structure of assembly **A3** reveals that the melamine-substituted aromatic ring carbon atoms are 4.05 Å apart,[8a] which is 0.75 Å less than the optimal distance measured from the crystal structure of the calix[4]arene–Ag^+ complex.[12a] Formation of the hydrogen-bonded assembly therefore leaves too little space for complexation of the Ag^+ ions in between the parallel aromatic rings of the calix[4]arene fragment.

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Insertion of Imines into Palladium–Acyl Bonds: Towards Metal-Catalyzed Alternating Copolymerization of Imines with Carbon Monoxide To Form Polypeptides**

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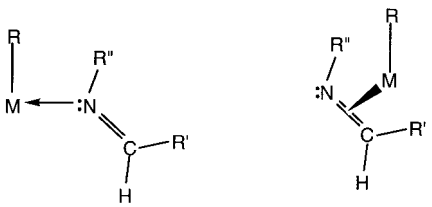
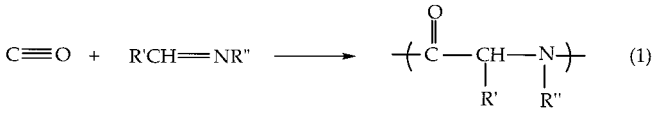
The insertion of unsaturated molecules into metal–carbon bonds is a critically important step in many transition-metal-catalyzed organic transformations. In particular, the insertion of alkenes and alkynes into metal–carbon bonds resulting in carbon–carbon bond formation has been extensively studied.[1] However, the analogous insertion of compounds with carbon–nitrogen multiple bonds has received far less attention: this is particularly true of imines.[2] The difference in insertion propensity of carbon–carbon and carbon–nitrogen multiple bonds can be attributed to the coordination characteristics of the respective molecules. Alkenes and alkynes form π-complexes with metals. For imines, σ-donation of the lone pair of electrons on the nitrogen is the preferred mode of interaction with the metal center (for example, structure **I**).[3] Since migratory insertion must be preceded by π coordination



I **II**

(R, R', R" = H, alkyl, aryl)

(structure **II**), the difficulty in achieving σ to π isomerization may be the reason for the paucity of imine insertions.[2] Herein we report the synthesis of amides by the insertion of imines into palladium(II)–acyl bonds. To our knowledge, this is the first direct observation of the insertion of imines into bonds between transition metals and carbon. The interest in this chemistry lies in the potentially new route to carbon–nitrogen bond formation. In particular, the alternating copolymerization of imines with carbon monoxide (in which the insertion of the imine into palladium–acyl bonds would be the key step in the chain growth sequence), if successful, should constitute a new procedure for the synthesis of polypeptides [Eq. (1)].[4]



(1)

Neutral palladium(II)–methyl complexes incorporating a range of bidentate phosphane and nitrogen ligands reacted with silver tetrafluoroborate in the presence of imines to form the corresponding imine-coordinated cationic complexes **1a**–**k** in excellent yields. The compound **1a** (L–L = 1,3-bis-(diphenylphosphanyl)propane) was isolated as a solid consisting of 91% **1a**·Et_2O and 9% [(dppp)$PdCl_2$] (the composition was determined by a combination of ^1H and ^{31}P NMR spectroscopy). A satisfactory elemental analysis (C,H) was obtained for a mixture of this composition. The complexes **1a**–**k** were found to be stable for over one month under nitrogen; there was no evidence of insertion of imine into the palladium–methyl bond.

The imine ligand was coordinated to the metal by σ donation of the lone pair of electrons on nitrogen (structure **I**). This was established from the ^1H and ^{13}C NMR spectra of the complexes. For example, in the ^1H NMR spectrum of complex **1c** (L–L = dppp, R = PhCH=NBz), recorded in $CDCl_3$, the CH protons of the coordinated imine appeared at $\delta = 8.20$ (dd, $J = 2$, 7.4 Hz) compared with $\delta = 8.29$ for the CH protons of the noncoordinated imine. The corresponding carbon appeared at $\delta = 167.89$ in the $^{13}C\{^1H\}$ NMR ($CDCl_3$) spectrum compared with $\delta = 160.69$ for the noncoordinated imine. On the other hand, π complexation has been shown to result in significant upfield shifts of these resonances.[3b]

