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Water-soluble Polymer-bound, Recoverable Palladium(0)-Phosphine Catalysts

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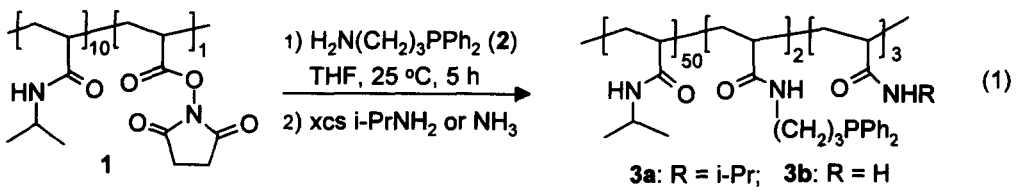
Abstract: The synthesis of a water-soluble polymer-bound Pd(0)-phosphine catalyst is described. This soluble polymeric catalyst is soluble in aqueous or mixed aqueous/organic media and has high activity in nucleophilic allylic substitution and in sp-sp^2 coupling reactions of aryl iodides with terminal alkynes. The catalyst can be recycled efficiently by solvent or thermal precipitation methods. © 1997 Elsevier Science Ltd.

There is a strong interest in developing reactive, selective catalysts that can be easily separated from products after a reaction. Two general strategies have been used. One approach uses insoluble or soluble polymer-supports.[1] A second strategy emphasizes the use of biphasic conditions as exemplified by fluorous biphasic and aqueous biphasic catalysis.[2,3] Here we describe our initial work with polymer-bound Pd(0)-phosphine catalysts based on the water-soluble polymer poly(*N*-isopropyl)acrylamide (PNIPAM).

PNIPAM-bound phosphine ligands were obtained by reaction of the amine **2** with poly(N-isopropyl)acryl-amide-*c*-(*N*-acryloxysuccinimide) (eq. 1).[4] We describe here allylic substitution reactions and sp-sp^2 coupling



1 **3a**: R = i-Pr; **3b**: R = H (1)

reactions using PNIPAM-bound Pd(0)-phosphine catalysts prepared from these soluble polymeric ligands. These polymer-supported catalysts are soluble in pure water or mixed aqueous media like H_2O/CH_3CN, H_2O/EtOH and H_2O/THF. These catalysts are recoverable by heating above PNIPAM's lower critical solution temperature (LCST) (H_2O) or by solvent precipitation, they are reusable and their reactivity mirrors that of their low molecular weight analog.

Pd-phosphine catalysts are widely used in synthesis and there are prior examples of water-soluble Pd catalysts.[5-8] As a result of our interests in water-soluble polymer supports,[9-11] we have begun to explore Pd derivatives of PNIPAM. PNIPAM itself has good solubility in water or mixed aqueous solvents. To incorporate phosphine ligands into PNIPAM, we prepared 1:10 copolymers of *N*-acryloxysuccinimide (NASI) with *N*-isopropylacrylamide using radical copolymerization.[4] These polymers were prepared in *t*-BuOH using AIBN as the initiator using a literature procedure.[12] The active ester groups in the resulting copolymer react (eq. 1) with 3-diphenylphosphinopropyl amine **2** to afford the polymeric phosphine ligand **3**. Ligand exchange

of $Pd(0)(dba)_2$ with **3** gave the corresponding PNIPAM-bound Pd(0) catalyst **4**.

