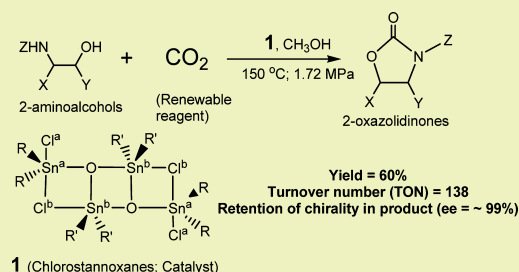# Synthesis of 2-Oxazolidinones by Direct Condensation of 2-Aminoalcohols with Carbon Dioxide Using Chlorostannoxanes

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Ⓢ *Supporting Information*

ABSTRACT: Synthesis of 2-oxazolidinones from 2-aminoalcohols and carbon dioxide (CO_2) in the presence of 1,3-dichloro-1,1,3,3-tetraalkyldistannoxanes (**1**) is reported. The influence of the change in substituent groups on the metal centers Sn^a and Sn^b of the catalyst (**1**) on the yields of the products was studied. Turnover numbers as high as 138 were obtained using the chlorostannoxane catalyst with all butyl substituents (**1a**) on both the metal centers. The activity of the catalyst **1a** on various substrates was studied and reported.

1 (Chlorostannoxanes; Catalyst)

Yield = 60%
Turnover number (TON) = 138
Retention of chirality in product (ee = ~99%)

KEYWORDS: *Carbon dioxide, Oxazolidinones, 2-Aminoalcohols, Chlorostannoxanes*

■ INTRODUCTION

Cyclic urethanes such as 2-oxazolidinones (2-OXZs) have been known for their use in various biological[1] and synthetic applications. Chiral 2-OXZs also known as Evans' auxiliaries[2−9] have been used as chiral auxiliaries in a wide range of asymmetric syntheses. Oxazolidinones have also been used as a new class of antibacterial agents that are active against pathogenic gram-positive bacteria.[10] Conventional synthesis of 2-OXZs from amino alcohols was generally done by phosgenation of corresponding 1,2-amino alcohols with phosgene or its derivatives.[11] Serious environmental pollution and equipment corrosion associated with phosgene have resulted in various alternative procedures such as oxidative cyclocarbonylation using CO/O_2,[12] but the potential of explosion hazard is one of the serious limitations of this process. In the light of the need for a "greener" synthetic process, an environmentally benign direct condensation of 2-aminoalcohols (2-AAs) with carbon dioxide (CO_2) will provide a better platform for the synthesis of 2-OXZs. Synthesis of 2-OXZs from 2-AAs using organometallic complexes was first reported by Matsuda and co-workers.[13] The harsh reaction conditions and benzene as cosolvent render this process uneconomical and nonecofriendly. An organotin catalyst, dibutyltin oxide, was reported for the synthesis of 2-OXZs using amino alcohols and CO_2 in the presence of N-methylpyrrolidone as cosolvent. This synthetic process employed relatively harsh reaction conditions (180 °C, 5 MPa) during the reaction period of 16 h.[14] Turnover number (TON) and turnover frequencies (TOF) of this catalyst were found to be very low with TON being 4−9 and TOF being 0.25−0.53. High temperatures, high pressures, and the need of stoichiometric amounts of catalysts in some processes have been a few of the concerns in previous reports.

Addressing these concerns, in this report, we studied the synthesis of 2-OXZs from 2-AAs and CO_2 in the presence of 1,3-dichloro-1,1,3,3-tetraalkyldistannoxanes (**1**; Figure 1) as catalysts.

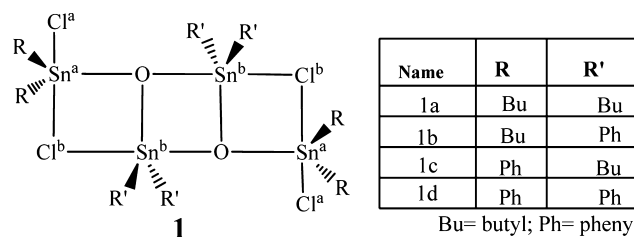| Name	R	R'
1a	Bu	Bu
1b	Bu	Ph
1c	Ph	Bu
1d	Ph	Ph

Bu = butyl; Ph = phenyl

Figure 1. Structure of chlorostannoxane catalysts.

