



Reductive carboxylation of alkyl halides with CO₂ by use of photoinduced SmI₂/Sm reduction system

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This paper is dedicated to Professor Henri Kagan, on the occasion of his 80th birthday

ABSTRACT

Upon visible-light irradiation, reductive carboxylation of alkyl halides takes place by using a SmI₂/Sm mixed system under atmospheric CO₂ to afford the corresponding carboxylic acids in good to excellent yields.

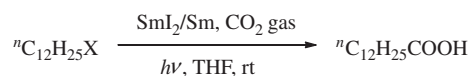
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Recently, the emission of carbon dioxide (CO₂) becomes serious problem as greenhouse gas. Although carbon dioxide is a potentially useful carbon resource, practical use in organic synthesis requires appropriate energy because of its energetical stability. In natural photosynthetic system, light energy is converted into chemical energy efficiently which is used to reduce CO₂ into carbohydrates.¹

During the last two decades, the use of low-valent rare earth species has been growing in synthetic organic chemistry; especially, samarium diiodide (SmI₂) is widely employed as a single-electron reducing agent in organic synthesis, because of its adequate reducing ability and suitable solubility in organic solvents such as THF.^{2,3} We have investigated novel photoinduced reductions with samarium diiodide, which occur upon visible-light irradiation since samarium diiodide absorbs the light of wavelength between 560 and 800 nm.⁴ Thus, we examined to apply this method to reductive coupling of alkyl halides with CO₂. Herein we report a novel reductive carboxylation of organic halides with CO₂ which can be established by visible-light irradiation (Scheme 1).⁵

First, we carried out the reductive carboxylation of *n*-dodecyl halide under various conditions (Table 1). SmI₂/Sm suspension was prepared in an ordinary way followed by adding 0.5 mmol of *n*-dodecyl halide, and the reaction mixture was irradiated with a xenon or tungsten lamp through Pyrex (*hν* >300 nm) under the atmosphere of CO₂. The photoinduced reductive carboxylation of *n*-dodecyl chloride with excess amounts of SmI₂/Sm took place successfully under the atmosphere of CO₂ affording tridecanoic acid in 68% yield (Entry 1). On the other hand, the carboxylation

did not proceed at all in the dark (Entry 2). Therefore, the visible-light irradiation is essential for this carboxylation. In the reactions using the pressurized CO₂ (Entries 3–5), the yields of the carboxylation product decreased in the increase of the CO₂ pressure.⁶ In these cases, the starting *n*-dodecyl chloride was recovered except for the formation of the carboxylic acid. These results suggest that the coordination of excess CO₂ to samarium reagents diminish the reducing ability of SmI₂/Sm. Next, the reductive carboxylation of *n*-dodecyl iodide with CO₂ (1 atm, bubbling) and SmI₂/Sm was examined in the presence of HMPA as an additive (Entries 6–8). The reaction using 1 equiv of HMPA afforded the reduced product, *n*-dodecane, in 37% yield with the recovery of the starting *n*-dodecyl iodide (Entry 6). In the case of 2 equiv of HMPA, the desired carboxylic acid was obtained in 31% yield with the formation of *n*-dodecane (46%) (Entry 7). However, the use of 3 equiv (or further excess amounts) of HMPA led to the exclusive formation of the reduced product, *n*-dodecane (~100%) (Entry 8). These results indicate that SmI₂/Sm/HMPA prefers the reduction to give *n*-dodecane, rather than the carboxylation. Upon irradiation with xenon lamp in the presence of bubbling CO₂, the reductive carboxylation of *n*-dodecyl chloride, bromide, and iodide was attempted, and tridecanoic acid was obtained in 14%, 42%, and 81% yields, respectively (Entries 9–11). In the dark, the reductive carboxylation of *n*-dodecyl iodide did not take place (Entry 12). By using *n*-dodecyl bromide as the substrate, the influence of the



Scheme 1.

