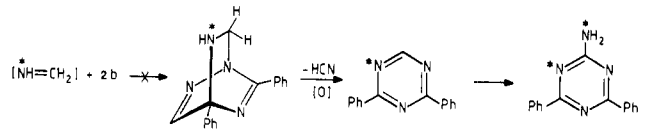
Scheme IV



16, which rearranges with expulsion of the hydride ion. The fate of this hydride ion is unknown, but due to the presence of many reducible double bonds, e.g., in **14** or **15**, reduction may occur. In any case the proposed mechanism explains the presence of the ring-labeled nitrogen atom derived from the amide ion and of the unlabeled exocyclic nitrogen derived from the nitrogen of the 1,2,4-triazine ring.

An alternative pathway to explain the formation of **4b**, involving as first step the nucleophilic addition of the anion of formamidine or aminocyan (both compounds previously found to be formed by amide-induced ring degradation of 1,2,4-triazines),[9] was considered, but this mechanism was excluded: reaction of **2b** with 1 equiv of potassium salt of formamidine, dissolved in liquid ammonia (free of amide ion) or with 1 equiv of potassium cyanamide (formed from aminocyan and 1 equiv of potassium amide) gave no detectable amounts of **4b**.

The possibility that **4b** is formed from **2b** by a Diels–Alder cycloaddition with inverse electron demand involving addition of methanimine, obtained as byproduct in the formation of 3,5-diphenyl-1,2,4-triazole (**3b**, see Scheme I) from **2b**, followed by loss of hydrogen cyanide, oxidation (by air) and subsequent amination (see above) was also taken into consideration (Scheme IV). Although this mechanism nicely explains the presence of the ^{15}N-label in the 1,3,5-triazine ring, it must be rejected, as this mechanism must lead to an amino compound, in which *both* amino group and ring nitrogen are ^{15}N-labeled; this has not been found.

Experimental Section

^1H NMR spectra were obtained with a Varian EM 390 with Me_4Si as internal standard. When measurements were made in liquid ammonia NH_3 was used as standard (adding 0.95 ppm converts the spectra to the Me_4Si scale). Mass spectra and ^{15}N-contents were determined on an AEI MS-902 mass spectrometer.

Amination Procedure for the Reaction of 1,2,4-Triazines 2a,b with Potassium Amide. To 20 mL of dry liquid ammonia in a 50-mL three-neck round-bottom flask equipped with a dry ice/acetone condenser were added a few crystals of ferric nitrate and 160 mg of potassium. After the mixture was stirred for 15 min at −33 °C the 1,2,4-triazine derivative (1 mmol) was added. The reaction was terminated after 24 h by the addition of 220 mg (4 mmol) of ammonium sulfate. After the ammonia was evaporated, the residue was thoroughly extracted with boiling chloroform. Separation of products was achieved by column chromatography on SiO_2 with chloroform for compounds **3b** and **4b** or chloroform–acetone (1:1) for compounds **3a** and **4a,c** as eluents.

The amination in ^{15}N-labeled liquid ammonia with ^{15}N-labeled potassium amide was carried out in the same manner.

Conversion of 2-Amino-4,6-diphenyl(^{15}N)-1,3,5-triazine (4b*) into 4,6-Diphenyl-1,3,5-triazin-6-one (9*). This conversion was performed by the same procedure as that described for the unlabeled compound.[12]

Conversion of 2-Amino-4-phenyl-1,3,5-triazine (4a) into 2,4-Diamino-6-phenyl-1,3,5-triazine (4c). 2-Amino-4-phenyl-1,3,5-triazine (1 mmol) was treated with 5 mmol of potassium amide in 20 mL of dry liquid ammonia. After 24 h the reaction was quenched with ammonium sulfate. The dry residue was extracted with boiling chloroform. Compound **4c** was purified by column chromatography (SiO_2, 1:1 chloroform–acetone). Yield of **4c**, 60%.

Preparation of 3,2′-Annelated 2-Phenylpyridines and Their Cyclopalladation Chemistry

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A series of 3,2′-polymethylene-bridged derivatives of 2-phenylpyridine has been prepared by thermolysis of *O*-allyloximes of 2,3-benzocycloalkanones. The electronic absorption and NMR spectra of these molecules may be related to the degree of nonplanarity of the system resulting from polymethylene bridging. These molecules react with palladium bis(acetylacetonate) and its hexafluoro derivative to give soluble, monomeric cyclopalladated products. Rates of cyclopalladation were measured for these systems as well as for 2-(phenyl-d_5)pyridine, and the results indicate the liklihood that for the less planar substrates the deprotonation step may show increasing importance over the electrophilic attack of palladium on the phenyl ring. The possible oxidative addition of palladium to a phenyl C–H bond cannot be ruled out.

The technique of bridging a biaryl system allows one to conveniently control the orientation of two covalently bonded aromatic rings with respect to one another. We have recently reported on the preparation and study of 3,3′-polymethylene-bridged derivatives of 2,2′-bipyridine,[1] 2,2′-biquinoline,[2] and 2,2′-bi-1,8-naphthyridine[3] as well as analogous bis-annelated derivatives of 2,2′;6′,2″-terpyridine.[4] An intriguing aspect of these molecules stems from our ability to control the orientation of the 1,4-bidentate chelating site by variation of the annelating bridge length. We have examined the effect of ligand conformation in coordination with copper(II),[5] ruthenium(II),[6]

