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Immobilized Sonogashira catalyst systems: new insights by multinuclear HRMAS NMR studies†

Tobias Posset,[a] Johannes Guenther,[b] Jacqueline Pope,[b] Thomas Oeser[a] and Janet Blümel*[b]

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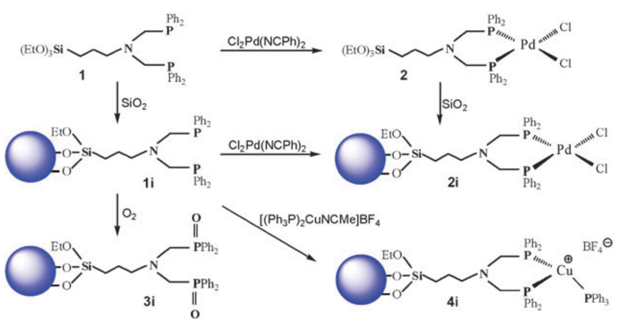
A new chelate phosphine linker and its Pd and Cu complexes have been synthesized and immobilized. The solvent impact on these immobilized species, their mobility, and coordination preferences have been studied *in situ* by HRMAS (High-Resolution Magic Angle Spinning) NMR. The catalyst recycling characteristics match the HRMAS results.

Metal catalyzed carbon–carbon bond forming reactions have dominated homogeneous catalysis over the last decade.[1] One of the most widely used catalytic reactions is the Sonogashira coupling of aryl halides with acetylenes, which is catalyzed by a Pd(0)/Cu(I) system.[2] However, detailed mechanistic studies remain scarce.[2] In homogeneous solution, mechanistic studies are complicated by the presence of many different species,[2] and it is often unclear whether palladium catalyzed reactions are achieved by tethered molecular entities, or metallic Cu[3] or Pd[4,5a,b] nanoparticles, or molecular Pd species in solution[5c] that form during the reaction. Catalyst immobilization helps to disentangle the different components and effects.[6] Furthermore, tethering the catalyst system to a solid support such as silica offers the advantage that, under the right conditions, the catalysts can easily be removed from the reaction mixture and recycled many times.[7] In this contribution, we will demonstrate that the line-narrowing HRMAS technique,[6–9] can provide valuable insights into structures of surface-bound linkers and catalysts and especially processes taking place at the liquid/solid interface.

The chelate ligand **1** (Scheme 1) has been synthesized in high yields by reacting $(EtO)_3Si(CH_2)_3NH_2$ with paraformaldehyde and $HPPh_2$.[10] This synthesis is very versatile and applicable to aryl amines and other phosphines HPR_2 (R = alkyl, aryl). Ligand **1** readily coordinates to a Pd center to form **2** (Scheme 1).[11] A single crystal X-ray structure[12] (Fig. 1) shows that **2** is nearly square planar at the metal center, the interplanar angle between the two selected planes Cl1/Cl2/Pd1 and P1/P2/Pd1 amounts to only 7.74(4)°. A strong pyramidalization at the nitrogen atom is indicated by a deviation of N1 by 0.469(3) Å out of the plane from its neighbouring carbon atoms.

The more rigid nature of the metal complex might be responsible for the virtual couplings[7a,9b] in ^{13}C NMR detectable for **2**,[11] but not for **1**.[10] Linker **1** and Pd complex **2** can be immobilized cleanly on silica[13] according to the standard procedure[7,9] to give **1i** and **2i** (Scheme 1). The dry material **1i** is oxidized to **3i** only slowly after days of exposure to air. **2i** can also be generated from **1i** by treating it with $Cl_2Pd(NCPh)_2$. The ^{31}P HRMAS spectra of **2i** in different solvents show one signal at 7.4 ppm, with the typical dependence of the linewidth on the polarity and viscosity of the solvent.[6,14]

The Cu component of the Sonogashira catalyst, **4i**, can be generated on silica by treating **1i** with $[(Ph_3P)_2CuNCMe]BF_4$ (Scheme 1). The PPh_3 and PPh_2 ^{31}P HRMAS signals of **4i** are found at 5.7 and −17.8 ppm, with the expected intensity ratio of 1 : 2. In contrast to the immobilized Pd component **2i**, for **4i** the ^{31}P HRMAS spectra in different solvents (Fig. 2) reveal



Scheme 1 Synthesis of Pd complex **2** and **1i–4i**.

