Synthesis and Solution Structure of Palladium Tris(*o*-tolyl)phosphine Mono(amine) Complexes

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The complex(es) resulting from a 1:4 mixture of $Pd_2(DBA)_3$ and $P(o-tol)_3$ react with aryl bromides or aryl iodides p-XC₆H₄R (X = Br, I; R = Me, *t*-Bu, OMe) to generate the corresponding halide dimers { $Pd[P(o-tol)_3](p-C_6H_4R)(\mu-X)$ }₂ (X = Br, R = *t*-Bu (1), Me (2), OMe (3); X = I, R = *t*-Bu (4), Me (5), OMe (6)) in 46–76% yield. Iodide dimer 5 reacts with AgOTf in acetonitrile to form the cationic bis(acetonitrile) complex { $Pd[P(o-tol)_3](p-C_6H_4-Me)(CH_3CN)_2$ }⁺OTf⁻ (8) which was treated in situ with LiCl to form the chloride dimer { $Pd[P(o-tol)_3](p-C_6H_4Me)(\mu-Cl)$ }₂ (9) in 93% yield. The *p*-tolyl halide dimers 2, 5, and 9 react with *N*-benzylmethylamine to generate the corresponding 1:1 palladium amine adducts Pd-[$P(o-tol)_3$]($p-C_6H_4Me$)[HN(Me)Bn]X (X = Cl (12), 85%; X = Br (13), 72%; X = I (14), 77%). Reaction of a mixture of Pd₂(DBA)₃ and $P(o-tol)_3$ with the haloamines 2-IC₆H₄(CH₂)₂N(H)Bn, 2-BrC₆H₄CH₂N(H)(p-tolyl), and 2-BrC₆H₄(CH₂)₃N(H)Bn gave the chelated palladium amine complexes Pd[$P(o-tol)_3$]($2-C_6H_4(CH_2)_2$ N(H)Bn]I (18, 71%), Pd[$P(o-tol)_3$][$2-C_6H_4CH_2$ N(H)(ptolyl)]Br (19, 77%), and Pd[$P(o-tol)_3$]($2-C_6H_4(CH_2)_3$ N(H)Bn]Br (21, 24%), respectively. Vari-

able-temperature ¹H and ³¹P NMR analysis of **12–14** and related complexes was consistent with hindered rotation about the P–C bonds, with predominant formation of the exo_2 -P(o-tol) conformer, and hindered rotation about the Pd–P bond with formation of three unequally populated rotamers.

Introduction

In 1983 Migita reported that $Pd[P(o-tol)_3]_2Cl_2$ (*o*-tol) = *o*-tolyl) served as an effective catalyst for the crosscoupling of aryl bromides with (diethylamino)stannane in toluene at 100 °C.¹ Despite the importance of aromatic amines in areas such as pharmaceuticals² and conductive polymers,³ and due to limitations in traditional methods for the synthesis of anilines,⁴ Pdcatalyzed C–N bond formation remained undeveloped for over a decade. However, recent work⁵ has led to the development of a tin-free Pd-catalyzed procedure for the conversion of aryl bromides⁶ to the corresponding anilines via reaction with free amine and sodium *tert*butoxide. For example, reaction of 5-bromo-*m*-xylene, *N*-benzylmethylamine (1.2 equiv), and sodium *tert*butoxide (1.4 equiv) with 2 mol % of Pd(DBA)₂ (DBA =

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dibenzylideneacetone) and 4 mol % of $P(o-tol)_3$ in toluene at 65 °C formed *N*-benzyl-*N*-methyl-3,5-xylidine in 84% yield (Scheme 1).^{6a} The corresponding reaction of aryl iodides⁷ and amines required higher temperatures and produced slightly lower yields of cross-coupled product than did aryl bromides.

The proposed catalytic cycle for the palladiumcatalyzed amination of aryl halides, based on Hartwig's mechanism for the cross-coupling of aminostannanes with aryl bromides, ^{5b,c} is shown in Scheme 2. The key steps include the cleavage of the aryl halide dimer **A** (X = Br, I) by free amine to form the corresponding palladium amine monomer **B** followed by deprotonation to generate the requisite three-coordinate palladium amide complex **C**. Due to the central role of the 1:1 palladium amine adducts **B** in the overall catalytic cycle, we have been interested in the factors which influence both the formation and reactivity of these complexes. Here we report on the synthesis and solution structure of a series of cyclic and acyclic palladium tris(*o*-tolyl)phosphine mono(amine) complexes.⁸

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⁽⁷⁾ Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 1133. (8) While this work was in progress, Hartwig and co-workers reported the syntheses of some palladium tris(*o*-tolyl)phosphine amine adducts: Paul, F.; Patt, J.; Hartwig, J. F. *Organometallics* **1995**, *14*, 3030.

9





Results and Discussion

Synthesis of the Palladium Aryl Bromide and **Iodide Dimers** { $Pd[P(o-tol)_3](Ar)(\mu-X)$ }₂. Hartwig has previously reported the synthesis of the aryl bromide dimers { $Pd[P(o-tol)_3](p-C_6H_4R)(\mu-Br)$ }₂ (R = t-Bu (1), Me (2), *n*-Bu) from the reaction of $Pd[P(o-tol)_3]_2$ with the corresponding aryl bromide.^{5b,c,8} However, we sought a synthesis of the aryl bromide dimers which did not require isolation of the bis(phosphine) complex Pd[P(otol)₃]₂. To this end, reaction of Pd₂(DBA)₃, P(o-tol)₃ (8 equiv), and 1-bromo-4-tert-butylbenzene (10 equiv) in benzene for 1 h led to the isolation of the palladium bromide dimer 1 in 69% yield (Scheme 3). A similar procedure was employed to synthesize the bromide dimers $2 \cdot \frac{1}{4}OEt_2$ (76%) and $\{Pd[P(o-tol)_3](p-C_6H_4OMe) (\mu$ -Br) $_{2}$ (3; 46%) and also the aryl iodide dimers {Pd- $[P(o-tol)_3](p-C_6H_4CMe_3)(\mu-I)\}_2$ (4; 52%), $\{Pd[P(o-tol)_3](p-C_6H_4CMe_3)(\mu-I)\}_2$ $C_{6}H_{4}Me(\mu-I)_{2}$ (5; 60%), and $\{Pd[P(o-tol)_{3}](p-C_{6}H_{4}OMe)(\mu-I)_{3}\}$ I) $_{2}$ (6; 51%).

In the syntheses of palladium bromide dimers **1–3**, reaction times of >1 h led to contamination of the desired aryl bromide dimer with the bis(phosphine) dibromide complex Pd[P(o-tol)₃]₂Br₂ (**7**),⁹ although the extent of contamination was dependent on the aryl bromide. For example, reaction of Pd₂(DBA)₃, P(o-tol)₃, and 1-bromo-4-*tert*-butylbenzene in benzene for 48 h formed only a trace (\leq 5%) of **7**, as determined by ¹H and ³¹P NMR analysis of the crude reaction mixtures. The analogous reaction of Pd₂(DBA)₃, P(o-tol)₃, and *p*-bromotoluene for 24 h gave a ~5:1 ratio of **1**:**7**, while reaction of Pd₂(DBA)₃, P(o-tol)₃, and *p*-bromoanisole for



24 h produced a ~1:1 mixture of **3**:7.¹⁰ ³¹P NMR analysis of the crude reaction mixtures in the syntheses of aryl iodide dimers **4**–**6** showed no evidence for formation of the diiodide mono(phosphine) dimer {Pd-[P(o-tol)_3]I(u-I)}₂.¹¹

8

Synthesis of Palladium Aryl Chloride Dimers. Due to the low cost and wide availability of aryl chlorides, the palladium-catalyzed cross-coupling of amines with aryl chlorides represents a significant and as yet unrealized transformation.¹² Because the palladium aryl chloride dimers $\{Pd[P(o-tol)_3](Ar)(\mu-Cl)\}_2$ are the potential intermediates in these transformations, we have also investigated their coordination chemistry. However, because the direct oxidative addition of aryl chlorides to Pd₂(DBA)₃/P(o-tol)₃-derived catalysts has not yet been demonstrated, palladium chloride dimers were generated via silver-mediated halide exchange from the corresponding bromide or iodide dimers. For example, when a suspension of iodide dimer 5 and AgOTf in CH₃CN was stirred for 2 min, a yellow solution of Pd[P(o-tol)₃](p-C₆H₄Me)(CH₃- $(CN)_2$ ⁺OTf⁻ (8) was formed and treated with LiCl without isolation (Scheme 4). The resulting creamcolored suspension was evaporated, extracted with toluene, and precipitated with hexane to give the aryl chloride dimer $\{Pd[P(o-tol)_3](p-C_6H_4Me)(\mu-Cl)\}_2$ (9) in 93% yield. Dimer 9 was characterized by ¹H NMR, ³¹P NMR, and elemental analysis. By a similar procedure, the chloride dimer $\{Pd[P(o-tol)_3](p-C_6H_4CMe_3)(\mu-Cl)\}_2$ (10) was formed from bromide dimer 1 via the bis-(acetonitrile) adduct $Pd[P(o-tol)_3](p-C_6H_4CMe_3)(CH_3 (CN)_{2}^{+}OTf^{-}$ (11).

