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Copper(I)-Catalyzed Four-Component Coupling Using Renewable Building Blocks of CO₂ and Biomass-Based Aldehydes

Qiumin Wu,^[a,b] Jinzhu Chen,^{*,[b]} Xuhong Guo^[a] and Yisheng Xu^{*,[a]}

^[a] State-Key Laboratory of Chemical Engineering, East China University of Science and Technology.
130 Meilong Rd., Shanghai 200237, P.R. China.
^[b] College of Chemistry and Materials Science, Jinan University. No. 601 Huangpu Avenue West,
Tianhe District, Guangzhou 510632, P.R. China.
*Corresponding author. E-mail address: <u>chenjz@jnu.edu.cn</u> (J. Chen), <u>yshxu@ecust.edu.cn</u> (Y. Xu);
Tel./Fax: (+86)-20-8522-0223.

Abstract: Both carbon dioxide (CO₂) and biomass-based molecules are recently regarded as renewable, abundant, environmentally benign, and attractive carbon-based feedstocks for organic synthesis. Therefore, a mild and efficient method for a synthesis of 1,3-oxazolidin-2-ones was developed through a green four-component coupling reaction by using CO₂, biomass-based aldehydes such as furfural and 5-hydroxymethylfurfural (HMF), terminal aromatic alkynes, and primary aliphatic amines with copper iodide as a catalyst. Twenty-four examples of furyl-substituted 1,3-oxazolidin-2-ones were obtained in 29–84% yields from the four-component coupling reaction. Moreover, the coupling reaction was applicable for the syntheses of furyl-containing bis-oxazolidinone and poly-oxazolidinone under mild conditions.

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1. INTRODUCTION

The growing carbon dioxide (CO₂) emissions has recently received much attentions due to global warming effect. It poses one of the opportunities for the transformation of CO₂ from industrial sources and the atmosphere to basic chemicals, together with a reduction of fossil fuel usage.^[1-5] In other words, as a renewable, inexpensive, abundant, non-toxic and C1 building block on earth, CO₂ has gained considerable concerns in the conversion into various significantly important chemicals and organic intermediates, such as cyclic carbonates,^[6-7] dimethyl carbonates,^[8-9] polycarbonates,^[10-11] polyurethane,^[12-13] methanol,^[14-15] formic acid,^[16-17] formats,^[18] formamides,^[18] carbamic acid(ester),^[19] oxazolidinones^[20] and others.^[21]

Among these CO₂-derived chemicals, the oxazolidinone framework constitutes a significant class of biological and pharmaceutical compounds. Therefore, oxazolidinone compounds are widely used in pharmaceutical chemistry and fine chemicals as versatile intermediates and chiral auxiliaries.^[22-23] Typically, oxazolidinones were employed as monoamine oxidase inhibitors,^[24] cholesteryl ester transfer protein inhibitors,^[25] and anticonvulsant drugs such as ethadione, paramethadione, and trimethadione.^[26] The preparation of oxazolidinones has been extensively investigated by using various reagents and catalytic system as shown in Scheme 1.^[27] From the perspective of green chemistry, the cycloaddition procedure for oxazolidinone preparation using CO₂ as a C1 source is more attractive in comparison with other processes. For example, the synthesis of oxazolidinone from CO₂ and propargylic amines through carboxylative cyclization were systematically examined by using various catalysts including transition metal catalysts of Pd,^[28] Ag,^[29] Au,^[30] Zn,^[31] and metal-free catalysts such as protic ionic liquids,^[32] superbases,^[33] N-heterocyclic carbene.^[134] Moreover, it is very inspiring for oxazolidinone synthesis by a three-

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component coupling between CO₂, propargylic alcohol and primary amine with transition-metal catalysts such as Ag,^[35] Cu,^[36] Ru,^[37] and tertiary phosphine,^[38] CuCl/ionic liquids,^[39] ionic liquids.^[40] Due to the fact that propargylamine can be prepared by a three-component coupling reaction between alkyne, amine and aldehyde (Scheme 1). Li and his co-workers reported the 1,3-oxazolidin-2-one synthesis from a multi-component coupling by using benzaldehyde and CO₂.^[41,42]



