

벤잘피롤린온의 광증감적 이성질화 반응

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Sensitized Photoisomerization of Benzalpyrrolinones

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요 약. 벤잘피롤린온 (*Z*-2, *Z*-4)을 직접 조사하거나 광증감제를 넣어 조사하니 광산소화되지 않고 광이성화 되었다. 단색광 (557 nm)을 사용하여 광증감제인 로즈벤잘 (rose bengal)만을 들뜨게 하여서 일어나는 벤잘피롤린온 (*Z*-2, *Z*-4 및 *E*-2) 들의 이성화에서는 삼중상태의 벤잘피롤린온이 관여하였다.

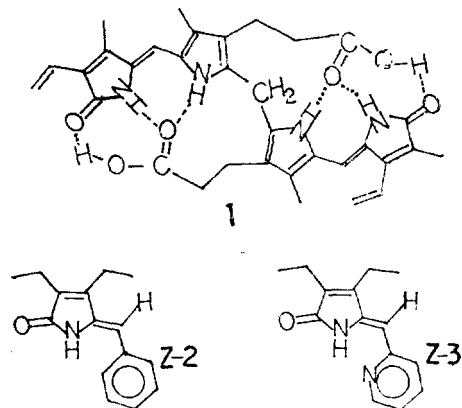
ABSTRACT. Rather than undergo photooxygenation, the *Z*-configuration benzalpyrrolinones (*Z*-2, *Z*-4) photoisomerized to the *E*-configuration isomers under direct or sensitized irradiation. Rose bengal sensitized photochemical stereoisomerization of benzalpyrrolinones (*Z*-2, *Z*-4 and *E*-2) with monochromatic light (at 557 nm, excitation of rose bengal only) showed that the triplet of benzalpyrrolinones was involved in the photoisomerization, since oxygen inhibited the photoisomerization.

1. INTRODUCTION

In connection with our interest in the photochemistry of bilirubin IX- α (1)¹ which is related to jaundice phototherapy, we have studied the photooxygenation of dipyrroles² and the photoisomerization of benzalpyrrolinones³ as model compounds for bilirubin IX- α . Even though the stereoisomerization of olefins in light belongs to the longest known and best investigated class of photochemical reaction, only a few reports concerned with photoisomerization of exocyclic double bond of mono- and dipyrroles have appeared.

Falk and collaborators reported that pyrromethenones⁴ and substituted benzalpyrrolinones⁵ were photoisomerized by direct irradiation.

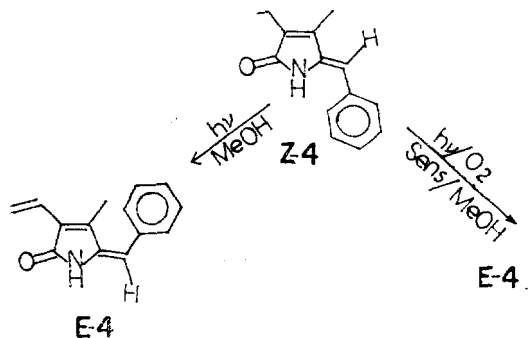
In our previous report³ benzalpyrrolinone 2 and pyridalpyrrolinone 3 were shown to be photoisomerized in a condition of photooxygenation or direct irradiation. The possibility of *Z* \rightleftharpoons *E* photoisomerization of bilirubin IX- α was also observed by excitation at 450 nm and other wavelengths⁶. In the present report we would like to report the reaction path of the sensitized photochemical stereoisomerization of benzalpyrrolinones *Z*-2, *E*-2 and *Z*-4.



