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ORIGINAL PAPER

Environmentally friendly transesterification and transacylation reactions under LiBr catalysis

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Abstract A room-temperature, convenient transesterification of various esters, induced by catalytic amounts of lithium bromide and diethylamine in a solvent-free environment, is described. Products are obtained in good purity by simple filtration to remove the catalyst and evaporation of the volatile portion. The procedure has also been successfully applied to transacetylation and aminolysis of esters.

Keywords Transesterification · Transacetylation · Aminolysis · Lithium bromide · Solvent-free

Introduction

In recent years, there has been an overwhelming increase in the number of reports on solvent-free [1, 2] reactions leading to development of the field into an important branch of "green chemistry". The advantages associated with such reactions include production of less chemical waste, less expense, and easier handling procedures. As a result, there are numerous recent reports on conducting efficient organic transformations in the absence of solvents [3–7].

Esters constitute one of the most important groups of compounds in industrial organic chemistry, because of their numerous applications as precursors for the preparation of dye carriers, solvents, plasticizers, artificial flavors, and polymers such as durable epoxy resins [8]. In addition, they play an important role as key intermediates in protection of hydroxyl functional groups in the course of multi-step synthetic procedures [9]. Traditional acid or base-catalyzed synthetic procedures for esters, however, suffer from drawbacks such as the harsh conditions required and the undesired reverse hydrolysis processes. Consequently, other efficient alternative methods have been developed in recent years for more convenient synthesis of esters [10–13]. One particularly useful approach in both academia and industry is the transesterification reaction, the process involving exchange of an alkoxy moiety between two carboxyl groups which is often superior to direct synthesis of esters from carboxylic acids and alcohols. The method finds special application in esterification of labile and difficult to separate carboxylic acids. In addition to synthetic applications, transesterification is applicable to the polymerization of lactones, the preparation of oils and fats, the curing of alkyd resins in the paint industry, and the preparation of polyesters [14, 15]. Beside the traditional acid and base-catalyzed transesterification procedures [16, 17], newer methods available in the literature involve the use of Lewis acidic reagents [18, 19], amine catalysts [20], metal alkoxides [21, 22], enzymes [23–25], organocatalysts [26, 27], and green solvents [28, 29]. Despite these, development of efficient procedures involving inexpensive recyclable catalytic systems under solvent-free conditions is still in demand.

In the framework of our investigation on aldehyde group manipulation reactions [30–32], we recently reported the use of mild Lewis acids for efficient room-temperature disproportionation reactions of aldehydes under "neutral conditions" [33]. In the latter communication we

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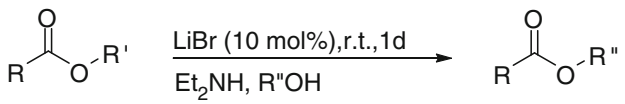
demonstrated that the reaction can selectively proceed toward the direct synthesis of methyl esters from aldehydes by choosing methanolic work-up. This observation could be rationalized by the attack of methanol on the "dimeric intermediate ester" and was supported by our obtaining amides or acids when diethylamine or water was used instead of methanol in the work-up step [34]. Based on these, we envisaged that the method could be further applied to transesterification reactions and we would like to report here a simple and convenient transesterification procedure conducted at room-temperature under LiBr catalysis [35] in a solvent-free environment (Scheme 1).

Results and discussion

We initiated our investigation on transesterification of benzyl benzoate with methanol in the presence of LiBr under a range of conditions. Optimum results were obtained when the reaction was conducted at room temperature in the presence of Et_2NH, catalytic amounts of LiBr (10 mol%), and no solvent. As a result 84% methyl benzoate was obtained in good purity after filtration to remove the catalyst and evaporation of the volatile portion (Table 1, entry 1). Ethanol behaved similarly, furnishing ethyl benzoate (entry 2). Under the same conditions, other aromatic esters could transesterify equally well within comparable time periods (entries 3–5). Alternatively, benzyl alcohol could successfully be used as a substitute for aliphatic alcohols in the procedure (entries 6–7). Interestingly, diethyl oxalate (entry 8) and diethyl carbonate (entry 9) could undergo mono substitution with benzyl alcohol leading to formation of moderate amounts of their respective transesterified products, whereas disubstituted products could be formed only in the presence of excessive amounts of benzyl alcohol. Secondary alcohols could be used as substitutes for benzyl alcohol at higher temperatures, giving 75% of the product (in reaction with isopropanol) after 20 h (entry 10). This lower reactivity was used to show the chemoselectivity of the process. As a result, in the presence of an equimolar mixture of methanol and isopropanol, benzyl benzoate led to exclusive formation of methyl benzoate with no formation of isopropyl benzoate (Scheme 2).