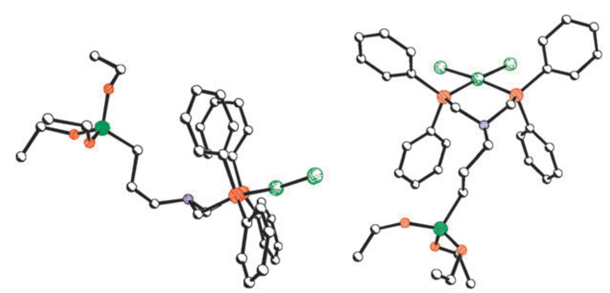


Fig. 1 Single crystal X-ray structure of Pd complex **2**.[12] Two different views (DCM inclusion and H atoms omitted for clarity).

[a] Institute of Organic Chemistry, University of Heidelberg, Im Neuenheimer Feld 270, 69120 Heidelberg, Germany
[b] Department of Chemistry, Texas A&M University, P.O. Box 30012, College Station, TX 77842-3012, USA. E-mail: bluemel@tamu.edu; Fax: +1 (979)845-5629; Tel: +1 (979)845-7749

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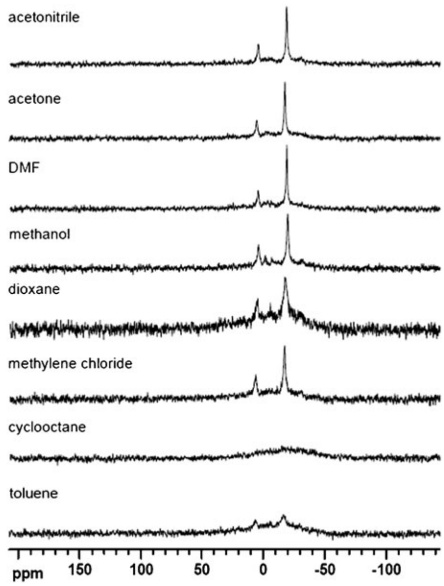
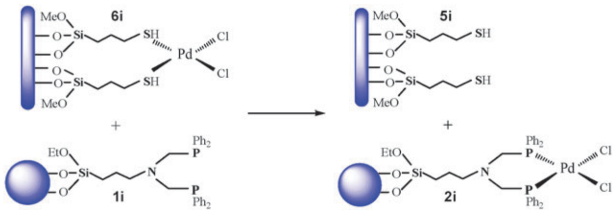


Fig. 2 ^{31}P HRMAS NMR spectra of **4i** in the indicated solvents.

that some polar solvents, such as dioxane, are able to replace the PPh_3 ligand at the Cu center, and the signal of uncoordinated PPh_3 can be seen in the corresponding spectra at about −6 ppm. This result reflects the tendency of Cu phosphine complexes to exchange ligands rapidly in solution.[15] However, this important involvement of the solvents has not been considered in detail previously with respect to possible leaching of the catalyst component from the support, or when contemplating the different activities of the catalyst in various solvents (see below). Therefore, in addition to classical CP/MAS,[16,17] HRMAS measurements are an indispensable tool for probing the interactions of catalyst precursors with the corresponding solvents prior to catalysis.

Fortunately, in spite of the potential exchange of the PPh_3 ligand by a solvent molecule, the Cu component of the Sonogashira catalyst system does not show substantial leaching tendencies when immobilized by a phosphine chelate linker.[6] However, the Pd component is known to leach substantially.[5,6] Therefore, in order to check the coordinating strength of ligand **1i** for the Pd complex, we sought to compare it with a thiol linker that is recognized as a strong transition metal scavenger.[5a] The modified silica **5i** (Scheme 2) has been obtained using $(MeO)_3Si(CH_2)_3SH$ (**5**) under the standard immobilization conditions.[7,9] Reaction of **5i** with $Cl_2Pd(NCPh)_2$ leads to **6i** (Scheme 2, structure according to ref. 5*a*). **5i** and **6i** are missing the ^{31}P probe for checking the completion of the coordination, but ^{13}C HRMAS[9d] can successfully be applied instead (Fig. 3).

