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HP-NMR Study of the Pd-Catalyzed Methoxycarbonylation of Styrene Using Monodentate and Bidentate Phosphane-Modified Systems

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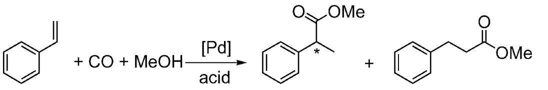
Catalytically active palladium systems bearing the monodentate phosphetane ligand **1** and diphosphane **2** were studied by multinuclear NMR and HP-NMR spectroscopy under methoxycarbonylation conditions. The reaction of the complex [PdCl$_2$(**1**)$_2$] (**1a**) with *p*TsOH yields the dimeric complex [PdCl(μ-Cl)(**1**)]$_2$ (**1b**), which was characterized by multinuclear NMR spectroscopy and X-ray crystallography. The isolated complex **1b** was tested as a precursor in the methoxycarbonylation of styrene, providing poor activity and enantioselectivity. Evidences for the protonation of ligand **1** under catalytic conditions were obtained. When complex [Pd(OTs)(OH$_2$)(*R*,*R*-bdpp)][OTs] (**2b**) was used as the catalyst precursor evidences for both hydride and methoxycarbonylation mechanisms were achieved. Two isomeric forms of [Pd(π-methylbenzyl)(*R*,*R*-bdpp)], **2h** and **2i**, were characterized by multinuclear NMR spectroscopy and DFT calculations. The results obtained by DFT calculations showed that the two most stable isomers contain the ligand bdpp in the "*chair*" conformation and that both isomers have very similar energies. The hydrido-carbonyl-bridged complex [Pd$_2$(μ-H)(μ-CO)(*R*,*R*-bdpp)$_2$][OTs] (**2e**) was also detected under catalytic conditions. Deuterium labeling experiments using [D$_4$]MeOH and GC-MS analysis of the unconverted substrate and products were performed and the results indicate that the styrene insertion step into the Pd–H bond of the catalyst is irreversible when the phosphetane containing system is used, whereas this step is reversible when the diphosphane precursor is used as the incorporation of deuterium was only observed in the latter case.

Introduction

Over the past two decades the asymmetric methoxycarbonylation of vinylarenes (Scheme 1) has been extensively studied as a route to obtain 2-arylpropionic acids, the most important class of nonsteroidal anti-inflammatory drugs.[1]



Scheme 1. Pd-catalyzed methoxycarbonylation of styrene.

The regioselectivity of these reactions is of critical importance when they are to be performed in an asymmetric manner, as only the branched product contains a chiral center. Catalysts containing bidentate diphosphane ligands have been frequently used for this reaction, but generally afford low regioselectivity to the branched product. However, a few successful examples have recently been reported.[2,3] Monodentate phosphorus ligands have recently received more attention because of their significant potential in various catalytic processes.[4] Interestingly, in the palladium-catalyzed methoxycarbonylation of styrene their use provides high regioselectivity to the branched ester.[5] This difference in regioselectivity was suggested to be due to the ability of monodentate ligands to coordinate to the palladium center in a *cis* or a *trans* manner.[6] Nevertheless, the study of the methanolysis step by van Leeuwen and coworkers, which was performed by varying the bite angle of diphosphanes, indicated that *cis* coordination of the phosphane ligands is required for this step to be efficient.[7] The dissociation/association of the phosphane ligands and the role of the acid counterion that is used have also been suggested to influence the regioselectivity.[8] van Leeuwen and coworkers have also demonstrated that the presence of electron-withdrawing substituents on diphosphane ligands can invert the regioselectivity of the methoxycarbonylation of styrene in favor of the branched ester.[3] Indeed, when comparing the results obtained with the DIOP ligand and with its analogue containing CF$_3$ substituents in the 3- and 5-positions they concluded that the formation of the

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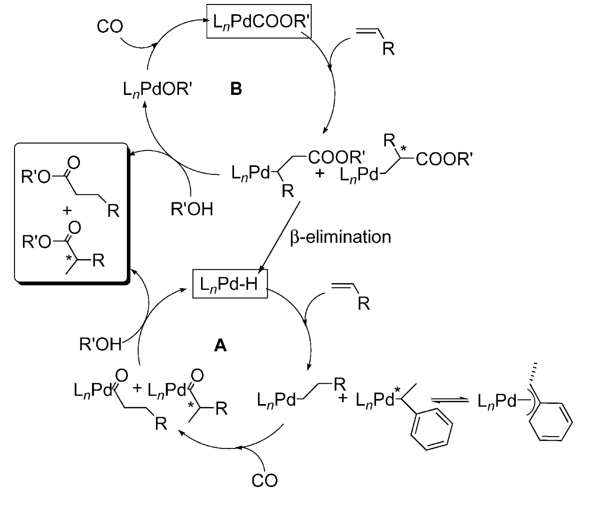
branched ester is favored when electron-poor diphosphanes are used.

Two mechanisms have been suggested for this reaction (Scheme 2).[9] The catalytic cycle can either start from a hydridopalladium complex (cycle A) or an (alkoxycarbonyl)-palladium species (cycle B). In the hydride cycle the first step is the insertion of the alkene into the Pd–H bond to form an alkyl complex, followed by coordination and migratory insertion of CO to produce a Pd–acyl species. Alcoholysis of the Pd–acyl species regenerates the Pd–H complex and yields the ester. Recent advances have been reported on this step using DFT calculation methods.[10] In the alkoxycarbonyl cycle the alkene is inserted into the Pd–carbon bond of the (alkoxycarbonyl)palladium complex, followed by alcoholysis to yield an alkoxypalladium complex and the ester. Coordination and migratory insertion of CO then regenerate the initial alkoxycarbonylpalladium complex. The production of the Pd–H species from complexes formed in cycle B was also demonstrated to occur through the β-elimination of an unsaturated ester after alkene insertion.[11] When the substrate is a vinylarene the branched-alkyl intermediate can be stabilized through the formation of a π-benzylic species with the two complexes in equilibrium.[6]



Scheme 2. Catalytic cycles proposed for the Pd-catalyzed methoxycarbonylation of styrene.

The co-existence of these two cycles was suggested to be the origin of the regioselectivity of these reactions.[12] On the basis of steric factors, the linear insertion of styrene is favored when the insertion occurs into a Pd–hydride bond whereas the branched insertion of styrene is favored when the insertion occurs into a Pd–alkoxycarbonyl bond.

Our recent reports on the use of monodentate phosphetane[5b] and diphosphane ligands[13] in the Pd-catalyzed methoxycarbonylation of styrene showed that these catalytic systems follow the general trend. In order to shed some light on the mechanism(s) operating for these systems, we report here our investigations using conventional and high-pressure NMR methods, DFT calculations, and deuterium labeling experiments. The ligand systems used for this study are shown in Figure 1. The choice of the ligands used here was obviously not motivated by their novelty, as both were previously reported in a number of asymmetric catalytic reactions, but as models for their typical behavior as mono- and bidentate phosphane ligands in this reaction in terms of regio- and enantioselectivity.[5b,13b]

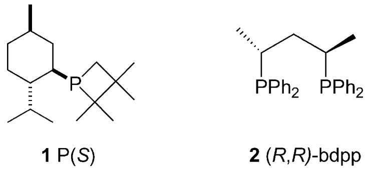


Figure 1. Ligands used in this study.

Results and Discussion

In order to investigate the behavior of the palladium catalytic systems containing the phosphetane **1** and the diphosphane **2** under methoxycarbonylation conditions, the reactivity of these systems was studied stepwise in the presence of the reagents present during the catalysis: MeOH, CO, and styrene. In the case of the monodentate phosphane system the reactivity of the Pd precursor **1a** towards *p*TsOH was also studied. The samples were heated to 323 K, the temperature at which conversions of the substrates were achieved for both systems.

Study of the Monophosphane System [PdCl$_2$(**1**)$_2$] (**1a**)/*p*TsOH Under Methoxycarbonylation Conditions

When [PdCl$_2$(**1**)$_2$] (**1a**) is used as the catalyst precursor the presence of acid is required.[5b] High regioselectivity to the branched ester was achieved (>99%) with the use of [PdCl$_2$(**1**)$_2$] (**1a**)/*p*TsOH but no enantioselectivity was induced under these conditions. In this report the reactivity of the complex **1a** towards *p*TsOH, CO, styrene, and methanol is studied stepwise.

Reaction of Complex 1a in CD$_3$OD/[D$_8$]THF in the Presence of pTsOH

In order to probe the stability of complex **1a** in the solvent mixture used during the catalytic reaction a solution of complex **1a** in CD$_3$OD/[D$_8$]THF was charged into a 5-mm NMR tube fitted with a Young's tap. The signals corresponding to the starting material are readily detected in ^{1}H and ^{31}P{^{1}H} NMR spectra that are acquired at room temperature. When the temperature is raised to 323 K no new signals are observed indicating that the complex **1a** is stable under these conditions. A solution of complex **1a** in CD$_3$OD/[D$_8$]THF was transferred into a 5-mm NMR tube and 5 equiv. of *p*TsOH was added. When a ^{31}P{^{1}H} NMR spectrum is acquired at room temperature (trace a, Figure 2) the signal at δ = 61 ppm corresponding to **1a** is readily detected. No other signals are detected at this temperature.

