Synthesis of $Fc^{9}CH_2Ph$ (Va). To a solution of 0.5 g of $NaBH_4$ in 30 ml of THF was added 0.3 g (0.61 mmole) of (IVa). The mixture was poured into water and extracted with ether. After evaporation of the extract the residue was recrystallized from hexane. Yield, 0.23 g (90%) of (Va).

Synthesis of $Fc^{9}CH_2(2,4,6\text{-}Me_3C_6H_2)$ (Vc) was carried out like the synthesis of (Va), from 0.32 g (0.57 mmole) of (IVc). Yield, 0.21 g (83%) of (Vc).

CONCLUSIONS

1. Secondary arylnonamethylferrocenylcarbinols have been synthesized.
2. Protonation of the carbinols forms an equilibrium mixture of diamagnetic (singlet) and paramagnetic (triplet) cations.

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SOLVENT-CONTROLLED REGIOSELECTIVITY IN THE ORTHO-PALLADATION OF BENZYLAMINES AND INTRAMOLECULAR EXCHANGE IN CYCLOPALLADATED LIGANDS

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One problem in the activation of C–H bonds (Y = N, O, P, S, etc.) involves the regioselectivity of the metallation reaction and the formation of different metallocycles:

$$HC^1{\sim}Y{\sim}C^2H + Pd(II) \rightarrow \overbrace{Pd-C^1{\sim}Y}{\sim}C^2H + HC^1{\sim}\overbrace{Y{\sim}C^2-Pd} \quad (1)$$

Several examples are known in which a change in the reaction conditions (such as solvent, catalyst, temperature, etc.) leads to a change in the reaction pathway for C–H bond activation and thus produces different Pd(II) complexes from the same organic ligand. For instance, palladation of 2-(2'-azaprop-1'-en-1'-yl)-8-methylquinoline (APMQ) upon treatment with Pd(II) chloride ($[Cl^-]/[Pd(II)] = 5.5$) in MeOH occurs exclusively at the sp^2-C–H bond in the 3-position, whereas treatment with Pd(II) acetate in $CHCl_3$ occurs at the sp^3-C–H bond in the methyl group in the 8-position [1]. The donor sites in these two reaction pathways are the imine and heterocyclic N atoms, respectively. In another paper [2], it was established that N-thiobenz-

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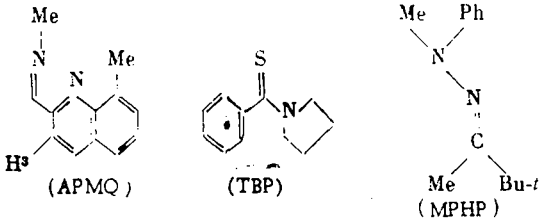
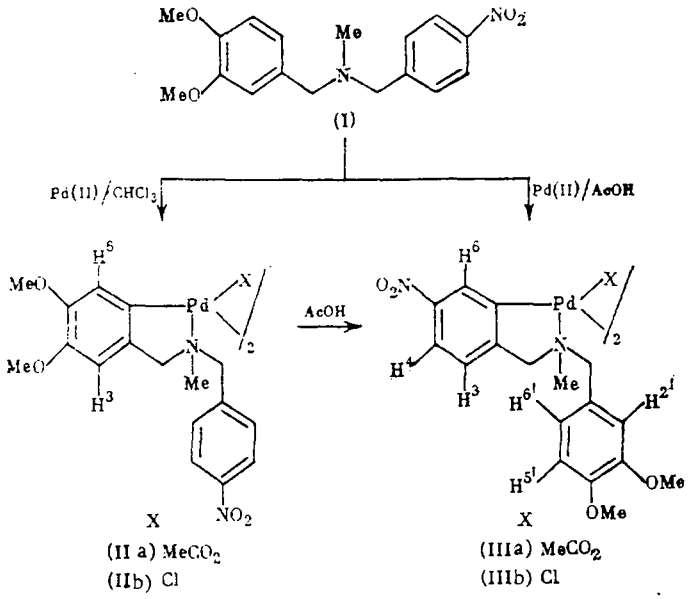
oylpyrrolidone (TBP) is activated at the sp^3-C—H bond of the pyrrolidone ring upon treatment with $PdCl_2$ in HMPA, and at the sp^2-C—H bond of the phenyl ring in MeOH solution.



