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HECK-MATSUDA REACTION UTILIZING IN-SITU GENERATED PALLADIUM ON ALUMINUM PHOSPHATE

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ABSTRACT. Pd on $AlPO_4$-catalyst was prepared by a one-pot process using $Pd(OAc)_2$ and $AlPO_4$ in methanol as solvent. The synthesized catalyst was used in the monoarylation of olefins via the Heck-Matsuda reaction. Several functionalized arylvinylphosphonates, cinnamic derivatives and benzalacetones could be obtained in good to excellent yields.

KEY WORDS: Arylvinylphosphonates, Benzalacetones, Cinnamic derivatives, Palladium on Aluminum phosphate, Kinetic studies

INTRODUCTION

Palladium colloids and nanoparticles have made important contributions as catalysts in cross-coupling reactions in recent decades [1-3]. Carrier materials for the immobilization of colloidal palladium catalysts used in cross-coupling reactions have equally received increasing attention in the literature in recent years. A cross-coupling reaction that has been increasingly investigated is the Matsuda-Heck reaction. Due to the easy accessibility of the diazonium salts required for this reaction as electrophilic compounds coupled with their reactivity, the mild reaction conditions employed and the excellent chemoselectivity towards a large number of functional groups, this reaction type has rendered this reaction of interest to industry and academia [4-13, 21].

High efficiency and good results have been achieved from the use of synthesized palladium/carbon catalysts [11, 14-16]. More recently however and based on the work of Felpin *et al.* [17, 20], we have developed efficient catalysts using Al_2O_3 as support. Recently, we have developed very efficient homemade catalysts using Al_2O_3 as support material based on the work of Felpin *et al.* [17, 20]. Using low concentrations of these catalysts and mild reaction conditions, we were able for the first time to achieve α,β,β-triarylation of methyl acrylate, single and double arylation of dimethyl itaconate in good yields. It is known that the tetrafluoroboric acid released during the reaction can promote side reactions and decomposition reactions [14, 18, 23, 24]. For this reason, carrier materials which, in addition to their carrier function, can also act as a base are to be regarded as particularly favorable [23, 24].

Within the scope of our work we have not only used aluminium oxide, which is well established as a carrier material in catalysis but we have also underscored the importance and use of aluminium phosphate as a possible carrier material, which until now has featured as a niche material in the literature. In addition, aluminum phosphate has found widespread use in medical applications as an antacid. In a recent work we could show the successful application of this catalyst system in the double arylation of different olefins [19]. Motivated by these results, we were eager to apply this catalyst system also to the monoarylation of olefins. In the present study, the monoarylation of common olefins such as acrylates, acrylamides, butenone and vinylphosphonates are investigated in more detail. The synthesis of the acid-labile benzalacetones should be possible, given the basic nature of the aluminium phosphate support material.

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EXPERIMENTAL

General remarks

NMR spectra were recorded on Bruker AC 250 and JEOL ECX 400 spectrometer. Chemical shifts in proton and carbon NMR spectra are reported in ppm relative to the TMS peak at 0.00 ppm or relative to $CDCl_3$ peak at 77.0 ppm, coupling constants (J) in Hz. Furthermore, some NMR spectra were recorded at the company NMR Consult Berlin. The samples were measured in 5 mm tubes using the NMR spectrometer VNMRS (Varian Inc., USA) at the measuring frequencies 500 MHz (1H), 126 MHz (13C, broadband decoupled). Infrared (IR) spectra were recorded as neat samples in ATR mode using a Spectrum One (Perkin-Elmer) spectrometer. Mass spectra were recorded on Bruker micro TOF-QII and Waters-micromass Quatro micro. Yields refer to isolated material determined to be pure by NMR-spectroscopy, mass spectrometry, and thin layer chromatography (TLC), unless specified otherwise in the text. For the purification via flash chromatography (FC): Merck Silica Gel 60 (240-400 Mesh) and Merck Aluminium oxide 90 active neutral (70-230 Mesh) were used. The scanning electron microscopy (SEM) image has been obtained with a Zeiss Gemini 1550 microscope.

The catalyst was dispersed onto a carbon adhesive tape. Diazonium salts used in this study were all known and prepared as described in the literature [22]. Solvents and chemicals were purchased from VWR or Aldrich and used as received. Activated charcoal (particle size ≤ 150 μm, 90%) and aluminum phosphate were purchased from Merck.