Analytically most indicative are the SCH_2 carbon signals, which prove that all thiol linkers are bound to the metal center. On coordinating the thiol to Pd, the S*C*H_2 carbon resonance shifts from about 29 to 25 ppm (Fig. 3), and the line becomes broader due to the restricted mobility enforced by the chelate formation. This also accounts for the broadening of the other CH_2 resonances on going from **5i** to **6i**. Due to the high spectral resolution, two sorts of OMe groups can be distinguished, the surface-bound (OMe′) and residual methoxy groups (OMe) at the silane.[17]



Scheme 2 The migration of the $PdCl_2$ fragment from **6i** to **1i**.

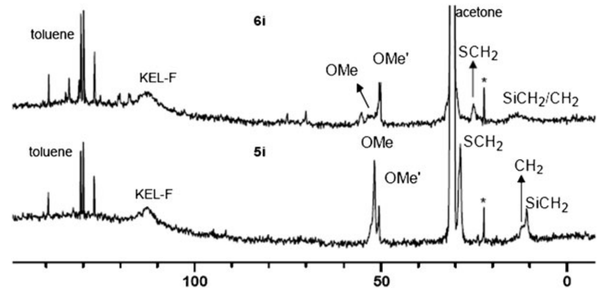


Fig. 3 ^{13}C HRMAS spectra (high power decoupling, 2 s pulse delay, acetone-d_6) of **5i** (bottom) and **6i** (top). * Denotes the CH_3 signal of residual toluene.

Mixing batches of **5i** and **2i** and stirring them in acetone overnight resulted in the top ^{31}P spectrum in Fig. 4. In contrast to our expectation, no traces of the uncoordinated phosphine **1i** with its ^{31}P signal at about −30 ppm could be detected. However, when mixing batches of **1i** and **6i** the formation of **2i** (Fig. 4, bottom trace) besides **1i** starts immediately. Following the process *in situ* by ^{31}P HRMAS spectroscopy, accumulating the FIDs over 3 h intervals (Fig. 4, middle section), reveals its timeline. Within 18 h practically all $PdCl_2$ fragments have migrated from the thiol to the chelate phosphine linkers. The process is continuous, as the signal of **1i** decreases, the signal of **2i** increases correspondingly. Therefore, we conclude that the chelate phosphine **1i** coordinates the Pd fragment even better than the thiol linkers.

The recycling results of the Sonogashira catalyst system with the immobilized Pd component **2i** and CuI added for each run[18] corroborate the HRMAS findings regarding the solvent influence and the coordination strength of the linkers. The thiol-bound catalyst **6i**, in combination with CuI, is the least active in dioxane and piperidine as solvents and produces only about 5% tolane in the first and 2% in the fourth run. The impact of the solvent on the catalyst activity of **2i** is shown in Fig. 5.[18] Dioxane propagates the most extensive leaching, which was determined to be quantitative by AAS measurements of the combined supernatants of the three runs. Offering additionally uncoordinated **1i** as the Pd scavenger on the surface leads to a catalyst that can be recycled four times until most of the activity is lost. Since the formation of Pd nanoparticles could be excluded by TEM measurements, Pd is leaching from the surface, as the HRMAS spectra suggest, and acting as a molecular species in solution, in accord with results on other Pd catalysts.[5b]

This contribution demonstrates that HRMAS NMR of immobilized catalysts in different solvents can give valuable insights into the nature and timescale of processes at the solid–liquid interface.

