



Photo-on-Demand Synthesis of Organic Chemicals from Tetrachloroethylene

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(別紙様式 3)

論 文 内 容 の 要 旨

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専 攻 化 学 専 攻

論文題目 (外国語の場合は、その和訳を併記すること。)

Photo-on-Demand Synthesis of Organic Chemicals from Tetrachloroethylene

(テトラクロロエチレンからの有機化学品の光オン・デマンド合成)

指導教員 大 西 洋

Carbamates, ureas, carbonates, esters, and amides, due to their structural diversity, are widely used in fields such as pharmaceuticals, agrochemicals, fragrances, and solvents, and possess significant application value. Currently, in the photo-on-demand reaction system using chloroform (CHCl_3) as the raw material, phosgene (COCl_2) was generated in situ as a reaction intermediate through a photo-oxidation reaction, and subsequently used to synthesize target products such as carbamates, N-substituted ureas, carbonates, esters, and amides. This method achieved the synthesis of the target products through the in situ generation and consumption of COCl_2 . However, this reaction system relied on COCl_2 , which is highly toxic and was historically used as a chemical weapon. COCl_2 has a C1 building block and is a colorless gas at room temperature, with the odor of rotten grass. Due to its difficulty in being perceived, once leakage occurs in laboratories or industrial production, inhalation by the human body can easily cause severe health hazards, even endangering life, thus leading to serious safety accidents. Therefore, the development of reaction systems that are free of COCl_2 or reduce its use is an important safety challenge at present. In addition, the synthesis of carbamates, N-substituted ureas, esters, and amides involves the use of mercury lamps, and mercury has potential hazards to the environment and humans.

To enhance safety in both laboratory and industrial production environments, it is necessary to develop safer reaction systems. Trichloroacetyl chloride (TCAC) has a C2 building block and is a colorless liquid at room temperature. Compared with gaseous COCl_2 , it is more easily perceived and has a strong chlorine odor. Once a leakage occurs, the human body can usually perceive it quickly and evacuate in time. Therefore, TCAC has a significant safety advantage over COCl_2 . In this study, on the premise of avoiding the use of COCl_2 and mercury lamps, tetrachloroethylene (TCE) was used as the raw material to explore a method for photo-on-demand generation of TCAC under a safer and more environmentally friendly 365 nm LED light source, and TCAC was further utilized to synthesize carbonates, esters, and amides. At the same time, in order to further reduce the generation of COCl_2 and improve the yield of TCAC, my study also optimized the reaction conditions. In addition, N-substituted trichloroacetamides (NTCAs) were used as substrates to synthesize carbamates and N-substituted ureas.

In order to avoid the use of COCl_2 , this study used TCE as the raw material to generate TCAC through a photo-oxidation reaction, and synthesized carbonates, esters, and amides. In addition, the use of mercury lamps has potential hazards to the environment and humans, and UV-C light causes a certain amount of photodecomposition of organic substrates and products. To avoid the use of mercury lamps, this study used a safer and more environmentally friendly LED light source (365 nm) and introduces chlorine gas (Cl_2) as an

initiator to achieve efficient generation of TCAC, thereby avoiding the potential hazards of mercury lamps to the environment and humans. In order to reduce the formation of COCl_2 and increase the yield of TCAC, this study optimized the reaction temperature and reaction time, reducing the formation of COCl_2 to 13% while increasing the yield of TCAC to 85%, effectively reducing the formation of COCl_2 while taking into account the yield of TCAC.

In the study of the synthesis of carbamates and N-substituted ureas, the application of N-substituted trichloroacetamides (NTCAs) 1–5 as reaction substrates was investigated, including 2,2,2-trichloro-N-(2,2,2-trifluoroethyl)acetamide (NTCA 1), N,N'-(methylenebis(4,1-phenylene))bis(2,2,2-trichloroacetamide) (NTCA 2), N,N'-(octafluorohexane-1,6-diyl)bis(2,2,2-trichloroacetamide) (NTCA 3), N-phenyl-2,2,2-trichloroacetamide (NTCA 4), N-(2,2,2-trichloroacetyl)benzamide (NTCA 5). Under basic conditions, NTCA 1, 2, and 3 each underwent condensation reactions with alcohols to afford the corresponding carbamates, while NTCA 1, 4, and 5 respectively reacted with amines to afford the corresponding N-substituted ureas. The experimental results for the synthesis of carbamates indicate that NTCA 2, lacking fluorine substituents and thus having weaker electron-withdrawing effects, may lead to a slower formation rate of the isocyanate intermediate, thereby extending the reaction time and reducing the yield. In contrast, NTCA 1 contains a $-\text{CF}_3$, which increases the electron-withdrawing ability, significantly shortening the reaction time and improving the yield. NTCA 3, with a greater number of fluorine, exhibits higher reactivity and conversion efficiency, achieving a yield of up to 85%. In the synthesis of N-substituted ureas, N-substituted ureas were obtained through reactions with amines, with the highest yield reaching 84%. The results showed that the yield of N-substituted urea obtained by using aniline in the 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)/acetonitrile (CH_3CN) system was relatively low, which may be due to the limited nucleophilicity of aniline. In contrast, in the sodium hydroxide (NaOH)/dimethyl sulfoxide (DMSO) system, the higher basicity and polarity of the medium significantly enhance the reaction efficiency and yield of aniline with NTCA 4.

