Notes

1,2,4-Triazole-Based Palladium Pincer Complexes. A New Type of Catalyst for the Heck Reaction

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Received July 22, 2003

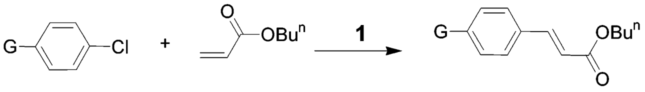
*Summary: The catalytic activity of a 1,2,4-triazole-based palladium(II) pincer complex (**1**) for the Heck reaction between aryl iodides, bromides, or chlorides and butyl acrylate is tested. A similar complex bearing an iodine on the benzene ring acts as substrate and catalyst.*

The Heck reaction[1] has become a widely used tool in organic synthesis, and the development of new catalysts is an ongoing activity. Although the Pd/P(*t*-Bu)$_3$ system has been shown to be an efficient catalyst even for aryl chlorides,[2] palladacycles represent the most extensively studied catalysts.[3] Two different palladacyclic systems are commonly used: *ortho*-metalated and *ortho,ortho*-metalated (pincer-type) complexes. Palladium *N*-heterocyclic carbene (NHC) catalysts have also been successfully used for this purpose.[4]

Pincer-type complexes bearing a pyrazole ring on the pendant ligands have been reported by van Koten.[5] These complexes are Lewis acids and catalyze Michael addition reactions. Other pincer ligands bearing *N*-heterocyclic carbenes based on imidazole have been reported by Crabtree for the Heck reaction catalysis.[6]

Herein we report the catalytic activity of PdI[η^3-(C$_6$H$_3$-2,6-(CH$_2$Tz)$_2$)-*N*,*C*,*N*] (**1**), a new type of catalyst for the Heck reaction. Compound **1** was synthesized by reacting palladium(II) acetate with 1,3-bis(1*H*-1,2,4-triazol-1-ylmethyl)benzene followed by treatment with potassium iodide.[7] Compound **1** is a tridentate and meridional complex ("pincer complex") that bears a 1,2,4-triazole ring on each of the pendant ligands. The presence of a heterocycle increases the chances of modifying the metal-binding stability, a factor that affects the catalytic activity. The third nitrogen atom of the 1,2,4-triazole ring could be able to form bimetallic complexes by coordination or formation of *N*-heterocyclic carbenes. The methylene group is an appropriate site to build a chiral catalyst,[5] and suitable functionalization of the benzene ring would allow the preparation of a dendritic catalyst.[8]

Table 1. Heck Reactions with Aryl Chlorides



entry	G	*T* (°C)	time (h)	TBAB (mol %)	**1** (mol %)	conversion
1	NO$_2$	125	70		0.5	12
2	NO$_2$	125	2	100	0.5	35
3	NO$_2$	140	40		0.5	13
4	NO$_2$	140	90	20	0.5	42
5	NO$_2$	140	2	100	0.5	73
6	NO$_2$	140	24	20	1	60
7	NO$_2$	140	2	100	1	71
8	NO$_2$	140	15	100	1	89
9	CH$_3$	140	25	100	0.5	43
10	OCH$_3$	140	15	100	0.5	9

The catalytic activity of compound **1** was successfully tested by reacting 4-bromobenzaldehyde and *n*-butyl acrylate, the most common test for the Heck reaction. An excellent yield (95%) was obtained by heating the reaction mixture at 125 °C for 15 h in dimethylacetamide in the presence of 0.5 mol % of **1** and sodium acetate as base.

Table 1 summarizes the reaction conditions and results obtained for aryl chlorides. An increase in the reaction temperature (compare entries 2 and 5) and the use of TBAB (Jeffery's protocol)[9] (compare entries 3 and 5) were essential to obtain satisfactory results. The higher yield was obtained after 15 h at 140 °C using a 100% of TBAB and 1% of catalyst mixture. Aryl chlorides with strong electron-releasing substituents remain poorly reactive compounds.

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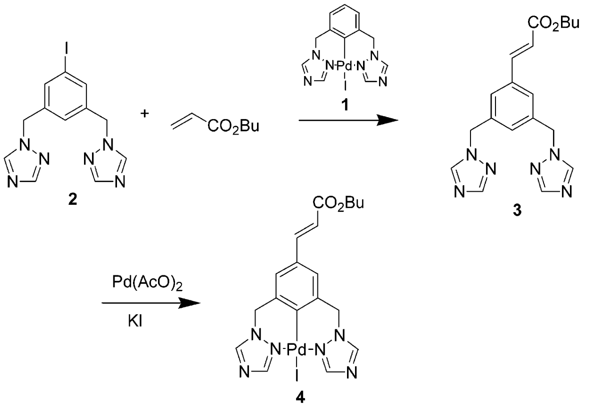
10.1021/om0340600 CCC: $25.00
Publication on Web 10/02/2003