Kinetic measurements

The progress of the reaction was monitored by measuring the gas evolution, which indicates the consumption of the diazonium salt, over time. For this purpose, the evolving gas was transferred into a measuring cylinder filled with water and the change in volume was recorded at an interval of 10 mL as a function of time. From the increase of the resulting reaction graphs the reaction rate and the Turn-over frequency (TOF) for different Heck reactions were determined. The program Origin 8.0. was used to evaluate the graphs.

General synthesis procedure A, for the preparation of functionalized benzalacetones by Pd /AlPO$_4$

$Pd(OAc)_2$ (0.1 mmol) and aluminum phosphate (5 mmol) were placed in methanol (15 mL) and stirred for 15 min at 25 °C. Buten-3-one (7.5 mmol), as well as the diazonium salt (5 mmol) were then added. After completion of the resulting gas evolution, the reaction mixture was filtered through Celite® 545 and the filter cake rewashed with ether (15 mL), and the filtrate poured onto 300 mL ice water. The aqueous phase was extracted 3 times with diethyl ether (25 mL). Then the combined organic phase was washed with water (30 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.
The following compounds were prepared analogous to the above general procedure:

*(E)-4-Methoxy-benzalacetone (**3a**).* Purification by flash chromatography (ethyl acetate-hexane 8:2 → 9:1) gave a green solid (0.72 g; 82%): IR (neat): ν = 1680, 1586, 1245, 988, 817 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 250 MHz): δ [ppm] = 2.36 (s, 3H); 3.84 (s, 3H); 6.60 (d, $^{3}J_{H\text{-}H}$= 17.5 Hz;1H); 6.91 (d, $^{3}J_{H\text{-}H}$=7.5 Hz, 2H); 7.48 (d, $^{3}J_{HH}$=17.5 Hz, 1H); 7.49 (d, $^{3}J_{HH}$=7.5 Hz, 2H); ^{13} C-NMR ($CDCl_3$, 100 MHz) δ [ppm] = 27.3, 55.3, 114.4, 124.9, 126.9, 129.9, 143.2, 161.5, 198.3; LC-MS (rel. int.): m/z = 177.2 $[M+H]^+$ (100).

*(E)-4-Methyl-benzalaceton (**3b**).* Purification by flash chromatography (ethyl acetate-hexane 8:2 → 9:1) gave a green solid (0.50 g; 63%): IR (neat): ν = 1663, 1609, 1254, 799 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 250 MHz): δ [ppm] = 2.37 (s, 6H); 6,68 (d, $^3J_{H\text{-}H}$=15.0 Hz,1H); 7.20 (d, $^3J_{HH}$ = 7.5 Hz, 2H); 7.44 (d, $^3J_{HH}$ = 7.5 Hz, 2H); 7.49 (d, $^3J_{HH}$ = 15.0 Hz,1H); ^{13} C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 21.4, 27.3, 126.1, 128.2, 129.6, 131.6, 140.9, 143.4, 198.3; LC-MS (rel. int.): m/z = 161.14 $[M+H]^+$ (100).

*(E)-4-Cyano-benzalacetone (**3c**).* Using 6 mol-% Pd. Purification by flash chromatography (ethyl acetate-hexane 8:2 → 9:1) gave a white solid (0.56 g; 65%): IR (neat): ν = 2224, 1665, 1364, 1253, 1208, 970, 957, 812 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 250 MHz): δ [ppm] = 2.42 (s, 3H); 6.80 (d, $^3J_{HH}$ = 17.5 Hz, 1H); 7.50 (d, $^3J_{HH}$ = 17.5 Hz, 1H); 7.65 (d, $^3J_{HH}$ = 10.0 Hz, 2H); 7.71 (d, $^3J_{HH}$ = 10.0 Hz, 2H); ^{13} C-NMR ($CDCl_3$, 100 MHz): δ [ppm] = 27.9, 113.4, 118.2, 128.5, 129.6, 129.7, 132.6, 138.7, 140.5, 140.6, 197.6; LC-MS (rel. int.): m/z = 172.1 $[M+H]^+$ (100).

General procedure B for the synthesis of functionalized arylvinylphosphonates with Pd /$AlPO_4$ as catalyst

$Pd(OAc)_2$ (0.075 mmol) and $AlPO_4$ (7.5 mmol) were suspended in methanol (37 mL) and stirred at 25 °C for 15 min. Diethyl vinylphosphonate (6 mmol), and the diazonium salt (7.5 mmol) were then added. The resulting reaction mixture was stirred for 12 h at 45 °C. The mixture was then concentrated under reduced pressure, and the residue taken up with ethyl acetate (59 mL), and filtered through Celite® 545. The filtrate was concentrated again and the residue purified by column chromatography on silica gel.

