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Interaction of substrate and catalyst during the formation of oxazolidinones from 2-aminoalcohols and diethyl carbonate using recyclable 1,3-dichlorodistannoxanes

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ABSTRACT

An efficient synthesis of oxazolidinone (OXZ) using 2-aminoalcohols (2AAs) and diethyl carbonate (DEC) as reagents in the presence of recyclable catalyst 1,3-dichloro-1,1,3,3-tetraalkyldistannoxane, $[(RR'SnCl)_2O]_2$ (**1**) is reported. 0.5 mol% (with respect to 2AA) of **1** provides OXZ quantitatively within 1 h at 80 °C with turnover frequency (TOF) of 200 h^{-1}. The observed TOF is much higher than the reported value (4 h^{-1}) of the most convenient and commercially feasible K_2CO_3 catalyst. Chiral 2AAs produce OXZs with 99% ee. Molar dependency of **1**, DEC and 2AA is found to be 1:2:2. Molar conductivities (Ω^{-1} cm^2 mol^{-1}) in DMSO at 25 °C are 6.41 for **1a** (R = R′ = Bu), 5.25 for **1b** (R = Bu, R′ = Ph), 2.87 for **1c** (R = Ph, R′ = Bu), and 2.21 for **1d** (R = R′ = Ph) which reveal the mobility of bridged Cl in **1** during reaction. The study of a broad range of substrates and reaction parameters supports a reaction pathway that begins with initial attack by –OH of the pre-formed 2-ethylcarbamato aminoalcohol (2ECA) of 2AA on Sn^b of **1** displacing the bridged Cl. Change in the reaction rates resulted due to various alkyl and aryl substituents on Sn provides better understanding of the distannoxane catalysis, which has not been attempted before for the said reaction.

1. Introduction

Oxazolidinones (OXZs) are a class of cyclic urethanes that have various important applications. One of the major applications of OXZs is as chiral auxiliaries [1] for asymmetric transformations. Utilizing the versatile properties of OXZs, several important pharmaceutical products [2], polymers [3], and significant organic molecules can be synthesized [4]. Thus, in terms of organic synthesis, OXZs belong to a very important class of chemicals. In particular, 3-substituted 2-OXZs have been reported to be useful as synthetic reagents, inhibitors, and additives, demonstrating antibacterial and fungicidal activity [5]. Thus, synthetic methods having high yields and reduction in the production costs for such an important class of molecule are a realistic goal of many research efforts.

The preparation of OXZs is well-documented in the literature using various starting materials, catalysts, and reaction conditions. For example, oxidative carbonylation is one of the commonly practiced methods known to produce OXZs with CO and oxygen as starting materials on Pd- and Cu-based catalyst systems with high efficiency [6]. However, costly palladium cannot provide the economic viability for the synthesis, and copper has considerable toxicity. OXZs have also been synthesized using carbon dioxide as the starting material either in catalytic [7] or non-catalytic pathways [8]. But inferior reaction yields and undesirable byproduct formation make the processes less interesting. Propargylamine and CO_2 produce corresponding OXZs with greater ease and with high yields in the presence of Pd [9] or Ru [10] and a heterogeneous catalyst [11]. Still, the acetylenic group holds the key for the success of the reaction and is thus applicable to only a narrow range of substrates. Use of costly palladium or ruthenium at catalyst loading of 5 mol% is another disadvantage of the process. A tosyl derivative of OXZ can be obtained in high yields from serine using a Grignard/CuX catalyst system [12]. A four-step synthetic method has been reported by Green and co-workers for a tyrosine-based OXZ

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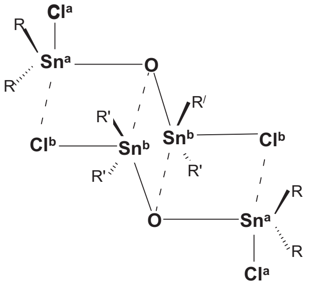

Dimeric structure of **1**

Name	R =	R/=
1a	Bu	Bu
1b	Bu	Ph
1c	Ph	Bu
1d	Ph	Ph

Scheme 1. OXZ formation from 2AA and DEC using **1**.

that can be used as a chiral auxiliary [13]. Selective rearrangement of certain carbamates also generates OXZ [14]. The rearrangement of specific propargylic *tert*-butylcarbamates, initiated by an efficient gold catalyst, has been reported for the synthesis of OXZ [15]. N-protected alkynylamines can be converted into alkylidene 2-OXZ under mild reaction conditions [16]. Cycloaddition of aziridines with isocyanates produces imino-OXZ [17], but the specific nature of the substrate and expensive catalyst system restricts the procedure from being widely practiced. Use of microwave irradiation as an energy efficient and "green" pathway to synthesize OXZ-2-ones starting with urea and ethanolamine and assisted by a catalytic amount of nitromethane has also been reported [18]. Trichloromethylchloroformate, a very reactive reagent, has been found to form OXZ, imidazolidinone and dioxolanone catalyzed by activated charcoal [19]. However, use of microwave irradiation and toxic trichloromethylformate severely limits these processes. Therefore, from the above discussion, it is evident that the synthesis of OXZs is specific to a substrate and catalyst, and lacks a broader scope.