This was confirmed in [3]. Palladation of the methylphenylhydrazone of pinacoline (MPHP) in C_6H_6 occurs at the Me—C group, whereas in MeOH in the presence of AcONa palladation occurs at the t-Bu group [4].* There have been no satisfactory attempts to explain the changes in the pathways of these reactions [1, 4].

In the present paper we report a new example of solvent-controlled regioselectivity in the palladation of a dibenzylamine derivative (I) upon treatment with Pd(II) acetate. Our interest in this particular reaction



system ($I/Pd(OAc)_2$) was stimulated by the kinetic results obtained in a study of ortho-palladation in ring-substituted N,N-dimethylbenzylamines [6, 7], as well as by the data obtained in a study of the equilibrium product distribution in exchange reactions involving cyclopalladated ligands [8]. Palladation rate measurements revealed that in $CHCl_3$ the reactivity (of the benzylamine derivative) decreases as the electron-withdrawing ability of the meta-substituent in the aromatic ring of the N,N-dimethylbenzylamine is enhanced, in the series $(MeO)_2$ > Me > H > MeO > Cl (Hammett reaction parameter $\rho = -1.6$), whereas in AcOH the series is reversed and electron poor substrates react more avidly ($\rho = +1.4$) [6, 7]. It would follow therefore, that kinetic control would result in the preferential palladation of electron rich substrates in $CHCl_3$ solution and of electron poor substrates in AcOH. Equilibrium studies in AcOH solution furthermore revealed [8] that thermodynamic control also favors palladation of electron poor ligands in a protic solvent. Thus, if a dibenzylamine derivative contains two phenyl rings, with different electron densities, both of which can be metallated, then in an aprotic solvent ($CHCl_3$) C—H activation is expected to take place in the more electron rich ring, whereas in a protic solvent (AcOH) palladation of the acceptor (electron withdrawing) Ph-group is expected. In order to confirm this hypothesis, we have synthesized the bifunctional amine (I), which contains two phenyl rings with different substituents (see Scheme above).

*One should mention in this regard asymmetric cyclopalladation reactions of prochiral substrates [5]. In these cases, however, the structures of the resulting palladacycles are identical for both enantiomers.

RESULTS AND DISCUSSION

Equimolar amounts of amine (I) and Pd(II) acetate were reacted in $CHCl_3$ solution for 1 day at 20°C. The color of the solution changed from brick-colored to yellow during this process and the reaction was accompanied by the formation of Pd(0). The yield of complex (IIa) was 64%. Reaction of (I) with Pd(II) acetate in AcOH was carried out for 4 h at 70°C. The yield of (IIIa) was 49%. The structures of (IIa) and (IIIa) were confirmed by elemental analysis, IR and PMR spectroscopy, as well as by reactions characteristic of these types of compounds. For example, treatment of (IIa) and (IIIa) with a solution of KCl in aqueous acetone led to the formation of the corresponding chlorides (IIb) and (IIIb).

The IR spectra of (IIa) and (IIIa) suggest bridging type coordination of the acetate ligands [9]: for (IIa) the characteristic bands are present at 1575 and 1415 cm^{-1}, along with the antisymmetric and symmetric NO_2 vibrational bands at 1520 and 1350 cm^{-1}, whereas for (IIIa) the first set of bands is at 1575 and 1420 cm^{-1}, the second set of bands at 1515 and 1340 cm^{-1}.

The PMR spectral parameters for free (I), the acetate complexes (IIa) and (IIIa), and the chloride complexes (IIb) and (IIIb) in the presence of pyridine-d_5 are summarized in Table 1. The latter reagent (pyridine) converts dimers into the corresponding monomer complexes of the type [Pd(C–N)(X)(Py)], in which the N atoms are oriented trans to one another, cf [10]. The spectra of the chloro complexes contain sufficient information concerning the structures of both isomers. The main feature is that the MeN signal in the spectra of (IIb) and (IIIb) is shifted downfield by 0.89 and 0.83 ppm, respectively, relative to the position of the signal for the free ligand (I). This is consistent with the presence of a Pd–N coordination bond. The CH_2N group protons appear as an AB quartet, which means that the Pd(II) plane is not a symmetry plane in the molecule. Finally, the position of the Pd–C σ-bond is easily ascertained based on an analysis of the spectra in the aromatic proton region. In the spectrum of (IIb) a singlet at 8.21 ppm (4H) corresponds to the protons in an unmetallated $C_6H_4NO_2$ ring, while singlets at 5.39 and 6.52 ppm belong to H^6 and H^3 in the palladated $(MeO)_2C_6H_2$ ring. The analogous region in the spectrum of (IIIb) consists of two well-resolved ABX spin systems, for the two rings (see Table 1). These data indicate in part that "double" palladation products, i.e., compounds containing simultaneously two Pd–C bonds in one complex (cf. [11]), are not formed in this case, just as was true for 2,6-diphenylpyridines.

