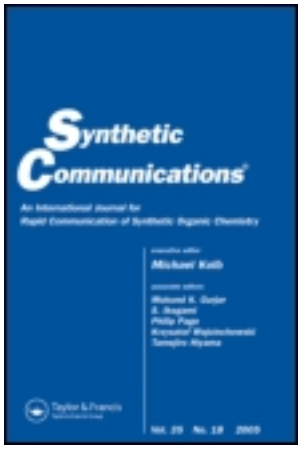

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FACILE AND MILD PROCESS FOR CHEMICAL FIXATION OF CO_2 TO 4-METHYLENE-1,3-OXAZOLIDIN-2-ONES UNDER SOLVENT-FREE CONDITIONS

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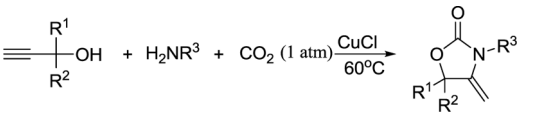
GRAPHICAL ABSTRACT



Abstract *4-Methylene-1,3-oxazolidin-2-ones were prepared via the cycloadditon reaction of propargylic alcohols with primary amines and CO_2 under atmospheric pressure at 60 °C in the absence of any additional solvent. This methodology affords an ecofriendly, mild, and easy approach to chemical fixation of CO_2.*

Keywords Carbon dioxide; chemical fixation; oxazolidinone; propargylic alcohol; solvent-free

Carbon dioxide (CO_2) is a major greenhouse gas, and a great deal of CO_2 is constantly emitted into the atmosphere from burning fossil fuels. The issue of recycling or removing CO_2 from industrial emissions is receiving increased attention. However, CO_2 is both an abundant and cheap nontoxic biorenewable resource. It is an attractive raw material for use in important industrial processes to replace toxic chemicals such as phosgene, isocyanates, or CO. Hence, chemical fixation of CO_2 into useful compounds attracts growing concern.[1]

1,3-Oxazolidin-2-ones constitute a very important class of heterocyclic compounds. They can be employed as multipurpose chiral synthons in asymmetric syntheses of biologically active compounds or their synthetic intermediates.[2] Chiral 1,3-oxazolidin-2-ones are widely used as chiral auxiliaries in many important asymmetric syntheses.[3] Moreover, some oxazolidinones such as DUP-105, DUP-721, and linezolid (Zyvox) have attracted interest as monodrug- or multidrug-resistant antibacterial agents.[4] The importance of these heterocyclic derivatives justifies the continuous efforts to develop novel approaches to their synthesis. A number of procedures to synthesize 2-oxazolidinones have been developed.[5]

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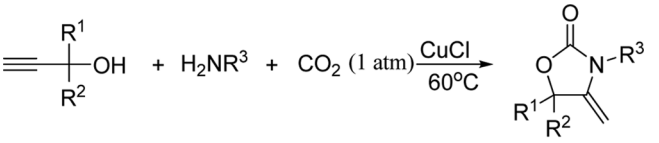


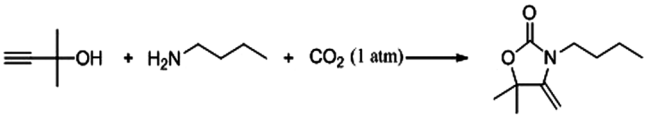
1 2 3

Scheme 1. Cycloaddition reaction of propargylic alcohols with amines in a CO_2 atmosphere under solvent-free conditions.

4-Methylene-1,3-oxazolidin-2-ones can be further transformed into synthetically useful derivatives because they bear an exocyclic double bond. It was reported that 4-methylene-1,3-oxazolidin-2-ones can be prepared via the cycloaddition of propargylic alcohols with primary amines and CO_2.[6] However, these reported protocols have suffered from drawbacks such as high temperature and high CO_2 pressure. Recently, we found that 4-methylene-1,3-oxazolidin-2-ones could be synthesized via the cycloaddition reaction of propargylic alcohols with primary amine in a CO_2 atmosphere under solvent-free conditions (Scheme 1).

