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PHOTOCHEMICAL REACTION OF 4,7-DIMETHYLBENZOFURAZAN USING LASER

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Abstract – 4,7-Dimethylbenzofurazan **1** was more reactive than other dimethylbenzofurazans, methylbenzofurazans and benzofurazan for short duration irradiation using a Xe lamp (Pyrex filter). Compound **1** was transformed by irradiation with the third harmonic of a Quanta-Ray Nd:YAG laser (355 nm) into (2*Z*,4*Z*)-2,5-dimethylhexa-2,4-dienedinitrile monoxide **2** in $CDCl_3$ at room temperature in excellent yield. With increasing temperature, the isomeric opened form compound **2** is thought to be thermally reverted to the original benzofurazan structure. The rate constant for this recyclization of **2** to **1** using $CHCl_3$ at 293 K was 1.16 x 10^{-5} s^{-1}. Irradiation of 1 in $CDCl_3$ yields photoproduct compound **2** with a quantum yield of 0.48, and a chemical yield of 99%. The yield of this photoreaction was dependant on the laser power and exposure time.

Benzofurazan has been shown to have numerous pharmacological and industrial applications.[1a-d] As a part of benzofurazan chemistry, the toxicity of benzofurazans in *Escherichia coli* has been reported to be caused by an increase in intracellular flux of superoxide on aerobic incubation.[2a] The superoxide production was confirmed using the cytochrome *c* reduction method and the formation of benzofurazan anion radicals in *E. coli* was followed by ESR spectroscopy.[2b]

4,7-Dimethylbenzofurazan **1** was transformed by $^1O_2$ into 4,7-dimethylbenzofurazan 4,7-endoperoxide, in excellent yields. The rate constant for the reaction of $^1O_2$ with compound **1** was determined by the quenching of luminescence to be 4.8 x 10^3 $M^{-1}S^{-1}$ using the third harmonic of a Quanta-Ray Nd:YAG laser. [3]

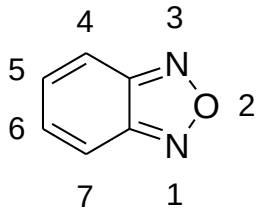


Figure1. Structure of benzofurazan

It is known that benzofurazan on irradiation with ultraviolet light gives are active nitrileoxide intermediate.[4] Nitrileoxide reacts with triethylphosphite to produce 1,4-dinitrile derivatives. Irradiation of benzofurazan in benzene yields an azepines and in methanol yields the corresponding *N*-substituted carbamate.[5] The photoreaction of benzofurazan and dimethyl acetylenedicarboxylate yields a mixture of isomeric isoxazoles.[6]

