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Palladium(0) allylic alkylation in a two-phase system or with a supported aqueous phase catalyst

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Abstract

The reaction of allylic carbonates with various acyclic and cyclic carbonucleophiles is catalyzed by the system $Pd(OAc)_2$ and $P(C_6H_4\text{-}m\text{-}SO_3Na)_3$ (or tppts) in a two-phase liquid medium H_2O-nitrile, the activity of the catalyst depending mainly on the nature of the nitrile, the temperature of the reaction and the ratio palladium/tppts. The same system $Pd(OAc)_2$ and $P(C_6H_4\text{-}m\text{-}SO_3Na)_3$ supported on silica catalyzes also this reaction. The formation of the active palladium species in the two cases is followed by ^{31}P NMR spectroscopy and discussed. Published by Elsevier Science B.V.

Keywords: Allylic substitution; Two-phase catalysis; Supported aqueous phase catalysis; Palladium; tppts

1. Introduction

There is a growing interest in metal catalyzed organic reactions in organic synthesis. Particularly palladium promoted organic reactions are now powerful tools in organic methodology, providing mild and selective routes to a great variety of valuable chemicals from basic organic precursors [1–7]. However one of the major problems in such homogeneous catalysis is the recovery of the molecular organometallic complexes, which is now necessary for economical, ecological and/or toxical reasons.

One of the most widely used palladium catalyzed transformation in organic chemistry is probably the alkylation of allylic substrates by carbo- and heteronucleophiles, the so-called ‘Tsuji–Trost reaction’, which occurs under very mild conditions with high regio- and stereoselectivity [8–10]. A possible solution to the recycling of the palladium catalyst is the use of a aqueous-organic two-phase system, the catalyst being ‘immobilized’ in the aqueous phase. Another elegant approach is the immobilization of the complex-containing aqueous phase on the surface of an hydrophilic inorganic oxide, the so-called ‘Supported aqueous phase catalysis’ or SAPC [11]. We used these two methodologies for the palladium-allylation of various carbonucleophiles.

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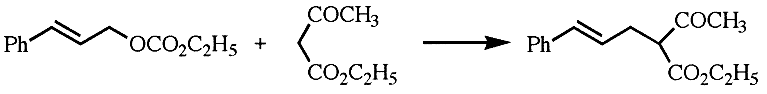
2. Results and discussion

2.1. Biphasic catalysis

We recently described the two-phase palladium-catalyzed allylic nucleophilic substitution reaction [12–16]. The optimization of the experimental conditions was performed using the alkylation of ethyl acetoacetate **2** by (E)-cinnamyl ethyl carbonate **1a** to give compound **3** as the test-reaction (Scheme 1), in the presence of $Pd(OAc)_2$ associated with the trisodium salt of the tri-(*m*-sulfophenyl)phosphine $P(C_6H_4\text{-}m\text{-}SO_3Na)_3$ (or tppts). The organic co-solvents of choice for this reaction are nitriles such as acetonitrile, butyronitrile or benzonitrile. $Pd(OAc)_2$ and $Pd_2(dba)_3$ are suitable precursors of palladium(0), although the former is preferred due to its good solubility in water. The highest activity is obtained using the ratio [Pd]/[tppts]≈1/5 and performing the reaction at 50°C. As expected, recycling of the catalyst is possible under these conditions by simple decantation and reuse of the aqueous solution, except when acetonitrile was used as the organic solvent; in this case, extraction of the product(s) with an organic solvent such as ethyl acetate was necessary before recycling of the aqueous phase containing the catalyst.