(1) Thummel, R. P.; Lefoulon, F.; Mahadevan, R. *J. Org. Chem.* **1985**, *50*, 3824.
(2) Thummel, R. P.; Lefoulon, F. *J. Org. Chem.* **1985**, *50*, 666.
(3) Thummel, R. P.; Lefoulon, F.; Cantu, D.; Mahadevan, R. *J. Org. Chem.* **1984**, *49*, 2208.
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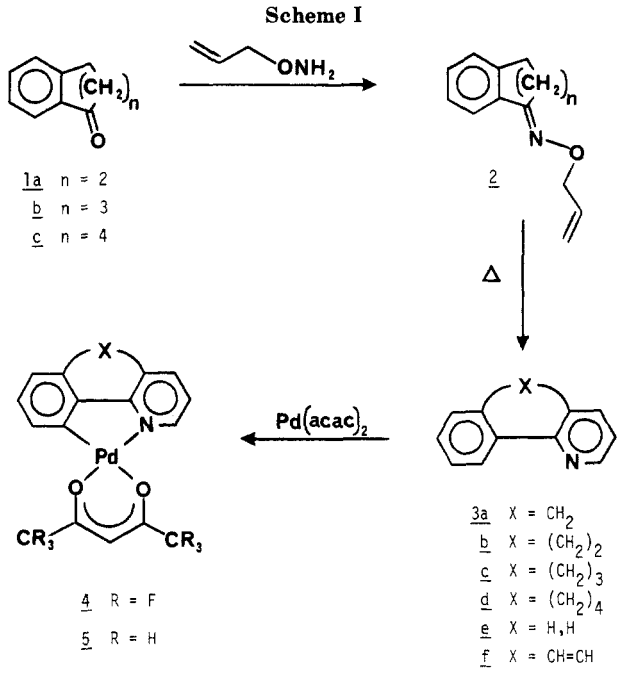
Scheme I



and dirhodium(I,I).[7] It appears that some flattening of the nonplanar ligands does occur upon coordination, resulting in strain that is absorbed partially by distortion of the bridge and partially by nonplanarity of the pyridine rings.

The 2-phenylpyridine molecule is a monodentate, which nevertheless can cyclometalate with species such as palladium, platinum, and rhodium to form five-membered rings. The reaction involves initial N-coordination with the metal followed by electrophilic attack on the 2′-position of the phenyl ring to form a covalent M–C bond. Our interest in conformational effects on coordination chemistry led us to explore the possible effects of conformation on this reaction by examining a series of 3,2′-annelated derivatives.

Synthesis

In 1983 Koyama and co-workers reported that the thermolysis of cycloalkanone oxime *O*-(allyl ethers) gave the corresponding 2,3-cycloalkenopyridines in moderate yields.[8] They reported the first synthesis of 5,6-dihydrobenzo[*h*]quinoline (**3b**), which is surprisingly unavailable via reduction of the parent benzo[*h*]quinoline.

Utilizing this methodology, we treated 1-benzosuberone (**1b**) and 1-benzocyclooctanone (**1c**) with *O*-allylhydroxylamine to obtain the oximes **2b** and **2c** in yields of 86% and 75%, respectively. Thermolysis of these oximes at 180–185 °C led to a multistep rearrangement resulting in the loss of H_2O and H_2 with the generation of the desired 3,2′-annelated 2-phenylpyridines **3c** and **3d** (Scheme I). Along with the previously known systems, **3a**,**b**,**e**,**f**, we now had in hand a series of substrates for cyclopalladation studies.

With the exception of **3a**, these 2-phenylpyridines reacted smoothly with palladium bis(hexafluoroacetylacetonate) (Pd[acac–F_6]$_2$) to provide the corresponding cyclopalladated series **4** as indicated in Scheme I. These materials were characterized by their elemental analyses as well as their 300-MHz ^{1}H NMR spectra. Each of the free ligands shows a clear doublet at low field for $H_{6'}$, which disappears upon cyclopalladation. The two protons held closest to the coordination site, $H_{5'}$ and $H_{6'}$ both experience upfield shifts as a result of complexation. The reaction of **3** with Pd[acac]$_2$ occurs more slowly, and the products show poorer solubility characteristics than their hexafluoro counterparts. Again **3a** was unreactive, and **3d** was too sluggish to readily afford pure product.

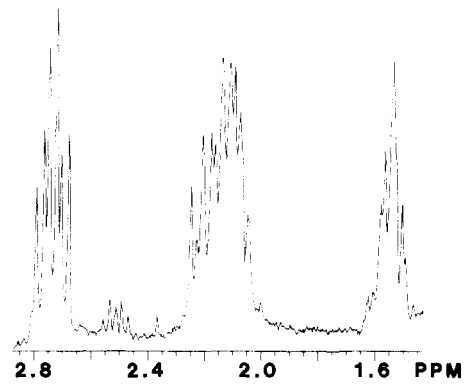


Figure 1. NMR spectrum of the bridge protons of **3d** (300 MHz, $CDCl_3$).

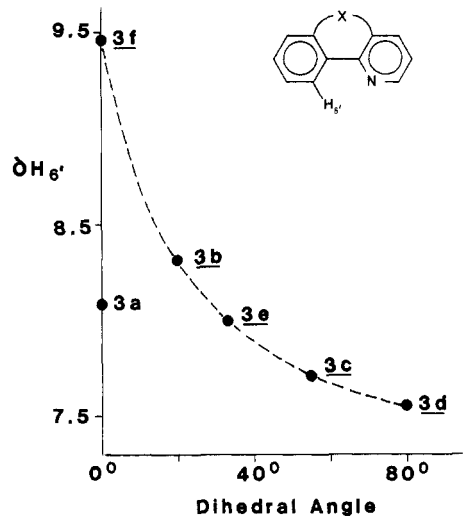


Figure 2. Correlation of the estimated dihedral angle and chemical shift of $H_{6'}$ for 3,2′-annelated 2-phenylpyridines.

