2, entries 9, 12 and 15).[17]

Considering the excellent results obtained in the bis-methoxycarbonylation of the aliphatic olefins **2d** and **2e** (table 2, entries 10 and 13), in order to evaluate how general this reaction is, alkenes with a double bond remote from the terminal methyl group, such as *trans*-3-octene **2f**, *cis*-4-octene **2g** and *trans*-4-octene **2h**, were also tested. Complete conversions of the *trans* olefins **2f** and **2h** have been achieved, obtaining the corresponding carbonylated products **3p** and **3r** with 92% and 76% isolated yields respectively (table 3, entry 1 and entry 3). Even if only 49% of *cis*-4-octene has been transformed in the carbonylated compound **3q**, almost all the product was recovered (table 3, entry 2). Finally, olefins containing a more internal double bond, such as unsaturated fatty acid methyl esters, were tested as substrates. While the methyl *trans*-9-octadecenoate **2j** has been fully converted, obtaining the bis-carbonylated product **3t** in 78% isolated yield (table 3, entry 5), with the methyl oleate **2i** a 50% of conversion was observed (table 3, entry 4).[18]

Table 3. Bis-methoxycarbonylation of aliphatic 1,2-disubstituted olefins **2f–2j**.

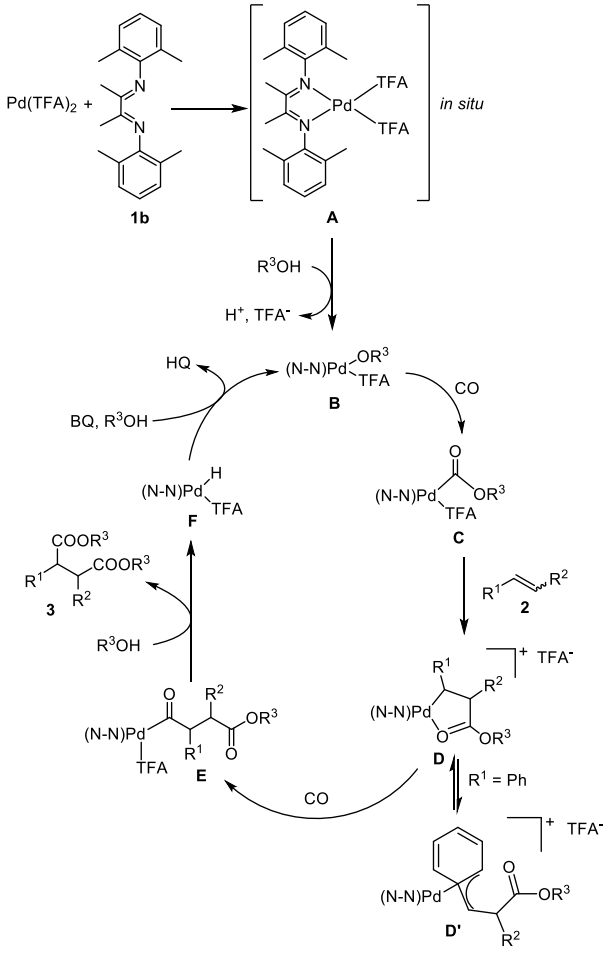


Entry[a]	2	3	Yield [%][b]
1			92
2			49[c] (91)[d]
3			76
4[e]			50[c] (92)[d]
5			78

[a] Reactions performed in autoclave at P_{CO} of 4 bar, with olefins **2f–2j** (2 mmol-scale), 2 mol% of $Pd(TFA)_2$, 2.2 mol% of **1b**, 2 mol% of *p*-TSA and 1.5 equiv. of BQ, in 7:1 MeOH/THF (0.5M) as the reaction medium, for 66 h. [b] Isolated yields after column chromatography. [c] Conversion of the 1,2-disubstituted olefins. [d] Isolated yield of product relative to the olefin conversion. [e] Reaction time 96 h.

All the products **3p-3t** were obtained with a total diastereospecificity and the *trans* aliphatic alkenes appear to be more reactive than the *cis* ones. This is the first time that the bis-alkoxycarbonylation of unsaturated fatty acid methyl esters, without isomerization of the double bond, yielding to methyl tricarboxylate compounds, is reported. Indeed, in literature, alkoxycarbonylations of internal olefins, such as 3-octene and 4-octene,[19] and of unsaturated fatty acids or fatty acid methyl esters,[20] lead to linear esters and to linear α,ω dicarboxylic acid diesters respectively, through a Pd-catalyzed isomerizing methoxycarbonylation process.