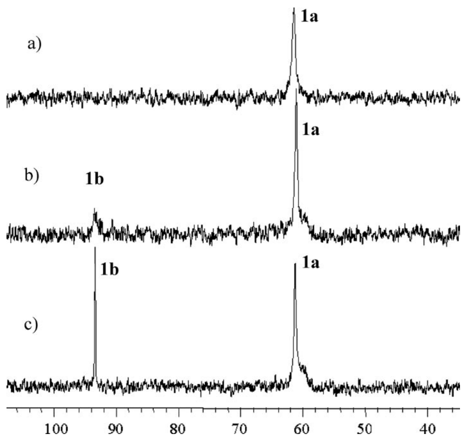


Figure 2. $^{31}P\{^1H\}$ Spectra of complex **1a** in CD_3OD/[D_8]THF in the presence of *p*TsOH (a) at 295 K, (b) after a few minutes at 323 K, and (c) after 2 h at 323 K.

However, when a $^{31}P\{^1H\}$ NMR spectrum is acquired at 323 K a new singlet resonance at δ = 93 ppm (trace b, Figure 2) is immediately detected. After 2 h at this temperature the intensity of this signal increases (trace c, Figure 2).When the sample was left for a few days at room temperature red and yellow crystals appeared from the solution. X-ray diffraction of both sets of crystals revealed that the yellow crystals corresponded to the starting material **1a**[5b] and that the red crystals corresponded to a new complex that was identified as *trans*-[PdCl(μ-Cl)(**1**)]$_2$ (**1b**). The molecular structure of **1b** is shown in Figure 3. Selected bond lengths and angles are listed in Table 1.

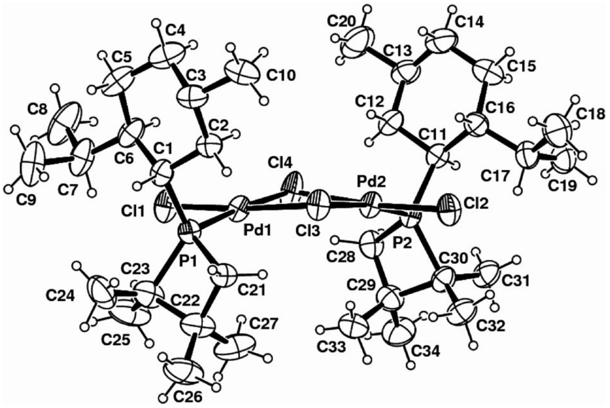


Figure 3. ORTEP diagram of the dinuclear complex **1b**. Ellipsoids drawn at the 35% probability level.

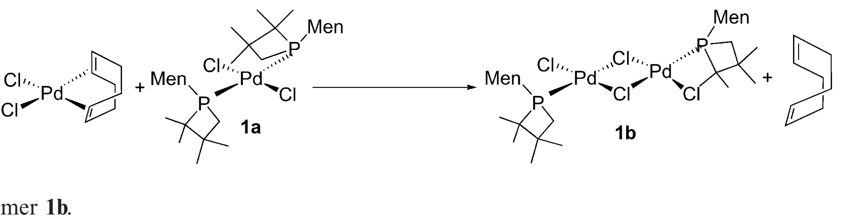
Table 1. Selected bond lengths [Å] and angles [°] for **1b**.

Selected bond lengths [Å]			
Pd(1)–P(1)	2.232(1)	Pd(2)–P(2)	2.224(1)
Pd(1)–Cl(1)	2.270(1)	Pd(2)–Cl(2)	2.273(2)
Pd(1)–Cl(3)	2.338(2)	Pd(2)–Cl(4)	2.302(2)
Pd(1)–Cl(4)	2.415(2)	Pd(2)–Cl(3)	2.480(1)
Selected angles [°]			
P(1)–Pd(1)–Cl(1)	90.37(5)	P(2)–Pd(2)–Cl(2)	91.01(5)
P(1)–Pd(1)–Cl(3)	94.57(5)	P(2)–Pd(2)–Cl(3)	171.74(6)
Cl(1)–Pd(1)–Cl(3)	175.97(7)	P(2)–Pd(2)–Cl(4)	92.00(5)
P(1)–Pd(1)–Cl(4)	174.17(6)	Cl(2)–Pd(2)–Cl(3)	92.66(5)
Cl(1)–Pd(1)–Cl(4)	89.55(5)	Cl(2)–Pd(2)–Cl(4)	173.96(8)
Cl(3)–Pd(1)–Cl(4)	85.74(6)	Cl(3)–Pd(2)–Cl(4)	85.04(5)
P(2)–Pd(2)–Cl(2)	92.27(5)	Pd(2)–Cl(4)–Pd(1)	94.87(5)

When some of these crystals were dissolved in CD_2Cl_2 the signal at δ = 93 ppm was again detected in the corresponding $^{31}P\{^1H\}$ NMR spectrum, demonstrating that **1b** is the species detected by NMR spectroscopy at 323 K. In the X-ray structure of **1b** both palladium centers exhibit a distorted square-planar geometry with mean coordination planes Cl(1)/P(1)/Cl(3)/Cl(4) and Cl(2)/P(2)/Cl(3)/Cl(4) forming a dihedral angle of 16.95(7)°. The Pd(1)–Cl(1) and Pd(2)–Cl(2) bond lengths were measured to be 2.267(1) and 2.273(2) Å, respectively, while the Pd–P bonds are 2.232(1) and 2.224(1) Å. As expected, from the higher *trans* influence of the phosphane ligands, the Pd(1)–Cl(4) and Pd(2)–Cl(3) bond lengths [2.415(2) and 2.480(1) Å, respectively] are significantly longer than those of Pd(1)–Cl(3) and Pd(2)–Cl(4) [2.338(1) and 2.302(1) Å, respectively] and the Pd–Cl bond lengths of the terminal chloride ligands are found to be shorter (ca. 2.27 Å) than those of the bridging chlorides. The bridging angles Pd(1)–Cl(3)–Pd(2) and Pd(2)–Cl(4)–Pd(1) are 92.27(5) and 94.87(5)°, respectively, while those at the metals inside the squared Pd_2Cl_2 fragment are narrower, being 85.74(5) and 85.04(5)°.The X-ray structure of the analogue compound bearing triphenylphosphane ligands was reported as a benzene solvate and exhibited similar structural features.[14]

In order to investigate the role of this complex during the catalysis, the synthesis of the dimer **1b** was performed by stirring a solution of [$PdCl_2$(COD)] and [$PdCl_2(\mathbf{1})_2$] (**1a**) for 2 h in dichloromethane at room temperature (Scheme 3).

The dimer was obtained in a pure form from recrystallization in hexane. When **1b** was tested as a catalytic precursor for the methoxycarbonylation of styrene, under the same catalytic conditions as those used for **1a**,[5b] the complex was found to be scarcely active. The complex **1b** af-



Scheme 3. Synthesis of dimer **1b**.

forded 12% of conversion, the chemo- and regioselectivity were 70 and 85%, respectively, and the enantiomeric excess was 8%. This latter result was interesting since no enantioselectivity was observed when complex **1a** was used as the catalyst precursor.

The formation of the dimer **1b** from **1a** requires the dissociation of phosphetane ligand **1** from this complex. However, no evidence for the presence of phosphetane **1** in solution could be obtained. The protonation of phosphane ligands in the presence of acid was previously reported under catalytic methoxycarbonylation conditions by Cole-Hamilton and coworkers, who elegantly used the properties of ligands to avoid the decomposition of vinylacetate in the presence of acids such as $MeSO_3H$.[15] Under these conditions the ligand is protonated and the resulting phosphonium salt is sufficiently acidic to protonate a palladium center and initiate the catalytic reaction. In this context, the reactivity of phosphetane **1** in an acidic medium was therefore investigated.

Reaction of the Phosphetane Ligand 1 in the Presence of pTsOH in CD_3OD

When a sample of **1** is dissolved in CD_3OD and charged into a 5-mm NMR tube fitted with a Young's tap and a $^{31}P\{^1H\}$ spectrum is acquired a signal is detected at δ = 18 ppm and readily assigned to the free ligand **1**. When *p*TsOH (0.5 equiv.) is added to the solution a new broad signal is observed at ca. 30 ppm in the corresponding $^{31}P\{^1H\}$ NMR spectrum. When a spectrum is acquired at 223 K the signal corresponding to **1** and a new signal at δ = 39.5 as a pseudo triplet with a 1:1:1 intensity pattern (trace a, Figure 4) are observed. The multiplicity of the signal at δ = 39.5 ppm suggests the formation of a new species containing deuterium with a P–D coupling of 70 Hz.

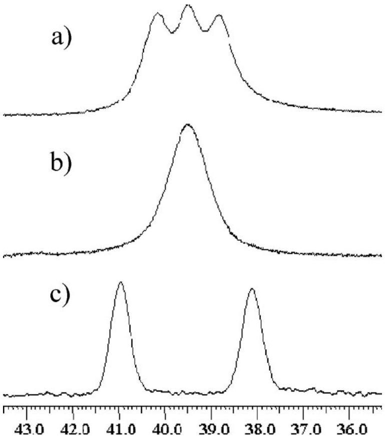


Figure 4. Selected region of $^{31}P\{^1H\}$ and ^{31}P NMR spectra of solutions containing phosphetane **1** + *p*TsOH (a) in CD_3OD at 223 K, (b) in CD_2Cl_2 at room temp., and (c) in CD_2Cl_2 at 223 K (^1H coupled spectrum).