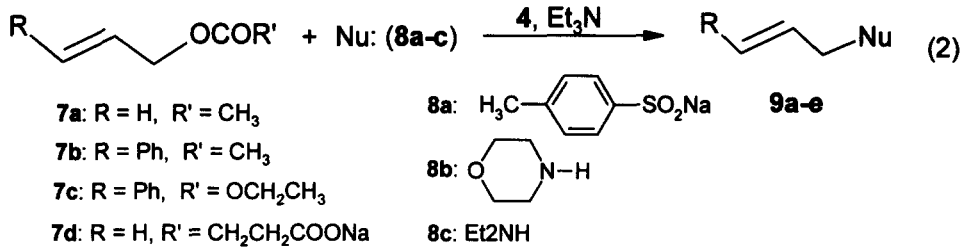
In a typical procedure, 10 g of poly[(NIPAM)-c-(NASI)] ($M_v = 5 \times 10^5$) **1** was dissolved in 150 mL of THF. Then 0.748 g of **2** in 10 mL of THF was added under N_2. The mixture was stirred at r.t. for 5 h and an excess of $^{i}PrNH_2$ or NH_3 was added to quench any unreacted active succinimide groups. Further stirring (r.t., 5 h) completed the reaction. Any solids at this point were removed by centrifugation. The product polymer **3** was isolated by precipitating the polymer using excess hexane. Two such reprecipitations yielded **3a** (soluble in mixed media) or **3b** (water-soluble) that was then used in the chemistry below. IR spectroscopy showed that **3** did not have any succinimide groups (no signals at 1810, 1780, 1735 cm^{-1}). The polymer **3** had a poor quality ^1H NMR spectrum with broad peaks at 1.13, 1.20-2.30, 2.60, 3.70, 4.00, 7.30-7.41. However, the ^{31}P NMR (D_2O) cleanly showed a broad singlet at δ -15.5 and a minor peak (< 5%) at δ 34 (which corresponds to the phosphine oxides). The golden-yellow Pd(0)-phosphine catalyst **4** was then formed from reaction **3** with $Pd(0)(dba)_2$ in THF using a **3**:Pd ratio of 4:1. Catalyst **4** was purified by reprecipitation as described above and had a new broad peak at δ17.0 besides the phosphine and phosphine oxide peaks in its ^{31}P NMR (CD_3OD) spectrum. We also prepared ligand $CH_3(CH_2)_2CONH(CH_2)_3PPh_2$ **5** from butyric anhydride and **2** for comparison purposes. Reaction of **5** with $Pd(0)(dba)_2$ as described above formed a low molecular weight Pd(0) complex **6** that served as a comparison to **4**.

Table 1 compares the activity of polymer-bound catalyst **4** with **6** in allylic substitution reactions (eq. 2).

Table 1 Results of allylic substitution reactions using PNIPAM-bound Pd(0) catalyst.[a]

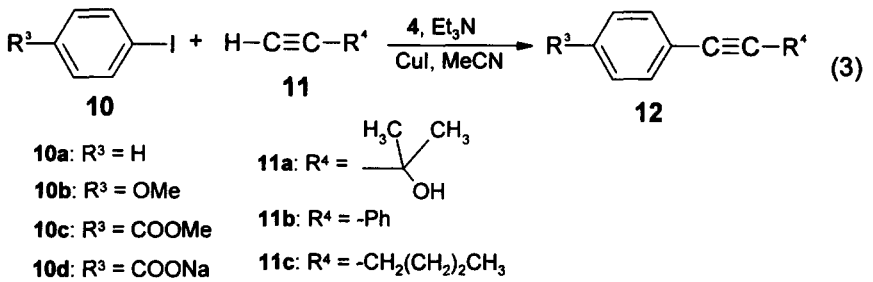
Run	Catalyst	Substrate	Nu:	Solvent	Temp (°C)	Time (h)	Product	Yield (%)
1	**6**	**7a**	**8a**	THF	35	4	**9a**	95
2	**4**	**7a**	**8a**	THF:H_2O	50	6	**9a**	94
3	**4**	**7d**	**8a**	H_2O	8	24	**9a**	91
4[c]	**4**	**7d**	**8a**	H_2O	8	24	**9a**	89
5[d]	**4**	**7b**	**8a**	THF:H_2O	50	6	**9b**	93
6	**4**	**7b**	**8a**	EtOH:H_2O	50	8	**9b**	94
7	**4**	**7b**	**8a**	CH_3CN:H_2O	50	8	**9b**	92
8	**4**	**7c**	**8b**	THF:H_2O	25	8	**9b**	94
9	**6**	**7b**	**8b**	THF:H_2O	25	5	**9c**	96
10	**4**	**7b**	**8b**	THF:H_2O	25	8	**9c**	96
11[b]	**4**	**7b**	**8b**	THF:H_2O	25	8	**9c**	93
12	**4**	**7d**	**8b**	H_2O	10	24	**9d**	86
13[b]	**4**	**7d**	**8b**	H_2O	10	24	**9d**	87
14	**4**	**7b**	**8c**	THF:H_2O	40	8	**9e**	88

