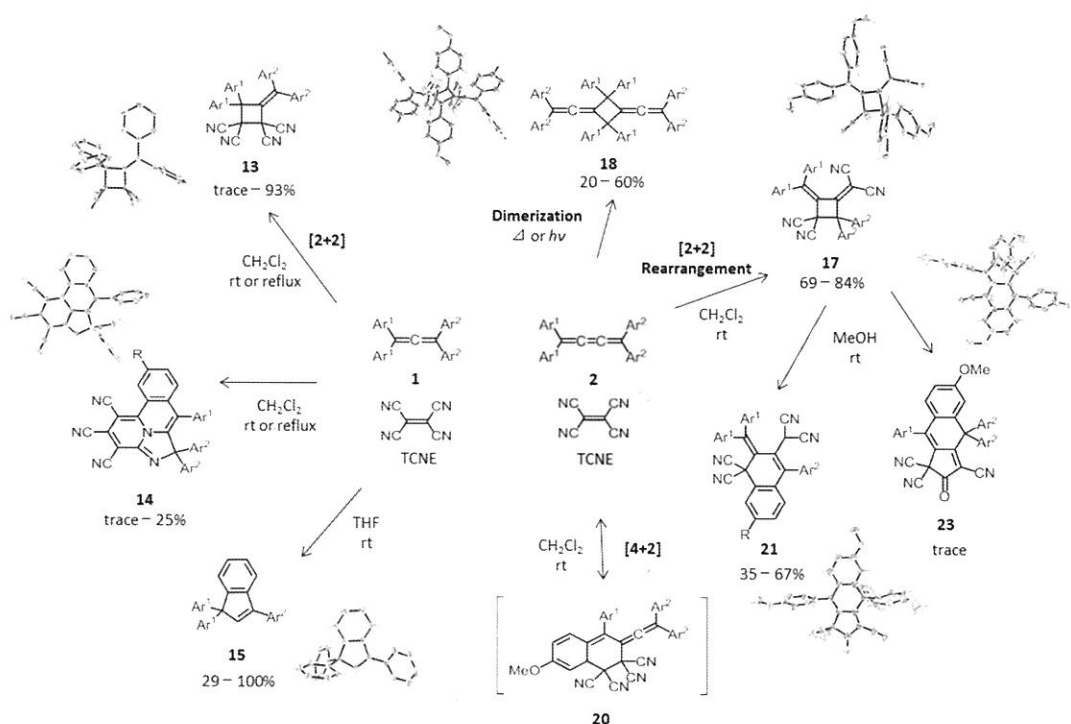


論文の要約

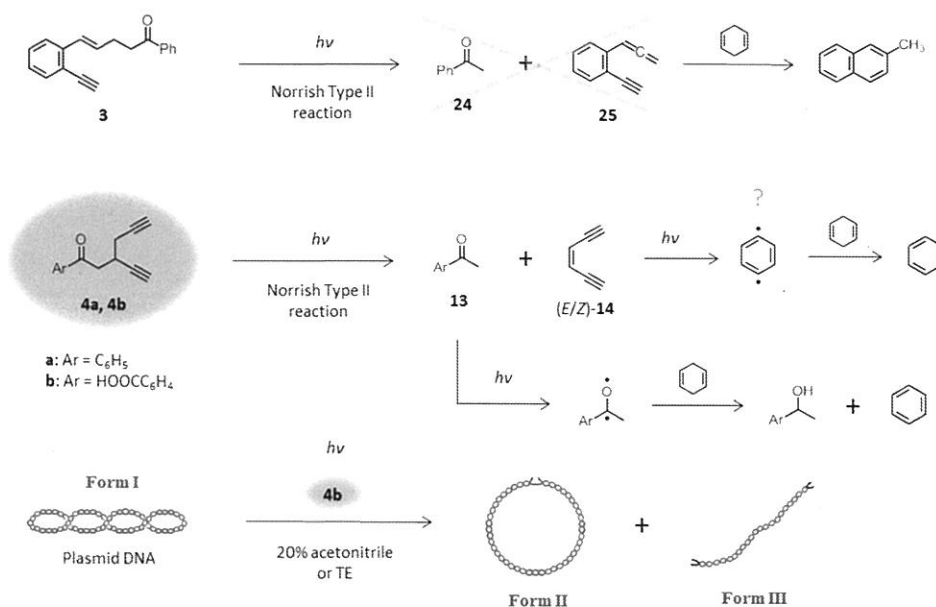
報告番号	甲 乙	第 229 号	氏名	小林 昭子
学位論文題目	Exploration of the Materials Science- and the Physiology-Oriented Chemistry of the sp-Carbon Rich Hydrocarbons, Allenes, Cumulenes and Acetylenes (アレン, クムレン, アセチレンのsp炭素を活用した新規機能性材料及び生理活性物質の創出)			

In the present study, I focused on the chemistry of sp-carbon atoms of unsaturated compounds such as allene, cumulene and acetylene. Especially, I interested in the organic functional materials and physiologically active substances with the use of consecutive C=C bonds and C≡C bonds.



