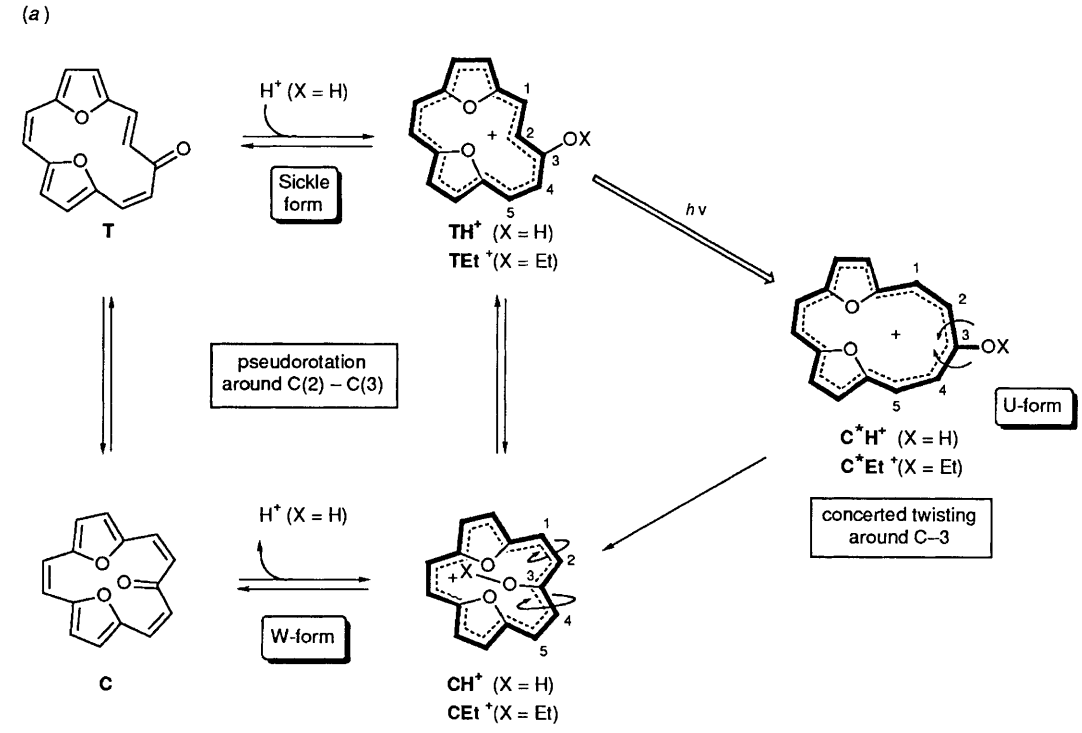
Photocyclic Processes of an Oxygen-bridged [15]Annulenyl Ion, whose State-to-state Changes are Very Similar to Those of Bacteriorhodopsin

Haru Ogawa,*[a] Hiroko Syouji,[a] Taiji Imoto,[a] Yuko Kato,[b] Yasuyoshi Nogami[b] and Toshitaka Koga[b]

[a] *Faculty of Pharmaceutical Sciences, Kyushu University 62, Fukuoka 812, Japan*
[b] *Daiichi College of Pharmaceutical Sciences, Fukuoka 815, Japan*

The photochemical behaviour of the hydroxy[15]annulenyl ion **TH**$^+$ and ethoxy[15]annulenyl ions (**TEt**$^+$) is described; **TH**$^+$ participates in a bacteriorhodopsin-like photocyclic process, giving very similar state-to-state changes in the transitions it undergoes.

On protonation, the conformationally flexible [15]annulenone **C** is in an equilibrium involving four chemical species **C**, **T**, **CH**$^+$ and **TH**$^+$ (Fig. 1*a*).[1] We have now found that (*i*) *trans*-annulenyl ion **TH**$^+$, a 14π Hückel aromatic ion, is converted into **CH**$^+$ by light most probably *via* **C*H**$^+$ (>360 nm, below −40 °C) in quantitative yield; (*ii*) the species **CH**$^+$ produced then rapidly reverts to **TH**$^+$ on warming above −20 °C. The species **CH**$^+$ is less planar and less aromatic than **TH**$^+$. It holds an inside OH group in place of the inside H of **TH**$^+$, and hence the pK_a value of **CH**$^+$ is lowered by 1.5 units