Attempts to isolate the bis(acetonitrile) adducts **8** and **11** by concentration of solvent or by precipitation with ether led to rapid decomposition. However, the corresponding cations $Pd[P(o tol)_3](p C_6H_4Me)(CD_3CN)_2]^+OTf^-$ (**8**-(CD_3CN)_2) and $Pd[P(o tol)_3](p C_6H_4CMe_3)(CD_3CN)_2]^+$.

 $\begin{array}{rcl} ArBr + L_2Pd^{(0)} & \longrightarrow Pd^{(l)}Br(L)_2 + Ar^{\cdot} \\ 2Pd^{(l)}Br(L)_2 & \longrightarrow 2Pd^{(l)}Br_2(L)_2 + L_2Pd^{(0)} \end{array}$

Ar: ____ ArH

(11) Reaction of PdI₂ and excess P(o-tol)₃ (2 equiv) forms only the mono(phosphine) diiodide complex $\{Pd[P(o-tol)_3]I(\mu-I)\}_2$ and none of the corresponding bis(phosphine) monomer (see Experimental Section). (12) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047.

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⁽¹⁰⁾ The origin of dibromide complex 7 is not clear. The reaction of p-bromoanisole with Pd₂(DBA)₃ and P(o-tol)₃ in C₆D₆ did not produce detectable quantities of the palladium bis(p-anisole) complex Pd[P(o-tol)₃]₂(p-anisole)₂ (as determined by 'H NMR) or its reductive-elimination product 4.4'-dimethoxybiphenyl (as determined by GCMS analysis), which suggests that 7 is not formed by disproportionation of **3**. Similarly, products derived from insertion of DBA into a palladium–anisyl bond followed by β -hydrogen elimination, such as PhCHCHC(O)C(p-anisyl)CHPh or PhCHCHC(O)CHC(p-anisyl)Ph, were not detected. Such a process would presumably lead to the formation of free HBr via reductive elimination from the initially formed palladium bromide hydride complex. However, GC–MS analysis of the reaction mixture indicated the presence of an electron transfer process. We thank a reviewer for suggesting this mechanism.



OTf⁻ (**11**-(CD₃CN)₂) were generated in CD₃CN and were analyzed without isolation by ¹H, ³¹P, and ¹⁹F NMR spectroscopy. The ¹H NMR spectrum of **8**-(CD₃CN)₂ at 75 °C displayed a singlet at δ 2.25 for the time-averaged P(*o*-tol)₃ methyl groups and a peak at δ 2.09 for the *p*-tolyl methyl group. As the temperature was lowered, the signals for the P(*o*-tol)₃ methyl groups broadened and split into three resonances at δ 3.11, 2.13, and 1.53 at -47 °C. In the ¹⁹F NMR spectrum of **8**-(CD₃CN)₂ no resonances were observed which could be assigned to coordinated OTf. Similar bis(acetonitrile) or bis(solvent) palladium complexes have been generated via reaction of palladium halide complexes with silver salts.¹³

Synthesis of Palladium Amine Complexes. Amines reacted rapidly (<1 min) with palladium halide dimers via cleavage of the halide bridge to produce monomeric palladium amine complexes (Scheme 5).8 For example, addition of N-benzylmethylamine (5 equiv) to a yellow benzene solution of the chloride dimer 9 gave a clear solution from which the 1:1 palladium amine adduct Pd[P(o-tol)₃](p-C₆H₄Me)[HN(Me)Bn]Cl (12) precipitated in 85% yield as a white microcrystalline solid. Amine adduct 12 was characterized by spectroscopy and by elemental analysis, and a trans orientation of the amine and phosphine ligands is inferred by analogy to the corresponding benzylamine derivative (see below). The ¹H NMR spectrum of **12** (CDCl₃, 55 °C) displayed a resonance at δ 2.07 for the methyl group of the *p*-tolyl ligand and a broad peak at δ 2.3 ($\omega_{1/2}$ = 70 Hz) for the methyl groups of the $P(o-tol)_3$ ligand. Coordination of amine to palladium was confirmed by resonances for the diastereotopic benzyl protons at δ 4.39 (br t, J = 12.4Hz) and 3.47 (dd, J = 7.0, 12.5 Hz). The presence of an NH proton was confirmed by a ¹H NMR resonance at δ 3.22, which diminished in intensity upon addition of D₂O.

The related 1:1 palladium bromide and iodide *N*benzylmethylamine adducts were more soluble than complex **12** and were synthesized by a modified procedure. Addition of *N*-benzylmethylamine to a yellow methylene chloride solution of bromide dimer **2** gave a clear solution. Concentration of the solution and addition of hexane gave the 1:1 palladium amine adduct Pd- $[P(o-tol)_3](p-C_6H_4Me)[HN(Me)Bn]Br$ (**13**) in 83% yield. Likewise, reaction of *N*-benzylmethylamine with the palladium iodide dimer led to the isolation of the amine adduct Pd[P(o-tol)_3](p-C_6H_4Me)[HN(Me)Bn]I (**14**) in 71% yield. Unlike the corresponding chloride (**12**) and bromide adducts (**13**), the room-temperature ¹H NMR



spectrum of **14** revealed an equilibrium mixture of **14** and **5** (~80:20) and HN(Me)Bn.¹⁴ An excess of *N*-benzylmethylamine (0.03 M) was required to effect complete conversion (>95% by ¹H NMR) of **5** to **14** in solution at room temperature.

Palladium amine adducts **13** and **14** were also formed as the exclusive products in the reaction of *N*-benzylmethylamine, $Pd_2(DBA)_3$, $P(o\text{-tol})_3$, and *p*-bromotoluene or *p*-iodotoluene, respectively, in C₆D₆. Isolation of **13** or **14** from the corresponding preparative-scale reactions was complicated by the comparable solubility of free DBA. However, the related amine adduct $Pd[P(o\text{-tol})_3]$ - $(p\text{-}C_6H_4OMe)[HN(CH_3)Bn]Br$ (**15**) was isolated in 51% yield from reaction of *p*-bromoanisole, *N*-benzylmethylamine, $Pd_2(DBA)_3$, and $P(o\text{-tol})_3$. The formation of the 1:1 palladium amine adducts **13–15** from mixtures of $Pd_2(DBA)_3$ and $P(o\text{-tol})_3$ is consistent with the intermediacy of the 1:1 amine adducts in the $Pd_2(DBA)_3/P(o\text{-tol})_3$ -catalyzed cross-coupling of aryl halides and amines.

Although the chloride adduct 12 was thermodynamically stable, the coordinated *N*-benzylmethylamine was kinetically labile and was readily displaced by free amine. For example, addition of benzylamine to a solution of **12** in CDCl₃ revealed resonances in the ¹H NMR spectrum after <1 min corresponding to benzylamine, N-benzylmethylamine, **12**, and Pd[P(o-tol)₃](p- C_6H_4Me)[H₂NBn]Cl (16), where K = [16][HN(Me)Bn]/[12][benzylamine] \approx 4 at 25 °C (Scheme 6).¹⁴ The ¹H NMR spectrum obtained after 15 min was identical with that obtained directly after addition of benzylamine, consistent with rapid approach to equilibrium. Likewise, addition of HN(Me)Bn to a CDCl₃ solution of 16 generated an equilibrium mixture of 12, 16, HN(Me)-Bn, and benzylamine. Pure 16 was isolated in 70% yield from reaction of benzylamine with 9, although the synthesis was complicated by formation of the bis-(benzylamine) complex Pd(p-C₆H₄Me)[H₂NBn]₂Cl.¹⁵

The stereochemistry of the 1:1 palladium amine adducts was determined from the ³¹P NMR spectra of the ¹⁵N-labeled benzylamine adducts Pd[P(o-tol)₃](p-C₆H₄Me)[H₂¹⁵NBn]Cl (**16**⁻¹⁵N) and Pd[P(o-tol)₃](p-C₆H₄-Me)[H₂¹⁵NBn]Br (**17**⁻¹⁵N). **16**⁻¹⁵N displayed a doublet in the ³¹P{¹H} NMR spectrum at δ 28.3 ($J_{PN} = 40.0$ Hz), while the bromide derivative **17**⁻¹⁵N displayed a doublet at δ 27.7 ($J_{PN} = 40.1$ Hz). The J_{PN} values observed for **16**⁻¹⁵N and **17**⁻¹⁵N are consistent with *trans*-phosphine

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⁽¹⁴⁾ The equilibrium constant for the formation of palladium amine adducts from the corresponding halide dimers is dependent on both the halide ligand and the amine: Widenhoefer, R. A.; Buchwald, S. L. *Organometallics* **1996**, *15*, 2755.

