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# **Cross-linked poly(4-vinylpyridine/styrene) copolymers** as a support for immobilization of ytterbium triflate

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Abstract—Eight cross-linked poly(4-vinylpyridine/styrene) (P/S) resins (as beads) were prepared by radical suspension polymerization. Ytterbium triflate was immobilized in the range of 0.10–0.24 mmol/g by mixing with the P/S resins. The ytterbium triflate-immobilized P/S resins exhibited good activity in two Lewis acid-catalyzed reactions. Low pyridine containing resins were recycled with no loss of activity, while a slight loss of activity was observed with the higher pyridine containing resins. © 2005 Elsevier Ltd. All rights reserved.

# 1. Introduction

Rare earth metal triflates (RE(OTf)<sub>3</sub>) including lanthanide (III) triflates (Ln(OTf)<sub>3</sub>) have been employed as mild Lewis acid in many organic transformations including aldol, Diels-Alder, Michael addition, aziridination, oxidation/ reduction, rearrangement and protection/deprotection reactions.<sup>1</sup> The use of these compounds has gained prominence not only due to their chemical versatility but also because of their stability in the presence of most polar functional groups and organic solvents including aqueous media. Moreover, RE(OTf)<sub>3</sub> are catalytically active in the presence of Lewis bases containing nitrogen, oxygen, phosphorous and sulfur atoms. These catalysts are used as homogeneous catalysts in organic solvents in most applications and since RE(OTf)<sub>3</sub> are more soluble in water than in common organic solvents, they can be recovered by aqueous extraction and reused.<sup>2</sup> Alternatively, immobilization of these catalysts on solid supports affords improved recycling and facile use in synthetic schemes, a consummate goal in catalyst development. Several methods for the immobilization of RE(OTf)<sub>3</sub> on polymer supports have been developed,<sup>3</sup> including microencapsulation using soluble polystyrene and lightly cross-linked polystyrene-supported scandium triflate. These immobilized catalysts were recycled without any loss of catalytic activity. However, while the microencapsulated catalysts has very good activity, a drawback to its use is the required precipitation

of the polymer for recovery of the catalyst.<sup>3c</sup> Similarly, the insoluble lightly cross-linked polystyrene/divinylbenzene (PS/DVB) copolymer-supported Sc(OTf)<sub>3</sub> has a short-coming in that it requires an intricate six step synthesis.<sup>3d</sup> Therefore, the development of solid polymeric support, that can be readily synthesized, possesses good activity and stability, and can be recycled efficiently would be of synthetic utility.

Recently, highly cross-linked polystyrene resins with pendant pyridine functional groups have been reported for immobilization of dirhodium tetracarboxylates.<sup>4,5</sup> The immobilization was considered to be due to both ligand coordination and physical encapsulation. Another example of catalyst immobilization on a pyridine-based polymer is the commercially available poly(4-vinylpyridine) supported osmium catalysts.<sup>6</sup> These two examples led us to speculate that cross-linked pyridine/styrene polymers could serve as potential supports for Ln(OTf)<sub>3</sub>. Herein, we describe the synthesis of a series of cross-linked poly(4-vinylpyridine/ styrene) copolymers, immobilization of Yb(OTf)<sub>3</sub> on these polymers, and their catalytic activity and reusability in two model reactions.

#### 2. Results and discussion

A series of cross-linked poly(4-vinylpyridine/styrene) copolymers (abbreviated as <sup>x</sup>P/S resins, where superscript x equates to % pyridine content) with varying ratios of styrene, 4-vinylpyridine and (cross-linker) 1,4-bis(4-vinylphenoxy)butane<sup>7</sup> were synthesized as beads by aqueous

*Keywords*: Lanthanide triflate; Poly(4-vinylpyridine/styrene); Catalyst immobilization.

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suspension radical polymerization in the presence of benzoyl peroxide (Scheme 1). Low cross-linked P/S resins **1a–1g** were prepared using 1 mol% of the 1,4-bis(4-vinyl-phenoxy)butane cross-linker. A highly cross-linked poly-(4-vinylpyridine) (abbreviated as  $^{90}$ P/DVB) resin **1h**, was prepared with 10% divinylbenzene as the cross-linker. All resins were sieved to a range of 40–400 mesh.



