Formation of Palladium Bis(amine) Complexes from Reaction of Amine with Palladium Tris(*o*-tolyl)phosphine Mono(amine) Complexes

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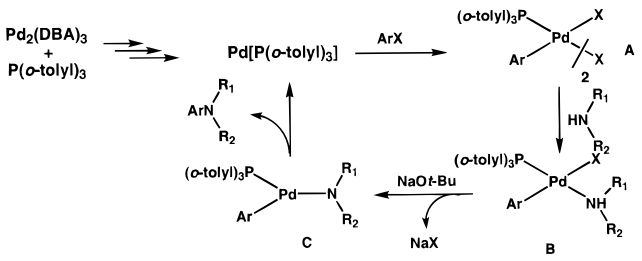
Palladium mono(benzylamine) complexes Pd[P(*o*-tolyl)$_3$](*p*-$C_6H_4CMe_3$)[H_2NBn]X (X = Cl (**7**), Br (**8**), I (**14**)) react reversibly with benzylamine in $CDCl_3$ at 25 °C via P(*o*-tolyl)$_3$ displacement to generate the corresponding bis(amine) derivatives *trans*-Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$X (X = Cl (**17**), $K_{eq} = 0.18 \pm 0.02$; Br (**16**), $K_{eq} = 0.14 \pm 0.01$; I (**18**), $K_{eq} = 0.10 \pm 0.01$). Complexes **16**−**18** were isolated from reaction of the palladium aryl halide dimers {Pd[P(*o*-tolyl)$_3$](*p*-$C_6H_4CMe_3$)(μ-X)}$_2$ (X = Cl (**4**), Br (**5**), I (**6**)) and excess benzylamine as the corresponding mono(benzylamine) solvate Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$X·H_2NBn (X = Br (**16**·H_2NBn), Cl (**17**·H_2NBn), I (**18**·H_2NBn)). IR and ^{1}H NMR spectroscopy of **16**·H_2NBn indicated the presence of N−H···X (X = N, Br, Pd) hydrogen bonds in both the solid state and solution. The equilibrium constant for the formation of **16** and P(*o*-tolyl)$_3$ from **8** and benzylamine ranged from 0.066 ± 0.005 in CD_2Cl_2 to 3.6 ± 0.3 in THF-d_8 and in C_6D_6 ranged from 0.90 ± 0.07 at 25 °C to 0.44 ± 0.04 at 77 °C ($\Delta G°_{298\ K} = 0.06 \pm 0.01$ kcal mol^{-1}; $\Delta H°_{298\ K} = -2.8 \pm 0.1$ kcal mol^{-1}; $\Delta S°_{298\ K} = -9 \pm 1$ eu). The equilibrium constants for the formation of the bis(amine) complexes Pd(*p*-$C_6H_4CMe_3$)[amine]$_2$Br from the reaction of Pd[P(*o*-tolyl)$_3$](*p*-$C_6H_4CMe_3$)[amine]Br and amine decreased in the order phenethylamine ≈ cyclohexylamine ≈ benzylamine ≈ (4-methylbenzyl)amine ≫ piperidine ≫ *N*-methylbenzylamine.

Introduction

We have shown that mixtures of $Pd_2(DBA)_3$ or Pd(DBA)$_2$ (DBA = dibenzylideneacetone) and P(*o*-tol)$_3$ (*o*-tol = *o*-tolyl) catalyze the conversion of aryl bromides[1] or aryl iodides[2] to anilines via reaction with free amine and sodium *tert*-butoxide.[3] In contrast to related palladium-catalyzed C−C bond-forming reactions,[4] aryl iodides required more forcing conditions and produced lower yields of anilines than did aryl bromides. In addition, while the cross-coupling protocol is effective in the case of unbranched secondary amines such as *N*-methylbenzylamine, both bulky secondary amines such as diisopropylamine and primary amines such as benzylamine produce low yields (∼0−25%) of cross-coupled product.[5]

The $Pd_2(DBA)_3$/P(*o*-tol)$_3$-catalyzed amination of aryl halides is believed to proceed by the initial oxidative addition of the aryl halide to the palladium mono(phosphine) complex Pd[P(*o*-tol)$_3$] to form the palladium halide dimer {Pd[P(*o*-tol)$_3$](Ar)(μ-X)}$_2$ (Scheme 1).[6] Reaction of the halide dimer with free amine then forms the corresponding palladium amine monomer Pd[P(*o*-tol)$_3$](Ar)[HNR_1R_2]X.[7] Deprotonation and reductive elimination from the three-coordinate palladium amido complex Pd[P(*o*-tol)$_3$](Ar)[NR_1R_2]X[6,8] forms the corresponding aniline derivative $ArNR_1R_2$ and regenerates the catalytically active mono(phosphine) complex.[9]

Scheme 1



In conjunction with our synthetic studies, we have investigated the stoichiometric reactions of the palladium tris(*o*-tolyl)phosphine halide dimers with amines in an effort to gain insight into the corresponding palladium-catalyzed amination of aryl halides.[10−12] For example, we have shown that the palladium halide dimers {Pd[P(*o*-tol)$_3$](*p*-C_6H_4Me)(μ-X)}$_2$ (X = Cl (**1**), Br (**2**), I (**3**)) react with *N*-benzylmethylamine to generate the corresponding 1:1 amine adducts Pd[P(*o*-tol)$_3$](*p*-

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(2) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 1133.

(3) See also: (a) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609. (b) Wolfe, J. P.; Rennels, R. A.; Buchwald, S. L. *Tetrahedron* **1996**, *20*, 7525.

(4) (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (c) de Meijere, A.; Meyer, F. E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379.

(5) We have recently found that mixtures of $Pd_2(DBA)_3$ and BINAP effectively cross-couple aryl bromides with primary amines: Wolfe, J. P.; Wagaw, S.; Buchwald, S. L. *J. Am. Chem. Soc.*, in press.

(6) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969.

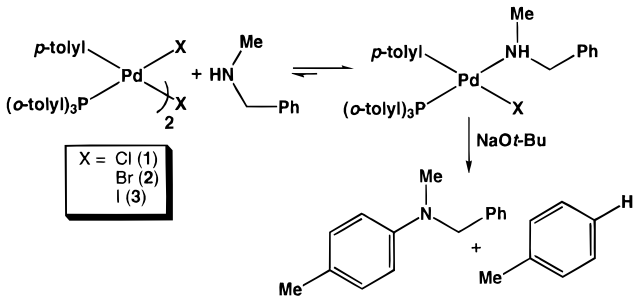
(7) Paul, F.; Patt, J.; Hartwig, J. F. *Organometallics* **1995**, *14*, 3030.

(8) (a) Loar, M. K.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4174. (b) Moravskiy, A.; Stille, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 4182. (c) Morrell, D. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1975**, *97*, 7262. (d) Ozawa, F.; Ito, T.; Yamamoto, A. *J. Am. Chem. Soc.* **1980**, *102*, 6457. (e) McCarthy, T. J.; Nuzzo, R. G.; Whitesides, G. M. *J. Am. Chem. Soc.* **1981**, *103*, 1676. (f) Komiya, S.; Albright, T. A.; Hoffmann, R.; Kochi, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 7255. (g) Komiya, S.; Albright, T. A.; Hoffmann, R.; Kochi, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 8440. (h) Tatsumi, K.; Hoffmann, R.; Yamamoto, A.; Stille, J. K. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1857.

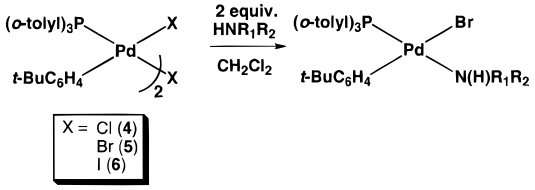
(9) Hartwig, J. F.; Paul, F. *J. Am. Chem. Soc.* **1995**, *117*, 5373.

