Photochemical Cleavage Reaction of 8-Quinolinyl Sulfonates That Are Halogenated and Nitrated at the 7-Position

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Received June 29, 2011; accepted August 15, 2011; published online August 23, 2011

Photochemical bond-cleavage reactions are potentially useful in chemistry, bioorganic chemistry and medicinal chemistry. We previously reported on a photochemical cleavage reaction of 8-quinolinyl sulfonate (8-QS) derivatives in aqueous solution at neutral pH, which we proposed to proceed *via* an excited triplet state. In this report, we report on the synthesis of some new photocleavable 8-QS derivatives, in which halogen atoms or a nitro group was introduced at the 7-position, in an attempt to improve photoreactive properties and to produce a red-shift in the irradiation wavelength. The introduction of bromine and iodine resulted in an acceleration in the photoreaction by about 1.5 times, possibly due to a heavy atom effect. It was also found that 7-nitro-8-QS absorbs at >360 nm, and, as a result, the S–O bond of this compound can be cleaved by photoirradiation with a fluorescent lamp in aqueous solution and on silicon surface.

Key words photolysis; 8-quinolinol; sulfonate; nitration; halogenation

Photochemical bond-cleavage reactions are potentially useful in organic chemistry, biological chemistry and chemical biology (*e.g.*; protection/deprotection in organic synthesis[1—4] and the uncaging of chemically masked or caged biorelevant molecules).[5—14] For example, the photolysis of sulfonic esters,[15—18] sulfonamides,[19—22] and sulfones[23,24] has been applied to photoresist materials,[16,20] protecting groups,[6,17,21,22] and other chemical reactions.[15,24,25]

We previously reported that substituted 8-quinolinyl sulfonates such as **1a**, **e** and **f** undergo photochemical S–O bond cleavage reactions to afford the corresponding 8-quinolinols (**2a**, **e**, **f**) and sulfonate (**3**) by photoirradiation of aqueous solutions at *ca.* 300 nm (Chart 1),[26—28] which was found during a study of Zn^{2+}-selective fluorescent probes having 8-quinolinol side chains.[26—29] A comparison of the photoreactivity of various 8-quinolinyl sulfonate (8-QS) derivatives suggested that the photoreaction efficiency is dependent on the nature of the substituent groups attached to the 8-quinolinol moiety rather than those on the sulfonate unit. In particular, the introduction of electron-withdrawing groups such as *N*,*N*-dialkylaminosulfonyl group contributes to an improved efficiency and a red shift in the irradiation wavelength.[25,26] Furthermore, a mechanistic study implied that this photolysis proceeds *via* homolytic cleavage of the S–O bond in the excited triplet state generated from the excited singlet state through intersystem crossing (ISC).[28]

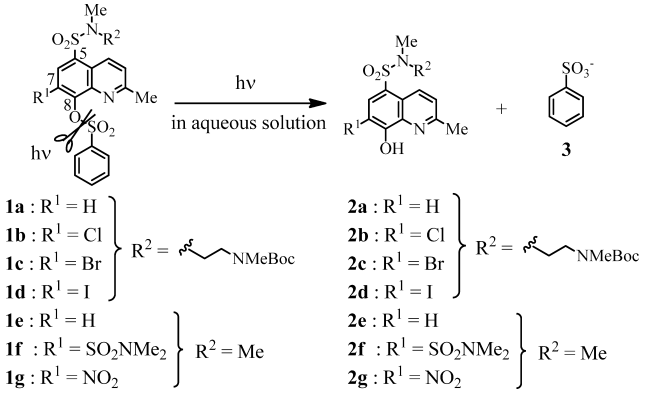

Chart 1. Photoreaction of 8-QS Derivatives (**1a**—**g**) in Aqueous Solution

One of the advantages of the photoreaction of 8-QS is that its photocleavage proceeds with negligible byproduct production. We recently reported on the design and synthesis of 8-QS-based photocleavable linkers **4** that consist (+)-biotin and dopamine moieties at both ends of the molecules (Chart 2).[30,31] This linker was fixed on an avidin-coated resin through a strong avidin-biotin complex, and a dopamine moiety was introduced at the other molecular end to trap specific receptors such as an anti-dopamine antibody. Subsequently, the 8-QS moieties were cleaved by photoirradiation at 313 nm, and the target complex of dopamine and the anti-dopamine antibody were isolated and identified.