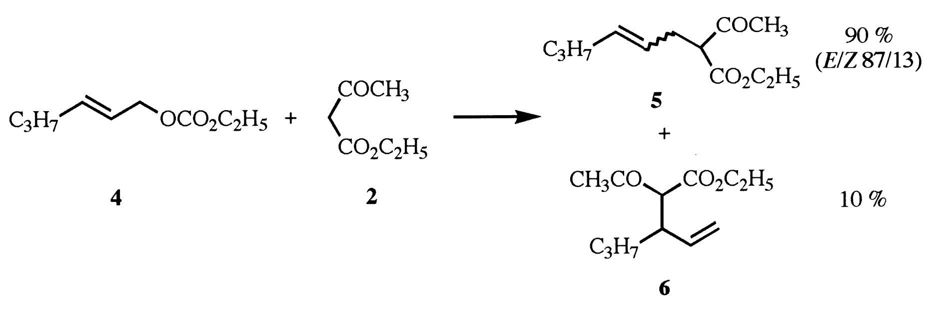
We also studied the reaction of ethyl acetoacetate **2** with (E)-methyl 2-hexenyl carbonate **4** in the presence of the catalyst $Pd(OAc)_2$/tppts in order to have a deeper insight into the regio- and stereoselectivity of the reaction (Scheme 2). Some selected results summarized in Table 1 show that the regioselectivity of the reaction was not affected by the ratio $Pd(OAc)_2$/tppts, the temperature of the reaction or the nature of the nitrile. We always observed the formation of the allylated products ethyl 2-acetyl-4-octenoate **5** and



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

Solvent (50 °C)	Isolated yields (%)
CH_3CN	1st cycle 80 2nd cycle 87
C_3H_7CN	1st cycle 95 2nd cycle 95
C_6H_5CN	1st cycle 94 2nd cycle 93 3rd cycle 90

Scheme 1.



Scheme 2.

Table 1
Reaction of ethyl acetoacetate **2** with methyl 2-hexenyl carbonate **4** in the presence of $Pd(OAc)_2$/tppts[a]

Solvent (l/l)	$Pd(OAc)_2$/tppts	T (°C)	Conv. (%)	**5** (%)	**6** (%)
CH_3CN/H_2O	1/4	50	0		
CH_3CN/H_2O	1/6	50	55	89	11
CH_3CN/H_2O	1/7.5	50	67	90	10
CH_3CN/H_2O	1/9	50	99	89	11
CH_3CN/H_2O	1/12	50	99	90	10
CH_3CN/H_2O	1/9	25	24	90	10
CH_3CN/H_2O	1/9	75	99	90	10
C_3H_7CN/H_2O	1/9	25	9	91	9
C_3H_7CN/H_2O	1/9	50	47	90	10
C_3H_7CN/H_2O	1/9	75	98	90	10
C_6H_5CN/H_2O	1/9	25	6	91	9
C_6H_5CN/H_2O	1/9	50	60	90	10
C_6H_5CN/H_2O	1/9	75	90	90	10

[a]Conditions: [**4**]/[**2**]/[$Pd(OAc)_2$]=25:35:1; [**4**]=0.5 mol l^{-1}; 24 h.

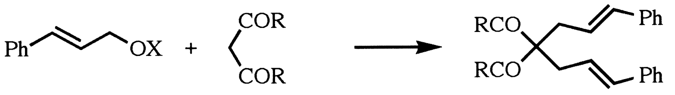
ethyl 2-acetyl-3-propyl-4-pentenoate **6** in a ratio 90:10, the linear compound **5** being a mixture of E/Z isomers in a ratio 87:13. However, the catalytic activity (and so the conversion) was deeply affected by some of these parameters. In a mixture of water acetonitrile as the two-phase system at 50°C, the highest activity was observed in this case for a ratio [tppts]/[$Pd(OAc)_2$] of 9. Using these conditions, we noticed that the conversion at 50°C was also dependent on the nature of the nitrile, the highest conversion being observed using acetonitrile. This could be related to the partial solubility of this nitrile in water. Effectively, benzonitrile–water and butyronitrile–water are true two-phase systems at 50°C; the transfer of the reactants from the organic phase to the aqueous phase for their transformation in the presence of the water-soluble palladium catalyst is thus probably the limiting step. Conversely, acetonitrile–water is not a true two-phase system at 50°C. This is confirmed by performing the reaction at various temperatures; if low conversion was obtained at 25°C even using water–acetonitrile, a complete conversion of the carbonate was observed by performing the reaction at 75°C even using butyronitrile or benzonitrile as the organic co-solvent; this could be correlated to a greater miscibility of the nitrile in water at this temperature.

Similar results were obtained using the branched 2-(vinyl)butyl ethyl carbonate as the π-allyl precursor.

