Photo-on-Demand Synthesis of Chloroformates and Vilsmeier Reagents with Chloroform: Their Applications to One-Pot Synthesis of Organic Chemicals

Liang, Fengying

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（クロロホルムを用いるクロロギ酸エステルとビルスマイヤー試薬の光オン・デマンド合成：有機化学薬品のワンポット合成への利用）

March 2021

Graduate School of Science, Kobe University

Fengying Liang

（ 梁 凤 英 ）

Photo-on-Demand Synthesis of Chloroformates and Vilsmeier Reagents with Chloroform: Their Applications to One-Pot Synthesis of Organic Chemicals

by

Fengying Liang

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A DISSERTATION

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Professor Tsuda Akihiko

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Abstract

Phosgene ($COCl_2$) is an extremely important C1 building block in organic synthesis. Beside its significant importance in a wide range of organic syntheses, it is well known that it has high toxicity owing to its high reactivity.

There are mainly two preparation methods of phosgene. As a general method, it is synthesized with carbon monoxide (CO) and chlorine (Cl_2) with activated carbon as a catalyst. This method has been used mainly in industry for a century. However, not only the produced $COCl_2$, both the reactants CO and Cl_2 also has high toxicity. With this reason, there is a potential risk of their leakage in the production processes. As an alternative safe method, $COCl_2$ can be produced from base-catalyzed decomposition of phosgene oligomers such as triphosgene (BTC) and diphosgene (TCF), which can be used as solid and liquid at room temperature, respectively. But recently, some research groups have reported that both BTC and TCF also need highly strict operations because they also have high toxicity.

Despite the high toxicity of $COCl_2$, it attracts organic chemists because of its many practical advantages in organic synthesis. It allows high yield syntheses without notable side products through the simple efficient organic reactions. Consequently, in situ production and consumption of $COCl_2$, which allows presence of a few amounts of $COCl_2$ formed temporally in the reaction system, are very important for the safety use of $COCl_2$. In this background, our research group recently developed a photo-on-demand synthesis of $COCl_2$ from $CHCl_3$, which is available in situ for a variety of organic syntheses.

In the present study, the above photochemical reaction has applied successfully to novel in situ UV photo-on-demand syntheses of chloroformates and Vilsmeier reagent with a chloroform ($CHCl_3$) solution. When a $CHCl_3$ solution containing an alcohol was exposed to UV light with a low-pressure mercury lamp

under O_2 bubbling, the corresponding chloroformate was obtained in practical high yield. Then, it further allowed one-pot conversion to carbonate and carbamate upon addition of an alcohol or amine, respectively, with or without an organic base to the sample solution. With similar procedures, Vilsmeier reagent, a general formylation reagent, was also obtained from a chloroform solution containing *N*,*N*-dimethylformamide (DMF) or *N*,*N*-dimethylacetamide(DMA). Their direct applications to the next reactions allowed one-pot synthesis of a lot of useful chemicals, such as aldehydes, acid chlorides, formates, ketones, and esters. In these novel in situ photo-on-demand syntheses, $CHCl_3$ plays dual roles of solvent and reactant. $COCl_2$ generated upon UV-irradiation in the $CHCl_3$ solution may consumed immediately in situ via the reaction with substrates dissolved in the $CHCl_3$.

The study was further extended to use visible light. In comparison with the reactions using the higher energy UV light, it has an advantage to decrease photochemical decompositions of the reaction substrates and/or products. The in situ photo-on-demand synthesis of Vilsmeier reagent with the visible light has been achieved upon addition of catalytic amounts of Cl_2 to the system. Under exposure to the visible light (LED lamp), Cl_2 causes a homolytic cleavage to give $Cl^{\bullet}$, which may extract $H^{\bullet}$ from $CHCl_3$ to accelerate radical chain reactions with O_2 to give $COCl_2$. The produced $COCl_2$ reacts immediately with DMF to give Vilsmeier reagent.

It is known that $CHCl_3$ undergoes oxidative photo-decomposition to give phosgene in analytical scale. However, this phenomenon has never been utilized in practical organic synthesis. The present study makes innovation, and provides many benefits to the chemical syntheses that use phosgene in both laboratory and industry.

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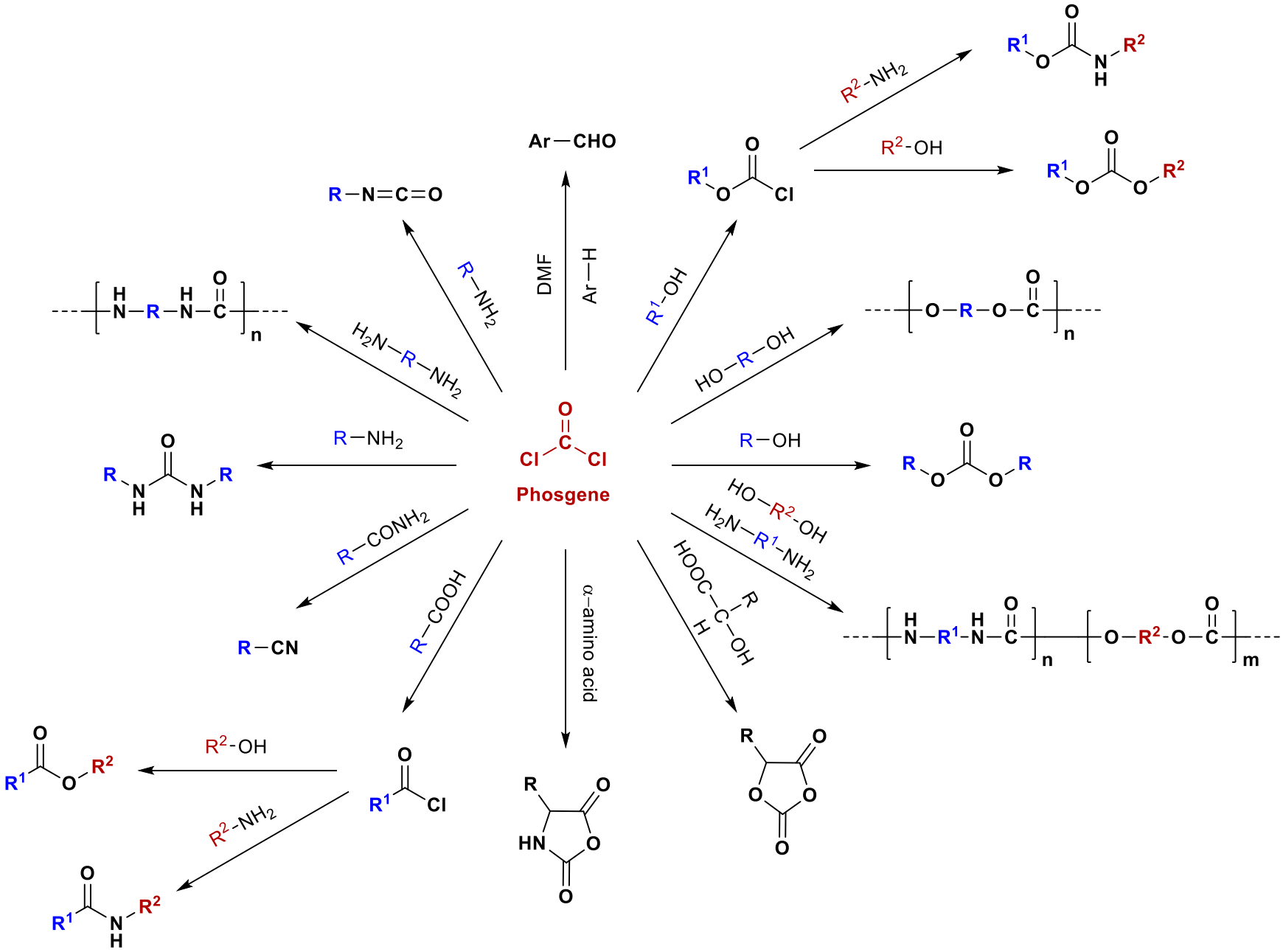
Chapter 1

General Introduction

1.1 Introduction of phosgene

Phosgene ($COCl_2$) is used as a highly reactive C1 building block in a variety of organic syntheses such as chloroformates, carbonates, carbamates, isocyanates, ureas, urethanes, and polymers (Scheme 1.1).[1] However, it is also well known that it has high toxicity, and also has a dark past history of being used as a chemical weapon in World War I.[2] With this reason, phosgene generally must be used by the on-demand and on-site production methods. There are mainly two methods to produce phosgene. (1) chemical reaction of carbon monoxide (CO) and chlorine (Cl_2) with a carbon catalyst (Scheme 1.2, reaction **I**)[3] and (2) decomposition of a phosgene oligomer (Scheme 1.2, reactions **II** and **III**)[4].

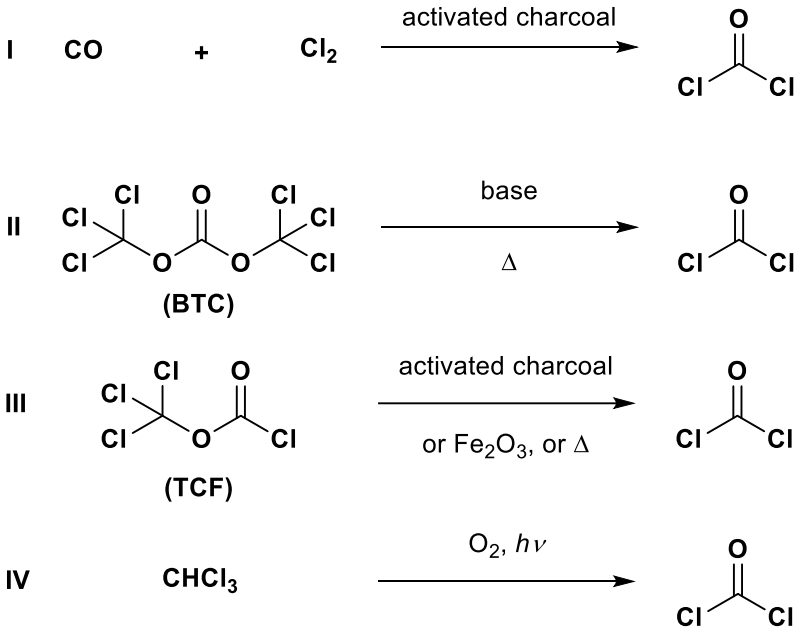
In 1812, John Davy mixed equal volume of CO and Cl_2, and the mixed gas was exposed to sunlight. A new gas was then generated, and he named it as "phosgene", which means "generated from light".[2a, 2b] Later, it was found that CO and Cl_2 react to give $COCl_2$ with a solid catalyst such as an activated charcoal, which is a more effective catalyst than the other catalysts.[2a, 2b] This protocol is also suitable for large scale production of phosgene, and it has a capacity of producing 5–80 tons per day even in a century ago.[2b] However, not only $COCl_2$, the reactants Cl_2 and CO are also highly toxic gases. Handling of the gas phase reactions has a potential risk of leakage.



Scheme 1.1 Applications of phosgene in organic syntheses.

As an alternative safe method, $COCl_2$ can be produced from catalytic decomposition of phosgene oligomers, such as triphosgene (BTC) and diphosgene (TCF). [4] BTC and TCF allow easy handling of the organic reactions compared with phosgene, due to their non-gaseous state at room temperature.[4a]

A base catalyst decomposes BTC to give 3 equiv. amount of phosgene (Scheme1.2, reaction **II**).[4] Further, metal salts and silica gel, having Lewis acid characters and active surfaces, also bring about decomposition of BTC over 200 °C to generate phosgene.[4b] Since BTC is a solid at room temperature, it allows versatile applications in organic synthesis with an advantage of in situ generation of phosgene in the solution. However, recently, Cotarca and co-workers have reported that BTC is also a highly toxic compound, and its vapor pressure is sufficiently high to be the toxic concentrations.[5a] It was also reported that BTC is indeed unstable in the presence of metal ion, charcoal, or nucleophiles.[5b] With these reasons, they claimed strict safety control of BTC like



Scheme 1.2 Synthetic reactions of phosgene.

phosgene.

Trichloromethyl chloroformate (TCF) so called diphosgene is a dense liquid at room temperature. It decomposes with a catalyst, such as activated charcoal or iron oxide, to give 2 equiv. amounts of phosgene (Scheme1.2, reaction **III**).[6] It also has an advantage of in situ generation of phosgene in the solution, and allows its applications to a variety of the phosgenation reactions. There are some reports to find different reactivities of TCF and phosgene in organic synthesis. Kurita and co-workers reported that TCF reacts with alkyl amino acids to give isocyanato acid chloride (O=C=NRCOCl) without addition of any other reagent, while phosgene needs an additional reagent, such as hydrogen chloride, thionyl chloride, or phosphorus pentachloride, to complete the reaction.[7] Although TCF has been utilized in many phosgenation reactions as a phosgene substitute, it is also a highly toxic compound that originally developed in chemical warfare of World War I.[6a] Hence, the chemical reactions with TCF must be performed at safe conditions as similar in the cases with phosgene.[6b]

Furthermore, there are many reports to show the characteristic higher reactivity of phosgene in comparison with BTC and TCF. For example, Pasquato and co-workers carried out substitution reactions of methanol to phosgene, BTC, and TCF, and found that the reaction with phosgene was extremely faster than that of BTC and TCF.[8] As shown in this example, phosgene, though having high toxicity, still has many advantages in terms of its high reactivity, high yield, simple easy post-processing, and low cost in organic synthesis. Consequently, innovative safe phosgenation reactions, which allow the in situ generation and immediate consumption of the generated phosgene, provide valuable reactions and related techniques in organic chemistry.[9] It can be expected that such reactions allow development of pseudo-phosgeneation reactions, which does not generate phosgene outside reaction system.

1.2 Photo-on-demand in situ generation of phosgene from chloroform

Chloroform ($CHCl_3$) is a widely used commercially available solvent in both laboratories and industries, and it is well known that it undergoes oxidative decomposition to give phosgene.[10]

The reaction of $CHCl_3$ with oxidative reagents has been investigated long years ago. In 1869, Emmerling and Lengyel reported a production method of phosgene from warmed chloroform with chromic acid mixture.[2a] They suggested a reaction scheme as follow:

$$2\,CHCl_3 + 3\,O \longrightarrow 2\,COCl_2 + H_2O + Cl_2$$

Although the reaction is too expensive in commercial purpose, it was a convenient method for supplying phosgene in laboratory scale experiments.[2a]

In addition to the reaction with an oxidative reagent, generation of phosgene from chloroform could be realized in a photochemical route. In 1848, Morson found that phosgene was generated from chloroform by irradiation of the sunlight under air.[11] In 1997, Oppenländer reported that a photooxidative decomposition of $CHCl_3$ with xenon excimer lamp (λ_{max} =172 nm) generates $COCl_2$, which was detected by IR spectroscopy.[12a] Later, Alapi and Dombi have reported the photolysis behaviors of chlorinated methanes in the presence of O_2 using a low-pressure mercury lamp as a light source.[12b] Their experimental results showed that the emission intensity at 184.9 nm of the low-pressure mercury lamp strongly contributes to the Cl–C bond cleavage of $CHCl_3$ to produce Cl radical. The generated $Cl^{\bullet}$ initiates the oxidative decomposition of $CHCl_3$ and finally affords $COCl_2$. With these knowledges, chloroform is expected to be a potential raw material of phosgene. However, such phenomena have not been noticed in organic synthesis. As a limited example, in 1966, Kawai obtained analytical

amounts of diphenyurea, when added aniline to a photo-decomposed $CHCl_3$ on the purpose of quantifying the generated $COCl_2$. [11c]

In 2012, Tsuda and co-workers (our group) reported the first example of using the photo-decomposed $CHCl_3$ containing $COCl_2$ to a variety of organic syntheses in practical scales (Scheme1.2, reaction **IV**).[13] Their reaction mechanism proposed for the oxidative photo-decomposition of $CHCl_3$ is shown in Scheme 1.3.[12b, 13a] They expected that $CHCl_3$ undergoes oxidative photo-decomposition through radical chain mechanism initiated by the C–Cl bond cleavage. In this reaction system, whole reactions were performed in a pseudo closed system (Figure 1.1), where the gaseous decomposed products generated from $CHCl_3$ were transferred to another vessel, containing a sample solution of substrate that reacts with $COCl_2$. With this system, a lot of chemicals, such as chlorinated organic compounds, HCl salts of amines, carbonates, polycarbonates,

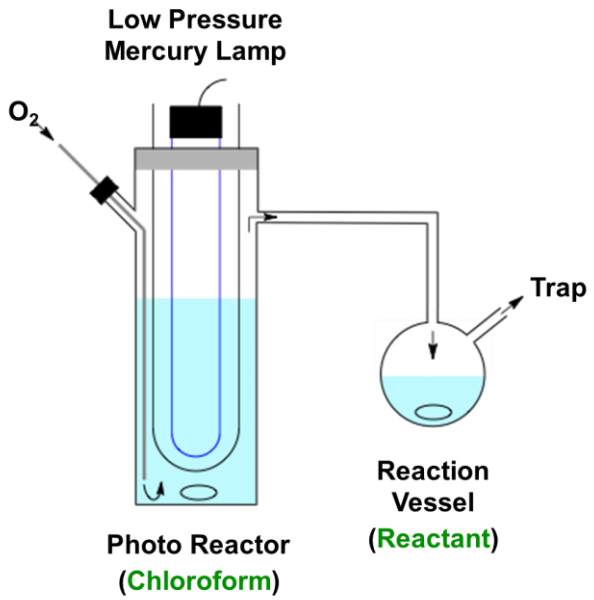
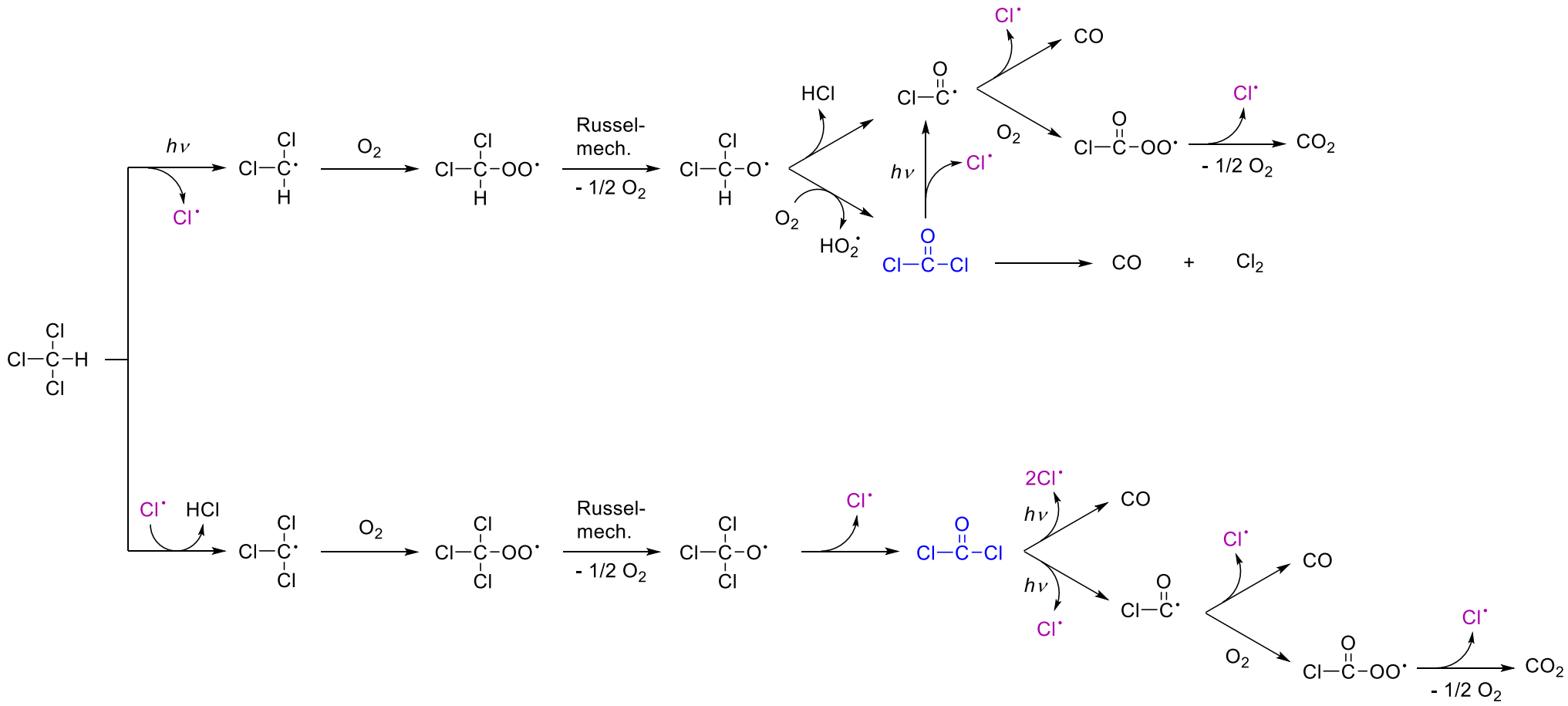


Figure 1.1 Schematic illustration of an experimental setup for photodecomposition of chloroform and for reactions of substrates with the photo-decomposed chloroform under flowing O_2.



Scheme 1.3 A possible reaction mechanism of oxidative photodecomposition of $CHCl_3$.

urea, were produced in practical high yields. This reaction system allowed the relatively safe phosgenation reactions in large scale with easy simple procedures. However, the transportation of the gaseous products, such as $COCl_2$, to another vessel provides the potential risk of the gas leakage. With this reason, the author has studied in this thesis a novel in situ photo-on-demand phosgenation reactions with a mixture solution of chloroform and reaction substrate with an expectation of no or less generation of phosgene from the reaction system.

1.3 Highlights and innovations of this work

In this thesis, novel photo-on-demand syntheses of chloroformate and Vilsmeier reagent have been developed.

Chapter 1 describes background and motivation of this study. Chapter 2 describes UV photo-on-demand in situ synthesis of chloroformate from a chloroform solution containing an alcohol. This photochemical reaction was discovered by the reevaluation of a general practice in chemistry using an alcohol as a stabilizer of chlorinated methanes. In this study, even in the presence of alcohol, $CHCl_3$ caused the oxidative photo-decomposition under exposure to UV light, resulting in the phosgenation reactions in situ. With an advantage of chloroform that serves as both reactant and solvent, a variety of the organic chemicals were synthesized through subsequent one-pot reactions.

Chapter 3 describes photo-on-demand in situ synthesis of Vilsmeier reagent (VR) with UV light from a chloroform solution containing *N*,*N*-dimethylformamide (DMF) or *N*,*N*-dimethylacetamide (DMA). The reactions provided VRs without notable side products in high yields, and their structures were characterized by single-crystal X-ray analysis. To the best of author′s knowledge, this is the first example of the crystallographic analysis of Vilsmeier reagent. This innovative reaction has many advantages for the synthesis and application of Vilsmeier reagent.

Chapter 4 describes in situ photo-on-demand synthesis of Vilsmeier reagent with visible light from a chloroform solution containing DMF and small amount of Cl_2 as a $Cl^{\bullet}$ resource. This reaction can greatly improve the practicality of the above photo-on-demand in situ synthesis of VR especially in industry.

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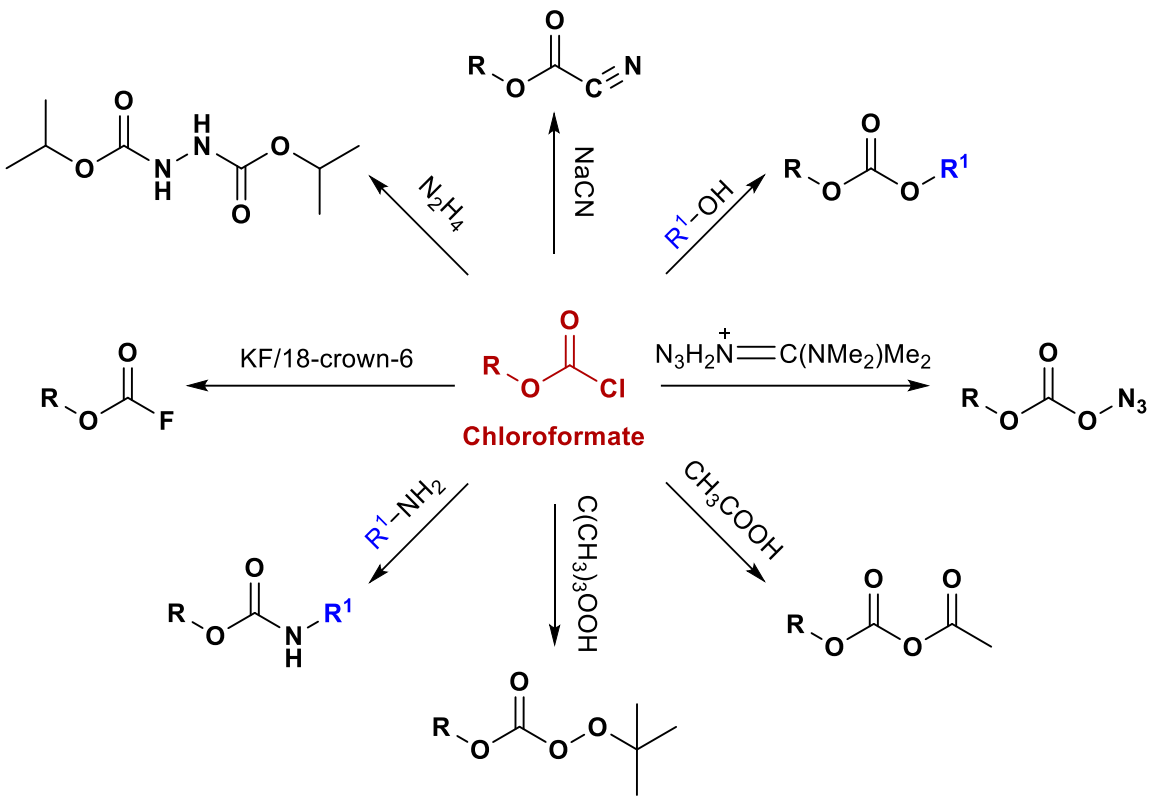
Chapter 2

Photo-on-Demand Synthesis of Chloroformates

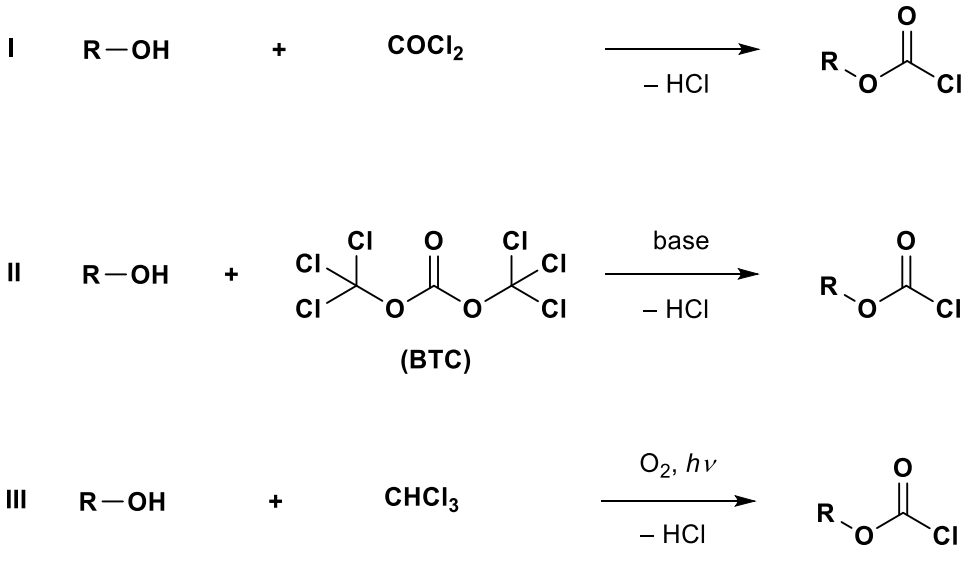
2.1 Introduction

Chloroformate, which plays important roles in organic synthesis (Scheme 2.1), is generally prepared from phosgene gas ($COCl_2$) and an alcohol (Scheme 2.2, reaction **I**).[1-6] Phosgene is a highly reactive C1 building block, but has high toxicity.[7] It is generally supplied by an on-demand production method that produces as much as needed when used in the synthesis. BTC, as a phosgene oligomer, allows in situ generation of phosgene in solution upon mixing with an organic base, and its subsequent rapid reaction with an alcohol gives the chloroformate (Scheme 2.2, reaction **II**).[8] However, as described in Chapter 1, it is also a toxic compound, and has to use in a strict safety-controlled condition.[9]

Recently, Tsuda and co-workers (our group) reported a photo-on-demand production of phosgene using only chloroform and O_2 gas.[10] This reaction allowed for syntheses of chloroformates in practical amounts with high yields through reaction of an alcohol with the photo-decomposed gas of chloroform (Scheme 2.2, reaction **III**). In that reaction system, the gas containing the produced phosgene must be transported from the photoreactor to another vessel that contains a solution of an alcohol (Chapter 1, Figure 1.1). Since the reaction has a potential risk of leakage, the author expected higher practical advantages for possible in situ photo-on-demand phosgenation reactions of alcohols with chloroform.



Scheme 2.1 Chemical reactions of chloroformates.



Scheme 2.2 Synthesis of chloroformate from alcohol with phosgene, triphosgene or chloroform.

It is known that an alcohol can be used as a stabilizer to prevent the decomposition of chloroform. In fact, commercially available chloroform contains 0.3 to 1.0% ethanol as a stabilizer.[11] Ethanol probably acts as a scavenger in the photo-decomposition of chloroform which proceeds through a radical mechanism, and further, it can remove small amount of the generated phosgene by formation of the chloroformate.[11b,11e,11f] For this reason, in the previous study, synthetic experiments were carried out by separating the photoreaction unit and the reaction vessel that were utilized in the photo-decomposition of chloroform and the chemical reaction of the generated gas with the substrate, respectively.[10] However, it is found herein that chloroformate is produced in situ with high yield upon photo-irradiation of a chloroform solution containing an alcohol with a low-

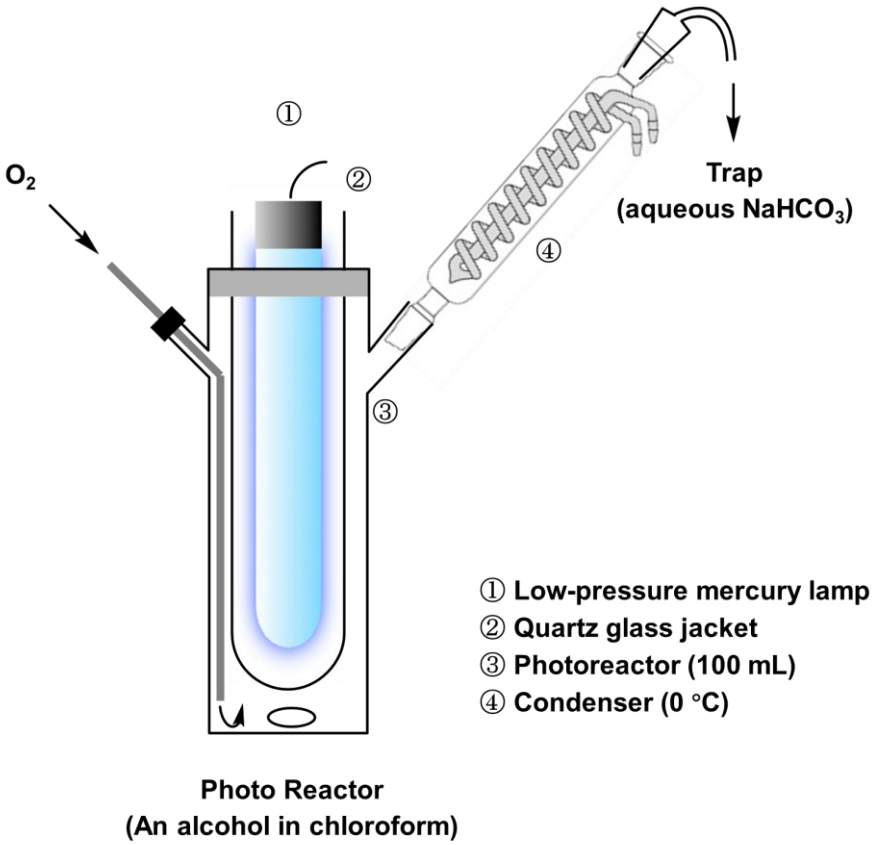


Figure 2.1 Schematic illustration of an experimental setup for photo-on-demand synthesis of chloroformate with a chloroform solution containing an alcohol.

pressure mercury lamp under O_2 bubbling (Figure 2.1).[12] It further allows one-pot chemical conversion of the resulting chloroformate to carbonates and carbamates.

2.2 Results and discussion

Photo-on-demand synthesis of chloroformates.

Low-pressure mercury lamps, which generally have low electric power consumption, mainly generate UV light with wavelengths of 184.9 and 253.7 nm, which cover electronic absorption bands of $CHCl_3$ due to σ–σ* and/or n–σ* transitions (Figure 2.2).[12,13] The lamp (20 W, ø24 mm × 120 mm), whose illuminance at 254 nm is 6.2–9.0 mW/cm^2 at 5 mm from the lamp, was inserted into the solution via a quartz glass jacket (ø28 mm) fixed in the center of a cylindrical flask (ø42 mm) (Figure 2.1).[10,12,14] Photochemical reactions were

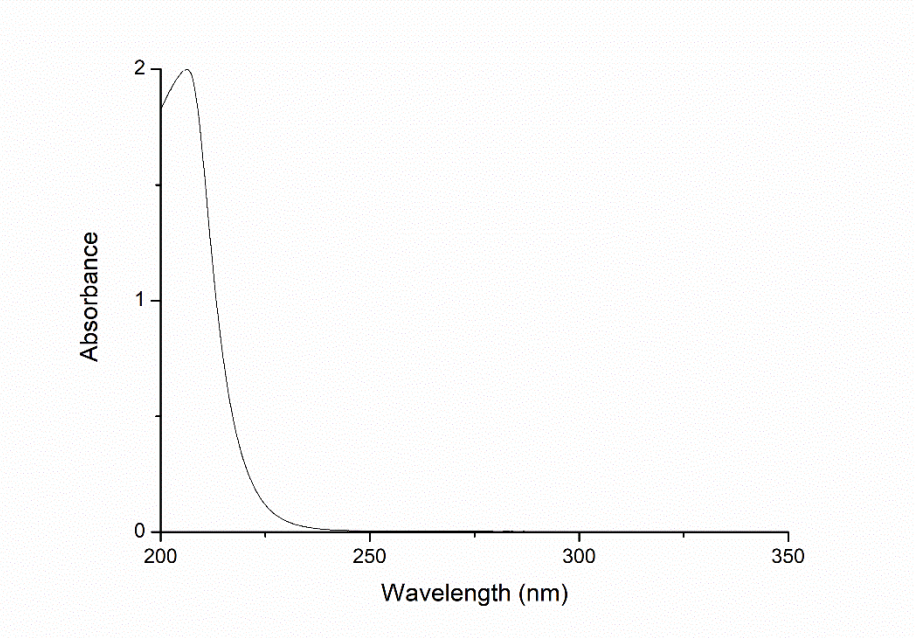
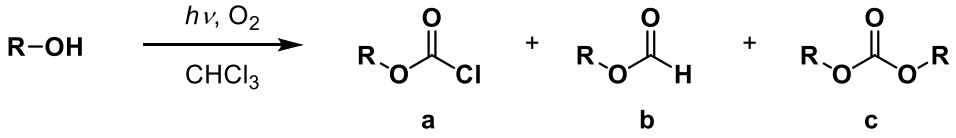


Figure 2.2 UV-Vis spectrum of $CHCl_3$ (λ_{max} = 206.4 nm) with the concentration of 4.33 × 10^{-2} M in CH_3CN at 293 K.

conducted with this reaction system under a steady flow of O_2 (25–50 mL/min) bubbled through 20 mL (250 mmol) of $CHCl_3$ containing 5–40 mmol of alcohol upon strong stirring of the sample solution at variable temperature. The reactions are demonstrated in a closed system, but the unreacted photo-decomposed gas from the system must be trapped outside with water containing a base such as $NaHCO_3$.

With this system, a $CHCl_3$ solution containing 20 mmol of EtOH was exposed to UV light at 30 °C (Table 2.1). The reaction, monitored by ^1H NMR spectroscopy, was completed in 2.5 h to give the corresponding chloroformate, formate, and carbonate in 51%, 3%, and 4% yields, respectively, without recovery (Table 2.1, entry 1). Elongation of the reaction time, however, led to a decrease of the product yield probably due to its photo-decomposition. When the reaction was performed with MeOH, the yield of the product also decreased dramatically without recovery (entry 2). It is expected that methyl chloroformate possibly produced is unstable under UV light, and its low boiling point also encourages vaporization around the lamp that generates both light and heat. In support of this hypothesis, the yield of the chloroformate increased to 60% with 1-propanol (entry 3). However, 2-propanol, a secondary alcohol, provided only the corresponding chloroformate and formate in 1% and 2% yields, respectively, without recovery, likely due to its low reactivity compared with 1-propanol and the photo-decomposition and thermal decomposition of the product (entry 4). No reactions were observed with phenol which has lower nucleophilicity compared with the primary alkyl alcohols. *tert*-Butyl alcohol, with a sterically crowded structure, also showed no reaction. This may due to its low reactivity and thermal decomposition of the corresponding chloroformate.[15] The yield of chloroformate increased to 73% with *n*-butanol (entry 5). The reactions also proceeded even with double the amount of alcohol (40 mmol, 3.0 g) and at lower temperature to give the chloroformate in 83% and 82% yields, respectively (entry 6 and 7, respectively). However, the reaction

Table 2.1 Photochemical synthesis of chloroformates with $CHCl_3$ solutions containing an alchohol.



entry	R−OH	amount (mmol)	temp. (°C)	time (h)	yield (%) [a]		
					a	**b**	**c**
1	CH_3CH_2OH	20	30	2.5	51	3	4
2	CH_3OH	20	30	6.5	7	2	-
3	$CH_3(CH_2)_2OH$	20	30	3.0	60	2	1
4	$(CH_3)_2CHOH$	10	30	2.0	1	2	-
5	$CH_3(CH_2)_3OH$	20	30	4.0	73	10	-
6	$CH_3(CH_2)_3OH$	40	30	7.0	83	1	-
7	$CH_3(CH_2)_3OH$	20	10	6.0	82	0.5	-
8	$CH_3(CH_2)_3OH$	20	50	5.0	7	7	-
9	$CH_3(CH_2)_5OH$	20	30	5.0	93	1	-
10	$H_3C(OCH_2CH_2)_3OH$	50	20	3.0	56	38	-
11	$H_3C(OCH_2CH_2)_3OH$	50	0	3.0	89	9	-

[a] Entries 1-9: ^1H NMR yields; entry 10: isolated yield.

decelerated dramatically at the higher temperature of 50 °C, which may accelerate vaporization of phosgene generated in $CHCl_3$ (entry 8). The highest yield of 93% was attained with 1-hexanol (entry 9). The photochemical reaction with triethylene glycol monomethyl ether (TEGM) at 20 °C also provided the

chloroformate in 56% yield but was accompanied by the formate in 38% yield (entry 10). Their ratio was dependent on the reaction temperature and changed to 89% and 9% when the reaction was performed at 0 °C (entry 11).

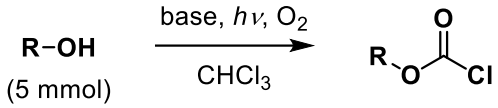
With respect to the mechanism of the reactions, it is expected that the chloroformate forms through the in situ reaction of the alcohol with phosgene generated through the oxidative photo-decomposition of chloroform. Further, as to the side products, the corresponding carbonate forms through the reaction of chloroformate with alcohol, while the formate ester may form through a radical reaction of photo-decomposed chloroformate generated upon breaking of the C–Cl bond with alcohol OH group. The latter formate ester was not produced in previous indirect method using the photo-decomposed gas of chloroform.[10]

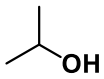
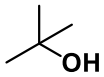
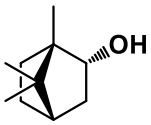
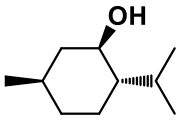
As to a related study, Hoggard and coworkers also reported a photochemical synthesis of chloroformate, where Amberlite IRA-900 in the chloride form, an anion exchange resin, catalyzes the photolysis of carbon tetrachloride in alcohol under exposure to visible and near-UV light to produce a mixture of corresponding dialkyl carbonate and alkyl chloroformate in 15% yield.[16] The above reaction developed in the present study is a more convenient method that allows gram-scale synthesis in practical high yield with a simple reaction system.

Photo-on-demand synthesis of chloroformates with base catalysts.

Organic bases, such as pyridine, triethylamine (TEA) and 4-dimethyl aminopyridine (DMAP), are generally used as a catalyst and a HCl scavenger in nucleophilic substitution reactions of alcohols.[17] Effects of the organic catalysts were further investigated in the photo-on-demand synthesis of chloroformate (Table 2.2). 2-Propanol provided the corresponding chloroformate only in 1% yield in the above photochemical reaction (Table 2.1, entry 4). However, when

Table 2.2 Photochemical synthesis of chloroformates with $CHCl_3$ solutions containing an alcohol and an organic base as a catalyst.



entry	R−OH	base	temp. (°C)	time (h)	^{1}H NMR yield (%)
1		pyridine (1 mmol)	0	6.0	52%
2		DMAP (2.5 mmol)	-15	5.0	70%[a]
3		pyridine (1 mmol)	30	2.0	89%
4		pyridine (2.5 mmol)	10	4.5	85%

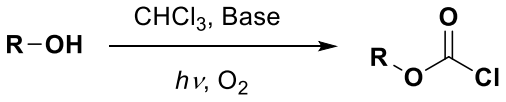
[a] The yield was estimated by its direct conversion to amide through the reaction with cyclohexylamine.

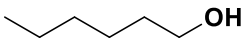
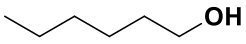
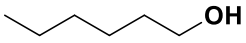
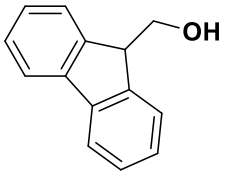
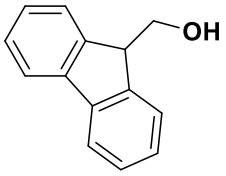
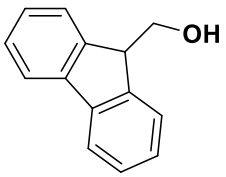
irradiated the UV light to a $CHCl_3$ solution containing a mixture of 2-propanol and catalytic 0.2 equiv. amount of pyridine, 2-propyl chloroformate was obtained in 52% yield (Table 2.2, entry 1). Then, *tert*-butanol, having sterically more crowded structure, was demonstrated. The photoreaction was performed at relatively low temperature, since the expected product *tert*-butyl chloroformate is thermally unstable.[15] In the presence of 0.5 equiv. DMAP, a stronger base than pyridine, *tert*-butyl chloroformate was produced in >70% yield (entry 2), while no reaction

was observed with pyridine at the same reaction conditions. (–)-Borneol, a sterically congested cyclic aliphatic alcohol, is a medicinally important compound.[18] When its chloroform solution without base was exposed to UV light at 30 °C, the corresponding chloroformate was obtained in 32% yield. However, in the presence of 0.2 equiv. amount of pyridine, the product yield was dramatically increased to 89% (entry 3). Although (–)-menthol, a natural chiral alcohol,[19] was less reactive without base, it provided corresponding chloroformate in 85% yield using 0.5 equiv. amount of pyridine, (entry 4).

Since the oxidative photo-decomposition of $CHCl_3$ generates HCl gas, which then protonates organic base, the author expected contribution of HCl salt of the base in the above reactions. Actually, there are some reports that use the HCl salt of amine as a catalyst in organic synthesis.[20] The author found herein that HCl salt of pyridine also accelerates formation of the chloroformate. Although 1-hexanol provided the corresponding chloroformate in 90% yield at 3 h without an additive (Table 2.3, entry 1), interestingly, the reaction was completed at shorter 2 h to provide the product in quantitative yield in the presence of only 0.03 equiv. amount of pyridine hydrochloride (entry 2). This result is same in the case with pyridine (entry 3). Although the observed acceleration mechanism is not clear at this stage, it is expected that the HCl salt of pyridine contributes as an acid or base catalyst of the reaction. Then, a remarkable effect with HCl salt of pyridine was observed in the reaction with 9H-fluorenylmethanol. A reaction without the salt provided the corresponding chloroformate in 40% yield after 3 h reaction (entry 4). However, addition of 0.1 equiv. amount of pyridine or the HCl salt of pyridine accelerated to complete the reaction only for 50 min with increasing the yield to ~83% (entries 5 and 6).

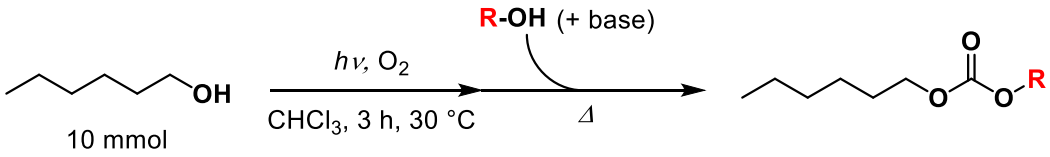
Table 2.3 Effects of pyridine and HCl salt of pyridine for the photochemical syntheses of chloroformates with $CHCl_3$ solutions containing an alcohol.

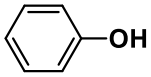
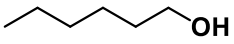
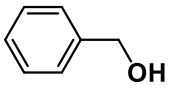
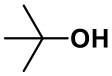
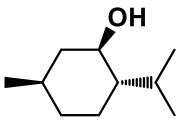
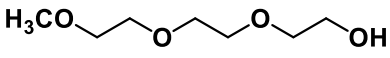


entry	R−OH	Temp. (°C)	Time (h)	Base	HCl Salt	^{1}H NMR Yield (%)
1	 (10 mmol)	30	3.0	-	-	90
2	 (10 mmol)	30	2.0	-	pyridine·HCl (0.3 mmol) (0.03 eq.)	99
3	 (10 mmol)	30	2.0	pyridine (0.3 mmol) (0.03 eq.)	-	99
4	 (5 mmol)	30	3.0	-	-	40
5	 (5 mmol)	30	0.8	pyridine (0.5 mmol) (0.1 eq.)	-	83
6	 (5 mmol)	30	0.8	-	pyridine·HCl (0.5 mmol) (0.1 eq.)	82

Next, with an advantage of using chloroform, which bifunctionally serves as reactant and solvent, one-pot syntheses of carbonates were demonstrated (Table

Table 2.4 One-pot syntheses of carbonates via photo-on-demand synthesis of a chloroformate.

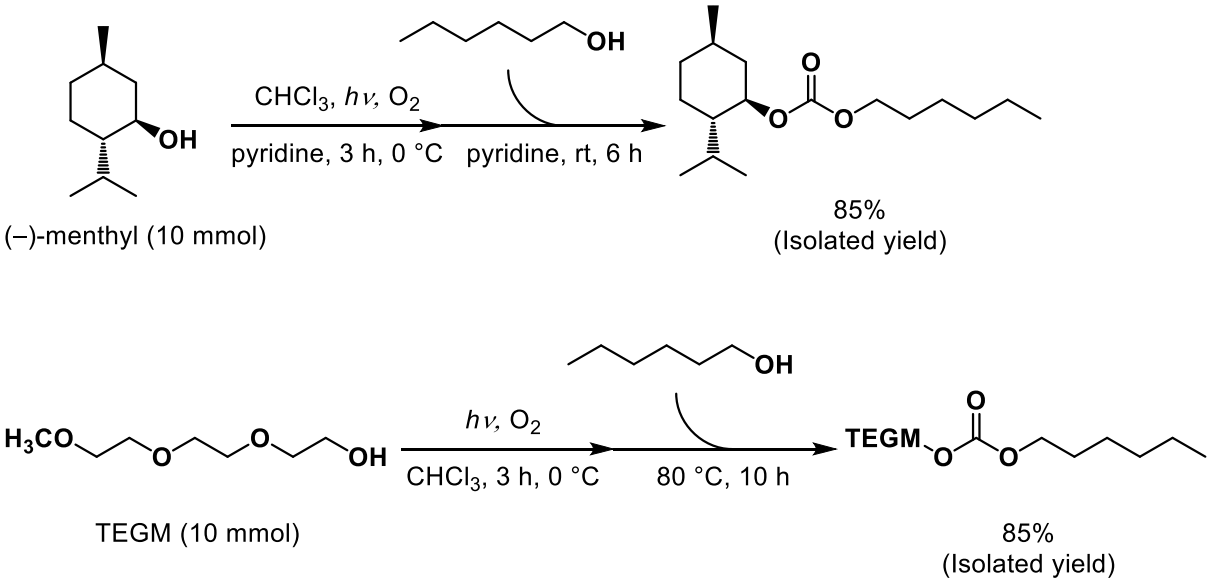


entry	R–OH	amount (eq.)	base (eq.)	temp. (°C)	time (h)	yield (%)
1		1.0	TEA (3.0)	r.t	1	56 [a]
2		1.5	-	90	15	95 [b]
3		1.5	-	90	20	87 [b]
4		3.0	Pyridine (1.0)	70	1	60 [b]
5		2.0	Pyridine (1.0)	70	1	4 [b]
6		1.2	-	130	10	54 [b]
7		1.5	-	90	14	50 [a]

[a] Isolated yield, [b] ^{1}H NMR yield.