Firstly, I have investigated the charge-transfer reactions of tetraaryllallene **1** and tetraaryl[3]cumulene **2** with tetracyanoethene (TCNE), a strong electron-accepting molecule. The reaction of allene **1** with TCNE at room temperature yielded the main four-membered ring compound **5** and the minor product **6**. Cyclobutane **5** was probably formed by [2+2] cycloaddition of the C=C bond of **1** with TCNE. On the other hand, **6** was determined by X-ray analysis to be a novel tetracyclic compound containing two nitrogens similar to a imidazo[1,5-*a*]pyridine and azaazulene derivatives. Several literatures show that imidazo[1,5-*a*]pyridine derivatives possess emission property and exhibit physiological activity, and azaazulene derivatives are also expected to use dye or antitumor agent. Actually, the solution of **6** displayed bright purple color and possessed long-wavelength absorption. In the case of the reaction of [3]cumulene **2** with TCNE at room temperature, a novel

four-membered ring compound **8** (a head-to-tail unsymmetrically substituted diaryllallene dimer) was formed by [2+2] cycloaddition of the central C=C bond of the [3]cumulene with TCNE in good yield; during this reaction, head-to-head symmetrically substituted diaryllallene dimer intermediate was formed. Unsymmetrical [3]cumulene also formed a small amount of another head-to-tail dimer **9**. Although allene dimer **8** was stable in nonpolar solvents, the four-membered ring of **8** cleaved to give the further-rearranged bicyclic and tricyclic compounds **10** and **11** in MeOH or CH₃CN. The MO calculations and cyclic voltammetry of products showed that the allene dimer **8** is assumed to produce a stable anion radical and may be a novel electron-accepting compound.



Secondly, I reported the development of novel DNA cleaving molecules possessing allene and acetylene. Ene-yne-allene and enediyne precursors are known to undergo either Myers-saito or Masamune-Bergman cyclization, with the produced diradical being able to abstract hydrogen from the phosphate backbone of DNA. I developed novel ene-yne-allene precursor **3** and enediyne precursor **4** possessing phototriggering functionality *via* a Norrish Type II reaction. The reaction of **3** under UV irradiation (≥ 280 nm) at room temperature could not yield acetophenone and ene-yne-allene; therefore Norrish Type II reaction was assumed to be not proceed. It was probably not easy for the $n\pi^*$ excited carbonyl oxygen to abstract the γ -hydrogen. On the other hand, enediyne precursor **5** afforded acetophenone **13** and (E/Z) -enediyne **14** under UV irradiation at room temperature through a Norrish Type II reaction, followed by hydrogen abstraction from 1,4-cyclohexadiene (CHD) to give benzene. Enediyne (Z) -**14** derived from **4** was assumed to undergo a Bergman cyclization and abstract hydrogen, but it was not clear from the current results whether (Z) -**14** formed the diradical intermediate. Because acetophenone itself abstracted hydrogen from CHD, the carbonyl oxygen of **4** was also expected to directly abstract hydrogen. In addition, **4** was able to cleave supercoiled DNA (Form I) to afford the nicked open circular Form II. As well, **4b**, which

possessed a carboxylic acid, was slightly soluble in water and effectively cleaved DNA to give Form II and linear Form III in TE without organic solvent.