The experiment was then repeated in CH_3OH and, after evaporation of the methanol, the residue was redissolved in CD_2Cl_2. In the $^{31}P\{^1H\}$ NMR spectrum at room temperature the signal at δ = 39.5 ppm is again detected as a broad singlet (trace b, Figure 4). When a ^1H-coupled ^{31}P NMR spectrum was acquired this signal was still detected as a broad resonance. In the corresponding ^1H NMR spectrum a new broad signal is observed at 7.4 ppm. In the ^1H-coupled ^{31}P NMR spectrum at 223 K the ^{31}P signal resonating at δ = 39.5 ppm exhibits a doublet multiplicity J_{P-H} = 470 Hz (trace c, Figure 4). In the ^1H NMR spectrum at 223 K the signal previously detected at 7.4 ppm exhibits a doublet multiplicity (J_{P-H} = 470 Hz). The value of the P–H coupling is characteristic of a compound containing a P–H moiety. The species corresponding to this signal was therefore identified as the protonated phosphetane **1**-H^+. Leoni et al. observed the formation of Cy_3PH^+ by addition of CF_3SO_3H to a solution of $[Pd(H)(OH_2)(PCy_3)_2]BF_4$ in $CDCl_3$ and [D$_8$]THF with J_{P-H} = 475 Hz, which is very similar to that observed for phosphetane **1**-H^+.[16] The values reported by McFarlane et al. for a series of protonated organophosphorus compounds are also in agreement with the coupling value measured for **1**-H^+.[17]

Reaction of Complex 1a in CD_3OD/[D$_8$]THF in the Presence of pTsOH and Carbon Monoxide (35 atm)

A solution of the precursor **1a** and *p*TsOH (5 equiv.) in a mixture of CD_3OD/[D$_8$]THF (ratio 1:1 in volume) was prepared and placed into a 10-mm high-pressure (HP) NMR tube. After pressurizing the tube with 35 atm of CO a $^{31}P\{^1H\}$ NMR spectrum was acquired at room temperature and the signal at δ = 61 ppm corresponding to the starting material **1a** was readily detected. At this temperature no other signals were detected and even at temperatures up to 323 K no changes were observed. The complex **1a** and *p*TsOH (5 equiv.) in CD_3OD/[D$_8$]THF were then stirred in a Schlenk tube overnight at 323 K and the solution was later transferred into the 10-mm high-pressure NMR tube. A first $^{31}P\{^1H\}$ NMR spectrum was acquired at room temperature before pressurizing with CO and two signals were detected: the signal at δ = 61 ppm (major), corresponding to the complex $[PdCl_2(\mathbf{3})_2]$ **1a**, and a singlet signal at δ = 93 ppm, previously identified as the dimer **1b** (trace a, Figure 5). In the ^1H NMR spectrum no hydride signals were observed. The tube was then charged with CO (35 atm) and the reaction was monitored by ^{31}P NMR spectroscopy. The decrease in intensity of the signal at δ = 93 ppm was apparent, while the signal at δ = 61 ppm remained unchanged (trace b, Figure 5). When the temperature was increased to 323 K the signal at δ = 93 ppm, corresponding to the dimer **1b**, was not observed and only the signal at δ = 61 ppm was detected (trace c, Figure 5).

After a few minutes at 323 K a new signal was detected at δ = 39.5 ppm, while the signal corresponding to **1a** remained unchanged (trace d, Figure 5). The signal at δ = 39.5 ppm is readily assigned to the protonated phosphetane **1**-H^+. At this point, in order to stabilize the palladium species involved in the reaction, the temperature was rapidly decreased to room temperature. The $^{31}P\{^1H\}$ NMR spectrum at this temperature reveals the presence of the starting complex **1a** and the protonated phosphetane **1**-H^+. No new signals are detected. When the experiment was repeated using ^{13}CO the same signals were detected in the $^{31}P\{^1H\}$

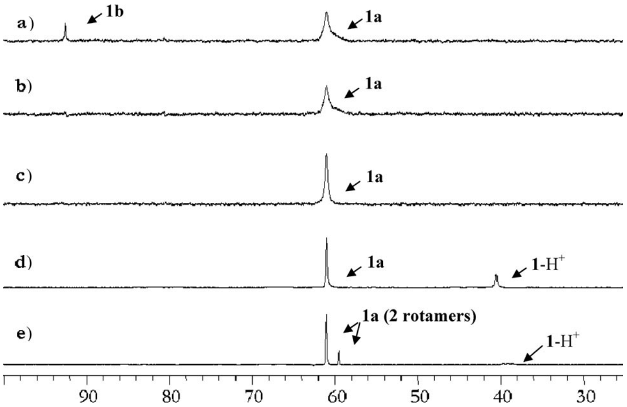


Figure 5. Sequence of $^{31}P\{^1H\}$ NMR spectra of complex **1a** + *p*TsOH in CD_3OD/[D$_8$]THF after overnight stirring at 323 K (a) at room temp. before pressurizing with CO, (b) at room temp. after pressurizing with 35 atm of CO, (c) at 323 K under 35 atm of CO, (d) after 5 min at 323 K under 35 atm of CO, and (e) at 223 K after warming at 323 K under 35 atm of CO.

NMR spectrum. In the corresponding $^{13}C\{^1H\}$ NMR spectrum at 323 K two singlet resonances are detected at δ = 185.0 and 186 ppm. The former signal was readily assigned to free CO. Although the chemical shift of the resonance at δ = 186 ppm is characteristic of a carbonyl ligand coordinated to palladium, its singlet multiplicity indicates that no phosphetane ligand is contained in this species. This latter signal is therefore assigned to a chlorocarbonylpalladium complex formed from the reaction of **1b** in the presence of CO. This assignment is in agreement with the disappearance of the ^{31}P signal of **1b** under CO pressure (Figure 5). When the temperature is decreased to 223 K the signal at δ = 61 ppm in the $^{31}P\{^1H\}$ NMR spectrum (trace e, Figure 5), corresponding to the starting material, is resolved into two singlets at δ = 61.2 and 59.7 ppm, corresponding to two rotameric forms of complex **1a** in solution.[5b] The signal at δ = 39 ppm appears as a pseudo triplet with a 1:1:1 intensity pattern, (J_{P-D} = 140 Hz), as expected for the P–D bond of **1**-D$^+$. In the $^{13}C\{^1H\}$ NMR spectra at 223 K the singlet signal at δ = 186 ppm is again detected. The identity of the corresponding species could not be determined. Several palladium–carbonyl complexes have been described under similar conditions.[18,19–21]

Reaction of Complex 1a in CD_3OD/[D_8]THF in the Presence of pTsOH, Styrene, and Carbon Monoxide (35 atm)

A solution of the precursor **1a** and *p*TsOH (5 equiv.) in CD_3OD/[D$_8$]THF as a mixture of solvents was stirred in a Schlenk tube overnight at 323 K. Styrene (20 equiv.) was added and the solution was transferred into the 10-mm HP-NMR tube. A first $^{31}P\{^1H\}$ spectrum was acquired at room temperature before pressurizing with CO. In the spectrum the signal at δ = 61 ppm {starting complex [PdCl$_2$(**1**)$_2$] (**1a**), major species} and a singlet signal at δ = 93 ppm (dimer **1b**) are detected. The tube was then charged with CO (35 atm) and the reaction was monitored by ^{31}P NMR spectroscopy. The signal at δ = 61 ppm remains unchanged while the signal corresponding to **1b** decreases in intensity. When the temperature is increased to 323 K the signal at δ = 61 ppm (**1a**) and a signal at δ = 39.5 ppm (**1**-H$^+$) are detected. The experiment was repeated using ^{13}CO and no changes were observed in the $^{31}P\{^1H\}$ spectrum. In the corresponding $^{13}C\{^1H\}$ NMR spectrum at 323 K four singlet resonances are detected at δ = 186.0, 185.0, 173.8, and 175.4 ppm. The former signal at δ = 186.0 ppm was previously detected in the absence of styrene. The signals at δ = 185.0, 173.8, and 175.4 ppm are readily assigned to free CO and to the linear and branched esters, respectively. The detection of the latter signals indicates that the methoxycarbonylation reaction is taking place. When the HP-NMR tube was cooled to 223 K no changes were detected in the $^{31}P\{^1H\}$ and $^{13}C\{^1H\}$ NMR spectra. It was concluded that the intermediates of the reaction were not stable enough to be detected by NMR spectroscopy under these conditions. However, since the precursor **1a** was detected throughout the HP-NMR spectroscopic study, it was concluded that only a small amount of this species reacted to form the Pd species that take part in the catalytic cycle.

Study of the Diphosphane System [Pd(OTs)(OH$_2$)(*R*,*R*)-bdpp][OTs] (2b) Under Methoxycarbonylation Conditions

The cationic complex [Pd(OH$_2$)(OTs)(*R*,*R*)-bdpp][OTs] (**2b**) was shown to be active in the absence of acid, affording enantioselectivity of up to 58% but with a regioselectivity to the branched ester of 16%.[13b]

The reactivity of the complex **2b** towards methanol, CO, and styrene was studied stepwise.

Reaction of Complex 2b in Methanol

In a 5-mm NMR tube fitted with a Young's tap a solution of complex **2b** in CD_2Cl_2 was prepared. When a ^1H NMR spectrum is acquired at room temperature five signals are observed in the aliphatic region at δ = 1.34 (dd, J_{PH} = 16 Hz and J_{HH} = 6.8 Hz, 6 H, Me), 2.29 (s, 6 H, MeTsO), 2.30 (m, 2 H, CH$_2$), 2.96 (m, 2 H, CH), and 4.38 (br. s, 2 H, H$_2$O) ppm. The latter signal is assigned to the coordinated water molecule. In the corresponding $^{31}P\{^1H\}$ NMR spectrum a single peak at δ = 27.9 ppm is detected. However, when the ^1H NMR spectrum of **2b** (Figure 6) is acquired in CD_3OD only four signals are detected in the aliphatic region at δ = 1.21 (dd, J_{PH} = 16 and J_{HH} = 7 Hz, 6 H, Me), 2.25 (tt, J_{PH} = 21 and J_{HH} = 6.8 Hz, 2 H, CH$_2$),

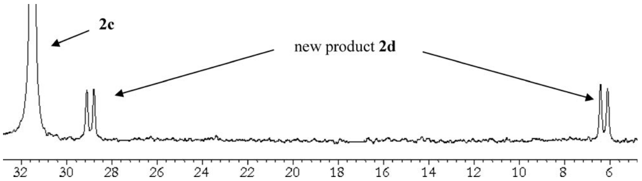


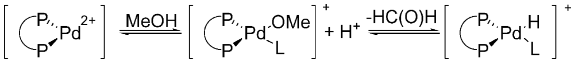
Figure 6. $^{31}P\{^1H\}$ NMR spectra of a solution containing **2b** in CD_3OD at 323 K.