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Table 1
Carboxylation of *n*-dodecyl halides with CO₂

$${}^n\text{C}_{12}\text{H}_{25}\text{X} \xrightarrow[h\nu, \text{THF, rt}]{\text{SmI}_2/\text{Sm, CO}_2 \text{ gas}} {}^n\text{C}_{12}\text{H}_{25}\text{COOH}$$

Entry	<i>hν</i>	X ^a	SmI ₂ /Sm (mmol)	CO ₂ gas (atm)	HMPA (mmol)	Time (h)	Yield (%) ^b
1	Xe lamp	Cl	3/6	1	—	6	68
2	Dark	Cl	3/6	1	—	6	0
3	Xe lamp	Cl	2/2	6	—	6	73 ^c
4	Xe lamp	Cl	2/2	18	—	6	34 ^c
5	Xe lamp	Cl	2/2	30	—	6	Trace ^c
6	Dark	I	2/2	Bubbling	2	1	Trace
7	Dark	I	2/2	Bubbling	4	1	31
8	Dark	I	2/2	Bubbling	6	1	— ^d
9	Xe lamp	Cl	3/3	Bubbling	—	6	14
10	Xe lamp	Br	3/3	Bubbling	—	6	42
11	Xe lamp	I	3/3	Bubbling	—	6	81
12	Dark	I	3/3	Bubbling	—	6	0
13	Xe lamp	Br	2/2	Bubbling	—	2	41
14	W lamp	Br	2/2	Bubbling	—	2	75
15	W lamp	Cl	2/2	Bubbling	—	2	48
16	W lamp	Cl	1.5/0.5	1	—	5	89
17	W lamp	Br	1.5/0.5	1	—	2	96
18	W lamp	I	1.5/0.5	1	—	1	97

^a *n*-Dodecyl halides (0.5 mmol) were used.^b Determined by GC.^c Autoclave bearing a glass window was used and photoirradiation was performed through the window.^d ¹²C₁₂H₂₆ was obtained quantitatively.

light sources on the carboxylation was investigated (Entries 13 and 14).

The use of tungsten lamp in place of xenon lamp resulted in the increase in the yield of tridecanoic acid.⁷ When the reductive carboxylation of *n*-dodecyl chloride was conducted under the atmosphere of CO₂ (without bubbling⁸) using SmI₂/Sm (1.5 mmol/0.5 mmol) upon irradiation with tungsten lamp, 89% of tridecanoic acid was obtained successfully (Entry 16). Under similar conditions, *n*-dodecyl bromide and iodide underwent reductive carboxylation, giving tridecanoic acid in excellent yields (Entries 17 and 18).⁹

To demonstrate the scope and limitation of the present method, the reductive carboxylation of several alkyl halides was examined under the optimized conditions (Table 2). From the materials science viewpoints, mono- or di-carboxylic acids containing long alkyl chains are important molecules as liquid crystals and Langmuir–Blodgett (LB) layers, because self assembly monolayers are formed based on hydrophobic interaction. Therefore, the reductive











carboxylation of docosanyl bromide and 1,10-dibromodecane was performed by using the present photoinduced SmI₂/Sm system, and the corresponding mono- and di-carboxylic acids were obtained in good yields, respectively (Entries 1 and 2).

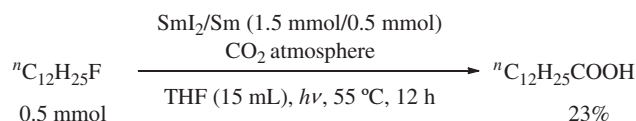
Secondary alkyl halides such as cyclohexyl halides also gave the corresponding carboxylic acid in moderate yields (Entries 3–5). In these reactions, bicyclohexyl was formed as a byproduct, most probably via the coupling of cyclohexyl radicals. In the case of benzyl chloride, it is very interesting that the corresponding carboxylic acid was obtained in 35% yield, despite benzyl radical is a very stable carbon radical species (Entry 6). In contrast, tertiary alkyl halides, for example, adamantyl iodide, underwent simple reduction to give the corresponding alkane and did not afford the desired carboxylic acid (Entry 7).