The reactivity of complexes **1a**–**k** towards carbon monoxide was examined by exposing them to an atmosphere of carbon monoxide at ambient temperature and a pressure of 3.4 bar. The results are summarized in Scheme 1. All the complexes reacted with carbon monoxide to form the corresponding palladium(II)–acyl species. However, the stability of these palladium–acyl species varied greatly. These complexes (**2**) could only be observed when the subsequent insertion of the imine into the palladium–acyl bond was slow or did not occur. ^{13}C-labeled carbon monoxide was used to facilitate characterization of the products: complexes formed with ^{13}CO are marked with an asterisk (*).

For complexes with nitrogen-donor ligands **1i**–**k** the corresponding palladium(II)–acyl complexes **2i**–**k** were formed in 16 h. The ^{13}C NMR resonance due to the carbonyl of the acyl group was observed at $\delta \approx 232$ for **2i***–**k*** as is typical for palladium(II)–acyl complexes.[5] There was no

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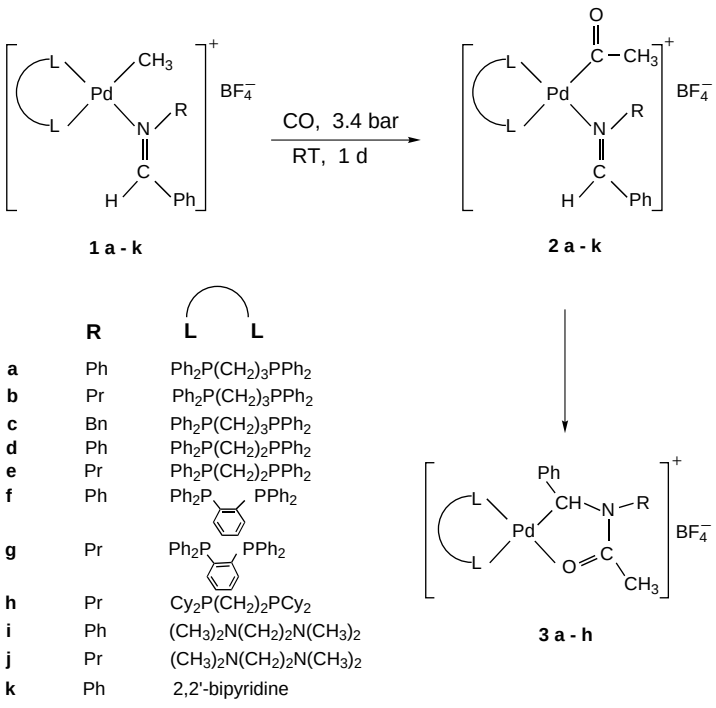

	R	L L
a	Ph	$Ph_2P(CH_2)_3PPh_2$
b	Pr	$Ph_2P(CH_2)_3PPh_2$
c	Bn	$Ph_2P(CH_2)_3PPh_2$
d	Ph	$Ph_2P(CH_2)_2PPh_2$
e	Pr	$Ph_2P(CH_2)_2PPh_2$
f	Ph	Ph_2P PPh_2
g	Pr	Ph_2P PPh_2
h	Pr	$Cy_2P(CH_2)_2PCy_2$
i	Ph	$(CH_3)_2N(CH_2)_2N(CH_3)_2$
j	Pr	$(CH_3)_2N(CH_2)_2N(CH_3)_2$
k	Ph	2,2'-bipyridine

Scheme 1. Reactions of **1** with CO and insertions of the C=N group into the metal–carbon bond to form an amide group. The carbonyl oxygen atom in complexes **3** coordinates to the palladium center.

evidence for the subsequent insertion of the coordinated imine into the palladium–acyl bond at ambient temperature.

