Advanced Synthesis & Catalysis

DOI: 10.1002/adsc.201400501

Selective Aryl α-Diimine/Palladium-Catalyzed Bis-Alkoxycarbonylation of Olefins for the Synthesis of Substituted Succinic Diesters

Francesco Fini,[a,*] Michela Beltrani,[a] Raffaella Mancuso,[b] Bartolo Gabriele,[b] and Carla Carfagna[a,*]

[a] Department of Biomolecular Sciences, University of Urbino, Piazza Rinascimento 6, 61029 Urbino (PU), Italy
Fax: (+39)-0722-303-306; phone: (+39)-0722-303-312; e-mail: fini_f@libero.it or carla.carfagna@uniurb.it
[b] Department of Chemistry and Chemical Technologies, University of Calabria, Via P. Bucci 12/C, 87036 Arcavacata di Rende (CS), Italy

Received: May 20, 2014; Revised: August 1, 2014; Published online: ■■ ■■, 0000

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201400501.

Abstract: Aryl α-diimine derivatives have been used, for the first time, as efficient new ligands for the palladium-catalyzed oxidative bis-alkoxycarbonylation reaction of olefins. The most active catalyst was formed *in situ* from bis(9-anthryl)-2,3-dimethyl-1,4-diazabutadiene and palladium(II) trifluoroacetate [$Pd(TFA)_2$]. 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 carbon monoxide (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 isopropyl alcohol as nucleophiles.

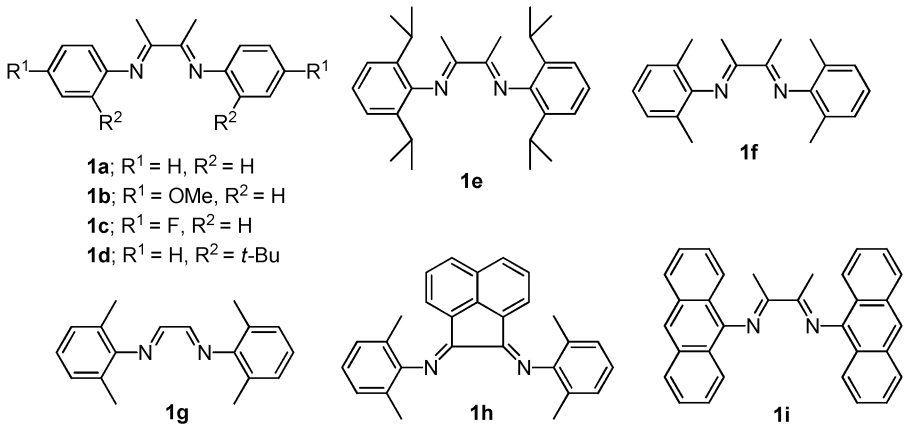
Keywords: alkenes; aryl α-diimine ligands; carbonylation; oxidative carbonylation; palladium; succinic acid esters

Introduction

Oxidative carbonylations are among the most important reactions in the field of palladium catalysis,[1] since the discovery targeted by Tsuji and co-workers in 1964,[2] followed by the contribution of Heck of 1972.[3] Carbonylations allow one 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[4] and in the syntheses of inhibitors of renin[5] and matrix metalloproteinase.[6] 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-alkoxycarbonylation of olefins. Even though the overall process has been widely recognized to be of high practical importance, only in recent times has it gained major attention both in the achiral[7] and asymmetric versions.[8] After the pioneering work by Heck,[3] a big leap was made by Chauvin et al. in 1990.[7h] 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, temperature 60–80 °C), to obtain dibutyl succinates with moderate selectivities.[7h] In 2001, Bianchini and co-workers reported a detailed study on the bis-alkoxycarbonylation of styrene, using pyridinimine ligands, $Pd(TFA)_2$ 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.[7k] Regarding the asymmetric counterpart, in the literature two different main approaches have been reported. Consiglio[8b,c] and Chan,[8h] using several chiral diphoshine palladium complexes, obtained dimethyl phenylsuccinate with high enantioselection, but modest conversion and selectivity, using BQ as oxidant under an elevated carbon monoxide pressure.[8c,h] 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.[8e,f,i] By running the bis-alkoxycarbonylation of different styrenes with high catalyst loadings under mild reaction conditions, moderate enan-

 © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim



Scheme 1. *N*,*N*-Diaryl DAB ligands **1a–i**.

tioinductions and yields were achieved.[8e,f,i] 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 α-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.[9] Despite their stability, accessibility,[10] 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,[8f,11] 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 $Pd(TFA)_2$ as palladium source, in a 1:1 mixture of methanol/THF as reaction medium and BQ as oxidizing agent.[12] Reactions were conducted under particularly mild conditions, under 4 bar of CO at 20 °C (Table 1).