**Scheme 1.** The preparation of P/S resins. Actual nitrogen (pyridine) content (mmol/g) found in experimental section (Table 5).

For lightly cross-linked resins, swelling in common organic solvents is an important factor in the success of solid-phase reactions.<sup>8</sup> The swollen volumes for these resins were determined by the syringe method<sup>9</sup> in several organic solvents (Table 1). All P/S resins displayed outstanding swelling in dichloromethane and modest swelling in methanol and acetonitrile. As expected the swelling of the high cross-linked PS/DVB resin **1h** was low and unaffected by the choice of solvent.

Immobilization of Yb(OTf)<sub>3</sub>, a representative Ln(OTf)<sub>3</sub> having relatively high acidity due to its small ionic radii,<sup>10</sup> onto P/S resins was achieved by shaking a suspension of P/S resins and Yb(OTf)<sub>3</sub> for 24 h in a 1:1 mixture of methanol/ dichloromethane (Scheme 2). This mixture is an optimal solvent for immobilization since Yb(OTf)<sub>3</sub> has good solubility and the resins also exhibit good swelling. The loading of Yb(OTf)<sub>3</sub> was determined by measuring the increase in the weight of the resulting resins, and verified by measuring the residual Yb(OTf)<sub>3</sub> in the filtrate. Yttebium triflate was immobilized into 200 mg of <sup>x</sup>P/S resins **1b–1g** and <sup>90</sup>P/DVB resin **1h** resulting in a loading of 0.10–0.24 mmol/g of <sup>x</sup>P/S(Yb) **2b–2g** and <sup>90</sup>P/DVB(Yb) **2h** (Table 1). Loading of Yb(OTf)<sub>3</sub> increased from <sup>10</sup>P/S to <sup>70</sup>P/S, and then decreased as the pyridine content was raised in <sup>90</sup>P/S and <sup>100</sup>P/S. The corresponding N/Yb ratio ranged

Table 1. Swollen volume of P/S resins and loading amounts of Yb(OTf)<sub>3</sub>



Scheme 2. Immobilization of Yb(OTf)3 into P/S resins.

between 9.2 and 52.0. No change in swelling of the  ${}^{x}P/S(Yb)$  resins was observed relative to the starting  ${}^{x}P/S$  resins.

Prior reports using soluble polymer supported  $Sc(OTf)_3$  have described that the interaction between  $Sc(OTf)_3$  and the phenyl groups of polystyrene may contribute to catalyst encapsulation.<sup>3c</sup> We prepared an insoluble cross-linked polystyrene resin **2a**, and applied the immobilization technique used to prepare resins **2b–2h**. However, no Yb(OTf)<sub>3</sub> was detected in this resin, confirming that phenyl groups residing within the resin do not play a major role in the immobilization, and the Yb(OTf)<sub>3</sub> immobilization on the <sup>x</sup>P/S resin occurs primarily by the ligand interaction between the metal and the pyridine moieties of each of the resins (Fig. 1).



Figure 1. IR spectrum of <sup>50</sup>P/S (1d, gray) and <sup>50</sup>P/S(Yb) (2d, black).

The key to the successful development of an immobilized catalyst requires that the twin goals of high activity and good stability be achieved. In the context of immobilized metal catalysts, contamination of the product by the homogeneous catalyst is a significant issue, therefore catalyst leaching should be kept to a minimum. Two preliminary tests were performed to determine the extent  $Yb(OTf)_3$  leaching from P/S resins and to determine the activity of the immobilized catalyst. First, the effect of solvent on catalyst leaching was determined by suspending

	Swollen volume (mL/g)				Loading <sup>a</sup>	N/Yb	
	CH <sub>2</sub> Cl <sub>2</sub>	MeOH	MeCN				
la	23.8	5.6	2.6	2a	0	_	
lb	19.6	4.6	2.7	2b	0.10	9.2	
lc	10.5	3.2	3.2	2c	0.15	18.9	
ld	18.3	6.5	2.9	2d	0.20	23.1	
le	10.4	6.6	4.1	2e	0.24	26.9	
lf	9.5	10.2	4.1	<b>2f</b>	0.23	35.7	
lg	10.7	11.7	5.2	2g	0.18	52.0	
lĥ	_		—	2h	0.23	36.5	

<sup>a</sup> mmol/g, Determined by weight increase.



Scheme 3.  $\beta$ -Amino ketone synthesis.

