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Aqueous media carboxylative cyclization of propargylic amines with CO_2 catalyzed by amphiphilic dendritic *N*-heterocyclic carbene–gold(I) complexes

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ABSTRACT

We prepared amphiphilic dendritic *N*-heterocyclic carbene (NHC)–gold(I) complexes having poly(ethylene glycol) units at the peripheral layer. By employing 1 mol % of the dendritic NHC–gold(I) catalyst, the aqueous media carboxylative cyclization of propargylic amines proceeded smoothly to provide the corresponding 2-oxazolidinone under atmospheric pressure of CO_2 at room temperature.

Development of green processes based on chemical fixation of carbon dioxide (CO_2) has received a great deal of interest in recent years because CO_2 could be used as a safe, inexpensive, and renewable C_1 building block to produce useful organic compounds.[1] One useful method in which CO_2 has been utilized as a substrate is through the carboxylative cyclization of propargylic amines with CO_2 to provide 2-oxazolidinones. For example, the carboxylative cyclization of propargylic amines has been found to proceed in the presence of organometallic complexes of ruthenium and palladium as catalysts under high CO_2 pressure.[2] Even in the absence of catalysts, this conversion has been successfully achieved under supercritical CO_2.[3] Recently, it was reported that *N*-heterocyclic carbene (NHC)–gold(I) complexes or silver acetate can catalyze the carboxylative cyclization of propargylic amines under atmospheric pressure of CO_2.[4]

Dendrimers are fascinating molecules due to their unique physical and chemical properties caused by their well-defined hyperbranched frameworks.[5] Metallodendrimers with a functional or catalytic site at their core have received considerable attention.[6] Their solubility and physical properties can be altered by peripheral modification.[7] For example, by the introduction of hydrophilic groups to the peripheral layer of a hydrophobic dendron, metal core dendrimers can become water-soluble[8] and afford unique catalytic activity.[9] We wish to report herein the synthesis of amphiphilic dendritic NHC–gold(I) complexes having poly(ethylene glycol) units at the peripheral layer, their application as catalysts to the aqueous media carboxylative cyclization of propargylic amines under atmospheric pressure of CO_2, and reuse of the catalyst in the sequential carboxylative cyclization by the successive addition of the propargylic amine. From the perspective of green chemistry, chemical fixation of CO_2 carried out in water is a very attractive field, as water is an environmentally benign solvent.[10]

The first- and the second-generation NHC–gold(I) core dendrimers having the tri(ethylene glycol) unit **2**G*n*[TEG] were synthesized as follows (Fig. 1, Scheme 1). A suspension of imidazole, poly(benzyl ether) dendritic bromide G*n*[TEG]–Br,[8a] and CsF–celite[11] in *N*,*N*-dimethylformamide (DMF) was stirred at 90 °C for 24 h. A mixture of the obtained dendritic imidazolium bromide **1**G*n*[TEG] and silver(I) oxide in 1,2-dichloroethane was stirred at 70 °C, and then stirred further after the addition of $AuCl(SMe_2)$ to the reaction mixture at room temperature to provide the corresponding NHC–gold(I) core dendrimer **2**G*n*[TEG]. All transformations were carried out in good chemical yields in both generations.

We then examined catalytic activity of the dendrimer **2**G*n*[TEG] ($n = 1, 2$) by performing the carboxylative cyclization of propargylic amines with CO_2 (Table 1). The procedure employed herein was Ikariya's synthetic sequence.[4a] Their result with the use of AuCl(IPr) (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) as a catalyst is shown in Table 1, entry 1.

