

Journal of Organometallic Chemistry, 436 (1992) C9–C12
Elsevier Sequoia S.A., Lausanne
JOM 22932PC

Preliminary communication

Palladium-assisted formation of carbon-carbon bonds. Stoichiometric synthesis of indenols and indenones. Catalytic synthesis of an indenol

José Vicente, José-Antonio Abad and Juan Gil-Rubio

Grupo de Química Organometálica, Departamento de Química Inorgánica, Universidad de Murcia, Aptdo. 4021, Murcia, 30071 (Spain)

(Received March 20, 1992)

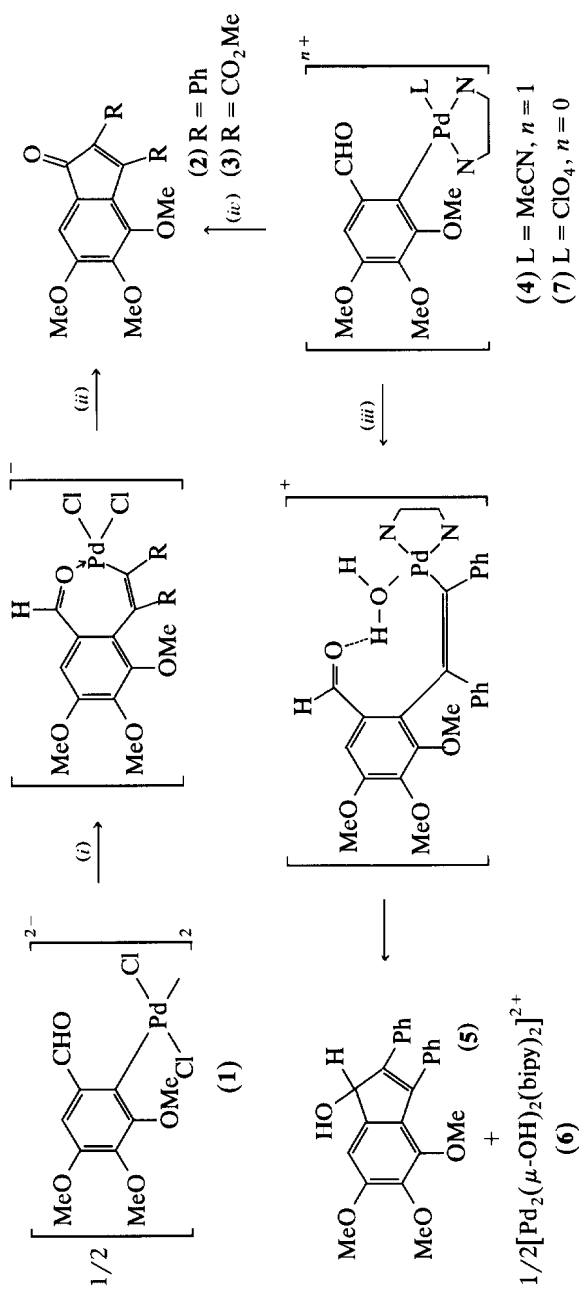
Abstract

Reactions of diphenylacetylene or dimethylacetylenedicarboxylate with $Q_2[Pd_2R_2Cl_2(\mu-Cl)_2]$ (**1**) [$Q = (PhCH_2)Ph_3P$; $R = 2,3,4$ -trimethoxy-6-formylphenyl] give metallic palladium and 2,3-diphenyl-, or 2,3-dimethylcarboxylate-, 5,6,7-trimethoxyindenone (**2** or **3**), respectively whereas diphenylacetylene reacts with $[PdR(bipy)(MeCN)]ClO_4$ (**4**), to give 2,3-diphenyl-5,6,7-trimethoxyindenol (**5**) and $[Pd_2(OH)_2(bipy)_2](ClO_4)_2$ (**6**). Catalytic synthesis of **5** is achieved by reaction of $[HgR_2]$, Ph_2C_2 , and $CuCl_2$ in the presence of $(Me_4N)_2[Pd_2Cl_6]$ (molar ratios 1:2:2:0.1).