S0276-7333(96)00316-0 CCC: $12.00

Scheme 2



Scheme 3

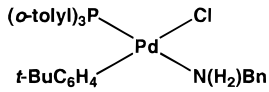
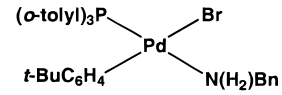
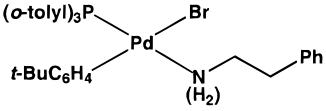
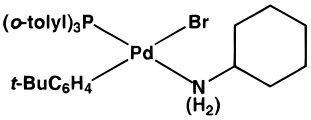
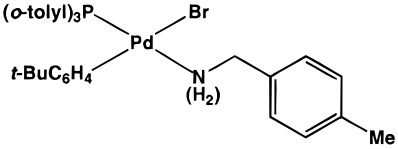
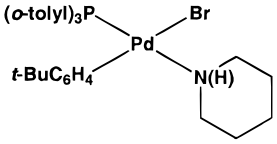
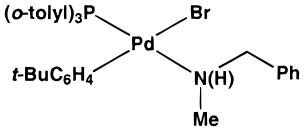
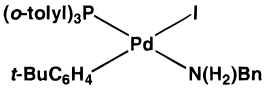


$C_6H_4Me)[HN(Me)Bn]X$ (X = Cl, Br, I) (Scheme 2).[10] These mono(amine) complexes react with sodium *tert*-butoxide to form mixtures of *N*-methyl-*N*-benzyl-*p*-toluidine and toluene.[11] We have also shown that the thermodynamics of the formation of 1:1 palladium amine adducts from palladium halide dimer and free amine were dependent on both the bridging halide ligand and the amine.[12] Because primary amines represent a particularly challenging substrate for the $Pd_2(DBA)_3$/P(*o*-tol)$_3$-catalyzed amination reaction,[5] we have continued to investigate the reactions of palladium aryl halide dimers with primary amines. Here we report that palladium mono(primary amine) complexes react reversibly with excess primary amine to form palladium bis(primary amine) complexes.

Results

Synthesis of Palladium Mono(amine) Complexes. The palladium tris(*o*-tolyl)phosphine mono(amine) complexes employed in this study were synthesized by reaction of the appropriate palladium *tert*-butylphenyl halide dimer {Pd[P(*o*-tol)$_3$](*p*-$C_6H_4CMe_3$)(μ-X)}$_2$ (X = Cl (**4**), Br (**5**), I (**6**)) with 2 equiv of the desired amine, as has been previously described (Scheme 3, Table 1).[7,10] By this procedure, the mono(amine) adducts Pd[P(*o*-tol)$_3$](*p*-$C_6H_4CMe_3$)[H_2NBn]X (X = Cl (**7**), Br (**8**)), Pd[P(*o*-tol)$_3$](*p*-$C_6H_4CMe_3$)[$H_2NCH_2CH_2$Ph]Br (**9**), Pd[P(*o*-tol)$_3$](*p*-$C_6H_4CMe_3$)[H_2NCy]Br (**10**), Pd[P(*o*-tol)$_3$](*p*-C_6H_4-CMe_3)[HNCH_2-4-C_6H_4Me]Br (**11**), Pd[P(*o*-tol)$_3$](*p*-C_6H_4-CMe_3)[piperidine]Br (**12**), and Pd[P(*o*-tol)$_3$](*p*-$C_6H_4CMe_3$)-[HN(Me)Bn]Br (**13**) were isolated in good yield. Reaction of the palladium aryl iodide dimer **6** with 2 equiv of benzylamine led to the exclusive formation of the mono(amine) derivative Pd[P(*o*-tol)$_3$](*p*-$C_6H_4CMe_3$)[H_2-NBn]I (**14**), as determined by ^{1}H and ^{31}P NMR spectroscopy. However, attempts to isolate **14** from the corresponding preparative-scale reaction produced a mixture of products, as evidenced by the presence of several *tert*-butyl peaks in the ^{1}H NMR spectrum of the isolated solid. Attempts to isolate or spectroscopically identify the mono(amine) complex Pd[P(*o*-tol)$_3$](*p*-C_6H_4-CMe_3)[NH_3]Br (**15**) from treatment of a solution of **5** in C_6D_6 with a 0.5 M solution of NH_3 in dioxane were unsuccessful.

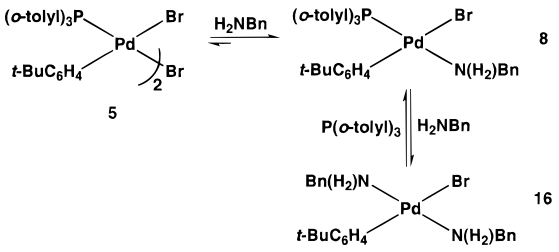
Table 1. Palladium Mono(amine) Complexes Formed from Reaction of Palladium Aryl Halide Dimers with Amine

Cmpd	structure	isolated yield
7		94
8		54
9		94
10		85
11		64
12		80
13		94
14		–

Conversion of Palladium Mono(amine) Complexes to Palladium Bis(amine) Complexes. Excess primary amine displaced the P(*o*-tol)$_3$ ligand from palladium tris(*o*-tolyl)phosphine mono(amine) complexes to form the corresponding bis(amine) complexes. For example, excess benzylamine (0.25 M) was added to a solution of palladium aryl bromide dimer **5** (~8 mM) in C_6D_6, and the resulting solution was monitored periodically by ^{1}H NMR spectroscopy at 25 °C. The initial spectrum revealed quantitative conversion of **5** to the mono(amine) complex **8**, as indicated by the appearance of a new *t*-Bu peak at δ 1.17 (Scheme 4). The *t*-Bu resonance corresponding to **8** slowly disappeared ($t_{1/2}$ = ~3 h)[13] with the formation of a 1:1 ratio of resonances corresponding to the equivalent methyl groups of free P(*o*-tol)$_3$ at δ 2.40 and a *t*-Bu group assigned to the

(10) Widenhoefer, R. A.; Zhong, H. A.; Buchwald, S. L. *Organometallics* **1996**, *15*, 2745.
(11) Widenhoefer, R. A.; Zhong, H. A.; Buchwald, S. L. *Abstracts of Papers*, 210th National Meeting of the American Chemical Society, Chicago, IL, Aug 1995; American Chemical Society: Washington, DC, 1995; INOR 70.
(12) Widenhoefer, R. A.; Buchwald, S. L. *Organometallics* **1996**, *15*, 2755.
(13) Kinetic studies have been performed: Widenhoefer, R. A.; Zhong, H. A.; Buchwald, S. L. Manuscript in preparation.

Scheme 4

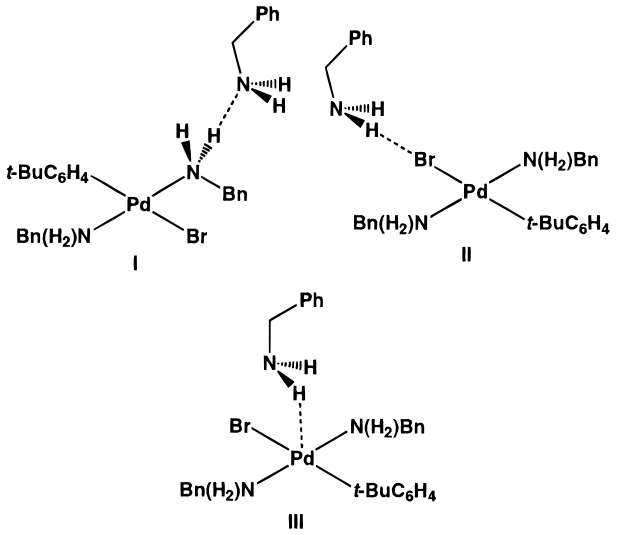


palladium bis(benzylamine) complex **16** at δ 1.27. No additional products or decomposition of the palladium amine complexes was observed throughout complete conversion of **8** to **16**. Addition of P(*o*-tol)$_3$ to solutions of **16** in C_6D_6 regenerated **8** and free benzylamine.

The ^{1}H NMR spectrum of **16** ($\sim$10 mM) displayed broad triplets at δ 3.81 (J = 7.1 Hz) and δ 2.4 (J = $\sim$7 Hz), corresponding to the benzylic protons and the amino protons, respectively, of the benzylamine ligands. Comparison of the intensity of these triplets to the intensity of the single *tert*-butyl resonance at δ 1.27 established the 2:1 ratio of benzylamine ligands to *tert*-butyl groups, while the equivalence of the benzylamine ligands is consistent with their *trans* orientation. Palladium bis(amine) complexes of the form Pd(amine)$_2$X$_2$ (X = halide, acetate) typically possess *trans* amine ligands,[14] and although *cis* palladium(II) bis(amine) complexes can be generated under certain conditions,[15] *cis* to *trans* isomerization is typically facile.[16] Addition of D_2O to a solution of **16** in C_6D_6 resulted in rapid deuterium exchange of the amino protons of the benzylamine ligands, as indicated by the disappearance of the δ 2.4 resonance and loss of coupling to the benzylic resonance at δ 3.81 in the ^{1}H NMR spectrum. The solution IR spectrum of **16** ($CDCl_3$) displayed bands at 3332 and 3274 cm^{-1} assigned to the antisymmetric and symmetric N−H stretching modes of the benzylamine ligands, respectively.[17]

In a preparative-scale reaction, a solution of palladium aryl bromide dimer **5** and excess benzylamine ($\sim$20 equiv, $\sim$1 M) in CH_2Cl_2 was stirred at room temperature for 12 h to give a clear solution. Evaporation of solvent and crystallization of the resulting yellow oil from THF/pentane at −30 °C gave the bis(amine) complex **16** as the mono(benzylamine) solvate Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$Br·H_2NBn (**16**·H_2NBn) in 99% yield as a white fibrous solid. Elemental analysis (C, H, N) established the 3:1 ratio of benzylamine units to PdArBr groups. The solid-state IR spectrum (KBr) displayed a broad N−H stretch at 3198 cm^{-1} with a shoulder at 3295 cm^{-1}, consistent with the presence of both free and

Chart 1. Potential Hydrogen-Bonding Modes in 16·H_2NBn



hydrogen-bonded NH_2 groups.[17] The solvated bis(amine) complex **16**·H_2NBn dissolved in C_6D_6 to form a 1:1 ratio of bis(amine) complex **16** and free benzylamine, as determined by ^{1}H NMR spectroscopy.