2.4). The chloroformate was initially prepared in the $CHCl_3$ solution. The lamp was then turned off, and the sample was stirred at 30–70 °C for 1–3 h to remove

the remaining photo-decomposed products such as phosgene and HCl from the system. Then, an equimolar amount of phenol, for example, with 3 equiv. TEA was added into the sample solution to give the corresponding asymmetric hexyl phenyl carbonate in 56% isolated yield (Table 2.4, entry 1). Alkyl alcohols, whose OH groups have relatively higher nucleophilicity than that of phenol, allowed substitution reactions with chloroformate without base. When 1.5 equiv. of 1-hexanol was added into the chloroform solution containing hexyl chloroformate, the corresponding carbonate was obtained in 95% isolated yield after heating of the sample solution at 90 °C for 15 h (entry 2), but the reaction did not proceed at room temperature and 50 °C. With a similar procedure, benzyl alcohol provided the asymmetric carbonate in 87% yield (entry 3). 2-Propanol did not react without base, but the corresponding asymmetric carbonate was obtained in 60% yield upon addition of pyridine (entry 4). *tert*-Butanol, having a sterically crowded structure, provided the carbonate only in 4% yield, even when using an organic



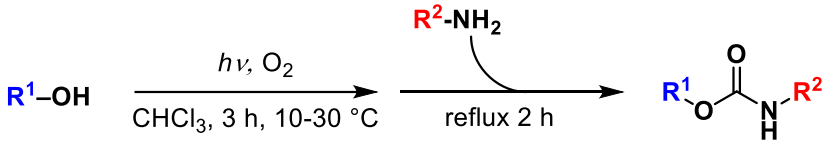
Scheme 2.3 Photo-on-demand synthesis of chloroformate and its subsequent one-pot synthesis of carbonate.

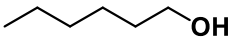
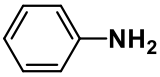
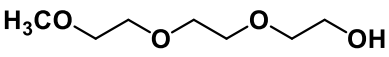
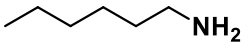
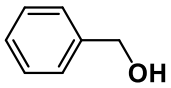
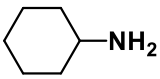
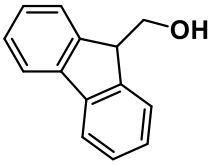
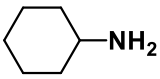
base catalyst (Table 2.4, entry 5). (–)-Menthol, a cyclic secondary alcohol, allowed the reaction at high temperature to give the corresponding asymmetric carbonate in 54% yield (entry 6). This carbonate could also be synthesized through opposite direction from (–)-menthyl chloroformate that prepared in Table 2.2 (entry 4) and 1-hexanol in 85% ^{1}H NMR yield (Scheme 2.3).

Surfactant molecules containing carbonate groups generally undergo biodegradation without generation of an acid in hydrolyzation.[21] Using 1-hexanol as the starting alcohol, an amphiphilic carbonate could be synthesized through the photochemical one-pot synthesis with TEGM in 50% yield (Table 2.4, entry 7). It is a nonionic surfactant molecule, and was also synthesized from TEGM (Scheme 2.3).

One of the most important uses of chloroformates is the introduction of *N*-protecting groups to amines.[3-5,22] For the next application, the one-pot synthesis of carbamates was demonstrated (Table 2.5). 1-Hexanol was photochemically converted to the corresponding chloroformate in $CHCl_3$, and then 1.2 equiv. amount of aniline was added to the sample solution. Substitution of the aniline with elimination of HCl occurred without base under reflux to give the carbamate in 70% yield (Table 2.5, entry 1). Using similar procedures, an amphiphilic carbamate was also synthesized without base starting from TEGM in 56% yield (entry 2). With respect to the mechanism, the molar equivalents of the added amine with respect to the chloroformate indicate that the HCl salt of the amine still allows for the nucleophilic substitution to chloroformate. This proposed mechanism is also supported by the reference in conventional synthesis of isocyanate with the HCl salt of amine and phosgene or phosgene oligomers at high temperature.[20b,20e] Finally, Cbz- and Fmoc- protections of an amine with this one-pot procedure were demonstrated. Benzyl alcohol and 9-fluorenemethanol, even though having strong absorption at UV region (Figure 2.3),

Table 2.5 One-pot syntheses of carbamates via photo-on-demand synthesis of a chloroformate.



entry	R^1–OH	R^2–NH_2 (eq.)	yield (%)
1		 (1.2)	70 [b]
2		 (1.2)	56 [a]
3		 (3.0)	76 [b]
4		 (6.0)	40 [b]

[a] Isolated yield, [b] ^{1}H NMR yield.

were photochemically converted to the chloroformates in $CHCl_3$. Since their chloroformates underwent thermal decomposition at relatively high temperature, addition of excess amounts of cyclohexylamine allowed the rapid reactions to give the corresponding carbamates in 76% and 40% yields, respectively (entries 3 and 4). The yield of the latter reaction is relatively low and highly dependent on the conditions probably due to the low solubility of 9-fluorenemethanol in $CHCl_3$.

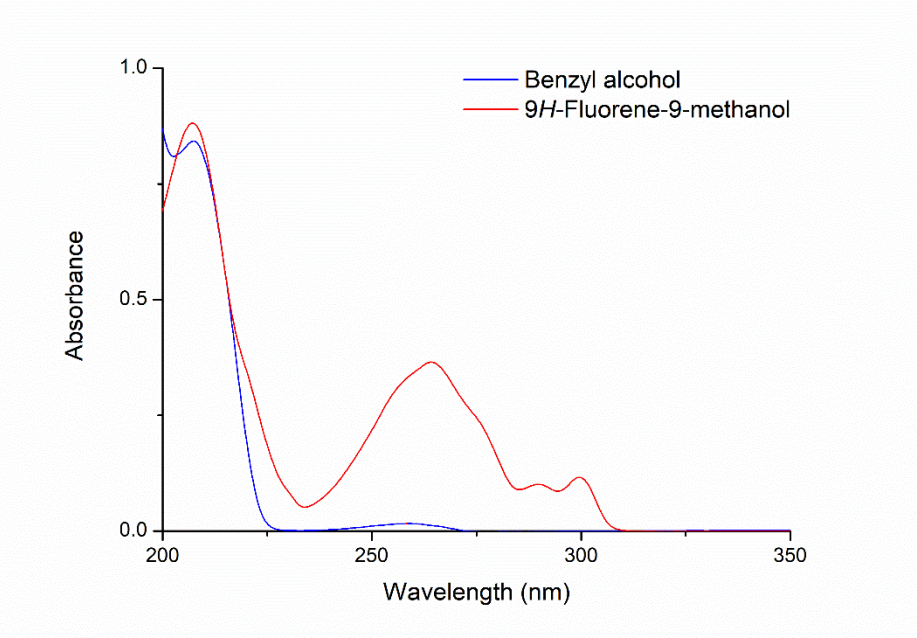
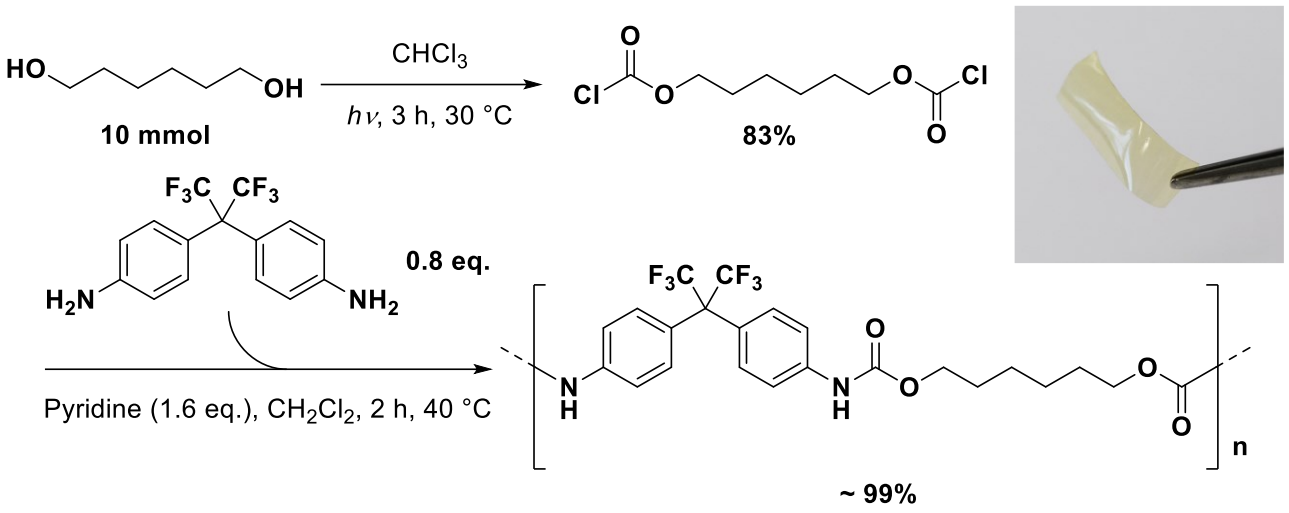


Figure 2.3 UV-Vis spectra of benzyl alcohol (λ_{max} = 207.6 and 258.6 nm) and 9*H*-fluorene-9-methanol (λ_{max} = 207.4, 264.2, and 299.8 nm) with the concentration of 1.22 × 10^{-4} M and 2.04 × 10^{-5} M, respectively, in CH_3CN at 293 K.

A one-pot synthesis of polyurethane with a bischloroformate, as prepared through photo-on-demand phosgenation of a diol, and a diamine has been demonstrated as a next application (Scheme 2.4). A $CHCl_3$ solution containing 1,6-hexandiol exposed to the UV light under O_2 bubbling to give its corresponding chloroformate in 83% yield. It was then reacted with 2,2-bis(4-aminophenyl)hexafluoropropane at 40 °C to give the corresponding polyurethane in high yield with an average molecular weight (M_w) of 5700 having a polydispersity index of M_w/M_n = 1.1, estimated by GPC. The polymer dissolved in THF formed a light yellow transparent film with high elasticity after slow evaporation of the solvent. The fluorine-containing polyurethanes are expected to have unique characters such as high antifouling property, weather resistance, and water resistance.[23]



Scheme 2.4 One-pot synthesis of a polyurethane via photo-on-demand synthesis of a bischloroformate.

2.3 Conclusions

This chapter described a novel in situ UV photo-on-demand synthesis of chloroformates with chloroform solutions containing an alcohol, and its subsequent application to the one-pot syntheses of carbonates and carbamates. Chloroform bifunctionally serves as a solvent and a reactant in this reaction system. Compared with conventional methods that use phosgene gas directly or phosgene oligomers indirectly for synthesizing chloroformates, this method has many advantages for practical organic syntheses in terms of safety, simplicity, operation, and cost. It will be an innovative chemical reaction for a variety of phosgenation reactions in both laboratory and industry.

2.4 Experimental section

2.4.1. Materials

Unless otherwise noted, reagents and solvents were used as received from Kishida Chemical Co., Ltd. [dichloromethane (>98.0%) and methanol (>99.5%)], Nacalai Tesque, Inc. [aniline (>99.0%), triethylamine (98.0%), t-butyl alcohol (>99.0%), 1-propanol (>99.5%), benzyl alcohol (>99.0%), 2-chloropyridine (>98.0%), 1,8-diazabicyclo[5,4,0]undec-7-ene (>97.0%), 1,2-dichloroethane (≥99.5%)], Wako Pure Chemical Industries, Ltd. [Na_2SO_4 (99.0%), $NaHCO_3$ (99.5–100.3%), ethanol (99.5%), pyridine (99.5%), 1-butanol (>99.0%), phenol (>99.0%), 4-dimethyl aminopyridine (>99.0%), 4,4'-(Hexafluoroisopropylidene)dianiline (>97.0%)], Tokyo Chemical Industry Co., Ltd. (TCI) [chloroform (>99.5%), 1-hexanol (>98.0%), isopropyl alcohol (>99.5%), hexylamine (>99.0%), triethylene glycol monomethyl ether (>98.0%), (–)-borneol (>95.0%), (–)-menthol (>99.0%), 2,6-dichloropyridine (>97.0%), cyclohexyl amine (>99.0%), 9-fluorenylmethanol (>98.0%), 1,6-hexanediol (>97.0%)], and Cambridge Isotope Laboratories, Inc. [$CDCl_3$ (D, 99.8%), DMSO-d_6 (D, 99.8%)]. For column chromatography, Wakogel (60N, particle size 38–100 μm, silica gel, irregular) was used. All products were unambiguously characterized by means of ^{1}H NMR spectroscopy in reference to the previous studies and the Sigma-Aldrich FT-NMR Library (ver. 4.0.10).[3,22,24]

2.4.2. Measurements and Calculations

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE 400 spectrometer and Bruker AVANCE 500 spectrometer, respectively, where chemical shifts (δ in ppm) were determined with respect to tetramethylsilane as the internal standard. ^{1}H NMR yields were determined by using 1,2-dichloroethane or dichloromethane as internal standards. Fourier transform infrared spectroscopy (FT-IR) was recorded on a JASCO FT/IR 4200. Fourier transform mass spectrometry (FT-MS) was performed on a Thermo Fisher Scientific LTQ Orbitrap. UV-Vis spectra were recorded on a JASCO V-670

spectrophotometer. Analytical HPLC was performed at 20 °C on a TOHSOH TSKgel G3000HHR column using a JASCO Type PU-2089 plus quaternary gradient pump, equipped with JASCO Type MD-2018 photodiode array detector, with THF as eluent.

2.4.3. Synthesis

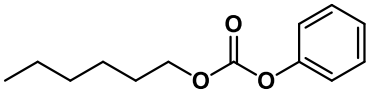
General.

Oxidative photo-decomposition of chloroform and its subsequent syntheses of carbonate and carbamate. A cylindrical flask (ø42 mm) equipped with a low-pressure mercury lamp (SEN Light Co., UVL20PH-6, 20 W, ø24×120 mm) was charged with a $CHCl_3$ solution. Heating of the sample solutions, if necessary, were performed with an aluminum block bath. The solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 0–50 °C for 2–7 h. The lamp was turned off, and the sample solution was stirred at 30–70 °C for 1–3 h. An alcohol (with or without a base) or an amine was then added to the sample solution, and the mixture was stirred for 1 h–overnight with or without heating of the sample solution.

In the case using a base, the resulting sample solution was washed with water and extracted with CH_2Cl_2 (20 mL×3). The organic layers were combined, dried over anhydrous Na_2SO_4, and evaporated to dryness. The corresponding carbonate or carbamate was obtained through vacuum distillation or silica gel column chromatography.

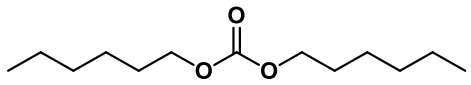
In the case without using a base, the corresponding carbonate was obtained through vacuum distillation of the resulting sample solution.

Synthesis of hexyl phenyl carbonate



Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Phenol (0.94 g, 10 mmol) and triethylamine (4.01 mL, 30 mmol) were then added to the flask, and the mixture solution was stirred at room temperature for 1 h. The sample solution was washed with water and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was subjected to a silica gel column chromatography with CH_2Cl_2 as an eluent to furnish hexyl phenyl carbonate as a colorless liquid in 56% yield (0.83 g, 5.6 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.38 (t, J = 8.0 Hz, 2H, CH_{Ar}), 7.24 (t, J = 8.4 Hz, 1H, CH_{Ar}), 7.18 (d, J = 7.6 Hz, 2H, CH_{Ar}), 4.25 (t, J = 6.8 Hz, 2H, CH_2), 1.78–1.71 (m, 2H, CH_2), 1.46–1.29 (m, 6H, CH_2), 0.91 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 153.8, 151.2, 129.4, 125.9, 121.1, 69.0, 31.4, 28.6, 25.4, 22.5, 14.0. IR (ATR): 3063, 2957, 2932, 2858, 1758, 1594, 1495, 1457, 1390, 1247, 1207, 1164, 1070, 1023, 946, 924, 903, 832, 804, 778, 731, 716, 704, 686 cm^{-1}. HRMS: m/z calculated for $C_{13}H_{18}O_3$+Na^+: 245.1148; $[M+Na]^+$ found 245.1147.

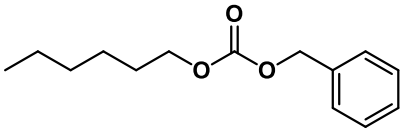
Synthesis of dihexyl carbonate



Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. 1-Hexanol (1.89 mL, 15 mmol) was then added to the flask, and the mixture solution was stirred at 90 °C for 15 h. Vacuum distillation of the resulting sample with a glass tube

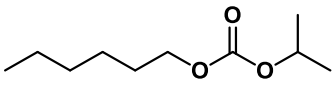
oven provided dihexyl carbonate as a colorless liquid in 56% yield (1.29 g, 5.6 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.12 (t, J = 6.4 Hz, 4H, CH_2), 1.70–1.63 (m, 4H, CH_2), 1.41–1.28 (m, 12H, CH_2), 0.89 (t, J = 6.8 Hz, 6H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 155.5, 68.0, 31.4, 28.7, 25.4, 22.5, 14.0. IR (ATR): 2957, 2930, 2860, 1744, 1468, 1402, 1252, 1064 cm^{-1}. HRMS: m/z calculated for $C_{13}H_{26}O_3$+H$^+$: 231.1966; [M+H]$^+$ found 231.1952.

Synthesis of benzyl hexyl carbonate



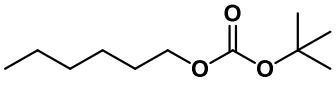
Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. Benzyl alcohol (1.55 mL, 15 mmol) was then added to the flask, and the mixture solution was stirred at 90 °C for 20 h. Vacuum distillation of the resulting sample with a glass tube oven provided benzyl hexyl carbonate as a colorless liquid in 74% yield (1.75 g, 7.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.40–7.33 (m, 5H, CH_{Ar}), 5.16(s, 1H, CH), 4.15 (t, J = 6.8 Hz, 2H, CH_2), 1.69–1.63 (m, 2H, CH_2), 1.38–1.28 (m, 6H, CH_2), 0.88 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 155.3, 135.4, 128.6, 128.5, 128.3, 69.5, 68.4, 31.4, 28.6, 25.4, 22.5, 14.0. IR (ATR): 2957, 2929, 2858, 1742, 1455, 1397, 1247, 1088, 1030, 970, 942, 908, 790, 753, 735, 696 cm^{-1}. HRMS: m/z calculated for $C_{14}H_{20}O_3$+H$^+$: 237.1496; [M+H]$^+$ found 237.1485.

Synthesis of hexyl isopropyl carbonate



Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. 2-Propanol (2.30 mL, 30 mmol) and pyridine (0.8 mL, 10 mmol) were then added to the flask, and the mixture solution was stirred at 70 °C for 1 h. The sample solution was washed with water and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. Vacuum distillation of the resulting sample with a glass tube oven provided hexyl isopropyl carbonate as a colorless liquid in 44% yield (0.83 g, 4.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.92–4.83 (m, 1H, CH), 4.11 (t, J = 6.8 Hz, 2H, CH_2), 1.70–1.62 (m, 2H, CH_2), 1.41–1.28 (m, 12H, CH_3 and CH_2), 0.89 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 154.8, 71.7, 68.0, 67.8, 31.4, 28.7, 25.4, 22.5, 21.8, 14.0. IR (ATR): 2958, 2933, 2861, 1739, 1468, 1388, 1257, 1182, 1094, 913, 792 cm^{-1}. HRMS: m/z calculated for $C_{10}H_{20}O_3$+H^+: 189.1496; $[M+H]^+$ found 189.1480.

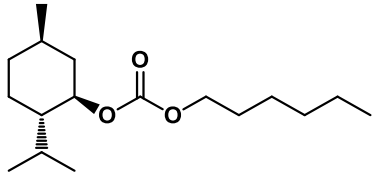
Synthesis of *tert*-butyl hexyl carbonate



Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. *tert*–Butanol (1.91 mL, 20 mmol) and pyridine (0.8 mL, 10 mmol) were then added to the flask, and the mixture solution was stirred at 70 °C for 1 h. The sample solution was washed

with water and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. Vacuum distillation of the resulting sample with a glass tube oven provided *tert*-butyl hexyl carbonate as a colorless liquid in 0.7% yield (0.14 g, 0.07 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.05 (t, J = 6.8 Hz, 2H, CH_2), 1.67–1.63 (m, 2H, CH_2), 1.49 (s, 9H, CH_3), 1.40–1.31 (m, 6H, CH_2), 0.89 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 153.7, 81.8, 67.2, 31.5, 28.7, 27.8, 25.5, 22.5, 14.0. IR (ATR): 2965, 2956, 2935, 2927, 1739, 1392, 1369, 1273, 1253, 1160, 1099, 874, 862 cm^{-1}. HRMS: m/z calculated for $C_{11}H_{22}O_3$+H$^+$: 203.1653; [M+H]$^+$ found 203.1637.

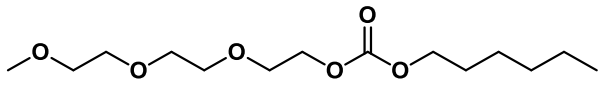
Synthesis of (–)-menthyl hexyl carbonate



Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. (–)-Menthol (1.87 g, 12 mmol) was then added to the flask, and the mixture solution was stirred at 130 °C for 10 h. Vacuum distillation of the resulting sample with a glass tube oven provided (–)-menthyl hexyl carbonate as a colorless liquid in 16% yield (0.46 g, 1.6 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.51 (td, J = 10.8, 4.4 Hz, 1H, CH), 4.12 (t, J = 6.8 Hz, 2H, CH_2), 2.09–2.04 (m, 1H, CH), 2.01–1.92 (m, 1H, CH), 1.70–1.27 (m, 12H), 1.10–0.89 (m, 12H), 0.79 (d, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 155.1, 78.1, 67.9, 47.0, 40.8, 34.1, 31.4, 28.7, 26.1, 25.4, 23.3, 22.5, 22.0, 20.7, 16.3, 14.0. IR (ATR): 2954, 2930, 2870, 1739, 1456, 1390, 1253, 1181, 981, 959 cm^{-1}. HRMS: m/z calculated for $C_{17}H_{32}O_3$+Na$^+$:

307.2244; $[M+Na]^+$ found 307.2271.

Synthesis of hexyl (2-(2-(2-methoxyethoxy)ethoxy)ethyl) carbonate

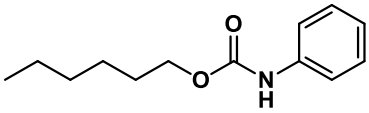


Method 1: Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. Triethylene glycol monomethyl ether (1.60 mL, 10 mmol) was then added to the flask, and the mixture solution was stirred at 90 °C for 13.5 h. Vacuum distillation of the resulting sample with a glass tube oven provided hexyl (2-(2-(2-methoxyethoxy)ethoxy)ethyl) carbonate as a colorless liquid in 50% yield (1.46 g, 5.0 mmol).

Method 2: Chloroform (20 mL, 250 mmol) and triethylene glycol monomethyl ether (1.60 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 0 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 60 °C for 2 h. 1-Hexanol (1.43 mL, 11.4 mmol) was then added to the flask, and the mixture solution was stirred at 80 °C for overnight. Vacuum distillation of the resulting sample with a glass tube oven provided hexyl (2-(2-(2-methoxyethoxy)ethoxy)ethyl) carbonate as a colorless liquid in 85% yield (2.50 g, 8.5 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.28 (t, J = 4.8 Hz, 2H, CH_2), 4.13 (t, J = 6.8 Hz, 2H, CH_2), 3.74–3.54 (m, 10H, CH_2), 3.38 (s, 3H, CH_3), 1.68–1.64 (m, 2H, CH_2), 1.39–1.29 (m, 6H, CH_2), 0.89 (t, J = 6.8 Hz, 3H, CH_3); ^{1}H NMR(400 MHz, D_2O, 293 K) : δ 4.19 (m, 2H, CH_2), 4.05 (t, J = 6.8 Hz, 2H, CH_2), 3.65 (m, 2H, CH_2), 3.58–3.54 (m, 6H, CH_2), 3.49–3.47 (m, 2H, CH_2), 3.24 (s, 3H, CH_3), 1.52 (m, 2H, CH_2), 1.26–1.12 (m, 6H, CH_2), 0.73 (t, J = 8.0 Hz, 3H, CH_3);

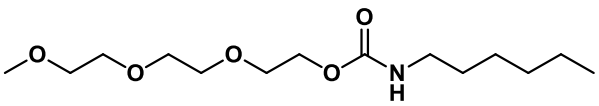
^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 155.3, 71.9, 70.6, 70.6, 70.7, 69.0, 68.3, 66.8, 59.0, 31.4, 28.6, 25.4, 22.5, 14.0. IR (ATR): 2954, 2926, 2872, 1743, 1457, 1399, 1254, 1102, 1027, 947, 877, 790 cm^{-1}. HRMS: m/z calculated for $C_{14}H_{28}O_6+H^+$: 293.1970; $[M+H]^+$ found 293.1965.

Synthesis of hexyl phenyl carbamate



Chloroform (20 mL, 250 mmol) and 1-hexanol (1.26 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. Aniline (1.09 mL, 12 mmol) was then added to the flask, and the mixture solution was stirred at 80 °C for 1.5 h. The sample solution was washed with water and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. Vacuum distillation of the resulting sample with a glass tube oven provided hexyl phenyl carbamate as a colorless liquid in 48% yield (1.06 g, 4.8 mmol). ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.39 (d, J = 7.6 Hz, 2H, CH_{Ar}), 7.30 (t, J = 6.4 Hz, 2H, CH_{Ar}), 7.06 (t, J = 7.2 Hz, 1H, CH_{Ar}), 6.59 (brs, 1H, NH), 4.16 (t, J = 6.8 Hz, 2H, CH_2), 1.70–1.63 (m, 2H, CH_2), 1.40–1.31 (m, 6H, CH_2), 0.90 (t, J = 6.8 Hz, 3H, CH_3). All ^1H NMR data are in agreement with the literature.[24]

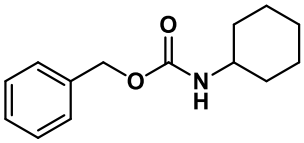
Synthesis of 2-(2-(2-methoxyethoxy)ethoxy)ethyl hexyl carbamate



Chloroform (20 mL, 250 mmol) and triethylene glycol monomethyl ether (1.60 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously

stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 20 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. Hexyl amine (1.59 mL, 12 mmol) was then added to the flask, and the mixture solution was stirred at 80 °C for 3 h. The sample solution was washed with water and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. Vacuum distillation of the resulting sample with a glass tube oven provided 2-(2-(2-methoxyethoxy)ethoxy)ethyl hexyl carbamate as a colorless liquid in 56% yield (1.63 g, 5.6 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.79 (brs, 1H, NH), 4.22 (t, J = 4.4 Hz, 2H, CH_2), 3.70–3.64 (m, 6H, CH_2), 3.57–3.54 (m, 2H, CH_2), 3.39 (s, 3H, CH_3), 3.16 (q, J = 6.8 Hz, 2H, CH_2), 1.51–1.44 (m, 2H, CH_2), 1.34–1.29 (m, 6H, CH_2), 0.88 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 156.4, 72.0, 70.6, 69.7, 63.8, 59.0, 41.0, 31.5, 29.9, 26.4, 22.6, 14.0. IR (ATR): 2954, 2926, 2872, 1743, 1457, 1399, 1254, 1102, 1027, 947, 877, 790 cm^{-1}. HRMS: m/z calculated for $C_{14}H_{29}NO_5$+H^+: 292.2129; $[M+H]^+$ found 292.2126.

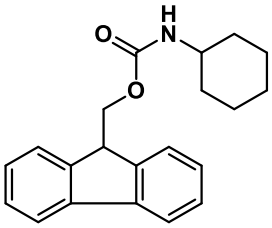
Synthesis of benzyl cyclohexyl carbamate



Chloroform (20 mL, 250 mmol) and benzyl alcohol (1.03 mL, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 20 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 1 h. Cyclohexylamine (3.43 ml, 30 mmol) was then added to the flask, and the mixture solution was stirred at 70 °C for 2 h. The sample solution was washed with water and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the

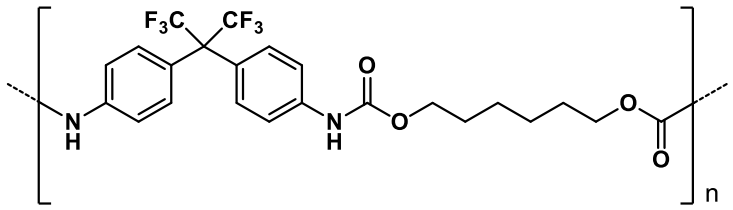
residue contains benzyl cyclohexyl carbamate in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.37–7.29 (m, 5H, CH_{Ar}), 5.08 (s, 2H, CH_2), 4.63 (s, 1H, NH), 3.54–3.47 (m, 1H, CH), 1.92 (d, *J* = 9.6 Hz, 2H, CH_2), 1.72–1.67 (m, 2H, CH_2), 1.63–1.57 (m, 2H, CH_2), 1.42–1.24 (m, 2H, CH_2), 1.22–1.08 (m, 2H, CH_2). All ^{1}H NMR data are in agreement with the literature.[22]

Synthesis of (9*H*-fluoren-9-yl)methyl cyclohexyl carbamate



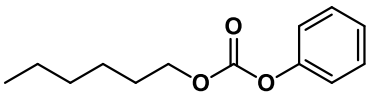
Chloroform (20 mL, 250 mmol), CH_3CN (10 mL, 192 mmol) and 9*H*-fluorenylmethanol (0.98 g, 5 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 20 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 3 h. Cyclohexylamine (1.72 ml, 15 mmol) was then added to the flask, and the mixture solution was stirred at 70 °C for 2 h. The sample solution was washed with water and extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4. ^{1}H NMR spectroscopy revealed that the resulting sample solution contains (9*H*-fluoren-9-yl)methyl cyclohexyl carbamate in 40% yield. It was then evaporated to leave a brown solid. It was washed with diethyl ether to afford (9*H*-fluoren-9-yl)methyl cyclohexyl carbamate as a white solid in 28% yield (0.45 g, 1.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.78 (d, *J* = 7.6 Hz, 2H, CH_{Ar}), 7.61(d, *J* = 7.2 Hz, 2H, CH_{Ar}), 7.40 (t, *J* = 7.2 Hz, 2H, CH_{Ar}), 7.32 (t, *J* = 7.2 Hz, 2H, CH_{Ar}), 4.63 (s, 1H, NH), 4.40 (d, *J* = 6.4 Hz, 2H, CH_2), 4.22 (t, *J* = 7.2 Hz, 1H, CH), 3.54–3.46 (m, 1H, CH), 1.97–1.93 (m, 2H, CH_2), 1.73–1.56 (m, 4H, CH_2), 1.41–1.10 (m, 4H, CH_2). All ^{1}H NMR data are in agreement with the literature.[3]

Synthesis of polyurethane



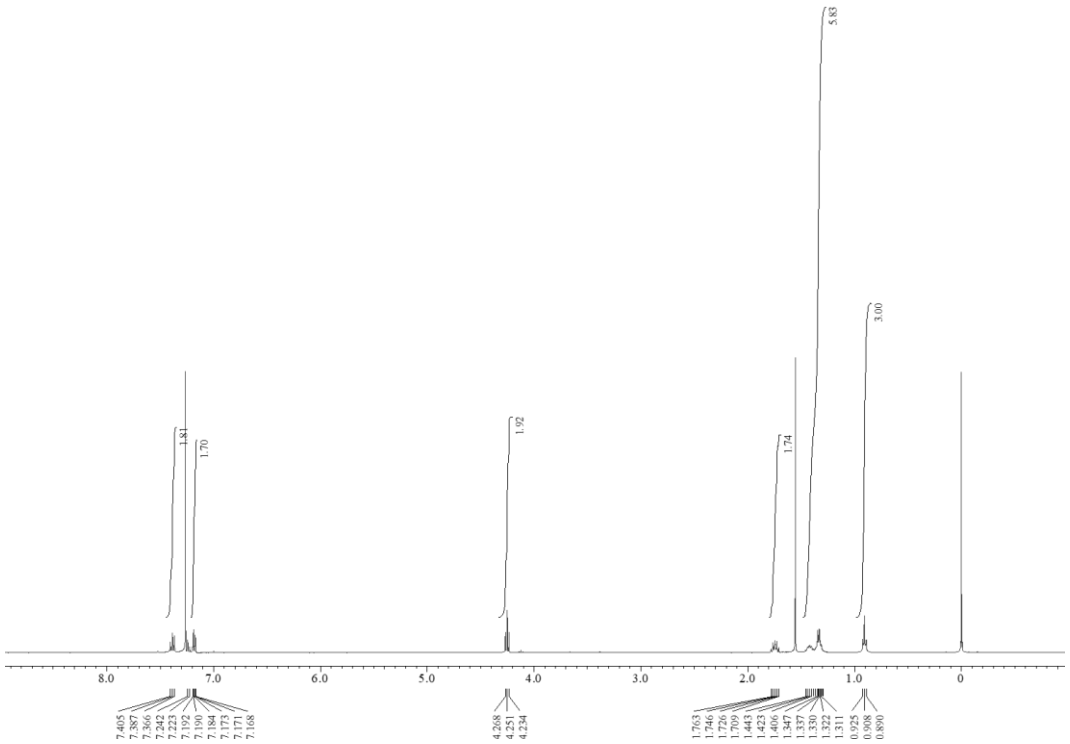
Chloroform (20 mL, 250 mmol) and 1,6-hexanediol (1.18 g, 10 mmol) were mixed in the cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (50 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 70 °C for 3 h. The resulting solution was added slowly to a 100 mL of CH_2Cl_2 solution containing 2,2-bis(4-aminophenyl)hexafluoropropane (2.67 g, 8 mmol). After then, pyridine (1.29 mL, 16 mmol) was added slowly, and the sample solution was refluxed for 2 h. The sample solution was evaporated to leave a pale yellow solid. It was washed with methanol to give the corresponding polyurethane in 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.85 (brs, 2H, NH), 7.54(d, J = 8.8 Hz, 4H, CH_{Ar}), 7.22 (d, J = 8.4 Hz, 4H, CH_{Ar}), 4.08 (t, J = 7.2 Hz, 4H, CH_2), 1.63 (brs, 4H, CH_2), 1.39 (brs, 4H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$, 293 K): δ 153.5, 140.0, 130.0, 125.6, 117.7, 64.2, 30.3, 28.3, 24.9. IR (ATR): 3304, 2950, 1706, 1600, 1524, 1418, 1331, 1204, 1171, 1068, 967, 929, 831, 769, 746, 736 cm^{-1}.

2.4.4. ^{1}H and ^{13}C NMR spectra of the compounds



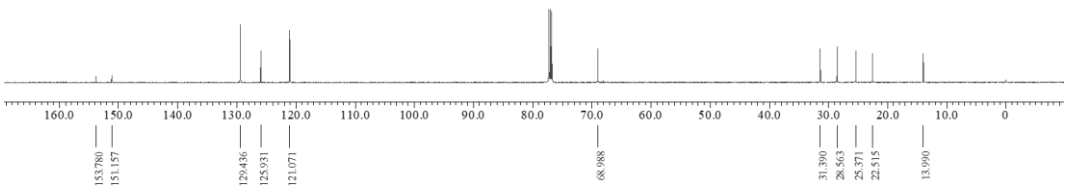
hexyl phenyl carbonate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

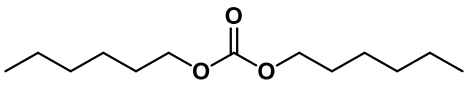


δ / ppm

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)

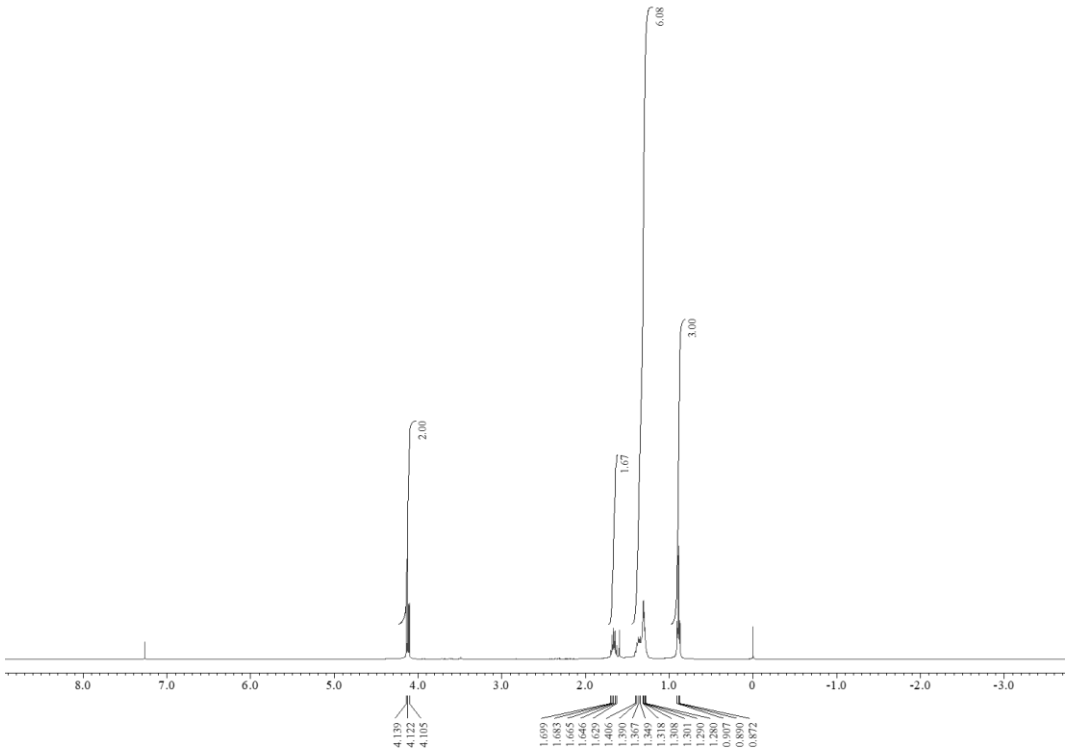


δ / ppm



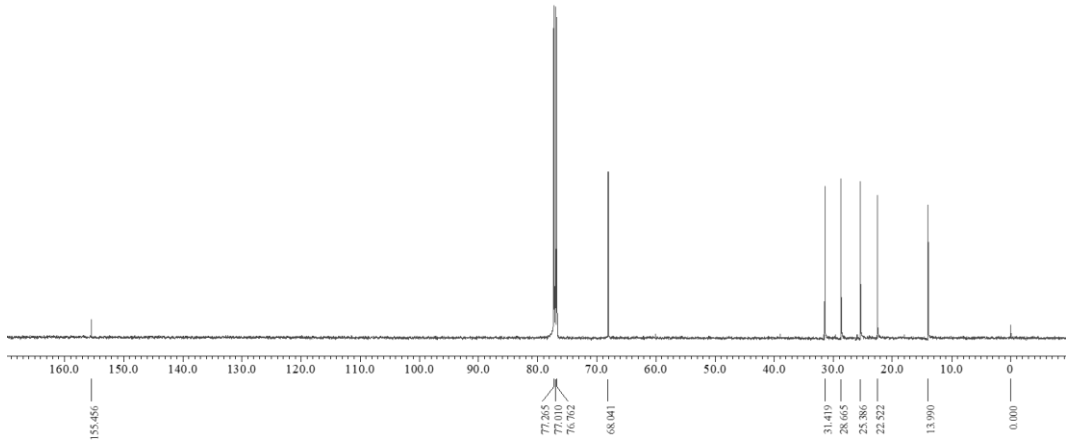
dihexyl carbonate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

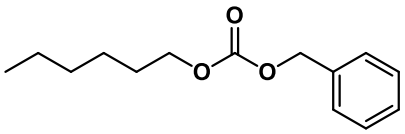


δ / ppm

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)

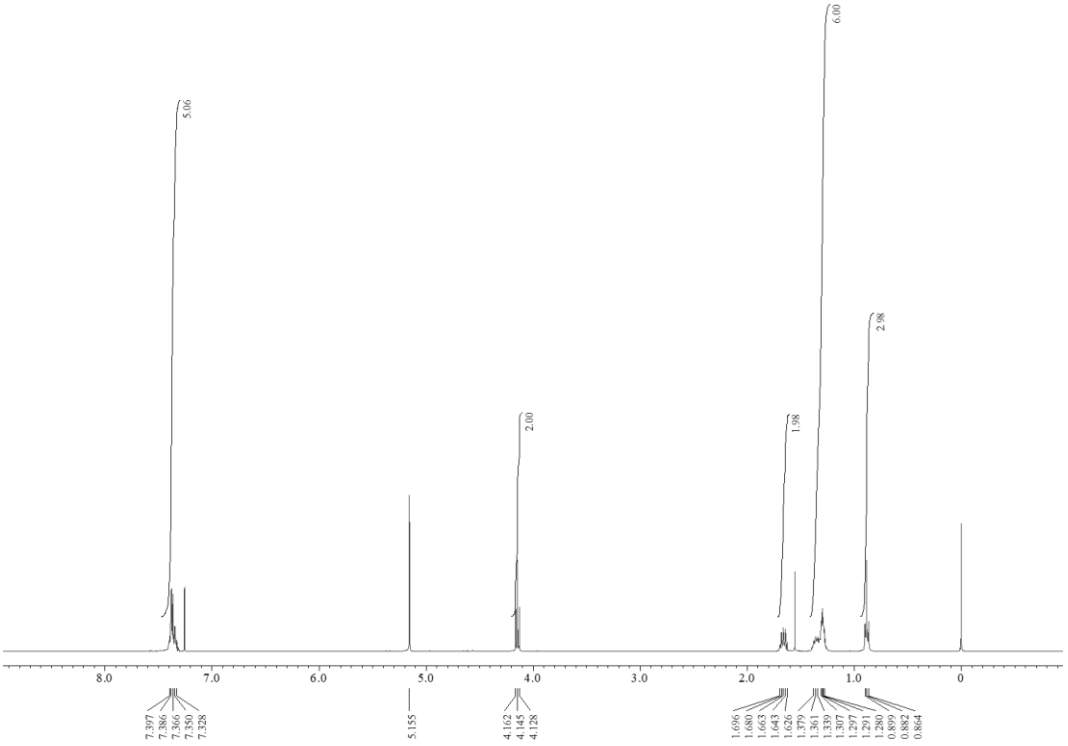


δ / ppm



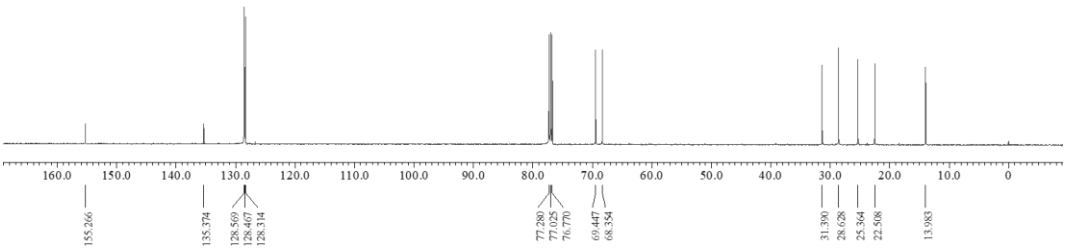
benzyl hexyl carbonate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

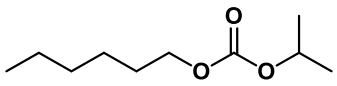


δ / ppm

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)

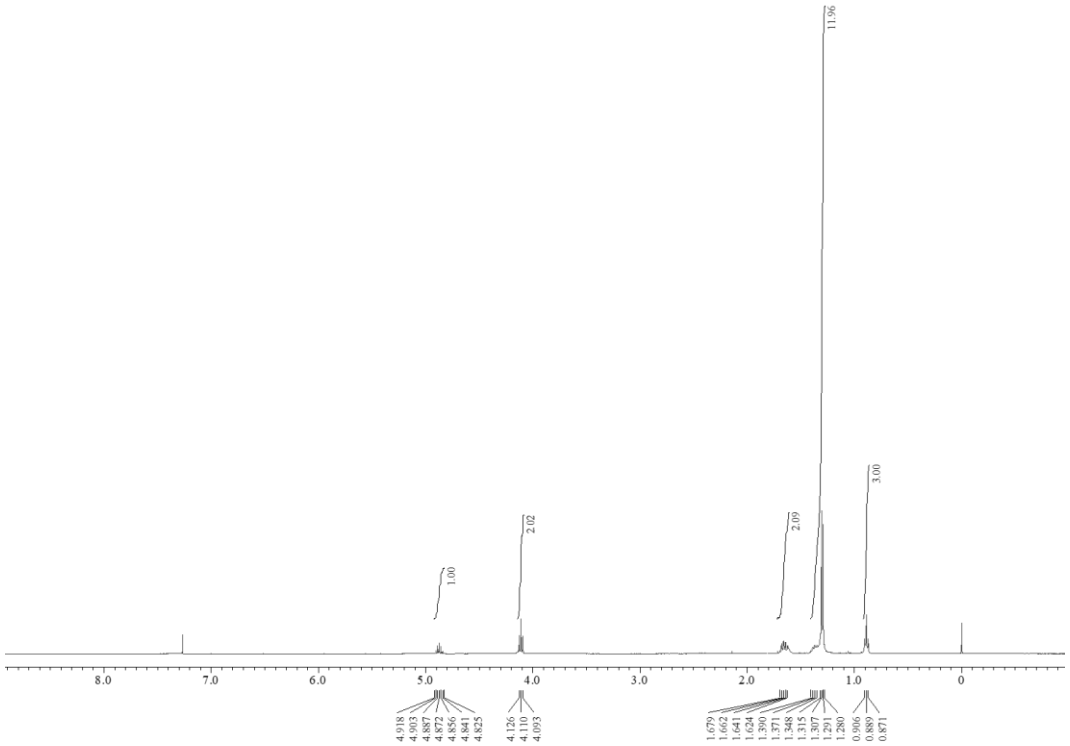


δ / ppm



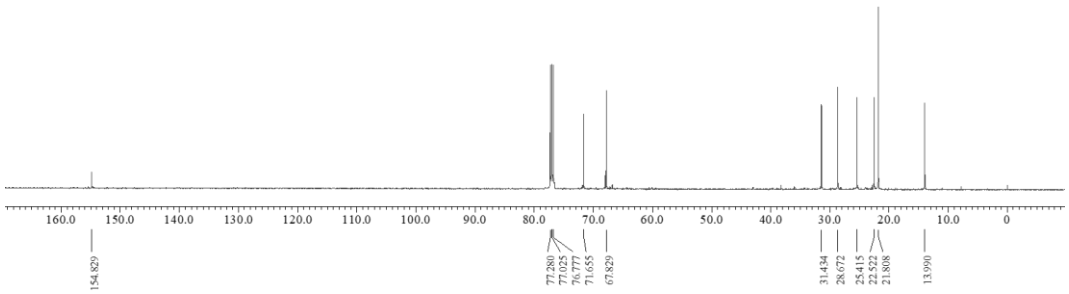
hexyl isopropyl carbonate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

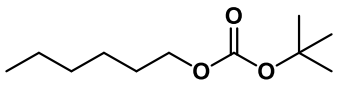


δ / ppm

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)

