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Photo-on-demand Phosgenation Reactions with Chloroform Triggered by Cl₂ upon Irradiation with Visible Light: Syntheses of Chloroformates, Carbonate Esters, and Isocyanates

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Chloroform (CHCl₃) upon bubbling with O₂ containing ~2% Cl₂ underwent oxidative photochemical conversion to phosgene (COCl₂) when exposed to a white LED light. Cl₂ may serve as a visible light-responsive radical initiator in the radical chain reactions of CHCl₃ and O₂. This photochemical reaction allowed both *in situ* and stepwise one-pot phosgenation reactions, which are simple and safe methods, without expensive apparatus. It can be applied to a variety of conventional organic syntheses using phosgene and phosgene oligomers.

Keywords: Visible light | Phosgenation | Chloroform

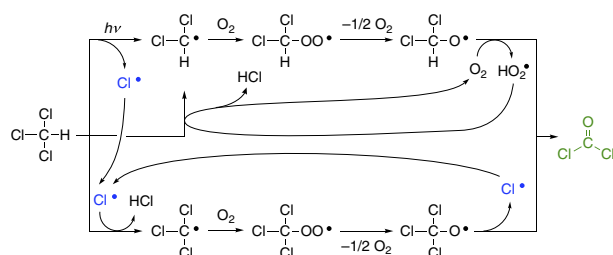
Photochemical synthesis with visible light is expected to play an important role for the design of sustainable chemical reactions with reductions of CO₂ emission and waste. It allows the use of light emitting diodes (LEDs) and sunlight as light sources, and also reduces photochemical degradation of the reaction substrates and/or products. There are a variety of photochemical reactions using visible light, most of which generally require a catalyst and/or reagent that are activated under visible light.^{1–3}

We previously reported that CHCl₃ under O₂ bubbling underwent oxidative photochemical conversion to produce COCl₂ upon exposure to UV-C light, mainly at 184.9 and 253.7 nm, generated from a low-pressure mercury lamp (LPML).⁴ COCl₂ is a highly reactive useful C1 building block in organic synthesis, but is a highly toxic gaseous compound at room temperature.^{5,6} The reaction may proceed through radical chain reactions triggered by C–Cl bond cleavage in CHCl₃ (Scheme 1).^{4,7} The generated Cl• extracts hydrogen from another CHCl₃ to produce Cl₃C•. It then reacts with O₂ to give COCl₂ with regeneration of Cl•. Meanwhile, Cl₂HC• may also react with O₂ to give COCl₂. With this photochemical reaction, we then developed *in situ* photo-on-demand synthesis methods for chloroformates and carbonate esters from CHCl₃ solutions containing alcohol with or without an organic base.^{8–10} Furthermore, we successfully demonstrated one-pot synthesis

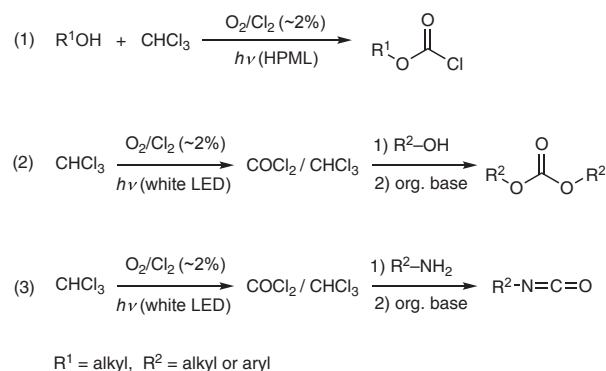
of isocyanates from primary amines with a prepared CHCl₃ solution containing COCl₂.¹¹ The substrates reacted with COCl₂ generated in CHCl₃ to give the products. These photochemical syntheses are safe, convenient, and inexpensive, but use LPML, which causes some unfavorable side reactions owing to the photo-decomposition of both reagents and products upon exposure to the high energy UV-C light. The use of mercury lamps should be avoided due to their large environmental impacts and health hazards.¹² This background motivated us to develop a novel photo-on-demand phosgenation reaction with lower-energy visible light.

It is known that chlorine (Cl₂), having a lowest-energy absorption band at around 300–500 nm with λ_{max} at 330 nm, undergoes homolytic cleavage to give 2 Cl• upon heating or irradiation of visible light.^{13,14} We expected that Cl₂ could become a visible light-responsive initiator of the radical chain reaction of CHCl₃,¹⁵ and found herein that CHCl₃ underwent oxidative photochemical conversion to COCl₂ under >300 nm light when a catalytic amount of Cl₂ was added to O₂ gas.¹⁶ In this study, we successfully applied this reaction to the *in situ* photo-on-demand synthesis of chloroformate with a mixture solution of CHCl₃ and alcohol (Scheme 2, reaction 1). Additionally, one-pot syntheses of carbonate esters and isocyanates were achieved with the CHCl₃ solution containing COCl₂ as prepared upon exposure to visible light (reactions 2 and 3, respectively).