2,3-Diaryllindenones with potential fluorescent and photofluorogenic properties have been prepared and studied as ligands for the strogen receptor [1]. Metal-mediated syntheses of 2,3-diphenylindenone have been achieved using diphenylacetylene and carbonyl complexes of Fe [2], Rh [3], or Ni [4]. In all these cases, the indenone carbonyl group comes from a coordinated carbon monoxide. Reaction of *ortho*-diiodobenzene with 3-hexyne in the presence of $[Pd(PPh_3)_4]$ as the catalyst and Zn as the reductant gives, under CO pressure, 2,3-diethylindenone [4]. Most of these reactions require high temperatures. Arylcarbonylmanganese complexes have been reacted with acetylenes to give indenols [5].

Organopalladium compounds are used in many organic reactions [6]; those involving orthometallated arylpalladium complexes and alkynes are of current interest [7,8]. However, neither the orthometallation of aromatic aldehydes nor the synthesis of orthoformylarylpalladium complexes had been described until our preliminary communication [9a] reporting the synthesis of several of such complexes by using organomercury compounds as transmetallating agents [9]. In this paper we describe the first method of preparing some 2,3-disubstituted-indenones or -indenols by using these arylpalladium(II) complexes. With our method the synthesis is achieved at room temperature.

Correspondence to: Professor J. Vicente.



Scheme 1. Proposed reaction pathways for the stoichiometric reactions. (i) + R₂C₂; (ii) - Pd, - Cl⁻, - HCl; (iii) + Ph₂C₂, + H₂O; (iv) + Ph₂C₂ - H⁺ - L - bipy - Pd.

We have used trimethoxyarylpalladium(II) derivatives in this research because this aryl moiety is present in organic molecules of pharmaceutical interest, for example the antileukemic lactones steganacin and steganagin [10], the antibacterial agent trimethoprim [11], and the cytotoxic colchicine [12].

Results and discussion

The stoichiometric reactions. Reactions of $Q_2[Pd_2R_2Cl_2(\mu-Cl)_2]$ (**1**) [$Q = (PhCH_2)Ph_3P$; $R = 2,3,4$ -trimethoxy-6-formylphenyl] [**9a**] with diphenylacetylene (1:10) or with dimethylacetylenedicarboxylate (1:2) give metallic palladium and indenone **2** (77%) or **3** (16%) [13] (see Scheme 1), respectively, whereas diphenylacetylene reacts in a 2:1 molar ratio with $[PdR(bipy)(MeCN)ClO_4]$ (**4**), obtained by reacting $[PdRCl(bipy)]$ [**9a**] with $AgClO_4$ in MeCN, to give the indenol **5** (67%) [13] and $[Pd_2(OH)_2(bipy)_2]ClO_4$ (**6**) [14], [15], **5** can also be obtained (73%) by reaction of Ph_2C_2 in 4:1 molar ratio with $[PdR(OCIO_3)(bipy)]$ (**7**) (prepared *in situ* by reacting (1:1) $[PdRCl(bipy)]$ [**9a**] with $AgClO_4$). The reactions were carried out without precautions to exclude atmospheric moisture.

The different behaviours of anionic complex **1** and cationic or neutral complexes **4** or **7** can be explained by the different nature of these complexes. In both kinds of reaction, it seems reasonable to assume that insertion of the alkyne into the palladium-carbon bond occurs (see Scheme 1); mono-insertion products of this type are formed in some reactions between arylpalladium(II) complexes and acetylenes [7]. However, the cationic intermediates formed from **4** or **7** should react very easily with nucleophiles such as adventitious moisture, giving an aqua-complex which should decompose to give the indenol **5**. The involvement of water in this process was tested by carrying out the reaction of **4** with Ph_2C_2 under anhydrous conditions, which gives the indenone **2** (62%). All these mono-insertion compounds are obtained even when a large excess of alkyne is used, which contrasts with the fact that di- and tri-insertion products are easily obtained in similar reactions with other arylpalladium complexes [7].