Table 2. Leaching test<sup>a</sup>

Entry	Solvent	(%) Conversion <sup>b</sup>	Loss of IR signal <sup>c</sup> (%)
1	CH <sub>2</sub> Cl <sub>2</sub>	3	0
2	MeCN	96	8
3	MeOH	100	49
4	$MeCN/CH_2Cl_2$ (1:1)	91	0
5	$MeOH/CH_2Cl_2$ (1:1)	95	47

<sup>a</sup> All reactions were carried out on a 0.1 mmol scale.

<sup>b</sup> Determined by HPLC.

<sup>c</sup> Calculated by IR integration of used P/S(Yb) resins.



**Figure 2.** Kinetics for the synthesis of **5** with resins (**2b–2h**) and Yb(OTf)<sub>3</sub> (10 mol%).—( $\bigcirc$ , Yb(OTf)<sub>3</sub>), ( $\diamondsuit$ , <sup>10</sup>P/S(Yb)), ( $\blacksquare$ , <sup>30</sup>P/S(Yb)), ( $\bigstar$ , <sup>50</sup>P/S(Yb)), ( $\checkmark$ , <sup>70</sup>P/S(Yb)), ( $\diamondsuit$ , <sup>70</sup>P/S(Yb)), ( $\diamondsuit$ , <sup>100</sup>P/S(Yb)), ( $\Box$ , <sup>90</sup>P/DVB(Yb)).

the immobilized catalyst in solvent for 30 min, followed by filtration, washing and drying. An IR technique was used as a semi-quantitative tool to determine the extent of leaching.<sup>†</sup> The degree of leaching was determined by comparing the IR

**Table 3.** Recycling results for the synthesis of  $5^{a}$ 

spectrums before and after the test. The <sup>x</sup>P/S(Yb) and <sup>90</sup>P/ DVB(Yb) resins were found to be stable in dichloromethane, acetonitrile, and methanol. In DMF, significant Yb(OTf)<sub>3</sub> was leached out from low pyridine-content <sup>x</sup>P/ S(Yb) resins **2b** and **2c**, while no leaching was observed in high pyridine-containing resins **2d–2h**. However, in 10% pyridine/dichloromethane, almost all the Yb(OTf)<sub>3</sub> was removed from all tested resins, further confirming the chelation of Yb(OTf)<sub>3</sub> by the pyridine moieties of the polymer.

Second, the activity of the catalyst and leaching of the catalyst was investigated in the context of a β-amino ketone synthesis<sup>11</sup> (Scheme 3) on  ${}^{50}$ P/S(Yb) resin 2d (Table 2). Since the resins contain pyridine moieties, the activity of the catalyst could be adversely affected by pyridine-catalyst interactions. However, we determined that the catalytic activity of Yb(OTf)3 is retained in a homogenous version of the probe reaction even in the presence of pyridine. In a nonpolar solvent such as methylene chloride, catalytic activity was low, but no discernable leaching of the catalyst was observed. In contrast, significant catalytic activity was obtained in acetonitrile and methanol solvents, but unacceptable levels of catalyst leaching were also observed. Since good activity is achieved in polar solvents and the catalyst is more stable in non-polar solvents, a mixed solvent system was required to optimize activity and stability. Using methanol/dichloromethane (1:1) or acetonitrile/dichloromethane (1:1), relatively low leaching of the catalyst was observed and 95% conversion to the desired β-amino ketone was obtained. An optimal solvent ratio of acetonitrile and dichloromethane was found to be 3:1, resulting in 95% conversion in 1 h with no apparent leaching of the catalyst; by comparison the homogeneous reaction was complete in 10 min under similar reaction conditions.

The entire array of the immobilized catalysts **2b–2h** were tested using the probe  $\beta$ -amino ketone synthesis consisting

Resin	1st	2nd	3rd	4th	5th	6th	7th	Ave.		
2b	98	98	98	97	98	98	98	98		
2c	99	98	98	98	98	97	98	98		
2d	95	95	95	95	95	95	95	95		
2e	96	96	95	93	93	88	92	93		
2f	89	85	82	79	83	72	84	82		
2g	86	82	80	76	74	72	81	79		
2h	91	75	84	86	89	89	88	87		

<sup>a</sup> All reactions were carried out on a 1 mmol scale, and conversion yield (%) was determined by HPLC.

