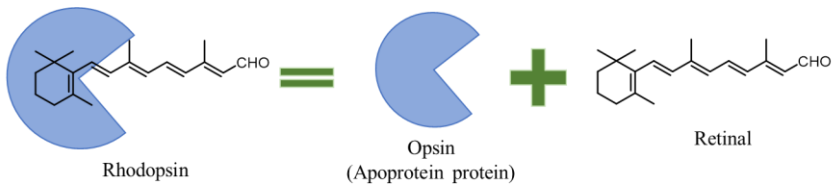
SYNTHESIS OF NOVEL ALL-*TRANS* RETINAL DERIVATIVES TO ELUCIDATION OF THE MOLECULAR MECHANISM FOR RHODOPSIN

Jiatong Lu [1], Masashi Ozawa[1], *Yuji Furutani[2], and *Yoshitomo Suhara[1]

[1]*Department of Bioscience and Engineering, Shibaura Institute of Technology, 307 Fukasaku, Minuma-ku, Saitama 337-8570, Japan*
[2]*Department of Life Science and Applied Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466-8555, Japan*
*Corresponding author : suhara@shibaura-it.ac.jp furutani.yuji@nitech.ac.jp

Background & Purpose

Rhodopsins are composed of the apoprotein opsin and the chromophore retinal and widely distributed in animal and microbial lineages, which are membrane proteins that play important roles in light responses such as vision in animal. Microbial rhodopsin isomerizes all-*trans* retinal (atRAL) to 13-*cis* form upon absorption of light which producing ion transport and light signal[1,2]. Time-resolved infrared spectroscopic analysis of the conformational change of the protein upon this isomerization to the 13-*cis* form should provide insight into the molecular mechanism of rhodopsin. However, the measurements are made with a mixture of heat release due to photoabsorption of the chromophore and structural changes due to its photoisomerization(Fig.1). Therefore, in order to analyze the spectral change to the 13-*cis* form due to photoisomerization, it is necessary to remove the spectral change for heat release. Interestingly, there are also reports of protein conformational changes induced without photoisomerization. Therefore, in this research, we planned to elucidate the molecular mechanism of rhodopsin by synthesizing and analyzing derivatives in which the 13th position of retinal fixed to the trans form not to isomerize to the 13-*cis* form.



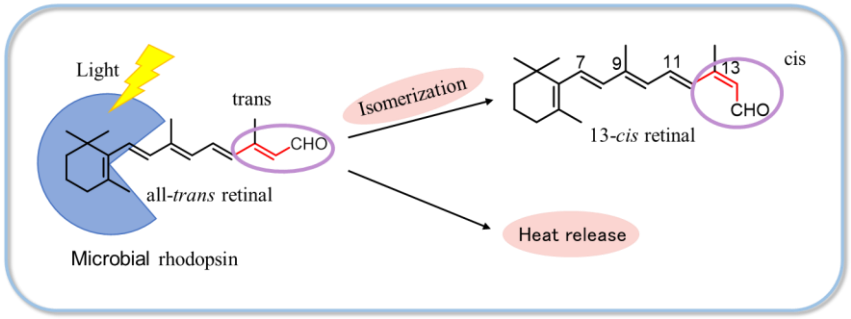


Fig. 1 Spectral changes due to photoabsorption-induced heat release and photoisomerisation of rhodopsin

Method

Since rhodopsin emits heat by absorbing light, the final spectrum is seen to be mixed with the spectrum of heat emission. In other words, it is not possible to measure the spectral change due to photoisomerization from all-trans-retinal to 13-*cis* rerinal. Therefore, to analyze the spectral changes caused by photoisomerization, it is necessary to remove the thermal emission spectral changes. By subtracting the spectral change of thermal emission, the spectral change of photoisomerization alone is obtained(Fig.2).

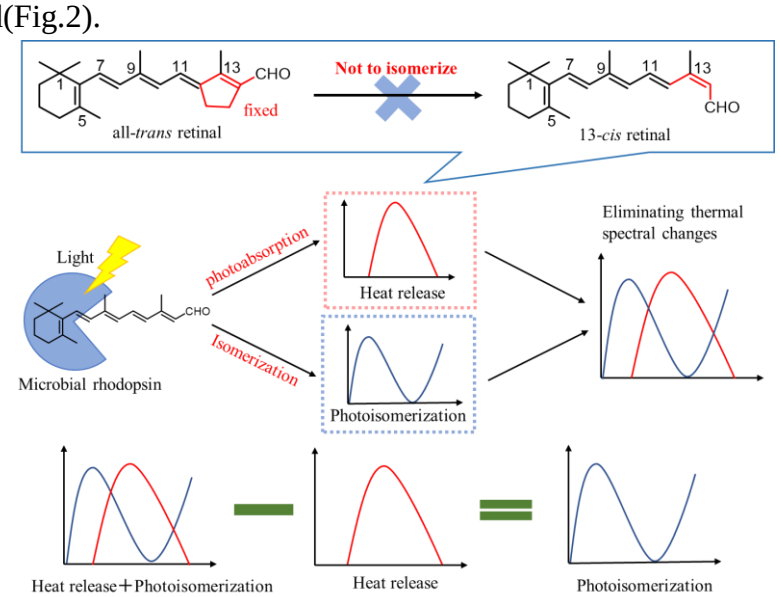


Fig. 2 Spectral changes due to photoabsorption-induced heat release and photoisomerisation of rhodopsin

Design of Compounds

Compounds **1-3** were designed in which the C-13 position was locked to the trans form with a carbocyclic compound to prevent the all-*trans* retinal isomerization reaction (Fig. 3).

