Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

# Molecular Iodine in Ionic Liquid: A Green Catalytic System for Esterification and Transesterification

Yiming Ren [a] & Chun Cai [a]

[a] Chemical Engineering College, Nanjing University of Science and Technology, Nanjing, China

Version of record first published: 06 May 2010

To cite this article: Yiming Ren & Chun Cai (2010): Molecular Iodine in Ionic Liquid: A Green Catalytic System for Esterification and Transesterification, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 40:11, 1670-1676

To link to this article: http://dx.doi.org/10.1080/00397910903161660

*Synthetic Communications*®, 40: 1670–1676, 2010
Copyright © Taylor & Francis Group, LLC
ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910903161660

# MOLECULAR IODINE IN IONIC LIQUID: A GREEN CATALYTIC SYSTEM FOR ESTERIFICATION AND TRANSESTERIFICATION

**Yiming Ren and Chun Cai**
*Chemical Engineering College, Nanjing University of Science and Technology, Nanjing, China*

***Esterification of carboxylic acids and transesterification of β-ketoesters with alcohols have been developed using a catalytic amount of iodine in polyethylene glycol (PEG) ionic liquid (IL 1000) to afford the corresponding esters in good yields. By simple separation of the ionic-liquid phase containing the iodine, the system of $I_2$/IL 1000 can be reused several times.***

***Keywords***: Esterification; ionic liquid; molecular iodine; transesterification

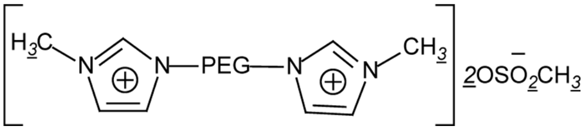
## INTRODUCTION

Esterification of carboxylic acids and transesterification of esters with alcohols play important roles in the production of organic esters, especially for some important products and intermediates in the laboratory and industry.[1–3] In addition, the esterification of carboxylic acids is a common and useful method for protecting carboxyl groups.[4,5] A number of procedures catalyzed by a variety of protic acids,[6,7] Lewis acids,[8,9] solid catalysts,[10,11] ionic liquids (ILs),[12,13] and enzymes[14] have been reported in the literature. However, many of these catalysts are expensive, difficult to prepare, toxic, and unsuitable for acid-sensitive functional groups or require longer reaction times and large amounts of solid supports, which would eventually result in the generation of a large amount of toxic waste.

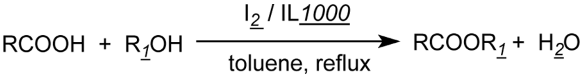
Recently, the use of molecular iodine has drawn considerable attention because it is an inexpensive, nontoxic, readily available catalyst for various organic transformations that affords the corresponding products in excellent yields with high selectivity. The mild Lewis acidity associated with iodine enhances its use in organic synthesis for several organic transformations that use stoichiometric levels to catalytic amounts. Owing to numerous advantages associated with this ecofriendly element, iodine has been explored as a powerful catalyst for various organic transformations.[15–22] Previously, molecular iodine had been explored as a powerful catalyst for esterification and transesterification reaction with good yields.[23–27] However, the reuse of iodine is difficult because it has good solubility in most organic solvents and

Received March 30, 2009.

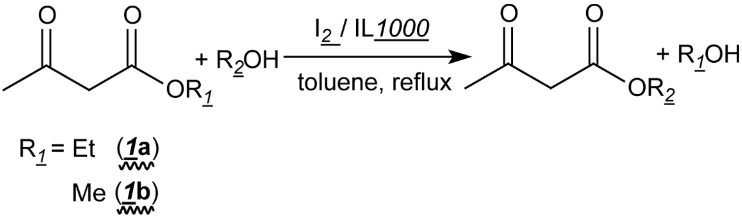
Address correspondence to Chun Cai, Chemical Engineering College, Nanjing University of Science and Technology, Nanjing 210094, China. E-mail: c.cai@mail.njust.edu.cn



Scheme 1. PEG ionic liquids.



Scheme 2. Iodine-catalyzed esterification in IL 1000.



