ORGANIC
LETTERS

2003
Vol. 5, No. 14
2445−2447

# Poly(4-*tert*-butylstyrene) as a Soluble Polymer Support in Homogeneous Catalysis

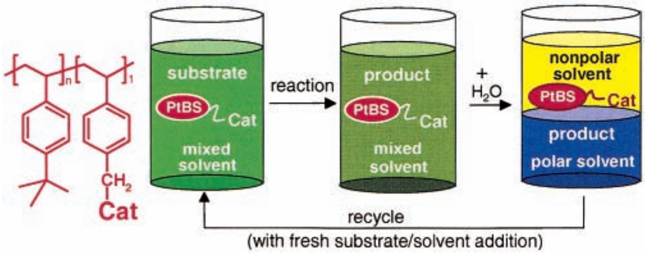
**David E. Bergbreiter* and Chunmei Li**

*Chemistry Department, Texas A&M University, P.O. Box 30012,*
*College Station, Texas 77842-3012*

*bergbreiter@tamu.edu*

**Received April 16, 2003**

## ABSTRACT



**Use of soluble poly(4-*tert*-butylstyrene) (PtBS) as a support in synthesis is demonstrated. These soluble polymers supported catalysts that were used in a monophasic medium. Subsequent separation of the catalysts after reaction was effected either by cooling- or by water-induced liquid/liquid-phase separation. Specific catalysts studied included both phosphine and DMAP nucleophilic catalysts. Low loadings of an azo dye quantified the efficiency of separation and recovery of these catalysts through multiple reaction cycles.**

Polymer supports are widely used in catalysis and synthesis. This chemistry has its origin in the solid-phase peptide synthesis strategy developed by Merrifield using cross-linked polystyrene.[1,2] Much of the subsequent work has continued to use similar insoluble polystyrene supports. However, soluble linear polymers, as well as dendrimers, are gaining increasing recognition because of their advantages in synthesis and characterization.[2−7] These soluble polymers can have the same separation advantages as insoluble supports when separation techniques such as membrane filtration, precipitation, and liquid/liquid-phase separation are used.[3] Here we describe a new type of soluble polystyrene support, poly(4-*tert*-butylstyrene), and show how catalysts on this alkylated polystyrene can be used under monophasic conditions but separated in the nonpolar phase of a biphasic solvent mixture.

Linear polystyrene has been used to support catalysts, substrates, and reagents.[2,4] It is most commonly recovered by solvent precipitation. Solvent precipitation is a general way to recover soluble polymers, but the excess solvents necessary for this process make this a less convenient and less Green procedure. Poly(4-*tert*-butylstyrene) (PtBS) is an alternative to polystyrene that can be prepared by radical polymerization of a commercial monomer. PtBS has received limited attention as a polymer support and as a component in block copolymers.[8] However, PtBS homopolymer has not generally been used as a support, presumably because it offers no advantages in separation if separation involves solvent precipitation chemistry. Here we show that the heptane solubility of PtBS makes it useful in liquid/liquid biphasic separations. PtBS and other alkylated polystyrenes are otherwise similar to PS, and such heptane solubility under biphasic separation conditions is a general strategy for separation and recovery of species bound to these polystyrene-like polymers. This possibility has also been noted by Plenio,

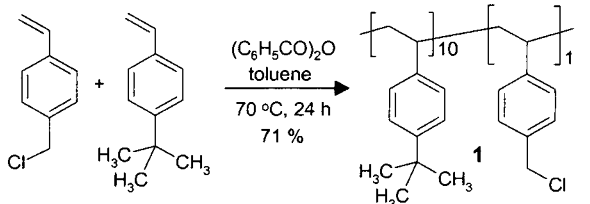
---

(1) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149.
(2) McNamara, C.; Dixon, M. J.; Bradley, M. *Chem. Rev.* **2002**, *102*, 3275−3300.
(3) Bergbreiter, D. E. *Chem. Rev.* **2002**, *102*, 3345−83.
(4) Dickerson, T. J.; Reed, N. N.; Janda, K. D. *Chem. Rev.* **2002**, *102*, 3325−3344.
(5) van Heerbeek, R.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Chem. Rev.* **2002**, *102*, 3717−3756.
(6) Toy, P. H.; Janda, K. D. *Acc. Chem. Res.* **2000**, *33*, 546−554.
(7) Vankelecom, I. F. J. *Chem. Rev.* **2002**, *102*, 3779−3810.

