Pyrrole Ring Cyclopalladation of Hydrazones Derived from *N*-(*p*-Toluenesulfonyl)-3-acetylpyrrole with Acetylhydrazine, Methyl Carbazate, and Semicarbazide

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Abstract

Hydrazones (HL) derived from *N*-(*p*-toluenesulfonyl)-3-acetylpyrrole with acetylhydrazine, methyl carbazate, and semicarbazide were cyclopalladated with lithium tetrachloropalladate in the presence of sodium acetate in methanol to give [PdClL]. The complex (HL = acetylhydrazone) reacted with a ligand (D) to give the adduct [PdClLD] (D = pyridine, triphenylarsine, tri-*p*-tolylphosphine, and n-butyldiphenylphosphine) or [PdClL(D)$_2$] (D = tri-n-butylphosphine). These complexes were characterized spectroscopically. Palladation is supposed to occur at 4-C of a pyrrole ring. In [PdClL] the cyclopalladated hydrazones act as a terdentate ligand coordinated through pyrrole 4-C, imino-N, and carbonyl-O atoms.

Introduction

Cyclometallation reactions occur usually with high regioselectivity and the products serve as useful intermediates in organic synthesis [1]. A wealth of examples of such reactions are known for benzene derivatives but only a small amount of information is available for similar reactions of compounds other than benzene derivatives [2]. Heteroaromatic compounds react often similarly to the related benzene derivatives but display unique abilities in pharmacology. Cyclometallated heteroaromatic compounds will become very useful intermediates for the preparation of new heteroaromatic derivatives [1]. We are interested in cyclometallation reactions of heteroaromatic compounds and have been investigating those reactions of pyrrole derivatives [3]. Acetylhydrazone of *N*-(*p*-toluenesulfonyl)-3-acetylpyrrole has been found to be cyclopalladated with lithium tetrachloropalladate and the results are described in this paper.

Results and Discussion

N-(*p*-Toluenesulfonyl)-3-acetylpyrrole (hereafter *p*-toluenesulfonyl is abbreviated as tosyl or Ts) was prepared by the methods reported for *N*-benzenesulfonyl-3-acetylpyrrole [4, 5]. The former reacted easily with acetylhydrazine, methyl carbazate, and semicarbazide to afford hydrazone derivatives (abbreviated as Hahp, Hmcp, and Hscp, respectively) (Table I). The hydrazones(HL) reacted with lithium tetrachloropalladate in the presence of sodium acetate in methanol to give [PdClL] (Table I).

In the infrared spectra (nujol mulls), ν(C=O) of the free ligands shifts to lower frequencies upon formation of the complexes (Table I) indicating coordination of the carbonyl groups. The amide II band of free Hahp at 1490 cm^{-1} shifts to 1527 cm^{-1} upon complexation confirming the coordination of the $-NHCOCH_3$ group [6]. The ν(N–H) bands of the –NHCOY groups persist in the complexes, although the spectral patterns change from those of the free ligands. This persistence confirms that the –NHCOY groups are not deprotonated. This is in contrast to the usual observation that under basic conditions an acylhydrazone is coordinated to a metal ion with deprotonation of the –NHCOY group [7].

The ^{1}H NMR spectra of the complexes (in dmso-d_6) show a broad signal due to the –NHCOY group (Table II), consistent with the above infrared spectral results. Integration of the ^{1}H NMR spectra indicates that one proton is lost in the region of aromatic proton resonances. For instance, free Hahp shows three signals due to a pyrrole ring at δ = 6.69dd, 7.14dd, and 7.36t ppm and upon formation of [PdClL] they are transformed to two doublets at 6.86 and 7.98 ppm (J(H–H) = 1.7 Hz). While the ^{13}C NMR spectrum of Hahp affords three peaks due to the proton-bearing carbon atoms of a pyrrole ring at δ = 112.3 ppm (J(C–H) = 176.5 Hz), 121.5(194.1) and 124.6(192.7), that of the complex gives two at 120.4(198.5) and 124.2(195.6). Of the spectral data of [PdCl(ahp)], the magnitude of J(H–H) suggests a H(2)–H(5) coupling and the J(C–H) values H(2)–C(2) and H(5)–C(5) couplings [8]. The probable structure for the complex is given in Fig. 1(a) (Y = CH_3). The bulky Ts substituent on a pyrrole ring N atom may favour this structure rather than the isomeric one with palladation at 2-C of the pyrrole ring. The coordination of Cl is

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TABLE I. Yields, Melting Points, Analytical Results, and Selected Bands of Infrared(IR) Spectra[a]