Scheme 1. Various methods for synthesis of oxazolidinone

In addition to CO₂, biomass is regarded as a renewable, abundant and attractive carbon-based feedstock as well as a promising alternative for fossil source.^[43] Typically, Yan and co-workers recently reported renewable heterocyclic compound synthesis from biomass-based carbohydrates, chitin and waste shrimp shells.^[44-45] In addition, both furfural and 5-hydroxymethylfurfural (HMF) are biomass-based versatile platform chemicals with high potential for the syntheses of bio-fuels and biomass-based fine chemicals such as levulinic acid,^[46-47] γ-valerolactone, 3,5-dihydroxymethylfurfural, 2,5-furandicarboxylic acid, 2,5-diformylfuran and so on.^[48] We thus

believe it should be very promising in term of green and high atomic efficiency for a four-component coupling reaction by using renewable building blocks of CO₂ and biomass-based furfural or HMF for the preparation of furyl-containing 1,3-oxazolidin-2-ones. However, compared with benzaldehyde, the presence of furan ring in the furfural and HMF makes them more reactive and unstable, and various complicated furan ring-related reactions such as Diels-Alder reaction,^[49] hydrolytic ring opening,^[50] hydrogenolytic ring opening,^[51] ring hydrogenation,^[52] furan ring polymerization,^[53-54] and humins formation^[55-56] were observed during their transformations. Furthermore, the presence of activated hydroxymethyl group in HMF makes it more difficult to become the desired product.^[56] It is thereby an urgent need but still a significant challenge to develop methodology for furfural- and HMF-related transformations. As far as we know, the synthesis of furyl-substituted 1,3-oxazolidin-2-ones *via* four-component coupling reaction by using biomass-based aldehydes such as furfural and HMF is barely reported and no systematic research has ever been described.



Scheme 2. CuI-promoted four-component coupling and three-component coupling reactions

Herein, we demonstrated the copper-promoted four-component coupling reactions by using renewable building blocks of CO₂ and biomass-based furfural or HMF for the preparation of furyl-substituted 1,3-oxazolidin-2-ones (Scheme 2). Our research revealed that the four-component

coupling reaction between terminal aromatic alkyne, primary aliphatic amine, CO₂, and biomassbased aldehyde afforded the desired 1,3-oxazolidin-2-one. In the case of aldehyde substrates, both furfural and HMF were applicable for the coupling reactions. For primary aliphatic amine reagents, even *tert*-butylamine with strong steric hindrance afforded the corresponding oxazolidinone. Moreover, we also reported the synthesis of furyl-substituted bis-oxazolidinone from dialkyne, as well as furyl-containing poly-oxazolidinone from dialkyne and diamine by using the coupling reactions. In terms of aromatic amine and secondary aliphatic amine, a three-component coupling between aromatic alkyne, amine and biomass-based aldehyde was observed to give furyl-substituted propargylamine without the participation of CO₂ (Scheme 2).

2. RESULTS & DISCUSSION

Initially, the optimization process was performed by using various copper salts for the model reaction of a four-component coupling reaction between phenylacetylene **1a**, biomass-based furfural **2a**, and cyclohexylamine **3a** under pressurized CO₂ to give furyl-substituted 1,3-oxazolidin-2-one **4a** (Table 1). Screening of various investigated copper salts indicates that CuI is the most effective catalyst for the coupling by producing the desired **4a** in 73% yield under the investigated conditions (Table 1, entries 1-5) with trace amount of 1,4-diphenylbuta-1,3-diyne (Supporting Information) as by-product. Evidently, the anion of cuprous salt catalyst (CuX, X = Cl, Br, I) plays an important role in the reaction and the promotion effect of the anion increases with the order of Cl⁻ < Br⁻ < l⁻, which is in line with the tendency of its leaving ability and nucleophilicity. Therefore, the leaving tendency of anion may presumably accelerate the formation of active Cu⁺ complex.^[32,57] Moreover, our control experiment demonstrates that **4a** was unobserved in the absence of any catalysts, further