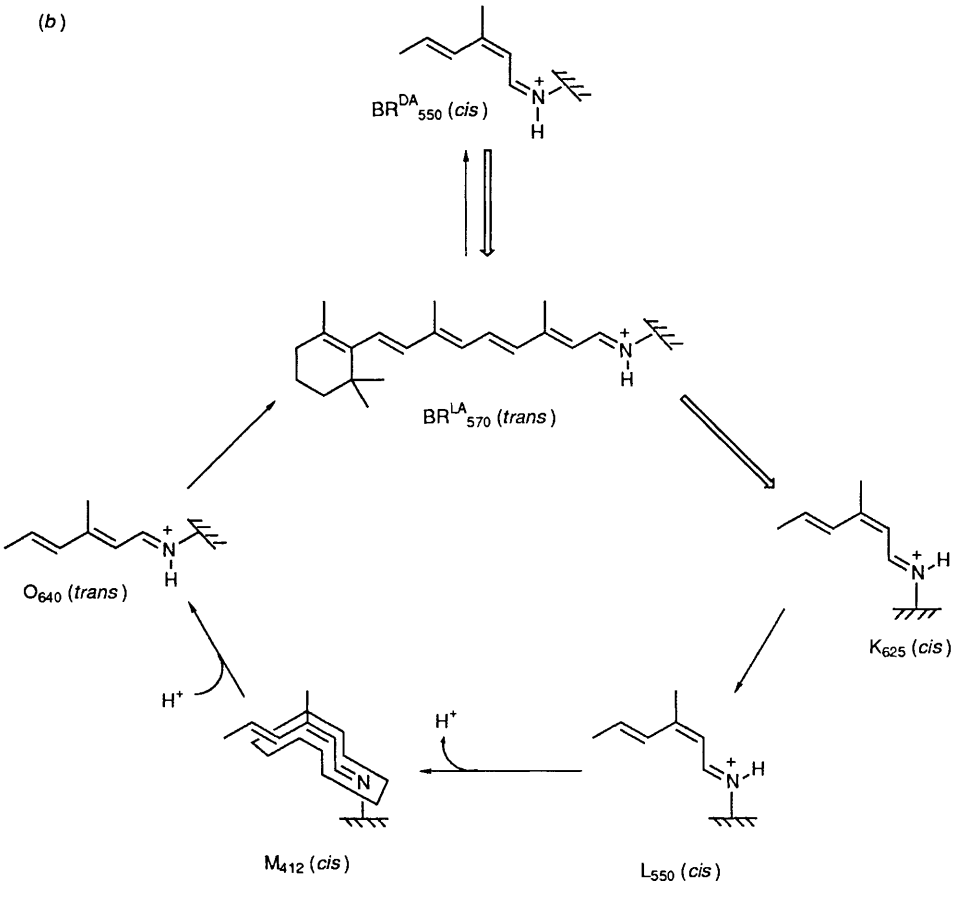


Fig. 1 Schematic comparison of the photo-cyclic processes of (*a*) the oxygen-bridged [15]annulenyl ion **TH**$^+$ and (*b*) bacteriorhodopsin (**bR**)[2] (LA and DA indicate light- and dark-adapted **bR**, respectively)