2. RESULTS AND DISCUSSION

2.1 Photoisomerization of Benzalpyrrolinones Z-4.

When Z-5-benzylidene-4-methyl-3-vinyl-3-pyrrolin-2-one (Z-4) in methanol ($5.1 \times 10^{-2} M$, 120 ml) in a quartz photocell was irradiated using a mercury arc lamp, photoisomerization of the substrate occurred as with Z-2³. The isolated Z-isomer was the same as the starting material according to uv, Mass spectra, ir, nmr and mp measurements. The characteristic nmr spectra (δ 6.45 in THF) for the E-isomer was also observed. The E-isomer was also thermodynamically less stable than Z-isomer (total yield 80 %, 20 % E, 80 % Z)



When a dilute methanolic solution of benzalpyrrolinone Z-4 containing rose bengal (3 mg%) was irradiated with a tungsten halogen lamp in a water cooled immersion photocell for the prepara-

tive photooxygenation, photoisomerization rather than photooxygenation was observed. The isolated isomers were identified as E- and Z-isomer. To make sure the above the result of photoisomerization and to resolve the problem further, the following experiment has been done.

2.2 Sensitized Photoisomerization with Monochromatic Light

When a methanolic solution of substrate Z-4 ($5.6 \times 10^{-5} M$, 3 ml) in a uv cuvette was irradiated with monochromatic light⁷ at 557 nm (rose bengal $\lambda_{max} = 557$ nm), no change of uv spectra of the substrate was observed. This control experiment showed that the substrate can not harvest energy from 557 nm irradiation in the absence of sensitizer. The methanolic solution of the substrate ($5.6 \times 10^{-5} M$, 3 ml) with rose bengal ($[RB] = 1.6 \times 10^{-5} M$) was irradiated as described in the control. The absorbance of the substrate ($\lambda_{max} = 342$ nm) was reduced. Developing the reaction mixture on TLC after evaporation of solvent, the only products were the Z- and E-isomers of 4, as was the case of preparative sensitized photoisomerization.

2.3 Triplet State as Intermediate

The sensitizer assists the isomerization, but singlet oxygen (1O_2) has not yet been excluded. To resolve this further the following competition and degassed experiment were carried out. Diphenylisobenzofuran is considered to be one of the best singlet oxygen acceptors⁸. A solution of 1,3-diphenylisobenzofuran (DPBF) in methanol ($3.4 \times 10^{-5} M$) with rose bengal ($1 \times 10^{-5} M$) and with/without "inhibitors" (Z-2 and Z-4, $7.0 \times 10^{-5} M$, $5.8 \times 10^{-5} M$ respectively) was irradiated at 577 nm using monochromatic light⁷ from a tungsten halogen lamp, 15 W. The pertinent results are given in Table 1. The photooxygenation was not effected by the "inhibitor", Z-2 and Z-4, until after 8 min irradiation. However, for longer irradiation times (16 min) both Z-2

and **Z-4** inhibited the protoxygenation of DPBF slowly (66.5 % for control, 56.4 % for **Z-2**, and 53.1 % for **Z-4**). This slow inhibition can be understood assuming that the triplet of rose bengal is quenched by **Z-2** or **Z-4** less effectively to give **E-2** or **E-4** (see below).

When the dilute methanolic solution of **Z-4**, **Z-2** and **E-2** ($[\text{substrate}] = 5.6 \times 10^{-5} M$) were irradiated with monochromatic light (at 557nm) with/without oxygen and sensitizer(rose bengal), the pertinent results are summarized in Tables 2~4.

When O_2 is removed from the reaction the photochemical isomerization was established

Table 1. Percentage of biphenylisobenzofuran transformed with/without inhibitors vs. Irradiation Time.

Irradiation time(min)	% Transformed		
	$w_0/\text{Inhibitor}$	$w/\text{Z-2}$	$w/\text{Z-4}$
1	4.2	4.9	4.3
4	17.0	17.4	16.3
8	31.5	31.8	31.4
16	66.5	56.4	53.1

Table 2. Percentage change of **Z-5**-benzylidene-4-methyl-3-vinyl-3-pyrrolin-2-one (**Z-4**) vs. irradiation time period.

Irradiation Time(min)	w_0/RB %	w/RB %	w/RB %, w_0/O_2
15	0	5.6	15.5
30	0	6.4	16.5
60	0	10.4	17.0
120	0	15.0	17.0
180	0	17.0	—

Table 3. Percentage change of **Z-3,4**-diethyl-5-benzylidene-3-pyrrolin-2-one (**Z-2**) vs. irradiation time period.