2.30 (s, 6 H, MeTsO), and 2.98 (m, 2 H, CH) ppm. The absence of a ^{1}H NMR signal for the coordinated water molecule was explained by the substitution of H_2O by CD_3OD to form the species [Pd(CD_3OD)(OTs)(*R*,*R*)-bdpp][OTs] (**2c**). In the corresponding ^{31}P{^{1}H} NMR spectrum a singlet resonance at δ = 31.5 ppm is detected.

When the sample in CD_3OD is heated to 323 K and the reaction is monitored by ^{31}P NMR spectroscopy two new signals are detected at δ = 29.5 and 6.8 ppm as two mutually coupled doublets ($^2J_{PP}$ = 52 Hz), indicating that the corresponding species contains two inequivalent phosphorus atoms.

After a few minutes at this temperature the conversion to this new species was measured to be 20%. When the sample was left at this temperature for a longer time the conversion was found to remain unchanged, suggesting that the new species **2d** was in equilibrium. In the corresponding ^{1}H NMR spectrum new aromatic and alkylic signals are detected and attributed to a new product containing a bddp ligand. However, no high field resonances could be detected.

The formation of the hydride species by the oxidation of MeOH into formaldehyde was previously proposed for these types of systems (Scheme 4).[18]



Scheme 4. Proposed route for the formation of the hydridopalladium species by the oxidation of MeOH into formaldehyde.

The absence of a hydride resonance in the ^{1}H NMR spectrum is attributed to rapid H/D exchange in CD_3OD. In an attempt to detect this signal the experiment was repeated in CH_3OH and in a mixture of CH_3OH/[D$_8$]THF, but no hydride signal could be observed because of the high intensity of the solvent peaks.

When the reaction was repeated in the presence of 5 equiv. of *p*TsOH the signals corresponding to the species **2d** were not detected, indicating that the formation of this complex was inhibited in the presence of *p*TsOH.

Reaction of Complex 2b in CD_3OD in the Presence of Carbon Monoxide (1 atm)

When a sample of **2b** is dissolved in CD_3OD and placed under 1 atm of carbon monoxide at room temperature only the signals corresponding to **2c** are detected in the corresponding ^{1}H and ^{31}P{^{1}H} NMR spectra. However, when the sample is heated to 323 K for a few minutes three new singlet signals at δ = 14.1, 17.5, and 17.8 ppm are detected in the ^{31}P{^{1}H} NMR spectrum (trace a, Figure 7). After 30 min at this temperature the signal at δ = 17.8 ppm is found to have increased in intensity (trace b, Figure 7) while the intensity of the signal corresponding to **2c** has decreased. The two other signals remain unchanged. Interestingly, no signals corresponding to the product observed at 323 K in the absence of CO are detected, indicating that **2d** is rapidly converted under these conditions.

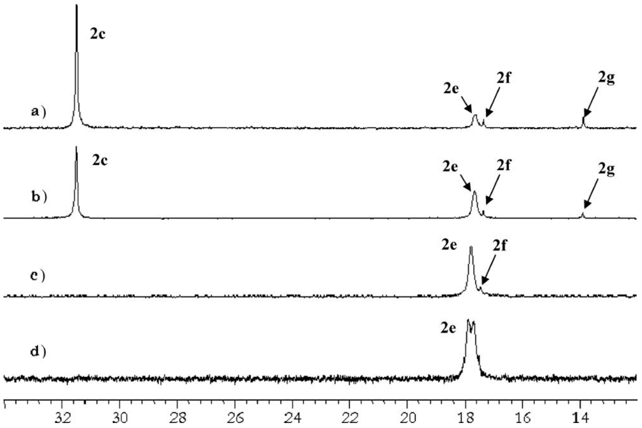
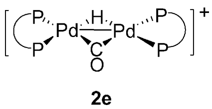


Figure 7. ^{31}P{^{1}H} NMR spectra of a CD_3OD solution containing complex **2b** in the presence of CO (1 atm) (a) after a few minutes at 323 K, (b) after 30 min at 323 K, (c) after 2 h at 323 K, and (d) after 4 h in the presence of ^{13}CO (1 atm) at 323 K.

After 2 h at 323 K only two resonances are visible in the ^{31}P{^{1}H} NMR spectrum with a signal at δ = 17.8 ppm corresponding to the main reaction product (ca. 95%) whereas the signal at δ = 17.5 ppm is detected as a minor product (ca. <5%) (trace c, Figure 7). At this point the signal corresponding to **2c** is not detected, indicating that full conversion has been reached. When the reaction is repeated using ^{13}CO the ^{31}P resonance at δ = 17.8 ppm exhibits an extra splitting and is detected as a broad doublet (J_{PC} = 32 Hz) (trace d, Figure 7). In the corresponding ^{1}H spectrum a new hydride signal is detected at δ = –4.92 ppm as a quintet (J_{PH} = 44 Hz) and in the ^{13}C{^{1}H} NMR spectrum a quintet resonance is detected at δ = 241.0 (J_{PC} = 32 Hz) ppm. The chemical shift of the latter signal suggests the presence of a bridging carbonyl between the two palladium centers. Elsevier and coworkers previously reported the formation of a dinuclear palladium hydrido-carbonyl complex using (*S*,*S*)-bdpp as the ligand.[19] Comparing the spectroscopic features reported by Elsevier et al., the major product of the reaction under these conditions was identified as the dimer [Pd$_2$(μ-H)(μ-CO)(*R*,*R*-bdpp)$_2$](OTs) (**2e**) (Figure 8). In this report, this species was shown to be unreactive in the presence of an alkene and its contribution to the catalytic outcome of the reaction was therefore discarded.



2e

Figure 8. Structure of the hydrido- and carbonyl-bridged palladium dimer **2e**.

Milstein et al. reported the synthesis of the analogue complex of **2e** with dippp and suggested that a hydridopalladium(II) and carbonylpalladium(0) fragment species are involved in the formation of this complex.[18] The absence of the signals corresponding to **2d** in the presence of CO suggested that this species was involved in the formation of the dimeric complex **2e**. It was therefore concluded that complex **2d** is a hydridopalladium(II) species. Two possible structures for **2d** are proposed in Figure 9.

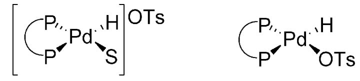


Figure 9. Proposed structures for species **2d**.

Reaction of Complex 2b in CD_3OD in the Presence of Carbon Monoxide (15 atm)

In order to study the effect of higher CO pressures the experiment was repeated using 15 atm of CO at room temperature and monitored by ^{31}P NMR spectroscopy. A few minutes after the introduction of the CO pressure at room temperature the previously detected signal at δ = 14.1 ppm was readily observed. After 30 min the signal at δ = 17.8 ppm corresponding to $[Pd(\mu\text{-}H)(\mu\text{-}CO)(R,R\text{-bdpp})]_2$ (**2e**) is observed. After 2 h the intensity of the signal corresponding to **2c** is found to have considerably decreased whereas the signal at δ = 17.5 ppm is found to increase in intensity. The species corresponding to the signals at δ = 17.8 and 14.1 ppm are the major reaction products under these conditions, indicating that the formation of these species is favored under higher CO pressures. In the $^{13}C\{^1H\}$ spectrum the signal at δ = 241 ppm corresponding to **2e** and two new signals at δ = 191.3 ppm (t, J_{PC} = 55 Hz) and 191.7 (br) ppm are detected. The chemical shifts of the two latter signals are characteristic of carbonyl ligands coordinated to a Pd center. These species are identified as $[Pd(R,R\text{-bdpp})(CO)]$ (**2f**) and $[Pd(R,R\text{-bdpp})(CO)_2]$ (**2g**), respectively. Analogue species were previously reported with very similar NMR spectroscopic features.[6,20,21] After 14 h at room temperature the signals corresponding to **2e** (major) and **2g** are again observed. A new singlet signal is also detected at δ = 41.5 ppm and is readily assigned to the phosphane oxide. In the corresponding ^1H NMR spectrum recorded at room temperature the hydride signal corresponding to **2e** is not detected. However, when the temperature is increased to 323 K the hydride signal at δ = –4.93 ppm is readily observed, indicating that H/D exchange occurs rapidly at this temperature.

Reaction of Complex 2b in CD_3OD in the Presence of Styrene

An NMR tube was charged with **2b** and 5 equiv. of styrene in CD_3OD and the reaction was monitored by ^{31}P NMR spectroscopy. At room temperature only the signal corresponding to **2c** is detected. When the temperature of the sample is raised to 323 K four new signals are detected as two sets of mutually coupled doublets at δ = 14.71 ($^2J_{PP}$ = 73.9 Hz), 17.9 ($^2J_{PP}$ = 73.2 Hz), 28.9 ($^2J_{PP}$ = 73.2 Hz), and 29.2 ($^2J_{PP}$ = 73.9 Hz) ppm, indicating the presence of two species containing two inequivalent phosphorus centers (trace a, Figure 10). The difference in intensities (1.4:1) indicates that the signals at δ = 29.2 and 14.7 ppm correspond to the major species, while the resonances at δ = 28.9 and 17.9 ppm correspond to the minor product of the reaction. After 30 min at this temperature the conversion reaches a maximum of ca. 30 %.