Despite the aforementioned potential of this methodology, low quantum yields of photochemical S–O bond cleavage and the relatively short photoirradiation wavelength (300—330 nm) may limit further applications. It is known that halogen atoms such as chlorine, bromine and iodine exhibit a heavy atom effect that facilitate ISC from the excited singlet state to the triplet state.[32] On the other hand, the nitro group is one of the strongest electron-withdrawing groups and frequently seen in photosensitize protecting groups. For example, the *o*-nitrobenzyl unit is often used as a photosensitive protecting groups in caged compounds[33] and the nitro group is known to induce a red-shift in the UV absorbance of the molecules. In this paper, we report on the photochemical properties of 8-QS derivatives having halogen atoms or a nitro group at the 7-position that were synthesized in order to improve the photoreactive efficiency and to produce a red shift in the irradiation wavelength (Chart 1), as followed by UV absorption spectrometry and ^{1}H-NMR measurement. The chemical modification of silicon (Si) wafers with 8-QS derivatives, and the photoreactivity conferred by this modifi-

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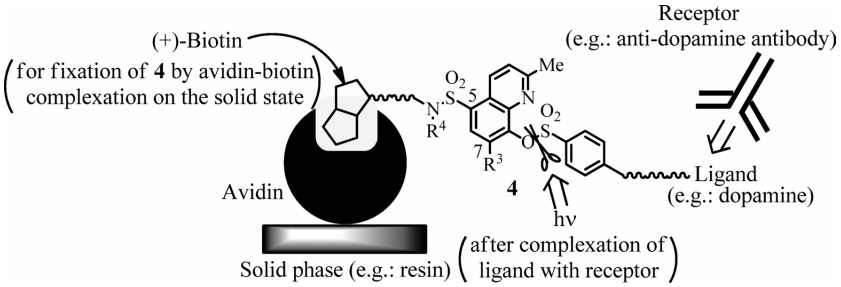


Chart 2. 8-QS Based Photocleavable Linker **4**

cation is also described.

Results and Discussion

Synthesis of 7-Haloganated and Nitrated 8-Quinolinyl Sulfonates The synthesis of 7-halo-8-quinolinyl sulfonates **1a**—**d** was carried out as shown in Chart 3.[26—29] The reaction of 5-chlorosulfonyl-8-hydroxyquinaldine (**5**)[26,28,29] with *N*-*tert*-butoxycarbonyl (Boc)-*N*,*N*′-dimethylethylenediamine (**7**) gave **2a**, reaction with *N*-chlorosuccinimide (NCS), *N*-bromosuccinimide (NBS), or *N*-iodosuccinimide (NIS) gave **2b**, **c**, and **d**, respectively. 7-Haloganated 8-quinolinols **2b**—**d** were reacted with benzenesulfonyl chloride to yield **1b**—**d**.

A conventional direct nitration of **2e** to **g** (H_2SO_4, HNO_3) was not successful (Chart 4). Therefore, a two step reaction (nitrosation with $NaNO_2$, HCl and oxidation with H_2O_2) gave **2g**, which was treated with benzenesulfonyl chloride to yield **1g**.

Photoreaction of 7-Halo-8-quinolinyl Sulfonates The photoreaction of **1b**—**d** was conducted by irradiation using a xenon (Xe) lamp at 290 nm in a 90/10 mixture of CH_3CN and *N*-(2-hydroxyethyl)piperazine-*N*′-2-ethanesulfonic acid (HEPES) buffer (pH 7.4) and the reaction was monitored by UV absorption spectrometer according to our previous report (Figs. 1, 2).[26—28] Figure 1 shows the UV absorption spectral changes of **1c**. The absorption at 290 nm of **1c** was reduced with increasing irradiation time with the isosbestic points at 267 nm and 315 nm. Similar results were obtained in the case of **1b** and **d**, while the photoreaction of **1b** was slower than that of **1d**. As shown in Fig. 2, the half life of **1a**—**d** were determined to be 9.0 min, 55.2 min, 5.4 min and 5.6 min, respectively, indicating that the photoreactivity of **1d** and **c** is *ca.* 1.5 times higher than that of **1a**.