The catalytic process. We have tried unsuccessfully to obtain **2** or **5** by reaction of R_2Hg and Ph_2C_2 using **1** and **7**, respectively, as catalysts. The expected compounds were obtained, but only in the amounts corresponding to the stoichiometric processes. This means that R_2Hg is able neither to oxidize Pd^0 nor to react with the hydroxo-complex **6** to regenerate the starting complexes. In order to prepare **2** catalytically we investigated the use of $CuCl_2$ as reoxidant [6]. However, the reaction of $[HgR_2]$, Ph_2C_2 , and $CuCl_2$ in the presence of $(Me_4N)_2[Pd_2Cl_6]$ (1:2:2:0.1 ratios) gives 62% of the indenol **5**. The result is unexpected because the diorganomercurial reacts with the palladium complex to give **1** [**9a**] and this compound reacts with Ph_2C_2 to give the indenone **2**. We suggest that $CuCl_2$, in addition to its role as oxidant, abstracts chloro-ligands from the intermediate **1** giving neutral or cationic palladium(II) species that would behave like **4** or **7**, and give the indenol. To the best of our knowledge neither catalytic syntheses of indenols nor reactions of anionic arylpalladium(II) with acetylenes has been reported [7]. A study of the mechanism of this process and of other ways to prepare indenones catalytically is now being undertaken.

Acknowledgement. We thank D.G.I.C.Y.T. (PB89-0430) for financial support. J.G. is grateful to the Spanish Ministerio de Educación y Ciencia for a Grant.