Properties of Annelated 2-Phenylpyridines. An examination of molecular models of the annelated 2-phenylpyridines **3a–d** indicates two interesting phenomena. The dihedral angle between the phenyl and pyridyl rings varies as a function of the annelating bridge length. The monomethylene-bridged system is planar while estimates for the remaining systems are 20° for **3b**, 55° for **3c**, and 80° for **3d**. An examination of the upfield region of the ^{1}H NMR for **3a–c** shows patterns that are consistent with equivalence of the geminal protons on either the α- or β-methylene groups. The upfield region for **3d** (Figure 1), however, shows three sets of peaks similar to what is observed for the analogous 3,3′-tetramethylene-2,2′-bipyridine.[1] The two triplets at lower field are attributed to one proton each on the α- and α'-methylene groups. These two protons both lie nearly in the plane of the adjacent aromatic ring and are therefore shifted downfield. Conversely, one proton on the β- and β'-methylene groups points toward the shielding region of the more remote

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(6) (a) Thummel, R. P.; Jahng, Y. *Inorg. Chem.* **1986**, *25*, 2527. (b) Thummel, R. P.; Lefoulon, F. *Inorg. Chem.*, in press. (c) Thummel, R. P.; Lefoulon, F., submitted for publication in *Inorg. Chem.*
(7) (a) Thummel, R. P.; Lefoulon, F.; Williamson, D.; Chavan, M. *Inorg. Chem.* **1986**, *25*, 1675. (b) Bear, J. L.; Chau, L. K.; Chavan, M. Y.; Lefoulon, F.; Thummel, R. P.; Kadish, K. M. *Ibid.* **1986**, *25*, 1514.
(8) Koyama, J.; Sugita, T.; Suzuta, Y.; Ire, H. *Chem. Pharm. Bull.* **1983**, *31*, 2601.

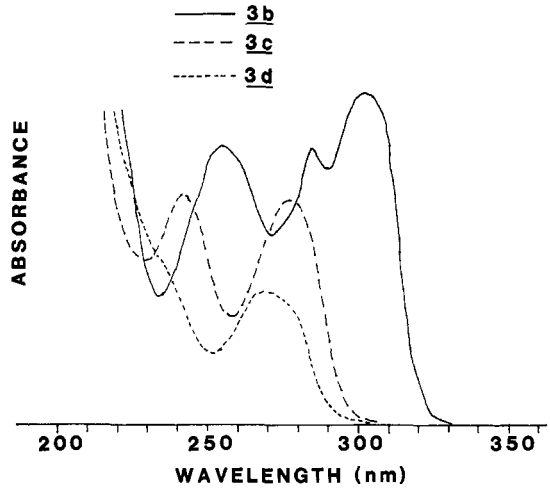


Figure 3. Ultraviolet absorption spectra of 3,2′-annelated 2-phenylpyridines.

aromatic ring and hence is shifted upfield, accounting for the signal at 1.55 ppm. The remaining four-bridge protons give rise to the overlapping multiplet at 2.0–2.3 ppm. Clear nonequivalence of these eight protons indicates that the molecule is conformationally rigid on the NMR time scale.

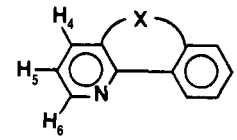
In an earlier study regarding the *N*-oxides of **3b** and **3c**, we were able to correlate changes in the chemical shift of the bay region proton ($H_{6'}$) upon N-oxidation with the dihedral angle of the system.[9] If we plot the chemical shift of $H_{6'}$ for **3b–d,f** vs. their estimated dihedral angle, we obtain the curve shown in Figure 2. Two interesting features of this curve can be pointed out. The $H_{6'}$ resonance for the unbridged system **3e** appears at 8.00 ppm, which would correlate to a dihedral angle of 33°. This value agrees quite well with an estimate of 30° made from the molar Kerr constant for this molecule.[10] In fact the value of 33° may be a little high since it does not account for the lack of a 2-alkyl inductive effect which would tend to shift $H_{6'}$ to higher field and hence smaller dihedral angle. The $H_{6'}$ resonance of **3a** appears at 8.09 ppm, which is substantially upfield from the resonance of 9.47 ppm observed for the analogous proton of the similarly planar benzo[*h*]quinoline (**3f**). A significant factor in this shift might be a decrease in deshielding due to $H_{6'}$ being pulled away from the deshielding region of the neighboring pyridine ring. Different inductive effects due to the bridges as well as rehybridization effects associated with the fused five-membered ring may also play an important role. In any event, the "bite" of **3a** is apparently large enough to preclude its cyclopalladation as will be discussed in the next section.

The ultraviolet absorption spectra for ligands **3b–d** are shown in Figure 3. As the system becomes less planar, the absorption intensity diminishes and the energy of absorption increases. These observations are consistent with diminished π-electron delocalization as a result of poorer overlap which in turn results from twisting about the single bond joining the two aromatic rings.

Cyclopalladation

For the cyclopalladated derivatives **4** and **5** the proton resonances of H_4 and H_6 on the pyridine ring can be readily identified (Table I) and give us some insight into the nature of the complexes. The chemical shift of H_4 should depend primarily on the electron density of the pyridine ring. Coordination typically depletes this electron density, and small downfield shifts are observed upon cyclopalladation. Very little difference results when the auxilliary ligand is changed from acac to acac–F_6, indicating that this species has little effect on the strength of the coordinative bond. A similar downfield shift is experienced by H_6 when the auxilliary ligand is acac, but this shift is compensated by an even larger upfield one when this ligand is acac–F_6. This additional shielding may be attributed to a through-space shielding induced by the trifluoromethyl groups. The greatest shielding is observed when comparing **4b** and **5b** where some flattening of the bridge coupled with approximate coplanarity of the aromatic rings may serve to push H_6 closer to the opposing trifluoromethyl group.

