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研究課題名(和文) A common and potentially prebiotic activating agent for phosphorylation of nucleosides and oligomerization of nucleotides and amino acids

研究課題名(英文) A common and potentially prebiotic activating agent for phosphorylation of nucleosides and oligomerization of nucleotides and amino acids

研究代表者

蟻 瑞欽 (Yi, Ruiqin)

東京工業大学・地球生命研究所・研究員

研究者番号：00860090

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研究成果の概要(和文)：塩化シアンは RNA とペプチドの合成を活性化することが提案されました。この研究では、RNA 重合のためのヌクレオチドの 5'-ホスホリミダゾールへの活性化と、ペプチドへのアミノ酸の活性化が実証されました。固相ペプチド合成における塩化シアン活性化アミノ酸重合も実証されており、産業におけるペプチド合成に利用できる可能性がある。RNA 重合のための5'-ホスホリミダゾールへの合成およびアミノ酸重合は、塩化シアンを使用したワンポット合成で起こることがわかっています。これらの結果は、塩化シアンがプレバイオティクス化学において非常に有用な活性化試薬であることを示唆しています。

研究成果の学術的意義や社会的意義

This study provides an understanding how RNA and peptides could evolve chemically starting from simple molecules to complex polymers under a one-single environment. The performed peptides synthesis affords an idea of the extension of the outcome from prebiotic chemistry to applicable chemistry.

研究成果の概要(英文)：cyanogen chloride was proposed to activate the synthesis of RNA and peptides. In this research, the activation of nucleotides to their 5'-phosphorimidazoles for RNA polymerization and activation of amino acids to peptides has been demonstrated. The cyanogen chloride activated polymerization of amino acids in the solid-phase peptide synthesis was also demonstrated, which could be used for the peptide synthesis in the industry. The activation of nucleotides to their 5'-phosphorimidazoles for RNA polymerization and amino acids polymerization has been found to occur in a one-pot synthesis using cyanogen chloride as a common activating agent. These results suggest that cyanogen chloride is a very useful activating reagent in the prebiotic chemistry.

研究分野：Prebiotic Chemistry

キーワード：The Origins of Life Amino acids RNA Peptides Polymerization Activating Chemistry

研究開始当初の背景

- (1) In the origins of life study, many studies have focused on the possible prebiotic synthetic pathways for some specific biomolecules, involving nucleotides, amino acids, and their corresponding oligomers. However, most of these pathways have relied on “discontinuous synthesis” models, which employ step-by-step chemical protocols or well-timed additional steps to favor specific targets.
- (2) To solve this problem in prebiotic synthesis, we have recently proposed to take a new approach of “continuous reaction networks”, in which a wide variety of compounds are constantly being formed, and reacting with each other to form new compounds. Based on the above consideration, we have recently demonstrated a continuous reaction network of nucleotides and RNA polymers. The next key question is whether this continuous model can enable the subsequent step towards the generation RNA polymers compatible with forming other important substrates, such as oligopeptides.

研究の目的

- (1) The primary purpose of this WAKATE project is to provide an understand of how RNA and peptides could evolve chemically starting from relatively simple molecules to complex polymers in a continuous manner under a single-pot environment.
- (2) More specifically, this project aims to demonstrate oligomerization of nucleotides to RNA and amino acids to peptides using cyanogen chloride as a chemical activator.

研究の方法

- (1) The activation of amino acids to peptides using cyanogen chloride as a chemical activator has been carried out. The intermediates formed in this mixture was observed by NMR spectroscopy to elucidate the reaction mechanism.
- (2) The peptide synthesis was be tested in the presence of nucleotides, to see if nucleotide 5'-phosphorimidazoles and peptides can be simultaneously formed under the same condition.
- (3) A solid-phase peptide experiment employing cyanogen chloride as an activating agent will be carried out and analyzed by HPLC.

研究成果

- (1) The activation of amino acids to peptides using cyanogen chloride was found to afford *N*-(aminocarbonyl)peptides see Figure 1. Deprotection of the urea group from *N*-(aminocarbonyl)peptides to obtain free peptide was success by the use of NO_2 . Repeating the processes of activation and deprotection can effectively extend the chain of oligopeptides. Twenty common amino acids were tested and most of them can be activated by this method.
- (2) Nucleotide 5'-phosphorimidazoles and peptides has been found to be generated simultaneously when cyanogen chloride was added into the solution of imidazole and nucleotides, and amino acids.

(3) A solid-phase peptide experiment employing cyanogen chloride as an activating agent has successfully achieved several types of free peptides in a highly pure form, indicating that this method has a potential possibility for the industry application.