Chemoselectivity was also observed when benzyl benzoate was treated with ethylene glycol under these conditions, leading to isolation of 75% of the mono-protected product 3-hydroxypropyl benzoate (entry 11). Because of the importance of transacetylation reactions [8, 39, 40], we extended the method to study the possibility of alcohol exchange in ethyl acetate under our conditions. The results, indicated in entries 12–13, clearly show that



Scheme 1

Table 1 LiBr catalyzed alcohol–alcohol exchange reactions of esters

Entry	RCOOR′	R″OH	RCOOR″	Yield (%)[a]	Ref.
1	$C_6H_5CO_2CH_2C_6H_5$	MeOH	**1a**	84	[20]
2	$C_6H_5CO_2CH_2C_6H_5$	EtOH	**1b**	82	[20]
3	(2-thienyl)CO_2–CH_2(2-thienyl)	MeOH	**1c**	92	[11]
4	(4-Me)$C_6H_4CO_2CH_2C_6H_5$	MeOH	**1d**	87	[11]
5	(4-Cl)$C_6H_4CO_2$–$CH_2C_6H_5$	MeOH	**1e**	93	[33]
6	$MeCO_2(CH_2)_3Me$	$C_6H_5CH_2OH$	**1f**	85	[27]
7	$MeCHClCO_2Et$	$C_6H_5CH_2OH$	**1g**	80	[36]
8	EtO_2CCO_2Et	$C_6H_5CH_2OH$	**1h**	76	[37]
9	$EtOCO_2Et$	$C_6H_5CH_2OH$	**1i**	74	[12]
10	$C_6H_5CO_2CHCH_2C_6H_5$	Me_2CHOH	**1j**	75[b]	[38]
11	$C_6H_5CO_2CH_2C_6H_5$	$HOCH_2CH_2OH$	**1k**	75	[13]
12	$MeCO_2Et$	$C_6H_5CH_2OH$	**1f**	82	[27]
13	$MeCO_2(CH_2)_3Et$	$Me(CH_2)_3OH$	**1l**	78	[38]

[a] Isolated yields

[b] Conducted at 58 °C

Scheme 2

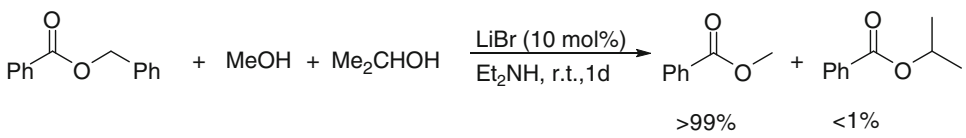
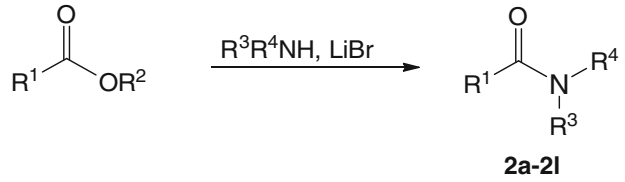


Table 2 LiBr catalyzed alcohol-amine exchanges



2a-2l

Entry	R^1	R^2	R^3, R^4	Product	Yield (%)[a]	Ref.
1	C_6H_5	$CH_2C_6H_5$	$(CH_2)_4$	**2a**	84	[45]
2	C_6H_5	$CH_2C_6H_5$	$(CH_2)_5$	**2b**	80	[38]
3	C_6H_5	$CH_2C_6H_5$	H, $(CH_2)_2Me$	**2c**	92	[38]
4	C_6H_5	$CH_2C_6H_5$	H, cyclohexyl	**2d**	87	[38]
5	C_6H_5	$CH_2C_6H_5$	H, $(CH_2)_4Me$	**2e**	90	[43]
6	C_6H_5	$CH_2C_6H_5$	H, $(CH_2)_2NH_2$	**2f**	92	[46]
7	C_6H_5	$CH_2C_6H_5$	H, $(CH_2)_2OH$	**2g**	92	[43]
8	C_6H_5CO	OEt	H, $(CH_2)_2OH$	**2h**	93	[42]
9	EtO_2C	OEt	H, $(CH_2)_2Me$	**2i**	93	[47]
10	EtO_2C	OEt	Et, Et	**2j**	98	[48]
11	EtO_2C	OEt	H, $(CH_2)_2Me$	**2k**[b]	91	[49]
12	Me	OEt	H, (*R*)-$CHMeC_6H_5$	**2l**	82	[50]