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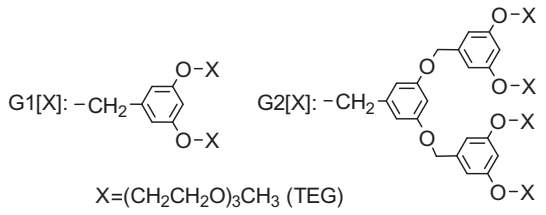
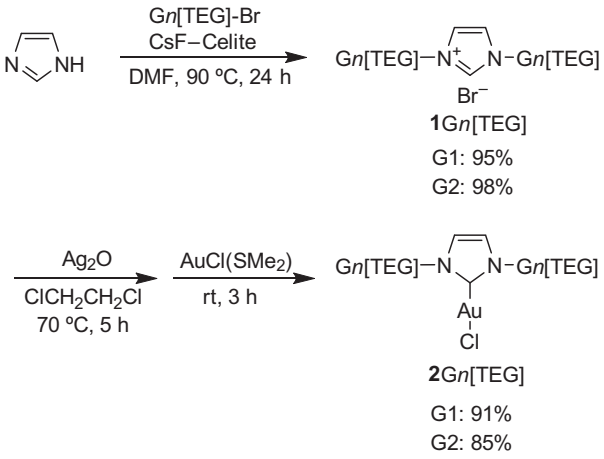
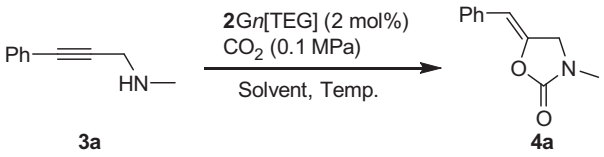


Figure 1. Structural formulas of G*n*[X] dendrons (*n* = 1, 2).



Scheme 1. Preparation of **2**G*n*[TEG] (*n* = 1, 2).

Table 1
Carboxylative cyclization of propargylic amine **3a** with CO_2 catalyzed by **2**G*n*[TEG][a]

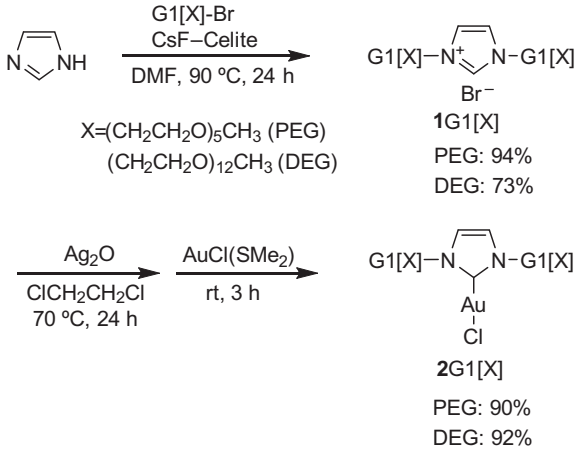


Entry	Au catalyst	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1[c]	AuCl(IPr)	MeOH	40	48	76
2	**2**G1[TEG]	MeOH	40	48	47
3	**2**G1[TEG]	MeOH	rt	48	82
4	**2**G2[TEG]	MeOH	rt	48	73
5	**2**G1[TEG]	H_2O	rt	24	85
6	**2**G2[TEG]	H_2O	rt	24	72
7	AuCl(IPr)	H_2O	rt	24	2
8[d]	AuCl(IPr)	H_2O	rt	24	1

[a] Reaction conditions: **2**G*n*[TEG] (2 mol %), **3a** (0.8 mmol), solvent (1 M based on **3a**), carried out at 40 °C or at room temperature for the indicated time under atmospheric pressure of CO_2 (0.1 MPa).
[b] Determined by integration of ^{1}H NMR absorptions referring to an internal standard.
[c] Cited from Ref. 4a.
[d] Carried out in the presence of 8 mol % of tri(ethylene glycol) dimethyl ether.