Ethyl acetoacetate (pK_a=10.25) and acetylacetone (pK_a=8.94) reacted with carbonate **4** under the same conditions (CH_3CN/H_2O 1/l, [palladium]/[tppts] 1/6, 50°C), but no reaction was observed with dimethylmalonate (pK_a=13.3); however addition of one equivalent of a base such as DBU (1,8-diazabicyclo[5,4,0]unde-7-ene) in this case gave the monoalkylated products (*n:iso*=67:13) with the formation of ca. 20% of the alcohol arising from the hydrolysis of the carbonate. The lack of reactivity of dimethyl malonate in the absence of a base compared to ethyl acetoacetate or acetylacetone may be correlated to its higher pK_a; the presence of water is unfavourable to the formation of the enolate and the presence of a very strong base such as DBU is needed.

We also used in this reaction various cyclic carbonucleophiles having low pK_a (Scheme 3). The C-alkylation of some of these compounds is sometimes difficult due to strong competitive O-alkylation reaction. We expected that the presence of water, known to inhibit the alkylation of π-allyl systems by nucleophiles such as alcohols would favor the C-alkylation reactions. Tetronic acid **7a** (pK_a=3.76), dimedone **7b** (pK_a=5.2), barbituric acid **7c** (pK_a=4.1) and 1,3-dimethyl barbituric acid **7d** (pK_a=4.4) reacted with cinnamyl ethyl carbonate **1a**, or with cinnamyl acetate **1b** in the presence of DBU, in a mixture nitrile/H_2O 1/l, at 50°C and with a ratio [palladium]/[tppts] 1/6, to give only the dialkylated products **8** in moderate to good chemical yields (Scheme 3).

Given the efficiency of our catalytic precursor system $Pd(OAc)_2$/tppts in water–nitrile medium, we investigated further the nature of the palladium species present in water, using ^{31}P NMR spectroscopy.



1 **7** **8**

X		R,R		Isolated yields %	
				CH_3CN	C_3H_7CN
b	$COCH_3$	**a**	$-CH_2O-$	34	32
b	$COCH_3$	**b**	$-CH_2CMe_2CH_2-$	30	40
a	CO_2CH_3	**c**	-NHCONH-	70	69
a	CO_2CH_3	**d**	-NMeCONMe-	62	59

Scheme 3.

Amatore et al. [17,18] have previously concluded from cyclic voltametry and ^{31}P NMR spectroscopy studies that the reduction of $Pd(OAc)_2$ to Pd(0) in the presence of PPh_3 occurred in a two step process, involving the fast formation of $Pd(OAc)_2(PPh_3)_2$, followed by the intramolecular reduction of Pd(II) to Pd(0) stabilized by phosphine ligands, with the concomitant formation of phosphine oxide. The same mechanism was proposed when the phosphine was tppts [19–21].

When a solution of $Pd(OAc)_2$ and 5 tppts was dissolved in D_2O at 25°C, we observed immediately three signals (Fig. 1): a sharp signal at δ=34.6 ppm characteristic of tppts oxide, a broad signal centered at δ=29.5 ppm characteristic of $Pd(OAc)_2(tppts)_2$ and a broad weak signal centered at δ=−2.0 ppm, but no peak corresponding to free tppts at δ=−5.6 ppm. With time, we observed the decrease of the intensity of the signal at δ=29.5 ppm and an increase of the signals at δ=34.6 and δ=−2.0 ppm, with concomitant shift of the latter peak to lower field. After 48 h, this peak appeared at δ=18.6 ppm, the signal at δ=29.5 ppm disappearing. No significant evolution was observed after 1 week. Formation of a peak at δ=23.7 ppm, characteristic of $PhPdI(tppts)_2$, by addition of an excess PhI to this solution, with concomitant disappearance of the signal at δ=18.6 ppm, was an indication that the latter signal is that of a palladium(0) complex $Pd(tppts)_n$. The time dependent shift of the related signal and its broadness is probably due to a fast exchange between tppts coordinated to palladium(0) in $Pd(tppts)_3$ and free tppts.

At 50°C, as expected, the reduction process is much faster (Fig. 2). If we observed effectively three signals at δ=34.6, 29.6 and −1.8 ppm after 3 min, the reaction was completed after 40 min with only two signals at δ=34.7 and 18.0 ppm.