In contrast to complexes **2i–k** with nitrogen-donor ligands, subsequent insertion of the coordinated imine occurred at ambient temperature in the phosphane-coordinated complexes **2a–h** to form **3a–h** (Scheme 1). The insertion resulted in the CH unit being attached to the imine the metal and the formation of a bond between nitrogen and the carbonyl group, resulting in the formation of an amide group. In addition, the carbonyl oxygen was coordinated to the palladium to form a stable five-membered ring. Similar chelates result from the insertion of alkenes into palladium(II)–acyl bonds.[5a, 6] The best result was obtained with compound **1a**. Exposing a solution of **1a** to carbon monoxide at a pressure of 3.4 bar for 1 d at ambient temperature yielded **3a** (or **3a***) as the only product (83% yield). The $^{31}P\{^1H\}$ NMR spectrum of complex **3a**, recorded in $CDCl_3$, showed two sets of doublets at $\delta = 0.19$ and 17.14 ($J = 70$ Hz), while that of **3a*** showed a doublet of doublets at $\delta = 0.08$ ($J = 9.2$, 70 Hz) and a doublet at 17.16 ($J = 70$ Hz). The observation of $^{31}P-^{13}C$ coupling for the upfield resonance indicates that the corresponding phosphorus atom was positioned *trans* to the weakly coordinated carbonyl group and confirms the existence of the chelate structure. The $^{13}C\{^1H\}$ NMR spectrum of **3a***, recorded in $CDCl_3$, showed the amide carbonyl resonance at $\delta = 181.64$ ($^3J_{P-C} = 9.4$ Hz). ^1H NMR spectrum in $CDCl_3$ of complex **3a** showed the methyl next to the carbonyl group at $\delta = 1.87$. The corresponding resonance in **3a*** appeared as a doublet ($J = 6.2$ Hz) at $\delta = 1.80$. The CH group of the inserted imine in complex **3a** showed up as a doublet of doublets at $\delta = 4.27$ ($J = 4.8$, 8.0 Hz), being coupled to the two nonequivalent phosphorus atoms. This resonance in **3a*** became a multiplet due to long range coupling to the carbonyl carbon. The IR spectrum of **3a** recorded in $CDCl_3$ exhibited an absorption band at 1630 cm^{-1} due to the coordinated carbonyl group of the amide. Finally, the compound **3a** was isolated as a solid consisting of 89.5% **3a** and 10.5% [(dppp)$PdCl_2$] (the composition was determined by ^{31}P NMR spectroscopy). Satisfactory elemental analysis (C, H) was obtained for a mixture of this composition.

The dppp complexes **1b** (R = PhCH=NPr) and **1c** (R = PhCH=NBz) were employed to examine the relative insertion propensities of benzaldehyde propyl imine and benzaldehyde benzyl imine. Both these imines showed a greater reluctance towards insertion into the corresponding palladium(II)–acyl bond than benzaldehyde phenyl imine (cf. **1a**). The observed yields of **3b** and **3c** were 50% and 20%, respectively. Additionally, the reactions were accompanied by significant decomposition and precipitation of metallic palladium. The above observations indicate that the insertion of an imine into a palladium(II)–acyl bond proceeds more readily when the nitrogen bears a phenyl rather than an alkyl substituent (also, see below). This difference may be due to higher σ-bonding ability of the nitrogen bearing a relatively electron-releasing alkyl substituent, thereby disfavoring the required isomerization from the σ to π complex (structure **I** to **II**).

The effect of the chelating phosphane upon the reaction was also examined. Like complex **1a**, the PhCH=NPh complexes **1d** (L–L = 1,2-bis(diphenylphosphanyl)ethane = dppe) and **1f** (L–L = 1,2-bis(diphenylphosphanyl)benzene = dppb), formed the imine-inserted products following conversion into the corresponding acyl species, albeit at lower yields (less than 30%). The sharply reduced ability of benzaldehyde propyl imine to undergo insertions (cf., **1b**) was not significantly altered by changing the structure of the coordinated bidentate phosphane. For example, complexes **1e** (L–L = dppe), **1g** (L–L = dppb), and **1h** (L–L = 1,2-bis(dicyclohexylphosphanyl)ethane = dcpe), could be converted into the corresponding palladium(II)–acyl species. However, the subsequent insertion of the imine into the palladium(II)–acyl bond was very slow and the imine-inserted product was formed only in low yields. In addition, the reactions were accompanied by precipitation of metallic palladium.

