Palladium-Catalyzed Cyclization of 6-Aminohex-1-yne

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Mechanistic details and limiting factors for the palladium-catalyzed addition of amines to alkynes (hydroamination) were studied, using the cyclization of 6-aminohex-1-yne to 2-methyl-1,2-dehydropiperidine as a specific example. The complex [Pd(Triphos)]$(CF_3SO_3)_2$ showed the highest catalytic activity of a series of structurally and electronically distinct palladium complexes. Several methods, such as calorimetry and in situ IR and NMR spectroscopy, were used to obtain evidence for a possible reaction cycle. It seems likely that (i) the substrate initially coordinates via the amine group and (ii) an intermediate is formed which is the product of a nucleophilic attack of the amine on a coordinated alkyne. Addition of an acid to the reaction mixture led to a strong increase in the reaction rate, probably by accelerating protolytic cleavage of the palladium−carbon bond in the intermediate complex.

Introduction

Catalytic C−N forming processes are of fundamental importance in organic chemistry. However, the direct addition of N−H bonds across the unsaturated carbon−carbon bond in alkenes or alkynes (hydroamination) remains challenging.[1] The industrial potential of hydroamination reactions is high, and *tert*-butylamine is produced on a large scale from ammonia and isobutene.[2] The catalyst employed in the commercial process is a zeolite which acts as a solid acid and activates the alkene by protonation. Therefore, the method is limited to alkenes that form a stable carbenium ion. Alternative approaches for hydroamination catalysts are based on activation of the amine group with group 1 metal bases[3−7] and group 3 to 4 metal complexes.[8−13] Catalysis by late transition metals[14−20] would be of particular interest for industrial applications. From the pioneering work of Reppe it is known that group 12 elements, especially cadmium and mercury, can catalyze the addition of secondary amines to acetylene to give the corresponding enamines.[21−23] More recently, a number of structurally different late transition metal complexes were found to be good catalysts for the intra- and intermolecular addition of amines to alkynes.[24−27] Examples are the cyclization of *o*-alkynylanilines to indoles with $PdCl_2$ [28,29] and of 1-aminoalk-*n*-ynes to pyrrolines (n = 3, 4) or 1,2-dehydropiperidines (n = 5) with $NaAuCl_4 \cdot 2H_2O$[30] or $[Ni(CO)_2(PPh_3)_2]$.[31]

The purpose of this study is to explore the potential of palladium complexes as hydroamination catalysts and to provide evidence for a possible reaction mechanism. The investigation is focused on palladium complexes,

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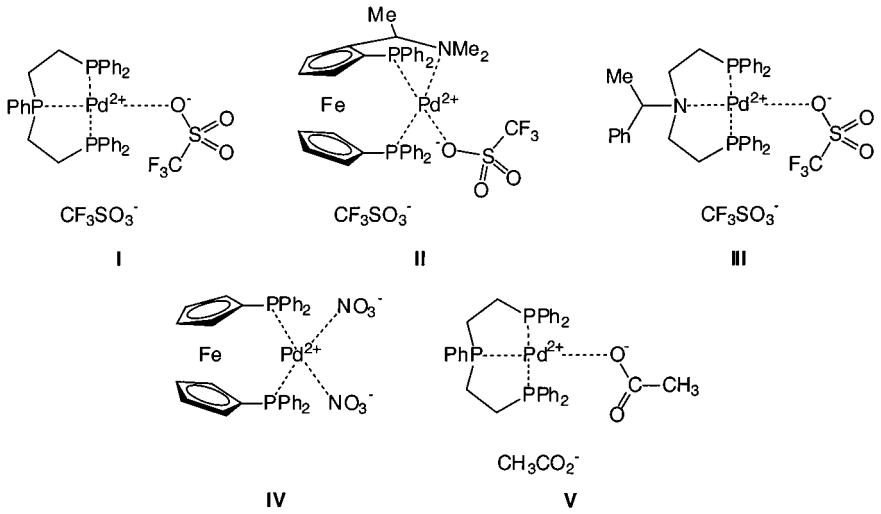
Scheme 1. Palladium Complexes Synthesized for This Study



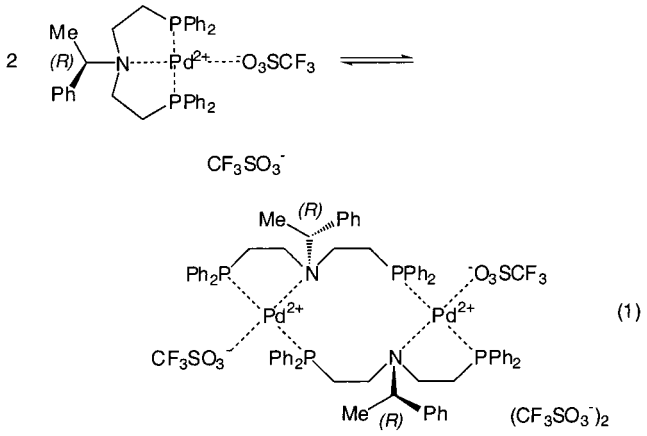
as the ligand sphere allows one to tune the catalytic properties of the metal center and enables the use of a variety of analytic tools for studying the reaction in and ex situ. Aiming at accelerating the rate of reaction, the limiting factors and, in particular, the rate-determining step and a possible resting state of the catalyst will be discussed.

Results and Discussion

Synthesis of Palladium Complexes. A series of closely related palladium complexes were synthesized to study the influence of the coordination sphere on the catalytic activity. The palladium complexes **I**−**V** as shown in Scheme 1 were prepared from $[PdCl_2(COD)]$ by displacement of the COD ligand by the corresponding phosphine ligand followed by halide abstraction with $AgCF_3SO_3$, $AgNO_3$, or $AgCH_3CO_2$. The complexes were fully characterized by multinuclear NMR, IR, FAB-MS, and elemental analysis. For $[Pd(Triphos)](CF_3SO_3)_2$ (**I**, Triphos = bis(2-diphenylphosphinoethyl)phenylphosphine), $[Pd(PPN)](CF_3SO_3)_2$ (**II**, PPN = *N*,*N*-dimethyl-1-[1′,2-bis(diphenylphosphino)ferrocenyl]ethylamine), $[Pd(PP)](NO_3)_2$ (**IV**, PP = 1,1′-bis(diphenylphosphino)-ferrocene), and $[Pd(Triphos)](CH_3CO_2)_2$ (**V**) the data were fully consistent with the structural formula given.

However, a comparison of the $^{31}P\{^1H\}$ NMR spectra of compound **I** and $[Pd(PNP)](CF_3SO_3)_2$ (**III**, PNP = *R*-*N*,*N*-bis(2-diphenylphosphinoethyl)-1-phenylethylamine) showed a different nature for the two complexes. In the spectrum of compound **I**, signals at 116.7 and 52.7 ppm in a 1:2 ratio could be assigned to the PPh and the two PPh_2 groups positioned *trans* to each other, respectively. The spectrum of **III** showed a complex multiplet centered at 42.7 ppm. The chemical shift indicates that the two PPh_2 groups in **III** were also arranged *trans* to each other. However, the higher order spectrum shows that the two PPh_2 groups were in a similar, but not equal environment. Simulation of the spectrum with gNMR[32] gave $\delta(^{31}P1) = 42.0(0.5)$ ppm, $\delta(^{31}P2) = 43.4(0.5)$ ppm and a coupling constant $J(^{31}P1,^{31}P2) = -91.8(12.4)$ ppm. The features of the ^{31}P NMR spectrum of **III** can in principle be explained by the presence of the chiral center in the molecule. Hindered rotation around the N−(CHMePh) bond would render the phosphorus atoms in **III** diastereotopic and hence nonequivalent.

However, closer inspection of the $^{13}C\{^1H\}$ NMR spectrum of **III** revealed 12 lines between 11.3 and 68.7 ppm in the region of aliphatic carbon atoms. The chiral center in the monomeric molecule would lead to only six inequivalent carbon atoms. Coupling to the ^{31}P nuclei is generally weak and would only be observed for the carbon atoms associated with the ethylene bridges, but not for the CHMePh group. The features in the $^{13}C\{^1H\}$ NMR spectrum can, however, be rationalized assuming the formation of a dimer according to eq 1. Molecular modeling showed that, because of steric limitations, the two 1-phenylethyl groups in the dimer can only be positioned *trans* to each other. As racemically pure phosphine was used, no center of symmetry can be present in the molecule. Thus, the two pairs of carbon atoms associated with the ethylene bridges are in a different environment and give rise to eight lines in the aliphatic carbon region. The two 1-phenylethyl groups give rise to a further four lines in the aliphatic carbon region, accounting for the total 12 lines in the $^{13}C\{^1H\}$ NMR spectrum of **III**. Further, the two PPh_2 groups attached to one palladium atom are in a different, but very similar environment in the dimer, giving rise to the higher order $^{31}P\{^1H\}$ NMR spectrum.