The reaction system for the *in situ* photo-on-demand synthesis with visible light was set up as follows. A mixture of O₂ and Cl₂ (~2%) gas was prepared in a three-necked flask (flask 1) containing Ca(ClO)₂ upon addition of aqueous HCl solution with a syringe pump under a steady flow of O₂ (0.1 L/min). The prepared O₂/Cl₂ gas was dried over a CaCl₂ column, and then injected into the next photoreactor (flask 2). A 100 W high-pressure mercury lamp (HPML) equipped with



Scheme 1. Proposed mechanism for oxidative photochemical conversion of CHCl₃ to COCl₂.



Scheme 2. Cl₂-triggered photo-on-demand phosgenation reactions with visible light developed in this study.

Table 1. *In situ* Photochemical synthesis of chloroformate from a CHCl_3 solution containing 1-hexanol with a 100 W high-pressure mercury lamp (HPML).

$\text{ROH} + \text{CHCl}_3 \xrightarrow[\text{time (h), T (}^\circ\text{C)}]{h\nu, \text{ gas}}$					$\text{R}-\text{O}-\overset{\text{O}}{\overset{\parallel}{\text{C}}}-\text{Cl} + \text{R}-\text{O}-\overset{\text{O}}{\overset{\parallel}{\text{C}}}-\text{O}-\text{R}$			
R = hexyl					1	2		
entry	gas	1-hexanol (mmol)	CHCl ₃ (mmol)	lamp	time (h)	T (°C)	yield (%) ^a	
							1	2
1	O ₂	10	250 (20 mL)	LPML ^c (20 W)	1	10	94	—
2	O ₂	10	250	HPML ^d (100 W)	1	10	—	—
3	O ₂ /Cl ₂ ^b	10	250	HPML ^d	1	10	>99	—
4	O ₂ /Cl ₂ ^b	10	250	— ^e	1	10	—	10
5	O ₂ /Cl ₂ ^b	10	250	room light	1	10	58	8
6	O ₂ /Cl ₂ ^b	30	625 (50 mL)	HPML ^d	5	20	>99	—

^a Determined by ^1H NMR analysis, ^b ~2% Cl_2 content, ^c quartz glass jacket, ^d borosilicate glass jacket, ^e dark

a water cooling system was inserted into the solution via a borosilicate glass jacket ($\phi 30 \text{ mm} \times 150 \text{ mm}$) fixed in the center of a cylindrical flask ($\phi 46 \text{ mm} \times 170 \text{ mm}$). The system thus allows irradiation by $>300 \text{ nm}$ light with a maximum intensity at 365 nm , whose illuminance is 37.1 mW/cm^2 . Alternatively, a commercially available 365 nm or white LED is attached to the outside of the cylindrical flask. The 365 nm LED with 2.25 W electrical power generates $355\text{--}375 \text{ nm}$ light with a maximum intensity at $\lambda = 365 \text{ nm}$, whose illuminance is 8.4 mW/cm^2 . The white LED generates $400\text{--}750 \text{ nm}$ light with a maximum intensity at $\lambda = 465 \text{ nm}$, and the illuminances of the 3 and 9 W lamps are 560 and 2000 lux, respectively.

As a reference reaction, according to our previous study,⁸ we demonstrated photochemical conversion of 1-hexanol to the corresponding chloroformate **1** with a 20 W LPML system (Table 1, Entry 1). When a CHCl_3 solution containing 1-hexanol under O_2 bubbling was exposed to the UV-C light, the chloroformate was obtained in 94% yield. The starting alcohol and/or product might undergo photo-decomposition to some extent, decreasing the product yield. With a 100 W HPML system instead of the LPML system, however, no reaction was observed (Entry 2). Interestingly, the reaction occurred upon mixing ~2% Cl_2 with the O_2 gas to give **1** in >99% yield (Entry 3). The observed increase in the product yield may result from cutting the higher energy UV light due to the borosilicate glass jacket. The reaction was then carried out in the dark, and the carbonate ester **2**, most likely formed through the reaction of **1** and alcohol, was obtained only in 10% yield (Entry 4). The reaction also proceeded under room light to give a mixture of **1** and **2** in 58 and 8% yields, respectively (Entry 5). A scale-up synthesis of **1** with the HPML was achieved by increasing the amounts of alcohol and CHCl_3 and raising the temperature to 20°C (Entry 6).

To develop a more convenient simple reaction system with lower energy consumption, the HPML was then replaced by a LED, which can generate 365 nm UV-A light. Initially, we quantitatively investigated the oxidative photochemical conver-

Table 2. Chemical estimation of COCl_2 generated from CHCl_3 under bubbling with O_2 containing Cl_2 (~2%) upon photo-irradiation with 365 nm and white LED.

