9 of Table I. The strong electronic bias in the catalyzed reaction is sufficient to overcome the steric bias which dominates relative olefin reactivities in the thermal reaction. The excellent control which characterizes our method for allylic carboxylation is epitomized by the two different structurally specific functionalizations possible with diene **7** (Scheme IV).

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(4) For a pertinent recent study on substituent effects in pericyclic reactions, see Gajewski, J. J. *J. Am. Chem. Soc.* **1979,** *101*, 4393.

(5) Ene adduct (1 g) is stirred vigorously with 10% aqueous KOH (15 mL) for 18 h to afford the α-hydroxymalonic acid **4** in nearly quantitative yield after acidification to pH 3 with HCl, extraction into ether, and evaporation of solvent.

(6) Cf. Corey, E. J.; Wollenberg, R. H. *Tetrahedron Lett.* **1976,** 4705. The α-hydroxymalonic acid **4** (1.0 mmol) is added to aqueous $NaIO_4$ (10 mL of 0.25 M) containing pyridine (15 μL). After vigorous stirring for 1 h, acid **5** is isolated, after acidification to pH 3 with HCl, by extraction into ether (2 × 20mL). For water-soluble products, the acidified reaction mixture is saturated with NaCl prior to extraction with ether. The acids **5** are methylated with diazomethane. Samples of the esters were purified for analysis by gas–liquid phase chromatography.

(7) The α-hydroxymalonic acid **4** (1.0 mmol) is stirred vigorously for 1 h with a solution of aqueous cerric ammonium nitrate (5 mL of 1.0 M) in acetonitrile (15 mL). The acid **5** is isolated, after dilution with water (100 mL), by extraction into ether (2 × 100 mL).

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Mary F. Salomon, Simon N. Pardo, Robert G. Salomon*
Department of Chemistry, Case Western Reserve University
Cleveland, Ohio 44106

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trans-Bromo(2-, 3-, and 4-pyridyl)bis(triethylphosphine)palladium(II) Complexes

Sir:

Oxidative addition reactions of 2- and 3-bromopyridines to tetrakis(triphenylphosphine)nickel(0) occurred in toluene at room temperature to afford the dinuclear nickel(II) complexes containing the carbon-bonded 2- and 3-pyridyl ligands, respectively.[1] The former complex is quite stable, but the latter is less stable and the corresponding 4-pyridylnickel(II) complex has not been obtained. On the other hand, tetrakis(triphenylphosphine)palladium(0) reacted with 2-, 3-, and 4-bromopyridines in toluene at 90 °C to produce stable complexes, $[PdBr(C_5H_4N\text{-}C^2)(PPh_3)]_2$ (**1a**), *trans*-$PdBr(C_5H_4N\text{-}C^3)(PPh_3)_2$ (**2a**), and *trans*-$PdBr(C_5H_4N\text{-}C^4)(PPh_3)_2$ (**3a**) in 55, 90, and 73% yields, respectively. These are the first examples of the carbon-bonded pyridyl complexes with palladium(II), although several pyridyl complexes with cobalt(III),[2] gold(I),[3] titanium(III),[4] and some other metals[5] as well as nickel(II)[1] have been reported so far.

Treatment of compounds **1a–3a** with triethylphosphine in diethyl ether at room temperature resulted in the *trans*-$PdBr(C_5H_4N\text{-}C^2$, $\text{-}C^3$, and $\text{-}C^4)(PEt_3)_2$ complexes (**1b, 2b,** and **3b,** respectively). They are all mononuclear[6] and trans since the methyl protons of triethylphosphine resonate as a 1:4:6:4:1 quintet and the proton-decoupled methylene carbons as a triplet with J(P–C) = 13 Hz. The trans structure is also supported by the existence of single ν(Pd–P) bands in the 330–320-cm^{-1} region. Thus these compounds are isomers.[7]

X-ray crystallographic studies[9] of the crystals of **1b, 2b,** and **3b** showed similar square-planar geometry around the palladium atom (Table I): the only significant difference in the bond lengths appears as the longer Pd–Br length of **3b** than those of **1b** and **2b,** although a reasonable rationalization is difficult. The substituents of the phosphorus atoms are staggered about the P–Pd–P sequence in **1b,** whereas they are almost eclipsed in **2b** and **3b.**

Table I. Some Results of Structure Analyses Including Bond Distances and Bond Angles around Pd[a]