(1)

A single-crystal X-ray analysis of **I** was performed to determine the steric requirements of the tridentate

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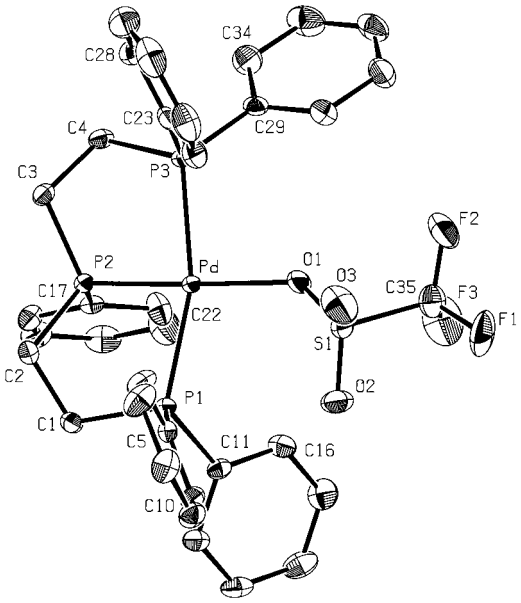


Figure 1. ORTEP[50] representation of the monocationic part of compound **I**·$CHCl_3$ in the solid state. Thermal ellipsoids are at the 50% probability level. Hydrogen atoms are omitted for clarity.

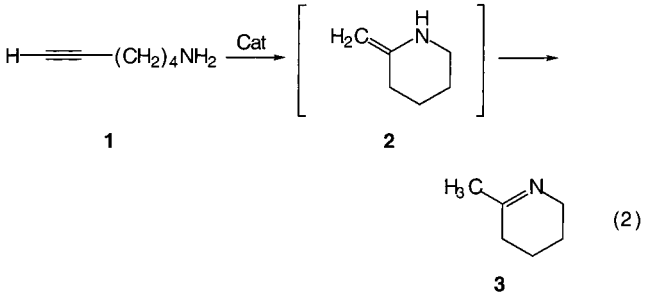
Table 1. Selected Interatomic Distances (Å) and Angles (deg) for I·$CHCl_3$

Pd−P1	2.3375(6)	P1−Pd−P2	82.38(2)
Pd−P2	2.2003(6)	P1−Pd−P3	164.14(2)
Pd−P3	2.3480(6)	P1−Pd−O1	99.88(6)
Pd−O1	2.134(2)	P2−Pd−P3	83.92(2)
P1−C1	1.856(3)	P2−Pd−O1	175.48(7)
P1−C5	1.813(3)	P3−Pd−O1	94.36(6)
P1−C11	1.805(2)	Pd−P1−C1	108.56(10)
P2−C2	1.814(3)	Pd−P1−C5	109.79(8)
P2−C3	1.814(3)	Pd−P1−C11	117.58(9)
P2−C17	1.813(3)	Pd−P2−C2	109.70(10)
P3−C4	1.836(3)	Pd−P2−C3	110.37(9)
P3−C23	1.811(3)	Pd−P2−C17	109.45(8)
P3−C29	1.812(3)	Pd−P3−C4	106.85(9)
S1−O1	1.457(2)	Pd−P3−C23	110.11(10)
S1−O2	1.427(2)	Pd−P3−C29	119.89(10)
S1−O3	1.421(2)	Pd−O1−S	135.82(12)
C1− C2	1.531(4)	O1−S1−C35	99.00(13)
C3−C4	1.533(4)	O2−S1−C35	104.63(13)
		O3−S1−C35	105.34(14)

phosphine ligand and to investigate the nature of the interaction between the anion and the palladium center. Suitable crystals of **I**·$CHCl_3$ were grown by slow evaporation of a chloroform solution of complex **I**. A perspective view of the complex is shown in Figure 1; selected bond lengths and angles are given in Table 1. The phosphine is coordinated in a tridentate fashion to the palladium center. The anticipated vacant coordination site *trans* to the PPh phosphorus atom is occupied by an oxygen atom (O1) of one trifluoromethanesulfonate anion. Thus, the geometry is based on the normal square-planar geometry of Pd^{II} centers. The rms deviation of all five fitted atoms defining the coordination plane (Pd, P1−P3, O1) amounts to 0.122(1) Å. The palladium−phosphorus and palladium−oxygen distances are Pd−P1 = 2.3375(6), Pd−P2 = 2.2003(6), Pd−P3 = 2.3480(6), and Pd−O1 = 2.134(2) Å. These distances are within the range of two similar palladium complexes with a square-planar $Pd^{II}(OP_3)$ coordination geometry [Pd(Triphos)](acac-F_6)$_2$ (Pd−O = 2.110(5) Å)[33] and the related [Pd(Triphos)]$(CF_3SO_3)_2$·C_6H_6 (Pd−O = 2.126(7) Å).[34] The bond lengths from palladium to P1 and P3, which are opposite to each other, are significantly longer than Pd−P2, clearly demonstrating the *trans*-influence of phosphorus.[35] Two ethylene bridges connect P2 with P1 and P3, respectively, to form two five-membered metallacycles with a nearly perfect envelope configuration. The angles P1−Pd−P2 (82.38(2)°), P2−Pd−P3 (83.92(2)°), and P1−Pd−P3 (164.14(2)°) are significantly smaller than 90° and 180°, respectively, indicating that steric strain is present in the metallacycles. The angles O1−Pd−P1 (99.88(6)°) and O1−Pd−P3 (94.36(6)°) are consequently larger than 90°, leaving additional space for coordination of the anion.

A search of the Cambridge Crystallographic Database[36] returned eight entries where $CF_3SO_3^-$ coordinates to a palladium(II) center (Table 2). The Pd−O bond distance in **I**·$CHCl_3$ (2.134(2) Å) is shorter than in those complexes where a C-ligand is situated *trans* (range Pd−O = 2.126(5)−2.271(7) Å, entries 1−5) and comparable to those complexes where a P-ligand is *trans* (range Pd−O = 2.118(2)−2.159(3) Å, entries 6−8). The relatively short Pd−O distance in **I**·$CHCl_3$ indicates a relatively strong Pd−O bond. As the counterion has to be displaced during catalysis, a large influence of the anion on the catalytic activity is expected. The S−O bond distance associated with the coordinated oxygen (S1−O1 = 1.457(2) Å) is significantly longer than the remaining S−O bonds (S1−O2 = 1.427(2), S1−O3 = 1.421(2) Å). At the same time the angle O−S−CF_3 is smaller for the coordinated oxygen atom (O1−S1−C35 = 99.0(1)°), relative to the uncoordinated oxygen atoms (O2−S1−C35 = 104.6(1)°, O3−S1−C35 = 105.3(1)°). However, the difference is too small to account for localized S−O and S═O bonds.

Catalytic Activity of the Palladium Catalysts. The activity of complexes **I**−**V** as catalysts for the direct addition of amines to alkynes was compared for the cyclization of 6-aminohex-1-yne (**1**). The cyclization of **1** first generates 2-methylene-piperidine (**2**) with an exocyclic double bond (eq 2). Subsequent 1,3-hydrogen shift occurs in situ and converts the enamine to the more stable isomeric imine 2-methyl-1,2-dehydropiperidine (**3**).



(2)

The catalytic activity of the complexes **I**−**V** ranges from 5.6(6) to 243(14) mol_{Sub}·$(mol_{Cat}$·$h)^{-1}$ (Figure 2). The

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(36) 3d Search and research Using the Cambridge Structural Database (1/2000, 215403 entries): Allen, F. H.; Kennard, O. *Chem. Des. Autom. News* **1993**, *8*, 1 and 31−37.