In order to avoid the use of mercury lamps, this study used TCE as a raw material and explored the method of generating TCAC under irradiation with a 365 nm LED light source. By introducing Cl_2 as an initiator and optimizing the reaction temperature and time, the yield of TCAC was effectively improved while the formation of COCl_2 was reduced. The experimental results showed that under the condition of $-20\text{ }^\circ\text{C}$, when the photoreaction time was extended to 5 hours, the yield of TCAC reached 85%, while the formation of COCl_2 was controlled at 13%. Further utilizing TCAC, carbonates were synthesized, with isolated yields ranging from 64% to 97%. In addition, during the experimental process, the formation of the

by-product CHCl_3 provided potential for resource recovery and reuse in this system. However, the formation of CHCl_3 is highly dependent on the reaction temperature, and its volatile nature leads to significant differences in the reaction conditions required for different target products, thereby bringing practical challenges to the efficient recovery of CHCl_3 .

In the study of ester synthesis, TCAC respectively reacted with sodium acetate, sodium laurate, lauric acid, and acetic acid to generate the corresponding mixed anhydrides, which then underwent condensation reactions with alcohols to achieve ester synthesis. The experimental results showed that the nucleophilicity of alcohols had a significant effect on the yield of esters and the formation of the by-product trichloroacetic acid esters (TCAEs). When the mixed anhydride formed from the reaction of TCAC with sodium acetate respectively reacted with 1-butanol and 2-propanol, which have relatively strong nucleophilicity, the isolated yields of the corresponding esters were relatively low (both 20%), while the amounts of the by-product TCAEs were relatively high (^1H NMR yields were 60% and 29%, respectively). In contrast, when fluoroalcohols or aromatic alcohols with weaker nucleophilicity were used, the isolated yields of the corresponding esters were 18–98%, and the formation of the by-product TCAEs was significantly reduced or even completely avoided. When sodium laurate or lauric acid containing an organic base reacted with TCAC to generate the corresponding mixed anhydrides, followed by reaction with phenol, the corresponding esters were obtained, with isolated yields of 48% and 62%, respectively, and no by-products were detected. In addition, when the mixed anhydride generated from the reaction of TCAC with acetic acid under basic conditions respectively reacted with 1-butanol and 2-propanol, which have relatively strong nucleophilicity, the isolated yields of the corresponding esters were significantly increased to 67% and 52%, and no TCAEs by-products were detected. This phenomenon may be attributed to the fact that the base in the system can rapidly capture the HCl released during the reaction process, maintaining the system in a weakly basic environment, thereby inhibiting the occurrence of side reactions and promoting the smooth progress of the esterification reaction between the mixed anhydride and an alcohol, effectively solving the problem of easily generating by-products TCAEs when using alcohols with relatively strong nucleophilicity. In the synthesis of amides, TCAC respectively reacted with sodium acetate, sodium laurate, sodium benzoate, acetic acid, lauric acid, and benzoic acid to generate the corresponding mixed anhydrides, which then underwent condensation reactions with amines to achieve the synthesis of amides. The experimental results showed that when butylamine and benzylamine respectively reacted with the mixed anhydrides, the isolated yields of the resulting amides were relatively low (18% and 31%, respectively), while the formation of the by-product trichloroacetamides (TCAAs)

was relatively high (^1H NMR yields were 70% and 34%, respectively). When aniline, *p*-toluidine, 4-fluoroaniline, 2,6-difluoroaniline, and pentafluoroaniline with weaker nucleophilicity respectively reacted with the mixed anhydrides, the isolated yields of the corresponding amides were 42–94%, and no by-products TCAAs were detected. The results showed that this reaction system was similar to the ester synthesis system, and when amines with weaker nucleophilicity were used, no by-products TCAAs were formed. Similarly, under basic conditions, when butylamine and benzylamine with relatively strong nucleophilicity respectively reacted with the mixed anhydrides, the isolated yields of the resulting amides were significantly increased to 68% and 71%, and no by-products TCAAs were detected.

In this study, under the premise of avoiding the use of COCl_2 , carbamates, N-substituted ureas, carbonates, esters, and amides were synthesized, improving the safety of the reaction. In order to avoid the use of mercury lamps, a safer and more environmentally friendly 365 nm LED light source was used, which effectively avoids the potential hazards of mercury lamps to the environment and humans. This study significantly improves the safety and environmental friendliness of the organic synthesis process, and has important practical significance and promotion value in both laboratory and industrial applications.