The following compounds were prepared according to the general procedure **B** and purified by column chromatography on silica gel:

*(E)-Diethyl-2-(aryl)vinylphosphonate (**4a**).* Chromatography eluent (ethyl acetate-hexane 8:2 → 9:1) gave a yellow oil (1.12 g; 88%). IR (neat): ν = IR: 1616, 1242, 1019, 957, 741 cm^{-1}; ^{1}H-NMR (DMSO-d6, 250 MHz): δ [ppm] = 1.26 (t,$^3J_{HH}$ = 7.5 Hz, 6H); 4.03 (pseudo-q, $^3J_{HH}$ = 7.5 Hz, 4H); 6.62 (t, $^3J_{HH}$ = 17.5 Hz, 1H); 7.34 (d, $^3J_{HH}$ = 17.5 Hz, 1H); 7.42 (m, 3H); 7.72 (m, 2H); ^{13}C-NMR (DMSO-d6, 100 MHz): δ [ppm] = 16.3 (J_{CP} = 6 Hz) , 61.3 (J_{CP} = 6 Hz), 114.9 (J_{CP} = 190 Hz), 128.0, 128.9, 130.3, 134.7 (J_{CP} = 23.2 Hz), 147.6 (J_{CP} = 6.8 Hz); ^{31}P-NMR (DMSO-d6, 100 MHz): δ [ppm] = 19.81; LC-MS (rel. int.): m/z = 241.16 $[M+H]^+$ (100).

*(E)-Diethyl-2-(4-fluoro-aryl)vinylphosphonate (**4b**).* Chromatography eluent (ethyl acetate-hexane 8:2 → 9:1) gave a yellow oil (1.38 g; quant.). IR (neat): ν = 1601, 1509, 1227, 1160, 1019, 959, 806, 571 cm^{-1}; ^{1}H-NMR (DMSO-d6, 250 MHz): δ [ppm] = 1.36 (t,$^3J_{HH}$ = 7.5Hz, 6H); 4.12 (pseudo-q, $^3J_{HH}$ = 7.5 Hz, 4H); 6.25 (t, $^3J_{HH}$ = 17.5 Hz, 1H); 7.11 (t, $^3J_{HH}$ = 7.5 Hz, 2H); 7.40 (d, $^3J_{HH}$ = 17.5 Hz, 1H); 7.55 (m, 2H);^{13}C-NMR (DMSO-d6, 100 MHz): δ [ppm]: 16.2 (J_{CP} = 6.2 Hz), 61.3 (J_{CP} = 5.3 Hz), 113.8 (J_{CP} = 192.8 Hz), 115.8 (J_{CP} = 21.8 Hz), 131.3, 131.5 (J_{CP} = 3 Hz), 146.3 (J_{CP} = 6.2 Hz), 163.15 (J_{CP} = 250 Hz); ^{31}P-NMR (DMSO-d6, 109.3 MHz): δ [ppm] = 19.69; LC-MS (rel. int.): m/z = 259.21 $[M+H]^+$ (100).

*(E)-Diethyl-2-(4-carboxymethyl-aryl)vinylphosphonate (**4c**).* Chromatography eluent (ethyl acetate-hexane 8:2 → 9:1) gave a brownish solid (1.46 g; 90%): IR (neat): ν = 1717, 1280, 1234, 1014, 961, 835, 758, 515cm^{-1}; ^{1}H-NMR (DMSO-d6, 250 MHz): δ [ppm] = 1.27 (t,$^3J_{HH}$ = 7.5Hz, 6H); 3.88 (s, 3H); 4.05 (pseudo-q, $^3J_{HH}$ = 7.5 Hz, 4H); 6.78 (t, $^3J_{HH}$ = 17.5 Hz, 1H); 7.47 (dd, $^3J_{HH}$ = 17.5 Hz, $^3J_{HP}$ = 22.5 Hz, 1H); 7.85 (d, $^3J_{HH}$ = 7.5 Hz, 2H); 7.98 (d, $^3J_{HH}$ = 7.5 Hz, 2H);^{13}C-NMR (DMSO-D6, 100 MHz): δ [ppm] = 16.2 (J_{CP} = 6 Hz), 48.0, 61.4 (J_{CP} = 6 Hz), 118.2 (J_{CP} = 189 Hz), 128.2, 129.6, 130.6, 139.1 (J_{CP} = 22.5 Hz), 146.1 (J_{CP} = 6 Hz), 165.8; ^{31}P-NMR (DMSO-D6, 109.3 MHz): δ [ppm] = 18.75; LC-MS (rel. int.): m/z = 299.24 $[M+H]^+$ (100).