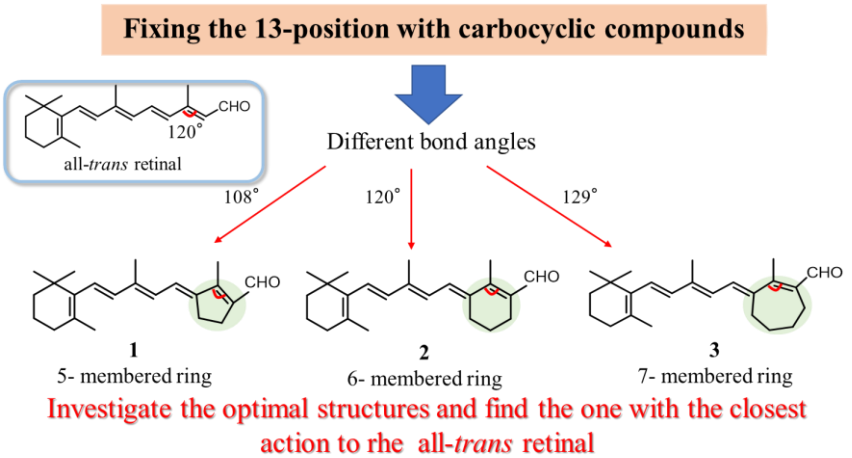
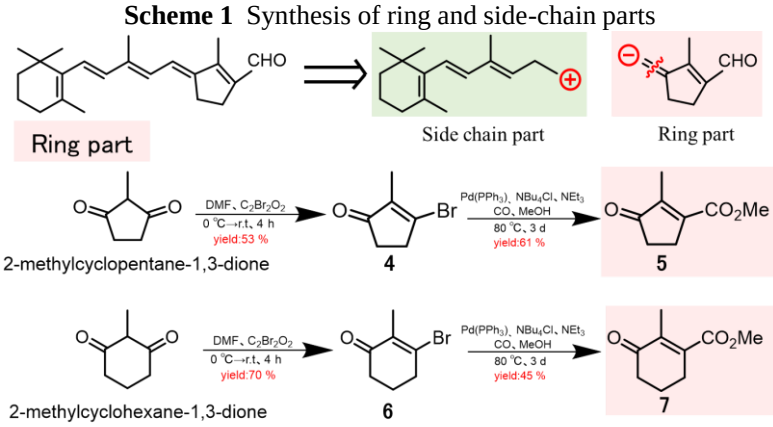


Fig. 3 Chemical structure of three kinds of retinal derivatives

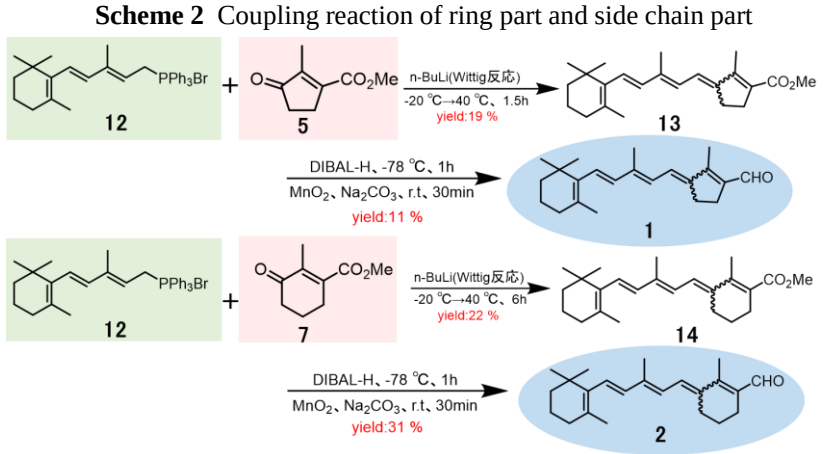
Synthesis

In order to synthesize retinal derivatives, we synthesize the side chain portion and the ring structure individually. Coupling in the final step synthesizes the desired derivative.

Scheme 1 Synthesis of ring and side-chain parts



Scheme 2 Coupling reaction of ring part and side chain part



Conclusion

Since the synthesis of objects **1** and **2** has been completed. We are currently working on the synthesis of compound **3**.

Reference

1) Hideaki E. Kato, Keiichi Inoue, et al. Nature. 2015, 521, 48–53
2) Keiichi Inoue, et al. Nature Communications. 2013, 1678, 1-10

Presenter imformation

Lu Jiatong
Shibaura Institute of Technology
Laboratory of organic synthesis and medical chemistry
1st year master's student