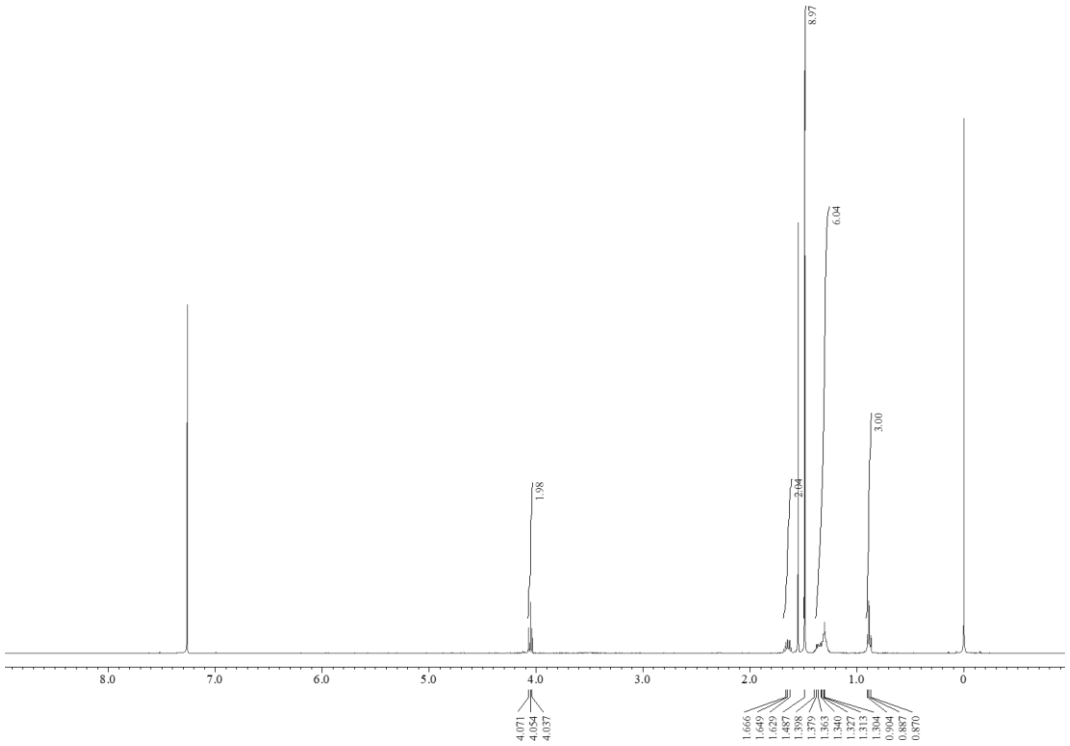


δ / ppm



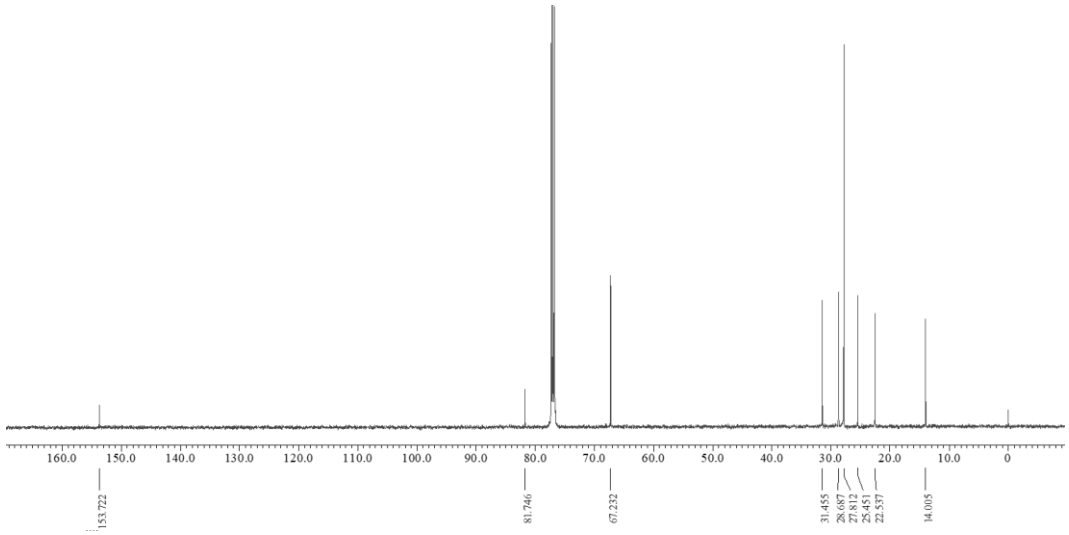
tert-butyl hexyl carbonate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

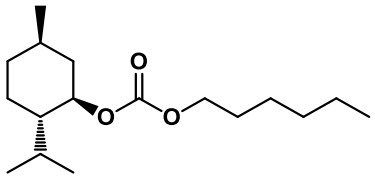


δ / ppm

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)

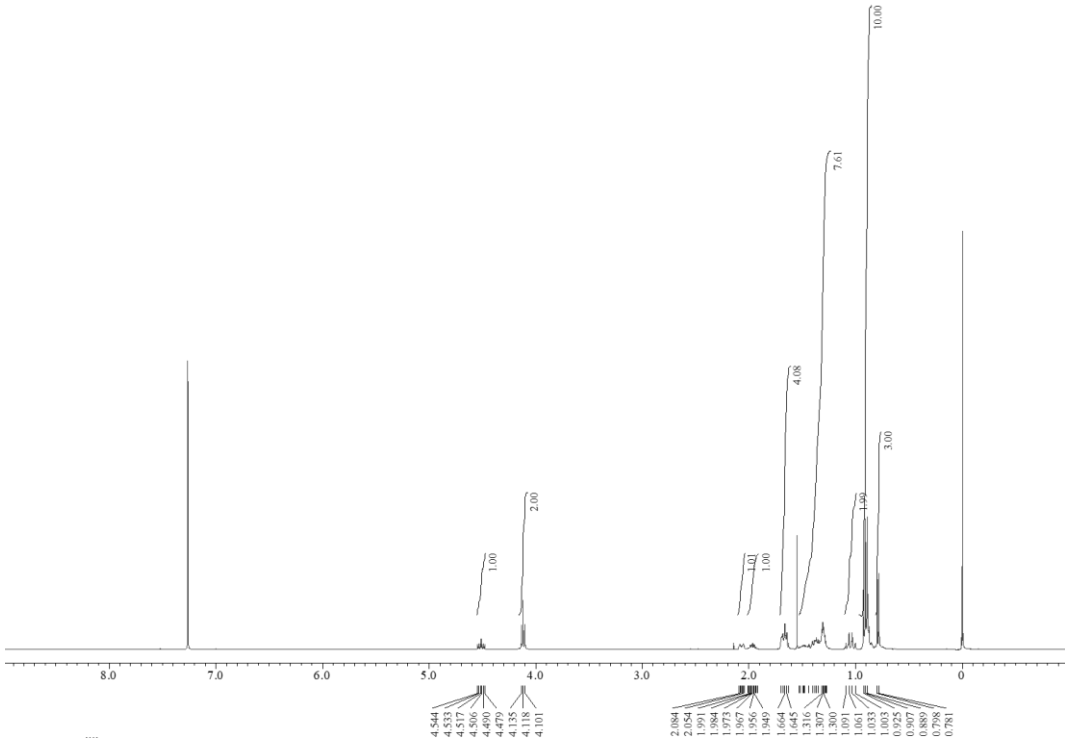


δ / ppm



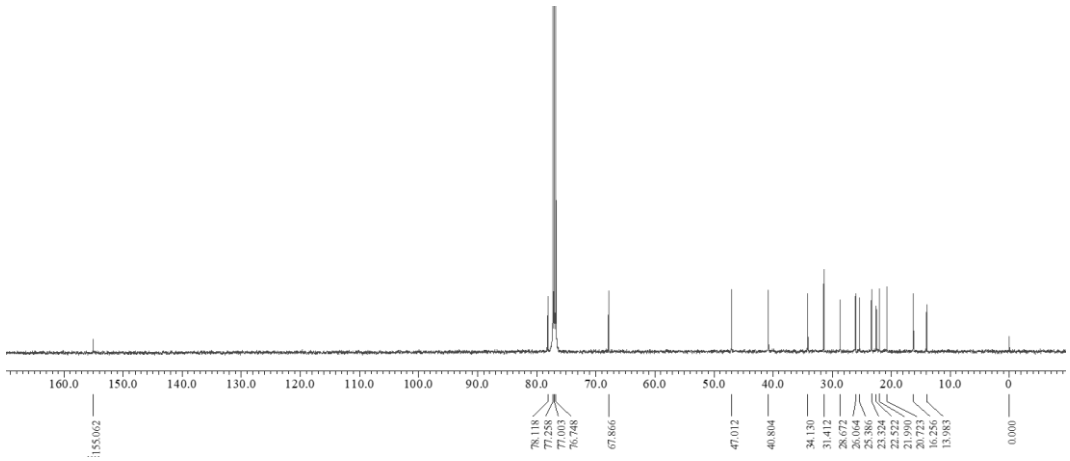
(–)-menthyl hexyl carbonate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

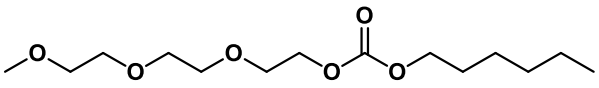


δ / ppm

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)

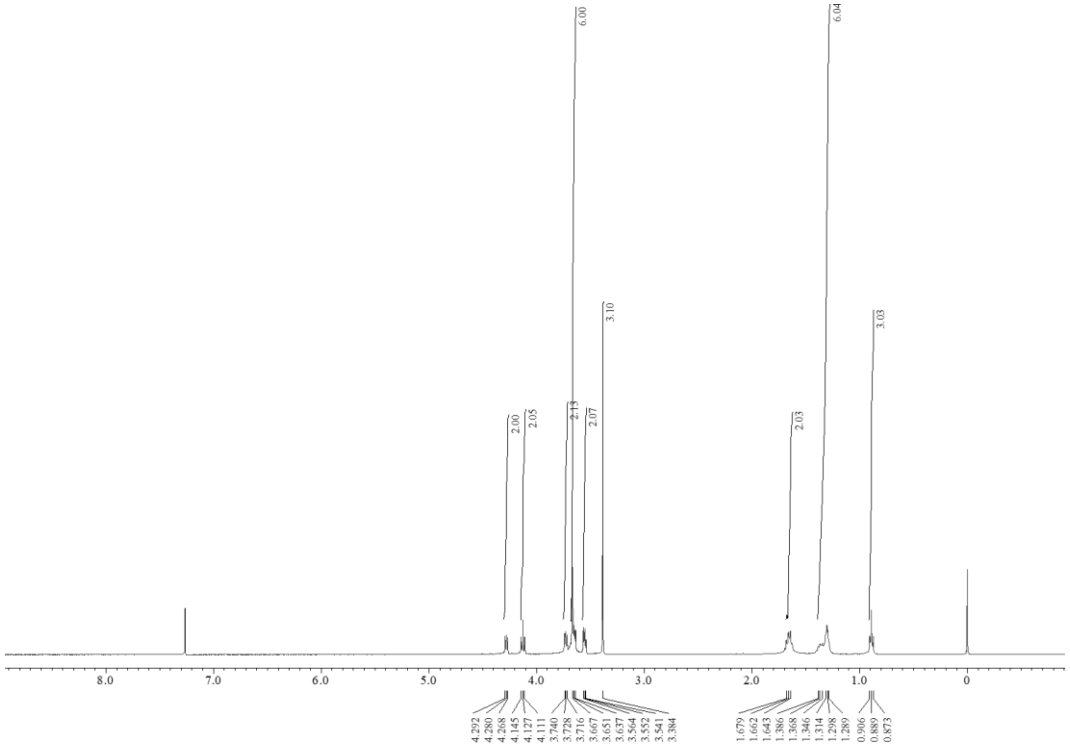


δ / ppm



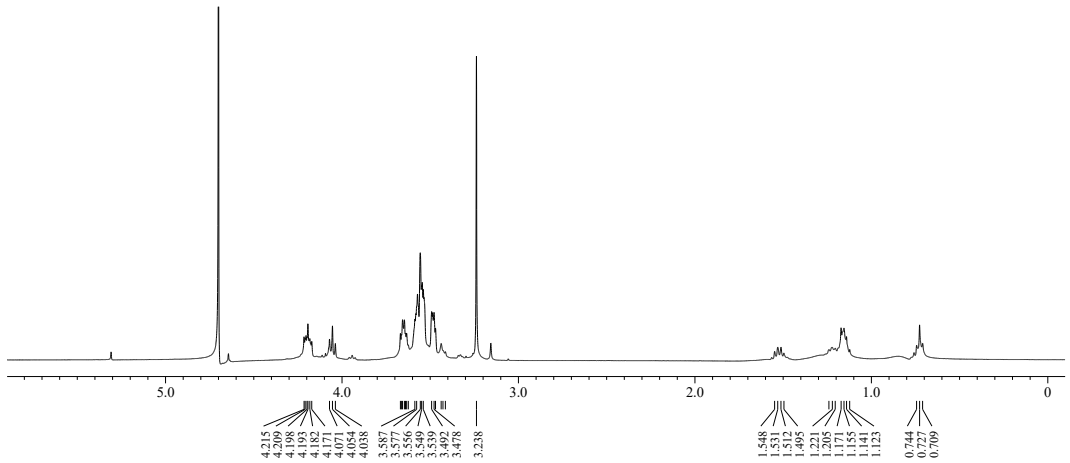
hexyl (2-(2-(2-methoxyethoxy)ethoxy)ethyl) carbonate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

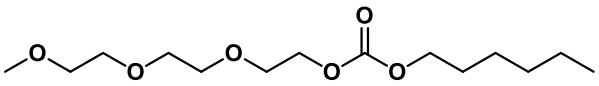


δ / ppm

^{1}H NMR (400 MHz, D_2O, 293 K)

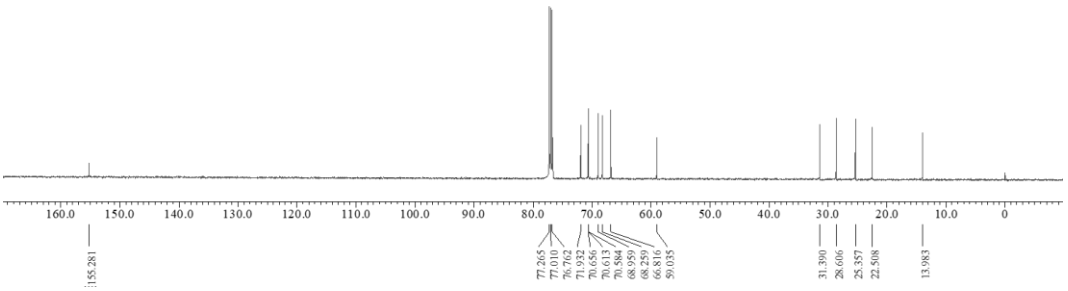


δ / ppm

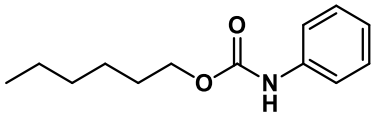


hexyl (2-(2-(2-methoxyethoxy)ethoxy)ethyl) carbonate

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)

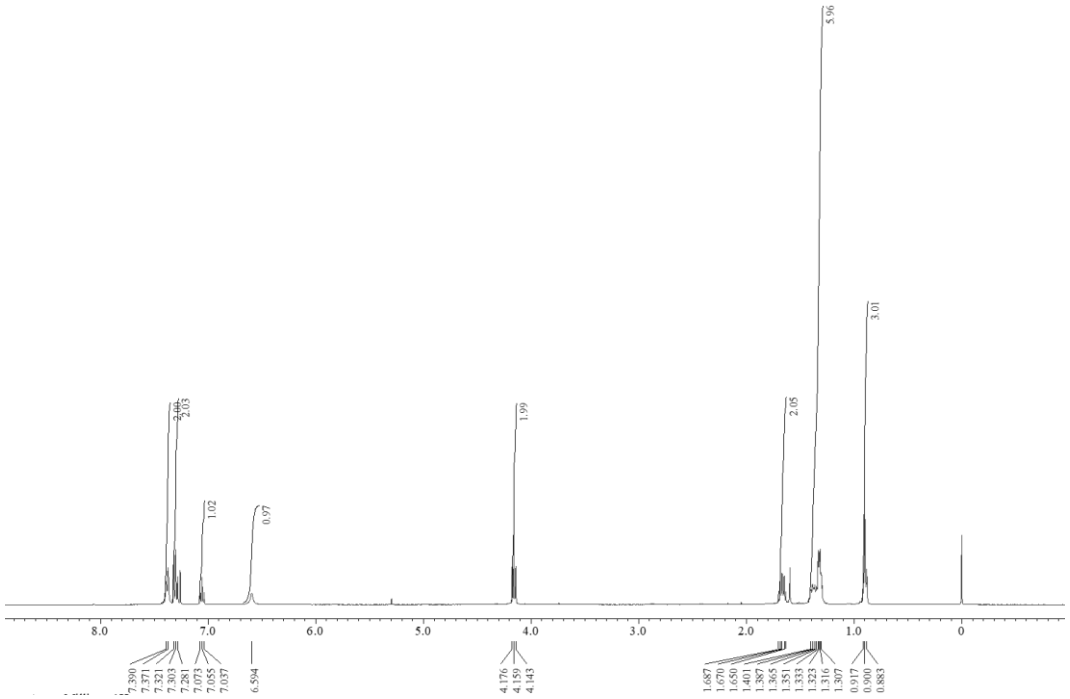


δ / ppm

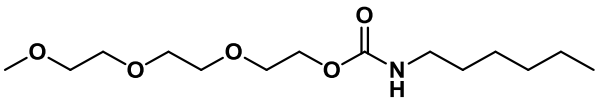


hexyl phenyl carbamate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

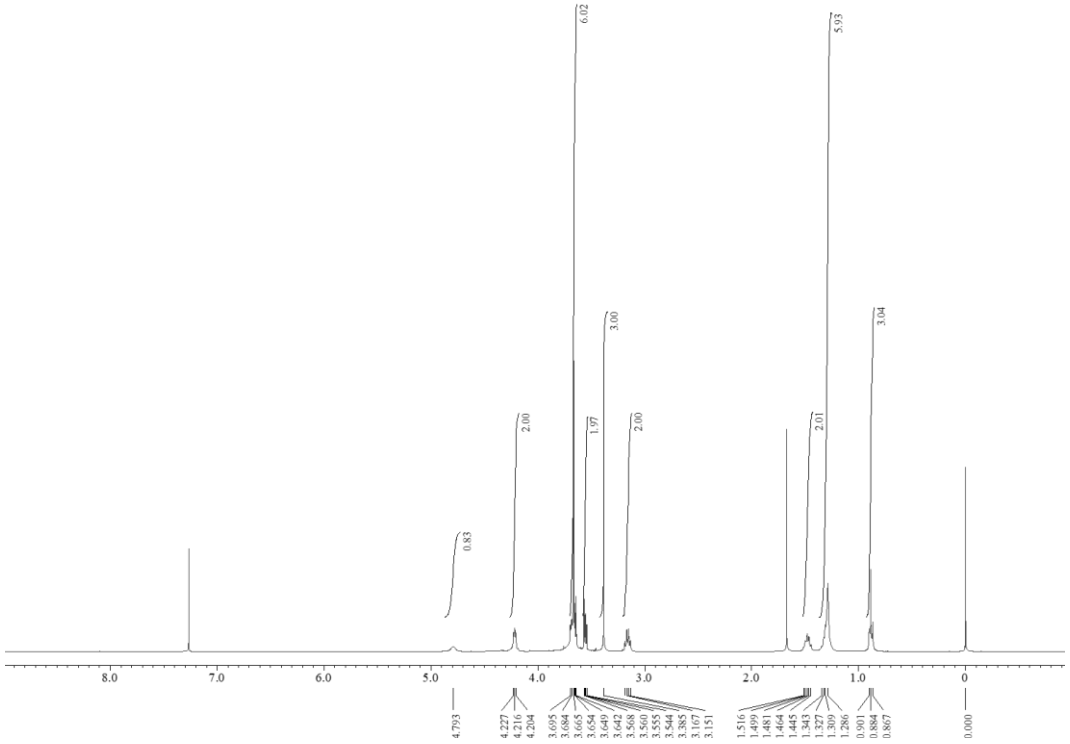


δ / ppm



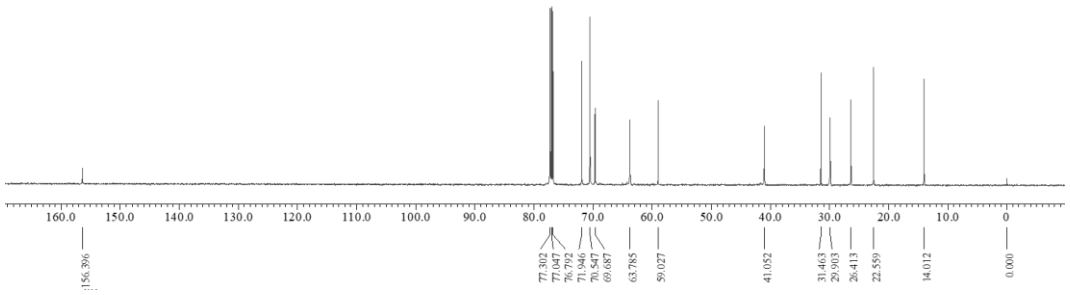
2-(2-(2-methoxyethoxy)ethoxy)ethyl hexyl carbamate

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)



δ / ppm

^{13}C NMR (125 MHz, $CDCl_3$, 293 K)



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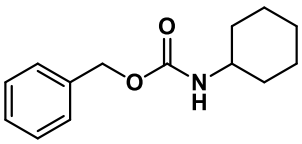
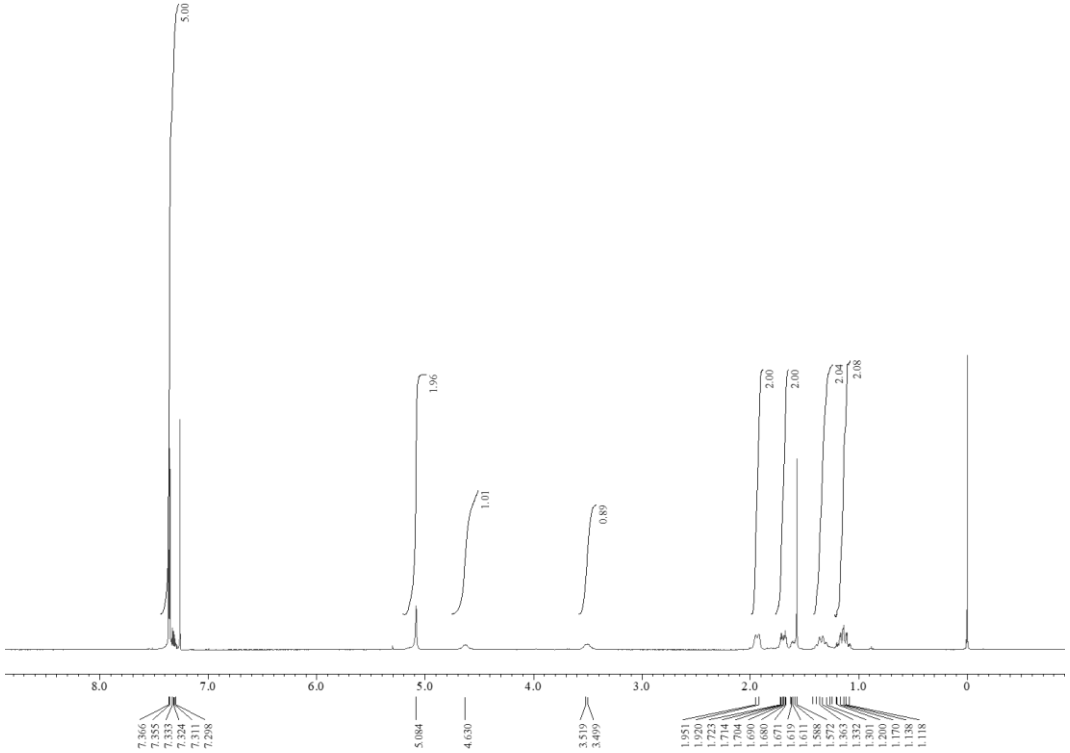
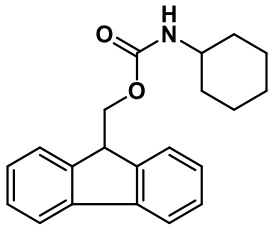


benzyl cyclohexyl carbamate

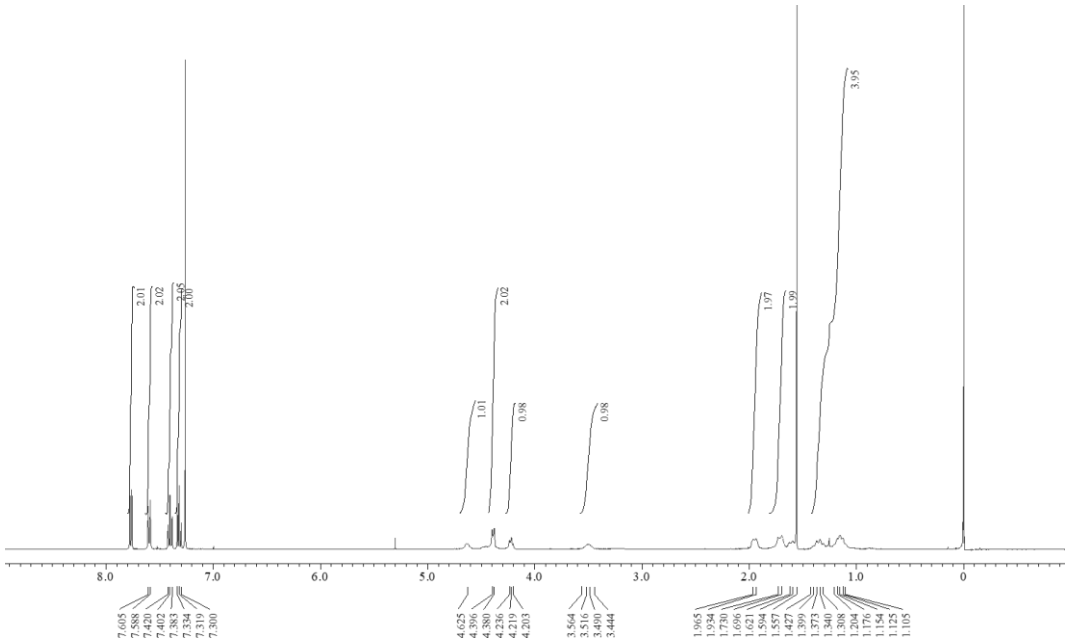
^{1}H NMR (400 MHz, $CDCl_3$, 293 K)



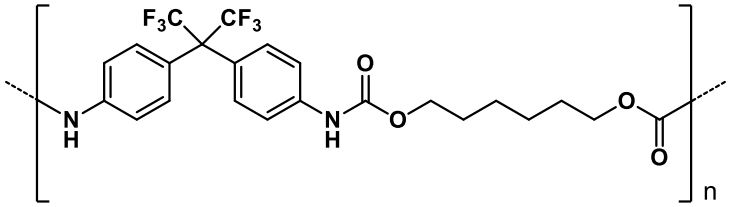


(9*H*-fluoren-9-yl)methyl cyclohexyl carbamate

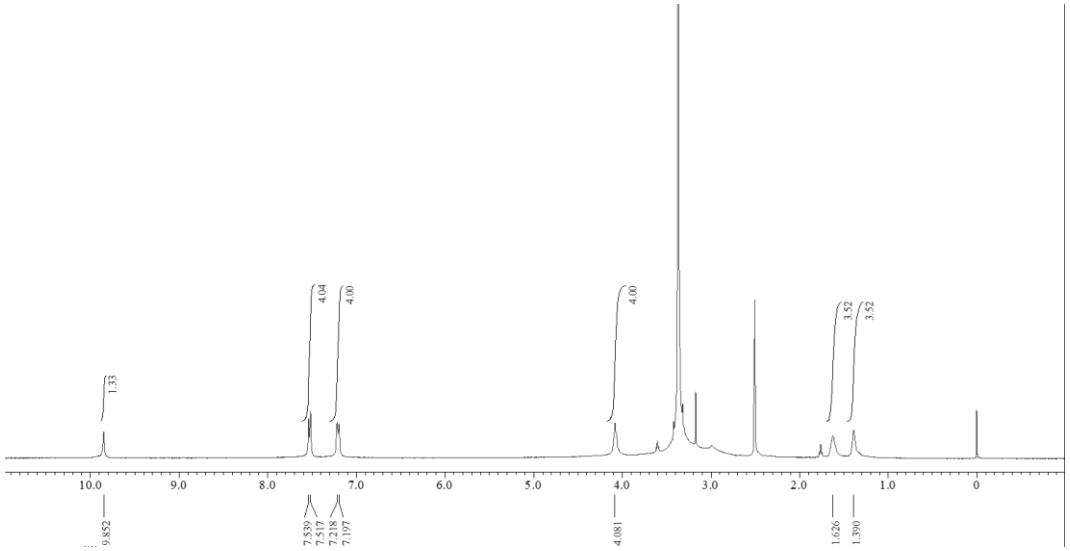
^{1}H NMR (400 MHz, $CDCl_3$, 293 K)



δ / ppm

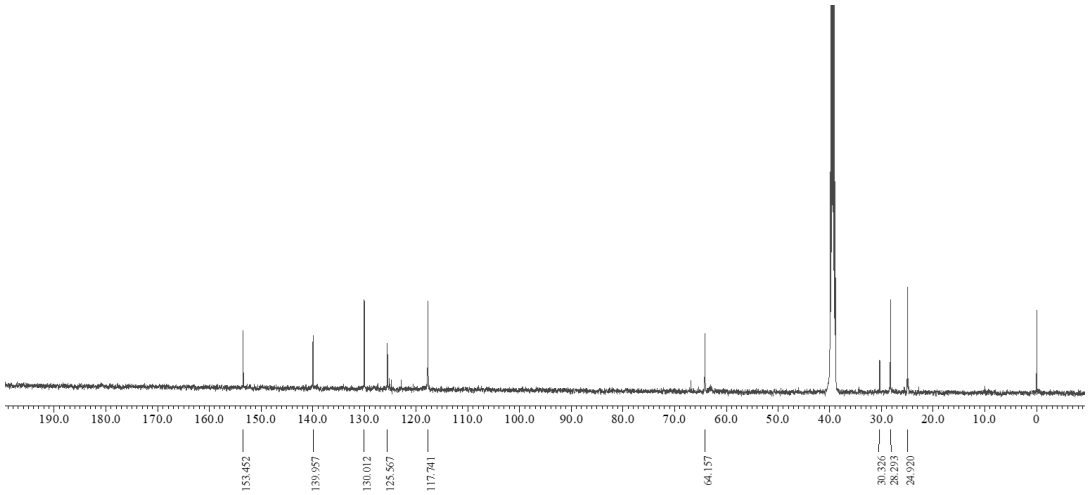


^{1}H NMR (400 MHz, DMSO-d_6, 293 K)



δ / ppm

^{13}C NMR (125 MHz, DMSO-d_6, 293 K)



δ / ppm

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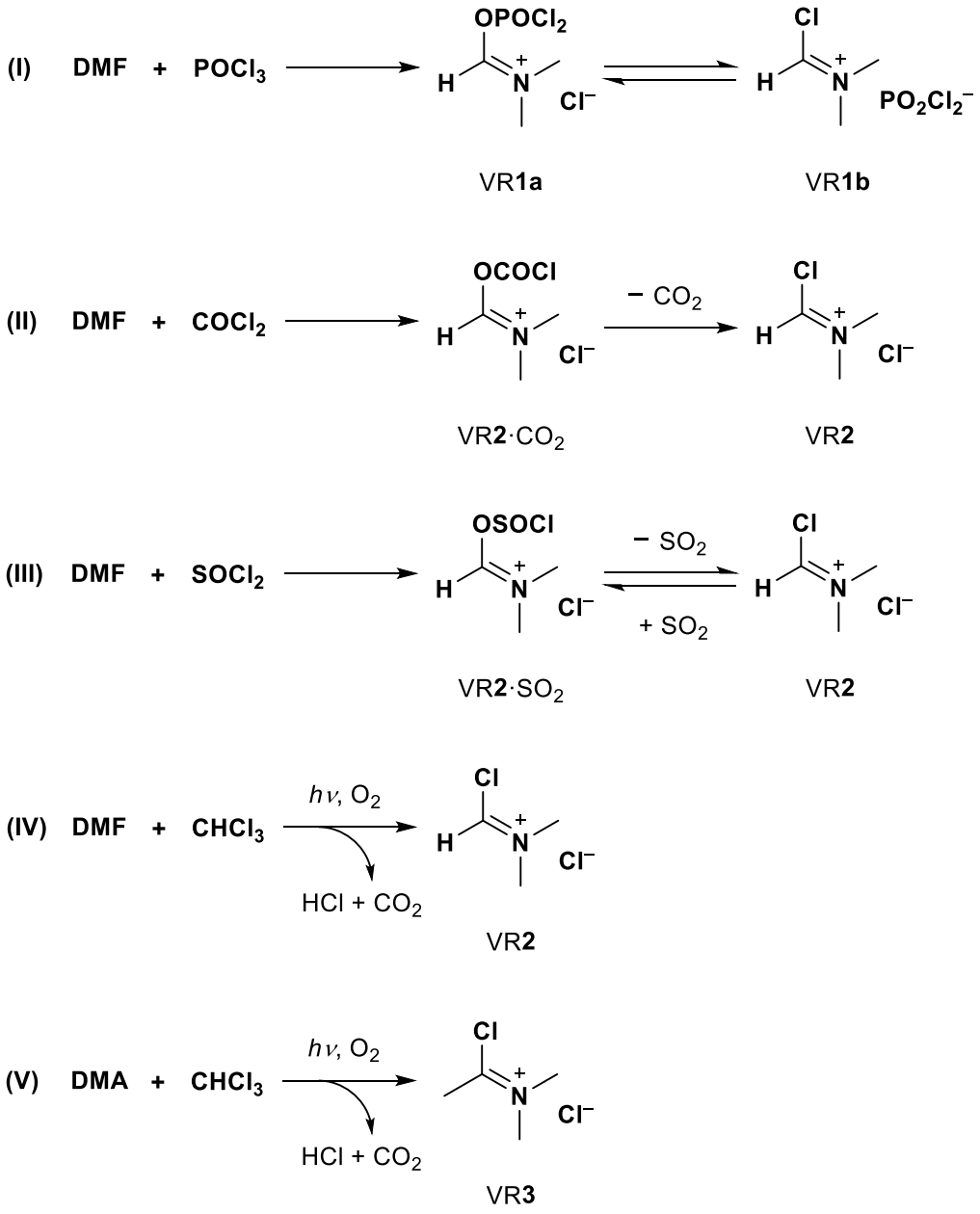
Chapter 3

UV Light Photo-on-Demand Synthesis of Vilsmeier Reagents with Chloroform

3.1 Introduction

The Vilsmeier reagent (VR), an iminium salt, was first reported a century ago.[1] It is used in a variety of organic syntheses, especially in formylation reactions.[1-3] The typical synthetic protocol for VR is the reaction of *N*,*N*-dimethylformamide (DMF) with phosphorus oxychloride ($POCl_3$) (Scheme 3.1, reaction **I**).[3,4] The produced VR is known to be in equilibrium between VR**1a** and VR**1b** due to intramolecular conversion of the anions. VR**1a** possesses higher reactivity than most of other VRs reported. However, $POCl_3$ has high toxicity and a corrosive nature. Furthermore, phosphorus-containing by-products formed after the reaction contaminate the product, and are known to be environmental pollutants.[3,5] Phosgene ($COCl_2$) is also available for synthesizing VR instead of $POCl_3$ (Scheme 3.1, reaction **II**). It reacts with DMF to give VR**2**·CO_2, which irreversibly decarbonates to form VR**2**.[3,6] In contrast to VR**1** prepared in reaction (**I**), there are fewer by-products generated in its synthetic applications. However, since $COCl_2$ is a gas at room temperature has high toxicity, organic synthesis with $COCl_2$ requires careful handling with special safety equipment.[7] For this reason, $COCl_2$ is produced through on-demand synthetic methods generally with CO and Cl_2 as raw materials.[8] In an alternative method to synthesize VR**2**, DMF is reacted with $SOCl_2$ to give VR**2**·SO_2, which is in equilibrium with VR**2** and SO_2



Scheme 3.1 Reactions of synthesizing Vilsmeier reagents.

(Scheme 3.1, reaction **III**).[3,9] $SOCl_2$ also has high toxicity and corrosive properties, and SO_2 gas generated in the reaction is an environmental air pollutant.[10] These three synthetic methods have been used widely in both

academic and industrial laboratories with few modifications. In addition to these reactions, as an innovative method without using hazardous reagents, Kimura and co-workers reported VR**2** synthesis with DMF and phthaloyl dichloride (OPC).[11] The reaction provides VR**2**, precipitated as a white solid in the sample solution, together with phthalic anhydride (PA) as a co-product. PA can be reconverted to OPC through reaction with 4-chlorobenzotrichloride in the presence of a $ZnCl_2$ catalyst. This method can produce VR**2** with higher quality compared with previous methods. However, VR**2**, which is very unstable in air, must be isolated from the sample solution when using it as a reagent for subsequent reactions. This background motivated the study to develop a novel artificially controllable on-demand synthesis method for VR**2** and its derivatives with high quality and efficiency by simple procedures using as few chemicals as possible.

In situ photo-on-demand synthesis of chloroformate with a mixed solution of chloroform and an alcohol without any other reagents was reported in Chapter 2.[12] The reactions were conducted in the solution with simple and easy procedures using only UV irradiation under O_2 bubbling. As a further extension of the reaction, this study has devolved a photo-on-demand in situ synthesis of Vilsmeier reagents (Scheme 3.1, reactions **IV** and **V**) with chloroform and their applications to one-pot syntheses of a variety of organic compounds, such as aldehydes, acyl chlorides, formates, ketones, esters, and amides.[13]

3.2 Results and discussions

3.2.1 In situ photo-on-demand synthesis of Vilsmeier reagent

An essentially same reaction system as with that described in Chapter 2 was employed for the photo-on-demand synthesis of Vilsmeier reagent. (Figure 2.1).

A Low-pressure mercury lamp was inserted into the reaction solution via a quartz glass jacket fixed in the center of a cylindrical flask.[12–14] Photochemical reactions were conducted with this reaction apparatus with vigorous stirring of the sample solution at 10–50 °C under a steady flow of O_2 (15–35 mL/min) bubbled through 20 mL (250 mmol) of $CHCl_3$ containing 5–50 mmol of DMF or DMA with or without a reaction substrate. The reactions were carried out in a closed system, but the unreacted photo-decomposed gas from the system was trapped outside with water containing a base such as $NaHCO_3$.

Initially, VR synthesis was demonstrated upon photo-irradiation of a $CHCl_3$ solution containing DMF at 30 °C. The reaction was monitored by ^1H NMR spectroscopy with $CDCl_3$ as the solvent. DMF peaks at δ = 2.97 and 2.88 ppm, and 8.02 ppm, corresponding to the *N*-methyl groups and the formyl group, respectively, decreased and new broad singlets at δ = 3.67 and 10.56 ppm

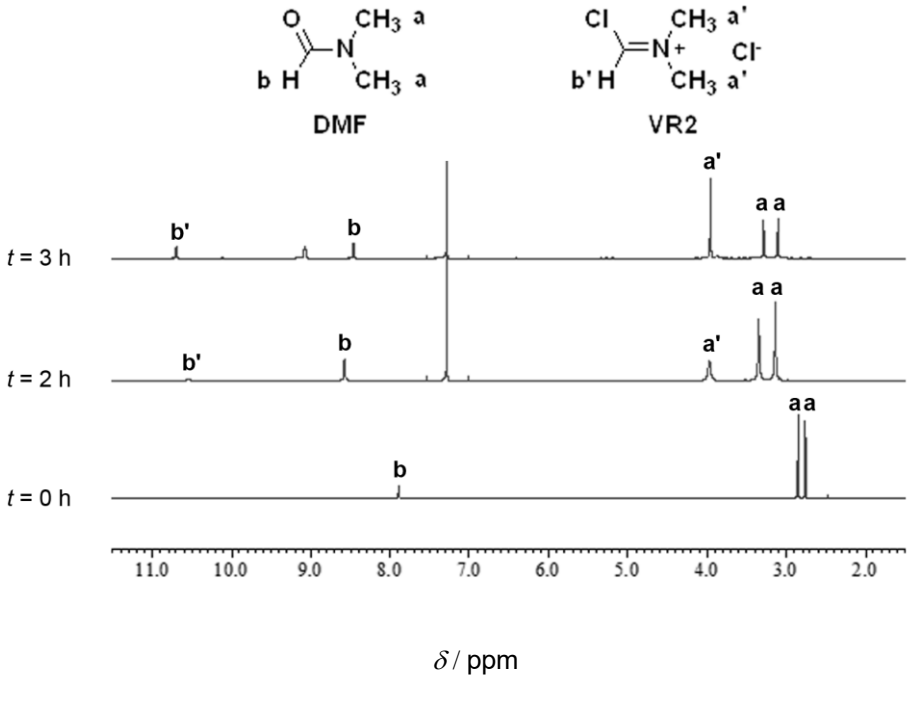
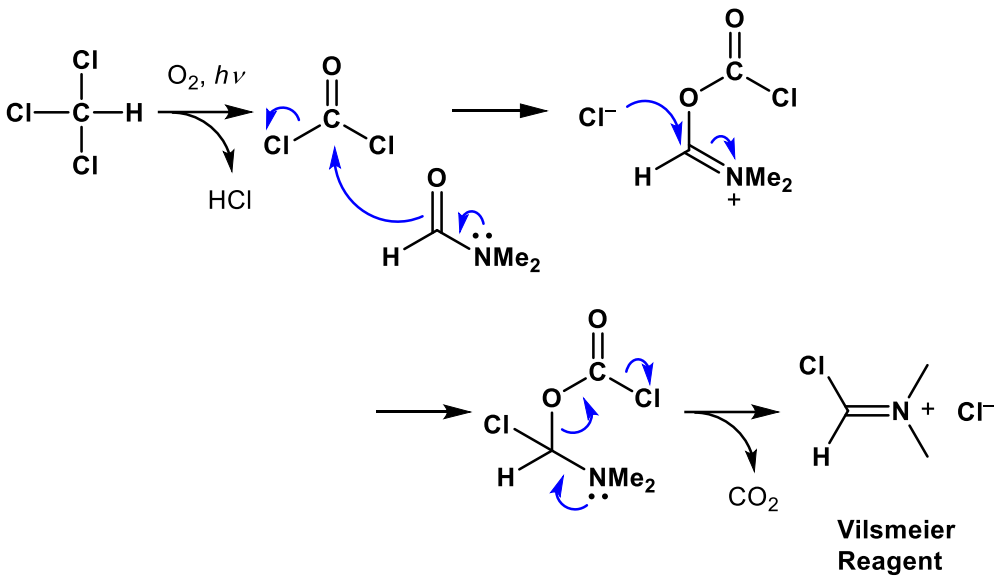


Figure 3.1 Time-course changes of DMF (20 mmol) in $CHCl_3$ (20 mL) upon photo-irradiation with a low-pressure mercury lamp under O_2 bubbling at 30 ºC monitored by ^1H NMR spectroscopy (400 MHz, $CDCl_3$). The $CDCl_3$ solutions for the measurement were prepared by collecting the sample solution at 0, 2, and 3 h.

increased (Figure 3.1). These two new peaks were consistent with those of VR**2** reported previously.[9a,11a,15] DMF may be converted to VR**2** by the following mechanism (Scheme 3.2): Oxidative photo-decomposition of $CHCl_3$ generates $COCl_2$ and HCl,[14,16] and then the generated $COCl_2$ immediately reacts in situ with DMF to give VR**2**·CO_2. The eliminated Cl^- then attacks the iminium cation to give a tetrahedral intermediate to result in formation of VR**2** after irreversible elimination of CO_2.



Scheme 3.2 A reaction mechanism expected for the photochemical formation of VR**2** from a $CHCl_3$ solution containing DMF.

In general, Vilsmeier reagents, especially VR**2**, are extremely moisture sensitive, and readily react with water to regenerate DMF and HCl. Even after isolating VR**2** in the purification process, DMF is still detected when analyzing VR**2** spectroscopically such as by NMR spectroscopy (see section **3.4.4**, ^1H and ^{13}C NMR spectra of VR**2**).[11a] For this reason, in order to estimate the true yield of VR**2** in the photoreaction, its one-pot conversion to an aldehyde was demonstrated through reaction with *N*-methylpyrrole, having high reactivity. The

yield of VR**2** could then be estimated from the yield of the product by ^{1}H NMR spectroscopy. For example, a mixture of 2- and 3-formyl-1-methylpyrroles **1a** was quantitatively obtained through the one-pot reaction with equiv. amounts (20 mmol) of DMF and *N*-methylpyrrole in $CHCl_3$ (20 mL, 250 mmol) (Table 3.2, entry 1). The total consumption of $CHCl_3$, including its vaporization, was estimated to be 43% (107 mmol) by ^{1}H NMR analysis after the reaction for 3 h at 30 ºC.

With this procedure, it was revealed that the yield of VR**2** was highly dependent on reaction conditions such as temperature, flow rate of oxygen gas, DMF concentration, and light intensity of the UV lamp. Figure 3.2a shows that the

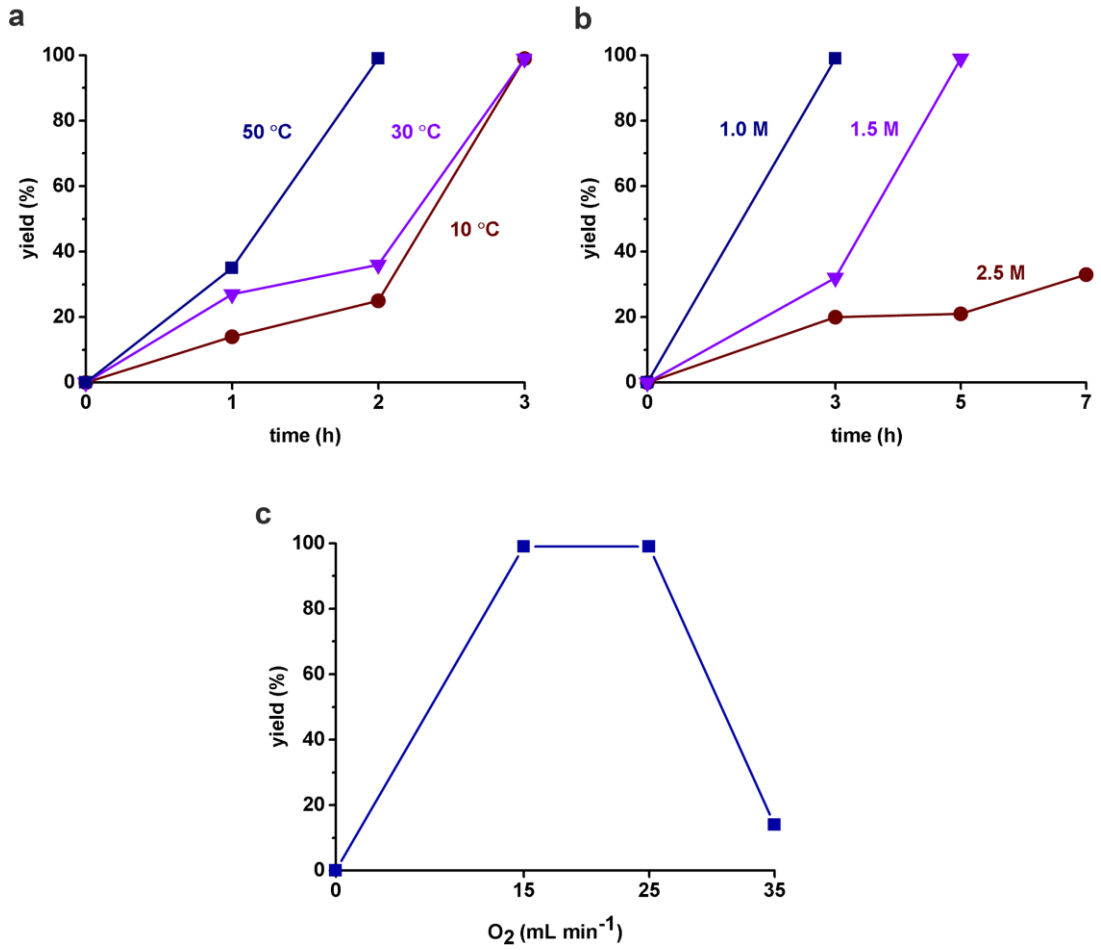


Figure 3.2 Plots of the yields of VR**2** formed upon photo-irradiation of $CHCl_3$ solutions containing DMF at variable a) temperature ([DMF] = 1.0 M, O_2 flow: 25 mL·min^{-1}), b) concentration of DMF (30 °C, O_2 flow: 25 mL·min^{-1}), and c) flow rate of O_2 gas ([DMF] = 1.0 M, 3 h, 30 °C).

formation of VR**2** is accelerated upon elevating the temperature. However, the reaction profiles with respect to time are nonlinear, which may result from acceleration of the reaction upon decreasing the reactant DMF. It can be expected that DMF more efficiently hindered the oxidative photo-decomposition of $CHCl_3$ than the produced VR**2**. This is supported by the fact that the rate of the reaction is clearly faster with a lower concentration of DMF in the $CHCl_3$ solution (Figure 3.2b). Although further investigation is necessary to elucidate the possible inhibition mechanism, it may result from the larger absorbance of 184.9 nm UV light by DMF than by VR**2**, and/or from DMF acting as a radical scavenger. The reaction is also dependent on the extent of oxidative photo-decomposition of $CHCl_3$, which can be controlled by the flow rate of oxygen. Although no reaction occurred without O_2, relatively high conversions of DMF to VR**2** were observed by slow bubbling (15–25 $mL \cdot min^{-1}$) of O_2 gas to the sample solution. In contrast, the conversion was dramatically decreased by fast bubbling of O_2 gas (35 $mL \cdot min^{-1}$), which may kick out the generated $COCl_2$ from the system before its reaction with DMF (Figure 3.2c).