Compound[b]	Yield (%)	Melting point[c] (°C)	Analysis, found(calc.) (%)			IR spectra (cm^{-1})	
			C	H	N	ν(C=O)	ν(Pd–X)
Hahp	87	165–166	56.44 (56.41)	5.38 (5.37)	12.76 (13.16)	1669	
Hmcp	93	200–201	53.92 (53.72)	5.13 (5.11)	12.22 (12.53)	1751	
Hscp	99	193–195	52.56 (52.49)	4.97 (5.03)	17.19 (17.49)	1692	
PdCl(ahp)·H_2O	93	197(dec)	37.50 (37.67)	3.65 (3.79)	8.81 (8.79)	1597	364
PdCl(mcp)	89	187(dec)	37.83 (37.83)	3.36 (3.39)	8.78 (8.82)	1638	358
PdCl(scp)	84	245(dec)	36.69 (36.46)	3.25 (3.28)	12.10 (12.15)	1666 1644	374
PdCl(ahp)(py)	34	185(dec)	44.70 (44.54)	3.98 (3.92)	10.32 (10.39)	1700	298
PdCl(ahp)($AsPh_3$)	49	181–183	51.67 (51.71)	3.97 (4.08)	5.44 (5.48)	1703	298
PdCl(ahp)($Ptol_3$)	55	193–196	56.67 (56.55)	4.80 (4.88)	5.26 (5.50)	1692	301
PdBr(ahp)($Ptol_3$)	46	187(dec)	53.20 (53.45)	4.57 (4.61)	4.96 (5.19)	1695	259
PdCl(ahp)($PBuPh_2$)	23	147–149	52.98 (53.00)	5.13 (5.02)	5.86 (5.98)	1702 1686	297
PdCl(ahp)(PBu_3)$_2$	39	149–153	54.42 (54.16)	8.27 (8.16)	4.67 (4.86)	1674	298
Pd(ahp-H)($Ptol_3$)	40	218–219	59.81 (59.38)	4.98 (4.98)	5.83 (5.77)	1598	

[a]Nujol mulls. X = Cl or Br. [b]Abbreviations: py = pyridine, $AsPh_3$ = triphenylarsine, $Ptol_3$ = tri-p-tolylphosphine, $PBuPh_2$ = n-butyldiphenylphosphine, and PBu_3 = tri-n-butylphosphine. [c]dec = decomposition.

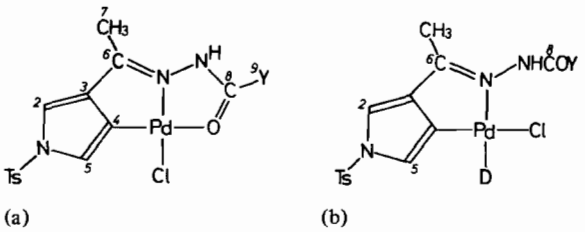

Fig. 1. Proposed structures for the complexes. Ts represents a *p*-toluenesulfonyl group; Y = CH_3, OCH_3, or NH_2; D = py, $AsPh_3$, $Ptol_3$, or $PBuPh_2$.

born out by the presence of strong ν(Pd–Cl) bands (Table I). Changes in chemical shifts of ^{13}C signals of the azomethine(6-C) and –NHCOY(8-C) groups should result from coordination of the two groups (Table II). The related structure (Fig. 1a, Y = OCH_3 or NH_2) is given for [PdClL] (L = mcp or scp), based on the spectroscopic data (Tables I and II). Conclusive evidence for the position of palladation requires an X-ray structural analysis.

[PdCl(ahp)]·H_2O reacted with a donor (D) to give [PdCl(ahp)D] (D = py, $AsPh_3$, $Ptol_3$, and $PBuPh_2$) or [PdCl(ahp)(PBu_3)$_2$] (Table I). The position of ν(C=O) bands in the infrared spectra of these adducts shows that the carbonyl groups are not coordinated, but coordination of Cl is inferred from the presence of strong ν(Pd–Cl) bands. Uncoordination of the –$NHCOCH_3$ group is also inferred from the 8-C chemical shift in the ^{13}C NMR spectra: the chemical shift is close to that of free Hahp. In the ^1H NMR spectra of [PdCl(ahp)D] only one signal is well separated from the complicated multiplets in the region of the aromatic proton resonances (Table II). The signal is remarkably well shielded compared with that of the parent [PdCl(ahp)]·H_2O. An aromatic ring current of D shields the 5-H of a pyrrole ring, based on the structure proposed in Fig. 1b. If palladation occurred at