<sup>†</sup> In addition to the IR bands of the <sup>x</sup>P/S resins, <sup>x</sup>P/S(Yb) and <sup>90</sup>P/DVB(Yb) resins show two broad bands 1252, 1154 cm<sup>-1</sup> and one sharp band at 1029 cm<sup>-1</sup> in the IR spectrum due to the triflate ligand.<sup>3c</sup> Since these Yb(OTf)<sub>3</sub>-specific IR bands do not overlap with the IR bands of the resins, the extent of leaching of Yb(OTf)<sub>3</sub> could be determined by relative comparison to polymer specific bands. To validate this IR technique, we prepared Yb(OTf)<sub>3</sub>-immobilized <sup>50</sup>P/S(Yb) resins with six different loadings (The loading amount was obtained by weight increase of the resin and confirmed by the amount of Yb(OTf)<sub>3</sub> in filtrates after immobilization), followed by an IR (1252 cm<sup>-1</sup>) integration. A linear correlation between the IR integration and ytterbium loading was obtained.

of aromatic imine **3** and vinyl silyl ether **4**. The kinetics (Fig. 2) and the conversion (Table 3) reveal that the reactivity of the Yb(OTf)<sub>3</sub>-immobilized catalyst is related to the ratio of N/Yb: higher activity is obtained at lower N/Yb ratios. Although lanthanides have weak interactions with heteroatoms, high pyridine concentration surrounding the metal might limit the accessibility of the metal to the substrate resulting in lower activity at high N/Yb ratios. This observation is comparable to the reported decrease in catalytic activity for a palladium/monophosphine polystyrene catalyst as the ligand to metal ratio was increased.<sup>12</sup>

Resins 2b, 2c and 2d containing 10-50% pyridine showed good activity and were recycled six times with no loss of activity (Table 3). However, resins 2e, 2f and 2g (70, 90 and 100% pyridine, respectively) had lower reactivity and exhibited a small decrease in activity after the sixth recycle. The highly cross-linked resin 2h was also recycled six times with no loss of activity. In particular, for the case of resin 2d, filtrates from the first three recycled reactions were analyzed for ytterbium by ICP-AES analysis to quantitate catalyst retention and leaching. A very small amount of vtterbium (detection limit corresponded to <0.2% of vtterbium on the catalyst) was observed in the three filtrates. Further corroboration was obtained by IR spectroscopy; integration of the IR spectra of resin 2d before and after use yielded no change. Finally, reaction curves and rates from six recycled reactions revealed that the activity of the immobilized catalyst is not altered after recycling. These observations show that there is no leaching of Yb(OTf)<sub>3</sub> during the reaction, as well as no loss of activity.

To demonstrate the versatility of the immobilized Yb(OTf)<sub>3</sub> resin, we chose to study its application in a second model reaction; the Diels–Alder reaction of imine **6** and ethyl vinyl ether for the synthesis of tetrahydroquinolines<sup>13</sup> (Scheme 4, Table 4). Three <sup>x</sup>P/S(Yb) resins with low N/Yb ratio (**2b**, **2c**, **2d**) were used under identical reaction conditions as that for  $\beta$ -amino ketone synthesis (Table 4). As observed in the former example, the order of reactivity was **2b**>**2c**>**2d**. Furthermore, these resins could be used five times without any loss of activity or alteration of the *trans/cis* ratio of products. These results show that the immobilized catalyst is not substrate-dependant, as the optimum conditions developed for the  $\beta$ -amino ketone synthesis of tetrahydroquinoline.



Scheme 4. Imino Diels-Alder reaction.

**Table 4.** Recycling results for the synthesis of  $7^{a}$ 

Resin	1st	2nd	3rd	4th	5th	Ave. ratio trans/cis <sup>b</sup>
2b	93	94	93	93	92	13/87
2c	90	92	91	92	92	13/87
2d	69	82	79	83	82	13/87

<sup>a</sup> All reactions were carried out on a 0.1 mmol scale, and data in table is % conversion determined by HPLC.

<sup>b</sup> The ratio was determined by HPLC and major product was proven to have *cis* configuration on the basis of correlation between coupling constants of four aliphatic protons.