⁽¹⁵⁾ The rate and extent of formation of bis(amine) complexes was dependent on both the amine and the halide ligand. We are currently investigating the formation of palladium bis(amine) complexes in detail as a potential chain-limiting step in the catalytic cross-coupling of aryl bromides and primary amines.

and amine ligands.¹⁶ For example, in a series of rhodium complexes containing amine and phosphine ligands, trans-J_{PN} ranged from 35 to 45 Hz, while cis- $J_{\rm PN}$ was consistently <5 Hz.^{16a}

Conformations and Interchange Mechanisms of M[**P**(*o*-tol)₃] **Complexes.** In his initial report, Migita noted that the P(o-tol)₃ ligand was crucial to the success of the palladium-catalyzed cross-coupling of aryl bromides and aminostannanes.¹ The use of $P(o-tol)_3$ has also been shown to produce higher reaction rates than PPh₃ in both the palladium-catalyzed Heck arylation reaction¹⁷ and Stille reaction.¹⁸ The enhanced activity of $P(o-tol)_3$ has typically been attributed to the steric bulk of the P(o-tol)₃ ligand, which promotes both phosphine lability and coordinative unsaturation of the metal.¹⁸ In addition, $P(o-tol)_3$ can also undergo cyclometalation of the o-methyl group with electrophilic transition metals^{17,19} to generate catalysts of unusually high activity. For example, Herrmann and Beller have recently shown that $P(o-tol)_3$ reacts with $Pd(OAc)_2$ to

form the acetate-bridged cyclometalated dimer {Pd[P(o-

tol)₂-o-C₆H₄CH₂](μ -OAc)₂, which was an extremely active catalyst for both the Heck arylation reaction²⁰ and the Suzuki cross-coupling reaction.²¹

Of the potential conformations available to rotationally restricted triaryl systems,²² two conformations of $P(o-tol)_3$ are accessible and have been observed in structurally characterized metal complexes. The exo₃ conformation²³ orients the three *o*-methyl groups toward the metal atom (exo), with each o-tolyl ring rotated approximately 60° off the M-P-ipso-C plane (Figure 1). The *exo*₂ conformation²⁴ possesses two *exo o*-tolyl groups in an orientation similar to those in the exo3 conformer, while the third *o*-methyl group is directed away from the metal atom (endo) with the o-tolyl ring rotated only slightly off the M–P–*ipso*-C plane (\sim 15°). The exo₂ conformation decreases the phosphine cone angle $\sim 35^{\circ}$ relative to the *exo*₃ conformation at the expense of approximately 9 kcal mol⁻¹ increased strain energy between the *o*-tolyl groups.²⁵ For example, Tolman calculated a cone angle for exo3-P(o-tol)3 of 195°

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Figure 1. The two-ring-flip mechanism for interconversion of the exo_3 and exo_2 conformations of the P(o-tol)₃ ligand, as viewed down the M–P axis.

from space-filling CPK models with a $M{-}P$ bond distance of 2.28 Å, 26 while a cone angle of 198° was determined from the crystal structure of the mercury perchlorate dimer {Hg[ClO₄][P(o-tol)₃](μ -Cl)}₂.²⁷ Conversely, a cone angle of 160° was calculated from the crystal structure of the exo₂-P(o-tol)₃ chromium dicarbonyl complex (p-xylene)Cr(CO)₂P(o-tol)₃.²⁸ Both the exo_3 and exo_2 P(o-tol)₃ conformers are chiral due to the screw axis generated by the propeller-like arrangement of the o-tolyl rings.

Because of the steric congestion about the o-tolyl rings, rotation about a single P-ipso-C bond requires correlated rotation about the other two P-ipso-C bonds. These rotations are often of sufficient energy to generate configurationally stable conformers and enantiomers on the NMR time scale. The mechanisms for the correlated rotation of sterically hindered triaryl systems were originally proposed by Kruland.²⁹ The lowest energy process for P-C bond rotation in $P(o-tol)_3$ complexes involves rotation of one ring (Figure 1, ring a) through the plane perpendicular to the M-P-*ipso*-C plane with correlated rotation of the other two rings (Figure 1, rings b and c) through the corresponding M-P-ipso-C planes.³⁰ This two-ring-flip mechanism²⁹ interconverts the exo₂ and exo₃ isomers and necessarily inverts the helicity of the phosphine; consecutive two-ring flips then leads to complete interchange of the o-tolyl rings.

Fluxional Behavior and Solution Structure of 13. The ¹H NMR spectrum of bromide adduct 13 in CD_2Cl_2 at -42 °C displayed a 1:1:1 ratio of three sets of P(o-tol)₃ methyl resonances at δ 3.30, 3.50, 3.27 (~8: 2:1), δ 2.39, 2.14, 2.26 (~8:2:1), and δ 1.54, 1.61, 1.58

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Figure 2. Variable-temperature ¹H NMR spectrum of the H-6 resonance of the *endo*-P(*o*-tol)₃ ring of **13** in CD_2Cl_2 . Temperatures are given in °C.

 $(\sim 8:2:1)$ ³¹ As the temperature was raised, the P(*o*-tol)₃ methyl resonances broadened and coalesced at 24 °C, forming a single broad resonance at δ 2.30 ($\omega_{1/2} = 95$ Hz) at 55 °C (CDCl₃). In addition, the -42 °C spectrum displayed a \sim 2:1:8 ratio of high-frequency peaks at δ 9.36 (dd, J = 7.33, 18.7 Hz), 8.71 (dd, J = 8.2, 18.1 Hz), and 8.36 (dd, J = 8.0, 17.6 Hz) (Figure 2), which integrated to one proton. As the temperature was raised, these resonances broadened and coalesced at \sim 15 °C (Figure 2), eventually forming a broad threeproton resonance at δ 7.5–8.0 at 55 °C (CDCl₃). The p-tolyl methyl resonance, which was observed as a sharp singlet at δ 2.05 at 55 °C in CDCl₃, broadened slightly but did not split upon cooling to -50 °C (CD₂Cl₂). Resonances corresponding to the coordinated amine were broadened and uninformative at low temperatures.

The ¹H NMR spectrum of **13** at -42 °C is consistent with two processes: (1) hindered rotation about the P–*ipso*-C bonds with predominant formation of the *exo*₂-P(*o*-tol)₃ conformer and (2) hindered rotation about the Pd–P bond with formation of three unequally populated rotamers (see below). The high-frequency resonance at δ 8.36 (dd, J = 8.0, 17.6 Hz, major isomer) is indicative of the *exo*₂-P(*o*-tol)₃ conformation as the H-6 proton of the *endo*-P(*o*-tol)₃ ring is forced into close proximity to the palladium d_z² orbital. The H-6 proton then experiences a downfield shift due to the paramagnetic anisotropy of the palladium atom.³² A similar chemical shift and J_{PH} value (δ 9.27 (d, J_{PH} = 16 Hz)) was



Figure 3. Pd-P bond rotamers of the exo_2 - $P(o-tol)_3$ ligand in **13** relative to the *p*-tolyl and bromide ligands, as viewed down the N-Pd-P axis (amine not shown).

observed for the H-6 proton of the *endo*-P(*o*-tol)₃ ring in the ¹H NMR spectrum of the palladium complex Pd-[P(*o*-tol)₃][hfac]₂ (hfac = 1,1,1,5,5,5-hexafluoro-2,4-pentanedionate).³³ Similarly, the bis(phosphine)palladium complex Pd[P(*t*-Bu₂Ph)]₂ displayed a resonance at δ 9.33 for the deshielded *ortho* phenyl protons.³⁴

The formation of a 1:1:1 ratio of $P(o-tol)_3$ methyl resonances at δ 3.30, 2.39, and 1.54 (major isomer) is expected for a static exo_2 - $P(o-tol)_3$ ligand. One *o*-methyl group is distinguished by its *endo* orientation; the two *exo-o*-methyl groups are inequivalent due to the helicity of the phosphine, which orients one *o*-methyl group toward an *endo-o*-tolyl ring and one *o*-methyl group toward an *exo-o*-tolyl ring (Figure 1). The failure to detect *p*-tolyl or $P(o-tol)_3$ methyl resonances which did not correlate with a high-field resonance indicates that the concentration of the *exo*₃ isomer (which would display *p*-tolyl and $P(o-tol)_3$ methyl resonances but no high-field resonance) must be small (<10%).

The 2:1:8 multiplicity of both the 1:1:1 P(o-tol)₃ methyl groups and the high-field H-6 endo-o-tolyl resonance of **13** in the ¹H NMR spectrum at -42 °C is consistent with hindered rotation about the Pd-P bond with the formation of three unequally populated rotamers. Three gauche rotamers of the P(o-tol)₃ ligand which differ in the relative orientation of the endo-P(o-tol)₃ ring to the cis-bromide and p-tolyl ligands are depicted in Figure 3. Presumably, the highest frequency H-6 endo-P(o-tol)₃ resonance (δ 9.36) corresponds to rotamer **13a**, in which the *endo* ring is in closest proximity to the d_{z^2} orbital. However, halide ligands have also been shown to induce downfield shifts in proximal aromatic resonances.³⁵ Hindered rotation of M-P bonds with formation of rotamers in metal complexes possessing bulky phosphine ligands has been observed. For example, the bis-(phosphine) carbonyl chloride complexes M[P(t-Bu)₂Et]₂-(CO)Cl (M = Ir,³⁶ Rh³⁷) displayed resonances corresponding to three rotamers in the low-temperature ³¹P NMR spectrum.