When the reaction is repeated using ^{13}C-labeled styrene (^{13}C enriched in α and β carbons of the vinyl unit) the signals at δ = 28.9 and 29.2 ppm exhibit an extra coupling and appear as a doublet of doublets ($^2J_{PP}$ = 73.2, J_{PC} = 12.3 Hz and $^2J_{PP}$ = 73.9, J_{PC} = 11.6 Hz, respectively) and the signals at δ = 14.71 and 17.9 ppm exhibit two extra couplings to ^{13}C and appear as a set of two doublet of doublet of doublets ($^2J_{PP}$ = 73.9, J_{PC} = 42.9, J_{PC} = 5.8 Hz and $^2J_{PP}$ = 73.2, J_{PC} = 42.2, J_{PC} = 5.0 Hz) (trace b, Figure 10). In the aliphatic region of the corresponding $^{13}C\{^1H\}$ NMR spectrum two doublets of doublets are observed at δ = 16.4 and 17.3 ppm (J_{CC} = 40, J_{PC} = 5.8 Hz and J_{CC} = 40, J_{PC} = 5 Hz, respectively) (trace a, Figure 11). At a lower field two sets of doublet of doublet of doublets at δ = 72.0 and 73.0 (J_{CC} = 40, J_{PC} = 42.9 Hz J_{PC} = 11.6 Hz and J_{CC} = 40, J_{PC} = 42.2 Hz J_{PC} = 12.3 Hz) ppm (trace b, Figure 11) are also

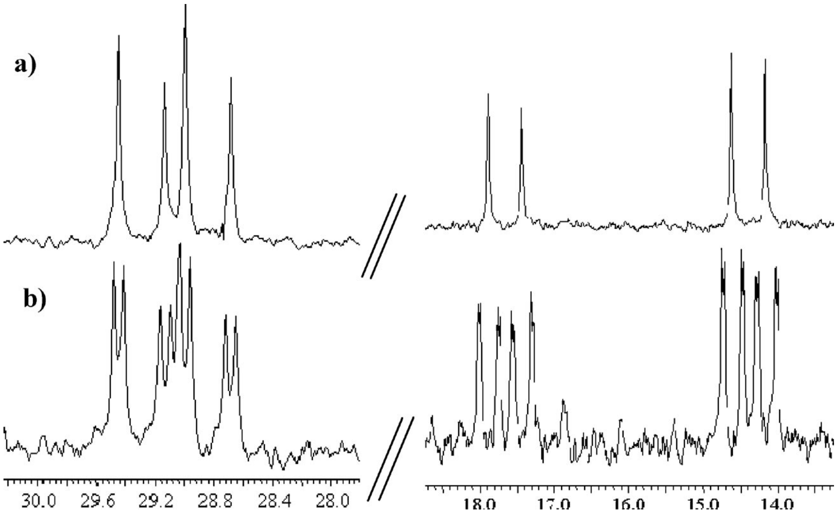


Figure 10. $^{31}P\{^1H\}$ NMR spectrum of a CD_3OD solution of complex **2b** at 323 K in the presence of: (a) styrene, (b) α,β-^{13}C-labeled styrene.

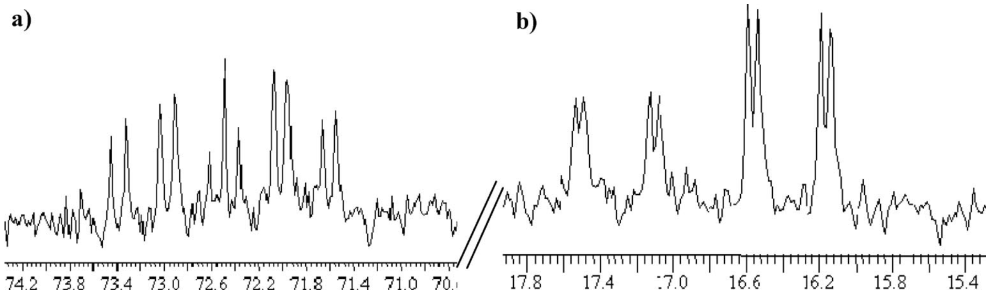


Figure 11. Selected regions of the $^{13}C\{^1H\}$ NMR spectrum of **2b** and styrene in CD_3OD at 323 K.

observed. The chemical shifts of the latter signals suggest the presence of allylic carbons. These observations indicate the formation of two η^3-π-benzylic species **2h** and **2i** with the formula [Pd(η^3-methylbenzyl)(*R*,*R*-bdpp)].

The insertion of styrene into Pd–H bonds to form η^3-π-benzylic species and the presence of these species in solution during the reaction of methoxycarbonylation of styrene was previously reported.[6,22] Musco and coworkers reported the characterization of a similar benzylic species using dppp as ligands with the selective formation of the *syn* complex [Pd(η^3-methylbenzyl)(dppp)] that exhibits a $^2J_{PP}$ value of 74 Hz.[23] However, because of the chiral nature of the diphosphane ligand used in this study the formation of 16 isomeric species is possible with four possible orientations of the methylbenzyl unit, two coordination modes (with either CH group in an *ortho* position to the vinyl unit of the phenyl ring), and two conformations of the bdpp ligand ("*boat*" and "*chair*") (Figure 12).

In order to establish the relative stability of these isomers their geometry was determined by means of DFT methods. The energies corresponding to the optimized structures of isomers **I**–**XVI** are indicated in Figure 12. All the species **I**–**XVI** were found to have similar energies, where the largest difference observed was 6.2 kcal mol^{-1}. The two most stable complexes were found to correspond to the complexes **III** and **IV**, which have very similar stabilities and in which the bdpp ligand adopts the "*chair*" conformation. These complexes correspond to the *syn* and *anti* isomers. Similar bond lengths were measured for these complexes (Figure 13): the Pd–C^1 bonds were measured as ca. 2.2 Å, the Pd–C^2 as ca. 2.35 Å, and Pd–C^3 as ca. 2.5 Å. The Pd–P bonds were found to be shorter when the phosphorus atom is in the

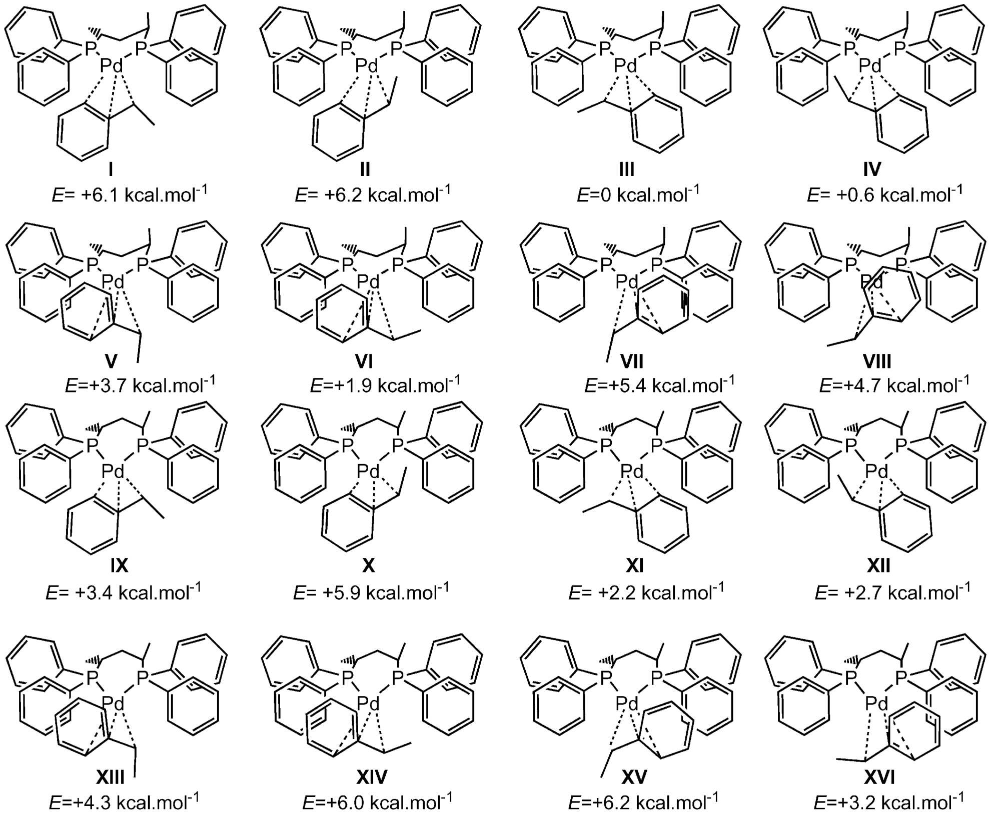


Figure 12. Possible isomers of [Pd(η^3-methylbenzyl)(*R*,*R*-bdpp)] and relative energies of the optimized structures. **I**–**VIII**: complexes with the dppp ligand in the "*chair*" conformation, **IX**–**XVI**: complexes with the dppp ligand in the "*boat*" conformation.

trans position to C^3 (ca. 2.3 Å) than when the phosphorus atom is *trans* to C^1 (ca. 2.4 Å). Note that isomer **VI**, which corresponds to a 180° rotation of the methylbenzyl unit with respect to **III**, is the third most stable and the only isomer that exhibits an energy difference with **III** and **IV** below 2 kcal mol^{-1}.