Keeping in mind the above results and the literature data,[4k,13,14,21,22] the catalytic cycle depicted in Scheme 2 is proposed, summarizing all the reactions involved in the bis-alkoxycarbonylation process. The (bis(2,6-dimethylphenyl)butane-2,3-diimine) palladium(II)bis(trifluoroacetate) catalyst **A** (Scheme 2, top) is formed *in situ* from the reaction between $Pd(TFA)_2$ and the ligand **1b** in THF.
With the intent of isolating and characterizing the catalyst, **A** was *ad hoc* synthesized, as reported in the Experimental Section. Because of the insolubility of **A** in the most common solvents and its degradation in DMSO, the NMR spectra were recorded in $CDCl_3$, after dissolving **A** in few microliters of hexafluoroisopropanol (HFIP).
From the ^1H NMR spectrum it appears that the signals of the protons H4, H5 and H7 of the complex **A** (Figure 1) are shifted downfield (about 0.10 - 0.30 ppm) respect to the free ligand **1b**, while the signal of H3 remains constant (Table S1, Supporting Information).



Scheme 2. Proposed catalytic cycle

Moreover, in the ^{13}C NMR spectrum all the carbon signals are shifted downfield (about 2.1 - 9.1 ppm) compared to free ligand **1b**, with the exception of the aromatic carbon C1 directly linked to the nitrogen atom that is shifted upfield (Table S2).

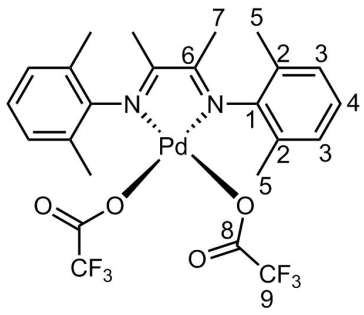


Figure 1. Complex **A**

The observed behaviour confirms the formation of the palladium complex and it is in agreement with the electron withdrawing effect of the metal center. Analogous complexes with bipyridine, phenanthroline or aryl α-diimine ligands have been previously reported.[23] Red/orange single crystals of **A·(CF$_3$)$_2$CHOH**, suitable for XRD analysis, were obtained by slow evaporation of the solvent, after dissolving the catalyst in a small amount of HFIP and adding $CHCl_3$. Complex **A** (Figure 2 and Table S3) displays the expected square-planar geometry, with two coordination sites of the Pd(II) centre occupied by the aryl α-diimine ligand and the other two sites by two trifluoroacetate ligands. The bonding parameters are similar to those previously found in analogous complexes.[23c,24] The angles between the planes of the two aromatic rings and the least-squares plane comprising Pd(1), N(1), N(2), O(1) and O(3) are 87.43(16)° and 83.68(15)°, respectively. Within the unit cell of **A·(CF$_3$)$_2$CHOH**, a hydrogen bond is present, involving the O(5)-H(5) group of the co-crystallized HFIP molecule and O(2), which belongs to one of the trifluoroacetate ligands of **A** [O(5)-H(5) 0.84 Å, H(5)···O(2) 1.91 Å, O(5)···O(2) 2.739(9) Å, <O(5)H(5)O(2) 169.3°].

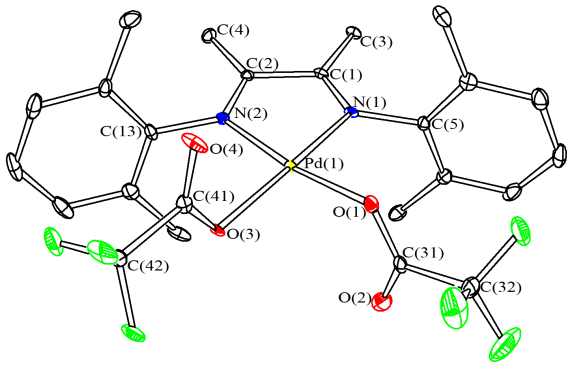
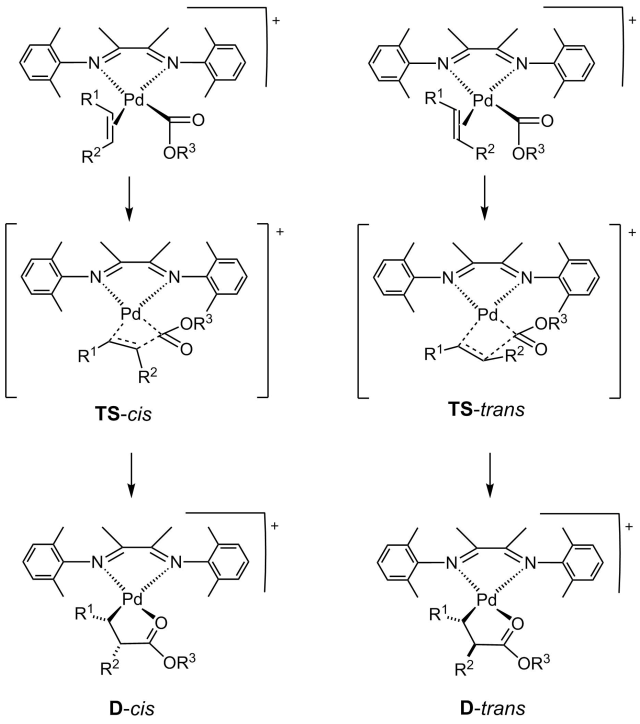


Figure 2. Molecular structure of Complex **A**. Displacement ellipsoids are at the 30% probability level. Hydrogen atoms have been omitted for clarity.

