Available online at www.sciencedirect.com

SCIENCE DIRECT®

Tetrahedron Letters 45 (2004) 5865–5867

Tetrahedron Letters

Poly(ethyleneglycol) (PEG): a rapid and recyclable reaction medium for the DABCO-catalyzed Baylis–Hillman reaction

S. Chandrasekhar,* Ch. Narsihmulu, B. Saritha and S. Shameem Sultana

Indian Institute of Chemical Technology, Hyderabad 500 007, India

Received 16 April 2004; revised 18 May 2004; accepted 28 May 2004

Abstract—PEG (400) has been used as a rapid and recyclable reaction medium for the Baylis–Hillman reaction with the conventional basic catalyst DABCO (20 mol %) with very good yields of products. Recyclability is achieved with no further addition of DABCO to the reaction medium over four runs without substantial loss in yields. Incidentally, DABCO is recycled for the first time in this transformation.

© 2004 Elsevier Ltd. All rights reserved.

The Baylis–Hillman reaction[1] is one of the very few reactions wherein atom economy[2] is perfectly preserved. Also this reaction results in a new C–C bond between an aldehyde and the α-carbon of an electron deficient olefin generating multifunctional building blocks for further synthetic manipulation.[3] Unfortunately, however, the applications and usefulness of this reaction in several cases are hampered by low yields, high concentration of catalyst and long reaction times (sometimes up to a week for less than 50% conversion). Also the reaction is generally inert to enones, α,β-substituted aldehydes and hindered aldehydes. To overcome these problems, several modifications have been attempted including new catalysts,[4] novel solvent media such as supercritical CO_2,[5] ionic liquids,[6] polar solvents,[7] ultrasound,[8] high pressure,[9] etc. Of all these methods, the ionic liquid medium is the only protocol which allows recycling of the solvent. However, recent findings have revealed that ionic liquids under the influence of a mild base like DABCO participate in a side reaction.[10] Also, the most ecofriendly solvent is not compatible with water, acrylates, which undergo hydrolysis in the presence of base. Thus, further methodologies are necessary to overcome these drawbacks. We recently found that poly(ethyleneglycol) is an efficient, recyclable reaction medium for the Heck reaction, catalytic hydrogenations and asymmetric dihydroxylation reactions.[11] Herein we report for the first time, poly(ethyleneglycol) (400) as a recyclable solvent medium for the rapid Baylis–Hillman reaction between unreactive aldehydes and activated olefins.

Our initial experiment was carried out between benzaldehyde (Table 1, entry 1) (2 mmol), ethyl acrylate (3 mmol) and DABCO (20 mol %) in poly(ethyleneglycol) (400 MW) at room temperature. To our surprise the reaction was found to be complete within 2 h and the product was isolated by extraction with ether (5 × 10 mL) (Scheme 1). Evaporation of the solvent and purification of the crude product by column chromatography yielded the required product in 92% yield; this represents an improvement on earlier methods with respect to reaction time, concentration of catalyst and increased yields. The reactivity of benzaldehyde with other activated olefins was also investigated. Treatment with acrylonitrile (entry 2) or methyl vinyl ketone (entry 3) and 20 mol % DABCO in PEG gave similar results with respect to time and yield (see Table 1).

4-Nitrobenzaldehyde (entries 4 and 5) reacted with ethyl acrylate and acrylonitrile resulting in the corresponding products in 96% and 93% yields after 2 h. 4-Fluorobenzaldehyde (entry 6) showed much faster reactivity in PEG forming the required product in 89% yield in 4 h, whereas the same reaction took over 60 h using trimethylamine.[7] The other aromatic and heteroaromatic aldehydes, 2-chloro-5-nitrobenzaldehyde (entry 7), 2-furaldehyde (entries 9 and 10) and 2-thiophenecarboxaldehyde (entry 11) showed the same consistency in

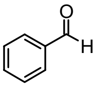
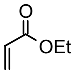
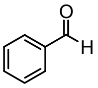
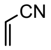
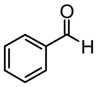
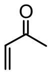
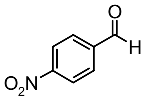
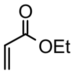
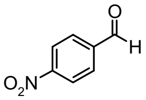
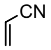
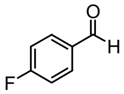
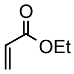
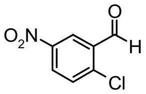
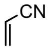
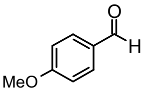
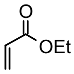
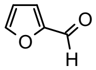
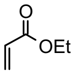
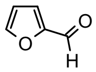
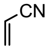
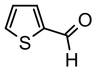
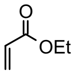
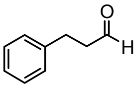
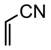
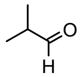
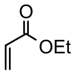
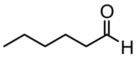
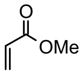
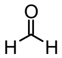
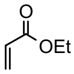
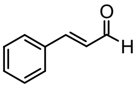
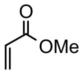
---

Keywords: PEG; DABCO; Baylis–Hillman reaction; Recyclability.