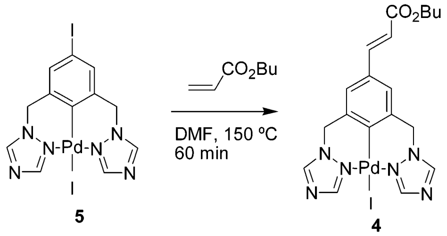
Table 2. Effect of TBAB and 18-Crown-6 after 6 h

additive (mol %)	TON	TOF (h^{-1})
none	28 000	4600
TBAB (100)	83 000	13 800
18-crown-6 (100)	86 000	14 300

Scheme 1. Synthesis of Palladium(II) Pincer Complex 4



Scheme 2. Autocatalysis of 5



Jeffery's protocol and the addition of 18-crown-6 were also tested for the reaction with 4-bromobenzaldehyde. Both the ammonium salt and the crown ether have a positive effect on the reaction, with the effect being slightly superior for the crown ether (see Table 2). The similar effect of both kinds of additives indicates that an anionic activation (acetate activation) is responsible for the increase in the reaction rate.

As indicated above, the existence of an appropriate functional group on the benzene ring of **1** would allow access to metallodendrimers. With this aim in mind, 1-iodo-3,5-bis(1*H*-1,2,4-triazol-1-ylmethyl)benzene (**2**) was reacted with *n*-butyl acrylate using **1** as a catalyst. Under these conditions the cinnamate derivative (**3**) was obtained; **3** was subsequently transformed into a new palladacycle (**4**), which is similar to **1** in having an ester group at the focal point (Scheme 1).

Compound **5**[7] undergoes the Heck reaction with *n*-butyl acrylate (Scheme 2). Compound **5** acts as the substrate and catalyst at the same time, yielding the metalated compound **4**. These two approaches, (i) Heck reaction and palladation and (ii) palladation and auto-Heck reaction, to compound **4** can be performed in a one-pot procedure by heating **2**, butyl acrylate, and palladium(II) acetate in acetic acid at 130 °C for 48 h. The drawback of this fast one-pot procedure is the consumption of 4 equiv of palladium(II) acetate.

In conclusion, we present a new type of catalyst for the Heck reaction of aryl iodides, bromides, and chlorides. The pincer ligand with an iodine atom at the phenyl substituent undergoes one-pot auto-Heck reaction yielding a new palladium(II) complex with acrylic derivative. This kind of catalyst may be prepared bearing stereogenic centers on the pendant ligands, and it can also be envisaged as a metalated building block for the synthesis of a dendritic catalyst. Asymmetric Heck reactions and the building of dendritic catalysts are currently under investigation in our laboratories.

Experimental Section

General Procedures. Unless otherwise stated, materials were commercially available and used without purification. Column chromatography was performed with Merck silica gel for flash columns (230−400 mesh). All reaction were run in oven-dried flasks under an argon atmosphere. ^{1}H and ^{13}C NMR spectra were performed in deuterated chloroform with a Varian-Inova 500 MHz instrument. NMR chemical shifts are given in parts per million (δ) relative to TMS as internal standard. EI-MS was recorded on a VG Autospect instrument.

General Method for the Heck Reactions. A dimethylacetamide (10 mL) suspension of the corresponding aryl halide (10 mmol), sodium acetate (11 mmol), PdI[η^3-(C_6H_3-2,6-(CH_2-Tz)$_2$)-*N*,*C*,*N*] (0.05 or 0.1 mmol), and, when appropriate, tetrabutylammonium bromide or 18-crown-6 (1.90 mmol) was degasified, and then butyl acrylate (14 mmol) was added. The new suspension was heated to 125 or 140 °C under stirring. For the analysis of the reaction, aliquots of 0.5 mL were taken and dissolved in 3.5 mL of dichloromethane. Then 5 mL of 5% HCl was added and the mixture stirred for 15 min. The organic layer was then separated and successively washed with water (15 mL), dried (Na_2SO_4), and evaporated under vacuum. Conversions of the reactions were estimated by ^{1}H NMR.

Butyl 3,5-Bis(1*H*-1,2,4-triazol-1-ylmethyl)cinnamate (3). The general method for the Heck reaction was followed using dimethylacetamide (10 mL), 1-iodo-3,5-bis(1*H*-1,2,4-triazol-1-ylmethyl)benzene (696 mg, 1.90 mmol), sodium acetate (171 mg, 2.09 mmol), tetrabutylammonium bromide (613 mg, 1.90 mmol), PdI[η^3-(C_6H_3-2,6-(CH_2Tz)$_2$)-*N*,*C*,*N*] (45 mg, 0.095 mmol), and 0.40 mL (2.66 mmol) of butyl acrylate. Reaction temperature: 125 °C. Reaction time: 44 h. All volatiles were evaporated under vacuum, and the product was purified by chromatography: a first fraction of an unidentified polymeric product was obtained using ethyl acetate as eluent, and a second fraction containing **3** was obtained using a mixture of ethyl acetate−ethanol, 19:1, as eluent. Yield: 490 mg (70%). Further purification could be achieved by crystallization from CH_2Cl_2−hexanes.