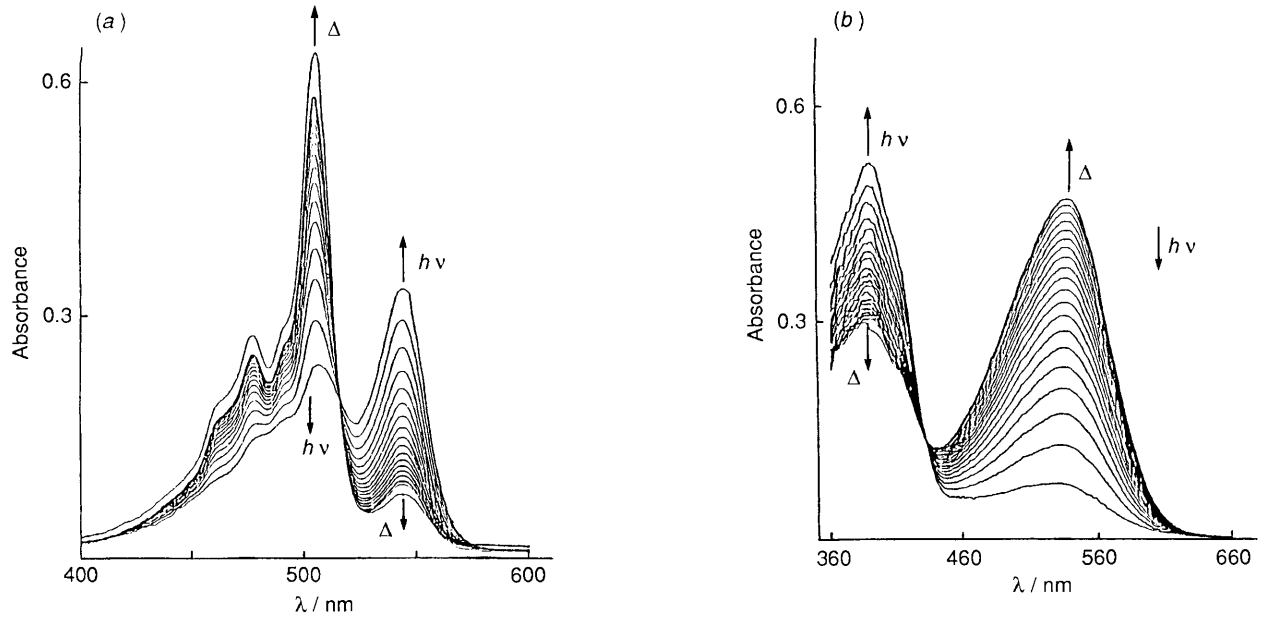


Fig. 2 Low-temperature UV–VIS spectra showing: (*a*) the **CH**$^+$ to **TH**$^+$ transition of the oxygen-bridged [15]annulenyl ion, in CH_2Cl_2 at −27 °C, time intervals 1.5 min, $[H^+]$ = 2.24 × 10^{-4} mol dm^{-3}. (*b*) The rates of the thermal relaxation of bacteriorhodopsin, the M_{412} to B_{568} transition, measured at pH 10.6, at −25 °C, in aqueous glycerine (66%), time intervals, 1.5 min.

(pK_a of **TH**$^+$ and **CH**$^+$ measured in CD_2Cl_2 at −60 °C: 5.2 and 3.7, respectively).

Fig. 1(*a*) shows state-to-state changes of the [15]annulenyl ion (X = H). It involves two chemical cyclic processes; one is a high quantum yield photo-isomerization, and the other a deprotonation–protonation sequence. The latter is joined to the former in the step of thermal relaxation (**CH**$^+$ to **TH**$^+$). The outer periphery of these two processes may lead to a sequential transformation $\hookrightarrow$**TH**$^+ \rightarrow$ **C*H**$^+ \rightarrow$ **CH**$^+ \rightarrow$ **C** $\rightarrow$ **T**$\hookrightarrow$, the net result of which can be represented, in principle, as a photochemical splitting of water.†[3] The annulenyl ion **TH**$^+$ may function as a model of bacteriorhodopsin because of highly efficient photoisomerization (**TH**$^+$ to **CH**$^+$) and rapid thermal relaxation (**CH**$^+$ to **TH**$^+$). Figs. 1(*a*) and 1(*b*) show the schematic analogy between these two processes.