Irradiation time(min)	Without RB	With RB	With RB without O_2
15	0	0	10.7
30	0	0.3	11.7
60	0	1.4	12.0
120	0	6.1	12.1

more quickly. In other words, oxygen inhibits the photoisomerization by competing with substrate for the triplet state of sensitizer or/and by quenching the triplet state of benzalpyrrolinones. The same results were obtained in chloroform solvent with rose bengal and 18-crown-9.

Thus a photoisomerization mechanism implicating triplet states is provided for substrates **Z-2** and **Z-4**.

Singlet oxygen is not responsible for the isomerization (see Fig. 1.).

The energy state of 1O_2 (22 kcal/mole) is too low to give energy to **Z-4** or **Z-2** for the isomerization, presumably. Whether the triplet state of benzalpyrrolinone **Z-4** is energetically lower than that of rose bengal (40~42 kcal/mole) is unclear, because the triplet state of benzalpyrrolinone **Z-4** is probably higher than that of bilirubin ($^3BR = 36 \text{ kcal/mole}$)¹⁰. Therefore the phantom triplets of **Z-4** or **Z-2** are probably involved.

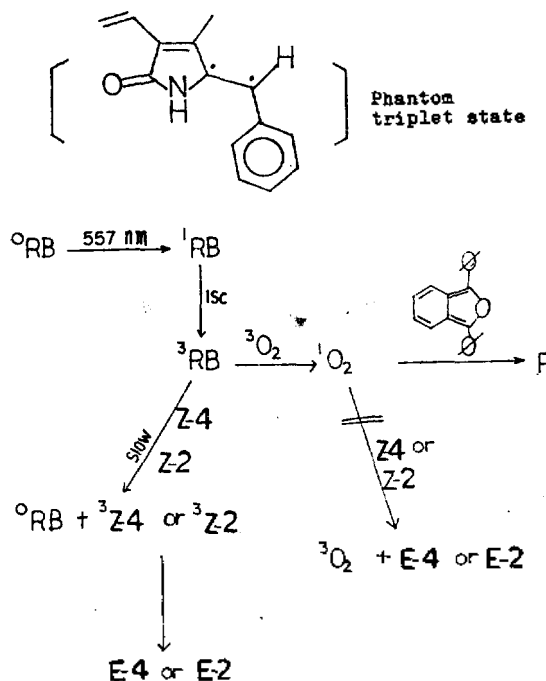


Fig. 1. Triplet state involvement in sensitized photoisomerization of benzalpyrrolinones.

This conclusion provides an explanation for fact that *Z*-4 or *Z*-2 inhibits the photooxygenation of DPBF slowly (or less effectively) by quenching the triplet state of sensitizer.

According to Hammond *et al.*,¹¹ sensitizers having low excitation energy function as photocatalyst *i.e.* in presence of these sensitizers the composition of the photostationary state approaches that of thermal equilibrium. To explain their work on the photochemical *cis-trans* isomerization of diphenylpropene, Hammond *et al.*, postulated a phantom triplet state whose energy is lower than that of either *trans*- or *cis*-diphenylpropene.

The composition of the photostationary states of *Z*-4 in the presence or in the absence of air are identical (83% *Z*, 17% *E*).

The *E*-isomer of 2 is slightly unstable to irradiation at 557 nm without sensitizer in methanol. With added sensitizer (RB) and excitation at 557 nm the reaction is faster than for the control. In the degassed system the reaction is very fast. The pertinent results are summarized in Table 4.

The observation shows that excited rose bengal assist the photoisomerization and that oxygen inhibits the reaction. The triplet state is involved again in the *E*⇌*Z* photoisomerization.

3. EXPERIMENTAL

3.1 General

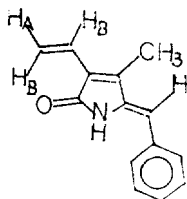
Table 4. Percentage change of *E*-3,4-diethyl-5-benzylidene-3-pyrrolin-2-one (*E*-2) vs. irradiation time period.

