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Polystyryl-supported TBD as an efficient and reusable catalyst under solvent-free conditions

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Received (in Corvallis, OR, USA) 30th June 2004, Accepted 10th September 2004
First published as an Advance Article on the web 19th October 2004

Polystyryl supported-TBD (PSTBD) is an efficient and reusable heterogeneous basic catalyst under solvent-free conditions for a variety of organic transformations such as 1,2-epoxide ring-opening, aldol-type condensation and Michael addition.

Currently, one of the most urgent challenges for organic chemists is the definition of more economically-advantageous and environmentally-friendly processes. To realize this goal, a central role is played by the use of: a) organic catalysts,[1] b) polymer-supported catalysts and/or reagents,[2] c) alternative reaction media.[3–5] For many years we have contributed in this field by focusing our research on the use of water[4] as reaction medium and on solvent-free conditions (SFC)[5] and on the definition of one-pot protocols to reduce the cost and the environmental impact of organic processes.[4,5b]

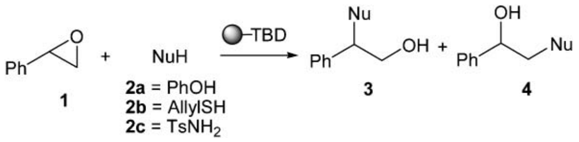
Much work has been done on the use of an organic catalyst both in organic solvent and SFC, and on the use of polymer-supported catalysts in organic media (dichloromethane or dimethylformamide, which are not green solvents).[2] Anchored catalysts have generally shown a lower efficiency which strongly depends on the swelling ability of the solvent employed as medium influencing reagents' accessibility to reactive sites.[2] To solve this problem the construction of flow-through reactors has been proposed.[6] For reaction under vapour phase another solution lies in the use of polymer-supported catalysts under continuous sCO_2- or vapour-flow conditions.[7] We are not aware of organic processes performed by employing a polystyryl-supported catalyst under SFC.

We hold that the use of an organic supported catalyst (metal-free, recoverable and reusable) under SFC (where an increased reactivity is achieved due to the intimacy of the reagents) is a new strategy to develop a chemically efficient, economical and environmentally-friendly organic chemistry. To demonstrate this idea we report in this communication the study of a series of fundamental chemical transformations such as: nucleophilic ring-opening of 1,2-epoxides, aldol and Knovenagel condensations, and Michael addition by using a catalytic amount of commercially available polystyryl-supported 1,5,7-triazabicyclo[4.4.0]dec-5-ene (PSTBD) under SFC together with the recovery and reuse of the catalyst.

The results of nucleophilic ring-opening of styrene oxide (**1**) by phenol (**2a**), allylthiol (**2b**), and *p*-toluensulfonamide (**2c**), using 5–10 mol% of PSTBD under SFC and those obtained in MeCN as a highly compatible solvent for the PSTBD swelling[8] are illustrated in Table 1. In all cases after the time required for the complete conversion under SFC, only small amounts of products were formed in MeCN. In DCM which is a less efficient swelling solvent[8] no reaction at all was observed.

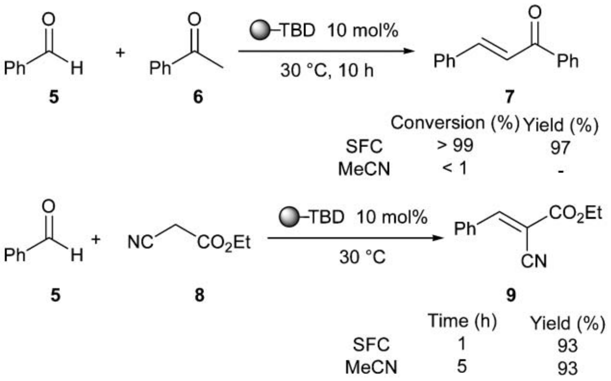
Benzaldehyde (**5**) (Scheme 1) reacted with acetophenone (**6**) at 30 °C and in the presence of 10 mol% of PSTBD to give the corresponding (*E*)-benzylidene benzophenone (**7**) in 97% yield after 10 h. No conversion at all was observed when the reaction was performed in MeCN. The significantly improved efficiency under SFC was confirmed when benzaldehyde (**5**) reacted with ethyl cyanoacetate (**8**). At 30 °C and in the presence of 10 mol% of PSTBD, it gave in 1 h the corresponding Knoevenagel condensation product **9** in 93% yield. In MeCN 5 h were needed to achieve the same yield.

Table 1 PSTBD-catalysed ring-opening of styrene oxide (**1**)



Exp	NuH/PSTBD (%)/M[a]	*T* (°C)	*t* (h)	C (%)[a]	**3/4**	Y (%)[a]
1	**2a**/10/SFC	80	24	>99	65/35	95
2	**2a**/10/MeCN	80	24	22	65/35	—
3	**2b**/5/SFC	30	0.5	>99	22/78	88
4	**2b**/5/MeCN	30	0.5	10	22/78	—
5	**2c**/10/SFC	80	10	>99	20/80	98[b]
6	**2c**/10/MeCN	80	10	10	20/80	—

[a] M = Reaction medium; C = Conversion (determined by GLC analysis); Y = Yield of the isolated products. [b] 17% of **3**, 68% of **4**, and 13% of bisadduct coming from double attack at β-position was also formed.

