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Selective Aryl alpha-Diimine/Palladium-Catalyzed Bis-Alkoxy- carbonylation of Olefins for the Synthesis of Substituted Succinic Diesters / Fini, Francesco; Beltrani, Michela; Mancuso, Raffaella; Gabriele, Bartolo; Carfagna, Carla. - In: ADVANCED SYNTHESIS & CATALYSIS. - ISSN 1615-4169. - ELETTRONICO. - 357:1(2015), pp. 177-184. [10.1002/adsc.201400501]

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# Selective Aryl $\alpha$ -Diimine/Palladium-Catalyzed Bis-Alkoxy carbonylation of Olefins for the Synthesis of Substituted Succinic Diesters

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Received: ((will be filled in by the editorial staff))

 Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/adsc.201#####>. ((Please delete if not appropriate))

**Abstract.** Aryl  $\alpha$ -diimine derivatives have been used, for the first time, as efficient new ligands for the palladium-catalyzed oxidative bis-alkoxy carbonylation reaction of olefins. The most active catalyst was formed in situ from *bis*-(9-anthryl)-2,3-dimethyl-1,4-diazabutadiene and Pd(TFA)<sub>2</sub>. This catalytic system was able to selectively convert olefins into succinic diesters in good yields (up to 97%) and low catalyst loading (up to 0.5 mol%) under mild reaction conditions (4 bar of CO at 20 °C in the presence of *p*-toluenesulphonic acid as additive and *p*-benzoquinone as oxidant). The optimized conditions could be successfully applied to both aromatic and aliphatic olefins, by using methanol, benzyl alcohol or isopropanol as nucleophiles.

**Keywords:** alkenes; aryl  $\alpha$ -diimine ligands; carbonylation; oxidative carbonylation; palladium; succinic acid esters

## Introduction

Oxidative carbonylations are among the most important reactions in the field of palladium catalysis,<sup>[1]</sup> since the discovery targeted by Tsuji and co-workers in 1964,<sup>[2]</sup> followed by the contribution of Heck of 1972.<sup>[3]</sup> Carbonylations allow to directly convert low value materials, like olefins or alkynes and carbon monoxide, into a number of highly valuable carbonylated compounds, useful in synthetic organic chemistry as well as pharmaceutical and medicinal chemistry.

Succinic acid and its derivatives are particularly important compounds, as they find application in material science<sup>[4]</sup> and in the syntheses of inhibitors of renin<sup>[5]</sup> and matrix metalloproteinase.<sup>[6]</sup> A particularly attractive method for the direct synthesis of succinic acid diesters from simple and readily available feedstocks consists in the Pd-catalyzed oxidative bis-alkoxy carbonylation of olefins. Even though the overall process has been widely recognized to be of high practical importance, only in recent times it has gained a major attention both in the achiral<sup>[7]</sup> and asymmetric version.<sup>[8]</sup> After the pioneering work by Heck,<sup>[3]</sup> a big leap was made by

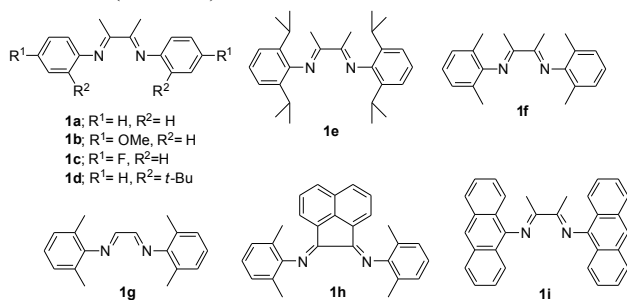
Chauvin et al in 1990.<sup>[7h]</sup> By employing butyl nitrite as the oxidizing agent, they were able to increase the catalytic efficiency up to 300 TON, under relatively mild reaction conditions ( $P_{CO} = 45$  bar, Temp. 60–80 °C), to obtain dibutyl succinates with moderate selectivities.<sup>[7h]</sup> In 2001, Bianchini and co-workers reported a detailed study on the bis-alkoxy carbonylation of styrene, using pyridinimine ligands, Pd(TFA)<sub>2</sub> as the palladium source and benzoquinone (BQ) as oxidant. However, only modest results in terms of conversion and yield could be achieved under their conditions.<sup>[7k]</sup> Regarding the asymmetric counterpart, in literature two different main approaches have been reported. Consiglio<sup>[8b,c]</sup> and Chan,<sup>[8h]</sup> with several chiral diphosphine palladium complexes, obtained dimethyl phenylsuccinate with high enantioselection, but modest conversion and selectivity, using BQ as oxidant under elevated carbon monoxide pressure.<sup>[8c,h]</sup> On the other hand, Inomata and Huang used chiral *N,N* and *N,S* ligands in combination with Pd[II]/Cu[I] salts and oxygen.<sup>[8e,f,i]</sup> By running the bis-alkoxy carbonylation of different styrenes with high catalyst loading under mild reaction conditions, moderate enantioinductions and yields were achieved.<sup>[8e,f,i]</sup> Although these contributions are important, an efficient methodology

for synthesizing succinic diesters with high conversion and selectivity, under mild reaction conditions has not been reported yet.