Although the spectrum of complex (IIb) does not contain any additional signals, the spectrum of (IIIb) does contain signals due to (IIb) as an impurity. Integration of the most intense of these signals at 8.21 ppm gives an estimate of the (IIb)/(IIIb) ratio equal to 77.6.

The PMR spectra of (IIa) and (IIIa) in the absence of pyridine-d_5 are extremely complex, due to the fact that the acetate dimers exist in boat-shaped structures [12]. Addition of a small excess of pyridine-d_5 greatly simplifies the spectra, which are then for the most part similar to the spectra of the chloride analogs (see Table 1). It should be noted, however, that in the case of (IIa) the unmetallated ring protons appear as an expected AA'BB' spin system, and not as a singlet, as is the case for (IIb). Comparison of the chemical shift values for (I), (IIa), and (IIb) leads us to conclude that the PdCl fragment is a stronger electron withdrawing acceptor than PdOAc. This conclusion is supported by the MeN chemical shift values in (IIa) and (IIb): 3.13 and 3.03 ppm, respectively.

The fact that complexes (III) are more thermodynamically stable than (II) was verified by the almost complete isomerization of (IIa) to (IIIa) over 4 h at 70°C in AcOH. This process may be regarded as an intramolecular exchange of cyclopalladated ligands, which is similar to intermolecular reactions which have been reported [13, 14].

The results obtained herein permit us to formulate a general rule concerning the selectivity of palladation of bifunctional benzylamine derivatives upon treatment with Pd(II) acetate: metallation products at the electron rich and electron poor rings can be prepared by carrying out the reactions in $CHCl_3$ or AcOH, respectively. This effect can be interpreted as follows: in the aprotic solvent $CHCl_3$ Pd(II) acetate behaves as a typical electrophile with respect to benzylamines [6, 7], which leads to the formation of products (II). In a protic solvent such as AcOH, in contrast, palladation of benzylamines is reversible, such that the thermodynamically more stable isomer (III) is accumulated under these reaction conditions. The reversibility of benzylamine palladation appears to be the key feature leading to coordination of Pd(II) with the most electron withdrawing acceptor phenyl group.

TABLE 1. PMR Spectral Parameters for (I)-(III) ((II) and (III) in the presence of pyridine-d_5; δ, ppm; J, Hz)

Compound	MeCOO	MeN	N—CH_2	N—CH_2	MeO *	MeOAr	NO_2Ar
(I)		2.24 s	3.58 s	3.65 s	3.83 s 3.86 s	6.80–7.03	7.45; 7.60; 8.11; 8.24 (AA'BB')
(IIa)	1.91 s	3.03 s	3.55; 3.68 4.02; 4.15 (AB q, J=13)	3.79; 3.82, 4.46; 4.59 (AB q, J=13)	3.45(5) 3.73(4)	5.45(H^6) 6.45(H^3)	7.98; 8.07; 8.17; 8.26 (AA'BB')
(IIb)	-	3.13 s	3.52; 3.66; 4.12; 4.26 (AB q, J=14)	3.73; 3.86, 4.78; 4.91 (AB q, J=13)	3.43(5) 3.74(4)	5.39(H^6) 6.52(H^3)	8.21 s
(IIIa)	1.93 s	2.96 s	3.54; 3.69, 4.19; 4.34 (AB q, J=15)	3.70; 3.82, 4.37; 4.49 (AB q, J=12)	3.85 3.88	6.93 d (J=8, $H^{5'}$); 6.99 dd (J=8.2, $H^{6'}$); 7.44 d (J=2, $H^{2'}$)	6.78 d (J=2, H^6), 6.81 d (J=8, H^3), 7.75 dd (J=8.2, H^4)
(IIIb)	-	3.07 s	3.50; 3.65; 4.29; 4.44 (AB q, J=15)	3.62; 3.75, 4.72; 4.85 (q, J=13)	3.86 3.87	7.03 d (J=8, $H^{5'}$); 7.06 dd (J=8.2, $H^{6'}$); 7.74 d (J=2, $H^{2'}$)	6.69 d (J=2, H^6), 6.8 d (J=8, H^3), 7.78 dd (J=8.2, H^4)

*In parentheses – position of the methoxy group.