There are several potential hydrogen-bonding interactions involving the NH_2 groups in crystalline **16**·H_2NBn, which may account for the observed solid-state IR spectrum. For example, the outer-sphere benzylamine molecule may function as a hydrogen bond acceptor to generate an N−H···N hydrogen bond with a ligated benzylamine molecule (**I**; Chart 1). In addition, an outer-sphere or ligated benzylamine molecule may form an N−H···Br hydrogen bond with a palladium bromide ligand (**II**). Similarly, an outer-sphere or ligated benzylamine molecule may form an N−H···Pd hydrogen bond with a filled palladium d orbital (**III**). Each type of hydrogen bonding (**I**−**III**) has been previously observed in platinum dichloride bis(amine) complexes.[17] However, our data are not sufficient to identify the specific hydrogen-bonding modes present in **16**·H_2NBn.

The hydrogen-bonding interactions involving the NH_2 group in crystalline **16**·H_2NBn also appears to persist in solution. Specifically, the ^{1}H NMR chemical shift of the NH_2 resonance of the benzylamine ligands of **16** in C_6D_6 was dependent on benzylamine concentration, which may indicate the formation of PdN−H···NH_2Bn hydrogen bonds in solution.[18] For example, the chemical shift of the NH_2 resonance of **16** in C_6D_6 ([**16**] = 6.7 mM) increased linearly from δ 2.29 to δ 3.0 with increasing benzylamine concentration from 6.7 mM to 0.40 M (Figure 1). At benzylamine concentrations greater than 0.40 M, the NH_2 resonance of **16** was obscured by the benzyl resonance of free benzylamine at δ 3.55. The ^{1}H NMR chemical shift of the NH_2 resonance of the benzylamine ligands of **16** was also dependent on methanol concentration, which may indicate the formation of PdN−H···OHMe bonds in solution.[19] For example, the chemical shift of the NH_2 resonance of **16** ([**16**] = [H_2NBn] = 6.7 mM) displayed an asymptotic approach to a limiting value of δ $\sim$2.75

(14) (a) Stephanson, T. A.; Morehouse, S. M.; Powell, A. R.; Heffer, J. P.; Wilkinson, G. *J. Chem. Soc.* **1965**, 3632. (b) Iball, J.; MacDougall, M.; Scrimgeour, S. *Acta Crystallogr.* **1975**, *B31*, 1672. (c) Goggin, P. L.; Goodfellow, R. J.; Reed, F. J. S. *J. Chem. Soc., Dalton Trans.* **1972**, 1298. (d) Shaplygin, I. S. Lazarev, V. B. *Zh. Neorg. Khim.* **1978**, *23*, 603. (e) Mirskova, I. S.; Sytov, G. A.; Skanazarova, I. M.; Avakyan, V. G.; Perchenko, V. N.; Nametkin, N. S. *Dokl. Akad. Nauk SSSR* **1977**, *237*, 346. (f) Mellor, J. W. *A Comprehensive Treatise on Inorganic and Theoretical Chemistry*; Longmans, Green: London, 1936; Vol. XV.

(15) Coe, J. S.; Lyons, J. R. *Inorg. Chem.* **1970**, *9*, 1775.

(16) (a) Lock, C. J. L.; Zvagulis, M. *Inorg. Chem.* **1981**, *20*, 1817. (b) Iball, J.; Scrimgeour, S. N. *Acta Crystallogr.* **1977**, *B33*, 1194. (c) Lock, C. J. L.; Speranzini, R. A.; Zvagulis, M. *Acta Crystallogr.* **1980**, *B39*, 1989. (d) Lock, C. J. L.; Zvagulis, M. *Acta Crystallogr.* **1980**, *B36*, 2140.

(17) (a) Chatt, J.; Duncanson, L. A.; Venanzi, L. M. *J. Inorg. Nucl. Chem.* **1958**, *8*, 67. (b) Chatt, J.; Duncanson, L. A.; Venanzi, L. M. *J. Chem. Soc.* **1955**, 4461. (c) Chatt, J.; Duncanson, L. A.; Venanzi, L. M. *J. Chem. Soc.* **1956**, 2712.

(18) Kollman, P. A.; Allen, L. C. *Chem. Rev.* **1972**, *72*, 283.

(19) A reviewer has suggested that the methanol concentration dependence of the amino resonance of **16** in the ^{1}H NMR spectrum could also result from methanol-promoted halide dissociation.

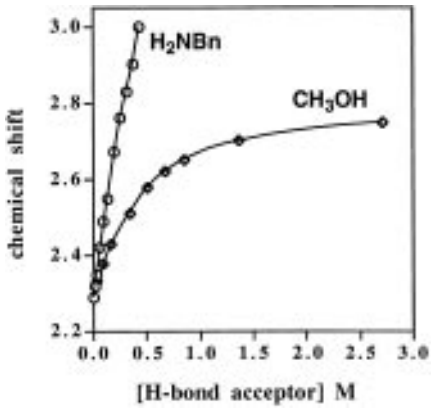


Figure 1. Benzylamine and methanol concentration dependence of the chemical shift of the NH_2 Resonance of **16** (6.7 mM) in C_6D_6 at 25 °C.

with increasing methanol concentration from 0 to 2.72 M (Figure 1).

The association constant for the formation of a 1:1 hydrogen-bonded adduct can often be derived from the dependence of the ^{1}H NMR chemical shift of the hydrogen bond donor on the concentration of the hydrogen bond acceptor via the Scatchard equation.[20] For example, the association constants for the formation of 1:1 hydrogen-bonded adducts of a low-valent transition-metal phenoxide or alkoxide complex and a phenol have been determined by ^{1}H NMR spectroscopy.[21] However, determination of the association constant for the formation of **16**·H_2NBn from **16** and benzylamine or for the formation of **16**·HOMe from **16** and methanol was precluded by the potential for multiple equilibria.[22] Likewise, attempts to obtain an association constant for the formation of **16**·H_2NBn by IR spectroscopy was precluded by the presence of intense aromatic C−H stretching bands corresponding to free benzylamine, which presumably obscured the hydrogen-bonded N−H stretching bands.

The stability of **16** in C_6D_6 solution was enhanced by the presence of benzylamine or methanol, possibly due to the presence of N−H···N or N−H···O hydrogen bonds, respectively. For example, while solutions of **16** (6.7 mM) in C_6D_6 which contained 6.7 mM benzylamine darkened within hours at room temperature, solutions of **16** (6.7 mM) in C_6D_6 which contained 0.30 M benzylamine or 1 M methanol showed no signs of decomposition after 2 weeks at room temperature. The instability of **16** in the absence of excess benzylamine precluded isolation of unsolvated **16**; attempted recrystallization of **16**·H_2NBn from a THF/pentane solution which contained no added benzylamine led to extensive decomposition and recovery of **16**·H_2NBn in low yield. Likewise, the low solubility and the instability of **16**·H_2NBn and related derivatives (see below) in the absence of a large excess of free amine precluded ^{13}C NMR analysis of these bis(amine) complexes.