In the last years, our group has extensively studied the catalytic behavior of Pd(II) complexes containing aryl  $\alpha$ -diimine (*N,N*-diaryl-diazabutadiene, DAB) ligands. Particularly interesting results have been obtained in the CO/styrene copolymerization reaction, leading to a copolymer of high tacticity with good yields.<sup>[9]</sup> Despite their stability, accessibility,<sup>[10]</sup> and efficacy as ligands to Pd, DAB ligands have not been used so far in the bis-alkoxycarbonylation of olefins. Considering our previous know-how, and the quite close structural analogy between DAB and the bisoxazoline ligands employed by Inomata and co-workers,<sup>[8f,11]</sup> we undertook an extensive study on the use of these proficient ligands in the palladium-catalyzed oxidative carbonylation of olefins to succinic acid diesters.

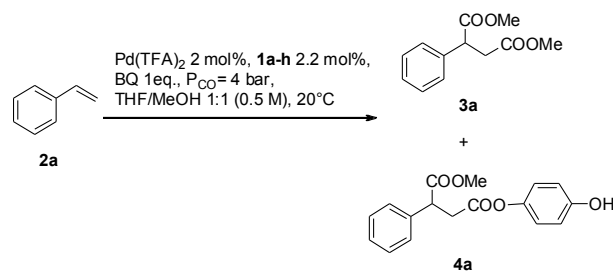
## Results and Discussion

Our initial experiments on the use of DAB ligands for the oxidative bis-alkoxycarbonylation of olefins were carried out on styrene using diaryl-DAB ligands **1a-h** (Scheme 1) and Pd(TFA)<sub>2</sub> as palladium source, in a 1:1 mixture of methanol/THF as reaction medium and BQ as oxidizing agent.<sup>[12]</sup> Reactions were conducted under particularly mild conditions, under 4 bar of CO at 20 °C (Table 1).



**Scheme 1.** *N,N*-diaryl DAB ligands **1a-i**.

**Table 1.** Bis-methoxycarbonylation reaction of styrene catalyzed by Pd(TFA)<sub>2</sub> with ligands **1a-h**. Effect of the ligand and BQ.



Entry <sup>a)</sup>	Ligand <b>1a-h</b>	t (h)	Conv. (%) <sup>b)</sup>	<b>3a:4a</b> ratio <sup>b)</sup>
1	--	42	<5	ND
2	<b>1a</b>	42	50	50:0
3	<b>1b</b>	170	40	40:0

4	<b>1c</b>	170	25	25:0
5	<b>1d</b>	72	40	40:0
6	<b>1e</b>	42	70	60:10
7	<b>1f</b>	72	90	75:15
8	<b>1g</b>	48	40	40:0
9	<b>1h</b>	72	85	65:20
10 <sup>c)</sup>	<b>1f</b>	21	≥98	87:13
11 <sup>d)</sup>	<b>1f</b>	42	≥98	65:35
12 <sup>e)</sup>	<b>1f</b>	42	30	28:2

<sup>a)</sup> Reaction performed in autoclave at P<sub>CO</sub> = 4 bar, with styrene (2 mmol-scale), 2 mol% of Pd(TFA)<sub>2</sub>, 2.2 mol% of **1a-h** and 1 eq. of BQ with THF/MeOH 1:1 (0.5M) as a reaction medium. <sup>b)</sup> Determined by using <sup>1</sup>H NMR analysis of a direct sample of the reaction mixture. <sup>c)</sup> Reaction performed with 1.5 eq. of BQ. <sup>d)</sup> Reaction performed with 0.5 mol% of Pd(TFA)<sub>2</sub>, 0.55 mol% of **1f** and 1.5 eq. of BQ. <sup>e)</sup> Reaction performed with 0.1 mol% of Pd(TFA)<sub>2</sub>, 0.11 mol% of **1f** and 1.5 eq of BQ.