Table 2. 3D Search and Research Using the Cambridge Structural Database[36]

entry	complex[a]	CSD−name	*d*(Pd−O) [Å]	*d*(S═O) [Å]
			trans Pd−C	
1	$[Pd((CC_5H_5)C(CH_3)_2CH_2)(PMe_3)(CF_3SO_3)]$[51]	BIXFET	2.21(1)	1.434[36]
			2.16(1)	1.429[36]
2	$[Pd(CO(CH_2)_2NEt_2)(NHEt_2)(CF_3SO_3)]$[52]	FMSEPD	2.271(7)	1.441(8)
3	$[Pd(COD)(CH_3)(CF_3SO_3)]$[53]	GOSKEE	2.126(5)	1.456[36]
4	$[Pd(C_{14}H_{27}N_2)(PEt_3)_2(CF_3SO_3)]$ (at 143 K)[54]	RUNCOS	2.184(4)	1.453(4)
5	$[Pd(C_{24}H_{29}O_{12})py_2(CF_3SO_3)]$ (at 173 K)[55]	ZOQLAS	2.147(5)	1.440(5)
			trans Pd−P	
6	$[Pd(Triphos)(CF_3SO_3)](CF_3SO_3)\cdot C_6H_6$[34]	RIDPOJ	2.126(7)	1.441(9)
7	$[Pd(DPPP)(H_2O)(CF_3SO_3)](CF_3SO_3)$[56]	YOSVOR	2.159(3)	1.469(4)
8	$[Pd_2(DPPP)_2(C_8H_4N_2)(CF_3SO_3)_2](CF_3SO_3)_2$[57]	ZAGDAM	2.118(2)	1.461[36]
			2.118(2)	1.461[36]
9	$I\cdot CHCl_3$		2.134(2)	1.457(2)

[a] $(CC_5H_5)C(CH_3)_2CH_2$, 2-(benzene-1,1-diyl)-2-methyl-propyl; $CO(CH_2)_2NEt_2$, 3-(diethylamino)propanoyl; $C_{14}H_{27}N_2$, 2-*p*-tolylazido-5-methylphenyl; $C_{24}H_{29}O_{12}$, *cis*,*cis*-1,2,3,4-tetrakis(methoxycarbonyl)-4-(2,3,4-trimethoxy-6-ethoxymethylphenyl)buta-1,3-dienyl; py, pyridyl; DPPP, 1,3-bis(diphenylphosphino)propane; $C_8H_4N_2$, μ_2-1,4-dicyanobenzene-*N*,*N*′.

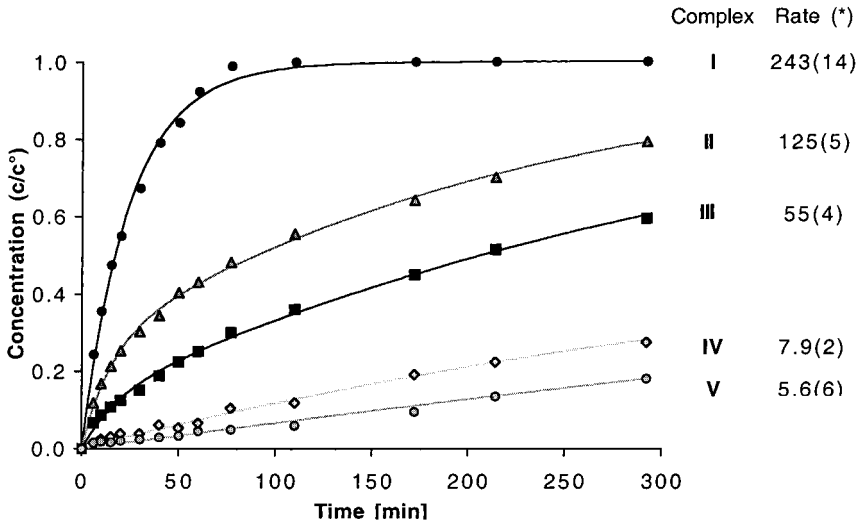

Figure 2. Time concentration diagram for the formation of **3** from **1** using the complexes **I**−**V** as catalysts. * The rate of reaction is given in $mol_{Sub}\cdot mol_{Cat}^{-1}\cdot h^{-1}$ for $t \rightarrow 0$.

differences in activity can be rationalized in part on the basis of the significant structural and electronic differences of these complexes. The highest activity was observed for **I**, whereas the lowest activity was observed for **V**. As the palladium cation has the same ligand sphere in the two complexes, the different activity must be due to the different anion ($CF_3SO_3^-$ and $CH_3CO_2^-$, respectively). In this respect, it was observed before that basic anions such as acetate lead to a low catalytic activity of late transition metal complexes in hydroamination reactions, whereas anions derived from sulfonic acids lead to an especially high activity.[24]

Formal replacement of the PPh group opposite the empty coordination site in **I** by a N(CHMePh) moiety gives complex **III**, which had an intermediate catalytic activity. The monomeric and the dimeric forms of **III** probably have similar catalytic activities, as the free coordination sites are in very similar environments and their number remains the same. The lower activity of **III** shows that a nitrogen ligand opposite the empty coordination site is less favorable than a phosphine ligand. It seems likely that this results from the strong *trans* effect[37] of the phosphine ligand, which weakens bonding of the substrate, the product, or an intermediate species to the metal center.

The activity of **IV**, containing a bidentate phosphine, was only slightly higher than that of **V** and much lower than of **I**. In contrast, **II**, with an additional amine group attached to one of the Cp rings, had a much higher catalytic activity than **IV**, but lower than **I**. The low activity of complex **IV** cannot fully be explained by the less favorable NO_3^- anion. The low activity also seems to be due to the ligand sphere, i.e., the bidentate phosphine. In contrast, tridentate ligands such as the phosphines in complexes **I** and **II** seem to be especially favorable. Substitution of a ligand *cis* to the empty coordination site has little electronic effect on the orbital involved in bonding of the substrate. The lower activity of **II** relative to **I** could be due to the different nature of the substituents attached to the coordinating atoms. The phenyl groups of the triphos ligand in **I** leave a narrow wedge which is favorable for approach of an unpolar substrate molecule, whereas the NMe_2 group in **II** is more polar and, thus, less favorable.

Mechanistic Studies. Substrate **1** can coordinate to the palladium center either via the amine or via the alkyne group (Scheme 2). To differentiate between the two bonding modes, the complex formation constant between **I** and **1** was determined using titration calorimetry (ITC). A solution of **1** in $CHCl_3$ was added incrementally to a solution of **I** in $CHCl_3$ and the heat

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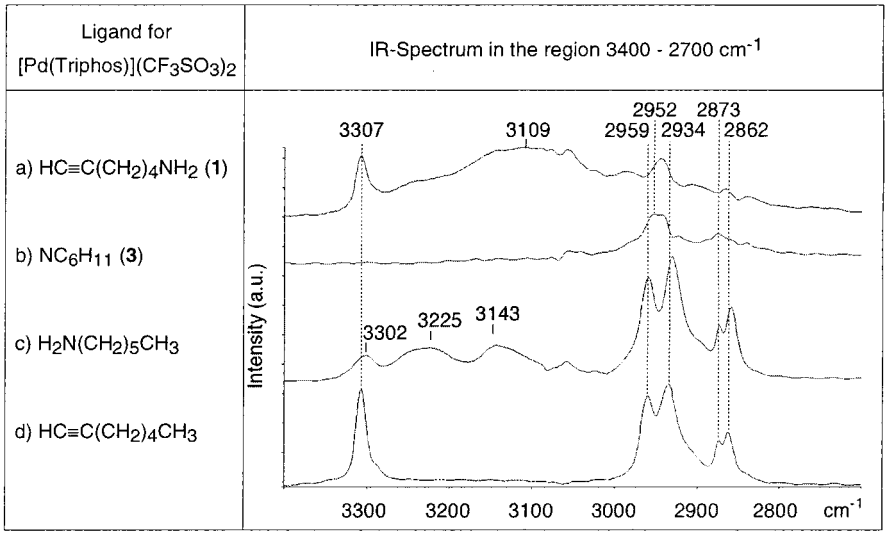
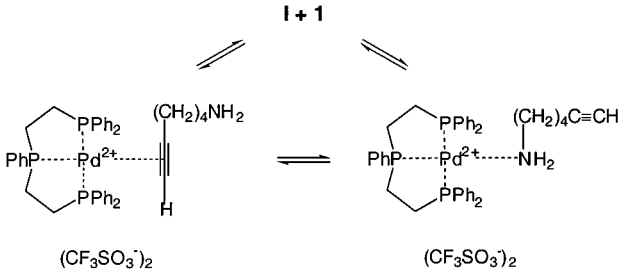


Figure 3. Infrared spectra of in situ 1:1 mixtures of [Pd(Triphos)]$(CF_3SO_3)_2$ (**I**) and various ligands. To facilitate analysis, the spectrum of **I** was subtracted from each of the infrared spectra obtained for mixtures **a**−**d**.