Table I. Selected ^{1}H NMR Data (δ) for 2-Phenylpyridines and Their Palladium Acetylacetonate Complexes (300 MHz, $CDCl_3$)



system	H_4	H_6
3e	7.59	8.64
5e	7.79	8.77
4e	7.84	8.48
3b	7.50	8.53
5b	7.56	8.85
4b	7.54	8.22
3c	7.53	8.60
5c	7.56	8.85
4c	7.57	8.52
3d	7.45	8.54
4d	7.90–7.71	

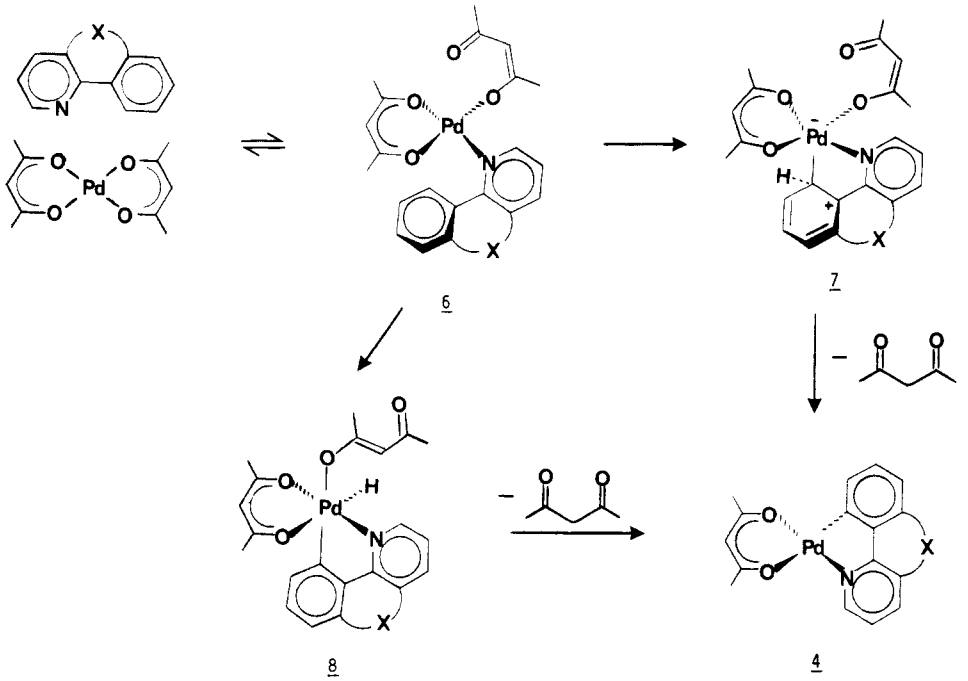
A generally accepted mechanism for the cyclopalladation of 2-phenylpyridines involves an initial rapid coordination of the pyridyl nitrogen to palladium, followed by electrophilic substitution by palladium at the 2′-carbon of the phenyl ring.[11] Several studies have addressed both the steric and electronic requirements for this process.

Selbin and co-workers studied a series of 14 derivatives of 2-phenylpyridine with various groups (CH_3, NO_2, OCH_3, halogen) substituted on the 2′-, 3′-, and 4′-positions of the phenyl ring.[12] The yields of the reaction of these ligands with $Pd(OAc)_2$ were cited as reflecting the relative ease of cyclopalladation and were consistent with an electrophilic attack of palladium on the phenyl ring. An earlier study with monosubstituted azobenzenes indicated that metalation occurred at the more activated benzene ring and thus supported the electrophilic nature of the reaction.[13]

The steric requirements for cyclopalladation of 2-phenylpyridine are relatively unstudied. One reason for this lack of study is the propensity for the formation of dimers in which two cyclopalladated species are bridged by ligands such as chloride or acetate. These dimers offer the possibility for syn and anti orientations of the phenyl and pyridine rings and are suggested to have a boat-like conformation.[14] Furthermore, the chloride-bridged dimers showed very poor solubility. Selbin and co-workers al-

(9) Thummel, R. P.; Jahng, Y. *J. Org. Chem.* **1985**, *50*, 3635.
(10) Huang, H. H. *Chem. Commun.* **1969**, 815.
(11) (a) Parshall, G. W. *Acc. Chem. Res.* **1970**, *3*, 139. (b) Bruce, M. I. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 73.
(12) Gutierrez, M. A.; Newkome, G. R.; Selbin, J. *J. Organomet. Chem.* **1980**, *202*, 341.
(13) Takahashi, H.; Tsuji, J. *J. Organomet. Chem.* **1967**, *10*, 511. See also: Hugentobler, M.; Klaus, A. J.; Mettler, H.; Rys, P.; Wehrle, G. *Helv. Chim. Acta* **1982**, *65*, 1202. Klaus, A. J.; Rys, P. *Helv. Chim. Acta* **1981**, *64*, 1452.
(14) Selbin, J.; Gutierrez, M. A. *J. Organomet. Chem.* **1983**, *93*, 104.

Scheme II



leviated these problems by conversion of the chloro-bridged dimers into monomeric dithiocarbamate derivatives, but unfortunately the formation of these secondary derivatives says little about the actual cyclometalation process.[15] Since 2-phenylpyridine reacts smoothly with palladium bis(acetylacetonate) and its hexafluoro derivative to provide a soluble monomeric species, we decided to use this reaction to probe the stereochemistry of cyclopalladation.

Scheme II outlines a possible mechanism for cyclopalladation. There is an initial rapid coordination of the phenylpyridine with Pd[acac]$_2$ to give the species **6**. Electrophilic attack of the vacant, axial palladium 5p$_z$ orbital on the π-sextet of the phenyl ring would lead to formation of the carbocation intermediate **7**. There is, of course, the possibility for π-complex formation preceding the σ bonding to palladium. Deprotonation of **7** with concomitant loss of the acac anion restores palladium to its square-planar 16-electron environment.