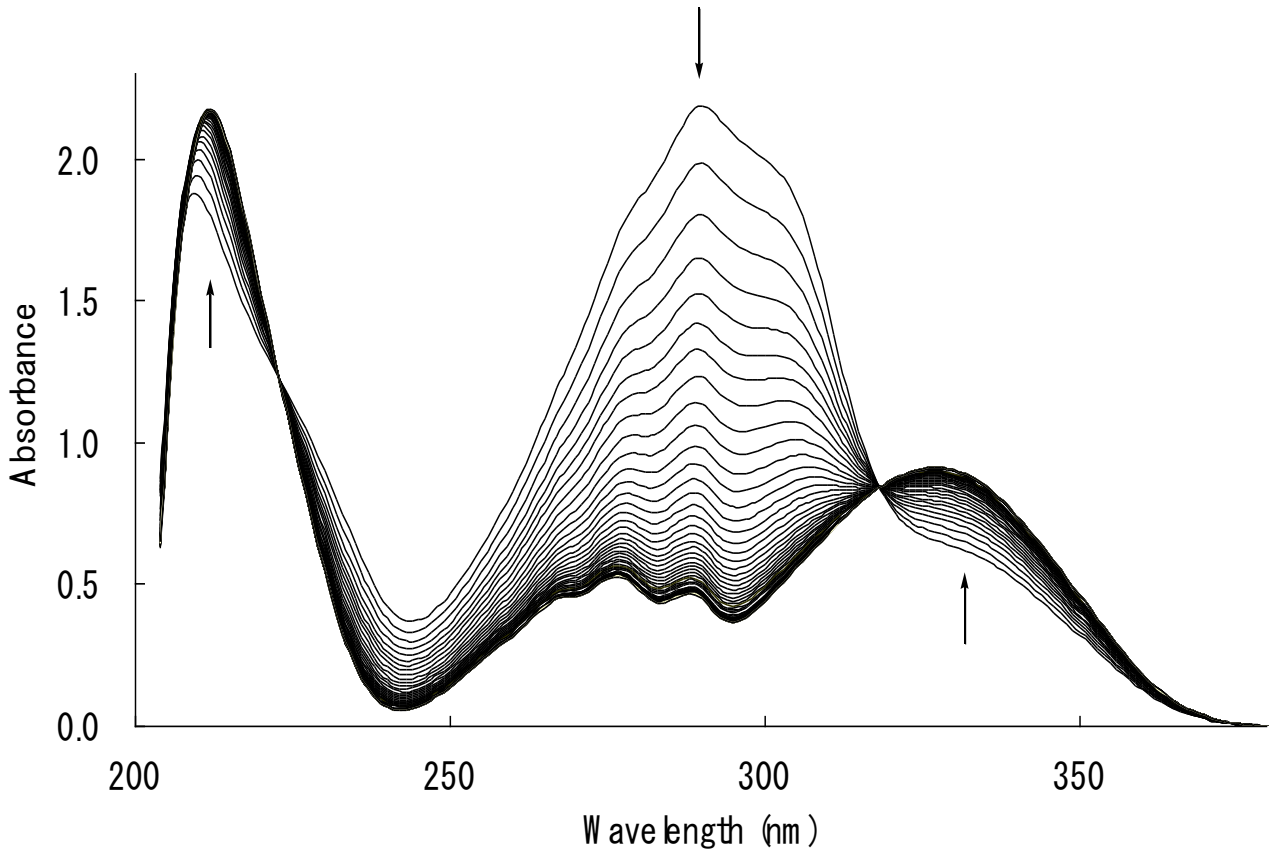


Figure 2. Change in absorption spectra of compound **1** (3.0×10^{-4} M) in MeOH after photoirradiation for 15 seconds using a 300 W Xe lamp (Pyrex filter)

The nitrileoxide intermediate is unstable at room temperature, therefore, the intermediate can be converted back to benzofurazan immediately.

Compound **1** in MeOH showed 5 UV maximum absorbance peaks at 213, 269, 277, 289 and 328 nm before irradiation. Absorbance peaks at 269, 277 and 289 and 328 nm may be ascribed to the π-π* transition of the benzofurazan ring.

Figure 2 shows the absorption spectral change of compound **1** in MeOH after irradiation. The UV/vis irradiation using of a 300 W Xe lamp (Pyrex filter) was examined for 15 seconds at room temperature. Irradiation causes a decrease of 328 nm and an increase 289 nm in the absorbance of **1**. The spectrum after irradiation gave only one peak at 289 nm between 230 and 370 nm. After irradiation with a Xe lamp light, the UV of photoproduct compound **2** then returned to that of compound **1** after being kept in the dark at 293 K for approximately 2 days. This absorption spectral change using compound **1** can easily occur even under room light or sun light.

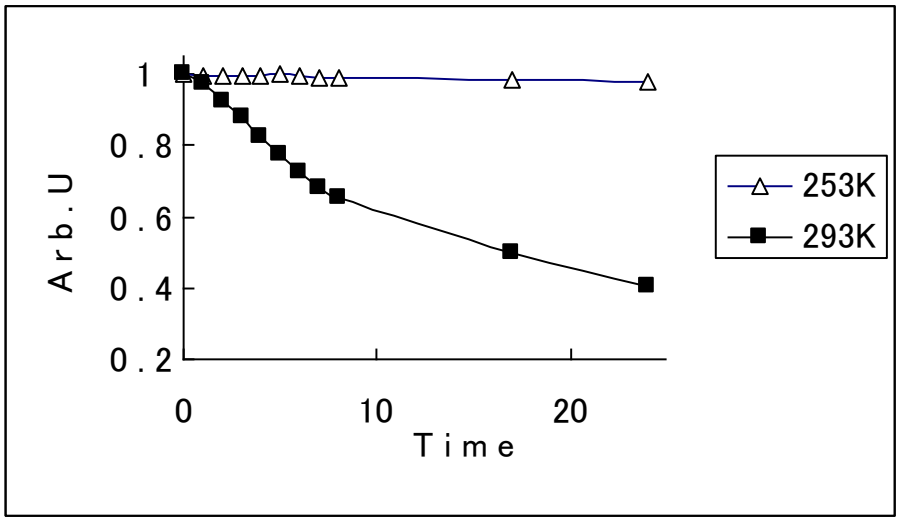


Figure 3. Stability of product **2** dependence on temperature observed upon photolysis of compound **1** in $CDCl_3$ using the third harmonic of a Quanta-Ray Nd:YAG laser (355 nm).