While no reaction took place in the absence of ligands, (Table 1, entry 1), the use of ligands **1a-c**, bearing unsubstituted or *para*-substituted aryl groups, (Scheme 1) did promote the formation of dimethyl succinate **3a**, with modest but encouraging conversions (Table 1, entries 2–4). Similar results were obtained with the mono-*ortho-t*-butyl substituted ligand **1d** (Table 1, entry 5). On the other hand, using the *ortho*-disubstituted-diaryl DAB ligands **1e-f**, bearing bulky *i*-propyl groups (**1e**) or methyl groups (**1f**) in the *ortho* positions of the aromatic rings (Scheme 1), good conversions were attained (Table 1, entries 6 and 7), albeit the desired compound **3a** was obtained in a mixture with 4-(4-hydroxyphenyl) 1-methyl 2-phenylsuccinate **4a** as by-product in different proportions. Formation of **4a** was clearly due to the participation of hydroquinone (formed by reduction of BQ under the reaction conditions) as nucleophile in the carbonylation reaction. Passing from ligand **1f** to **1g** and **1h**, bearing diverse diimine backbones, no beneficial effects were noted (Table 1, compare entry 7 with entries 8 and 9). On the other hand, when the amount of benzoquinone was increased (up to 1.5 equiv), a complete conversion was achieved, with a **3a:4a** ratio of 87:13, with the *ortho*-dimethyl disubstituted ligand **1f** (Table 1 entry 10). The efficiency of the Pd(TFA)<sub>2</sub>/**1f** catalyst was assessed by performing the bis-alkoxycarbonylation reaction with a significantly lower catalyst loading. With 0.5 mol% of catalyst, a complete conversion was reached after 42 h reaction time, although the amount of **4a** increased (up to 65:35; Table 1, entry 11). With 0.1 mol% of catalyst, a 30% conversion of styrene was observed after 42 h (Table 1, entry 12).

With these preliminary data in hand, an extensive optimization study of the reaction conditions was carried out, aimed, in particular, at improving the selectivity of the process toward the desired product **3a**. Full details of this study are given in the Supporting Information (Table S1), while representative results are shown in Table 2.

**Table 2.** Representative results on the Pd(TFA)<sub>2</sub>/DAB-catalyzed bis-methoxycarbonylation of styrene carried out under different reaction condition.

Entry <sup>a)</sup>	Ligand Pd(TFA) <sub>2</sub>	Additive	t (h)	Conv. (%) <sup>b)</sup>	3a:4a ratio <sup>b)</sup>
1	<b>1f</b> 0.5 mol%	--	42	≥98	75:25
2	<b>1f</b> 0.5 mol%	<i>p</i> -TSA 2.0 mol%	42	90	80:10
3	<b>1f</b> 0.1 mol%	--	42	25	25:0
4	<b>1f</b> 0.1 mol%	<i>p</i> -TSA 0.5 mol%	42	75	65:10
5	<b>1i</b> 0.5 mol%	<i>p</i> -TSA 2.0 mol%	66	≥98	95:5
6	<b>1i</b> 0.1 mol%	<i>p</i> -TSA 0.5 mol%	66	45	45:0
7 <sup>c)</sup>	<b>1i</b> 0.5 mol%	<i>p</i> -TSA 2.0 mol%	66	85	80:5
8 <sup>c)</sup>	<b>1i</b> 0.1 mol%	<i>p</i> -TSA 0.5 mol%	66	25	25:0

<sup>a)</sup> Reaction performed in autoclave at P<sub>CO</sub> of 4 bar, with styrene **2a** (2 mmol-scale), 0.5 or 0.1 mol% of Pd(TFA)<sub>2</sub>, 0.55 or 0.11 mol% of **1f** or **1i**, and 1.5 eq. of BQ, with MeOH/THF 7:1 (0.5M) as the reaction medium. <sup>b)</sup> Determined by using <sup>1</sup>H NMR analysis on a direct sample of the reaction mixture. <sup>c)</sup> Reaction performed in a Schlenk tube at atmospheric pressure of CO.

From this investigation, a beneficial effect of increasing the MeOH/THF ratio on selectivity emerged: in fact, using **1f** as ligand in a 7:1 MeOH/THF mixture as reaction medium, the **3a:4a** ratio was 75:25 (Table 2, entry 1; to be compared with entry 11 of Table 1). Moreover, the use of *p*-toluenesulphonic acid (*p*-TSA) as additive (in a 4 to 5 molar ratio with palladium) caused a significant improvement in the efficiency of the process (Table 2, entries 2 and 4): in particular, lowering the catalyst loading down to 0.1 mol%, a catalytic TON of 750 and a TOF of 18 h<sup>-1</sup> were achieved, with a **3a:4a** ratio of 65:10 (compare entry 4 in Table 2 with entry 12 in Table 1). Continuing the process of optimization, we also tested the new ligand *bis*-(9-anthryl)-2,3-dimethyl-1,4-diazabutadiene **1i** recently synthesized by our group for the Pd catalyzed CO/styrene copolymerization.<sup>[9a]</sup> This ligand led to the best results in terms of styrene conversion (>98%) and selectivity toward **3a** (95%), as shown in Table 2, entry 5.<sup>[13]</sup> Remarkably, the catalyst Pd(TFA)<sub>2</sub>/**1i** was active even at atmospheric pressure of CO (Table 2, entries 7–8).

We next investigated the generality of this new efficient and selective catalytic system in the bis-

alkoxycarbonylation reaction with different vinyl arenes and aliphatic olefins (Table 3).