Scheme 2. Equilibrium between Coordination of 1 to the Palladium Center in I via the Amine Lone Pair or via the Alkyne π-System



generated upon mixing the solutions was measured. Close to a molar ratio of **1**/**I** = 1, the heat developed dropped to zero. For the complex formation, a reaction enthalpy $\Delta H° = -71.0(7)$ kJ·mol^{-1} and an equilibrium constant $K = 4.2(1.4) \times 10^6$ mol·dm^{-3} were calculated. For the complexation of hexylamine (formally replacing C≡CH in **1** by C_2H_5) to **I** a very similar $\Delta H° = -69.8(7)$ kJ·mol^{-1} and a slightly smaller equilibrium constant $K = 1.1(0.3) \times 10^6$ mol·dm^{-3} were determined. In contrast, no heat evolution was detected when a solution of heptyne (formally replacing NH_2 in **1** by CH_3) was added to a solution of **I**.

The similar complex formation constant of **1** and hexylamine indicates that, during catalysis, the initial interaction of **1** with the palladium center occurs via coordination of the nitrogen lone pair to the palladium center. The low heat flow observed for coordination of heptyne is due to either a very small complex formation constant, i.e., a weak coordination of π(C≡C) to the palladium center, or a very small $\Delta H°$ of the reaction.

The coordination of the substrate to the palladium center was also studied with IR spectroscopy. For this purpose, a solution of **I** in $CDCl_3$ was prepared, 1 equiv of **1** added, and the mixture (**a**) immediately analyzed by IR spectroscopy. For comparison reasons, the corresponding spectra of solutions containing (**b**) a mixture of **I** and **3**, (**c**) a mixture of **I** and hexylamine, and (**d**) a mixture of **I** and heptyne were also measured. To facilitate the analysis, the spectrum of the parent complex **I** (signals due to ν_{st}(CH) at 3063, 2965, and 2929 cm^{-1}) was subtracted from each of the spectra obtained for **a**−**d**. The C−H stretching region proved suitable for an assignment and interpretation of the signals (Figure 3).

Solution **a** showed an intense broad signal ranging from 3300 to 2850 cm^{-1} and signals at 3307 and 2941 cm^{-1} with a lower intensity. The signal at 3307 cm^{-1} is easily assigned to the alkyne ν_{st}(≡CH) by comparison with the spectrum of **d**. No change in the frequency relative to the parent heptyne was observed, whereas a decrease in intensity and a slight broadening indicates weak interaction of the C≡CH moiety. A solution of hexylamine in $CDCl_3$ did not show a signal that could be assigned to ν_{st}(NH), whereas in CD_3CN it was observed as a weak band at 3385 cm^{-1}. Upon coordination of hexylamine to **I** ($CDCl_3$, **c**) three additional broad signals appeared at 3302, 3225, and 3143 cm^{-1}, which were assigned to the NH protons, indicating that the amine group strongly interacts with the palladium center. The signals due to coordinated amine were not detected for solution **a** so that simple coordination of the amine group to the palladium can be excluded. The broad signal and a decrease of the intensity of the alkyne signal in mixture **a** relative to mixture **d** indicate that both functionalities may be involved in the interaction of **I** and **1**. Presumably, the amine is coordinated to the palladium center via the NH_2 group and the alkyne moiety is involved in a weak interaction as, for example, hydrogen bonding.[38] A mixture of product molecule **3** and **I** (**b**) showed a completely different IR spectrum and clearly cannot account for the observations in **a**.

To identify the palladium species present during catalysis, a 100-fold excess of **1** was added to a solution of **I** in $CDCl_3$ and a $^{31}P\{^1H\}$ NMR spectrum of the mixture taken. Only two signals were detected at 102.8 and 45.2 ppm, which are assigned to the PPh moiety and the two PPh_2 groups of a new palladium complex **VI**. To identify this complex, a series of comparison samples was prepared and a $^{31}P\{^1H\}$ NMR spectrum of each mixture taken (Table 3). The spectrum of a mixture of **I** and 1 equiv of **1** (entry 2) showed intense signals at

(38) Desiraju, G. R.; Steiner, T. *The Weak Hydrogen Bond*; Oxford University Press: Oxford, 1999.

Table 3. $^{31}P\{^1H\}$ NMR Signals Observed for Mixtures of [Pd(Triphos)]X_2 (X = $CF_3SO_3^-$, $CH_3CO_2^-$) and Various Ligands[c]

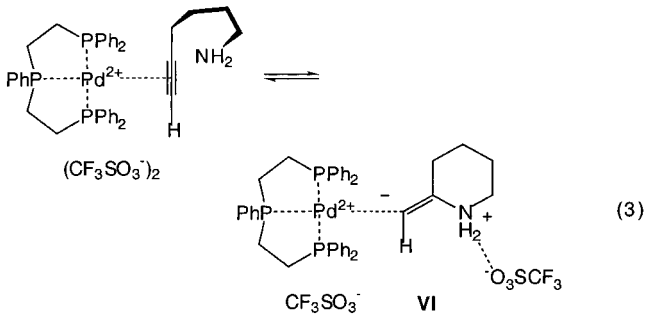
entry	ligand for [Pd(Triphos)]$(CF_3SO_3)_2$	δ(P1) [ppm]	δ(P2/3) [ppm]	assignment
1	—	**116.7**	**52.7**	[Pd]$-^-O_3SCF_3$
2	1 equiv of $H{\equiv}C(CH_2)_4NH_2$ (**1**)	116.7	52.7	[Pd]$-^-O_3SCF_3$
		109.5	**53.9**	[Pd]$-NC_6H_{11}$
		102.7	45.2	[Pd]$-^-C{=}C-NR_3^+$
3	100 equiv of $HC{\equiv}C(CH_2)_4NH_2$ (**1**)	**102.8**[a]	**45.2**[a]	[Pd]$-^-C{=}C-NR_3^+$
4	1 equiv of NC_6H_{11} (**3**)	116.7	52.7	[Pd]$-^-O_3SCF_3$
		109.5	**53.8**	[Pd]$-NC_6H_{11}$
5	1 equiv of $H_2N(CH_2)_5CH_3$	116.8	53.0	[Pd]$-^-O_3SCF_3$
		108.7	**53.9**	[Pd]$-NH_2$Hex
6	(1) 1 equiv of $HC{\equiv}C(CH_2)_4CH_3$	116.7	52.5	[Pd]$-^-O_3SCF_3$
	(2) 1 equiv of NEt_3	112.7	47.5	[Pd]$-NEt_3$
		102.9	**45.3**	[Pd]$-^-C{=}C-NR_3^+$
7	(1) 1 equiv of NEt_3	112.6	47.5	[Pd]$-NEt_3$
	(2) 1 equiv of $HC{\equiv}C(CH_2)_4CH_3$	**103.0**	**45.3**	[Pd]$-^-C{=}C-NR_3^+$
8	1 equiv of $HC{\equiv}C(CH_2)_4CH_3$	**116.7**	**52.7**	[Pd]$-^-O_3SCF_3$
9	1 equiv of NEt_3	**112.3**	**47.2**	[Pd]$-NEt_3$
entry	ligand for [Pd(Triphos)]$(CH_3CO_2)_2$	δ(P1) [ppm]	δ(P2/3) [ppm]	assignment
10	—	**112.8**	**47.4**	[Pd]$-^-O_2CCH_3$
11	1 equiv of $HC{\equiv}C(CH_2)_4NH_2$ (**1**)	**112.8**	**47.4**	[Pd]$-^-O_2CCH_3$
12	100 equiv of $HC{\equiv}C(CH_2)_4NH_2$ (**1**)	112.8	47.3	[Pd]$-^-O_2CCH_3$
		102.7 [b]	**45.3** [b]	[Pd]$-^-C{=}C-NR_3^+$

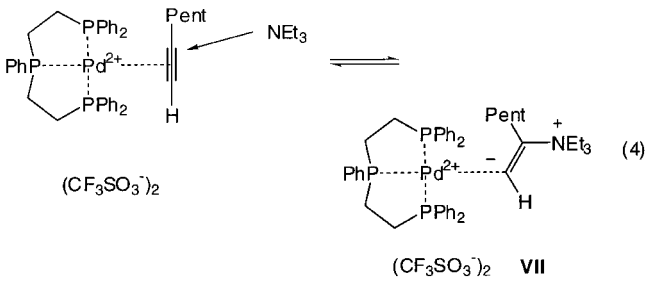
[a] **102.8** t ($J(^{31}P,^{31}P)$ = 17.7 Hz); **45.2** d ($J(^{31}P,^{31}P)$ = 17.8 Hz). [b] **102.7** t ($J(^{31}P,^{31}P)$ = 17.8 Hz); **45.3** d ($J(^{31}P,^{31}P)$ = 14.9 Hz). [c] The chemical shift of the main component in each reaction mixture is given in bold; [Pd] denotes $[Pd(Triphos)]^{2+}$.