The presence of a single $P(o-tol)_3$ resonance at δ 2.33 in the ¹H NMR spectrum of **13** at 55 °C is consistent with rapid rotation about both the Pd–C and Pd–P bonds. Although P–C rotation in $P(o-tol)_3$ complexes is typically of higher energy than M–P rotation, the

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Figure 4. Potential diastereomers of **13** as viewed down the N-Pd-P bond. Diastereomers are related horizontally by inversion of phosphine helicity and vertically by amine inversion; enantiomers are related diagonally.

simultaneous coalescence of all nine $P(o-tol)_3$ methyl resonances indicates that the two processes possess comparable rotational barriers. The simultaneous coalescence of the $P(o-tol)_3$ methyl resonances may result from correlated P-C and Pd-P rotation due to intermeshing of the phosphine o-tolyl rings with the p-tolyl ligand. The presence of diastereotopic benzyl protons of the coordinated HN(Me)Bn ligand at 55 °C requires that chirality of the amine be static on the NMR time scale.

Although hindered Pd-P bond rotation has precedence and adequately accounts for the 2:1:8 isomer ratio observed in the low-temperature ¹H NMR spectrum of 13, hindered Pd-P bond rotation is not required to produce the observed isomers. For example, because both the phosphine and the amine are chiral on the NMR time scale, two sets of diastereomers of 13 are possible (Figure 4). In addition, three geometric isomers, two of which possess *cis*-amine and phosphine ligands, are also possible (Figure 5). As a result, a combination of diastereomers and geometric isomers could account for the observed 2:1:8 ratio of isomers in **13**. In an effort to probe for the presence of these potential isomers, we investigated the variable-temperature ³¹P{¹H} NMR spectrum of **16**-¹⁵N, which possesses an achiral, ¹⁵N-labeled amine.

The ${}^{31}P{}^{1}H$ NMR spectrum of 16- ${}^{15}N$ at -42 °C displayed a \sim 2:1.3:1 ratio of doublets at δ 27.6 ($J_{\rm PN}$ = 36.8 Hz), 26.9 ($J_{\rm PN}$ = 35.6 Hz), and 23.9 ($J_{\rm PN}$ = 37.4 Hz), consistent with trans phosphine and amine ligands (Figure 6). As the temperature was raised, these doublets collapsed and eventually formed a doublet at δ 26.4 ($J_{\rm PN}$ = 40.1 Hz) at 35 °C. In addition, a small doublet at δ 27.1 (J_{PN} = 36.6 Hz) was observed at -33 °C which accounted for <10% of the total isomers and may correspond to a small amount of an *exo*₃-P(*o*-tol)₃ isomer. The presence of multiple isomers which all possess trans-phosphine and amine ligands in the lowtemperature ³¹P NMR spectrum of 16-¹⁵N suggests that the low-temperature isomers of 13 also correspond to neither geometric isomers nor diastereomers. The failure to observe diastereomers in 13 as a result of amine chirality indicates that either one set of diastereomers is highly favored relative to the second set or that chirality at nitrogen does not significantly perturb the chemical shifts of the P(o-tol)₃ proton resonances.

Amine adducts 12 and 14 displayed temperaturedependent ¹H NMR behavior analogous to that displayed by bromide derivative 13; at -42 °C, each complex displayed three high-frequency H-6 endo-P(otol)₃ resonances (Table 1) along with the corresponding $P(o-tol)_3$ methyl resonances. Because the chemical shifts for the $P(o-tol)_3$ methyl groups were similar for each complex, the coalescence temperature $(T_c; Table$ 1) is directly related to the rotational barrier for each complex. Comparison of T_c values (Table 1) reveals that $T_{\rm c}$ increased in the order 12 < 13 < 14, which corresponds to the van der Waals radius of the *cis*-halide ligand (Cl (1.75 Å) < Br (1.85 Å) < I (1.96 Å)],³⁸ presumably due to increased steric interaction of the $P(o-tol)_3$ ligand with increasing halide size. The steric bulk of ancillary ligands has been shown to increase the rotational barriers of P-C and M-P bonds of PPh3 and P(o-tol)₃ complexes.³⁹

Chelated Palladium Amine Complexes. Palladacyclic amine complexes are of interest as potential intermediates in the Pd-catalyzed intramolecular amination of haloamines.⁴⁰ A series of chelating palladium amine complexes was synthesized in a one-pot procedure analogous to that employed in the synthesis of **17**. For example, reaction of Pd₂(DBA)₃, P(*o*-tol)₃, and *N*-benzyl-*o*-iodophenethylamine in benzene for 24 h at room tem-

perature led to the isolation of the six-membered palla-

dacycle $Pd[P(o-tol)_3][2-C_6H_4(CH_2)\dot{N}(H)Bn]I$ (**18**) in 71% yield. By a similar procedure, the five-membered palladacyles $Pd[P(o-tol)_3][2-C_6H_4(CH_2)\dot{N}(H)p-tolyl]Br$ (**19**)

and $Pd[P(o-tol)_3][2-C_6H_4(CH_2)^{15}N(H)Ph]Br ($ **20**) and the

seven-membered palladacycle $Pd[P(o-tol)_3][2-C_6H_4(CH_2)_3-$

 $\dot{N}(H)Bn]Br$ (21) were also isolated.

The ¹H NMR spectra of the five-membered palladacycles were similar to those of the corresponding acyclic derivatives. For example, 20 displayed a 1:2.6:2.6 ratio of high-field resonances at δ 9.54 (br d, J = 17.2 Hz), 8.78 (dd, J = 7.05, 15.5 Hz), and 8.28 (dd J = 8.6, 17.5 Hz) in the low-temperature ¹H NMR spectrum (Figure 7, Table 1), and a 2.6:2.6:1 ratio of doublets at δ 36.8 $(J_{\rm PN} = 36.3 \text{ Hz}), 34.1 (J_{\rm PN} = 37.0 \text{ Hz}), \text{ and } 28.7 (J_{\rm PN} =$ 36.3 Hz) in the low-temperature ${}^{31}P{}^{1}H$ NMR spectrum (Figure 7, Table 1). Complexes 18 and 21 were somewhat unusual, as only a single isomer was detected by low-temperature ¹H and ³¹P NMR spectroscopy. As was anticipated, chelation promotes coordination of amine to the palladium atom. For example, the ¹H NMR spectrum of iodide complex 18 at 55 °C showed no evidence for amine dissociation and formation of a palladium iodide dimer, in contrast to the acyclic iodide derivative 14, which was \sim 35% dissociated at room temperature.

The chelated amine complexes **18–20** displayed higher coalescence temperatures (T_c) for the P(*o*-tol)₃ methyl resonances than did the corresponding acyclic derivatives (Table 1). In the chelated amine complexes, the

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Figure 5. Potential geometric isomers of 13.



Figure 6. Variable-temperature ${}^{31}P{}^{1}H$ NMR spectra of **16**- ${}^{15}N$ in CDCl₃. Temperatures are given in °C.

aryl ring is forced to lie in or near the coordination plane.⁴¹ Although this orientation may not produce excessive ground-state interaction between the H-6 proton of the palladium-bound aryl ligand and the phosphine-bound *o*-tolyl groups due to potential intermeshing, rotation about the Pd–P or P–C bonds will clearly produce a high-energy interaction. Conversely, the palladium: bound *p*-tolyl ligand of the corresponding acyclic amine complexes is able to rotate about the P–C bond and adopt an orientation perpendicular to the coordination plane either in the ground state or as a transition state for Pd–P and/or P–C rotation.⁴² The very high coalescence temperature (85 °C) of **18** apparently results from the combination of the large iodide ligand and the chelated aryl ring.

Conclusions

Reaction of aryl bromides or aryl iodides with a mixture of $Pd_2(DBA)_3$ and $P(o-tol)_3$ can be employed to

generate gram quantities of the corresponding palladium halide dimers in a single step as pure material. These halide dimers undergo a rapid bridge cleavage reaction with amines to form the corresponding 1:1 palladium amine adducts which possess trans phosphine and amine ligands. The amine complexes are also formed as the exclusive product in the reaction of Pd2- $(DBA)_3$ and $P(o-tol)_3$ with any halide and amine. Variable-temperature ¹H and ³¹P NMR analysis of the palladium amine adducts was consistent with hindered rotation about the P-C bonds, with predominant formation of the exo₂-P(o-tol)₃ conformer and hindered rotation about the Pd-P bond. The barriers for rotation about the P-C and Pd-P bonds were sensitive to the steric bulk of the ligands *cis* to the phosphine ligand. We are currently investigating the effect of both the halide ligand and the amine on the equilibrium formation and reactivity of the 1:1 palladium amine adducts and the relevance of these processes on the Pd-catalyzed cross-coupling of amines and aryl halides. In addition, we are investigating the formation of palladium bis-(amine) complexes as a potential chain-limiting step in the catalytic process.