2.2. Supported aqueous phase catalysis

Although SAPC has been successfully used in hydroformylation of heavy or functionalized olefins [22–26], selective hydrogenation of α,β-unsaturated aldehydes [27] and asymmetric hydrogenation [28–30], no example of the use of palladium(0)-based SAPC appeared in the literature since our preliminary communication [31].

The supported palladium catalyst was prepared as exemplified in Scheme 4. The palladium acetate (0.1 mmol) and tppts (0.5 mmol) were dissolved in 3 ml of degazed water at 25°C for 1.5 h; the solution was then poured onto 1 g of porous silica (Grace, S_{BET}=185 m^2g^{-1}, pore diameter: 24 nm, pore volume=1.2 ml g^{-1}), previously evacuated at 200°C. After 2 h at room temperature, the water was evacuated to give the SAP catalyst SAP25P as a yellow powder. Using the same procedure, but maintaining the solution of $Pd(OAc)_2$/tppts at 50°C, gave the SAP catalyst SAP50P. The palladium content of the catalysts was ca. 0.76 wt.%. We also prepared similarly a palladium/tppts catalyst immobilized on a non-porous silica (Degussa, Aerosil 200, S_{BET}=225 m^2g^{-1}) SAP25NP; the palladium content of this dry solid was ca. 0.74 wt.%.

The prepared catalysts were examined for their ability to catalyze the allylic alkylation of methylene active compounds using the reaction-test (Scheme 1). The catalytic test was conducted as follow: 0.2 g of the

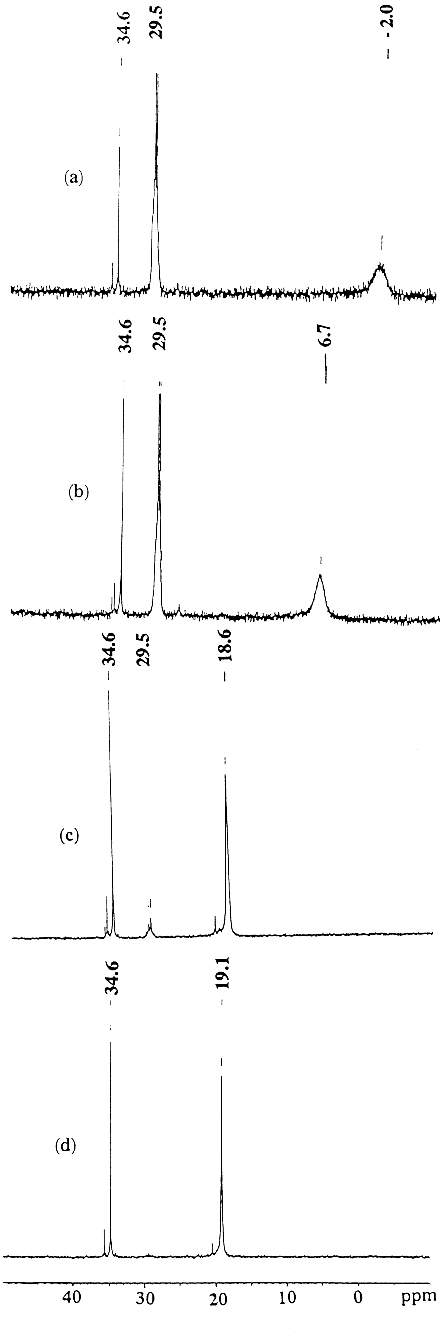


Fig. 1. Evolution with time of the ^{31}P NMR spectrum of $Pd(OAc)_2$+5 tppts in D_2O at 25°C; (a) 3 mn; (b) 45 mn; (c) 48 h; (d) 7 days.