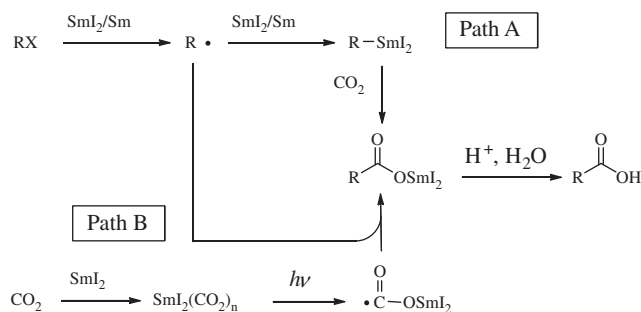
Moreover, the reductive coupling of alkyl fluoride such as *n*-dodecyl fluoride was attempted (Scheme 2). Under similar conditions, the desired reductive carboxylation of *n*-dodecyl fluoride did not proceed at all even upon visible-light irradiation; however, elevated temperature led to the formation of tridecanoic acid (23%) along with *n*-dodecane (34%) and 1-dodecene (4%).¹⁰

In this reductive carboxylation, two possible pathways are considered as shown in Scheme 3. Path A includes (1) generation of alkylsamarium species (RSmX₂) by the reduction of alkyl halides with SmI₂/Sm; (2) carboxylation of the alkylsamarium species with CO₂ to form samarium salt of carboxylic acids; (3) protonation of the salt to produce carboxylic acids during workups. Path B involves (1) single-electron transfer to alkyl halides from SmI₂/Sm to generate alkyl radical species; (2) coordination of CO₂ to SmI₂^{11,12} and photoinduced electron transfer to generate radical

Table 2
Reductive carboxylation of alkyl halides^a

Entry	Substrates	Products	Time (h)	Yield (%) ^b
1	ⁿ C ₂₂ H ₄₅ Br	ⁿ C ₂₂ H ₄₅ COOH	6	74
2	Br(CH ₂) ₁₀ Br	HOOC(CH ₂) ₁₀ COOH	6	76
3			5	45
4			6	50
5			1.5	31
6			4.5	35
7			4.5	—

^a Reaction conditions: alkyl halides (0.5 mmol), SmI₂/Sm (1.5 mmol/0.5 mmol), CO₂ (1 atm, atmosphere), THF (15 mL), rt, *hν* (tungsten lamp, 500 W).^b Determined by ¹H NMR.**Scheme 2.**



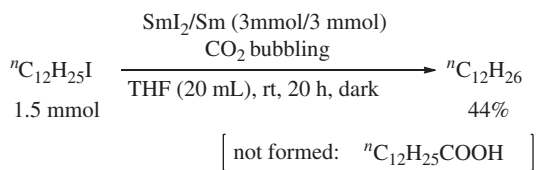
Scheme 3.

anion species of CO_2 ; (3) radical coupling of the alkyl radical species with the radical anion species of CO_2 and the following protonation to produce carboxylic acids.

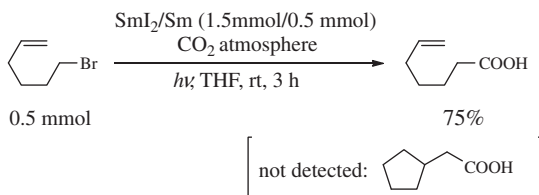
To get insight into the reaction pathway, we examined the reaction of *n*-dodecyl iodide with CO_2 (1 atm) in the presence of SmI_2/Sm in the dark, which provided *n*-dodecane (44%) without formation of the desired tridecanoic acid (Scheme 4). The formation of *n*-dodecane can be explained by the protonation of *n*-dodecylsamarium diiodide ($^{12}\text{C}_{12}\text{H}_{25}\text{SmI}_2$) during aqueous workups. If Path A is present, *n*-dodecylsamarium diiodide ($^{12}\text{C}_{12}\text{H}_{25}\text{SmI}_2$) may react with CO_2 to give tridecanoic acid. However, no formation of tridecanoic acid suggests that Path A is not a real pathway for this reductive carbonylation.¹³ Although the reaction of Scheme 4 also involves the generation of *n*-dodecyl radical as an intermediate, the dark condition inhibits the generation of radical anion of CO_2 , resulting in no formation of tridecanoic acid.

To get some information about the rate for the carboxylation process, we next examined the photoinduced reductive carboxylation of 5-hexenyl bromide with CO_2 in the presence of SmI_2/Sm , which afforded 6-heptenoic acid in good yield without the formation of cyclic carboxylic acid (Scheme 5). Since the rate for 5-*exo* cyclization of 5-hexenyl radical is reported to be $2.3 \times 10^5 \text{ s}^{-1}$ (25 °C),¹⁴ the rate for the carboxylation of carbon radical is estimated to be more than 10^7 s^{-1} (25 °C).