Photo-on-demand VR synthesis was also possible with *N*,*N*-dimethylacetamide (DMA) (Scheme 3.1, reaction **V**). Using similar conditions to those for the synthesis of VR**2**, VR**3**, which has a methyl group on the iminium carbon, was successfully obtained with quantitative conversion, and isolated in 66% yield as a white crystalline solid. In contrast to the case of VR**2**, which could be stored for only a couple of days even in a closed bottle at low temperature, the obtained VR**3** was relatively stable under air, and could be stored for several months under the same conditions as VR**2** in a closed bottle at low temperature. This stability most likely originated from the attached methyl group that may allow hyperconjugation with the $C=N^+$ group as well as steric protection of the iminium carbon.

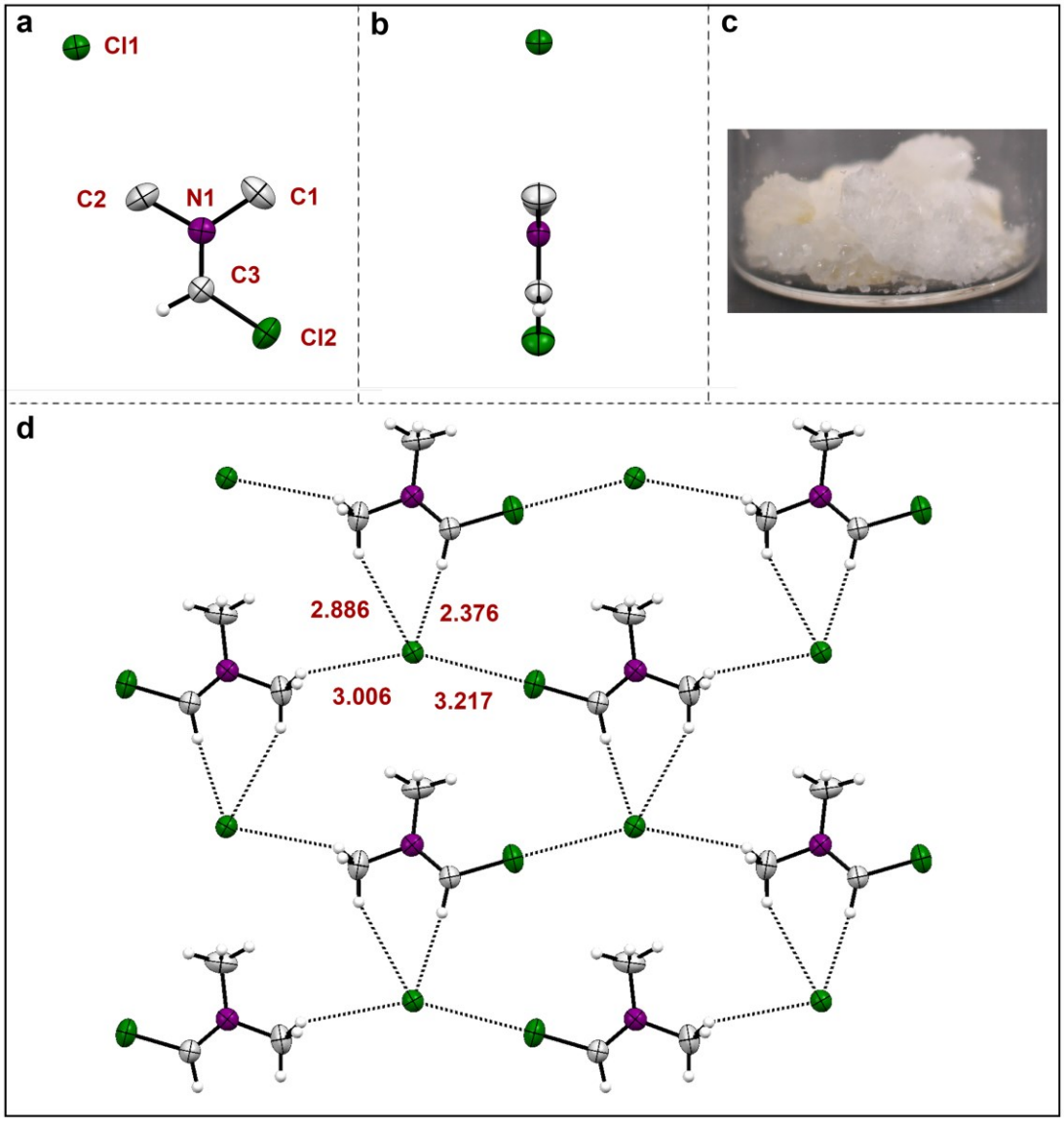


Figure 3.3 Single-crystal X-ray structure of VR**2**. a) Top view, b) side view of the crystal structure, c) a photo of crystalline VR**2**, d) the crystal packing structure viewed from the crystallographic axis *b*. Color code: grey, C; purple, N; green, Cl; white, H.

Since the photochemical reactions of DMF and DMA with $CHCl_3$ allowed formation of VR**2** and VR**3**, respectively, without notable by-products, the sample obtained after the reaction provided single crystals amenable to analysis by X-ray crystallography (Figure 3.3 and 3.4). Their crystallographic data are summarized in Table 3.1. To the best of author′s knowledge, this is the

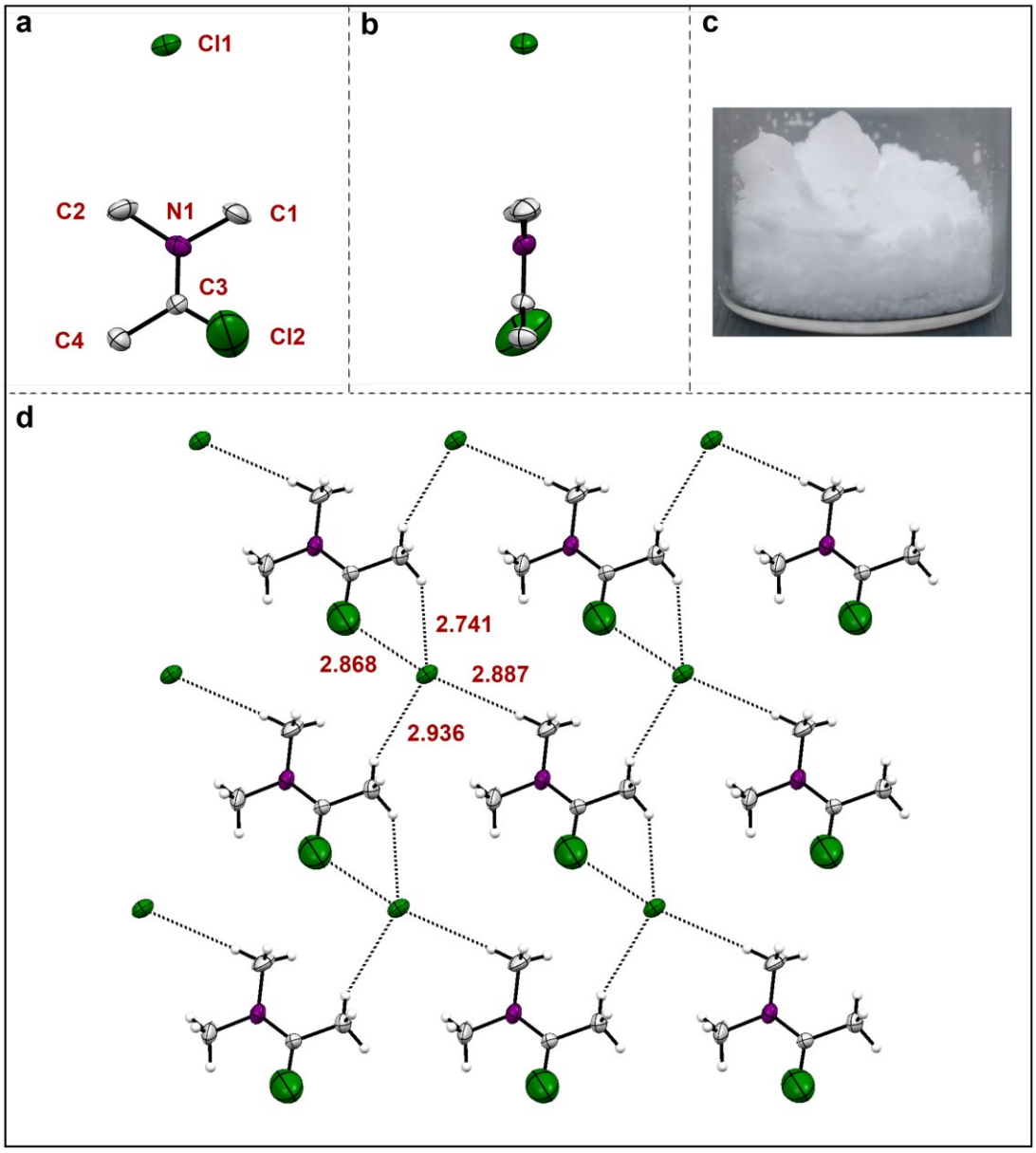


Figure 3.4 Single-crystal X-ray structure of VR**3**. a) Top view, b) side view of the crystal structure, c) a photo of crystalline VR**3**, d) the crystal packing structure viewed from the crystallographic axis *b*. Color code: grey, C; purple, N; green, Cl; white, H.

first example of the crystallographic analysis of VR. The X-ray crystallographic analysis showed that VR**2** adopts a planar conformation with a bond length of the iminium group (C3–N1) of 1.266 Å (Figure 3.3a and 3.3b). The length observed is almost same as that (1.273 Å) for diethylmethyleneiminium chloride

Table 3.1 Crystallographic data for single crystals of VR**2** and VR**3**.

Crystals	VR**2**	VR**3**
CCDC deposit No.	2054184	2054219
Formula	C_3H_7ClNCl	C_4H_9ClNCl
Formula weight	128 g·mol^{-1}	142 g·mol^{-1}
Temperature	193(2) K	173(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	orthorhombic	monoclonic
Space group	*Pnma*	$P\,2_1$
a	8.9156(11) Å	6.7141(14) Å
b	6.6747(8) Å	6.7510(14) Å
c	10.4483(12) Å	7.2786(15) Å
α	90 °	90 °
β	90 °	96.812(2) °
γ	90 °	90 °
Volume	621.77(13) Å^3	327.59(12) Å^3
Z	4	2
Density (calculated)	1.367 mg·m^{-3}	1.440 mg·m^{-3}
Absorption coefficient	0.910 mm^{-1}	0.871 mm^{-1}
F(000)	264 e	148 e
Crystal size	0.285 × 0.200 × 0.143	0.220 × 0.200 × 0.180
2θ range	3.00 to 27.46 °	2.818 to 27.765 °
Index ranges	$-11 \le h \le 10$, $-8 \le k \le 7$, $-9 \le l \le 13$	$-7 \le h \le 8$, $-8 \le k \le 8$, $-9 \le l \le 5$
Goodness-of-fit on F^2	1.587	2.169
Final R indices [$I>2\sigma(I)$]	$R1$ = 0.0363, $wR2$ = 0.1035	$R1$ = 0.0964, $wR2$ = 0.2593
R indices (all data)	$R1$ = 0.0364, $wR2$ = 0.1039	$R1$ = 0.1022, $wR2$ = 0.2667
Largest diff. peak and hole	0.658 and -0.334 e·Å^{-3}	0.707 and -1.534 e·Å^{-3}

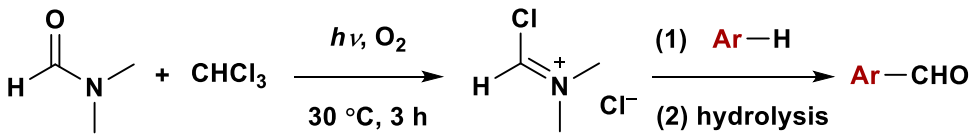
($H_2C{=}NEt_2^+Cl^-$) reported previously.[17] The iminium cation is separated from the counter Cl^- ion by the *N*–methyl groups (C1–N1 and C2–N1 = 1.461 and 1.469 Å, respectively). In the crystal packing structure shown in Figure 3.3d, counter Cl^- ions are surrounded by multiple C–H groups (bond lengths = 2.376–3.006 Å), in

which the observed CH–Cl^- interactions are stronger at the acidic hydrogen attached on the iminium-carbon bearing Cl group. Furthermore, Cl^- ions are situated in the 2D network structure of the iminium ions with Cl–Cl distances of 3.217 Å, indicating halogen bonding.[18] Similar structural features are observed in the crystal structure of VR**3**, having a methyl group on the iminium-carbon. It also has a planar structure with a C=N^+ distance of 1.286 Å (Figure 3.4a and 3.4b). The slightly longer bond length than that of VR**2** may be ascribed to the steric repulsion between the methyl groups (C1 and C4) and/or hyperconjugation between the methyl and iminium groups. In the crystal packing structure, counter Cl^- ions are also surrounded by multiple C–H groups with distances of 2.741–2.936 Å, which are shorter than those observed in VR**2** (Figure 3.4d). The halogen bonding between Cl^- and iminium-Cl with a distance of 2.868 Å also supports formation of a 2D-network structure.

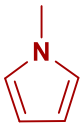
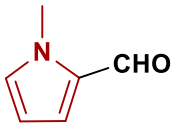
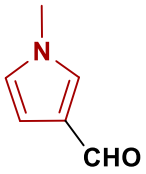
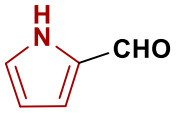
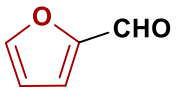
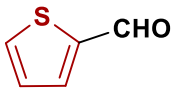
3.2.2 One-pot syntheses of Aldehydes and Ketones

The photo-on-demand in situ synthesis of VR with $CHCl_3$, which plays dual roles as reagent and solvent, has a strong advantage for utilization in one-pot organic syntheses. Initially, one-pot formylation reactions of aromatic compounds were conducted by extended applications of the reaction with 1-methylpyrrole as described above (Table 3.2). As a general experimental procedure, VR**2** was prepared through the photo-on-demand phosgenation reaction of DMF (20 mmol) in $CHCl_3$ (250 mmol, 20 mL) at 30 °C. After elevating the temperature to remove possible remaining reactive species such as $COCl_2$ and HCl, the aromatic substrate (5–10 mmol) was added to the sample solution. After the reaction at 0–70 °C for 0.5–16.0 h, the product was hydrolyzed with alkaline aqueous solution, such as saturated Na_2CO_3, to give the formyl compound. For example, 5-membered heterocyclic compounds, 1*H*-pyrrole, furan, and thiophene provided

Table 3.2 One-pot synthesis of aldehydes with VR**2** prepared upon photo-irradiation of a $CHCl_3$ solution containing DMF.

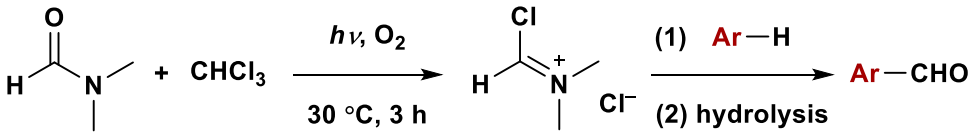


VR2 **1**

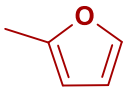
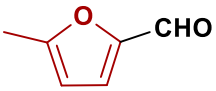
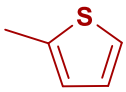
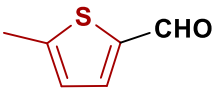
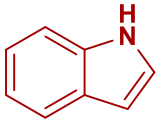
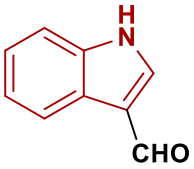
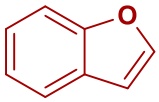
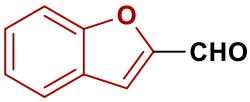
entry	Ar—H	temp. (°C)	time (h)	product	yield
1		70	0.5	 **1a**	92%[a] 73%[b]
				 **1a'**	8%[a] 8%[b]
2		70	1.0	 **1b**	82%[a] 53%[b]
3		r.t.	2.5	 **1c**	60%[a] 53%[b]
4		70	6.0	 **1d**	38%[a] 23%[b]

[a] ^{1}H NMR yield. [b] isolated yield.

Table 3.2 (continued) One-pot synthesis of aldehydes with VR**2** prepared upon photo-irradiation of a $CHCl_3$ solution containing DMF.



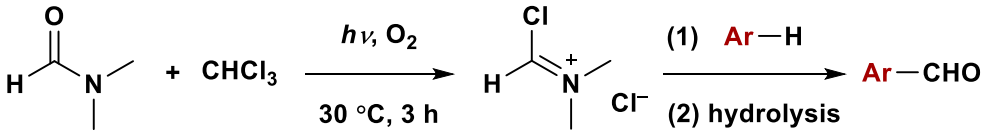
VR**2** **1**

entry	Ar—H	temp. (°C)	time (h)	product	yield
5		0	1.0	 **1e**	79%[a] 76%[b]
6		70	0.5	 **1f**	98%[a] 95%[b]
7		r.t.	18.0	 **1g**	86%[a] 71%[b]
8		100	20.0	 **1h**	26%[b]

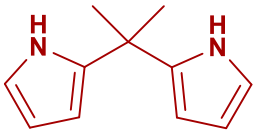
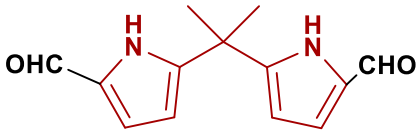
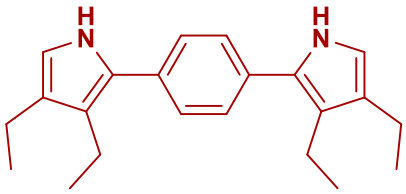
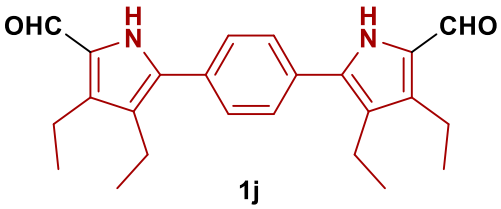
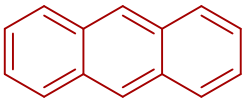
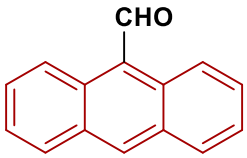
[a] ^{1}H NMR yield. [b] isolated yield.

2-formyl products in 82, 60, and 38% NMR yields, respectively (**1b**–**1d**). Substitution with an electron-donating CH_3 group on the heterocyclic compounds

Table 3.2 (continued) One-pot synthesis of aldehydes with VR**2** prepared upon photo-irradiation of a $CHCl_3$ solution containing DMF.



VR**2** **1**

entry	Ar—H	temp. (°C)	time (h)	product	yield
9		70	1.0	 **1i**	92%[a] 85%[b]
10		70	0.5	 **1j**	66%[b]
11		70	16	 **1k**	50%[a] 50%[b]

[a] ^{1}H NMR yield. [b] isolated yield.

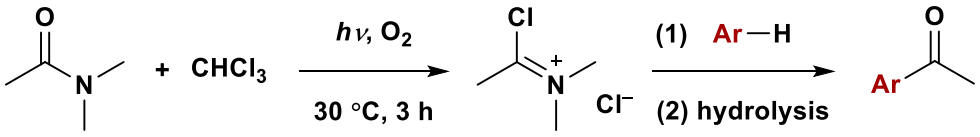
increased the product yields, likely due to the acceleration of the electrophilic substitution reaction with VR (cf. **1a** and **1b**, **1c** and **1e**, and **1d** and **1f**). Indole with its larger aromatic structure also allowed formylation at the 3-position in 86% yield, but benzofuran provided the 2-formyl product in relatively low yield (**1g** and **1h**, respectively). Since VR**2** efficiently reacted with 1*H*-pyrrole, one-pot

formylation reactions of bispyrroles, which are utilized for fabricating functional supramolecular architectures and macrocyclic rings, were demonstrated.[19] Bispyrrole derivatives, including an aliphatic and an aromatic bridge, both provided the corresponding bisformyl products in high yields (**1i** and **1j**). Anthracene, having a larger π-conjugation structure without heteroatom, also reacted with VR**2** to give the 9-formylation product in 50% yield (**1k**).

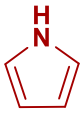
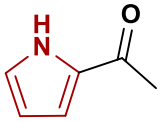
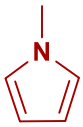
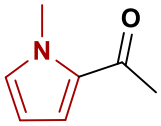
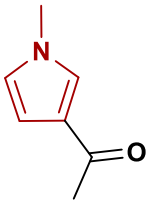
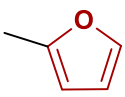
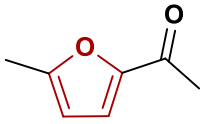
Using a similar procedure to the above formylation reactions, VR**3** was prepared through the photo-on-demand phosgenation reaction of DMA (20 mmol) in $CHCl_3$ (250 mmol, 20 mL) at 30 °C. However, its reactivity was clearly lower than that of VR**2**, probably due to the effects of the methyl group substituted on the iminium-carbon as described above. After the work-up process, an aromatic substrate (5 mmol) was added to the sample solution and stirred for a relatively long time. One-pot syntheses of ketones were achieved (Table 3.3), but the yields of the products were lower than in the formylation with VR**2**, likely due to the lower reactivity of VR**3**. For example, pyrrole provided the 2-acetyl product (**2a**) in 28% yield, but 1-methylpyrrole improved the combined yield of the 2- and 3-acetyl products to >99% (**2b**). Although no reactions were observed with either furan or thiophene, 2-methylfuran reacted with VR**3** to give the corresponding ketone (**2c**) in 48% yield after reaction at room temperature for 144 h.

In a plausible reaction mechanism, VR causes an electrophilic substitution reaction to the aromatic substrate to give an iminium salt through C–C bond formation. It was then hydrolyzed with alkaline aqueous solution to provide the corresponding formyl-substituted compounds with elimination of dimethylamine (Scheme 3.3).[20]

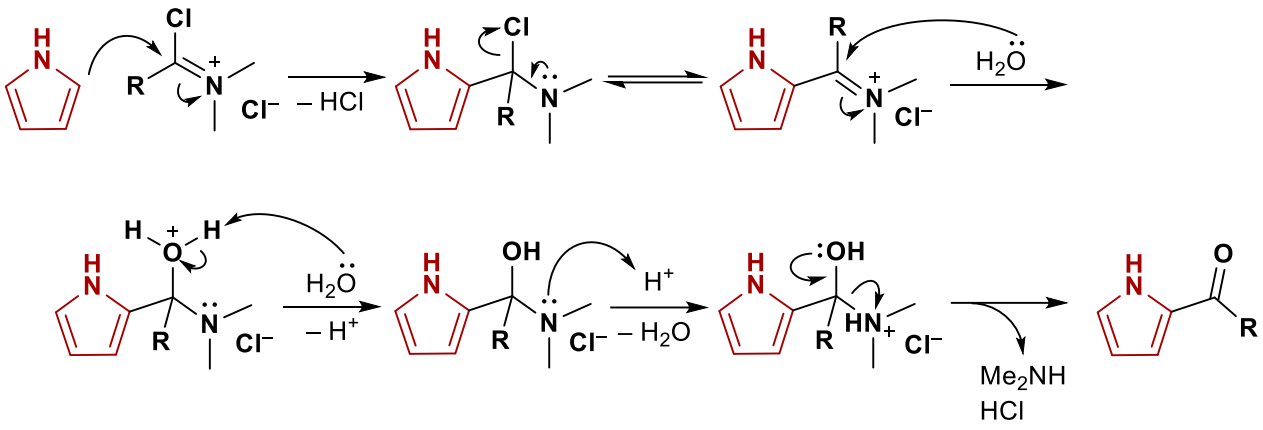
Table 3.3 One-pot synthesis of ketones with VR**3** prepared upon photo-irradiation of a $CHCl_3$ solution containing DMA.



VR3 **2**

entry	Ar—H	temp. (°C)	time (h)	product	yield
1		r.t.	21	 **2a**	28%[a] 28%[b]
2		r.t.	156	 **2b**	53%[a] 31%[b]
				 **2b'**	47%[a] 37%[b]
3		r.t.	144	 **2c**	48%[a] 37%[b]

[a] ^{1}H NMR yield. [b] isolated yield.

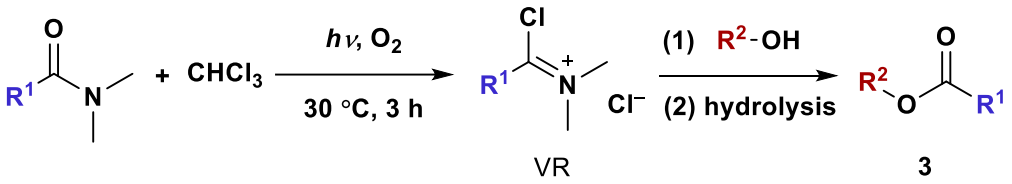


Scheme 3.3 A reaction mechanism proposed for the formation of aldehyde and ketone with Vilsmeier reagent (R = H or CH_3).

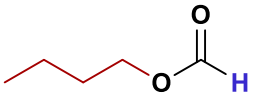
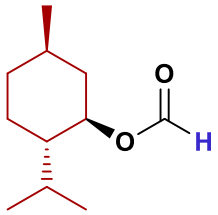
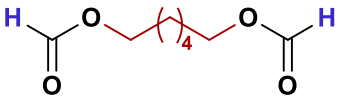
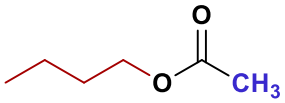
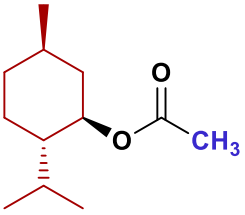
3.2.3 One-pot syntheses of formates and esters

O-formylation of alcohols is one of the protection methods of OH group. Vilsmeier reagent is known as a chemoselective formylation reagent for primary and secondary alcohols.[21] VR**2** and VR**3** were available for the one-pot syntheses of formates and esters, respectively (Table 3.4). As a general procedure, these products were synthesized with one-pot addition of an alcohol (5–10 mmol) to the VR**2** or VR**3**, prepared through the photo-irradiation of a $CHCl_3$ (20 mL) solution containing DMF or DMA (20 mmol) under O_2 bubbling at 30 °C. In the reaction with VR**3**, whose reactivity is lower than that of VR**2**, 1.2 equiv. amounts of organic base such as pyridine were also added to the sample solution as a catalyst. With a solution containing VR**2**, 1-BuOH was successfully converted to *n*-butyl formate in 92% yield (**3a**). A similar reaction proceeded with (–)-menthol, a secondary alcohol, to give (–)-menthyl formate quantitatively (**3b**). 1,6-Hexanediol provided the corresponding bisformate in 96% yield (**3c**). On the other hand, with a $CHCl_3$ solution containing VR**3**, 1-BuOH and (–)-menthol were converted to butyl acetate and (–)-menthyl acetate in 80% and 63% yields,

Table 3.4 One-pot synthesis of formates and esters with VR**2** or VR**3** prepared upon photo-irradiation of a $CHCl_3$ solution containing DMF or DMA, respectively.



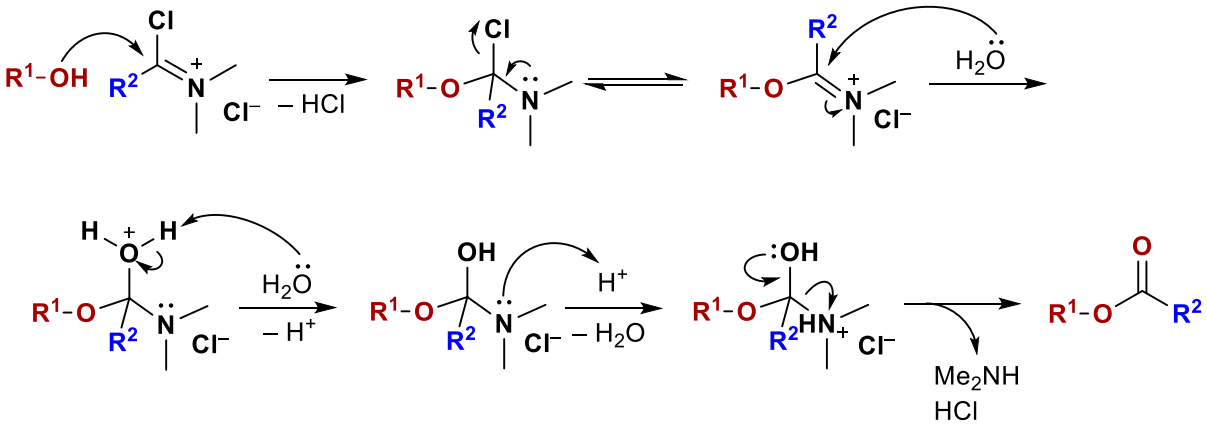
VR 3

entry	R^2-OH	pyridine (equiv.)	temp. (°C)	time (h)	product	yield
1	1-butanol	-	r.t.	1	 3a	92%[a] 87%[b]
2	(–)-menthol	-	r.t.	1	 3b	99%[a] 70%[b]
3	1,6-hexanediol	-	r.t.	1	 3c	96%[a] 44%[b]
4	1-butanol	1.2	10	1	 3d	80%[a] 41%[b]
5	(–)-menthol	1.2	50	1	 3e	63%[a] 51%[b]

[a] ^{1}H NMR yield. [b] isolated yield.

respectively (**3d** and **3e**).

A presumed mechanism for the formation of formate and ester from the reaction of VR with an alcohol is shown in Scheme 3.4. VR initially reacts with an alcohol to form an iminium salt through substitution of the iminium-Cl group, and its subsequent hydrolysis allows formation of the corresponding formate and ester.[20]

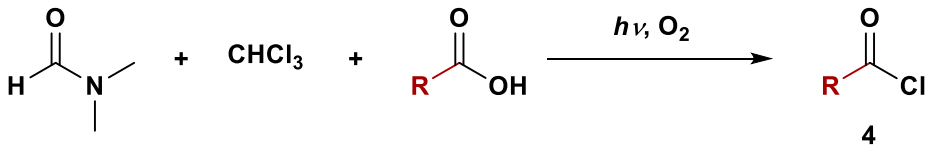


Scheme 3.4 A reaction mechanism proposed for the formation of formate and ester with Vilsmeier reagent (R^2 = H or CH_3).

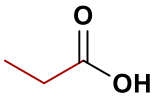
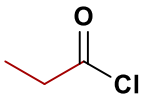
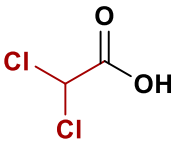
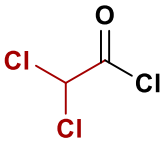
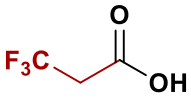
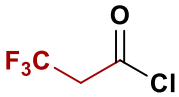
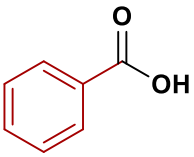
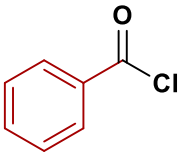
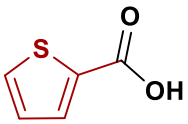
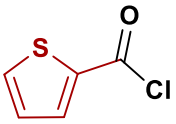
3.2.4 One-pot syntheses of acyl chlorides

Acyl chlorides are key building blocks to synthesize esters and amides. It is known that carboxylic acids convert to the corresponding acyl chlorides through reaction with phosgene in the presence of DMF. Here, it could be expected that the oxidative photochemical conversion of $CHCl_3$ to $COCl_2$ would allow an in situ photo-on-demand synthesis of the acyl chloride with a $CHCl_3$ solution containing a carboxylic acid and catalytic amounts of DMF. As a general procedure, the photo-on-demand synthesis was carried out through photo-irradiation of a $CHCl_3$ (250 mmol, 20 mL) solution containing a carboxylic acid and

Table 3.5 Photochemical in situ synthesis of acyl chlorides with $CHCl_3$ solutions containing carboxylic acid and DMF.

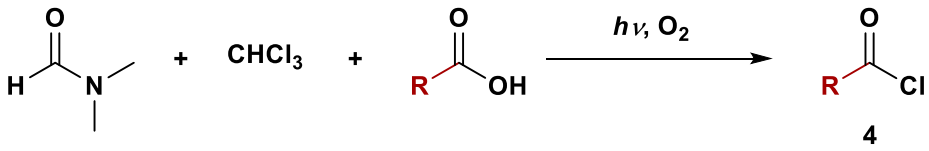


4

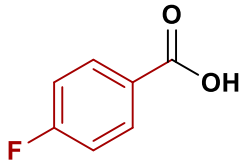
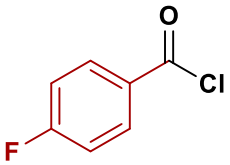
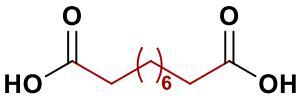
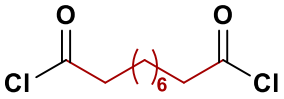
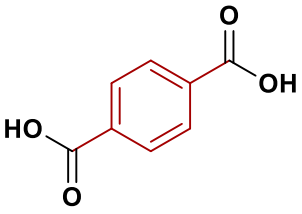
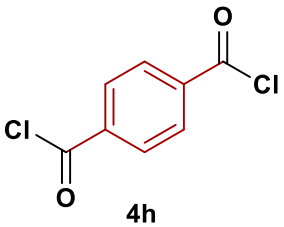
entry	RCOOH	temp. (°C)	time (h)	product	yield
1		30	3.0	 4a	90%[a] 86%[b]
2		30	3.0	 4b	99%[a] 7%[b]
3		30	3.0	 4c	99%[a] 44%[b]
4		30	3.0	 4d	99%[a] 83%[b]
5		30	3.0	 4e	93%[a] 50%[b]

[a] ^{1}H NMR yield. [b] isolated yield.

Table 3.5 (continued) Photochemical in situ synthesis of acyl chlorides with $CHCl_3$ solutions containing carboxylic acid and DMF.



4

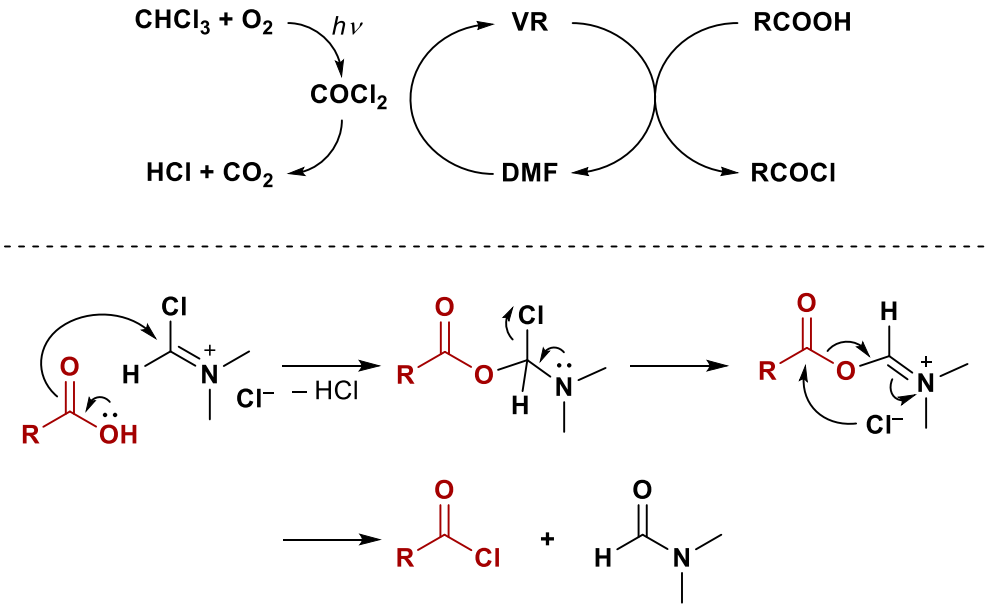
entry	RCOOH	temp. (°C)	time (h)	product	yield
6		30	3.5	 4f	99%[a] 58%[b]
7		30	4.5	 4g	99%[a] 44%[b]
8		30	6.0	 4h	82%[a] 79%[b]

[a] ^{1}H NMR yield. [b] isolated yield.

0.5–2.0 equiv. amount of DMF at 30 °C under O_2 bubbling. Propanoic acid, an aliphatic carboxylic acid, provided propionyl chloride (**4a**) in 90% NMR yield (86% isolated yield) (Table 3.5, entry 1). Dichloroacetic acid and 3,3,3-trifluoropropionic acid, having higher acidity (lower nucleophilicity), also resulted in formation of the corresponding acyl chlorides in quantitative yields (**4b** and **4c**). Efficient conversions were observed with aromatic carboxylic acids such as benzoic acid and 2-thiophenecarboxylic acid (**4d** and **4e**). 4-Fluorobenzoic acid, having an

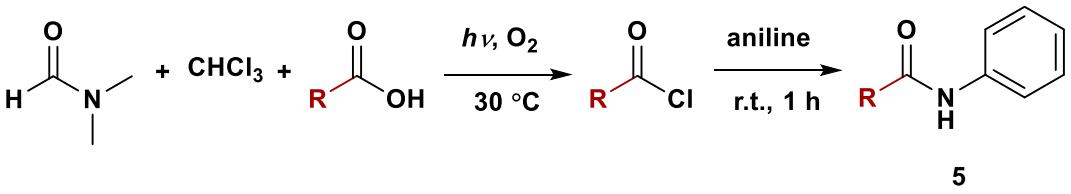
electron-withdrawing F group (**4f**), also provided the corresponding acid chloride in quantitative yield. This reaction was also available for substrates having multiple carboxyl groups such as sebacic acid and terephthalic acid, whose acyl chlorides are utilized for fabricating polyamides and polyesters. They provided the corresponding acyl chlorides in quantitative and 82% yields, respectively (**4g** and **4h**). Notable differences between NMR and isolated yields, observed especially in the substrates bearing electron withdrawing group, may result from decomposition of the acyl chloride in the process of isolation.

A possible reaction mechanism for the photo-on-demand synthesis of the acyl chlorides is shown in Scheme 3.5. $COCl_2$ generated through oxidative photo-decomposition of $CHCl_3$ reacts with DMF to give VR**2** with elimination of HCl and CO_2. The generated VR**2** then reacts with the carboxylic acid to form an iminium salt that substitutes the iminium-Cl group. Subsequent nucleophilic substitution of the eliminated Cl^- with the carbonyl group provides the corresponding acyl chloride with regeneration of DMF. In support of this proposed mechanism,

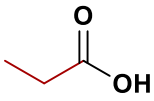
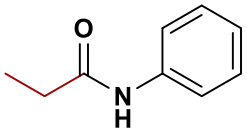
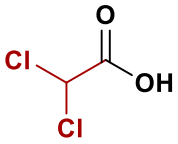
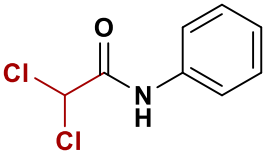
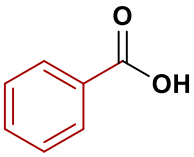
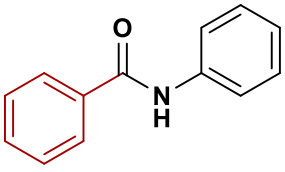
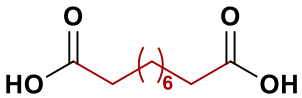
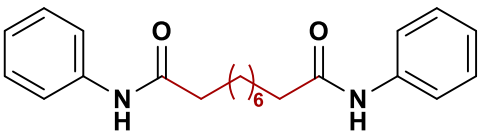


Scheme 3.5 (Top) A schematic illustration of the reaction mechanism expected for formation of acyl chloride from $CHCl_3$ and carboxylic acid in the presence of DMF upon photo-irradiation. (Bottom) A reaction mechanism proposed for the reaction of carboxylic acid and VR**2**.

Table 3.6 One-pot synthesis of amides with acyl chlorides prepared upon photo-irradiation of $CHCl_3$ solutions containing carboxylic acids.



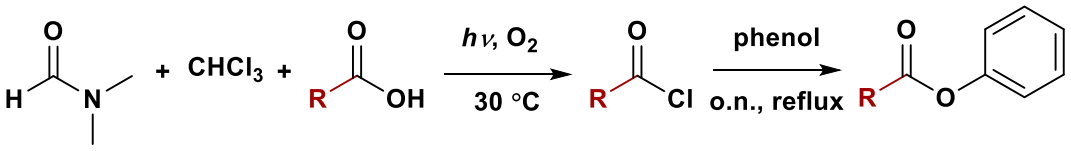
5

entry	RCOOH	product	yield (%)
1		 5a	63[a] 50[b]
2		 5b	93[a] 67[b]
3		 5c	99[a] 93[b]
4		 5d	93[b]

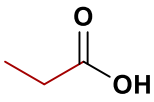
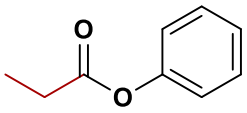
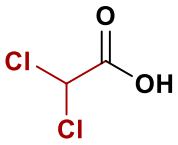
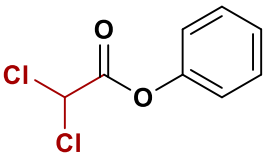
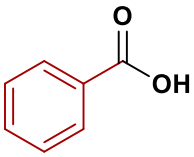
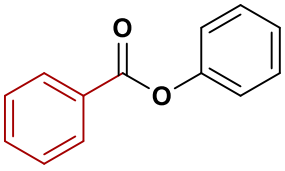
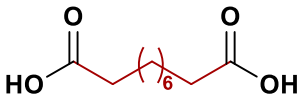
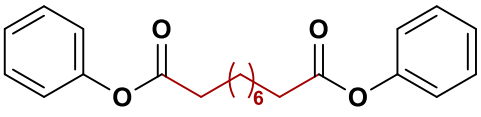
[a] ^{1}H NMR yield. [b] isolated yield.

the reaction of benzoic acid with a smaller amount of DMF (0.1 equiv.) was demonstrated. The reaction proceeded to give the acyl chloride quantitatively,

Table 3.7 One-pot synthesis of esters with acyl chlorides prepared upon photo-irradiation of $CHCl_3$ solutions containing carboxylic acids.



6

entry	RCOOH	product	yield (%)
1		 6a	60[a] 60[b]
2		 6b	55[a] 42[b]
3		 6c	73[a] 49[b]
4		 6d	98[a] 76[b]

[a] ^{1}H NMR yield. [b] isolated yield.

but was clearly decelerated compared to the case using 0.5 equiv. DMF, indicating that DMF acts as a catalyst in this reaction.

With the advantage of the photo-on-demand synthesis of acyl chlorides with a $CHCl_3$ solution containing a catalytic amount of DMF, the sample solution was further applied to the one-pot synthesis of amides and esters (Tables 3.6 and 3.7, respectively). When 2.0–5.0 equiv. amounts of aniline or phenol were added directly to the as-prepared sample solution containing the acyl chloride, the corresponding amides and esters were obtained in high yields. However, the yields of most of the esters were lower than the corresponding amides. This may be due to the different reactivities of aniline and phenol. Thermal decomposition and/or vaporization of the acyl chlorides may occur under reflux conditions for the longer reaction times required for synthesizing esters. Benzoic acid and sebacic acid having relatively high boiling points provided the corresponding esters in 73% and 98% yields, respectively.

3.3 Conclusions

In this chapter, the author found a novel in situ photo-on-demand synthesis of VRs with a $CHCl_3$ solution containing DMF or DMA. This procedure enables the synthesis of VRs easily as well as safely without highly toxic corrosive reagents such as $POCl_3$, $SOCl_2$, and $COCl_2$. The reaction generates a $CHCl_3$ solution containing VR without notable by-products simply by photo-irradiation under O_2 bubbling. Since the main by-products are gaseous HCl and CO_2, which are immediately discharged out of the system, VRs could be isolated readily as a crystalline solid capable of subjecting to X-ray crystallographic analysis.

Taking an advantage of $CHCl_3$, which plays dual roles as reagent and solvent, it enabled the one-pot syntheses of organic chemicals such as aldehydes, acyl chlorides, formates, ketones, esters, and amides. This photochemical reaction provides enormous advantages in terms of efficiency, safety, cost, and

environmental impact, and is expected to create much innovation in a variety of organic syntheses in both academia and industry.

3.4 Experimental Section

3.4.1 Materials

Unless otherwise noted, reagents and solvents were used as received from Kishida Chemical Co., Ltd. [dichloromethane (>98%), ethyl acetate (>99%) and *n*-hexane (>95.0%)], Nacalai Tesque, Inc. [thiophene (≥99%), anthracene (>96.0%), propionic acid (≥97.0%), 1,2-dichloroethane (≥99.5%)], Wako Pure Chemical Industries, Ltd. [Na_2SO_4 (99.0%), $NaHCO_3$ (99.5–100.3%), Na_2CO_3 (99.5%), NaOH (97.0%), *N*,*N*-dimethylformamide (>99.5%), chloroform (>99.7%), benzoic acid (>99.5%), 1-butanol (>99.0%), pyridine (>99.5%), phenol (>99.0%)], Tokyo Chemical Industry Co., Ltd. (TCI) [*N*,*N*-dimethylacetamide (>99.0%),1-methylpyrrole (>99.50%), furan (>99.0%), 2-methylfuran (>98.0%), 2-methylthiophene (>97.0%), 2,3-benzofuran (>99.0%), 1*H*-indole (>99.0%), 2,2-dichloroacetic acid (>98.0%), 3,3,3-trifluoropropanoic acid (>98.0%), 2-thiophenecarboxylic acid (>98.0%), 4-fluorobenzoic acid (>98.0%), sebacic acid (>98.0%), terephthalic acid (>99.0%), (–)-menthol (>99.0%), 1,6-hexanediol (>97.0%), aniline (>98.0%)], Sigma-Aldrich Co. LLC [1*H*-pyrrole (>98.0%)]. and Cambridge Isotope Laboratories, Inc. [$CDCl_3$ (D, 99.8%), DMSO-d_6 (D, 99.8%)]. For column chromatography, Wakogel (60N, particle size 38–100 μm, silica gel, irregular) was used. 5,5'-Dimethyldipyrromethane and 1,4-bis(3,4-diethyl-1*H*-pyrrol-2-yl)benzene were synthesized according to the literature methods.[22,23] All products synthesized in this study were unambiguously characterized by means of ^{1}H and ^{13}C NMR in reference to the previous studies and the Sigma-Aldrich FT-NMR Library (ver. 4.0.10).[24-48]

3.4.2 Measurements and Calculations

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE 400 spectrometer, where chemical shifts (δ in ppm) were determined with respect to tetramethylsilane as an internal standard. ^{19}F NMR spectra were recorded on Bruker AVANCE 400 spectrometer, where chemical shifts (δ in ppm) were determined with respect to hexafluorobenzene as an external standard. ^{1}H NMR yields were determined by using 1,2-dichloroethane, dichloromethane or *n*-hexane as internal standards. Fourier transform infrared spectroscopy (FT-IR) was recorded on a JASCO FT/IR 4200. Fourier transform mass spectrometry (FT-MS) was performed on a Thermo Fisher Scientific LTQ Orbitrap. The single-crystal X-ray diffraction data of single crystals were collected on a Bruker APEX II Ultra CCD diffractometer using MoKα radiation (λ = 0.71073 Å). The data were collected at 193 or 173 K and the structures were resolved by direct methods and refined by full-matrix least-squares on F2 (SHELXL97). The X-ray single-crystal structures of the Vilsmeier reagents reported in this study have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition numbers CCDC 2054184, *N*,*N*-dimethylchloroformiminium chloride (VR**2**); CCDC 2054219, 1-chloro-*N*,*N*-dimethylethaniminium chloride (VR**3**).

3.4.3 Synthesis

General procedure

One-pot synthesis of aldehydes. A cylindrical flask (ø42 mm × 120 mm) equipped with a low-pressure mercury lamp (SEN Light Co., UVL20PH-6, 20 W, ø24×120 mm) was charged with a 20 mL of $CHCl_3$ solution containing 20 mmol of *N*,*N*-dimethylformamide (DMF). The solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C with a water

bath for 2 h. An aromatic substrate was added to the sample solution, and the mixture was stirred for 0.5–20 h with or without heating of the sample solution. The resulting sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4, and evaporated to dryness. The corresponding aldehyde was obtained through silica gel column chromatography or washing with an appropriate solvent.

One-pot synthesis of ketones. A cylindrical flask equipped with a low-pressure mercury lamp was charged with a 20 mL of $CHCl_3$ solution containing 20 mmol of *N*,*N*-dimethylacetamide (DMA). The solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h to generate a yellow solid. $CHCl_3$ (8 mL) was added to dissolve the precipitates. An aromatic substrate was then added to the sample solution, and the mixture was stirred for 21–156 h at room temperature. The resulting sample solution was neutralized with an alkaline aqueous solution and extracted with CH_2Cl_2 (20 mL×3) or ethyl acetate (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4, and evaporated to dryness. The corresponding ketone was obtained through silica gel column chromatography.

One-pot synthesis of formates. A cylindrical flask equipped with a low-pressure mercury lamp was charged with a 20 mL of $CHCl_3$ solution containing 20 mmol of DMF. The solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. An aliphatic alcohol was then added to the sample solution, and the mixture was stirred at room temperature for 1 h. The resulting sample solution was neutralized with a saturated Na_2CO_3 aqueous

solution (30 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4, and evaporated to dryness. The corresponding formate was isolated through distillation.