(E)-Diethyl-2-(4-acetyl-aryl)vinylphosphonate ***(4d)***. Chromatography eluent (ethyl acetate-hexane 8:2 → 9:1) gave a yellow oil (1.34g; 88%). IR (neat): ν = 1682, 1243, 1018, 955, 833, 806, 588 cm^{-1}; ^{1}H-NMR (DMSO-d6, 250 MHz): δ [ppm] = 1.24 (t,$^{3}J_{HH}$ = 7.5Hz, 6H); 2.57 (s, 3H); 4.02 (pseudo-q, $^{3}J_{HH}$ = 7.5 Hz, 4H); 6.76 (t, $^{3}J_{HH}$ = 17.5 Hz, 1H); 7.42 (dd, $^{3}J_{HH}$ = 17.5 Hz, $^{3}J_{HP}$= 22.5 Hz, 1H); 7.82 (d, $^{3}J_{HH}$ = 7.5 Hz, 2H); 7.95 (d, $^{3}J_{HH}$ = 7.5 Hz, 2H); ^{13}C-NMR (DMSO-d6, 100 MHz): δ [ppm] = 16.3 (J_{CP} = 6 Hz), 26.9, 61.4 (J_{CP} = 6 Hz), 117.1 (J_{CP} = 180 Hz), 128.2, 128.7, 138.9, 139.0 (J_{CP} = 23.3 Hz), 146.2 (J_{CP} = 6 Hz), 197.5; ^{31}P-NMR (DMSO-d6, 109.3 MHz): δ [ppm] = 18.85; LC-MS (rel. int.): m/z = 283.20 [M+H]$^{+}$ (100).

General procedure C, for the monoarylation of olefins with Pd /AlPO$_4$ catalyst

0.2 mmol Pd(OAc)$_2$ (0.2 mmol), AlPO$_4$ (10 mmol) and the olefin (10 mmol) were suspended in MeOH (30 mL) at 25°C and a stirred for 30 min to reduce the palladium. After reduction, the diazonium salt (10 mmol) was added to the suspension and stirred. After completion of the reaction (gas evolution), the reaction mixture was filtered through a G3 frit containing Celite® 545 and the filtrate was poured into ice water (300 mL). Unless otherwise described, the aqueous phase was then extracted three times with dichloromethane (50 mL). The combined organic phase was washed once with ice water (50 mL), dried over magnesium sulfate, and activated charcoal was added. The desiccant and activated carbon were filtered off over a G3 frit containing Celite® 545. After removal of the excess solvent in vacuo, the residue was weighed and the isolated yield was characterized by the analytical methods.

The following compounds were prepared analogous to procedure C:

(E)-Methyl-3-(4-methoxyphenyl)acrylate ***(5a)***. The reaction time was 7.4 min. A white solid (1.35 g, 70%) was obtained. IR (ATR): v 2950, 2842, 1715, 1602, 1512, 1288, 1254, 1170, 1026, 984, 838, 823, 769 cm^{-1}; 1H NMR (500 MHz, chloroform-d): δ 7. 65 (d, $^{3}J_{HH}$ = 16.0 Hz, 1H), 7.47 (d, $^{3}J_{HH}$ = 8.5 Hz, 2H), 6.90 (d, $^{3}J_{HH}$ = 8. 5 Hz, 2H), 6.31 (d, $^{3}J_{HH}$ = 16.0 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H); 13C- NMR (126 MHz, chloroform-d): δ 167.69, 161.33, 144.46, 129.66, 127.06, 115.21, 114.27, 55.31, 51.51 ppm; LC-MS: m/z (intensity): 193 [MH]+ (20), 151 (100).

(E)-Methyl-3-(4-nitrophenyl)acrylate ***(5b)***. The product precipitated and the work-up deviated from the general working instruction. The reaction mixture was dissolved in MeOH (X ml) and activated carbon was added. The activated carbon was filtered off over a G3 frit through Celite® 545. After removal of the excess solvent in vacuo, the residue was worked up as described in the general procedure C. Yellow-brown solid (1.88 g, 91 %). IR (ATR): v 2957, 1722, 1510, 1343, 1314, 1193, 1172, 847, 706 cm-1; 1H NMR (300 MHz, chloroform-d): δ 8.25 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H), 7.70 (d, $^{3}J_{HH}$ = 16.0 Hz, 1H), 7.67 (d, $^{3}J_{HH}$ = 8. 7 Hz, 2H), 6.57 (d, $^{3}J_{HH}$ = 16.0 Hz, 1H), 3.84 (s, 3H) ppm; 13C NMR (126 MHz, chloroform-d): δ 166.44, 148.49, 141.88, 140.45, 128.51, 123.90, 122.06, 52.31 ppm; GC-MS: m/z (intensity): 207 [M] (18), 176 (100).

