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PII: S0040-4020(16)30015-1

DOI: 10.1016/j.tet.2016.01.015

Reference: TET 27422

To appear in: *Tetrahedron*

Received Date: 18 October 2015

Revised Date: 2 January 2016

Accepted Date: 8 January 2016

Please cite this article as: Liu H, Hua R, Conversion of carbon dioxide into 2-oxazolidinones and 2(3*H*)-oxazolones catalyzed by 2,2',2'-terpyridine, *Tetrahedron* (2016), doi: 10.1016/j.tet.2016.01.015.

Graphical Abstract

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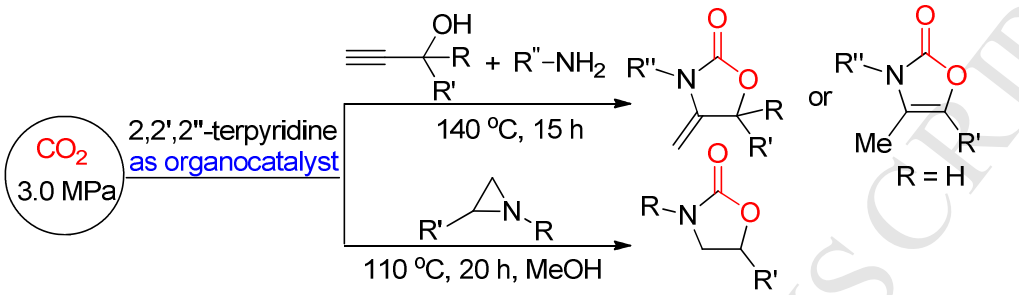

Conversion of carbon dioxide into 2-oxazolidinones and 2(3*H*)-oxazolones catalyzed by 2,2',2''-terpyridine

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Abstract:

The catalytic activation of pyridines as organocatalysts in the three-component cycloaddition of CO_2, propargyl alcohol and primary amine was investigated, and 2,2',2''-Terpyridine was found to be the efficient organocatalyst to afford 4-methylene-2-oxazolidinones or 2(3*H*)-oxazolones in good to high yields. 2,2',2''-Terpyridine also showed high catalytic activity in the coupling reaction of CO_2 with aziridines bearing either electron-donating or electron-withdrawing *N*-substitutents to give substituted 2-oxazolidinones in high yields.

Key Words: Carbon dioxide; 4-Methylene-2-oxazolidinones; 2-Oxazolidinones; 2(3*H*)-Oxazolones, Pyridine; 2,2',2''-Terpyridine

1. Introduction

Substituted 2-oxazolidinones are one of the important five-membered heterocyclic compounds, which not only show interesting biological and physiological activities,[1] but also have been applied as intermediates in the synthesis of other functional compounds.[2] In particular, chiral 2-oxazolidinones have been widely applied as chiral auxiliaries in asymmetric syntheses,[3] and substituted 4-methylene-2-oxazolidinones are the good synthons for the formation of spiro compounds.[4] Owing to the importance of 2-oxazolidinones, a variety of methods were developed for their selective synthesis.[5] Among recent reported synthetic methods, the reaction of CO_2 with propargylamines,[6] or the three-component cycloaddition of CO_2, propargyl alcohols and primary

amines giving 4-methylene-2-oxazolidinones,[7] or the coupling reaction of CO_2 with aziridines affording 2-oxazolidinones[8] are the most interesting and promising synthetic methods from the viewpoint of developing CO_2 as carbon source, since the transformation of CO_2 into the value-added organic compounds is a very important and a hot research topic in organic synthetic chemistry and green chemistry.

Recent years, attempts have been made in our group to develop the efficient catalyst systems including not only transition metal complexes,[9] but also organic compounds[10] as catalysts to transfer CO_2 into organic compounds. In continuation of our interest in developing efficient catalysts in the transformation of CO_2 into the value-added organic compounds, we are interested in the synthesis of 4-methylene-2-oxazolidinones from the three-components cycloaddition of CO_2, propargyl alcohols and primary amines in the presence of pyridine and its derivatives as organocatalysts. Because there are only two papers reporting such transformation by using PBu_3[7(b)] and guanidine[7(h)] as organocatalysts, and however 2,2',2''-terpyridine was found to be the efficient organocatalyst in our group in the coupling reaction of CO_2 with epoxides giving cyclic carbonates.[10(b)]

