Photocatalytic Monofluorination of Benzene by Fluoride via Photoinduced Electron Transfer with 3-Cyano-1-methylquinolinium

Kei Ohkubo,[†] Atsushi Fujimoto,[†] and Shunichi Fukuzumi^{*,†,‡}

[†]Department of Material and Life Science, Graduate School of Engineering, Osaka University and ALCA, Japan Science and Technology Agency (JST), 2-1 Yamada-oka, Suita, Osaka 565-0871, Japan

[‡]Department of Bioinspired Science, Ewha Womans University, Seoul 120-750, Korea

Supporting Information

ABSTRACT: The photocatalytic fluorination of benzene occurs under photoirradiation of an oxygen-saturated acetonitrile (MeCN) of the 3-cyano-1-methylquinolinium ion (QuCN⁺) containing benzene and tetraethylammonium fluoride tetrahydrofluoride (TEAF·4HF) with a xenon lamp (500 W) attached to a colored-glass filter ($\lambda < 290$ nm) to yield fluorobenzene and hydrogen peroxide. The quantum yield of formation of fluorobenzene was 6%. Nanosecond laser flash photolysis measurements were performed to elucidate the mechanistic details for photocatalytic fluorination. Transient absorption spectra taken after the nanosecond laser excitation at 355 nm of a degassed MeCN solution of QuCN⁺ and benzene exhibited absorption bands due to QuCN[•] ($\lambda_{max} = 500$ nm) and the benzene dimer radical cation ($\lambda_{max} = 900$ nm), which were generated by photoinduced electron transfer from benzene to the singlet excited state of QuCN⁺. The decay rate of the transient absorption band due to the benzene dimer radical cation was accelerated by the addition of TEAF·4HF. The observed rate constant increased with increasing concentration of TEAF·4HF. The rate constant of the electrophilic addition of



fluoride to the benzene radical cation was determined to be $9.4 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$. Thus, the photocatalytic reaction is initiated by intermolecular photoinduced electron transfer from benzene to the single excited state of QuCN⁺. The benzene radical cation formed by photoinduced electron transfer reacts with the fluoride anion to yield the F-adducted radical. However, QuCN[•] can reduce O₂ to O₂^{•-}, and this is followed by the protonation of O₂^{•-} to afford HO₂[•]. The hydrogen abstraction of HO₂[•] from the F-adduct radical affords fluorobenzene and H₂O₂ as the final products.

INTRODUCTION

Aromatic fluorination reactions have merited special attention because of useful application in materials science, the chemical industry, and medicine.^{1–10} Fluorinated substitution has been carried out by the Balz-Schiemann reaction using HBF₄ with HNO₃, which requires an amino group.^{11,12} Direct substitution of the fluorine group on the benzene ring is also known by electrochemical fluorination and the use of XeF₂; however, their synthetic utility has been limited because of low yield and poor selectivity.^{13–21} In particular, it has been difficult to perform selective monofluorination of aromatic compounds. The best oxidant is obviously dioxygen from the standpoint of green chemistry.^{22–24}

Radical cations produced by photoinduced electron-transfer reactions are known to react with nucleophiles to form various adducts.^{25–38} Among aromatic radical cations, the benzene radical cation is a very strong electrophile. Thus, the electron-transfer oxidation of benzene is expected to undergo an efficient nucleophilic aromatic substitution. The nucleophilic substitution of aromatic radical cations has been mainly investigated in the gas phase.^{39–46} However, the electron-transfer oxidation of benzene in solution is relatively difficult because of the high one-electron oxidation potential of benzene, $E_{ox} = 2.48$ V versus SCE in acetonitrile

(MeCN).^{37,47,48} We have recently found that the 3-cyano-1methylquinolinium ion (QuCN⁺) has an extremely strong oxidizing ability to oxidize benzene easily by electron transfer upon photoexcitation in MeCN.³⁷ The reduced radical of QuCN⁺ (QuCN[•]) as a product of photoinduced electron transfer is readily oxidized by O₂ to regenerate QuCN⁺. Thus, QuCN⁺ can be an effective photocatalyst for the fluorination of benzene with O₂ via electron-transfer oxidation of benzene with a weak nucleophile, the fluoride anion. The nucleophilic addition of the fluoride anion to radical cations would enable selective fluorination via the electron-transfer oxidation of substrates. However, there has been no report on the selective monofluorination of aromatic compounds via electron-transfer oxidation using oxygen as an oxidant.