Deeming and Rothwell have invoked an axial attack on palladium by the C_{10}–H bond of benzo[*h*]quinoline, but they propose attack on the higher energy $d_{x^2-y^2}$ orbital, which would require cyclometalation in the coordination plane.[16] They subsequently studied the cyclopalladation of a series of 8-substituted and 2,8-disubstituted quinolines where a different mechanism is very likely functioning.

Inspection of a model of **6** indicates that an orthogonal orientation of the two aromatic rings such as would exist in the case of **3d** should provide the best overlap for electrophilic attack of the phenyl π-sextet on the axial palladium 5p$_z$ orbital. Thus, if the formation of **7** is rate determining, we would expect **3d** to react most rapidly. To evaluate this possibility, we undertook a kinetic study of the cyclopalladation process. Although the rate of reaction of **3** with Pd[acac–F$_6$]$_2$ is too rapid to be easily followed spectrophotometrically, the analogous reaction with Pd[acac]$_2$ occurs at a convenient rate in butanol at 110 °C. Assuming a steady-state concentration of **6** and utilizing pseudo-first-order conditions, we measured the rates shown in Table II. The rate differences along the series **3b–d**

Table II. Kinetic Data for the Reaction of 2-Phenylpyridines with Pd[acac]$_2$ in Butanol at 110 ± 0.5 °C

compd	$k_{obsd} \times 10^5$, s^{-1}	compd	$k_{obsd} \times 10^5$, s^{-1}
3b	8.72	**3e**	5.37
3c	5.55	**3f**	6.55
3d	3.54	**11**	3.59

are less than 3-fold, with the least planar system **3d** reacting the slowest. The unbridged **3e** reacts at about the same rate as **3c** in accord with their similar conformations. The monomethylene-bridged **3a** is unreactive with either reagent due to the large bite angle caused by the short bridge that pulls the two aromatic rings toward itself. The corresponding 3,3′-methylene-2,2′-bipyridine will act as a bidentate ligand with ruthenium.[6c,17]

If the stereochemical assumption we have made above is valid, our results are inconsistent with rate-determining attack of the palladium 5p$_z$ orbital on the phenyl ring. One alternative explanation would require the deprotonation step to become rate determining. In this case the thermodynamic stability of the products **4** would correlate better with the observed rates in that **3d**, which reacts the slowest, gives rise to the most distorted complex **4**.

A second explanation would invoke direct palladium insertion into the ortho C–H bond of the phenyl ring, leading to an octahedral species **8** that would then loose acetylacetone in a cis fashion to generate the cyclopalladated product. The prerequisite geometry leading from **6** to **8** might require overlap of the ortho C–H bond with the axial 5p$_z$ orbital such that a planar orientation of the ligand would be more favorable. To provide further insight into this process we looked for the existence of a kinetic isotope effect.

The prerequisite substrate 2-(phenyl-d_5)pyridine (**11**) was prepared by the reaction of (phenyl-d_5)magnesium bromide with pyridine *N*-oxide followed by dehydration in acetic anhydride of the resulting *N*-hydroxy intermediate[18,19] (eq 1). The structure of **11** was verified by the

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(16) Deeming, A. J.; Rothwell, J. P. *Pure Appl. Chem.* **1980**, *52*, 649.
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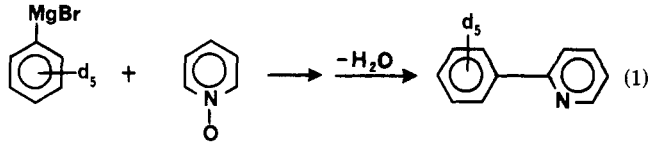
complete absence of phenyl protons in the ^1H NMR.



9 10 11

When **11** was treated with Pd[acac]$_2$, the rate was slower than that observed for **3e** (k_H/k_D = 1.5), indicating a small kinetic isotope effect. Unfortunately it is not clear which of the two alternative mechanisms is most consistent with this result.

In general, one would expect k_H/k_D to be greater than 3.0 if the second step was rate determining in a normal electrophilic aromatic substitution. Small effects, k_H/k_D = 1–2, are frequently observed for reactions in which the first step is rate determining.[20,21] Thus for the parent system, 2-phenylpyridine, it appears that the formation of **7** is slow while deprotonation to give **4** is more rapid. As we proceed along the series **3b–d**, it is not unlikely that the deprotonation step becomes slower due to the strain inherent in **4** while formation of **7** might, in fact, become geometrically more favorable. We hypothesize that if deuterium-substituted analogues of **3b–d** were available, the value of k_H/k_D would increase as the ligand became less planar due to increasing importance of the second step.

Our data still do not rule out the oxidative addition pathway proceeding via intermediate **8**. Few data are available regarding primary isotope effects for such a process, but relatively small values in the range of k_H/k_D = 1–2 do not appear unreasonable.[22]

Cyclopalladated species such as **4** and **5** are known to undergo a variety of synthetically useful ligand-exchange reactions. Future studies in this area will examine the effect of conformation on these processes.