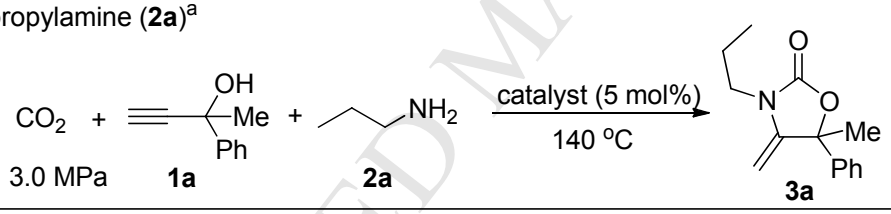
2. Results and discussion

The three-component cycloaddition of CO_2, 2-phenyl-3-butyn-2-ol (**1a**) and *n*-propylamine (**2a**) was performed in an autoclave with stirring under different conditions to examine the catalytic activity of pyridines and to find out the optimal conditions. A mixture of **1a**, **2a** (2.0 equiv) and pyridine or its derivatives (0.05 equiv) was placed in a 25-mL of autoclave, and CO_2 (3.0 MPa of initial pressure) was pressurized directly to the autoclave under air atmosphere at ambient temperature, and then the autoclave was heated at 140 ^oC (oil bath temperature). As summarized in Table 1, without any catalyst, the expected reaction also took place, and the desired 5-methyl-4-methylene-5-phenyl-3-*n*-propyloxazolidin-2-one (**3a**) was formed in 17% GC yield after 24 h (entry 1), but the use of 5 mol% pyridine as organocatalyst could greatly increase the yield to 50% (entry 2). The substituted pyridine derivatives at 2- position, such as 2-methylpyridine

(entry 3, 58%), 2-(*N*,*N*-dimethyl)pyridine (entry 4, 46%) displayed similar catalytic activity as pyridine as organocatalyst (entry 2, 50%), and 2-aminopyridine was found to have considerably higher catalytic activity for the formation of **3a** (entry 5, 68%). Under the similar reaction conditions, the use of 2,2',2''-terpyridine yielded **3a** in decent yield (entry 6, 87%). However, the use of MeCN or toluene as solvent was proven to be improper for the transformation (Table 1, entries 7-8). Interestingly, under solvent-free conditions, the yield of **3a** was nearly unaffected when the reaction time was shortened to 15 h (Table 1, entry 9 *vs* entry 6). Although at the same reaction time when the oil bath temperature was reduced to 110 °C, or the pressure of CO_2 was decreased to 1.0 MPa, the yields of **3a** were dramatically decreased to 38% and 59%, respectively (Table 1, entries 10-11). Therefore, the reaction conditions indicated in entry 9 of Table 1 were chosen as the optimal conditions for the following present three-component cycloaddition reactions.

Table 1

Optimizing reaction conditions for cycloaddition of carbon dioxide, 2-phenyl-3-butyn-2-ol (**1a**) and *n*-propylamine (**2a**)[a]