(E)-Methyl-3-(2-nitrophenyl)acrylate ***(5c)***. Column chromatographic purification (cyclohexane : ethyl acetate = 9:1, 8:2). Yellow solid (1.88 g, 91%). IR (ATR): v 2956, 1718, 1520, 1345, 1332, 1292, 1208, 1196, 1180, 975, 756 cm-1; 1H NMR (500 MHz, chloroform-d): δ 8. 12 (d, $^{3}J_{HH}$ = 15.8 Hz, 1H), 8.04 (d, $^{3}J_{HH}$ = 8.0 Hz, 1H), 7.68 - 7.65 (m, 1H), 7.64 (d, $^{3}J_{HH}$ = 8.0 Hz, 1H), 7.57 - 7.53 (m, 1H), 6.37 (d, $^{3}J_{HH}$ = 15.8 Hz, 1H), 3.83 (s, 3H) ppm; 13C NMR (126 MHz, chloroform-d) δ 165.17, 147.31, 139.12, 132.49, 129.54, 129.29, 128.10, 123.89, 121.86, 50.99 ppm; LC-MS: m/z (intensity): 208 [MH]$^{+}$ (19), 176 (100).

(E)-3-(4-methoxyphenyl)acrylonitrile ***(6a)***. Reaction temperature 40 °C and the reaction time was 2.8 h. Work-up was carried out according to the general procedure C. Yellow solid (0.94 g, 59 %). IR (ATR): v 3059, 2974, 2937, 2844, 2215, 1603, 1510 1275, 1252, 1176, 1023, 986, 846,

807 cm-1; 1H NMR (500 MHz, chloroform-d): δ 7.39 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 7.33 (d, $^3J_{HH}$ = 16.6 Hz, 1H), 6. 91 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 5.71 (d, $^3J_{HH}$ = 16.5 Hz, 1H), 3.84 (s, 3H) ppm; 13C NMR (126 MHz, chloroform-d): δ 162.02, 149.99, 129.04, 126.32, 118.66, 114.49, 93.34, 55.43 ppm; LC-MS: m/z (intensity): 160 $[MH]^+$ (100).

*(E)-3-(4-methoxyphenyl)acrylamide (**7a**).* Reaction temperature 60 °C and the reaction time was 46 min. Since the product precipitated during hydrolysis, it was filtered through a G4 frit. After removal of the excess water on the freeze dryer, the residue was weighed and the isolated yield was characterized by the analytical methods. White solid (1.19 g, 67%). IR (ATR): v 3463, 3359, 3170, 1662, 1595, 1388, 1253, 1174, 1026, 1016, 989, 829, 771 cm-1; 1H NMR (500 MHz, DMSO-d6): δ 7. 50 (d, ^3JHH = 8.5 Hz, 2H), 7.46 (s, 1H), 7.36 (d, $^3J_{HH}$ = 15.8 Hz, 1H), 7. 00 (s, 1H), 6.96 (d, $^3J_{HH}$ = 8.5 Hz, 2H), 6.46 (d, $^3J_{HH}$ = 15.8 Hz, 1H), 3.78 (s, 3H) ppm; 13C NMR (126 MHz, DMSO-d6): δ 167. 11, 160.36, 139.00, 129.17, 127.44, 119.77, 114.41, 55.29 ppm; LC-MS: m/z (intensity): 178 $[MH]^+$ (11), 161 (100).

RESULTS AND DISCUSSION

Based on our previous results, the range of applications of aluminum phosphate as a carrier material should be further investigated.

Aluminum phosphate is insoluble in water and alcohols and is commonly used in the pharmaceutical field as an antacid, i.e., acid scavenger. Little is written about the use of $AlPO_4$ in connection with Mizoroki-Heck reaction, as a functional support material and catalyst. In this respect, we set out to obtain a bifunctional catalyst in which the $AlPO_4$ can act both as a support material for the catalytic species and as a potential base in Heck-Matsuda reaction. To this end, 2 mol% $Pd(OAc)_2$ was reacted with 1 equivalent of $AlPO_4$ (based on diazonium salt) in MeOH for 15 min to give a Pd/ $AlPO_4$ - containing 7.8 wt%. As a starting point of our investigations, we first studied the reaction of 4-methoxybenzene tetrafluoroborate **1a** with butenone **2**, as depicted in our previous work (Table 1) [18]. It was known from then on that both the 4-methoxybenzalacetone **3a** the butenone **2** tend to undergo acid-catalyzed side reaction and also resulted in the decomposition of **3a**.