The photoreaction of **1b**—**d** (irradiated at 290 nm) was also followed by ^{1}H-NMR (Figs. 3, 4). Figure 3 shows the change in the ^{1}H-NMR spectrum of **1c** upon photoirradiation at 290 nm using a Xe lamp in a 90/10 mixture of CD_3CN and D_2O (100 mM HEPES at pD 7.4). As shown in Fig. 3, the ^{1}H signals of **1c** have nearly disappeared after 4 h and **1c** is almost quantitatively converted into **2c** with negligible byproduct production. The time course for the photoreactions of **1a**—**d** are summarized in Fig. 4, indicating that the photoreaction of 7-Cl derivative **1b** was slower than that of **1a** and that **1c** and **1d** are more reactive than **1a**. These results suggest that the introduction of heavy atoms such as bromine and iodine at the 7-position of **1c** and **d** somehow accelerates photochemical cleavage reaction of 8-QS, possibly due to their stronger heavy atom effect than that of chlorine in **1b**.[32,34] We assume that the heavy atom effect and/or electron-withdrawing effect (inductive effect) of chlorine in **1b**

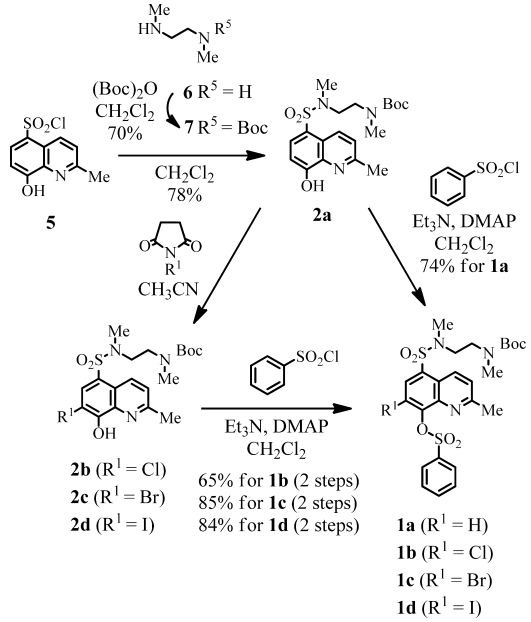


Chart 3. Syntheses of **1a** and 7-Halo-8-QS Derivatives **1b**—**d**

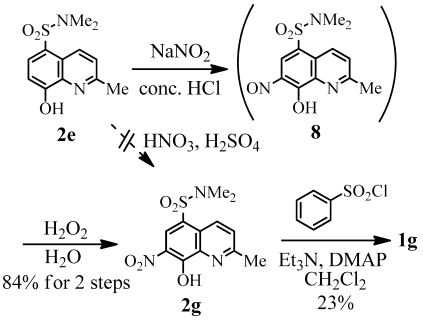


Chart 4. Synthesis of 7-Nitro-8-QS **1g**

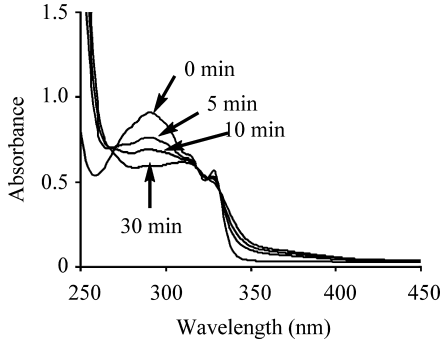


Fig. 1. Change in UV Absorption Spectra of 50 μM **1c** upon Photoirradiation at 290 nm in 90/10 CH_3CN/10 mM HEPES (pH 7.4 with I=0.1 ($NaNO_3$)) at 25 °C

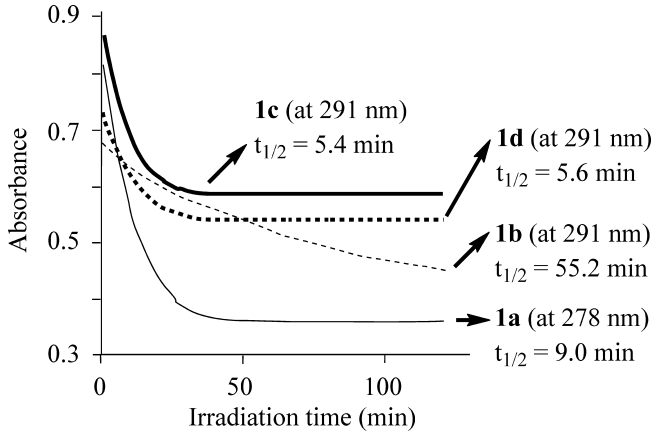


Fig. 2. Change in UV Absorbance of **1a** (Plain Curve), **1b** (Dashed Curve), **1c** (Bold Curve) and **1d** (Dashed Bold Curve) against Photoirradiation Time (Photoirradiation at 290 nm)

