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Tsuji–Trost allylations with palladium recovery by phosphines/Pd(0)-triolefinic macrocyclic catalysts

Anna Serra-Muns, Roser Pleixats *

Chemistry Department, Universitat Autònoma de Barcelona, Cerdanyola del Vallès, 08193-Barcelona, Spain

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Dedicated to Prof. Pelayo Camps Garcia on the occasion of his 65th birthday

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ABSTRACT

The allylation of several nitrogen and oxygen based nucleophiles with ethyl cinnamyl carbonate under mild conditions is described. The processes take place in the absence of added base and in the presence of the precatalytic system Pd(0)-triolefinic macrocycle/1,1′-bis(diphenylphosphino)ferrocene. The macrocyclic ligand plays a key role in the recovery of the metal in the form of the initial macrocyclic complex.

1. Introduction

The palladium(0)-catalyzed allylation of nucleophiles (the Tsuji–Trost reaction) is the displacement of a leaving group from an allylic framework by a nucleophile under Pd(0) catalysis. It constitutes a powerful method for C–C and C-heteroatom bond formation which has gained high recognition in organic synthesis due to its versatility, broad scope and easy experimental procedure [1]. Although many leaving groups in the allyl system have been reported in the literature for the in situ generation of cationic η^3-allylic palladium complexes, the acetoxy and the alcoxycarbonyloxy groups have remained the most popular since the corresponding acetates and mixed carbonates are very reactive and easily available. Allylic carbonates offer advantages over acetates as addition of external base is not required for pronucleophiles which are more acidic than alcohols in the reaction medium. The alcoxide anion formed in situ as counter-anion of the electrophilic η^3-allyl palladium intermediate generates the conjugate base of the pronucleophile and the allylation takes place formally in neutral medium. Therefore, they have been the most extensively used substrates for this kind of reaction since 1982 [1k]. We have described the palladium(0)-catalyzed allylation of several highly acidic and non nucleophilic compounds using allylic carbonates [2]. The Tsuji–Trost reaction has also been broadly applied to the allylation of ambident nucleophilic heterocycles [1j], frequently providing higher regioselectivities than classical alkylation methods. Extensive work on this subject has been reported by the group of Moreno-Mañas [3]. The classical catalytic systems in Tsuji–Trost reactions involve the use of palladium(0) (e.g., $Pd(PPh_3)_4$, $Pd_2(dba)_3$) or palladium(II) (e.g., $Pd(OAc)_2$) precursors and phosphine ligands to stabilize the intermediate cationic η^3-allyl complex, these ligands being either present in the precursor complex or added externally.

Some years ago in the group of Moreno-Mañas we serendipitously discovered [2c] air- and moisture-stable phosphine-free azamacrocyclic triolefinic palladium(0) complexes of the type **Pd-1** (Scheme 1). The preparation [4,5] of the required 15-membered triolefinic macrocycles **1**, their coordination properties [5,6] with transition metals, and the activity of **Pd-1** as recyclable catalysts [5,7] has been reported. Thus, complexes **Pd-1** were active in Suzuki cross-couplings with activated aryl iodides [7a]. Polymeric versions (polystyrene-grafted catalyst [7a] and macrocycle-based polypyrrole-modified electrodes [7e]) were efficiently recovered and reused. Activated and deactivated aryl iodides were good substrates for Suzuki couplings under catalysis by recyclable silica hybrid materials containing macrocyclic complexes covalently anchored [7d,f,g]. Although these results were promising, the activity in Suzuki couplings was limited to aromatic iodides. The cross-coupling between arenediazonium salts and potassium organotrifluoroborates [7h], the Mizoroki-Heck reactions with arenediazonium tetrafluoroborates as electrophilic partners [7c],

* Corresponding author. Tel.: +34 93 581 2067; fax: +34 93 581 1265.
E-mail address: roser.pleixats@uab.cat (R. Pleixats).

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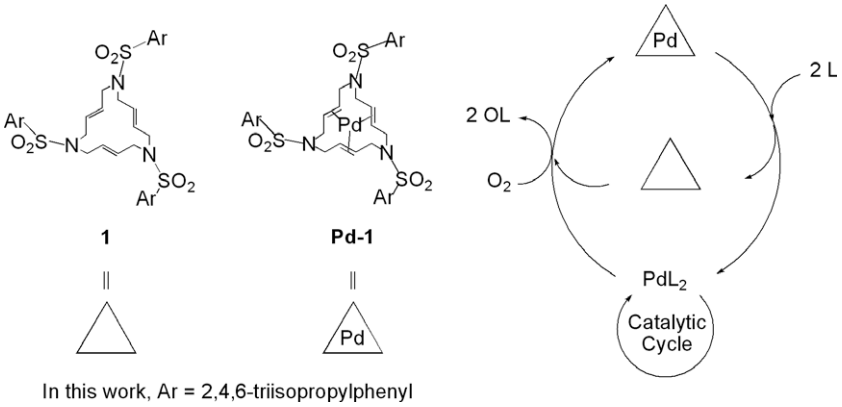


Scheme 1. Triolefinic azamacrocycles **1** and the corresponding Pd(0) complexes **Pd-1**. The role of **1** and **Pd-1** in a catalytic cycle in the presence of phosphine ligands.

and the hydroarylation of alkynes in ionic liquids [7b] catalyzed by these macrocyclic complexes have also been described. On the other hand, complexes **Pd-1** were not active in telomerisation of butadiene in the presence of methanol. However, upon addition of phosphines, the reaction took place and the catalytic species could be recycled up to four times by addition of fresh phosphine at each time [8]. Subsequent studies showed that **Pd-1** complexes reacted with monodentate or bidentate phosphines to furnish PdL_n complexes [9]. After catalysis came to an end, if the phosphine was oxidized, palladium(0) reverted to the free macrocycle ligand, thus preventing agglomeration and precipitation of palladium black and remaining available for a new run, which required addition of fresh phosphine but not fresh palladium (Scheme 1). Later on, we performed successful Suzuki cross-couplings on aryl and heteroaryl bromides and chlorides by using a catalytic system that was a combination of a bulky aliphatic σ-donor phosphine with a macrocyclic complex of type **Pd-1** [10]. The addition of highly nucleophilic and sterically demanding phosphines allowed activation of the more challenging bromides and chlorides [11], and the macrocycle **1** allowed the recovery of the metal in the form of the initial macrocyclic complex. Subsequent kinetic and mechanistic studies were undertaken in collaboration with Jutand on the first step of this Suzuki process, that is, the oxidative addition of aryl halides to the PdL_n complexes generated in situ from a Pd(0)-triolefinic macrocyclic complex and phosphines [12]. This investigation emphasized the key role played by the unsaturated macrocyclic ligands **1** on the kinetics of the oxidative addition.

With all these precedents in mind, we decided to test the palladium(0)-catalyzed allylation using a catalytic precursor system consisting of a mixture of complex **Pd-1** and a phosphine, with the aim to achieve the recovery of the metal in the form of the macrocyclic complex. Preliminary experiments [9] performed in the NMR tube revealed that, as in the telomerisation processes previously mentioned, the presence of a phosphine ligand was required to achieve the allylation reaction. The disappearance of **Pd-1** complexes upon addition of phosphines, with concomitant appearance of free macrocycle **1** and PdL_n species, was observed by NMR. These in situ formed PdL_n intermediates would react with the allylic substrates to form the cationic η^3-allyl palladium complexes. Now, we present herein the results of the reactions of ethyl cinnamyl carbonate with several nitrogen and oxygen-based nucleophiles.

2. Experimental

2.1. General remarks

Experiments were carried out with standard high-vacuum and Schlenk techniques. THF was stored over potassium hydroxide for one day and then dried by distillation from sodium-benzophenone ketyl just before use. ^{1}H NMR spectra (250 or 360 MHz) and ^{13}C NMR (62.5 or 90 MHz) were usually recorded on a Bruker DPX-250 or on a Bruker DPX-360. Chemical shifts (δ, ppm) are referenced to Me_4Si (^{1}H and ^{13}C). The abbreviations used are *s* for singlet, *d* for doublet, *dd* for double doublet, *t* for triplet, *q* for quartet, *dt* for double triplet, and *m* for multiplet. IR data were obtained on a Bruker Tensor 27 spectrophotometer with ATR Golden Gate. Mass spectra (MS-ESI and HRMS-ESI) were recorded at the Servei d'Anàlisi de la Universitat Autònoma de Barcelona using an Esquire 3000 quadrupole instrument and a MicroTOFQ Bruker Daltonic operating in the positive ion mode (ES+) at a probe tip voltage of 3 kV. Elemental analyses were performed at the Servei d'Anàlisi de la Universitat Autònoma de Barcelona. Macrocycle **1** and its palladium(0) complex **Pd-1** were prepared as previously reported [7a].

2.2. Preparation of allylation products

2.2.1. General procedure: Preparation of N-cinnamyl-N-methylaniline, *4a*

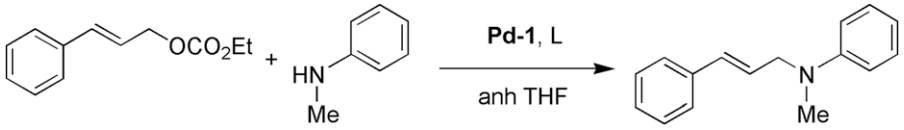
Ethyl cinnamyl carbonate **2** (58 mg, 0.281 mmol), **Pd-1** (25 mg, 0.022 mmol) and dppf (15.7 mg, 0.028 mmol) were added into a Schlenk flask. Three vacuum/argon cycles were made. *N*-methylaniline **3a** (31 μL, 0.989 g/mL, 0.281 mmol) and anhydrous and degassed THF (3 mL) were added. The mixture was magnetically stirred at room temperature under argon for 22 h. The solvent was evaporated and the residue was purified by flash-chromatography (silica gel) with hexane-ethyl acetate 97:3, to afford **4a** [13] as an oil (53 mg, 86% yield); ^{1}H NMR ($CDCl_3$) δ = 2.97 (s, 3H), 4.07 (d, *J* = 5.5 Hz, 2H), 6.23 (dt, *J* = 15.7 and 5.4 Hz, 1H), 6.51 (d, *J* = 15.7 Hz, 1H), 6.75 (m, 3H), 7.22 (m, 7H); ^{13}C NMR ($CDCl_3$) δ = 38.1, 55.0, 112.8, 116.7, 125.9, 126.5, 127.5, 128.7, 129.3, 131.4, 137.1, 149.7. Then, a mixture **Pd-1:1** 97:3 (15 mg, 94% recovery) was eluted.

2.2.2. Preparation of allylation products *4b–k*

The other compounds **4** were prepared in a similar manner (see Table 2 for differences in experimental conditions).

*2.2.2.1. N-cinnamyl-N-methyl-4-chloroaniline, **4b**.* Eluent: hexane–ethyl acetate 97:3–90:10; IR (ATR): ν = 3026, 1596, 1499, 1448, 1355, 1199, 1116, 964, 808 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 2.96 (s, 3H), 4.04 (d, *J* = 5.2 Hz, 2H), 6.19 (dt, *J* = 15.7 and 5.4 Hz, 1H), 6.48 (d, *J* = 15.7 Hz, 1H), 6.67 (d, *J* = 9.0 Hz, 2H), 7.16 (d, *J* = 9.0 Hz, 2H), 7.31 (m, 5H); Anal. Calc. for $C_{16}H_{16}NCl$: C, 74.55; H, 6.26; N, 5.43. Found: C, 73.98; H, 6.33; N, 5.09%.

Table 1
Optimization of Tsuji–Trost reaction between ethyl cinnamyl carbonate, **2**, and *N*-methylaniline, **3a**.

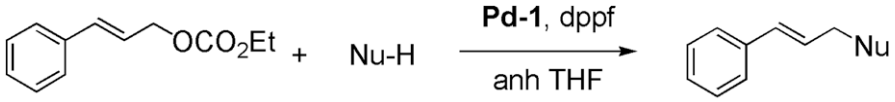


2 **3a** **4a**

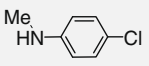
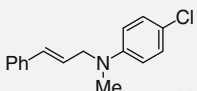
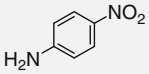
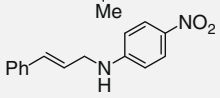
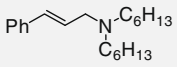
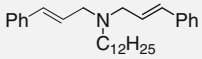
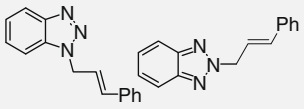
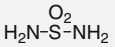
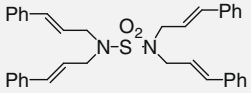
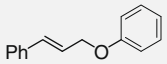
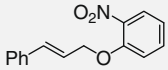
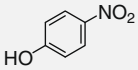
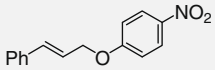
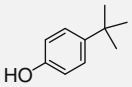
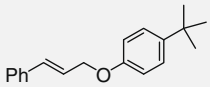
Entry[a]	L	Equivalents (L)[b]	Time (h)	Conversion (%)[c]	Yield **4a** (%)[d]	**Pd-1**:**1**[e]
1	PCy_3[f]	2.0	15	70	70	0:100
2	dppb	2.3	24	60	55	0:100
3	PPh_3	2.0	24	100	89	87:13
4	PPh_2(*o*-tolyl)	2.0	20	100	72	97:3
5	dppe	2.0	3	100	69	85:15
6	dppf	1.3	22	100	86	97:3

[a] [**2**] = 0.09–0.10 M, **2**:**3a** = 1:1, 5% molar of **Pd-1**, anhydrous and degassed THF, argon atmosphere, room temperature.
[b] Equivalents of L with respect to **Pd-1**.
[c] Conversion determined by ^{1}H NMR.
[d] Isolated yields of **4a** by chromatography.
[e] Ratio **Pd-1**:**1** determined by ^{1}H NMR in the recovered mixture separated from **4a** by chromatography.
[f] Commercial solution of PCy_3 in toluene (20% w/w) was used.

Table 2
Tsuji–Trost reactions between ethyl cinnamyl carbonate **2** and *N*- and *O*-nucleophiles **3** to give allylation products **4**.



2 **3** **4**

Entry[a]	T	Time (h)	Carbonate **[2]**	Nucleophile	**3**	2:3	Product	**4**	Yield (%)[b]	**Pd-1**:**1**[c]
1	r.t.	15	0.09		**3b**	1:1		**4b**	70	86:14
2	r.t.	15	0.08		**3c**	1:1		**4c**	21[d,e]	81:19
3	r.t.	20	0.09	$HN(C_6H_{13})_2$	**3d**	1:1		**4d**	90[f]	50:50
4	r.t.	20	0.08	$H_2NC_{12}H_{25}$	**3e**	1:1		**4e**	73[f,g]	19:81
5	r.t.	20	0.09		**3f**	1:1		**4f 4'f**	33 58	0:100
6	r.t.	14	0.25		**3g**	5:1		**4g**	49	0:100
7	refl.	21	0.10		**3h**	1:0.9		**4h**	100	92:8
8	refl.	21	0.11		**3i**	1:0.9		**4i**	29[d]	56:44
9	refl.	21	0.11		**3j**	1:0.9		**4j**	58[d]	55:45
10	r.t.	15	0.13		**3k**	1:0.9		**4k**	78	88:12

[a] 5% molar of **Pd-1**, 5% molar of dppf, anhydrous and degassed THF, argon atmosphere.
[b] Isolated yields of **4** by chromatography.
[c] Ratio **Pd-1**:**1** determined by ^{1}H NMR in the recovered mixture separated from **4** by chromatography.
[d] Other secondary products are obtained (see text).
[e] 23% conversion of **3c**.
[f] Yield determined by ^{1}H NMR integration on the eluted fraction by chromatography.
[g] Yield based on **2.**

2.2.2.2. N-cinnamyl-4-nitroaniline, ***4c*** *[2a,14].* Eluent: hexane–ethyl acetate 80:20–70:30; ^{1}H NMR ($CDCl_3$) δ = 4.04 (dd, J = 5.7 and 1.5 Hz, 2H), 4.68 (br s, 1H), 6.26 (dt, J = 16.0 and 5.7 Hz, 1H), 6.60 (m, 3H), 7.31 (m, 5H), 8.10 (d, J = 9.2 Hz, 2H).

2.2.2.3. N-cinnamyl-N, N-dihexylamine, ***4d****.* Eluent: hexane–ethyl acetate 96:4; IR (ATR): ν = 2927, 2857, 1465, 1376, 782 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.88 (t, J = 6.6 Hz, 6H), 1.28 (m, 12H), 1.47 (m, 4H), 2.45 (m, 4H), 3.24 (d, J = 6.5 Hz, 2H), 6.28 (dt, J = 15.7 and 6.5 Hz, 1H), 6.50 (d, J = 15.7 Hz, 1H), 7.28 (m, 5H); ^{13}C NMR ($CDCl_3$) δ = 14.2, 22.8, 27.1, 27.4, 32.0, 54.1, 56.8, 126.4, 127.3, 128.2, 128.6, 132.1, 137.4. HRMS (ESI): m/z = 302.2839 (calcd for $C_{21}H_{35}N$ + H: 302.2842).

2.2.2.4. N, N-dicinnamyl-N-dodecylamine, ***4e****.* Eluent: hexane–ethyl acetate 90:10; IR (ATR): ν = 3025, 2923, 2852, 1599, 1494, 1449, 1362, 1317, 1150, 965, 742, 692, 659, 629 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.88 (t, J = 6.6 Hz, 3H), 1.25 (m, 18H), 1.52 (m, 2H), 2.50 (m, 2H), 3.30 (d, J = 6.5 Hz, 4H), 6.30 (dt, J = 15.7 and 6.7 Hz, 2H), 6.52 (d, J = 15.7 Hz, 2H), 7.27 (m, 10H); MS-ESI: m/z = 418 [M+H]$^+$; HRMS (ESI): m/z = 418.3462 (calcd for $C_{30}H_{44}N$: 418.3468).

2.2.2.5. 1-Cinnamylbenzotriazole, ***4f*** *and 2-cinnamylbenzotriazole,* ***4′f****.* Eluent: hexane–ethyl acetate 100:0–95:5; **4f** [3f]: ^{1}H NMR ($CDCl_3$) δ = 5.36 (d, J = 6.2 Hz, 2H), 6.36 (dt, J = 15.7 and 6.2 Hz, 1H), 6.65 (d, J = 15.7 Hz, 1H), 7.35 (m, 7H), 7.54 (dt, J = 8.4 and 1.1 Hz, 1H), 8.05 (dt, J = 8.4 and 1.1 Hz, 1H); **4′f** [3f]: ^{1}H NMR ($CDCl_3$) δ = 5.50 (dd, J = 6.7 and 1.2 Hz, 2H), 6.55 (dt, 15.8 and 6.6 Hz, 2H), 6.79 (d, J = 15.8 Hz, 1H), 7.34 (m, 7H), 7.88 (m, 2H).

2.2.2.6. N, N, N′, N′-tetracinnamylsulfamide, ***4g*** *[2b].* Eluent: hexane–ethyl acetate 100:0–90:10; IR (ATR): ν = 3026, 2924, 2852, 1495, 1448, 1322, 1145, 966, 902, 746, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 4.03 (d = 6.5 Hz, 8H), 6.23 (dt, J = 15.8 and 6.7 Hz, 4H), 6.55 (d, J = 15.8 Hz, 4H), 7.29 (m, 20H).

2.2.2.7. (Cinnamyloxy)benzene, ***4h*** *[15].* Eluent: hexane–ethyl acetate 100:0–98:2; ^{1}H NMR ($CDCl_3$) δ = 4.69 (d, J = 5.7 Hz, 2H), 6.41 (dt, J = 16.0 and 5.7 Hz, 1H), 6.73 (d, J = 16.0 Hz, 1H), 6.96 (m, 3H), 7.32 (m, 7H).

2.2.2.8. 1-Cinnamyloxy-2-nitrobenzene, ***4i*** *[16].* Eluent: hexane–ethyl acetate 98:2–90:10; ^{1}H NMR ($CDCl_3$) δ = 4.86 (d, J = 5.5 Hz, 2H), 6.39 (dt, J = 16.0 and 5.5 Hz, 1H), 6.79 (d, J = 16.0 Hz, 1H), 7.1–7.6 (m, 8H), 7.85 (dd, J = 8.0 and 1.5 Hz, 1H); MS: m/z = 255 [M$^+$].

2.2.2.9. 1-Cinnamyloxy-4-nitrobenzene, ***4j*** *[17].* Eluent: hexane–ethyl acetate 100:0–90:10; IR (ATR): ν = 2927, 1590, 1515, 1495, 1339, 1255, 1108, 996, 970, 854, 789, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 4.80 (d, J = 6.0 Hz, 2H), 6.38 (dt, J = 16.0 and 6.0 Hz, 1H), 6.76 (d, J = 16.0 Hz, 1H), 7.01 (d, J = 9.2 Hz, 2H), 7.32 (m, 5H), 8.21 (d, J = 9.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 69.2, 114.7, 122.8, 125.8, 126.5, 128.2, 128.6, 134.1, 135.9, 163.5. HRMS (ESI): m/z = 278.0782 (calcd for $C_{15}H_{13}NO_3$ + Na: 278.0788).

2.2.2.10. 1-Cinnamyloxy-4-tert-butylbenzene, ***4k****.* Eluent: hexane–ethyl acetate 100:0–97:3; IR (ATR): ν = 2960, 2926, 1513, 1260, 1016, 799, 744, 692 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.34 (s, 9H), 4.72 (d, J = 5.8 Hz, 2H), 6.46 (dt, J = 15.9 and 5.7 Hz, 1H), 6.63 (d, J = 15.9 Hz, 1H), 6.94 (d, J = 8.6 Hz, 2H), 7.2-7.4 (m, 5H), 7.45 (d, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ = 31.7, 34.2, 68.8, 114.3, 124.9, 126.4, 126.7, 127.9, 128.7, 132.9, 136.6, 143.7, 156.5; HRMS (ESI): m/z = 289.1552 (calcd for $C_{19}H_{22}O$ + Na: 289.1563).

3. Results and discussion

We initially studied the reaction between ethyl cinnamyl carbonate, **2**, and *N*-methylaniline, **3a**, in the presence of a 5% molar of **Pd-1** (see Scheme 1, Ar = 2, 4, 6-triisopropylphenyl) and several phosphine ligands (aromatic and aliphatic monodentate phosphines; bidentate phosphines) (Table 1). In all cases the reactions were performed under inert atmosphere, with equimolar amounts of reagents, in anhydrous and degassed tetrahydrofuran at room temperature. Treatment of the crude mixtures by column chromatography through silica gel permitted the obtention of moderate to good yields of *N*-cinnamyl-*N*-methylaniline, **4a**, and also the recovery of a mixture of palladium(0) complex **Pd-1** and the free macrocycle **1** in the molar ratios mentioned in Table 1. The recovery of macrocycle was nearly quantitative in all cases (if we consider the sum of its free and metal coordinated forms). ^{1}H NMR spectra distinguish very well free macrocycles from their palladium(0) complexes since free macrocycles present signals for the olefinic protons at δ ca. 5.50–5.80, whereas in palladium complexes strong upfield shifts are observed, up to δ ca. 2.50–4.40 depending of the proton considered [2c,5]. When the aliphatic and bulky monodentate tricyclohexylphosphine (Table 1, entry 1) and the bidentate 1,4-bis(diphenylphosphino)butane (Table 1, entry 2) were used, partial conversion and total decomplexation was observed (ratio **Pd-1**:**1** of 0:100). Fortunately, using triphenylphosphine, PPh_2(*o*-tolyl), 1,2-bis(diphenylphosphino)ethane (dppe) or 1,1′-bis(diphenylphosphino)ferrocene (dppf) as ligands, full conversions and good yields of **4a** were achieved (Table 1, entries 3–6), monodentate PPh_2(*o*-tolyl) (entry 4) and bidentate dppf (entry 6) providing almost complete recovery of the metal in the form of **Pd-1** (ratio **Pd-1:1** of 97:3). Taking into account the best compromise between isolated product yield and palladium recovery, the conditions of entry 6 were adopted for subsequent experiences with other nucleophiles (but 1.0 equivalent of bidentate phosphine with respect to palladium was used instead of 1.3 equivalents in further experiments). The recovered mixture **Pd-1:1** 97:3 of entry 6 was used in a second run under the same conditions to afford complete conversion of the substrates to **4a** in the given time (85% isolated yield of **4a**; a 96:4 mixture of **Pd-1**:**1** was recovered).

To extend the scope of the reaction we first tested other aromatic secondary and primary amines such as 4-chloro-*N*-methylaniline (**3b**) and 4-nitroaniline (**3c**) (Table 2, entries 1 and 2, respectively), as well as secondary and primary aliphatic amines such as di-*n*-hexylamine (**3d**) and *n*-dodecylamine (**3e**) (Table 2, entries 3 and 4, respectively). Using the secondary amine **3b**, *N*-cinnamyl-*N*-methyl-4-chloroaniline, **4b**, was obtained in 70% isolated yield and quite good recovery of palladium was achieved (Table 2, entry 1). Highly acidic and non-nucleophilic 4-nitroaniline (**3c**) (pKa value in DMSO: 20.9, as compared with methanol: 29.0) [18] reacted at room temperature with the carbonate **2** under palladium catalysis, presumably through its conjugate base [2], but *N*-cinnamyl-4-nitroaniline, **4c**, was obtained in low yield due to a low conversion (76% of **3c** was recovered) and to decomposition of allylic carbonate **2** during the reaction (Table 2, entry 2). Minor amounts of secondary products derived from **2** such as cinnamyl alcohol and cinnamaldehyde were also obtained. The yields of **4c** were not improved with other phosphine ligands such as PPh_3 and PPh_2(*o*-tolyl). Allylation of aniline derivatives under palladium catalysis has previously been reported with *N*-allylpyridinium salts [19], allylic carbonates [2a] and allylic alcohols [20].

A more nucleophilic secondary aliphatic amine **3d** afforded **4d** in good yield in a room temperature reaction (Table 2, entry 3) and the primary amine **3e** gave the diallylation product **4e** under similar conditions when equimolar amounts of reagents were used

(73% yield with respect to **2**) (Table 2, entry 4). Unfortunately, the recovery of the palladium complex was inferior in these cases (ratios **Pd-1:1** of 50:50 and 19:81 for entries 3 and 4). However, it must be taken into account that palladium is catalytic and the **Pd-1** complex acts as a precatalyst and metal reservoir. Thus, all the recovered mixtures containing complexed palladium are useful to be reused in a second run.

The reaction with an ambident nucleophilic heterocycle such as benzotriazole (**3f**) under these mild conditions provided a mixture of the regioisomers **4f** and **4′f** derived from the allylation at N-1 and N-2 positions in an excellent 91% global yield and a selectivity of 1:1.8 in favour of **4′f** (Table 2, entry 5). Although the macrocycle **1** was fully recovered uncomplexed, it is worth to mention that previous essays in our group [3f] with the same nucleophile in refluxing dioxane under $Pd(PPh_3)_4$ catalysis afforded a mixture of compounds with lower yields and a lower regioselectivity (ratio **4f:4′f** of 1:1.4). Later on, Sinou [21] reported also mixtures of regioisomers in the allylation of **3f** with a carbonate derived from an unsaturated carbohydrate. Benzotriazole has been found to form palladium complexes [22]. The competition of **3f** with our macrocycle as ligand for the metal could be on the origin of the recovery of fully uncomplexed macrocycle **1**. Tetraallylation of highly acidic and non nucleophilic sulfamide was achieved in the absence of external base using an excess of the carbonate (**2:3** ratio of 5:1) at room temperature (Table 2, entry 6). Decomplexation of **Pd-1** after the reaction was also observed. It is worth to mention that although reactions of sulfamide with carbonyl groups and with nitriles are well precedented [23], this is not so for alkylations, and substituted sulfamides are best prepared by nucleophilic attack of amines on the sulphur atom with elimination of ammonia [24]. Next, we turned to oxygen-based nucleophiles such as phenol (**3h**), 2-nitrophenol (**3i**), 4-nitrophenol (**3j**) and 4-*tert*-butylphenol (**3k**) (Table 2, entries 7–10, respectively). For **3h**, **3i** and **3j** the reaction mixture was heated at reflux in order to enhance the reaction rate. Ether **4h** was obtained from phenol in quantitative yield (Table 2, entry 7). For the electron-poor and more acidic nitrophenols **3i** and **3j** (pKa = 10.8 for **3j** in DMSO) [18], the isolated yields were modest and secondary products derived from the carbonate **2** were detected by GC–MS, such as cinnamyl alcohol and cinnamyl ethyl ether (Table 2, entries 8 and 9). For the more electron-rich phenol **3k**, good yield of **4k** was achieved at room temperature (Table 2, entry 10). The recovery of **Pd-1** varies depending on the nucleophile (ratio **Pd-1:1** from 98:2 for phenol to 55:45 for 4-nitrophenol). In all cases the O-allylation products were obtained as in other previously reported synthesis of allylic aryl ethers from allylic carbonates and phenols under palladium catalysis [25] although C-allylation of naphthols and benzene polyols by allyl alcohols [26] and allylic carbonates [25b] has also been described.

4. Conclusion

Mixtures of macrocyclic triolefinic palladium(0) complex **Pd-1** and 1,1′-bis(diphenylphosphino)ferrocene (5% molar of Pd, 1:1 molar ratio of Pd/dppf) have been successfully used as precatalytic system for the allylation of several nitrogen and oxygen based nucleophiles with ethyl cinnamyl carbonate in the absence of base. The reactions take place under mild conditions, in tetrahydrofuran at room temperature (or under reflux in few cases). The nucleophiles tested include secondary and primary aliphatic and aromatic amines, benzotriazole, sulfamide and several phenols. The presence of the phosphine is required for the allylation reaction to take place, the in situ formed Pd(L-L) species acting as catalyst. It is worth noting that the macrocyclic ligand **1** plays a key role in the recovery of the metal in the form of the initial **Pd-1** complex, which can be separated by chromatography and reused in a subsequent run.

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