Experimental Section

Nuclear magnetic resonance spectra were obtained on a Varian Associates FT-80 spectrometer or Nicolet NT-300 WB spectrometer in $CDCl_3$, and chemical shifts are reported in parts per million downfield from Me_4Si. Infrared spectra were obtained on a Perkin-Elmer 330 spectrophotometer. Ultraviolet spectra were obtained on a Perkin-Elmer 1330 spectrophotometer. Mass spectra were obtained by direct sample introduction into a Hewlett-Packard 5970 Series mass selective detector coupled with a Hewlett-Packard 5890A gas chromatograph equipped with a 12-m cross-linked methyl silicone capillary column programmed from 60 to 280 °C at 20 °C/min with helium as the carrier gas. 1-Tetralone, 1-benzosuberone, 4-azafluorene, and bromobenzene-d_5 were purchased from Aldrich Chemical Co. 1-Benzocyclooctanone was prepared according to the method of Huisgen and Rapp.[23] 5,6-Dihydrobenzo[*h*]quinoline was prepared according to the method of Koyama et al.[8] The Pd[acac]$_2$ was purchased from Alfa Chemical Co., and the Pd[acac-F_6]$_2$ was prepared according to the procedure of Siedle et al.[24]

1-Benzosuberone Oxime *O*-(Allyl ether) (2b). A mixture of 2.0 g (12.5 mmol) of 1-benzosuberone, 1.35 g (12.5 mmol) of *O*-allylhydroxylamine hydrochloride,[8] 1.02 g of anhydrous NaOAc, and 1.2 g of anhydrous Na_2CO_3 in EtOH (30 mL) was refluxed for 6 h. After concentration, the residue was extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over $MgSO_4$, and concentrated to give a pale yellow liquid, which was purified by Kugelrohr distillation to afford 2.31 g (86%) of **2b**, bp 95-97 °C (0.18 mm). GC analysis indicated the presence of two isomers. Chromatography on silica gel eluting with hexane afforded 1.2 g of one pure isomer and 0.8 g of a mixture of both isomers. Major component: ^1H NMR (80 MHz) δ 7.46–7.08 (m, Ar-H), 6.32–5.12 (ABC pattern, C*H*=CH_2) 4.69 (d, OCH_2, *J* = 5.5 Hz), 2.72 (m, 4 H, α-CH_2), 1.68 (m, 4 H, β-CH_2); IR (thin film) 3060, 3003, 2910, 2843, 1603, 1480, 1448, 1342, 1310, 1018, 913, and 753 cm^{-1}; MS, *m/e* 215 (M, 41), 214 (M – 1, 100), 200 (15), 143 (30), 132 (29), 129 (60), 128 (57), 116 (59), 115 (53), 104 (26). The minor component showed spectral properties similar to those given for the major fraction.

1-Benzocyclooctanone Oxime *O*-(Allyl ether) (2c). A solution of 1.0 g (6 mmol) of 1-benzocyclooctanone, 1.0 g (9 mmol) of *O*-allylhydroxylamine hydrochloride,[8] and 0.36 g (9 mmol) of NaOH in absolute EtOH (25 mL) was refluxed for 24 h. After concentration, the residue was extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with water, dried over $MgSO_4$, and concentrated to give a pale yellow oil. Chromatography on silica gel, eluting with CCl_4, provided 1.0 g (73%) of **2c** as a 2:5 mixture of syn and anti isomers as indicated by GC analysis and 0.3 g of unreacted ketone. The ^1H NMR (300 MHz) of the mixture of isomers showed two sets of peaks, data are given for the major set: δ 7.30–6.96 (m, 4 H, ArH), 6.12–5.08 (ABC pattern CHCH_2), 4.67 (d, OCH_2, *J* = 5.5 Hz), 2.74 (m, 4 H, α-CH_2), 1.67 (m, 2 H, γ-CH_2), 1.53 (m, 4 H, β-CH_2); IR (thin film) 3060, 3015, 2920, 2850, 1450, 1342, 1150, 1025, 915, 780 cm^{-1}; both isomers showed almost identical MS, *m/e* 229 (M), 212, 170, 157, 129.

3,2′-Trimethylene-2-phenylpyridine (3c). A sealed glass tube (12 mm × 130 mm, 1.2-mm wall) containing 1.0 g (4.65 mmol) of **2b** was heated at 180–185 °C for 50 h. The tube was cooled and opened, and 5 mL of $CHCl_3$ was added. The $CHCl_3$ solution was extracted with 5% HCl. This aqueous phase was made basic with 50% NaOH and extracted with CH_2Cl_2. After drying over $MgSO_4$, the CH_2Cl_2 was evaporated to give a yellow oil that was purified by Kugelrohr distillation to afford 0.10 g (13%) of **3c**, bp 110–115 °C (0.15 mm), and 0.15 g of 1-benzosuberone. Compound **3c** gave the following spectral properties: ^1H NMR (300 MHz) δ 8.60 (d, H_6, $J_{5,6}$ = 4.8 Hz), 7.72 (d, $H_{6'}$, $J_{5',6'}$ = 8.1 Hz), 7.53 (d, H_4, $J_{4,5}$ = 7.6 Hz), 7.34 (dt, $H_{4'}$), 7.23 (d, $H_{3'}$), 7.18 (dd, H_5), 2.53 (t, α-CH_2, *J* = 7.0 Hz), 2.49 (t, α′-CH_2, *J* = 7.0 Hz), 2.23 (quintet, β-CH_2, *J* = 7.0 Hz); ^{13}C NMR (75 MHz) δ 158.5, 147.6, 140.1, 139.3, 136.3, 135.0, 128.7 (2C), 128.4, 126.8, 122.0, 33.0, 31.0, 30.3; IR (thin film) 3060, 2920, 2850, 1595, 1582, 1559, 1445, 1421, 1020, 750 cm^{-1}; MS, *m/e* 196 (M + 1, 11), 195 (M, 97), 194 (M – 1, 100), 180 (49), 168 (22), 167 (49), 166 (17), 152 (15), 83 (53).