There are three possible forms of the annulenyl ions, designated as 'U,' 'W' and 'sickle' (Fig. 1*a*). **TH**$^+$ adopts the 'sickle' form (see Fig. 1*a*) before irradiation, since **TH**$^+$ exhibited one inner proton NMR signal at extremely high field (δ −3.41, d, *J* 14.1 Hz). On irradiation (visible light >360 nm, 500 W projector lamp), at −60 °C in CD_2Cl_2 **TH**$^+$ was completely isomerized into **CH**$^+$. The ^{1}H NMR spectrum at −60 °C exhibited a simple pattern owing to the twofold symmetry of **CH**$^+$, and the inner proton doublet of **TH**$^+$ was no longer present. Also, we have found that (*i*) **TEt**$^+$ (X = Et, in Fig. 1*a*), prepared from annulenone **C** and $[Et_3O]^+PF_6^-$, could undergo photo-isomerization (**TEt**$^+$ to **CEt**$^+$) in quantitative yield; (*ii*) rapid **CEt**$^+$ to **TEt**$^+$ thermal relaxation took place on warming above −40 °C. The high quantum yield photoisomerization followed by rapid decay of **CH**$^+$ or **CEt**$^+$ led us to postulate that the U-shaped species (**C*H**$^+$ or **C*Et**$^+$) exists as a transient isomer. A single concerted twisting[4] around the C-3 centre of **C*H**$^+$ or **C*Et**$^+$ (as indicated by arrows in Fig. 1*a*) leads the 'U'-form into the 'W'-form (**CH**$^+$ or **CEt**$^+$). That **CEt**$^+$ adopts the W instead of the U form was supported by a diamagnetic ^{1}H NMR chemical shift difference for the OEt groups in **TEt**$^+$ and **CEt**$^+$ (*i.e.* Δδ = 4.6 ppm for the CH_3 and 2.5 ppm for the CH_2 group). The differences are large enough to show that the OEt groups of **TEt**$^+$ and **CEt**$^+$ occupy their positions at the outside and the inside of the perimeter, respectively.‡

The rates of thermal back isomerization (**CH**$^+$ to **TH**$^+$ or **CEt**$^+$ to **TEt**$^+$) could be measured by UV–VIS spectroscopy in

† Unless water does not participate with both cyclic processes in Fig. 1 (*a*) and 1 (*b*), no net chemical changes will be produced as shown below.

a			*b*		
TH$^+$	$\xrightarrow{h\nu}$	**CH**$^+$	**TH**$^+$	$\xrightarrow{h\nu}$	**CH**$^+$
CH$^+$	$\rightarrow$	**C** + H^+	**CH**$^+$	$\rightarrow$	**C** + H^+
C	$\rightarrow$	**T**	**C**	$\rightarrow$	**T**
T + H_2O	$\rightarrow$	**TH**$^+$ + OH^-	**T** + H^+	$\rightarrow$	**TH**$^+$
H_2O	$\xrightarrow{h\nu}$	$H^+ + OH^-$	no net chemical reaction		

The photoisomerization process of the annulenyl ion **TEtH**$^+$ is devoid of a protolytic equilibrium due to *O*-alkylation; and hence it contains only thermal and photochemical equilibria. From the thermodynamic and kinetic points of view, the photocyclic process of the annulenyl ion **TH**$^+$ is indeed a good active site model of bacteriorhodopsin. In order to use the process as a real working model of bacteriorhodopsin, we need chemical auxiliary or auxiliaries that work as H^+ channels or some liquid membrane experiments, such as were reported in ref. 3.

‡ Since the equilibrium is drastically affected by light, H^+ concentration or temperature, dramatic spectral changes could be detected by UV–VIS and ^{1}H NMR spectroscopy. **TEt**$^+$: δ_H (270 MHz; CD_3CN) furan H 9.59 (1H, d, *J* 4.29 Hz), 9.40 (1H, d, *J* 4.29 Hz), 9.34 (1H, d, *J* 4.29 Hz) and 9.30 (1H, d, *J* 4.29 Hz); outer-H 10.16 (1H, d, *J* 14.35 Hz), 9.64 (1H, d, *J* 12.54 Jz), 9.48 (1H, d, *J* 11.71 Hz), 9.34 (1H, d, *J* 11.71 Hz) and 8.76 (1H, d, *J* 12.54 Hz); inner H −3.97 (1H, d, *J* 14.35 Hz); CH_2CH_3 1.83 (2H, t, *J* 6.93 Hz); CH_2CH_3 5.19 (3H, q, *J* 6.93 Hz); λ_{max}/nm (CH_2Cl_2) 342 (ε 111) 600 dm^3 mol^{-1} cm^{-1}), 358 (116700) and 516 nm (38000): **CEt**$^+$ δ_H (500 MHz; CD_3COCD_3, at −90 °C) furan H 9.68 (2H, d, *J* 3.81 Hz) and 9.64 (2H, d, *J* 4.40 Hz); *cis*-H 9.12 (2H, d, *J* 9.54 Hz), 9.53 (2H, d, *J* 10.27 Hz) and 9.60 (2H, singlet-like); CH_2CH_3 0.524 (2H, t, *J* 6.60 Hz); CH_2CH_3 −0.657 (3H, q, *J* 6.60 Hz); λ_{max}/nm (CH_2Cl_2) 360 (ε 138000 dm^3 mol^{-1} cm^{-1}) and 552 nm (28000).