		1a 2a	[Cu]			
	+ 00		12			
		3a		4a 🎽		
Entry	Catalyst	Т	P _{CO2}	t	Solvent	4a Yield ^b
	[mol%]	[°C]	[MPa]	[h]		[%]
1	CuSCN (30)	75	0.5	12	EtOH	0
2	Cu(OTf) ₂ (30)	75	0.5	12	EtOH	3
3	CuCl (30)	75	0.5	12	EtOH	27
4	CuBr (30)	75	0.5	12	EtOH	54
5	CuI (30)	75	0.5	12	EtOH	73
6	CuI (10)	75	0.5	12	EtOH	44
7	CuI (20)	75	0.5	12	EtOH	70
8	CuI (40)	75	0.5	12	EtOH	63
9	CuI (30)	55	0.5	12	EtOH	10
10	CuI (30)	65	0.5	12	EtOH	18
11	CuI (30)	85	0.5	12	EtOH	65
12	CuI (30)	95	0.5	12	EtOH	63
13	CuI (30)	75	0.1	12	EtOH	59
14	CuI (30)	75	1.0	12	EtOH	76
15	CuI (30)	75	1.5	12	EtOH	70
16	CuI (30)	75	2.0	12	EtOH	71
17	CuI (30)	75	2.5	12	EtOH	71
18	CuI (30)	75	0.5	8	EtOH	64
19	CuI (30)	75	0.5	10	EtOH	73
20	CuI (30)	75	0.5	14	EtOH	60
21	CuI (30)	75	0.5	16	EtOH	72
22	CuI (30)	75	0.5	12	Toluene	18
23	CuI (30)	75	0.5	12	H ₂ O	34
24	CuI (30)	75	0.5	12	EtOAc	55
25	CuI (30)	75	0.5	12	THF	63

Table 1. Optimization for the copper-promoted four-component coupling reaction betweenphenylacetylene, furfural, CO_2 and cyclohexylamine^a

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^{*a*}Reaction conditions: **1a** (102 mg, 1.0 mmol), **2a** (192 mg, 2.0 mmol), **3a** (198 mg, 2.0 mmol), catalyst (10-40 mol% relative to **1a**), CO₂ (0.1-2.5 MPa), solvent (0.11 mL), reaction temperature (55-75 °C), reaction time (8-16 h). ^{*b*}Based on **1a** and determined by HPLC using external standard method with mobile phase of CH₃OH and H₂O (V_{CH3OH}:V_{H2O} = 1:1).

indicating the excellent promotion effect of the CuI on the coupling reaction. The influence of catalyst loading level on the coupling reveals that 4a yields are smoothly increased to a maximum with an optimum CuI loading amount of 30 mol% relative to the 1a (Table 1, entries 5-8). As expected, the effect of reaction temperature was observed to dramatically raise the 4a yield from 10% at 55 °C to 73% at 75 °C under the investigated conditions (Table 1, entries 5, 9-10), reflecting a remarkable promotion effect of temperature on the coupling reaction. However, a further increase of temperature leads to a slightly reduced 4a yield (Table 1, entries 5, 11-12). The influence of initial CO₂ pressure on the reaction reveals that an enhancement of CO₂ pressure from atmospheric pressure to 0.5 MPa improve the 4a yield from 59% to 76% (Table 1, entries 5, 13-14), showing a requirement of higher CO₂ concentration to promote the coupling reaction. When the CO₂ pressure is high enough to smoothly accomplish the coupling reaction, a further increased CO₂ pressure above 0.5 MPa shows very limited effect on the coupling reaction (Table 1, entries 5, 13-17). The influence of reaction time on the coupling shows an optimum of 12 h for the reactions (Table 1, entries 5, 18-21). Besides, the reaction is strongly dependent on the reaction media in which ethanol is the best for the reaction. Generally, the 4a yields obtained from polar solvents such as EtOH, THF, EtOAc and H₂O are much higher than that obtained from nonpolar solvents such as toluene (Table 1, entries 5, 22-25).

To probe the scope of the coupling reaction, various aromatic alkynes **1**, amines **3** and biomassbased aldehydes **2** were systematically investigated under the optimized conditions. In general, both biomass-based furfural **2a** and HMF **2b** were converted smoothly into the corresponding products by using the optimized conditions at hand (Table 2). In the case of the coupling of *para*-substituted phenylacetylene **1a** with furfural **2a**, cyclohexylamine **3a** and CO₂, the yields of target oxazolidinones





^{*a*}Reaction conditions: alkyne **1** (1.0 mmol), amine **3** (2.0 mmol), aldehyde **2** (2.0 mmol), CuI (57 mg, 0.3 mmol), EtOH (0.11 mL), CO₂ (0.5 MPa), 75 °C, 12 h. Isolated oxazolidinone yields based on **1**. ^{*b*}Reaction conditions: 1,3-diethynylbenzene (1.0 mmol), **2** (4.0 mmol), cyclohexylamine (4.0 mmol),

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CuI (0.3 mmol), EtOH (0.11 mL), CO2 (1.0 MPa), 75 °C, 36 h.