Scheme 5

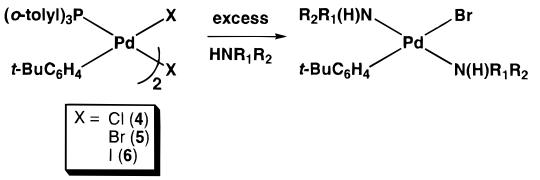
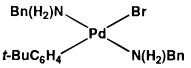
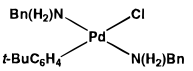
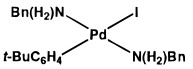
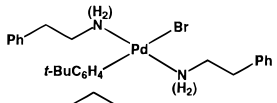
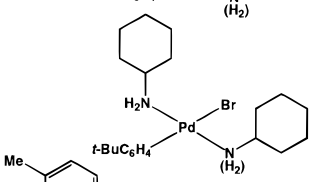
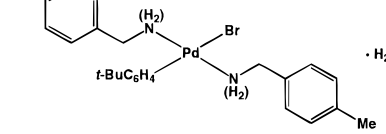
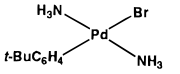
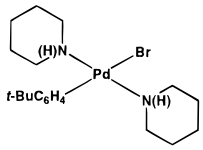


Table 2. Palladium Bis(amine) Complexes Formed From Reaction of Palladium Aryl Halide Dimers with Amine

Cmpd	structure		Isolated yield[a]
16		· H_2NBn	99
17		· H_2NBn	97
18		· H_2NBn	99
19		· H_2NCH$_2$CH$_2$Ph	84
20		· H_2NCy	89
21		· H_2NCH$_2$-4-C$_6$H$_4$Me	89
22		· NH_3	92
23		–	[a]

[a] Not isolated; detected in solution by ^{1}H NMR spectroscopy.

Synthesis of Palladium Bis(amine) Complexes Related to 16·H_2NBn. A series of palladium bis(amine) complexes were isolated from the reaction of the appropriate palladium aryl halide dimer and excess primary amine by procedures analogous to that employed in the synthesis of **16**·H_2NBn. For example, reaction of excess benzylamine with palladium aryl chloride dimer **4** or the aryl iodide dimer **6** led to isolation of the mono(benzylamine)-solvated bis(benzylamine) complexes Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$Cl·H_2NBn (**17**·H_2NBn) and Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$I·H_2NBn (**18**·H_2NBn), respectively (Scheme 5, Table 2). The spectroscopy of complexes **17** and **18** was analogous to that observed for the bromide derivative **16**. Iodide

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(23) (a) Seligson, A. L.; Trogler, W. C. *J. Am. Chem. Soc.* **1991**, *113*, 2520. (b) The cone angle for methylbenzylamine has not been determined. A cone angle of ~127° can be approximated by comparison to known cone angles for the related secondary amines HN(Me)Ph (126°) and NH(Me)-*n*-Pr (127°).

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Table 3. Temperature and Solvent Dependence of K_{eq} for the Formation of 16 and P(*o*-tol)$_3$ from the Reaction of 8 and Benzylamine at 25 °C

entry no.	solvent	temp, °C	K_{eq}
1	C_6D_6	25	0.90 ± 0.07
2	C_6D_6	40	0.70 ± 0.06
3	C_6D_6	55	0.57 ± 0.05
4	C_6D_6	65	0.51 ± 0.05
5	C_6D_6	77	0.44 ± 0.04
6	THF-d_8	25	3.6 ± 0.3
7	dioxane-d_8	25	1.8 ± 0.2
8	toluene-d_8	25	0.63 ± 0.05
9	CD_2Cl_2	25	0.066 ± 0.005
10	$CDCl_3$	25	0.14 ± 0.01

derivative **18** was particularly unstable in C_6D_6 solution in the absence of excess benzylamine and darkened within minutes at room temperature.

Reaction of palladium bromide dimer **5** with excess phenethylamine, cyclohexylamine, (4-methylbenzyl)-amine, or ammonia led to the isolation of the corresponding mono(amine)-solvated palladium bis(amine) complexes Pd(*p*-$C_6H_4CMe_3$)[$H_2NCH_2CH_2Ph$]$_2$Br (**19**·H_2-NCH_2CH_2Ph), Pd(*p*-$C_6H_4CMe_3$) [H_2NCy]$_2$Br·H_2NCy (**20**·H_2NCy), Pd(*p*-$C_6H_4CMe_3$)[H_2NCH_2-4-C_6H_4Me]$_2$Br·H_2-NCH_2-4-C_6H_4Me (**21**·H_2NCH_2-4-C_6H_4Me), and Pd(*p*-$C_6H_4CMe_3$)[NH_3]$_2$Br·NH_3 (**22**·NH_3), respectively. A *trans* orientation of the amine ligands in complexes **19**−**21** was inferred due to the equivalence of the amine ligands in the respective ^{1}H NMR spectra and by analogy to related bis(amine) complexes.[14] However, the ^{1}H NMR spectrum of **22** provided no information concerning the stereochemistry of the amine ligands due to the broadness of the ligated amine NH resonances. As a result, a *trans* configuration of the amine ligands in **22** was tentatively assigned. The reaction of palladium bromide dimer **5** and excess piperidine in C_6D_6 formed the corresponding bis(amine) complex Pd(*p*-$C_6H_4CMe_3$)-[piperidine]$_2$Br (**23**), as evidenced by the appearance of resonances corresponding to free P(*o*-tol)$_3$ at δ 2.40 and a new *tert*-butyl resonance at δ 1.30 in the ^{1}H NMR spectrum. However, the unfavorable equilibrium constant for conversion of **12** to **23** precluded isolation of **23** (see below).

Thermodynamics of the Interconversion of Palladium Mono- and Bis(amine) Complexes. The formation of palladium bis(amine) complexes from reaction of amine and palladium aryl halide dimer represents a potential turnover limiting step in the corresponding $Pd_2(DBA)_3$/P(*o*-tol)$_3$-catalyzed amination of aryl halides.[1−3] As a result, the thermodynamics and kinetics[13] of the conversion of palladium mono(amine) to bis(amine) complexes were investigated in greater detail by ^{1}H NMR spectroscopy. For example, a solution of mono(amine) complex **8** (~16 mM) and excess benzylamine (0.115 M) in $CDCl_3$ was monitored periodically by ^{1}H NMR spectroscopy at 25 °C. After 3 days, an equilibrium 1.0:1.5 mixture of **8**:**16** had formed which corresponds to an equilibrium constant of K_{eq} = [**16**]-[P(*o*-tol)$_3$]/[**8**][benzylamine] = 0.14 ± 0.01 at 25 ± 1 °C (Table 3).

The equilibrium constant for the conversion of **8** to **16** displayed a moderate solvent effect and increased overall by a factor of 55 in the order CD_2Cl_2 (K_{eq} = 0.066 ± 0.006) < $CDCl_3$ < toluene-d_8 < benzene-d_6 < dioxane-d_8 < THF-d_8 (K_{eq} = 3.6 ± 0.3) (Table 3). The large equilibrium constant in oxygenated solvents such as dioxane-d_8 and THF-d_8 may result from the ability of the solvent to serve as a hydrogen-bond acceptor.[17] The equilibrium constant for the conversion of **8** to **16** in C_6D_6 was temperature-dependent and ranged from 0.90 ± 0.07 at 25 °C to 0.44 ± 0.04 at 77 °C (Table 3). A van't Hoff plot of the data provided the thermodynamic parameters: $\Delta H° = -2.8 \pm 0.1$ kcal mol^{-1}; $\Delta S° = -9 \pm 1$ eu.

The equilibrium constants for the conversion of mono-(amine) to bis(amine) complexes were determined as a function of the halide ligand (Table 4). For example, K_{eq} was determined in $CDCl_3$ at 25 °C for the formation of chloride derivative **17** from reaction of **7** and benzylamine (K_{eq} = 0.18 ± 0.02) and for the formation of the iodide complex **18** from the reaction of **14** and benzylamine (K_{eq} = 0.10 ± 0.01) (Table 4). Similarly, the equilibrium constants for the conversion of mono-(amine) to bis(amine) complexes were determined as a function of the amine (Table 4). Specifically, K_{eq} was determined in C_6D_6 at 25 °C for the formation of **19** from the reaction of **9** and phenethylamine (1.1 ± 0.1), **20** from the reaction of **10** and cyclohexylamine (1.1 ± 0.1), **21** from the reaction of **11** and (4-methylbenzyl)amine (0.50 ± 0.04), and **23** from the reaction of **12** and piperidine ((18 ± 2) × 10^{-3}).