[a]Reactions were run on a 10 mmol scale under N_2 with 1% Pd, 0.2 M substrate and [substrate]: [Nu:]: Et_3N = 1:1.3:1.5. H_2O was 20% by volume in mixed solvents. Yields are isolated yields. [b]A recovered catalyst was used and the yield is the average yield for 5 recycles. [c]Recovered catalyst was used. [d]A recovered catalyst was used and the yield is the average yield for 10 recycles.



The reactions were carried out homogeneously in H_2O or mixed solvents THF/ H_2O, CH_3CN/ H_2O or EtOH/ H_2O. Both allyl acetates and carbonates reacted smoothly with sodium p-toluene sulfinate or a secondary amine in the presence of **4** or **6** to afford **9** in high yield. Compared to **6** (Table 1, run 1, 9), the PNIPAM-bound catalyst **4** has essentially the same activity. Recycling of catalyst **4** is simple. Solvent precipitation (adding the reaction mixture into hexane) leads to quantitative recovery of the catalyst. The recovered catalyst can be dissolved in fresh solvents and reused (Table 1, runs 4,5,11,13). We have shown that the catalyst was recycled 10 times (run 5) and the average yield is 93%. In water, precipitation of **4b** can be accomplished by heating to room temperature (above **4b**'s LCST). However, the lower reaction temperature required by **4b**'s LCST leads to longer reaction times in this solvent. There was a very modest loss in activity of **4** after 15 recycling steps. The ^{31}P NMR spectrum at this point suggests that this loss in activity is the result of some adventitious oxidation of the phosphine ligand.

'We also carried out cross-coupling reactions of terminal alkynes with aryl iodides catalyzed by **4** (eq. 3, Table 2). Cross coupling takes place smoothly in the presence of 0.5% CuI cocatalyst and 1.5 equiv of Et_3N. The PNIPAM-bound catalyst **4**'s activity is again barely distinguishable from that of **6** (Table 2) for this coupling reaction. However, **4** can be recycled (Table 2, run 3) and the use of **4** facilitates product isolation.



In summary, water-soluble PNIPAM-bound Pd(0)-phosphine complexes that can be recovered and reused by solvent or thermal precipitation methods can be readily synthesized. These soluble polymer-bound catalysts have advantages of easy product isolation and high activity. These catalysts can be used in pure water or, when substrate solubility dictates, in mixed aqueous solvents. Further studies of derivatives of PNIPAM as ligands are continuing in our laboratory.

Table 2 Cross-coupling reactions using PNIPAM-bound Pd(0) catalysts.[a]

Run	Catalyst	Substrates	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	**6**	**10a 11a**	MeCN	50	3	93
2	**4**	**10a 11a**	MeCN:H_2O	55	8	92
3[c]	**4**	**10a 11a**	MeCN:H_2O	55	8	93
4	**4**	**10b 11a**	MeCN:H_2O	55	8	96
5	**4**	**10b 11b**	MeCN:H_2O	55	6	92
6	**4**	**10b 11c**	MeCN:H_2O	60	8	88
7	**4**	**10c 11a**	MeCN:H_2O	55	8	95
8[d]	**4**	**10d 11a**	H_2O	10	36	91
9[c,d]	**4**	**10d 11a**	H_2O	10	36	89

[a] Reactions were run on a 10 mmol scale under N_2 with [Pd]:aryl iodide:alkyne:Et_3N = 1:100:150:150 with 0.5% CuI cocatalyst. [b]These are isolated yields. [c]Recovered catalyst was used. [d]K_2CO_3 was used as the base and the solvent contained 5% CH_3CN.

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