In conclusion, we have observed, for the first time, the insertion of the C=N bond of imines into palladium(II)–acyl bonds. The insertions resulted in the formation of palladium(II)–alkyl species with amide bonds. Moreover, the carbonyl group of the amide was coordinated to the metal to form a five-membered ring. It is interesting to note that while imine insertion into palladium(II)–acyl bonds was observed, the corresponding insertion into palladium(II)–alkyl bonds did not occur. Almost certainly, the formation of the very strong amide linkage constituted the added driving force in the former reaction. A comparison of the insertion propensity of imines with different groups on the nitrogen showed that benzaldehyde phenyl imine was far superior to benzaldehyde propyl imine and benzaldehyde benzyl imine. The effect of the nature of the auxiliary bidentate ligand on the metal was also investigated. No imine insertion was observed with bidentate nitrogen-donor ligands at ambient temperature.

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Insertion was, however, observed with bidentate phosphane ligands.

For the alternating copolymerization of imine with carbon monoxide to proceed, the subsequent insertion of carbon monoxide into the palladium(II)–carbon bond of the imine-inserted product must occur. In preliminary experiments, we did not observe carbon monoxide insertion in species **3a** at ambient temperature. We ascribe our failure to the strong binding of the carbonyl group of the amide fragment to the metal, thereby preventing the coordination of an incoming carbon monoxide molecule. While a similar coordination of the carbonyl group also occurs in the intermediates involved in the alternating copolymerization of alkenes and carbon monoxide,[5a, 6, 7] the difference lies in the greater negative charge and, therefore, stronger coordinating ability of the carbonyl oxygen of an amide fragment. Interestingly, the insertion of carbon monoxide apparently occurs readily in analogous species where the amide carbonyl is not coordinated to the metal.[8]

Experimental Section

Synthesis of **1a**–**k**: A solution of $AgBF_4$ in acetonitrile was added to a solution of $L_2Pd(Me)(Cl)$ (1 equiv) and imine (1 equiv) in dichloromethane. After this had been stirred for 15 min, the AgCl was removed by filtration. The resulting complex was isolated by removing the solvent and drying under reduced pressure for 1 d.

Reaction of **1a**–**k** with carbon monoxide: The complex **1a**–**k** (0.10 g) was dissolved in $CDCl_3$ and placed in a 22 mL Parr bomb, which was then charged with 3.4 bar of carbon monoxide. The mixture was allowed to stand at ambient temperature for 1 d. The excess carbon monoxide was then released, the solution filtered to remove any metallic palladium, and the product characterized by ^1H, $^{31}P\{^1H\}$, and $^{13}C\{^1H\}$ NMR spectroscopy. Reactions were also run with ^{13}C-labeled carbon monoxide.

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Maracin and Maracen: New Types of Ethynyl Vinyl Ether and α-Chloro Divinyl Ether Antibiotics from *Sorangium cellulosum* with Specific Activity Against Mycobacteria**

Martina Herrmann, Bettina Böhlendorf, Herbert Irschik, Hans Reichenbach, and Gerhard Höfle*

Dedicated to Professor Meinhart H. Zenk on the occasion of his 65th birthday

Even in highly developed industrial countries, tuberculosis is still one of the most common causes of death due to infection.[1] The causative pathogen, *Mycobacterium tuberculosis*, can only be completely eliminated by a lengthy course of treatment despite the use of highly active antibiotic combination preparations (rifampicin, streptomycin, isoniazide etc.), since its growth is particularly slow and it is protected by a wax-containing cell wall.[2] The same is true for leprosy which is also caused by mycobacteria.[3] In AIDS, increasing occurrence of multiresistant *M. tuberculosis* strains and atypical mycobacterial infections is a particular danger.[2, 4] New types of antibiotics are urgently needed to treat such infections, in order to aid patients in individual cases and in the long term, to prevent the spread of resistant pathogen strains.

During a screening program using the nonpathogenic *Mycobacterium phlei* as indicator organism, we discovered

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