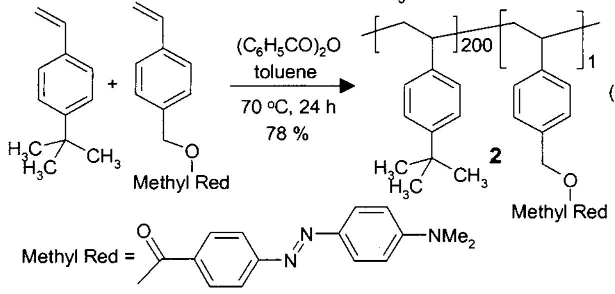
10.1021/ol034655r CCC: $25.00

who has used a cyclohexane as a solvent for a *p*-methylstyrene support.[9]

Poly(4-*tert*-butylstyrene) supports were prepared using radical copolymerization (eq 1). Chloromethyl styrene or dye-labeled polystyrene were used as comonomers.



(1)



(2)

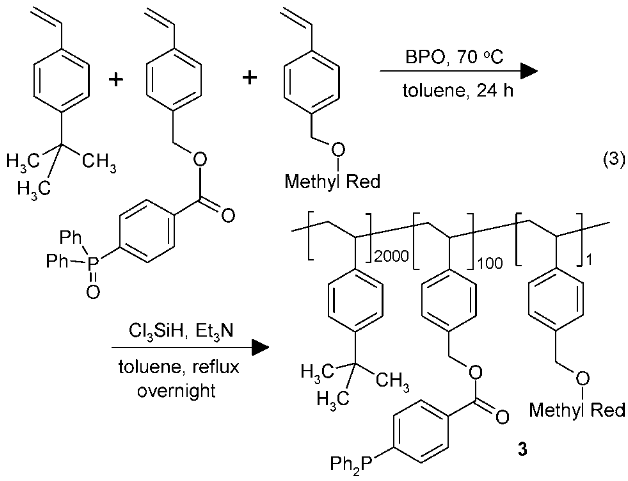
The product copolymer was isolated by solvent precipitation using methanol. In the case of the dye-labeled copolymer **2**, this solvent precipitation was quantitative on the basis of the absence of dye label in the supernatant.

Solvent precipitation can be used with PtBS, but there is no advantage to using PtBS over polystyrene if this technique is used to recover the polymer. Fortunately, two other techniques are available: thermomorphic separations of a polar/nonpolar mixed solvent system or a technique we have termed latent biphasic chemistry.[10−15] An alkylated polystyrene like poly(*tert*-butylstyrene) is more useful than polystyrene in either of these techniques. In both techniques, the reactions involving the polymer support occur in a monophasic mixture. Separation occurs in a subsequent biphasic mixture on the basis of the phase-selective solubility of an alkylated polystyrene like PtBS in heptane or cyclohexane rather than in a polar organic solvent. Thermomorphic systems use solvent mixtures that are miscible hot and biphasic cold. Latent biphasic separations use miscible solvent mixtures at the cusp of immiscibility to run a reaction.[12−15] In these cases, phase separation occurs at the end of the reaction by the addition of a small amount of another solvent or by the addition of some other perturbant. Either technique can be used with PtBS, but this paper focuses on the use of a latent biphasic system using heptane and ethanol because the nucleophile-catalyzed reactions we used were most conveniently run at room temperature.

The copolymer obtained in eq 2 was characterized by GPC. It had an $M_n$ of 23 000 Da and an $M_w$ of 48 000 Da. It was readily soluble in heptane. Moreover, this dye-labeled poly(*tert*-butylstyrene) was phase selectively soluble in heptane when another polar phase was present. Specifically, when **2** was first dissolved in heptane and then mixed with an equal volume of either DMF or 90% aqueous ethanol, a biphasic mixture formed with a yellow heptane phase. Heating either of these biphasic solutions to 70 °C produced a monophasic mixture. Cooling these thermomorphic mixtures of polymer and solvents back to room temperature reformed the biphasic solution. UV−visible spectroscopic analysis of the nonpolar and polar phases of the product biphasic mixture ($\lambda_{max}$ and the $\epsilon$ of the dye were 427 nm and 26 000, respectively) showed no detectable ($<0.5\%$) dye in the aqueous ethanol phase. The copolymer **2** was also readily separable in a latent biphasic system. The copolymer **2** dissolved in a miscible mixture (1:1, vol:vol) of heptane and EtOH. Addition of 10 vol % water produced a biphasic mixture with the dye-labeled polymer exclusively in the less polar heptane-rich phase ($>99.5\%$ selective solubility).