Taking up the description of the catalytic cycle, reaction of **A** with the alcohol allows the formation of the active species **B** and the insertion of CO leads to the alkoxycarbonyl-palladium complex **C** (Scheme 2). The successive coordination and insertion of the

alkene in **C** affords the 5-membered palladacycle **D**. In the case of *cis*- or *trans*-β-methylstyrene, where R^1 is a phenyl ring, the η^3-allylic intermediate **D'** could be in equilibrium with **D**.[14, 25] In any case, further CO insertion gives the complex **E**. Intermediates similar to **D**,[22] **D'**[21] and **E**[21b] have been previously isolated and characterized by us through stoichiometric model reactions. Finally, a nucleophilic attack of the alcohol on the carbonyl linked to Pd in the intermediate **E**, leads to the final product **3** and the palladium hydride complex **F**. Benzoquinone regenerates the active species **B** closing the catalytic cycle (Scheme 2).[26]

The conservation of the *trans* or *cis* geometry of the 1-2 disubstituted alkene, in the palladacycle intermediate **D**, can be explained through a concerted *syn* addition of the Pd-alkoxycarbonyl moiety to the olefin C=C bond (Scheme 3).[22a,27] The resulting four-membered transition states **TS**-*trans* and **TS**-*cis*, depicted in Scheme 3, account for the diastereospecificity of the bis-alkoxycarbonylation reaction.



Scheme 3. *Syn* addition of the Pd-alkoxycarbonyl fragment to the *cis* or *trans* olefins

The proposed catalytic cycle (Scheme 2) allows us to figure out also the causes for the formation of by-products **4**, occurring in the reactions between β-methylstyrenes and *i*-PrOH as nucleophile (Scheme 1). Considering the 2-1 regioselectivity of the insertion of the β-methylstyrenes[22a] into the Pd-alkoxycarbonyl bond of complex **C** (Scheme 2), the formation of both compounds **3** and **4** may results from a competition between isopropanol and hydroquinone (formed during the catalytic cycle) to act as nucleophiles towards the intermediate **E**. The smaller steric hindrance of hydroquinone compared to isopropanol makes the first one more reactive, but being the *i*-PrOH present in great excess, the succinate esters **3** and the by-products **4** are formed in almost equal quantities. Furthermore, from the structure of **4a** and **4b** it can be deduced that, while in the highly hindered intermediate **E** there is a competition between the two nucleophiles, in the intermediate **F** only the *i*-PrOH, present in greater amounts, reacts regenerating the active species **B** (Scheme S1, Supporting Information). This information on the catalytic cycle could be useful to design the synthesis of succinates with two different ester functionalities.

DFT studies are underway to better understand all steps of the catalytic cycle.

Conclusions

An efficient method for the Pd-catalyzed bis-alkoxycarbonylation of 1,2-disubstituted olefins **2** to give 2,3-disubstituted-succinic diesters **3** has been developed, using $Pd(TFA)_2$ as palladium source, bis-(2,6-dimethylphenyl)-2,3-dimethyl-1,4-diazabutadiene as ligand and *p*-benzoquinone as oxidant. The process is diastereospecific, due to the *syn* addition of the olefinic double bond to the alkoxycarbonyl palladium intermediate **C**. Moreover the high selectivity of the reaction and the nearly quantitative yields with aromatic, cyclic and aliphatic olefins using methanol or benzyl alcohol as nucleophiles, under particularly mild reaction conditions (4 bar of CO at 20°C), demonstrate the high efficiency of our catalytic system. For the first time the bis-alkoxycarbonylation reaction of 1,2-dialkyl substituted olefins and of unsaturated fatty acid methyl esters has been successfully realized, obtaining the corresponding products stereospecifically, in good to excellent yields. In particular, if one of the substituents on the double bond is a methyl or an ethyl group the best results were achieved (yields up to 96%), while with alkenes bearing a more internal double bond, the results are slightly less satisfactory and the *trans* olefins resulted to be more reactive than the *cis* ones.