Chlorostannoxanes are efficient robust catalysts that have been used in various synthetic processes such as in polyester synthesis,[15] urethane[16] and polyurethane[17] synthesis, ring-opening polymerization,[18] cyclic carbonate synthesis,[19] and transesterification[20,21] reactions. One of the major features of **1** is that it possesses two degenerate metal centers Sn^a and Sn^b.[20,22] These multi-active catalytic centers offer several advantages over other catalysts. One of the advantages is the ability to control Lewis acidity of the catalysts by changing the substituents on the metal centers. Exploring the catalytic abilities of chlorostannoxanes, we recently reported the synthesis of 2-OXZs[23] from 2-AAs and diethyl carbonates under relatively mild temperatures (80 °C) and in very less

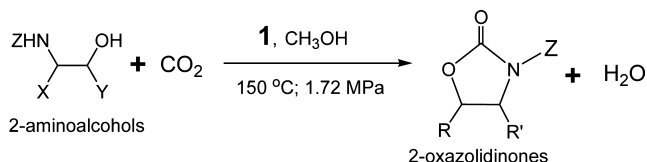time (1 h). These catalysts were found to be efficient with turnover frequencies (TOF) as high as 200 h^{-1}.

In this report, we have studied the synthesis of 2-OXZs from 2-aminoalcohols (2-AAs) and CO_2 in the presence of chlorostannoxanes while using methanol as cosolvent (Scheme 1). We are able to produce considerable turnover numbers

Scheme 1. General Reaction of 2-Oxazolidinone (2-OXZ) Synthesis

ZHN, OH + CO_2 $\xrightarrow[\text{150 °C; 1.72 MPa}]{\textbf{1}, CH_3OH}$ 2-oxazolidinones + H_2O

2-aminoalcohols

(TONs) as high as 138 over the reaction period of 6 h. Owing to the capability of change in the activity of the catalysts to the change in substituent groups on the metal centers, we have studied this change in activity over a period of time using two different substituents (butyl and phenyl) at Sn^a and Sn^b centers of chlorostannoxanes (Figure 1).
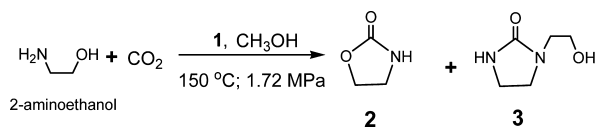
■ EXPERIMENTAL SECTION

General Procedure. In general, the reaction was performed in a PARR 5500 high pressure reactor fitted with a 50 mL stainless steel autoclave. 2-Aminoalcohol (0.0041 mol), methanol (0.05 mol), and **1** (0.000017 mol) were added to the autoclave, and the reaction mixture was purged with CO_2 two times before finally adding about 1.72 MPa of CO_2. The reactor was then heated to the required temperature and was allowed to stand at that temperature until the completion of stipulated time. After this, the reactor was cooled in an ice/water bath, and gas was released. The reaction mixture was collected using methanol and was analyzed using gas chromatography/mass spectrometry (GC/MS) technique.

■ RESULTS AND DISCUSSION

Initially, we studied the influence of time on the catalytic activity of **1a**−**1d** using 2-aminoethanol as the substrate (Scheme 2). We observed that the yield of corresponding 2-

Scheme 2. Synthesis of 2-Oxazolidinone from 2-Aminoethanol and CO_2

H_2N OH + CO_2 $\xrightarrow[\text{150 °C; 1.72 MPa}]{\textbf{1}, CH_3OH}$ **2** + **3**

2-aminoethanol

oxazolidinone has gradually increased reaching its maximum yield in about 6 h. At the same time, as observed in the GC/MS analysis (Figure S4−S7, Supporting Information), a side product **3** formed in considerable yields with an increase in time. Figure 2 indicates the activity of catalyst **1a** over the conversion of 2-aminoethanol. An increase in total conversion of the molecule with an increase in formation of products **2** and **3** was observed. No other side products were observed in this process.

Further, activity of the catalysts was studied in the presence of various substituents on the metal centers Sn^a and Sn^b. As reported in our previous studies toward the synthesis of oxazolidinones[23] from amino alcohols and diethyl carbonates and also the synthesis of cyclic carbonates[19] from epoxides and carbon dioxide, we were able to observe a trend in the change
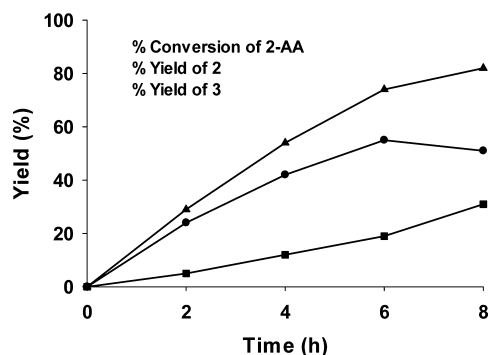