decreases with the complexity of substituted groups on the phenylacetylene molecule. Notably, both the electron-donating groups, including methyl 4c, ethyl 4g and methoxyl 4e, and electronwithdrawing groups such as chlorine 4i are well-tolerated in the reaction system. Similar results were also observed in the coupling of *para*-substituted phenylacetylene 1a with HMF 2b, cyclohexylamine 3a and CO₂. Notably, the methyl-substituted phenylacetylene with methyl group on *meta*-position of the benzene 4k gives the same yield when compared with the *para*-substituted product 4a, which demonstrates that the coupling yield is presumably not affected by the position of the methyl group when furfural 2a participates in the reaction. In addition to phenylacetylene and substituted phenylacetylene, 2-ethynylthiophene and 2-ethynylpyridine are applicable for the coupling reactions, yielding thiophene-substituted oxazolidinone **4m** and pyridine-substituted oxazolidinone **4p**, respectively. Moreover, the coupling reaction was performed very well with 1,3-diethynylbenzene to give the desired furyl-containing bis-oxazolidinone products 5a and 5b, further suggesting the widespread applicability of the coupling towards aromatic terminal alkyne substrates. However, aliphatic terminal alkyne of 1-octyne was inapplicable to the coupling reactions under the investigated condition, presumably due to its low acidity.^[58-59] Notably, the four-component coupling reactions between phenylacetylene 1a, butylamine, CO₂ with biomass-based aldehydes including both furfural and HMF show relatively low yields of furyl-containing 1,3-oxazolidin-2-ones (32-50%, 4u-v, Table 2) if compared with the 1,3-oxazolidin-2-one yields from the coupling reactions with benzaldehyde (85%).^[41] Moreover, the variation of the yields of furyl-substituted 1,3-oxazolidin-2one products (4a-z, Table 2) are irregular when compared with those of benzaldehyde-participated

1,3-oxazolidin-2-one syntheses.^[41] Finally, the furfural- and HMF-participated CO₂-fixation reactions generally show low yields of target products than those from high reactive substrates such as epoxide, aziridine, 2-aminoethanol and terminal alkyne or those through a domino reaction substrate including terminal propargyl alcohol, propargylic amine, o-alkynylaniline derivatives etc.^[60-62] These results can presumably be attributed to the instability of furan ring.^[63] According to the reported references, the furan ring opening reactions,^[51] furan ring polymerization,^[53-54] and polymeric humins formations^[55-56] occurred constantly in the furfural- and HMF-involved reactions. Particularly, polymeric humins can neither be analyzed by HPLC nor be quantified according to their composition.^[64-65] In addition to biomass-based furfural and HMF, aldehydes including 5-methyl-2-furaldehyde, 5-ethyl-2-furaldehyde and 5-chloro-2-furaldehyde were investigated for the four-component coupling with moderate to low yield of the desired 1,3-oxazolidin-2-ones **5c-e** as shown in Table 2.

Encouraged by the wide scope of alkynes, we further investigated the effect of amine substrate on the 1,3-oxazolidin-2-one preparation. Not surprisingly, the coupling reactions show a very broad substrate scope to primary amines regardless of the participation of furfural **2a** or HMF **2b**. Typical primary aliphatic amines, such as *n*-propylamine, *n*-butylamine and *n*-octylamine give the corresponding 1,3-oxazolidin-2-ones in 32~70% yields (**4q-v**, Table 2), presumably owing to the strong adsorption of primary amines towards CO₂ under mild conditions. ^[66] The coupling reaction with benzylamine was also performed smoothly with decent yields of the corresponding target products (**4w-x**, Table 2). Notably, *tert*-butylamine, with strong steric-hindrance effect, shows limited effect on the coupling by producing the corresponding oxazolidin-2-one with reasonable yields (**4yz**, Table 2). However, in the case of aniline, propargylic amine products **6a-b** (Table 3) were observed

Table 3. Synthesis of various propargylamines *via* CuI-promoted three-component coupling betweenphenylacetylene, amine and biomass-based aldehyde. a



^{*a*}Reaction conditions: **1a** (1.0 mmol), **2** (2.0 mmol), **3** (2.0 mmol), CuI (57 mg, 0.3 mmol), EtOH (0.11 mL), 75 °C, 12 h. Isolated propargylamine yields based on **1a**. ^{*b*}Reaction conditions: 1,3-diethynylbenzene (1.0 mmol), **2** (4.0 mmol), aniline (4.0 mmol), CuI (0.3 mmol), EtOH (0.11 mL), 75 °C, 36 h. Isolated bis-propargylic amine yields based on 1,3-diethynylbenzene.