CHCl_3		$h\nu, \text{O}_2/\text{Cl}_2$ (~2%) 1.5 h, 20 °C	vapor	chloroformate + carbonate	
			EtOH		
			solution	1 + 2	
			1-hexanol		

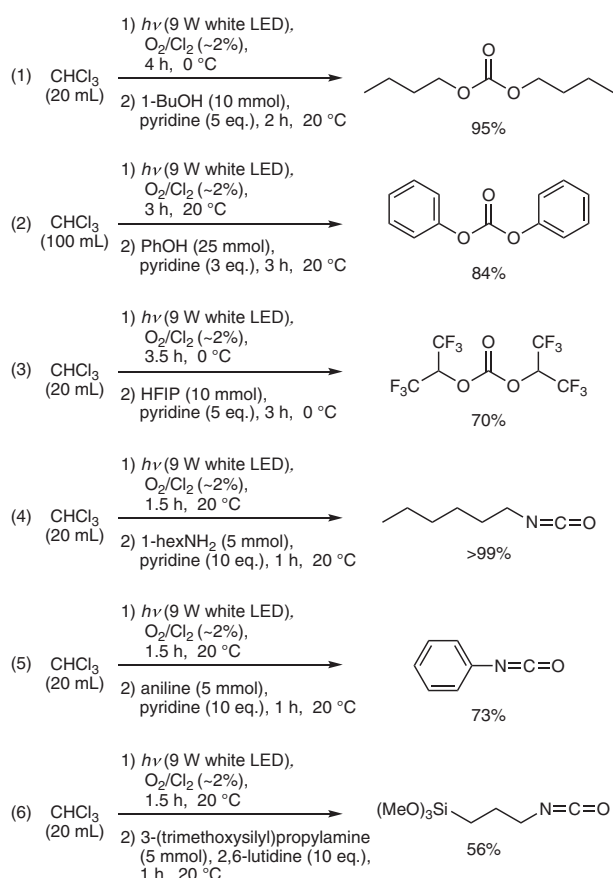
entry	lamp	CHCl ₃ (mmol)	Estimated COCl ₂ (mmol)		conversion (%) ^a
			solution	vapor	
1	365 nm LED (2.25 W)	375 (30 mL)	26	11	9.9
2	white LED (3 W)	375 (30 mL)	16	11	7.2
3	white LED (9 W)	375 (30 mL)	26	21	12.5
4	LPML ^b (20 W)	375 (30 mL)	26	25	13.6

^a Determined by ^1H NMR analysis, ^b quartz glass jacket

sion of CHCl_3 to COCl_2 by varying the LED lamp. The produced COCl_2 dissolved in CHCl_3 and that vaporized into the gas phase could be estimated separately by chemical trapping with an alcohol. When 30 mL of CHCl_3 under O_2/Cl_2 bubbling was exposed to 365 nm light with a 2.25 W LED at 20°C for 1.5 h , it afforded 9.9% conversion to COCl_2 (Table 2, Entry 1). Furthermore, white light generated from a 3 W LED gave COCl_2 with 7.2% conversion (Entry 2). The observed conversion increased to 12.5% by increasing the light intensity with a 9 W LED (Entry 3). This yield is comparable to that with the 20 W LPML system (Entry 4).

Next, the above *in situ* photochemical conversion of CHCl_3 to COCl_2 was applied to the one-pot syntheses of carbonate esters and isocyanates (Scheme 3).¹⁷ When a 1:5 mixture of 1-BuOH and pyridine was added to the as-prepared CHCl_3 solution containing COCl_2 , dibutyl carbonate was obtained in 95% yield. PhOH, a lower nucleophilic aromatic alcohol, also reacted to give diphenyl carbonate in 84% yield. Hexafluoroisopropyl alcohol (HFIP), which is expected to have lower nucleophilicity than PhOH judging from their pK_a values (9.3 and 10.0, respectively),^{18,19} provided the corresponding carbonate ester in 70% yield. This method was further available to the synthesis of isocyanates. A sequential addition of hexylamine and pyridine to the as-prepared CHCl_3 solution containing COCl_2 resulted in formation of the isocyanate in >99% yield. With the same procedure, aniline, an aromatic amine, was converted to the corresponding isocyanate in 73% yield. 3-(Trimethoxysilyl)propylamine, which readily undergoes hydrolysis condensation with water under acidic conditions, also provided the corresponding isocyanates in 56% yield.

In this study, we found that oxidative photochemical conversion of CHCl_3 to COCl_2 occurred upon exposure to visible light while bubbling with O_2 containing ~2% Cl_2 . The visible light caused Cl-Cl bond cleavage to generate Cl^\bullet , which may be an initiator to trigger the radical chain reactions of CHCl_3 and O_2 . This reaction allows photo-on-demand generation of COCl_2 in CHCl_3 , which is practically applicable to *in situ* and stepwise one-pot phosgenation reactions. It is expected to replace a variety of conventional organic synthetic



Scheme 3. Stepwise one-pot photochemical syntheses of carbonate esters and isocyanates with CHCl_3 and alcohols or primary amines with a 9 W white LED.

reactions using phosgene and phosgene oligomers, and reduce the environmental impacts.

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