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Oxidative Alkoxycarbonylation of Alkynes by Means of Aryl α-diimine Palladium(II) Complexes as Catalysts

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

[a] Department of Biomolecular Sciences, University of Urbino "Carlo Bo", Piazza del Rinascimento 6, 61029 Urbino (PU), Italy; e-mail: fini_f@libero.it; Fax: (+39) 0722 303306; Tel: (+39) 0722 303302
[b] Department of Industrial Chemistry "T. Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna (BO), Italy; e-mail: carla.carfagna@unibo.it
[c] Department of Chemical and Pharmaceutical Sciences, University of Trieste, Via Licio Giorgieri 1, 34127 Trieste (TS), Italy
[d] Department of Chemistry and Chemical Technologies, University of Calabria, Via P. Bucci 12/C, 87036 Arcavacata di Rende (CS), Italy

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Abstract. The straightforward *in situ* synthesized Bis-(2,6-diisopropyl)-acenaphthenequinonediimine palladium triflate catalyst was generally employed for both the mono-alkoxycarbonylation of terminal alkynes, and the bis-alkoxycarbonylation of 1,2-disubstituted alkynes by using mild reaction conditions (P_{CO}= 4 bar, Temp. 20°C). Utilizing low catalyst loading (down to 0.5 mol%), a variety of propiolic esters were synthesized with good to excellent isolated yields. Most importantly the system was very efficient not only with methanol but also with a range of different alcohols, starting from the less hindered benzyl alcohol to the most ones, such as isopropanol and *tert*-butanol. In addition aromatic and aliphatic 1,2-disubstituted alkynes were converted into maleic acid derivatives, together with acid-catalyzed isomerization reaction, showing modest to good selectivity and excellent combined yields. In particular 3-hexyne showed a satisfactory degree of selectivity for the maleic diesters of methanol, and benzyl alcohol, obtaining the corresponding products with good isolated yields.

Keywords: alkynes; aryl α-diimine ligands; carbonylation; oxidative carbonylation; palladium; propiolic and maleic acid esters

Introduction

Oxidative carbonylations are among the most important reactions in organometallic and organic chemistry.[1] These processes enable the direct conversion of raw materials, such as olefins and alkynes, into high value added carbonylated products starting from the simplest C-1 unit, that is, carbon monoxide.[1] Depending on the nature of the substrate and reaction conditions, different carbonylated products can be obtained in one step under the promoting action of a metal catalyst and in the presence of an external oxidant. Acetylenic substrates, in particular, have proved to be very useful and versatile starting materials in oxidative carbonylation reactions, usually carried out in the presence of a Pd-based catalytic system.[1]

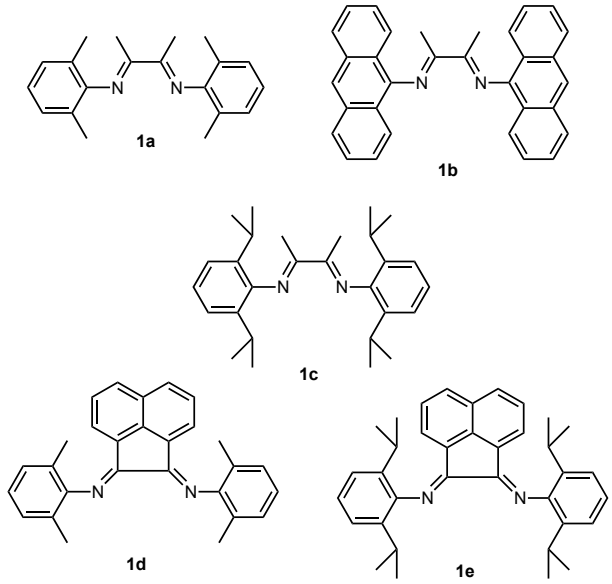
The oxidative carbonylation of simple, unfunctionalized alkynes may basically lead to two different kind of products, that are, dicarbonylated products (maleates and/or fumarates) and monocarbonylated products (propiolic esters and 2-ynamides).[2] The first oxidative carbonylation of alkynes was reported by Tsuji and co-workers in 1964, who described the conversion of acetylene into muconyl and maleic acid chloride by using a stoichiometric amount of $PdCl_2$.[3] Later on, they synthesized propiolic esters by using 5 mol% of $PdCl_2$ in combination with $CuCl_2$ as the oxidant to close the catalytic cycle.[4] During the last four decades various methodologies for the catalytic oxidative carbonylation of alkynes to maleates,[5] haloacrylates and alkoxyacrylates,[6] 2-ynoates[7] and 2-ynamides,[8] have been reported, mostly based on the use of Pd(II) as the catalytic species and oxygen as the external oxidant. These processes have been conveniently applied to variously functionalized alkynes, affording a variety of different compounds, such as numerous carbonylated heterocycles.[1,9]