A cursory examination of other PtBS copolymers suggests that the separations achieved with the thermomorphic or latent biphasic strategies described above are general, though exceptions exist. For example, the catalysts described below all were successfully recovered in heptane. A copolymer formed from 4-*tert*-butylstyrene and vinyl pyridine also was selectively soluble in heptane under thermomorphic conditions using heptane−aqueous EtOH or heptane−DMF on the basis of UV−visible analysis using a dye-labeled PtBS. However, alkylated pyridinium salts of this copolymer were mainly or exclusively in the DMF (polar) phase under similar conditions.

Poly(4-*tert*-butylstyrene) copolymers containing nucleophilic catalysts or ligands can be prepared by copolymerization or by modification of **1** (eq 3).



(3)

A triarylphosphine was attached to a poly(4-*tert*-butylstyrene) support and then used to catalyze the Michael addition of

---

(8) Gravert, D. J.; Datta, A.; Wentworth, P., Jr.; Janda, K. D. *J. Am. Chem. Soc.* **1998**, *120*, 9481−9495.

(9) Datta, A.; Plenio, H. *Chem. Commun.* **2003**, in press.

(10) Bergbreiter, D. E.; Liu, Y.-S.; Osburn, P. L. *J. Am. Chem. Soc.* **1998**, *120*, 4251−4252.

(11) Bergbreiter, D. E.; Osburn, P. L.; Frels, J. D. *J. Am. Chem. Soc.* **2001**, *123*, 11105−11106.

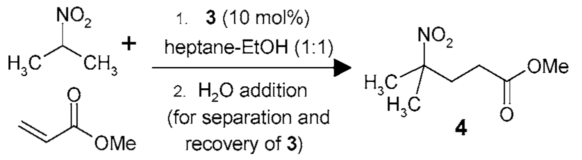
(12) Bergbreiter, D. E.; Osburn, P. L.; Smith, T.; Li, C.; Frels, J. D. *J. Am. Chem. Soc.* **2003**, *125*, 6254−6260.

(13) Deng, G.-J.; Fan, Q.-H.; Chen, X.-M.; Liu, D.-S.; Chan, A. S. C. *Chem. Commun.* **2002**, 1570−1571.

(14) Abatjoglou, A. G.; Peterson, R. R.; Bryant, D. R. *Chem. Ind.* **1996**, *68*, 133−139 described this process as phase decantation.

(15) Scurto, A. M.; Aki, S. N. V. K.; Brennecke, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 10276−10277.

2-nitropropane to methyl acrylate (eq 4). In this chemistry, the phosphine oxide was attached to the polymer and subsequently reduced to the active phosphine catalyst once the polymer was formed. The nucleophilic polymer-bound catalyst **3** also included some methyl red-labeled comonomer that served as a colorimetric tag to facilitate studies of the extent of recycling of the polymeric catalyst.

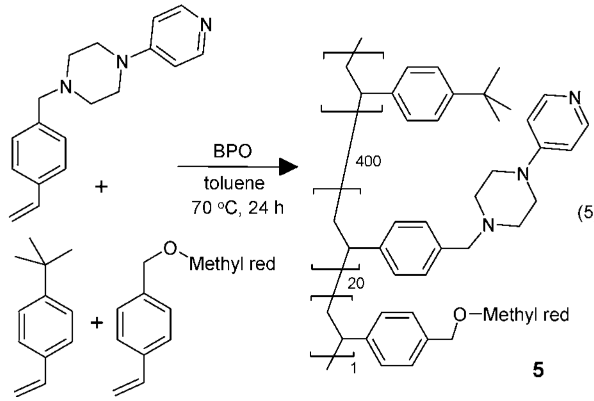


(4)