Furthermore, under our reaction conditions, olefin isomerization is not observed, as often happens in Pd catalyzed processes.[3f] In conclusion our bis-alkoxycarbonylation appears to be very general since it can be applied to a large number of different types of 1,2-disubstituted olefins.

The high reactivity of the catalytic system is probably due to the conformation of the palladium intermediates having the aryl rings of the ligand **1b** almost perpendicular to the Pd coordination plane, because of the presence of substituents in the *ortho* positions.[21] This conformation probably favours the leaving of the succinate ester products **3**, enhancing the efficiency of the reactions. The structure of palladium catalyst **A** has been fully identified by NMR and XRD analysis. Based on the above results and the organometallic palladium intermediates,

previously isolated and characterized by us in model reactions, a catalytic cycle, explaining the complete diastereoselectivity of the process, has been proposed. The use of the bulky isopropyl alcohol as nucleophile has allowed us to draw some further conclusions about the mechanism of the catalytic process.

Experimental Section

General methods and materials

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. ^{19}F NMR were recorder on a Varian Mercury Plus VX 400 (^{19}F: 376 MHz), using $CDCl_3$ as solvent. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet, dd = double doublets, dq = double quartets, td = triple doublets. Mass spectra were recorded on a LC-MS apparatus Agilent Ion-Trap 6310A 2795, using electrospray (ES+ or ES-) ionisation techniques. Carbon monoxide (Cp grade 99.99%) was supplied by Air Liquide, *p*-benzoquinone was purchased by Sigma-Aldrich and was recrystallized from n-heptane/EtOH mixture, olefins **2a–2j** were purchased from Sigma-Aldrich, Alfa Aesar or TCI, filtered off a plug of neutral Al_2O_3 and used without further purification. Anhydrous THF was distilled from sodium-benzophenone, methanol was distilled from $Mg(OMe)_2$ and isopropyl alcohol was distilled from CaH_2. $Pd(TFA)_2$ was weighted in an analytical balance without excluding moist and air. All other chemicals were purchased from Sigma-Aldrich and used without further purification. Ligand **1a** was synthesized by our group according to a previously reported procedure.[14] Ligands **1b** and **1c**, used in the optimization reaction, were synthesized according to previously reported procedure.[28] Compounds **3a, 3d, 3g, 3i** were already known and the spectral date are identical to the previously reported literature data (see supporting information for more details).[13a,4c,29]

CCDC.1588018 (complex **A·(CF$_3$)$_2$CHOH** and CCDC.1588019 (compound **4b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Typical procedure for the bis-alkoxycarbonylation reaction of 1,2-disubstituted olefins.

In a nitrogen flushed Schlenk tube, equipped with a magnetic stirring bar, the respective olefins **2a**–**j** (2 mmol) and the alcohol R^3OH (3.5 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 $Pd(TFA)_2$ (13.3 mg, 0.04 mmol) and THF (0.5 mL) were added in sequence. After the mixture turned in a red/brown color (20 min), the ligand **1b** (12.8 mg, 0.044 mmol) was added. The mixture was left under stirring for 10 min, turning in a dark orange color. The olefin solution and the formed catalyst was injected in sequence in a nitrogen flushed autoclave, equipped with a magnetic stirring bar, containing benzoquinone (325 mg, 3 mmol) and *p*-TSA·H_2O (7.6 mg, 0.04 mmol). After 10 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 the room temperature (20°C) for 66 h. The autoclave was vented off, flushed with nitrogen and the reaction mixture was directly analyzed by ^{1}H NMR to determine the conversion of the olefins **2**. The crude was then dried under reduced pressure and filtered off a plug of silica gel, washing with CH_2Cl_2/Et_2O 1:1 (150 mL) finally the solution was dried up in vacuum. Then NaOH 1M (30 mL) was added and the solution was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic solution was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The product was eventually obtained after column chromatography on silica gel (Petroleum ether/CH_2Cl_2 50:50 then 20:80; if benzyl alcohol was used as nucleophiles: Petroleum ether/CH_2Cl_2 70:30 then 50:50).

(2R*,3R*)-Dibenzyl 2-methyl-3-phenylsuccinate (3b): Following the general procedure, compound **3b** was obtained as a white powder; yield: 92% (0.715 g). ^{1}H NMR δ 7.47–7.27 (m, 13H), 7.14–7.07 (m, 2H), 5.22 (d, J = 12.4 Hz, 1H), 5.13 (d, J = 12.4 Hz, 1H), 4.94 (s, 2H), 4.02 (d, J = 11.0 Hz, 1H), 3.46 (dq, J = 11.0, 6.8 Hz, 1H), 1.40 (d, J = 6.8 Hz, 3H). ^{13}C NMR δ 173.8, 171.9, 136.5, 135.61, 135.56, 128.6, 128.5, 128.43, 128.37, 128.2, 128.0, 127.93, 127.91, 127.7, 66.6, 66.2, 54.9, 43.7, 16.4. ESI-MS: m/z=389 $[M+H]^+$.