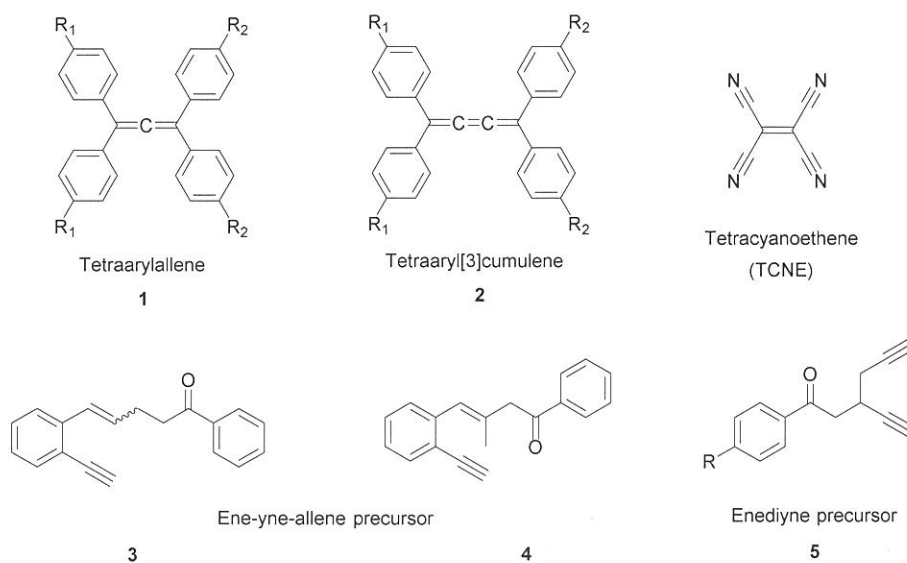
In summary, I explored the chemistry and utility of sp-carbon atoms of allene/cumulene and acetylene. To contribute to growth of the rich chemistry of these compounds, further study including the investigation of the properties and reactivity of other higher cumulenes and the development of novel precursors such as 9- or 10-membered ring ene-yne-allene and enediyne with phototriggering functionalities are in progress.

論文内容要旨

報告番号	甲 先 第 229 号	氏 名	小林（上田）昭子
学位論文題目	Exploration of the Materials Science- and the Physiology-Oriented Chemistry of the sp-Carbon Rich Hydrocarbons, Allenes, Cumulenes and Acetylenes (アレン, クムレン, アセチレンのsp炭素を活用した新規機能性材料及び生理活性物質の創出)		
<p>内容要旨</p> <p>sp-Carbon atoms of unsaturated organic compounds, especially allene/cumulene and acetylene, are unique and these synthesis and reactivity have been reported in several reviews. Consecutive C=C bonds of allene or cumulene and C≡C bond of acetylene are contained in many organic functional materials and physiologically active substances. For example, radialene and ketene dimer are expected to be used as organic electronics materials and dyes. Cumulene also draws attention as a novel organometallic catalyst and functional polymer. On the other hand, 1,2,4-heptatriene-6-yne and 1,5-hexadiyne-3-ene are generally known as potent antitumor agents. Recently, various functional ene-yne-allene and enediyne precursors have been developed. In addition, several literatures reported metal catalyzed syntheses of physiologically active hetero rings from aminoallene. Despite the fact that the chemistry of these compounds has been studied fairly extensively, the rich chemistry of these unsaturated molecules is yet to be revealed. In the present study, I focused on the two aspects of charge-transfer reactions of allene/[3]cumulene with electron acceptor and development of physiologically active substances possessing allene or acetylene moiety.</p> <p>Allenes (propadienes) are the simplest cumulated diene and the central carbon is sp-hybridized. The synthesis and chemistry of allene have attracted attention because of the unique strained structure possessing axial chirality and interesting reactivity. Several literatures showed that allene precursors are useful for syntheses of physiologically active substances, dye molecules and polymer molecules. In addition, cumulenes are the homologous series of hydrocarbons that contain three or more sequential double bonds sharing the sp-hybridized carbon atoms. The consecutive sp-hybridized carbon atoms of cumulene are very unique and may lead to a wide variety of reactions; particularly, the chemistry of [3]cumulenes (butatrienes) has been investigated. For example, a [3]cumulene possessing an electron withdrawing group such as Cl as a terminal group thermally dimerizes to a [4]radialene. Early studies showed that tetraphenyl[3]cumulene photodimerizes to a head-to-tail dimer at the terminal C=C bond of two molecules of the [3]cumulene. Recently, nickel-catalyzed cycloaddition of tetramethyl[3]cumulene yielded not only octamethyl[4]radialene but also dodecamethyl[6]radialene. On the other hand, tetraphenyl[3]cumulene, which is more stable than tetramethyl[3]cumulene, was unreactive even in the presence of a nickel(0) catalyst.</p>			

Firstly, I have investigated the charge-transfer reactions of tetraaryllallene (**1**) / tetraaryl[3]cumulene (**2**) with tetracyanoethene (TCNE). The ethane, TCNE, was discovered in 1957 as the simplest of the symmetrical percyanoalkene. Not only was it found to be extremely reactive and to undergo a series of addition and substitution reactions, but also the forerunner of the cyano-based acceptor molecules known to date. It is well established that the π -orbitals of the alkene group in TCNE possess low-lying energies and thus TCNE lead to a wide variety of reactions.

