A Simple and Efficient Procedure for Transesterification Catalyzed by Indium Triiodide

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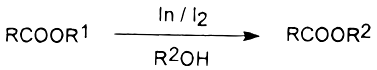
Transesterification is an important reaction which has wide applications[1] in academic as well as industrial research. Thus, a number of procedures catalyzed by a variety of protic and Lewis acids, organic and inorganic bases, enzymes, and antibodies have been developed.[1,2] Surprisingly, in all these reports although there are many examples of transesterification of esters to the corresponding analogues with higher alcohol moieties, examples of reverse transformations are not adequately included. During the course of our recent investigation we sought a transesterification of a menthyl ester to methyl or ethyl ester. However, our attempts with several reported reagents including $AlCl_3$ and $Ti(OPr^r)_4$ failed to produce a satisfactory result. Moreover, some of these reagents, particularly organotin compounds, are highly toxic. Thus, we felt the necessity of an efficient transesterification procedure with general applicability involving simple operations and a nontoxic reagent.

The reactions involving indium metal[3] and its halides[4] have been the subject of current interest because of their great potential in organic synthesis. During our recent endeavor[5] with indium-mediated reactions we have observed a very significant effect of indium triiodide in the transesterification process. This prompted us to initiate a systematic investigation on InI_3-catalyzed transesterification reactions, and herein we wish to disclose our results (Scheme 1)

In a typical experimental procedure, the ester was heated under reflux in a desired alcohol[6] in the presence of indium triiodide, prepared in situ by stirring indium metal and iodine in that particular alcohol at room temperature for half an hour. The reaction was monitored by TLC, and after completion, excess alcohol was stripped off and the residue was extracted with ether. The ether extract, after being washed with sodium thiosulfate and brine, was evaporated to furnish the product.

Scheme 1



$$RCOOR^1 \xrightarrow[R^2OH]{In / I_2} RCOOR^2$$

A wide range of structurally varied carboxylic esters including open-chain, cyclic, and aromatic ones underwent transesterification with a variety of alcohols by this procedure. The results are summarized in Table 1. The reaction proceeds smoothly with primary (methanol, ethanol, and benzyl alcohol), secondary (2-propanol), as well as tertiary alcohols (*tert*-butyl alcohol), although transesterification with *tert*-butyl alcohol and benzyl alcohol have been carried out under sonication. Conversions from methyl ester to higher homologues and from higher esters to lower homologues are achieved with uniform efficiency by this procedure. Particularly, transformation of menthyl ester to methyl ester (entries 12 and 13), which is very difficult to accomplish by other methods, indicates the efficacy of this reagent. Transesterification to *tert*-butyl ester (entries 5 and 6), which is often problematic in acid-catalyzed reactions, is also realized by this reagent. This procedure is also suitable for transesterification of a chiral ester without any racemization (entries 14 and 15). Several functional groups such as double bond (entries 16, 17, 22, and 23), nitro (entry 21), methoxyl (entries 20 and 23), and hydroxyl (entries 14 and 15) remain unaffected under the present reaction conditions.

Although the reaction proceeds well with a catalytic amount (0.3−0.5 equiv) of indium triiodide, the reactions are quite slow. However, reaction times are substantially reduced when 1.5 equiv of InI_3 is used. The reactions are, in general, very clean giving very high yields, and no side product has been isolated. The transesterification of aliphatic esters is usually complete within 5−6 h, but aromatic esters took longer (25−30 h).

In conclusion, the present procedure using indium triiodide provides a very efficient method for transesterification. The notable advantages of this method are: (a) operational simplicity; (b) easy availability and nontoxic nature of the reagent; (c) general applicability; (d) mild reaction conditions (tolerance to several sensitive functionalities during transesterification), and (e) high yield. We believe this will present a better and more practical alternative to the existing methodologies and will find useful applications in organic synthesis.

Experimental Section

General. The carboxylic esters are obtained commercially or prepared from the corresponding acids by a standard method. The esters and alcohols are distilled before use. Indium metal (Ingot, SRL, India) was cut into small slices and used directly without any treatment. Iodine crystal was used as obtained commercially.

General Procedure for Transesterification. Representative Procedure. Methyl phenyl acetate (150 mg, 1 mmol) was heated at reflux with a solution of indium triiodide in 2-propanol, prepared[7] in situ by stirring indium metal slices (173 mg, 1.5 mmol) and iodine (571 mg, 2.25 mmol) in dry 2-propanol (6 mL) at room temperature (25 °C) for half an hour. After the

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[1] (a) Fujita, T.; Tanaka, M.; Norimine, Y.; Suemune, H. *J. Org. Chem.* **1997**, *62*, 3824. (b) Shapiro, G.; Marzi, M. *J. Org. Chem.* **1997**, *62*, 7096.

[2] Otera, J. *Chem. Rev.* **1993**, *93*, 1447, and references therein.

[3] (a) Cintas, P. *Synlett* **1995**, 1087. (b) Li, C. J.; Chen, D. L.; Lu, Y. O.; Haberman, J. X.; Mague, J. T. *J. Am. Chem. Soc.* **1996**, *118*, 4216. (c) Paquette, L. A.; Mitzel, T. M. *J. Org. Chem.* **1996**, *61*, 8799. (d) Fujiwara, N.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2318. (e) Isaac, M. B.; Paquette, L. A. *J. Org. Chem.* **1997**, *62*, 5333.