Recently, we developed a novel catalytic system, consisting of a palladium source with 1,4-diaryl-2,3-diazabutadiene (DAB) ligands, able to promote the carbonylation of olefins to succinic diesters with high selectivity and efficiency[10] as well as the copolymerization of styrene with CO to yield a

copolymer with a high degree of tacticity.[11] In this paper, we have studied the activity of this catalytic system in the oxidative carbonylation reaction of both terminal and internal alkynes. We have found that our catalyst, in a suitably modified form, is also able to efficiently promote the oxidative monocarbonylation of terminal alkynes to propiolate esters and of internal alkynes to maleic derivatives (diesters and their cyclic isomers) under particularly mild reaction conditions (4 bar CO, 20 °C) and using benzoquinone (BQ) as external oxidant.

Results and Discussion

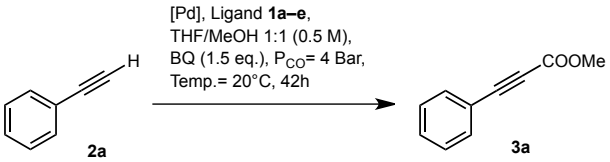
To begin with, an extensive work of optimization has been carried out testing common sources of palladium such as $Pd(TFA)_2$ and $(PhCN)_2PdCl_2$ and DAB ligands **1a–e** (Scheme 1).[12]



Scheme 1. *N*,*N*-Diaryl dimine ligands tested in the reaction optimization process **1a–e**.

The initial reaction conditions were similar to those previously reported for the bis-alkoxycarbonylation of olefins,[10] consisting of 4 bar of CO at 20 °C in THF/MeOH (1:1, v/v) as the reaction medium, in the presence of of 5 mol % of $Pd(TFA)_2$/**1a** as catalyst and 1.5 equiv of BQ as oxidizing agent. With phenylacetylene **2a** as the substrate, no conversion was observed, proving that alkynes are less reactive compared with olefins under these conditions (Table 1, entry 1). We accordingly tested a potentially more reactive catalytic species, consisting of $(PhCN)_2Pd(OTf)_2$/**1a**, which has been generated *in situ* from $(PhCN)_2PdCl_2$, 2 equiv of AgOTf and ligand **1a**. This system was indeed very effective, and was able to promote the smooth conversion of **2a** (80%) into the corresponding oxidative mono-carbonylation product (methyl phenylpropiolate, **3a**), after 42 h, with a catalyst loading as low as 0.5 mol%, (Table 1, entry 2).

Table 1. Optimization study for the oxidative carbonylation of the phenylacetylene **2a**.



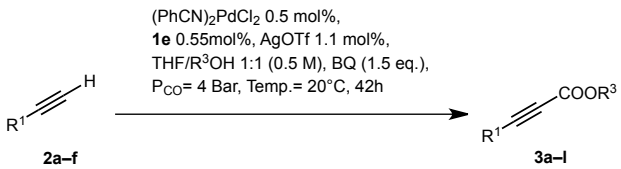
Entry[a]	Pd(II) [mol%]	Ligand **1a–e** [mol%]	Ag(I) [mol%]	Conv. [%][b]
1	$Pd(TFA)_2$ 5	**1a** 5.5	--	<5
2	$(PhCN)_2PdCl_2$ 0.5	**1a** 0.55	AgOTf 1.1	80
3	$(PhCN)_2PdCl_2$ 0.5	--	AgOTf 1.1	55
4	$(PhCN)_2PdCl_2$ 0.5	**1a** 0.55	--	<5
5	--	**1a** 0.55	AgOTf 1.1	<5
6	$(PhCN)_2PdCl_2$ 0.5	**1a** 0.55	$AgPF_6$ 1.1	10
7	$(PhCN)_2PdCl_2$ 0.5	**1a** 0.55	$AgSO_3CH_3$ 1.1	70
8[c]	$(PhCN)_2PdCl_2$ 0.5	**1a** 0.55	AgOTf 1.1	40
9[d]	$(PhCN)_2PdCl_2$ 0.5	**1a** 0.55	AgOTf 1.1	80
10	$(PhCN)_2PdCl_2$ 0.5	**1b** 0.55	AgOTf 1.1	45
11	$(PhCN)_2PdCl_2$ 0.5	**1c** 0.55	AgOTf 1.1	>95
12	$(PhCN)_2PdCl_2$ 0.5	**1d** 0.55	AgOTf 1.1	30
13	$(PhCN)_2PdCl_2$ 0.5	**1e** 0.55	AgOTf 1.1	>95
14	$(PhCN)_2PdCl_2$ 0.1	**1c** 0.11	AgOTf 0.22	25
15	$(PhCN)_2PdCl_2$ 0.1	**1e** 0.11	AgOTf 0.22	80
16[e]	$(PhCN)_2PdCl_2$ 0.5	**1e** 0.55	AgOTf 1.1	65
17[f]	$(PhCN)_2PdCl_2$ 2	**1e** 2.2	AgOTf 4.5	>95