Scheme 3. Iodine-catalyzed transesterification in IL 1000.

easy sublimation at high temperature. Recently, we reported a facile method for recovery and reuse of iodine by polyethylene glycol (PEG) ionic liquid.[28] The PEG ILs (Scheme 1) and toluene have the advantages of both homogeneous and heterogeneous phases at different temperatures (biphasic conditions at lower temperatures and monophasic at higher temperatures) with the ease of product as well as catalyst separation. Here, we report our successful approach for transesterification and direct esterification using a catalytic amount of iodine in the PEG IL (Schemes 2 and 3).

## RESULTS AND DISCUSSION

First, the reaction of acrylic with methanol was explored to search for the optimal conditions, such as the amount of catalysts and the reaction temperature (Table 1). The reaction temperature had a great influence on the reaction. A poor yield was obtained when the reaction proceeded at room temperature (Table 1, entry 1). Increasing the reaction temperature could remarkably enhance both reaction yield and rate, perhaps because the IL and toluene formed a homogeneous phase at high temperature. The results showed that an appreciable amount of $I_2$ was 3 mol% to acrylic (Table 1, entry 7). A longer reaction time was necessary and less yield was obtained with less $I_2$. An increase in the amount of $I_2$ did not lead to an improvement in yield (Table 1, entry 6). However, in the absence of iodine, few products were synthesized (Table 1, entry 10). The reaction was also explored in several PEG ILs (Table 1, entry 7); the results showed that all the PEG ILs had good yields for the reaction. However, IL 1000 and toluene have both homogeneous and heterogeneous phases at different temperatures, and the system of IL 1000/toluene change to two phases is faster than other PEG ionic liquids system at room temperature.

**Table 1.** Studies on the reaction of acrylic with methanol in IL 1000

| Entry | $I_2$ (mol%) | T (°C) | Yield (%)[a] |
|---|---|---|---|
| 1 | 3 | r.t. | 12 |
| 2 | 3 | 70 | 51 |
| 3 | 3 | 80 | 59 |
| 4 | 3 | 90 | 72 |
| 5 | 3 | 100 | 83 |
| 6 | 4 | 110 | 91 |
| 7[b] | 3 | 110 | 90, 89, 87, 85<br>88[c]<br>90[d]<br>89[e] |
| 8 | 2 | 110 | 73 |
| 9 | 1 | 110 | 44 |
| 10 | 0 | 110 | Trace |

[a] Isolated yields.
[b] The system of $I_2$/IL 1000 was run for four consecutive cycles.
[c] IL 400 was used.
[d] IL 2000 was used.
[e] IL 4000 was used.

Under the optimized reaction conditions, we investigated the reaction of carboxylic acids with various alcohols (Table 2). Both aromatic and aliphatic alcohols reacted efficiently with carboxylic acids promoted by $I_2$ in IL 1000. Table 2 shows how the aromatic alcohols, with different substituents such as chloro, nitro, methoxy, and methyl, were converted to the corresponding esters in excellent yields. However, aromatic alcohols with electron-donating groups gave the corresponding

**Table 2.** Direct esterification of carboxylic acids with alcohols using iodine as catalyst in IL 1000[a]

| Entry | Carboxylic acid | Alcohol | Yield (%)[b] |
|---|---|---|---|
| 1 | $CH_3COOH$ | $C_6H_5CH_2OH$ | 85 |
| 2 | $CH_3COOH$ | 2-$MeC_6H_4CH_2OH$ | 91 |
| 3 | $CH_3COOH$ | 4-$MeOC_6H_4CH_2OH$ | 92 |
| 4 | $CH_3COOH$ | 2-$ClC_6H_4CH_2OH$ | 82 |
| 5 | $CH_3COOH$ | 3-$NO_2C_6H_4CH_2OH$ | 80 |
| 6 | $CH_3COOH$ | $(CH_3)_2CHOH$ | 90 |
| 7 | $CH_3COOH$ | $CH_3OH$ | 92 |
| 8 | $CH_3COOH$ | *c*-$C_6H_{11}OH$ | 90 |
| 9 | $CH_3COOH$ | *n*-$C_4H_9OH$ | 94 |
| 10 | $CH_3COOH$ | *t*-$C_4H_9OH$ | 61 |
| 11 | *n*-$C_{10}H_{21}COOH$ | $CH_3OH$ | 91 |
| 12 | $C_2H_5COOH$ | *n*-$C_9H_{19}OH$ | 93 |
| 13 | $C_2H_5COOH$ | $(CH_3)_2CHOH$ | 90 |
| 14 | *n*-$C_8H_{17}COOH$ | $CH_3OH$ | 91 |
| 15 | $C_6H_5COOH$ | $CH_3OH$ | Trace |
| 16 | 4-$NO_2C_6H_4COOH$ | $CH_3OH$ | Trace |

[a] All reactions were carried out with 3 mol% of iodine in refluxing toluene for 6 h.
[b] Isolated yields.