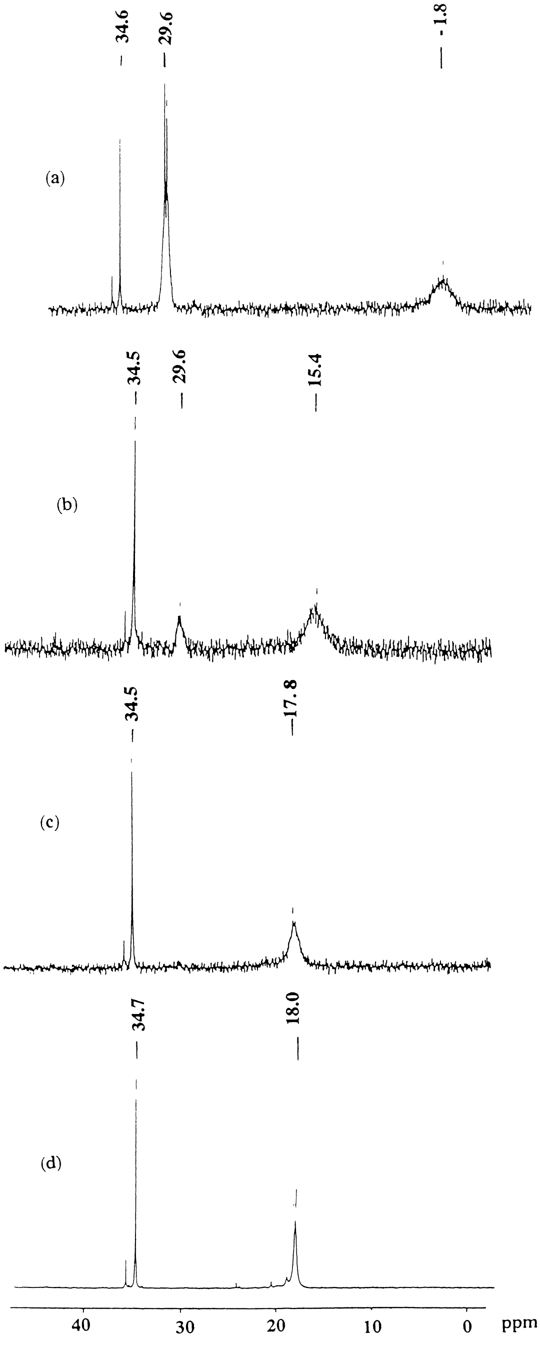


Fig. 2. Evolution with time of the ^{31}P NMR spectrum of $Pd(OAc)_2$+5 tppts in D_2O at 50°C; (a) 0 mn; (b) 11 mn; (c) 40 mn; (d) 30 h.

$$\underset{0.1\ \text{mmol}}{Pd(OAc)_2} + \underset{0.5\ \text{mmol}}{\text{tppts}} \xrightarrow[\text{T °C}]{H_2O\ (3\ \text{mL})} \text{Pd(0) complex} \xrightarrow[\text{then drying}]{\text{Silica (1 g)}} \text{Pd SAP Catalyst}$$

Scheme 4.

dry catalytic system was transferred in a Schlenk tube and a controlled amount of water was added via a syringe. Then a solution of ethyl acetoacetate (3.6 mmol, 30 equiv) and (E)-cinnamyl ethyl carbonate (3.0 mmol, 25 equiv) in the nitrile (6 ml) was added via a syringe, and the reaction mixture was brought to 80°C. Analytical samples were analyzed by gas chromatography after addition of an internal standard (geraniol), the reactant conversion and product yield being determined from standard curves established using authentic samples.

The catalytic properties of SAP25P was first studied as a function of the water content of the solid, the reaction being performed at 80°C, with acetonitrile as the organic solvent (Fig. 3(a)). Although the conversion of carbonate was nearly quantitative after ca. 24 h, the reaction was slow; after 8 h, the conversion was only 40–50% whatever the initial water content of the solid. If the activity of the SAP and the two-phase catalyst are similar, one can notice that:

- the stability of the catalyst under the SAP conditions is higher than under the homogeneous two-phase conditions. If precipitation of black particles was observed after 6 h in the latter case, no significant metal leaching could be detected in the former case (that is less than 0.5% of initial Pd found in the solution at the end of the reaction).
- the SAP25P catalyst is highly selective in the formation of the desired monoalkylated product, only traces of dialkylated product being observed after 24 h. On the opposite, the biphasic system leads to large amounts of cinnamyl alcohol, which is not the case for the SAPC.
- the SAP25P catalyst can be recycled. After removal of the liquid phase and washing with acetonitrile, the recovered solid is able to completely convert a similar solution of the reactants under the same conditions.