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要 旨			
申請者（舍乐木格）が提出した学位論文を、本研究科の学位論文評価基準に照らして審査するために、物理化学講座教員（大西）・有機化学講座教員（松原と田村）・有機化学と応用化学に深い造詣をもつ研究科外審査委員（森）からなる審査委員会を組織した。令和7年8月8日15時10分から審査委員全員の出席のもとで学位論文発表会を開催し、発表30分に続いて60分にわたって論文内容と関係学術分野に関する口頭試問をおこなった。試問終了後ただちに審査委員会を開催して、学位論文評価基準が定める以下の5項目について各委員の心証を意見交換し、ついで可否を判定した。 (1) 専攻分野に関する高度な学術的価値を有する研究結果を含むこと さまざまな官能基をもつ多種多様な有機化合物を自在に合成することは、基礎科学としての有機化学における最重要課題であると同時に、研究成果の社会還元をめざす学術である応用化学において中核的な意義を有する。これを実現するひとつの方策は、どのような反応物とも反応を起こしうる中間体化学種を利用することである。このような中間体の典型としてホスゲン（COCl_2）がある。非常に強い求電子剤であるホスゲンは、さまざまな炭酸エステル・尿素化合物・酸塩化物などを高収率で生産する優れた中間体である。しかし、広汎な有機物質と強く反応する中間体として好ましい性質は、人体をはじめとする生物体を強く浸食する毒性と表裏一体である。事実、ホスゲンは第一次世界大戦で実戦使用された化学兵器でもある。舍乐木格氏はホスゲンを代替する中間体として塩化トリクロロアセチル（CCl_3COCl）に注目し、この中間体をテトラクロロエチレン（C_2Cl_4）からオンデマンドに生成する光化学反応の反応条件を最適化して、生成した塩化トリクロロアセチルを中間体とする有用化合物合成を実証する学位研究をおこなった。学位論文2章と3章の内容はアメリカ化学会（ACS）が発行する <i>The Journal of Organic Chemistry</i> 誌ならびに <i>ACS Omega</i> 誌に上梓され、これまで計8回引用された。有機化学と応用化学において高度な学術的価値をもつと認められる。			

氏名 舍乐木格

(2) 先行研究や関連研究をふまえて適切な課題設定をおこなっていること

ホスゲン中間体の単離と保存に起因する危険を回避する方策として、津田明彦らはクロロホルム (CHCl_3) を炭素源として光誘起ラジカル反応によってホスゲンを生成消費を反応容器内に限定する光オンデマンド合成法を開拓してきた。舍乐木格氏がこの合成法をふまえて、炭素源をクロロホルムからテトラクロロエチレンに切り替え、ホスゲンの生成を抑制しつつ、塩化トリクロロアセチルを生成する光誘起ラジカル反応の開発に挑戦したことは適切である。

(3) 課題に対して適切な研究方法を選択し研究を実施していること

反応工程の対人危険性と環境負荷を抑制するために、気化しやすいホスゲン (沸点 8°C) を、常温液体である塩化トリクロロアセチル (沸点 115°C) で置き換えるアイデアは適切である。塩化トリクロロアセチルといえども反応性が高く、有害な化合物であることに配慮して、単離と保存を必要としない光オンデマンド合成法を利用したことによって、高度な安全設備を整備しにくい小規模事業所などにおいて利用しやすい合成法を構築できた。さらに、テトラクロロエチレンを塩化トリクロロアセチルに変換するラジカル反応の開始剤として塩素ガス (Cl_2) を利用することで、励起光源を水銀灯 (深紫外光源) から LED (近紫外光源) に転換することを可能にした。これらの要素技術を統合して窒素置換尿素・エステル・アミドなどを合成し、本手法が有用化合物の安全な合成に役立つことを実証した。

(4) 研究結果を適切に考察し結論を得ていること

本学位論文が提案する合成法の核は、テトラクロロエチレンを高収率で塩化トリクロロアセチルへ転換する光誘起ラジカル反応である。ラジカル反応は目的とする生成物以外の副生成物を与える短所をもつ。本研究においては、いったん生成した塩化トリクロロアセチルがホスゲンへ転化する副反応が問題となった。舍乐木格氏は反応温度を下げることでホスゲン生成を抑制し、炭素-炭素共有結合の開裂に必要な熱エネルギー供給をコントロールすることの有用性を考察した。

(5) 章立て・引用を含めて論理的で明瞭な記述をおこなっていること

研究背景 (1 章)・窒素置換トリクロロアセトアミドを出発物とする窒素置換尿素化合物の合成 (2 章)・テトラクロロエチレンを炭素源とする塩化トリクロロアセチルの光オンデマンド合成 (3 章)・塩化トリクロロアセチルを出発物とするカーボネイト (3 章) およびエステルとアミド化合物 (4 章) の合成・総括 (5 章) からなる学位論文 (160 ページ) の章立ては適切である。各章ともに目的・実験手順・実験結果・先行研究との比較にもとづく考察が順序よく英語で記述されている。先行研究に対する十分な検索と適切な引用がなされている。

【結論】以上の認識にもとづいて本審査委員会は、舍乐木格氏が提出した学位論文が学位論文評価基準をみたし、有機化学と応用化学の発展に寄与する成果として学位授与にふさわしい内容をもつと全員一致で判定した。