One-pot synthesis of esters. A cylindrical flask equipped with a low-pressure mercury lamp was charged with a 20 mL of $CHCl_3$ solution containing 20 mmol of DMA. The solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h to generate a yellow solid. $CHCl_3$ (8 mL) was added to dissolve the precipitates. A mixture of alcohol and pyridine was then added to the sample solution, and stirred at 10–50 °C for 1 h. The resulting sample solution was neutralized with a NaOH aqueous solution (3 M, 30 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4, and evaporated to dryness. The corresponding ester was obtained through silica gel column chromatography.

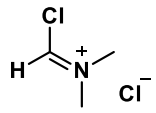
Synthesis of acyl chlorides. A cylindrical flask equipped with a low-pressure mercury lamp was charged with a 20 mL of $CHCl_3$ solution containing 5–20 mmol of DMF and 10 mmol of carboxylic acid. The solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3–6 h. The lamp was turned off, and the sample solution was stirred at 30–50 °C for 2 h. The corresponding acyl chloride was isolated through distillation.

One-pot synthesis of *N*-phenyl amides. A cylindrical flask equipped with a low-pressure mercury lamp was charged with a 20 mL of $CHCl_3$ solution containing 5–10 mmol of DMF and 10 mmol of carboxylic acid. The solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3.0–4.5 h. The lamp was turned off, and the sample solution was stirred at 30–50 °C for 2 h. Aniline (50 mmol) was then added slowly, and the sample solution

was stirred at room temperature for 1 h. The corresponding amide was obtained through silica gel column chromatography or washing with an appropriate solvent.

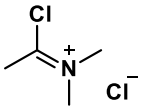
One-pot synthesis of phenyl ester. A cylindrical flask equipped with a low-pressure mercury lamp was charged with a 20 mL of $CHCl_3$ solution containing 5–10 mmol of DMF and 10 mmol of carboxylic acid. The solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3.0–4.5 h. The lamp was turned off, and the sample solution was stirred at 30–50 °C for 2 h. Phenol (20 mmol) disssolved in 2 mL of $CHCl_3$ was then added slowly and refluxed for overnight. The sample solution was evaporated to dryness, and washed with hot water (> 65 °C, 30 mL×7). The corresponding ester was obtained through silica gel column chromatography, recrystallization, or washing with an appropriate solvent.

Synthesis of *N*,*N*-dimethylchloroformiminium chloride (VR2)



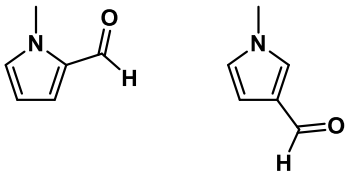
Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Vacuum distillation of the resulting sample with a glass tube oven provided *N*,*N*-dimethylchloroformiminium chloride (VR**2**) as a white crystalline solid in 69% yield (1.76 g, 13.9 mmol). ^{1}H NMR (400 MHz, CDCl3, 293 K): δ 3.96 (s, 6H, CH_3), 10.95 (s, 1H). ^{13}C NMR (100 MHz, CDCl3, 293 K): δ 166.1, 46.3.

Synthesis of 1-chloro-*N*,*N*-dimethylethaniminium chloride (VR3)



Chloroform (20 mL, 250 mmol) and DMA (1.85 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Vacuum distillation of the resulting sample with a glass tube oven provided *N*,*N*-dimethylchloroformiminium chloride (VR**3**) as a white crystalline solid in 66% yield (1.86 g, 13.2 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 3.26 (s, 6H, CH_3), 2.65 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 175.1, 38.7, 18.5.

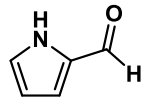
Synthesis of 1-methylpyrrole-2-carbaldehyde (1a) and 1-methylpyrrole-3-carbaldehyde (1a')



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 1-Methylpyrrole (0.89 mL, 10 mmol) was then added slowly at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 1 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts was dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 1-methylpyrrole-2-carbaldehyde (**1a**) and 1-

methylpyrrole-3-carbaldehyde (**1a'**) in 92% and 8% yields, respectively. It was then subjected to silica gel column chromatography (ethyl acetate/CH_2Cl_2, v/v=1:10) to afford **1a** and **1a'** as yellow liquids in 73% yield (0.80 g, 7.3 mmol) and 8% yield (0.09 g, 0.8 mmol), respectively. Their ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[24] 1-Methylpyrrole-2-carbaldehyde (**1a**): ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.55 (s, 1H, CHO), 6.91 (dd, J = 4.0, 1.6 Hz, 1H, CH_{Ar}), 6.88 (brs, 1H, CH_{Ar}), 6.22 (dd, J = 4.0, 2.4 Hz, 1H, CH_{Ar}), 3.96 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 179.6, 132.1, 132.0, 124.2, 109.5, 36.5. 1-Methylpyrrole-3-carbaldehyde (**1a'**): ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.73 (s, 1H, CHO), 7.24 (t, J = 1.6 Hz, 1H, CH_{Ar}), 6.64–6.62 (m, 2H, CH_{Ar}), 3.72 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 185.3, 129.8, 126.7, 124.4, 108.6, 36.7.

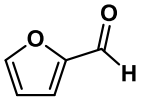
Synthesis of 1*H*-pyrrole-2-carbaldehyde (1b)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 1*H*-pyrrole (0.74 mL, 10 mmol) was added slowly at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 1 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^1H NMR spectroscopy revealed that the residue contains 1*H*-pyrrole-2-carbaldehyde (**1b**) in 82% yield. It was then subjected to silica gel column chromatography (ethyl acetate/CH_2Cl_2, v/v=1:10) to afford **1b** as a yellow liquid in 53% yield (0.51 g, 5.3 mmol). ^1H and

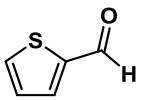
^{13}C NMR spectra are in agreement with those reported in the literature.[25] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.54 (s, 1H, CHO), 7.14–7.12 (m, 1H, CH_{Ar}), 7.00–6.98 (m, 1H, CH_{Ar}), 6.37–6.35 (m, 1H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 179.5, 132.8, 127.1, 122.0, 111.4.

Synthesis of furan-2-carbaldehyde (1c)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Furan (0.73 mL, 10 mmol) was then added slowly at 0 °C, and the sample solution was stirred at room temperature for 2.5 h. The sample solution was then neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains furan-2-carbaldehyde (**1c**) in 60% yield. It was then subjected to silica gel column chromatography (CH_2Cl_2) to afford **1c** as a light yellow liquid in 53% yield (0.51 g, 5.3 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[26] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.68 (s, 1H, CHO), 7.71–7.70 (m, 1H, CH_{Ar}), 7.27 (dd, J = 3.2, 0.8 Hz, 1H, CH_{Ar}), 6.62 (dd, J =3.2, 1.2 Hz, 1H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 177.9, 153.0, 148.1, 121.0, 112.6.

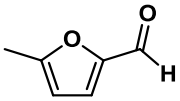
Synthesis of thiophene-2-carbaldehyde (1d)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a

cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Thiophene (0.79 mL, 10 mmol) was added slowly at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 6 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains thiophene-2-carbaldehyde (**1d**) in 38% yield. It was then subjected to silica gel column chromatography (CH_2Cl_2) to afford **1d** as a light yellow liquid in 23% yield (0.25 g, 2.25 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[27] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.95 (s, 1H, CHO), 7.80–7.77 (m, 2H, CH_{Ar}), 7.24 (dd, J = 4.8, 3.6 Hz, 1H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 183.1, 144.0, 136.4, 135.2, 128.4.

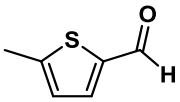
Synthesis of 5-methyl-2-furaldehyde (1e)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 2-Methylfuran (0.9 mL, 10 mmol) was then added slowly, and stirred for 1 h at 0 °C. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 5-methyl-2-furaldehyde (**1e**) in 79% yield. It was then subjected to silica gel column chromatography (CH_2Cl_2) to afford **1e** as a yellow

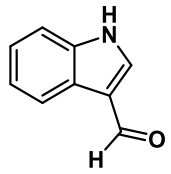
liquid in 76% yield (0.84 g, 7.6 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[28] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.52 (s, 1H, CHO), 7.17 (d, J = 3.6 Hz, 1H, CH_{Ar}), 6.24 (dd, J = 3.6, 0.8 Hz, 1H, CH_{Ar}), 2.43 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 176.9, 159.8, 151.9, 123.9, 109.5, 14.1.

Synthesis of 5-methylthiophene-2-carboxaldehyde (1f)



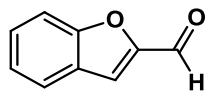
Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 2-Methylthiophene (0.97 mL, 10 mmol) was added slowly at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 0.5 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 5-methylthiophene-2-carboxaldehyde (**1f**) in 98% yield. It was then subjected to silica gel column chromatography (*n*-hexane/CH_2Cl_2, v/v=1:10) to afford **1f** as a light yellow liquid in 95% yield (1.2 g, 9.5 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[29] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.81 (s, 1H, CHO), 7.60 (d, J = 4.0 Hz, 1H, CH_{Ar}), 6.90–6.88 (m, 1H, CH_{Ar}), 2.58 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 182.7, 151.7, 142.0, 137.4, 127.1, 16.2.

Synthesis of 1*H*-indole-3-carbaldehyde (1g)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 1*H*-indole (1.17 g, 10 mmol) dissolved in 1 mL of DMF was added slowly at 0 °C, and stirred at room temperature for 18 h. The sample solution was then neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4. ^{1}H NMR spectroscopy revealed that the resulting sample solution contains 1*H*-indole-3-carbaldehyde (**1g**) in 86% yield. It was then evaporated to leave a brown solid. The residue was washed with CH_2Cl_2 to give **1g** as a light pink solid in 71% yield (1.03 g, 7.1 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[30] ^{1}H NMR (400 MHz, DMSO-d_6, 293 K): δ 12.16 (brs, 1H, NH), 9.96 (s, 1H, CHO), 8.30 (s, 1H, CH_{Ar}), 8.13 (d, J = 6.8 Hz, 1H, CH_{Ar}), 7.54 (d, J = 7.2 Hz, 1H, CH_{Ar}), 7.30–7.21 (m, 2H, CH_{Ar}). ^{13}C NMR (100 MHz, DMSO-d_6, 293 K): δ 184.9, 138.4, 137.0, 124.0, 123.4, 122.0, 120.7, 118.1, 112.3.

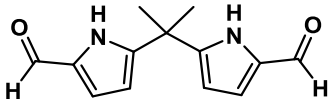
Synthesis of 2-benzofuran-carboxaldehyde (1h)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned

off, and the sample solution was stirred at 50 °C for 2 h. 2,3-Benzofuran (1.1 mL, 10 mmol) dissolved in 10 mL of DMF was added slowly at 0 °C, and then, the temperature was gradually elevated to 100 °C. The sample solution was stirred at 100 °C for 20 h. It was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was subjected to silica gel column chromatography (*n*-hexane/CH_2Cl_2, v/v=1:2) to afford 2-benzofuran-carboxaldehyde (**1h**) as a yellow liquid in 26% yield (0.39 g, 2.6 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[31] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.89 (s, 1H, CHO), 7.77 (d, *J* = 8.0 Hz, 1H, CH_{Ar}), 7.62 (d, *J* = 8.8 Hz, 1H, CH_{Ar}), 7.58 (d, *J* = 1.2 Hz, 1H, CH_{Ar}), 7.56–7.51 (m, 1H, CH_{Ar}), 7.38–7.7.34 (m, 1H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 179.8, 156.3, 152.7, 129.2, 126.7, 124.2, 123.7, 117.8, 112.7.

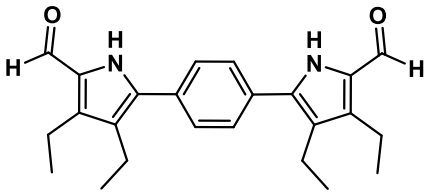
Synthesis of 5,5'-(propane-2,2-diyl)bis(1*H*-pyrrole-2-carbaldehyde) (1i)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 5,5'-Dimethyldipyrromethane (0.44 g, 2.5 mmol) dissolved in 5 mL of $CHCl_3$ was added slowly at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 1 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue

contains 5,5'-(propane-2,2-diyl)bis(1*H*-pyrrole-2-carbaldehyde) (**1i**) in 92% yield. It was then subjected to silica gel column chromatography (ethyl acetate/CH_2Cl_2, v/v=1:5) to afford **1i** as a yellowish white solid in 85% yield (0.49 g, 2.1 mmol). ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[32] ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 10.25 (brs, 2H, NH), 9.32 (s, 2H, CHO), 6.89 (dd, J = 3.6, 2.4 Hz, 2H, CH_{Ar}), 6.24 (dd, J = 4.0, 2.8 Hz, 2H, CH_{Ar}), 1.75 (s, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 179.4, 147.9, 132.6, 122.6, 108.3, 36.3, 28.3.

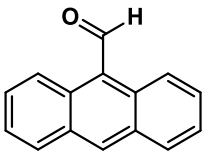
Synthesis of 5,5'-(1,4-phenylene)bis(3,4-diethyl-1*H*-pyrrole-2-carbaldehyde) (1j)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 1,4-Bis(3,4-diethyl-1*H*-pyrrol-2-yl)benzene (580 mg, 1.81 mmol) dissolved in 20 mL of $CHCl_3$ was added slowly at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 0.5 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. The crude product was recrystallized by CH_2Cl_2/MeOH, and dried under vacuum to give 5,5'-(1,4-phenylene)bis(3,4-diethyl-1*H*-pyrrole-2-carbaldehyde) (**1j**) as a light yellow solid in 66% yield (450 mg, 1.2 mmol). ^1H and ^{13}C NMR spectra are in agreement with those reported in

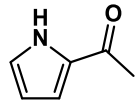
the literature.[33] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.66 (s, 2H, CHO), 9.18 (brs, 2H, NH), 7.58 (s, 4H, CH_{Ar}), 2.84 (q, J = 7.6 Hz, 4H, CH_2), 2.68 (q, J = 7.6 Hz, 4H, CH_2), 1.31 (t, J = 7.6 Hz, 6H, CH_3), 1.21 (t, J = 7.6 Hz, 6H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 177.2, 138.8, 135.7, 128.7, 127.7, 125.0, 17.7, 17.3, 17.1, 15.9.

Synthesis of anthracene-9-carbaldehyde (1k)



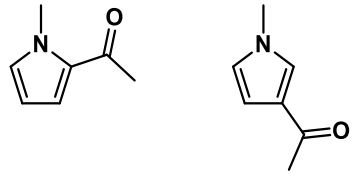
Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Anthracene (0.98 g, 5 mmol) dissolved in 30 mL of $CHCl_3$ was added slowly at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 16 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains anthracene-9-carbaldehyde (**1k**) in 50% yield. It was then subjected to silica gel column chromatography (*n*-hexane/CH_2Cl_2, v/v=1:1) to afford **1k** as a yellow solid in 50% yield (0.51 g, 2.5 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[34] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 11.55 (s, 1H, CHO), 9.02 (dd, J = 9.2, 0.8 Hz, 2H, CH_{Ar}), 8.73 (s, 1H, CH_{Ar}), 8.10 (d, J = 8.4 Hz, 2H, CH_{Ar}), 7.72–7.68 (m, 2H, CH_{Ar}), 7.59–7.55 (m, 2H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 193.0, 135.2, 132.1, 131.1, 129.3, 129.1, 125.7, 124.7, 123.5.

Synthesis of 2-acetyl pyrrole (2a)



Chloroform (20 mL, 250 mmol) and DMA (1.85 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h to generate a yellow solid. Then, $CHCl_3$ (8 mL) was added to dissolve the precipitates. 1*H*-pyrrole (0.74 mL, 10 mmol) was added slowly at 0 °C, and then, stirred at room temperature for 21 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with ethyl acetate (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 2-acetyl pyrrole (**2a**) in 28% yield. It was then subjected to silica gel column chromatography (ethyl acetate/CH_2Cl_2, v/v=1:10) to afford **2a** as a colorless crystal in 28% yield (0.30 g, 2.8 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[35] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.26 (brs, 1H, NH), 7.02 (td, J = 2.4, 1.2 Hz, 1H, CH_{Ar}), 6.92–6.90 (m, 1H, CH_{Ar}), 6.30–6.27 (m, 1H, CH_{Ar}), 2.43 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 188.1, 132.2, 124.7, 116.8, 110.6, 25.4.

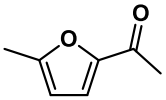
Synthesis of 2-acetyl-1-methylpyrrole (2b) and 3-acetyl-1-methylpyrrole (2b')



Chloroform (20 mL, 250 mmol) and DMA (1.85 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with

O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h to generate a yellow solid. Then, $CHCl_3$ (8 mL) was added to dissolve the precipitates. 1-Methylpyrrole (0.45 mL, 5 mmol) was added slowly at 0 °C, and then, stirred at room temperature for 156 h. The sample solution was then neutralized with a NaOH aqueous solution (3M, 30 mL) at 0 °C, and extracted with ethyl acetate (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 2-acetyl-1-methylpyrrole (**2b**) and 3-acetyl-1-methylpyrrole (**2b'**) in 53% and 47% yields, respectively. It was then subjected to silica gel column chromatography (ethyl acetate/CH_2Cl_2, v/v=15:100) to afford **2b** and **2b'** as yellow liquids in 31% yield (0.19 g, 1.5 mmol) and 37% yield (0.23 g, 1.9 mmol), respectively. Their ^{1}H and ^{13}C NMR spectra are in agreement with those recorded in the Sigma-Aldrich FT-NMR Library (ver. 4.0.10). 2-Acetyl-1-methylpyrrole (**2b**): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 6.95 (dd, J = 4.4, 2.0 Hz, 1H, CH_{Ar}), 6.79 (t, J = 2.0 Hz, 1H, CH_{Ar}), 6.13 (dd, J = 4.0, 2.4 Hz, 1H, CH_{Ar}), 3.94 (s, 3H, CH_3), 2.43 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 188.61, 130.92, 130.86, 119.71, 107.85, 37.61, 27.06. 3-Acetyl-1-methylpyrrole (**2b'**): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.23 (t, J = 1.6 Hz, 1H, CH_{Ar}), 6.58 (d, J = 2.0 Hz, 2H, CH_{Ar}), 3.69 (s, 3H, CH_3), 2.39 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 193.5, 126.8, 126.1, 123.3, 109.5, 36.6, 27.1.

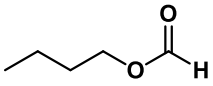
Synthesis of 2-acetyl-5-methyl furan (2c)



Chloroform (20 mL, 250 mmol) and DMA (1.85 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned

off, and the sample solution was stirred at 50 °C for 2 h to generate a yellow solid. Then, $CHCl_3$ (8 mL) was added to dissolve the precipitates. 2-Methylfuran (0.45 mL, 5 mmol) was added slowly at 0 °C, and then, stirred at room temperature for 144 h. The sample solution was neutralized with a NaOH aqueous solution (3M, 30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^1H NMR spectroscopy revealed that the residue contains 2-acetyl-5-methyl furan (**2c**) in 48% yield. It was then subjected to silica gel column chromatography (ethyl acetate/CH_2Cl_2, v/v=1:20) to afford **2c** as a yellow oil in 39% yield (0.24 g, 3.9 mmol). ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[36] ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.10 (d, J = 3.6 Hz, 1H, CH_{Ar}), 6.16 (dd, J = 3.6, 0.8 Hz, 1H, CH_{Ar}), 2.43 (s, 3H, CH_3), 2.40 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 186.1, 157.9, 151.5, 119.5, 109.0, 25.7, 14.1.

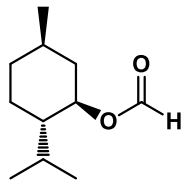
Synthesis of butyl formate (3a)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 1-Butanol (0.93 mL, 10 mmol) was added slowly at 0 °C, and then, stirred at room temperature for 1 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^1H NMR spectroscopy revealed that the residue contains butyl formate (**3a**) in 92% yield. Atmospheric distillation of the residue afforded **3a** as a colorless liquid in 87% yield (0.89 g, 8.7 mmol). ^1H and ^{13}C NMR spectra are in agreement with those

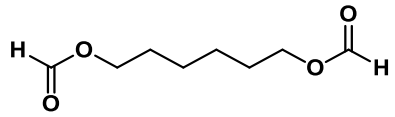
recorded in the Sigma-Aldrich FT-NMR Library (ver. 4.0.10). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.06 (s, 1H, CHO), 4.17 (t, J = 7.6 Hz, 2H, CH_2), 1.69–1.62 (m, 2H, CH_2), 1.45–1.36 (m, 2H, CH_2), 0.95 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 161.2, 63.8, 30.5, 19.1, 13.6.

Synthesis of (–)-menthyl formate (3b)



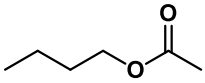
Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. (–)-Menthol (1.56 g, 10 mmol) dissolved in 2 mL of $CHCl_3$ was added slowly at 0 °C, and then, stirred at room temperature for 1 h. The sample solution was neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains (–)-menthyl formate **(3b)** in 99% yield. Vacuum distillation of the residue afforded **3b** as a colorless liquid in 70% yield (1.28 g, 7.0 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[37] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.08 (s, 1H, CHO), 4.81 (td, J = 10.8, 4.0 Hz, 1H, CH), 2.04–1.99 (m, 1H, CH), 1.96–1.85 (m, 1H, CH), 1.73–0.81 (m, 7H), 0.93 (d, J = 5.2 Hz, 3H, CH_3), 0.91 (d, J = 6.0 Hz, 3H, CH_3), 0.78 (d, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 160.9, 74.2, 46.8, 40.9, 34.1, 31.4, 26.0, 23.2, 22.0, 20.8, 16.1.

Synthesis of hexane-1,6-diyl diformate (3c)



Chloroform (20 mL, 250 mmol) and DMF (1.56 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. 1,6-Hexanediol (0.59 g, 5 mmol) dissolved in 15 mL of $CHCl_3$ was added slowly at 0 °C, and then, stirred at room temperature for 1 h. The sample solution was then neutralized with a saturated Na_2CO_3 aqueous solution (30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains hexane-1,6-diyl diformate (**3c**) in 96% yield. Vacuum distillation of the residue afforded **3c** as a colorless liquid in 44% yield (0.38 g, 2.2 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.06 (s, 1H, CHO), 4.17 (t, J = 6.4 Hz, 4H, CH_2), 1.73–1.64 (m, 4H, CH_2), 1.45–1.38 (m, 4H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 161.2, 63.8, 28.4, 25.5. IR (ATR): 2938, 2863, 1716, 1160 cm^{-1}. HRMS: m/z calcd for $C_8H_{14}O_4$+Na^+: 197.0784; $[M+Na]^+$ found: 197.0783.

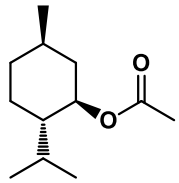
Synthesis of *n*-butyl acetate (3d)



Chloroform (20 mL, 250 mmol) and DMA (1.85 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h to generate a yellow solid. Then, $CHCl_3$ (8 mL) was added to dissolve the precipitates. A mixture of 1-butanol (0.46 mL, 5 mmol) and pyridine (0.48 mL, 6 mmol) was added slowly at

0 °C, and then, stirred at 10 °C for 1 h. The sample solution was neutralized with a NaOH aqueous solution (3M, 30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains *n*-butyl acetate (**3d**) in 80% yield. It was then subjected to silica gel column chromatography (CH_2Cl_2) to afford **3d** as a colorless liquid in 41% yield (0.24 g, 2.0 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those recorded in the Sigma-Aldrich FT-NMR Library (ver. 4.0.10). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.07 (t, J = 6.8 Hz, 2H, CH_2), 2.05 (s, 3H, CH_3), 1.65–1.55 (m, 2H, CH_2), 1.43–1.34 (m, 2H, CH_2), 0.94 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 171.3, 64.4, 30.7, 21.0, 19.1, 13.7.

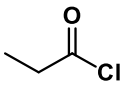
Synthesis of (–)-menthyl acetate (3e)



Chloroform (20 mL, 250 mmol) and DMA (1.85 mL, 20 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h to generate a yellow solid. Then, $CHCl_3$ (8 mL) was added to dissolve the precipitates. A 2 mL of $CHCl_3$ solution containing (–)-menthol (0.78 g, 5 mmol) and pyridine (1.6 mL, 20 mmol) was added slowly at 0 °C, and then, stirred at 50 °C for 1 h. The sample solution was neutralized with a NaOH aqueous solution (3M, 30 mL) at 0 °C, and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains (–)-menthyl acetate (**3e**) in 63% yield. It was then

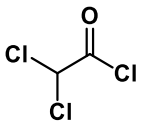
subjected to silica gel column chromatography (*n*-hexane/CH_2Cl_2, v/v=5:1) to afford **3e** as a colorless liquid in 51% yield (0.58 g, 2.5 mmol). ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[38] ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 4.68 (td, *J* = 10.8, 4.4 Hz, 1H, CH), 2.04 (s, 3H, CH_3), 2.02–1.96 (m, 1H, CH), 1.92–1.81 (m, 1H, CH), 1.71–0.81 (m, 7H), 0.91 (d, *J* = 2.0 Hz, 3H, CH_3), 0.89 (d, *J* = 2.8 Hz, 3H, CH_3), 0.77 (d, *J* = 6.8 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 170.7, 74.2, 47.0, 40.9, 34.3, 31.4, 26.3, 23.5, 22.0, 21.4, 20.8, 16.4.

Synthesis of propionyl chloride (4a)



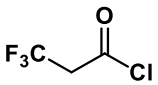
Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and propionic acid (0.67 mL, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 2 h. ^1H NMR spectroscopy revealed that the resulting sample solution contains propionyl chloride (**4a**) in 90% yield. Atmospheric distillation of the sample solution afforded **4a** as a colorless liquid in 86% yield (0.8 g, 8.6 mmol). ^1H and ^{13}C NMR spectra are in agreement with those recorded in the Sigma-Aldrich FT-NMR Library (ver. 4.0.10). ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 2.96 (q, *J* = 7.6 Hz, 2H, CH_2), 1.235 (t, *J* = 7.2 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 174.7, 40.9, 9.5.

Synthesis of 2,2-dichloroacetyl chloride (4b)



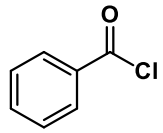
Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and 2,2-dichloroacetic acid (0.82 mL, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3.5 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 2 h. ^{1}H NMR spectroscopy revealed that the resulting sample solution contains 2,2-dichloroacetyl chloride (**4b**) in 99% yield. Atmospheric distillation of the sample solution afforded **4b** as a colorless liquid in 7% yield (0.11 g, 0.7 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those recorded in the Spectral Database for Organic Compounds (SDBS).[39] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 6.12 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 165.5, 70.1.

Synthesis of 3,3,3-trifluoropropanoyl chloride (4c)



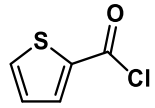
Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and 3,3,3-trifluoropropanoic acid (0.88 mL, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 2 h. ^{1}H NMR spectroscopy revealed that the resulting sample solution contains 3,3,3-trifluoropropanoyl chloride (**4c**) in 99% yield. Atmospheric distillation of the sample solution afforded **4c** as a colorless liquid in 66% yield (0.96 g, 6.6 mmol). ^{1}H and 19F NMR spectra are in agreement with those reported in the literature.[40] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 3.77 (q, J = 9.2 Hz, 2H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 164.2, 123.0 (d), 50.3 (q). ^{19}F NMR (376 MHz, $CDCl_3$, 293 K): δ –64.15, –64.12, –64.10.

Synthesis of benzyl chloride (4d)



Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and benzoic acid (1.28 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. ^{1}H NMR spectroscopy revealed that the resulting sample solution contains benzyl chloride (**4d**) in 99% yield. Vacuum distillation of the sample solution afforded **4d** as a colorless liquid in 83% yield (1.17 g, 8.3 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[41] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.14 (dd, J = 8.4, 1.2 Hz, 2H, CH_{Ar}), 7.69 (t, J = 7.6 Hz, 1H, CH_{Ar}), 7.52 (t, J = 8.0 Hz, 2H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 168.4, 135.3, 133.3, 131.4, 129.0.

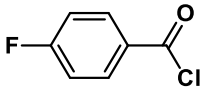
Synthesis of 2-thiophenecarbonyl chloride (4e)



Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and 2-thiophenecarboxylic acid (1.28 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. ^{1}H NMR spectroscopy revealed that the resulting sample solution contains 2-thiophenecarbonyl chloride (**4e**) in 93% yield. Vacuum distillation of the sample solution afforded **4e** as a colorless liquid in 50% yield (0.73 g, 5 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those recorded in the Spectral Database for Organic Compounds (SDBS).[42] ^{1}H NMR

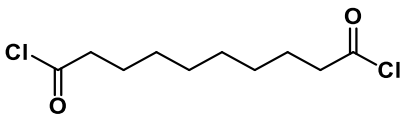
(400 MHz, $CDCl_3$, 293 K): δ 7.99 (dd, J = 4.0, 1.2 Hz, 1H, CH_{Ar}), 7.84 (dd, J = 5.2, 1.6 Hz, 1H, CH_{Ar}), 7.21 (dd, J = 4.8, 4.0 Hz, 1H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 159.7, 138.0, 137.7, 137.4, 128.7.

Synthesis of 4-fluorobenzoyl chloride (4f)



Chloroform (30 mL, 250 mmol), DMF (0.78 mL, 10 mmol), and 4-fluorobenzoic acid (1.4 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3.5 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. ^1H NMR spectroscopy revealed that the resulting sample solution contains 4-fluorobenzoyl chloride (**4f**) in 99% yield. Vacuum distillation of the sample solution afforded **4f** as a colorless liquid in 58% yield (0.92 g, 5.8 mmol). ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[41] ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.19–8.14 (m, 2H, CH_{Ar}), 7.22–7.17 (m, 2H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 168.4, 167.0 (d), 134.3 (d), 129.6 (d). ^{19}F NMR (376 MHz, $CDCl_3$, 293 K): δ –100.82, –100.80, –100.79, –100.78, –100.77, –100.76, –100.74.

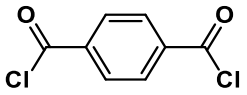
Synthesis of sebacoyl chloride (4g)



Chloroform (20 mL, 250 mmol), DMF (0.78 mL, 10 mmol), and sebacic acid (2.02 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 4.5 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. ^1H NMR spectroscopy revealed that the resulting sample solution contains

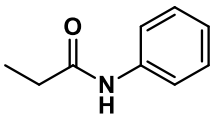
sebacoyl chloride (**4g**) in 99% yield. Vacuum distillation of the sample solution afforded **4g** as a colorless liquid in 44% yield (1.05 g, 4.4 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those recorded in the Spectral Database for Organic Compounds (SDBS).[43] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 2.89 (t, J = 7.6 Hz, 4H, CH_2), 1.74–1.67 (m, 4H), 1.37–1.30 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 173.8, 47.0, 28.8, 28.3, 25.0.

Synthesis of terephthaloyl dichloride (4h)



Chloroform (30 mL, 250 mmol), DMF (1.56 mL, 20 mmol), and terephthalic acid (1.66 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 6 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. ^{1}H NMR spectroscopy revealed that the resulting sample solution contains terephthaloyl dichloride (**4h**) in 82% yield. Vacuum distillation of the sample solution afforded **4h** as a colorless liquid in 79% yield (1.6 g, 7.9 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[44] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.26 (s, 4H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 167.5, 138.3, 131.4.

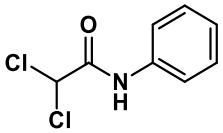
Synthesis of *N*-phenylpropionamide (5a)



Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and propionic acid (0.67 mL, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at

30 °C for 2 h. Aniline (4.6 mL, 50 mmol) was added slowly at 0 °C, and then, stirred at room temperature for 1 h. The sample solution was washed with water (30 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains *N*-phenyl propionamide (**5a**) in 63% yield. It was then subjected to silica gel column chromatography (*n*-hexane/CH_2Cl_2, v/v=1:2) to afford **5a** as a yellow solid in 50% yield (1.2 g, 8.1 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those reported in the literature.[45] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.52 (d, J = 8.0 Hz, 2H, CH_{Ar}), 7.32 (t, J = 7.6 Hz, 2H, CH_{Ar}), 7.10 (t, J = 7.2 Hz, 1H, CH_{Ar}), 2.43 (q, J = 7.6 Hz, 2H, CH_2), 1.26 (t, J = 7.6 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 171.9, 137.9, 129.0, 124.2, 119.7, 30.8, 9.7.

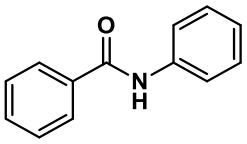
Synthesis of 2,2-dichloro-*N*-phenylacetamide (5b)



Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and 2,2-dichloroacetic acid (0.82 mL, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3.5 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 2 h. Aniline (4.6 mL, 50 mmol) was added slowly at 0 °C, and then, stirred at room temperature for 1 h. The sample solution was washed with water (30 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts was dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 2,2-dichloro-*N*-phenylacetamide (**5b**) in 93% yield. It was then subjected to silica gel column chromatography (CH_2Cl_2) to afford **5b** as a yellow solid in 67% yield (1.36 g, 6.7 mmol). ^{1}H and

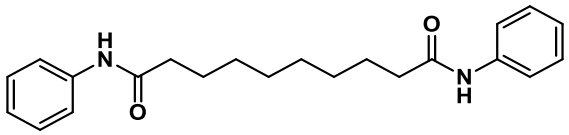
^{13}C NMR spectra are in agreement with those reported in the literature.[46] ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.09 (brs, 1H, NH), 7.57 (d, J = 7.6 Hz, 2H, CH_{Ar}), 7.39 (t, J = 7.2 Hz, 2H, CH_{Ar}), 7.21 (t, J = 7.6 Hz, 1H, CH_{Ar}), 6.04 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 161.7, 136.2, 129.2, 125.7, 120.2, 66.9.

Synthesis of *N*-phenylbenzamide (5c)



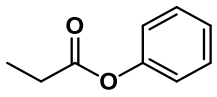
Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and benzoic acid (1.28 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Aniline (4.6 mL, 50 mmol) was added slowly at 0 °C, and then, stirred at room temperature for 1 h. The sample solution was washed with water (30 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic extracts were dried over anhydrous Na_2SO_4. ^{1}H NMR spectroscopy revealed that the sample solution contains *N*-phenylbenzamide (**5c**) in 99% yield. It was then evaporated to leave an orange solid. The residue was washed with a 20: 1 mixture solution of *n*-hexane and CH_2Cl_2 to afford **5c** as a yellow solid in 93% yield (1.84 g, 9.3 mmol). ^{1}H and ^{13}C NMR spectra are in agreement with those recorded in the Sigma-Aldrich FT-NMR Library (ver. 4.0.10). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.89 (d, J = 7.2 Hz, 2H, CH_{Ar}), 7.79 (brs, 1H, NH), 7.66 (d, J = 7.6 Hz, 2H, CH_{Ar}), 7.58–7.49 (m, 3H, CH_{Ar}), 7.39 (t, J = 7.2 Hz, 2H, CH_{Ar}), 7.16 (t, J = 7.6 Hz, 2H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 165.7, 137.9, 135.0, 131.9, 129.1, 128.8, 127.0, 124.6, 120.2.

Synthesis of N^1,N^{10}-diphenyldecanediamide (5d)



Chloroform (20 mL, 250 mmol), DMF (0.78 mL, 10 mmol), and sebacic acid (2.02 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 4.5 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Aniline (4.6 mL, 50 mmol) was added slowly at 0 °C, and stirred at room temperature for 1 h to give a precipitate. It was then collected through filtration, and washed with methanol to give N^1,N^{10}-diphenyldecanediamide (**5d**) as a white solid in 93% yield (3.29 g, 9.3 mmol). ^{1}H NMR (400 MHz, DMSO-d_6, 293 K): δ 9.83 (brs, 2H, NH), 7.59 (d, J = 7.6 Hz, 4H, CH_{Ar}), 7.27 (t, J = 7.2 Hz, 4H, CH_{Ar}), 7.01 (t, J = 7.6 Hz, 2H, CH_{Ar}), 2.86 (t, J = 7.2 Hz, 4H, CH_2), 1.60–1.57 (m, 4H, CH_2), 1.30 (m, 8H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6, 293 K): δ 171.1, 139.2, 122.8, 118.9, 36.3, 28.6, 28.6, 25.0. IR (ATR): 3310, 2928, 2851, 1655, 1597, 1534, 1442, 755, 712, 687. cm^{-1}. HRMS: m/z calcd for $C_{22}H_{28}N_2O_2$+H$^+$: 353.2224; [M+H]$^+$ found: 353.2216.

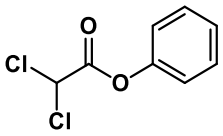
Synthesis of phenyl propionate (6a)



Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and propionic acid (0.67 mL, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 2 h. Phenol (1.88 g, 20 mmol) dissolved in 2 mL of $CHCl_3$ was added slowly at 0 °C, and then, refluxed for overnight. ^{1}H NMR spectroscopy revealed

that the sample solution contains phenyl propionate (**6a**) in 60% yield. It was then evaporated to dryness, and washed with hot water (> 65 °C, 30 mL×7). The organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was subjected to silica gel column chromatography (CH_2Cl_2) to afford **6a** as a colorless liquid in 60% yield (0.91 g, 6.0 mmol). ^1H and ^{13}C NMR spectra are in agreement with those recorded in the Spectral Database for Organic Compounds (SDBS).[47] ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.37 (t, J = 7.6 Hz, 2H, CH_{Ar}), 7.22 (t, J = 7.2 Hz, 1H, CH_{Ar}), 7.09 (d, J = 8.0 Hz, 2H, CH_{Ar}), 2.62 (q, J = 7.2 Hz, 2H, CH_2), 1.27 (t, J = 7.6 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 172.9, 150.8, 129.4, 125.7, 121.5, 27.8, 9.1.

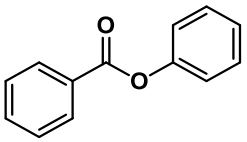
Synthesis of phenyl 2,2-dichloroacetate (6b)



Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and 2,2-dichloroacetic acid (0.82 mL, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3.5 h. The lamp was turned off, and the sample solution was stirred at 30 °C for 2 h. Phenol (1.88 g, 20 mmol) dissolved in 2 mL of $CHCl_3$ was added slowly at 0 °C, and then, refluxed for overnight. ^1H NMR spectroscopy revealed that the sample solution contains phenyl 2,2-dichloroacetate (**6b**) in 55% yield. It was then evaporated to dryness, and washed with hot water (> 65 °C, 30 mL×7). The organic layer was dried over anhydrous Na_2SO_4, and evaporated to dryness. The residue was subjected to silica gel column chromatography (*n*-hexane/CH_2Cl_2, v/v=1:1) to afford **6b** as a crystalline white solid in 42% yield. ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[46] ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.43 (t, J = 7.6 Hz, 2H, CH_{Ar}), 7.30 (t, J = 7.6

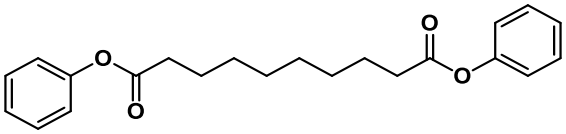
Hz, 1H, CH_{Ar}), 7.19 (d, *J* = 8.4 Hz, 2H, CH_{Ar}), 6.16 (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 163.0, 150.1, 129.7, 126.8, 120.7, 64.2.

Synthesis of phenyl benzoate (6c)



Chloroform (20 mL, 250 mmol), DMF (0.4 mL, 5 mmol), and benzoic acid (1.28 g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 3 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Phenol (1.88 g, 20 mmol) dissolved in 2 mL of $CHCl_3$ was added slowly at 0 °C, and then, refluxed for overnight. ^1H NMR spectroscopy revealed that the sample solution contains phenyl benzoate (**6c**) in 73% yield. It was then evaporated to dryness, and washed with hot water (> 65 °C, 30 mL×7) to leave a yellow solid. It was further recrystallized with methanol/CH_2Cl_2 to afford **6c** as a colorless crystal in 49% yield (0.97 g, 4.9 mmol). ^1H and ^{13}C NMR spectra are in agreement with those reported in the literature.[48] ^1H NMR (400 MHz, $CDCl_3$, 293 K): δ 8.22 (d, *J* = 8.4 Hz, 2H, CH_{Ar}), 7.64 (tt, *J* = 7.2, 1.6 Hz, 1H, CH_{Ar}), 7.52 (t, *J* = 7.2 Hz, 2H, CH_{Ar}), 7.44 (t, *J* = 7.2 Hz, 2H, CH_{Ar}), 7.28 (t, *J* = 7.6 Hz, 1H, CH_{Ar}), 7.23 (d, *J* = 8.4 Hz, 2H, CH_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 165.2, 151.0, 133.6, 130.2, 129.6, 129.5, 128.6, 125.9, 121.7.

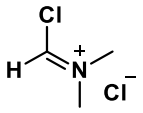
Synthesis of diphenyl sebacate (6d)



Chloroform (20 mL, 250 mmol), DMF (0.78 mL, 10 mmol), and sebacic acid (2.02

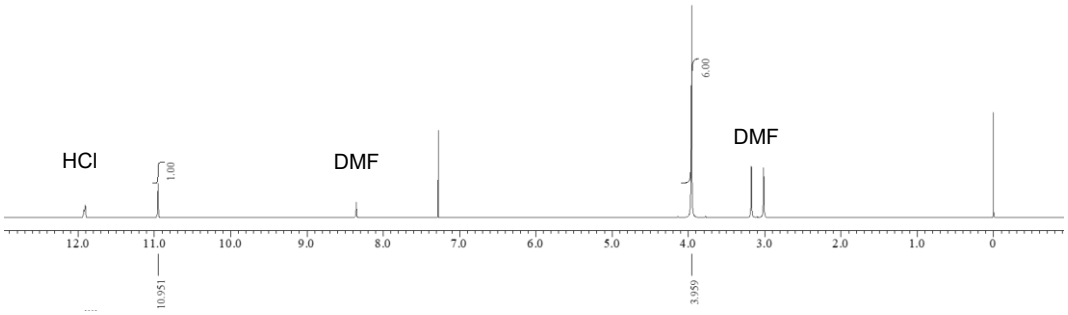
g, 10 mmol) were mixed in a cylindrical flask. The sample solution was vigorously stirred upon bubbling with O_2 (25 mL/min) under exposure to the light at 30 °C for 4.5 h. The lamp was turned off, and the sample solution was stirred at 50 °C for 2 h. Phenol (1.88 g, 20 mmol) dissolved in 2 mL of $CHCl_3$ was added slowly at 0 °C, and then, refluxed for overnight. ^{1}H NMR spectroscopy revealed that the sample solution contains diphenyl sebacate (**6d**) in 98% yield. It was then evaporated to dryness, and washed with hot water (> 65 °C, 30 mL×7) to leave a yellow solid. It was further washed with methanol to afford **6d** as a white solid in 76% yield (2.68 g, 7.6 mmol). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 7.37 (t, J = 8.0 Hz, 4H, CH_{Ar}), 7.22 (t, J = 7.2 Hz, 2H, CH_{Ar}), 7.08 (d, J = 8.0 Hz, 4H, CH_{Ar}), 2.56 (t, J = 7.2 Hz, 4H, CH_2), 1.80–1.72 (m, 4H, CH_2), 1.45–1.40 (m, 8H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, 293 K): δ 172.3, 150.7, 129.4, 125.7, 121.6, 34.7, 29.1, 29.0, 24.9. IR (ATR): 2930, 2852, 1743, 1590, 1483, 1360, 1288, 1194, 1130, 763, 711, 689 cm^{-1}. HRMS: m/z calcd for $C_{22}H_{26}O_4$+H^+: 355.1904; $[M+H]^+$ found: 355.1904.

3.4.4 ^{1}H and ^{13}C NMR spectra of products



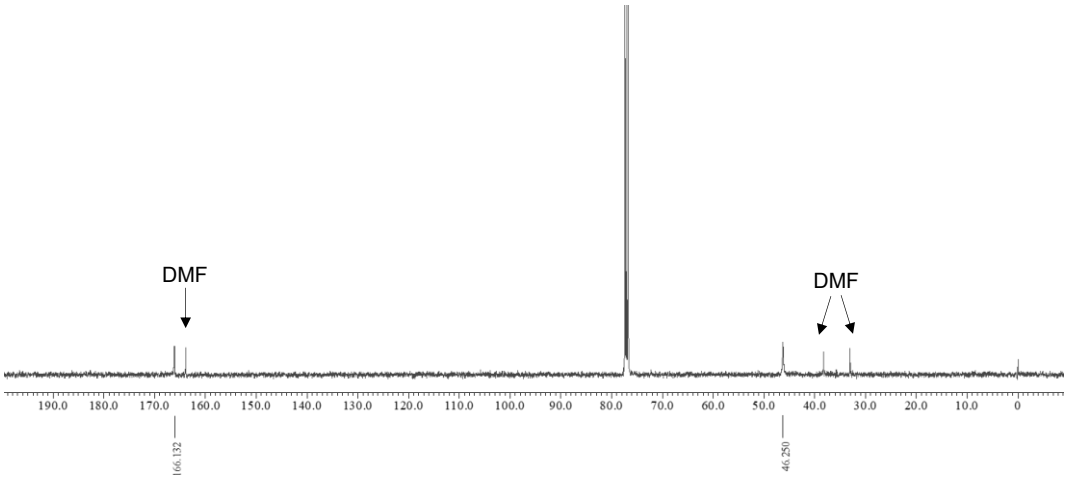
N,*N*-dimethylchloroformiminium chloride (VR**2**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

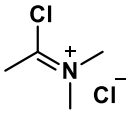


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

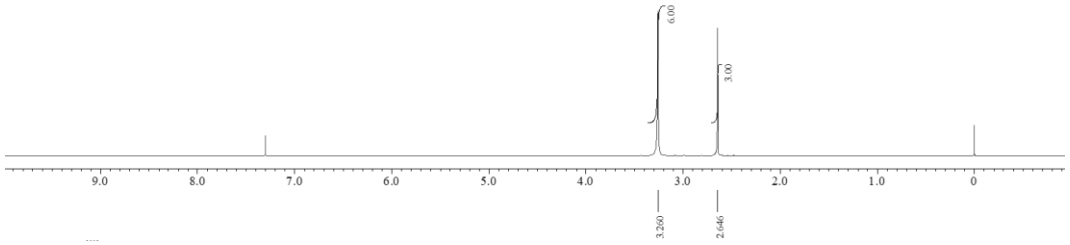


δ / ppm



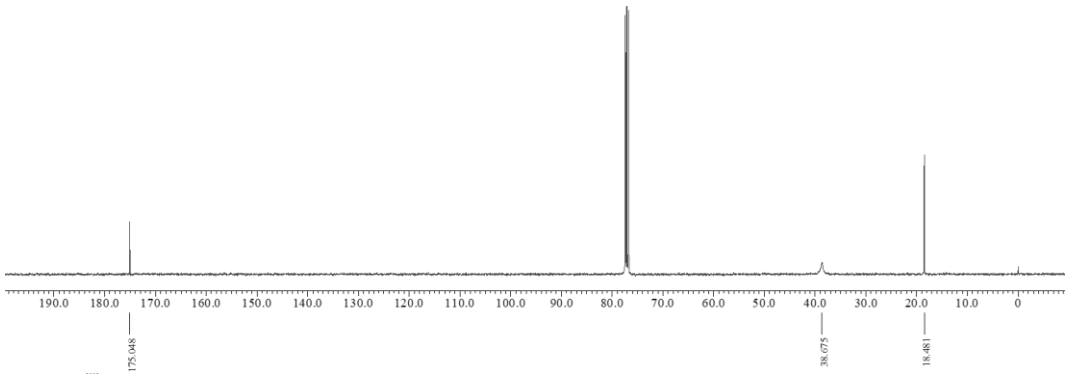
1-chloro-*N*,*N*-dimethylethaniminium chloride (VR**3**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

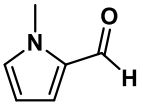


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

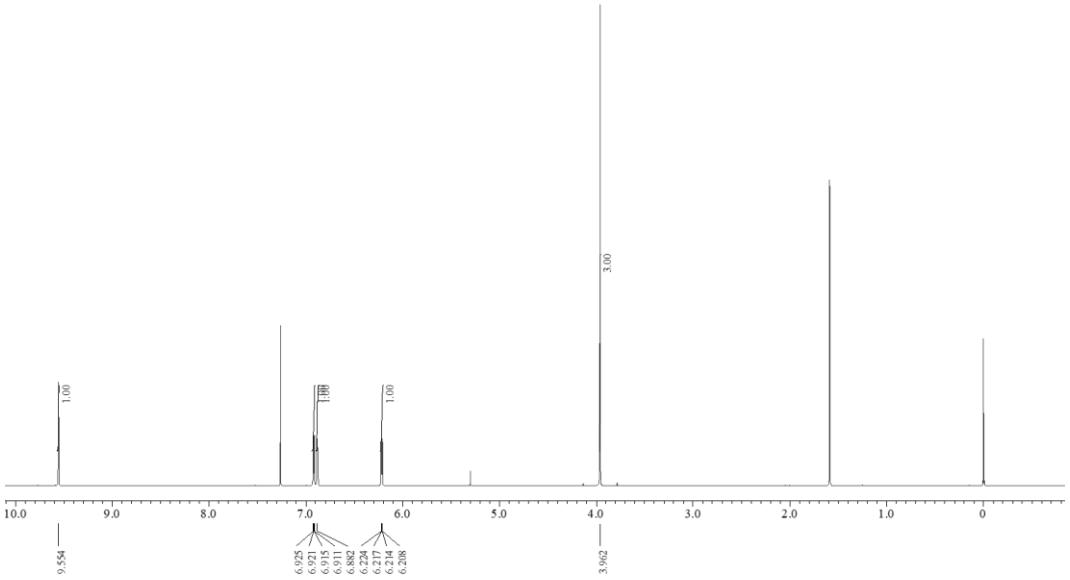


δ / ppm



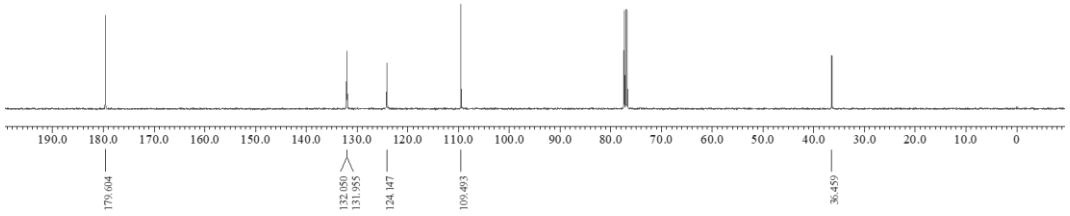
1-methylpyrrole-2-carbaldehyde (**1a**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

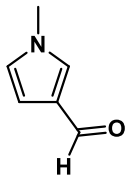


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K).