We performed the same experiments with the catalyst SAP50P. If its activity was quite similar to that of SAP25P without added water, this activity increased with the water content of the solid, reaching a plateau at 22 wt.% water (Fig. 3(b)). The selectivity was again very high and close to 100%.

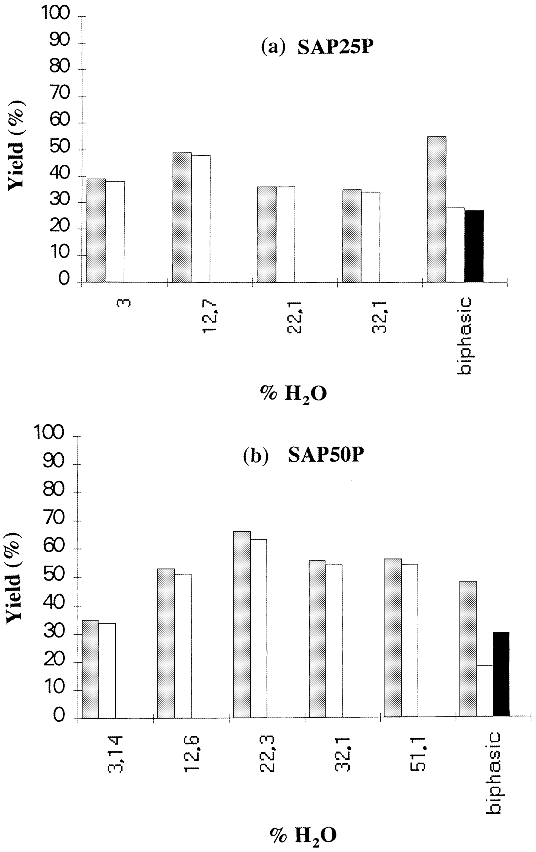


Fig. 3. Influence of the water content of solid catalyst (0.76% Pd) on its catalytic properties in the allylic alkylation of ethyl acetoacetate with (E)-cinnamyl ethyl carbonate using: (a) SAP25P; (b) SAP50P. Conditions: m_{catal}=200 mg, T=80°C, 8 h of reaction, solvent CH_3CN. (▨) Carbonate conversion (%); (□) Monoalkylated product yield (%); (■) Cinnamyl alcohol yield (%).

The catalyst SAP25NP, obtained from a non-porous silica, was used under the same conditions. The observed activity for reaction 1 was quite similar to those reported for catalyst SAP25P, as was the stability toward formation of palladium particles and metal leaching (<1 ppm Pd in the supernatant solution, i.e. <0.3% of the Pd present on the solid). So, it seems that the presence of mesopores is not necessary for this reaction under these conditions.

The activity of SAP50P for this reaction of alkylation is strongly dependent upon the nature of the nitrile. Thus, it becomes several order of magnitudes higher in benzonitrile and is strongly dependent on the water content of the solid. So, no carbonate conversion occurred within 3 h with a catalyst containing 3 wt.% H_2O, but complete carbonate conversion was achieved within 1 h with a selectivity close to 100% with a catalyst containing 30–50 wt.% H_2O; this is in quite contrast with the time for complete conversion (24 h) necessary when acetonitrile was used as the solvent. However, above 50 wt.% H_2O, the activity of the catalyst SAP50P decreased, and we simultaneously observed that the solid was poorly dispersed in the liquid phase and that the solution became shallow. This could be due to some leaching of water from the solid and explained the difficulties encountered to obtain in this case reproductible results.

A study of the nature of the surface phosphinated species was performed by ^{31}P NMR spectroscopy. With a water content lower than 15 wt.%, the spectra of the samples SAP25P are very broad, avoiding identification of the surface phosphinated species. Conversely, with a H_2O content of 23 wt.%, the spectrum is very close to the solution spectrum ((Fig. 4(a)). When this sample was heated at 80°C for 2 h, we observed three signals at δ=33.0 ppm (tppts oxide), 29.1 ppm and 14.0 ppm (Fig. 4(b)); after 15 h, the signal at δ=29.1 ppm disappeared