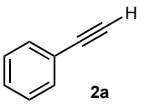
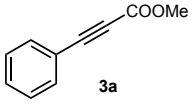
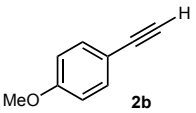
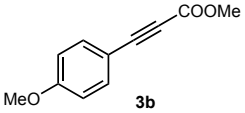
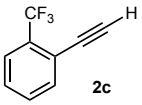
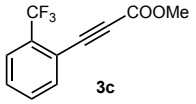
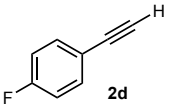
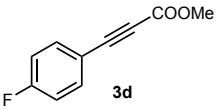
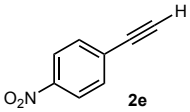
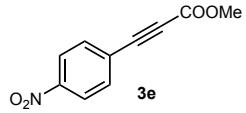
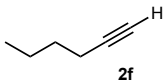
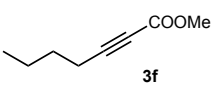
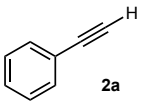
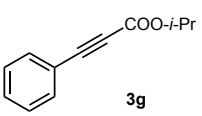
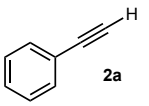
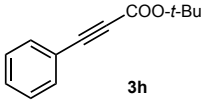
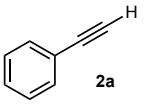
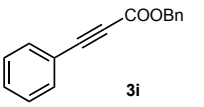
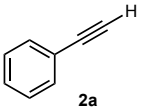
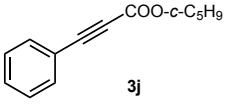
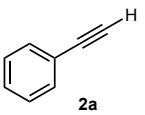
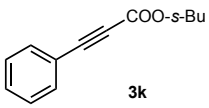
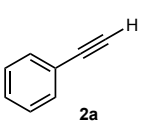
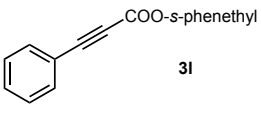
[a] Reaction performed in autoclave at P_{CO} = 4 bar, with phenylacetylene **2a** (2 mmol-scale), Pd(II) 5 mol%, 0.5 mol% or 0.1 mol% (0.10, 0.01 mmol or 0.002 mmol), ligand **1a–e** 5.5 mol%, 0.55 mol% or 0.11 mol% (0.11 mmol, 0.011 mmol or 0.0022 mmol), Ag(I) 1.1 mol% or 0.22 mol% (0.022 or 0.0044 mmol) and the 1.5 eq of BQ (3 mmol) with THF/MeOH 1:1 (0.5 M) as reaction medium at 20°C, for 42 h. [b] Determined by direct ^1H NMR analysis of a sample of the reaction mixture. [c] Reaction performed at 8 bar of CO. [d] Reaction performed at 60°C. [e] Reaction performed in a Schlenk tube at atmospheric pressure of CO (balloon). [f] Reaction performed in a Schlenk tube at atmospheric pressure of CO (balloon) with **2a** (2 mmol), $(PhCN)_2PdCl_2$ 2 mol% (0.04 mmol), ligand **1e** 2.2 mol% (0.044 mmol) and AgOTf 4.5 mol% (0.09 mmol) with the stated time, oxidant and temperature.

By performing the reaction in the absence of the ligand, only 55% of conversion was obtained (Table 1, entry 3). No reaction occurred without AgOTf or in the absence of the palladium source (Table 1, entries 4 and 5). No improved results with respect to that of Table 1, entry 2, were observed using $AgPF_6$ or $AgSO_3CH_3$ as the Ag(I) source (Table 1, entries 6 and 7, respectively) or increasing the temperature to 60°C (Table 1, entry 8) and the pressure of CO to 8 bar (Table 1, entry 9). A possible optimization of the nature of the ligand was also taken into consideration (Table 1, entries 10–13, ligands **1b–e**). Ligands **1b** and **1d** were less effective than ligand **1a**, although **1b** was the best ligand tested for the bis-alkoxycarbonylation of olefins.[10] (Table 1, entries 10 and 12, respectively). On the other hand, ligands **1c** and **1e** turned out to be quite effective, bringing the reaction to completion, probably due to the high steric hindrance at the *ortho* positions of the aryl moiety (Table 1, entries 11 and 13, respectively). By lowering the catalyst loading down to 0.1 mol%, the efficiency of the process was further tested with both ligands **1c** and **1e** (Table 1 entries 14 and 15). In these cases the two results were quite different, and only the catalytic specie bearing the bis(2,6-diisopropyl)-acenaphthenequinonediimine (diaryl-BIAN) ligand **1e** retained most of its activity by converting **2a** into **3a** in 80% yield, with a TON of 800 and TOF of 9.5 h^{-1}, (entry 15). We finally tested our system at atmospheric pressure of CO; as can be seen from the results reported in Table 1, entry 16, a certain degree of reactivity was preserved by using 0.5 mol% of catalyst loading (65% conversion), meanwhile complete conversion of the starting material was achieved by slightly increasing the loading of the *in situ* synthesized catalyst $(PhCN)_2Pd(OTf)_2$/**1e** up to 2 mol% (entry 17). This latter result show that our system is significantly efficient even under an atmospheric pressure of CO, allowing the use of simple Schlenk tube equipped with a balloon as a CO reservoir (Table 1, entries 15–17).

