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Transesterification of *N*-Acyloxazolidinones with Alcohol by Lanthanum(III) Iodide

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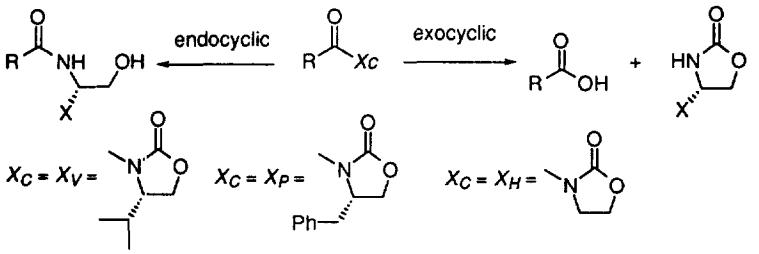
Abstract: Transesterification of *N*-acyloxazolidinones by treatment with an alcohol and lanthanum(III) iodide gives the corresponding esters in good to excellent yields under mild conditions with negligible racemization.

2-Oxazolidinones[1] are widely used as chiral auxiliaries, and resulting degree of asymmetric induction can be high in carbon-carbon bond formations such as aldol reaction,[2] alkylation,[3] acylation[4] and Diels-Alder reaction.[5] Non-chiral *N*-acyloxazolidinones are also good building blocks for highly asymmetric reactions catalyzed by chiral catalysts.[6] After the stereospecific reaction with the chiral auxiliary, the oxazolidinone needs to be removed from the product without damaging the stereogenic centers in the molecule. Cleavage of the auxiliary can be either exo- or endocyclic. The nucleophilic cleavage of unhindered *N*-acyl derivatives undergoes exocyclic cleavage to give the desired products (Scheme 1).[7] However, when R is larger or α-branched, the undesired endocyclic cleavage of the oxazolidinone ring is predominant with basic reagents. The endocyclic oxazolidinone cleavage can be avoided using lithium hydroperoxide[7a] as a nucleophile instead of a hydroxide; regioselective exocyclic cleavage occurs for oxazolidinone-derived carboximides. The use of this reagent on a large scale may however be hazardous because of its explosive nature. Exocyclic cleavage with metal alkoxides, e.g., lithium,[3, 5a] magnesium,[8] and titanium,[9] yields esters successfully.

Scheme 1



We now found that selective exocyclic cleavage of *N*-acyloxazolidinones with an alcohol catalyzed by lanthanum(III) iodide proceeded smoothly to give corresponding esters under mild conditions. We would like to present preliminary results of the transesterification of chiral and non-chiral *N*-acyloxazolidinones by the lanthanum(III) iodide/alcohol method.[10]

On treatment of the cycloadduct bearing oxazolidinone (X_V) (**1**) with lanthanide(III) iodide (LnI_3)[11] in the presence of an alcohol, the corresponding ester (**2**) was obtained in moderate to good yields at room temperature (Scheme 2). The chiral oxazolidinone group (HX_V) can be recovered and reused. We first surveyed the reaction of the oxazolidinone (**1**) with methanol or benzyl alcohol using LaI_3, CeI_3, SmI_3, and YbI_3. Table 1 summarizes the results of the reaction. LaI_3 and CeI_3 effectively catalyzed the exocyclic

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transesterification with both methanol and benzyl alcohol to produce the corresponding esters; quantitative yields of the esters were obtained using LaI_3. SmI_3 and YbI_3 were also effective for the transesterification with methanol, but gave poor yields of the ester with benzyl alcohol. As benzyl esters, which are readily converted to the acids, are more synthetically important, the uses of SmI_3 and YbI_3 were not appropriate for the reaction. $LaCl_3$ and $LaBr_3$ mediated the transesterification moderately but not so effective as the iodide. With *tert*-butyl alcohol, endocyclic cleavage of the oxazolidinone ring occurred exclusively. It is worthy to note that the reaction proceeded without using basic lanthanum alkoxide.[12] Considering that the conventional transesterification of *N*-acyloxazolidinones was carried out with metal alkoxides, the LaI_3 /alcohol method is characteristic.