## 3. Conclusion

A series of P/S resins were prepared by suspension polymerization and used as polymeric supports to immobilize  $Yb(OTf)_3$ . These resins are inexpensive and can be readily prepared and the immobilized catalysts can be recycled without any loss of activity. Although we have demonstrated the use of these resins in preparation of a  $\beta$ -amino ketone and tetrahydroquinoline, the development of immobilized lanthanide triflate clearly provides a clean route for preparing many potentially useful compounds. With the current emphasis on green chemistry, the use of pyridine-based polymers to immobilize other metal-based catalysts affords an interesting area for further research.

### 4. Experimental

# 4.1. General methods

All chemicals were obtained from commercial suppliers and were used without further purification unless otherwise stated. All of the glassware used in the solid-phase reactions was silanized by treating with Sigmacote<sup>®</sup>. Flash chromatography was carried out using Merck silica gel 60 (230-400 mesh). Preparative TLC was carried out on Merck 60 F254 plates (0.5 mm) eluting with ethyl acetate/hexanes. FT-IR spectra were recorded using a Thermo Nicolet AVATA 360 spectrometer equipped with a Golden Gate single reflection diamond ATR accessory. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded using a Varian INOVA-399 (400 MHz) and calibrated using residual undeuterated solvent as an internal reference. High performance liquid chromatography (HPLC) was performed using a Hitachi system: L-5000 LC controller, 655A variable wavelength UV monitor, 655A-12 liquid chromatograph, and D-2000 chromatointegrator. HPLC conditions: Vydac 201SP column (5 µm RP C18) 4.6 mm  $\times$  250 mm, acetonitrile/water isocratic 65:35 (for compound 5), 50:50 (for compound 7), flow: 1 mL min<sup>-1</sup>, detection UV ( $\lambda$ =254 nm), injection loop 20 µL. High-resolution mass spectra (HRMS) were recorded at The Scripps Research Institute using an IonSpec Ultima high-resolution FTMS instrument (MALDI-FTMS) and low-resolution mass spectra were obtained using electrospray ionization (ESI).

## 4.2. General procedure for synthesis of P/S resins

 $^{50}$ P/S resin (1d). The aqueous phase used for the suspension polymerization reactions was prepared by dissolving acacia gum (30 g) and NaCl (10 g) in deionized water (1 L). This solution was then filtered to remove insoluble impurities, and degassed for 15 min under vacuum while being sonicated. A 300 mL flange flask equipped with 3-necked lid and mechanical stirrer was charged with 250 mL of the above aqueous solution. To this preheated solution at 50 °C was added a homogeneous solution of styrene (13.81 mL, 120.6 mmol), freshly-distilled 4-vinylpyridine (13.00 mL, di(4-vinylphenoxy)-butane 120.6 mmol). (710 mg, 2.41 mmol), benzoyl peroxide (292 mg, 1.21 mmol) and chlorobenzene (8 mL) prepared by gentle warming. The suspension was stirred at 500 rpm and 50 °C for about 3-5 min with monitoring droplet size. Once the desired droplet size was formed, the stirring rate was reduced to 250 rpm and the reaction flask was heated to 80 °C for 6 h. After cooling, the polymer was filtered with 400-meshed sieve and washed several times with warm water, followed by a methanol. The resultant beads were washed by continuous extraction in Soxhlet apparatus with THF overnight and sequentially washed with 50% MeOH/THF

and MeOH and dried under vacuum to give 12.76 g of pale yellow resin. The dried resin was sieved to give 11.54 g of the <sup>50</sup>P/S resin (**1d**, 49%) in the 40–400 mesh size. Nitrogen content (mmol/g) of **1d** was obtained from elemental analysis to be 4.48 mmol/g (Table 5); FTIR:  $\nu_{max}$  (cm<sup>-1</sup>) 3024, 2920, 1596, 1557, 1493, 1451, 1414; Anal. Calcd for C<sub>7.70</sub>H<sub>7.72</sub>N<sub>0.50</sub>O<sub>0.02</sub>: C, 85.96; H, 7.23; N, 6.51. Found: C, 82.99; H, 7.35; N, 6.28: other P/S resins were prepared in the same manner.