With these data in hand, we extended the process to several aromatic (**2a–e**) and aliphatic (**2f**) alkynes by performing the reaction under conditions able to guarantee full conversion of the substrates (0.5–2 mol% of catalyst, under 4 bar of CO at 20°C, for 42 h; Table 2).

Table 2. Substrate scope of the mono-alkoxycarbonylation of alkynes **2a–f**.



Entry[a]	Alkynes 2a–f	Products 3a–l	Yield [%][b]
1			90
2			82
3			62
4			78
5[c]			55[d]
6			72[e]
7[f]			74
8[g]			81
9[h]			83
10[i]			92
11[j]			75
12[k]			68

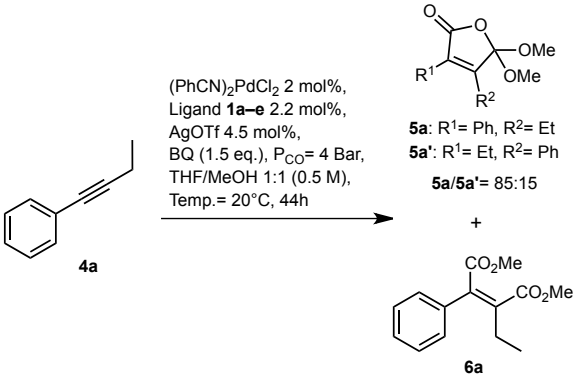
[a] Reaction performed in autoclave at P_{CO} = 4 bar, with alkynes **2a–f** (2 mmol-scale), $(PhCN)_2PdCl_2$ 0.5 mol% (0.01 mmol), ligand **1e** 0.55 mol% (0.011 mmol), AgOTf

1.1 mol% (0.022 mmol) and 1.5 eq of BQ (3 mmol) with THF/R^3OH 1:1 (0.5 M) as reaction medium at 20°C, for 42 h. [b] Isolated yields after column chromatography. Unless otherwise noted, substrate conversion was quantitative. [c] Reaction performed with 2 mol% of catalyst loading. [d] Conversion of the alkyne **2e** was 60%. [e] Isolated yield of the main product **3f** is reported. [f] Reaction performed by using *i*-PrOH in place of methanol. [g] Reaction performed by using *t*-BuOH in place of methanol. [h] Reaction performed by using BnOH in place of methanol. [i] Reaction performed by using *c*-C_5H_9OH in place of methanol. [j] Reaction performed by using *s*-BuOH in place of methanol. [k] Reaction performed by using *s*-phenethanol in place of methanol.

As can be seen from Table 2, good to excellent results were obtained in term of isolated yields of the corresponding propiolate methyl esters **3a–f**, the best outcome being achieved with phenylacetylene **2a** (affording 90% yield of **3a**, Table 2 entry 1). Arylacetylenes **2b**–**d**, bearing electron donating– (*p*-OMe) or electron withdrawing (*o*-CF_3, *p*-F) groups, were compatible with the catalytic system, with the corresponding products **3b**–**d** obtained in fair to good isolated yields (62–82%, entries 2–4). The reaction could also be applied to a substrate bearing a strong electron-withdrawing group, such as *p*-NO_2 (**2e**), which was converted into **3e** in 69% isolated yield working with a catalyst loading of 2 mol% (Table 2, entry 5). An aliphatic alkyne, such as 1-hexyne, was also reactive under the standard conditions and let to methyl 2-hexynoate **3f** in 72% yield, although in a mixture with methyl (*E*)-3-methoxy-2-heptenoate (12% yield, Table 2, entry 6).[13] Our method could also be successfully applied to higher alcohols (including benzyl alcohol isopropanol, cyclopentanol, *sec*-butanol, *sec*-phenethanol, as well as a hindered tertiary alcohols such as *tert*-butanol) using phenylacetylene **2a** as model substrate (Table 2, entries 7–12). Indeed the corresponding propiolate **3g–l** were attained in good to excellent yields, demonstrating the broadness of this methodology (Table 2, entries 7–12).