(2R*,3R*)-Diisopropyl 2-methyl-3-phenylsuccinate (3c): Following the general procedure, compound **3c** was obtained as a colorless oil; yield: 40% (0.232 g). ^{1}H NMR δ 7.37–7.31 (m, 2H), 7.30–7.19 (m, 3H), 4.99 (hept, J = 6.3 Hz, 1H), 4.72 (hept, J = 6.3 Hz, 1H), 3.71 (d, J = 11.2 Hz, 1H), 3.20 (dq, J = 11.2, 6.8 Hz, 1H), 1.28 (d, J = 6.8 Hz, 3H), 1.23 (d, J = 6.3 Hz, 3H), 1.13 (d, J = 6.3 Hz, 3H), 1.01 (d, J = 6.3 Hz, 3H), 0.83 (d, J = 6.2 Hz, 3H). ^{13}C NMR δ 173.9, 171.9, 137.1, 128.6, 128.5, 127.7, 68.5, 67.7, 55.6, 44.0, 21.9, 21.63, 21.59, 21.4, 16.5. ESI-MS: m/z=293 $[M+H]^+$.

(2S*,3R*)-Dibenzyl 2-methyl-3-phenylsuccinate (3e): Following the general procedure, compound **3e** was obtained as a colorless oil; yield: 90% (0.699 g). ^{1}H NMR δ 7.43–7.26 (m, 13H), 7.20–7.14 (m, 2H), 5.17 (d, J = 12.4 Hz, 1H), 5.12 (d, J = 12.4 Hz, 1H), 5.08 (d, J = 12.6 Hz, 1H), 5.03 (d, J = 12.6 Hz, 1H), 3.90 (d, J = 11.4 Hz, 1H), 3.30 (dq, J = 11.4, 7.3 Hz, 1H), 1.02 (d, J = 7.3 Hz, 3H). ^{13}C NMR δ 175.4, 172.9, 136.3, 135.98, 135.89, 129.0, 128.62, 128.59, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 66.60, 66.59, 54.5, 42.5, 15.5. ESI-MS: m/z=389 $[M+H]^+$.

(2S*,3R*)-Diisopropyl 2-methyl-3-phenylsuccinate (3f): Following the general procedure, compound **3f** was obtained as a colorless oil; yield: 50% (0.292 g). ^{1}H NMR δ 7.35–7.24 (m, 5H), 5.03 (hept, J = 6.3 Hz, 1H), 4.94 (hept, J = 6.3 Hz, 1H), 3.69 (d, J = 11.4 Hz, 1H), 3.09 (dq, J = 11.4, 7.3 Hz, 1H), 1.28 (d, J = 6.3 Hz, 3H), 1.24 (d, J = 6.3 Hz, 3H), 1.21 (d, J = 6.3 Hz, 3H), 1.05 (d, J = 6.2 Hz, 3H), 0.94 (d, J = 7.3 Hz, 3H). ^{13}C NMR δ 175.3, 172.7, 136.9, 128.8, 128.5, 127.6, 68.3, 68.0, 54.7, 42.8, 21.9, 21.80, 21.76, 21.4, 15.6. ESI-MS: m/z=293 $[M+H]^+$.

(1R*,2S*)-Dibenzyl cyclohexane-1,2-dicarboxylate (3h): Following the general procedure, compound **3h** was obtained as a colorless oil; yield: 80% (0.564 g). ^{1}H NMR δ 7.40–7.28 (m, 10H), 5.08 (d, J = 12.4 Hz, 2H), 5.03 (d, J = 12.4 Hz, 2H), 2.95–2.88 (m, 2H), 2.12–2.01 (m, 2H), 1.86–1.75 (m, 2H), 1.59–1.35 (m, 4H). ^{13}C NMR δ 173.5, 136.1, 128.5, 128.24, 128.17, 66.3, 42.7, 26.3, 23.8. ESI-MS: m/z=353 $[M+H]^+$.

(2R*,3S*)-Dimethyl 2-methyl-3-pentylsuccinate (3j): Following the general procedure, compound **3j** was obtained as a pale yellow oil; yield: 92% (0.423 g). ^{1}H NMR δ 3.68 (s, 3H), 3.67 (s, 3H), 2.73–2.62 (m, 2H), 1.70–1.54 (m, 1H), 1.43–1.31 (m, 1H), 1.31–1.17 (m, 6H), 1.12 (d, J = 6.7 Hz, 3H), 0.85 (t, J = 6.8 Hz, 3H). ^{13}C NMR δ 175.5, 174.8, 51.9, 51.7, 48.7, 42.2, 31.7, 30.8, 27.2, 22.5, 15.3, 14.1. ESI-MS: m/z=231 $[M+H]^+$.