Experimental Section

General Methods. Palladium halides, Pd₂(DBA)₃, aryl halides, amines, and phosphines were manipulated in air. All other manipulations and all reactions were performed under an 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 a septum. NMR spectra were obtained on a Varian XL-300 spectrometer in CDCl₃ at ambient temperature unless otherwise noted. ¹H and $^{13}C{^{1}H}$ (75.6 MHz) spectra were referenced relative to the residual solvent peak. Room-temperature ³¹P NMR (96 MHz) spectra were referenced relative to external 85% H₃PO₄; lowtemperature ³¹P NMR spectra were referenced relative to external PPh₃ in CDCl₃ (δ –4.69). Probe temperatures were calibrated with a 0.3% solution of HCl in methanol. IR spectra were recorded on a Perkin-Elmer Model 6000 FTIR spectrometer. Elemental analyses were performed by E+R Analytical 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. THF- d_8 and dioxane- d_8 were distilled from Na/K alloy, methylene chloride and methylene chloride- d_2 were distilled from CaH₂, and CDCl₃ was distilled from P₂O₅. Pd₂(DBA)₃ (Strem),⁴³ P(*o*-tol)₃ (Strem), 1-bromo-4-*tert*-butylbenzene (Fluka), 1-iodo-4-*tert*-butylbenzene (Lancaster), *p*-bromotoluene (Aldrich), *p*-iodotoluene (Lancaster), *p*-bromoanisole (Aldrich), and *p*-iodoanisole (Aldrich) were used as received. LiI (Aldrich), LiCl (Mallinckrodt), and LiBr (Aldrich) were dried at 80 °C under vacuum prior to use. *N*-Benzylmethylamine and benzylamine were purchased from Aldrich and were distilled from CaH₂ under N₂ prior to use.

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		-	-		
cmpd	temp (°C)	H-6 <i>endo</i> -P(<i>o</i> -tol) ₃ resonance (δ)	$P(o-tol)_3$ methyl resonances (δ)	isomer ratio	<i>T</i> _c (±5 °C) ^{<i>a</i>}
12	-42 ^b	9.33 (dd, J = 8.3, 17.6 Hz) 8.71 (dd, J = 7.8, 18.0 Hz) 8.34 (dd, J = 7.9, 17.0 Hz)	3.35, 2.00, 1.42 3.12, 2.11, 1.41 3.15, 2.24, 1.43	1.5 1 10	0 ^{<i>b</i>}
13	-42^{b}	9.36 (dd, J = 7.2, 18.6 Hz) 8.71 (dd, J = 7.1, 18.1 Hz) 8.36 (dd, J = 7.8, 17.6 Hz)	3.50, 2.14, 1.61 3.27, 2.26, 1.58 3.30, 2.39, 1.54	2.5 1 8.4	25 ^b
14	-16 ^b	9.46 (dd, J = 8, 18 Hz) 8.7 br 8.42 (dd, J = 8, 18 Hz)	3.32, 1.93, 1.37 3.48, 2.03, 1.48	5 1 5	55 ^c
18	-42^{b}	9.49 (dd, J = 8.2, 18.1 Hz)	3.17, 1.51, 0.83		65^d
19	-42 ^b	9.54 (br d, <i>J</i> = 18 Hz) 8.78 (dd, <i>J</i> = 8.4, 17.7 Hz) 8.38 (dd, <i>J</i> = 7.8, 17.7 Hz)	2.85, 1.32, 1.53 3.12, 1.82, 1.58 2.73, 1.94, 1.55	1 2.6 2.6	65 ^d
20	8 ^c	9.54 (br d, J = 17.2 Hz) 8.73 (dd, J = 7.1, 15.5 Hz) 8.28 (dd, J = 8.6, 17.5 Hz)	2.82, 1.30, 1.52 3.11, 1.92, 1.57 2.66, 1.79, 1.55	1 2.6 2.6	85 ^d
21	8 ^c	9.50 (dd, J = 7.8, 16.5 Hz)	3.18, 1.98, 0.92		

^a Coalescence temperature for P(o-tol)₃ methyl resonances. ^b CD₂Cl₂. ^c CDCl₃. ^d Toluene-d₈.



Figure 7. H-6 resonance of the *endo*-P(*o*-tol)₃ ring in the ¹H NMR spectrum (top) and ³¹P{¹H} NMR spectrum (bottom) of **20** at -42 °C in CD₂Cl₂.

Benzylamine- ${}^{15}N$ (Isotech) and aniline- ${}^{15}N$ (Cambridge Isotope Laboratories) were used as received. *N*-benzyl-*o*-iodophenethylamine and *N*-benzyl-3-(*o*-bromophenyl)propylamine were synthesized by published procedures.^{7a}

{**Pd[P(o-tol)**₃](*p*-C₆H₄CMe₃)(μ -Br)}₂ (1).⁸ A purple solution of Pd₂(DBA)₃ (1.5 g, 1.6 mmol), P(*o*-tol)₃ (2.0 g, 6.6 mmol), and *p*-tert-butyl bromobenzene (3.2 g, 14.7 mmol) in 80 mL of benzene was stirred at room temperature for 1 h. The resulting green-brown solution was filtered through Celite, and benzene was evaporated under vacuum. Addition of Et₂O (100 mL) to the oily residue formed a precipitate over 4 h, which was filtered, washed with Et₂O, and dried under vacuum to give 1 (1.4 g, 69%) as a yellow powder. ¹H NMR (55 °C): δ 7.24, 7.11, 7.03, 6.68, 6.48 (d, *J* = 8.2 Hz), 2.14 [br, 9 H, P(*o*-tol)₃], 1.08 (C₆H₄CMe₃). ³¹P{¹H} NMR: δ 28.7 (br). Anal.





Calcd (found) for $C_{62}H_{68}Br_2P_2Pd_2$: C, 59.68 (59.78); H, 5.49 (5.51); Br, 12.81 (12.62).

{**Pd**[**P**(*o*-tol)₃](*p*-C₆H₄Me)(μ -Br)}₂ (2).⁸ Reaction of Pd₂-(DBA)₃ (500 mg, 0.55 mmol), P(o-tol)₃ (700 mg, 2.3 mmol), and 4-bromotoluene (1.4 g, 8.2 mmol) using a procedure analogous to that used to prepare **1** led to the isolation of **2** (480 mg, 76%) as a bright yellow powder which contained 0.4 Et₂O/Pd by ¹H NMR analysis. ¹H NMR (55 °C): δ 7.65 (br), 7.26 (m), 7.07 (br), 6.58 (br), 6.30 (d, J = 7.71 Hz), 2.18 [br, 9 H, P(o-tol)₃], 1.98 (C₆H₄Me). ³¹P{¹H</sup>} NMR: δ 28.4 (br).

{**Pd**[**P**(*o*-tol)₃](*p*-**C**₆**H**₄**OMe**)(*µ*-**Br**)}₂ (**3**). Reaction of Pd₂-(DBA)₃ (250 mg, 0.27 mmol), P(*o*-tol)₃ (330 mg, 1.1 mmol), and 4-bromoanisole (510 mg, 2.7 mmol) using a procedure analogous to that used to prepare **1** led to the isolation of **3** (152 mg, 46%) as a bright yellow powder which contained traces (<5%) of Et₂O by ¹H NMR analysis. ¹H NMR (55 °C): δ 7.55 (br), 7.29 (m), 7.06 (br), 6.59 (br), 6.15 (d, *J* = 7.95 Hz), 3.53 (C₆H₄*OMe*), 2.19 [br, 9 H, P(*o*-tol)₃]. ³¹P{¹H} NMR: δ 28.2. Anal. Calcd (found) for C₅₆H₅₆Br₂O₂P₂Pd₂: C, 56.26 (56.53); H, 4.72 (4.96); Br, 13.37 (13.58).

{**Pd**[**P**(*o*-tol)₃](*p*-C₆H₄CMe₃)(*µ*-I)₂ (4). A solution of Pd₂-(DBA)₃ (250 mg, 0.27 mmol), P(*o*-tol)₃ (330 mg, 1.1 mmol), and *p*-*tert*-butyliodobenzene (700 mg, 2.7 mmol) in 15 mL of benzene was stirred at room temperature for 30 min. The resulting green-brown solution was filtered through Celite, and the solution was concentrated to 10 mL under vacuum. Addition of Et₂O (50 mL) formed an orange precipitate over 4 h, which was collected, washed with Et₂O, and dried under vacuum to give **4** (190 mg, 52%) as a pale orange powder. ¹H NMR (55 °C): δ 7.24, 7.10 (br), 6.88 (br), 6.50 (d, *J* = 8.33 Hz), 2.10 [br, 9 H, P(*o*-tol)₃], 1.08 (C₆H₄CMe₃). ³¹P{¹H} NMR: δ 25.8 (br). Anal. Calcd (found) for C₆₂H₆₈I₂P₂Pd₂: C, 55.50 (55.32); H, 5.11 (5.14); I, 18.92 (19.08).