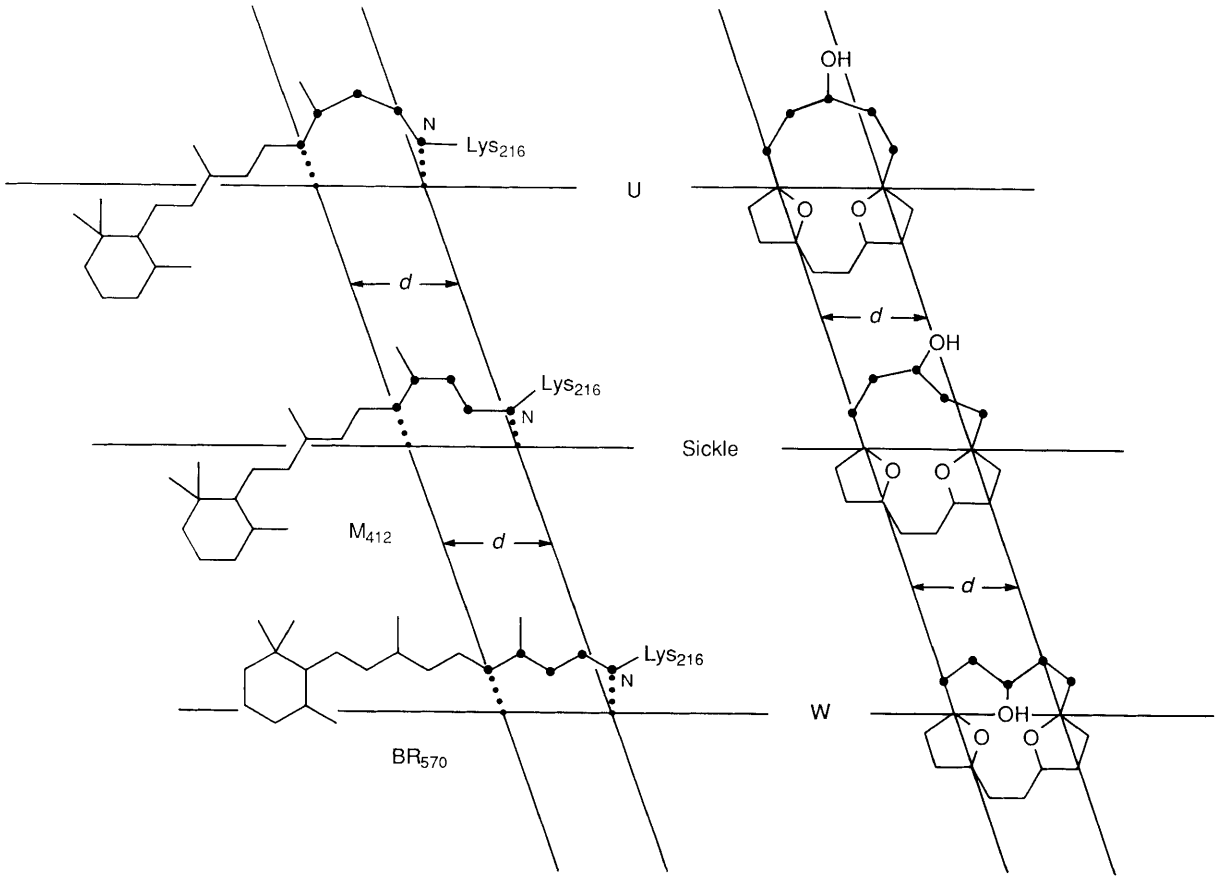


Fig. 3 Comparison of the flexible segments of the polyene chain of bacteriorhodopsin and of the oxygen-bridged [15]annulenyl ion. Both have five sequential sp^2-atom centres in common as the unit undergoing rapid conformational changes, designated by U, sickle and W. The conformational changes of this unit produce a cyclic pK_a change with a high turnover number.