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*-*tert*-butyl substituted ligand **1d** (Table 1, entry 5). On the other hand, using the *ortho*-disubstituted-diaryl DAB ligands **1e** and **1f**, bearing bulky isopropyl 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 $Pd(TFA)_2$/**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).

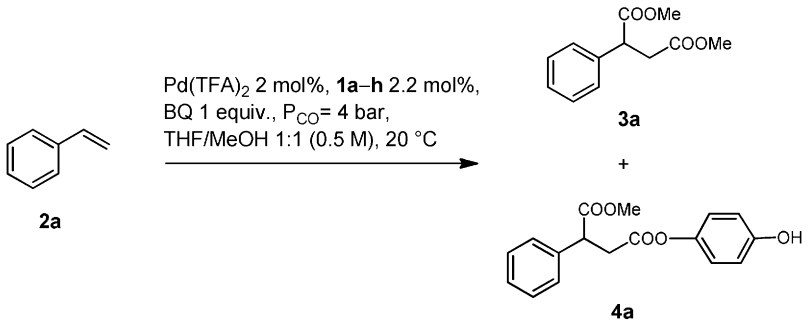
With these preliminary data in hand, an extensive optimization study of the reaction conditions was carried out, aimed, in particular, at improving the selectivity of the process toward the desired product **3a**. Full details of this study are given in the Supporting Information (Table S1), while representative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

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

 © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

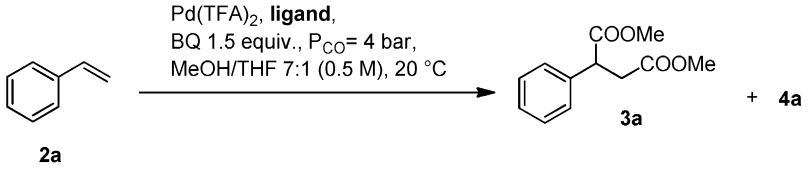
Table 1. Bis-methoxycarbonylation reaction of styrene catalyzed by $Pd(TFA)_2$ with ligands **1a–h**. Effect of the ligand and BQ.



Entry[a]	Ligand **1a–h**	Time [h]	Conversion [%][b]	**3a**:**4a** ratio[b]
1	–	42	<5	ND
2	**1a**	42	50	50:0
3	**1b**	170	40	40:0
4	**1c**	170	25	25:0
5	**1d**	72	40	40:0
6	**1e**	42	70	60:10
7	**1f**	72	90	75:15
8	**1g**	48	40	40:0
9	**1h**	72	85	65:20
10[c]	**1f**	21	≥ 98	87:13
11[d]	**1f**	42	≥ 98	65:35
12[e]	**1f**	42	30	28:2

[a] Reaction performed in autoclave at $P_{CO}=4$ bar, with styrene (2 mmol scale), 2 mol% of $Pd(TFA)_2$, 2.2 mol% of **1a–h** and 1 equiv. of BQ with THF/MeOH 1:1 (0.5 M) as reaction medium.
[b] Determined by direct ^1H NMR analysis of a sample of the reaction mixture.
[c] Reaction performed with 1.5 equiv. of BQ.
[d] Reaction performed with 0.5 mol% of $Pd(TFA)_2$, 0.55 mol% of **1f** and 1.5 equiv. of BQ.
[e] Reaction performed with 0.1 mol% of $Pd(TFA)_2$, 0.11 mol% of **1f** and 1.5 equiv. of BQ.

Table 2. Representative results on the $Pd(TFA)_2$/DAB-catalyzed bis-methoxycarbonylation of styrene carried out under different reaction conditions.