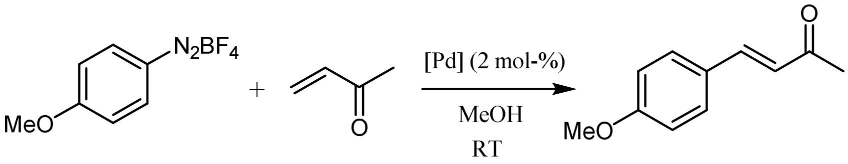
In order to ascertain the efficacy of this catalyst system we compared it with other catalysts in previous work in terms of yield, reaction rate, reaction time and initial time. The catalysts considered were, on the one hand, palladium acetate in the presence of calcium carbonate as acid scavenger with and without pre-reduction, palladium acetate with activated carbon and calcium carbonate as acid scavenger, and palladium acetate with aluminum phosphate, each with pre-reduction. For this purpose, 2 mol% palladium(II) acetate was used in each case.

In comparison, both systems exhibited comparable chemoselectivities and yields. However, in this system as opposed to that of $Pd(OAc)_2$, only 1.5 equivalents of butenone were required [18]. No decomposition of the benzalacetones formed was observed, which tends to support the bifunctional character of aluminum phosphate as a carrier and base.

The supported systems (entries 3 and 4, Table 1) showed, in addition to the highest yields, the shortest initial times accompanied by the highest turnover rates and catalytic activities. Thus, the $Pd(OAc)_2/AlPO_4$ system is characterized by a 65% higher catalytic activity compared to the $Pd(OAc)_2$ and by a 40% higher catalytic activity compared to the supported $Pd(OAc)_2/C$ system. Further more detailed differences can be worked out by examining the reaction profiles.

As can be seen from Figure 1, the reaction with the $Pd(OAc)_2/AlPO_4$ system, in contrast to the other catalyst systems, shows a largely linear reaction course. While the $Pd(OAc)_2/C$ system shows a shoulder-like formation towards the end of the reaction, indicating a more significant catalyst change; a trend not observable in the case of the $Pd(OAc)_2/AlPO_4$-system.

Table 1. Comparison of catalytic systems



1a **2** **3a**

Entry	Catalyst	Pre-reduction	Initial time [s]	Conversion rate 10^{-2} [mmol/s]	TOF [h^{-1}]	Yield [%]
1	$Pd(OAc)_2$[a]	No	53	2.07	745	74[b]
2	$Pd(OAc)_2$[a]	Yes	40	1.82	655	66[b]
3	$Pd(OAc)_2/C$[a]	Yes	23	2.43	875	82[b]
4	$Pd(OAc)_2/AlPO_4$	Yes	19	3.41	1228	82
5	Pd/C Heraeus Type U-01218	no	n.d.	n.d.	n.d.	5

[a]additional use of 0.5 eq. $CaCO_3$, [b]Ref. 18.

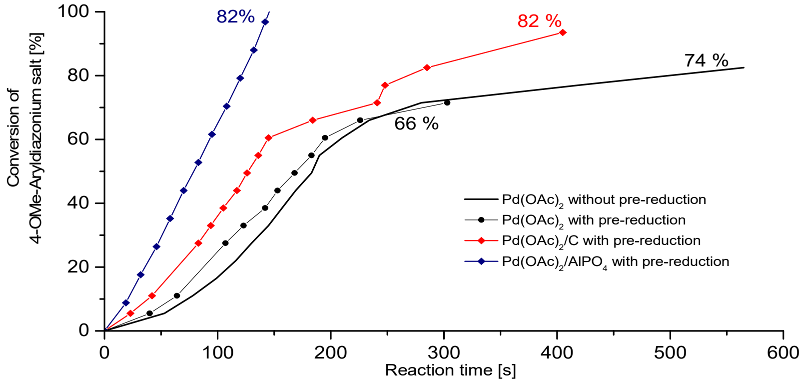


Figure 1. Conversion course of the utilized Pd-catalysts.

Strikingly, hardly any conversion was obtained when a commercially available catalyst from Heraeus was used (Entry 5, Table 1).

A significant decrease in product yield was also observed with unsupported pre-reduced $Pd(OAc)_2$, which was of even greater magnitude when it was pre-reduced over 2 h and a metal mirror was visible on the inside of the reaction flask.