Encouraged by these results, we went further to explore the reactivity of internal alkynes. We started our investigation with inexpensive and readily available 1-phenyl-1-butyne **4a**. Considering the expected lower reactivity of an internal alkyne with respect to a 1-alkyne, the experiments were performed with 2 mol% of the *in situ* generated $(PhCN)_2Pd(OTf)_2$/**1a** catalyst; the obtained results are shown in Table 3.[14]

Table 3. Representative results for the optimization of the bis-alkoxycarbonylation of 1-phenyl-1-butyne **4a**.



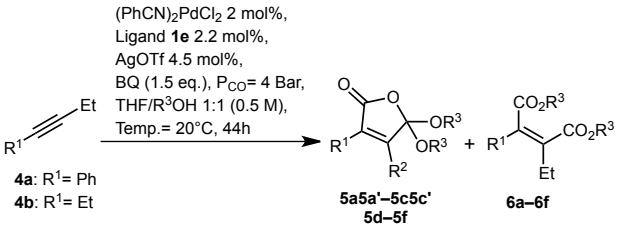
Entry[a]	Ligand **1a–1e**	P_{CO} (bar)	Conv.[b] (%)	**5a5a'**:**6a** ratio[b]
1	--	4	<5	--
2	**1a**	4	80	2:1
3[c]	--	1	<5	--
4[c]	**1a**	1	40	1:1
5[d]	**1a**	8	>98	1:1
6	**1b**	4	83	1:1
7	**1c**	4	87	1:1
8	**1d**	4	82	2:1
9	**1d**	8	>98	3:2
10	**1e**	4	>98	4:3
11[e]	**1e**	4	44	1:1

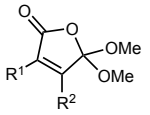
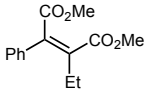
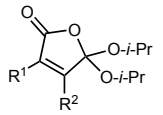
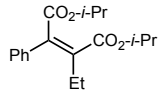
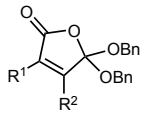
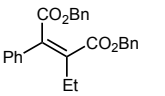
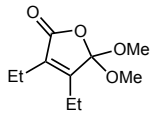
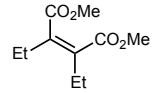
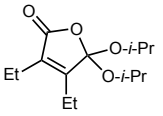
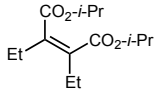
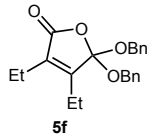
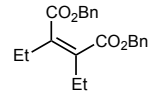
[a] Reaction performed in autoclave at P_{CO} = 4 bar, with alkyne **4a** (2 mmol-scale), $(PhCN)_2PdCl_2$ 2 mol% (0.04 mmol), ligands **1a–e** 2.2 mol% (0.044 mmol), AgOTf 4.5 mol% (0.09 mmol) and 1.5 eq of BQ (3 mmol) with THF/MeOH 1:1 (0.5 M) as reaction medium at 20°C, for 44 h. [b] Determined by direct ^{1}H NMR analysis of a sample of the reaction mixture. [c] Reaction performed in a Schlenk tube at atmosferic pressure of CO (balloon). [d] Reaction performed at 60°C and 8 bar of CO. [e] Reaction performed with $(PhCN)_2PdCl_2$ 0.5 mol% (0.01 mmol), ligand **1e** 0.55 mol% (0.011 mmol) and AgOTf 1.1 mol% (0.022 mmol).

Under 4 bar of CO, the oxidative carbonylation of **4a** gave a conversion of the starting material of 80% into a mixture of isomeric products. In particular together with the maleic diesters **6a**, two regioisomeric cyclic products **5a** and **5a'** were obtained with a ratio of 85/15 (Table 3).[5g,15] They were detected only by ^{13}C NMR due to their close chemical resemblance. The ratio between the mixture of cyclic regioisomers **5a5a'** and the maleic diester **6a** was 2/1 (Table 3, entry 2). Conversely the reaction performed without the ligand **1a** gave no reaction at all (Table 3, entries 1 and 3). Under the atmospheric pressure of CO, the system was poorly active and **4a** was converted only for 40% with a **5a5a'**:**6a** ratio of 1:1 (Table 3, entry 4). The increase of the temperature up to 60 °C and the pressure of CO up to 8 bar increased the conversion of the alkyne **4a** with a concomitant effect on the **5a5a'**:**6a** ratio (Table 3, entry 5, to be compared with entry 2). We then changed the nature of the ligand, as can be seen from the results reported in Table 3,

entries 6–10. All the other tested ligands **1b**–**e** were more active than **1a** (entry 2): in particular, a quantitative conversion of **4a** was observed with ligands **1e**, by using 2 mol% of catalyst loading, at 4 bar of CO (Table 3, entries 10 and 11). Under the optimized conditions, an isolated yield of 48% and of 41% for the regioisomeric mixture **5a5a'** and for the maleic esters **6a** could be respectively achieved (Table 4, entry 1).