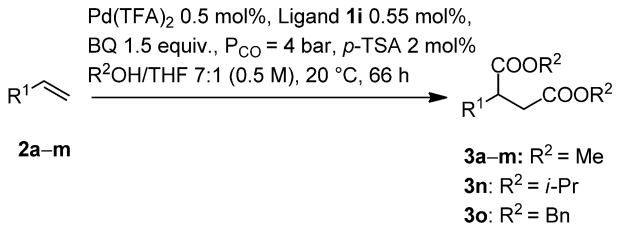


Entry[a]	**Ligand/**amount of $Pd(TFA)_2$	Additive	Time [h]	Conversion [%][b]	**3a**:**4a** ratio[b]
1	**1f/**0.5 mol%	–	42	≥ 98	75:25
2	**1f/**0.5 mol%	*p*-TSA (2.0 mol%)	42	90	80:10
3	**1f/**0.1 mol%	–	42	25	25:0
4	**1f/**0.1 mol%	*p*-TSA (0.5 mol%)	42	75	65:10
5	**1i/**0.5 mol%	*p*-TSA (2.0 mol%)	66	≥ 98	95:5
6	**1i/**0.1 mol%	*p*-TSA (0.5 mol%)	66	45	45:0
7[c]	**1i/**0.5 mol%	*p*-TSA (2.0 mol%)	66	85	80:5
8[c]	**1i/**0.1 mol%	*p*-TSA (0.5 mol%)	66	25	25:0

[a] Reaction performed in an autoclave at P_{CO} of 4 bar, with styrene **2a** (2 mmol scale), 0.5 or 0.1 mol% of $Pd(TFA)_2$, 0.55 or 0.11 mol% of **1f** or **1i**, and 1.5 equiv. of BQ, with MeOH/THF 7:1 (0.5 M) as the reaction medium.
[b] Determined by direct ^1H NMR analysis on a sample of the reaction mixture.
[c] Reaction performed in a Schlenk tube at atmospheric pressure of CO.

 © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

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



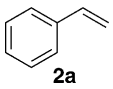
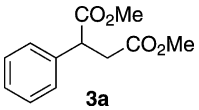
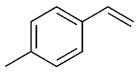
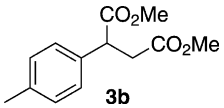
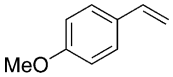
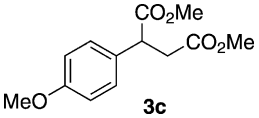
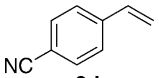
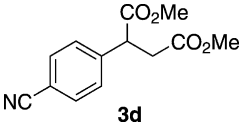
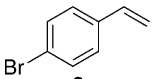
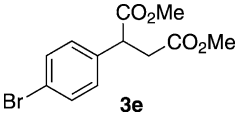
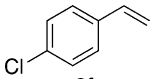
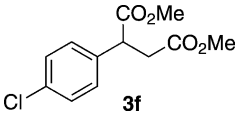
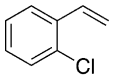
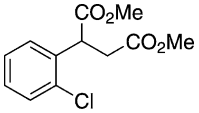
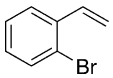
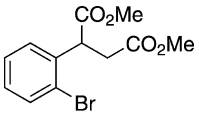
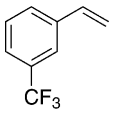
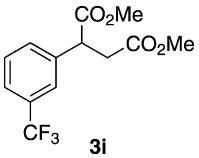
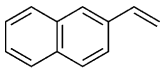
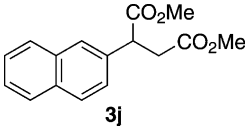
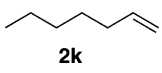
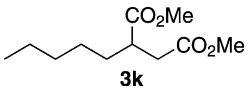
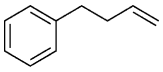
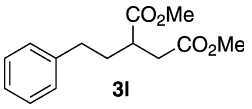
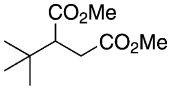
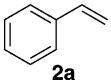
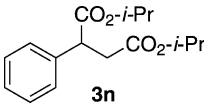
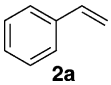
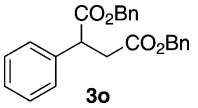
Entry[a]	2a–l	3a–n	Yield [%][b]
1	 2a	 3a	91
2	 2b	 3b	97
3[c]	 2c	 3c	88[d]
4	 2d	 3d	90[d]
5	 2e	 3e	96
6	 2f	 3f	91
7	 2g	 3g	75[e] (94)
8	 2h	 3h	45[e] (91)
9	 2i	 3i	85
10[f]	 2j	 3j	87[d]
11[f]	 2k	 3k	92