We report herein that 3-cyano-1-methylquinolinium perchlorate $(QuCN^+ClO_4^-)^{37}$ acts as an efficient photocatalyst for the selective monofluorination of benzene with tetraethylammonium fluoride tetrahydrogen fluoride salt (TEAF·4HF) as a fluorine source and O_2 as an oxidant under photoirradiation to produce fluorobenzene without further fluorination. The

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photocatalytic reaction is initiated by photoinduced electron transfer from benzene to the singlet excited state of QuCN⁺. The photocatalytic mechanism is clarified by detecting radical intermediates involved in the photocatalytic reactions with the use of laser flash photolysis. The present study provides a unique fluorination pathway of aromatic hydrocarbons with fluoride and oxygen as a green oxidant.

EXPERIMENTAL SECTION

Materials. 1-Methyl-3-cyanoquinolinium iodide (QuCN⁺I⁻) was prepared by the reaction of 3-cyanoquinoline with methyl iodide in acetonitrile, converted to the perchlorate salt (QuCN⁺ClO₄⁻) by the addition of magnesium perchlorate to QuCN⁺I⁻ in methanol and purified by recrystallization from methanol.^{49,50} Potassium ferrioxalate used as an actinometer was prepared according to the literature and purified by recrystallization from hot water.^{51,52} Benzene, fluorobenzene, chlorobenzene, bromobenzene, and iodobenzene used as substrates were obtained commercially. Tetraethylammonium fluoride tetrahydrofluoride (TEAF·4HF) was purchased from Tokyo Chemical Industry Co., Ltd. Acetonitrile was spectral grade, obtained commercially and used without further purification. Deuterated [²H₃] acetonitrile (CD₃CN) was obtained from Euri SO-TOP, CEA, France, and used as received.

Reaction Procedure. A CD_3CN solution (0.6 cm³) containing QuCN⁺ClO₄⁻ (2.0 × 10^{-3} M) and TEAF·4HF $(5.0 \times 10^{-2} \text{ M})$ in a sample tube sealed with a rubber septum was saturated with oxygen by bubbling with oxygen through a stainless steel needle for 5 min. Then, benzene (1.2 μ mol, 2.0 × 10^{-2} M) or halogenated benzene (1.2 μ mol, 2.0 × 10^{-2} M) was added to the solution. The solution was then irradiated with a 500 W xenon lamp (Ushio Optical model X SX-UID 500XAMQ) through a colored-glass filter transmitting λ > 290 nm at room temperature. After photoirradiation, the corresponding oxygenated product was identified and quantified by a comparison of the ¹H NMR spectra with that of an authentic sample. The¹H NMR measurements were performed on a Japan Electron Optics JMN-AL300 (300 MHz) NMR spectrometer. The yield of H₂O₂ was determined by titration with excess NaI (100 mm). The amount of I_3^- formed was then determined from the UV–vis spectrum ($\lambda_{max} = 361$ nm, ε_{361} nm $= 2.5 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$).^{53,54}

Quantum Yield Determinations. A standard actinometer (potassium ferrioxalate)⁵¹ was used for the quantum yield determination of the QuCN⁺ photosensitized fluorination of a benzene with oxygen and fluoride anions. A square quartz cuvette (10 mm i.d.) that contained an MeCN solution (3.0 cm³) of QuCN⁺ClO₄⁻ (5.0×10^{-3} M), TEAF 4HF (5.0×10^{-2} M), and benzene $(0-1.0 \times 10^{-1} \text{ M})$ was irradiated with $\lambda = 334$ nm monochromatized light from a Shimadzu RF-5300PC fluorescence spectrophotometer. Under the conditions of actinometry experiments, the actinometer and QuCN⁺ absorbed essentially all of the incident light of $\lambda = 334$ nm. The light intensity of monochromatized light of $\lambda = 334$ nm was determined to be 1.2×10^{-8} einstein s⁻¹. The photochemical reaction was monitored using a Shimadzu GC-17A gas chromatograph and a Shimadzu MS-QP5000 mass spectrometer. The quantum yields were determined from the increase in the quantity of fluorinated benzene derivatives.

Photophysical Measurements. UV-visible absorption measurements were performed using a Hewlett-Packard 8453 spectrophotometer. Steady-state fluorescence spectra were recorded in a FluoroMax-4 equipped with a 150 W xenon lamp. Time-resolved florescence measurements were made with the technique of time-correlated single-photon counting (TCSPC) in a FluoroMax-4-TCSPC. Samples were excited with a 350 nm NanoLED with a fwhm of 1.4 ns and a repetition rate of 100 MHz.