**Table 3.** Scope of the bis-alkoxycarbonylation reaction of aryl and alkyl olefins.

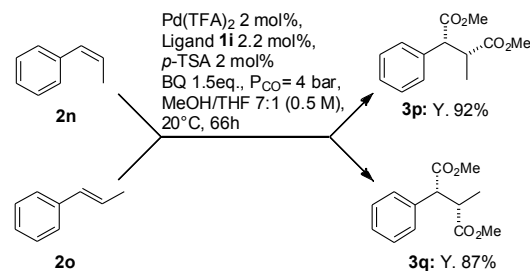
Entry <sup>a)</sup>	2a-l	3a-n	Yield (%) <sup>b)</sup>
1			91
2			97
3 <sup>c)</sup>			88 <sup>d)</sup>
4			90 <sup>d)</sup>
5			96
6			91
7			75 <sup>e)</sup> (94)
8			45 <sup>e)</sup> (91)
9			85
10 <sup>f)</sup>			87 <sup>d)</sup>
11 <sup>f)</sup>			92
12 <sup>f)</sup>			77
13 <sup>g)</sup>			53 <sup>e)</sup> (95)
14 <sup>h)</sup>			92
15 <sup>h)</sup>			94

<sup>a)</sup> Reactions performed in autoclave at a P<sub>CO</sub> of 4 bar, with olefins **2a-l** (2 mmol-scale), 0.5 mol% of Pd(TFA)<sub>2</sub>, 0.55

mol% of **1i**, 2 mol% of *p*-TSA and 1.5 eq. of BQ, in 7:1 MeOH/THF (0.5M) as the reaction medium, for 66 h.<sup>b)</sup> Isolated yields after column chromatography.<sup>c)</sup> Reaction performed with 1 mol% catalyst loading and 2 mol% of *p*-TSA in 7:1 MeOH/THF (0.25M) as the reaction medium.<sup>d)</sup> The presence of a small amount of by-products **4** (less than 7%) in the crude mixture was detected by <sup>1</sup>H NMR.<sup>e)</sup> Conversion of the  $\alpha$ -olefins and, in parenthesis, isolated yields of the converted product are reported.<sup>f)</sup> Reaction performed with 1 mol% catalyst loading.<sup>g)</sup> Reaction performed with 2 mol% catalyst loading.<sup>h)</sup> Reaction performed with 2 mol% catalyst loading, using *i*-PrOH or BnOH in place of methanol.

The succinic acid methyl esters **3a–l** were obtained in good to excellent yields, regardless the different electronic character of the substituents on the aromatic ring (Table 3, entries 1–10). The best isolated yield (97%) was achieved using *p*-methyl styrene as substrate (Table 3, entry 2). While with olefin **2c**, bearing a strong  $\pi$ -donating group, such as *p*-OMe, a slight increase of catalyst loading under more diluted conditions was needed to minimize the formation of by-product **4c**, obtaining **3c** in 88% yield (Table 3, entry 3). *p*-Br, *p*-Cl, and *m*-CF<sub>3</sub> substituents were quite well tolerated in the reaction, with the corresponding esters **3e**, **3f**, and **3i** being obtained with excellent yields (Table 3, entries 5, 6 and 9, respectively). However, vinyl arenes **2g** and **2h**, bearing *o*-Cl and *o*-Br substituents, respectively, were less reactive, and incomplete conversion was observed, even though the selectivity toward diesters **3g** and **3h** was still high (Table 3, entries 7 and 8). 2-vinylnaphthalene **2j** and aliphatic olefins, such as 1-heptene **2k** and 1-(but-3-enyl)benzene **2l**, were in general less reactive than styrenes, and a slight increase of catalyst loading (up to 1 mol%) was necessary to achieve satisfactory results in terms of isolated yield and selectivity in the corresponding succinic diesters **3j–l** (Table 3, entries 10–12). Even with an aliphatic olefin hindered in alpha position,<sup>[14]</sup> such as 3,3-dimethyl-1-butene **2m**, the carbonylated product **3m** was obtained with 95% yield over a converted starting material of 53% (Table 3, entry 13), with 2 mol% of catalyst loading. A survey of different alcohols as nucleophiles in place of methanol was made to prove the broadness of the methodology and to synthesize different products with orthogonal cleavable *i*-propyl- and benzyl- ester groups (**3n–o**), very useful in synthetic organic and medicinal chemistry (Table 3 entries 13–14).