Table 3. (Continued)

Entry[a]	2a–l	3a–n	Yield [%][b]
12[f]	 2l	 3l	77
13[g]	 2m	 3m	53[e] (95)
14[h]	 2a	 3n	92
15[h]	 2a	 3o	94

[a] Reactions performed in autoclave at a P_{CO} of 4 bar, with olefins **2a–l** (2 mmol scale), 0.5 mol% of $Pd(TFA)_2$, 0.55 mol% of **1i**, 2 mol% of *p*-TSA and 1.5 equiv. of BQ, in 7:1 MeOH/THF (0.5 M) as the reaction medium, for 66 h.

[b] Isolated yields after column chromatography.

[c] Reaction performed with 1 mol% catalyst loading and 2 mol% of *p*-TSA in 7:1 MeOH/THF (0.25 M) as the reaction medium.

[d] The presence of a small amount of by-products **4** (less than 7%) in the crude mixture was detected by ^{1}H NMR.

[e] Conversion of the α-olefins and, in parenthesis, isolated yields of the converted product are reported.

[f] Reaction performed with 1 mol% catalyst loading.

[g] Reaction performed with 2 mol% catalyst loading.

[h] Reaction performed with 2 mol% catalyst loading, using *i*-PrOH or BnOH in place of methanol.

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^{-1} 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.[9a] 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.[13] Remarkably, the catalyst $Pd(TFA)_2$/**1i** was active even at atmospheric pressure of CO (Table 2, entries 7 and 8).

We next investigated the generality of this new efficient and selective catalytic system in the bis-alkoxycarbonylation reaction with different vinylarenes and aliphatic olefins (Table 3).

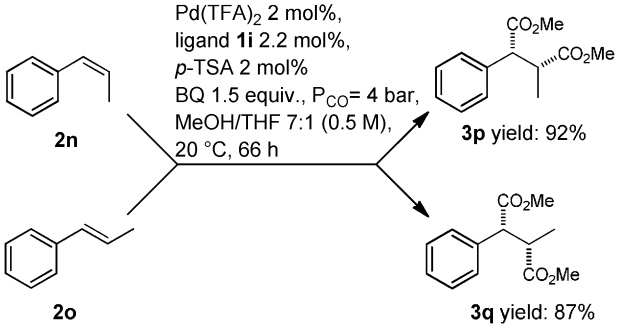
© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

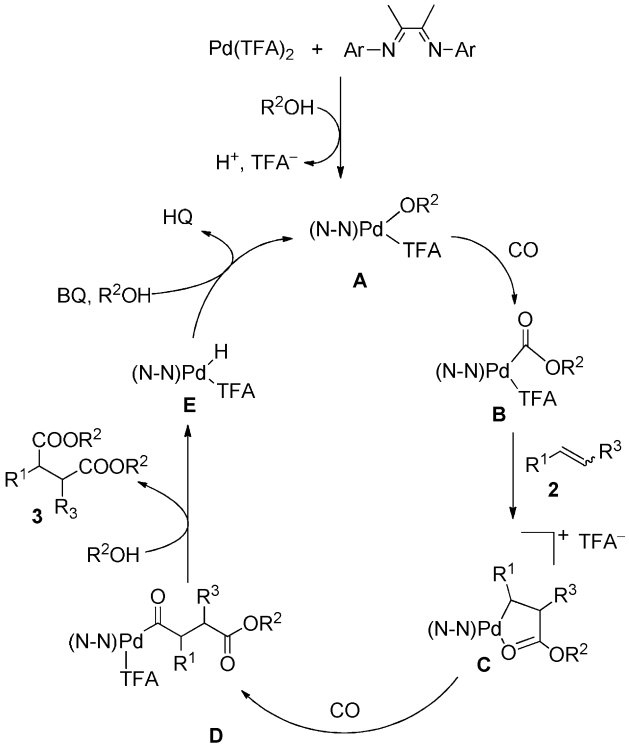
The succinic acid methyl esters **3a–l** were obtained in good to excellent yields, regardless of the different electronic character of the substituents on the aromatic ring (Table 3, entries 1–10). The best isolated yield (97%) was achieved using *para*-methylstyrene as substrate (Table 3, entry 2). While with olefin **2c**, bearing a strong π-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_3 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, vinylarenes **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-Vinylnaphtalene **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 the alpha position,[14] 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 isopropyl and benzyl ester groups (**3n** and **3o**), very useful in synthetic organic and medicinal chemistry (Table 3 entries 13 and 14). Isopropyl alcohol and benzyl alcohol were reactive enough to cause complete styrene conversion, even though with a higher catalyst loading [2 mol% of $Pd(TFA)_2$/**1i**; Table 3, entries 13 and 14].[15]