First, by employing 2 mol % of the first-generation catalyst **2**G1[TEG], the carboxylative cyclization of *N*,*N*-methyl(3-phenylpropargyl) amine **3a** was carried out under atmospheric pressure of CO_2 (0.1 MPa) in methanol at 40 °C for 48 h. However in this case, the reaction proceeded heterogeneously to provide the corresponding 2-oxazolidinone **4a** in a rather low chemical yield (47%; Table 1, entry 2). In contrast, by employing **2**G1[TEG] as a catalyst at room temperature, **4a** was obtained in a fair chemical yield (82%; Table 1, entry 3). Generally, poly(ethylene glycol) derivatives have higher solubility in a polar protic solvent by lowering the temperature.[12] The fair chemical yield in entry 3 was probably due to good solubility of **2**G1[TEG] in methanol at room temperature. We subsequently performed this carboxylative cyclization catalyzed by the second-generation catalyst **2**G2[TEG]. However the chemical yield of **4a** when using **2**G2[TEG] was somewhat lower than that with the use of the first-generation **2**G1[TEG], probably due to steric hindrance of the second-generation dendron (Table 1, entries 3 and 4). Next, by employing the first-generation **2**G1[TEG] in water, the aqueous media carboxylative cyclization proceeded smoothly to provide **4a** in a shorter time (24 h, 85%; Table 1, entry 5). However, also in these cases carried out in water, the chemical yield for the second-generation **2**G2[TEG] was somewhat lower than that for the first-generation **2**G1[TEG] (Table 1, entries 5 and 6). On the other hand, by employing AuCl(IPr) as a catalyst in water at room temperature, the chemical yield of **4a** was poor (2%; Table 1, entry 7). Under these reaction conditions, even with the addition of 8 mol % of tri(ethylene glycol) dimethyl ether with the same amount of TEG moieties of **2**G1[TEG], **4a** was obtained in only 1% yield (Table 1, entry 8). From these results, it can be concluded that the inclusion of NHC–gold(I) complex with an amphiphilic dendrimer is essential to the aqueous media carboxylative cyclization of propargylic amines with CO_2.

We next synthesized the first-generation of other amphiphilic dendritic NHC–gold(I) catalysts having either penta(ethylene glycol) or dodeca(ethylene glycol) units at the peripheral layer **2**G1[PEG] and **2**G1[DEG], which were prepared according to the procedure similar to that used for **2**G1[TEG] (Scheme 2).[13] All transformations were carried out in fair chemical yields for both catalysts.[14]

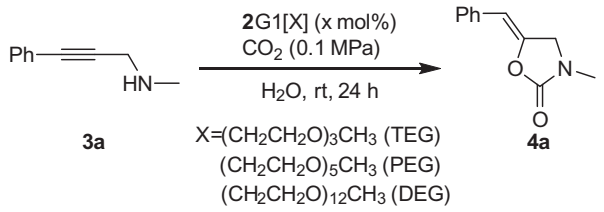


Scheme 2. Preparation of **2**G1[X].

As shown in Table 2, by employing three amphiphilic dendritic NHC–gold(I) catalysts **2**G1[X] (X = TEG, PEG, DEG), respectively, the aqueous media carboxylative cyclization of **3a** with CO_2 was carried out at room temperature for 24 h. As a result, the dendritic NHC–gold(I) catalyst having the penta(ethylene glycol) unit **2**G1[PEG] afforded the highest chemical yield (Table 2, entries 3 and 4). Even in the case of using 1 mol % of the catalyst, **2**G1[PEG] afforded a fair chemical yield of **4a** (82%; Table 2, entry 4).

We subsequently performed the aqueous media carboxylative cyclization of various propargylic amines by employing 1 mol % of the dendritic NHC–gold(I) catalysts having penta(ethylene glycol) units **2**G1[PEG], as shown in Table 3.[15] In the cases of the internal propargylic amines except for **3a**, the carboxylative cyclization reactions were carried out for 48 h to provide the corresponding 2-oxazolidinones **4** in acceptable chemical yields

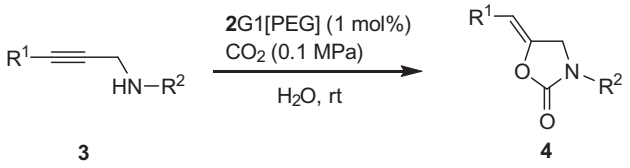
Table 2
Aqueous media carboxylative cyclization of propargylic amine **3a** with CO_2 catalyzed by **2**G1[X][a]