the temperature range of −60 to −30 °C, and obeyed first-order kinetics. Low activation energies were obtained {**CEt**$^+$ to **TEt**$^+$ isomerization, E_a = 11.9 kcal mol^{-1} in acetone; **CH**$^+$ to **TH**$^+$ isomerization, E_a = 10.3 kcal mol^{-1} in CD_2Cl_2 at $-\log[H^+] = 4.6$ (CF_3COH as H^+ donor); 1 cal = 4.184 J}. The results suggest that the single 'bicycle pedal motion' on the C(2)–C(3) bond of (**CH**$^+$ or **CEt**$^+$) (*i.e.* the W to sickle isomerization) is a very favoured process, the C(2)–C(3) and C(4)–C(5) bonds being kept nearly parallel each other when the segment adopts the W form.

Finally, the following considerations indicate how the photo-cyclic processes of the annulenyl ion **TH**$^+$ are schematically and kinetically analogous to those of bacteriorhodopsin (**bR**),[4] whereas their chemical origins are quite different (for the kinetic analogy, see Fig. 2). In the **bR** cycle, all the *cis–trans*-isomerizations of the retinylidene Schiff's base take place only at a specific segment, *i.e.* at the sequential five sp^2 atoms including the Schiff's base N atom (encircled in Fig. 1*b*). The segment functions not only as a centre of photochemical and thermal isomerizations, but also as a susceptible centre for the protonation–deprotonation sequence. The segment being placed in a heavily packed protein space, both termini of the segment should be kept at an almost constant distance apart throughout the conformational changes[5] (Fig. 3). Under such a constraint, concerted twistings or bicycle pedal motions become responsible for causing *cis–trans* isomerization in the segment.[5] In a similar way, annulenone **C** has a segment of five sp^2 carbon atoms, both termini of which are also kept at an almost constant distance apart by the di-furyl-ethene bridge as is the case in the protein matrix of **bR**. The carbonyl group of **C** exists as a susceptible centre for the protonation–deprotonation sequence. The inside oxygen bridges put suitable strains in the segment to drive a rapid regeneration of **TH**$^+$ *via* two possible pathways.§

We have, therefore, found that a light-driven cycle could be written schematically for the first time from the field of annulenone chemistry. The transitions of the cycle are very similar to those of **bR**. To sum up the particular properties of the annulenyl ion photo-cycle: (*i*) the highly efficient photo-isomerization can produce a considerable pK_a difference; (*ii*) the thermal relaxation rates are as high as those of **bR** (see Fig. 1*b*); and (*iii*) the photo-cycle involves a 14π Hückel aromatic system with suitable inside bridges, and hence is stable and repeatable as many times as we required.

We acknowledge a Grant-in-Aid from the Ministry of Education of Japan (01571156).

Received, 14th May 1990; Com. 0/02129F

References

1 H. Ogawa, M. Inoue, T. Imoto, I. Miyamoto, H. Kato, Y. Taniguchi, Y. Nogami and T. Koga, *J. Chem. Soc., Chem. Commun.* 1989, 118, and references cited therein.
2 F. Derguini, D. Dunn, L. Eisenstein, K. Nakanishi, K. Odashima, V. J. Rao, L. Sastry and J. Termini, *Pure Appl. Chem.*, 1986, **58**, 719.
3 P. Haberfield, *J. Am. Chem. Soc.*, 1987, **109**, 6177; 6178.
4 W. Stoeckenius and R. A. Bogomolni, *Annu. Rev. Biochem.* 1982, **52**, 587.
5 R. S. H. Liu, D. Mead and A. E. Asato, *J. Am. Chem. Soc.*, 1985, **107**, 6609; and references cited therein.

§ There are two possible pathways to revert to **TH**$^+$ from **CH**$^+$ in Fig. 1(*a*), *i.e. via* the direct return path **CH**$^+$ to **TH**$^+$ and *via* the **CH**$^+$ → **C** → **T** → **TH**$^+$ path. Which way is operative is not determined *a priori*.