References and notes

- 1 G.M. Anstead, R.J. Altenbach, S.R. Wilson and J.A. Katzenellenbogen, *J. Med. Chem.*, 31 (1988) 1316; G.M. Anstead, S.R. Wilson, R. Scott and J.A. Katzenellenbogen, *J. Med. Chem.*, 32 (1989) 2163.
- 2 I.R. Butler, W.R. Cullen, W.E. Lindsell, P.N. Preston and S.J. Rettig, *J. Chem. Soc., Chem. Commun.*, (1987) 439; I.R. Butler, J.E. Elliott and J. Houde Jr., *Can. J. Chem.*, 67 (1989) 1308; I.R. Butler, *Can. J. Chem.*, 68 (1990) 1979.
- 3 P. Hong, B. Cho and H. Yamazaki, *Chem. Lett.*, (1979) 339.
- 4 L. Liebeskind and M.S. South, *J. Org. Chem.*, 45 (1980) 5426.
- 5 L.S. Liebeskind, J.R. Gasdaska, J.S. McCallum and S.J. Tremont, *J. Org. Chem.*, 54 (1989) 669; R.C. Cambie, M.R. Metzler, P.R. Rutledge and P.D. Woodgate, *J. Organomet. Chem.*, 381 (1990) C26.
- 6 R.F. Heck, *Palladium Reagents in Organic Synthesis*, Academic Press, New York, 1985.
- 7 T. Hosokawa, C. Calvo, H.B. Lee and P.M. Maitlis, *J. Am. Chem. Soc.*, 95 (1973) 4914; F. Maassarani, M. Pfeffer and G. Le Borgne, *Organometallics*, 6 (1987) 2029; *ibid.*, 6 (1987) 2043; M. Pfeffer, *Recl. Trav. Chim. Pays-Bas*, 109 (1990) 567.
- 8 G. Wu, A.L. Rheingold, S.J. Geib and R.F. Heck, *Organometallics*, 6 (1987) 1941.
- 9 (a) J. Vicente, J.A. Abad, M.A. Stiakaki and P.G. Jones, *J. Chem. Soc., Chem. Commun.*, (1991) 137; (b) J. Vicente, M.D. Bermúdez, J. Escribano, M.P. Carrillo and P.G. Jones, *J. Chem. Soc., Dalton Trans.*, (1990) 3083; (c) J. Vicente, M.T. Chicote, M.D. Bermúdez, M.J. Sánchez-Santano and P.G. Jones, *J. Organomet. Chem.*, 354 (1988) 381, and refs. therein.
- 10 F.E. Ziegler, I. Chliwner, K.W. Fowler, S.J. Kanfer, S.J. Kuo and N.D. Sinha, *J. Am. Chem. Soc.*, 102 (1980) 790; K. Tomioka, T. Ishiguro, H. Mizuguchi, N. Komeshima, K. Koga, S. Tsukagoshi, T. Tsuruo, T. Tashiro, S. Tanida and T. Kishi, *J. Med. Chem.*, 34 (1991) 54, and refs. therein.
- 11 J.H. Chan, and B. Roth, *J. Med. Chem.*, 34 (1991) 550, and refs. therein.
- 12 I. Ringel, D. Jaffe, S. Alerhand, O. Boye, A. Muzafar and A. Brossi, *J. Med. Chem.*, 34 (1991) 3334.
- 13 **2**, **3** and **5** gave satisfactory elemental analyses. Selected spectroscopic data: IR (Nujol) in cm^{-1} ; NMR chemical shifts (CDCl_3) in ppm relative to internal tetramethylsilane; coupling constants in Hz. **2**: $\nu(\text{CO})$: 1700; ^1H : δ 7.35 (m, br, 5H, Ph), 7.17 (m, 5H, Ph), 7.09 (s, 1H, C_6H), 3.92, 3.88, and 3.30 (s, 3H, MeO); ^{13}C : δ 195.5 (CO), 61.1, 61.0, and 56.6 (MeO); m/z 372 (M^+ , 71%), 215 (100%), 213 (39%), 113 (40%), 108 (38%), 107 (46%). **3**: $\nu(\text{CO})$: 1736, 1716 and 1693; ^1H : δ 7.02 (s, 1H, C_6H), 4.01, 3.93, 3.91, 3.89, and 3.84 (s, 3H, Me); ^{13}C : δ 189.6 (C=O), 61.7, 61.0 and 56.7 (MeO), 52.7 and 52.1 (CO_2Me); m/z 336 (M^+ , 51%), 305 (19%), 219 (100%), 218 (57%), 167 (32%). **5**: $\nu(\text{OH})$: 3525; ^1H : δ 7.35 (m, 5H, Ph), 7.22 (m, 5H, Ph), 7.10 (s, 1H, C_6H), 5.58 (d, $^3J(\text{HH}) = 8$, 1H, CHOH), 3.94, 3.84, and 3.28 (s, 3H, MeO), and 1.85 (d, 1H, OH); ^{13}C : 77.3 (CHOH), 61.2, 61.0, and 56.4 (MeO); m/z 374 (M^+ , 100%), 359 (31%), 215 (32%), 113 (39%).
- 14 This compound could not be purified and characterized in solution due to its extreme insolubility. However, analytical and IR data [$\nu(\text{OH})$ at 3380 cm^{-1}] point to a formulation such as $[\text{Pd}_2(\text{OH})_2(\text{bipy})_2](\text{ClO}_4)_2$ (Found C, 31.69; H, 2.39; N, 7.39. Calc. C, 33.78; H, 2.90; N, 6.85). The synthesis and X-ray structure of a similar complex, $[\text{Pd}_2(\text{OH})_2(\text{Ph}_2\text{P}(\text{CH}_2)_3\text{PPh}_2)_2][\text{BF}_4]_2$, [15] appeared during the preparation of this paper.
- 15 C. Pisano, G. Consiglio, A. Sironi and M. Moret, *J. Chem. Soc., Chem. Commun.*, (1991) 421.