**Table 3.** Transesterification of β-ketoesters with alcohols using iodine as catalyst in IL 1000[a]

| Entry | β-Ketoester | Alcohol | Yield (%)[b] |
|---|---|---|---|
| 1 | **1a** | $n$-$C_3H_7OH$ | 70 |
| 2 | **1a** | $(CH_3)_2CHOH$ | 68 |
| 3 | **1a** | $n$-$C_4H_9OH$ | 80 |
| 4 | **1a** | $s$-$C_4H_9OH$ | 76 |
| 5 | **1a** | $t$-$C_4H_9OH$ | 51 |
| 6 | **1a** | $c$-$C_6H_{11}OH$ | 71 |
| 7 | **1a** | $n$-$C_8H_{17}OH$ | 80 |
| 8 | **1a** | $C_6H_5CH_2OH$ | 75 |
| 9 | **1b** | $n$-$C_4H_9OH$ | 81 |
| 10 | **1b** | $t$-$C_4H_9OH$ | 53 |
| 11 | **1b** | $c$-$C_6H_{11}OH$ | 70 |
| 12 | **1b** | $C_6H_5CH_2OH$ | 72 |

[a] All reactions were carried out with 3 mol% of iodine in refluxing toluene for 6 h.
[b] Isolated yields.

products in better yields than those with electron-withdrawing groups. The reaction of *t*-BuOH under the same conditions gave only the corresponding ester in moderate yield (Table 2, entry 10). We next examine the transesterification of β-ketoesters with various alcohols with $I_2$/IL 1000 (Table 3). Table 3 showed that the various β-ketoesters were gained in good yields. Similarly, the reaction of *t*-BuOH under the same conditions gave only the corresponding esters in moderate yields because of the steric hindrance of *t*-BuOH (Table 3, entries 5 and 10). However, in cases where a carboxylic acid group is directly attached to an aromatic ring, such as benzoic acid (Table 2, entries 15 and 16), there was almost no reaction.

The recycling performance of iodine in the IL 1000 was investigated in the reaction of acrylic acid and methanol. The data listed in Table 1 showed that $I_2$/IL 1000 could be reused four times with satisfying results.

In conclusion, we have developed a simple, inexpensive, and effective method for the esterification and transesterification using a catalytic amount of iodine in IL. The advantages of the present reaction are the elimination of metals and toxic reagents, operational simplicity, and good yields of products. Moreover, the simple experimental procedure, combined with ease of recovery and reuse of iodine, is expected to contribute to the development of a green strategy for the other iodine-catalyzed reaction. Further studies on the reuse of iodine are now in progress.

## EXPERIMENTAL

Infrared (IR) spectra were recorded on a Bomem MB154S infrared analyzer. $^1H$ NMR were recorded with Bruker Advance RX300. Electrospray ionization–mass spectrometry (ESI-MS) results were recorded on a Themo Finningan Trace TSQ. Reagents were obtained from commercial sources. Commercially available reagents were used without further purification. Products are all known compounds and were identified by comparing of their physical and spectra data with those reported in the literature.