109.5 and 53.9 ppm. These can be assigned to formation of the cyclization product **3** and its coordination to the palladium center (see entry 4). Additional weaker signals at 116.7/52.7 and 102.7/45.2 ppm can be assigned to the parent palladium complex **I** and the unknown intermediate **VI**, respectively. Coordination of hexylamine to **I** gave rise to a pair of signals at 108.7/53.9 ppm (entry 5), while addition of heptyne to **I** did not give a shift of the ^{31}P signals relative to **I** (entry 8), indicating no or only weak coordination of the alkyne moiety to palladium.

The chemical shift of the signals in the ^{31}P NMR spectrum of the mixture of hexylamine and **I** indicates that the amine is coordinated via the lone pair to the palladium. It can be excluded that the amine is oxidatively added to the palladium center in stoichiometric quantities, as this would give rise to a large shift of the ^{31}P NMR signals. However, this does not preclude oxidative addition in the catalytic cycle.

On the other hand, **VI** could be the result of an intramolecular nucleophilic attack (eq 3). In this respect, it is known that a nucleophilic attack of an amine on coordinated alkenes or alkynes is possible.[39] To test this hypothesis, 1 equiv of heptyne and 1 equiv of NEt_3 were added in succession to a solution of **I**. Complex **VII** formed in situ according to eq 4[40] and gave rise to a pair of signals in the $^{31}P\{^1H\}$ NMR spectrum at exactly the same chemical shift as the unknown intermediate **VI** (entry 6). Thus, the direct environment of the palladium center must be very similar in both intermediates and is assigned the moiety $[(Triphos)Pd^{2+}{\leftarrow}CH^-{=}CR-NR'_3{}^+]$ with R = alkyl, R′ = H, alkyl. The groups R and R′ are different in **VI** and **VII**, but the distance of 4 and 5 bonds to the phosphorus nuclei is too big to have an effect on their chemical shift. Additional low-intensity signals in the spectrum of **VII** are readily assigned to the parent palladium complex and coordination of NEt_3 to palladium. To prove that the formation of intermediate **VII** is an equilibrium reaction, the order of adding the ligands was reversed, adding first triethylamine and subsequently heptyne (entry 7). In this mixture complex **VII** was observed in about the same concentration as before, confirming that its formation is an equilibrium reaction.



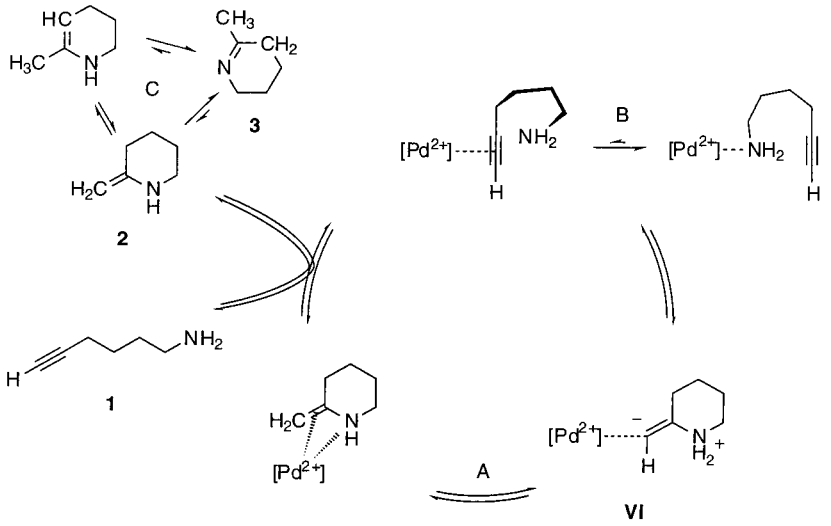


To investigate why **V** has a much lower activity in the cyclization of **1**, the same sequence of $^{31}P\{^1H\}$ NMR experiments was performed with this complex. For all samples, except when 100 equiv of **1** was added to **V**, only the ^{31}P signals due to the parent complex **V** were observed. For the latter mixture, a pair of signals at 102.7/45.3 ppm was noticed (entry 12). The chemical shift was equal to the shift observed for **VI** and **VII** and

(39) Akermark, B.; Bäckvall, J.-E.; Zetterberg, K. *Acta Chem. Scand. B* **1982**, *36*, 577.

(40) For a related platinum complex see: Ambüehl, J.; Pregosin, P. S.; Venanzi, L. M.; Ughetto, G.; Zambonelli, L. *Angew. Chem., Int. Ed. Engl.* **1975**, *44*, 369.

Scheme 3. Reaction Mechanism Proposed for the Cyclization of 1



indicates the formation of the same cationic intermediate. Thus, even strong donor ligands such as NEt_3 are unable to displace the acetate ion from its coordination to the palladium center. A large excess of **1** is required to shift the equilibrium toward displacement of the acetate ion from the primary coordination sphere. Thus, in addition to the basic nature of the acetate ion mentioned before, its ability to strongly coordinate to the palladium center could explain the low catalytic activity of **V**.

A likely reaction sequence for the addition of amines to alkynes catalyzed by palladium is shown in Scheme 3, using as a specific example the cyclization of **1**. Initial coordination of substrate **1** to the palladium center occurs via the amine. The complex isomerizes so that the alkyne group becomes coordinated to the metal center. This renders the π-system susceptible to a nucleophilic attack of the nitrogen lone pair which gives the 2-ammonio alken-1-yl complex **VI**. Protolytic cleavage of the metal−carbon bond leads to desorption of **2** and regenerates the catalyst. Subsequently, the enamine **2** isomerizes in situ to the more stable imine **3**. This reaction sequence is proposed based on the observations described above and reports that zinc(II) salts were also good catalysts for the cyclization of aminoalkynes.[24] For the latter, an alternative mechanism, where the amine is added oxidatively to the zinc center, is not possible.[41] For palladium, the tridentate phosphine ligands used in this study inevitably make the oxidative addition of H−N (or other H−X) more difficult in comparison with bi- or monodentate ligands. Accordingly, the mechanism proposed is not necessarily applicable to hydroamination reactions involving palladium complexes with bi- and monodentate ligands as encountered in other organic syntheses.[16,17,42]

Complex **VI** was identified as the palladium species that occurs in the highest concentration during the palladium-catalyzed cyclization of **1**. Two explanations for the high concentration seem likely: Complex **VI** could be a resting state and not be directly involved in the catalytic cycle, or the subsequent step, protolytic cleavage of the palladium−carbon bond, is the rate-limiting step. If the latter hypothesis were valid, a higher concentration of protons in the catalytic mixture should accelerate the reaction. Therefore, trifluoromethane sulfonic acid was added to the catalytic mixture. With addition of 1 equiv of CF_3SO_3H relative to palladium, the rate of reaction doubled from 243(14) to 435(15) (Figure 4). When higher concentrations of CF_3SO_3H were employed, the rate of reaction increased further; however, the increase in rate was less. For a mixture of **1**:**I**:CF_3SO_3H = 100:1:100 the reaction was complete within 5 min and the rate of reaction could only be estimated (ca. 1800 $mol_{Sub}\cdot(mol_{Cat}\cdot h)^{-1}$). In contrast, even small amounts of a base (here LiN^iPr_2) inhibited the reaction completely.

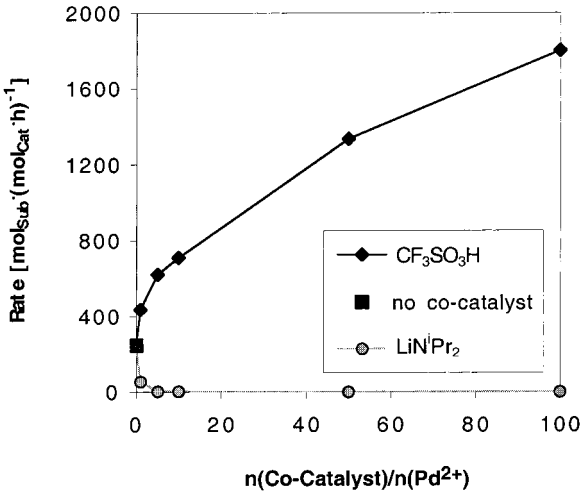


Figure 4. Initial rate of reaction for the cyclization of 6-aminohex-1-yne (**1**) using the catalyst [Pd(Triphos)]$(CF_3SO_3)_2$ (**I**) in the presence of CF_3SO_3H or LiN^iPr_2 as cocatalyst.