by CuI-promoted three-component coupling of phenylacetylene **1a**, aniline and biomass-based aldehydes **2**. We speculated that low pK_a of propargylic amine **6a-b** inhibits the nucleophilic attack of nitrogen atom in the **6a-b** to CO₂ and prohibits the subsequent hydrogen transfer from NH group in **6a-b** to the oxygen atom of CO₂. ^[67-70] From the point of view, the pKa and the number of activated hydrogen atoms are the most important factors, jointly determining the types of the coupling reaction. Besides, the furyl-containing bis-propargylic amines **6c-d** were successfully synthesized by the coupling of 1,3-diethynylbenzene, aniline and aldehyde **2**. Finally, secondary aliphatic amines, including diethyl amine and pyrrolidine, undergoes a three-component assembly with phenylacetylene and biomass-based aldehydes **2** to give the corresponding furyl-containing propargylic amines 6e-h under the investigated conditions (Table 3).

Previously, phenyl-substituted bis-oxazolidinone was prepared copper-catalyzed fourcomponent coupling between phenylacetylene, benzaldehyde, diamine hydrochloride salt and CO₂; while, phenyl-containing poly-oxazolidinone was synthesized from 1,3-diethynylbenzene, benzaldehyde, diamine hydrochloride salt and CO2.^[42] In our case, in addition to the synthesis of furyl-containing bis-oxazolidinone products 5a and 5b, we further investigated the preparation of furyl-containing poly-oxazolidinone 7 by the CuI-coupling of 1,3-diethynylbenzene furfural, 1,6hexanediamine and CO₂ (Scheme 3). It is worth mentioning that various attempts were made to dissolve the black and hard solid of furyl-containing poly-oxazolidinone 7 with solvents such as H₂O, CH₂Cl₂, THF and DMF but without any success. Figure 1 shows a solid state ¹³C-NMR spectrum of the 7. The characteristic signal of carbonyl in the oxazolidinone ring was observed at 154 ppm. $^{[41,42]}$ While, the free carbons on the benzene ring of 7 shows specific peaks at 126 and 130 ppm. Besides, three signals at 112, 144 and 151 ppm are ascribed to the carbon atoms on the furan rings.^[42] The symmetric carbons on the hexyl bridge show signal at 27 ppm and the peak at 44 ppm is assigned to the terminal carbon atoms of hexyl bridge bonded to the nitrogen on the oxazolidinone ring. Therefore, our above experimental results demonstrate that CuI can efficiently promote four-component coupling reaction between aromatic terminal alkyne 1, primary aliphatic amine 3, CO₂ and biomassbased aldehyde such as furfural 2a and HMF 2b to give furyl-substituted 1,3-oxazolidin-2-one 4 (Table 2). In addition, furyl-containing bis-oxazolidinone 5a, 5b and poly-oxazolidinone 7 were synthesized by the investigated catalytic system under the optimized reaction conditions. While, CuIpromoted three-component coupling reaction was observed between aromatic terminal alkyne 1, primary aromatic amine or secondary aliphatic amine 3 and biomass-based aldehyde 2 to yield furyl-



Scheme 3. Synthesis of furyl-containing poly-oxazolidinone



Figure 1. The solid state ¹³C CP/MAS NMR spectrum of furyl-containing poly-oxazolidinone 7 recorded at a MAS rate of 75 MHz.

substituted propargylic amine. Besides, the furyl-substituted bis-propargylic amines **6c-d** were obtained by the CuI-promoted three-component coupling system. Notably, the isolated furyl-substituted 1,3-oxazolidin-2-ones and furyl-substituted propargylic amines are quite stable although they were prepared from unstable furfural or HMF, indicating their potential applications in the productions of various organic chemicals and stable intermediates.

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Scheme 4. Proposed reaction mechanisms

Two tentative reaction pathways for the copper-promoted four-component coupling were proposed in Scheme 4.^[41,67,71-72] For the path a, Cu(I) species initially reacts with a terminal alkyne to give a terminal copper-acetylide intermediate **8** presumably with the help of amine. Evidently, the leaving tendency of anion for cuprous salt (CuX, X = Cl, Br, I) may promote the formation of the intermediate 8. This assumption is in accord with our experimental observations (Table 1, entries 3–5). The imine **9**, forms by aldehyde **2** and primary aliphatic amine **3**, is attacked by the intermediate **8** to yield copper-complex which then undergoes demetallation to release secondary propargylamine **10**. A subsequent carboxylation of **10** under the atmosphere of CO₂ gives intermediate **11**, again, with the help of amine. While, Cu(I) species-promoted cyclization of intermediate **11** results in the formation of heterocyclic oxazolidinone product **4**. In the case of path b, the carbamic acid ammonium

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salt 12, obtained from the amine 3 and CO₂, attacks aldehyde group of furfural 2a or HMF 2b to give intermediate 13. A subsequent capture of 13 by copper-acetylide 8 promotes the generation of intermediate 11; while, the product 4 is obtained by Cu-promoted cyclization of 11.