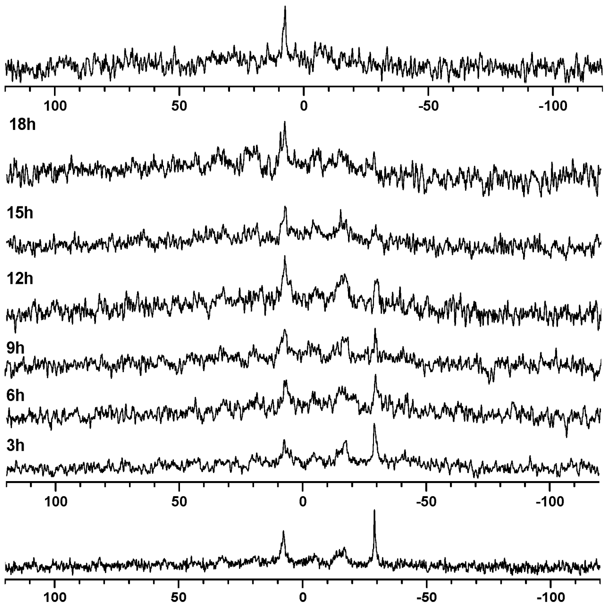


Fig. 4 ^{31}P HRMAS spectra. Top: batches of **2i** and **5i** after being stirred together in acetone overnight. Bottom: batches of **6i** and **1i**, stirred for several minutes. Middle section: spectra recorded at the given time intervals after mixing batches of **1i** and **6i** in acetone.

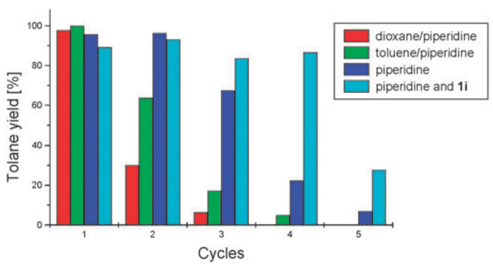


Fig. 5 Recycling characteristics of **2i** in the indicated solvents. CuI and the substrates PhI and PhCCH are added for each cycle.[18]

