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Copper-catalyzed C–C bond-forming transformation of CO₂ to the alcohol oxidation level: selective synthesis of homoallylic alcohols from allenes, CO₂, and hydrosilanes
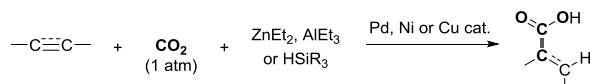
Yosuke Tani, Kazunari Kuga, Tetsuaki Fujihara,* Jun Terao and Yasushi Tsuji*

A highly selective carbon–carbon bond-forming transformation of carbon dioxide (CO_2) to the alcohol oxidation level has been disclosed. By employing a copper/bisphosphine catalyst system and hydrosilanes as the mild and easy-to-handle reducing agents, various allenes react with CO_2 to give homoallylic alcohols regioselectively. Esters and other reducible functionalities on the allenes remain intact during the reaction, while CO_2 is reduced to the alcohol oxidation level.
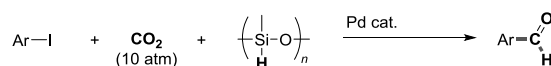
Carbon dioxide (CO_2) is at the highest oxidation level of carbon. Owing to its abundance and non-toxic, stable, and inert nature, the chemical transformation of CO_2 to lower oxidation levels (*i.e.*, the carboxylic acid, aldehyde, and alcohol oxidation levels)[1] has been one of the central challenges in chemistry.[2] In particular, C–C bond-forming reactions using CO_2 have afforded various value-added organic compounds.[3] However, the products obtained from these reactions have been limited to carboxylic acids or their derivatives, *i.e.*, at the carboxylic acid oxidation level.[4,5] Even in the presence of stoichiometric amounts of reactive reducing agents such as $ZnEt_2$,[5b–5d] $AlEt_3$,[5d,e] and hydrosilanes,[5a] only carboxylic acids were provided through hydrocarboxylation reactions of alkynes,[5a,5b] styrenes,[5c] allenes,[5d] and 1,3-dienes[5e] (Scheme 1a). Quite recently, CO_2 was converted to the aldehyde oxidation level; benzaldehyde derivatives were afforded by the Pd-catalyzed reaction of aryl iodides, CO_2 (10 atm), and a hydrosilane (Scheme 1b).[6]

As for transformation of CO_2 to the alcohol oxidation level, its catalytic conversion to methanol has been intensively studied in the presence of various reducing agents.[7] However, without a C–C bond-forming event, the product is limited to methanol. Herein, we report the selective synthesis of homoallylic alcohols (**2**) from CO_2 with allenes (**1**)[8,9] by employing a copper catalyst and a hydrosilane[10,11] (Scheme 1c).
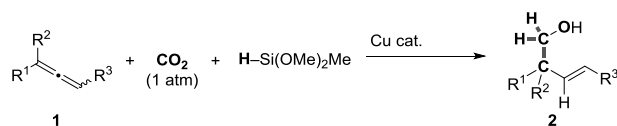
**Scheme 1** C–C bond-forming transformation of CO_2 to different oxidation levels.

To the best of our knowledge, this is the first example of the transformation of CO_2 to the alcohol oxidation level with concomitant C–C bond formation.[12] Importantly, CO_2 is reduced to the alcohol oxidation level chemoselectively, with esters or other reducible functionalities on the allenes being intact. Previously, a formal addition of hydroxymethyl (CH_2OH) group onto allenes was reported by Krische, who used methanol instead of CO_2 with hydrosilanes in the presence of an Ir catalyst.[13] However, there has been no C–C bond-forming synthesis of alcohols directly from the CO_2 oxidation level.

First, the reaction of 1-methyl-1-(2-phenethyl)allene (**1a**, 0.25 mmol) with CO_2 (1 atm) and a hydrosilane was examined in the presence of a copper catalyst (Table 1). We used 1.5 mmol of hydrosilane, which corresponds to 2.0 equiv for the required amount to provide the homoallylic alcohol **2a** since three H atoms were incorporated into the product. Initially, various ligands were evaluated employing $HSi(OMe)_2Me$ as the hydrosilane. Xy-Xantphos[14] was identified as the best ligand, affording **2a** in 99% GC yield and in 84% isolated yield after column chromatography (entry 1). In stark contrast to
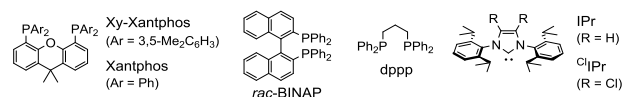
Table 1 Effect of catalytic system on the synthesis of **2a**[a]
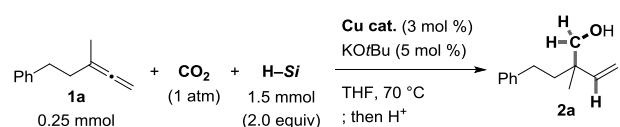
Entry	Cu cat.	H–Si	Yield (%)[b]
1	Xy-Xantphos / CuCl	HSi(OMe)₂Me	99 (84)[c]
2[d]	Xy-Xantphos / CuCl	HSi(OMe)₂Me	96
3	Xantphos / CuCl	HSi(OMe)₂Me	92
4	*rac*-BINAP / CuCl	HSi(OMe)₂Me	85
5	dppp / CuCl	HSi(OMe)₂Me	73
6	IPrCuCl	HSi(OMe)₂Me	62
7	ᶜˡIPrCuCl	HSi(OMe)₂Me	67
8	Xy-Xantphos / CuCl	HSi(OEt)₃	83
9	Xy-Xantphos / CuCl	PMHS	35