To prove the reaction pathways outlined in Scheme 4, control experiments were performed as shown in Scheme 5. To examine the path a mechanism, we repeated the coupling reaction between phenylacetylene 1a, furfural 2a and cyclohexylamine 3a under optimized conditions with N₂ instead of CO₂ and, to our expectation, the secondary propargylamine 14 was obtained with a moderate isolated yield of 63% (Scheme 5). However, a CuI-promoted direct carboxylative cyclization of 14 leads to a low yield of 59% for the target product 4a (Scheme 5a). While, an enhanced 4a yield up to 83% was observed only when cyclohexylamine was employed to the carboxylative cyclization reaction (Scheme 5b). The above results suggest that the amine presumably catalyzes the carboxylation step of the 14 as an organic base and/or participated in the formation of active Cu species to promote the subsequent cyclization step. Previously, He and co-workers reported 2oxazolidinone syntheses from propargylic amines and CO2 at atmospheric pressure by using Cu(II)substituted polyoxometalate-based ionic liquids.^[73] The bifunctional Cu(II) catalyst simultaneously activate both two substrates of propargylic amine and CO₂, thus effectively promoting the carboxylative cyclization. Therefore, the combination of cyclohexylamine and CuI may promote carboxylative cyclization of 14 in our case (Scheme 5b). In the case of the investigation of path b mechanism (Scheme 4), we obtained a 91% yield of carbamic acid ammonium salt 15 from CO2 and cyclohexylamine (Scheme 5), which promotes the chemical fixation of CO₂ and accordingly increases the CO₂ concentration in the reaction system. The quantitative formation of 15 was proved by ${}^{13}C$ {H} NMR analysis due to the presence of the characteristic signal of carbonyl at 159 ppm (Figure

S38, Supporting Information). CuI-promoted three-component coupling of **15**, phenylacetylene **1a**, and furfural **2a** gives the target product **4a** with a yield of 73% (Scheme 5c). Therefore, both path a and b may competitively occur depending on the reaction conditions.



Scheme 5. Control experiments for 4a synthesis



Figure 2. a) Cu 2p XPS and b) Cu LMM of the recovered catalyst

To investigate the active species of the Cu catalyst, the catalyst was collected and recovered after the reaction and further analyzed by X-ray photoelectron spectra (XPS). As showed in Figure 2a, Cu2p XPS shows two peaks centered at the binding energies of 932.7 eV and 952.5 eV without any satellite peaks, indicating the absence of Cu²⁺ species.^[74] Due to the overlap of Cu⁰ and Cu⁺ in the Cu2p XPS spectra, the Cu LMM spectra was carried out for further characterization. The peaks with kinetic energy located at 918.5 and 916.0 eV were assigned to metallic copper and Cu⁺ species, respectively,^[75] thus suggesting the presence of both Cu⁰ and Cu⁺ species during the catalytic cycle as described in the Scheme 4.^[76] The Cu⁺ species can be assigned to copper-acetylide intermediate 8 (Scheme 4); while, Cu⁰ species can presumably attributed to the Cu⁰ complex or Cu⁰ nanoparticles.^[77,78] Notably, Cu⁰-nanoparticles were reported for propargylamine synthesis through three-component coupling of aldehyde, amine and alkyne.^[78] To investigate the catalytic activity of the recovered Cu-containing materials, the catalyst residue was isolated from reaction medium by filtration, washed thoroughly with ethanol, dried under the vacuum, and then applied to the next run of the four-component coupling reaction. To our surprise, the desired 1,3-oxazolidi-2-one 4a was obtained with the yield of 21%, which is low if compared with the 76% yield of 4a in the first run.