These observations confirm the hypothesis that complex **VI** occurs in a high concentration because protolytic cleavage of the palladium−carbon bond is a slow step in the catalytic cycle. It seems likely that the acid leads to faster protonation of the alkenyl-carbon in **VI** and thus facilitates formation of enamine **2** (Scheme 3, A). Rate-limiting cleavage of the metal−carbon bond was

(41) Müller, T. E.; Pleier, A.-K. *J. Chem. Soc., Dalton Trans.* **1998**, *4*, 583.
(42) Hahn, C.; Spiegler, M.; Herdtweck, E.; Taube, R. *Eur. J. Inorg. Chem.* **1999**, 435.

also predicted in a recent theoretical study on hydroamination reactions.[43] However, in the cyclization of **1** the protons could also be involved in two further steps of the catalytic cycle (Scheme 3, B and C).

(i) The substrate initially coordinates via the amine lone pair rather than the alkyne group. Isomerization and coordination of the alkyne is necessary prior to the nucleophilic attack. Reversible protonation of the amine group shifts the equilibrium—which is on the side of the amine—toward coordination of the alkyne.

(ii) Protons catalyze the isomerization of enamines to the corresponding imines. Thus, in the cyclization of **1** the concentration of free intermediate **2** will be lower in acidic conditions. If desorption of **2** from the palladium center is slow, addition of an acid will lead to a faster desorption of the product and acceleration of the overall process.

Conclusions

The activity of palladium complexes for the cyclization of 6-aminohex-1-yne (**1**) to 2-methyl-1,2-dehydropiperidine (**3**) was investigated. The highest activity in the series of complexes studied was observed for [Pd(Triphos)]$(CF_3SO_3)_2$ (**I**). Initial coordination of **1** to the palladium center probably occurs via the amine group. Isomerization and coordination of the alkyne group enables the subsequent nucleophilic attack of the amine lone pair on the CC π-system. This leads to the 2-ammonioalken-1-yl complex **VI**, which was the predominant palladium species (>99%) in the catalytic mixture, as shown by ^{31}P NMR spectroscopy. The high concentration of the complex indicates that the subsequent step, protolytic cleavage of the Pd−C bond in **VI**, is rate limiting. Addition of trifluoromethanesulfonic acid to the catalytic mixture drastically accelerated the overall reaction. Thus, protons act as cocatalysts in the palladium-catalyzed addition of the amine N−H bond to the CC triple bond in **1**. In summary, it seems likely that the key step of the reaction is the coordination of the triple bond to the metal center, which enables nucleophilic attack of the free electron pair on nitrogen on the CC π-system. The findings presented in this study are in excellent agreement with a recent theoretical study on the molecular background of hydroamination reactions.[43]

Experimental Section

Materials and Methods. All reactions involving air- and/or water-sensitive compounds were performed using standard Schlenk techniques. Solvents were obtained dry from Aldrich. Catalysts and other chemicals not described in the Experimental Section were purchased from Aldrich, Fluka, or Strem and used as received. The compounds 6-aminohex-1-yne (**1**),[41] [Pd(PP)]$(NO_3)_2$ (**IV**),[41] and [Pd(Triphos)]$(CH_3CO_2)_2$ (**V**) [24] were prepared as described in the respective reference.

Physical and Analytical Methods. ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded on a Bruker AM 400 and referenced in ppm relative to the solvent shift[44] or tetramethylsilane. GC analyses were performed on a HP 5730A gas chromatograph equipped with a Supelco Amine (3m × 1/8 S.S., 25% CW-400 + 2.5% KOH on Chrom-W-AW) column. Infrared spectra were obtained on a Perkin-Elmer 2000 FT-IR spectrometer from solutions in $CDCl_3$ or KBr disks. Mass spectroscopic analyses were performed on a Finnigan MAT 311A by the fast atom bombardment (FAB) method. Elemental analyses were performed by the Microanalytical Laboratory of the Technische Universität München. Isothermal titration calorimetry was performed using a MCS-JTC instrument (Microcal, MA) and applying corrections obtained from blind titrations to account for the heats of dilution.

Preparations. [Pd(Triphos)]$(CF_3SO_3)_2$ (I). The complex [$PdCl_2$(COD)] (40 mg, 0.14 mmol) was dissolved in CH_2Cl_2 (10 cm^3), and a solution of bis(2-diphenylphosphinoethyl)phenylphosphine (Triphos, 75 mg, 0.14 mmol) in CH_2Cl_2 (5 cm^3) added. The volatiles were removed in vacuo, the residue of [PdCl(Triphos)]Cl was redissolved in CH_2Cl_2 (10 cm^3), a solution of $AgCF_3SO_3$ (72 mg, 0.28 mmol) in CH_3CN (2 cm^3) was added, and the mixture was stirred at room temperature overnight. A white precipitate formed, which was removed by filtration, and the volume of the filtrate was reduced in a partial vacuum. Addition of Et_2O yielded a light yellow solid, which was recrystallized from CH_2Cl_2/pentane and dried in vacuo.

Yield: 0.11 g, 85%. Found: C, 46.2; H, 3.5. Calcd for $C_{36}H_{33}F_6O_6P_3PdS_2$: C, 46.2; H, 3.5. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 116.7 (s, 1P, PPh), 52.7 (s, 2P, PPh_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$): 134.7 to 123.9 (mm, Ph), 29.8 (d, $^1J(^{13}C, ^{31}P)$ 35 Hz, CH_2), 28.4 (t, $^{1/3}J(^{13}C, ^{31}P)$ 17 Hz, CH_2). ^1H NMR ($CDCl_3$): 8.19 (dd, 2H, Ph), 7.74−7.48 (mm, 23H, Ph), 3.37 (sept, 2H, CH_a), 3.11 (dd, $^2J(^1H, ^{31}P)$ 55 Hz, $^3J(^1H, ^{31}P)$ 15 Hz, $CH_{a'}$), 3.00 (m, 2H, CH_b), 2.25 (b, 2H, $CH_{b'}$). IR: 3058 (m), 2965 (w), 2920 (w), 1485 (m), 1437 (s), 1324 (m), 1266 (vs), 1158 (s), 1105 (s), 1030 (vs), 999 (m), 830 (m), 747 (m), 725 (m), 709 (m), 690 (m), 637 (vs), 572 (m) cm^{-1}. *m/z* (FAB): 789 ($M^+ - CF_3SO_3$), 640 ($M^+ - 2CF_3SO_3$).

[Pd(PPN)]$(CF_3SO_3)_2$ (II). The complex [$PdCl_2$(COD)] (52 mg, 0.18 mmol) was dissolved in CH_2Cl_2 (10 cm^3) and a solution of *N*,*N*-dimethyl-1-[1′,2-bis(diphenylphosphino)ferrocenyl]-ethylamine (PPN, 0.11 g, 0.18 mmol) in CH_2Cl_2 (5 cm^3) added. The volatiles were removed in vacuo, the residue redissolved in CH_2Cl_2, a solution of $AgCF_3SO_3$ (93 mg, 0.36 mmol) in CH_3CN (5 cm^3) added, and the mixture stirred for 1 h. The mixture was filtered and the volume of the filtrate reduced in a partial vacuum. The product was precipitated with Et_2O, recrystallized from CH_2Cl_2/pentane, and dried in vacuo.

Yield: 0.13 g, 70% black microcrystals. Found: C, 44.4; H, 3.7; N, 1.5. Calcd for $C_{41}H_{38}Cl_2F_6FeNO_6P_2PdS_2$: C, 44.2; H, 3.4; N, 1.3. $^{31}P\{^1H\}$ NMR (CD_3CN/CD_3NO_2): 54.2 (s), 48.9 (s). ^1H NMR (CD_3CN): 7.7−7.3 (mm, 25H, Ph), 4.2 (m, 7H, Cp), 2.7 (m, 6H, NMe_2), 1.7 (m, 3H, Me). IR: 3058 (w), 1481 (w), 1437 (s), 1279 (vs), 1256 (vs), 1166 (vs), 1120 (w), 1098 (m), 1030 (vs), 998 (w) cm^{-1}. *m/z* (FAB): 881 ($M^+ - CF_3SO_3$).