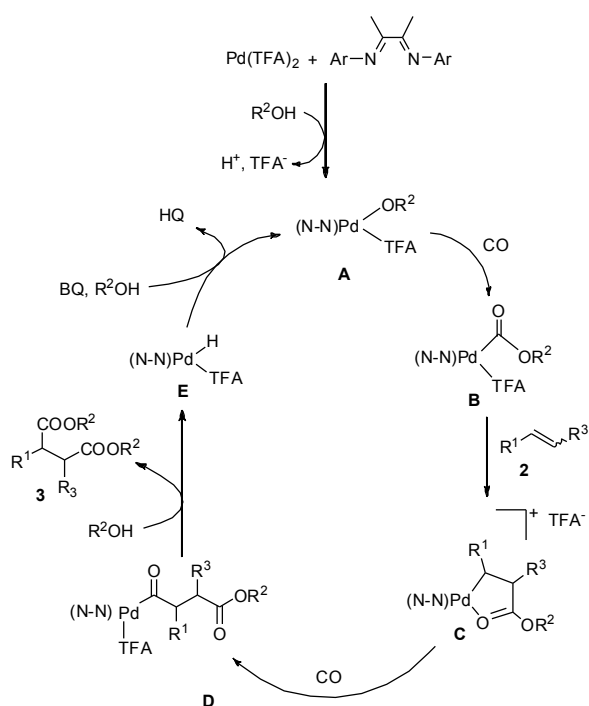
Isopropanol and benzyl alcohol were reactive enough to cause complete styrene conversion, even though with a higher catalyst loading (2 mol% of Pd(TFA)<sub>2</sub>/**1i**; Table 3, entries 13 and 14).<sup>[15]</sup> Regarding internal olefins, while no reaction was observed using the initial reaction conditions reported in Table 1, and ligands **1a** and **1b**, the carbonylation performed with Pd(TFA)<sub>2</sub>/**1i** (2 mol%) allowed a complete conversion of *cis*- and *trans*- $\beta$ -methylstyrene (Scheme 2)



**Scheme 2.** Bis-alkoxycarbonylation reaction with 1,2-disubstituted olefins **2n**, **2o**.

The resulting products **3p** and **3q** were achieved in good isolated yields of 92% and 87% respectively, with total diastereoselectivity (Scheme 2). The geometry of compounds **3p** and **3q** comes from a *syn* overall addition of the carboxyl moieties to the olefin.<sup>[16]</sup> This process, in agreement with a generally accepted mechanism, pass through a concerted *syn* addition of the Pd-carbonyl fragment of the catalyst to the olefin double bond, via a four-membered transition state.<sup>[11,17]</sup>

According to the above results and literature data,<sup>[7k,9,11]</sup> we can propose for the reaction the mechanism shown in Scheme 3. The first step of the process is the formation of the active species **A** from the reaction between Pd(TFA)<sub>2</sub>, the DAB ligand and the alcohol.<sup>[18]</sup> Insertion of CO leads to the alkoxy carbonylpalladium complex **B**, which, after insertion of the alkene **2**, affords the 5-membered palladacycle intermediate **C**,<sup>[11]</sup> however formation of an  $\eta^3$ -allylic intermediate in equilibrium with **C** cannot be ruled out.<sup>[9]</sup> In any case, further CO insertion to give complex **D**, followed by nucleophilic displacement by the alcohol, leads to the final product **3** and palladium hydride complex **E**. Finally, the intervention of benzoquinone regenerates the active species **A** thus closing the catalytic cycle.<sup>[12]</sup>



**Scheme 3.** Proposed catalytic cycle.

The main parameters that influence our bis-alkoxycarbonylation method are: the type of ligand, the presence of *p*-TSA and the ROH/THF ratio. While the last parameter mainly affects the ratio of compounds **3/4**, the roles played by the *p*-TSA and the ligand are more complex. First of all, the sulfonic acid has clearly two effects: it increases the **3/4** ratio and enhances the catalytic efficiency (TON and TOF). In particular, it appears that *p*-TSA decreases the amount of the phenate anion in equilibrium with hydroquinone, suppressing the formation of product **4**. Moreover, as reported by Bianchini et al.,<sup>[7k]</sup> the acid stabilizes the intermediate complex **E** (Scheme 3) and improves the oxidizing ability of BQ, avoiding the formation of palladium black.<sup>[7k]</sup> Regarding the ligand, catalytic species generated from ligands bearing *ortho*-disubstituted aryl rings, such as **1f** and **1i**, appear to be more active than the other ones. This is probably due to the particular conformation of the *in situ* formed complexes. In fact, with ligands **1f** and **1i**, strong steric interactions between the substituents of the diimines backbone and the phenyl rings constrain the aryls to arrange almost perpendicularly with respect to the palladium mean coordination plane.<sup>[9]</sup> This conformation affects the coordination of the aromatic olefin making possible a  $\pi$  stacking interaction in the olefin insertion transition states that could be the origin of the high productivity found both in the CO/vinyl arene copolymerization<sup>[9]</sup> and in the bis-alkoxycarbonylation reaction reported here. With the *ortho*-disubstituted aryl ligand **1e** the reaction still occurs but the conversion was not satisfactory (70%, Table 1 entry 6) probably due to the highly bulky *i*-propyl groups on the aryls which cause a difficult access of the olefin and CO to the

catalytic center.<sup>[9]</sup> Conversely the methyl groups in the Pd(TFA)<sub>2</sub>/**1f** catalyst have the exact size to promote the reaction to completion, but the selectivity towards MeOH or HQ, to achieve **3:4** in good ratio, still lacks (Table 1 entry 7 and 10).<sup>[9]</sup> Finally the complete conversion and selectivity observed in the bis-alkoxycarbonylation reaction with Pd(TFA)<sub>2</sub>/**1i** catalyst (Table 2, entry 5) can be ascribed to the precise steric hindrance of the anthryl moieties and to a greater ability of complex **D** (Scheme 3) to undergo alcoholysis by ROH rather than cleavage by hydroquinone.