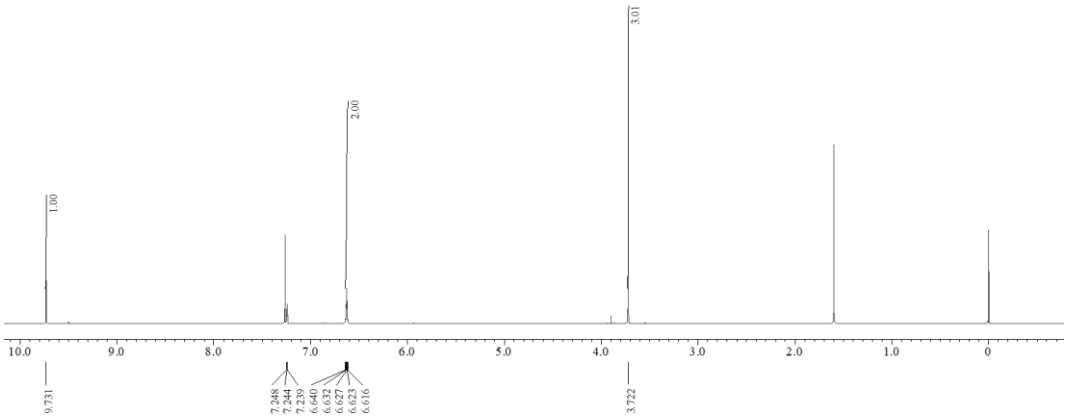


δ / ppm



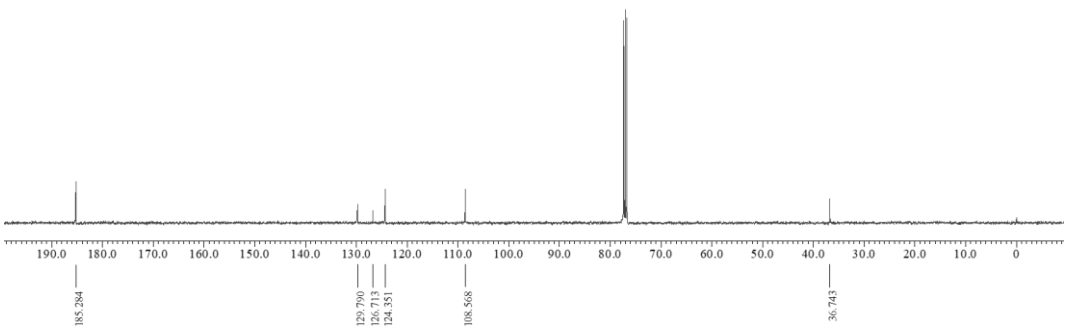
1-methylpyrrole-3-carbaldehyde (**1a'**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

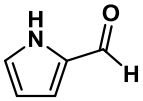


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K).

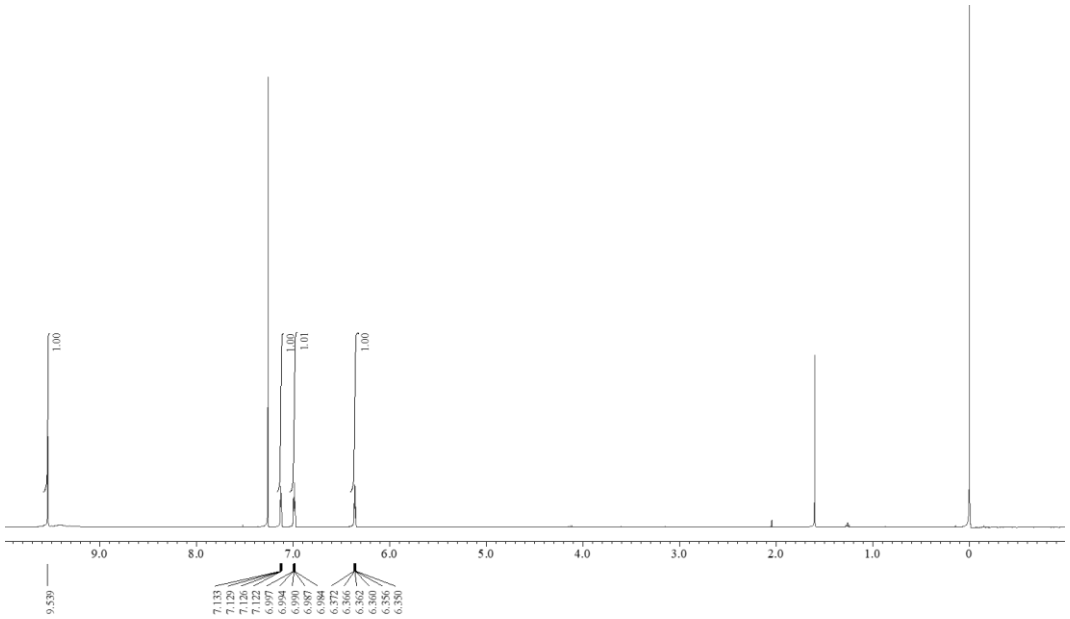


δ / ppm



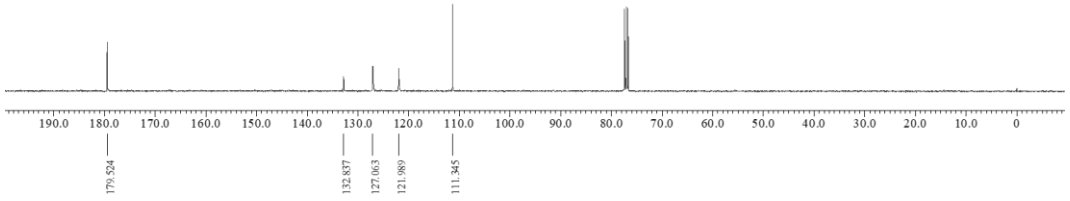
1*H*-pyrrole-2-carbaldehyde (**1b**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

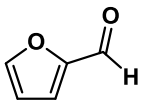


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

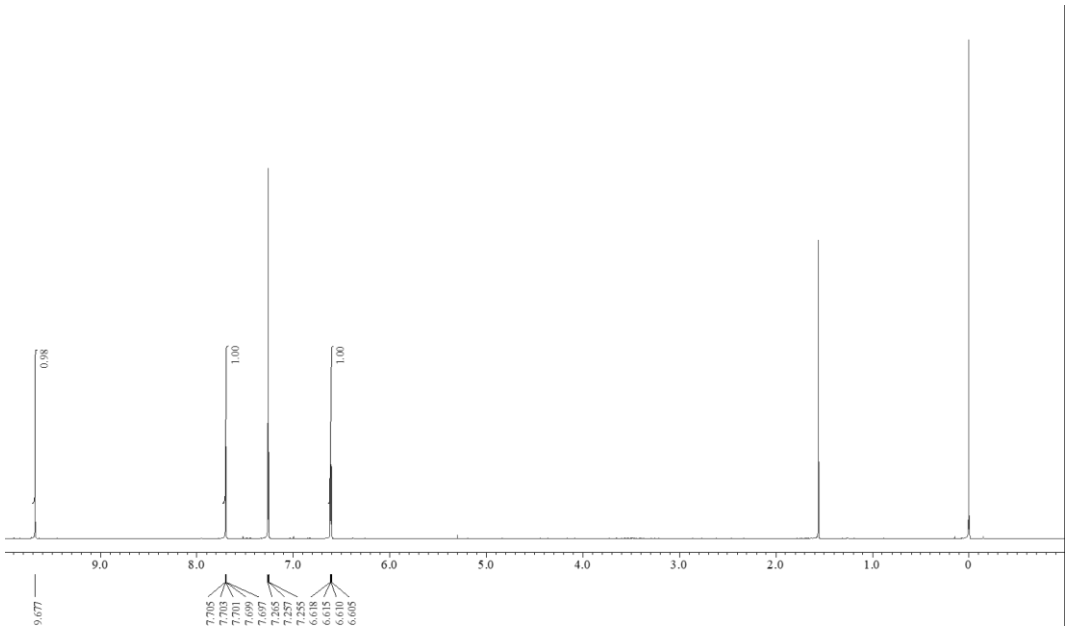


δ / ppm



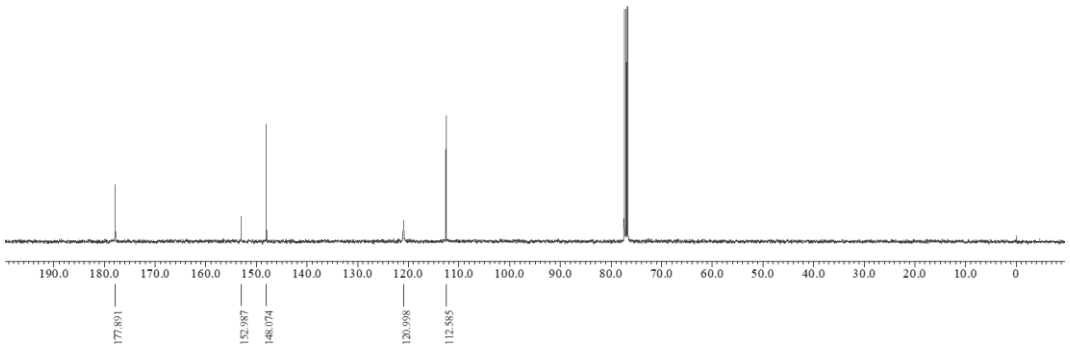
furan-2-carbaldehyde (**1c**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

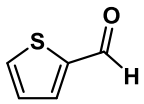


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

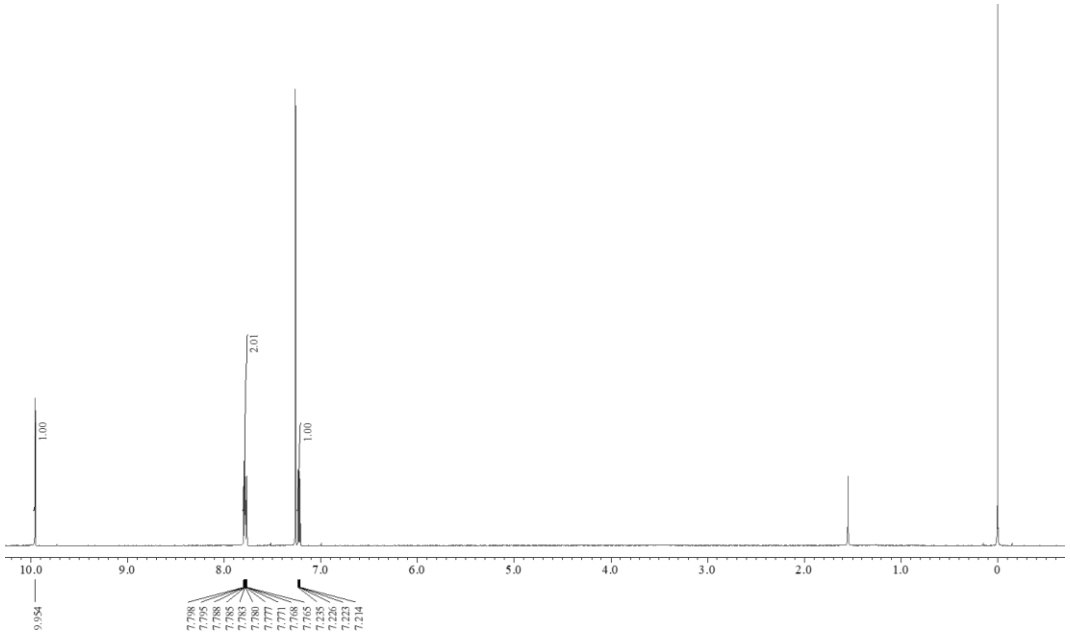


δ / ppm



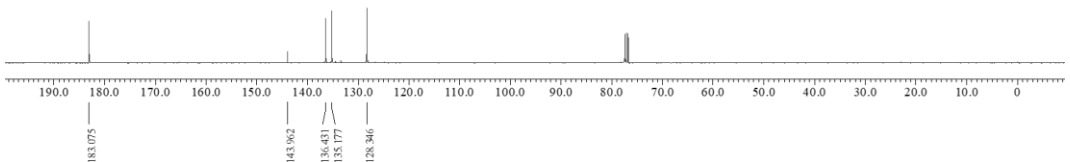
thiophene-2-carbaldehyde (**1d**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

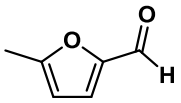


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

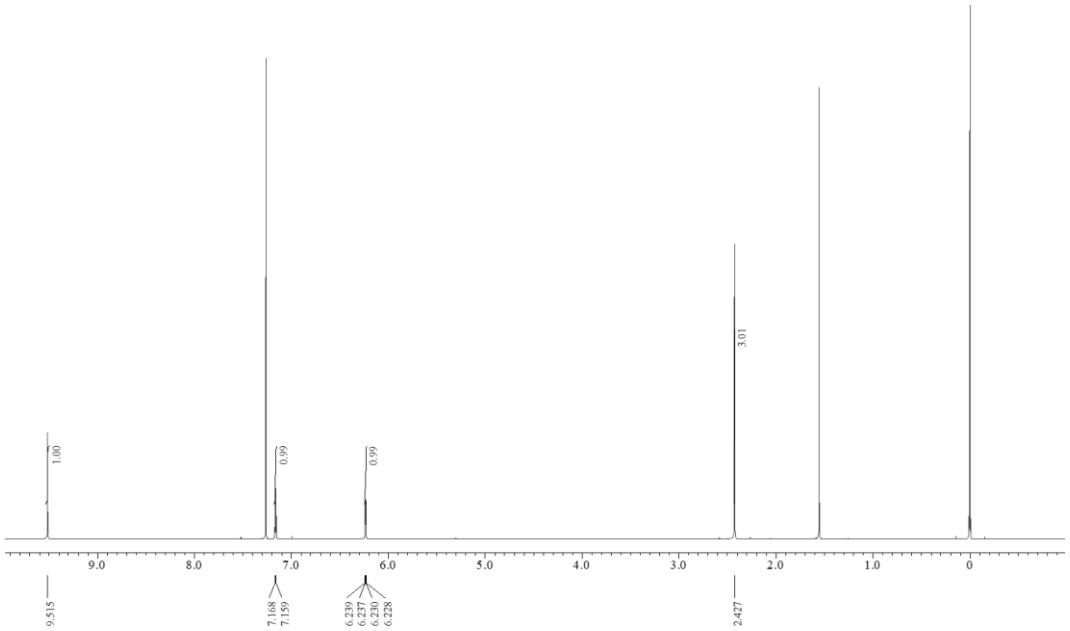


δ / ppm



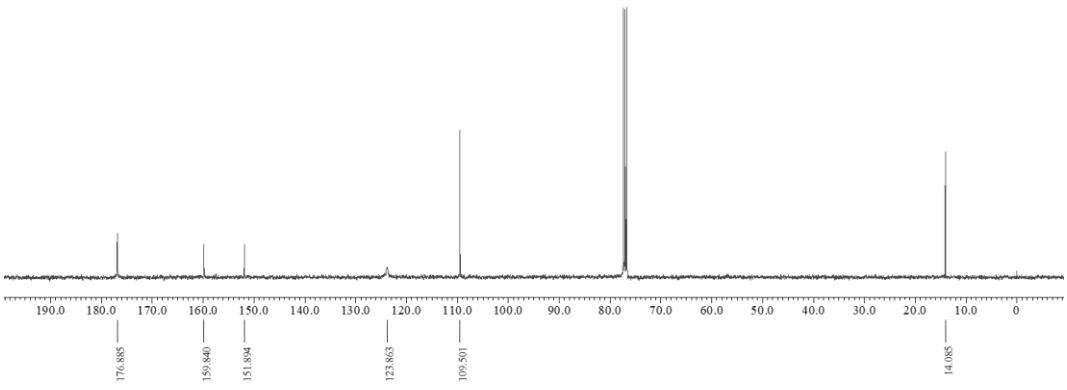
5-methyl-2-furaldehyde (**1e**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

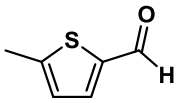


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

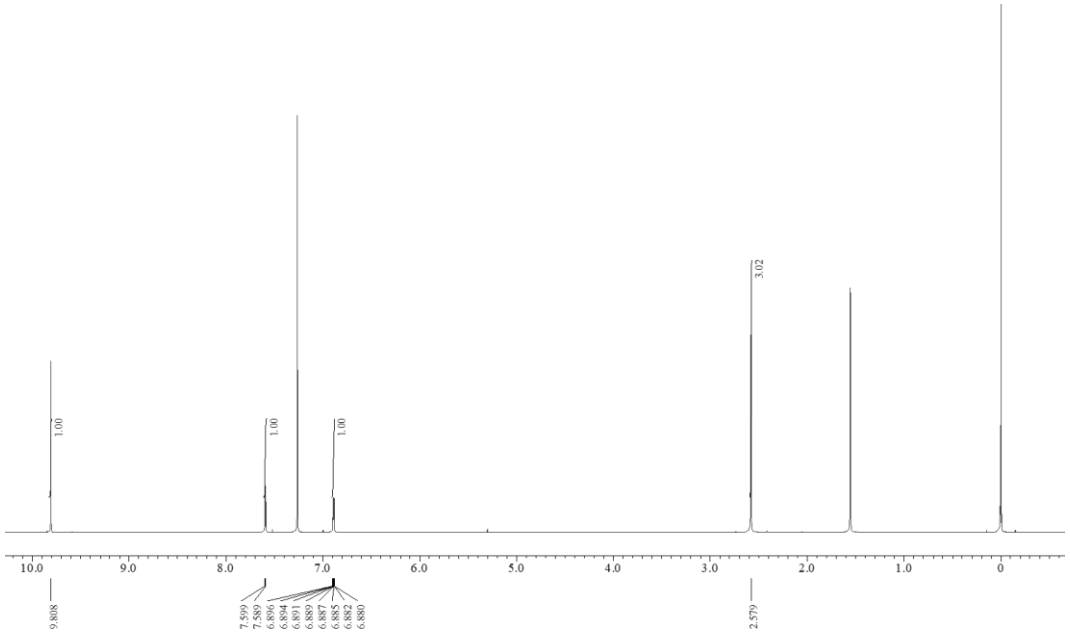


δ / ppm



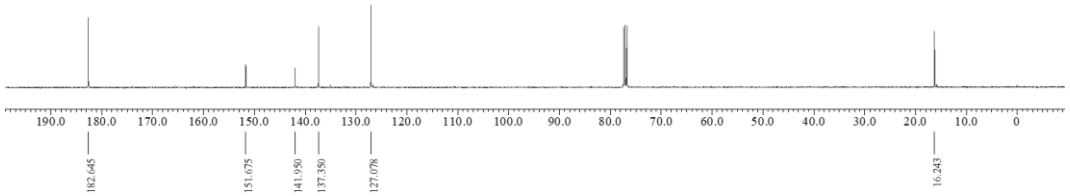
5-methylthiophene-2-carboxaldehyde (**1f**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

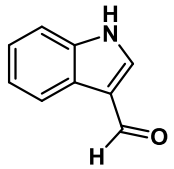


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

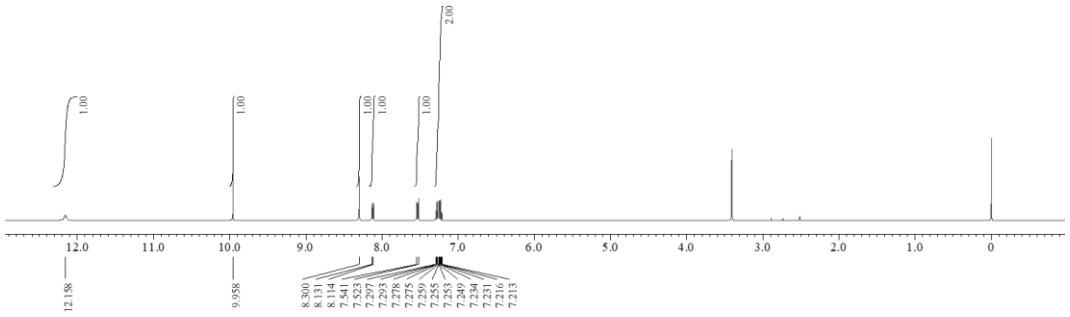


δ / ppm



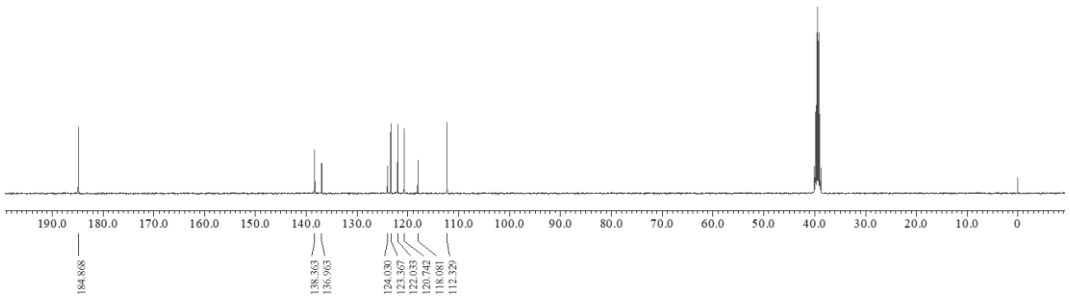
1*H*-indole-3-carbaldehyde (**1g**)

^{1}H NMR (400 MHz, DMSO-d_6, 293 K)

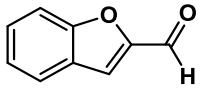


δ / ppm

^{13}C NMR (100 MHz, DMSO-d_6, 293 K)

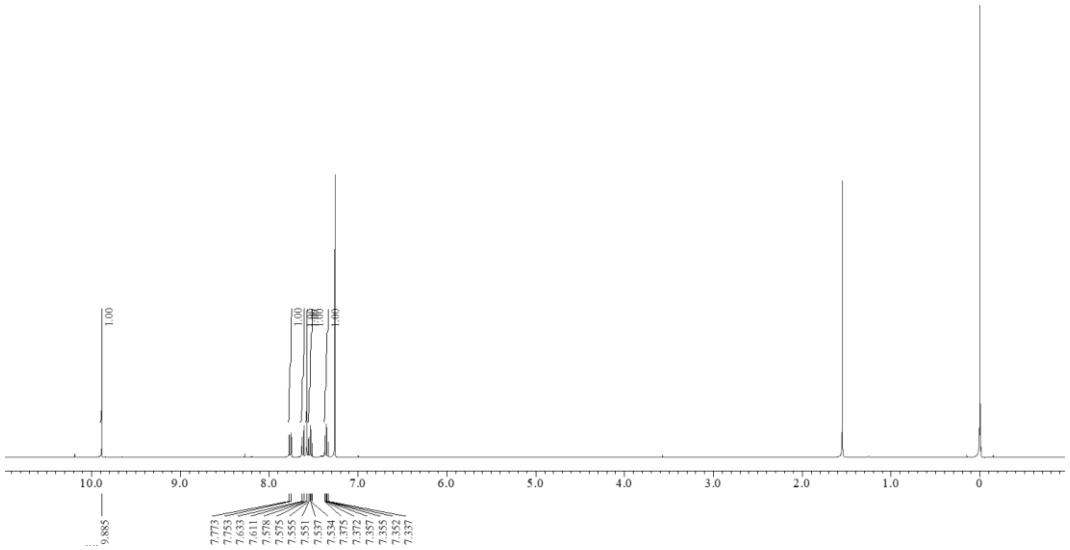


δ / ppm



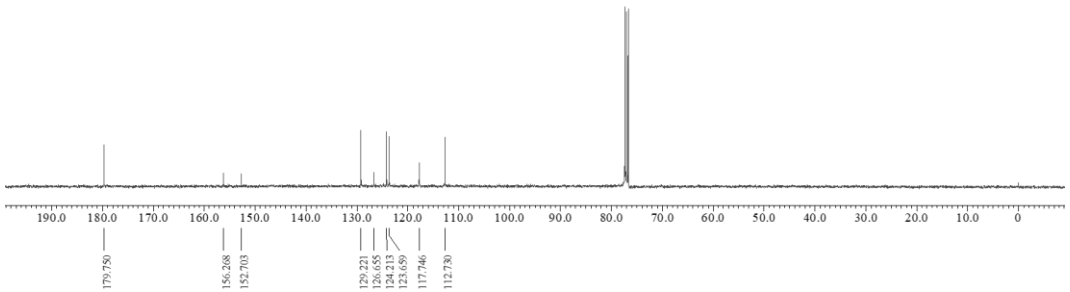
2-benzofuran-carboxaldehyde (**1h**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

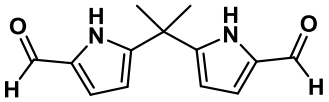


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

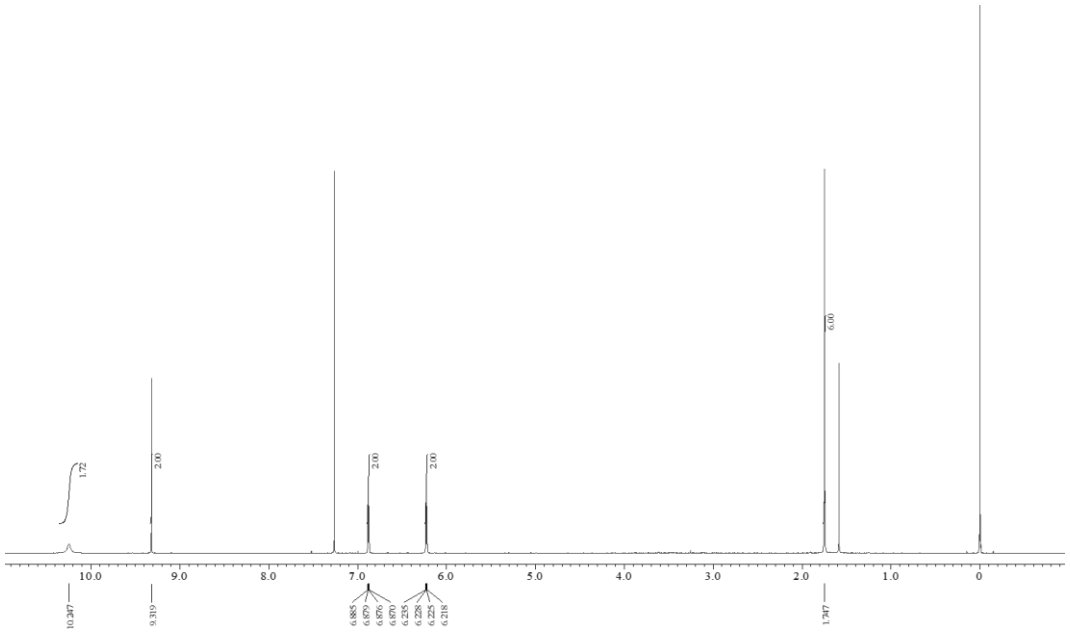


δ / ppm



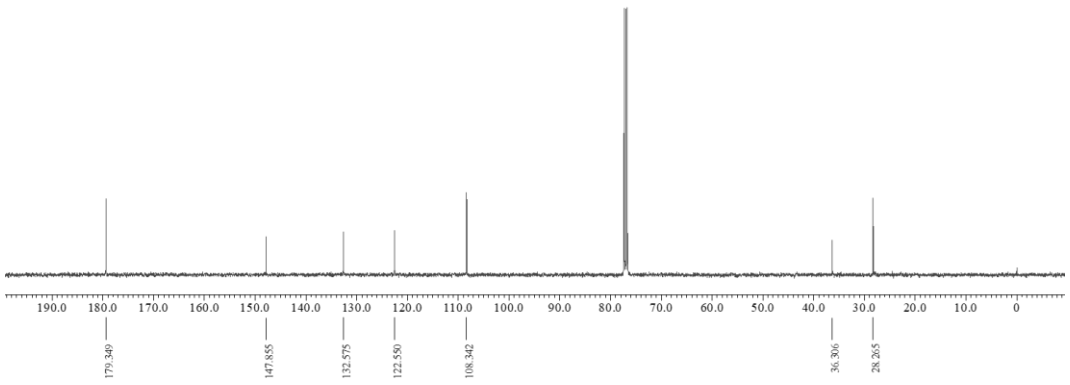
5,5'-(propane-2,2-diyl)bis(1*H*-pyrrole-2-carbaldehyde) (**1i**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

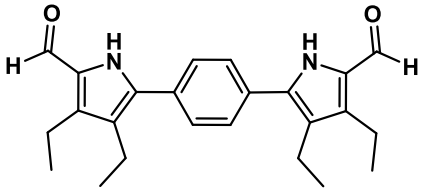


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

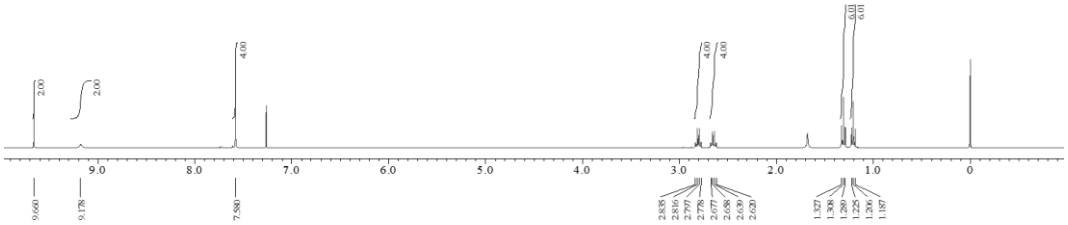


δ / ppm



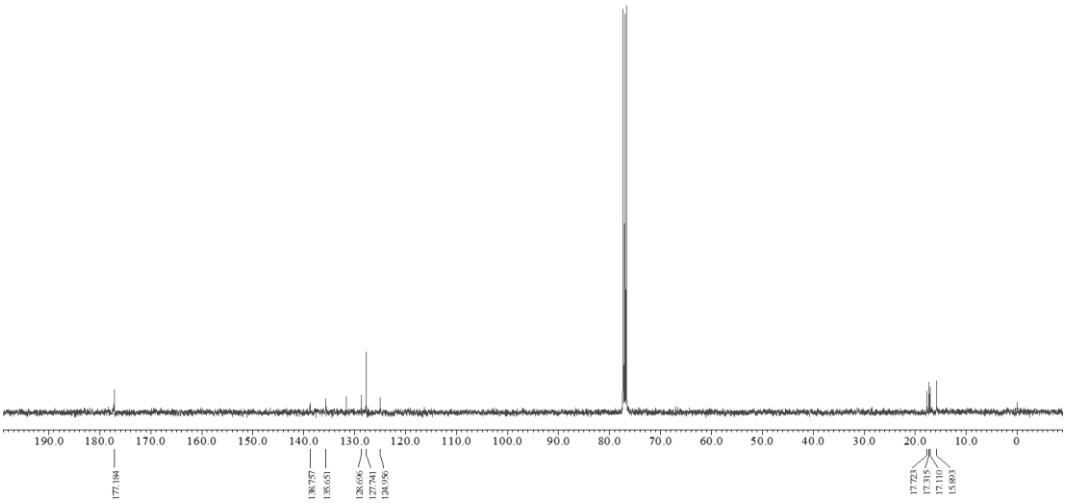
5,5'-(1,4-phenylene)bis(3,4-diethyl-1*H*-pyrrole-2-carbaldehyde) (**1j**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

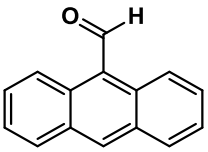


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

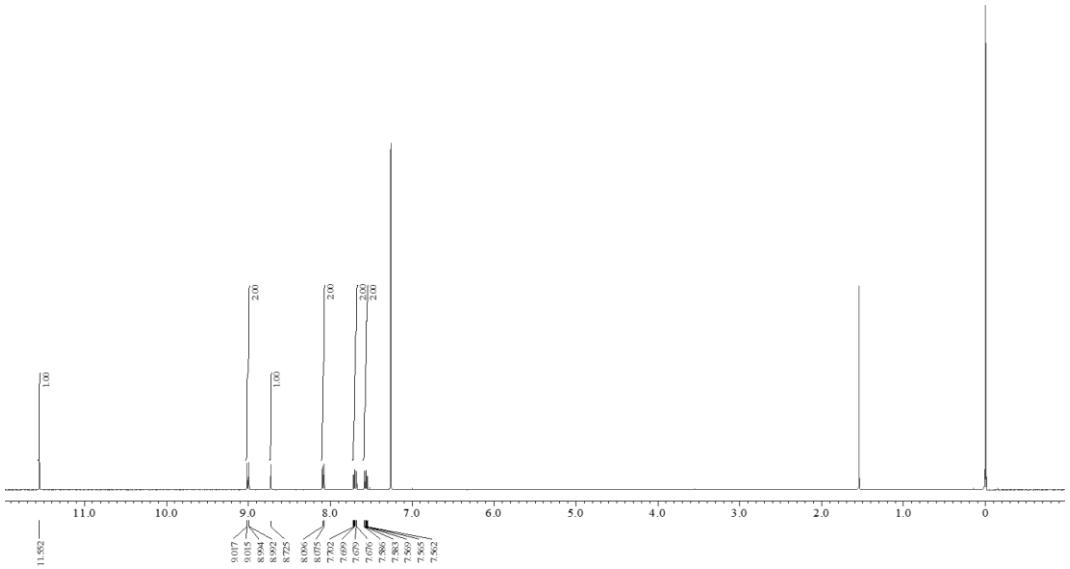


δ / ppm



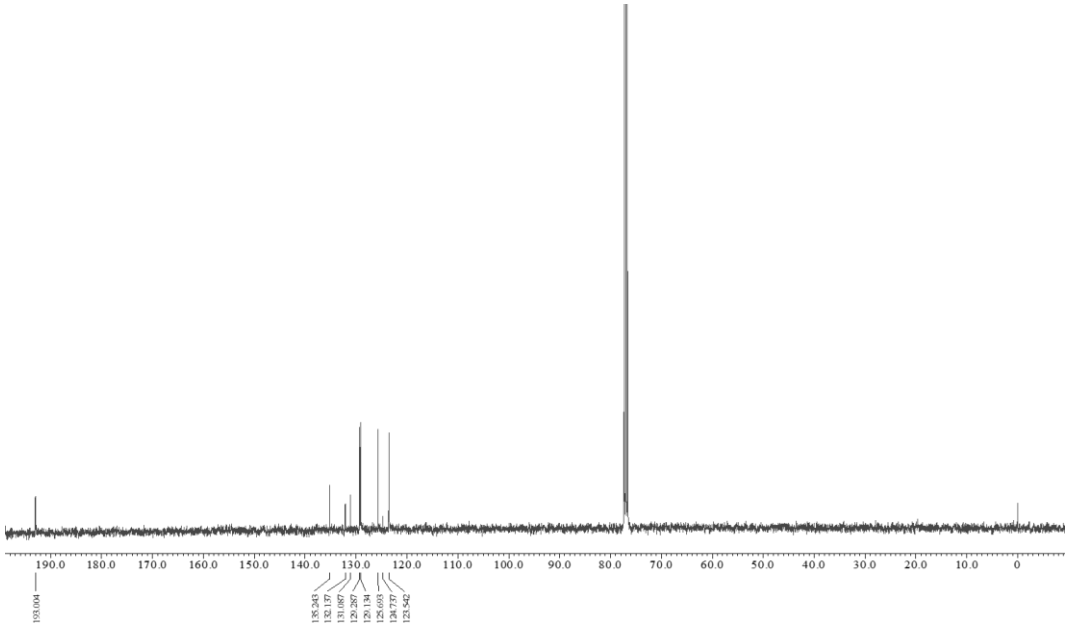
anthracene-9-carbaldehyde (**1k**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

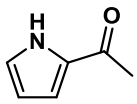


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

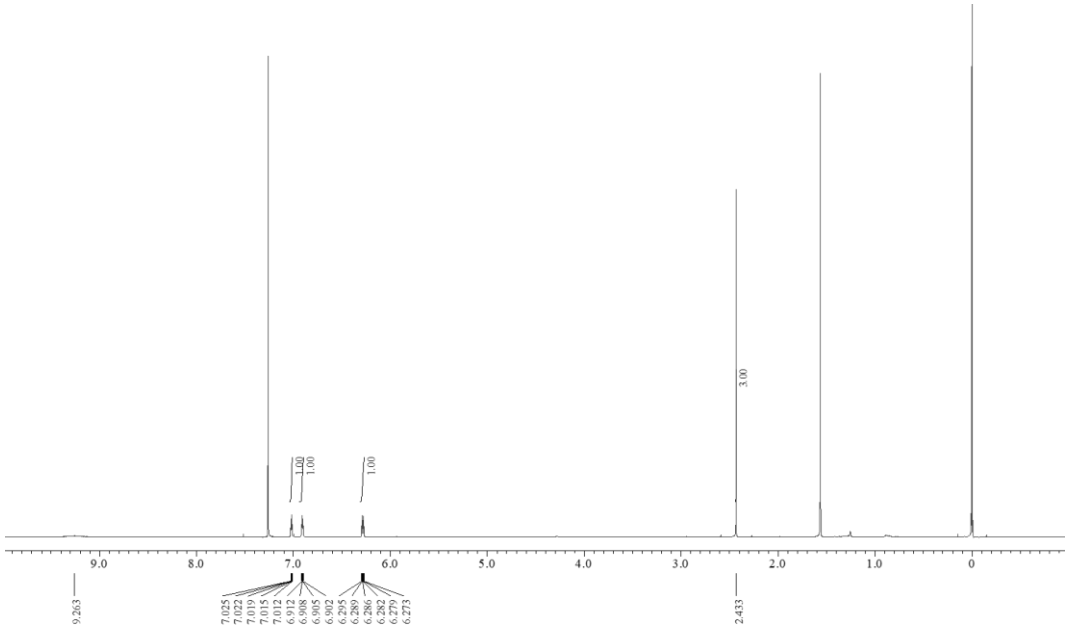


δ / ppm



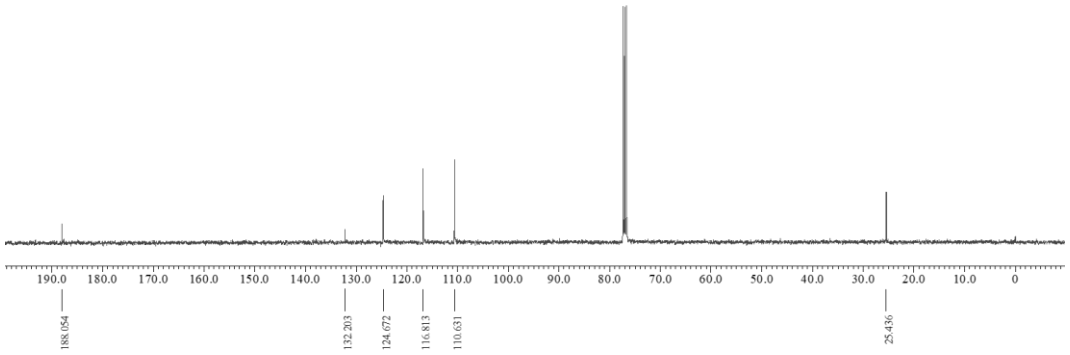
2-acetyl pyrrole (**2a**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

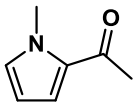


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

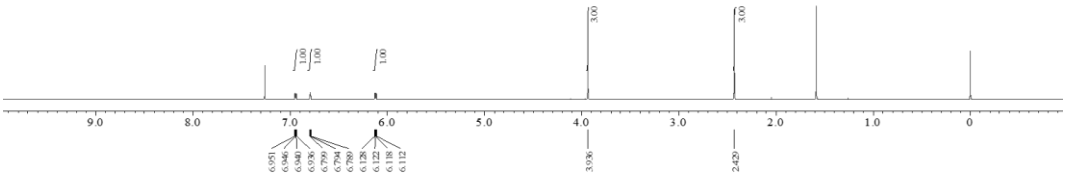


δ / ppm



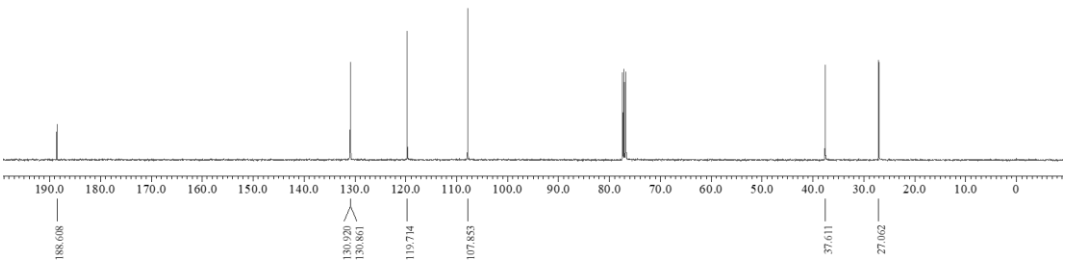
2-acetyl-1-methylpyrrole (**2b**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

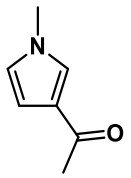


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K).

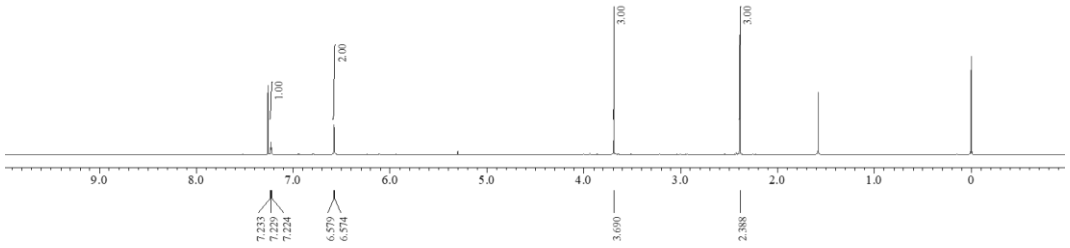


δ / ppm



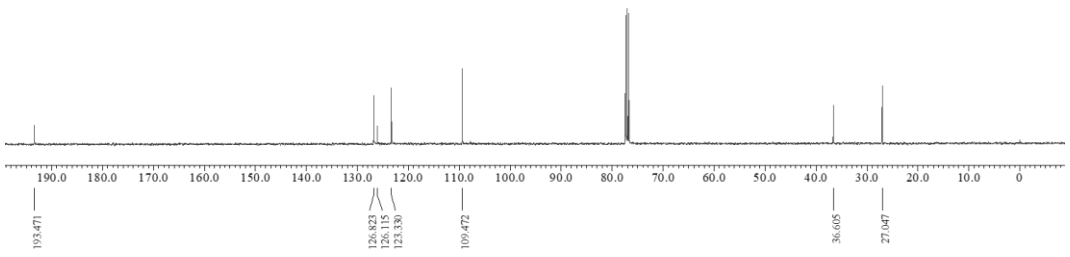
3-acetyl-1-methylpyrrole (**2b'**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

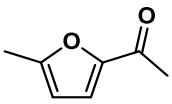


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

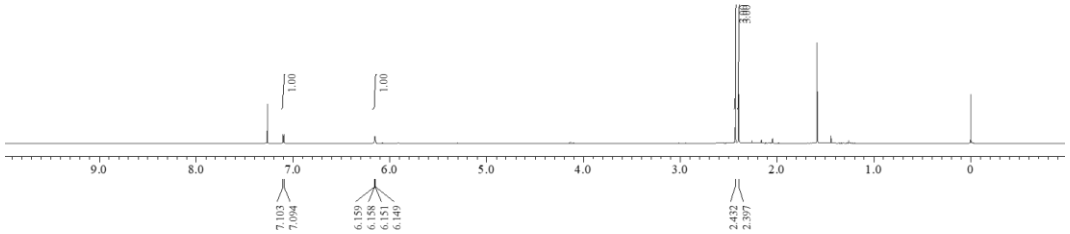


δ / ppm



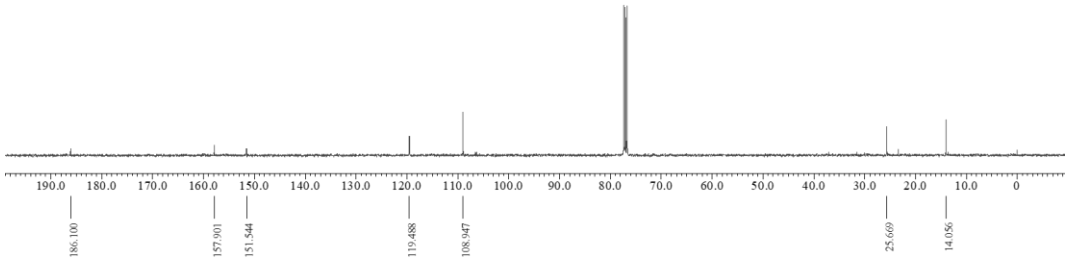
2-acetyl-5-methyl furan (**2c**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

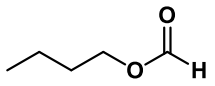


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

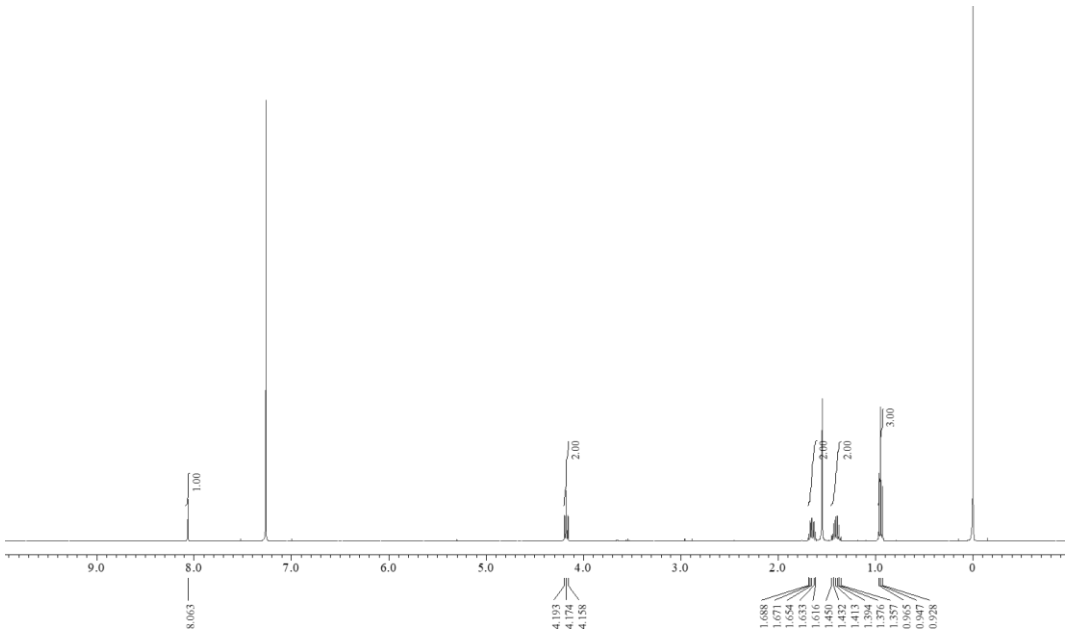


δ / ppm



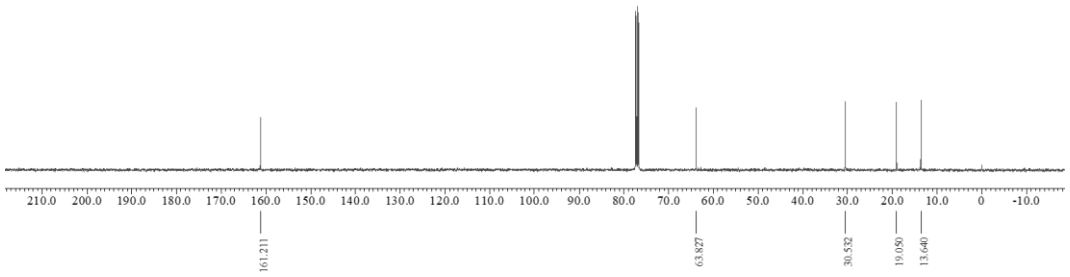
butyl formate (**3a**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

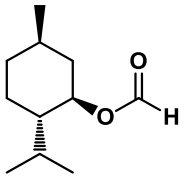


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

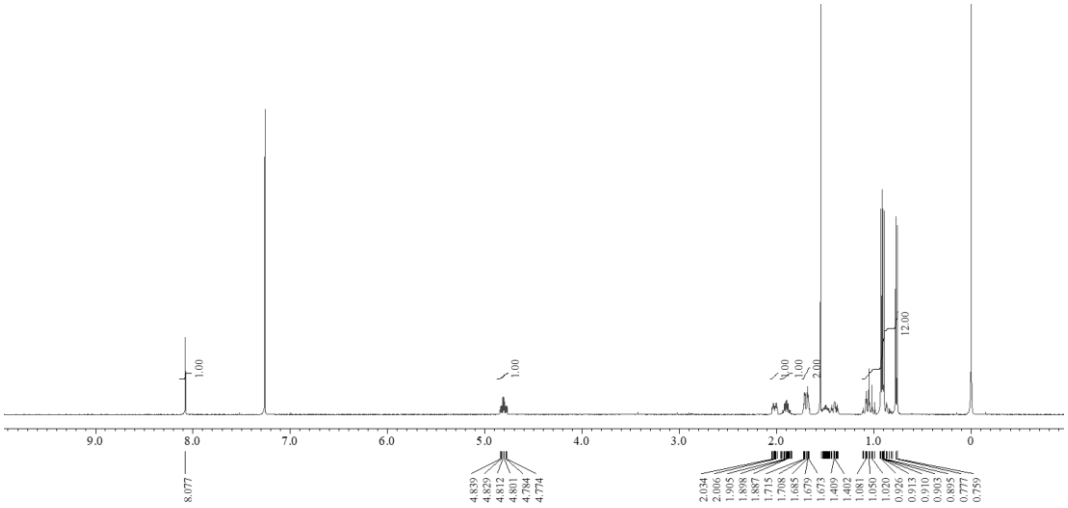


δ / ppm



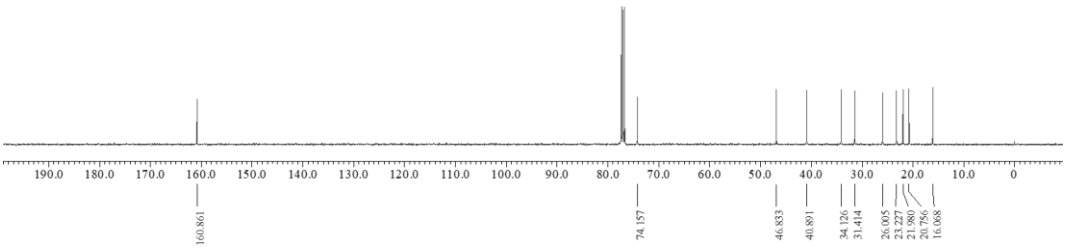
(–)-menthyl formate (**3b**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

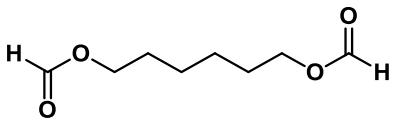


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K).