3. CONCLUSION

In summary, we demonstrated a CuI-promoted four-component coupling for 1,3-oxazolidin-2-one synthesis by using terminal aromatic alkyne, primary aliphatic amine, and renewable building blocks of CO₂ and biomass-based aldehyde under a green and mild conditions. A series of furyl-containing 1,3-oxazolidin-2-ones, bis-oxazolidinones and poly-oxazolidinone were prepared by the coupling reaction. Two reaction pathways were proposed and further proved by control experiments. Moreover, a three-

component coupling was observed between terminal aromatic alkyne, aromatic amine or secondary aliphatic amine, and biomass-based aldehyde to give furyl-substituted propargylamine without the participation of CO₂.

4. EXPERIMENTAL SECTION

4.1. Synthetic procedure

Synthesis of 1,3-oxazolidin-2-one 4

The coupling reaction was carried out in a 25 mL-stainless steel autoclave. The autoclave reactor was successively loaded with a magnetic stir bar, CuI (57 mg, 0.3 mmol), phenylacetylene (102 mg, 1.0 mmol), furfural (192 mg, 2.0 mmol), cyclohexylamine (198 mg, 2.0 mmol) and EtOH (0.11 mL). After flushing the autoclave with CO₂ three times, the CO₂ pressure was kept at 0.5 MPa at ambient temperature. The reaction was carried out in an oil bath at 75 °C for 12 h with a stirring speed of 600 rpm. The reaction vessel was then cooled down to ambient temperature conditions and the reaction mixture was filtered with filter membrane (0.45 µm). The resulting filtrate was concentrated by rotavapor and the crude product was further purified by a flash column chromatography on silica gel (v/v, cyclohexane/EtOAc = 25:1) to afford **4a** as a white flaked solid with the yield of 76% (246 mg). ¹H NMR (400 MHz, 25 °C, CDCl₃, Figure S1, Supporting Information) δ 7.54 (d, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 6.49–6.38 (m, 2H), 5.53 (s, 1H), 5.34 (s, 1H), 3.69–3.57 (m, 1H), 1.84–1.55 (m, 6H), 1.08 (dddt, *J* = 25.8, 16.6, 13.3, 8.4 Hz, 4H). ¹³C NMR (101 MHz, 25 °C, CDCl₃, Figure S1, Supporting Information) δ 154.17, 150.39, 144.63, 143.51, 133.45, 128.50, 128.45, 127.01, 110.88, 110.09, 103.87, 55.95, 54.16, 30.43, 29.63, 25.78, 25.75,

25.18). MS (ESI, Figure S37, Supporting Information): Anal. Calcd. for $C_{20}H_{21}NO_3$: m/z = 324.1600 [MH⁺], Found: m/z = 324.1595 [MH⁺].

Synthesis of bis-oxazolidinone 5

The bis-oxazolidinone **5a** was obtained similarly as depicted above in the production of **4a** by using CuI (57 mg, 0.3 mmol), furfural (384 mg, 4.0 mmol), cyclohexylamine (396 mg, 4.0 mmol), 1,3-diethynylbenzene (126 mg, 1.0 mmol), CO₂ (1.0 MPa) and EtOH (0.11 mL). The product **5a** was obtained as orange solid with the yield of 43% by flash column chromatography (cyclohexane/EtOAc = 10:1). ¹H NMR (400 MHz, 25 °C, CDCl₃, Figure S25, Supporting Information) δ 7.55 (s, 1H), 7.51–7.47 (m, 2H), 7.45 (d, *J* = 1.1 Hz, 2H), 7.31–7.27 (m, 1H), 6.49 (dd, *J* = 3.2, 0.5 Hz, 2H), 6.42 (dd, *J* = 3.2, 1.9 Hz, 2H), 5.54 (d, *J* = 1.8 Hz, 2H), 5.37 (d, *J* = 1.8 Hz, 2H), 3.64 (ddd, *J* = 12.2, 10.3, 3.8 Hz, 2H), 1.72 (dtd, *J* = 34.4, 30.5, 13.0 Hz, 10H), 1.45 (s, 2H), 1.36–1.18 (m, 4H), 1.07–0.85 (m, 4H). ¹³C NMR (101 MHz, 25 °C, CDCl₃, Figure S25, Supporting Information) δ 154.21, 150.29, 144.71, 143.52, 133.58, 128.74, 128.41, 127.09, 110.94, 110.20, 103.88, 55.99, 54.18, 30.44, 29.65, 27.01, 25.80, 25.78, 25.21. MS (ESI, Figure S61, Supporting Information): Anal. Calcd. for C₃₄H₃₆N₂O₆: m/z = 569.2652 [MH⁺], Found: m/z = 569.2651 [MH⁺].