[Pd(PNP)]$(CF_3SO_3)_2$·CH_3CN (III). The complex [$PdCl_2$(COD)] (0.13 g, 0.46 mmol) was dissolved in CH_2Cl_2 (25 cm^3), and a solution of R(+)-*N*,*N*-bis(2-diphenylphosphinoethyl)-1-phenylethylamine (PNP, 0.25 g, 0.46 mmol) in CH_2Cl_2 (10 cm^3) was added. The volatiles were removed in vacuo, the residue redissolved in CH_2Cl_2, a solution of $AgCF_3SO_3$ (0.12 g, 0.46 mmol) in CH_3CN (5 cm^3) added, and the mixture stirred for 1 h. The latter part of the procedure was repeated adding a solution of $AgCF_3SO_3$ (0.12 g, 0.46 mmol) in CH_3CN (5 cm^3) and stirring the mixture for 1 h. The mixture was then filtered and the volume of the filtrate reduced in a partial vacuum. The product was precipitated with Et_2O, recrystallized from CH_2Cl_2/pentane, and dried in vacuo.

Yield: 0.37 g, 85% yellow powder. Found: C, 48.4; H, 4.1; N, 2.4. Calcd for $C_{40}H_{40}F_6N_2O_6P_2PdS_2$: C, 48.5; H, 4.1; N, 2.8. $^{31}P\{^1H\}$ NMR (CD_3CN): 42.0(0.5), 43.4(0.5), $J(^{31}P,^{31}P) = -91.8$-(12.4). ^{19}F NMR (CD_3CN): −16.5 (s). $^{13}C\{^1H\}$ NMR (CD_3CN): 137.7−129.5 (mm, Ph), 68.6 (s), 67.8 (s), 63.6 (s), 58.9 (s), 39.5 (s), 31.1 (s), 29.6 (s), 24.5 (s), 23.6 (s), 14.3 (s), 13.2 (s), 11.3

(43) Senn, H. M.; Blöchl, P. E.; Togni, A. *J. Am. Chem. Soc.* **2000**, *122*, 4098.
(44) Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.

Table 4. Crystallographic Data for I·$CHCl_3$

chem formula	$C_{35}H_{33}F_3O_3P_3PdS$, CF_3O_3S, $CHCl_3$
fw	1058.46
color/shape	yellow/fragment
cryst size (mm)	0.28 × 0.25 × 0.15
cryst syst	monoclinic
space group	$P2_1/n$ (No. 14)
a (Å)	10.0166(1)
b (Å)	26.7427(5)
c (Å)	16.6381(3)
β (deg)	104.373(1)
V (Å^3)	4317.4(1)
Z	4
T (K)	123
ρ_{calcd} (g cm^{-3})	1.628
μ (mm^{-1})	0.893
F_{000}	2128
θ-range (deg)	1.98−25.37
data collected (h,k,l)	±12, ±32, ±20
no. of reflns collected	29 015
no. of indep rflns/R_{int}	7850 (all)/0.0312
no. of obsd rflns ($I>2\sigma(I)$)	7182 (obsd)
no. of params refined	659
R1 (obsd/all)	0.0308/0.0352
wR2 (obsd/all)	0.0679/0.0699
GOF (obsd/all)	1.052/1.052
max/min $\Delta\rho$ (e Å^{-3})	+0.94 /−0.75

(s). ^{1}H NMR (CD_3CN): 8.05−7.18 (mm, 25H, Ph), 4.38 (q, 1H, CH), 4.20 (q, 1H, CH_aH_b), 3.85 (b, 1H, CH_aH_b), 3.67 (m, 2H, CH_aH_b), 3.41 (m, 2H, CH_aH_b), 3.20 (m, 1H, CH_aH_b), 3.01 (m, 1H, CH_aH_b), 2.20 (s, 3H, CH_3CN), 1.63 (d, 3H, CH_3). IR: 3057 (m), 2990 (m), 2929 (m), 2328 (m), 2300 (m), 1484 (m), 1455 (m), 1436 (s), 1258 (vs), 1224 (s), 1157 (vs), 1104 (s), 1030 (vs), 997 (s) cm^{-1}. m/z (FAB): 800 ($M^+ - CF_3SO_3$), 651 ($M^+ - 2\ CF_3SO_3$).

X-ray Structure Determination of Complex I·$CHCl_3$. Details of the X-ray experiment, data reduction, and final structure refinement calculation are summarized in Table 4. Crystals of complex **I**·$CHCl_3$ suitable for X-ray structure determination were grown by slow evaporation of a saturated solution of **I** in chloroform. Preliminary examination and data collection were carried out on a kappa-CCD system (Nonius Mach3) equipped with a rotating anode (NONIUS FR591; 50 kV; 60 mA; 3.0 kW) and graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Data collection was performed at 123 K with an exposure time of 48 s per film (φ- and ω-scan, oscillation modus, $\Delta\varphi/\Delta$ = 1.0°). A total of 29 015 reflections were collected.[45] After merging, 7850 independent reflections remained and were used for all calculations. The data were corrected for Lorentz and polarization effects. Corrections for absorption and decay effects were not applied. The unit cell parameters were obtained by full-matrix least-squares refinements of 24 372 reflections with the program Scalepack.[46] The structure was solved by a combination of direct methods and difference Fourier syntheses.[47] All non-hydrogen atoms of the asymmetric unit were refined with anisotropic thermal displacement parameters. All hydrogen atoms were found in the difference Fourier map and refined freely with individual isotropic thermal displacement parameters. Full-matrix least-squares refinements were carried out by minimizing $\sum w(F_o^2 - F_c^2)^2$ with the SHELXL-97 weighting scheme and stopped at maximum shift/err < 0.001.[48] Neutral atom scattering factors for all atoms and anomalous dispersion corrections for the non-hydrogen atoms were taken from *International Tables for Crystallography*.[49] All other calculations (including ORTEP graphics) were done with the program PLATON.[50] Calculations were performed on a PC workstation (Intel Pentium II) running LINUX.

Catalysis. In a typical procedure, a mixture of [Pd(Triphos)]-$(CF_3SO_3)_2$ (3.3 mg, 3.5 μmol) and toluene (10 cm^3) was heated at reflux and the reaction started by addition of 6-aminohex-1-yne[41] (**1**) (40 mm^3, 0.35 mmol). At regular intervals, small samples were taken and analyzed by gas chromatography. For the experiments given in Figure 2 3.3 mg of [Pd(Triphos)]$(CF_3SO_3)_2$, 3.6 mg of [Pd(PPN)]$(CF_3SO_3)_2$, 3.3 mg of [Pd(PNP)]$(CF_3SO_3)_2$, 3.0 mg of [Pd(PP)]$(CF_3SO_3)_2$, and 2.7 mg of [Pd(Triphos)]-$(CH_3CO_2)_2$ were used. For the experiments given in Figure 4, the same amounts (3.3 mg of [Pd(Triphos)]$(CF_3SO_3)_2$, 40 mm^3 of 6-aminohex-1-yne, and 15 cm^3 of toluene) were used, and the cocatalyst trifluoromethanesulfonic acid (3.5, 18, 35, 176, 351 μmol) or LiN^iPr_2 (3.5, 18, 35, 176, 351 μmol) was added to the catalytic mixture within 2 min of the reaction being started.

In Situ IR Experiments. Mixture a. The complex [Pd-(triphos)]$(CF_3SO_3)_2$ (7.3 mg, 7.8 × 10^{-3} mmol) was dissolved in a solution of 6-aminohex-1-yne (8.8 × 10^{-4} cm^3, 7.8 × 10^{-3} mmol) in $CDCl_3$ (0.21 cm^3) and the IR spectrum taken against $CDCl_3$ as the background.

Mixture b. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (7.2 mg, 7.7 × 10^{-3} mmol) was dissolved in a solution of 2-methyl-1,2-dehydropiperidine (8.7 × 10^{-4} cm^3, 7.7 × 10^{-3} mmol) in $CDCl_3$ (0.20 cm^3) and the IR spectrum taken against $CDCl_3$ as the background.

Mixture c. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (7.4 mg, 7.9 × 10^{-3} mmol) was dissolved in a solution of *n*-hexylamine (1.0 × 10^{-3} cm^3, 7.9 × 10^{-3} mmol) in $CDCl_3$ (0.21 cm^3), and the IR spectrum taken against $CDCl_3$ as the background.

Mixture d. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (7.1 mg, 7.6 × 10^{-3} mmol) was dissolved in a solution of 1-heptyne (1.0 × 10^{-3} cm^3, 7.6 × 10^{-3} mmol) in $CDCl_3$ (0.20 cm^3) and the IR spectrum taken against $CDCl_3$ as the background.