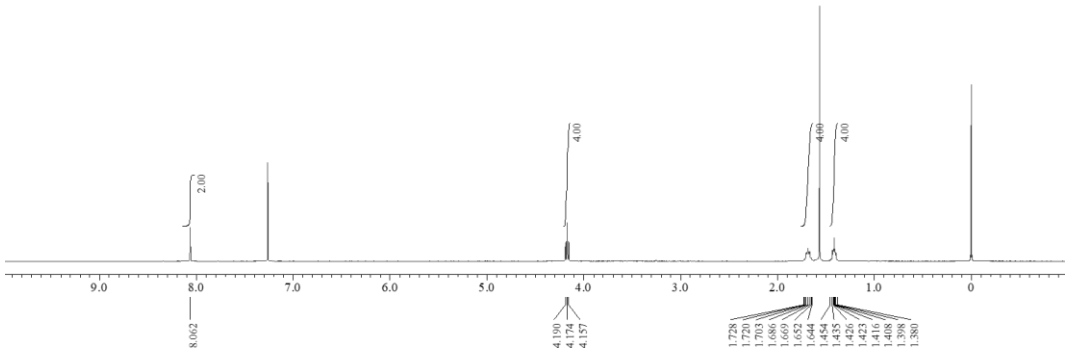


δ / ppm



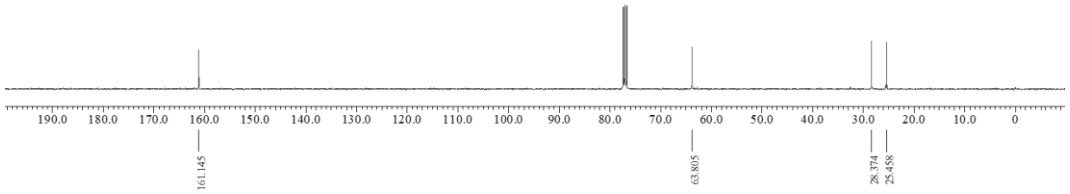
hexane-1,6-diyl diformate (**3c**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

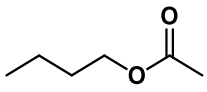


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

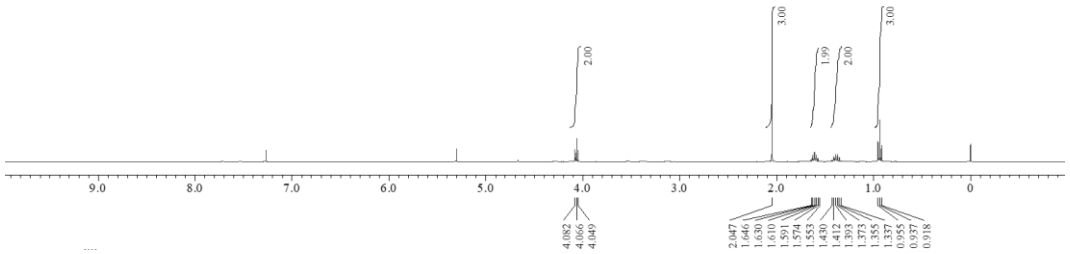


δ / ppm



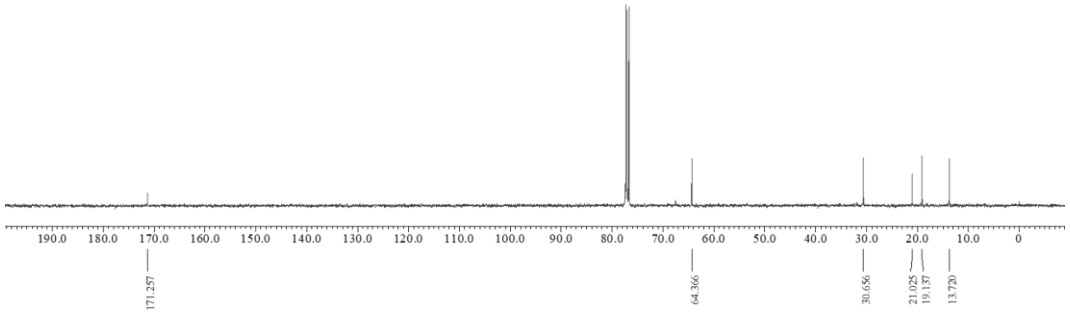
n-butyl acetate (**3d**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

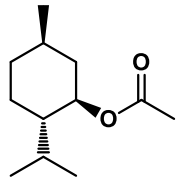


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

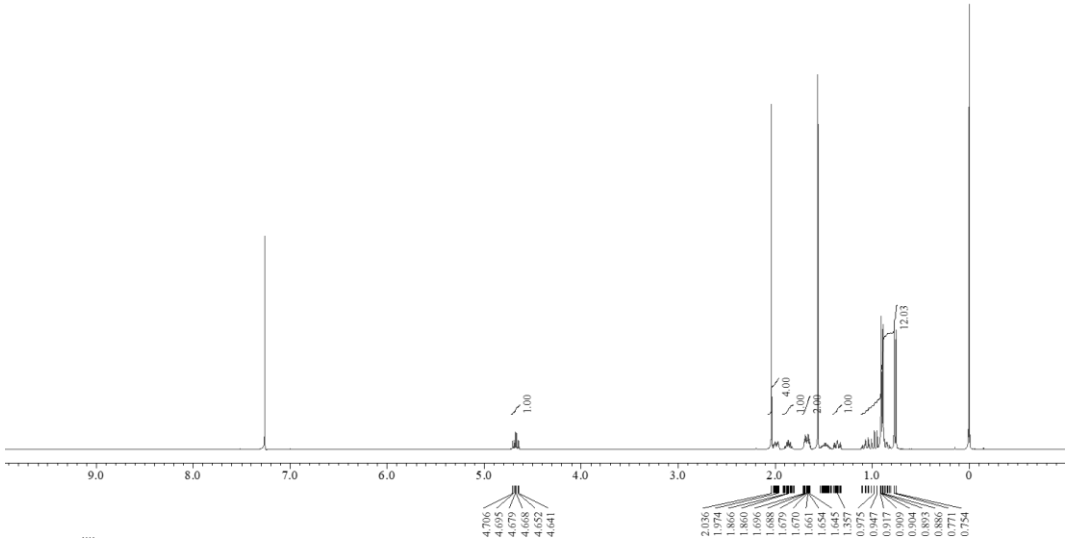


δ / ppm



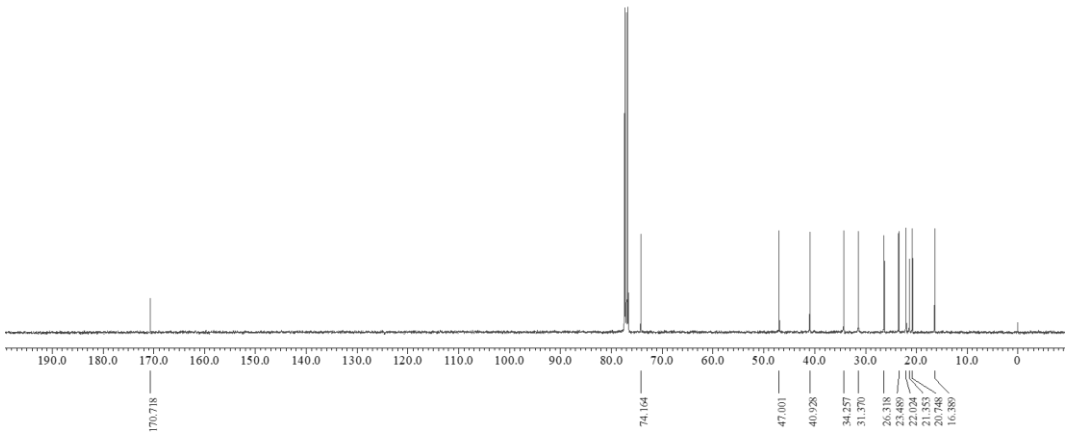
(–)-menthyl acetate (**3e**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

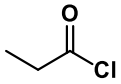


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

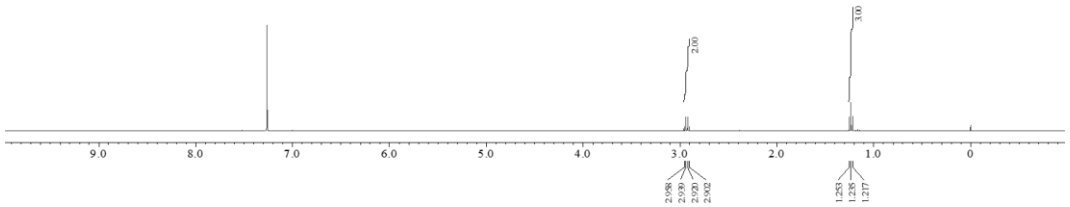


δ / ppm



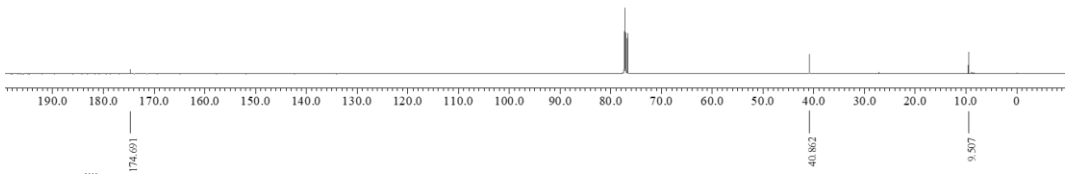
propionyl chloride (**4a**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

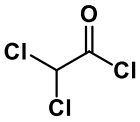


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

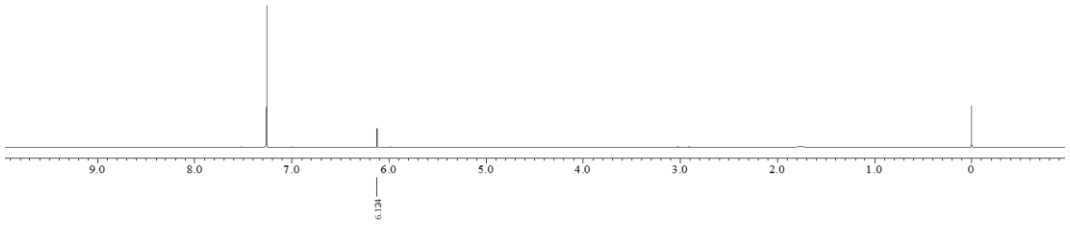


δ / ppm



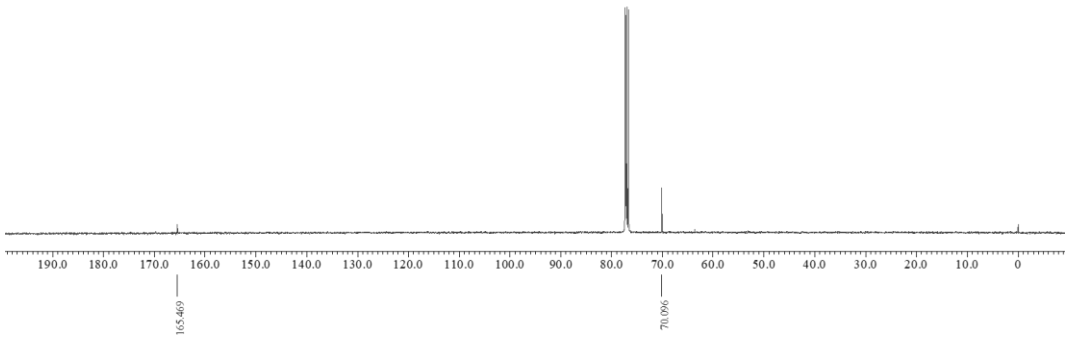
2,2-dichloroacetyl chloride (**4b**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

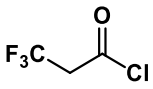


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

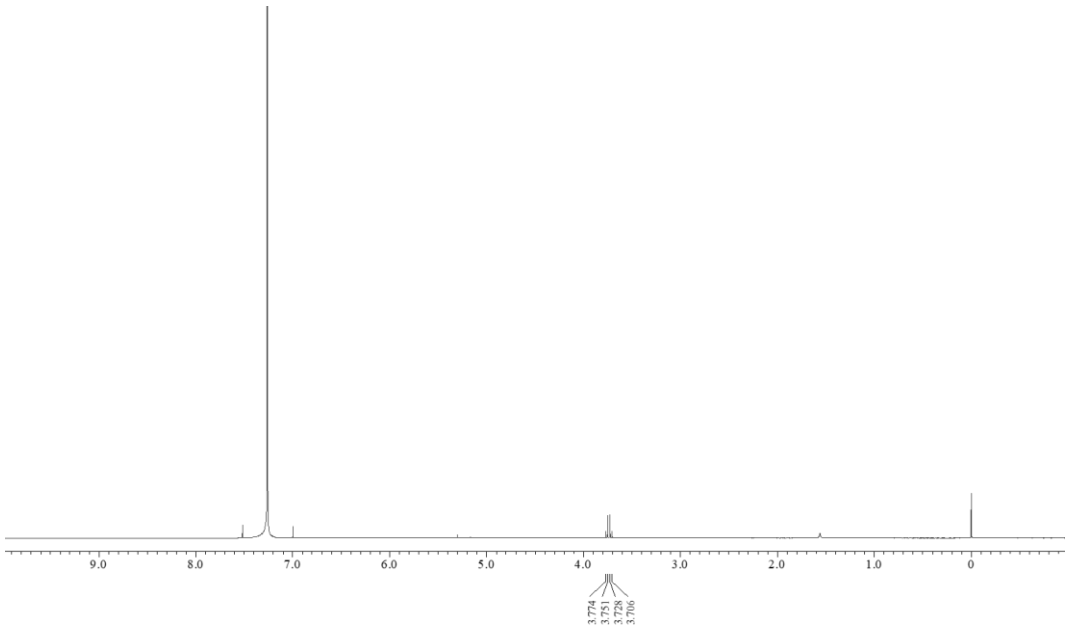


δ / ppm



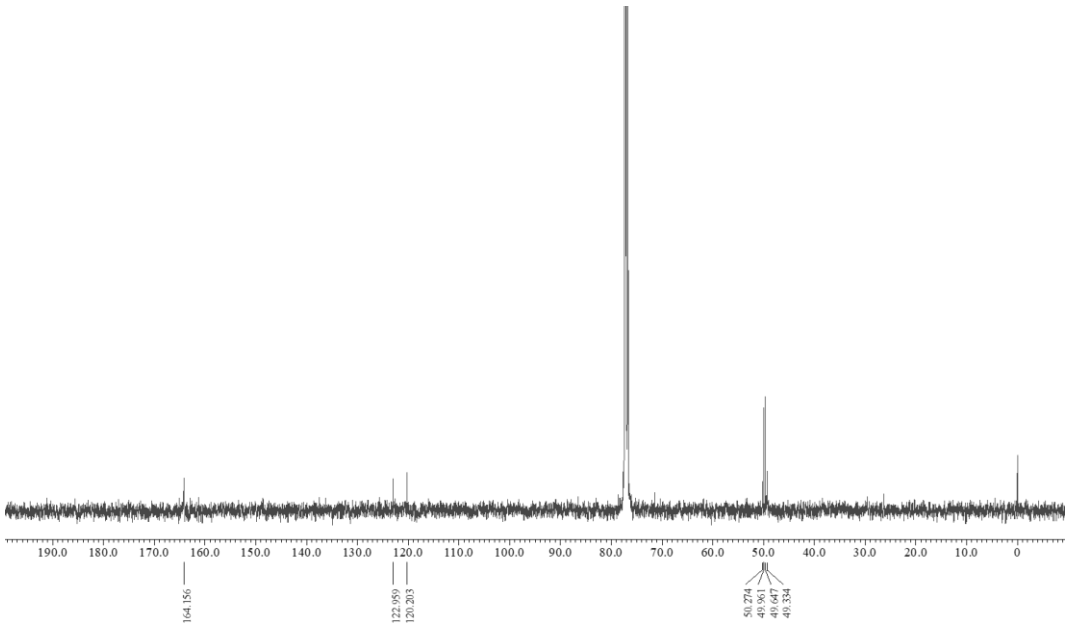
3,3,3-trifluoropropanoyl chloride (**4c**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

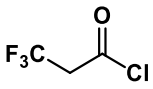


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

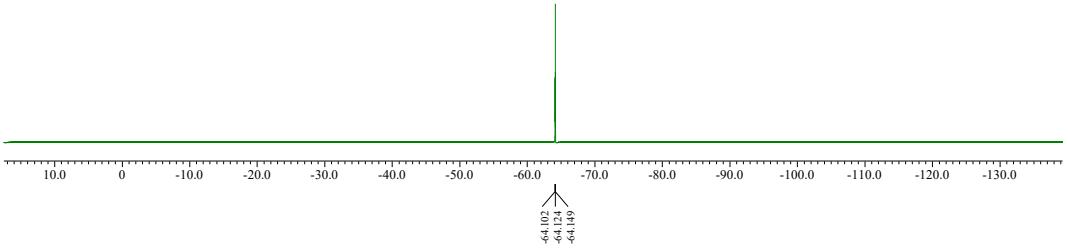


δ / ppm

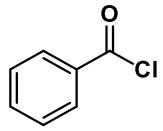


3,3,3-trifluoropropanoyl chloride (**4c**)

^{19}F NMR (376 MHz, $CDCl_3$, 293 K)

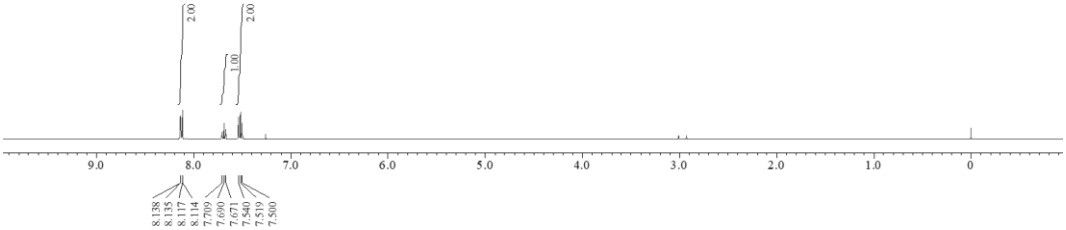


δ / ppm



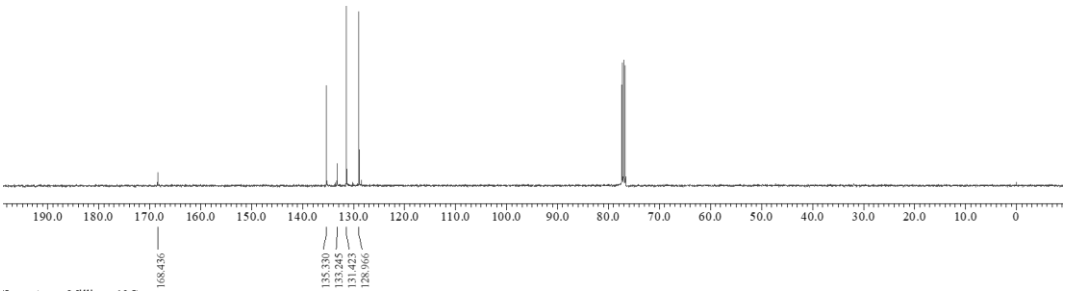
benzyl chloride (**4d**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

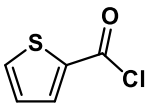


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

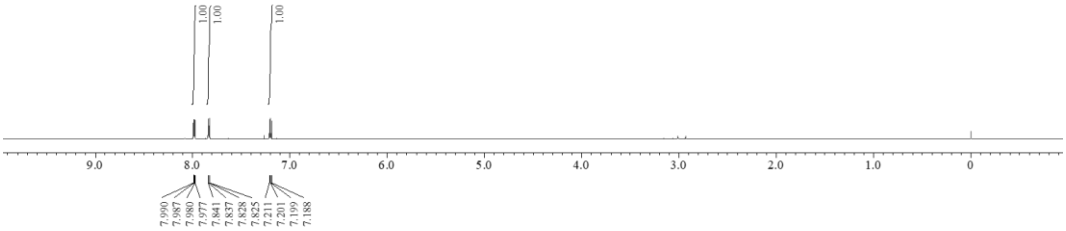


δ / ppm



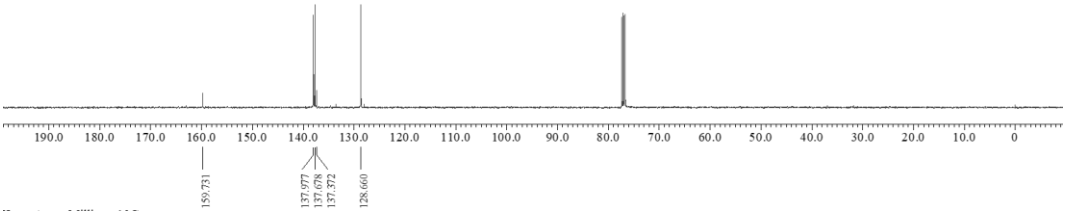
2-thiophenecarbonyl chloride (**4e**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

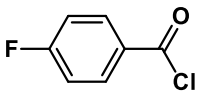


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

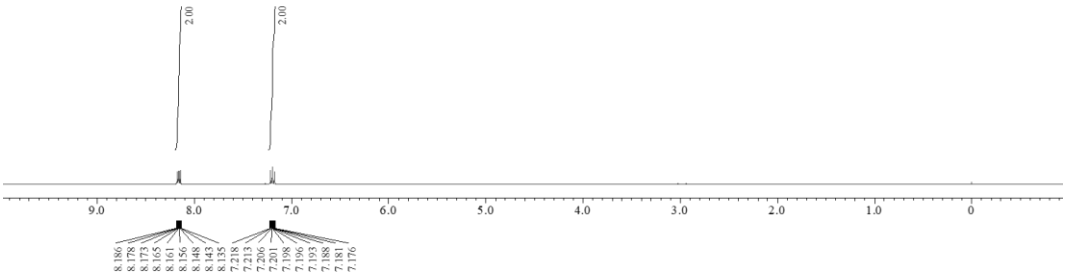


δ / ppm



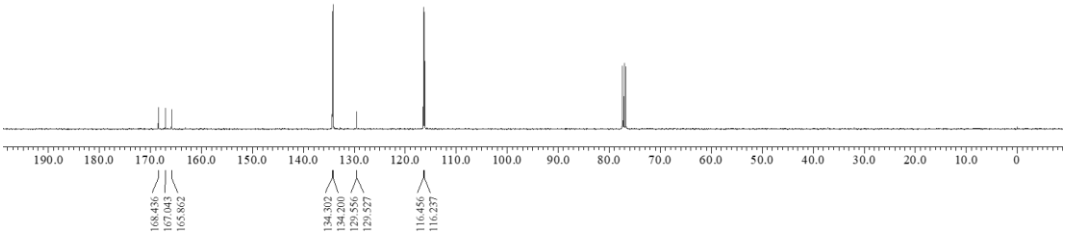
4-fluorobenzoyl chloride (**4f**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

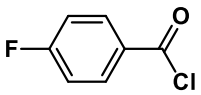


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

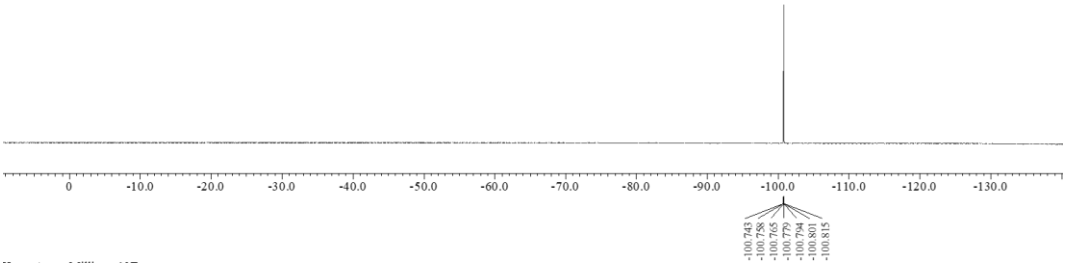


δ / ppm

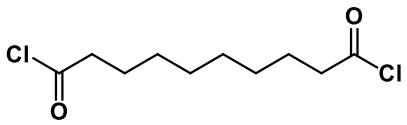


4-fluorobenzoyl chloride (**4f**)

^{19}F NMR (376 MHz, $CDCl_3$, 293 K)

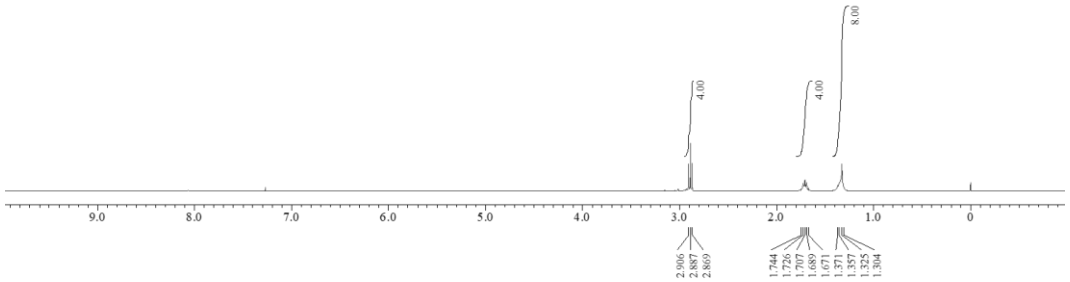


δ / ppm



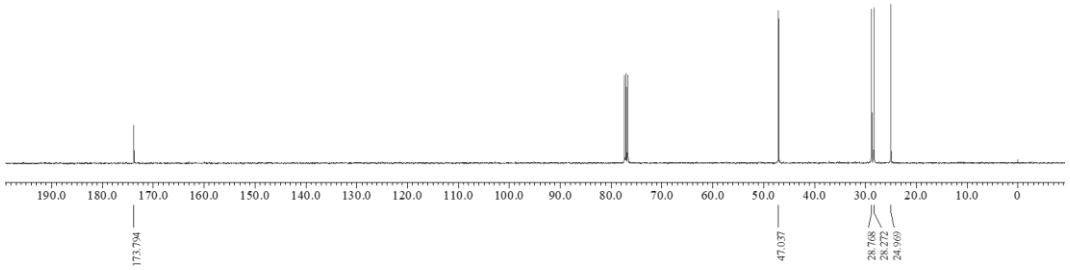
sebacoyl chloride (**4g**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

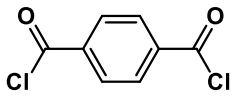


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

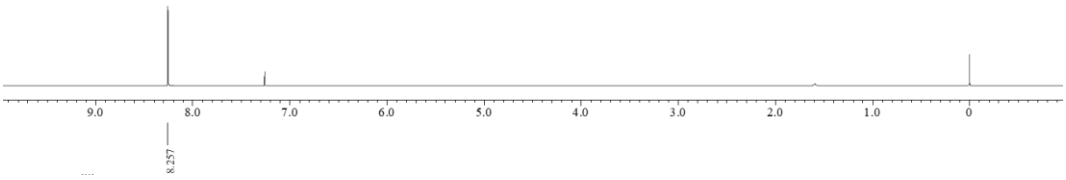


δ / ppm



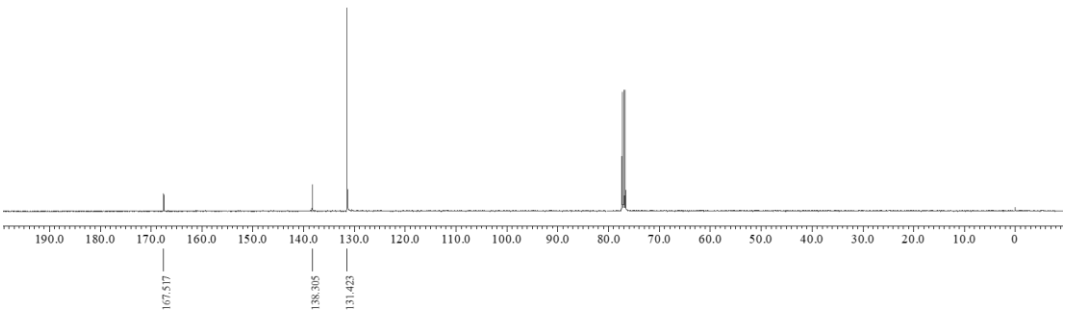
terephthaloyl dichloride (**4h**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

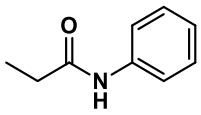


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

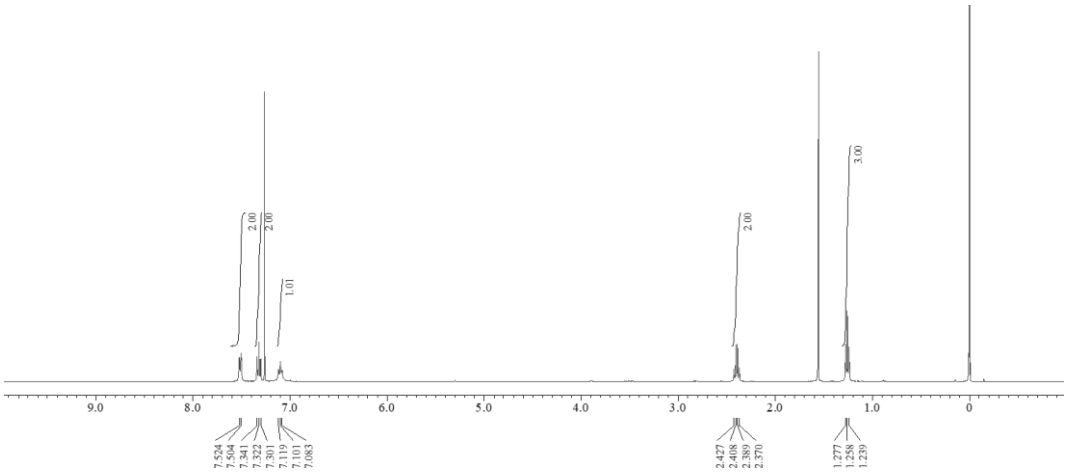


δ / ppm



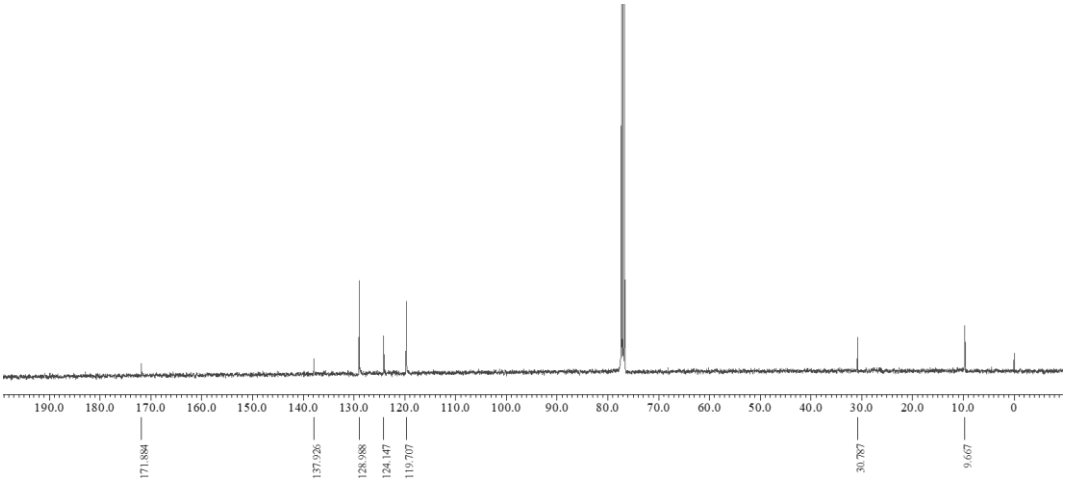
N-phenyl propionamide (**5a**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

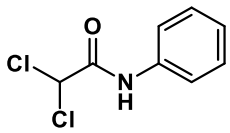


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

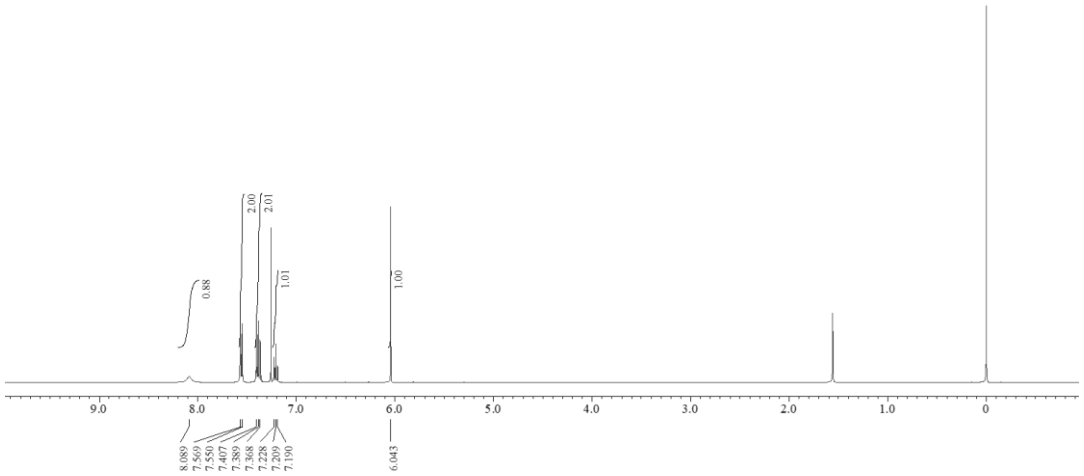


δ / ppm



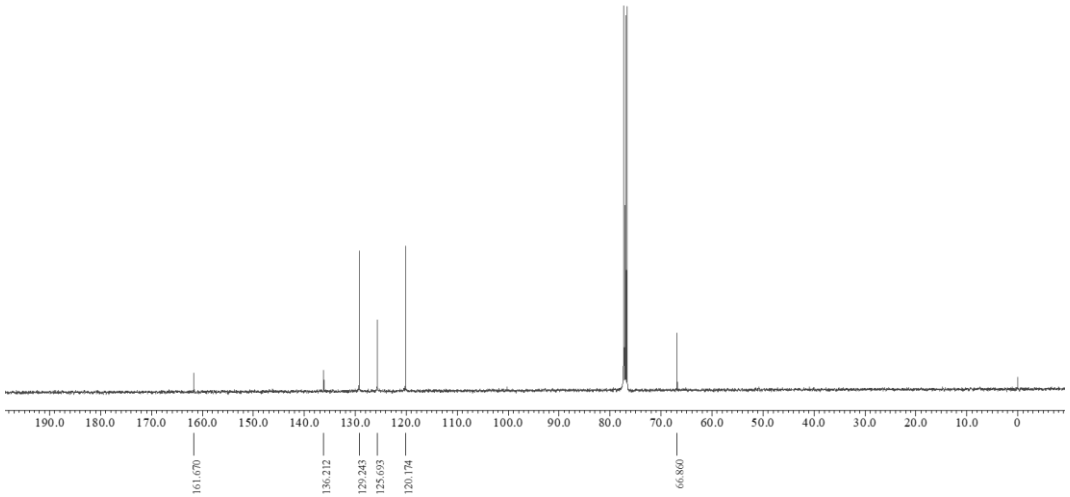
2,2-dichloro-*N*-phenylacetamide (**5b**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

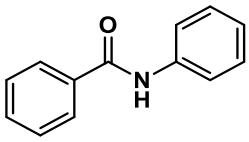


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

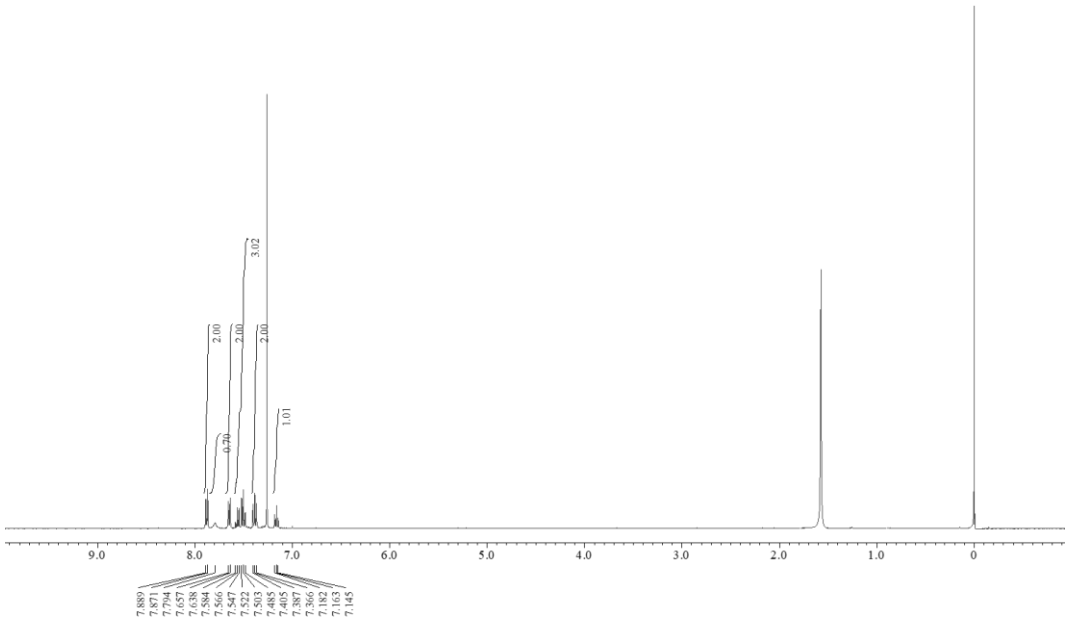


δ / ppm



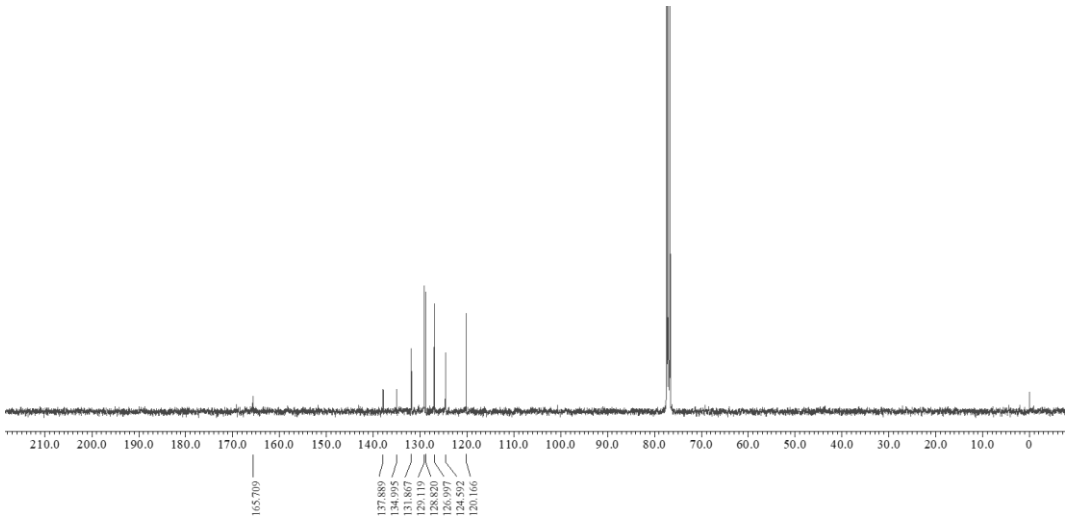
N-phenyl benzamide (**5c**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

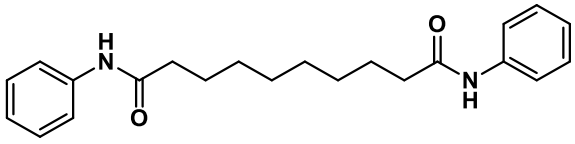


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

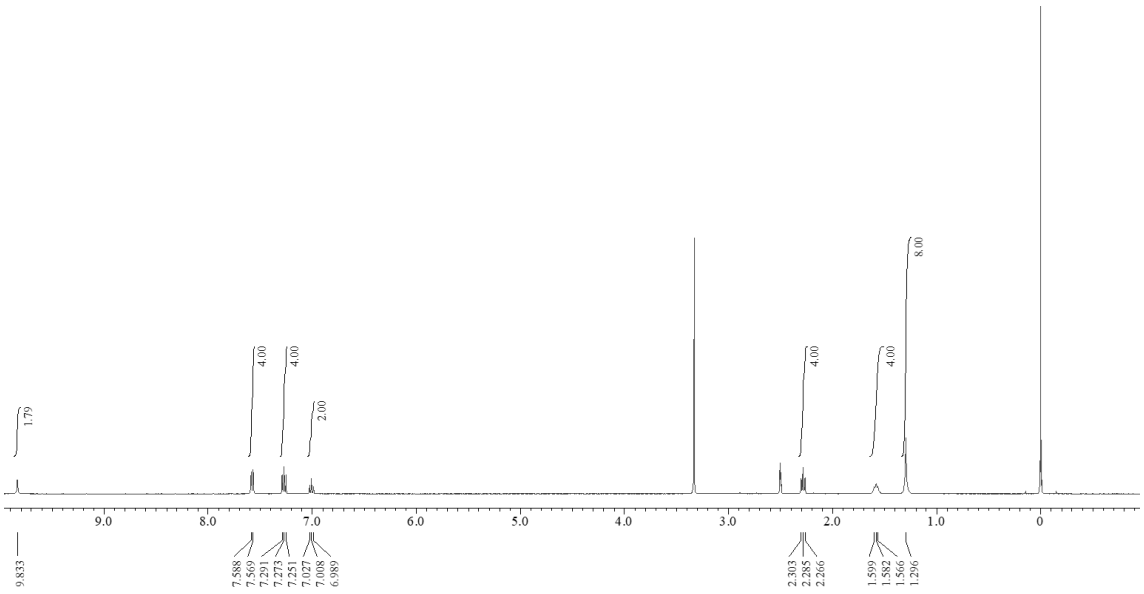


δ / ppm



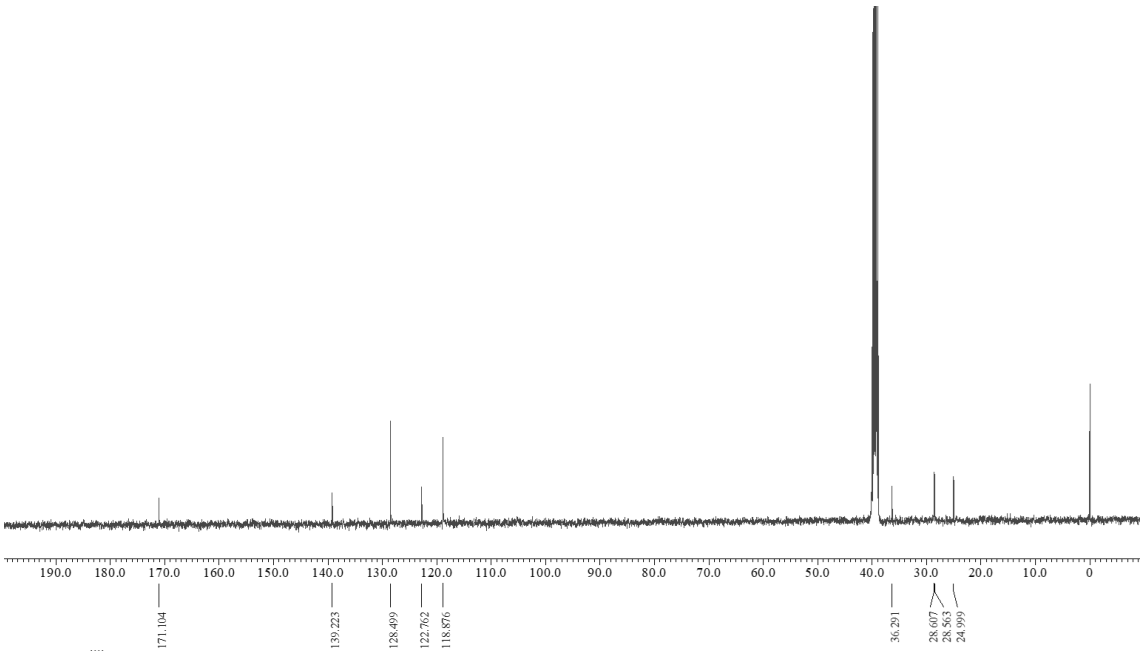
N^1,N^{10}-diphenyldecanediamide (**5d**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