[a] Conditions: **1a** (0.25 mmol), Cu cat. (3 mol %), KO*t*Bu (5 mol %), a hydrosilane (1.5 mmol), in THF (0.50 mL) under CO₂ (1 atm, closed) at 70 °C for 18 h. [b] Yield was determined by GC analysis using an internal standard. [c] Isolated yield is shown in parenthesis. [d] For 20 min.
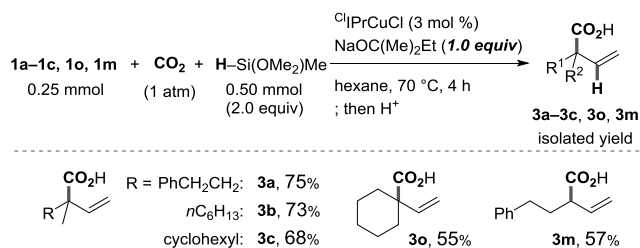
reported hydrocarboxylation reactions,[5] no product at the carboxylic acid oxidation level was detected under the present conditions. Present reaction was fast, reaching completion within 20 min (entry 2). Other bidentate phosphine ligands such as Xantphos,[14] BINAP[14] and dppp[14] gave **2a** in 92%, 85% and 73% yields, respectively (entries 3–5). Employing an *N*-heterocyclic carbene (NHC) ligand IPr[14] or ᶜˡIPr,[14] the yield was decreased (entries 6 and 7). In a survey of hydrosilanes using Xy-Xantphos as the ligand, HSi(OEt)₃ afforded **2a** in slightly lower yield (entry 8), whereas PMHS[14] was ineffective possibly owing to its large steric bulk (entry 9).

With these optimized conditions in hand, various allenes were employed in the reaction (Table 2). The corresponding homoallylic alcohols (**2b**–**2n**) were obtained regioselectively, and the resulting terminal olefin moieties of **2b**–**2m** were preserved without undergoing hydrosilylation by the remaining hydrosilane. 1,1-Disubstituted allenes (**1b**–**1d**) provided **2b**–**2d** in good to high isolated yields (entries 1–3). It is noteworthy that various ester functionalities on the allenes (**1e**–**1h**) remained intact without any indication of reduction to the corresponding diols (judging from GCMS and ¹H NMR analyses), whereas CO₂ was reductively incorporated into the homoallylic alcohol moieties. Thus, homoallylic alcohols bearing a primary alkyl acetate (**2e**, entry 4), primary alkyl isobutyrate (**2f**, entry 5), methyl benzoate moiety (**2g**, entry 6),

Table 2 Synthesis of homoallylic alcohols (**2**) from **1**[a]
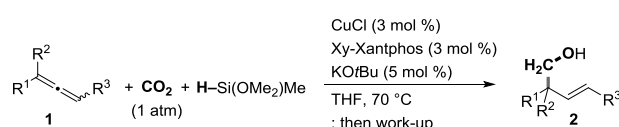
Entry	Allene: **1**		Product: **2**		Yield (%)[b]
1[c]		**1b**		**2b**	73
2[c]		**1c**		**2c**	68
3[c]		**1d**		**2d**	59
4		**1e**		**2e**	86
5		**1f**		**2f**	62
6		**1g**		**2g**	75
7		**1h**		**2h**	52
8[d]		**1h**		**2h'**	74
9		**1i**		**2i**	62
10[c]		**1j**		**2j**	75
11		**1k**		**2k**	72
12		**1l**		**2l**	21
13[e]		**1m**		**2m**	30
14[f]		**1n**		**2n**	48

[a] Conditions: **1** (0.25 mmol), CuCl (3 mol %), Xy-Xantphos (3 mol %), KO*t*Bu (5 mol %), HSi(OMe)₂Me (2.0 mmol), in THF (0.50 mL) under CO₂ (1 atm, closed) at 70 °C for 18 h. [b] Isolated yield of **2**. [c] HSi(OMe)₂Me (1.5 mmol) was used. [d] By modified workup procedure.[15] [e] DTBM-Xantphos[14] (3 mol %) was used as the ligand. [f] dppBz[14] (3 mol %) was used as the ligand.

Scheme 2 Cu-catalyzed hydrocarboxylation of allenes.

and an ethyl ester functionality in the proximity of the reaction site (**2h**, entry 7) were obtained in good to high isolated yields. The product **2h** seemed labile during the workup procedure, but could be isolated as the γ-lactone **2h'** in higher yield (entry 8).[15] The carbamate functionality in **1i** was also retained in the reaction (entry 9). Unfortunately, a substrate bearing an amide functionality afforded the corresponding product in low yield.[15] Aryl bromide (**1j**) and alkene (**1k**) moieties were tolerated to give **2j** and **2k** in 75% and 72% yields, respectively (entries 10 and 11). Phenyl-substituted (**1l**) and mono-substituted (**1m**) allenes gave the corresponding alcohols (**2l** and **2m**) in low yields though substrates were fully consumed (entries 12 and 13). A tri-substituted allene (**1n**) also converted to the product (**2n**) in moderate yield (entry 14).