Secondly, I focused on DNA cleaving molecules possessing allene and acetylene. Natural ene-yne-allene and enediyne precursors such as calicheamicin, dynemicin and neocarzinostatin are known to be DNA cleaving molecules derived from bacteria. These precursors can undergo either Myers-Saito or Masamune-Bergman cyclization, with the produced diradical being able to abstract hydrogen from the phosphate backbone of DNA. However, these precursors are toxic to not only tumor cells but also normal cells; therefore, they are not effective antitumor agents. Alternatively, ene-yne-allene and enediyne precursors with various functionalities have been designed and reported in several reviews. Early studies showed that an enediyne constrained in a 10-membered ring could easily undergo Bergman cyclization at room temperature. Following this, a water-soluble 10-membered ring enediyne possessing hydroxyl groups was prepared and found to undergo a Bergman cycloaromatization at 37 °C. It was also found to cleave double-stranded DNA. A bicyclic enediyne was also synthesized. Although it was stable at room temperature, cyclization only occurred at elevated temperatures. In addition, ene-yne-allenes and enediynes possessing photo-triggering functionalities have attracted attention. Recently, Suzuki and co-workers developed novel enediyne model compounds with photochemically removable protecting groups such as *o*-nitrobenzyl ester and ether. In this study, I report the synthesis of ene-yne-allene (**3**, **4**) and enediyne precursors (**5**) possessing photo-triggering functionality *via* a Norrish Type II reaction. In addition, I have extended the photochemistry of **3–5** and explored its use as novel DNA cleaving molecules.



論文審査の結果の要旨

報告番号	甲 先 第 229 号	氏 名	小 林 昭 子
審査委員	主査 今 田 泰 嗣 副査 右 手 浩 一 副査 河 村 保 彦		
学位論文題目 Exploration of the Materials Science- and the Physiology-Oriented Chemistry of the sp-Carbon Rich Hydrocarbons, Allenes, Cumulenes and Acetylenes (アレン, クムレン, アセチレンのsp炭素を活用した新規機能性材料及び生理活性物質の創出)			
審査結果の要旨 <p>本博士論文は, sp混成軌道の炭素を鍵原子とした基本的な炭化水素 (アレン, クムレン, アセチレンなど) の付加反応性を解明したものである。併せて, それらの分子の光励起でエンジインやエンインアレンの生成に続く活性ジラジカルの発生を期待し, 分子生物学分野でも関心を持たれているDNA損傷活性の発現に展開した。</p> <p>標題の化合物群は, p性に富んだ炭素原子を有し, 高い付加反応性や光反応性が期待できる。また, それらの化合物を構成する化学結合の集積は, 分子軌道の更なる相関を生じるため新たな反応性が期待されるが, そうした観点の知見は欠けていた。</p> <p>本学位論文提出者は, 標題化合物の前述の特徴を考慮する一方, 電荷移動反応に関する知見が殆どないことに着目し, 二重結合の数を系統的に変化させたアレン, クムレン類の当該反応を精査した。反応性評価は主に物質分析の手法により, 生成物分離と優れた結晶化手法により多数の単結晶X線構造解析を成し遂げた。その結果, 発光材料や分子触媒など機能性材料並びに有機化学の発展に資すると期待される多くの新規な有機分子を見出すと共に, 構造と反応性並びに反応機構を明らかにした。</p> <p>また, これらの熱反応に対し光励起状態の反応性解明の観点から, 基本的な有機光反応として知られるNorrish Type II反応を用い, 光照射で二重結合を生じる構造要素を標題分子の新たなデザインに包含させた。そして, 光照射によるエンジインやエンインアレンの生成を狙った。後者はさらに検討を要したが, 前者は室温でのバグマン環化が誘起できた。とりわけ, カルボキシル基をエンジイン前駆体に導入し水溶性を賦与するとともに, 当該前駆体の光照射・環化・活性ジラジカルの生成でϕX174RFIプラスミドDNAの二重螺旋がForm III (鎖状構造) へ損傷できることを見出した。</p> <p>以上本研究は, 従来比較的不安定なため知見の乏しかったsp炭素による炭化水素分子の新たな化学反応を開拓するとともに, 材料科学や分子生物学に資する知見を見出したものであり, 本論文は博士 (工学) の学位授与に値するものと判定する。</p>			