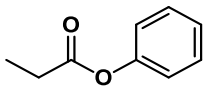


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

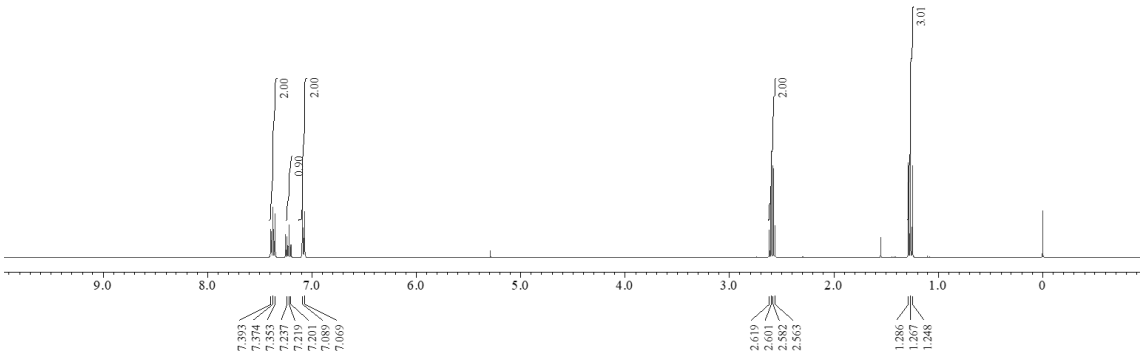


δ / ppm



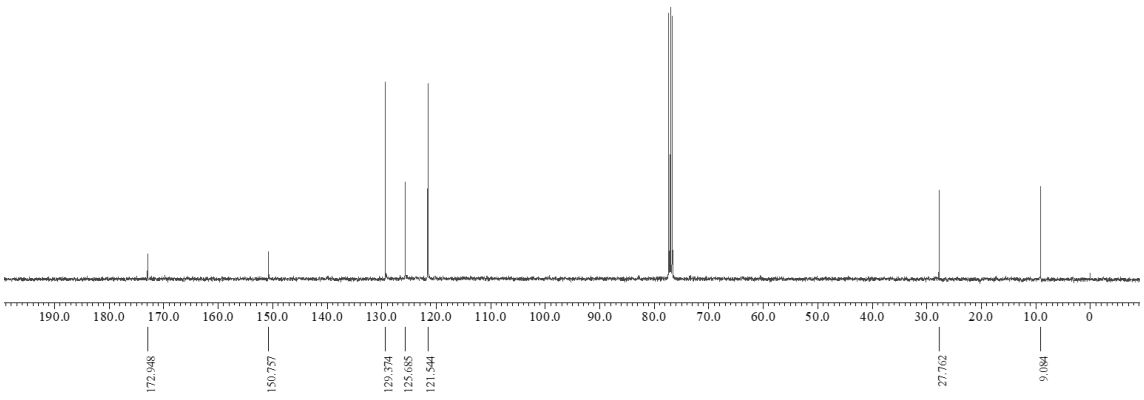
phenyl propionate (**6a**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

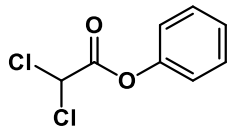


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

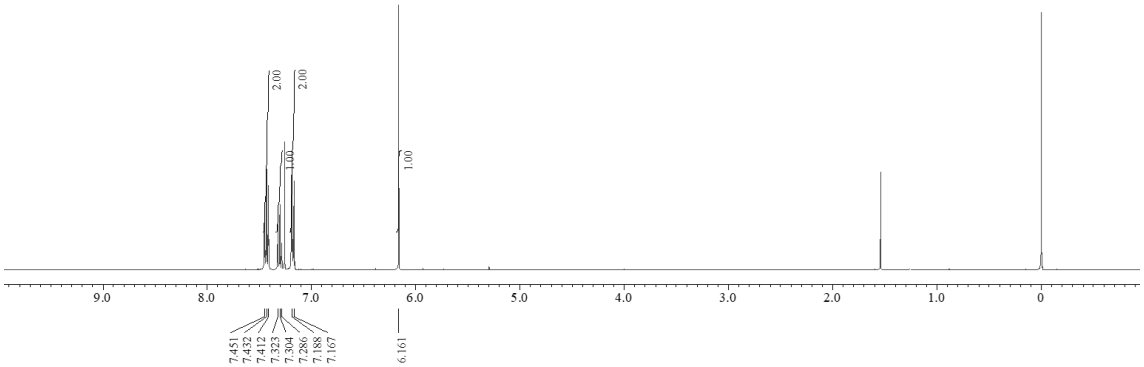


δ / ppm



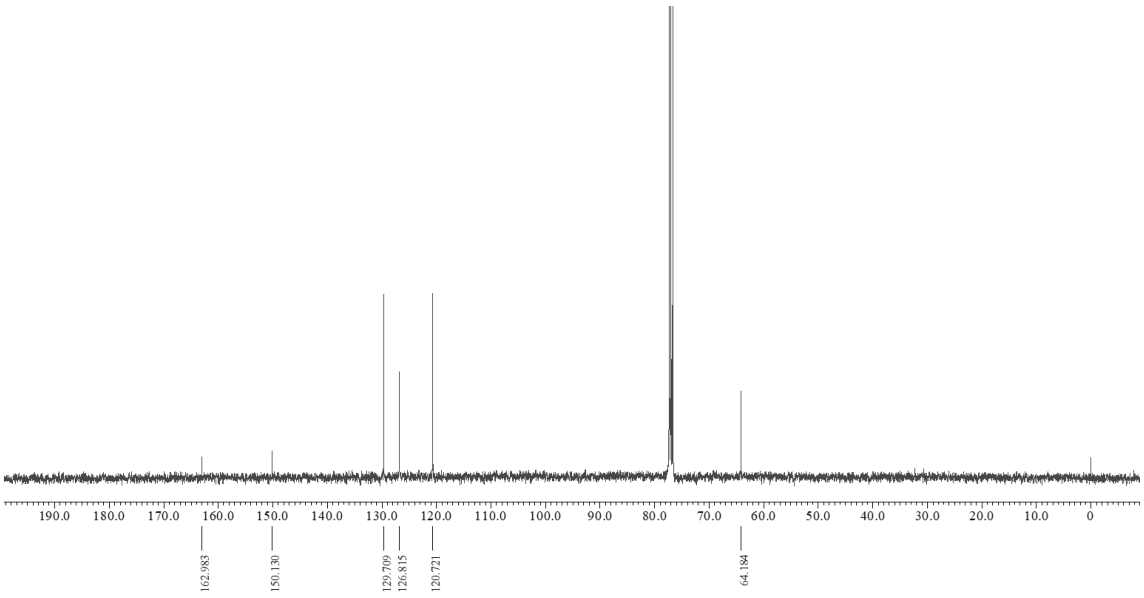
phenyl 2,2-dichloroacetate (**6b**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

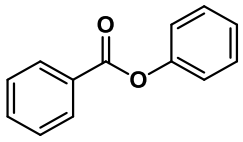


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

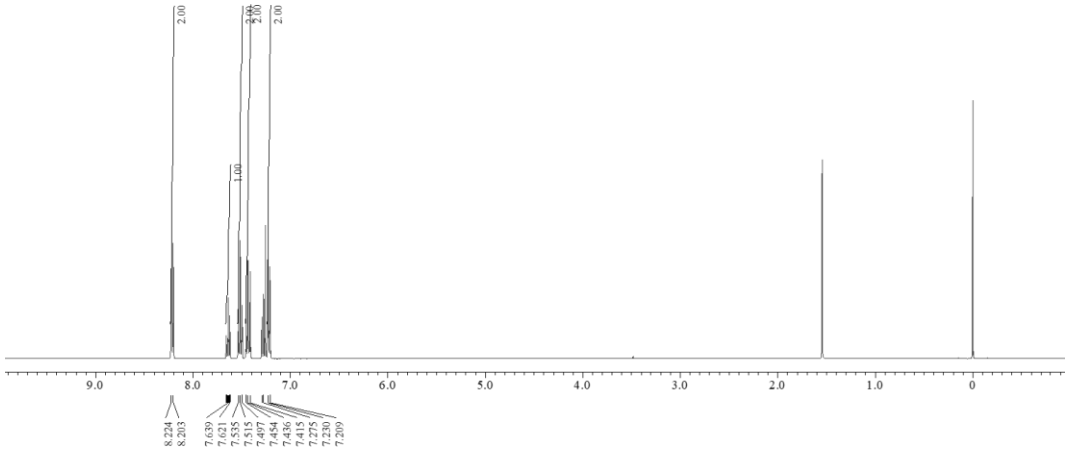


δ / ppm



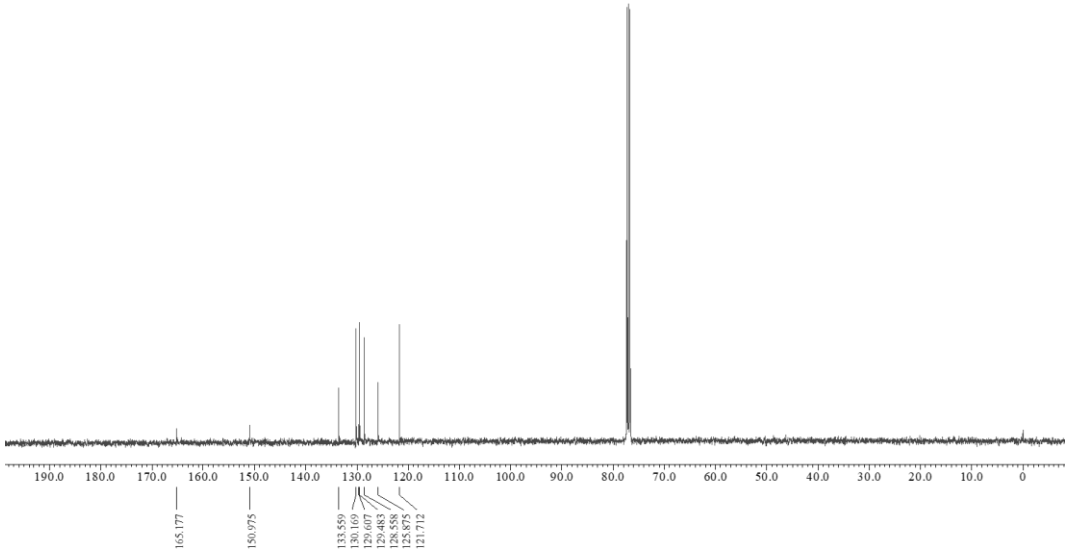
phenyl benzoate (**6c**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

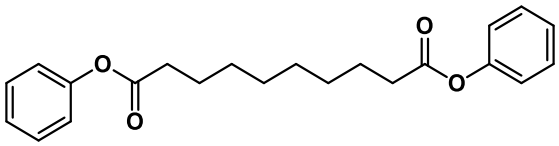


δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)

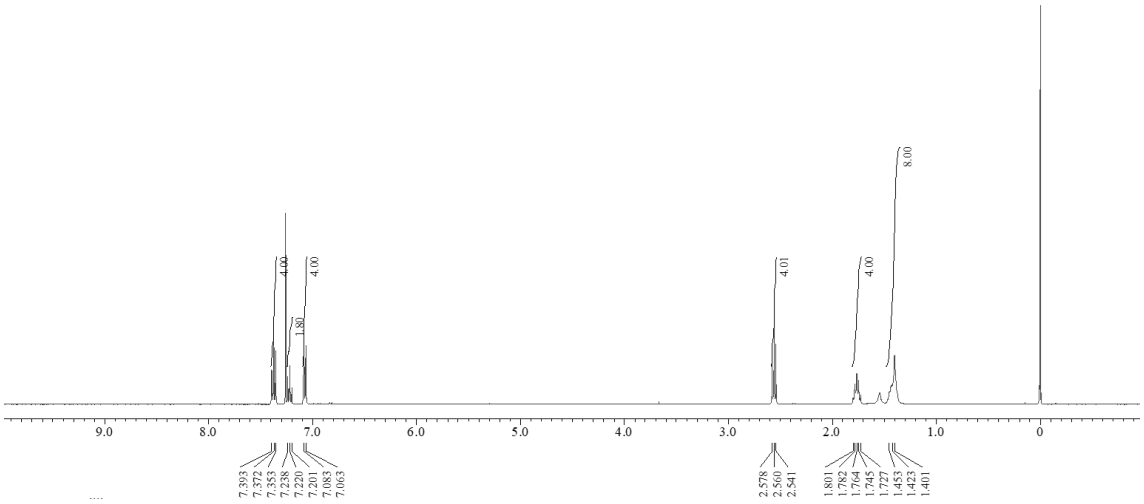


δ / ppm



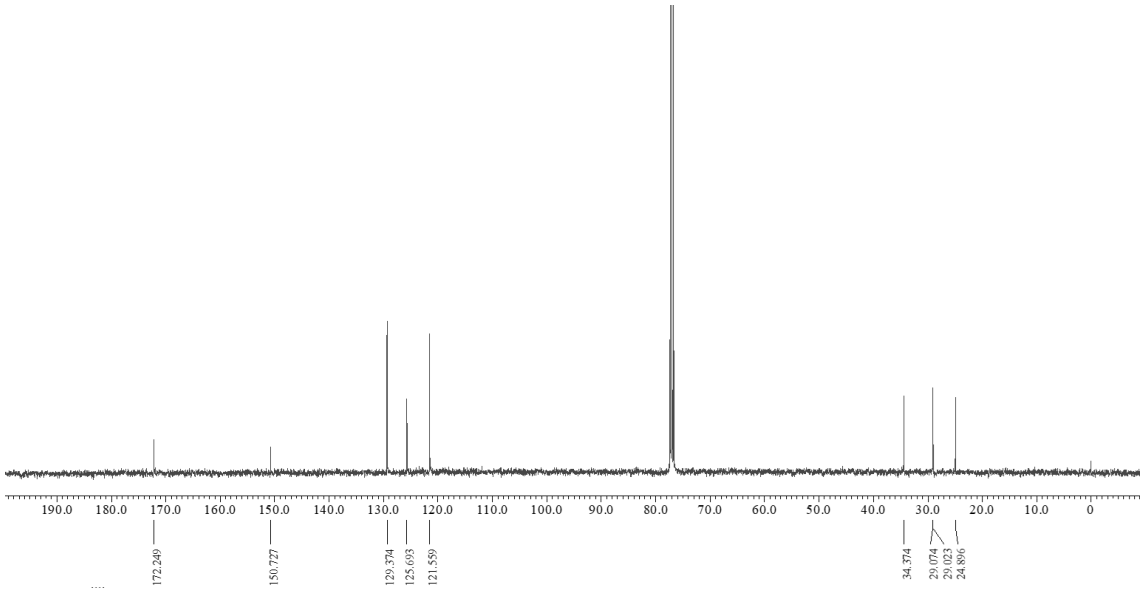
diphenyl sebacate (**6d**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)



δ / ppm

^{13}C NMR (100 MHz, $CDCl_3$, 293 K)



δ / ppm

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Chapter 4

Visible Light Photo-on-Demand Synthesis of Vilsmeier Reagents with Chloroform

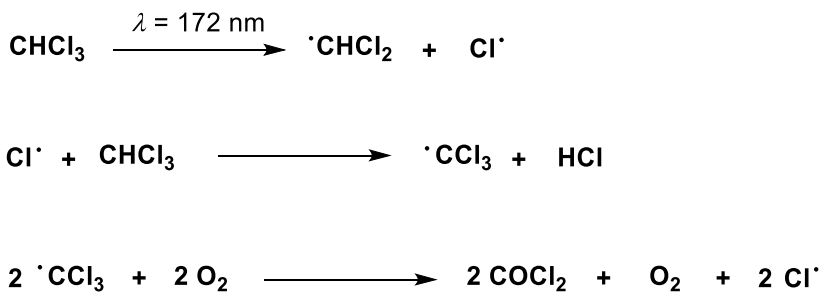
4.1 Introduction

Visible light promoted chemical reactions have attracted considerable attention in organic synthesis, because they are expected to play an important role in addressing environmental issues such as reduction of CO_2 emission.[1] In comparison with the reactions with higher energy UV light, it has an advantage to decrease photochemical decompositions of the reaction substrates and/or products, since the visible light hardly breaks covalent bonds such as carbon–carbon, carbon-hydrogen, carbon–heteroatom, carbon–halogen bonds. However, the reactions with visible light, generally, need a catalyst and/or reagent that is activated by the photo-irradiation.

The production method of Vilsmeier reagent (VR), described in Chapter 3, has not changed essentially for a century. As an extension of the UV photo-on-demand synthesis of VR with $CHCl_3$ and DMF (Chapter 3), the author has attempted to develop a novel in situ photo-on-demand synthesis of VR with the visible light. There are a few reports for the photochemical synthesis of VR with visible light. Stephenson and co-workers reported that a DMF solution containing tetrabromomethane (CBr_4) and $Ru(bpy)_3Cl_2$ as a photoredox catalysis provided Br-containing VR, a brominated version of VR**2**, upon visible light irradiation (blue LED with λ_{max} = 435 nm).[2] Later, McCallum and Barriault demonstrated the photochemical synthesis of the brominated VR**2** through irradiation of UV-A light

(365 nm LED) to a mixture solution of CBr_4 and DMF without the catalyst.[3] Although the brominated VR**2** shows similar chemical properties with VR**2**, CBr_4 used in that reaction is relatively expensive reagent and is also toxic and a cancer suspect agent.[4] The iodinated VR**2** was also synthesized with visible light from CHI_3 and DMF, and it was further available to an iodination reaction of alcohol.[5] However, to the best of author's knowledge, no example has been reported for the photochemical synthesis of the original VR**2**, a commonly used Vilsmerier reagent, with visible light.

It has been reported that the oxidative photo-degradations of chlorinated methanes such as $CHCl_3$ and CH_2Cl_2 might cause radical chain reactions with O_2 initiated by $Cl^{\bullet}$.[6] Oppenländer reported that 172 nm UV irradiation of $CHCl_3$ resulted in C–Cl bond cleavage to give $^{\bullet}CHCl_2$ and $Cl^{\bullet}$ (Scheme 4.1).[6a] The generated $Cl^{\bullet}$ further extracts hydrogen from another $CHCl_3$ to produce $^{\bullet}CCl_3$ through formation of HCl. The produced $^{\bullet}CCl_3$ then reacts with O_2 to give $COCl_2$ with regeneration of $Cl^{\bullet}$. Alapi and Dombi also reported the photo-decomposition of the chlorinated methanes upon irradiation of 184.9 nm UV light.[6b] They also claimed that $Cl^{\bullet}$ plays a key role in the photolysis of the chlorinated methanes. These studies suggested that the oxidative transformation of $CHCl_3$ to $COCl_2$ is promoted by the reagents that can generate $Cl^{\bullet}$ under exposure to the visible light.



Scheme 4.1 Oxidative photodecomposition of $CHCl_3$.

It is well-known that chlorine (Cl_2), having the lowest energy absorption band at around 300–400 nm with λ_{max} at 330 nm,[7] brings about homolytic cleavage to give $2Cl^{\bullet}$ upon visible light-irradiation or heating as an energy source to overcome the energy barrier.[8] With such characteristic property of Cl_2, the author developed herein a novel in situ photo-on-demand synthesis of Vilsmeier reagent with the visible light. Chloroform underwent oxidative photo-decomposition upon exposure to the visible light under bubbling of a mixture gas of O_2 and Cl_2. Then, the reaction allowed in situ photo-on-demand synthesis of Vilsmeier reagent, capable of applying to the one-pot synthesis of aldehydes.

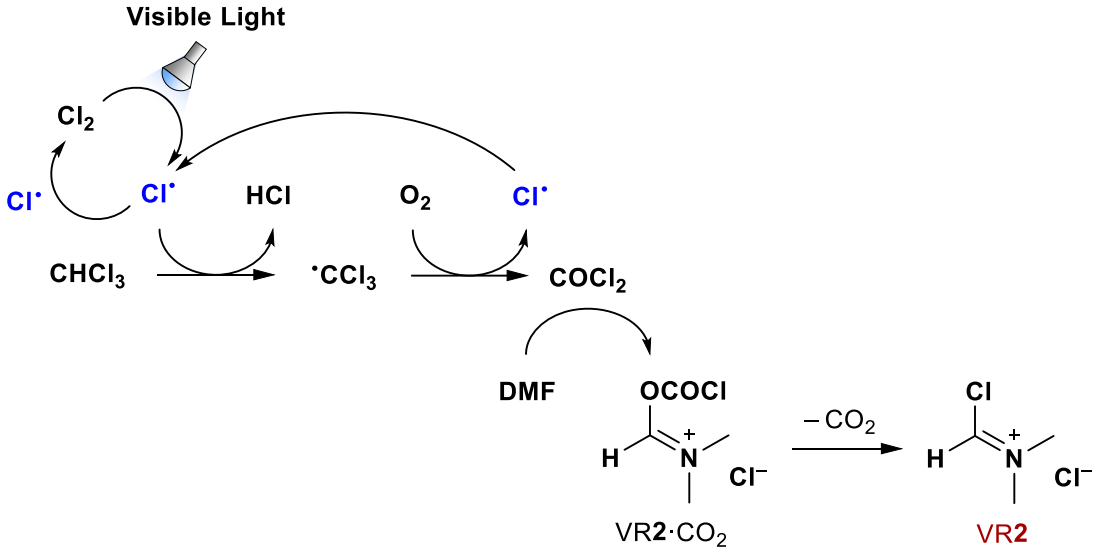
4.2 Results and discussion

A reaction system for the in situ photo-on-demand synthesis of Vilsmeier reagent (VR) with visible light was set up as follow: A mixture of O_2 and Cl_2 gas was prepared in a three-necked flask (flask 1) containing 15−60 mmol of $Ca(ClO)_2$ upon addition of aqueous HCl solution with a syringe pump under steady flow of O_2 (15−35 mL/min). O_2/Cl_2 gas prepared was dried through a $CaCl_2$ column, and then, injected to a next photoreactor (flask 2), which contains 20−300 mmol of DMF and 20−300 mL of $CHCl_3$. This reaction system allows in situ photo-on-demand synthesis of VR under visible light irradiation (4W or 9W LED lamp) in a closed system. While the photo-decomposed gas unreacted or generated in the course of reaction was trapped with an aliphatic alcohol and alkaline aqueous solution such as $NaHCO_3$ (aq.).

Initially, for the synthesis of VR**2** with visible light (Table 4.1, entry 1), O_2/Cl_2 gas was transferred to the flask 2, containing a mixture solution of $CHCl_3$ (20 mL) and DMF (20 mmol). The sample solution was photo-irradiated at 30 °C for 3 h with a commercially available white LED light (4 W), which emits 400–700 nm visible light, attached outside the flask. After turning off the light, the sample

solution was stirred at 50 °C for 2 h to remove possible gaseous products, such as $COCl_2$, HCl and Cl_2. An equivalent amount of *N*-methylpyrrole for DMF was then added to the sample solution to produce the corresponding aldehyde. The yield of VR could be estimated from the yield of this aldehyde in ^1H NMR spectroscopy. Then, it was found that VR**2** formed at least in 90% yield in this reaction conditions.

A possible reaction mechanism for the formation of VR with visible light in this system is proposed in Scheme 4.2. Initially, Cl_2, generated from the reaction of $Ca(ClO)_2$ with HCl (aq.), undergoes homolytic cleavage to give $Cl^{\bullet}$ under exposure to visible light. The generated $Cl^{\bullet}$ then extracts hydrogen from $CHCl_3$ to provide $^{\bullet}CCl_3$ and HCl. $^{\bullet}CCl_3$ then reacts with O_2 to give $COCl_2$, through regeneration of $Cl^{\bullet}$, which allows radical chain reactions. The generated $COCl_2$ reacts with DMF to produce VR**2**·CO_2, which forms VR**2** after irreversible elimination of CO_2.



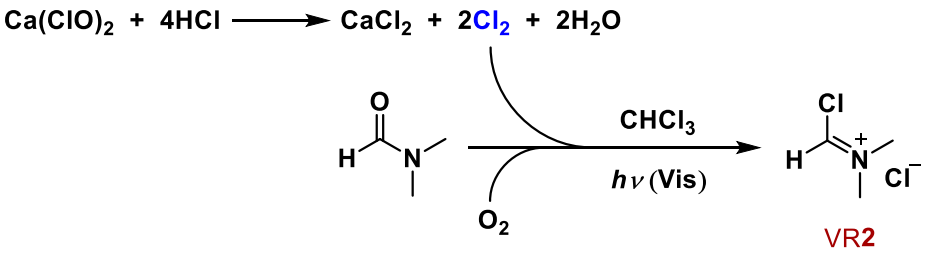
Scheme 4.2 A possible reaction mechanism of visible light photo-on-demand synthesis of Vilsmeier reagent with a chloroform and DMF initiated by Cl_2.

The reactions were demonstrated in various conditions. Then, it was found that the yield of VR is highly dependent on temperature, O_2 flow rate, and intensity of the light (Table 4.1). The yield of VR was increased to 97% with 4 W lamp at 50 °C (entry 2). However, no reaction was observed at 10 °C (entry 3). The observed temperature effects may originate from the bond cleavage of Cl_2 caused upon photo-irradiation and/or heating. The flow rate of O_2 gas, which allows the reaction with $^{\bullet}CCl_3$ to give $COCl_2$, also affects the yield of VR (entries 1, 4 and 5). Oxygen deficiency in the reaction system caused decrease of the product yield. With an expectation to enhance the bond cleavage of Cl_2, the photoreaction was further performed with a 9 W LED lamp. The reaction provided VR in higher yield (96%) compared with the case of 4 W LED lamp (entries 1 and 6). Then, the highest 98% yield was attained at 50 °C under O_2 flow at 25 mL/min with a 9 W LED lamp (entry 7).

Next, with an objective to scale-up the synthesis of VR, the reaction was demonstrated with larger amount of DMF according to the above best conditions in temperature, O_2 flow, and light intensity, but the yield of VR was decreased to ~22% (entries 8 and 9). These results suggest that there is a threshold of the concentration of DMF in the reaction. It is expected that DMF prevents oxidative photo-decomposition of $CHCl_3$ as a radical scavenger or a light absorber. Based on these experimental results and the mechanistic considerations, the concentration of DMF in $CHCl_3$ was adjusted to 1.0 mol/L (same with entries 5–7). Then, the scale-up was attained in 83% product yield with a 300 mL of $CHCl_3$ solution containing 0.3 mol of DMF (entry 10).

This synthetic system was further available to the one-pot synthesis of aldehyde. After the photochemical preparation of VR**2** in $CHCl_3$ by following the best conditions described above (Table 4.1, entry 7), an aromatic substrate was added to the sample solution. Subsequent hydrolysis reaction with aqueous NaOH provided the corresponding aldehyde (Table 4.2). No notable differences

Table 4.1 Cl_2 initiated visible light photo-on-demand synthesis of VR**2** with a $CHCl_3$ solution containing DMF.

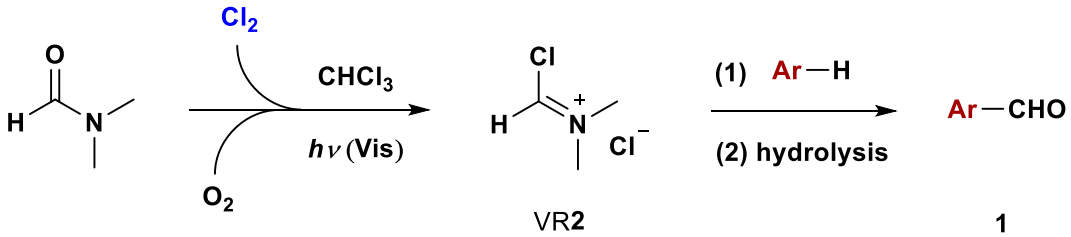


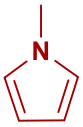
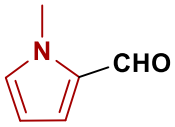
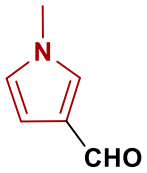
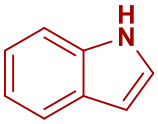
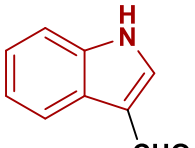
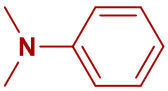
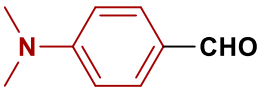
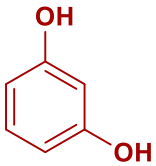
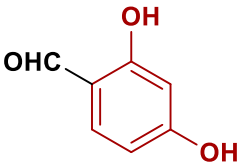
entry	O_2 (mL/min)	flask 1[a]			flask 2				Yield of VR (%)[b]
		$Ca(ClO)_2$ (mmol)	HCl (aq)		DMF (mmol)	$CHCl_3$ (mL)	temp. (°C)	LED lamp	
			amount (M, mL)	speed (mL/h)					
1	35	15	7 M (8.6 mL)	4.3	20	20	30	4 W	90
2	35	15	7 M (8.6 mL)	4.3	20	20	50	4 W	97
3	35	15	7 M (8.6 mL)	4.3	20	20	10	4 W	0
4	15	15	7 M (8.6 mL)	4.3	20	20	30	4 W	65
5	25	15	7 M (8.6 mL)	4.3	20	20	30	4 W	96
6	35	15	7 M (8.6 mL)	4.3	20	20	30	9 W	96
7	25	15	7 M (8.6 mL)	4.3	20	20	50	9 W	98
8	25	15	7 M (8.6 mL)	4.3	30	20	50	9 W	33
9	25	15	7 M (8.6 mL)	4.3	50	20	50	9 W	22
10	25	60	7 M (34.4 mL)	4.3	300	300	50	9 W	83

[a] Reaction temperature: 30 °C.

[b] The yields of VR were estimated by its reaction product with 1-methylpyrrole in ^1H NMR spectroscopy.

Table 4.2 Cl_2 initiated visible light photo-on-demand synthesis of VR**2** with a $CHCl_3$ solution containing DMF and its one-pot conversion of aldehyde.



entry	Ar—H	temp. (°C)	time (h)	product	^{1}H NMR yield
1		70	0.5	 **1a**	87%
				 **1a'**	11%
2		r.t.	2.0	 **1b**	42%
3		r.t.	2.0	 **1c**	57%
4		30	1.5	 **1d**	71%

were observed in the yields of the products in comparison with the reactions using UV light described in Chapter 3.

With respect to the mechanism of synthesizing aldehyde, Vilsmeier reagent reacts with the substrate to give an iminium salt with generation of HCl. The formed iminium salt then converts to the corresponding aldehyde with eliminations of amine and HCl through hydrolysis reaction.

The author noticed herein that the product yield is also highly dependent on the hydrolysis conditions. There are a few reports to examine the conditions of the hydrolysis at the final work-up process of Vilsmeier formylation reaction. Experimental results by varying pH of the added water (not shown) suggested that, relatively strong alkaline conditions seem to be favorable for converting the substrate to the aldehyde when using nitrogen-containing aromatic substrates (Table 4.2, entries 1−3). Interestingly, although resorcinol bearing two OH groups showed no conversion to the aldehyde in the strong alkaline conditions, the reaction proceeded in acidic conditions (entry 4). These differences may be ascribed to the electrophilicity of the iminium salt formed through the reaction of VR and aromatic substrate (Chapter 3, Scheme 3.3).

4.3 Conclusions

This chapter described a novel visible light photo-on-demand synthesis of Vilsmeier reagent from a chloroform solution containing DMF. To the best of author′s knowledge, this is the first example of photochemical synthesis of VR**2** with visible light. In this reaction, Cl_2 provides $Cl^{\bullet}$ upon exposure to visible light to initiate the oxidative photo-decomposition of $CHCl_3$ through radical chain reactions. Since all the side products generated in this reaction are gases at room temperature, one can prepare a $CHCl_3$ solution containing VR in high purity. It allows subsequent one-pot synthesis of aldehyde. This method needs no special equipment, and the experiment can be easily as well as safely performed in the

closed system. This novel photochemical reaction will be valuable in both laboratory and industry.

4.4 Experimental section

4.4.1 Materials: Unless otherwise noted, reagents and solvents were used as received from Kishida Chemical Co., Ltd. [dichloromethane (>98%), ethyl acetate (>99%), *n*-hexane (>95.0%)], Nacalai Tesque, Inc. [1,2-dichloroethane (≥99.5%), hydrochloric Acid (35%), calcium hypochlorite (hightest)], Wako Pure Chemical Industries, Ltd. [Na_2SO_4 (99.0%), $NaHCO_3$ (99.5–100.3%), NaOH (97.0%), *N*, *N*-dimethylformamide (>99.5%), chloroform (>99.7%)], Tokyo Chemical Industry Co., Ltd. (TCI) [1-methylpyrrole (>99.50%), 1*H*-indole (>99.0%), *N*,*N*-dimethyl aniline (>98.0%), resorcinol (>99.0%)], and Cambridge Isotope Laboratories, Inc. [$CDCl_3$ (D, 99.8%), DMSO-d_6 (D, 99.8%)]. For column chromatography, Wakogel (60N, particle size 38–100 μm, silica gel, irregular) was used. All products were unambiguously characterized by means of ^{1}H NMR in reference to the previous studies and the Sigma-Aldrich FT-NMR Library (ver. 4.0.10).[9-10]

4.4.2 Measurements and Calculations: ^{1}H NMR spectra were recorded on Bruker AVANCE 400 spectrometer, where chemical shifts (δ in ppm) were determined with respect to tetramethylsilane as an internal standard. ^{1}H NMR yields were determined by using 1,2-dichloroethane or dichloromethane as internal standards.

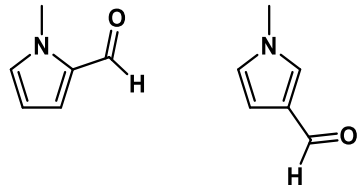
4.4.3 Synthesis

General procedure

Photochemical synthesis of VR2 with visible light and its application to one-pot synthesis of aldehydes. 15–60 mmol of $Ca(ClO)_2$ was charged to a three-

necked round bottom flask (flask 1), equipped with a syringe pump. Flask 1 was further connected to a two-necked round bottom flask (flask 2) via a calcium chloride tube. Flask 2 was charged with a solution containing 20–300 mmol of *N*, *N*-dimethylformamide (DMF) and 20–300 mL of $CHCl_3$. Under steady flow of O_2 (25–35 mL/min), an aqueous HCl solution (7M) was continuously added to flask 1 by a syringe pump at 30 °C. The solution in flask 2 was vigorously stirred under irradiation of white light with a LED lamp (4W or 9W) at 30–50 °C. After the addition of HCl (aq.), the flask 2 was exposed to the light for additional 1 h. After turning off the light, the sample solution was stirred for 2 h under O_2 bubbling to remove unreacted reactive species from the system. An aromatic substrate was then added to flask 2 containing the sample solution at 0 °C, and the mixture was stirred for 1.0–2.0 h with or without heating. The resulting sample solution was then hydrolyzed with NaOH (aq., 2M) and extracted with CH_2Cl_2 (20 mL×3). The organic layers were combined, dried over anhydrous Na_2SO_4, and evaporated to dryness. The yield of the corresponding aldehyde was estimated by ^1H NMR spectroscopy in comparison with an internal standard.

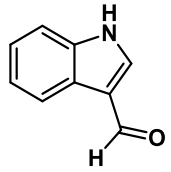
Syntheses of 1-methylpyrrole-2-carbaldehyde (1a) and 1-methylpyrrole-3-carbaldehyde (1a')



Flask 1 was charged with 15 mmol of $Ca(ClO)_2$, while flask 2 was charged with a solution containing 20 mmol of DMF and 20 mL of $CHCl_3$. Under steady flow of O_2 (25 mL/min), an aqueous HCl solution (7M, 8.6 mL) was continuously added to flask 1 by a syringe pump at a speed of 4.3 mL/h at 30 °C. The solution in flask 2 was vigorously stirred under irradiation of white light with a LED lamp (9W) at 50 °C. After the addition of HCl (aq.), the flask 2 was exposed to the light for

additional 1 h. After turning off the light, the sample solution was stirred for 2 h under O_2 bubbling to remove unreacted reactive species from the system. 1-Methylpyrrole (1.78 mL, 20 mmol) was then added to flask 2 containing the sample solution at 0 °C. The sample solution was stirred while gradually elevating temperature, and then, refluxed for 1.0 h. The resulting sample solution was then hydrolyzed with NaOH (aq., 2M, 25 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 1-methylpyrrole-2-carbaldehyde (**1a**) and 1-methylpyrrole-3-carbaldehyde (**1a'**) in 87% and 11% yield, respectively. It was then subjected to silica gel column chromatography (ethyl acetate/CH_2Cl_2, v/v=1:10) to afford **1a** and **1a'** as yellow liquids in 78% yield (1.71 g, 15.7 mmol) and 9% yield (0.21 g, 1.9 mmol), respectively. Their ^{1}H NMR spectra are in agreement with those reported in the literature.[9] 1-Methylpyrrole-2-carbaldehyde (**1a**): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.55 (s, 1H, CHO), 6.91 (dd, J = 4.0, 1.6 Hz, 1H, CH_{Ar}), 6.88 (brs, 1H, CH_{Ar}), 6.22 (dd, J = 4.0, 2.4 Hz, 1H, CH_{Ar}), 3.96 (s, 3H, CH_3). 1-Methylpyrrole-3-carbaldehyde (**1a'**): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.73 (s, 1H, CHO), 7.24 (t, J = 1.6 Hz, 1H, CH_{Ar}), 6.64-6.62 (m, 2H, CH_{Ar}), 3.72 (s, 3H, CH_3).

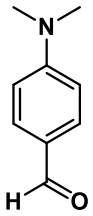
Synthesis of 1*H*-indole-3-carbaldehyde (1b)



VR was prepared with a same procedure as mentioned above. 1*H*-indole (0.59 g, 5 mmol) was dissolved in 2 mL of DMF, and then added to the flask 2 slowly at 0 °C. The sample solution was stirred at room temperature for 2 h. The resulting sample solution was then hydrolyzed with NaOH (aq., 2M, 25 mL) and extracted

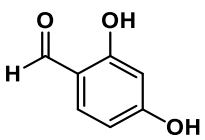
with CH_2Cl_2 (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4. ^{1}H NMR spectroscopy revealed that the sample solution contains 1*H*-indole-3-carbaldehyde (**1b**) in 42% yield. ^{1}H NMR spectrum is in agreement with that reported in the literature.[10] ^{1}H NMR (400 MHz, DMSO-d_6, 293 K): δ 12.16 (brs, 1H, NH), 9.96 (s, 1H, CHO), 8.30 (s, 1H, CH_{Ar}), 8.13 (d, J = 6.8 Hz,1H, CH_{Ar}), 7.54 (d, J = 7.2 Hz,1H, CH_{Ar}), 7.30–7.21 (m, 2H, CH_{Ar}).

Synthesis of 4-(*p*-dimethylamino)benzaldehyde (1c)



VR was prepared with a same procedure as mentioned above. *N*,*N*-dimethylaniline (0.63 mL, 5 mmol) was then added to the flask 2 slowly at 0 °C. The sample solution was stirred at room temperature for 2 h. The resulting sample solution was then hydrolyzed with NaOH (aq., 2M, 28 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 4-(*p*-dimethylamino)benzaldehyde (**1c**) in 57% yield. ^{1}H NMR spectrum is in agreement with that recorded in the Sigma-Aldrich FT-NMR Library (ver. 4.0.10). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 9.74 (s, 1H, CHO), 7.75 (d, J = 8.8 Hz, 2H, CH_{Ar}), 6.72 (d, J = 8.8 Hz, 2H, CH_{Ar}), 3.09 (s, 6H, CH_3).

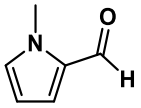
Synthesis of 2,4-dihydroxybenzaldehyde (1d)



VR was prepared with a same procedure as mentioned above. Resorcinol (0.55

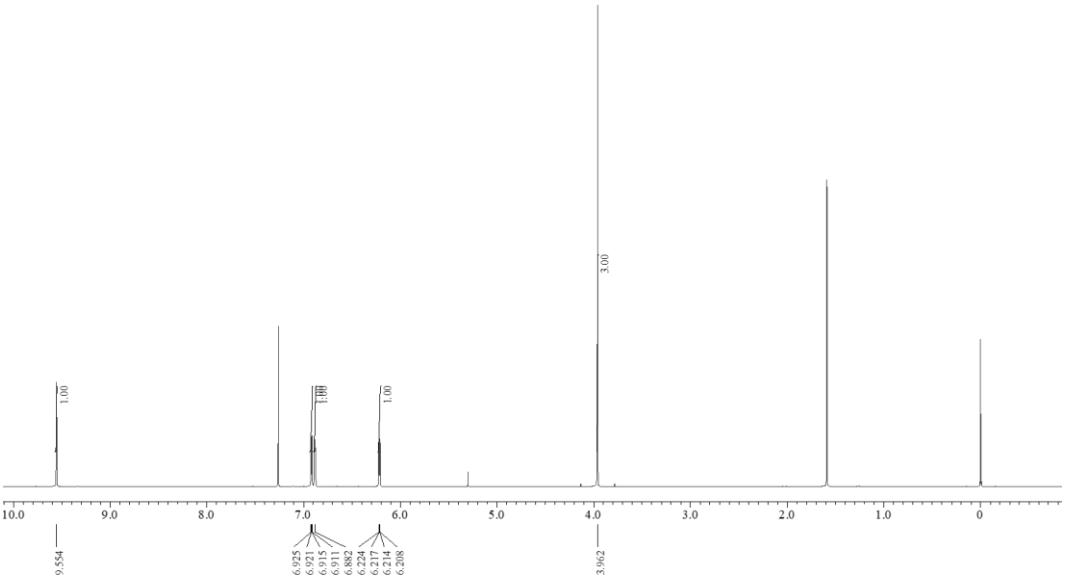
g, 5 mmol) was dissolved in 2 mL of DMF, and then added to the flask 2 slowly at 0 °C. The sample solution was stirred at 30 °C for 2 h. The resulting sample solution was then hydrolyzed with NaOH (aq., 2M, 21 mL) and extracted with CH_2Cl_2 (20 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated to dryness. ^{1}H NMR spectroscopy revealed that the residue contains 2,4-dihydroxybenzaldehyde (**1d**) in 71% yield. ^{1}H NMR spectrum is in agreement with that recorded in the Sigma-Aldrich FT-NMR Library (ver. 4.0.10). ^{1}H NMR (400 MHz, $CDCl_3$, 293 K): δ 11.43 (s, 1H, OH), 9.72 (s, 1H, CHO), 7.44 (d, J = 8.8 Hz, 1H, CH_{Ar}), 6.50 (dd, J = 8.8, 2.4 Hz,1H, CH_{Ar}), 6.39 (d, J = 2.4 Hz, 1H, CH_{Ar}), 5.80 (s, 1H, OH).

4.4.4 ^{1}H NMR spectra of products

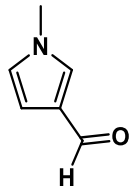


1-methylpyrrole-2-carbaldehyde (**1a**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

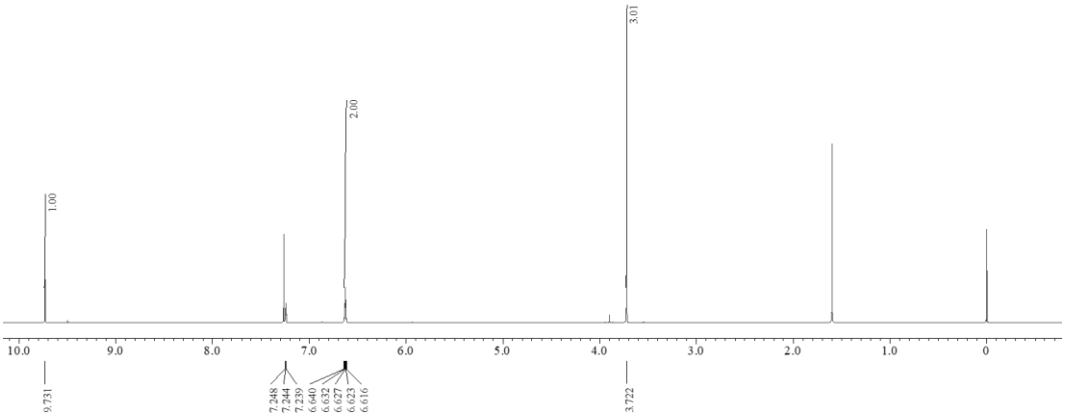


δ / ppm

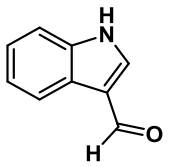


1-methylpyrrole-3-carbaldehyde (**1a'**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

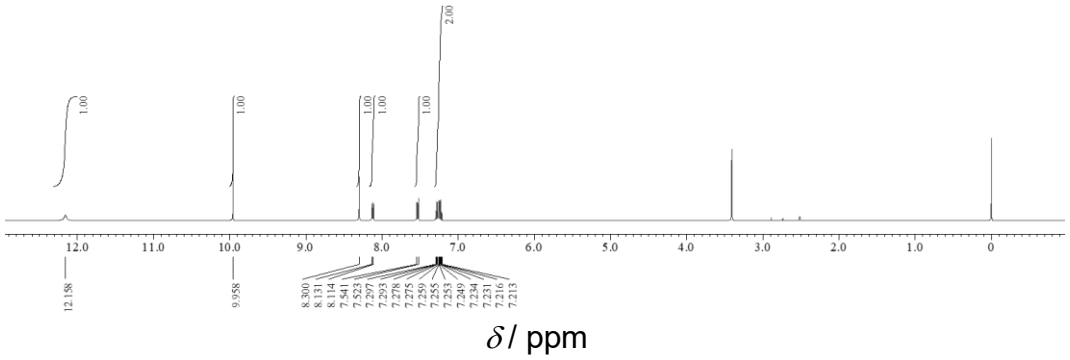


δ / ppm

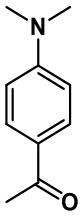


1*H*-indole-3-carbaldehyde (**1b**)

^{1}H NMR (400 MHz, DMSO-d_6, 293 K)

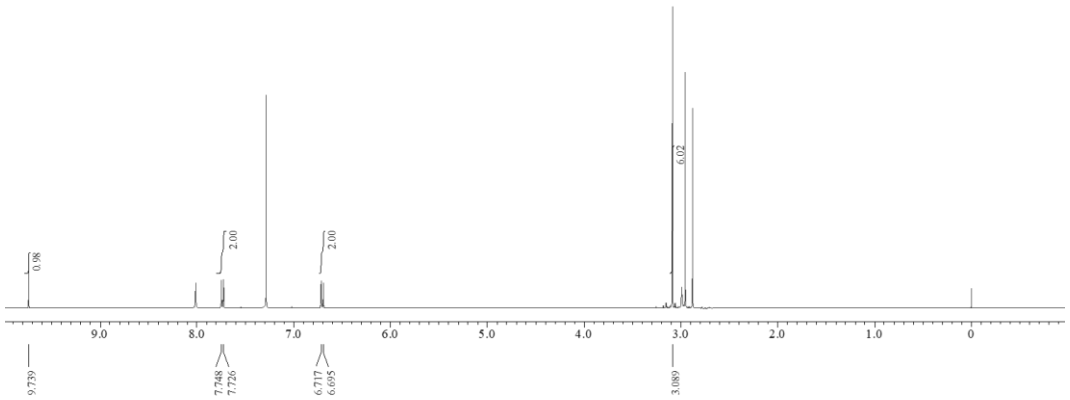


δ / ppm

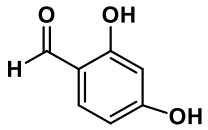


1-(4-(dimethylamino)phenyl)ethan-1-one (**1c**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)

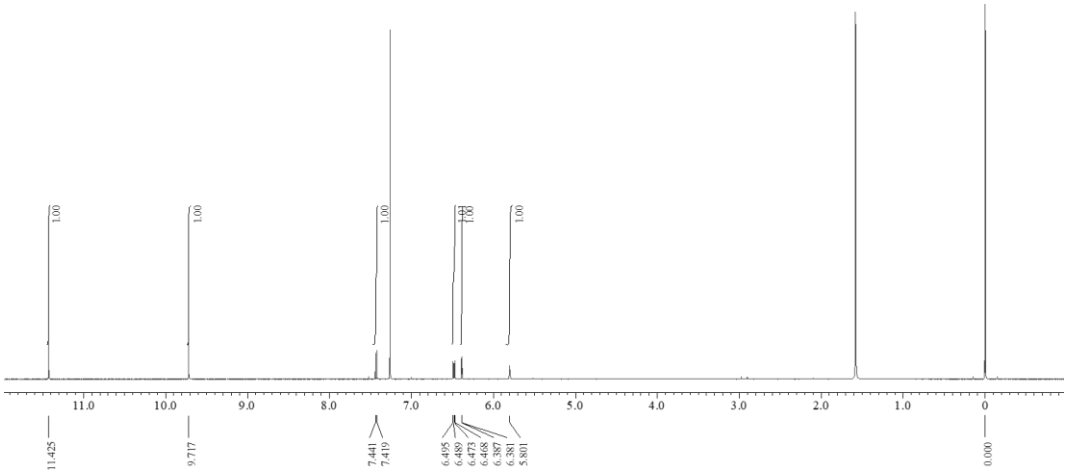


δ / ppm



2,4-dihydroxybenzaldehyde (**1d**)

^{1}H NMR (400 MHz, $CDCl_3$, 293 K)



δ / ppm

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Publications

1. F. Liang, M. Yanai, Y. Suzuki, A. Tsuda. Photo-on-Demand Synthesis of Chloroformates with a Chloroform Solution Containing an Alcohol and Its One-Pot Conversion to Carbonates and Carbamates. *Org. Lett.* **2020**, *22*, 3566-3569.

2. F. Liang, K. Eda, T. Okazoe, A. Wada, N. Mori, K. Konishi, A. Tsuda. Photo-on-demand Synthesis of Vilsmeier Reagents with Chloroform and their Applications to One-pot Organic Syntheses. (Has been submitted)