Irradiation Time (min)	%		
	<i>w/o</i> /RB	<i>w</i> /RB	<i>w</i> /RB+ degassed
15	—	1.0	≥30
30	—	1.7	—
60	—	3.5	—
120	1.3	7.1	—

The benzalpyrrolinones used for photoisomerization were prepared in this laboratory. Solvents were reagent grade unless otherwise specified. Nuclear magnetic resonance (nmr) spectra were measured in deuteriochloroform on a Varian A-60 or Perkin-Elmer R-24B. Chemical shifts are reported in parts per million (δ) downfield from TMS as an internal standard. The following descriptive abbreviations are used: *s*=singlet, *d*=doublet, *br*=broad and *m*=multiplet. Mass spectra were determined on a Jeol JMS-07 instrument at 12 or 70 eV. Visible and uv spectra were recorded on a Cary-14 spectrophotometer. Infrared spectra were obtained from sample in chloroform with a Beckman IR-8 spectrophotometer. The plates used for preparative thin layer chromatography (TLC, 20×20 cm) were prepared with *ca.* 8 g of absorbent (0.05~0.2 mm silica gel F, M. Woelm, Eschwege) giving a layer thickness of 1 mm. Preparative photoisomerization was accomplished in a quartz photocell (120 ml) using a mercury arc lamp (Hanovia 8A-1 quartz). Preparative sensitized photochemistry was carried out in a water-cooled pyrex immersion well apparatus with circulating oxygen using a 500 w tungsten-halogen lamp (Sylvania 500 Q/CL). Kinetic sensitized photoisomerization studies were accomplished in uv cell (1cm path, 3 ml) using 10 nm bandpass monochromatic light from a Bausch and Lomb Monochromator (model 33-86-07) equipped with 15 w tungsten lamp. For degassed experiment, a pyrex to quartz fused 10 mm quartz cell was subjected to at least three cycles of freeze-pump-thaw treatment at a pressure of 4.0×10^{-6} torr.

3.2 Synthesis of *Z*-5-Benzylidene-4-methyl-3-vinyl-3-pyrrolin-2-one (*Z*-4). Benzalpyrrolinone *Z*-4 was prepared by the method of Plieninger, *et al.*,¹² m.p 170~171°C (lit m.p 170~171°C); only one spot on analytical TLC

in $\text{CHCl}_3/\text{Et}_2\text{O}$ (6:4); nmr(CDCl_3) δ 2.17(*s*, 3H, CH_3), 5.43(*2d*, 1H, $J=4\text{ Hz}$, $J=8\text{ Hz}$, A proton), 6.10 (*s*, 1H, exocyclic vinyl CH=), 6.38 (*m*, 2H, B protons), 7.33 (*m*, 5H, phenyl), 8.20 (*br. s*, 1 H, NH); mass spectra, *m/e* (rel. intens.), 211(M^+ , 100 %), 196(16 %), 182 (33%), 167(33); uv(methanol), $\lambda_{\text{max}}=342\text{ nm}$, $\epsilon_{342}=2.9 \times 10^4$; ir(cm^{-1} , chloroform), 3507(free NH), 3257(NH hydrogen), 3057(CH=), 3017 (CH=), 1693(C=O), 1623 (C=C).



For preparation of benzalpyrrolinone **Z-2** and **E-2** see the previous report³.