	1b	**2b**	**3b**
crystal system	triclinic	monoclinic	orthorhombic
space group	$P\bar{1}$	$P2_1/c$	$Pn2_1a$
bond distances, Å			
Pd–C	1.993 (6)	1.998 (6)	2.030 (17)
Pd–Br	2.524 (1)	2.522 (1)	2.563 (3)
Pd–P	2.313 (3)	2.322 (2)	2.328 (5)
	2.314 (2)	2.323 (2)	2.325 (4)
bond angles, deg			
P–Pd–P	175.88 (8)	176.71 (7)	171.1 (2)
Br–Pd–C	178.2 (2)	178.2 (2)	178.1 (5)
P–Pd–Br	88.36 (6)	89.77 (5)	89.0 (2)
	95.55 (6)	90.37 (5)	92.8 (1)
P–Pd–C	89.9 (2)	90.1 (1)	89.8 (5)
	86.2 (2)	89.8 (2)	88.6 (5)

[a] Esd's are given in parentheses.

To compare basicities of these complexes, titration with perchloric acid was performed in dioxane-water (1:1 by volume) at 25 °C and μ = 0.1 ($NaClO_4$), and the pK_a values for the conjugate acids of **1b** and **2b** were determined to be 8.04 and 5.47, respectively. Basicity of **1b** is astonishingly stronger than that of uncoordinated pyridine (pK_a = 4.47). Unfortunately the solubility of **3b** in the mixed solvent was not enough in the presence of added sodium perchlorate to give an accurate pK_a value. For the sake of comparison, acid titration was carried out in the absence of sodium perchlorate in the same mixed solvent and the pK_a values obtained were 7.44, 5.01, and 5.38 for **1b, 2b,** and **3b,** respectively, indicating that **3b** is a stronger base than **2b.**

^{1}H and ^{13}C NMR chemical shifts were determined and assigned as is shown in Figure 1 on the basis of the C–H and C–P coupling patterns and of the selected decoupling data. In each case the carbon atom bonded to palladium resonates at remarkably lower field compared with the corresponding carbon in uncoordinated pyridine. The ortho (adjacent) carbons also show 5.6–10.2-ppm downfield shifts, but the para carbons in **1b** and **2b** show ~6-ppm upfield shifts, while the meta carbons show smaller change. The change of the shieldings of the pyridine-ring carbons on σ bonding to palladium is quite similar to that observed for the phenyl-ring carbons in some phenylplatinum(II) complexes.[10]

With the aim of gaining some insight into the nature of chemical bonds in these complexes, we carried out MO calculations based on the CNDO/2 method of the simplified model complexes, *trans*-$PdCl(2\text{-}, 3\text{-}, \text{and } 4\text{-pyridyl})(PH_3)_2$. Standard values[11] were used for CNDO/2 parameters asso-

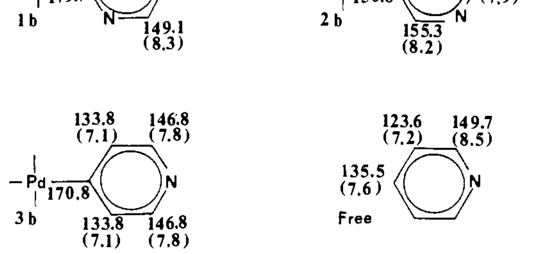

Figure 1. ^{13}C and ^{1}H (in parentheses) shieldings in complexes **1b, 2b,** and **3b** (both of δ_C and δ_H from Me_4Si).

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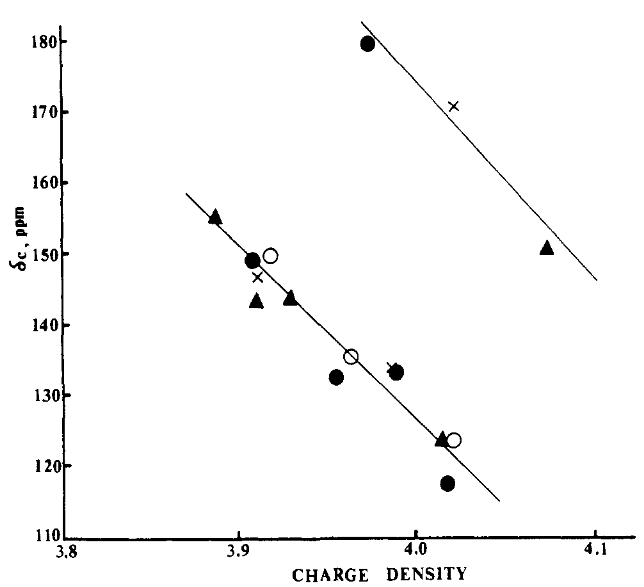

Figure 2. Observed ^{13}C shieldings for uncoordinated pyridine (○), complexes **1b** (●), **2b** (▲), and **3b** (×) vs. the calculated charge densities, the upper straight line referring to the quaternary carbons bonded to palladium and the lower one to the other ring carbons.

ciated with the H, C, N, P, and Cl atoms, while those of Pd were estimated using the experimental data[12] $\frac{1}{2}(I_\mu + A_\mu)$, 4d, 8.33, 5s, 4.135, and 5p, 1.835 eV, and $-\beta_\mu^\circ$, 4d, 20.00, 5s, 8.47, 5p, 3.76 eV, where I, A, and β° stand for the valence state ionization potential, electron affinity, and bonding parameter, respectively, and μ is the subscript associated with each atomic orbital.