## Conclusion

We have developed an efficient method for the Pd-catalyzed bis-alkoxycarbonylation of olefins **2** to give succinic diesters **3** in good yields and high selectivity, under particularly mild reaction conditions (4 bar of CO at 20 °C). Various substituted aryl  $\alpha$ -diimine ligands have been used for the first time in this kind of reaction, together with Pd(TFA)<sub>2</sub> as palladium source, alcohols as nucleophiles and 1,4-benzoquinone as oxidant. In particular, the 9-anthryl ligand **1i** gave the best results in terms of substrate conversion and product yield, with low catalyst loading (0.5–2 mol%). The optimized reaction conditions could be successfully applied to both aromatic and aliphatic olefins, with different alcohols as nucleophiles, including the sterically hindered *i*-PrOH. The enantioselective version of our bis-alkoxycarbonylation is currently under investigation in our laboratories.

## 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 <sup>1</sup>H NMR taking a direct sample of the crude mixture. <sup>1</sup>H NMR and <sup>13</sup>C NMR were recorded on a Bruker Avance 200 spectrometer (<sup>1</sup>H: 200 MHz, <sup>13</sup>C: 50 MHz), using CDCl<sub>3</sub> as solvent. Chemical shifts are reported in the  $\delta$  scale relative to residual CHCl<sub>3</sub> (7.26 ppm) for <sup>1</sup>H NMR and to the central line of CDCl<sub>3</sub> (77.10 ppm) for <sup>13</sup>C NMR. <sup>13</sup>C NMR were recorded with <sup>1</sup>H broadband decoupling. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptet, m = multiplet, dd = double doublets, br = broad. Mass spectra were recorded on a LC-MS apparatus Waters 2795, Micromass ZQ using electrospray (ES+) ionisation techniques. Carbon monoxide (Cp grade 99.99%) was supplied by Air Liquide, benzoquinone was purchased by Sigma-Aldrich and was recrystallized from n-heptane/EtOH mixture, olefins **2a-o** were purchased from Sigma-Aldrich or Alfa Aesar or TCI, filtered off a plug of neutral Al<sub>2</sub>O<sub>3</sub> and used without further purification. Anhydrous THF was distilled from sodium-benzophenone, and methanol was distilled from Mg(OMe)<sub>2</sub>. Pd(TFA)<sub>2</sub> was weighed in an analytical balance without excluding moist and air. All other chemicals were purchased from Sigma-Aldrich and used without further purification. Ligands **1a-h**, used in the optimization reaction were synthesized according to previously reported procedure.<sup>[10]</sup> Ligand **1i** was

synthesized by our group according to a previously reported procedure.<sup>[9a]</sup> Compounds **3a–f,j,l** were already known and the spectral data are identical to the previously reported literature data (see supporting information for more details).<sup>[81]</sup>

### Typical Procedure for the bis-alkoxycarbonylation reaction of olefins.

In a nitrogen flushed Schlenk tube, equipped with a magnetic stirring bar, the Pd(TFA)<sub>2</sub> (3.3 mg, 0.01 mmol) and THF (0.5 mL) were added in sequence. After the mixture turned in a red/brown color (20 min), the ligand **1i** (4.8 mg, 0.011 mmol) was added. The mixture was left stirring for 10 min, turning in a dark-green color. The formed catalyst was injected in a nitrogen flushed autoclave, equipped with a magnetic stirring bar, containing benzoquinone (325 mg, 3 mmol) and p-TSA·H<sub>2</sub>O (7.6 mg, 0.04 mmol) in MeOH (3.5 mL). After 10 min of stirring, olefins **2a–o** (2 mmol) were added in one portion in the reaction mixture. 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 <sup>1</sup>H NMR to determine the conversion and the ratio of the product **3** and **4**. The crude was then dried under reduced pressure and filtered off a plug of silica gel, washing with CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O 8:2 (25 mL) finally the solution was dried up in vacuum. The product was eventually obtained after column chromatography on silica gel (Petroleum ether/CH<sub>2</sub>Cl<sub>2</sub> 50:50 then 30:70).

### Dimethyl 2-(2-chlorophenyl)succinate **3g**.

Following the general procedure, compound **3g** was obtained as a pale yellow oil in 94% of isolated yield (over a conversion of 75% of 2-chlorostyrene **2g**, determined by <sup>1</sup>H NMR analysis on a direct sample of the reaction mixture). <sup>1</sup>H NMR δ 7.47–7.13 (m, 4H), 4.60 (dd, *J* = 9.8, 5.1 Hz, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 3.13 (dd, *J* = 17.0, 9.8 Hz, 1H), 2.65 (dd, *J* = 17.0, 5.1 Hz, 1H). <sup>13</sup>C NMR δ 172.9, 171.7, 135.6, 133.6, 130.0, 128.9, 128.8, 127.3, 52.4, 51.9, 44.0, 36.4. ESI-MS *m/z* 257 [M+H]<sup>+</sup>.