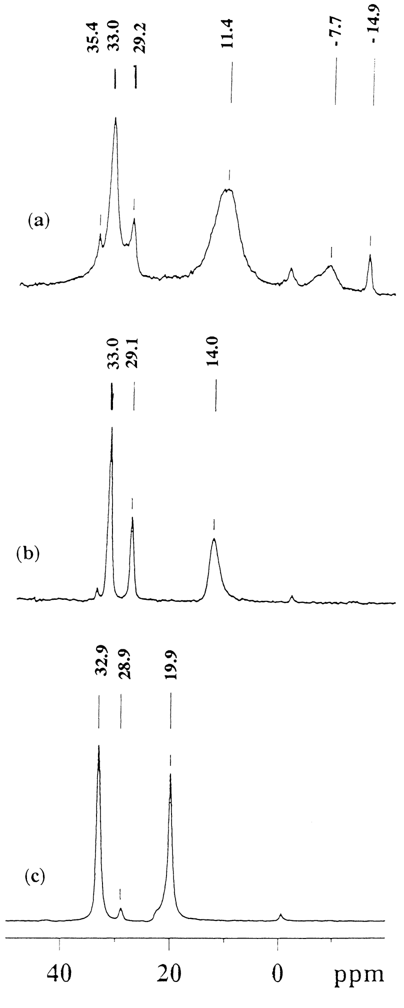


Fig. 4. Evolution with time of the ^{31}P MAS NMR spectrum of solid SAP25P (23 wt.% H_2O): (a) at 25°C; (b) maintained at 80°C for 2 h; (c) maintained at 80°C for 62 h.

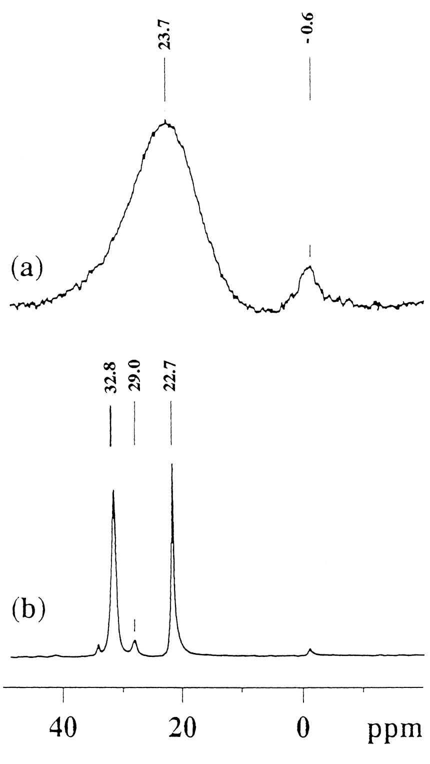


Fig. 5. ^{31}P MAS NMR spectrum of solid SAP50P (3 wt.% H_2O): (a) as such; (b) after addition of water prior to spectrum recording.

and the third peak was shift at 19.9 ppm (Fig. 4(c)), a phenomenon characteristic of the rapid exchange between tppts coordinated to Pd(tppts)$_3$ and free tppts. Analysis of the surface species of solid SAP25P containing 3 wt.% H_2O was possible after addition of a small amount of water directly in the rotor, just before recording the spectrum. We observed effectively in this case that reduction of Pd(II) to Pd(0) was a slow process.

In the case of catalyst SAP50P prepared by contacting silica with an aqueous solution of Pd(OAc)$_2$+5 tppts preheated at 50°C, the surface complex is as expected essentially Pd(tppts)$_3$, even when the water content is low (Fig. 5).

3. Conclusion

Immobilization of the system Pd(OAc)$_2$ and $P(C_6H_4$-*m*-$SO_3Na)_3$ (or tppts) in water either in a two-phase liquid medium H_2O-nitrile supported on silica gave a catalytic system which is active in the reaction of allylic carbonates with ethyl acetoacetate and other carbonucleophiles (Trost–Tsuji reaction). The activities as well as the recyclability of these catalytic systems depend upon various factors such as the ratio palladium/tppts, the nature of the organic solvent, the miscibility of the nitrile and the water, the water content of the solid in the case of the SAP catalyst. The palladium SAP catalyst seems more promising than the homogeneous two-phase catalyst; work is now in progress to extend this methodology to other palladium-catalyzed reactions.

References

[1] G. Wilkinson, F.G.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, vol. 8, Pergamon Press, Oxford, 1982.