(2R*,3S*)-Dibenzyl 2-methyl-3-pentylsuccinate (3k): Following the general procedure, compound **3k** was obtained as a colorless oil; yield: 89% (0.681 g). ^{1}H NMR δ 7.39–7.28 (m, 10H), 5.14–5.05 (m, 4H), 2.81–2.69 (m, 2H), 1.69–1.55 (m, 1H), 1.41–1.30 (m, 1H), 1.26–1.15 (m, 6H), 1.13 (d, J = 6.6 Hz, 3H), 0.82 (t, J = 6.8 Hz, 3H). ^{13}C NMR δ 174.6, 174.0, 135.90, 135.88, 128.60, 128.58, 128.5, 128.34 (2C), 128.32, 66.5, 66.4, 48.7, 42.3, 31.5, 30.7, 27.1, 22.4, 15.1, 14.0. ESI-MS: m/z=383 $[M+H]^+$.

(2R*,3S*)-Diisopropyl 2-methyl-3-pentylsuccinate (3l): Following the general procedure, olefin **2d** were converted for 42%, obtaining compound **3l** as a pale orange oil with 43% of yield (0.103 g) over the converted olefin. ^{1}H NMR δ 5.10–4.96 (m, 2H), 2.67–2.56 (m, 2H), 1.69–1.57 (m, 1H), 1.44–1.34 (m, 1H), 1.34–1.18 (m, 18H), 1.12 (d, J = 6.5 Hz, 3H), 0.86 (t, J = 6.4 Hz, 3H). ^{13}C NMR δ 174.6, 173.9, 67.9, 67.8, 48.9, 42.6, 31.7, 30.8, 27.1, 22.5, 22.0 (2C), 21.94, 21.88, 15.3, 14.1. ESI-MS: m/z=287 $[M+H]^+$.

(2S*,3S*)-Dimethyl 2-methyl-3-pentylsuccinate (3m): Following the general procedure, compound **3m** was obtained as a pale yellow oil; yield: 96% (0.442 g). ^{1}H NMR δ 3.66 (s, 3H), 3.65 (s, 3H), 2.78 (dq, J = 7.3, 8.3 Hz, 1H), 2.67 (dt, J = 4.4, 8.6 Hz, 1H), 1.64 – 1.46 (m, 2H), 1.34 – 1.18 (m, 6H), 1.16 (d, J = 7.1 Hz, 3H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR δ 175.8, 175.4, 51.9, 51.7, 47.5, 40.9, 31.8, 28.7, 26.6, 22.5, 14.3, 14.1. ESI-MS: m/z=231 $[M+H]^+$.

(2S*,3S*)-Dibenzyl 2-methyl-3-pentylsuccinate (3n): Following the general procedure, compound **3n** was obtained as a colorless oil; yield: 97% (0.742 g). ^{1}H NMR δ 7.40–7.27 (m, 10H), 5.13–4.99 (m, 4H), 2.89 (dq, J = 7.1, 1.1 Hz, 1H), 2.78 (dt, J = 4.1, 8.7 Hz, 1H), 1.73–1.48 (m, 2H), 1.33–1.21 (m, 6H), 1.19 (d, J = 7.1 Hz, 3H), 0.85 (t, J = 6.8 Hz, 3H). ^{13}C NMR δ 175.1, 174.6, 136.1, 136.0, 128.60, 128.57, 128.4, 128.31, 128.27, 128.25, 66.5, 66.4, 47.5, 40.95, 31.8, 28.7, 26.6, 22.5, 14.3, 14.1. ESI-MS: m/z=383 $[M+H]^+$.

(2S*,3S*)-Diisopropyl 2-methyl-3-pentylsuccinate (3o): Following the general procedure, olefin **2e** were converted for 65%, obtaining compound **3o** as a pale orange oil with 46% of yield (0.170 g) over the converted olefin. ^{1}H NMR δ 5.07–4.92 (m, 2H), 2.72 (dq, J = 7.1, 8.3 Hz, 1H), 2.62 (td, J = 4.1 8.7 Hz, 1H), 1.64–1.46 (m, 2H), 1.38–1.17 (m, 18H), 1.14 (d, J = 7.1 Hz, 3H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR δ 174.9, 174.3, 67.8, 67.7, 47.6, 41.1, 31.8, 28.6, 26.5, 22.5, 21.87, 21.85, 21.82, 21.77, 14.3, 14.1. ESI-MS: m/z=287 $[M+H]^+$.