Laser Flash Photolysis. Measurements of nanosecond transient absorption spectra in the photochemical reactions of QuCN⁺ with benzene, TEAF·4HF, and O₂ in MeCN were performed according to the following procedures. Typically, the nitrogen-saturated MeCN solution containing benzene (10 mM-1.0 M) and QuCN⁺ (40 μ M) was excited with a Nd:YAG laser (Continuum, SLII-10, 4–6 ns fwhm) at λ = 355 nm with a power of 10 mJ/pulse. Photoinduced events were monitored by the use of a continuous Xe lamp (150 W) and an InGaAs-PIN photodiode (Hamamatsu 2949) as a probe light and a detector, respectively. The output from the photodiodes and a photomultiplier tube was recorded with a digitizing oscilloscope (Tektronix, TDS3032, 300 MHz). The transient spectra were recorded for fresh solutions in each laser excitation. All experiments were performed at 298 K.

Theoretical Calculations. Density functional theory (DFT) calculations were performed with Gaussian 09.⁵⁵ The calculations were performed on a 32-processor QuantumCube at the B3LYP/6-311+G(d,p) level of theory by applying the polarizable continuum model (PCM) using the integral equation formalism variant (IEF-PCM). Electronic charges were obtained by natural population analysis (NPA).

RESULTS AND DISCUSSION

The photoinduced fluorination of benzene occurs under the photoirradiation of an oxygen-saturated acetonitrile (MeCN) solution containing QuCN⁺ ClO₄⁻ (2.0 mM), benzene (20 mM), and TEAF·4HF (50 mM) with a xenon lamp (500 W) through a colored-glass filter transmitting $\lambda > 290$ nm to yield fluorobenzene and hydrogen peroxide (H₂O₂) (eq 1). The time course of the photocatalytic reaction is shown in Figure 1.



The yield of fluorobenzene after 50 min of photoirradiation was 20% with a 40% conversion of benzene, which was determined by GC-MS and ¹H NMR analyses. H_2O_2 was detected by an iodometric titration. Phenol was also detected as a side product because of the photocatalytic oxygenation of benzene with QuCN⁺ in the presence of a small amount of H_2O containing MeCN.^{36,56–58} No further fluorination occurred under the present reaction conditions. When benzene was replaced by fluorobenzene as a substrate, no fluorination occurred to yield difluorobenzene. The quantum yield of the formation of fluorobenzene (Φ) was determined from the initial rate of product formation by the use of potassium ferrioxalate as a standard actinometer (Experimental Section).^{51,52} The Φ value increased with increasing concentration of benzene to approach a limiting value (Φ_{∞}) (Figure 2). Such a saturated dependence of Φ on the benzene concentration is expressed by



Figure 1. Irradiation time profiles of the photoinduced fluorination of benzene (2.0×10^{-2} M) in O₂-saturated MeCN (0.6 mL) containing TEAF·4HF (5.0×10^{-2} M) at 298 K; [QuCN⁺ ClO₄⁻] = 2.0×10^{-3} M. Benzene, black; hydrogen peroxide, blue; fluorobenzene; red; phenol, orange.



Figure 2. Plot of quantum yield vs $[C_6H_6]$ for the formation of fluorobenzene in the photofluorination of benzene (0–100 mM) with TEAF·4HF (50 mM) and QuCN⁺ (2.0 mM) in O₂-saturated MeCN at 298 K.

$$\Phi = \frac{\Phi_{\infty} K_{obs} [C_6 H_6]}{1 + K_{obs} [C_6 H_6]}$$
(2)

where K_{obs} is the quenching constant. The K_{obs} value can be converted to the corresponding rate constant (k_{obs}) provided that the lifetime of the excited state involved in the reaction (τ) is known as eq 3.

 $k_{\rm obs} = K_{\rm obs} \tau^{-1} \tag{3}$

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From the curve fitting using eq 2 in Figure 2, the values of Φ_{∞} and $K_{\rm obs}$ were determined to be 6.0% and 90 M⁻¹, respectively. The $k_{\rm obs}$ value was determined to be 1.0×10^{10} s⁻¹ as calculated from eq 3 using $\tau = 9.0$ ns for ¹QuCN^{+*}.⁵⁹ The pertinent data of the photoinduced fluorination of benzene and halogenated benzene are summarized in Table 1.