In a nucleophilic Michael reaction, the supported catalyst **3** was first dissolved in heptane. Then, an equal volume of an ethanol solution of the substrates was added. The resultant reaction occurred in a homogeneous mixture of ethanol and heptane. Unlike thermomorphic systems that we studied earlier, elevated temperatures were not required. After 24 h at 25 °C, a small amount (<10 vol %) of water was added to induce phase separation. The product was isolated from the ethanol phase. UV−visible spectroscopy showed that all the PtBS-bound catalyst was in the nonpolar heptane-rich phase, an observation that correlated with a simple visual inspection of color of the two phases of this latent biphasic system. Liquid/liquid phase separation then separated this product phase from the catalyst-containing phase. The addition of a fresh ethanol solution of nitropropane and methylacrylate to this heptane solution of the polymer-bound phosphine catalyst was all that was required for a subsequent cycle of the catalytic reaction. The isolated yields of Michael addition product **4** through the first five cycles were 31.5, 56.7, 69.0, 72.5, and 71.1%. As can be seen, the initially low yield increases with increasing cycle number. This is because the product has some solubility in heptane. Thus, the product in the first cycle only represents the product that partitions into the aqueous ethanol phase. As the cycle number increases, the heptane phase eventually gets saturated with the product and the isolated yield from the aqueous ethanol phase increases. This effect has been noted in other biphasic systems both by us and others.[16] The yields in the later cycles of this repetitive reaction were similar to those seen if the same reaction were catalyzed by triphenylphosphine.[17]

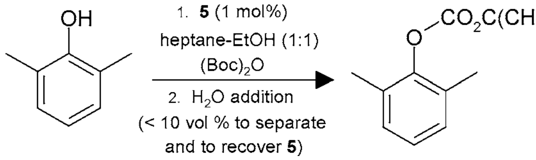
A second nucleophilic catalyst supported by PtBS is the polymer-bound (dimethylamino)pyridine analogue we supported earlier on poly(*N*-alkylacrylamide)s. The synthesis of this polymer-bound catalyst is shown in eq 5.

This second example of a nucleophilic catalyst (**5**) was used to catalyze formation of a t-Boc derivative of 2,6-dimethylphenol (eq 6). In this case, the extent of recovery of the catalyst and the yields of product were directly comparable to those seen with the thermomorphic systems we described earlier.[18] The isolated yield for the first five cycles of this reaction were 34.3, 60.9, 82.2, 94.6, and 99%. As was true in thermomorphic systems or in the latent biphasic chemistry with **5** described above, partitioning of product into the nonpolar heptane phase produced lower isolated yields of product in the early cycles. In this case, we reused catalyst **5** through 20 cycles.



(5)

Isolation and recycling of the catalyst was achieved using the procedures described above for the phosphine catalyst. Yields after the first few cycles were essentially quantitative (ca. 93% average for each of 20 cycles). Separation of the polymer from the aqueous ethanol phase was quantitative as judged by either visual observation or UV−visible spectroscopic analysis.



(6)

To summarize, poly(4-*tert*-butylstyrene) copolymers are effective soluble polymer supports that can readily be recycled as heptane solutions after their use in a homogeneous reaction using liquid/liquid biphasic separations. While some copolymers (e.g., copolymers with alkylpyridinium groups) are not selectively soluble in alkane solvents, ongoing work in our group will address this through the synthesis of even more lipophilic alkylated polystyrene derivatives.

**Acknowledgment.** Support of this work by the R. A. Welch Foundation, the National Science Foundation (CHE-0010103), and ArQule is gratefully acknowledged. We thank Professor Plenio of Darmstadt University for sharing with us some of his group's preliminary work on novel transition metal catalysts supported on linear poly(4-methylstyrene).

**Supporting Information Available:** Procedures for the synthesis of the chloro-methylstyrene-c-poly(4-*tert*-butylstyrene) copolymer, catalyst **3**, and catalyst **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL034655R

---

[16] Kollhofer, A.; Plenio, H. *Chem. Eur. J.* **2003**, *9*, 1416−1425.

[17] White, D. A.; Baizer, M. M. *Tetrahedron Lett.* **1973**, *37*, 3597−3600.

[18] Bergbreiter, D. E.; Osburn, P. L.; Li, C. *Org. Lett.* **2002**, *4*, 737−740.