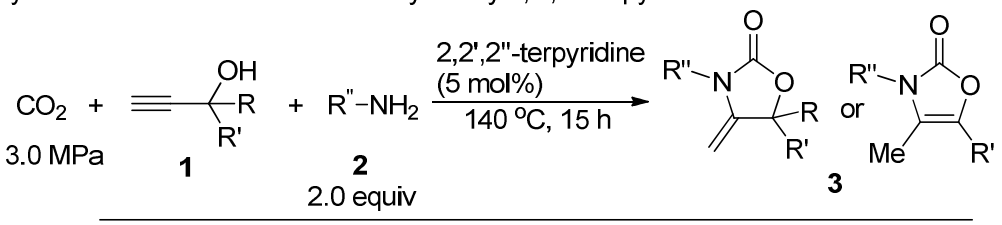


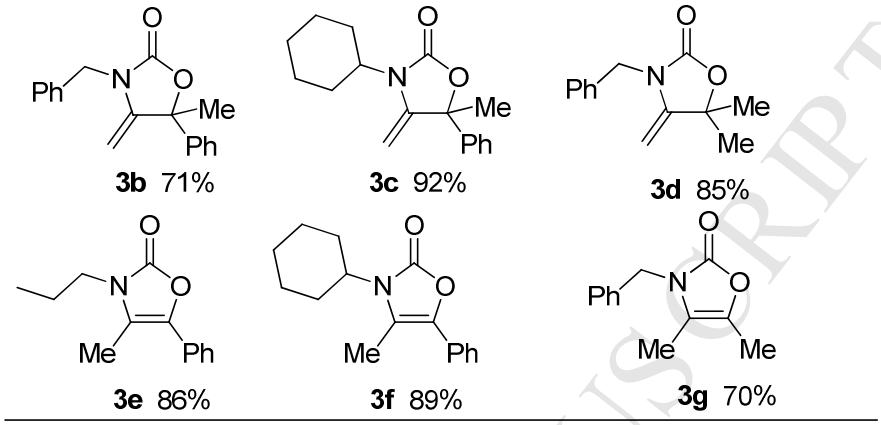
Entry	Catalyst	Time (h)	Solvent	GC Yield (%)[b]
1	—	24	—	17
2	pyridine	24	—	50
3	2-methylpyridine	24	—	56
4	2-dimethylaminopyridine	24	—	46
5	2-aminopyridine	24	—	68
6	2,2',2''-terpyridine	24	—	87
7	2,2',2''-terpyridine	24	MeCN	63
8	2,2',2''-terpyridine	24	toluene	56
9	2,2',2''-terpyridine	15	—	87 (85)
10[c]	2,2',2''-terpyridine	15	—	38
11[d]	2,2',2''-terpyridine	15	—	59

[a] The reactions were carried out using 2.0 mmol of **1a**, 4.0 mmol of **2a** and 5 mol % of catalyst in a 25-mL autoclave with 3.0 MPa of CO_2.
[b] GC yields of **3a** are based on **1a** by using *n*-$C_{18}H_{38}$ as internal standard, and isolated yield in parenthesis.
[c] at 100 °C.
[d] 1.0 MPa of CO_2.

Table 2

Synthesis of 2-oxazolidinones catalyzed by 2,2',2"-terpyridine[a]



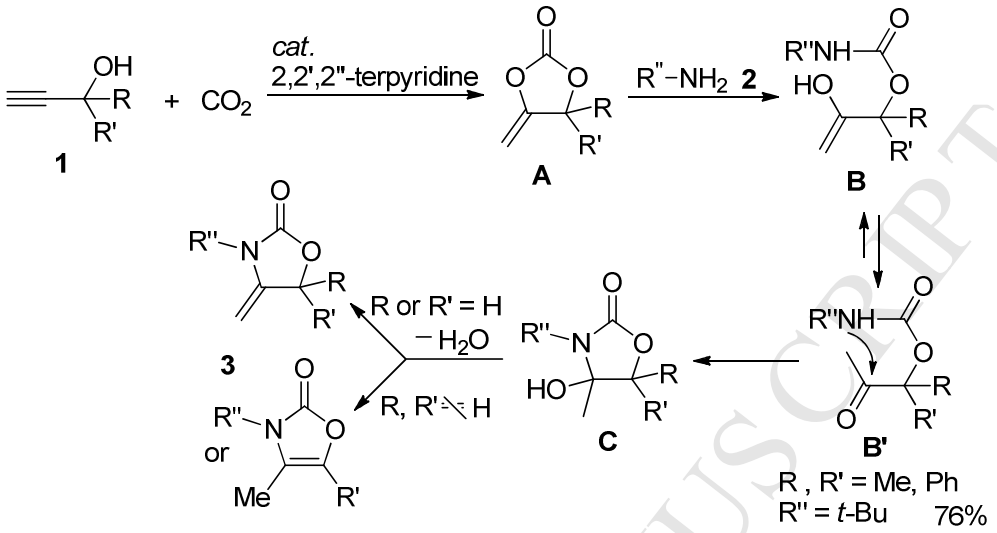


[a] Reactions were carried out using 2.0 mmol of **1**, 4.0 mmol of **2**, and the yield of **3** is isolated yields.

As shown in Table 2, the cycloaddition reactions of CO_2, **1a** with benzylamine, or cyclohexylamine gave the corresponding 4-methylene-2-oxazolidinones (**3b**-**c**) in 71% and 92% yields, respectively. The reaction of 2-methyl-3-butyn-2-ol with CO_2 and benzylamine produced the expected cyclic compound **3d** in good yield. In the cases of 1-phenyl-2-propyn-1-ol or 3-butyn-2-ol used, the reactions afforded *multi*-substituted 2(3*H*)-oxazolone derivatives (**3e**-**g**) instead of the expected 4-methylene-2-oxazolidinone derivatives. However, when anilines (*e.g.* phenylamine, 4-methylaniline) or internal propargyl alcohols were used, the corresponding 2-oxazolidinones or 2(3*H*)-oxazolones could not be formed.