Entry	X	**2**G1[X] (x mol %)	Yield[b] (%)
1	TEG	2	85
2	TEG	1	60
3	PEG	2	87
4	PEG	1	82
5	DEG	2	84
6	DEG	1	72

[a] Reaction conditions: **2**G1[X] (1 or 2 mol %), **3a** (0.8 mmol), H_2O (1 M based on **3a**), carried out at room temperature for 24 h under atmospheric pressure of CO_2 (0.1 MPa).
[b] Determined by integration of ^{1}H NMR absorptions referring to an internal standard.

Table 3
Aqueous media carboxylative cyclization of various propargylic amines with CO_2 catalyzed by **2**G1[PEG][a]



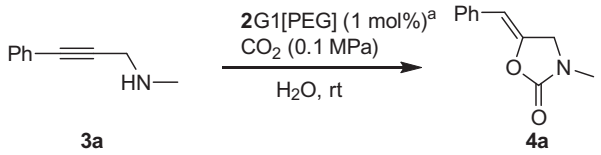
Entry	Substrate	R^1	R^2	Time (h)	Product	Yield[b] (%)
1	**3a**	C_6H_5	CH_3	24	**4a**	82
2	**3b**	4-$CH_3C_6H_4$	CH_3	48	**4b**	87
3	**3c**	CH_3	$C_6H_5CH_2$	48	**4c**	74
4	**3d**	C_2H_5	$C_6H_5CH_2$	48	**4d**	72
5[c]	**3e**	H	CH_3	72	**4e**	49

[a] The reaction conditions were the same as those indicated in Table 2.
[b] Determined by integration of ^{1}H NMR absorptions referring to an internal standard.
[c] 2 mol % of **2**G1[PEG] was used.

(Table 3, entries 2–4). The reaction of a substrate having a terminal alkyne unit, *N*-methylpropargylamine **3e**, gave the corresponding 2-oxazolidinone **4e** in a rather low chemical yield, even when the reaction was carried out for 72 h through the use of 2 mol % of **2**G1[PEG] (49%; Table 3, entry 5).[16–18]

Finally, the reusability of the catalyst **2**G1[PEG] was examined in the sequential carboxylative cyclization by the successive addition of the propargylic amine **3a** (Table 4). The carboxylative cyclization of **3a** catalyzed by 1 mol % of **2**G1[PEG] was carried out at room temperature for 24 h to provide the corresponding 2-oxazolidinone **4a** in an 82% chemical yield, as mentioned above (Table 4, entry 1). In a separate run, after **3a** was initially reacted with CO_2 through the use of 1 mol % of **2**G1[PEG] for 24 h, **3a** was subsequently added to the reaction mixture, and the reaction was continued for 24 h (total 48 h). As a result, **4a** was obtained in an 87% chemical yield (TON 174; Table 4, entry 2). In the run of entry 3, the further successive addition of **3a** after 48 h allowed us to obtain **4a** in a 70% chemical yield (TON 210; Table 4, entry 3). From

Table 4
Sequential carboxylative cyclization by the successive addition of **3a**[a]



Entry	Successive addition of **3a**[b]	Time (h)	Yield[c] (%)	TON
1	–	24	82	82
2	After 24 h	48	87	174
3	After 24 and 48 h	72	70	210

[a] The initial reaction conditions were the same as those indicated in Table 2.
[b] **3a** (0.8 mmol) was added successively.
[c] Based on total volume of **3a**. Determined by integration of ^{1}H NMR absorptions referring to an internal standard.

these results, it can be concluded that **2**G1[PEG] maintains its catalytic activity after the initial and second round carboxylative cyclizations of **3a**, and that the catalyst **2**G1[PEG] can be reused by the successive addition of **3a**.