### Dimethyl 2-(2-bromophenyl)succinate **3h**.

Following the general procedure, compound **3h** was obtained as a pale yellow oil in 91% of isolated yield (over a conversion of 45% of 2-bromostyrene **2h**, determined by <sup>1</sup>H NMR analysis on a direct sample of the reaction mixture). <sup>1</sup>H NMR δ 7.61–7.54 (m, 1H), 7.30–7.21 (m, 2H), 7.18–7.07 (m, 1H), 4.63 (dd, *J* = 10.0, 4.9 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.12 (dd, *J* = 17.0, 10.0 Hz, 1H), 2.68 (dd, *J* = 17.0, 5.0 Hz, 1H). <sup>13</sup>C NMR δ 172.9, 171.7, 137.4, 133.4, 129.1, 128.8, 128.0, 124.3, 52.5, 52.0, 46.4, 36.7. ESI-MS *m/z* 301 [M+H]<sup>+</sup>.

### Dimethyl 2-(3-(trifluoromethyl)phenyl)succinate **3i**.

Following the general procedure, compound **3i** was obtained as a colorless oil in 85% of isolated yield. <sup>1</sup>H NMR δ 7.59–7.40 (m, 4H), 4.15 (dd, *J* = 5.5 Hz, 9.8 Hz, 1H), 3.66 (s, 3H), 3.64 (s, 3H), 3.21 (dd, *J* = 9.7, 17.0 Hz, 1H), 3.21 (dd, *J* = 5.5, 17.0 Hz, 1H). <sup>13</sup>C NMR δ 172.8, 171.6, 138.7, 131.30 (q, *J* = 1.1 Hz), 131.28 (q, *J* = 32.4 Hz), 129.5, 124.74 (q, *J* = 3.7 Hz), 124.69 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 272.4 Hz), 52.6, 52.0, 46.9, 37.4. ESI-MS *m/z* 291 [M+H]<sup>+</sup>.

### Dimethyl 2-pentylsuccinate **3k**.

Following the general procedure, but performing the reaction with 1 mol% catalyst loading (6.6 mg, 0.02 mmol of Pd(TFA)<sub>2</sub> and 9.6 mg, 0.022 mmol of **1i**) compound **3k** was obtained as a colorless oil in 92% of isolated yield. <sup>1</sup>H NMR δ 3.70 (s, 3H), 3.68 (s, 3H), 2.93–2.64 (m, 2H), 2.44

(dd, *J* = 15.9, 4.6 Hz, 1H), 1.72–1.43 (m, 2H) 1.39–1.13 (m, 6H), 0.97–0.79 (m, 3H); <sup>13</sup>C NMR δ 175.7, 172.7, 51.8, 51.7, 41.1, 35.7, 31.8, 31.4, 26.5, 22.3, 13.9. ESI-MS *m/z* 217 [M+H]<sup>+</sup>.

### Dimethyl 2-*tert*-butylsuccinate **3m**.

Following the general procedure, but performing the reaction with 2 mol% of catalyst loading (13.3 mg, 0.04 mmol of Pd(TFA)<sub>2</sub> and 19.2 mg, 0.044 mmol of **1i**), compound **3m** was obtained as a pale yellow oil in 95% of isolated yield (over a conversion of 53% of 3,3-methyl-1-butene **2m**). <sup>1</sup>H NMR δ, 3.66 (s, 3H), 3.63 (s, 3H), 2.85–2.39 (m, 3H), 0.93 (s, 3H); <sup>13</sup>C NMR δ 174.8, 173.3, 51.9, 51.4, 51.3, 32.7, 27.9.; ESI-MS *m/z* 203 [M+H]<sup>+</sup>.

### Diisopropyl 2-phenylsuccinate **3n**.

Following the general procedure, but performing the reaction with 2 mol% catalyst loading (13.3 mg, 0.04 mmol of Pd(TFA)<sub>2</sub> and 19.2 mg, 0.044 mmol of **1i**) and using *i*-PrOH as alcohol, compound **3n** was obtained as a colourless oil in 92% of isolated yield. <sup>1</sup>H NMR δ 7.26 (br s, 5H), 4.98 (hept, *J* = 6.3 Hz, 1H), 4.97 (hept, *J* = 6.2 Hz, 1H), 4.01 (dd, *J* = 5.5, 10.2 Hz, 1H), 3.12 (dd, *J* = 10.2, 16.7 Hz, 1H), 2.60 (dd, *J* = 5.5, 16.7 Hz, 1H), 1.22 (d, *J* = 6.3 Hz, 3H), 1.19 (d, *J* = 6.2 Hz, 3H), 1.16 (d, *J* = 6.2 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 3H); <sup>13</sup>C NMR δ 172.4, 171.0, 138.0, 128.7, 127.7, 127.4, 68.4, 68.1, 47.5, 38.2, 21.7, 21.7, 21.4; ESI-MS *m/z* 278 [M+H]<sup>+</sup>.