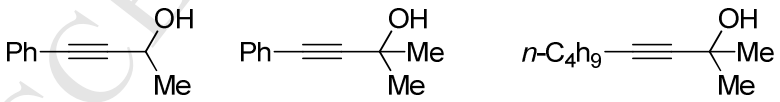
On the basis of the reported catalytic system[7(a), 7(f), 7(i)], and our results, a proposed mechanism for the formation of 4-methylene-2-oxazolidinones or 2(3*H*)-oxazolones is depicted in Scheme 1, which includes the formation of α-methylene cyclic carbonate as intermediate **A** in the presence of 2,2',2"-terpyridine, and its nucleophilic addition reaction with primary amine to give *N*-alkylcarbamate **B'**, subsequent cyclization by intramolecular nucleophilic addition reaction and dehydration reaction affording 4-methylene-2-oxazolidinones or 2(3*H*)-oxazolones, depending upon

the substituents R and R'. In the case of **1a** and *tert*-butylamine employed, intermediate **B'** was isolated in 76% yield,[11] possibly due to the steric hindrance of *t*-butyl group to restrain the further transformation of **B'** to **C**. These obtained results support partly the proposed mechanism.



Scheme 1. Proposed mechanism for the formation of 4-methylene-2-oxazolidinones and 2(3*H*)-oxazolones.

It should be noted that when internal propargylic alcohols, such as 1,3-diphenylpropargylic alcohol, 2-methyl-4-phenyl-3-butyn-2-ol and 2-methyl-3-octyn-2-ol (Scheme 1) were subjected to the optimized reaction conditions, the desired 2(3*H*)-oxazolones and 4-methylene-2-oxazolidinones could not be obtained.



Scheme 2. Internal propargylic alcohols.

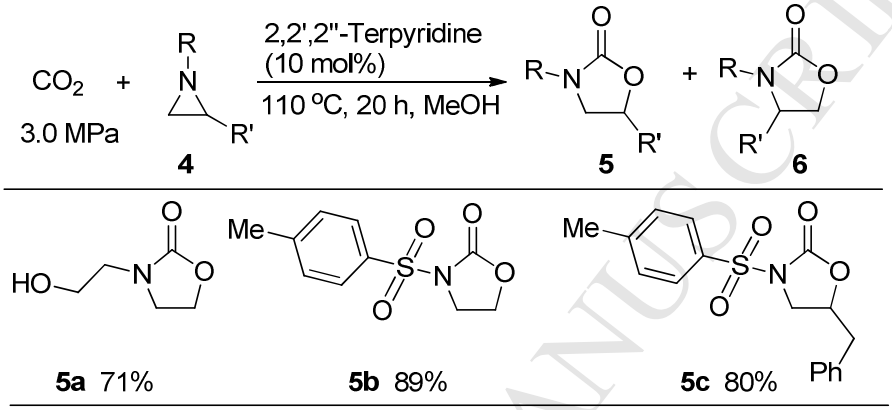
As mentioned-above, the coupling reaction of CO_2 with aziridines has also been one of the interesting and important reactions to construct 2-oxazolidinone ring, even aziridines are usually limited and difficult to be prepared. Therefore, in this work, the catalytic activity of 2,2',2"-terpyridine in the reaction of CO_2 with aziridines was also briefly investigated.

It was found that the reaction of *N*-(2-hydroxyethyl)aziridine (**4a**) with CO_2 under the same

reaction conditions (Table 2) afforded the expected product of 3-(2-hydroxyethyl)oxazolidin-2-one (**5a**) in very low yield (< 5%). After re-optimizing reaction conditions, **5a** could be obtained in 71% yield by using 10 mol% of 2,2',2''-terpyridine as catalyst and methanol as solvent at 110 ^{o}C for 20 h (Table 3).

Table 3

Coupling reactions of aziridines with CO_2 catalyzed 2,2',2''-terpyridine[a]



[a] Reactions were carried out using 3.0 mmol of **4** in 2.0 mL of MeOH, and yield of 5 is isolated yield.

