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題目(和文)	9,10-ジ（ピペラジニル）アントラセンを基にした生体適合性の粘度応答性蛍光プローブの開発
Title(English)	Development of Biocompatible Viscosity-Responsive Fluorescent Probes Based on 9,10-Di(piperazinyl)anthracene
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学位種別(和文)	博士論文
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種別(和文)	要約
Type(English)	Outline

This dissertation, entitled “Development of Biocompatible Viscosity-Responsive Fluorescent Probes Based on 9,10-Di(piperazinyl)anthracene（9,10-ジ（ピペラジニル）アントラセンを基にした生体適合性の粘度応答性蛍光プローブの開発）”, deals with the development of viscosity-responsive fluorescent probes based on 9,10-di(piperazinyl)anthracene and the imaging results using these probes.

Microviscosity has attracted significant interest due to its influence on various biologically relevant processes. Since the mechanical methods are not suitable for measuring the viscosity in microenvironments, visualization of viscosity using small molecular fluorescent probes that respond to viscosity has been explored. In this context, TICT-based fluorescent molecules are frequently used as viscosity-responsive probes. In this study, the author focused on the molecules that undergo conformational changes at MECI as a viscosity-responsive unit in order to minimize sensitivity to the environmental factors other than the viscosity. Indeed, the author developed 9,10-di(piperazinyl)anthracene and its derivatives for biocompatible viscosity-responsive probes (Figure 1). As a result, it was found that introduction of oligo(ethylene glycol) chains on 9,10-di(piperazinyl)anthracene unit provided biocompatibility to the molecules, and demonstrated their potential for use in viscosity-targeted imaging of biologically important targets under various conditions.

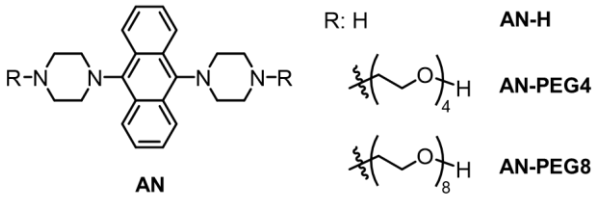

Figure 1. Molecular structure of **AN**.

This dissertation consists of the following six chapters. In chapter 1, entitled “General Introduction”, the characteristics of viscosity-responsive emissive molecules are overviewed in terms of environment-responsive fluorescent probes. The challenges in developing viscosity-responsive fluorescent probes suitable for use in cellular systems are highlighted, and the limitations of the conventional probes and recent approaches to address these limitations are described. Then, taking into consideration this background, the objectives of this study and the novel molecular design are described.

Chapter 2, entitled “Synthesis and Photophysical Properties of 9,10-Di(piperazinyl)anthracene and Its Derivatives Directed Toward Biocompatible Probes”, describes

synthesis and photophysical properties of the molecules developed in this study. The synthetic methods to afford **AN** were established, and the conditions for inapplicable reactions are also described. Then, for the use in aqueous environments, protonation at the amino group of the molecules is also investigated, and their optical properties are studied from both experimental and computational perspectives. The modification of the side chain did not significantly affect the fluorescence properties, indicating that appropriate modification of the side chain can be designed for each purpose.

Chapter 3, entitled "Dense and Acidic Organelle Visualization in Living Cells and Responsiveness to Intracellular Biological Processes", describes the results of investigation on living cell imaging using the probes developed in this study. Various cell experiments have revealed that the molecule bearing oligo(ethylene glycol) chains exhibit low cytotoxicity and cell membrane permeability, and it can selectively stain acidic and dense organelles. Furthermore, the fluorescence response to biological processes within cells was demonstrated, indicating their utility as viscosity-responsive fluorescent probes.

Chapter 4, entitled "Control of Sensitivity to Micelles/Vesicles by length of Monodisperse Oligo(Ethylene Glycol) Substituted to 9,10-Di(piperazinyl)anthracene", describes the responsiveness of the developed molecules in solutions containing micelles and vesicles. 9,10-Di(piperazinyl)anthracene and oligo(Ethylene Glycol)-substituted derivatives increased their emission intensity in the presence of micelles, regardless of the type of surfactants. In contrast, the sensitivity to vesicles was exhibited variably. In conclusion, the results demonstrate that the sensitivity to micelles and vesicles is influenced by the pH of the solution and the length of the side chain, and the reason why background-free staining was achieved in cell imaging in Chapter 3 is discussed.

Chapter 5, entitled "Label-Free Visualization of Multiphase Coacervates by Targeting Viscosity", describe the visualization of coacervates. While the coacervates have attracted considerable attention in terms of a chemical model of liquid-liquid phase separation, coacervate-selective label-free visualization has not been fully established probably due to no-specific target for this purpose. Here, the author achieved the visualization of coacervates by targeting their characteristic high viscosity, and the multiphase coacervates can be distinguishably observed utilizing fluorescence lifetime.

In chapter 6, as "conclusion and perspective", the summary of the dissertation and future prospects in the relevant fields are described. Despite the various challenges present in this field,

the development of viscosity-responsive probes is one important research issue from the perspective of organic chemistry. The author summarizes the current situation on this point and points out the need for standardizing terminology, which is currently somewhat confusing. Finally, the author provides future perspectives on the biological significance of viscosity, an area that has yet to be fully addressed.