We initially examined the reaction of 2-methylbut-3-yn-2-ol (**1a**) and *n*-butylamine (**2a**) in a CO_2 atmosphere to optimize the reaction condition, and the results are summarized in Table 1. A series of metal salts was screened to drive the cycloadditon reaction at 60 °C for 24 h in which the ratio of propargylic alcohol to primary amine was 1:2. As can be seen from Table 1, cuprous salts could catalyze the reaction, and cuprous chloride was better then cuprous iodide and cuprous bromide (entries 1–3). Only trace amounts of 3-butyl-5,5-dimethyl-4-methyleneoxazolidin-2-one were

Table 1. Optimizing reaction conditions for cycloaddition of propargylic alcohols with amines in a CO_2 atmosphere[a]



1a 2a 3a

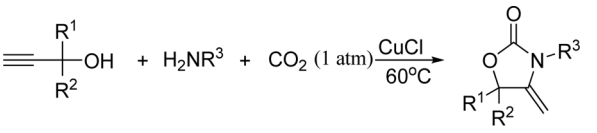
Entry	Temperature (°C)	Alcohol/amine	Catalyst	Yield[b] (%)
1	60	1:2	CuI	72
2	60	1:2	CuBr	75
3	60	1:2	CuCl	81
4	60	1:2	$FeCl_2$	Trace
5	60	1:2	$ZnCl_2$	0[c]
6	60	1:1	CuCl	68
7	60	1:3	CuCl	81
8	80	1:2	CuCl	80
9	40	1:2	CuCl	55

[a]Condition: 2-methylbut-3-yn-2-ol (2 mmol), *n*-butylamine (2–6 mmol), catalyst (0.1 mmol).
[b]Isolated yields based on 2-methylbut-3-yn-2-ol.
[c]2-Methylbut-3-yn-2-ol remained unchanged.

obtained with the catalysis of ferrous chloride, and zinc chloride could not promote the reaction at all (entries 4 and 5). When the ratio of alcohol to amine was regulated to 1:1, the yield decreased to 68% (entry 6), and raising the quantity of amine could not further improve the cycloaddition reaction (entry 7). When the reaction was carried out at 80 °C (entry 8), the isolated yield was unchanged, while the yield was only 55% at 40 °C (entry 9). Therefore, the best reaction conditions were as follows: 2-methylbut-3-yn-2-ol (**1a**; 2 mmol), *n*-butylamine (**2a**; 4 mmol), cuprous chloride (0.1 mmol) as catalyst, a temperature of 60 °C, and a reaction time of 24 h.

We then explored the generality and scope of the reaction (Table 2). A variety of primary amines were employed to react with 2-methylbut-3-yn-2-ol (**1a**) in an atmosphere of CO_2 under the optimal reaction conditions. As the results showed, the steric hindrance of the substituents on the primary amines could affect the cycloaddition significantly. Thus, when *n*-, *sec*-, and *tert*-butylamine were employed, *n*-butylamine (**2a**) yielded the best result (81% isolated yield; entry 1), but no desired product was detected when *tert*-butylamine was used (entry 3). Allylamine (**2c**) and cyclohexylamine (**2d**) could also proceed efficiently with yields of 77% and 83% respectively (entries 4 and 5). However, aniline could not react at all, and **1a** was recovered (entry 6). Various propargylic alcohols, such as 1-ethynylcyclohexanol (**1b**), 2-phenylbut-3-yn-2-ol (**1c**), 3,4-dimethylpent-1-yn-3-ol (**1d**), and 3-methylnon-1-yn-3-ol (**1e**) successfully unterwent cycyloaddition with *n*-butylamine (**2a**) in the atmosphere of CO_2 under the given conditions. The corresponding 4-methylene-1,3-oxazolidin-2-ones **3e–h** could be obtained in 63–84% yields (entries 7–10). However,

Table 2. Synthesis of 4-methylene-2-oxazolidinones from corresponding propargylic alcohols and primary amines in a CO_2 atmosphere[a]