3,2′-Tetramethylene-2-phenylpyridine (3d). The same procedure was followed as described above for **3c** using 0.7 g (3.06 mmol) of **2c**. The crude yellow oil obtained (0.6 g) was chromatographed on silica gel eluting with CH_2Cl_2–hexane (1:4). The later fractions provided 0.12 g (20%) of solid material that was recrystallized from C_6H_{12}–$CHCl_3$ (4:1): mp 112–113 °C; ^1H NMR (300 MHz) δ 8.54 (dd, H_6, $J_{5,6}$ = 4.7, $J_{4,6}$ = 1.2 Hz), 7.56 (d, $H_{6'}$, $J_{5',6'}$ = 7.7 Hz), 7.45 (d, H_4, $J_{4,5}$ = 7.3 Hz), 7.38–7.22 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$, H_5), 2.79–2.68 (m, 2 H), 2.25–2.05 (m, 4 H), 1.61–1.49 (m, 2 H); ^{13}C NMR (75 MHz) δ 158.0, 146.9, 142.0, 139.2, 137.7, 137.1, 129.3, 128.9, 128.6, 125.9, 122.6, 32.4, 31.9, 29.3 29.0; IR (KBr) 3050, 3038, 2905, 2825, 1570, 1558, 1440, 1435, 1420, 1278, 1138, 783, 748 cm^{-1}; MS, *m/e* 210 (M + 1, 6.4), 209 (M, 42), 208 (13), 181 (26), 180 (100), 167 (11), 152 (13).

2-(Phenyl-d_5)pyridine (11).[18,19] A Grignard reagent was generated in dry THF in the normal fashion from 2.43 g (15 mmol) of bromobenzene-d_5 and 0.35 g (15 mmol) of Mg turnings. To this reagent was slowly added a solution of 1.43 g (15 mmol) of pyridine *N*-oxide in 10 mL of THF. The mixture was stirred for 40 min and then allowed to stand overnight. It was hydrolyzed with a solution of 0.55 g of NH_4Cl in 1.5 mL of H_2O. The supernatant liquid was decanted, and the residue was washed with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and evaporated to give 1.50 g of material that was dissolved in 8 mL of Ac_2O and refluxed for 4 h. The Ac_2O was removed by distillation, and the residue was made basic with 50% NaOH and extracted with CH_2Cl_2. The CH_2Cl_2 solution was dried over $MgSO_4$ and evaporated to give 0.80 g of an oil that was chromatographed on 20 g of silica gel, eluting with hexane–CH_2Cl_2 (4:1). The latter fractions provided 0.2 g of **11**, which was further purified by preparative gas chromatography on a $^1/_4$ in. × 5 ft

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column of 5% Carbowax 20M + 5% KOH on Chromsorb W (80–100 mesh) at 120 °C and 30 mL/min helium flow: ^{1}H NMR (300 MHz) δ 8.69 (d, H_6, $J_{5,6}$ = 4.6 Hz), 7.72 (m, H_4, H_5), 7.21 (m, H_3).

General Procedure for Cyclopalladation. A solution of ligand and Pd[acac–F_6]$_2$ in hexane was refluxed for 2 h, or a suspension of ligand and Pd[acac]$_2$ in MeOH was refluxed for 12 h. A yellow precipitate, which appeared almost immediately, was collected and washed with cold hexane to give the cyclopalladated product.

Reaction of Pd[acac–F_6]$_2$ with 2-Phenylpyridine. Treatment of 47 mg of 2-phenylpyridine with 50 mg of Pd[acac-F_6]$_2$ provided 64 mg (95%) of **5e**: mp 192–193 °C (lit.[24] mp 193 °C): ^{1}H NMR (300 MHz) δ 8.48 (dd, H_6, J = 5.7, 0.7 Hz), 7.84 (dt, H_4, J = 7.5, 0.9 Hz), 7.62 (d, $H_{2'}$,[25] J = 8.1 Hz), 7.37–7.30 (m, 2 H), 7.19–7.11 (m, 3 H), 6.08 (s, =C*H*).

Reaction of Pd[acac–F_6]$_2$ with 5,6-Dihydrobenzo[*h*]quinoline. Treatment of 30 mg of **3b** with 30 mg of Pd[acac–F_6]$_2$ provided 27 mg (95%) of **5b** as yellow crystals: mp 206–207 °C; ^{1}H NMR (300 MHz) δ 8.22 (dd, H_6, J = 5.7, 1.2 Hz), 7.54 (dd, H_4, J = 7.7, 1.2 Hz), 7.11–6.98 (m, 3 H), 6.85 (dd, $H_{5'}$, J = 7.4, 0.8 Hz), 6.13 (s, =C*H*), 2.98 (m, CH_2CH_2). Anal. Calcd for $C_{18}H_{11}F_6NO_2Pd$: C, 43.79; H, 2.25; N, 2.84. Found: C, 44.24; H, 2.29; N, 2.83.

Reaction of Pd[acac–F_6]$_2$ with 3,2′-Trimethylene-2-phenylpyridine. Treatment of 50 mg of **3c** with 50 mg of Pd[acac–F_6]$_2$ provided 80 mg (93%) of **5c** as yellow crystals: mp 162–163 °C: ^{1}H NMR (300 MHz) δ 8.52 (dd, H_6, J = 5.3, 1.0 Hz), 7.57 (d, H_4, J = 8.0 Hz), 7.22 (dd, $H_{3'}$, J = 7.3, 1.0 Hz), 7.03 (dd, H_5, J = 7.8, 5.5 Hz), 6.93–6.86 (overlapping m, H_4, and $H_{5'}$), 6.10 (s, =C*H*), 3.04 (t, 4 H, J = 5.7 Hz, ArCH_2), 2.4 (m, 2 H, $CH_2CH_2CH_2$). Anal. Calcd for $C_{19}H_{13}F_6NO_2Pd$: C, 44.95; H, 2.58; N, 2.76. Found: C, 45.18; H, 2.58; N, 2.76.