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 $Pd(TFA)_2$/**1i** (2 mol%) allowed a complete conversion of *cis*- and *trans*-β-methylstyrene (Scheme 2).

The resulting products **3p** and **3q** were obtained 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.[16] This process, in agreement with a generally accepted mechanism, passes through a concerted *syn* addition of the Pd-carbonyl fragment of the catalyst to the olefin double bond, *via* a four-membered transition state.[11,17]



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



Scheme 3. Proposed catalytic cycle.

According to the above results and literature data,[7k,9,11] we can propose the reaction mechanism shown in Scheme 3. The first step of the process is the formation of the active species **A** from the reaction between $Pd(TFA)_2$, the DAB ligand and the alcohol.[18] Insertion of CO leads to the alkoxycarbonyl-palladium complex **B**, which, after insertion of the alkene **2**, affords the 5-membered palladacycle intermediate **C**,[11] however formation of an η^3-allylic intermediate in equilibrium with **C** cannot be ruled out.[9] 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

 © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

regenerates the active species **A** thus closing the catalytic cycle.[12]

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 sulphonic 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.,[7k] the acid stabilizes the intermediate complex **E** (Scheme 3) and improves the oxidizing ability of BQ, avoiding the formation of palladium black.[7k] 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 diimine backbones and the phenyl rings constrain the aryls to arrange almost perpendicularly with respect to the palladium mean coordination plane.[9] This conformation affects the coordination of the aromatic olefin making possible a π stacking interaction in the olefin insertion transition states that could be the origin for the high productivity found both in the CO/vinylarene copolymerization[9] 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 isopropyl groups on the aryls which cause a difficult access of the olefin and CO to the catalytic center.[9] Conversely the methyl groups in the $Pd(TFA)_2$/**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, is still lacking (Table 1 entry 7 and 10).[9] Finally the complete conversion and selectivity observed in the bis-alkoxycarbonylation reaction with $Pd(TFA)_2$/**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.

Conclusions

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). Variously substituted aryl α-diimine ligands have been used for the first time in this kind of reaction, together with $Pd(TFA)_2$ 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 techniques. 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 Brucker Avance 200 spectrometer (^{1}H: 200 MHz, ^{13}C: 50 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 $CDCl_3$ (77.10 ppm) for ^{13}C NMR. ^{13}C NMR were recorded with ^{1}H broadband decoupling. The following abbreviations were used to explain the multiplicities: s = singlet, 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^+) ionization 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_2O_3 and used without further purification. Anhydrous THF was distilled from sodium-benzophenone, and methanol was distilled from $Mg(OMe)_2$. $Pd(TFA)_2$ was weighed in an analytical balance without excluding moisture 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 the previously reported procedure.[10] Ligand **1i** was synthesized by our group according to a previously reported procedure.[9a] Compounds **3a–f**, **j**, **l** were already known and the spectral date are identical to the previously reported literature data (see the Supporting Information for more details).[8i]

Typical Procedure for the Bis-alkoxycarbonylation Reaction of Olefins

In a nitrogen-flushed Schlenk tube, equipped with a magnetic stirring bar, $Pd(TFA)_2$ (3.3 mg, 0.01 mmol) and THF (0.5 mL) were added in sequence. After the mixture had turned to 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, changing to a dark-green color. The formed catalyst

© 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

was injected 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) in MeOH (3.5 mL). After 10 min of stirring, the respective olefin **2a–o** (2 mmol) was added in one portion into the reaction mixture. The autoclave was flushed three times with CO and pressurized to 4 bar of carbon monoxide. The reaction mixture 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 and the ratio of the products **3** and **4.** The crude material was then dried under reduced pressure and filtered through a plug of silica gel, washing with CH_2Cl_2/Et_2O 8:2 (25 mL) and finally the solution was evaporated under vacuum. The product was eventually obtained after column chromatography on silica gel (petroleum ether/CH_2Cl_2 50:50 then 30:70).