Photoirradiation of the absorption band of QuCN⁺ (λ_{ex} = 350 nm) results in fluorescence in MeCN at 430 nm. The fluorescence lifetimes were determined by time-resolved fluorescence decay measurements as shown in Figure 3a. The



Figure 3. (a) Fluorescence decays of QuCN⁺ at 430 nm with benzene (0-10 mM) in deaerated MeCN containing H₂O (100 mM). A pale gray line denotes the instrument response. Excitation wavelength, 350 nm. (b) Plot of fluorescence decay rate constant (k_{obs}) vs benzene concentration.

Table 1. Product Yields for the Photocatalytic Fluorination of Benzene Derivatives and Rate Constants of Photoinduced Electron Transfer from Substrates to ¹QuCN^{+*} (k_q) and the Addition Reaction of F⁻ to Substrate Radical Cations (k_F) in MeCN

| substrate | conv., % | product | yield, % | <i>k</i> _q , M ^{−1} s ^{−1} | <i>k</i> _F , M ^{−1} s ^{−1} |
|-----------|----------|---------------------|-------------------|---|---|
| | 40 [| ✓ ^F 20 (| → ^{OH} 4 | 1.1 × 10 ¹⁰ | 9.4 × 10 ⁹ |
| F | 39 | no fluorinatio | on | 1.0 × 10 ¹⁰ | 7.7 × 10 ⁹ |
| CI | 34 | | 7 | 1.1 × 10 ¹⁰ | 7.0 × 10 ⁹ |
| Br | 25 | F Br | 6 | 1.2 × 10 ¹⁰ | 3.4 × 10 ⁹ |
| | trace | no fluorination | | 1.3 × 10 ¹⁰ | |

fluorescence decay rate constant of ¹QuCN^{+*} (k_{obs}) increased with an increase in the concentration of benzene (0–10 mM). The quenching rate constant (k_q) was determined from the slope of k_{obs} versus [C_6H_6] to be 1.1 × 10¹⁰ M⁻¹ s⁻¹ (Figure 3b), which is close to the rate constant determined from the quantum yield dependence on the benzene concentration (Figure 2) given by eqs 2 and 3. Thus, the rate-determining step is photoinduced electron transfer from benzene to ¹QuCN^{+*}.

The free-energy change of photoinduced electron transfer from benzene to ¹QuCN^{+*} was determined from the oneelectron oxidation potential of benzene ($E_{ox} = 2.48$ V vs SCE),^{36,46,47} the one-electron reduction potential of QuCN⁺ ($E_{red} = -0.60$ V vs SCE),⁵⁷ and the singlet excited energy of QuCN⁺ ($^{1}E^{*} = 3.32$ eV)³⁶ using eq 4 to be negative ($\Delta G_{et} = -0.24$ eV).

$$\Delta G_{\rm et} = e(E_{\rm ox} - E_{\rm red}) - {}^{\rm L}E^* \tag{4}$$

Thus, the photocatalytic fluorination of benzene is made possible by the electron-transfer oxidation of benzene by ${}^{1}QuCN^{+*}$. The rate constants of quenching of ${}^{1}QuCN^{+*}$ by halogenated benzenes were also determined, and the values are summarized in Table 1. (Data are shown in Supporting Information Figures S1–S4.) ${}^{1}QuCN^{+*}$ was also efficiently quenched by fluorobenzene, which is a reason that the conversion of benzene was limited in the photocatalytic fluorination of benzene (Figure 1).

The occurrence of photoinduced electron transfer from benzene to ¹QuCN⁺* was confirmed by nanosecond laser flash photolysis measurements. Nanosecond laser excitation at 355 nm of QuCN⁺ in deaerated MeCN containing benzene (1.0 M) afforded a transient absorption spectrum at 0.4 μ s, in which new absorption bands appeared at 520 and 900 nm as shown in Figure 4a. The transient absorption band at 520 nm is assigned to the one-electron reduced QuCN⁺ (QuCN[•]).^{36,60} The near-IR absorption around 900 nm is assigned to the benzene dimer radical cation.^{36,57,61} The absorption bands at 520 and 900 nm decay, obeying second-order kinetics resulting from the bimolecular back electron transfer from QuCN[•] to the benzene dimer radical cation or the benzene radical cation. When TEAF.4HF was introduced into the QuCN⁺/benzene system, the broad absorption due to the benzene dimer radical cation disappeared as shown in Figure 4b, whereas the absorption band at 520 nm due to QuCN[•] remained. The decay time profile in the presence of TEAF·4HF obeyed first-order kinetics. The observed decay rate constant (k_{obs}) increased linearly with increasing concentration of TEAF 4HF as shown in the inset of Figure 4b. The rate constant of the reaction of the benzene dimer radical cation or the benzene radical cation with fluoride ($k_{\rm F}$) was determined to be 9.4 × 10⁹ M⁻¹ s⁻¹ from the slope shown in the inset of Figure 4b. No quenching of the benzene dimer radical cation was observed when TEAF·4HF was replaced by tetra-n-butylammonium chloride or bromide under otherwise the same experimental conditions. Thus, no photocatalytic chlorination and bromination of benzene occurred with QuCN⁺. The rate constants of the benzene radical cation and halogenated benzene radical cations with TEAF·4HF were also determined to be $1.0 \times 10^{10} - 1.3 \times 10^{10}$ M^{-1} s⁻¹, respectively (Table 1) (data are shown in Figures S5– S7 in Supporting Information). No dependence of k_{a} on the free-energy change of electron transfer was observed because the k_q values are close to the diffusion rate constant in MeCN