This observation is associated with the fact that the freshly reduced palladium particles in solution without firm fixation tend to form agglomerates, which leads to a decrease in the reactivity of the catalytic Pd(0) species. In order to generate a highly reactive system, it is necessary to ensure a fine distribution of the catalyst on the support material, so that the palladium particles are easily accessible during the reaction. Such a distribution is present in the case of freshly generated $Pd(OAc)_2/C$ and $Pd(OAc)_2/AlPO_4$.

To better understand the reactivity differences between the catalysts, the respective immobilized catalysts were qualitatively examined in more detail using electron microscopy. As can be seen from the SEM images, palladium clusters are present in the case of the in situ generated immobilized palladium catalysts (Figure 2A and 2C). The commercially available palladium on activated carbon from Heraeus (Figure 2B) is present as a very coarse, compact distribution. This explains why the product conversion using the commercially available catalyst was much lower (only 5% conversion) than that using the freshly generated Pd(OAc)$_2$/C or the Pd(OAc)$_2$/AlPO$_4$ system.

The SEM images of the differently supported pre-reduced catalysts show large differences in morphology. It is well known that both the size distribution of the metal crystallites, as well as the type of support have a great influence on the performance of the immobilized catalysts. Significant differences in morphological structure were observed for Pd(OAc)$_2$/AlPO$_4$ (Figure 2C).

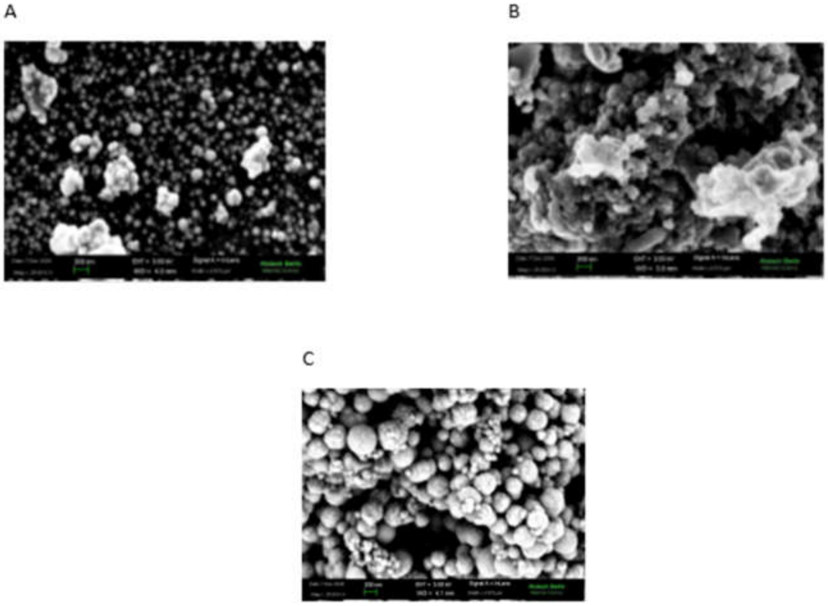


Figure 2. SEM-Pictures: A. Pd(OAc)$_2$/C; B. Pd/C Hearaeus Type U 01218; C. Pd(OAc)$_2$/AlPO$_4$.

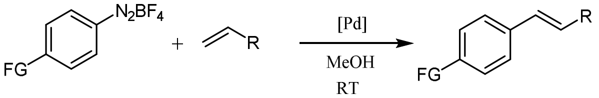
The supported palladium is present in the form of spheres of maximum surface area, which are finely sandwiched by the AlPO$_4$ support. The nature and the form of the large surface area, explain the observed excellent reactivity of the system. Compared to the Pd/C prepared in situ, the Pd clusters formed in the presence of aluminum phosphate as a support material appear larger.

A much more active Pd catalyst is obtained with AlPO$_4$ as support material in spite of the larger particle sizes compared to that of activated carbon most likely speaks for the positive synergistic effect of aluminum phosphate as a support material in catalysis.