TABLE II. Selected Data of ^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR Spectra of the Ligands and Complexes [a]

Compound	^1H NMR, δ (ppm) (J (Hz))				^{13}C NMR, δ (ppm) (J(P–C) (Hz))					^{31}P[d]
	N–H	2-H	5-H	4-H	2-C	5-C	4-C	6-C	8-C	
Hahp	9.5br	7.36t (2.2)	7.14dd (3.2, 2.2)	6.69dd (3.3, 1.6)	121.8	119.5	111.4	145.4	174.0	
Hmcp[b]	9.9br	7.58t (1.9)	7.22dd (3.2, 2.2)	6.53dd (3.2, 1.5)	122.2	120.2	111.7	145.0	154.8	
Hscp[b]	9.2br	7.62t (1.6)	7.21dd (3.2, 2.2)	6.84dd (3.1, 1.3)	122.2	119.8	112.4	140.2	157.8	
PdCl(ahp)·H_2O[b]	10.2br	7.98d (1.7)	6.86d (1.7)		124.2	120.4		166.8	180.7	
PdCl(mcp)[b]	9.6br	8.02d (1.7)	6.87d (1.7)		124.6	120.4		154.5	181.2	
PdCl(scp)[b]	8.3br	7.87d (1.7)	6.83d (1.7)		122.8	120.0		155.4	176.2	
PdCl(ahp)(py)	9.3br	[c]	6.18d (1.5)		120.9	117.8		168.3	174.4	
PdCl(ahp)($AsPh_3$)	9.6br	[c]	5.28d (2.0)		120.7	122.0		160.1	172.6	
PdCl(ahp)($Ptol_3$)	9.7br	[c]	5.19dd (1.5, 0.7)		120.4	122.4d (10.3)		168.1	171.8	34.3
PdBr(ahp)($Ptol_3$)	9.7br	[c]	5.20dd (1.5, 0.7)		120.3	122.2d (10.4)		167.8	172.3	34.5
PdCl(ahp)($PBuPh_2$)	9.5br	[c]	5.26dd (1.6, 0.5)		120.4	121.9d (10.4)		167.8	171.7	30.6
PdCl(ahp)(PBu_3)$_2$	8.9br	7.42d (1.8)	6.43br		120.9	119.4t (6.6)		144.7	173.9	4.2
Pd(ahp-H)($Ptol_3$)		6.91d (1.5)	5.01d (1.5)		118.3	122.4d (6.2)		155.3	182.3d (6.2)	27.4

[a]Solvent used was $CDCl_3$ unless otherwise noted. TMS(tetramethylsilane) was used as an internal standard. d = doublet, t = triplet, and br = broad. Numbering of protons and carbons are given in Fig. 1. [b]In dimethylsulfoxide-d_6(dmso-d_6). DSS(sodium 2.2-dimethyl-2-silapentanesulfonate) was used as an internal standard for ^1H chemical shifts and dmso-d_6 chemical shift (δ = 39.5 ppm) was used as a reference peak for ^{13}C chemical shifts. [c]Overlapped with other aromatic ring proton resonances. [d]vs. 85% H_3PO_4.

2-C of a pyrrole ring, no proton of the pyrrole ring would be in the shielding region of such an aromatic ring current. An additional small splitting (0.5–0.7 Hz) of the signal should result from an H–P coupling since there is no such splitting when D = py or $AsPh_3$. The $^{13}C\{^1H\}$ NMR spectra are also complicated in the region of the aromatic carbon resonances and only the signals of 2-C and 5-C are identified (Table II). In the complexes with a phosphine ligand J(C–P) is operative for the signals of 5-C.

In the ^1H NMR spectrum of [PdCl(ahp)(PBu_3)$_2$] the chemical shift of 5-H is very different from those of [PdCl(ahp)D] discussed just above. In the PBu_3 complex shielding due to an aromatic ring current of D is not expected and the 5-H signal resides at a lower field. An appearance of the 5-C signal as a triplet in the $^{13}C\{^1H\}$ NMR and a single peak of the $^{31}P\{^1H\}$ NMR spectrum indicate that the two PBu_3 molecules are equivalent. The two PBu_3 are, therefore, *trans* to each other and ahp is bound to a palladium atom only through a 4-C atom, namely the complex is formulated as *trans*-[PdCl(η^1-ahp)(PBu_3)$_2$]. The different ν(C=O) frequency (Table I) from those of [PdCl(ahp)D] presumably reflects the different coordination mode of ahp. Uncoordination of the 3-substituent is evident from the fact that the ^{13}C chemical shifts of 6-C and 8-C of the substituent are near to those of free Hahp.