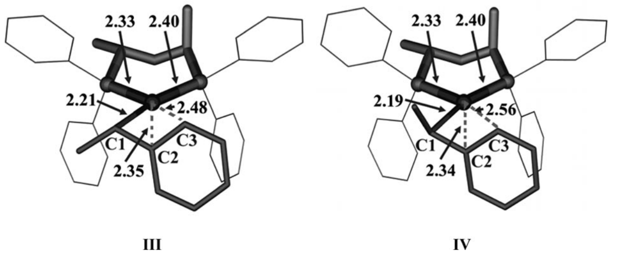


Figure 13. Structure of the most stable isomers of [Pd(η^3-methylbenzyl)(*R*,*R*-bdpp)].

On the basis of these results the complexes **III** and **IV** are the lowest energy isomers and hence are the most likely to be detected by NMR spectroscopy. We therefore propose that isomers **III** and **IV** correspond to the complexes previously identified as **2h** and **2i**, respectively. The small difference in energy between these two species is in agreement with the ratio that is close to 1:1 that was measured by integration of the NMR signals.

Reaction of Complex 2b in CD_3OD in the Presence of Styrene and Carbon Monoxide (1 atm)

An NMR tube was first charged with a CD_3OD solution of **2b** and 20 equiv. of styrene. CO was bubbled through the solution for ca. 5 min and the reaction was monitored by ^{31}P NMR spectroscopy. When a $^{31}P\{^1H\}$ NMR spectrum was recorded at room temperature the signals corresponding to **2c** and the π-benzylic species **2h** and **2i** were immediately detected, as well as a new set of mutually coupled doublets at δ = 28.7 (J_{PP} = 73 Hz) and 15.0 (J_{PP} = 73 Hz) ppm. When the temperature is raised to 323 K these latter signals are not observed and the intensity of the signals corresponding to **2h** and **2i** are found to rapidly increase under these conditions. When the reaction is repeated using ^{13}CO at room temperature the resonances at δ = 28.7 and 15.0 ppm appear as doublet of doublets, exhibiting an extra P–C coupling of 12 Hz. In the corresponding $^{13}C\{^1H\}$ NMR spectrum three peaks are detected in the carbonyl region of the spectrum: a large singlet at δ = 185 ppm that is assigned to free CO, a triplet resonance at δ = 173.4 (J_{PC} = 12 Hz) ppm, and a singlet at δ = 169.3 ppm. Although the chemical shift of these signals are characteristic of a carbonyl group of an organic compound, the observation of a P–C coupling for the signal at δ = 173.4 ppm indicates that this signal corresponds to a Pd species containing two phosphorus centers. Furthermore, the value of J_{PC} (12 Hz) confirms that this species corresponds to the species previously observed in the $^{31}P\{^1H\}$ NMR spectrum. The formation of terminal carbonyls or acyls can be discarded considering that their resonances usually have higher chemical shifts. The spectroscopic features of this species are found to be very similar to those reported by van Leeuwen and coworkers for an allylic species observed when styrene was used as the olefin.[12c]

The complex corresponding to these signals was identified as the methyl 2-benzylacetate species **2j** described in Figure 14. The multiplicity of the ^{13}C signal at δ = 173 ppm is proposed to be a doublet of doublet with a similar coupling constant $J_{P,C}$ = 12 Hz.

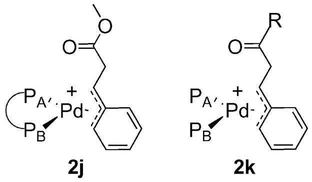


Figure 14. Pd(benzyl) species **2j** and **2k** detected by NMR spectroscopy.

The formation of this species can be explained by insertion of styrene into a Pd–COOMe bond, implying that a mechanism based on the Pd–COOMe species was active under these conditions. At 323 K, in contrast with the results obtained in the absence of CO, the signal corresponding to **2c** is observed to rapidly disappear. When the sample was left at this temperature for several hours no new ^{31}P signals were detected. After 24 h at this temperature the sample was cooled to room temp. and the signals for **2h**, **2i**, and **2e** were readily detected. When the reaction is performed in the presence of ^{13}CO a singlet signal at δ = 202.2 ppm is detected and readily assigned to CO/styrene co-oligomers. After a few hours at 323 K the carbonyl signal corresponding to the linear and branched esters at δ = 175.25 and δ = 176.9 (ratio b/l = 0.25) ppm are observed. After 12 h at this temperature a new carbonyl signal is detected at δ = 213.1 ppm (t, J_{PC} = 9 Hz) indicating that this signal arises from a new Pd species containing two phosphorus centers. The J_{PC} value is similar to that observed for the species **2j**, suggesting a long-range coupling to the phosphorus atom. The π-benzyl-ketone complex **2k** (Figure 14), which can be formed by the insertion of styrene into a Pd–acyl bond, matches the NMR signals observed.[24] After 24 h new carbonyl signals at δ = 212.05 (s), 210.4 (s), and 200.5 (s) ppm corresponding to CO/styrene co-oligomers are detected.[25] The detection of co-oligomers indicates that methanolysis and a chain-transfer reaction are competing under these conditions.

Reaction of Complex 2b in CD_3OD in the Presence of Styrene and Carbon Monoxide (15 atm)

A 10-mm HP-NMR sapphire tube was charged with a solution of complex **2b** in CD_3OD, and 50 equiv. of styrene was added. The NMR tube was pressurized with 15 atm of a mixture of ^{12}CO and ^{13}CO. After a few minutes at room temperature the signals corresponding to **2c** and the carbonylpalladium(0) **2g** were detected as the major products. Small signals corresponding to the benzylpalladium complexes **2h** and **2i** and two new mutually coupled doublet signals are also detected at δ = 28.1 and 25.6 ($^2J_{PP}$ = 42 Hz) ppm. In the corresponding $^{13}C\{^1H\}$ NMR spectrum only the signal corresponding to free CO is detected at this stage. When the temperature is increased to 323 K the ^{31}P signals corresponding to **2c**, the benzylpalladium complexes **2h** and **2i**, the palladium dimer **2e**, the carbonylpalladium(0) **2g**, and phosphane oxide are observed. At this temperature the signal for **2c** is found to decrease in intensity whereas the signals corresponding to the dimer **2e** and benzyl species **2h** and **2i** are observed to rapidly increase in intensity. The detection of these complexes indicates that these species are stable under methoxycarbonylation conditions. In the carbonyl region of the $^{13}C\{^1H\}$ NMR spectrum, signals corresponding to the linear and branched esters, free CO, and oligomers at δ = 202 and 210 ppm are readily detected. No new signals were detected under these conditions.

Deuterium Labeling Experiments in the Methoxycarbonylation of Styrene Using [PdCl$_2$(1)$_2$] (1a)/pTsOH and [Pd(OH$_2$)(OTs)(R,R)-bdpp][OTs] (2b) as Catalyst Precursors

In order to gain information on the mechanism involved in these reaction systems a set of catalytic experiments was completed using [D$_4$]MeOH and a GC-MS analysis of the ester products and unconverted styrene.

When the phosphetane containing complex **1a** was used as a catalyst precursor 10% conversion was achieved with total regioselectivity to the branched ester. A GC-MS analysis of the unconverted styrene revealed that no incorporation of deuterium had occurred during the catalytic reaction. This indicated that the insertion of styrene is not reversible under these conditions. When GC-MS analysis of the branched ester is performed the molecular peak is *m*/*z* = 168, which is consistent with the incorporation of four deuterium atoms into this product, corresponding to one molecule of [D$_4$]MeOH. No further incorporation of deuterium was observed, which is in agreement with the previous observations showing that no deuterium is incorporated into the styrene. These results are in agreement with those reported by Heil and coworkers using the complex [PdCl$_2$(PPh$_3$)$_2$] as the catalyst precursor.[26] Interestingly, the same authors reported that in the presence of SnCl$_2$ in the catalytic reaction, deuterium incorporation was observed in both the substrate and the reaction products, indicating a different behavior during the styrene insertion/β-elimination step of the reaction.[26,27]

When the diphosphane complex **2b** was used as the catalyst precursor 50% conversion was achieved with the formation of 85% of the linear ester and 10% of the branched product. A GC-MS analysis of the unconverted styrene revealed that incorporation of up to three deuterium atoms had occurred and that only a small proportion of the styrene in solution did not contain deuterium (Table 2).

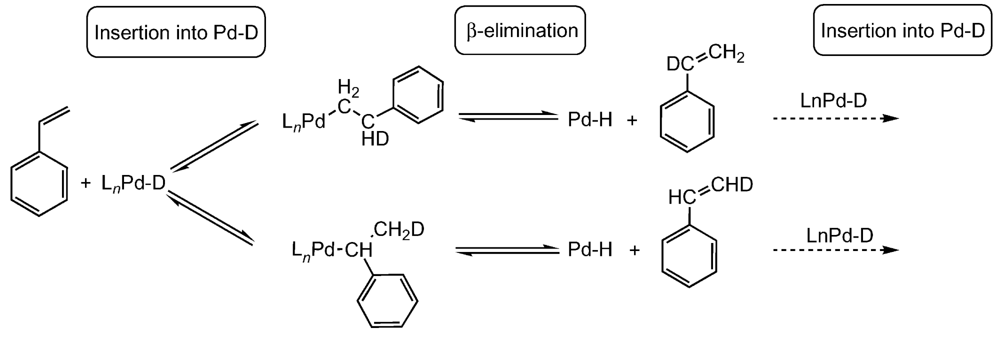
Table 2. Isotopomers of the products and substrate after catalytic methoxycarbonylation with [D$_4$]MeOH.

