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Investigation of photoreaction for 2-nitrobenzofuran and its 3-methyl derivative

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ABSTRACT

Aromatic nitro compounds undergo various photoreactions such as photosubstitution, photoredox reactions, photodissociation, and photoinduced nitro–nitrite rearrangements. The reaction mechanisms for these photoreactions, especially nitro–nitrite rearrangement reactions have never been completely understood. It was originally assumed that the potential cause for a nitro–nitrite rearrangement originates from the twisted dihedral angle between the plane of the nitro group and the plane of the aromatic ring [O.L. Chapman et al., J. Am. Chem. Soc. 88 (1966) 5550–5554]. Although the majority of aromatic nitro compounds have coplanar conformation and undergo nitro–nitrite rearrangement, no studies clearly substantiate this theory. This study reports on the photochemical reactions of 2-nitrobenzofuran and the effects of 3-methyl substituent on the compound. The results show that a nitro–nitrite rearrangement selectively occurs in deaerated acetonitrile solution for the photoreactions of 2-nitrobenzofuran. Moreover, nitro–nitrite rearrangement might occur in the photoreaction of 3-methyl-2-nitrobenzofuran. The quantum yield of degradation for 3-methyl-2-nitrobenzofuran was higher than that for 2-nitrobenzofuran, indicating that the methyl substituent at the 3-position changes the photoreactivity of 2-nitrobenzofuran.

1. Introduction

Aromatic nitro compounds are known to undergo various photoreactions induced by UV, such as photosubstitution, photoredox reactions, photodissociation and photo-induced nitro–nitrite rearrangements [1–24]. While photosubstitution and photoredox reactions were well investigated [1–12], photodissociation and nitro–nitrite rearrangement reactions have not been completely elucidated [11–24]. This is due to the fact that nitro–nitrite rearrangements and photodissociation reactions have low reaction efficiencies, which makes it difficult to observe any of the short-lived reaction intermediates. Consequently, the mechanism of nitro–nitrite rearrangements has also never been sufficiently explained. Chapman et al. originally proposed a reaction mechanism that involved nitro–nitrite rearrangement, which arose from an $n\pi^*$ excited state due to the specific conformations of the nitro group and aromatic ring [14]. In this particular conformation, the nitro group is positioned almost perpendicular to the plane of the aromatic ring due to the steric hindrance from its adjacent substituents. This causes deconjugation of the aromatic ring with the nitro group. In the following proposed reaction mechanism shown in Scheme 1, an oxaziridine ring is formed as an intermediate. This three-membered ring immediately collapses and generates a nitrite group, which converts into a phenoxy radical and nitric oxide radical through the cleavage of the O—N bond.

Conversely, Lippert and Kelm have also observed a rearrangement of the nitro group in the photoreaction of 4-fluoronitrobenzene [18]. 4-Fluoronitrobenzene was irradiated by UV in benzene solvent, and it was proposed that 4-fluorophenol, 4-fluoronitrophenol, and 4-fluorobiphenyl are produced as photoproducts. They proposed that this occurred due to a predissociation mechanism, where the C—N bond in 4-fluoronitrobenzene dissociates in its excited state. The cleavage of the C—N bond resulted in the generation of a nitrogen dioxide radical and a phenyl radical. The oxygen atom on the nitrogen dioxide radical could rebind to the phenyl radical and produce nitrosobenzene derivatives. The collapse of nitrosobenzene generated a phenoxy radical and nitric oxide. The reaction mechanism proposed by

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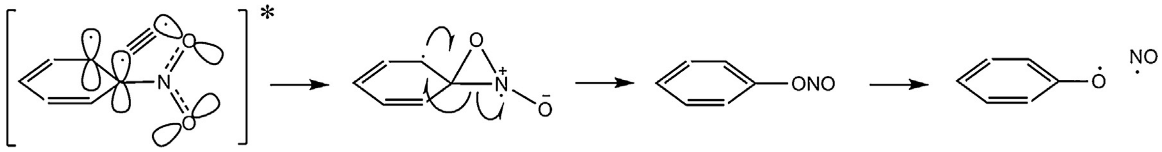


Scheme 1. Reaction mechanism proposed by Chapman et al. for nitro–nitrite rearrangement.

Lippert and Kelm is shown in Scheme 2. Lippert and Kelm further stated that the presence of 4-fluorobiphenyl as a byproduct in this reaction system indicated that a phenyl radical was generated in the photoreaction of 4-fluoronitrobenzene.

Photochemical reactions play an important role in aromatic nitro compounds. For example, the photoreactions of flutamide, which is used as an anticancer drug used for prostate cancer treatment [25], have been investigated from different perspectives in pharmacology, photochemistry, and photophysics. [26–28]. When this medication was prescribed, patients often experienced photodermatosis as a rare, adverse side effect [29–30]. This photoinduced skin disorder was believed to be due to the irradiation of sunlight, which prompted further investigation on the photoreactivity of flutamide. Through *in vitro* experiments, it was determined that certain photoreactions of flutamide that included nitro–nitrite rearrangements and photoreductions were caused by UV irradiation [26–28]. The causal relationship between the photoreactivity of flutamide and photodermatosis are still being investigated. In another example, nitro polycyclic aromatic hydrocarbons (NPAHs) were widely investigated, which were known as harmful air pollutants [31,32]. Several examples of the hydrocarbon structures for NPAHs include pyrene, anthracene, and chrysene. The mechanism for the generation of NPAHs was studied owing to their significant toxicity as a mutagen and carcinogen. It was suggested that a succession of radical reactions was initially caused by an addition reaction of a nitrate or a hydroxyl radical. The photodecomposition of various NPAHs was also investigated to estimate its half-life on the ground surface [32].