<sup>0</sup>P/S resin (**1a**). 17.28 g (64%, 40–400 mesh). FTIR:  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3025, 2920, 1601, 1492, 1451;

<sup>10</sup>P/S resin (**1b**). 9.05 g (36%, 40–400 mesh). FTIR:  $\nu_{max}$  (cm<sup>-1</sup>) 3025, 2918, 1598, 1493, 1451; Anal. Calcd for C<sub>8.10</sub>H<sub>8.12</sub>N<sub>0.10</sub>O<sub>0.02</sub>: C, 90.76; H, 7.64; N, 1.30. Found: C, 89.85; H, 8.10; N, 1.73:

<sup>30</sup>P/S resin (**1c**). 16.15 g (67%, 40–400 mesh). FTIR:  $\nu_{max}$  (cm<sup>-1</sup>) 3025, 2919, 1597, 1557, 1493, 1452, 1415; Anal. Calcd for C<sub>7.90</sub>H<sub>7.92</sub>N<sub>0.30</sub>O<sub>0.02</sub>: C, 88.36; H, 7.43; N, 3.91. Found: C, 84.97; H, 7.12; N, 3.75:

<sup>70</sup>P/S resin (**1e**). 13.06 g (51%, 40–400 mesh). FTIR:  $\nu_{max}$  (cm<sup>-1</sup>) 3025, 2920, 1596, 1557, 1493, 1452, 1414; Anal. Calcd for C<sub>7.50</sub>H<sub>7.52</sub>N<sub>0.70</sub>O<sub>0.02</sub>: C, 83.59; H, 7.03; N, 9.10. Found: C, 81.13; H, 7.20; N, 7.68:

<sup>90</sup>P/S resin (**1f**). 14.10 g (55%, 40–400 mesh). FTIR:  $\nu_{max}$  (cm<sup>-1</sup>) 3025, 2920, 1596, 1557, 1414; Anal. Calcd for C<sub>7.30</sub>H<sub>7.32</sub>N<sub>0.90</sub>O<sub>0.02</sub>: C, 81.20; H, 6.83; N, 11.67. Found: C, 76.95; H, 7.39; N, 10.98:

<sup>100</sup>P/S resin (**1g**). 14.40 g (57%, 40–400 mesh). FTIR:  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3025, 2920, 1596, 1557, 1414; Anal. Calcd for C<sub>7.20</sub>H<sub>7.22</sub>N<sub>1.00</sub>O<sub>0.02</sub>: C, 80.01; H, 6.73; N, 12.96. Found: C, 74.74; H, 6/97; N, 11.99:

<sup>90</sup>P/DVB resin (**1h**). 3.85 g (51%, 40–400 mesh). FTIR:  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 3026, 2925, 1597, 1557, 1415; Anal. Calcd for C<sub>8.30</sub>H<sub>8.50</sub>N<sub>0.90</sub>O<sub>0.20</sub>: C, 80.85; H, 6.91; N, 10.16. Found: C, 74.82; H, 7.49; N, 10.92:

#### 4.3. Immobilization procedure

Each 200 mg of eight resins (1a-1h) was placed in 5 mLvial containing 50 mg of Yb(OTf)<sub>3</sub>. 4 mL of methanol/ dichloromethane (1:1) cosolvent was added to the vial. After being tightly capped, these vials were shaken for 24 h at room temperature. The resultant resins were collected in a plastic syringe equipped with a polyethylene frit and washed with methanol/dichloromethane (1:1) solvent several times, and dried under reduced pressure to give Yb(OTf)<sub>3</sub>immobilized resins (2a: 200 mg, 2b: 213 mg, 2c: 220 mg, 2d: 229 mg, 2e: 235 mg, 2f: 233 mg, 2g: 225 mg, 2h: 233 mg).

 Table 5. Nitrogen (pyridine) content (mmol/g)