{ $Pd[P(o-tol)_3](p-C_6H_4Me)(\mu-I)$ }₂ (5).⁸ Reaction of Pd₂-(DBA)₃ (250 mg, 0.27 mmol), P(o-tol)₃ (330 mg, 1.1 mmol), and

p-iodotoluene (0.6 g, 2.7 mmol) using a procedure analogous to that used to prepare **4** led to the isolation of **5** (207 mg, 60%) as a pale orange powder which contained traces (<5%) of Et₂O by ¹H NMR analysis. ¹H NMR (55 °C): δ 7.34, 7.07 (br), 6.73 (br), 6.32 (d, J = 6.38 Hz), 2.11 [br, 9 H, P(o-tol)₃], 1.98 (C₆H₄*Me*). ³¹P{¹H} NMR: δ 25.5 (br). Anal. Calcd (found) for C₅₆H₅₆I₂P₂Pd₂: C, 53.48 (53.45); H, 4.49 (4.65); I, 20.18 (20.19).

{**Pd[P(o-tol)_3]**(*p*-C₆H₄OMe)(μ -I)}₂ (6). Reaction of Pd₂-(DBA)₃ (250 mg, 0.27 mmol), P(*o*-tol)₃ (330 mg, 1.1 mmol), and *p*-iodoanisole (900 mg, 3.8 mmol) using a procedure analogous to that used to prepare **4** led to the isolation of **6** (180 mg, 51%) as a pale orange powder which contained traces (<5%) of Et₂O by ¹H NMR analysis. ¹H NMR (55 °C): δ 7.25 (m), 7.08 (br), 6.75 (br), 6.17 (d, J = 7.46 Hz), 3.53 (s, 3 H, C₆H₄O*Me*), 2.14 [br, 9 H, P(*o*-tol)₃]. ³¹P{¹H} NMR: δ 25 (br). Anal. Calcd (found) for C₅₆H₅₆I₂O₂P₂Pd₂: C, 52.16 (52.01); H, 4.38 (4.54); I, 19.68 (19.97).

{**Pd[P(o-tol)_3]I(µ-I)**}₂. A solution of PdI₂ (200 mg, 0.55 mmol), LiI (162 mg, 1.21 mmol), and P(*o*-tol)₃ (380 mg, 1.25 mmol) in MeOH (7 mL) was heated at reflux for 30 min. The resulting brown suspension was cooled to room temperature, filtered in air, washed with methanol (20 mL) and Et₂O (20 mL), and dried under vacuum to give {Pd[P(*o*-tol)₃]I₂}₂ (357 mg, 97%) as a dark brown powder. ¹H NMR: δ 9.21, 7.47, 7.14, 3.26, 1.90, 1.55. ³¹P{¹H} NMR: δ 30.6 (br). Anal. Calcd (found) for C₄₂H₄₂I₄P₂Pd₂: C, 37.95 (37.65); H, 3.26 (3.11); I, 38.19 (38.09).

Pd[P(o-tol)_3]_2Br₂ (7).⁹ Reaction of PdBr₂ (200 mg, 0.75 mmol), LiBr (140 mg, 1.61 mmol), and P(o-tol)₃ (514 mg, 1.70 mmol) using a procedure analogous to that used to prepare {Pd[P(o-tol)_3]I_2}₂ led to the isolation of 7 (623 mg, 100%) as an orange powder. ¹H NMR: δ 9.21, 8.85, 7.22, 7.10, 2.97 (br), 1.95 (br), 1.60. ³¹P{¹H} NMR: δ 20.2, 19.4 (~1:1).

{**Pd[P(o-tol)_3]**(*p*-C₆H₄Me)[**CD**₃**CN**]₂}⁺**OTf**⁻ (**8**-(**CD**₃**CN**)₂). Silver triflate (3 mg, 1×10^{-2} mmol) was added to a suspension of **5** (5 mg, 4×10^{-3} mmol) in CD₃CN (0.75 mL), and the mixture was shaken for 1 min. The resulting yellow solution of **8**-(CD₃CN)₂ was filtered into an NMR tube and analyzed without isolation. ¹H NMR (CD₃CN, 75 °C): δ 7.68 (m), 7.48 (t, J = 7.5 Hz), 7.33 (t, J = 7.5 Hz), 7.28 (t, J = 7.5 Hz), 6.56 (t, J = 7.5 Hz), 2.34 [br s, 9 H, P(*o*-tol)₃], 2.10 (s, 3 H, C₆H₄*Me*). ³¹P{¹H</sup>} NMR (CD₃CN, 50 °C): δ 25.2.

{**Pd**[**P**(*o*-tol)₃](*p*-C₆H₄Me)(*µ*-Cl)}₂ (9). A suspension of 5 (220 mg, 0.17 mmol) and AgOTf (94 mg, 0.37 mmol) in 5 mL of CH₃CN was stirred at room temperature for 5 min. The resulting yellow solution was decanted from the gray precipitate, which was extracted with an additional 5 mL of CH₃CN. LiCl (500 mg, 12.7 mmol) was added to the combined extracts, and the resulting suspension was stirred at room temperature for 2 days. Acetonitrile was evaporated under vacuum, and the residue was extracted with toluene and filtered through Celite. Evaporation of toluene and addition of Et₂O (5 mL) gave a pale yellow solution. Dropwise addition of pentane (10 mL) formed a yellow precipitate, which was washed with Et₂O and pentane and dried under vacuum to give 9 (175 mg, 93%) as a pale yellow powder. ¹H NMR: δ 7.68 (br, 3 H), 7.27 (t, J = 7.05 Hz, 3 H), 7.08 (m, 6 H), 6.48 (br, 2 H), 6.30 (d, J = 7.72Hz, 2 H), 2.22 [s, 9 H, P(o-tol)₃], 1.98 (s, 3 H, C₆H₄Me). ³¹P- $\{^1H\}$ NMR: δ 28.8. Anal. Calcd (found) for $C_{56}H_{56}Cl_2P_2Pd_2$: C, 62.59 (62.34); H, 5.25 (5.53); Cl, 6.60 (6.71)

{**Pd**[**P**(*o*-tol)₃](*p*-C₆H₄CMe₃)(μ -Cl)₂ (10). Reaction of 1 (410 mg, 0.33 mmol) and AgOTf (169 mg, 0.66 mmol), followed by treatment with LiCl (750 mg, 17.8 mmol) using a procedure analogous to that used to prepare **9**, led to the isolation of **10** (216 mg, 57%) as a yellow powder. ¹H NMR (55 °C): δ 7.70 (br, 3 H), 7.25 (m, 3 H), 7.08 (br, 6 H), 6.59 (br), 6.47 (d, J = 7.76 Hz), 2.17 [br, 9 H, P(*o*-tol)₃], 1.07 (C₆H₄CMe₃). ³¹P{¹H} NMR: δ 28.2. Anal. Calcd (found) for C₆₂H₆₈Cl₂P₂Pd₂: C, 64.26 (64.48); H, 5.91 (6.17); Cl, 6.12 (6.11).

{**Pd[P(o-tol)_3](p-C_6H_4CMe_3)[CD_3CN]_2**}⁺**OTf**⁻ (11-(**CD**_3-**CN)_2**). Reaction of silver triflate (5 mg, 2×10^{-2} mmol) and 1 (7 mg, 6×10^{-3} mmol) in CD₃CN (0.80 mL) using a procedure

analogous to that used to generate **8**-(CD₃CN)₂ formed **11**-(CD₃-CN)₂, which was analyzed without isolation by NMR. ¹H NMR (CD₃CN, 50 °C): δ 7.64 (m), 7.49 (t, J = 7.5 Hz), 7.28 (m), 6.75, 6.72, 6.67 (m), 2.16 [br s, 9 H, P(*o*-tol)₃], 1.32 (s, 3 H, C₆H₄*CMe*₃). ³¹P{¹H} NMR (CD₃CN, 50 °C): δ 25.2.