Figure 2. Variation in total conversion and product yields with time using **1a** (2-AA = 2-aminoalcohol).

in activity of the catalysts with change in substituents on the catalysts, **1a**, **1b**, **1c**, and **1d**, at various durations of the reactions (Figure 2; Figures S2−S1 to S3−S3, Supporting Information). An all butyl-substituted **1a** was found to be highly active followed by the catalyst **1b** (Figure S2−S1, Supporting Information) that has butyl substituents on Sn^a and phenyl substituents on Sn^b. Further, the activity of catalyst **1c** (Figure S3−S2, Supporting Information) with phenyl substituents on Sn^a and butyl substituents on Sn^b was found to be lower than **1b** but higher than an all phenyl substituted chlorostannoxane **1d** (Figure S3−S3, Supporting Information). The nondegeneracy of metal centers and varying butyl and phenyl substituents influence the electronic and steric environment of the catalysts and in turn their activity. The observed change in the activity of the catalyst could be due to the change in Lewis acidity of the Sn centers and the solubility of the catalyst in the solvent system caused by various substituents. The decrease in solubility may be a result of change in polarity of the catalyst due to change in substituents.[22]

A further study in the presence of **1a** catalyst using 2-aminoethanol as a representative substrate indicated that the yield of the product increases with an increase in the amount of the catalyst. We were able to observe a first-order dependence on the concentration of the catalyst (Figure S4−S4, Supporting Information).
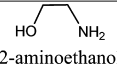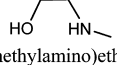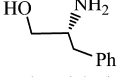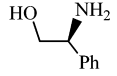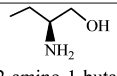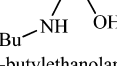
In the presence of the **1a** catalyst and using 2-aminoethanol as representative substrate, we studied the effect of change in substrate concentration using four different concentrations of the substrates (Figure S4−S5, Supporting Information). We were able to observe that the change in concentration of the substrate does not have a great influence as there is not a steep change in the yields of the product with change in substrate concentration.

Over a range of 100−250 psi (0.7−1.72 MPa) pressure, an increase in pressure has resulted in an increase in yield of the product. As shown in Figure S5−S6 (Supporting Information), we were able to observe that the increase in yields of the product with increase in pressure could be of first order.

In addition to 2-aminoethanol, the ability of the catalyst **1a** to synthesize 2-OXZs from various other substrates was studied. Table 1, indicates the yields of the products obtained.

Substitution on the carbon adjacent to the amine group did not make a huge difference as was seen in the case of 2-phenylalaninol. Gas chromatograms of all the corresponding reactions products are provided in Figures S5−S7 to S8−S11 of the Supporting Information. As shown in the table, GC/MS

Table 1. List of Various Substrates Studied

Entry	Substrate	Yield %	%ee*
1	HO─NH$_2$ 2-aminoethanol	55	-
2	HO─HN─ 2-(methylamino)ethanol	56	-
3	R-2-phenylalaninol (HO, NH$_2$, Ph)	60	99
4	R-2-phenylglycinol (HO, NH$_2$, Ph)	50	99
5	S-2-amino-1-butanol (OH, NH$_2$)	53	99
6	N-n-butylethanolamine (Bu─NH─OH)	52	-

(2-aminoalcohol 0.0041 mol; **1a** 0.000017; CH$_3$OH 0.05 mol; 1.72 Mpa; 150 °C; 6 h;)
(*calculated using GC-MS)

measurements for the determination of %ee indicated that the optical purity of the products was maintained.

In this synthetic process, we observed the formation of dimethyl carbonate (($CH_3O)_2CO$) (Figure S8−S12, Supporting Information), possibly due to the reaction of methanol (CH_3OH) and CO_2. On the basis of our previous studies toward the synthesis of 2-oxazolidinones from 2-amino alcohols and diethyl carbonate using chlorostannoxanes,[23] we assume that the same pathway is followed in these reactions, too (Figure S8−S13, Supporting Information).

Using chlorostannoxane catalysts, we were able to produce considerable amounts of 2-oxazolidinones from 2-AAs and CO_2 at high turnover numbers (TON = 138), which are novel as the previous works were reported to have used high catalyst amounts to get good yields. As reported previously, the Lewis acidity of the chlorostannoxanes changes with a change in the substituents on the metal centers. We were able to observe a similar kind of trend in the influence of the nature of the catalyst with change in time and observed the fact that catalytic activity changes in the order of **1a** > **1b** > **1c** >**1d**.

ASSOCIATED CONTENT

Ⓢ Supporting Information
Plots corresponding to the activity of the catalysts and gas chromatograms of the reaction mixtures of various substrate. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

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