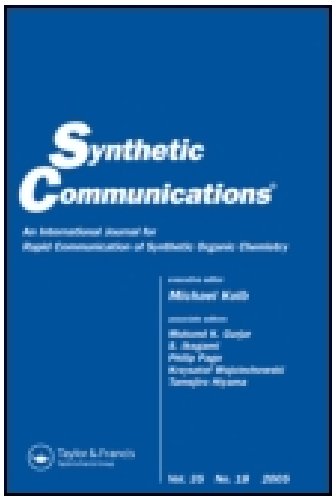

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A Simple and Convenient Procedure for the Conversion of Esters to Secondary Amides

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A Simple and Convenient Procedure for the Conversion of Esters to Secondary Amides

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ABSTRACT

An improved procedure has been developed for the direct conversion of carboxylic esters to secondary amides by simple treatment with primary amines in presence of indium triiodide.

Key Words: Esters; Secondary amides; Indium triiodide; Amines.

The preparation of amides from the corresponding carboxylic acids and their derivatives is a very useful process in organic synthesis.[1] As reactions of carboxylic acids themselves with ammonia or amines to provide the corresponding amides are of not much preparative value,[2]

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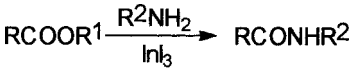
other derivatives of acids particularly acyl halides, acid anhydrides, and esters are most commonly used. However, limitations are associated with the use of acyl halides and acid anhydrides and thus esters are preferred. Usually, reactions with esters require strongly basic or acidic catalysts. Although, quite a number of methods are reported for the conversion of esters to amides,[3] most of these have serious drawbacks with regard to toxicity of the reagent particularly those involving tin compounds,[3b,3c] operational simplicity and efficiency. Thus, in recent times other approaches involving *N*-acylimidazoles[4a,4b] and *N*-acylbenzotriazoles[4c] have been demonstrated which also are not very simple and cost effective. Hence, there is a scope for further improvement of this procedure. Recently, we have reported very useful applications of indium triiodide in transesterification,[5a] acylation,[5b] hydrolysis of esters,[5c] and direct conversion of THP ether to acetate[5d] and we wish to disclose here its another successful use in the conversion of ester to secondary amide.

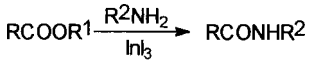


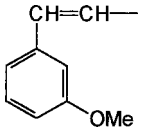
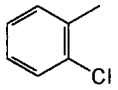
The experimental procedure is very simple. A carboxylic ester was heated (room temperature stirring did not lead to any reaction) with a primary amine in presence of a catalytic amount of indium triiodide for a certain period of time (TLC). Usual workup and purification furnished pure amide.

Several structurally varied carboxylic esters are converted to the corresponding amides by treatment with primary amines by this procedure. The results are reported in Table 1. The yields are very high. Both aromatic and non-aromatic amines such as aniline and benzyl amine have been used. This procedure is quite compatible with several sensitive functionalities such as, chloro, methoxy, and C=C bond.

The reaction is catalytic and proceeds even with 5 mol% of indium triiodide although the reaction is relatively slow. The reaction does not proceed at all in the absence of indium triiodide. It was also observed that indium alone is not capable to catalyze the process whereas, iodine pushes the conversion to the extent of 5–10% under similar conditions. Indium triiodide is thus essential for an efficient reaction. However, this procedure is not very effective for the preparation of primary and tertiary amides using ammonia and secondary amine, respectively.

Table 1. Conversion of carboxylic esters to secondary amides.



Entry	R	R^1	R^2	Time (h)	Yield (%)[a]
1	$PhCH_2$	Me	$PhCH_2$	7	92
2	Ph	$PhCH_2$	$PhCH_2$	7.5	90
3	$PhCH_2$	Menthyl	$PhCH_2$	8	93
4	$PhCH_2$	*i*-Pr	$PhCH_2$	8	92
5		Me	$PhCH_2$	5.5	87
6	Ph_2CH	Me	$PhCH_2$	7.5	90
7	$CH_3(CH_2)_{14}$	Et	$PhCH_2$	8.5	91
8		Me	$PhCH_2$	7.5	83
9	$PhCH_2$	Me	Ph	8.5	90
10	Ph_2CH	Me	Ph	9	85
11	$CH_3(CH_2)_{16}$	Et	Ph	8	91
12	Ph	CH_2Ph	Ph	9	93
13	CH_3	CH_2Ph	Ph	8.5	91

[a]Yields refer to those of pure isolated products fully characterized by comparison of their spectral (IR and NMR) data and melting point of those reported.

In conclusion, the present procedure provides an efficient methodology for the conversion of a carboxylic ester to a secondary amide. The operational simplicity, no involvement of toxic reagents and high yield make this procedure a practical alternative to the existing methods.[3,4]

GENERAL EXPERIMENTAL PROCEDURE

A carboxylic ester (1 mmol) was heated at an oil bath temperature of 110–120°C in a primary amine (2 cm^3) in presence of catalytic amount of indium triiodide (20 mol%), freshly prepared by stirring indium and iodine in THF.[6] After the reaction was over (TLC), the reaction mixture was

extracted with ether and the ether extract was washed successively with aqueous hydrochloric acid (1N) to remove excess amine, brine, and dried over Na_2SO_4. Evaporation of solvent left a crude solid which was purified by recrystallization from ether–petroleum ether (60–80°C) solvent mixture to furnish pure amide. The same procedure is followed for the conversion of all carboxylic esters to the corresponding amides listed in Table 1. Most of these amides are known compounds and are easily identified by their melting points and spectral data. New compounds are also in good agreement with their spectral and analytical data.

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