A solution of the mono(*N*-methylbenzylamine) complex **13** in C_6D_6 which contained 0.25 M *N*-methylbenzylamine displayed no evidence for the formation of the corresponding palladium bis(amine) complex Pd(*p*-C_6H_4-CMe_3)[HN(Me)Bn]$_2$Br (**24**) by ^{1}H NMR spectroscopy; no *t*-Bu resonances were observed in the region δ 1.20−1.30, and the resonance for free P(*o*-tol)$_3$ was not observed. Making the assumption that P(*o*-tol)$_3$ or *tert*-butyl resonances resulting from 5% conversion of **13** to **24** would be observed in the ^{1}H NMR spectrum, we can estimate an equilibrium constant for the conversion of **13** and *N*-methylbenzylamine to **24** and P(*o*-tol)$_3$ of ≤4 × 10^{-5} at 25 °C. Our inability to satisfactorily characterize the mono(amine) complex **15** precluded determination of the equilibrium constant for conversion of **15** to bis(amine) complex **22**.

Discussion

Hydrogen Bonding in Transition-Metal Amine Complexes. The NH_2 groups of palladium aryl halide bis(amine) complexes such as **16** readily form hydrogen bonds in both the solid state and in solution. Likewise, the proclivity of an NH_x (x = 1−3) group of a transition-metal amine complex to serve as hydrogen bond donor has been documented for complexes of Rh,[25] Co,[26] Ru,[27] Fe,[28] Pt, and Pd.[17] In addition, transition-metal complexes possessing halide,[29] phenoxide, and alkoxide[30] and hydroxide[31] ligands also display a strong tendency to form hydrogen bonds. Of particular relevance, Chatt and co-workers observed the formation of PtN−H···Cl,

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Table 4. Amine and Halide Dependence of K_{eq} for the Formation of Palladium Bis(amine) Complexes and P(*o*-tol)$_3$ From the Reaction of the Corresponding Mono(amine) Complex and Amine at 25 °C

entry no.	amine	mono(amine)	bis(amine)	cone angle[a]	pK_a[b]	solvent	K_{eq}
1	H_2NBn	**7**	**17**	106	9.32	$CDCl_3$	0.18 ± 0.02
2	H_2NBn	**14**	**18**	106	9.32	$CDCl_3$	0.10 ± 0.01
3	$H_2NCH_2CH_2Ph$	**9**	**19**	106	9.87	C_6D_6	1.1 ± 0.1
4	H_2NCy	**10**	**20**	115	10.64	C_6D_6	1.1 ± 0.1
6	$H_2NCH_2C_6H_4Me$	**11**	**21**	106		C_6D_6	0.50 ± 0.04
6	piperidine	**12**	**23**	121	11.12	C_6D_6	0.018 ± 0.002
7	HN(Me)Bn	**13**	**24**	~127		C_6D_6	$\leq 4 \times 10^{-5}$

[a] Cone angles from ref 23. [b] pK_a from ref 24.

PtN−H···O(dioxane), and PtN−H···Pt hydrogen bonds in a series of platinum dichloride bis(amine) complexes and platinum dichloride mono(amine) complexes Pt(amine)(L)Cl_2 (L = neutral two-electron donor) by IR spectroscopy.[17] Significantly, they observed that the NH_2 group of a ligated primary amine was a more effective hydrogen bond donor than was the NH group of a ligated secondary amine. Likewise, the NH_x group of a platinum bis(amine) complex was a better hydrogen bond donor than was the NH_x group of the corresponding mono(amine) mono(phosphine) complex. In accord with these observations, hydrogen bond formation was evident both in the solid state and in solution for palladium bis(amine) complexes such as **16**, while no evidence for hydrogen bond formation was observed in the corresponding mono(amine) mono(phosphine) complexes **7**−**14**.

In addition to spectroscopic studies, amine complexes possessing either an N−H···X (X = Cl, Br, I) hydrogen bond between an NH_x group and a neighboring halide ligand or an N−H···M hydrogen bond between an NH_x group and a filled transition-metal d orbital have been structurally characterized by X-ray crystallography. For example, the platinum *cis*-dichloride bis(cycloalkylamine) complexes $Pt(Cl)_2[H_2NCH(CH_2)_n]$ (n = 2,[32] 3,[33] 5[34]] formed a three-dimensional lattice via intermolecular N−H···Cl bonds, while the iridium monohydride mono(amine) bis(phosphine) complexes $Ir(H)(CH_3)I[NH(SiMe_2CH_2PR_2)_2]$ (R = Ph, *i*-Pr) form inner-sphere N−H···I hydrogen bonds.[35] Similarly, the tungsten tricarbonyl monochloride diaminobenzene complexes $W(CO)_3(Cl)[\eta^3$-*o*-$C_6H_3ClCH_2NH$-*o*-$C_6H_4NCHAr]$ form both inner-sphere and intermolecular N−H···Cl hydrogen bonds.[36] The unusual diplatinum salt $[N(n\text{-}Pr)_4]_2[PtCl_4]\cdot$*cis*-$[PtCl_2(NH_2Me)_2]$ formed both intermolecular N−H···Cl−Pt and N−H···Pt bonds in the solid state,[37] while the platinum phenylamido monohydride complex $PtH(NHPh)(PEt_3)_2$ dimerized with close N−H···Pt intermolecular contacts.[38]

Transition-metal amine complexes possessing N−H···N hydrogen bonds between the NH_x group of a ligated amine and an outer-sphere amine molecule have not been structurally characterized. However, transition-metal amine complexes possessing N−H···O hydrogen bonds between the NH_x group of a ligated amine and an oxygen atom acceptor have been structurally characterized. For example, the palladium bis(phenoxide) bis(pyrrolidine) complex $Pd(OPh)_2[HN(CH_2)_4]_2$ formed a dimer in the solid state via four intramolecular PdN−H···O(Ar)Pd hydrogen bonds.[39] The corresponding bis(phenol) solvate $Pd(OPh)_2[HN(CH_2)_4]_2\cdot 2HOPh$ crystallized in the form of a one-dimensional polymeric chain via intermolecular N−H···O(phenol) bonds.[40] The platinum dichloride monoammine mono(phosphine) complex $PtCl_2(NH_3)(PMe_3)$ formed an isolable 2:1 18-crown-6 adduct, $PtCl_2(NH_3)(PMe_3)\cdot{}^1/_2(C_{12}H_{24}O_6)$, in which all three hydrogen atoms of the ammine ligand formed N−H···O hydrogen bonds with the crown ether oxygen atoms.[37] The piperidine tetracarbonyl trimethyl phosphite complexes $M(CO)_4[P(OMe)_3]$(piperidine) (M = Mo,[41] Cr[42]) form inner-sphere N−H···O hydrogen bonds to a single phosphite oxygen atom.

Thermodynamics of Palladium Bis(amine) Formation. Although quantitative thermodynamic data are limited, a P−Pd^{II} bond is typically considered stronger than the corresponding N−Pd^{II} bond. For example, the enthalpy for cleavage of the chloride bridge in the palladium allyl chloride dimer $\{[\eta^3$-$CH_2C(Me)CH_2]Pd(\mu$-$Cl)\}_2$ with triphenylphosphine was ~5 kcal mol^{-1} greater than the corresponding bridge-cleavage reaction employing piperidine.[43] The thermodynamic preference for a P−Pd^{II} bond over a N−Pd^{II} bond has been attributed to the more favorable overlap of the sp^2d palladium orbital with the diffuse phosphorus sp^3 hybrid

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orbital relative to the more compact nitrogen sp^3 hybrid orbital.[44] The effect of $d\pi-d\pi$ back-bonding on the stability of the M−P bond of a transition metal and a trialkyl- or triarylphosphine is not clear.[45] However, conversion of **8** + benzylamine to **16** + P(*o*-tol)$_3$ was slightly exothermic ($\Delta H \approx -3$ kcal mol^{-1}), which may result in part from the large cone angle of the P(*o*-tol)$_3$ ligand (θ = 195°)[46,47] relative to benzylamine (θ = 106°).[23a]

The coordination or dissociation of an amine serves as a key step in a variety of transition-metal-catalyzed processes.[48] As a result, there has been an effort to correlate both the basicity and steric bulk of an amine to the kinetic or thermodynamic binding affinity.[23a,49] For example, we have recently shown that the binding constants K_b (determined relative to *N*-benzylmethylamine) for the reaction of amine with **1** to form the palladium mono(amine) complexes Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$Me)(amine)Cl were dependent on both the basicity and steric bulk of the amine.[12] Specifically, for sterically small amines with cone angles less than ~120°, the relative binding constant of the amine was dominated by the basicity of the amine, while for larger amines, the K_b value became sensitive to the steric bulk of the amine, consistent with the presence of a steric threshold.[50,51] The presence of a steric threshold has been observed in the correlation of the transition-metal binding affinities of both phosphines[50] and amines[51] with the respective cone angles.