* Corresponding author. Tel.: +91-40-7193434; fax: +91-40-27160512; e-mail: srivaric@iict.res.in

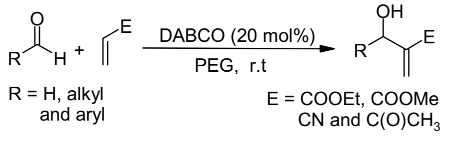
0040-4039/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2004.05.153

Table 1. DABCO-catalyzed Baylis–Hillman reaction in PEG

Entry	Aldehyde	Activated olefin	Time (h)	Yield (%)[a]
1			2.0	92
2			1.5	94
3			3.0	89
4			2.0	96
5			2.0	93
6			4.0	89
7			1.5	94
8			3.0	40
9			3.0	91
10			2.5	91
11			3.0	90
12			5.0	75
13			4.0	86
14			4.5	80
15			4.0	72
16			4.0	65

[a] Isolated yields. Products were characterized by ^{1}H NMR and mass spectroscopy.

faster reactivity and very good product yields. However, the yield was dramatically reduced for the reaction between the electron-rich aldehyde, 4-methoxybenzaldehyde (entry 8) and ethyl acrylate (Table 1).



Scheme 1.

Table 2. Reusability of PEG and DABCO for the Baylis–Hillman reaction between 4-nitrobenzaldehyde and ethyl acrylate

Run	1	2	3	4
Time (h)	2	6	16	24
Isolated yield (%)	96	92	95	89

The same trend of acceleration was also observed in the reactivity of aliphatic aldehydes. 3-Phenylpropanal (entry 12), isobutyraldehyde (entry 13) and hexanal (entry 14) underwent the Baylis–Hillman reaction with activated olefins in PEG resulting in 75%, 86% and 80% yields, respectively. To check the efficiency of the transformation, formaldehyde (entry 15) and *trans*-cinnamaldehyde (entry 16) were also subjected to the Baylis–Hillman reaction with acrylates in PEG to provide good yields of the desired products.

The recyclability of the reaction was investigated and revealed the important observation that no additional catalyst was required for subsequent runs. After completion of the reaction between 4-nitrobenzaldehyde, ethyl acrylate and DABCO (20 mol %), the reaction mixture was extracted with ether (5 × 10 mL), concentrated in vacuo and purified by column chromatography to give the product in 96% yield. For the next run, the reactants were added and stirred without adding DABCO. The reaction was complete in 6 h affording the product in an excellent 92% yield. The third and fourth runs were repeated without addition of catalyst, however, on these occasions extended reaction times were necessary (see Table 2).

In conclusion, this communication describes for the first time, the Baylis–Hillman reaction in (PEG), a recyclable solvent medium. Also DABCO was found to be recycled efficiently over four runs.

Acknowledgements

C.N., B.S. and S.S.S. thank CSIR, New Delhi for financial support. IICT Communication No.: 030514.

References and notes

1. (a) Baylis, A. B.; Hillman, M. E. D. German Patent 2,155,113, 1972; *Chem. Abstr.* **1972**, *77*, 34174q; (b) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653; (c) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001; (d) Langer, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 3049.
2. Trost, B. M. *Science* **1991**, *254*, 1471.
3. Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811.
4. (a) Aggarwal, V. K.; Mereu, A. *Chem. Commun.* **1999**, 2311; (b) Rezgui, F.; El Gaied, M. M. *Tetrahedron Lett.* **1998**, *39*, 5965; (c) Kawamura, M.; Kobayashi, S. *Tetrahedron Lett.* **1999**, *40*, 1539; (d) Basavaiah, D.; Krishnamacaryulu, M.; Rao, A. J. *Synth. Commun.* **2000**, *30*, 2061; (e) Leadbeater, N. E.; Van der Pol, C. J. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2831; (f) Shi, M.; Jiang, J.-K.; Li, C.-Q. *Tetrahedron Lett.* **2002**, *43*, 127.
5. Rose, P. M.; Clifford, A. A.; Rayner, C. M. *Chem. Commun.* **2002**, 968.
6. Rosa, J. N.; Afonso, A. M.; Santos, A. G. *Tetrahedron* **2001**, *57*, 4189.
7. (a) Auge, J.; Lubin; Lubineau, A. *Tetrahedron Lett.* **1994**, *35*, 7947; (b) Yu, C.; Liu, B.; Hu, L. *J. Org. Chem.* **2001**, *66*, 5413; (c) Aggarwal, V. K.; Dean, D. K.; Mereu, A.; Williams, R. *J. Org. Chem.* **2002**, *67*, 510; (d) Cai, J.; Zhou, Z.; Zhao, G.; Tang, C. *Org. Lett.* **2002**, *4*, 4723.
8. Coelho, F.; Almeida, W. P.; Veronese, D.; Mateus, C. R.; Lopes, E. C. S.; Rossi, R. C.; Silvera, G. P. C.; Pavam, C. H. *Tetrahedron* **2002**, *58*, 7437.
9. (a) Hill, J. S.; Isaacs, N. S. *Tetrahedron Lett.* **1986**, *27*, 5007; (b) Nolte, R. J.; Scheeren, H. W. *Tetrahedron* **1996**, *52*, 8307; (c) Hayashi, Y.; Okado, K.; Ashimine, I.; Shoji, M. *Tetrahedron Lett.* **2002**, *43*, 8683.
10. Aggarwal, V. K.; Emme, I.; Mereu, A. *Chem. Commun.* **2002**, 1612.
11. (a) Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S. S.; Reddy, N. R. K. *Org. Lett.* **2002**, *4*, 4399; (b) Chandrasekhar, S.; Narsihmulu, Ch.; Sultana, S. S.; Reddy, N. R. K. *Chem. Commun.* **2002**, 1716; (c) Chandrasekhar, S.; Narsihmulu, Ch.; Chandrasekhar, G.; Shyamsunder, T. *Tetrahedron Lett.* **2004**, *45*, 2421; (d) Chandrasekhar, S.; Shyamsunder, T.; Chandrasekhar, G.; Narsihmulu, Ch. *Synlett* **2004**, 522.