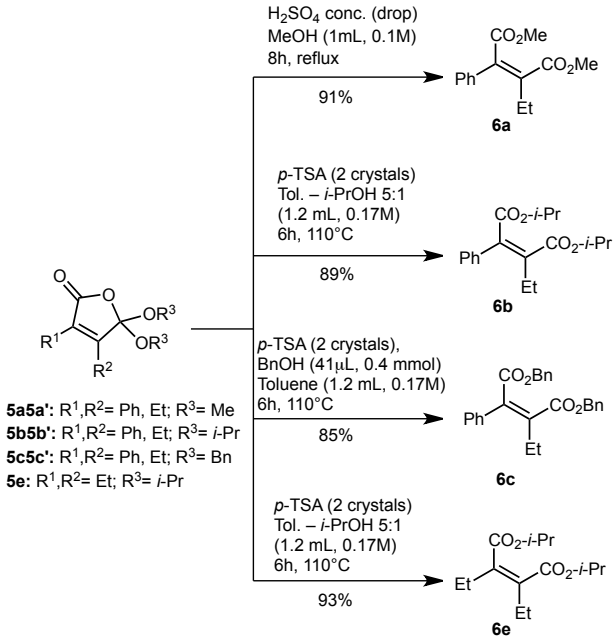
Table 4. Bis-alkoxycarbonylation of **4a**, **4b** by using different alcohols.



Entry[a]	Alkynes **4a, 4b**	Alcohols R^3OH	**5a5a'–5c5c', 5d–5f** [%][b]	**6a–6f** [%][b]	Total Yield **6a–f** [%][b]
1	**4a**	MeOH	 **5a**: R^1= Ph, R^2= Et; **5a'**: R^1= Et, R^2= Ph; **5a**:**5a'**= 85/15; Y. 48%	 **6a** Y. 41%	85[c]
2	**4a**	*i*-PrOH	 **5b**: R^1= Ph, R^2= Et; **5b'**: R^1= Et, R^2= Ph; **5b**:**5b'**= 75/25; Y. 40%	 **6b** Y. 43%	79[c]
3	**4a**	BnOH	 **5c**: R^1= Ph, R^2= Et; **5c'**: R^1= Et, R^2= Ph; **5c**:**5c'**= 75/25; Y. 41%	 **6c** Y. 38%	73[c]
4	**4b**	MeOH	 **5d** Y. 9%	 **6d** Y. 72%	72
5	**4b**	*i*-PrOH	 **5e** Y. 41%	 **6e** Y. 50%	88[c]
6	**4b**	BnOH	 **5f** Y. 9%	 **6f** Y. 83%	83

[a] Reaction performed in autoclave at P_{CO} = 4 bar, with alkynes **4a** or **4b** (2 mmol-scale), $(PhCN)_2PdCl_2$ 2 mol% (0.04 mmol), ligands **1e** 2.2 mol% (0.044 mmol), AgOTf 4.5 mol% (0.09 mmol) and 1.5 eq of BQ (3 mmol) with THF/R^3OH 1:1 (0.5 M) as reaction medium at 20°C, for 44 h. [b] Isolated yields after column chromatography. [c] Overall yield after carbonylation of **4a**, **4b** followed by acid-catalyzed isomerization of **5a5a'–5c5c'**, **5e** into **6a–c, 6e**.

It is worth noting that, as already reported for an analogous compound by some of us,[5g] the mixture **5a5a'** can be easily converted into **6a** in 91% isolated yield by acid-catalyzed isomerization in MeOH (Scheme 2, Top).