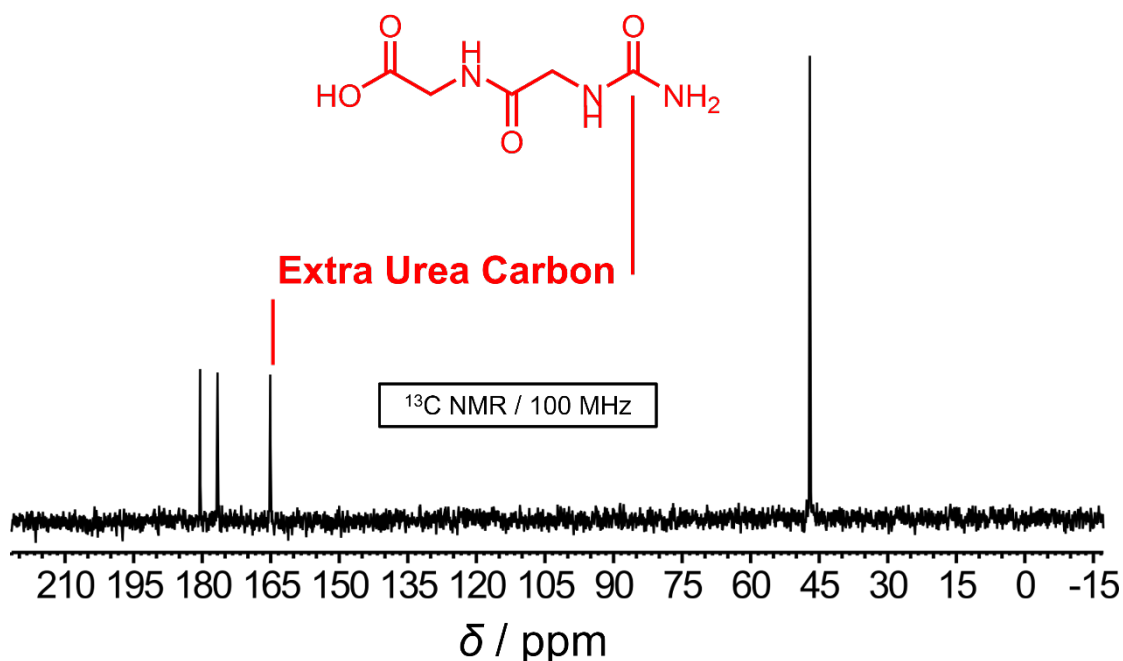


Figure 1. The ^{13}C NMR of *N*-(aminocarbonyl)glycine dimer.

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1. **Ruiqin Yi***, Mike Mojica, Albert C Fahrenbach, H James Cleaves, Ramanarayanan Krishnamurthy*, Charles L Liotta*. Carbonyl Migration in Uronates Affords a Potential Prebiotic Pathway for Pentose Production. *JACS Au* **2023**, 3(9), 2522-2535.
2. **Ruiqin Yi***, Tony Z. Jia, Markus Meringer, Luke K. Marshall, Chen Chen, Shawn Erin McGlynn, Albert C. Fahrenbach and H. James Cleaves II*. Alternating co-synthesis of glycol nucleic acid (GNA) monomers with dicarboxylic acids via drying. *ChemComm* **2023**, 59(45), 6865-6868.
3. **Ruiqin Yi***, Ryan Kern, Pamela Pollet, Huacan Lin, Ram Krishnamurthy*, Charles L. Liotta*. Erythrose and Threose: Carbonyl Migrations, Epimerizations, Aldol, and Oxidative Fragmentation Reactions Under Plausible Prebiotic Conditions. *Chemistry—A European Journal* **2023**, 29(8), e202202816.
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5. 主な発表論文等

〔雑誌論文〕 計4件（うち査読付論文 4件/うち国際共著 4件/うちオープンアクセス 1件）

1. 著者名 Yi Ruiqin, Kern Ryan, Pollet Pamela, Lin Huacan, Krishnamurthy Ramanarayanan, Liotta Charles L.	4. 巻 29
2. 論文標題 Erythrose and Threose: Carbonyl Migrations, Epimerizations, Aldol, and Oxidative Fragmentation Reactions under Plausible Prebiotic Conditions	5. 発行年 2023年
3. 雑誌名 Chemistry A European Journal	6. 最初と最後の頁 1~12
掲載論文のDOI (デジタルオブジェクト識別子) 10.1002/chem.202202816	査読の有無 有
オープンアクセス オープンアクセスとしている (また、その予定である)	国際共著 該当する
1. 著者名 Afrin Rehana, Chen Chen, Sarpa Davide, Sithamparam Mahendran, Yi Ruiqin, Giri Chaitanya, Mamajanov Irena, Cleaves H. James, Chandru Kuhan, Jia Tony Z.	4. 巻 223
2. 論文標題 The Effects of Dehydration Temperature and Monomer Chirality on Primitive Polyester Synthesis and Microdroplet Assembly	5. 発行年 2022年
3. 雑誌名 Macromolecular Chemistry and Physics	6. 最初と最後の頁 2200235 ~ 2200235
掲載論文のDOI (デジタルオブジェクト識別子) 10.1002/macp.202200235	査読の有無 有
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 該当する
1. 著者名 Saha Arpita, Yi Ruiqin, Fahrenbach Albert C., Wang Anna, Jia Tony Z.	4. 巻 12
2. 論文標題 A Physicochemical Consideration of Prebiotic Microenvironments for Self-Assembly and Prebiotic Chemistry	5. 発行年 2022年
3. 雑誌名 Life	6. 最初と最後の頁 1595 ~ 1595
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1. 著者名 Yi Ruiqin, Jia Tony Z, Meringer Markus, Marshall Luke K., Chen Chen, McGlynn Shawn E, Fahrenbach Albert C., Cleaves H. James	4. 巻 未知
2. 論文標題 Alternating co-synthesis of glycol nucleic acid (GNA) monomers with dicarboxylic acids via drying	5. 発行年 2023年
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掲載論文のDOI (デジタルオブジェクト識別子) 10.1039/D2CC06818D	査読の有無 有
オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 該当する

〔学会発表〕 計0件

〔図書〕 計0件

〔産業財産権〕

〔その他〕

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6. 研究組織

	氏名 (ローマ字氏名) (研究者番号)	所属研究機関・部局・職 (機関番号)	備考
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7. 科研費を使用して開催した国際研究集会

〔国際研究集会〕 計0件

8. 本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関
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