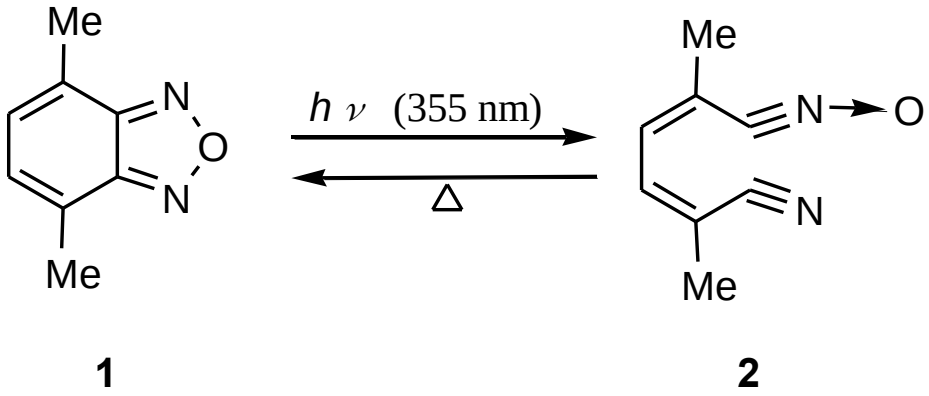
From the analysis using 289 nm in the absorbance of **1**, temperature affects the reversion of substrate compound **1** from photoproduct compound **2** in Figure 3. With decreasing temperature (253 K), compound **2** is more stable, with increasing temperature (293 K), isomeric opened form compound **2** is thought to thermally revert to the original benzofurazan structure. In the case of 5,6-dimethylbenzofurazan, we could not confirm the big change in absorbance at room temperature under the same condition. 4-Methylbenzofurazan, 5-methylbenzofurazan and 4,5-dimethylbenzofurazan did confirm a small change in absorbance at room temperature after two minutes of photoirradiation.

Using a Xe lamp, photoproduct compound **2** can be isolated with preparative TLC. FT-IR shows the presence of two CN functions on compound **2** at room temperature (2215, 2277 cm^{-1}). In the case of 4-methylbenzofurazan (photoproduct: 2218, 2280 cm^{-1}) or 4,5-dimethylbenzofurazan (photoproduct:

2213, 2262 cm^{-1}), we could not isolate the photoproduct. The two CN functions can be confirmed using $CHCl_3$ as a reaction solvent at room temperature with difficulty, though only after a long period of irradiation. These weak signals disappeared for short time. The two CN functions of the photoproducts of benzofurazan, 5-methylbenzofurazan and 5,6-dimethylbenzofurazan could not be confirmed by IR signals in the presence of two CN functions at room temperature during such a short irradiation time (15 seconds).

However compound **1** was more reactive in that short reaction time, and CN absorptions for photoproduct compound **2** were remarkably more stable and had a strong intensity in the analysis of the infrared spectrum. The photoreactivity of benzofurazan, 5-methylbenzofurazan and 5,6-dimethylbenzofurazan may be lower than that of 4,7-dimethylbenzofurazan for such a short irradiation at room temperature.

Using the third harmonic of a Quanta-Ray Nd:YAG laser (355 nm) at room temperature, UV irradiation of colorless compound **1** in $CDCl_3$ through N-O and C-C bonds cleavage, light yellow isomeric open form, which is thermally reverted to the original benzofurazan structure. Irradiation of **1** in $CDCl_3$ yields (2*Z*, 4*Z*)-2,5-dimethylhexa-2,4-dienedinitrile monoxide **2** with a quantum yield of 0.48, and a chemical yield of 99%. (Scheme 1)



1 **2**

Scheme 1

Chemical yield was calculated by ^1H NMR integration and the only organic product detectable by ^1H NMR. Compound **2** can be converted back to **1** almost as slow as that of benzofurazan (lit. 5, 2 x 10^{-5} s^{-1} at 293 K). The rate constant for this recyclization of **2** to **1** using $CHCl_3$ at 293 K is 1.16 x 10^{-5} s^{-1}, using MeOH at 293 K is 2.69 x $10^{-5}s^{-1}$. Photoproduct compound **2** in $CHCl_3$ was more stable than in MeOH. We have studied compound **1** in $CDCl_3$ by the third harmonic of a Quanta-Ray Nd:YAG laser in the range of 355 nm at various laser powers. The dependence on laser power enhanced the yield of product **2** as shown in Figure 4.