Pd[P(*o***-tol)₃](***p***-C₆H₄Me)[HN(CH₃)Bn]Cl (12).** *N***-Benzylmethylamine (263 mg, 2.2 mmol) was added to a yellow solution of 9** (200 mg, 0.19 mmol) in 10 mL of C₆H₆ and stirred at room temperature for 15 min, and the resulting clear solution was allowed to stand at room temperature. A white precipitate formed over 2 h, which was filtered, washed with ether, and dried under vacuum to give **12** (207 mg, 85%) as a white microcrystalline solid. ¹H NMR (55 °C): δ 7.63 (br), 7.51 (d, *J* = 3.4 Hz), 7.38 (m), 7.34, 7.29 (t, *J* = 7.5 Hz), 7.09 (m), 6.36 (m), 4.39 [br t, *J* = 12.4 Hz, 1 H, HN(CH₃)C*H*₂Ph], 3.47 [dt, *J* = 12.5, 7 Hz, HN(CH₃)C*H*₂Ph], 3.22 [br s, 1 H, *H*N(CH₃)-Bn], 2.46 [d, *J* = 6.0 Hz, 3 H, HN(CH₃)Bn], 2.22 [br, 9 H, P(*o*tol)₃], 2.03 (s, C₆H₄*Me*). ³¹P{¹H} NMR: δ 27.9. IR (Nujol): 3261 cm⁻¹. Anal. Calcd (found) for C₃₆H₃₉CINPPd: C, 65.66 (65.92); H, 5.97 (6.07); N, 2.13 (2.10).

Pd[P(*o***-tol)₃](***p***-C₆H₄Me)[HN(CH₃)Bn]Br (13).** *N***-Benzylmethylamine (160 mg, 1.32 mmol) was added to a yellow solution of 2** (150 mg, 0.13 mmol) in 5 mL of CH₂Cl₂ and 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 **13** (148 mg, 83%) as a pale yellow microcrystalline solid. ¹H NMR (55 °C): δ 7.84, 7.37, 7.29 (t, *J* = 7 Hz), 7.10, 6.38, 4.40 [br s, 1 H, HN(CH₃)C*H*₂Ph], 4.35 [br s, 1 H, *H*N(CH₃)Bn], 3.42 [br s, 1 H, HN(CH₃)C*H*₂Ph], 2.46 [br s, 3 H, HN(CH₃)Bn], 2.18 [br, 9 H, P(*α*-tol)₃], 2.05 (s, 3 H, C₆H₄*Me*). ³¹P{¹H</sup>} NMR: δ 27.9. IR (Nujol): 3257 cm⁻¹. Anal. Calcd (found) for C₃₆H₃₉-BrNPPd: C, 61.51 (61.63); H, 5.59 (5.83); N, 1.99 (2.06).

Pd[P(*o***-tol)₃](***p***-C₆H₄Me)[HN(CH₃)Bn]I (14). Reaction of 5 (220 mg, 0.18 mmol), and** *N***-benzylmethylamine (212 mg, 1.75 mmol) using a procedure analogous to that used to prepare 13** led to the isolation of **14** (186 mg, 71%) as a pale yellow microcrystalline solid. ¹H NMR (~80:20 ratio of **14**:5): δ 7.37, 7.29, 7.05, 6.4, 4.48 [br, 1 H, HN(CH₃)C*H*₂Ph], 3.47 [br, 1 H, HN(CH₃)C*H*₂Ph], 3.22, [br, 6 H, P(*o*-tol)₃], 2.48 [br, 3 H, HN(CH₃)Bn], 2.04 (s, 3 H, C₆H₄Me), 1.50 [br s, 3 H, P(*o*-tol)₃], *H*N(CH₃)Bn not observed. ³¹P{¹H} NMR {CDCl₃ [0.05 M HN(Me)Bn]}: δ 28.1. IR (Nujol): 3253 cm⁻¹. Anal. Calcd (found) for C₃₆H₃₉ClNPPd: C, 57.65 (57.53); H, 5.24 (5.48); N, 1.87 (2.14).

Pd[P(o-tol)₃](p-C₆H₄OMe)[HN(CH₃)Bn]Br (15). A purple solution of Pd₂(DBA)₃ (150 mg, 0.16 mmol), P(o-tol)₃ (250 mg, 0.82 mmol), p-bromoanisole (313.1 mg, 1.6 mmol), and benzyl-(methyl)amine (235 mg, 1.9 mmol) in 5 mL of benzene was stirred at room temperature for 2 days. The resulting greenbrown suspension was filtered through Celite, and the residue was extracted with CH₂Cl₂ (50 mL) and evaporated under vacuum. Addition of Et₂O (20 mL) to the resulting oily residue formed a yellow precipitate, which was filtered, washed with Et₂O and pentane, and dried under vacuum to give 15 (120 mg, 51%) as a pale yellow powder. ¹H NMR (C_6D_6 , 75 °C): δ 7.80, 7.20, 7.05, 6.88, 6.36, 4.55 [br, HN(Me)CH₂Ph], 3.50 [br, HN(Me)CH₂Ph], 3.29 (s, C₆H₄OMe), 3.18 [br, HN(Me)CH₂Ph], 2.33 [br, P(o-tol)₃], 2.25 [br, HN(*Me*)Bn]. ${}^{31}P{}^{1}H$ NMR: δ 27.9 (br). IR (Nujol): 3258 cm⁻¹. Anal. Calcd (found) for C₃₆H₃₉-BrNOPPd: C, 60.14 (60.35); H, 5.47 (5.79); N, 1.95 (1.95).

Pd[P(o-tol)₃](p-C₆H₄Me)[H₂NBn]Cl (16). Reaction of **9** (150 mg, 0.14 mmol) and benzylamine (74 mg, 0.7 mmol) using a procedure analogous to that used to prepare **13** led to the isolation of **16** (127 mg, 70%) as a pale yellow microcrystalline solid, which contained traces (≤5%) of hexane by ¹H NMR analysis. ¹H NMR (50 °C): δ 7.74 (br, 3 H), 7.28 (t, *J* = 6.4 Hz, 3 H) 7.21 (m, 3 H), 7.11 (m, 7 H), 6.58 (br s, 2 H), 6.46 (d, *J* = 7.3 Hz, 2 H), 3.75 (br, 2 H, H₂NCH₂Ph), 2.91 (br, 2 H, H₂NCH₂Ph), 2.21 [br s, 9 H, P(*o*-tol)₃], 2.07 (s, 3 H, C₆H₄Me).

³¹P{¹H} NMR: δ 28.3. Anal. Calcd (found) for C₃₅H₃₇-ClNPPd: C, 65.23 (65.03); H, 5.78 (5.93); N, 2.17 (2.31).

Pd[P(*o***-tol)₃](***p***-C₆H₄Me)[H₂¹⁵NBn]Cl (16⁻¹⁵N). Small amounts (<0.5 mL) of benzylamine⁻¹⁵N were added via syringe to a solution of 9** (7 mg, 6×10^{-3} mmol) in CDCl₃ (0.75 mL) and monitored after each addition by ¹H NMR spectroscopy. Addition of 1.4 mL of benzylamine⁻¹⁵N generated **16**⁻¹⁵N, which contained ~5% **9** by ¹H NMR analysis. ³¹P{¹H} NMR (50 °C): δ 28.1 (d, J_{PN} = 40.0 Hz).

Pd[P(*o***-tol)₃](***p***-C₆H₄Me)[H₂NBn]Br (17). Reaction of 2 (100 mg, 0.09 mmol), and benzylamine (19 mg, 0.18 mmol) using a procedure analogous to that used to prepare 13** led to the isolation of **17** (82 mg, 69%) as a pale yellow microcrystalline solid which contained traces (≤5%) of hexane by ¹H NMR analysis. ¹H NMR (50 °C): δ 7.80 (br s, 3 H), 7.31 (t, *J* = 7.9 Hz, 3 H), 7.24 (s, 5 H), 7.12 (br s, 6 H), 6.63 (br s, 2 H), 6.51 (br s, 2 H), 3.79 (br, 2 H, H₂NCH₂Ph), 2.98 (br, 2 H, H₂-NCH₂Ph), 2.20 [br s, 9 H, P(*o*-tol)₃], 2.09 (s, 3 H, C₆H₄*Me*). ³¹P-{¹H</sup>} NMR: δ 28.9. Anal. Calcd (found) for C₃₅H₃₇BrNPPd: C, 61.02 (61.25); H, 5.41 (5.32).

Pd[P(o-tol)₃](p-C₆H₄Me)[H₂¹⁵NBn]Br (17-¹⁵N). Reaction of benzylamine-¹⁵N and 2 (7 mg, 6×10^{-3} mmol) in CDCl₃ (0.75 mL) using the procedure employed in the synthesis of 16-¹⁵N formed 17-¹⁵N. ³¹P{¹H} NMR: δ 28.9 (d, $J_{PN} = 40.1$ Hz).