^{1}H NMR (δ, $CDCl_3$): 8.13 (s, 2H), 8.01 (s, 2H), 7.60 (d, 1H, $J = 15$ Hz), 7.37 (s, 2H), 7.16 (s, 1H), 6.41 (d, 1H, $J = 15$ Hz), 5.36 (s, 4H), 4.21 (m, 2H), 1.68 (m, 2H), 1.43 (m, 2H), 0.97 (m, 3H). ^{13}C NMR (δ, $CDCl_3$): 166.4, 152.5, 143.2, 142.5, 136.5, 136.3, 128.5, 127.3, 120.4, 64.7, 52.8, 30.6, 19.1, 13.7. MS (EI) *m*/*z*: 366.4 (M^+). Anal. Calcd for $C_{19}H_{22}N_6O_2$ (366.42): C, 62.28; H, 6.05; N, 22.94. Found: C, 62.01; H, 6.26; N, 23.25.

Compound 4. **From Butyl 3,5-Bis(1*H*-1,2,4-triazol-1-ylmethyl)cinnamate (3).** A modification of the method described in ref 7 was followed, using butyl 3,5-bis(1*H*-1,2,4-triazol-1-ylmethyl)cinnamate (**3**) (115 mg, 0.314 mmol), palladium acetate (71 mg, 0.314 mmol), and acetic acid (10 mL). After evaporation of acetic acid, 15 mL of dichloromethane and a solution of potassium iodide (261 mg, 1.57 mmol) in 15 mL of water were added, and the mixture was stirred for 16 h at room temperature. The organic layer was then separated and successively washed with water (15 mL), dried (Na_2SO_4), and evaporated under vacuum to give **4**. Yield: 161 mg (86%). Further purification could be achieved by crystallization from CH_2Cl_2−hexanes.

From Compound 5.[7] The general method for the Heck reactions was followed, using DMF (5 mL) as solvent, **5** (449 mg, 0.75 mmol), sodium acetate (73 mg, 0.83 mmol), and butyl acrylate (0.15 mL, 1.05 mmol). Reaction temperature: 125 °C. Reaction time: 2 h. All volatiles were evaporated under vacuum, and the product was purified by gradient chromatography using dichloromethane−ethyl acetate (3:1 to 1:1) as eluent. Yield: 302 mg (67%). Further purification could be achieved by crystallization from CH_2Cl_2−hexanes.

From 1-Iodo-3,5-bis(1*H*-1,2,4-triazol-1ylmethyl)benzene (2). A solution of **2** (250 mg, 0.67 mmol), sodium acetate (65 mg, 0.75 mmol), palladium acetate (170 mg, 0.75 mmol), and butyl acrylate (0.25 mL, 1.75 mmol) in acetic acid (15 mL) was stirred and heated at 130 °C for 12 h. Then, three portions of palladium acetate (170 mg, 0.75 mmol) were added every 12 h. After filtration of the black palladium(0) formed, the acetic acid was evaporated and dichloromethane (20 mL) and a solution of potassium iodide (600 mg, 3.61 mmol) in 20 mL of water were successively added. Stirring was maintained for 16 h at room temperature. The organic layer was then separated and successively washed with water (15 mL), dried (Na_2SO_4), and evaporated under vacuum. The product was purified by chromatography using dichloromethane−ethyl acetate, 3:1. Yield: 281 mg (70%).

^{1}H NMR (δ, $CDCl_3$): 8.85 (s, 2H), 8.36 (s, 2H), 7.61 (d, 1H, $J = 16$ Hz), 7.27 (s, 2H), 6.45 (d, 1H, $J = 16$ Hz), 5.47 (br s, 4H), 4.22 (m, 2H), 1.70 (m, 2H), 1.45 (m, 2H), 0.98 (m, 3H). ^{13}C NMR (δ, $CDCl_3$): 166.8, 158.4, 147.4, 143.6, 142.6, 135.0, 132.2, 126.0, 118.7, 64.6, 55.4, 30.7, 19.1, 13.8. MS (EI) *m*/*z*: 471.3 (M^+). Anal. Calcd for $C_{19}H_{21}IN_6O_2Pd$ (598.73): C, 38.11; H, 3.54; N, 14.04. Found: C, 37.90; H, 3.86; N, 14.48.

Acknowledgment. This work was supported by the Consejería de Ciencia y Tecnología de Castilla-La Mancha (Project PAI-02-013). J.G. is indebted to the Junta de Comunidades de Castilla-La Mancha for a grant.

Supporting Information Available: NMR and MS spectra of compounds **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM0340600