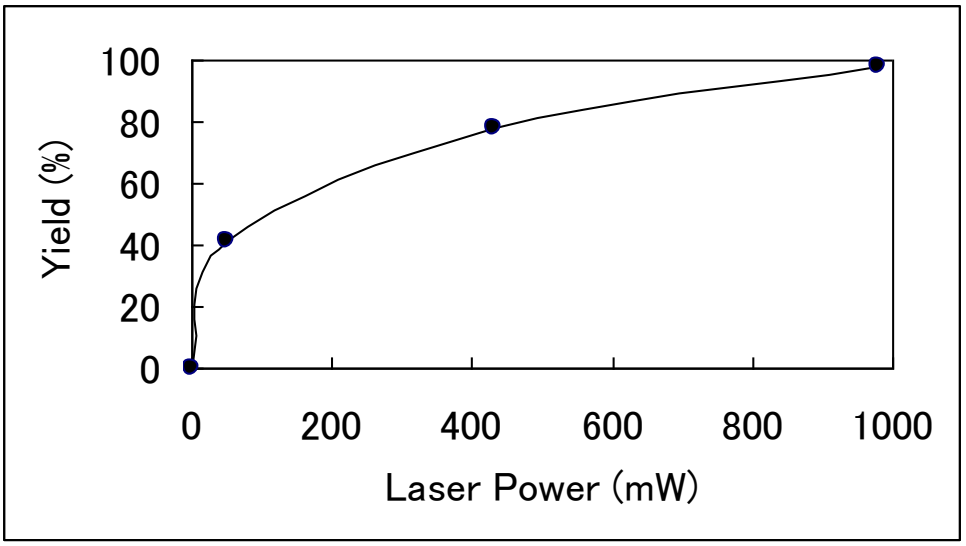


Figure 4. Laser power dependence of the yield of Product **2** in photolysis of Compound **1** in $CDCl_3$. Exposure time was 60 minutes.

With increasing laser power, the yield amount of product **2** was increased sharply. At a laser power of 980 mW for 60 minutes, chemical yield attained 99%. The laser power could control the synthesis of the open ring form photoproduct.

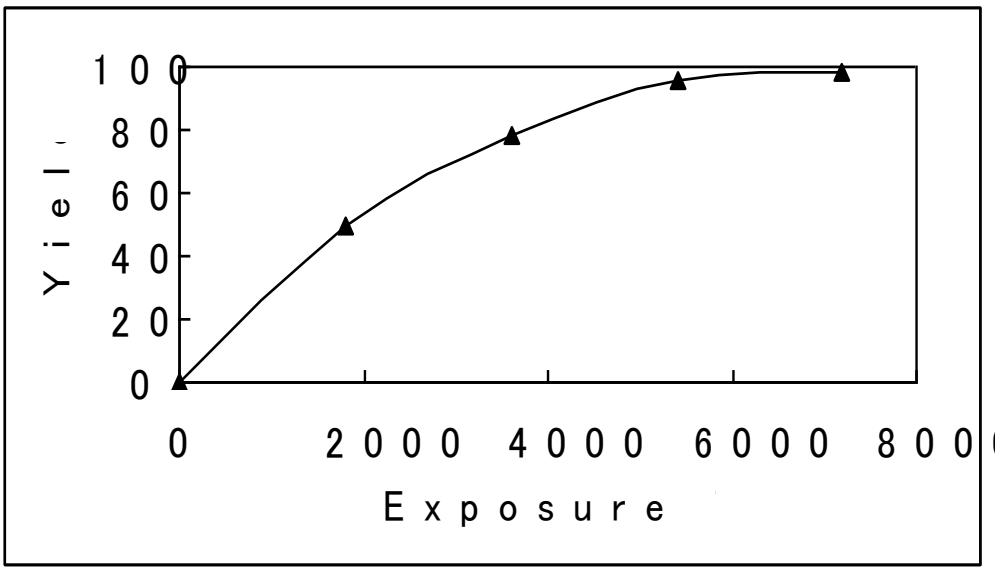


Figure 5. Exposure time dependence of the yield of Product **2** in photolysis of Compound **1** in $CDCl_3$. Laser power was 430 mW.