1 **2** **3**

Entry	R^1	R^2	R^3	Product	Yield[b] (%)
1	Me	Me	*n*-Bu	**3a**	81
2	Me	Me	*s*-Bu	**3b**	70
3	Me	Me	*t*-Bu	NO	0[c]
4	Me	Me	Allyl	**3c**	77
5	Me	Me	Cy	**3d**	83
6	Me	Me	Ph	NO	0[d]
7		$-C_5H_{10}-$	*n*-Bu	**3e**	84
8	Me	Ph	*n*-Bu	**3f**	87
9	Me	*i*-Pr	*n*-Bu	**3g**	69
10	Me	n-C_5H_{13}	*n*-Bu	**3h**	63
11	H	Me	*n*-Bu	NO	0[d]
12	H	H	*n*-Bu	NO	0[d]

[a]Reagents and conditions: alcohol **1** (2 mmol), amine **2** (4 mmol), CuCl (0.1 mmol), 60 °C, 24 h.
[b]Isolated yield based on alcohol.
[c]No desired product detected.
[d]Alcohol remained unchanged.

no desired products were detected when *n*-butylamine reacted with secondary or primary propargylic alcohols (entries 11 and 12), which suggested that such reaction seems to be specific only for tertiary alcohols.

In conclusion, we have disclosed that 4-methylene-1,3-oxazolidin-2-ones could be synthesized via the cycloadditon reaction of propargylic alcohols with primary amines and CO_2 under atmospheric pressure in the absence of any additional solvent. The solvent-free methodology described herein is an ecofriendly, mild, and easy approach to chemical fixation of CO_2.

EXPERIMENTAL

All starting materials and catalysts were commercially purchased and used without further purification. ^{1}H NMR spectra were recorded on a Bruker DRX-400 spectrometer using $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on a Shimadzu GCMS-QP5050A at an ionization voltage of 70 eV equipped with a DB-WAX capillary column (internal diameter = 0.25 mm, length = 30 m). Infrared (IR) spectra were recorded on an Analect RFX-65A spectrometer.

General Procedure for the Preparation of 4-Methylene-1,3-oxazolidin-2-ones

A mixture of propargylic alcohol (2 mmol), amine (4 mmol), and catalyst (0.1 mmol) was stirred under atmospheric CO_2 pressure at the selected temperature for the required reaction time. When the reaction was complete, the residuel was flushed with Et2O (3×10 mL). The products were purified by column chromatography (gel, petroleum ether/ethyl acetate, 6:1) and identified by ^{1}H NMR, mass and IR.

Data

3-Butyl-5,5-dimethyl-4-methyleneoxazolidin-2-one (3a). Orange oil; MS: $m/z = 183$ (M^+, 34), 141 (27), 128 (43), 96 (31), 84 (18), 43 (10), 32 (24), 28 (100); IR (KBr, v/cm^{-1}): 2985, 2877, 1733, 1681; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.93 (t, $J = 7.4$ Hz, 3H), 1.29–1.41 (m, 2H), 1.40–1.63 (m, 8H), 3.42 (t, $J = 7.4$ Hz, 2H), 3.96 (d, $J = 2.8$ Hz, 1H), 4.05 (d, $J = 2.8$ Hz, 1H).

3-*sec*-Butyl-5,5-dimethyl-4-methyleneoxazolidin-2-one (3b). Orange oil; MS: $m/z = 183$ (M^+, 18), 128 (100), 110 (22), 84 (48), 41 (13); IR (KBr, v/cm^{-1}): 2981, 2881, 1767, 1674; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.85–0.90 (m, 3H), 1.34–1.39 (m, 3H), 1.45 (s, 6H), 1.60–1.64 (m, 2H), 3.78–3.84 (m, 1H), 3.94 (d, $J = 2.8$ Hz, 1H), 4.15 (d, $J = 2.8$ Hz, 1H).