In summary, by employing amphiphilic dendritic NHC–gold(I) catalysts, the aqueous media carboxylative cyclization of propargylic amines with CO_2 proceeded at room temperature to provide the corresponding 2-oxazolidinones in acceptable chemical yields. Furthermore, the dendritic NHC–gold(I) catalyst could be reused in the sequential carboxylative cyclization by the successive addition of the propargylic amine.

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13. *Preparation of **2**G1[PEG]:* A suspension of **1**G1[PEG] (672 mg, 0.505 mmol) and silver(I) oxide (151.8 mg, 0.655 mmol) in 1,2-dichloroethane (5 mL) was stirred at 70 °C for 24 h under an argon atmosphere. After cooling to room temperature, $AuCl(SMe_2)$ (149 mg, 0.506 mmol) was added to the reaction

mixture. The resulting mixture was stirred at room temperature for 3 h under an argon atmosphere. The reaction mixture was concentrated to dryness, and the residue was filtered through Celite to remove insoluble materials. After evaporation of the filtrate, the residue was purified with silica gel column chromatography (ethyl acetate–methanol = 3:1 as an eluent) to obtain **2**G1[PEG] (669 mg, 0.452 mmol) in a 90% yield.

14. *Selected data:* **2**G1[PEG] Pale yellow oil; IR (neat) 2872, 1594, 1447, 1349, 1298, 1246, 1119, 949, 851 cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) δ 6.87 (s, 2 H), 6.49 (d, J = 2.1 Hz, 4 H), 6.45 (t, J = 2.1 Hz, 2H), 5.26 (s, 4 H), 4.09 (t, J = 4.7 Hz, 8 H), 3.83 (t, J = 4.7 Hz, 8 H), 3.73–3.62 (m, 56 H), 3.56–3.52 (m, 8 H), 3.37 (s, 12 H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 171.2, 160.4, 136.9, 120.9, 107.1, 101.5, 71.9, 70.7, 70.6, 70.5, 70.5, 70.5, 69.5, 67.6, 59.0, 55.2; Anal. Calcd for $C_{61}H_{104}AuClN_2O_{24}$: C, 49.44; H, 7.07; N, 1.89; Cl, 2.39. Found: C, 49.54; H, 7.09; N, 1.77; Cl, 2.21.
15. *General procedure:* To a Schlenk-tube were successively added **2**G1[PEG] (0.008 mmol), degassed water (0.8 mL) and a propargylic amine (0.8 mmol) under an argon atmosphere, and the inside of the Schlenk-tube was replaced with CO_2 (0.1 MPa). The carboxylative cyclization of the propargylic amine with CO_2 proceeded by the stirring of the resulting mixture at room temperature. After 24–48 h, methanol and dichloromethane were added to homogenize the reaction mixture. The chemical yield was determined by integrating ^1H NMR absorptions referring to an internal standard (3-hydroxybenzyl alcohol (1 mmol)), which was added to the homogenized aqueous solution.
16. As an example of a primary amine, 1-ethynylcyclohexylamine did not afford the corresponding 2-oxazolidinone.
17. 2-Oxazolidinones **4a**,[4a] **4c**,[19] **4d**,[19] and **4e**[4a] are known compounds, and their NMR spectra are in accordance with those reported in the literature.
18. *Compound **4b*** White powder; mp 133.4–134.5 °C; IR (KBr) 2916, 2862, 1782, 1697, 1435, 1412, 1273, 1088, 1034, 841 cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) δ 7.45 (d, J = 8.1 Hz, 2 H), 7.13 (d, J = 8.0 Hz, 2 H), 5.48 (t, J = 2.0 Hz, 1 H), 4.31 (d, J = 2.0 Hz, 2 H), 2.99 (s, 3 H), 2.33 (s, 3 H); ^{13}C NMR (100 MHz; $CDCl_3$) δ 155.7, 140.8, 136.5, 130.6, 129.1, 128.0, 102.7, 50.7, 30.3, 21.1; Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found: C, 70.95; H, 6.44; N, 6.79.
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