EXPERIMENTAL

PMR spectra were recorded on Bruker CXP-100 and Tesla BS-467 spectrometers using $CDCl_3$ solutions versus HMDS as internal standard; chemical shifts are reported relative to TMS. IR spectra were obtained for KBr pellets on a JASCO-200 spectrophotometer. Pd(II) acetate was prepared according to [15].

1-(3',4'-Dimethoxyphenyl)-2-methyl-3-(4'-nitrophenyl)-2-azapropane (I). a) A mixture of 10 mmoles 3,4-dimethoxybenzylamine ("Merck") and 10 mmoles 4-nitrobenzaldehyde ("Fluka") was dissolved in 25 ml absolute benzene and 4Å molecular sieves were added. The solution was kept for 2 h at 20°C, then passed through a short column filled with SiO_2. The benzene was evaporated and the residue was recrystallized from ether. Yield 1.8 g (60%) of light yellow crystals of the Schiff base, 1-(3',4'-dimethoxyphenyl)-3-(4'-nitrophenyl)-2-azaprop-2-ene, mp 93°C. IR spectrum (ν, cm^{-1}) 1640 (C=N), 1520 and 1340 (NO_2). PMR spectrum (δ, ppm; J, Hz) 3.82 s and 3.85 s (MeO) 4.78 d (CH_2, J = 1.5), 6.83 s (MeOAr), 7.78-8.28 (AA'BB', NO_2Ar) and 8.40 t (N=CH, J = 1.5).

b) A solution of 4.6 mmoles of the corresponding Schiff base in 70 ml EtOH was prepared and ca. 0.7 g $NaBH_4$ was added to it with stirring; the mixture was stirred an additional 1 h, then acidified with 1 N HCl and the solvent was removed *in vacuo*. The residue was washed with benzene and treated with 40% NaOH to a strongly basic reaction point. After extraction with ether, drying over NaOH, and solvent removal the yield of oily product was 0.8 g (80%), 1-(3',4'-dimethoxyphenyl)-3-(4'-nitrophenyl)-2-azapropane, mp of the chlorohydrate, 187°C. IR spectrum (ν, cm^{-1}) 1520 and 1345 (NO_2). PMR spectrum (δ, ppm) (free base) 3.72 s (C^1H_2), 3.85 m (OCH_3, C^3H_2), 6.80 m (MeOAr), 7.42-8.22 (AA'BB', NO_2Ar).

c) To 4.3 mmoles of the resulting secondary amine cooled with ice was added 1.2 g of 85% HCOOH through a condenser, followed by 0.8 g of 20% CH_2O. The mixture was heated for 2 h on a water bath until no more CO_2 was evolved. The cooled mixture was then treated with conc. HCl and evaporated to dryness; the residue was washed with benzene and ether, treated with 25% NaOH, and extracted with ether. After concentration *in vacuo* the yield of (I) was 1 g (75%), as an oil, R_f 0.7 (Silufol; alcohol:NH_4OH = 4:1). IR spectrum (ν, cm^{-1}): 1520 and 1345 (NO_2). PMR spectrum, see Table 1.