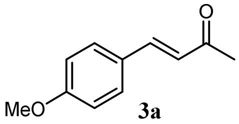
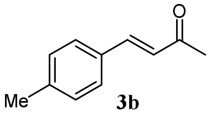
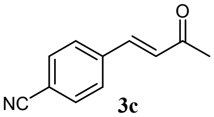
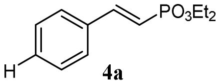
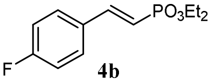
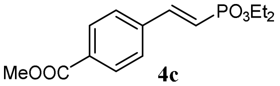
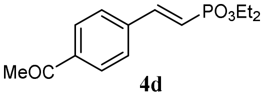
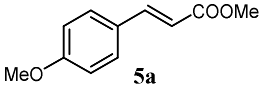
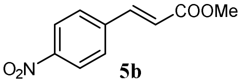
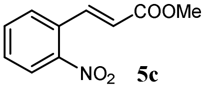
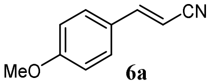
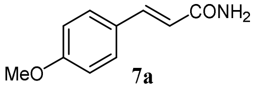
The significantly higher catalytic activity of the Pd(OAc)$_2$/AlPO$_4$-system may be attributed to the greater stability of the Pd particles and the occurrence of concentration effects due to local enrichment. Associated with this is the partial reduction in the activation energy due to the support. Furthermore, there also appears to be a concentration of the dissolved reactants at the interface due to interactions with the polar or charged units at the interface.

The significantly higher catalytic activity of the Pd(OAc)$_2$/AlPO$_4$-system may be attributed to the greater stability of the Pd particles and the occurrence of concentration effects due to local enrichment. Associated with this is the partial reduction in the activation energy due to the support. Furthermore, there also appears to be a concentration of the dissolved reactants at the interface due to interactions with the polar or charged units at the interface.

Table 2. Monoarylation of olefins via Heck-Matsuda reaction using $Pd(OAc)_2/AlPO_4$



1 **3, 4-8**

Entry	R (Olefin)	FG	Product	Procedure	Yield [%]
1	COMe	4-OMe	 **3a**	A	82
2	COMe	4-Me	 **3b**	A	65
3	COMe	4-CN	 **3c**	A	65[a]
4	PO_3Et_2	H	 **4a**	B	88
5	PO_3Et_2	4-F	 **4b**	B	100
6	PO_3Et_2	4-COOMe	 **4c**	B	90
7	PO_3Et_2	4-COMe	 **4d**	B	88
8	COOMe	4-OMe	 **5a**	C	70
9	COOMe	4-NO2	 **5b**	C	91
10	COOMe	2-NO2	 **5c**	C	91
11	CN	4-OMe	 **6a**	C	59
12	$CONH_2$	4-OMe	 **7a**	C	67

[a] use of 6 mol-% of catalyst.

Another advantage of the $Pd(OAc)_2/AlPO_4$ catalyst is that, in contrast to other catalyst systems described above, the use of calcium carbonate as an acid scavenger for the tetrafluoroboric acid generated during the reaction can be dispensed with. In analogy to the earlier results of Beller and Felpin, this catalyst cannot be used again after the reaction [14, 16].

Encouraged by this result, our next step was to look at the use of this catalyst in the preparation of other monoarylated olefins. To this end, we investigated reactions with vinyl phosphonates, methyl acrylate, acrylamides, and acrylonitrile, in addition to other functionalized benzalacetones (Table 2).

As shown in Table 2, functionalized benzalacetones could be obtained in good yields using this novel catalyst system (entries 1-3). As shown in previous studies, 6 mol% of the palladium catalyst was required to prepare 4-cyanobenzalacetones [18].

Arylvinylphosphonates represent important synthetic building blocks in organic chemistry. Thus, both monoarylations and biarylations of vinyl phosphonates have been described using Heck-Matsuda reactions [19, 21]. To this end, diethyl vinylphosphonate was reacted with various functionalized aryl diazonium salts using 1 mol% of the palladium formed in situ on aluminum phosphate at 45 °C in methanol as solvent (Table 2, entries 4-7). As shown in Table 2, the corresponding functionalized arylvinylphosphonates were obtained in excellent yields and stereoselectivity.

However, the applicability of the new catalytic system was not limited to butenone and diethylvinylphosphonate. Reactions with methyl acrylate, acrylonitrile and the corresponding acrylamides were equally unproblematic. In all cases, the corresponding monoarylated reaction products were obtained in good to very good yields.

CONCLUSION

In the present work, we were able to demonstrate the synthetic potential of the $Pd(OAc)_2/AlPO_4$ catalyst system in the Heck-Matsuda reaction, which has been rather neglected so far. Compared to conventionally used catalysts such as palladium acetate or an in situ generated palladium on carbon, the present catalyst system exhibits a significantly higher catalytic activity, which could be verified by kinetic studies. Electron-miscroscopic studies proved the formation of immobilized palladium clusters. The newly developed catalyst system was successfully used in the synthesis of functionalized benzalacetones, cinnamic esters, cinnamic amides and arylvinylphosphonates, which are valuable synthetic building blocks in organic synthesis. The arylation of acrylonitrile was also feasible. It was shown that the aluminum phosphate has bifunctionality as a support material and base in the Heck-Matsuda reaction.

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