[a] Isolated yields

[b] For this product the EtO group of R^1 is also replaced with $NH(CH_2)_2Me$

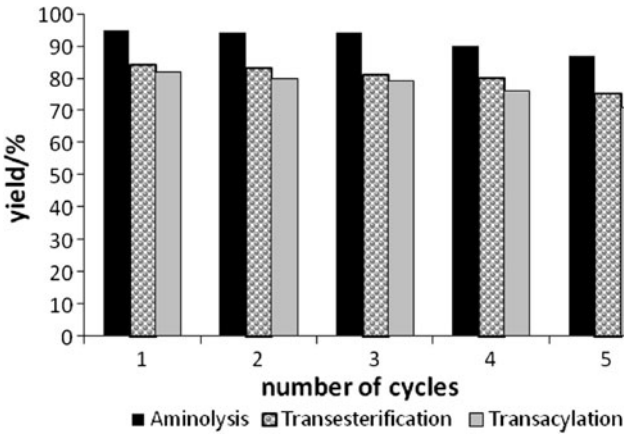


Fig. 1 Efficient recovery of the catalyst

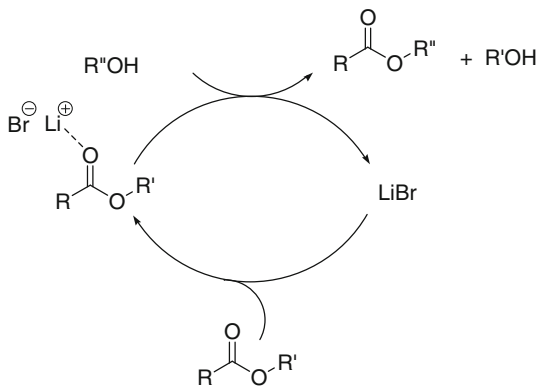


Fig. 2 Proposed mechanism

benzylic or aliphatic alcohols can efficiently be used as substitutes for the ethyl alcohol moiety in ethyl acetate.

Next, control experiments were carried out to evaluate the role of the amine on transesterification of benzyl benzoate. Omission of the amine from the reaction medium led to no product formation and the starting ester was quantitatively recovered. Replacement of Et_2NH with Et_3N only prolonged the reaction time. Instead, when a cyclic secondary amine (pyrrolidine) was employed, aminolysis of the substrate was observed leading to formation of phenyl(pyrrolidin-1-yl)methanone, in which the alcohol residue is substituted with the cyclic amine (Table 2, entry 1). This result persuaded us to investigate more aminolysis reactions of esters, which are a common method of amide bond formation and are normally carried out under extreme conditions [41, 42]. Therefore, development of efficient and novel procedures to conduct these reactions under mild conditions would be of interest [43, 44].

The transacylation process was again efficiently observed when other cyclic secondary (entry 2) or primary amines (entries 3–5) were used in the reaction. Use of ethylenediamine only gave the monoprotected product (entry 6). Alternatively, when 2-aminoethanol was subjected to the conditions, preferential reaction of the amino group was observed (entries 7–8). Under these conditions, diethyl oxalate underwent mono substitution to give its respective semiamide products (entries 9–10) while double *N*-alkylation occurred only if excessive quantities of the amine were used (entry 11). Interestingly, for the reaction of ethyl acetate with (*R*)-1-phenylethanamine only formation of the respective amide product was observed; in this reaction the stereochemistry of the chiral starting amine was retained (entry 12).

On completion of each reaction the volatile portion of the mixture was evaporated, the solid residue was washed with toluene, and LiBr was separated by simple filtration. The separated LiBr was dried under vacuum and used in next five reactions without significant loss of activity, as shown in Fig. 1 for aminolysis of benzyl benzoate with *n*-propylamine, transesterification of benzyl benzoate with methanol, and transacetylation of ethyl acetate with benzyl alcohol. Application of the results to triglycerides for the preparation of biodiesels is under investigation in our laboratory.

Based on the observed results, a mechanistic pathway can be suggested in which LiBr is recycled continuously throughout the course of the reaction (Fig. 2). This hypothesis is supported by recovery of the catalyst by

simple filtration and its direct efficient reuse in subsequent reactions without significant loss of activity.

In summary, we have demonstrated that LiBr, a very stable and mild reagent to handle, can efficiently cause solvent-free transesterification of various esters at room temperature. The conditions were successfully applied to transacetylation and aminolysis of esters also. Recycling of the catalyst and environmental safety of the process are additional advantages of this method.

Experimental

IR spectra were recorded using KBr disks on a Bruker Vector-22 infrared spectrometer. ^{1}H NMR spectra were obtained on a FT-NMR Bruker Ultra Shield^{TM} (500 MHz) or Bruker AC 80 MHz instrument as $CDCl_3$ solutions using TMS as the internal standard reference. Mass spectra were obtained on a Finnigan Mat 8430 apparatus. Starting esters were prepared via Tishchenko dimerization of aldehydes [33] or purchased from commercial sources.

Typical transesterification procedure

A suspension of an ester (10 mmol), an alcohol (30 mmol), Et_2NH (20 mol%, 2 mmol), and LiBr (10 mol%, 1 mmol) was mixed at room temperature until TLC or GC experiments showed completion of the reaction. LiBr was separated by simple filtration and the ester product was isolated from the filtrate by evaporation of the volatile portion. The identity of the products was confirmed by spectroscopic methods and comparison with published data [11–13, 20, 27, 33, 36–38].

Typical aminolysis procedure

A suspension of an ester (10 mmol), an amine (13 mmol), and LiBr (10 mol%, 1 mmol) was mixed at room temperature until TLC or GC experiments showed completion of the reaction. LiBr was separated by simple filtration and the amide product was isolated from the filtrate by evaporation of the volatile portion. The identity of the products was confirmed by spectroscopic methods and comparison with published data [38, 42, 43, 45–50].

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