[2] E.W. Abel, F.G.A. Stone, G. Wilkinson (Eds.), Comprehensive Organometallic Chemistry II, vol. 12, Pergamon Press, Oxford, 1995.

[3] B.M. Trost, I. Fleming, G. Pattenden (Eds.), Comprehensive Organic Synthesis, vol. 3, Pergamon Press, Oxford, 1991.

[4] B.M. Trost, T.R. Verhoeven, in: G. Wilkinson, F.G.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, vol. 8, Pergamon Press, Oxford, 1982, 799 pp.

[5] R.F. Heck, in: B.M. Trost, F.G.A. Stone, M.F. Semmelhack (Eds.), Comprehensive Organic Synthesis, vol. 4, Pergamon Press, Oxford, 1991, 833 pp.

[6] J. Tsuji, Palladium Reagents and Catalysts: Innovations in Organic Synthesis, Wiley, Chichester, 1995.

[7] R.F. Heck, Palladium Reagents in Organic Synthesis, Academic Press, London, 1985.

[8] S.A. Goldeski, in: B.M. Trost, I. Fleming, G. Pattenden (Eds.), Comprehensive Organic Synthesis, vol. 3, Pergamon Press, Oxford, 1991, 585 pp.

[9] P.J. Harrington, in: E.W. Abel, F.G.A. Stone, G. Wilkinson (Eds.), Comprehensive Organometallic Chemistry, vol. 12, Pergamon Press, Oxford, 1995, 959 pp.

[10] C.G. Frost, J. Howarth, J.M. Williams, Tetrahedron: Asymmetry 3 (1992) 1089.

[11] M.E. Davis, Chemtech (1992) 498.

[12] M. Safi, D. Sinou, Tetrahedron Lett. 32 (1991) 2025.

[13] E. Blart, J.P. Genêt, M. Safi, M. Savignac, D. Sinou, Tetrahedron 50 (1994) 505.

[14] S. Sigismondi, D. Sinou, M. Pérez, M. Moreno-Manas, R. Pleixats, M. Villarroya, Tetrahedron Lett. 35 (1994) 7085.

[15] C. Goux, S. Sigismondi, D. Sinou, M. Pérez, M. Moreno-Manas, R. Pleixats, M. Villarroya, Tetrahedron 52 (1996) 9521.

[16] S. Sigismondi, D. Sinou, J. Mol. Catal 116 (1996) 289.

[17] C. Amatore, A. Jutand, M.A. M'Barki, Organometallics 11 (1992) 3009.

[18] C. Amatore, E. Carre, A. Jutand, M.A. M'Barki, Organometallics 14 (1995) 1818.

[19] F. Monteil, Ph. Kalck, J. Organomet. Chem. 482 (1994) 45.

[20] G. Papadogianakis, J.A. Peters, L. Maat, R.A. Sheldon, J. Chem. Soc., Chem. Commun. (1995) 1105.

[21] C. Amatore, E. Blart, J.P. Genêt, A. Jutand, S. Lemaire-Audoire, M. Savignac, J. Org. Chem. 60 (1995) 6829.

[22] J.P. Arhancet, M.E. Davis, J.S. Merola, B.E. Hanson, Nature 339 (1989) 454.

[23] I.T. Horvath, Catal. Lett. 6 (1990) 43.

[24] I. Gou, B.E. Hanson, I. Toth, M.E. Davies, J. Organomet. Chem. 403 (1991) 221.

[25] I. Gou, B.E. Hanson, I. Toth, M.E. Davies, J. Mol. Catal. 70 (1991) 363.

[26] G. Fremy, E. Monflier, J.F. Carpentier, Y. Castanet, A. Mortreux, J. Catal. 162 (1996) 339.

[27] E. Fache, C. Mercier, N. Pagnier, B. Despeyroux, P. Panster, J. Mol. Catal. 79 (1993) 117.

[28] K.T. Wan, M.E. Davis, Nature 370 (1994) 449.

[29] K.T. Wan, M.E. Davis, J. Catal. 148 (1994) 1.

[30] K.T. Wan, M.E. Davis, J. Catal. 152 (1995) 25.

[31] P. Schneider, F. Quignard, A. Choplin, D. Sinou, New J. Chem. 20 (1996) 545.