3-Allyl-5,5-dimethyl-4-methyleneoxazolidin-2-one (3c). Orange oil; MS: m/z = 167 (M^+, 90), 122 (100), 108 (96), 82 (50), 55 (57), 41 (48), 28 (68); IR (KBr, v/cm^{-1}): 2988, 2941, 1734, 1648; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.50 (s, 6H), 3.97 (d, $J = 2.8$ Hz, 1H), 4.04–4.06 (m, 3H), 5.10–5.22 (m, 2H), 5.68–5.89 (m, 1H).

3-Cyclohexyl-5,5-dimethyl-4-methyleneoxazolidin-2-one (3d). White solid, mp 54–56 °C; MS: $m/z = 209$ (M^+, 23), 128 (100), 112 (15), 84 (45), 55 (17), 41 (15); IR (KBr, v/cm^{-1}): 2934, 2859, 1733, 1682; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.09–1.19 (m, 1H), 1.27–1.35 (m, 2H), 1.44 (6H, s), 1.65 (d, $J = 9.4$ Hz, 3H), 1.80 (d, $J = 10.4$ Hz, 2H), 2.02–2.05 (m, 2H), 3.52 (1H, m), 3.95 (d, $J = 2.8$ Hz, Hz, 1H), 4.16 (d, $J = 2.8$ Hz, 1H).

3-*n*-Butyl-5,5-pentamethylene-4-methyleneoxazolidin-2-one (3e). White solid, mp 60–62 °C; MS: $m/z = 223$ (M^+, 38), 181 (58), 168 (100), 122 (25), 112 (38), 55 (11), 41 (13); IR (KBr, v/cm^{-1}): 2940, 2868, 1730, 1672; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.92 (t, $J = 7.4$ Hz, 3H), 1.23–1.84 (m, 14H), 3.41 (t, $J = 7.2$ Hz, 2H), 3.92 (d, $J = 2.4$ Hz, 1H), 4.00 (d, $J = 2.4$ Hz, 1H).

3-Butyl-5-methyl-4-methylene-5-phenyloxazolidin-2-one (3f). Orange-red oil; MS: $m/z = 245$ (M^+, 20), 190 (22), 158 (100), 144 (100), 129 (32), 97 (65), 77 (23), 41 (8); IR (KBr, v/cm^{-1}): 2934, 2868, 1760; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.88–0.94 (m, 3H), 1.30–1.34 (m, 2H), 1.55–1.60 (m, 2H), 1.85 (s, 3H), 3.42–3.51 (m, 2H), 4.08 (d, $J = 2.8$ Hz, 1H), 4.22 (d, $J = 3.2$ Hz, 1H), 7.31–7.45 (m, 5H).

3-Butyl-5-isopropyl-5-methyl-4-methyleneoxazolidin-2-one (3g). Orange-red oil; MS: $m/z = 211$ (M^+, 32), 169 (90), 126 (29), 112 (100), 84 (10), 55 (14), 41 (22); IR (KBr, v/cm^{-1}): 2970, 2879, 1775, 1673; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.88–0.99 (m, 9H), 1.30–1.36 (m, 2H), 1.44 (s, 3H), 1.53–1.57 (m, 2H), 1.80–1.82 (m, 1H), 3.31–3.38 (m, 1H), 3.43–3.57 (m, 1H), 3.91 (d, $J = 2.8$ Hz, 1H), 4.08 (d, $J = 2.8$ Hz, 1H).

3-Butyl-5-hexyl-5-methyl-4-methyleneoxazolidin-2-one (3h). Dark-red oil; MS: $m/z = 253$ (M^+, 5), 169 (100), 126 (25), 113 (30), 98 (38), 55 (10), 41 (12); IR (KBr, v/cm^{-1}): 2930, 2865, 1675; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 0.85 (t, $J = 6.8$ Hz, 3H), 0.93 (t, $J = 7.2$ Hz, 3H), 1.23–1.35 (m, 10H), 1.44–1.64 (m, 5H), 3.42 (M, 2H), 3.90 (d, $J = 2.8$ Hz, 1H), 4.07 (d, $J = 2.8$ Hz, 1H).

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