It is worth note that there are only two reported efficient catalyst systems for the reaction of CO_2 with *N*-tosylaziridines [*N*-(*p*-toluenesulfonyl)aziridine] to give 5-substituted oxazolidin-2-ones **5**[8(l)] or 4-substituted oxazolidin-2-ones **6** with high regioselectvity.[8(b)] On the basis of the results in Table 3, 2,2',2''-terpyridine has been demonstrated to be the simple organocatalyst for the coupling reactions of CO_2 with *N*-tosylaziridine or 2-phenyl-1-tosylaziridine to give the corresponding 2-oxazolidinone in high yields. More importantly, in the case of 2-benzyl-1-tosylaziridine used, the reaction occurred with high regioselectivity to form 5-benzyl-3-tosyl-oxazolidin-2-one (**5c**) in 80% isolated yield, and only trace amount (< 1%) of 4-benzyl-3-tosyl-oxazolidin-2-one (**6c**) was determined in the reaction mixture by GC-MS. Therefore, 2,2',2''-terpyridine has been proven to be an efficient organocatalyst for the selective synthesis of 5-substituted oxazolidin-2-ones *via* the cycloaddition of CO_2 to aziridines having electron-withdrawing *N*-substitutent.

3. Conclusion

Results reported in this paper have demonstrated that 2,2',2''-terpyridine is an efficient organocatalyst to catalyze the three-component cycloaddition reaction of CO_2, propargyl alcohols and primary amines affording 4-methylene-2-oxazolidinones or *multi*-substituted 2(3*H*)-oxazolones depending on the structures of propargyl alcohols, and the coupling reaction of CO_2 with aziridines producing 2-oxazolidinones, providing an alternatively simple, and metal-free organocatalytic system for the transformation of CO_2 into the value-added organic compounds.

4. Experimental section

4.1. General Methods

All organic starting materials are analytically pure and used without further purification. All reactions were carried out without any particular precautions to moisture or oxygen. Nuclear magnetic resonance (NMR) spectra were recorded using $CDCl_3$ as solvent at 298 K. ^{1}H NMR (300 MHz & 400 MHz) chemical shifts (δ) were referenced to internal standard TMS (for ^{1}H, δ = 0.00 ppm). ^{13}C NMR (75 MHz & 101 MHz) chemical shifts were referenced to internal solvent $CDCl_3$ (for ^{13}C, δ = 77.16 ppm). Gas chromatography (GC) analyses were performed on a GC instrument (capillary 25m column). Mass spectra (MS) were obtained on a low-resolution GC/MS spectrometer with a PEG-25M column resonance.

4.2. General experimental procedure for the three-components cycloaddition of CO_2, propargyl alcohol and primary amine catalyzed by 2,2',2''-terpyridine: A mixture of propargyl alcohol (2.0 mmol), primary amine (4.0 mmol) and 2,2',2''-terpyridine (0.1 mmol) was charged in a 25-mL autoclave, and then CO_2 was introduced at an initial pressure of 3.0 MPa at room temperature. The autoclave was heated at 140 ^{o}C (oil bath temperature) with stirring for 15 h. After the reaction, the autoclave was cooled to room temperature, and CO_2 was released slowly. The obtained mixture was dissolved in CH_2Cl_2 (10 mL), and was then concentrated to *ca*. 1.0 mL. The desired product **3** was obtained by flash column chromatography on silica gel with petroleum ether

as eluent.

4.3. General experimental procedure for the coupling reaction of CO_2 with aziridines in the presence of 2,2',2''-terpyridine affording 2-oxazolidinones (5a–c): A mixture of aziridines (3.0 mmol), 2,2',2"-terpyridine (0.3 mmol) and methanol (2.0 mL) was charged in a 25-mL autoclave, and then CO_2 was introduced at an initial pressure of 3.0 MPa at room temperature. The autoclave was heated at 110 ^{o}C (oil bath temperature) with stirring for 20 h. After the reaction, the autoclave was cooled to room temperature, and CO_2 was released slowly. The obtained mixture was then concentrated to *ca*. 1.0 mL. The desired product **5** was obtained by flash column chromatography on silica gel with petroleum ether as eluent.

4.4. Characterization data of products

All the products (**3a-g** and **5a-c**) were known compounds and identified by their ^{1}H-NMR, ^{13}C-NMR and GC-MS (see Supporting Information).

Acknowledgments

This project was supported by the National Basic Research Program of China (973 Program, 2011CB201405).

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11. The characterization data are reported in Supporting Information.