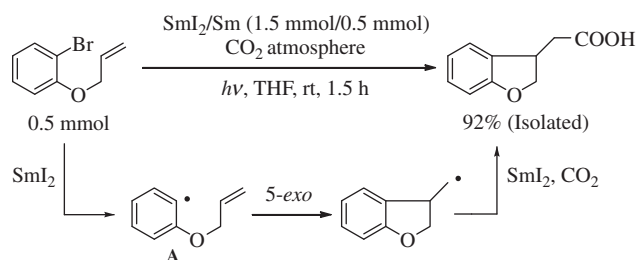
Since 5-*exo* cyclization of aryl radicals such as **A** is known to be very fast process ($k = 6.3 \times 10^9 \text{ s}^{-1}$ (30 °C)),¹⁵ it is of great interest to examine the reductive carbonylation of *o*-allyloxy-bromobenzene (Scheme 6). Upon photoirradiation, *o*-allyloxy-bromobenzene reacted with CO_2 in the presence of SmI_2/Sm to afford the corresponding cyclic carboxylic acid in excellent yield. The reaction



Scheme 4.



Scheme 5.



Scheme 6.

proceeded via the generation of the aryl radical, 5-*exo* cyclization, and carboxylation with CO_2 .

In summary, atmospheric CO_2 is found to react with alkyl halides efficiently using SmI_2/Sm mixed system. Photoirradiation is indispensable for this reaction and resides the potential to develop various synthetic reactions by following natural photosynthetic systems.

Acknowledgments

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- In a 20 mL of three-necked glass flask (Pyrex) equipped with a cooler, an N_2 inlet and CO_2 bubbling tube were placed under the atmosphere of nitrogen, Sm powder (6 mmol, 0.902 g), 1,2-diiodoethane (2 mmol, 0.846 g), and THF (10 mL). The resulting mixture was stirred magnetically for 1.5 h to prepare a SmI_2/Sm reagent, and then CO_2 was introduced into the vessel via tube. Upon irradiation with a Xe lamp (500 W), haloalkane (0.5 mmol) was added to the mixture, and then the reaction was continued for another 6 h. The reaction

- temperature was kept at rt by cooling with flowing water. After the decomposition of excess SmI_2/Sm with air, and then 1 mol L^{-1} HCl, the product was extracted with ether. The extracts were dried (MgSO_4) and concentrated in vacuo affording products. The yields of the known carboxylic acids were determined by GC or ^1H NMR. The isolation of the carboxylic acids was performed by preparative TLC (Silica gel, hexane–ethyl acetate as eluent). Oxalic acid or its salt were not detected.
- The reactions were performed using a 50 mL stainless steel autoclave equipped with glass windows.
 - The quantity of light of tungsten lamp is larger than that of xenon lamp in the wavelength of 450–650 nm, which is effective for activation of SmI_2 .
 - The presence of excess amounts of CO_2 (CO_2 bubbling condition) diminished the reducing ability of SmI_2 , most probably due to the coordination of CO_2 to SmI_2 .
 - In the absence of Sm metal, the reductive carboxylation of *n*-dodecyl iodide with SmI_2 proceeds to give the corresponding carboxylic acid in 63% yield.
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 - To get some information about $\text{SmI}_2\text{-CO}_2$ complex, SmI_2/Sm in THF under the atmosphere of CO_2 was monitored by UV–vis spectra. After preparing SmI_2/Sm (0.1 M) in THF, 5 mL of CO_2 gas was flowed into the mixture from inlet side by syringe, followed by 5 min stirring. Then, the UV–vis spectra were measured in 1×10^{-3} M using 1 mm-wavelength cell. After measurement, 10 and 15 mL of CO_2 gas were added in turn and the UV–vis spectra were measured continuously in the same way. From the series of UV–vis spectra, the absorption of peaks at 350 and 420 nm were slightly reduced.
 - The dark reaction in the presence of HMPA afforded the carboxylic acid in 31% yield (Table 1, Entry 7). From these results, it is reasonable to consider that the organosamarium species is stabilized in the presence of HMPA and it reacts with CO_2 to give the carboxylic acid. Therefore, the reaction using HMPA may proceed by Path A.
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