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10 Synthesis of the chelate phosphine ligand **1**: $(EtO)_3Si(CH_2)_3NH_2$ (0.58 g, 2.63 mmol) is dissolved in 20 ml of toluene and $(CH_2O)_x$ (0.19 g, 5.26 mmol) and Ph_2PH (0.98 g, 5.26 mmol) are added. The suspension turns into a clear solution within 2 h after heating to 60 °C, and is stirred overnight at this temperature. The solvent is removed *in vacuo*, and 1.40 g (2.27 mmol, yield 85%) of **1** results as a clear, viscous liquid. $\delta(^1H)$ (500.1 MHz, C_6D_6) 7.53–7.04 (m, H_{aryl}), 3.76 (q, $^3J_{HH}$ 7.0 Hz, OCH_2), 3.63 (d, $^3J_{PH}$ 3.4 Hz, PCH_2), 3.00 (t, $^3J_{HH}$ 7.1 Hz, CH_2CH_2N), 1.75 (quint., $^3J_{HH}$ 7.6 Hz, $CH_2CH_2CH_2$), 1.57 (t, $^3J_{HH}$ 7.0 Hz, CH_3), 0.65 (t, $^3J_{HH}$ 8.1 Hz, $SiCH_2$); $\delta(^{13}C)$ (125.8 MHz, C_6D_6) 139.14 (d, $^1J_{PC}$ 13.7 Hz, C_i), 133.54 (d, $^2J_{PC}$ 18.5 Hz, C_o), 128.63 (d, $^3J_{PC}$ 6.6 Hz, C_m), 128.55 (s, C_p), 59.64 (t, $^3J_{PC}$ 9.0 Hz, CH_2CH_2N), 59.23 (dd, $^1J_{PC}$ 9.3 Hz, $^3J_{PC}$ 5.6 Hz, CH_2P), 58.43 (s, OCH_2), 20.31 (s, $CH_2CH_2CH_2$), 18.62 (s, CH_3), 8.33 (s, $SiCH_2$); $\delta(^{31}P)$ (121.5 MHz, C_6D_6) −28.2; MS (EI, 70 eV) *m*/*z* 432.1 [M^+–PPh_2], 199.1 [PPh_2^+]; MS (HR-EI) *m*/*z* (%, calc.) 432.2098 (100.00, 432.2124) [M^+–PPh_2].
11 Synthesis of Pd complex **2**: $(C_6H_5CN)_2PdCl_2$ (0.074 g, 0.19 mmol) is dissolved in 10 ml of toluene. Ligand **1** (0.119 g, 0.19 mmol), in 5 ml of toluene, is added dropwise at ambient temperature, and the orange mixture is stirred for 2 h. Then the solution is concentrated to about 5 ml and 10 ml of pentane is added. Hereby, a yellow precipitate forms that is washed two times with 5 ml of pentane and dried *in vacuo*. Complex **2** is obtained in quantitative yield (0.148 g, 0.19 mmol). $\delta(^1H)$ (500.1 MHz, $CDCl_3$) 8.87–7.35 (m, H_{aryl}), 3.74 (q, $^3J_{HH}$ 7.0 Hz, OCH_2), 3.32 (dd, $^2J_{PH}$ 4.1 Hz, $^4J_{PH}$ 2.5 Hz, PCH_2), 2.63 (t, $^3J_{HH}$ 7.2 Hz, CH_2CH_2N), 1.46 (quint., $^3J_{HH}$ 7.0 Hz, $CH_2CH_2CH_2$), 1.15 (t, $^3J_{HH}$ 7.0 Hz, CH_3), 0.38 (t, $^3J_{HH}$ 7.9 Hz, $SiCH_2$); $\delta(^{13}C)$ (125.8 MHz, $CDCl_3$) 133.85 (virt. t, $^3J_{PC}$ 5.0 Hz, C_m), 131.43 (s, C_p), 128.92(t, $^1J_{PC}$ 57.3 Hz, $^3J_{PC}$ 7.0 Hz, C_i), 128.58 (virt. t, $^{2/4}J_{PC}$ 5.9 Hz, C_o), 65.08 (t, $^3J_{PC}$ 10.0 Hz, CH_2CH_2N), 58.45 (s, OCH_2), 56.58 (dd, $^1J_{PC}$ 46.4 Hz, $^3J_{PC}$ 1.7 Hz, PCH_2), 18.56 (s, $CH_2CH_2CH_2$), 18.29 (s, CH_3), 7.66 (s, $SiCH_2$); $\delta(^{31}P)$ (121.5 MHz) 7.59 (C_6D_6), 7.79 ($CDCl_3$); MS (FAB) *m*/*z* 795.1 [M^+], 760.1 [M^+–Cl], 723.2 [M^+–2Cl], 538.1 [M^+–2Cl–PPh_3], 305.0 [$PdPPh_2^+$]; HRMS (FAB) *m*/*z* (%, calc.) 793.1024 (18.3%, 793.1056) [M^+], 758.1420 (99.8%, 758.1367) [M^+–Cl], 723.1647 (23.5%, 723.1679) [M^+–2Cl]; UV/VIS λ (ε) 260 nm (17645), 324 nm (5235).
12 CCDC 795029. Crystal data of **2**: orthorhombic, space group $P2_12_12_1$, Z = 4, 489 parameters, T = 100(2) K, $C_{37}H_{49}Cl_6N_1O_3P_2Pd_1Si_1$ (964.90), a = 11.2996(7), b = 13.4269(8), c = 28.789(2) Å, V = 4367.9(5) Å^3, D_c = 1.467 g cm^{-3}, F_{000} = 1976, μ = 0.928 mm^{-1}, 46 007 refl. measd, 10 832 unique (R_{int} 0.034), final R_1 = 0.034, wR_2 = 0.078, absolute structure parameter (Flack value) −0.011(18). We found two molecules of dichloromethane (DCM) as crystal inclusion. Disorder effects were refined at one ethyl group (85 : 15% multiplicity) and at one DCM molecule (50 : 50% multiplicity)†.
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18 Reaction temperature 25 °C; surface coverage of **2i**: 10.6 molecules per 100 nm^2; ratio solvent:piperidine 2 : 1; **2i** : **1i** 1 : 1; ratio Pd : Cu : PhI : PhCCH 0.04 : 0.05 : 1.00 : 1.50; PhI concentration 1.6 mmol l^{-1}; maximal reaction time per cycle 6 h.