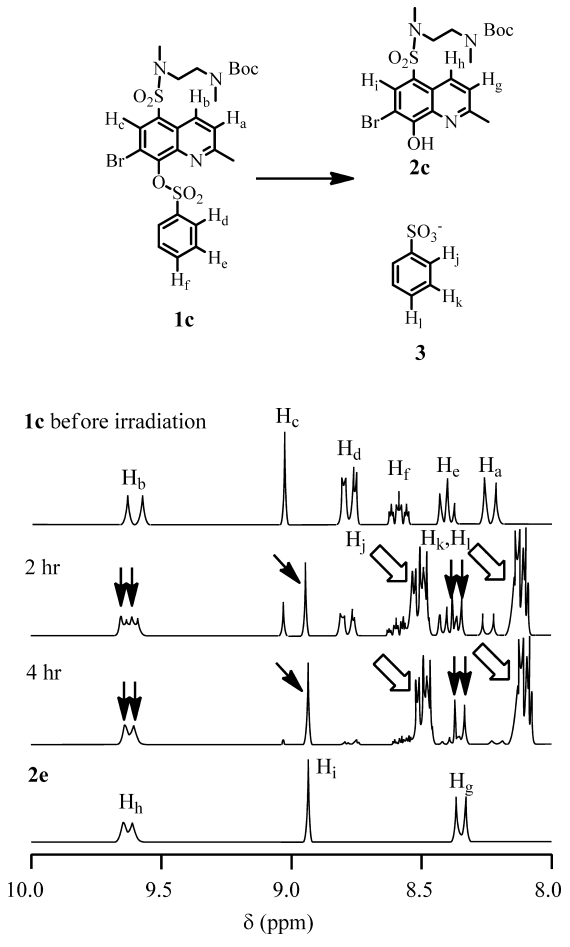


Fig. 3. Change in ^{1}H-NMR Spectra (Aromatic Region) of 1 mM **1c** upon UV Irradiation at 290 nm in 90/10 CD_3CN/100 mM HEPES (pD 7.4 with I=0.1 ($NaNO_3$)) at 25 °C

Plain and hollow arrows indicate ^{1}H signals of **2c** and **3**, respectively.

are compensated by its electron-donating effect (resonance effect), resulting in the lower photoreactivity of **1b** than **1a**, **c** and **d**.[35]

Photoreaction of 7-Nitro-8-quinolinyl Sulfonates In our previous work,[27,28] we reported that the introduction of electron-withdrawing groups such as *N*,*N*-dialkylaminosul-

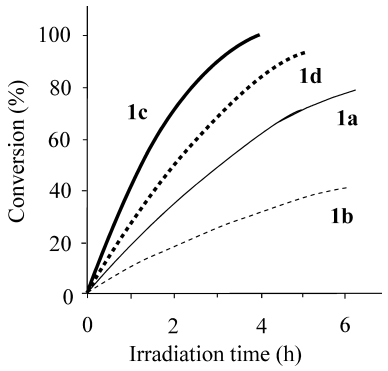


Fig. 4. Conversion of the Photoreaction Followed by ^{1}H-NMR Spectra of **1a** (Plain Curve), **1b** (Dashed Curve), **1c** (Bold Curve) and **1d** (Dashed Bold Curve) against Irradiation Time

Photoirradiation was conducted at 290 nm in 90/10 CD_3CN/100 mM HEPES (pD 7.4 with I=0.1 ($NaNO_3$)) at 25 °C.

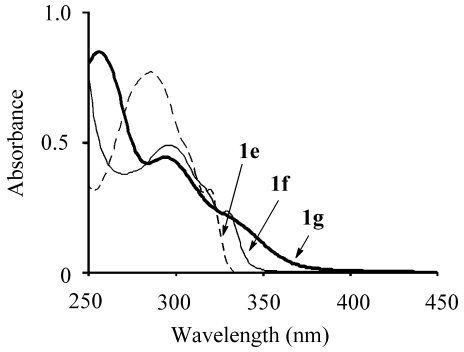


Fig. 5. UV Absorption Spectra of 50 μM **1e**—**g** in 90/10 CH_3CN/20 mM HEPES (pH 7.4 with I=0.1 ($NaNO_3$)) at 25 °C

Dashed, plain and bold lines indicate UV absorption spectra of **1e**—**g**, respectively.

fonyl group (**1f**) induces a red-shift in the UV absorption spectrum (plain curve in Fig. 5). Furthermore, the UV absorption spectrum of 7-nitro substrate **1g** is extended to *ca.* 380 nm, as shown by the bold curve in Fig. 5.