The equilibrium constants for the formation of palladium bis(amine) complexes from the corresponding mono(amine) complex and free amine were also dependent on the steric bulk of the amine (Table 3). For example, the equilibrium constant for the formation of **16** from the reaction of **8** and benzylamine was $\geq 2 \times 10^4$ times larger ($\Delta\Delta G° \geq 6$ kcal mol^{-1}) than K_{eq} for the formation of **24** from reaction of **13** and *N*-methylbenzylamine. In addition, despite limited data points, the correlation between the equilibrium constant and the cone angle of the amine was consistent with the presence of a steric threshold. For example, a plot of log K_{eq} versus cone angle for the formation of **16** from **8** and benzylamine (θ = 106°, pK_a = 9.32), **19** from **9** and phenethylamine (θ = 106°, pK_a = 9.87), **20** from **10** and cyclohexylamine (θ = 115°, pK_a = 10.64), **23** from **12** and piperidine (θ = 121°, pK_a = 11.12), and **24** from **13** and *N*-methylbenzylamine ($\theta \approx 127°$)[24b] revealed that log K_{eq} was independent of amine cone angles below 115° and decreased linearly with increasing cone angle above 115° (Figure 2). Unfortunately, the limited range of basicities for amines of comparable cone angle precluded a detailed investigation of the relationship between K_{eq} and amine basicity.

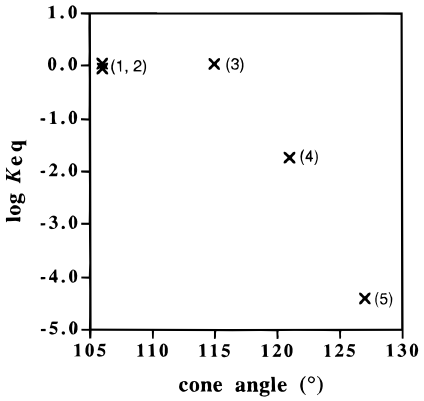

Figure 2. Plot of log K_{eq} versus amine cone angle for the formation of **16** from **8** and benzylamine (1), **19** from **9** and phenethylamine (2), **20** from **10** and cyclohexylamine (3), **23** from **12** and piperidine (4), and **24** from **13** and *N*-methylbenzylamine (5) in C_6D_6 at 25 °C.

The efficiency of the tin-free Pd$_2$(DBA)$_3$/P(*o*-tol)$_3$-catalyzed amination of aryl halides is halide-dependent; aryl iodides required more forcing conditions and produced lower yields of anilines than did aryl bromides.[1−3] We have therefore probed the influence of the halide ligand on both the formation and reductive elimination of palladium mono(amine) complexes in an effort to elucidate the origin of this halide effect in the corresponding catalytic reaction.[10−12] For example, the equilibrium constants for reaction of diisopropylamine with palladium aryl halide dimers **1**−**3** at 25 °C in CD_2Cl_2 to form the corresponding amine monomers Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$Me)[HN(*i*-Pr)$_2$]X (X = Cl, Br, I) were halide dependent and decreased overall by a factor of $\sim 2.3 \times 10^3$ ($\Delta\Delta G° = \sim 4.6$ kcal mol^{-1}) in the order Cl > Br ≫ I. Similarly, the equilibrium constants for the formation of palladium bis(amine) derivatives from mono(amine) complexes and free amine were halide-dependent and decreased in the order Cl > Br > I. However, the magnitude of this halide effect was considerably smaller than was observed in the dimer cleavage reactions. For example, the equilibrium constant for formation of the iodide complex **18** from **14** and benzylamine was ~2 times smaller than K_{eq} for the formation of the corresponding chloride complex **17** from **7** and benzylamine.

Conclusions

We have shown that palladium tris(*o*-tolyl)phosphine mono(primary amine) aryl halide complexes are converted to the corresponding palladium bis(primary amine) aryl halide complexes upon treatment with

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excess primary amine. These palladium bis(amine) complexes are prone to form hydrogen bonds involving the NH_2 groups of the palladium-bound amine ligands both in the solid state and in solution. In benzene-d_6 at 25 °C, the free energy for conversion of mono(primary amine) complexes to bis(primary amine) complexes is <0.1 kcal mol^{-1}. The corresponding conversion of mono(secondary amine) complexes to bis(secondary amine) complexes was considerably less favorable ($\Delta\Delta G° \geq 2.4$ kcal mol^{-1}). The greater tendency of primary amines to form palladium bis(amine) complexes relative to secondary amines and the failure of palladium aryl halide bis(amine) complexes to generate detectable quantities of aromatic amine upon treatment of sodium *tert*-butoxide may contribute to the ineffectiveness of primary amines as substrates in the corresponding Pd/P(*o*-tol)$_3$-catalyzed amination of aryl halides. We are continuing to investigate the kinetics and mechanism of the formation of palladium bis(amine) complexes from palladium mono(amine) derivatives in an effort to further evaluate this process as a turnover-limiting step in the corresponding Pd/P(*o*-tol)$_3$-catalyzed amination of aryl halides.

Experimental Section

General Methods. All manipulations and reactions were performed under an inert atmosphere of nitrogen or argon in an inert atmosphere glovebox or by standard Schlenk techniques. Preparative-scale reactions were performed in flame- or oven-dried Schlenk tubes equipped with a stirbar, side-arm joint, and septum. NMR experiments were performed in oven-dried 5 mm thin-wall NMR tubes fitted with a rubber septum. ^{1}H NMR spectra were obtained on a Varian XL-300 or Unity-300 spectrometer and were referenced relative to the residual proton resonance of the solvent. ^{31}P NMR spectra were obtained on a Varian XL-300 (121 MHz) and were referenced relative to external H_3PO_4. IR spectra were recorded on a Perkin-Elmer FTIR spectrophotometer. Elemental analyses were performed by E+R Microanalytical Laboratories (Corona, NY).

Diethyl ether, hexane, pentane, benzene, and benzene-d_6 were distilled from purple solutions of sodium and benzophenone under argon or nitrogen. Toluene-d_8, THF-d_8, and dioxane-d_8 were distilled from Na/K alloy. Methylene chloride and methylene chloride-d_2 were distilled from CaH_2; $CDCl_3$ was distilled from P_2O_5. Amines (Aldrich) were either purchased as anhydrous grade and used as received or were distilled from CaH_2 under Ar prior to use.

Equilibrium measurements for the conversion of mono(amine) to bis(amine) complexes conducted at 25 °C were conducted at ambient laboratory temperature; periodic temperature measurement indicated a variation of ≤1 °C throughout approach to equilibrium. Experiments conducted at 40 °C were performed in a constant-temperature oil bath maintained at ± 0.5 °C or in the probe of a preheated NMR spectrometer calibrated with an ethylene glycol thermometer and maintained at ±0.5 °C throughout data acquisition. Experiments conducted at 55−77 °C were performed in the probe of a preheated NMR spectrometer. Estimation of error limits for equilibrium constants and the corresponding free energy values was performed as previously described.[12]

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[H$_2$NBn]Cl (7). A solution of benzylamine (20 μL, 20 mg, 0.2 mmol) and **4** (106 mg, 0.09 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 10 min. The resulting colorless solution was concentrated to 1 mL under vacuum and diluted with 20 mL of hexane. Cooling the solution via concentration to 10 mL under vacuum formed a white precipitate, which was filtered, washed with hexane, and dried under vacuum to give **7** (118 mg, 94%) as a white, microcrystalline solid. ^{1}H NMR ($CDCl_3$, 50 °C): δ 7.80 (br, 3 H), 7.32 (t, J = 6.5 Hz, 3 H), 7.25−7.07 (m, 11 H), 6.67 (m, 4 H), 3.81 (br t, J = 7.1 Hz, 2 H, H_2NCH_2Ph), 2.96 (br, 2 H, H_2NCH_2Ph), 2.16 [br s, 9 H, P(*o*-tol)$_3$], 1.16 (s, 9 H, $C_6H_4CMe_3$). ^{31}P{^{1}H} NMR ($CDCl_3$, 25 °C): δ 26.9. Anal. Calcd (found) for $C_{38}H_{43}BrNPPd$: C, 66.48 (66.71); H, 6.31 (6.51).

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[H$_2$NBn]Br (8). Reaction of benzylamine (30 μL, 29 mg, 0.27 mmol) and **5** (150 mg, 0.12 mmol) using a procedure analogous to that used to prepare **7** led to the isolation of **8** (95 mg, 54%) as a yellow powder. ^{1}H NMR ($CDCl_3$, 50 °C): δ 7.80 (br, 3 H), 7.22 (m, J = 6.4 Hz, 3 H), 7.07 (m, 4 H), 6.69 (s, 4 H), 3.82 (br t, J = 8 Hz, 2 H, H_2NCH_2Ph), 3.01 (br, 2 H, H_2NCH_2Ph), 2.15 [br s, 9 H, P(*o*-tol)$_3$], 1.17 (s, 3 H, $C_6H_4CMe_3$). ^{31}P{^{1}H} NMR ($CDCl_3$, 25 °C): δ 27.2. Anal. Calcd (found) for $C_{38}H_{43}BrNPPd$: C, 62.43 (62.23); H, 5.93 (5.99).