We have studied compound **1** in $CDCl_3$ by the third harmonic of a Quanta-Ray Nd:YAG laser in the range of 355 nm at various exposure times. The dependence on exposure time enhanced the yield of

product **2** as shown in Figure 5. Increasing exposure time induces an increase in the yield amount of product **2**. At an exposure time of 7,200 seconds using a laser power of 430 mW, the chemical yield attained 99%.

Exposure time could control the synthesis of the open ring form photoproduct. On this photoreaction of photoproduct **2** from compound **1** in Figure 5, this photoreaction obeys a first–order rate and the rate approximates the equation below: 1-exp (-0.00045 x t).

4,7-dimethylbenzofurazan **1** was transformed by irradiation with the third harmonic of a Quanta-Ray Nd:YAG laser (355 nm) into (2*Z*,4*Z*)-2,5-dimethylhexa-2,4-dienedinitrile monoxide in $CDCl_3$ at room temperature in excellent yield. Compound **1** was more reactive in such a short reaction time compared to dimethyl and methylbenzofurazan. Product (2*Z*,4*Z*)-2,5-dimethylhexa-2,4-dienedinitrile monoxide was almost as stable as dinitriles from benzofurazan at room temperature. The presence of 4 and 7-position Me must be important for the stability of the dinitrile monoxide structure and reactivity of this photoreaction. The laser power and exposure time can control this photoreaction. Comparing light sources, for example a Xe lamp, or an Hg lamp, such a low power and short exposure time gave a good yield using a laser.

EXPERIMENTAL

UV absorption spectra were measured using a JASCO UV/VIS Spectrophotometer V-550. Melting points were determined with a Yanagimoto micromelting point apparatus and are uncorrected. The IR spectra were recorded on a JASCO Fourier Transform Infrared spectrophotometer FT/IR-4100. The ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a JEOL FT NMR spectrometer JNR-ECX500 with TMS as the internal standard. The MS spectra were recorded on a JEOL Mass Spectrometer JMS-GCmate. Substrate compound **1** was prepared as previously described.[7]

A solution of 5.0 mg of 4.7-dimethylbenzofurazan dissolved in 0.5 mL $CDCl_3$ put into a 5 mm OD NMR tube. A laser beam was irradiated through the orifice of the NMR tube directly, not through the tube glass. The beam size was 12 mm in diameter. Chemical yield was calculated by ^{1}H NMR integration (99%). Quantum yield was calculated by values of exposure time, laser power, laser wavelength and chemical yield. Rate constant was calculated by UV absorbance at 289 nm from compound **2** to compound **1**.

After photoreaction, it was purified by preparative TLC (Merck, Silica gel plate 60 F_{254} Art. 1.05717) to give (2*Z*,4*Z*)-2,5-dimethylhexa-2,4-dienedinitrile monoxide **2**, (*n*-hexane/ CH_2Cl_2 (3:2)). The product was extracted with CH_2Cl_2, and dried using air carefully afforded a light yellow powder. Before UV absorption spectra were recorded, a solution of 4.7-dimethylbenzofurazan in MeOH was stored in the dark for 24 hours. Product **2** mp 93 ^{o}C. IR ($CHCl_3$) cm^{-1}: ν2215, 2277, ^{1}H-NMR (δ, ppm, $CDCl_3$), 2.06(3H, s), 2.13(3H, s), 6.86(2H, s), ^{13}C-NMR (δ, ppm, $CDCl_3$), 20.4, 22.3, 112.9, 116.3, 117.3, 129.6,

136.3, 139.7, FAB-low-resolution mass spectrum (m/z) 149(M+1).

Starting material **1** showed melting point and resonances; mp 68 °C. ^{1}H-NMR (δ, ppm, $CDCl_3$), 2.60(6H, s), 7.00(2H, s), ^{13}C-NMR (δ, ppm, $CDCl_3$), 17.2, 124.4, 129.7, 150.4.

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