The photoreactions of nitro-substituted aromatic hydrocarbons have also been thoroughly examined [1–20,26–28]. In the photoreactions of nitro-substituted aromatic heterocycles, R. Hunt and S. T. Reid specifically investigated the photorearrangements of five-membered nitroheteroaromatic systems such as 2-nitrofuran and 2-nitropyrrole. In their study, 2-nitrofuran was irradiated in methanol and produced 3-hydroxyimino-2-oxo-2,3-dihydrofuran [19–20]. An analogue photoproduct was produced from the photorearrangement of 2-nitropyrrole [19]. Moreover, irradiation of 3-methyl-2-nitrofuran caused rearrangement occurred at 5-position which produced 5-hydroxyimino-3-metylfuran-2(5H)-one [20]. These photorearrangements are similar to those of nitro-olefins [21–23]. In this study, irradiation experiments of 2-nitrobenzofuran derivatives were conducted to investigate the photochemistry of nitro-substituted aromatic heterocycles. In 2-nitrobenzofuran, the nitro group and aromatic ring are arranged in a coplanar conformation. Some investigations show that aromatic nitro compounds with a coplanar conformation undergo nitro–nitrite rearrangements [13,17–20] Conversely, Y. Kitamura and T. Matsuura explained the photochemistry of a hindered nitrobenzene [24], 2,6-dialkyl-substituted nitrobenzene, by referring to the mechanism developed by Chapman et al. Although nonsubstituted nitrobenzenes undergo photoreduction in hydrogen-donating solvent [1,2], their study shows that nitro–nitrite rearrangements can also occur with photoreduction if 2,4,6-trimethylnitrobenzene is irradiated in 2-propanol solvent.

To date, no studies clearly indicate whether the nitro–nitrite rearrangement would occur if the aromatic ring and nitro group existed in a coplanar conformation. The effects of the methyl substituent at the 3-position of 2-nitrobenzofuran were also examined. An investigation into the photochemical reactions of 2-nitrobenzofuran and its 3-methyl derivative would clarify the relationship between the dihedral angle and nitro–nitrite rearrangement. Moreover, this study would provide additional insight into the photoreactions of nitro-substituted heteroaromatic compounds. This could potentially lead to the design of photostable aromatic nitro compounds and expand the usage of aromatic nitro compounds into the fields of material and pharmaceutical sciences.

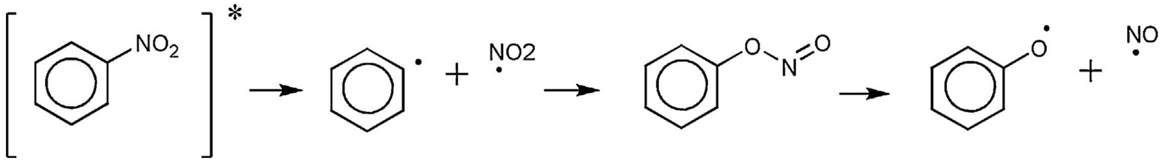
2. Materials and methods

2.1. Chemicals

All reagents and solvents were reagent grade and used as-received in synthetic procedures. High-performance liquid chromatography (HPLC) grade acetonitrile (Nacalai Tesque) was used as the reaction solvent for the irradiation experiments. Compounds 1a, 2a, and 1 g were prepared according to previous literatures [33,34]. The synthesis procedures were shown in Supplementary information.

2.2. Instruments and equipment

In preparative experiments, a high-pressure mercury arc lamp (UVL-100HA-100P; Riko) was used as the light source. A super-high-pressure mercury lamp (UI–501C, Ushio Inc.) was used for qualitative experiments and the determination of quantum yields. All ^{1}H NMR and ^{13}C NMR spectra were obtained with a JOEL ECS-400 instrument, and all IR spectra were obtained with a JASCO FT/IR-400 instrument. GC–MS analyses were performed with a Hewlett-Packard HP6890/5793MSD instrument. The absorption spectra were recorded with a Hitachi U-2310 spectrophotometer. HPLC was performed with a Shimadzu LC-6AD equipped with a normal phase column (Kanto Chemical, Mightysil Si60, 250 mm × 4.6 mm × 5 μm). The mobile phase consisted of hexane and ethyl acetate in a 4:1 composition ratio. The photoproducts were detected by a UV–vis detector (Shimadzu, SPD-10A UV–vis detector). The detection wavelength of the photoreactions was set at 313 nm with a flow rate of 1 mL/min. To separate the racemic



Scheme 2. Reaction mechanism proposed by Lippert and Kelm for the rearrangement of the nitro group.