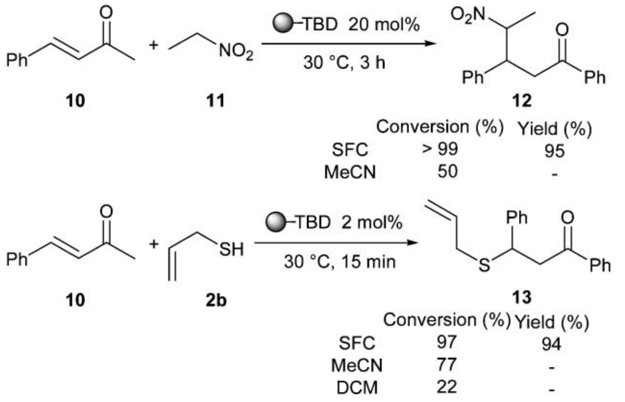


Scheme 1 PSTBD-catalysed condensations of benzaldehyde (**5**).

Similar results were obtained in the Michael reaction of (*E*)-benzylidene acetone (**10**) with nitroethane (**11**) (Scheme 2).† While in only 3 h the complete conversion to γ-nitroketone **12** was obtained under SFC, only 50% of this product was formed in MeCN. Allylthiol (**2b**) reacted with **10** in only 15 min under SFC by using 2 mol% of PSTBD at 30 °C to give β-allylthio-ketone **13** (Scheme 2). In MeCN after the same reaction time a 77% conversion was reached while in DCM only 22% of **13** was formed. Also in this case the reaction medium dramatically influenced the reactivity and SFC are showed again to be the most efficient conditions for promoting the reaction.

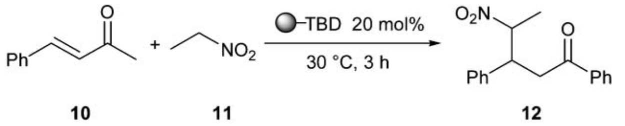
It is noteworthy that the same reactions performed under SFC by using non-supported base (TBD) gave closely comparable results both in terms of reaction times and isolated yields of products proving that under SFC the anchoring of TBD to the

DOI: 10.1039/b409808k



Scheme 2 PSTBD-catalysed additions on (*E*)-benzylidene acetone (**10**).

Table 2 Reuse of recovered PSTBD in the Michael addition of (*E*)-benzylidene acetone (**10**) with nitroethane (**11**)



Entry	Conversion (%)	Yield (%)
1	>99	95
2	97	95
3	98	95
4	90	88
5	>99[a]	95

[a] after PSTBD regeneration.

polymeric support did not result in a significant drop of the catalytic efficiency, as it usually happens in organic solvents.[2b]

The recovery and reuse of PSTBD is illustrated for the reaction of (*E*)-benzylidene acetone (**10**) with nitroethane (**11**) (Table 2). After the first run ethyl acetate was added to the reaction mixture and the catalyst was recovered by filtration and then reused. After 4 runs only a slight deceleration effect was observed. A complete reactivation of PSTBD was performed by washing the recovered material with aqueous ammonia solution. After this treatment in the fifth run the same efficiency as in the first run was again obtained.

In conclusion SFC, with respect to organic reaction media, has proved to significantly improve the efficiency of PSTBD in a variety of general organic transformations.

The approach here presented represents a novel use of polymer-supported organic catalysts and we believe that this strategy would be profitably applied to the development of continuous flow reactors, avoiding the use of solvent to isolate the products.

The Ministero dell'Istruzione dell'Università e della Ricerca (MIUR) and the Università degli studi di Perugia are thanked for financial support within the funding projects: COFIN, COFIN-LAB (CEMIN) and FIRB 2001.

Notes and references

† Typical experimental procedure for the reaction of **10** with **11** under SFC: a vial equipped with a magnetic stirrer was charged with PSTBD (75 mg, ~0.2 mmol (8.0–8.5 N/g)) and then (*E*)-benzylidene acetone (**10**) (146 mg, 1.0 mmol) and nitroethane (**11**) (79 mg, 1.05 mmol) were consecutively added. The reaction mixture was left under stirring in air atmosphere at 30 °C. After 3 h ethyl acetate was added and the heterogeneous mixture was left under stirring for additional 30 min and then solid PSTBD was separated by Büchner filtration from the organic layer, washed with additional ethyl acetate, dried under vacuum and reused. The organic layer was evaporated under reduced pressure to give the corresponding γ-nitroketone **12** in 95% yield in >98% purity.Reactions in organic solvents were performed by using 2.0 mL of MeCN or DCM.

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