Figure 4. (a) Transient absorption spectrum observed upon 355 nm nanosecond laser excitation of QuCN⁺ (40μ M) with benzene (1.0 M) in deaerated MeCN at 298 K taken after 0.4 μ s. (b) Decay time profiles of absorbance at 900 nm in the presence of TEAF·4HF (0, 0.1, 0.2, and 0.5 mM). Kinetic traces were drawn by single-exponential curve fitting. (Inset) k_{obs} vs [TEAF·4HF].

because of the highly exergonic photoinduced electron-transfer reactions.

On the basis of the above-mentioned results, the photocatalytic mechanism is proposed as shown in Scheme 1, where the photocatalytic reaction is initiated by photoinduced electron transfer from benzene to ¹QuCN^{+*}. The benzene radical cation, formed by photoinduced electron transfer, exists in equilibrium with the benzene dimer radical cation because of the large excess of benzene. The benzene radical cation reacts with the fluoride of TEAF-4HF to yield the F-adduct radical. However, radical QuCN[•], formed by the photoinduced electron transfer with ¹QuCN^{+*}, can reduce O₂ to O₂^{•-}, and this is followed by the protonation of O₂^{•-} to afford HO₂^{•.62} The hydrogen abstraction of HO₂[•] from the F-adduct radical yields fluorobenzene and H₂O₂ (Scheme 1).⁶⁴ The formation of phenol as a side product (Figure 1) is ascribed to the addition of OH⁻ to the benzene radical cation.

Figure 5 shows electronic charges of the radical cations calculated by the DFT method to clarify the reason that no photofluorination of fluorobenzene and iodobenzene occurred as shown in Table 1. In the case of benzene radical cation, OH⁻ can attack toward the carbon nucleus with a positive charge (+0.081 shown in Figure 5a). However, the electronic positive charge of the fluorobenzene radical cation is mainly localized on the ipso carbon (+0.609) rather than on the other carbons (-0.196 for the ortho postion, -0.151 for the meta position, and +0.056 for the para position) as a result of the electronwithdrawing effect of the fluorine atom (Figure 5b). F⁻ of TEAF-4HF may attack toward the ipso carbon to form the 1,1difluorocyclohexadienyl radical. Then, C-F bond cleavage occurs to yield a starting material, fluorobenzene, without fluorination (Scheme 2). In contrast, the iodobenzene radical cation has no positive charge on the carbon atoms as a result of Scheme 1. Photocatalytic Mechanism of the Fluorination of Benzene with QuCN⁺





Figure 5. Electronic charges on the carbon and halogen atoms of radical cations of (a) benzene, (b) fluorobenzene, (c) chlorobenzene, (d) bromobenzene, and (e) iodobenzene obtained by natural population analyses (NPA). The geometry optimizations were carried out with density functional theory at the B3LYP/6-311+G(d,p) level by applying the polarizable continuum model (PCM) using the integral equation formalism variant (IEF-PCM).

Scheme 2



the strong electron-donating effect of the iodine atom (Figure 5e). Thus, there is no chance to form a C–I bond in the reaction between the iodobenzene radical cation and F^- .

CONCLUSIONS

The use of QuCN⁺ as an organic photocatalyst has enabled us to accomplish the photoinduced fluorination of benzene using molecular O_2 as an oxidant and TEAF·4HF as an F source. The reactive intermediates in the photocatalytic reaction were successfully detected by laser flash photolysis measurements to clarify the photocatalytic mechanism.

ASSOCIATED CONTENT

S Supporting Information

Transient absorption spectral data to determine rate constants. Complete author list for ref 55. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*Fax: +81-6-6879-7370. E-mail: fukuzumi@chem.eng.osaka-u. ac.jp.

Notes

The authors declare no competing financial interest.

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