2-Aminoalcohols (2AAs), which can be derived from their corresponding amino acids, are very useful substrates in the context of OXZ synthesis. They provide a much wider scope, and thus they are the focus of the present work. The synthesis involves cyclilization of 2AAs with organic carbonates or equivalent molecules in the presence of catalysts. The catalyst can be alkali-based or an equivalent, Lewis acidic, or transition metal-based [20]. Alkoxide catalysts require drastic reaction conditions that may damage the chirality, if present, of the final product [21] and may also produce other undesirable byproducts. Diethyl carbonate (DEC) in the presence of K_2CO_3 as a catalyst can produce the product at satisfactory yields [22]. It is noteworthy that 2AAs can also be converted to OXZ using alkali catalyst at the expense of cyclic carbonate [23] by transesterification method. However, use of DMF as solvent, long reaction time and moderate yields are major drawbacks for this process [24].

Considering all of the above-mentioned concerns, a simple, economically viable catalytic method that can be used for synthesizing a broad range of OXZs in good yields is still a major challenge. We have tried to address these concerns by using 1,1,3,3-tetraalkyl/aryl-1,3-dichloro distannoxane (**1**, 0.5 mol%) as an efficient, robust, and recyclable catalyst that can generate OXZ from the corresponding 2-aminoalcohols (2AA) in the presence of DEC in short time (1 h), under mild reaction conditions (80 °C) and in the absence of any additional solvent (Scheme 1). Turn over frequency (TOF) of the process is as high as 200 h^{-1} and the purity of the product is more than 98%. This is a significant improvement in comparison to one of the most efficient synthetic methods of OXZ production where TOF of 4 h^{-1} is achieved using K_2CO_3 as catalyst [20].

Catalysts **1** have been used in a number of places in organic syntheses: namely, in polyester synthesis [25], urethane [26] and polyurethane [27] synthesis, ring opening polymerization [28], esterification and transesterification [29] reactions, etc. They (**1**) show unique advantages in terms of reaction rate, product and catalyst separation, and high reaction yields when compared to the conventional Lewis acid-base catalysts like metal alkoxides or trihalides [29]. We have also demonstrated an efficient green process of transesterification reaction of polyhydric alcohol by varying lipophilicity of **1** [30]. Very recently, for the first time, we have established a synthetic method of producing biodiesel from triglycerides using **1** in supercritical CO_2 [31]. One of the major features of **1** is that it possesses multi-active catalytic centers with controllable Lewis acidity, offering several advantages over other catalysts [29,32]. This unique feature and versatility of **1** have encouraged us to study several unexplored areas such as OXZs synthesis.

In this report, we have studied a series of 2AAs, both chiral and achiral, in order to understand the structure-reactivity relationship (Scheme 1). Interestingly, recovered catalyst (**1**) shows efficiency in producing OXZ similar to that of the original one. Additionally, the reaction kinetics and the possible mechanism of the catalytic pathway have been discussed. The present work also addresses for the first time the effect of substituents on Sn to understand the mechanistic route of OXZ formation using **1**. The proposed mechanistic route is different compared to other literature reported distannoxane catalyzed [27,29,33] reactions where mostly alkyl and bridging groups of the catalyst are varied. As diethyl carbonate, a congener of carbon dioxide, is considered as a green solvent/reagent, the present findings will also contribute to the field of sustainable development for OXZ synthesis.

2. Experimental

2.1. General

Chemicals are purchased from Aldrich Chemical Company, USA and used without further purification unless otherwise specified. Solvents are purified by standard purification procedures before use in the reactions [34]. Reaction products are analyzed by Gas Chromatography (Shimadzu, GC 2010) using a DB-5 column (J&W Scientific). ^1H NMR spectra are obtained with a 300 MHz Varian FT spectrometer using deuterated solvent as the lock. The spectra are collected at 25 °C and chemical shifts (δ, ppm) are referenced to residual solvent peak ($CDCl_3$ δ, ^1H, 7.26 ppm). ^{119}Sn NMR has been recorded using a Bruker AV500 in $CDCl_3$. Electrospray ionization mass spectra (ESI-MS) are recorded using a Micromass Q-TOF mass spectrometer. Infra Red (IR) spectra are recorded using a Perkin Elmer, Spectrum 100 instrument. The elemental analyses (C, H) are carried out with a Perkin-Elmer 2400 C elemental analyzer (accuracy ±0.3%). Amount of tin was estimated using inductively coupled plasma optical emission spectroscopy (ICP-OES), Perkin Elmer, model 4300 DV (detection limit 1 ppm). Chloride is estimated using an Ion Chromatography (Metrohm) method (detection limit 1 ppb). Enantiomeric excess is measured in Shimadzu LC 2010 HPLC using Daicel's CHIRALPAK®AD-H column.

Catalysts are synthesized according to an established procedure [30]. Chlorine and Sn are determined according to published methods [35].

2.2. Preparation of oxazolidinone

In a typical reaction, 257 g (2.18 mol) of DEC, 73.3 g (0.49 mol) (S)-phenylalaninol and 1.2 g (0.001 mol) catalyst **1a** are combined in a three-necked round bottom flask equipped with a 12″ Vigreux condenser and heated at 80 °C for 1 h. The initial heterogeneous solution slowly becomes homogenous within 10 min. The progress