## Typical Procedure for the Synthesis of IL 1000

Methylsulfonyl chloride (10 mL) was added to a solution of PEG 1000 (60 mmol) and triethylamine (120 mmol) in toluene (200 mL) within 30 min under a nitrogen atmosphere. The mixture was stirred at room temperature. After 3 h, the mixture was filtered. The filtrate was added to 1-methylimidazol (120 mmol), and the mixture was stirred at 86 °C for 17 h. After the reaction, the IL layer was separated and washed with petroleum ether (3 × 10 mL). Evaporation of solvent under reduced pressure gave the desired pure product IL 1000 in 80% yield. $^1$H NMR (500 MHz, $CDCl_3$, δ): 2.85 (s, 6H, $2OSO_2CH_3$), 3.70–3.76 [m, 97H, $(OCH_2CH_2)_n$], 3.82 (s, 6H, $2NCH_3$), 7.52 (s, 2H, 2CH), 7.59 (s, 2H, 2CH), 8.81 (s, 2H, 2CH); ESI-MS: 448.17, $M^{++}/2$, n = 16), 470.20, $M^{++}/2$, n = 17, 492.20, $M^{++}/2$, n = 18, 514.27, $M^{++}/2$, n = 19, 558.27, $M^{++}/2$, n = 21, 580.30, $M^{++}/2$, n = 22, 602.33, $M^{++}/2$, n = 23, 624.36, $M^{++}/2$, n = 24, 646.36, $M^{++}/2$, n = 25, 668.37, $M^{++}/2$, n = 26, 690.43, $M^{++}/2$, n = 27, 712.43, $M^{++}/2$, n = 28, 153.07 (100); IR (KBr, $cm^{-1}$): 3447, 3153, 2985, 1447, 1352, 1205, 1117, 1060, 858, 587.

## General Procedure for Esterification

$I_2$ (0.06 mmol) was added to a solution of carboxylic acid (2 mmol), alcohol (1 mL), and toluene (1.5 mL) in IL 1000 (1 mL). The mixture was refluxed for the specified time and monitored by thin-layer chromatography (TLC). After the reaction, the mixture was cooled to room temperature, and the upper toluene containing the expected product was separated by decantation. The toluene was evaporated, and the pure products were obtained via purification through column chromatography. The bottom phase was the IL containing the iodine and the produced water. The system of $I_2$/IL 1000 was reused after removal of the water under reduced pressure.

## General Procedure for Transesterification

$I_2$ (0.06 mmol) was added to a solution of β-ketoester (2 mmol), alcohol (2.5 mmol), and toluene (1.5 mL) in IL 1000 (1 mL). The mixture was refluxed for the specified time and monitored by TLC or gas chromatography (GC). After the reaction, the mixture was cooled to room temperature, and the upper toluene containing the expected product was separated by decantation. The toluene was evaporated, and the pure products were obtained via purification through column chromatography. The bottom phase was the IL containing the iodine. The system of $I_2$/IL 1000 was reused in subsequent runs without further purification.

## REFERENCES

1. Otera, J. *Esterification*; Wiley-VCH: Weinheim, 2003.
2. Otera, J. Esterification. *Chem. Rev.* **1993**, *93*, 1449–1470.
3. Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; VCH: New York, 1999; pp. 1932–1941.

4. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley: New York, 1999; pp. 269–453.
5. Haslam, E. Recent developments in methods for the esterification and protection of the carboxyl group. *Tetrahedron* **1980**, *36*, 2409.
6. Rehberg, C. E.; Fischer, C. H. Preparation and properties of the n-alkyl acrylates. *J. Am. Chem. Soc.* **1944**, *66*, 1203.
7. Wang, B.; Ming, Y. L.; Shuan, S. J. Ionic liquid-regulated sulfamic acid: Chemoselective catalyst for the transesterification of β-ketoesters. *Tetrahedron Lett.* **2003**, *44*, 5037.
8. Ranu, B. C.; Dutta, P.; Sarkar, A. A simple and efficient procedure for transesterification catalyzed by indium triiodide. *J. Org. Chem.* **1998**, *63*, 6027.
9. Barbosa, S. L.; Dabdoub, M. J.; Hurtado, G. R.; Klein, S. I.; Baroni, A. C. M.; Cunha, C. Solvent-free esterification reactions using Lewis acids in solid-phase catalysis. *Appl. Catal. A* **2006**, *313*, 146.
10. Madje, B. R.; Patil, P. T.; Shindalkar, S. S.; Benjamin, S. B.; Shingare, M. S.; Dongare, M. K. Facile transesterification of β-ketoesters under solvent-free condition using borate zirconia solid acid catalyst. *Catal. Commun.* **2004**, *5*, 353.
11. Bhagiyalakshmi, M.; Priya, S. V.; Mabel, J. H.; Palanichamy, M.; Murugesan, V. Effect of hydrophobic and hydrophilic properties of solid acid catalysts on the esterification of maleic anhydride with ethanol. *Catal. Commun.* **2008**, *9*, 2007.
12. Gui, J.; Cong, X.; Liu, D.; Zhang, X.; Hu, Z.; Sun, Z. Novel Brønsted acidic ionic liquid as efficient and reusable catalyst system for esterification. *Catal. Commun.* **2004**, *5*, 473.
13. Li, X.; Eli, W.; Li, G. Solvent-free synthesis of benzoic esters and benzyl esters in novel Brønsted acidic ionic liquids under microwave irradiation. *Catal. Commun.* **2008**, *9*, 2264.
14. Cordova, A.; Janda, K. D. A highly chemo- and stereoselective synthesis of β-keto esters via a polymer-supported lipase-catalyzed transesterfication. *J. Org. Chem.* **2001**, *66*, 1906.
15. Bandgar, B. P.; Shaikh, K. A. Molecular iodine–catalyzed efficient and highly rapid synthesis of bis(indolyl)methanes under mild conditions. *Tetrahedron Lett.* **2003**, *44*, 1959.
16. Saeeng, R.; Sirion, U.; Sahakitpichan, P.; Isobe, M. Iodine catalyzes *C*-glycosidation of D-glucal with silylacetylene. *Tetrahedron Lett.* **2003**, *44*, 6211.
17. Phukan, P. Iodine as a very powerful catalyst for three-component synthesis of protected homoallylic amines. *J. Org. Chem.* **2004**, *69*, 4005.
18. Phukan, P. Iodine as an extremely powerful catalyst for the acetylation of alcohols under solvent-free conditions. *Tetrahedron Lett.* **2004**, *45*, 4785.
19. Banik, B. K.; Fernandez, M.; Alvarez, C. Iodine-catalyzed highly efficient Michael reaction of indoles under solvent-free condition. *Tetrahedron Lett.* **2005**, *46*, 2479.
20. Ishihara, M.; Togo, H. An efficient preparation of 2-imidazolines and imidazoles from aldehydes with molecular iodine and (diacetoxyiodo)benzene. *Synlett* **2006**, 227.
21. Das, B.; Chowdhury, N.; Damodar, K. Iodine-catalyzed efficient conjugate addition of pyrroles to α,β-unsaturated ketones. *Tetrahedron Lett.* **2007**, *48*, 2867.
22. Rao, W.; Tay, A. H. L.; Goh, P. J.; Choy, J. M. L.; Ke, J. K.; Chan, P. W. H. Iodine-catalyzed allylation of 1,3-dicarbonyl compounds with allylic alcohols at room temperature. *Tetrahedron Lett.* **2008**, *49*, 122.
23. Ramalinga, K.; Vijayalakshmi, P.; Kaimal, T. N. B. A mild and efficient method for esterification and transesterification catalyzed by iodine. *Tetrahedron Lett.* **2002**, *43*, 879.
24. Chavan, S. P.; Shivasankar, K.; Sivappa, R.; Kale, R. Zinc-mediated transesterification of β-ketoesters and coumarin synthesis. *Tetrahedron Lett.* **2002**, *43*, 8583.

25. Chavan, S. P.; Kale, R. R.; Shivasankar, K.; Chandake, S. I.; Benjamin, S. B. A simple and efficent method for transesterification of β-ketoesters catalysed by iodine. *Synthesis* **2003**, 2695.
26. Bosco, J. W. J.; Agrahari, A.; Saikia, A. K. Molecular iodine–catalyzed selective acetylation of alcohols with vinyl acetate. *Tetrahedron Lett.* **2006**, *47*, 4065.
27. Ahmed, N.; Lier, J. E. Molecular iodine in isopropenyl acetate (IPA): A highly efficient catalyst for the acetylation of alcohols, amines, and phenols under solvent-free conditions. *Tetrahedron Lett.* **2006**, *47*, 5345.
28. Ren, Y. M.; Cai, C. A green procedure for the protection of carbonyl compounds catalyzed by iodine in ionic liquid. *Tetrahedron Lett.* **2008**, *49*, 7110.