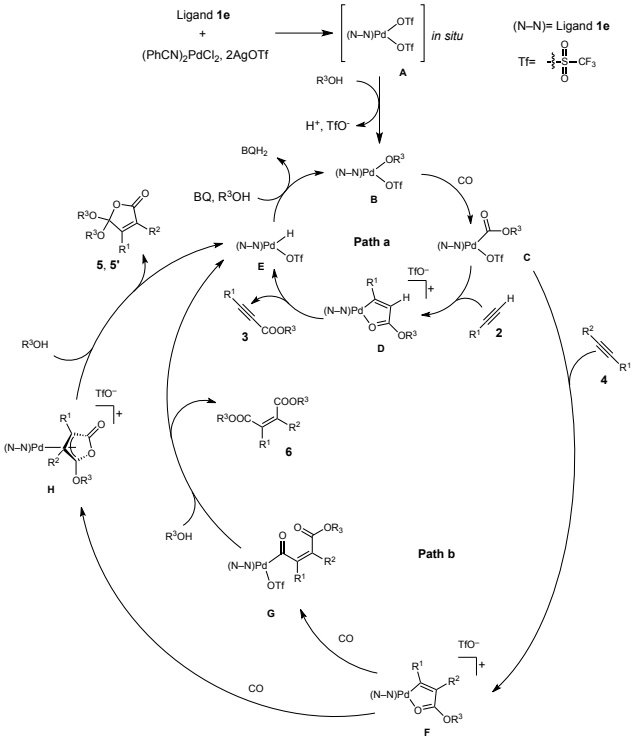


Scheme 2. Isomerization of **5a5a'–5c5c'** and **5e** into maleic acid esters **6a–c, 6e** by means of Brönsted acid catalysis.

Thus, the combined carbonylation/isomerization process allowed the selective synthesis of the maleic diester **6a** in 85% overall yield (Table 4, entry 1). Moreover the bis-alkoxycarbonylation of **4a** with other alcohols, such as *i*-PrOH and BnOH was also successful, in both cases the ratio between the obtained cyclic regioisomers **5b**:**5b'** and **5c**:**5c'** was 75:25 (table 4 entries 2 and 3), meanwhile the ratios between the mixture of cyclic isomers and the maleic diesters **5b5b'**:**6b** and **5c5c'**:**6c** were of 1:1, with good isolated yields of 40%, 43%, 41% and 38% respectively (Table 4 entries 2 and 3). Mixtures of regioisomers **5b5b'** and **5c5c'** were isomerized in acid-catalyzed conditions (Scheme 2). Since the isomerization condition used for **5a5a'** was not suitable, an optimization of the process was carried out (Scheme 2). By replacing concentrated sulfuric acid with *p*-TSA and choosing carefully the reaction medium, the transformation of cyclic regioisomers **5b5b'**, **5c5c'** were brought to completion with good isolated yield (89% and 85%, Scheme 2, center),

attaining the maleic diesters **6b–c** with good overall isolated yields (72% and 88%, Table 4, entries 2 and 3). Interestingly, the carbonylation of the aliphatic internal alkyne 3-hexyne **4b**, was more selective towards the formation of the alkyl maleates **6** with respect to the analogous reactions with **4a** (compare entries 4 and 6 with entries 1–3, Table 4). By using MeOH and BnOH as alcohols, **4b** was converted into maleic esters **6d** and **6f** with a minimum amount of cyclic compounds **5d** and **5f** (isolated yields of 9%). **6d** and **6f** were directly obtained by the carbonylation process, with 72% and 83% of isolated yields (entries 4 and 6). Conversely the bis-alkoxycarbonylation of **4b**, with the more sterically demanding *i*-PrOH as alcohol, produced a mixture of **5e** and **6e** with ca. 1:1 ratio and isolated yields of 41% and 50% respectively (Table 4, entry 5). The isomerization of **5e**, by using *p*-TSA, brought the formation of maleic diester **6e** with 93% isolated yield (Scheme 2, bottom) and an overall carbonylation/isomerization yield of 88% (table 4, entry 5).

With all this data in hand, and according to the existing knowledge on Pd-catalyzed oxidative carbonylation of alkynes,[1-9] we propose the catalytic cycles shown in Scheme 3 to justify the mono- and the bis-alkoxycarbonylation outcomes of terminal and 1,2-disubstituted alkynes under our conditions (in particular, pathway **a** refers to the monocarbonylation reaction, pathway **b** to the dicarbonylation process). Ligand **1e** and $(PhCN)_2PdCl_2$, in combination with 2 eq. of AgOTf, in situ generate $(PhCN)_2Pd(OTf)_2$/**1e** (Scheme 3, **A**).[16] The subsequent intervention of the alcohol R^3OH forms complex **B**, which is the catalytically active species for terminal and internal alkynes.[16] Upon sequential insertion of carbon monoxide and the alkynes **2** or **4** into **B**, the key five-membered palladacycle intermediates **D** (pathway **a**) or **F** (pathway **b**) are formed. In the case of complex **D**, the relative anti-periplanar position of the hydrogen atom with respect to palladium atom favours a fast hydrogen β-elimination, generating the propiolate ester **3** and the palladium hydride complex **E** (pathway **a**). On the other hand palladacycle intermediate **F** undergoes a second carbon monoxide addition to give complex **G** followed by nucleophilic attack by the alcohol to the carbonyl of the acylpalladium moiety. Displacement of palladium would then lead to the maleate product **6** and palladium hydride **E**. Alternatively an intramolecular rearrangement/cyclization, after a CO insertion in 5 position of **F**, could lead to the η^3-allylpalladium intermediate **H**.[15] The regioselective nucleophilic attack of the alcohol R^3OH to the C-5 of **H** eventually results in the formation of dialkoxyfuranones **5** and **5'** and palladium hydride **E**.