Di-μ-acetatobis[(2-methyl-(4'-nitrophenylmethyl)aminomethyl-4,5-dimethoxyphenyl-C^1,N)palladium(II)] (IIa). To a solution of (I) (1.32 mmoles) in 8 ml $CHCl_3$ (purified initially to remove EtOH) was added 8 ml of a solution of Pd(II) acetate (1.32 mmoles) in $CHCl_3$, and the resulting mixture was maintained at 20°C for 24 h. The mixture was filtered to remove the metallic palladium deposit, 20 ml H_2O was added, and the aqueous extract was treated with 10 ml $CHCl_3$: the organic extracts were combined and washed twice with water, then dried over $MgSO_4$. After filtration the solvent was evaporated under vacuum to ca. 13 ml volume and then 15 ml hexane was added slowly while stirring the solution with a magnetic stirrer; this led to the formation of a yellow precipitate. The precipitate was filtered, washed with hexane, and dried under vacuum. Yield 405 mg (IIa) (64%), mp 170-172°C (dec). (IIa) is moderately soluble in organic solvents ($CHCl_3$, C_6H_6) upon heating. Found: C 48.2; H 4.7%. $C_{38}H_{44}N_4O_{12}Pd_2$. Calculated: C 47.5; H 4.6%.

Di-μ-chlorobis[(2-methyl-(4'-nitrophenylmethyl)aminomethyl-4,5-dimethoxyphenyl-C^1,N)palladium(II)] (IIb). a) To a solution of (IIa) (0.45 mmole) in 15 ml acetone was added 10 ml of aqueous KCl. The resulting precipitate was washed with water and dried over NaOH. Yield 0.153 g (IIb) (69%), mp 119-121°C (dec.). Found: C 41.2; H 5.0; N 5.6%. $C_{34}H_{38}N_4O_8Cl_2Pd_2 \cdot 4H_2O$. Calculated: C 41.4; H 4.7; N 5.7%.

b) Complex (IIb) could also be prepared via treatment of the chlorohydrate of (I) with Pd(II) acetate in $CHCl_3$, as follows: chlorohydrate of (I) (0.91 mmole) in 10 ml $CHCl_3$ was mixed with 10 ml of a solution of $Pd(OAc)_2$ (0.80 mmole) in $CHCl_3$ and the resulting solution filtered. The mixture was kept at 20°C for 24 h. The crystalline deposit was removed by filtration, washed with hexane, and dried under vacuum. Yield 0.25 g (69%) of (IIb).

Di-μ-acetatobis[(2-methyl-(3',4'-dimethoxyphenylmethyl)aminomethyl-5-nitrophenyl-C^1,N)-palladium(II)] (IIIa). a) $Pd(OAc)_2$ (1.46 mmoles) was dissolved with slight heating in 15 ml AcOH. After filtration the solution was treated with 1.46 mmoles (I) in 15 ml $CHCl_3$ and the resulting mixture was heated at 70°C for 4 h. A small amount of Pd(0) was formed. The mixture was filtered, 15 ml each $CHCl_3$ and H_2O were added, and the aqueous layer was washed with 15 ml $CHCl_3$; the combined organic layers were then washed twice with 20 ml portions of water. After drying over $MgSO_4$ the solvent was evaporated under vacuum and the residue yielded 0.34 g of

(IIIa) (49%) by column chromatography ($SiO_2/CHCl_3$). In contrast to isomer (IIa), complex (IIIa) is extremely soluble in most organic solvents; mp 144-151°C (dec). Found: C 47.0; H 4.5; N 5.7%. $C_{38}H_{44}N_4O_{12}Pd_2$. Calculated: C 47.5; H 4.6; N 5.8%.

b) The dimeric complex (IIa) (0.105 mmole) was dissolved with heating in 5 ml C_6H_6 and 5 ml AcOH was added, the mixture was heated at 70°C for 4 h and then worked up as described above in Part a). Yield 51%.

Di-μ-chlorobis[(2-methyl-(3',4'-dimethoxyphenylmethyl)aminomethyl-5-nitrophenyl-C^1,N)-palladium(II)] (IIIb). This was prepared by treatment of a solution of (IIIa) in acetone with an aqueous solution of KCl or by thermostatting a suspension of (IIb) in a mixture of C_6H_6/AcOH at 70°C, according to the methods reported above; mp 125-129°C (dec). Found: C 45.0; H 4.3; N 6.1%. $C_{34}H_{36}N_4O_8Cl_2Pd_2$. Calculated: C 44.7; H 4.2; N 6.1%.

CONCLUSIONS

Cyclometallation of 1-(3',4'-dimethoxyphenyl)-2-methyl-3-(4'-nitrophenyl)-2-azapropane upon treatment with Pd(II) acetate occurs at the electron rich dimethoxy-substituted aromatic ring in $CHCl_3$ solution, and at the electron poor nitrophenyl ring in AcOH solution.

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