Dimethyl 2-(2-chlorophenyl)succinate (3g): Following the general procedure, compound **3g** was obtained as a pale yellow oil; yield: 94% (over a conversion of 75% of 2-chlorostyrene **2g**, determined by ^{1}H NMR analysis on a direct sample of the reaction mixture). ^{1}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); ^{13}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 $[M+H]^+$.

Dimethyl 2-(2-bromophenyl)succinate (3h): Following the general procedure, compound **3h** was obtained as a pale yellow oil; yield: 91% (over a conversion of 45% of 2-bromostyrene **2h**, determined by ^{1}H NMR analysis on a direct sample of the reaction mixture). ^{1}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); ^{13}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 $[M+H]^+$.

Dimethyl 2-(3-(trifluoromethyl)phenyl)succinate (3i): Following the general procedure, compound **3i** was obtained as a colorless oil; yield: 85%. ^{1}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); ^{13}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 $[M+H]^+$.

Dimethyl 2-pentylsuccinate (3k): Following the general procedure, but performing the reaction with 1 mol% catalyst loading [6.6 mg, 0.02 mmol of $Pd(TFA)_2$ and 9.6 mg, 0.022 mmol of **1i**] compound **3k** was obtained as a colorless oil; yield: 92%. ^{1}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); ^{13}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 $[M+H]^+$.

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 $Pd(TFA)_2$ and 19.2 mg, 0.044 mmol of **1i**], compound **3m** was obtained as a pale yellow oil; yield: 95% (over a conversion of 53% of 3,3-methyl-1-butene **2m**). ^{1}H NMR: δ = 3.66 (s, 3H), 3.63 (s, 3H), 2.85–2.39 (m, 3H), 0.93 (s, 9H); ^{13}C NMR: δ = 174.8, 173.3, 51.9, 51.4, 51.3, 32.7, 27.9; ESI-MS: m/z = 203 $[M+H]^+$.

Diisopropyl 2-phenylsuccinate (3n): Following the general procedure, but performing the reaction with 2 mol% catalyst loading [13.3 mg, 0.04 mmol of $Pd(TFA)_2$ and 19.2 mg, 0.044 mmol of **1i**] and using *i*-PrOH as the alcohol, compound **3n** was obtained as a colorless oil; yield: 92%. ^{1}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); ^{13}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 $[M+H]^+$.

Dibenzyl 2-phenylsuccinate (3o): Following the general procedure, but performing the reaction with 2 mol% catalyst loading [13.3 mg, 0.04 mmol of $Pd(TFA)_2$ and 19.2 mg, 0.044 mmol of **1i**] and using BnOH as the alcohol, compound **3o** was obtained as a colorless oil; yield: 94%. ^{1}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); ^{13}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 $[M+H]^+$.

(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 $Pd(TFA)_2$ and 19.2 mg, 0.044 mmol of **1i**], compound **3p** was obtained as a pale yellow wax; yield: 92%. ^{1}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); ^{13}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 $[M+H]^+$.

(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 $Pd(TFA)_2$ and 19.2 mg, 0.044 mmol of **1i**], compound **3q** was obtained as a pale yellow oil; yield: 87%. ^{1}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); ^{13}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 $[M+H]^+$.

Acknowledgements

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

References

[1] For recent reviews, see: a) X.-F. Wu, H. Neumann, M. Beller, *ChemSusChem* **2013**, *6*, 229; b) X.-F. Wu, H. Neumann, M. Beller, *Chem. Rev.* **2013**, *113*, 1; c) B. Gabriele, R. Mancuso, G. Salerno, *Eur. J. Org. Chem.* **2012**, 6825; d) Q. Liu, H. Zhang, A. Lei, *Angew. Chem.* **2011**, *123*, 10978; *Angew. Chem. Int. Ed.* **2011**, *50*, 10788; e) J. Liu, J. Chen, W. Sun, C. Xia, *Chin. J. Catal.* **2010**, *31*, 1; f) A. Brennfuehrer, H. Neumann, M.

 © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Beller, *ChemCatChem* **2009**, *1*, 28; g) A. Brennführer, H. Neumann, M. Beller, *Angew. Chem.* **2009**, *121*, 4176; *Angew. Chem. Int. Ed.* **2009**, *48*, 4114; h) C. F. J. Barnard, *Organometallics* **2008**, *27*, 5402–5422; i) B. Gabriele, G. Salerno, M. Costa, *Top. Organomet. Chem.* **2006**, *10*, 1397–1421; j) C. Godard, B. K. Muñoz, A. Ruiz, C. Claver, *Dalton Trans.* **2008**, 853.

[2] J. Tsuji, M. Morikawa, J. Kijitsuji, *J. Am. Chem. Soc.* **1964**, *86*, 4851.

[3] R. F. Heck, *J. Am. Chem. Soc.* **1972**, *94*, 2712.

[4] a) C. Livage, C. Egger, G. Ferey, *Chem. Mater.* **2001**, *13*, 410; b) M. A. Carnahan, M. W. Grinstaff, *Macromolecules* **2001**, *34*, 7648; c) Z. Qiu, T. Ikehara, T. Nishi, *Macromolecules* **2002**, *35*, 8251; d) S. Okajima, R. Kondo, K. Toshima, S. Matsumura, *Biomacromolecules* **2003**, *4*, 1514; e) T. Dong, K. Shin, B. Zhu, Y. Inoue, *Macromolecules* **2006**, *39*, 2427; f) M. A. Carnahan, M. W. Grinstaff, *Macromolecules* **2006**, *39*, 609.

[5] a) K. Yoshikawa, K. Inoguchi, T. Morimoto, K. Achiwa, *Heterocycles* **1990**, *31*, 1413; b) Y. Ito, T. Kamijo, H. Harada, F. Matsuda, S. Terashima, *Tetrahedron Lett.* **1990**, *31*, 2731; c) K. Inoguchi, T. Morimoto, K. Achiwa, *J. Organomet. Chem.* **1989**, *370*, C9; d) H. Jendralla, *Tetrahedron Lett.* **1991**, *32*, 3671; e) B. Kammermeier, G. Beck, W. Holla, D. Jacobi, B. Napierski, H. Jendralla, *Chem. Eur. J.* **1996**, *2*, 307.

[6] a) M. Whittaker, C. D. Floyd, P. Brown, A. J. H. Gerain, *Chem. Rev.* **1999**, *99*, 2735; b) M. P. Sibi, H. Hasegawa, *Org. Lett.* **2002**, *4*, 3347.

[7] a) D. M. Fenton, P. J. Steinwand, *J. Org. Chem.* **1972**, *37*, 2034; b) D. E. James, L. F. Hines, J. K. Stille, *J. Am. Chem. Soc.* **1976**, *98*, 1806; c) D. E. James, J. K. Stille, *J. Am. Chem. Soc.* **1976**, *98*, 1810; d) J. K. Stille, R. Divakaruni, *J. Org. Chem.* **1979**, *44*, 3474; e) G. E. Morris, D. Oakley, D. A. Pippard, D. J. H. Smith, *J. Chem. Soc. Chem. Commun.* **1987**, 410; f) D. Milstein, *Acc. Chem. Res.* **1988**, *21*, 428; g) J. Tsuji, *Synthesis* **1990**, 739; h) P. Bréchot, Y. Chauvin, D. Commereuc, L. Saussine, *Organometallics* **1990**, *9*, 26; i) S. Toda, M. Miyamoto, H. Kinoshita, K. Inomata, *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3600; j) E. Drent, J. A. M. van Broekhoven, M. J. Doyle, *J. Organomet. Chem.* **1991**, *417*, 235; k) C. Bianchini, H. Man Lee, G. Mantovani, A. Meli, W. Oberhauser, *New J. Chem.* **2002**, *26*, 387.