(2S*,3S*)-Dimethyl 2-butyl-3-ethylsuccinate (3p): Following the general procedure, compound **3p** was obtained as a colorless oil; yield: 92% (0.424 g). ^{1}H NMR δ 3.64 (s, 3H), 3.63 (s, 3H), 2.70–2.57 (m, 2H), 1.75–1.50 (m, 4H), 1.35–1.09 (m, 4H), 0.84 (t, J = 7.1 Hz, 6H). ^{13}C NMR δ 175.4, 175.1, 51.68, 51.67, 48.0, 46.2, 29.1, 28.9, 22.7, 22.2, 13.95, 11.3. ESI-MS: m/z=231 $[M+H]^+$.

(2R*,3S*)-Dimethyl 2,3-dipropylsuccinate (3q): Following the general procedure, compound **3q** was obtained as a colorless oil; yield: 91% (0.205g) over a conversion of 49% of *cis*-4-octene **2g**, determined by ^{1}H NMR analysis on a direct sample of the reaction mixture. ^{1}H NMR δ 3.69 (s, 6H), 2.70–2.59 (m, 2H), 1.67–1.51 (m, 2H), 1.37–1.17 (m, 6H), 0.87 (t, J = 7.1 Hz, 6H). ^{13}C NMR δ 175.1, 51.7, 48.4, 33.2, 20.8, 14.0. ESI-MS: m/z=231 $[M+H]^+$.

(2S*,3S*)-Dimethyl 2,3-dipropylsuccinate (3r): Following the general procedure, compound **3r** was obtained as a pale yellow oil; yield: 76% (0.350 g). ^{1}H NMR δ 3.65 (s, 6H), 2.72–2.63 (m, 2H), 1.63–1.48 (m, 4H), 1.36–1.16 (m, 4H), 0.89 (t, J = 7.3 Hz, 6H). ^{13}C NMR δ 175.3, 51.7, 46.6, 31.4, 20.3, 14.1. ESI-MS: m/z=231 $[M+H]^+$.

(8R*,9S*)-Trimethyl heptadecane-1,8,9-tricarboxylate (3s): Following the general procedure, compound **3s** was obtained as a colorless oil after column chromatography on silica gel (Petroleum ether/CH_2Cl_2 30:70 then CH_2Cl_2, in this case the previous extraction with NaOH 1M / CH_2Cl_2 was not carried out due to **3s** water solubility); yield: 92% (0.381g) over a conversion of 50% of methyl oleate **2i**, determined by ^{1}H NMR analysis on a direct sample of the reaction mixture. ^{1}H NMR δ 3.69 (s, 6H), 3.66 (s, 3H), 2.67–2.57 (m, 2H), 2.29 (t, J = 7.5 Hz, 2H), 1.65–1.52 (m, 4H), 1.38–1.13 (m, 22H), 0.87 (t, J = 6.9 Hz, 3H). ^{13}C NMR δ 175.0, 174.98, 174.4, 51.7 (2C), 51.5, 48.47, 48.45, 34.1, 31.9, 30.97, 30.91, 29.40, 29.39, 29.24, 29.19, 29.0 (2C), 27.40, 27.35, 24.9, 22.7, 14.2. ESI-MS: m/z=415 $[M+H]^+$.

(8R*,9R*)-Trimethyl heptadecane-1,8,9-tricarboxylate (3t): Following the general procedure, compound **3t** was obtained as a pale yellow oil after column chromatography on silica gel (Petroleum ether/CH_2Cl_2 30:70 then CH_2Cl_2, in this case the previous extraction with NaOH 1M / CH_2Cl_2 was not carried out due to **3t** water solubility); yield: 78% (0.647 g). ^{1}H NMR δ 3.66 (s, 9H), 2.72–2.61 (m, 2H), 2.29 (t, J = 7.5 Hz, 2H), 1.64–1.49 (m, 6H), 1.34–1.16 (m, 20H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR δ 175.38, 175.36, 174.4, 51.80, 51.79, 51.6, 46.82, 46.80, 34.2, 31.97, 29.7, 29.51, 29.47, 29.35, 29.28, 29.25, 29.17 (2C), 27.04, 27.01, 25.0, 22.8, 14.3. ESI-MS: m/z=415 $[M+H]^+$.

(2R*,3R*)-1-(4-hydroxyphenyl)-4-methyl-3-methyl-2-phenylsuccinate (4a): Following the general procedure, compound **4a** was obtained as a pale yellow oil after column chromatography on silica gel (CH_2Cl_2 then Et_2O/CH_2Cl_2 5:95, in this case the previous extraction with NaOH 1M / CH_2Cl_2 was not carried out due to **4a** water solubility); yield: 46% (0.315 g). ^{1}H NMR δ 7.44–7.39 (m, 2H), 7.36–7.26 (m, 3H), 6.85–6.71 (m, 4H), 4.77 (hept, J = 6.3 Hz, 1H), 4.00 (d, J = 10.9 Hz, 1H), 3.30 (dq, J = 6.8, 10.9 Hz, 1H), 1.39 (d, J = 6.8 Hz, 3H), 1.05 (d, J = 6.3 Hz, 3H), 0.86 (d, J = 6.2 Hz, 3H). ^{13}C NMR δ 174.2, 171.9, 154.1, 143.6, 136.1, 128.8, 128.6, 128.1, 122.1, 116.1, 68.3, 55.1, 43.9, 21.5, 21.3, 16.4. ESI-MS: m/z=341 $[M-H]^-$.

(2S*,3R*)-1-(4-hydroxyphenyl)-4-methyl-3-methyl-2-phenylsuccinate (4b): Following the general procedure, compound **4b** was obtained as a white powder after

column chromatography on silica gel (CH_2Cl_2 then Et_2O/CH_2Cl_2 5:95, in this case the previous extraction with NaOH 1M / CH_2Cl_2 was not carried out due to **4b** water solubility); yield: 41% (0.281 g). ^{1}H NMR δ 7.44–7.29 (m, 5H), 6.82–6.69 (m, 4H), 5.06 (hept, J = 6.2 Hz, 1H), 3.96 (d, J = 11.4 Hz, 1H), 3.19 (dq, J = 11.4, 7.3 Hz, 1H), 1.27 (d, J = 6.5 Hz, 3H), 1.25 (d, J = 6.5 Hz, 3H), 1.01 (d, J = 7.3 Hz, 3H). ^{13}C NMR δ 175.3, 172.5, 153.4, 144.4, 136.2, 129.2, 128.7, 128.1, 122.4, 116.0, 68.4, 54.5, 42.9, 21.9, 21.8, 15.6. ESI-MS: m/z=341 $[M-H]^-$.

***Ad hoc* synthesis of catalyst A: (bis(2,6-dimethylphenyl)butane-2,3-diimine)palladium(II)bis(trifluoroacetate):** In a nitrogen flushed Schlenk tube, equipped with a magnetic stirring bar, the $Pd(TFA)_2$ (13.3 mg, 0.04 mmol) and THF (0.5 mL) were added in sequence. After the mixture turned in a red/brown color (20 min), the ligand **1b** (11.8 mg, 0.0404 mmol) was added. The mixture was left under stirring for 10 min, turning in a dark orange color. The solvent was removed under vacuum. The complex **A** was obtained as a orange powder; yield: 91% (0.023 g). The NMR spectra are recorded dissolving the catalyst in 50µL of HFIP and then adding $CDCl_3$. ^{1}H NMR δ 7.35–7.23 (m, 2H), 7.15 (d, J = 7.6 Hz, 4H), 2.35 (s, 12H), 2.19 (s, 6H). ^{13}C NMR δ 180.3, 163.6 (q, $^2J_{CF}$ = 38 Hz), 140.6, 130.0, 129.4 (2C), 114.4 (d, $^1J_{CF}$ = 287 Hz), 18.99, 17.5. ^{19}F NMR δ -75.1.

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[16] To reduce the amount of the by-product **4b**, two less bulky ligands, having only one ortho-substituent on the aryl ring, i.e. Ar_2DABMe_2 with Ar = naphthyl and Ar_2DABMe_2 with Ar = 2-(*tert*-butyl)-benzyl, were tested, but in both cases the conversions were lower (60% and 30% respectively) and the ratio **3f**/**4b** was about the same. This is a further evidence of the need to use an aryl α-diimine ligand having two *ortho*-substituents in each aromatic ring.

[17] Various parameters were changed to improve conversions and isolated yields of bis-alkoxycarbonylation of *trans*-2-octene with i-PrOH: catalyst loading (up to 5 mol%); pressure of CO (1 bar); amount of p-TSA (ranging from 0 to 5%) and olefin concentration (0.25M), but none of them had a positive effect on the reactions.

[18] Using the oleic acid as substrate for the bis-methoxycarbonylation reaction, performing the reaction in the same conditions reported in table 3, a conversion of 50% was achieved, obtaining the methyl tricarboxylate product **3s** (table 3) and the 9,10-methoxycarbonylated oleic acid (9R*,10S*)-9,10-bis(methoxycarbonyl)octadecanoic acid in a 80:20 ratio respectively.

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Diastereospecific Bis-Alkoxycarbonylation of 1,2-disubstituted Olefins Catalyzed by Aryl α-Diimine Palladium(II) Catalysts

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