Precursor	Styrene	Linear ester	Branched ester
1a	M	–	M + 4
2b	M	M + 4	M + 4
	M + 1	M + 5	M + 5
	M + 2	M + 6	M + 6
	M + 3		

The main isotopomer contained one and two deuterium atoms while a small percentage was found to have incorporated three deuterium atoms. These results support the assumption that the Pd–hydride route is operative under these conditions and indicate that the insertion of styrene into the Pd–H bond of the catalyst is reversible. This result is in accordance with those reported by Consiglio et al., which concluded that a Pd–H mechanism was operative in this reaction, based on deuterium labeling experiments using a Pd/DIOP system.[28]

An analysis of the different fragments detected by MS showed that no deuterium had been incorporated in the phenyl moiety of the styrene molecule and thus indicated that the deuterium incorporation had taken place at the vinylic moiety of the molecule. The incorporation of up to three deuterium atoms can thus be explained by styrene insertion into the Pd–D bond of the catalyst followed by β-elimination, yielding a Pd–H species and a molecule of styrene containing one deuterium atom (Scheme 5). If this process is repeated the incorporation of new deuterium atoms can occur.

A GC-MS analysis of the esters formed under these conditions revealed that the product contains between four and six deuterium atoms with the major products including four



Scheme 5. Proposed mechanism for deuterium incorporation into the substrate during the Pd-catalyzed methoxycarbonylation of styrene.

deuterium atoms and corresponding to the incorporation of one molecule of $[D_4]MeOH$. Very similar distributions of isotopomers were observed for both esters. The formation of these isotopomers can be explained by the addition of one molecule of $[D_4]MeOH$ to the substrate that already contains between nought and two deuterium atoms. Analysis of the fragments suggests that incorporation of one deuterium atom into the phenyl ring of both ester products had occurred. The mechanism required to perform such an incorporation must involve the breakage of an sp^2 C–H bond of the phenyl group followed by H/D exchange.

These deuterium labeling experiments indicated that insertion of styrene into the Pd–H bond of the catalysts is reversible or irreversible, depending on whether the reaction is catalyzed by the monodentate or bidentate system **1a** or **2b**, respectively.

Conclusions

Systems bearing monodentate ligand **1** and diphosphane **2** were studied under methoxycarbonylation conditions. In the presence of *p*TsOH complex **1a** was shown to yield the dimeric complex **1b**, which was characterized by multinuclear NMR spectroscopy and X-ray crystallography. The isolated complex **1b** was tested as a precursor in the methoxycarbonylation of styrene and showed poor activity and enantioselectivity, and could not account for the catalytic results obtained when **1a** was used as the precursor. Evidences for the protonation of ligand **1** under catalytic conditions were obtained. When the reaction was studied with complex **2b** as the precursor evidences for both hydride and methoxycarbonylation mechanisms were obtained for the methoxycarbonylation of styrene under these conditions. The detection of CO/styrene co-oligomers also indicated that methanolysis and chain transfer reactions were in competition. Two isomeric forms of [Pd(π-methylbenzyl)(*R*,*R*-bdpp)], **2h** and **2i**, were characterized by multinuclear NMR spectroscopy and DFT calculations were used to discriminate between the 16 possible geometries for these species. The results obtained by DFT calculations showed that the more stable isomers contain the ligand bdpp in a "*chair*" conformation and have very similar energies. The detection of these species under high CO pressure indicates that isomerisation towards the branched-alkyl intermediates is a high energy process. This is in agreement with the poor regioselectivity to the branched ester achieved with this system under catalytic conditions. The hydrido- and carbonyl-bridged complex **2e** was also detected under catalytic conditions and this species was shown to be stable in the presence of styrene. This complex was previously reported as being a resting state during the reaction. Deuterium labeling experiments using $[D_4]MeOH$ and GC-MS analysis of the unconverted substrate and products showed that under methoxycarbonylation conditions no deuterium incorporation into the substrate occurs when the catalyst precursor **1a** is used, but that incorporation of up to three deuterium atoms occurs when the reaction is performed with **2b** as the precursor. These results indicate that the styrene insertion step into the Pd–H bond of the catalyst is irreversible when the phosphetane-containing system is used whereas this step is reversible when the diphosphane precursor is used. Such a result is of great importance for the understanding of the regioselectivity of the reaction.

Experimental Section

General: All palladium complexes were synthesized using standard Schlenk techniques under a nitrogen atmosphere. Diethyl ether, toluene, and THF were distilled from sodium/benzophenone and dichloromethane was distilled from P_2O_5. All solvents were deoxygenated before use. The phosphetane **1**[29a] and the palladium complexes $[PdCl_2(NCPh)_2]$,[29b] [PdCl2(COD)],[29c] *trans*-$[PdCl_2(\mathbf{1})_2]$ (**1a**),[5b] [PdCl$_2$(*R*,*R*-BDPP)] (**2a**),[29d] and [Pd(H$_2$O)(OTs)(*R*,*R*-BDPP)][OTs] (**2b**)[29d] were prepared according to literature methods. All other reagents were used as received from commercial suppliers. Deuterated solvents used for routine NMR spectroscopic measurements were dried with molecular sieves. ^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR spectra were recorded with a Varian Mercury 400 spectrometer (400.14, 100.63, and 161.98 MHz, respectively). Chemical shifts were referenced to either TMS as an internal standard (^1H and $^{13}C\{^1H\}$ NMR spectra) or 85% H_3PO_4 as an external standard ($^{31}P\{^1H\}$ NMR spectra). High-pressure NMR experiments (HP-NMR) were carried out in a 10-mm (diameter) sapphire tube with a titanium cap and the spectra were recorded using a Varian 300 MHz spectrometer.

HP-NMR Measurements: In a typical experiment, an NMR tube was charged under N_2 with a solution of the palladium precursor (0.04 mmol), *p*TsOH (when needed, 0.4 mmol), and styrene (0.8 mmol) in a mixture of deuterated solvents $CD_3OD/[D_8]THF$ (2 mL). The tube was then pressurized with CO to the desired pressure.

Deuterium Labeling Experiments with [D$_4$]MeOH: These catalytic experiments were carried out in a Berghof autoclave, and the reaction mixtures were magnetically stirred and electrically heated. A solution of the palladium precursor, acid (when required), and styrene in a THF/$[D_4]MeOH$ mixture (1:1, 5 mL) were introduced into the evacuated autoclave. Carbon monoxide was introduced and the system was then heated. Stirring was initiated once thermal equilibrium had been reached. Once the reaction was complete the autoclave was cooled to room temperature and depressurized. The product was filtered in a short column of celite and the solvent was removed under vacuum. The reaction conditions using complex **1a** as the precursor were: [Pd] = 0.015 mmol, Pd/styrene = 1:200, Pd/*p*TsOH = 1:10, time = 24 h, THF/CD_3OD = 1:1 (5 mL), 60 °C, P_{CO} = 35 atm. The reaction conditions using complex **2a** as the precursor were: [Pd] = 0.015 mmol, Pd/styrene = 1:100, time = 6 h, THF/CD_3OD, 1:1 (5 mL), T = 90 °C, 30 atm.

Synthesis of [PdCl(μ-Cl)(1)]$_2$ (1b): A solution of $[PdCl_2(COD)]$ (35.8 mg, 0.12 mmol) in dichloromethane (5 mL) was added to a solution of **1a** (89.5 mg, 0.12 mmol) in dichloromethane (5 mL). The reaction was left to stir at room temperature overnight. The solution was concentrated under vacuum and ethyl ether (3 mL) was added to precipitate the complex. The orange solid was recrystallized from hexane to obtain complex **1b** as red crystals. Yield 65 mg (58%). ^1H NMR (CD_2Cl_2, 400.13 MHz): δ = 0.82 (d, $^3J_{HH}$ = 7 Hz, CH_3), 0.97 (d, $^3J_{HH}$ = 7 Hz, CH_3), 1.01 (s, CH_3), 1.02 (d, $^3J_{HH}$ = 7 Hz, CH_3), 1.11 (m, CH_2), 1.26 (d, $^2J_{HH}$ = 18 Hz, CH), 1.51 (d, $^2J_{HH}$ = 21 Hz, CH), 1.56 (s, CH_3), 1.65 (m, CH_2), 1.71

(s, CH_3), 1.90 (m, CH_2), 2.64 (m, CH) ppm. ^{13}C NMR (CD_2Cl_2, 100.63 MHz): δ = 17.8 (s, CH_3), 20.1 (s, CH_3), 22.6 (s, CH_3), 23.8 (s, CH_3), 25.0 (s, CH_3), 25.2 (CH_2), 25.9 (d, J_{PC} = 16 Hz, CH_3), 28.3 (s, CH_3), 31.6 (s, CH), 34.0 (d, J_{PC} = 13 Hz, CH_2), 34.5 (s, CH_2), 36.4 (d, J_{PC} = 11 Hz, CH), 36.7 (s, 1 C), 42.3 (s, CH), 45.7 (broad, CH) ppm. ^{31}P NMR (CD_2Cl_2, 161.98 MHz): δ = 94.5 (s) ppm.

X-ray Data Collection and Structure Determination of $[PdCl_2(1)]_2$ (1b): Data collection for crystal structure analysis was carried out at 293(2) K with an Enraf Nonius CAD4 single crystal diffractometer (Mo-K_α radiation, λ = 0.71073 Å). Cell refinement, indexing, and scaling of all the data set were performed using the programs Denzo and Scalepack.[30] The structure was solved by direct methods and subsequent Fourier analyses[31] and refined by the full-matrix least-squares method based on F^2 with all observed reflections.[31] A difference Fourier map revealed a molecule of CH_2Cl_2 with chlorines disordered over two positions (occupancies 0.55/0.45, hydrogen atoms not assigned) in the asymmetric unit. All the calculations were performed using the WinGX System, version 1.70.01.[32]

Crystal Data: $C_{35}H_{66}Cl_6P_2Pd_2$, M_r = 974.32 g mol^{-1}, monoclinic, space group $P2_1$, a = 11.279(3) Å, b = 14.873(3) Å, c = 14.891(3) Å, β = 109.58(3)°, V = 2353.5(9) Å^3, Z = 2, D_c = 1.375 g cm^{-3}, μ(Mo-K_α) = 1.194 mm^{-1}, F(000) = 1000, θ range = 2.00–28.70°. Final R_1 = 0.0450, wR_2 = 0.1140, S = 0.910 for 439 parameters and 29446 reflections, 11528 unique [R(int) = 0.0330], of which 8091 with $I > 2\sigma(I)$, max positive and negative peaks in ΔF map 0.720, –0.442 e Å^{-3}. Flack parameter = –0.01(3).