The ^{13}C NMR chemical shift is known to be correlated with the charge density on a given carbon atom in a molecule.[13] As is seen in Figure 2, the plot of observed ^{13}C shieldings for pyridine carbons against the calculated charge densities gave two straight lines, one for the carbon atoms bonded to palladium and the other for other carbons inclusive of those in uncoordinated pyridine. The specific behavior of the quaternary carbons might be caused by the contribution of dσ orbital to the Pd-C bond.

From the standpoint of valence-bond theory, the back-donation from palladium might be largest in the case of **1b**, since the carbon atom adjacent to nitrogen in uncoordinated pyridine has the lowest charge density and hence the highest electron acceptability as evidenced by the ^{13}C chemical shielding (Figure 1).

Compounds **2a, 3a,** and $PdCl[C_5H_3(6\text{-}Cl)\text{-}C^2](PPh_3)_2$, which was obtained as a mononuclear complex from the reaction between $Pd(PPh_3)_4$ and 2,6-dichloropyridine, react with carbon monoxide in THF at room temperature to afford the acyl complexes in high yields, which in turn readily react with methanol in the absence of base to yield methyl nicotinate, methyl isonicotinate, and methyl 6-chloropicolinate, respectively. On the contrary, the triethylphosphine complexes **1b, 2b,** and **3b** as well as the dinuclear complex **1a** are not carbonylated under the same conditions. Catalysis of **1a** for the cross-coupling reaction between 2-chloropyridine and methylmagnesium bromide and other reactions of the pyridylpalladium(II) complexes will be reported elsewhere.

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Kiyoshi Isobe, Eiko Kai, Yukio Nakamura
Kichisuke Nishimoto, Toshio Miwa, Shinichi Kawaguchi*
Department of Chemistry, Faculty of Science
Osaka City University, Sumiyoshi-ku, Osaka 558, Japan

Kenji Kinoshita, Kazumi Nakatsu*
Department of Chemistry, Faculty of Science
Kwansei Gakuin University, Nishinomiya
Hyogo 662, Japan

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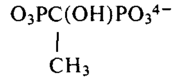
Structural Characterization of a ^{99}Tc-Diphosphonate Complex. Implications for the Chemistry of ^{99m}Tc Skeletal Imaging Agents

Sir:

Diagnostic nuclear medicine involves the investigation, development, production, and use of radiopharmaceuticals, i.e., γ-ray-emitting isotopes in specific chemical forms designed to concentrate in specific organs of the body. Subsequent scanning of the organs with a γ-ray camera provides valuable diagnostic and prognostic data by an essentially noninvasive technique.[1-3] ^{99m}Tc has been the isotope of choice for diagnostic nuclear medicine because of its optimal nuclear properties, its diverse chemistry, and its general availability.[4-8] Several X-ray structural determinations of technetium complexes have recently appeared,[4,9-12] but none have involved ligands that form the basis of clinically useful ^{99m}Tc radiopharmaceuticals. This communication reports the structural characterization of a ^{99m}Tc complex with methylenediphosphonate (MDP), the simplest member of the class of diphosphonate ligands which is used in the preparation of efficacious ^{99m}Tc skeletal imaging agents and ^{99m}Tc myocardial infarct imaging agents.[1-5,7,13-15] The constitutions of the clinically used diphosphonates MDP and HEDP (1-hydroxyethylidenediphosphonate) are shown below along with that of the

$O_3POPO_3^{4-}$
PYP

$O_3PCH_2PO_3^{4-}$
MDP


$O_3PC(OH)(CH_3)PO_3^{4-}$
HEDP

related ligand pyrophosphate (PYP). While it is generally assumed that ^{99m}Tc complexes of these three ligands are avid bone seekers because the coordinated phosphonate or phosphate ligand still has considerable affinity for calcium, the chemistry of these systems is very complex and no coherent theory explaining their in vivo mechanism(s) of action has yet been developed. In large part this situation obtains because, until now, there has been no firm information as to the possible mode(s) of bonding and interaction between diphosphonate ligands and technetium. In this communication we report on the preparation and structure of a ^{99}Tc-MDP complex.

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