千葉大学
CHIBA UNIVERSITY

RESEARCH NEWS STORY

January 14, 2026
Chiba University

Bis-Pseudoindoxyls: A New Class of Single Benzene-Based Fluorophores for Bioimaging Applications

Researchers developed bis-pseudoindoxyls, compact fluorophores with red-shifted absorption and fluorescence, which can be utilized for time-resolved bioimaging

Fluorescent dyes enable the visualization of biomolecular localization and dynamics in living systems. To date, no single benzene-based fluorophores with absorption and emission at wavelengths above 600 nm, the ideal wavelength for bioimaging, have been developed. To address this challenge, researchers from Japan have developed bis-pseudoindoxyls. Owing to its unique red-shifted absorption and fluorescence properties, this dye holds promise for applications in red-light-based bioimaging studies.

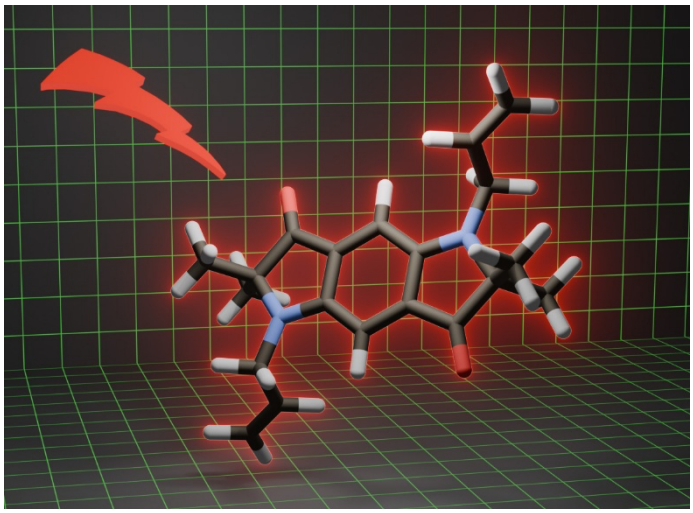

Image title: Bis-Pseudoindoxyl: A New Fluorophore for Bioimaging
Image caption: Single benzene-based fluorophores with absorption wavelengths above 600 nm are ideal for bioimaging. Recently, scientists from Japan have developed bis-pseudoindoxyls, which exhibit red-region absorption and emission. This compact fluorophore is ideal for long-term live-cell imaging of lipid droplets in the red spectral region.
Image credit: Professor Tetsuhiro Nemoto from Chiba University, Japan
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Fluorophores are chemical compounds or molecules that absorb light energy at one wavelength and re-emit it as light at a longer, lower-energy wavelength, acting as glowing tags or markers. The absorption process is known as excitation, and the re-emission is visible as fluorescent light, which makes these molecules crucial for biological imaging, diagnostics, and tracing cellular molecules like proteins or lipids under normal or various infectious conditions.

Fluorophores with red-light absorption properties are ideal for bioimaging. Red light refers to wavelengths above 600 nm, and in this range, the natural absorption capacity of chromophores inside our body, like DNA and proteins, is reduced. Therefore, fluorescent probes with absorption bands in this region are specifically excited. Recently, fluorophores featuring a single benzene ring as the core structure, known as single benzene-based fluorophores (SBBFs), have attracted increasing attention due to their small molecular size and excellent biocompatibility. However, no SBBF with absorption wavelengths above 600 nm has been reported to date.

To address this challenge, a team of scientists led by Professor Tetsuhiro Nemoto from the Graduate School of Pharmaceutical Sciences, Chiba University, Japan, has developed a new class of single benzene-based fluorophores, bis-pseudoindoxyls. The team comprised Tomohiro Yazawa and Akiko Takaya from the Graduate School of Pharmaceutical Sciences, Chiba University, and Masaya Nakajima from the Graduate School of Pharmaceutical Sciences, the University of Tokyo, Japan. Their research findings were made available online on November 10, 2025, and were published in Volume 27, Issue 46 of the journal *Organic Letters* on November 21, 2025.

A pseudoindoxyl scaffold is a unique bicyclic chemical structure with a five-membered nitrogen-containing ring fused to a six-membered benzene ring at its core. It is found in complex natural products that exhibit distinctive light absorption and emission properties. *"Based on this understanding, our collaborators and our team conducted computational predictions of the photophysical properties of various pseudoindoxyl derivatives and explored new synthetic approaches to this framework,"* explains Dr. Nemoto. Based on this, the core scaffold of the molecule, 14CO25NH, was developed. This was further modified chemically to develop 14CO25Nallyl. Among all the synthesized dyes, this molecule was the most suitable for bioimaging due to its properties.

To test its suitability for bioimaging, the researchers conducted live cell imaging using 14CO25Nallyl as a red-light-excitable fluorescent dye. It was used for successful visualization of lipid droplet formation inside live cells during *Salmonella* infection. The dye showed low cytotoxicity and sufficient aqueous solubility, properties that make it suitable for live-cell bioimaging.

The dye exhibits some unique properties. *"This fluorophore itself exhibits a blue color. It is also expected to find applications as a pigment material. In addition, compared with known molecules that possess comparable red-light absorption properties, it features a smaller molecular size and superior cell membrane permeability,"* says Prof. Nemoto. Red light in the visible region offers deeper tissue penetration and lower phototoxicity than shorter-wavelength light.

Due to its advantageous properties, this dye holds promise for applications in red-light-based bioimaging studies and as a functional coloring agent. Talking about the implications of the study, Dr. Nemoto mentions, *"This study has laid the groundwork for creating new dye molecules that remain compact in size while still being able to absorb and emit long-wavelength light. By using this dye framework, we expect to open up new possibilities for developing medical technologies, including near-infrared light-based diagnostics and photodynamic therapy."*

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About Professor Tetsuhiro Nemoto from Chiba University, Japan

Dr. Tetsuhiro Nemoto currently serves as a Professor at the Graduate School of Pharmaceutical Sciences, Chiba University, Japan. He completed his Ph.D. at the University of Tokyo, Japan. His research focuses on the development of innovative methodologies and catalytic reactions in the field of synthetic organic chemistry. His lab utilizes computational chemistry techniques to design functional molecules with biological activities and to develop them synthetically. Over the years, he has published 153 papers that have been cited more than 4,200 times. He is affiliated with prestigious academic societies, such as the Society of Synthetic Organic Chemistry, Japan, and the Chemical Society of Japan.

Funding:

This work was financially supported by JSPS KAKENHI (Grant Number 23K24004, Tetsuhiro Nemoto), AMED-CREST (Grant Numbers 24gm1610004 and 25gm1610004, Akiko Takaya, Tetsuhiro Nemoto), and the Futaba Memorial Foundation (Tetsuhiro Nemoto, Tomohiro Yazawa).

Reference:

Title of original paper: Bis-Pseudoindoxyls: A Compact Fluorophore with Red-Shifted Absorption and Fluorescence for Bioimaging Applications
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Journal: *Organic Letters*
DOI: 10.1021/acs.orglett.5c04305

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