Scheme 2

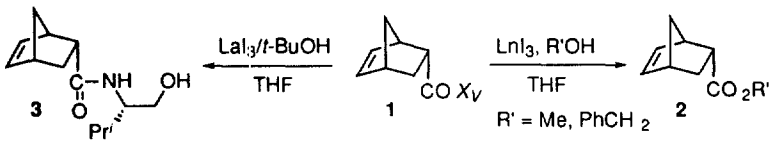


Table 1. Transesterification of the oxazolidinone (**1**) with alcohol by lanthanide(III) iodide[a]

Ln	R'OH	Yield (%) of ester (**2**)[b]
La	MeOH	quant.
	$PhCH_2OH$	99
Ce	MeOH	quant.
	$PhCH_2OH$	77
Sm	MeOH	86
	$PhCH_2OH$	8
Yb	MeOH	88
	$PhCH_2OH$	34

[a]The oxazolidinone (**1**) (1.0 mmol), LnI_3 (0.1-1.0 mmol), R'OH (3.0 mmol); in THF, rt, 15 h. [b]Determined by GC.

As LaI_3 revealed to be most effective for the transesterification, we next examined the reaction of various *N*-acyloxazolidinones with benzyl alcohol using LaI_3. The results are summarized in Table 2. With non hindered oxazolidinones the selective exocyclic cleavage occurred to give the esters quantitatively in each oxazolidinone group (X_V, X_P, or X_H) (runs 1-3). With hindered and α-branched oxazolidinones, the transesterification with benzyl alcohol depended on the structure of oxazolidinone group. The reaction with the oxazolidinones X_V produced the esters in good yields (runs 4-6 and 9), while with the oxazolidinones X_P the yields of the esters were not satisfactory, the starting oxazolidinones being recovered(runs 4, 6, and 9). The methyl esters could be obtained in high yields even in the reaction with the hindered oxazolidinones X_P and more sterically demanded oxazolidinones (run 11) using methanol instead of benzyl alcohol. Racemization scarcely occurred (less than 0.1 %) during the course of the transesterification with the chiral R groups (runs 5-6, 8-10). The transesterification of the β-hydroxy carboximide accompanied the retro-aldol reaction giving the aldehyde and benzyl propanoate instead(run 7).

Scheme3

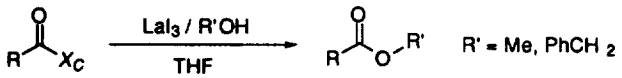
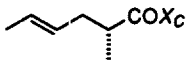
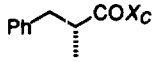
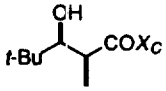


Table 2. Transesterification of *N*-Acyloxazolidinone with LaI_3 / $PhCH_2OH$[a]

Run	RCOX_C	Yield (%) of ester [b]		
		X_C = X_V	X_P	X_H
1	PhCOX_C	89	81	93
2	$PhCH_2CO X_C$	93	78	95
3	$CH_3(CH_2)_5CO X_C$	77	quant.	quant.
4	*t*-BuCOX_C	93	28	-
5		79	76	-
6		88	55	-
7		-[c]	-[c]	-
8		quant.	90	quant.
9		85	37	-
10		20	trace	-
11[d]		quant.[e]	quant.[e]	-

[a]Oxazolidinone (1.0 mmol), LaI_3 (0.1-1.0 mmol), $PhCH_2OH$ (3.0 mmol); in THF, rt, 15-60 h. [b]Determined by GC. [c]Benzyl propanate (60-95%) and pivalaldehyde (60-95%) were produced. [d]Methanol was used instead of benzyl alcohol. [e]The methyl ester was a product.

In conclusion, the advantages of the transesterification method are 1) LaI_3 is readily prepared from La metal and iodine in THF and inexpensive, 2)The reaction procedure is simple, just mixing oxazolidinone, alcohol and LaI_3, 3) The reaction can be catalytically carried out, and 4) No attendant side reactions including

racemization occur in the reaction.

The following provides a typical experimental procedure for the transesterification of *N*-acyloxazolidinones with benzyl alcohol/LaI_3. To a THF (26 ml) solution of LaI_3 (0.1 M, 2.6 mmol) was added benzyl alcohol (0.84 g, 7.8 mmol) at room temperature and the resulting solution was stirred for 10 min. The oxazolidinone (**1**) (0.65 g, 2.6 mmol) was then added to the mixture and stirred at the same temperature for 15 h. The mixture was treated with water, extracted with diethyl ether (30 ml X 3). The ethereal solution was washed with aq. $Na_2S_2O_3$, and dried over $MgSO_4$. Evaporartion of the solvent left a pale yellow residue which was subjected to column chromatography on silica gel; hexane/ethyl acetate = 12 : 1 elueted the ester (**2**) (0.59 g, 2.6 mmol, 99-100%) and ethyl acetate eluted the oxazolidinone (HX_V) (0.29 g, 2.26 mmol, 87 %).

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