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[H$_2$NCH$_2$CH$_2$Ph]Br (9). Reaction of **5** (106 mg, 0.085 mmol), and phenethylamine (20 mg, 0.17 mmol) using a procedure analogous to that used to prepare **7** led to the isolation of **9** (118 mg, 94%) as a white microcrystalline solid. ^{1}H NMR ($CDCl_3$, 50 °C): δ 7.80 (br, 3 H), 7.30 (t, J = 6.5 Hz, 3 H), 7.15−7.06 (m, 11 H), 6.87 (m), 6.66 (m), 2.93 (br, 2 H, $H_2NCH_2CH_2Ph$), 2.71 (m, 4 H, H_2NCH_2-CH_2Ph + $H_2NCH_2CH_2Ph$), 2.14 [br s, 9 H, P(*o*-tol)$_3$], 1.17 (s, 9 H, $C_6H_4CMe_3$). ^{31}P{^{1}H} NMR ($CDCl_3$, 25 °C): δ 28.9. Anal. Calcd (found) for $C_{39}H_{45}BrNPPd$: C, 62.87 (62.96); H, 6.09 (6.26).

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[H$_2$NCy]Br (10). Reaction of **2** (100 mg, 0.08 mmol) and cyclohexylamine (20 μL, 17 mg, 0.16 mmol) using a procedure analogous to that used to prepare **7** led to the isolation of **10** (99 mg, 85%) as a white microcrystalline solid. ^{1}H NMR (C_6D_6, 50 °C): δ 8.11 (br, 3 H), 7.05 (d, J = 7.4 Hz), 7.01 (m), 6.92 (m), 6.77 (d, J = 7.7 Hz), 2.55 [br, 3 H, $NH_2CH(CH_2)_5$ + α-CH], 2.32 [br s, 9 H, P(*o*-tol)$_3$], 1.70 (br, 2 H, β-CH_2), 1.36 (br, 2 H, β-CH_2), 1.17 (s, 9 H, $C_6H_4CMe_3$), 0.90 (br, 3 H, γ-CH_2 + δ-CH_2), 0.72 (br, 3 H, γ-CH_2 + δ-CH_2). ^{31}P{^{1}H} NMR ($CDCl_3$, 25 °C): δ 28.6. Anal. Calcd (found) for $C_{37}H_{47}BrNPPd$: C, 61.46 (61.70); H, 6.55 (6.43).

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[H$_2$NCH$_2$-*p*-C$_6$H$_4$Me]Br (11). Reaction of (4-methylbenzyl)amine (21 μL, 19 mg, 0.16 mmol) and **5** (100 mg, 0.08 mmol) using a procedure analogous to that used to prepare **7** led to the isolation of **11** (78 mg, 64%) as a yellow microcrystalline solid. ^{1}H NMR (C_6D_6, 50 °C): δ 7.05 (d, J = 7.64 Hz), 6.93 (br), 6.81 (s), 6.04 (s), 3.70 (br s, 2 H, $H_2NCH_2C_6H_4CH_3$), 2.65 (br, 2 H, $H_2NCH_2C_6H_4CH_3$), 2.40 [br s, 9 H, P(*o*-tol)$_3$], 2.03 (br s, 2 H, $H_2NCH_2C_6H_4CH_3$), 1.18 (s, 3 H, $C_6H_4CMe_3$). ^{31}P{^{1}H} NMR ($CDCl_3$, 25 °C): δ 28.2. Anal. Calcd (found) for $C_{39}H_{45}BrNPPd$: C, 62.87 (62.64); H, 6.09 (6.11).

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[piperidine]Br (12). Reaction of **5** (100 mg, 0.08 mmol) and piperidine (25 μL, 22 mg, 0.25 mmol) using a procedure analogous to that used to prepare **7** led to the isolation of **12** (91 mg, 80%) as a white microcrystalline solid. ^{1}H NMR (C_6D_6, 50 °C): δ 8.05 (br, 3 H), 7.05 (d, J = 7.33 Hz), 6.91 (m), 6.80 (d, J = 7.41 Hz), 3.55 [br s, 1 H, $HN(CH_2)_5$], 3.13 (br d, J = 12.6 Hz, 2 H), 2.64 (br d, J = 11.7 Hz, 2 H), 2.33 [br s, 9 H, P(*o*-tol)$_3$], 1.18 (s, 9 H, $C_6H_4CMe_3$), 1.01 (br d, J = 11.7 Hz, 3 H), 0.80 (br, 3 H). ^{31}P{^{1}H} NMR ($CDCl_3$, 25 °C): δ 28.8 (br). Anal. Calcd (found) for $C_{36}H_{45}$-BrNPPd: C, 60.98 (61.09); H, 6.40 (6.49).

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[HN(Me)Bn]Br (13). Reaction of **5** (100 mg, 0.08 mmol) and methylbenzylamine (20 mg, 0.2 mmol) using a procedure analogous to that used to prepare **7** led to the isolation of **13** (118 mg, 94%) as yellow blocks. ^{1}H NMR (C_6D_6, 50 °C): δ 7.80 (br, 3 H), 7.42 (m), 7.19 (d, J = 7.4 Hz), 7.05 (d, J = 7.5 Hz), 6.90 (m), 6.69 (m), 4.50 (br t, $J \approx 7$ Hz, 1 H, HN(Me)CH_2Ph), 3.41 (br s, 1 H, $HN(Me)CH_2Ph$), 2.96 (br, 1 H, HN(Me)CH_2Ph), 2.27 [br s, 9 H, P(*o*-tol)$_3$], 1.15 (s, 9 H, $C_6H_4CMe_3$). Anal. Calcd (found) for $C_{39}H_{45}BrNPPd$: C, 62.87 (62.82); H, 6.09 (6.11).

Pd[P(*o*-tol)$_3$](*p*-C$_6$H$_4$CMe$_3$)[H$_2$NBn]I (14). Benzylamine was added in small portions (<0.5 μL) to a solution of **6** (7

mg, 5×10^{-3} mmol) in $CDCl_3$ (0.7 mL), and the mixture was monitored by ^1H NMR spectroscopy after each addition. Addition of 1.5 μL (0.01 mmol) of benzylamine generated **14**, which was >95% pure by ^1H NMR spectroscopy and was characterized without isolation. ^1H NMR ($CDCl_3$, 50 °C): δ 7.80 (br, 3 H), 7.22 (m, J = 6.4 Hz, 3 H), 7.07 (m, 4 H), 6.69 (s, 4 H), 3.82 (br t, J = 8 Hz, 2 H, H_2NCH_2Ph), 3.01 (br, 2 H, H_2NCH_2Ph), 2.15 [br s, 9 H, P(*o*-tol)$_3$], 1.17 (s, 3 H, $C_6H_4CMe_3$). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 25 °C): δ 27.2.

Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$Br·H_2NBn (16·H_2NBn). A solution of **5** (250 mg, 0.20 mmol) and benzylamine (825 μL, 810 mg, 7.6 mmol) in CH_2Cl_2 (8 mL) was stirred overnight at room temperature to give a colorless solution. Solvent was evaporated under vacuum, and the residue was dissolved in THF (3 mL) and diluted with pentane (10 mL). Cooling the resulting solution to −30 °C overnight produced a precipitate which was filtered, washed with pentane, and dried under vacuum to give **16**·H_2NBn (260 mg, 99%) as a white fibrous solid. ^1H NMR (C_6D_6, 25 °C): in addition to resonances corresponding to free benzylamine (δ 7.15, 3.55, and 0.79), resonances were observed at δ 7.13−6.85 (10 H), 3.81 (t, J = 7.0 Hz, 4 H, H_2NCH_2Ph), 2.4 (br t, $J \approx 7$ Hz, 4 H, H_2NCH_2Ph), 1.27 (s, 9 H, $C_6H_4CMe_3$). IR (KBr): 3295, 3198, 3106, 2958, 1581, 1496, 1454, 1360, 1160, 1116, 990, 817, 751, 700 cm^{-1}. IR ($CDCl_3$): ν_{N-H} 3333, 3275 cm^{-1}. Anal. Calcd (found) for $C_{31}H_{40}BrN_3Pd$: C, 58.09 (57.85); H, 6.29 (6.26); N, 6.56 (6.33).

Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$Cl·H_2NBn (17·H_2NBn). Reaction of **4** (95 mg, 0.08 mmol) and benzylamine (300 μL, 294 mg, 2.7 mmol) using a procedure analogous to that used to prepare **16**·H_2NBn gave **17**·H_2NBn (95 mg, 97%) as a white fibrous solid. ^1H NMR (C_6D_6, 25 °C): in addition to resonances corresponding to free benzylamine (δ 7.15, 3.55, and 0.79), resonances were observed at δ 7.13−6.85 (10 H), 3.86 (t, J = 7.1 Hz, 4 H, H_2NCH_2Ph), 2.68 (t, J = 7.1 Hz, 4 H, H_2NCH_2Ph), 1.27 (s, 9 H, $C_6H_4CMe_3$). IR (KBr): 3302, 3186, 3059, 2959, 1589, 1483, 1454, 1009, 991, 816, 751, 699 cm^{-1}. IR ($CDCl_3$): ν_{N-H} 3333, 3275 cm^{-1}. Anal. Calcd (found) for $C_{31}H_{40}ClN_3Pd$: C, 62.42 (62.46); H, 6.76 (6.93); N, 7.04 (6.94).

Pd(*p*-$C_6H_4CMe_3$)[H_2NBn]$_2$I·H_2NBn (18·H_2NBn). Reaction of **6** (100 mg, 0.075 mmol) and benzylamine (300 μL, 294 mg, 2.7 mmol) employing a procedure analogous to that used to prepare **16**·H_2NBn gave **18**·H_2NBn (101 mg, 99%) as yellow needles. ^1H NMR (C_6D_6, 25 °C): in addition to resonances corresponding to free benzylamine (δ 7.15, 3.55, and 0.79) resonances were observed at δ 7.13−6.85 (10 H), 3.76 (t, J = 7.3 Hz, 4 H, H_2NCH_2Ph), 2.28 (br t, J = ~7 Hz, 4 H, H_2NCH_2Ph), 1.27 (s, 9 H, $C_6H_4CMe_3$). IR (KBr): 3262, 3186, 3119, 2963, 1583, 1454, 980, 816, 753, 701 cm^{-1}. IR ($CDCl_3$): 3329, 3271 cm^{-1}. Anal. Calcd (found) for $C_{31}H_{40}IN_3Pd$: C, 54.12 (54.31); H, 5.86 (6.05); N, 6.11 (6.02).

Pd(*p*-$C_6H_4CMe_3$)[$H_2NCH_2CH_2Ph$]$_2$Br·$H_2NCH_2CH_2Ph$ (19·$H_2NCH_2CH_2Ph$). A solution of **5** (100 mg, 0.08 mmol) and phenethylamine (200 μL, 193 mg, 1.6 mmol) in THF (2 mL) was stirred overnight at room temperature to give a colorless solution. Solvent was evaporated under vacuum, and the residue was crystallized from Et_2O/pentane (1/6) to give **19**·$H_2NCH_2CH_2Ph$ (92 mg, 84%) as a white solid. ^1H NMR (C_6D_6, 25 °C): in addition to resonances corresponding to free phenethylamine (δ 2.68 (t, J = 6.8 Hz), 2.45 (t, J = 6.8 Hz), and 0.51), resonances were observed at δ 7.11, 7.08, 7.06, 7.03, 6.81 (d, J = 6.8 Hz), 2.71 (t, J = 7.3 Hz, 2 H, $H_2NCH_2CH_2Ph$), 2.39 (t, J = 7.4 Hz, 2 H, $H_2NCH_2CH_2Ph$), 2.71 (br, 2 H, $H_2NCH_2CH_2Ph$). IR ($CDCl_3$): ν_{N-H} 3325, 3270 cm^{-1}. Anal. Calcd (found) for $C_{34}H_{46}BrN_3Pd$: C, 59.79 (59.61); H, 6.79 (6.86); N, 6.15 (6.13).

Pd(*p*-$C_6H_4CMe_3$)[H_2NCy]$_2$Br·H_2NCy (20·H_2NCy). A solution of **5** (100 mg, 0.08 mmol) and cyclohexylamine (200 μL, 173 mg, 1.8 mmol) in THF (2 mL) was stirred overnight to give a colorless solution. Solvent was evaporated under vacuum, and the residue was crystallized from hexane (10 mL) at −30 °C to give **20**·H_2NCy (97 mg, 89%) as white needles. ^1H NMR (C_6D_6, 25 °C): δ 7.31 (d, J = 8.3 Hz, 2 H), 7.23 (d, J = 8.3 Hz, 2 H), 2.72 (tt, J = 3.8, 10.8 Hz, 2 H, α-CH), 1.91 (d, J = 10.6 Hz, 4 H), 1.40 1.35, 1.28 (s, 9 H, $C_6H_4CMe_3$), 0.92 (d, J = 12.2 Hz), 0.65 (m). IR ($CDCl_3$): ν_{N-H} 3319, 3261 cm^{-1}. Anal. Calcd (found) for $C_{28}H_{52}BrN_3Pd$: C, 54.50 (54.61); H, 8.49 (8.69); N, 6.81 (6.59).

Pd(*p*-$C_6H_4CMe_3$)[H_2NCH_2-*p*-C_6H_4Me]$_2$Br·H_2NCH_2-*p*-C_6H_4Me (21·H_2NCH_2-*p*-C_6H_4Me). Reaction of **5** (100 mg, 0.08 mmol) and (4-methylbenzyl)amine (300 μL, 294 mg, 2.7 mmol) employing a procedure analogous to that used to prepare **20**·H_2NCy gave **21**·H_2NCH_2-*p*-C_6H_4Me (97 mg, 89%) as white needles. ^1H NMR (C_6D_6, 25 °C): in addition to resonances corresponding to free (4-methylbenzyl)amine (δ 7.15, 3.59, 2.14, and 0.70), resonances were observed at δ 7.13−6.85 (aromatic, 10 H), 3.84 (t, J = 7.05 Hz, 4 H, $H_2NCH_2C_6H_4Me$), 2.49 (br t, 4 H, $H_2NCH_2C_6H_4Me$), 2.14 (s, 3 H, $H_2NCH_2C_6H_4Me$), 1.28 (s, 9 H, $C_6H_4CMe_3$). IR ($CDCl_3$): ν_{N-H} 3230, 3272 cm^{-1}. Anal. Calcd (found) for $C_{34}H_{46}BrN_3Pd$: C, 59.79 (59.54); H, 6.79 (6.81); N, 6.15 (6.02).

Pd(*p*-$C_6H_4CMe_3$)[NH_3]$_2$Br·NH_3 (22·NH_3). A 0.5 M solution of ammonia in dioxane (5 mL, 2.5 mmol) was added to solid **5** (100 mg, 0.08 mmol) and stirred for 5 min. The resulting colorless solution was allowed to stand overnight at room temperature to form a colorless precipitate, which was filtered, washed with pentane, and dried under vacuum to give **22**·NH_3 (55 mg, 92%) as white needles. ^1H NMR (C_6D_6, 25 °C): in addition to the resonance corresponding to free NH_3 (δ 0.50), resonances were observed at δ 7.07 (d, J = 8.55 Hz, 2 H), 7.03 (d, J = 8.55 Hz, 2 H), 2.14 (br s, 3 H, NH_3), 1.25 (s, 9 H, $C_6H_4CMe_3$). IR ($CDCl_3$): ν_{N-H} 3376, 3282 cm^{-1}. Anal. Calcd (found) for $C_{10}H_{22}BrN_3Pd$: C, 32.41 (32.14); H, 5.98 (5.87).

Thermodynamics of the Conversion of 8 + H_2NBn to 16 + P(*o*-tol)$_3$. Benzylamine (10 μL, 0.09 mmol) was added via syringe to an NMR tube containing a solution of **5** (7.0 mg, 0.011 mmol) and P(*o*-tol)$_3$ (29.4 mg, 0.097 mmol) in C_6D_6 (0.70 mL). The tube was shaken, and its contents were analyzed periodically by ^1H NMR at 25 °C. The concentrations of **8** and **16** were determined by integrating the *tert*-butyl resonances for **8** (δ 1.17) and **16** (δ 1.27) and from the mass balance. The concentration of free benzylamine was determined from the mass balance. The equilibrium constant for the conversion of **8** to **16** was determined according to the formula K_{eq} = [**8**][P(*o*-tol)$_3$]/[**16**][benzylamine]. Related equilibrium constants were determined by analogous procedures.

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