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Preliminary communication

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

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Abstract

Reactions of diphenylacetylene or dimethylacetylenedicarboxylate with $Q_2[Pd_2R_2Cl_2(\mu\text{-}Cl)_2]$ (**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-Diarylindenones 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.

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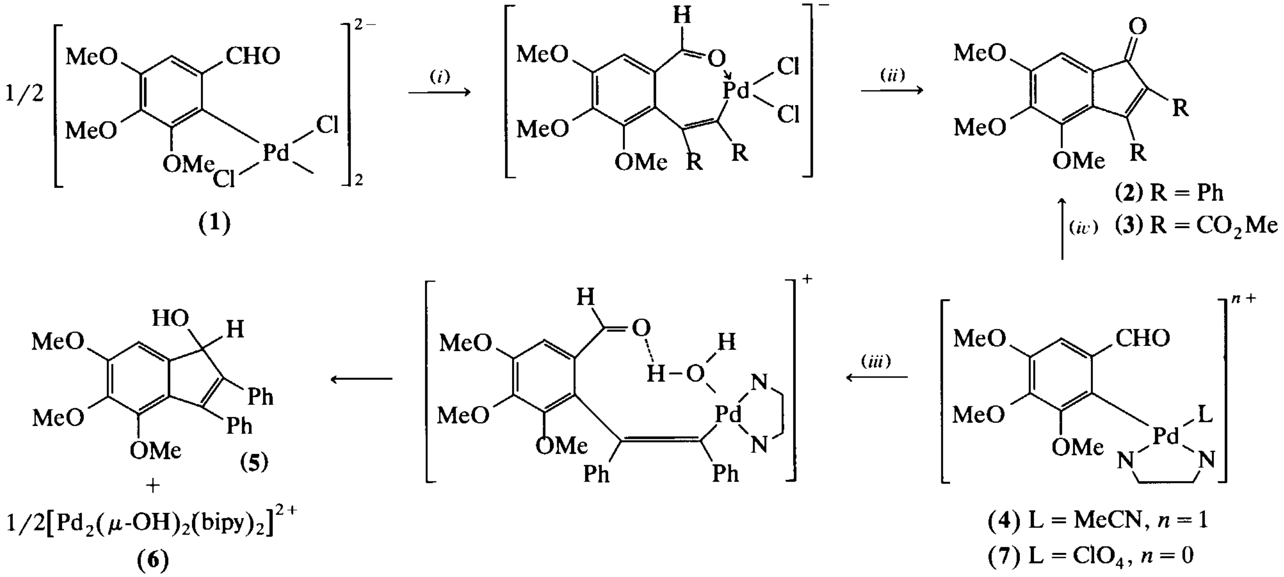

Scheme 1. Proposed reaction pathways for the stoichiometric reactions. (*i*) $+R_2C_2$; (*ii*) $-Pd$, $-Cl^-$, $-HCl$; (*iii*) $+Ph_2C_2$, $+H_2O$; (*iv*) $+Ph_2C_2$ $-H^+ - L - bipy - Pd$.

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 steganangin [10], the antibacterial agent trimethoprim [11], and the cytotoxic colchicine [12].

Results and discussion

The stoichiometric reactions. Reactions of $Q_2[Pd_2R_2Cl_2(\mu\text{-}Cl)_2]$ (**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 $[Pd_2(OH)_2(bipy)_2](ClO_4)_2$ (**6**) [14], [15], **5** can also be obtained (73%) by reaction of Ph_2C_2 in 4:1 molar ratio with $[PdR(OClO_3)(bipy)]$ (**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.

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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**: ν(CO): 1700; ^{1}H: 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**: ν(CO): 1736, 1716 and 1693; ^{1}H: 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**: ν(OH): 3525; ^{1}H: δ 7.35 (m, 5H, Ph), 7.22 (m, 5H, Ph), 7.10 (s, 1H, C_6H), 5.58 (d, ^3J(HH) = 8, 1H, *C*HOH), 3.94, 3.84, and 3.28 (s, 3H, MeO), and 1.85 (d, 1H, O*H*); ^{13}C: 77.3 (*C*HOH), 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 [ν(OH) at 3380 cm^{-1}] point to a formulation such as $[Pd_2(OH)_2(bipy)_2](ClO_4)_2$ (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, $[Pd_2(OH)_2\{Ph_2P(CH_2)_3PPh_2\}_2][BF_4]_2$, [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.