Computational Details: Structure optimizations were carried out using the Amsterdam Density Functional (ADF2006.01) program developed by Baerends et al.[33] The numerical integration scheme used was developed by te Velde et al.[34] The geometry optimization procedure was based on the method reported by Versluis and Ziegler.[35] The functional applied was BP86, in which the local exchange-correlation potential was combined with the nonlocal Becke's exchange correction[36] and Perdew's correlation correction.[37] Relativistic effects were included through the zero-order regular approximation (ZORA) formalism.[38] For all atoms a Slater-type orbital (STO) basis set of triple-ζ quality with a polarization function was used. A value of 4.5 for the numerical integration parameter was employed.

Supporting Information (see also the footnote on the first page of this article): Coordinates of the optimized geometries and the corresponding energies for species **I**–**XVI** and the GC-MS spectra of the products corresponding to the deuterium labeling experiments.

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[1] *Ullmann's Encyclopedia of Industrial Chemistry* (Ed.: W. Gerhartz), vol. 3, VCH, Weinheim, **1985**, p. 41.

[2] H. Ooka, T. Inoue, S. Itsumo, M. Tanaka, *Chem. Commun.* **2005**, 1173.

[3] E. Guiu, M. Caporali, B. Muñoz, C. Müller, M. Lutz, A. L. Spek, C. Claver, P. W. N. M. van Leeuwen, *Organometallics* **2006**, *25*, 3102.

[4] F. Lagasse, H. Kagan, *Chem. Pharm. Bull.* **2000**, *48*, 315.

[5] a) G. Consiglio, S. C. A. Nefkens, C. Pisano, F. Wenzinger, *Helv. Chim. Acta* **1991**, *74*, 323; b) B. K. Muñoz, C. Godard, A. Marinetti, A. Ruiz, J. Benet-Buchholz, C. Claver, *Dalton Trans.* **2007**, 5524.

[6] I. del Río, C. Claver, P. W. N. M. van Leeuwen, *Eur. J. Inorg. Chem.* **2001**, 2719 and references cited therein.

[7] P. W. N. M. van Leeuwen, M. A. Zuideveld, B. H. G. Swennenhuis, Z. Freixa, P. C. J. Kamer, K. Goubitz, J. Fraanje, M. Lutz, A. L. Spek, *J. Am. Chem. Soc.* **2003**, *125*, 5523.

[8] I. del Río, N. Ruiz, C. Claver, *Inorg. Chem. Commun.* **2000**, *3*, 166.

[9] a) T. Fuchikami, K. Ohishi, I. Ojima, *J. Org. Chem.* **1983**, *48*, 3803; b) G. Cavinato, L. Toniolo, *J. Organomet. Chem.* **1990**, *398*, 187; c) D. Milstein, *Acc. Chem. Res.* **1988**, *21*, 428; d) M. Kanawa, S. Nakamura, E. Watanabe, H. Urata, *J. Organomet. Chem.* **1997**, *542*, 185.

[10] a) E. Zuidema, C. Bo, P. W. N. M. Van Leeuwen, *J. Am. Chem. Soc.* **2007**, *129*, 3989; b) S. M. A. Donald, S. A. Macgregor, V. D. Settels, J. Cole-Hamilton, G. R. Eastham, *Chem. Commun.* **2007**, *6*, 562.

[11] S. Otsuka, A. Nakamura, T. Yoshida, M. Naruto, K. Ataka, *J. Am. Chem. Soc.* **1973**, *95*, 3180.

[12] a) B. E. Ali, H. Alper, *J. Mol. Catal.* **1993**, *80*, 377; b) C. Pisano, A. Mezzetti, G. Consiglio, *Organometallics* **1992**, *11*, 20; c) G. P. C. M. Dekker, C. J. Elsevier, K. Vrieze, P. W. N. M. van Leeuwen, C. F. Roobeek, *J. Organomet. Chem.* **1992**, *430*, 357.

[13] a) C. Godard, A. Ruiz, C. Claver, *Helv. Chim. Acta* **2006**, *89*, 1610; b) B. K. Muñoz, PhD Thesis, **2007**, Universitat Rovira i Virgili, Tarragona, Spain.

[14] C. Sui-Seng, F. Bélanger-Gariépy, D. Zargarian, *Acta Crystallogr., Sect. E* **2003**, *59*, 618.

[15] . A. J. Rucklidge, G. E. Morris, A. M. Z. Slawin, D. J. Cole-Hamilton, *Helv. Chim. Acta* **2006**, *89*, 1783.

[16] P. Leoni, M. Sommovigo, M. Pasquali, S. Midollini, D. Braga, P. Sabatino, *Organometallics* **1991**, *10*, 1038.

[17] a) W. McFarlane, R. F. M. White, *J. Chem. Soc. C* **1969**, 744; b) G. Olah, W. McFarlane, *J. Org. Chem.* **1969**, *34*, 1832.

[18] a) M. Portnoy, D. Milstein, *Organometallics* **1994**, *13*, 600; b) M. Portnoy, F. Frolow, D. Milstein, *Organometallics* **1991**, *10*, 3960.

[19] I. Tóth, C. J. Elsevier, *Organometallics* **1994**, *13*, 2118.

[20] I. Toth, C. J. Elsevier, *J. Chem. Soc., Chem. Commun.* **1993**, 529.

[21] a) P. J. Pérez, J. C. Calabrese, E. Bunel, *Organometallics* **2001**, *20*, 337b) R. Trebbe, R. Goddard, A. Rufinska, K. Seevogel, K. Porschke, *Organometallics* **1999**, *18*, 2466.

[22] F. C. Rix, M. Brookhart, P. S. White, *J. Am. Chem. Soc.* **1996**, *118*, 2436.

[23] G. Gatti, J. A. López, C. Mealli, A. Musco, *J. Organomet. Chem.* **1994**, *483*, 77.

[24] E. Drent, P. H. M. Budzelaar, *Chem. Rev.* **1996**, *96*, 663.

[25] M. Brookhart, F. C. Rix, J. M. De Simone, J. C. Barborak, *J. Am. Chem. Soc.* **1992**, *114*, 5894.

[26] C. Benedek, S. Tőrös, B. Heil, *J. Organomet. Chem.* **1999**, *586*, 85.

[27] C. Benedek, G. Szalontai, A. Gömöry, S. Tőrös, B. Heil, *J. Organomet. Chem.* **1999**, *579*, 147.

[28] G. Consiglio, S. C. A. Nefkens, C. Pisano, *Inorg. Chim. Acta* **1994**, *220*, 273.

[29] a) A. Marinetti, L. Ricard, *Tetrahedron* **1993**, *49*, 10291; b) J. R. Doyle, P. E. Slade, H. B. Jonassen, *Inorg. Synth.* **1960**, *6*, 216; c) D. Drew, J. R. Doyle, *Inorg. Synth.* **1972**, *13*, 52; d) C. Bianchini, A. Meli, G. Müller, W. Oberhauser, E. Passaglia, *Organometallics* **2002**, *21*, 4965.

[30] Z. Otwinowski, W. Minor, *Processing of X-ray Diffraction Data Collected in Oscillation Mode, Methods in Enzymology*, vol. 276: *Macromolecular Crystallography*, part A, 307–326 (Eds.:

C. W. Carter Jr., R. M. Sweet), Academic Press, New York, **1997**.

[31] G. M. Sheldrick, *SHELX97 Programs for Crystal Structure Analysis (Release 97–2)*, University of Göttingen, Germany, **1998**.

[32] L. J. Farrugia, *J. Appl. Crystallogr.* **1999**, *32*, 837.

[33] a) E. J. Baerends, D. E. Ellis, P. Ros, *Chem. Phys.* **1973**, *2*, 41; b) E. J. Baerends, P. Ros, *Chem. Phys.* **1973**, *2*, 52; c) E. J. Baerends et al. ADF2004.01; SCM, *Theoretical Chemistry*, Vrije Universiteit, Amsterdam, The Netherlands, http://www.scm.com: **2004**; d) C. F. Guerra, J. G. Snijders, G. te Velde, E. J. Baerends, *Theor. Chem. Acc.* **1998**, *99*, 391.

[34] a) P. M. Boerrigter, G. te Velde, E. J. Baerends, *Int. J. Quantum Chem.* **1988**, *33*, 87; b) G. te Velde, E. J. Baerends, *J. Comput. Chem.* **1992**, *99*, 84.

[35] L. Versluis, T. Ziegler, *J. Chem. Phys.* **1988**, *88*, 322.

[36] A. D. Becke, *Phys. Rev. A* **1988**, *38*, 3098.

[37] a) J. P. Perdew, *Phys. Rev. B* **1986**, *34*, 7406; b) J. P. Perdew, *Phys. Rev. B* **1986**, *33*, 8822.

[38] a) E. van Lenthe, E. J. Baerends, J. G. Snijders, *J. Chem. Phys.* **1993**, *99*, 4597; b) E. van Lenthe, E. J. Baerends, J. G. Snijders, *J. Chem. Phys.* **1994**, *101*, 9783; c) E. van Lenthe, A. Ehlers, E. J. Baerends, *J. Chem. Phys.* **1999**, *110*, 8943.

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