Synthesis of propargylamine 6

The propargylamine **6a** was obtained similarly as depicted above in the production of **4a** by using CuI (57 mg, 0.3 mmol, 30 mmol% relative to alkyne), furfural (192 mg, 2.0 mmol), aniline (186 mg, 2.0 mmol), phenylacetylene (102 mg, 1.0 mmol) and EtOH (0.11 mL) under nitrogen atmosphere. The desired propargylamine **6a** was obtained as orange oil with the yield of 66% (v/v, cyclohexane/EtOAc = 25:1). ¹H NMR (400 MHz, 25 °C, CDCl₃, Figure S27, Supporting Information) δ 7.50–7.47 (m, 2H), 7.42 (s, 1H), 7.33–7.31 (m, 3H), 6.49 (d, *J* = 3.2 Hz, 1H), 6.35 (dd, *J* = 3.1, 1.9

Hz, 1H), 5.08 (s, 1H), 2.77–2.54 (m, 4H), 1.11 (t, *J* = 7.2 Hz, 6H). ¹³C NMR (101 MHz, 25 °C, CDCl₃, Figure S27, Supporting Information) δ 152.65, 142.55, 131.94, 128.41, 128.35, 123.13, 110.17, 109.07, 85.90, 84.49, 52.04, 45.07, 13.44. MS (ESI, Figure S63, Supporting Information): Anal. Calcd. for C₁₉H₁₅NO: m/z = 274.1232 [MH+], Found: m/z = 274.1225 [MH+]

Synthesis of poly-oxazolidinone 7

The poly-oxazolidinone 7 was obtained similarly as depicted above in the production of **4a** by using CuI (57 mg, 0.3 mmol), furfural (384 mg, 4.0 mmol), 1,6-hexanediamine (232 mg, 2.0 mmol), 1,3-diethynylbenzene (126 mg, 1.0 mmol), CO₂ (3 MPa) and EtOH (0.11 mL) at 75 °C for 2 days in the autoclave. The poly-oxazolidinone **7** was obtained as hard and black solid after filtration and washed thoroughly with H₂O, CH₂Cl₂, THF, DMF by Soxhlet extractions.

4.2. Characterization techniques

¹H and ¹³C{¹H} NMR spectra were recorded on a Bruker Advance 300 at 400 MHz for ¹H and 101 MHz for ¹³C with CDCl₃ and DMSO-d₆ as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts were showed in parts per million (ppm, δ scale) downfield from TMS at 0.00 ppm and referenced to the CDCl₃ at 7.26 ppm for ¹H, and 77.16 ppm for ¹³C, respectively. In the case of DMSO-d₆, chemical shifts referenced to 2.50 ppm for ¹H and 39.52 ppm for ¹³C. The solid-state ¹³C NMR spectra were recorded on a Bruker Advance III at 75 MHz. High-resolution mass spectra were obtained by ESI on a SCIEX X500R QTOF. X-ray photoelectron spectra (XPS) and Auger electron spectroscopy were performed on a Kratos Ultra system using an Al K α radiation source. The binding energies for each spectrum were calibrated with a C 1s spectrum of 284.6 eV.

5. ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the Wiley Publications website at DOI:

XXXX. ¹H and ¹³C {¹H} NMR spectra, high-resolution mass spectra of the products (PDF).

6. AUTHOR INFORMATION

Corresponding Author

*E-mail address: <u>chenjz@jnu.edu.cn.</u> Tel.: (+86)-20-8522-0223, Fax: (+86)-20-8522-0223 (J. Chen),

*E-mail address: <u>yshxu@ecust.edu.cn</u> (Y. Xu)

ORCID

Jinzhu Chen: 0000-0002-6475-1431

Yisheng Xu: 0000-0001-8245-9787

Notes

The authors declare no competing financial interest.

7. ACKNOWLEDGEMENTS

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Keywords: biomass • carbon dioxide fixation • copper • multi-component coupling • oxazolidinone

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Copper(I)-Catalyzed Four-Component Coupling Using Renewable Building Blocks of CO2

and Biomass-Based Aldehydes

Qiumin Wu, Jinzhu Chen, Xuhong Guo and Yisheng Xu



Furyl-containing oxazolidinone, bis-oxazolidinone and poly-oxazolidinone were obtained by copperpromoted four-component coupling using renewable building blocks of CO₂ and biomass-based aldehydes.