[4] (a) Loh, T.-P.; Pei, J.; Lin, M. *J. Chem. Soc., Chem. Commun.* **1996**, 2315. (b) Loh, T.-P.; Pei, J.; Cao, G.-Q. *J. Chem. Soc., Chem. Commun.* **1996**, 1819. (c) Miyai, T.; Inoue, K.; Yasuda, M.; Baba, A. *Synlett* **1997**, 699. (d) Loh, T.-P.; Pei, J.; Vekoh, K. S.; Cao, G.-Q.; Li, X.-R. *Tetrahedron Lett.* **1997**, *38*, 3465.

[5] Ranu, B. C.; Majee, A. *J. Chem. Soc., Chem. Commun.* **1997**, 1225.

[6] The alcohol was taken in excess for a clean and smooth reaction. The use of just 1 equiv of alcohol leads to charring, and the reactions are messy. The presence of a cosolvent such as benzene also fails to provide a satisfactory result.

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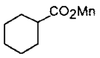
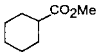
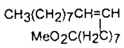
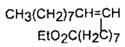
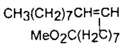
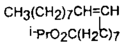
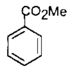
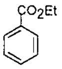
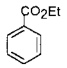
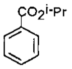
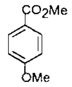
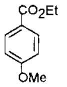
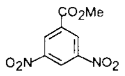
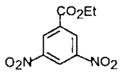
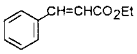
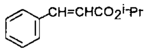
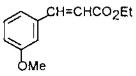
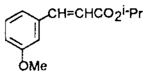
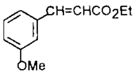
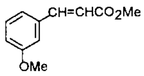
Table 1. InI_3-Catalyzed Transesterification

entry	carboxylic ester	alcohol	time(h)	product	yield(%) [a]
1	$PhCH_2CO_2Me$	i-PrOH	6	$PhCH_2CO_2{}^{i}\text{-}Pr$	90
2	$PhCH_2CO_2{}^{i}\text{-}Pr$	MeOH	5.5	$PhCH_2CO_2Me$	86
3	$PhCH_2CH_2CO_2Me$	i-PrOH	6	$PhCH_2CH_2CO_2{}^{i}\text{-}Pr$	89
4	$PhCH_2CH_2CO_2{}^{i}\text{-}Pr$	MeOH	6	$PhCH_2CH_2CO_2Me$	85
5	$PhCH_2CO_2Me$	t-BuOH	18[b]	$PhCH_2CO_2{}^{t}\text{-}Bu$	70
6	$PhCH_2CH_2CO_2Me$	t-BuOH	22[b]	$PhCH_2CH_2CO_2{}^{t}\text{-}Bu$	68
7	$PhCH_2CO_2{}^{t}\text{-}Bu$	MeOH	6.5	$PhCH_2CO_2Me$	84
8	$CH_3(CH_2)_{16}CO_2Et$	i-PrOH	5	$CH_3(CH_2)_{16}CO_2{}^{i}\text{-}Pr$	88
9	$CH_3(CH_2)_{14}CO_2Et$	MeOH	4.5	$CH_3(CH_2)_{14}CO_2Me$	85
10	$PhCH_2CO_2Me$	$PhCH_2OH$	12[b]	$PhCH_2CO_2CH_2Ph$	89
11	$PhCH_2CO_2CH_2Ph$	MeOH	12	$PhCH_2CO_2Me$	88
12	$PhCH_2CO_2Mn$	MeOH	6.5	$PhCH_2CO_2Me$	84
13		MeOH	7		82
14	d(+)-Diethyl tartarate	i-PrOH	7	d(+)-Diisopropyl tartarate	87
15	s(-)-Diethyl lactate	MeOH	7	s(-)-Dimethyl lactate	82
16	 $CH_3(CH_2)_7CH{=}CH$ $MeO_2C(H_2C)_7$	EtOH	6.5	 $CH_3(CH_2)_7CH{=}CH$ $EtO_2C(H_2C)_7$	84
17	 $CH_3(CH_2)_7CH{=}CH$ $MeO_2C(H_2C)_7$	i-PrOH	6	 $CH_3(CH_2)_7CH{=}CH$ $^{i}\text{-}PrO_2C(H_2C)_7$	85
18		EtOH	24		70
19		i-PrOH	30		72
20		EtOH	30		86
21		EtOH	32		84
22		i-PrOH	26		87
23		i-PrOH	25		88
24		MeOH	25		90

[a] Yields refer to those of pure isolated products, fully characterized by spectral data. [b] The reaction was carried out under sonication.

reaction was over (6 h, monitored by TLC) excess alcohol was distilled off at reduced pressure and the residue was extracted with ether. The ether extract was washed successively with a solution of sodium thiosulfate, brine, and dried Na_2SO_4. Evaporation of ether produced the crude product which was purified by column chromatography over silica gel to furnish pure isopropyl phenyl acetate (oil, 160 mg, 90%) which is in full agreement with spectral data of an authentic sample.

This procedure is followed for transesterification of all the substrates included in Table 1, except those of methyl phenyl acetate (entry 5) and methyl phenyl propionate (entry 6) with *tert*-butyl alcohol and methyl phenyl acetate with benzyl alcohol (entry 10) which were carried out under sonication in an ultrasonic cleaner (Julabo, Germany).

All the products are known compounds and are easily identified by comparison of their spectra with those of authentic samples.[8]

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(7) Han, Y.; Huang, Y.-Z. *Tetrahedron Lett.* **1995**, *36*, 7277.

(8) Pouchert, C. J. *The Aldrich Library of NMR Spectra*, 2nd ed.; Aldrich Chemical Co., Inc.: Milwaukee, 1983; Vols. 1 and 2.