Scheme 3. Proposed Catalytic cycle.

In both pathways **a** and **b**, the reconversion of **E** into the catalytically active species **B** occurs upon the intervention of the oxidant (BQ, which is reduced to H_2BQ, Scheme 3).[17] The theoretical studies concerning both mechanisms are currently underway and will be reported in due course.

Conclusion

We have found that the complex generated in situ from $(PhCN)_2PdCl_2$ with ligand Bis-(2,6-diisopropyl)-acenaphthenequinonediimine **1e** is an excellent catalytic precursor for realizing the oxidative mono-alkoxycarbonylation of terminal alkynes **2** to propiolate esters **3** as well as the oxidative bis-alkoxycarbonylation of internal alkynes **4** to maleic diesters **6** in combination with an acid-catalyzed isomerization reaction. Eventually both propiolic esters **3** and maleic diesters **6** have been obtained with good overall isolated yields from inexpensive alkynes **2** and **4**. The carbonylation processes occur under particularly mild conditions (4 bar CO, 20 °C) in the presence of an alcohol as nucleophile, including MeOH, benzyl alcohol, secondary alcohols or sterically hindered tertiary alcohols, and benzoquinone as oxidant, demonstrating the broadness of the process towards the synthesis of several esters of propiolic and maleic acids.

Experimental Section

Typical procedure for the mono-alkoxycarbonylation reaction of terminal alkynes. In a nitrogen flushed dried Schlenk tube equipped with a magnetic stirring bar were added in sequence the $(PhCN)_2PdCl_2$ (3.8 mg, 0.01 mmol) and THF (2 mL). After the mixture turned in a red/brown color (20 min), the ligand **1e** (5.5 mg, 0.011 mmol) was added and the mixture was left stirring for 10 min, turning in a dark orange color. AgOTf (5.8 mg, 0.022 mmol) was added in one portion and the catalyst mixture turned in a light orange color with the development of yellowish solid. The preformed catalyst $(PhCN)_2Pd(OTf)_2$/**1e** was then injected in a nitrogen flushed autoclave containing benzoquinone (325 mg, 3 mmol) in the stated alcohol R^3OH (2 mL). After 10 min the respective alkyne **2a–f** (2 mmol) was added in one portion in the reaction mixture by using a syringe. The autoclave was flushed three times with CO and pressurized with 4 bar of carbon monoxide. The reaction was vigorously stirred at room temperature (20°C) for 42 h. After the stated time the autoclave was vented off, flushed with nitrogen and the reaction mixture was directly analyzed by ^1H NMR to determine the conversion of the starting alkyne. The crude was then dried under reduced pressure and filtered off a plug of silica gel, washing with CH_2Cl_2 (100 ml). Finally the solution was dried up in vacuum. Products **3a–l** were eventually obtained after flash column chromatography on silica gel (Petroleum Ether/CH_2Cl_2 50:50 then 30:70).

Typical procedure for the bis-alkoxycarbonylation reaction of 1,2-disubstituted alkynes 4a, 4b. In a nitrogen flushed Schlenk tube equipped with a magnetic stirring bar were added in sequence the $(PhCN)_2PdCl_2$ (15.3 mg, 0.04 mmol) and THF (2 mL). After the mixture turned in a red/brown color (20 min), the ligand **1e** (22.0 mg, 0.044 mmol) was added and the mixture was left stirring for 10 min, turning in a dark orange color. AgOTf (23.1 mg, 0.09 mmol) was added in one portion and the catalyst mixture turned in a light orange color with the development of yellowish solid. The preformed catalyst was injected in a nitrogen–flushed autoclave containing benzoquinone (325 mg, 3 mmol) in the stated alcohols R^3OH (2 mL). After 10 min the alkyne **4a** or **4b** (2 mmol) was added in one portion in the reaction mixture by using a syringe. 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 44 h. After the stated time the autoclave was vented off, flushed with nitrogen and the reaction mixture was directly analyzed by ^1H NMR to determine the conversion of **4a** and **4b** and the ratio **5b**:**5b'**, **5c**:**5c'** and **5a5a'–5c5c':6a–c**, **5d–5f:6d–f** (the ratio **5a**:**5a'** was determined by ^{13}C NMR on the purified mixture). The crude was then dried under reduced pressure, 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 mixtures **5a5a'–5c5c'** and products **5d–5f**, **6a–f** were eventually obtained after flash column chromatography on silica gel (Petroleum ether/CH_2Cl_2 50:50 then 30:70). **5a5a'–5c5c'** were used for the acid-catalyzed isomerization without further purification.

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Oxidative Alkoxycarbonylation of Alkynes by Means of Aryl α-diimine Palladium(II) Complexes as Catalysts

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