Pd[P(o-tol)₃][2-C₆H₄(CH₂)₂N(H)Bn]I (18). A purple suspension of Pd₂(DBA)₃ (200 mg, 0.21 mmol), P(o-tol)₃ (370 mg, 1.1 mmol), and 2-IC₆H₄(CH₂)₂N(H)Bn (535 mg, 0.57 mmol) in 20 mL of benzene was stirred at room temperature for 24 h. The resulting green-brown suspension was filtered through Celite, and benzene was evaporated under vacuum. Addition of Et₂O (10 mL) to the oily residue formed a white precipitate, which was filtered, washed with Et₂O, and dried under vacuum to give 18 (368 mg, 71%) as a yellow powder which was \geq 95% pure by ¹H NMR analysis. **18** was further purified by recrystallization from CH₂Cl₂/hexane. ¹H NMR (0 °C): 9.49 (dd, J = 8.2, 18.1 Hz), 7.4–6.3 (m, aromatic), 5.49 (br s, 1 H, NH, identified by D_2O exchange), 3.93 (dd, 1 H, J = 4.2, 13.8 Hz), 3.53 (dt, 1 H, J = 6.4, 13.2 Hz), 3.17 [s, 3 H, P(o-tol)₃], 2.81 (m, 2 H), 2.05 (br t, J = 9.3 Hz), 1.51 [s, 3 H, P(o-tol)₃], 0.83 [s, 3 H, P(o-tol)₃]. ³¹P NMR: δ 29.1. IR (Nujol): 3241 cm⁻¹. Anal. Calcd (found) for C₃₆H₃₇INPPd: C, 57.81 (57.63); H, 4.99 (4.84); N, 1.87 (1.80).

N-(p-tolyl)-o-bromobenzylamine. A suspension of 2-bromobenzyl bromide (5 g, 20.1 mmol), p-toluidine (10.7 g, 100 mmol), and K₂CO₃ (14 g, 100 mmol) in 20 mL of THF was refluxed for 18 h. After the suspension was cooled to room temperature, water (50 mL) and Et₂O were added and the layers were separated. The aqueous layer was extracted with Et_2O (3 \times 75 mL), and the combined Et_2O fractions were dried (MgSO₄) and concentrated using a rotary evaporator. The residue was chromatographed (SiO2, hexane/ethylacetate, (2/ 1) with 1% Et₃N), and the first band to elute was collected to give N-(p-tolyl)-o-bromobenzylamine (4.7 g, 85%) as a yellow oil which solidified upon standing. ¹H NMR: δ 7.55 (dd, J =2.2, 8.2 Hz, 1 H), 7.39 (dd, J = 2.0, 7.7 Hz, 1 H), 7.23 (dt, J = 2.0, 7.7 Hz, 1 H), 7.10 (dt, J = 1.8, 7.4 Hz, 1 H), 6.97 (d, J = 8.3 Hz, 2 H), 6.52 (d, J = 8.2 Hz, 2 H), 4.36 (s, 2 H), 4.05 (br s, 1 H), 2.22 (s, 3 H). ${}^{13}C{}^{1}H$ NMR: δ 145.6, 138.5, 132.9, 129.9, 129.3, 128.7, 127.6, 127.0, 123.4, 113.2, 48.8, 20.5. Anal. Calcd (found) for C₁₄H₁₄BrN: C, 60.89 (60.98); H, 5.11 (5.21).

 $\mathbf{Pd}[\mathbf{P}(o \cdot \mathbf{tol})_3][2 \cdot C_6 \mathbf{H}_4 \mathbf{CH}_2 \mathbf{N}(\mathbf{H})(p \cdot \mathbf{tolyl})]\mathbf{Br}$ (19). Reaction of $\mathbf{Pd}_2(\mathbf{DBA})_3$ (200 mg, 0.44 mmol), $\mathbf{P}(o \cdot \mathbf{tol})_3$ (290 mg, 0.95 mmol), and 2-Br- $C_6 \mathbf{H}_4 \mathbf{CH}_2 \mathbf{N}(\mathbf{H})(p \cdot \mathbf{tolyl})$ (345 mg, 1.25 mmol) using a procedure analogous to that used to prepare **18** gave **19** (260 mg, 77%). ¹H NMR (-42 °C): δ 9.54 (br d, J = 17 Hz), 8.78 (dd, J = 7.92, 17.6 Hz), and 8.38 (dd, J = 7.72, 17.6 Hz) (1:2.6:2.6, 1 H), 7.50–6.80 (m, 17 H), 6.2–6.5 (m, 3 H), 5.26 (dd, J = 6.3, 15.0 Hz), 5.16 (dd, J = 5.6, 14.6 Hz), and 4.94 (dd, J = 6.6, 15.3 Hz) (1:2.6:2.6, 1 H), 4.20 (br d, J = 15.3 Hz, 1 H), 3.12, 2.85, and 2.73 [2.6:1:2.6, 3 H, P(*o*-tol)₃], 2.26, 2.20, and 2.17 [2.6:2.6:1, 3 H, *p*-toly1], 1.94, 1.82, and 1.32 [2.6: 2.6:1, 3 H, P(*o*-tol)₃], 1.58, 1.55, 1.53 [2.6:2.6:1, 3 H, P(*o*-tol)₃]. IR (Nujol): 3187 cm⁻¹. ³¹P{¹H} NMR (96 MHz, CDCl₃, -42 °C): δ 37.3, 35.1, and 29.4 (2.6:2.6:1). Anal. Calcd (found) for C₃₅H₃₅BrNPPd: C, 61.20 (61.22); H, 5.14 (5.37); N, 2.04 (1.95).

Pd[P(o-tol)₃][2-C₆H₄(CH₂)¹⁵N(H)Ph]Br (20). A suspension of 2-bromobenzyl bromide (0.6 g, 2.4 mmol), aniline- ^{15}N (1 g, 11 mmol), and K₂CO₃ (1.4 g, 10 mmol) in 5 mL of THF was refluxed for 2 h. After the suspension was cooled to room temperature, water (5 mL) and Et₂O (5 mL) were added and the layers were separated. The aqueous layer was extracted with Et₂O (3 \times 5 mL), and the combined Et₂O fractions were dried (MgSO₄) and concentrated under vacuum to give a mixture of ¹⁵*N*-phenyl-*o*-bromobenzylamine-¹⁵*N*⁴⁴ and aniline- ^{15}N . The resulting oil was diluted to 5 mL with C₆H₆, and 1.5 mL of this solution was added via syringe to a solution of Pd2-(DBA)₃ (150 mg, 0.16 mmol) and P(*o*-tol)₃ (200 mg, 0.66 mmol) in C_6H_6 (10 mL). The resulting mixture was stirred for 2 h to form a brown solution, which was filtered through Celite and concentrated to 1 mL under vacuum. Addition of Et₂O (20 mL) formed a tan precipitate over 4 h, which was filtered, washed with Et₂O, and dried under vacuum to give **20** (113 mg, 51%) based on Pd) as a yellow powder which contained $\sim 5\%$ Et₂O by ¹H NMR analysis. ¹H NMR (0 °C): δ 9.54 (dd, J = 6.8, 17.2 Hz), 8.73 (dd, J = 7.05, 15.5 Hz), and 8.28 (dd J = 8.6, 17.5 Hz) (1:2.6:2.6, 1 H), 7.5–6.8 (m, 12 H), 6.6–5.8 (m, HN + aromatic, 3 H), 5.26 (dd, J = 7.2, 13.8 Hz), 5.17 (dd, J = 7.1, 14.2 Hz), and 4.95 (dd, J = 7.4, 13.7 Hz) (1:2.6:2.6, 1 H), 4.25 (d, J = 13.9 Hz, 1 H), 3.11, 2.82, and 2.66 [2.6:1:2.6, 3 H, P(otol)3], 1.92, 1.79, and 1.30 [2.6:2.6:1, 3 H, P(o-tol)3], 1.57, 1.55, and 1.52 [2.6:2.6:1, 3 H, P(o-tol)₃]. ³¹P{¹H} NMR (-42 °C): δ 36.8 (d, $J_{\rm PN} = 36.3$ Hz), 34.1 (d, $J_{\rm PN} = 37.0$ Hz), and 28.7 (d, $J_{\rm PN} = 36.3$ Hz) (2.6:2.6:1).

Pd[P(*o***-tol)₃](2-C₆H₄(CH₂)₃N(H)Bn]Br (21).** Reaction of Pd₂(DBA)₃ (410 mg, 0.88 mmol), P(*o*-tol)₃ (530 mg, 1.74 mmol), and 2-BrC₆H₄(CH₂)₃N(H)Bn (570 mg, 1.90 mmol) using a procedure analogous to that used to prepare **18** led to the isolation of **21** (150 mg, 24%) as a white powder. ¹H NMR: δ 9.6 (br, 1 H), 7.6–7.0, 6.8–6.2 (m, 8 H), 4.14 (s, 1 H), 4.01 (s, 2 H), 3.18 (s, 3 H), 3.10 (s, 2 H), 2.96 (s, 1 H), 3.36 (s, 1 H), 1.98 (s, 1 H), 1.77 (s, 1 H), 1.53 (s, 1 H), 0.92 (s, 3 H). ³¹P{¹H} NMR (50 °C): δ 28.5 (br). IR (Nujol): 3227 cm⁻¹. Anal. Calcd (found) for C₃₇H₃₉BrNPPd: C, 62.15 (61.87); H, 5.50 (5.43); N, 1.96 (2.13).

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