Treatment of [PdCl(ahp)($Ptol_3$)] with silver salt under basic conditions gave [Pd(ahp-H)($Ptol_3$)] (ahp-H denotes the ligand where a proton is lost from ahp). The absence of ν(N–H) in the infrared and the disappearance of the broad N–H signal in the ^1H NMR spectra indicate that the $-NHCOCH_3$ group is deprotonated and the low ν(C=O) value reveals the coordination of the carbonyl group. The

different feature of the ^{13}C chemical shifts of 6-C and 8-C from those of the complexes discussed above (Table II) suggests that ahp-H adopts another mode of coordination. The coupling between P and 8-C is, for instance, indicative of the carbonyl coordination. The $-NHCOCH_3$ group should be coordinated in a mode similar to that observed usually for acylhydrazone complexes formed under basic conditions [7].

Experimental

(1) Preparation of N-Tosyl-3-acetylpyrrole

N-Tosyl-3-acetylpyrrole was prepared according to the method reported for *N*-benzenesulfonyl-3-acetylpyrrole [4, 5] and tosyl chloride was used instead of benzenesulfonyl chloride.

N-Tosylpyrrole: Yield, 62%. Melting point (m.p.) 103–104 °C. *Anal.* Found: C, 59.71; H, 5.03; N, 6.36. Calc. for $C_{11}H_{11}NO_2S$: C, 59.71; H, 5.01; N, 6.33%. ^1H NMR ($CDCl_3$): 6.27t, 7.15t ppm ($J = 2.3$ Hz) (pyrrole ring protons).

N-Tosyl-3-acetylpyrrole: Yield, 78%. m.p. 90–91 °C. Found: C, 59.29; H, 4.98; N, 5.29. Calc. for $C_{13}H_{13}NO_3S$: C, 59.30; H, 4.98; N, 5.32%. ^1H NMR ($CDCl_3$): 6.67dd ppm ($J = 1.6$, 3.3 Hz), 7.14dd(2.2, 3.4), 7.75t(1.9) (pyrrole ring protons).

(2) Preparation of Hahp, Hmcp, and Hscp

Yields, melting points, and analytical results are summarized in Table I.

A mixture of 5 mmol of *N*-tosyl-3-acetylpyrrole, 5 mmol of acetylhydrazine, and 0.1 ml of acetic acid in 30 ml of ethanol was heated on a steam bath for 1 h and the mixture was left standing at room temperature overnight. Crystals were collected, washed with cold ethanol, and dried in air. Hmcp was prepared similarly from methyl carbazate instead of acetylhydrazine. Hscp was obtained similarly upon mixing in stoichiometry an ethanol solution of *N*-tosyl-3-acetylpyrrole and an aqueous solution of semicarbazide hydrochloride neutralized with sodium acetate in advance.

(3) Preparation of the Complexes

[PdClL] (L = ahp, mcp, and scp)

A mixture of 1 mmol of HL, 1 mmol of lithium tetrachloropalladate (prepared *in situ* from 2 mmol of lithium chloride and 1 mmol of palladium chloride), and 1 mmol of sodium acetate in 40 ml of methanol was stirred overnight at room temperature. The yellow precipitate obtained was washed with methanol and dried in air.

[PdCl(ahp)D] and [PdCl(ahp)(PBu_3)$_2$]

A mixture of 1 mmol of [PdCl(ahp)] and 1 mmol of D (or 2 mmol of PBu_3) in 40 ml of dichloromethane was stirred on a hot plate for several hours until a nearly clear solution had been obtained. The solution was filtered, concentrated to a small volume, and mixed with n-hexane to give a precipitate. The precipitate was washed with n-hexane and dried in air.

[Pd(ahp-H)($Ptol_3$)]

A solution of 1 mmol of [PdCl(ahp)($Ptol_3$)] in 30 ml of acetone was stirred with 1 mmol of 1,8-diazabicyclo[5.4.0]-7-undecene and 0.5 mmol of silver(I) oxide for 4 h and filtered. The filtrate was concentrated to dryness and extracted with dichloromethane. The extract was treated with Florisil and concentrated to a small volume. Upon addition of n-hexane a precipitate formed, which was washed with n-hexane and dried in air.

Measurements

Some ^1H and ^{13}C NMR spectra were recorded on a HITACHI R-90H NMR spectrometer. Other measurements were carried out by the methods reported previously [3].

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