Reaction of Pd[acac–F_6]$_2$ with 3,2′-Tetramethylene-2-phenylpyridine. Treatment of 21 mg of **3d** with 50 mg of Pd[acac–F_6]$_2$ provided 43 mg (83%) of **5d** as a yellow solid: mp 132–133 °C; ^{1}H NMR (300 MHz) δ 7.90–7.71 (overlappings m, 3 H), 7.41 (d, 1 H, J = 7.7 Hz), 7.25 (dd, H_5, J = 7.4, 5.8 Hz), 6.65 (d, $H_{5'}$, J = 5.8 Hz), 6.45 (s, =CH), 2.78–2.71 (m, 1 H), 2.26–1.90 (m, 4 H), 1.42–1.23 (m, 2 H), 0.89 (t, 1 H, J = 12.3 Hz). A suitable sample for elemental analysis could not be prepared.

Reaction of Pd[acac–F_6]$_2$ with Benzo[*h*]quinoline. Treatment of 40 mg of **3f** with 40 mg of Pd[acac–F_6]$_2$ provided 34 mg (92%) of a yellow solid: mp 268–270 °C; ^{1}H NMR (300 MHz) δ 8.69 (d, H_2, J = 5.3 Hz), 8.31 (d, H_4, J = 7.8 Hz), 7.76 (d, 1 H, J = 8.8 Hz), 7.63–7.47 (overlapping m, 5 H), 6.21 (s, =C*H*). Anal. Calcd for $C_{18}H_9F_6NO_2Pd$: C, 43.97; H, 1.84; N, 2.85. Found: C, 43.85; H, 1.84; N, 2.83.

Reaction of Pd[acac]$_2$ with 2-Phenylpyridine. Treatment of 66 mg of 2-phenylpyridine (**3e**) with 65 mg of Pd[acac]$_2$ provided 86 mg (86%) of yellow crystals: mp 242–243 °C; ^{1}H NMR (300 MHz) δ 8.77 (d, H_6, J = 5.6 Hz), 7.79 (t, H_4, J = 8.1 Hz), 7.62 (overlapping d and t, 2 H), 7.42 (dd, 1 H), 7.21–7.09 (overlapping m, 3 H), 5.40 (s, =C*H*), 2.11 (s, CH_3), 2.06 (s, CH_3).

Reaction of Pd[acac]$_2$ with 5,6-Dihydrobenzo[*h*]quinoline. Treatment of 64 mg of **3b** with 61 mg of Pd[acac]$_2$, followed by evaporation of the MeOH solvent and recrystallization of the residue from CH_3OH–$CHCl_3$ (1:1), provided 90 mg (92%) of yellow needles: mp 171–172 °C; ^{1}H NMR (300 MHz) δ 8.85 (dd, H_6, J = 5.4, 1.3 Hz), 7.56 (coincidental d, H_4 and $H_{3'}$), 7.05–6.99 (m, 2 H), 6.89 (dd, $H_{5'}$, J = 7.3, 0.7 Hz), 5.38 (s, =C*H*), 2.06 (overlapping t, CH_2CH_2), 2.09 (s, CH_3), 2.04 (s, CH_3).

Reaction of Pd[acac]$_2$ with 3,2′-Trimethylene-2-phenylpyridine. Treatment of 110 mg of **3c** with 85 mg of Pd[acac]$_2$ followed by cooling and the addition of an equal volume (10 mL) of $CHCl_3$ provided 82 mg (81%) of yellow needles, mp 165–166 °C; ^{1}H NMR (300 MHz) δ 8.85 (d, H_6, J = 5.2 Hz), 7.56 (coincidental d, H_4 and $H_{3'}$), 7.05–6.99 (m, 2 H), 6.89 (d, $H_{5'}$, J = 7.4 Hz), 5.37 (s, =C*H*), 3.07 (overlapping t, α-CH_2), 2.08 (s, CH_3), 2.06 (masked quintet, β-CH_2), 2.04 (s, CH_3).

Reaction of Pd[acac]$_2$ with Benzo[*h*]quinoline. Treatment of 70 mg of **3f** with 85 mg of Pd[acac]$_2$ provided 86 mg (85%) of yellow crystals: mp 213–214 °C (lit.[26] mp 214–215 °C); ^{1}H NMR (300 MHz) δ 8.91 (d, H_2, J = 4.8 Hz), 8.23 (d, H_4, J = 8.2 Hz), 7.75–7.72 (overlapping d, 2 H), 7.57–7.44 (m, 4 H), 5.45 (s, =C*H*), 2.16 (s, CH_3), 2.11 (s, CH_3).

Kinetic Measurements. A stock solution of ligand was prepared by dissolving an appropriate amount [ca. 12-fold excess: 1.8×10^{-3} mol of ligand in 25 mL of *n*-BuOH (Fisher certified grade)]. A fresh stock solution of Pd[acac]$_2$ (ca. 1.5×10^{-4} M) was prepared from 25 mL of *n*-BuOH and ca. 1.1 mg of Pd[acac]$_2$ prior to each set of kinetic runs.

A Perkin-Elmer 330 spectrophotometer was equilibrated and calibrated from 500 to 350 nm for *n*-BuOH against the visible source. Both substrate and reagent show no absorbance in this region. An equal volume (usually 20 mL) of the substrate and Pd[acac]$_2$ solution was mixed well in a 50-mL round-bottomed flask, and the resulting mixture was placed in a thermostated bath at 110 ± 0.5 °C. Every 30 or 60 min, a 3-mL aliquot was removed from the flask and placed in a 1 × 1 × 3 cm cuvette, which was immediately scanned over the range from 500 to 350 nm. The aliquot was then returned to the reaction flask. Rate data for cyclopalladation were obtained by monitoring absorbance increases at 300 or 380 nm. First-order rate constants, k, were calculated on the basis of a least-squares fit (uniform weighting) to the relation

$$\ln |A_\infty - A_t| = -k_t + \ln (A_\infty - A_0)$$

where A_∞ and A_0 are the final and initial absorbances, respectively. A_t is the absorbance measured at time t.

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