4.3.1. 3-(Naphthalen-1-yl)-1-phenyl-3-phenylamino-propan-1-one (5). Compound 3 (23 mg, 0.10 mmol) and 4 (29 mg, 0.15 mmol) were added to a vial containing acetonitrile/dichloromethane (3 mL, 3:1, v/v) and 0.01 mmol of <sup>x</sup>P/S(Yb) resins (2b, 100 mg; 2c, 68 mg; 2d, 50 mg; 2e, 41 mg; 2f, 43 mg; 2g, 56 mg; 2h, 44 mg). After shaking for 1 h at room temperature, reaction mixture was filtered with a plastic syringe equipped with a polyethylene frit. The filtrate was used for HPLC analysis and purified with preparative TLC for further analysis. The filtered <sup>x</sup>P/ S(Yb) resins was washed with acetonitrile/dichloromethane (v/v=3:1) three times, and dried under reduced pressure. These recovered  ${}^{x}P/S(Yb)$  resins were reused up to six times more in the same procedure. After six-time reuse, the filtrate was used for another leaching test (as mentioned below) as well as HPLC analysis: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  3.53 (dd, J= 16.8, 8.4 Hz, 1H), 3.62 (dd, J = 16.6, 4.2 Hz, 1H), 4.80–5.20 (br s, 1H), 5.81 (dd, J=8.2, 4.2 Hz, 1H), 6.53 (dd, J=8.6, 1.0 Hz, 2H), 6.63 (tt, J = 8.0, 0.9 Hz, 1H), 7.03 (dd, J = 8.6,7.4 Hz, 2H), 7.34–7.41 (m, 3H), 7.48–7.58 (m, 3H), 7.69 (d, J = 7.2 Hz, 1H), 7.73 (d, J = 8.4 Hz, 1H), 7.85–7.90 (m, 3H), 8.19 (d, J = 8.8 Hz, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  44.9, 50.8, 114.0, 118.1, 122.3, 123.6, 125.6, 125.8, 126.5, 127.9, 128.2, 128.7, 129.1, 129.3, 130.5, 133.5, 134.1, 136.6,

**4.3.2. 4-Ethoxy-2-phenyl-1,2,3,4-tetrahydroquinoline** (7).<sup>13</sup> Compound **6** (18 mg, 0.10 mmol) and ethyl vinyl ether (29  $\mu$ L, 0.30 mmol) were used as reactants. The procedure and reaction scale was the same as the synthesis of **5**. <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.23 (t, J=7.0 Hz, 3H), 2.06 (ddd, J=12.0, 12.0, 12.0 Hz, 1H), 2.39 (ddd, J=12.4, 5.7, 2.7 Hz, 1H), 3.50–3.58 (m, 1H), 3.64–3.72 (m, 1H), 3.97 (br s, 1H), 4.51 (dd, J=11.6, 2.8 Hz, 1H), 4.80 (dd, J=10.4, 5.6 Hz, 1H), 6.49 (dd, J=8.0, 0.8 Hz, 1H), 6.72 (td, J=7.4, 1.1 Hz, 1H), 7.03 (tm, J=7.2 Hz, 1H), 7.28–7.46 (m, 6H); MS (ESI) m/z 254 [M+H]<sup>+</sup>, 208. (see Ref. 13 for <sup>13</sup>C NMR).

137.4, 198.2; HRMS (MALDI-FTMS) m/z = 35275.1514

 $[M+Na]^+$ , calcd for C<sub>25</sub>H<sub>21</sub>NONa = 374.1515.

#### 4.4. Activity and leaching tests

**4.4.1. Test I (ligand-exchange with solvent).** One millilitre of dichloromethane was added to 2 mL vial containing 20 mg of **2d**. After shaking for 30 min, the resin was collected in a plastic syringe equipped with a polyethylene frit and quickly washed with the same solvent twice, and dried under reduced pressure. A small amount of the resin was employed to obtain IR spectra. Leaching tests in methanol, acetonitrile, DMF and 10% pyridine/dichloromethane were performed in the same manner as described above.

**4.4.2. Test II (activity and ligand-exchange with substrates and products).** To a suspension of **2d** (50 mg, 0.01 mmol) and dichloromethane (2.5 mL) in a reaction vial was added **3** (23 mg, 0.10 mmol) and **4** (29 mg, 0.15 mmol).

	1b	1c	1d	1e	1f	1g	1h
Theoretical	0.92	2.79	4.65	6.49	8.30	9.25	8.36
Experimental	1.24	2.68	4.48	5.48	7.84	8.56	7.79

After shaking for 1 h, the resin was collected in a plastic syringe equipped with a polyethylene frit and quickly washed with the same solvent twice, and dried under reduced pressure. A small amount of the resin was employed to obtain IR spectra. Leaching tests in methanol, acetonitrile, methanol/ dichloromethane (1:1) and acetonitrile/dichlromethane (1:1) were performed in the same manner as described above (% Conversion was determined by HPLC).

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# Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2005.01.068.

# **References and notes**

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