3.3 Photoisomerization of Benzalpyrrolinones **Z-4** and **Z-2**

Z-5-Benzylidene-4-methyl-3-vinyl-3-pyrrolin-2-one (Z-4) in methanol ($5.1 \times 10^{-2}\text{ M}$, 120 ml) in a quartz photocell was irradiated using a mercury arc lamp (Hanovia 8A-1 quartz) for 2 hrs. The reaction was monitored by change in the uv spectra. Evaporation of the solvent at room temperature gave the photoproduct mixture. The mixture was separated by preparative TLC on silica gel. The two separated compounds were recrystallized from pyridine-water. The compounds turned out to be the *E*- and *Z*-isomers as expected. The isolated *Z*-isomer was identified as starting material by: nmr (CDCl_3) 2.17(*s*, 3H, CH_3), 5.43(*2d*, 1H, $J=4\text{ Hz}$, $J=8\text{ Hz}$), 6.10 (*s*, 1H, exocyclic vinyl CH=), 6.38(*m*, 2H,) 7.33(*m*, 5H, phenyl), 8.20 (*br. s*, 1H, NH). The mass spectra are same as the starting materl. The other produced was identified as the *E*-isomer by nmr (CDCl_3), δ 2.27(*s*, 3H, CH_3), 5.57(*m*, 1H,), 6.22(*s*, 1H, methine hydrogen), 6.53(*m*, 2H),

7.42(*m*, 5H, phenyl) and its facile conversion back to the *Z* isomer. Same procedure was used for **Z-2**.

3.4 Thermal Stability

The *Z*-isomer (for example, **Z-2**, 1 mg) was placed) in a melting point capillary, melted at 145~150 °C and maintained for 30 min. After cooling the melting point was measured again. No change in melting point was observed. Furthermore, TLC showed only one spot. The *E*-isomer (1 mg) were treated as mentioned above. The melting point (115 °C) was lower than that of pure *E*-isomer (138 °C for **E-2**) after heating. TLC showed two spots which correspond to the *Z*- and *E*-isomer of **2**.

3.5 Sensitized Photoisomerization with Broad Spectrum Light Source.

preparative sensitized photoisomerization of **Z-4** has been done according to the previous method for **Z-2**.³

3.6 Sensitized Photoisomerization with Monochromatic Light Source.

Quenching by Benzalpyrrolinones. Diphenylisobenzofuran (DPBF, 2.31 mg) was dissolved in methanol in a 25 ml flask. One milliliter of the solution and 5 ml of rose bengal stock solution ($2.0 \times 10^{-5}\text{ M}$) were combined and diluted with methanol to 10 ml in a volumetric flask. Two milliliters of the solution in 1 cm path uv cell were irradiated at 557 nm using monochromatic light (control experiment).

Benzalpyrrolinone **Z-2** (0.799 mg, $3.5 \times 10^{-3}\text{ mmole}$) was dissolved in a 10 ml volumetric flask. Two milliliters of the solutionon, 1 ml of DPBF solution and 5 ml of rose bengal stock solution were diluted to 10 ml in a volumetric flask with methanol.

For vinylbenzalpyrrolinone **Z-4** 0.820 mg ($3.9 \times 10^{-3}\text{ mmole}$) of the sample were dissolved in methanol in a 10 ml flask. One and one half milliliters of the soution, 1 ml of DPBF solution

and 5 ml of rose bengal stock solution were diluted to 10 ml in a volumetric flask with methanol. Two milliliters of the final solutions were irradiated as in control experiment. The results are given in *Table 1*.

Effect of Oxygen. Benzalpyrrolinone *Z-2* (0.344 mg, 1.5×10^{-3} mmole) was dissolved in methanol in 25 ml volumetric flask. The solution (2.8 ml) in a uvcell (1 cm path) without sensitizer was irradiated at 557 nm with monochromatic light (control). No change was observed in the absorption spectra for 2 hrs.

The rest of the solution (22 ml) was diluted to 25 ml in a flask with rose bengal solution (1 ml, 4×10^{-4} M) and methanol. The final solution (2.8 ml) was irradiated under aerobic conditions (same uv cell as control). Two and eight tenths milliliters of the final solution were placed in a vacuum-designed uv cell as control) and degassed by the freeze-pump-thaw method at 3.0×10^{-6} torr for 3 cycles. The solution under aerobic or anaerobic condition were irradiated and monitored by uv spectroscopy. The results are reported in *Table 3*. For *Z-4* and *E-2*, the same procedures were used (see *Table 2, 4*).

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