[8] a) C. Pisano, S. C. A. Nefkens, G. Consiglio, *Organometallics* **1992**, *11*, 1975; b) S. C. A. Nefkens, M. Sperrle, G. Consiglio, *Angew. Chem.* **1993**, *105*, 1837; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1719; c) M. Sperrle, G. Consiglio, *J. Mol. Catal. A* **1999**, *143*, 263; d) M. Sperrle, G. Consiglio, *Chem. Ber. Recl.* **1997**, *130*, 1557; e) Y. Ukaji, M. Miyamoto, M. Mikuni, S. Takeuchi, K. Inomata, *Bull. Chem. Soc. Jpn.* **1996**, *69*, 735; f) S. Takeuchi, Y. Ukaji, K. Inomata, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 955; g) K. Saigo, *Tetrahedron Lett.* **1998**, *39*, 7529; h) L. Wang, W. Kwok, J. Wu, R. Guo, T. T.-L. Au-Yeung, Z. Zhou, A. S. C. Chan, K.-S. Chan, *J. Mol. Catal. A* **2003**, *196*, 171; i) Y.-X. Gao, L. Chang, H. Shi, B. Liang, K. Wongkhan, D. Chaiyaveij, A. S. Batsanov, T. B. Marder, C.-C. Li, Z. Yang, Y. Huang, *Adv. Synth. Catal.* **2010**, *352*, 1955.

[9] a) C. Carfagna, G. Gatti, P. Paoli, B. Binotti, F. Fini, A. Passeri, P. Rossi, B. Gabriele, *Organometallics* **2014**, *33*, 129; b) C. Carfagna, G. Gatti, P. Paoli, P. Rossi, *Organometallics* **2009**, *28*, 3212; c) C. Carfagna, G. Gatti, L. Mosca, A. Passeri, P. Paoli, A. Guerri, *Chem. Commun.* **2007**, *43*, 4540.

[10] S. D. Ittel, L. Johnson, M. Brookhart, *Chem. Rev.* **2000**, *100*, 1169.

[11] C. Carfagna, G. Gatti, L. Mosca, P. Natanti, P. Paoli, P. Rossi, B. Gabriele, G. Salerno, *Dalton Trans.* **2011**, *40*, 6792.

[12] a) H. Grennberg, A. Gogoll, J.-E. Bäckvall, *Organometallics* **1993**, *12*, 1790; b) Other quinones were tested but only benzoquinone was able to function as oxidant.

[13] By using the same optimized reaction conditions reported in Table 2, bis-oxazoline and diphosphine ligands, in combination with $Pd(TFA)_2$, were not active in the bis-alkoxycarbonylation of the styrene, see Table S2 in the Supporting Information.

[14] Isoprene and 4-vinylcyclohexene 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 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% isolated yield.

[16] T. Aratani, K. Tahara, S. Takeuchi, Y. Ukaji, K. Inomata, *Chem. Lett.* **2007**, *36*, 1328.

[17] C. Carfagna, G. Gatti, L. Mosca, P. Paoli, A. Guerri, *Helv. Chim. Acta* **2006**, *89*, 1660.

[18] Ancillary experiments were conducted to support the proposed catalytic cycle. Ligand **1i** was added to a THF solution of $Pd(TFA)_2$ and benzoquinone, to avoid a relatively fast decomposition. After removing the solvent from the reaction mixture, the ^1H NMR, recorded in $CDCl_3$, showed signals attributable to the precatalyst $[(N–N)Pd(THF)_2]^{2+}[TFA^-]_2$. Unfortunately the addition of methanol produced an immediate decomposition of the complex to palladium black.

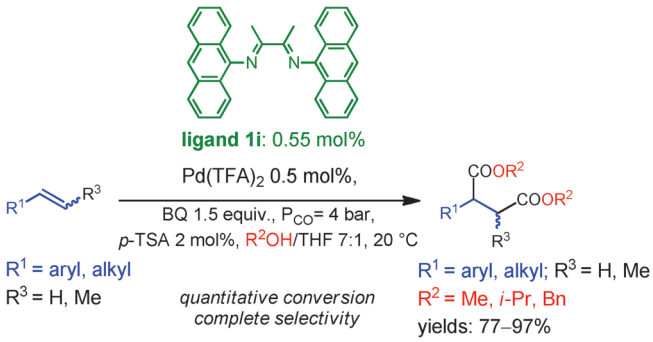
 © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

Selective Aryl α-Diimine/Palladium-Catalyzed Bis-Alkoxycarbonylation of Olefins for the Synthesis of Substituted Succinic Diesters

Adv. Synth. Catal. **2014**, *356*, 1 – 9

Francesco Fini,* Michela Beltrani, Raffaella Mancuso, Bartolo Gabriele, Carla Carfagna*



 © 2014 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim