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A Copper- and Amine-Free Sonogashira Reaction of Aryl Halides Catalyzed by 1,3,5-Triaza-7-phosphaadamantane Palladium Systems

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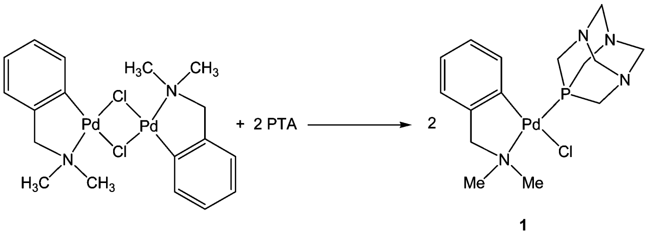
The monomeric complex [Pd(dmba)Cl(PTA)] [dmba = N,C-chelating 2-(dimethylaminomethyl)phenyl; PTA = 1,3,5-triaza-7-phosphaadamantane] has been obtained and its crystal structure has been established by X-ray diffraction. Conditions for an efficient copper- and amine-free catalyzed Sonogashira reaction of aryl bromides and chlorides with terminal alkynes by [Pd(dmba)Cl(PTA)] and Pd(OAc)$_2$/PTA have been developed. It is worthwhile noting that a relatively low palladium catalyst loading has been employed.

1. Introduction

The Sonogashira cross-coupling reaction is well-known as being one of the most important and utilized reactions for the construction of carbon−carbon bonds, in particular for the formation of alkynes.[1−7] This method has been applied for the synthesis of natural products, bioactive compounds, and materials.[8−20] The most commonly used catalytic systems for this transformation include PdCl$_2$(PPh$_3$)$_2$, PdCl$_2$/PPh$_3$, and Pd(PPh$_3$)$_4$ together with CuI as the cocatalyst and large amounts of amines as the solvents or cosolvents. However, the presence of CuI can result in the formation of some Cu(I) acetylides in situ that can readily undergo oxidative homocoupling reactions of alkynes.[21−23] In addition, amines such as piperidine, diethylamine, and triethylamine required in most Sonogashira reactions add to the environmental burden. Herrmann reported a procedure for the Sonogashira reaction of aryl bromides under copper-free conditions, but it was necessary to use air-sensitive and pyrophoric P(t-Bu)$_3$ as a ligand, although the coupling did proceed with only 0.5 mol % of palladium and ligand.[24] Recently, Nájera has disclosed a palladacycle catalyst for the cross-coupling of aryl bromides and iodides with terminal alkynes under copper- and amine-free conditions.[25,26] However, this methodology requires relatively harsh conditions (110 °C). On the other hand, the preparation by Fairlamb et al. of some monomeric cyclometalated palladium(II) complexes and their use in the Sonogashira reactions of aryl halides with phenyl acetylene (in the presence and absence of Cu(I) salts) has also been reported.[27]

Scheme 1



In the present study our initial aim was to synthesize an organopalladium complex derived from the N,C-chelating 2-(dimethylaminomethyl)phenyl (dmba) and the known phosphine 1,3,5-triaza-7-phosphaadamantane (PTA) and the study of its catalytic activity in Sonogashira reactions under copper- and amine-free conditions. We have also done this catalytic study with the system Pd(OAc)$_2$/PTA. The PTA ligand is unique due to its small steric demand (cone angle similar to PMe$_3$), its resistance to oxidation, and its solubility in a wide variety of solvents. The synthesis of PTA was first reported in 1974,[28] but the coordination chemistry of this ligand has been explored

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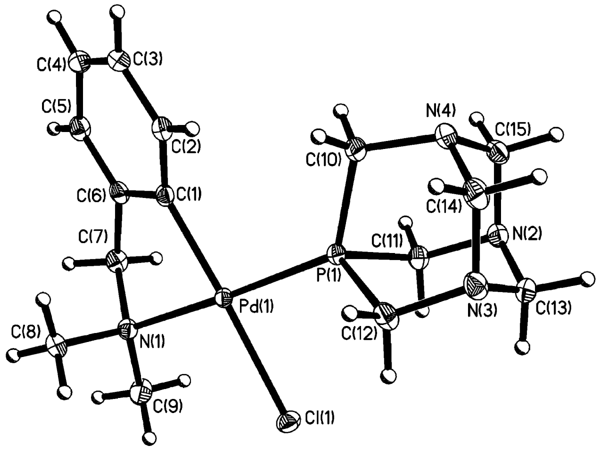

Figure 1. ORTEP of complex **1** showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

Table 1. Selected Distances (Å) and Bond Angles (deg) for Complex 1

bond distances		bond angles	
Pd(1)−C(1)	2.0086(16)	C(1)−Pd(1)−N(1)	80.82(6)
Pd(1)−N(1)	2.1467(14)	C(1)−Pd(1)−P(1)	97.27(5)
Pd(1)−P(1)	2.2260(4)	N(1)−Pd(1)−P(1)	172.84(4)
Pd(1)−Cl(1)	2.3983(4)	C(1)−Pd(1)−Cl(1)	175.38(5)
		N(1)−Pd(1)−Cl(1)	95.01(4)
		P(1)−Pd(1)−Cl(1)	86.621(15)

Table 2. Hydrogen Bonds [Å and deg] for Complex 1[a]

D−H···A	*d*(D−H)	*d*(H···A)	*d*(D···A)	∠(DHA)
C(5)−H(5)···Pd(1)#1	0.95	3.29	3.7391(17)	111.0
C(7)−H(7B)···Cl(1)#1	0.99	2.60	3.5530(17)	161.9
C(11)−H(11B)···N(3)#1	0.99	2.62	3.555(2)	157.7
C(2)−H(2)···Cl(1)#2	0.95	2.90	3.6304(18)	134.7

[a] Symmetry transformations used to generate equivalent atoms: #1 $x+1$, y, z; #2 x, $-y+1/2$, $z-1/2$.

only recently[29] and, as far as we know, only one organopalladium compound containing PTA has ever been reported, [Pd(salicylaldiminato)(Me)(PTA)].[30] The unique adamantane-type phosphine that has been used until now in coupling reactions is 1,3,5,7-tetramethyl-2,4,8-trioxa-6-phenyl-6-phosphaadamantane.[31] It is worthwhile noting that a relatively low palladium catalyst loading has been employed in our reactions.

2. Results and Discussion

2.1. Synthesis and Characterization of [Pd(dmba)Cl(PTA)]. In dichloromethane, the dimeric complex [Pd(dmba)(μ-Cl)]$_2$ reacts at room temperature with 2 equiv of PTA to yield the monomeric complex [Pd(dmba)Cl(PTA)] (**1**) (Scheme 1) in a very high yied. The structure was assigned on the basis of microanalytical and NMR data. Complex **1** is an air-stable solid, and the thermal analysis shows that it decomposes above 220 °C in a dynamic N_2 atmosphere. Complex **1** shows a singlet resonance at −46 ppm in its $^{31}P\{^1H\}$ NMR spectrum, consistent for palladium compounds containing PTA acting as a P-donor ligand.[29] The ^1H NMR spectrum of complex **1** shows the PTA-*trans*-to-NMe_2 ligand arrangement, as can be inferred from the small, but significant, coupling constants $^4J_{P-H}$ (ranging from 2.4 to 2.7 Hz) of the NMe_2 and the CH_2N protons with the phosphorus atom.[32,33] The proton NMR spectrum shows also a singlet resonance and an AB quartet (ca. 12.7 Hz geminal H−H coupling) due to the NCH_2P and NCH_2N methylene groups of the PTA ligand, respectively. The presence of only a singlet for the NCH_2P methylene protons, although rather unusual since two-bond P−H coupling would be expected, has also been recently observed in [Au(C≡CR)(PTA)] complexes.[34] By use of 2D (HETCOR) and $^1H\{^{31}P\}$ NMR spectra we could unambiguously confirm the assignment of the PTA ligand protons. In the ^{13}C NMR spectrum of complex **1** the resonances due to NCH_2N and PCH_2N are observed as doublets at δ 73 and 52 ppm, respectively, due to coupling to ^{31}P.

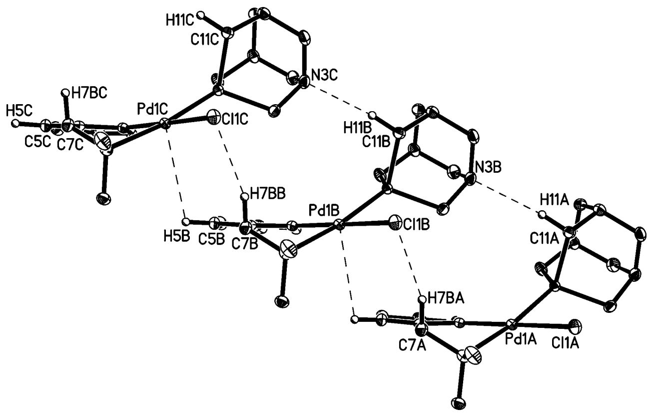

Figure 2. Schematic showing the zigzag chain formed by hydrogen bonding in complex **1**.

Scheme 2

$$\mathrm{Ar{-}X\ +\ R{-}{\equiv}{-}H\ \xrightarrow[-\,HX]{cat.\ [Pd]}\ Ar{-}{\equiv}{-}R}$$

R = alkyl, aryl; X = Br, Cl

The structure of **1** is shown in Figure 1. Selected bond distances and bond angles are given in Table 1. Coordination at palladium is approximately square planar, although the angles around palladium deviate from 90° due to the bite angle of the cyclometalated ligand. The C(1)−Pd−N(1) angle of 80.82(6)° is within the normal range for such complexes.[35,36] The PTA ligand is *trans* to the nitrogen donor due to the difficulty of coordinating a phosphine *trans* to an aryl ligand in palladium complexes (i.e., the destabilizing effect known as *transphobia*).[37] The cyclometalated ring is puckered with the nitrogen atom significantly out of the plane defined by the palladium and carbon atoms, a feature that is quite commonly observed in cyclometalated dmba complexes. The Pd−C bond length is essentially the same as that reported in [Pd(*o*-$C_6H_4CH_2NMe_2$)(PCy_3)(TFA)].[36] The Pd−P distance of 2.2260(4) Å is very

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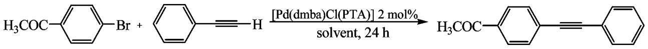
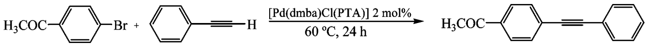
Table 3. Sonogashira Coupling of 4-Bromoacetophenone with Phenylacetylene: Solvent Study



entry	solvent	temperature (°C)	yield (%)[a]
1	acetonitrile	60	92
2	acetone	60	82
3	tetrahydrofuran	60	66
4	toluene	60	48

[a] Determined by GC. Conditions: 1.0 equiv of aryl bromide, 1.5 equiv of phenylacetylene, 1.5 equiv of Cs_2CO_3, 4.0 mL of solvent, 60 °C, 24 h.

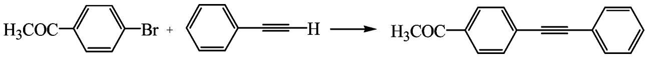
Table 4. Screening of Bases for Sonogashira Coupling of 4-Bromoacetophenone with Phenylacetylene



entry	base	yield (%)[a]
1	Cs_2CO_3	92
2	K_2CO_3	68
3	Et_3N	45

[a] Determined by GC. Conditions: 1.0 equiv of aryl bromide, 1.5 equiv of phenylacetylene, 1.5 equiv of base, 4.0 mL of CH_3CN, 60 °C, 24 h.

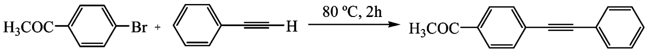
Table 5. Effect of the Copper Additive on the Efficiency of Sonogashira Coupling of 4-Bromoacetophenone with Phenylacetylene



entry	CuI (mol %)	yield (%)[a]
1	0.0	50
2	0.5	46
3	1.0	44

[a] Determined by GC. Conditions: 1.0 equiv of aryl bromide, 1.5 equiv of phenylacetylene, 1.5 equiv of Cs_2CO_3, 4.0 mL of CH_3CN, 2.5 mol % of catalyst [Pd(dmba)Cl(PTA)], 80 °C, 2 h.

Table 6. Sonogashira Coupling of 4-Bromoacetophenone: Influence of the Ratio $Pd(OAc)_2$:PTA



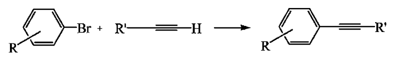
entry	catalyst	ligand	molar ratio	yield (%)[a]
1	$Pd(OAc)_2$	PTA	1:1	50
2			1:2	72
3			1:3	88
4			1:4	28
5			1:5	12

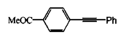
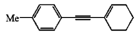
[a] Determined by GC. Conditions: 1.0 equiv of aryl bromide, 1.5 equiv of phenylacetylene, 1.5 equiv of Cs_2CO_3, 4.0 mL of CH_3CN, 2.5 mol % of $Pd(OAc)_2$, 80 °C, 2 h.

similar to those found in *cis*-$[PdCl_2(PTA)_2]$,[38] and it is almost 0.1 Å shorter than that observed in $[Pd(dmba)Cl(PPh_3)]$ of 2.321 Å.[39] This last observation is consistent with the smaller cone angle (103°) and more basic nature of PTA as compared to PPh_3.[30] In the crystal, a three-dimensional macromolecular network structure is observed built up by hydrogen bonding, which involves the PTA ligand, the coordinated chloride, the dmba, and even the metal center (Table 2 and Figure 2), the C(5)−H(5)···Pd(1) interaction being a rather weak one.[40]

2.2. Sonogashira Reaction of Aryl Halides Catalyzed by PTA Palladium Systems. Complex **1** and $Pd(OAc)_2$/PTA were screened for catalytic activity in the cross-coupling of aryl bromides or aryl chlorides with terminal alkynes under copper- and amine-free conditions (Scheme 2).

Table 7. Sonogashira Coupling of Aryl Bromides with Terminal Alkynes



entry	product	cat.	yield (%)[a]	entry	product	cat.	yield (%)[a]
1		1	100	21		1	96
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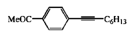
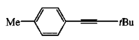
3		1	100	23		1	100
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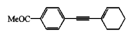
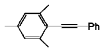
5		1	100	25		1	76
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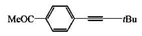
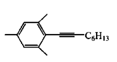
7		1	100	27		1	45
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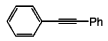
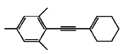
9		1	70	29		1	75
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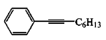
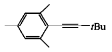
11		1	100	31		1	80
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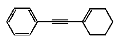
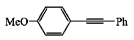
13		1	98	33		1	60
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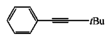
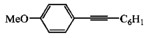
15		1	100	35		1	88
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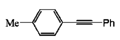
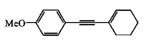
17		1	70	37		1	80
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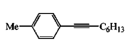
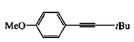
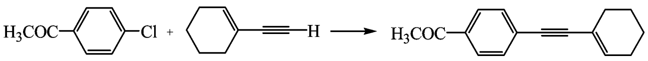
19		1	92	39		1	100
20		2	99	40		2	100

[a] Determined by GC. Conditions: 1.0 equiv of aryl bromide, 1.5 equiv of alkyne, 1.5 equiv of Cs_2CO_3, 4.0 mL of CH_3CN, 2.5 mol % of [Pd], 80 °C, 24 h.

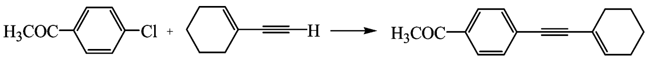
Table 8. Sonogashira Coupling of 4-Chloroacetophenone with 1-Ethynylcyclohexene: Solvent Study



entry	solvent	temperature (°C)	yield (%)[a]
1	acetonitrile	80	66
2	acetone	60	26
3	dioxane	100	35
4	tetrahydrofuran	60	23
5	toluene	100	40

[a] Determined by GC. Conditions: 1.0 equiv of aryl chloride, 1.5 equiv of 1-ethynylcyclohexene, 1.5 equiv of Cs_2CO_3, 4.0 mL of solvent, 3 mol % of $Pd(OAc)_2$, 9 mol % PTA, 24 h.

Table 9. Screening of Bases for Sonogashira Coupling of 4-Chloroacetophenone with 1-Ethynylcyclohexene

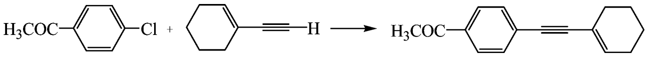


entry	base	yield (%)[a]
1	Cs_2CO_3	66
2	K_2CO_3	15
3	K_3PO_4	10
4	Et_3N	14

[a] Determined by GC. Conditions: 1.0 equiv of aryl chloride, 1.5 equiv of 1-ethynylcyclohexene, 1.5 equiv of base, 4.0 mL of acetonitrile, 3 mol % of $Pd(OAc)_2$, 9 mol % PTA, 80 °C, 24 h.

For preliminary optimization of the reaction conditions, we first studied the reaction of 4-bromoacetophenone and phenylacetylene under nitrogen at 60 °C in the presence of 2 mol % of complex **1** with respect to the aryl bromide. The solvents

Table 10. Sonogashira Coupling of 4-Chloroacetophenone with 1-Ethynylcyclohexene: Influence of TBAB



entry	equiv of TBAB	yield (%)[a]
1	0	66
2	0.1	68
3	0.5	74
4	1.0	90
5	1.5	95
6	2.0	86

[a] Determined by GC. Conditions: 1.0 equiv of aryl chloride, 1.5 equiv of 1-ethynylcyclohexene, 1.5 equiv of Cs_2CO_3, 4.0 mL of acetonitrile, 3 mol % of $Pd(OAc)_2$, 9 mol % PTA, 80 °C, 24 h.

used were toluene, acetonitrile, acetone, and tetrahydrofuran (Table 3). The best conversion was obtained when acetonitrile was used (entry 1), although in acetone the yield was also high (82%, entry 2).

Another important initial goal was to find a suitable base that would effect the desired reaction. Surprisingly, commonly used tertiary amine bases such as triethylamine gave inferior results (Table 4). Gratifyingly, however, both Cs_2CO_3 and K_2CO_3 were effective as bases, with Cs_2CO_3 being the more reactive (92%, entry 1).

Another important observation was also made during our initial experiments. The presence of copper cocatalyst (added prior to the start of the reaction) has a deleterious effect on the desired transformation (Table 5), an effect that has been found previously by Buchwald et al.[41]

For the catalytic system $Pd(OAc)_2$/PTA we have also optimized the ratio palladium:phosphine (Table 6). The molar ratio 1:3 showed the best activity (entry 3).

After preliminary optimization of the reaction conditions, we tested the catalytic activity of complex **1** and the mixture $Pd(OAc)_2$/PTA (1:3 molar ratio, catalyst **2**) in the Sonogashira coupling of aryl bromides with terminal alkynes in acetonitrile at 80 °C, 24 h (the reaction time was not optimized) and Cs_2CO_3 as base, and the results are summarized in Table 7. A relatively low palladium catalyst loading was used (2.5 mol % [Pd]).

In the case of the reaction of the activated 4-bromoacetophenone with terminal alkynes the yields of products with both catalytic systems (entries 1−8) were excellent (100%). Excellent conversions were also obtained in the case of bromobenzene (entries 9−16) and the deactivated 4-bromotoluene (entries 17−24), except when phenylacetylene was used (ca. 70% yield) due to partial formation of the homocoupling product (Glaser-type reaction). The cross-coupling of sterically hindered aryl bromides (bromomesitylene) also proceeded quite well with both catalytic systems (entries 25−32). When the electronically deactivated substrate 4-bromoanisole is used (a good indicator of optimal catalyst performance) also good conversions were obtained (entries 33−40).

Due to our excellent results with the arylbromides, then we decided to study also the activity of catalysts **1** and **2** in the cross-coupling of the less reactive aryl chlorides with terminal alkynes. For preliminary optimization of the reaction conditions, we first studied the reaction of 4-chloroacetophenone and 1-ethynylcyclohexene with catalyst **2** ($Pd(OAc)_2$/PTA in 1:3 molar ratio) in different solvents (Table 8) and different bases (Table 9). The best solvent was acetonitrile (Table 8, entry 1) and the best base Cs_2CO_3 (Table 9, entry 1).

On the other hand, recent studies have shown that the presence of tetrabutylamonium bromide (TBAB) can be crucial to obtain good conversions in cross-coupling of aryl chlorides.[42,43] Therefore, we have also studied the influence of TBAB in the reaction of 4-chloroacetophenone and 1-ethynylcyclohexene with catalyst **2** (Table 10), the best result being observed for 1.5 equiv of TBAB (entry 5). The presence of copper cocatalyst has a deleterious effect on the desired transformation (Table 11), as observed also with the aryl bromides (vide supra).

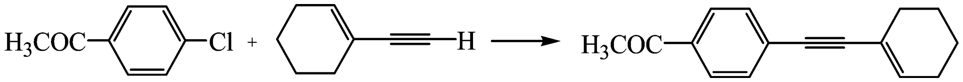
After preliminary optimization of the reaction conditions, we tested the catalytic activity of complex **1** and the mixture $Pd(OAc)_2$/PTA (1:3 molar ratio, catalyst **2**) in the Sonogashira coupling of aryl chlorides with terminal alkynes in acetonitrile at 80 °C, 24 h (the reaction time was not optimized), Cs_2CO_3 as base, and TBAB. The results are summarized in Table 12. A relatively low palladium catalyst loading was used (3 mol % [Pd]).

In the case of the reaction of the activated aryl chlorides with terminal alkynes the yields of products with both catalytic systems (entries 1−24) were excellent. Good conversions were also obtained in the case of chlorobenzene (entries 25−32). We have also tried with heterocyclic chlorides, such as 4-chloropyridine, with excellent results (100% yields, entries 33−40). It is worthwhile noting that these last coupling products are of biological importance.[44] It must also be noticed that no metallic palladium was observed.

In summary, we have established in this paper that both systems **1** and **2** based on the PTA ligand catalyze the Sonogashira reaction of aryl bromides and chlorides with excellent results in the absence of amine and CuI. The results are better than those obtained in systems based on $P(t\text{-}Bu)_3$[45,46] such as $[Pd(allyl)Cl]_2/P(t\text{-}Bu)_3$ (2.5 mol %/10 mol %),[46] for which the coupling between 4-chloroacetophenone and phenylacetylene was 50% yield.

On the other hand, we have observed that our systems behave with an efficiency similar to that found for $Pd(PA\text{-}Ph)_2\cdot dba$ (PA-Ph = 1,3,5,7-tetramethyl-2,4,8-trioxa-6-phenyl-6-phosphaadamantane),[31] the unique adamantane-type phosphine that has been

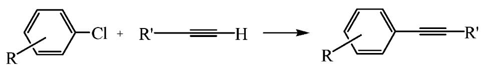
Table 11. Effect of the Copper Additive on the Efficiency of Sonogashira Coupling of 4-Chloroacetophenone with 1-Ethynylcyclohexene

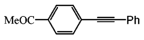
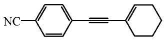
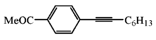
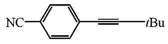
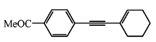
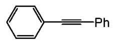
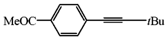
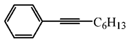
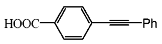
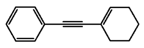
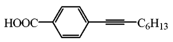
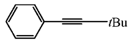
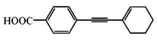
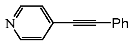
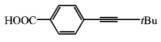
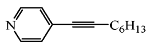


entry	mol % of CuI	yield (%)[a]
1	0.0	78
2	1.5	66
3	3.0	64
4	6.0	54
5	9.0	48

[a] Determined by GC. Conditions: 1.0 equiv of aryl chloride, 1.5 equiv of 1-ethynylcyclohexene, 1.5 equiv of Cs_2CO_3, 1.5 equiv of TBAB, 4.0 mL of acetonitrile, 3 mol % of $Pd(OAc)_2$, 9 mol % PTA, 80 °C, 6 h.

Table 12. Sonogashira Coupling of Aryl Chlorides with Terminal Alkynes



entry	product	cat.	yield (%)[a]	entry	product	cat.	yield (%)[a]
1		1	80	21		1	100
2		2	80	22		2	100
3		1	100	23		1	100
4		2	98	24		2	100
5		1	100	25		1	50
6		2	95	26		2	50
7		1	100	27		1	60
8		2	100	28		2	58
9		1	100	29		1	66
10		2	100	30		2	65
11		1	100	31		1	70
12		2	100	32		2	72
13		1	100	33		1	100
14		2	100	34		2	100
15		1	100	35		1	100
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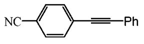
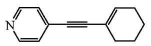
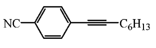
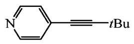
17		1	100	37		1	100
18		2	100	38		2	100
19		1	100	39		1	100
20		2	100	40		2	100

[a] Determined by GC. Conditions: 1.0 equiv of aryl chloride, 1.5 equiv of alkyne, 1.5 equiv of Cs_2CO_3, 1.5 equiv of TBAB, 4.0 mL of acetonitrile, 3 mol % of [Pd], 80 °C, 24 h.

Table 13. Crystal Data and Summary of Data Collection and Refinement for Complex 1

formula	$C_{15}H_{24}ClN_4PPd$
fw	433.20
cryst syst	monoclinic
a (Å)	6.0478(3)
b (Å)	17.7771(8)
c (Å)	15.6673(7)
α (deg)	90
β (deg)	92.531(2)
γ (deg)	90
volume (Å^3)	1682.78(14)
temperature	100(2)
space group	$P2(1)/c$
Z	4
μ(mm^{-1})	1.358
no. of reflns collected	18 270
no. of indep reflns	3444
R(int)	0.0168
R1 [$I > 2\sigma(I)$][a]	0.0181
wR$_2$ (all data)[b]	0.0465

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$, $wR2 = [\sum[w(F_o^2 - F_c^2)^2]/\sum w(F_o^2)^2]^{0.5}$. [b] $w = 1/[\sigma^2((F_o^2) + (aP)^2 + bP]$, where $P = (2F_c^2 + F_o^2)/3$ and a and b are constants set by the program.

used until now in coupling reactions. Furthemore complex **1** is one of the palladacycle complexes that are more active in this type of cross-coupling reactions together with those prepared by Nájera[25] and Herrmann,[47] being able to catalyze Sonogashira reactions with aliphatic alkynes and even aryl chlorides.

3. Experimental Section

Instrumental Measurements. The C, H, and N analyses were performed with a Carlo Erba model EA 1108 microanalyzer. Decomposition temperatures were determined with a SDT 2960 with a TA Instruments DSC-TGA at a heating rate of 5 °C min^{-1} with the solid samples under nitrogen flow (100 mL min^{-1}). The ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Bruker AC 200E, a Bruker AC 300E, or a Bruker AV 400 spectrometer, using $SiMe_4$ and H_3PO_4 as standards. Infrared spectra were recorded on a Perkin-Elmer 1430 spectrophotometer using Nujol mulls between polyethylene sheets. Mass spectra (positive-ion FAB) were recorded on a VG AutoSpecE spectrometer and measured using 3-nitrobenzyl alcohol as the dispersing matrix. GC analyses were performed on a CEinstruments GC 8000 fitted with a 30 m SPB column.

Materials. The starting complex $[Pd(dmba)(\mu\text{-}Cl)]_2$ and the PTA ligand were prepared by procedures described elsewhere.[48,49] Solvents were dried by the usual methods.

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Preparation of Complex [Pd(dmba)(PTA)(Cl)] (1). To a solution of $[Pd(dmba)(\mu\text{-}Cl)]_2$ (300 mg, 0.543 mmol) in dichloromethane (15 mL) was added PTA (170.8 mg, 1.086 mmol). The resulting solution was stirred at room temperature for 1 h 30 min and then concentrated under vacuum. The addition of hexane caused the precipitation of a white solid, which was collected by filtration, washed with hexane, and air-dried.

Data for Complex 1. Yield: 96%. Anal. Calcd for $C_{15}H_{24}N_4ClPPd$: C, 41.6; H, 5.6; N, 12.9. Found: C, 41.7; H, 5.8; N, 12.9. Mp: 225 °C dec. ^1H NMR ($CDCl_3$): δ ($SiMe_4$) 7.06−6.99 (m, 4 H, aromatics of dmba), 4.54 (AB q, $J = 12.7$ Hz, 6 H, NCH_2N), 4.47 (s, 6 H, CH_2P), 3.89 (d, 2 H, CH_2N of dmba, $J_{HP} = 2.4$ Hz), 2.68 (d, 6 H, NMe_2, $J_{HP} = 2.7$ Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ ($SiMe_4$) 148.8, 147.8, 135.9, 126.0, 124.7, 123.5 (aromatics dmba), 73.3 (d, $J = 6.9$ Hz, NCH_2N of PTA), 72.6 (d, $J = 3.3$ Hz, CH_2N of dmba), 52.3 (d, $J = 16.1$ Hz, NCH_2P of PTA), 50.1 (d, $J = 2.7$ Hz, NMe_2 of dmba). ^{31}P NMR ($CDCl_3$): δ (H_3PO_4) −46.51 (s). Positive-ion FAB mass spectrum: m/z 397 $(M - Cl)^+$.

General Procedure for the Sonogashira Reaction. All reactions were performed in a Radleys carousel adapted for rigorous inert atmosphere reactions. To a mixture of the appropriate aryl halide (1 mmol), the appropriate base (1.5 mmol), and the solvent (4 mL) was added the Pd catalyst (2.5 mol % de [Pd] for the aryl bromides and 3.0 mol % de [Pd] for the aryl chlorides), and in some cases tetrabutylamoniun bromide ((1.5 mmol) was added (only for the aryl chloride reactions). The resultant mixture was then heated at 80 °C for 30 min, and then the corresponding alkyne (1.5 mmol) was added. Stirring was continued at 80 °C under nitrogen for the corresponding reaction times indicated in the tables, after which time an aliquot of 0.2 mL was extracted, to which H_2O (0.5 mL) was added to quench the reaction. The aqueous layer was extracted with toluene (4 × 1 mL). To the organic extract was added hexadecane (0.204 mmol, internal standard), and then the mixture was dried over $MgSO_4$. The conversion to product was determined by GC.

X-ray Crystal Structure Analysis. Crystal of complex **1** was mounted in inert oil on glass fibers and transferred to the cold gas stream of the diffractometer (Bruker Smart Apex CCD). Data were collected using monochromated Mo Kα radiation in ω mode. Absorption correction was based on multiscans (program SADABS). The structures were refined anisotropically.[50] Hydrogen atoms were included using rigid methyl groups or a riding model.

Acknowledgment. This work was supported by the Dirección General de Investigación del Ministerio de Ciencia y Tecnología (Project No. CTQ2005-09231-C02-01/BQU), Spain, and the Fundación Séneca de la Comunidad Autónoma de la Región de Murcia (Project No. 00448/PI/04).

Supporting Information Available: X-ray crystallography data for complex **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM060636K

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