In Situ NMR Experiments. Mixture 1. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 × 10^{-3} mmol) was dissolved in $CDCl_3$ (0.6 cm^3) and ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra taken.

^{1}H NMR ($CDCl_3$): 8.19 (dd, 2H, Ph), 7.74−7.48 (mm, 23H, Ph), 3.37 (sept, 2H, CH_a), 3.11 (dd, ^2J(^{1}H, ^{31}P) 55 Hz, ^3J(^{1}H, ^{31}P) 15 Hz, $CH_{a'}$), 3.00 (m, 2H, CH_b), 2.25 (b, 2H, $CH_{b'}$). ^{13}C-{^{1}H} NMR ($CDCl_3$): 134.7 to 123.9 (mm, Ph), 29.8 (d, ^1J(^{13}C, ^{31}P) 35 Hz, CH_2), 28.4 (t, $^{1/3}J$(^{13}C, ^{31}P) 17 Hz, CH_2). ^{31}P{^{1}H} NMR ($CDCl_3$): δ 116.7 (s, 1P, PPh), 52.7 (s, 2P, PPh_2).

Mixture 2. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 × 10^{-3} mmol) was dissolved in $CDCl_3$ (0.5 cm^3), 6-aminohex-1-yne (6.3 × 10^{-4} cm^3, 5.5 × 10^{-3} mmol) in $CDCl_3$ (0.1 cm^3) added, and a ^{31}P{^{1}H} NMR spectrum taken.

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$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 109.5 (s, 1P, PPh), 53.9 (s, 2P, PPh_2), small signals at 116.7, 102.7, 52.7, and 45.2.

Mixture 3. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (0.5 cm^3), 6-aminohex-1-yne (6.3 $\times$ 10^{-2} cm^3, 0.55 mmol) in $CDCl_3$ (0.1 cm^3) added, and ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra taken.

^1H NMR ($CDCl_3$): δ 2.73 (t, 2H, **1**, CH_2-N), 2.21 (dt, 2H, **1**, $CH_2-C{+}C$), 1.96 (t, 1H, **1**, HC+C), 2.32 (s, 2H, **1**, NH_2), 1.58 (q, 4H, **1**, CH_2-CH_2), small signals due to **2**, **3**, and **VI**. $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 84.6 (s, **1**, C2), 68.8 (s, **1**, C1), 41.7 (s, **1**, C6), 32.6 (s, **1**, C5), 26.1 (s, **1**, C4), 18.5 (s, **1**, C3), small signals due to **2**, **3**, and **VI**. $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 102.8 (t, $J(^{31}P, ^{31}P)$ = 17.7 Hz, 1P, PPh), 45.2 (d, $J(^{31}P, ^{31}P)$ = 17.8 Hz, 2P, PPh_2).

Mixture 4. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (0.5 cm^3), 2-methyl-1,2-dehydropiperidine (6.3 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) in $CDCl_3$ (0.1 cm^3) added, and a $^{31}P\{^1H\}$ NMR spectrum taken.

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 109.5 (s, 1P, PPh), 53.8 (s, 2P, PPh_2), small signals at 116.7 and 52.7.

Mixture 5. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (0.5 cm^3), *n*-hexylamine (7.3 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) in $CDCl_3$ (0.1 cm^3) added, and a $^{31}P\{^1H\}$ NMR spectrum taken.

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 108.7 (s, 1P, PPh), 53.9 (s, 2P, PPh_2), small signals at 116.8 and 53.0.

Mixture 6. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (1 cm^3), hept-1-yne (7.3 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) and triethylamine (7.7 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) were added, and ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were taken.

^1H NMR ($CDCl_3$): δ 7.94−7.85 (m, 9H, Ph), 7.46−7.36 (m, 16H, Ph), 3.28 (m, 4H, PCH_2), 3.11 (q, $J(^1H, ^1H)$ = 7.2 Hz, 6H, NCH_2), 2.20 (m, 4H, PCH_2), 2.10 (m, 2H, CH_2), 1.94 (s, 1H, CH), 1.31 (t, $J(^1H, ^1H)$ = 7.5 Hz, 9H, NCH_3), 1.11 (m, 4H, CH_2), 0.81 (q, $J(^1H, ^1H)$ = 7.7 Hz, 2H, CH_2), 0.67 (t, $J(^1H, ^1H)$ = 7.1 Hz, 3H, CH_3). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 132.2−129.5 (mm, Ph), 47.2 (s, NCH_2), 31.4 (s, CH_2), 30.0 (s, CH_2), 22.7 (s, CH_2), 21.7 (s, CH_2), 14.4 (s, CH_3), 9.1 (s, NCH_2CH_3). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 102.9 (s, 1P, PPh), 45.3 (s, 2P, PPh_2), small signals at 116.8, 112.7, 52.5, and 47.5.

Mixture 7. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (1 cm^3), triethylamine (7.7 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) and hept-1-yne (7.3 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) were added, and a $^{31}P\{^1H\}$ NMR spectrum was taken.

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 103.0 (s, 1P, PPh), 45.3 (s, 2P, PPh_2), small signals at 112.6 and 47.5.

Mixture 8. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (0.5 cm^3), heptyne (7.3 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) in $CDCl_3$ (0.1 cm^3) added, and a $^{31}P\{^1H\}$ NMR spectrum taken.

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 116.7 (s, 1P, PPh), 52.7 (s, 2P, PPh_2).

Mixture 9. The complex [Pd(triphos)]$(CF_3SO_3)_2$ (5.2 mg, 5.5 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (1 cm^3), triethylamine (7.7 $\times$ 10^{-4} cm^3, 5.5 $\times$ 10^{-3} mmol) added, and a $^{31}P\{^1H\}$ NMR spectrum taken.

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 112.3 (s, 1P, PPh), 47.2 (s, 2P, PPh_2).

Mixture 10. The complex [Pd(triphos)]$(CH_3CO_2)_2$ (2.2 mg, 2.9 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (0.6 cm^3), and ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were taken.

^1H NMR ($CDCl_3$): 8.34 (dd, 2H, Ph), 7.85 (quart, 4H, Ph), 7.70 (quart, 4H, Ph), 7.60−7.44 (mm, 15H, Ph), 5.30 (s, 2H, CH_2Cl_2), 4.08 (sept, 2H, CH_a), 3.13 (dd, $^2J(^1H, ^{31}P)$ 58 Hz, $^3J(^1H, ^{31}P)$ 15 Hz, $CH_{a'}$), 2.75 (m, 2H, CH_b), 2.22 (b, 2H, $CH_{b'}$). $^{13}C\{^1H\}$ NMR ($CDCl_3$): 134.6−125.0 (mm, Ph), 30.3 (td, $^1J(^{13}C, ^{31}P)$ 33 Hz, $^{2/3}J(^{13}C, ^{31}P)$ 6 Hz, $PhP-CH_2$), 28.6 (dt, $^{1/3}J(^{13}C, ^{31}P)$ 16 Hz, $^2J(^{13}C, ^{31}P)$ 8 Hz, Ph_2P-CH_2). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 112.3 (s, 1P, PPh), 47.2 (s, 2P, PPh_2).

Mixture 11. The complex [Pd(triphos)]$(CH_3CO_2)_2$ (2.2 mg, 2.9 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (0.5 cm^3), 6-aminohex-1-yne (3.3 $\times$ 10^{-4} cm^3, 2.9 $\times$ 10^{-3} mmol) in $CDCl_3$ (0.1 cm^3) added, and a $^{31}P\{^1H\}$ NMR spectrum taken.

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 112.8 (s, 1P, PPh), 47.4 (s, 2P, PPh_2).

Mixture 12. The complex [Pd(triphos)]$(CH_3CO_2)_2$ (2.2 mg, 2.9 $\times$ 10^{-3} mmol) was dissolved in $CDCl_3$ (0.5 cm^3), 6-aminohex-1-yne (3.3 $\times$ 10^{-2} cm^3, 0.29 mmol) in $CDCl_3$ (0.1 cm^3) added, and a $^{31}P\{^1H\}$ NMR spectrum taken.

$^{31}P\{^1H\}$ NMR ($CDCl_3$): δ 102.7 (t, $J(^{31}P, ^{31}P)$ = 17.8 Hz, 1P, PPh), 45.3 (d, $J(^{31}P, ^{31}P)$ = 14.9 Hz, 2P, PPh_2), small signals at 112.8 and 47.3.

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Supporting Information Available: Tables of crystal and data collection parameters, atomic coordinates, bond lengths, bond angles, and thermal displacement parameters for **I**·$CHCl_3$ in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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