### Dibenzyl 2-phenylsuccinate **3o**.

Following the general procedure, but performing the reaction with 2 mol% catalyst loading (13.3 mg, 0.04 mmol of Pd(TFA)<sub>2</sub> and 19.2 mg, 0.044 mmol of **1i**) and using BnOH as alcohol, compound **3o** was obtained as a colourless oil in 94% of isolated yield. <sup>1</sup>H NMR δ 7.51–7.09 (m, 15H), 5.10 (br s, 4H), 4.18 (dd, *J* = 9.9, 5.5 Hz, 1H), 3.29 (dd, *J* = 16.9, 10.0 Hz, 1H), 2.77 (dd, *J* = 16.9, 5.5 Hz, 1H); <sup>13</sup>C NMR δ 172.7, 171.3, 137.5, 135.8, 135.7, 128.9, 128.6, 128.50, 128.33, 128.28, 128.2, 127.9, 127.8, 66.8, 66.7, 47.4, 37.8. ESI-MS *m/z* 375 [M+H]<sup>+</sup>.

### (2*R*\*,3*R*\*)-Dimethyl 2-methyl-3-phenylsuccinate **3p**.

Following the general procedure, but performing the reaction with 2 mol% of catalyst loading (13.3 mg, 0.04 mmol of Pd(TFA)<sub>2</sub> and 19.2 mg, 0.044 mmol of **1i**), compound **3p** was obtained as a pale yellow wax in 92% of isolated yield. <sup>1</sup>H NMR δ 7.36–7.21 (m, 5H), 3.81 (d, *J* = 10.9 Hz, 1H), 3.65 (s, 3H), 3.40 (s, 3H), 3.24 (dq, *J* = 10.9, 6.8 Hz, 1H), 1.28 (d, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR δ 174.3, 172.5, 136.6, 128.4, 128.1, 127.6, 54.6, 51.9, 51.3, 43.6, 16.2; ESI-MS *m/z* 237 [M+H]<sup>+</sup>.

### (2*S*\*,3*R*\*)-Dimethyl 2-methyl-3-phenylsuccinate **3q**.

Following the general procedure, but performing the reaction with 2 mol% of catalyst loading (13.3 mg, 0.04 mmol of Pd(TFA)<sub>2</sub> and 19.2 mg, 0.044 mmol of **1i**), compound **3q** was obtained as a pale yellow oil in 87% of isolated yield. <sup>1</sup>H NMR δ 7.44–7.25 (m, 5H), 3.81 (d, *J* = 11.4 Hz, 1H), 3.77 (s, 3H), 3.67 (s, 3H), 3.21 (dq, *J* = 11.3, 7.3 Hz, 1H), 0.99 (d, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR δ 176.0, 173.6, 136.2, 128.8, 128.3, 127.7, 54.1, 52.0, 51.9, 42.2, 15.3; ESI-MS *m/z* 237 [M+H]<sup>+</sup>.

## Acknowledgements

This work was supported by Ministero dell'Università e della Ricerca (PRIN n. 2008A7P7YJ).

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- [13] By using the same optimized reaction conditions reported in Table 2, bis-oxazoline and diphosphine ligands, in combination with Pd(TFA)<sub>2</sub>, were not active in the bis-alkoxycarbonylation of the styrene, see Table S2 in the Supporting Information.
- [14] Isoprene and 4-vinyl-cyclohexene-monoxide were also tested in the bis-alkoxycarbonylation of styrene. Although conversions of 90% and 20% were achieved, respectively (with 2 mol% of catalyst loading), in both cases a complex mixtures of products were attained.
- [15] Using the more sterically hindered *t*-BuOH as nucleophile the reaction was much slower, even with 2 mol% of catalyst loading. A conversion of 40% of **2a** was attained leading to the 4,4'-1,4-phenylene 1-tert-butyl bis(2-phenylsuccinate) in 35% of isolated yield.
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- [18] Ancillary experiments were conducted to support the proposed catalytic cycle. Ligand **1i** was added to a THF solution of Pd(TFA)<sub>2</sub> and benzoquinone, to avoid a relatively fast decomposition. After removing the solvent from the reaction mixture, the <sup>1</sup>H NMR, recorded in CDCl<sub>3</sub>, showed signals attributable to the precatalyst [(N-N)Pd(THF)<sub>2</sub>]<sup>2+</sup>[TFA<sup>-</sup>]<sub>2</sub>. Unfortunately the addition of methanol produced an immediate decomposition of the complex to palladium black.



Selective Aryl  $\alpha$ -Diimine/Palladium-Catalyzed  
Bis-Alkoxy carbonylation of Olefins for the  
Synthesis of Substituted Succinic Diesters

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