We found that by increasing the amount of the base from 5 mol % to 1.0 equiv with ^{Cl}IPr as the ligand, the product could be completely switched from **2** to β,γ-unsaturated carboxylic acid **3** (Scheme 2).[15] The hydrocarboxylation of allenes was previously reported by Iwasawa and Takaya employing a Pd catalyst and the highly reactive and pyrophoric $AlEt_3$ as the reducing agents.[5d] In the present work, we realized the hydrocarboxylation with a Cu catalyst utilizing a mild and easy-to-handle hydrosilane as the reducing agent. The product **3a** was isolated in 75% yield without the formation of **2a** (Scheme 2). Similarly, other 1,1-disubstituted allenes (**1b**, **1c** and **1o**), as well as a mono-substituted allene **1m**, selectively provided the corresponding acids (**3b**, **3c**, **3o**, and **3m**) in moderate to good yields. The use of a stoichiometric amount of base is a key for the selective formation of **3**. Thus, products at two different oxidation levels (**2** and **3**) were selectively prepared by simply adjusting the equivalence of base in the Cu-catalyzed reactions.

Possible catalytic cycles are shown in Scheme 3. Copper hydride **A** is generated by the reaction of copper chloride with a base and a hydrosilane (step 0).[5a,16] Addition of **A** across a terminal double bond of allene **1** with the Cu atom at the less hindered site generates allylcopper intermediate **B** (step 1), which reacts with CO_2 regioselectively at the γ-position via six-membered transition state to give copper carboxylate **C** (step 2).[4a] For the synthesis of homoallylic alcohols (**2**), carboxylate **C** could be further reduced[15] by the hydrosilane to copper alkoxide **E** via the silyl copper ketal derivative **D** (steps 3 and 4). Finally, σ-bond metathesis of **E** with the hydrosilane provides silyl ether **F** and regenerates **A** as the active catalyst species (step 5). Protonation (workup) of **F** affords homoallylic alcohol **2** as the alcohol product. In the hydrocarboxylation reaction (Scheme 2), the base traps copper carboxylate **C** to prevent

further reduction (step 6), and protic workup of **G** affords carboxylic acid **3**.
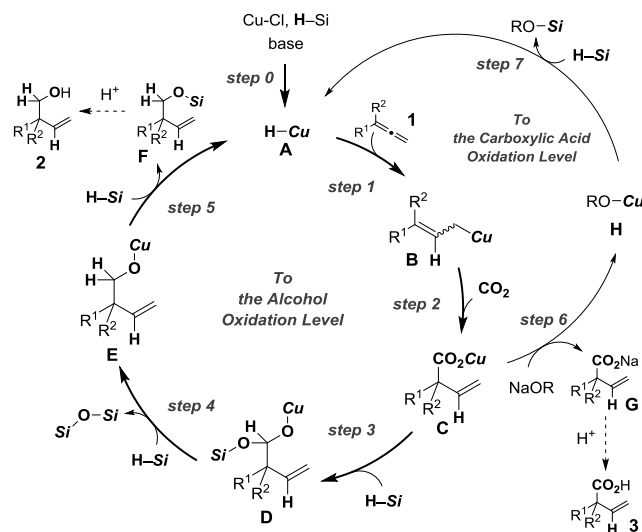
Scheme 3 Possible reaction mechanisms.

In conclusion, we have developed a selective C–C bond-forming transformation of CO_2 to the alcohol oxidation level for the first time. Allenes react with CO_2 and a mild and easy-to-handle hydrosilane to afford homoallylic alcohols regioselectively. A wide range of esters on the allenes remains unchanged during the reaction although CO_2 is reduced to the alcohol oxidation level, representing the distinctive chemoselectivity of the transformation. The oxidation level of the products can be switched to give β,γ-unsaturated carboxylic acids as the products by simply using the stoichiometric amounts of base with a tuned catalyst system. Further experiments elucidating the reaction mechanisms and developing enantioselective reactions are now on going.

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14 Abbreviations: Xy-Xantphos = 4,5-bis(bis(3,5-dimethylphenyl)phosphino)-9,9-dimethylxanthene; Xantphos = 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene; BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl; dppp = 1,3-bis(diphenylphosphino)propane; IPr = 1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene; [Cl]IPr = 1,3-bis(2,6-diisopropylphenyl)-4,5-dichloroimidazole-2-ylidene; PMHS = poly(methylhydrosiloxane); DTBM-Xantphos = 4,5-bis(bis(3,5-di-*tert*-butyl-4-methoxyphenyl)phosphino)-9,9-dimethylxanthene; dppBz = 1,2-bis(diphenhylphosphino)benzene.

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