Based on these observations, the photoreaction of **1g** was carried out by irradiation at 360 nm, at which the absorption of **1e** and **f** is very weak. Figure 6 shows the photoreaction of **1g**, as followed by UV absorption spectrometry. With increasing irradiation time, the absorbance at 346 and 420 nm is considerably increased, eventually reaching that of **2g**. The fact that isosbestic points around 298 nm and 321 nm were observed strongly suggests that **1g** was converted into **2g** with minimum byproduct production, when the photoirradiation is conducted at 360 nm. For comparison, the photoreaction of **1e** (R^1=H, dashed curve in Fig. 6b) and **1f** (R^1=SO_2NMe_2, plain curve in Fig. 6b) was very slow when the photoirradiation was made at the same wavelength.[36]

The photoreaction of **1g** irradiated at 360 nm by a Xe lamp was also analyzed by ^{1}H-NMR in a 90/10 mixture of CD_3CN and D_2O (100 mM HEPES at pD 7.4) at 25 °C. As shown in Fig. 7, **1g** was converted into **2g** after photoirradiation for 3 h. Considering the combined UV absorption and ^{1}H-NMR results, it can be concluded that **1g** was converted into **2g** with minimum byproduct production by photoirradiation at 360 nm.

Quantum Yields for Photolysis of 8-Quinolinyl Sulfonate Derivatives The quantum yields (Φ) for the photol-

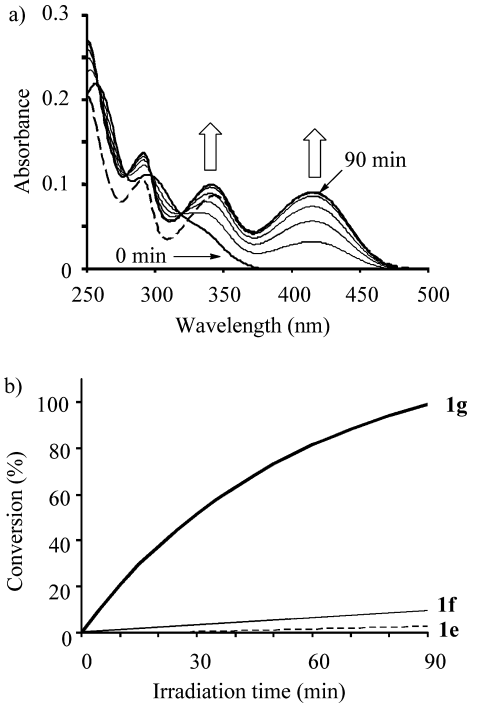


Fig. 6. (a) Change in UV Absorption Spectra of 10 μM **1g** upon UV Irradiation at 360 nm in 90/10 CH_3CN/10 mM HEPES (pH 7.4 with I=0.1 ($NaNO_3$)) at 25 °C

For comparison, UV absorption spectrum of **2g** in indicated with a dashed curve.

(b) Conversion of the Photoreaction of **1e** (Dashed Curve), **1f** (Plain Curve), and **1g** (Bold Curve) against Irradiation Time under Xe Lamp at 360 nm

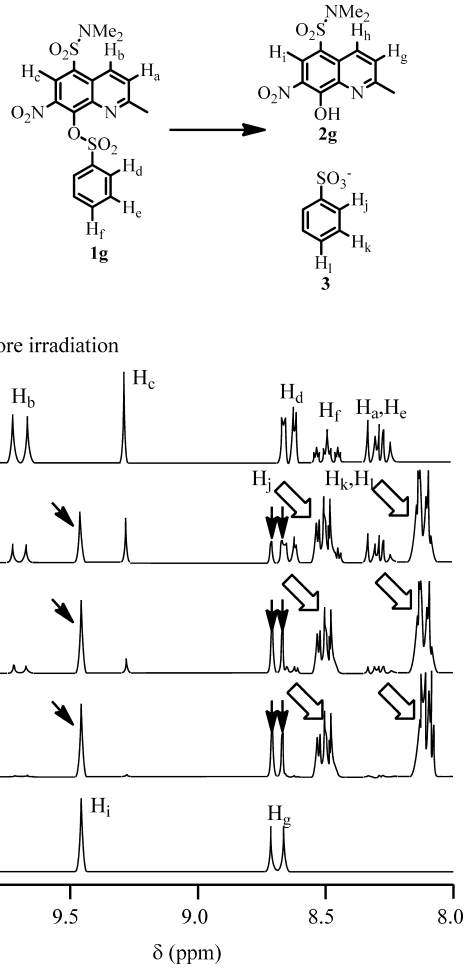


Fig. 7. Change in ^{1}H-NMR Spectra (Aromatic Region) of 1 mM **1g** upon UV Irradiation at 360 nm in 90/10 CD_3CN/100 mM HEPES (pD 7.4 with I=0.1 ($NaNO_3$)) at 25 °C

Plain and hollow arrows indicate ^{1}H signals of **2g** and **3**, respectively.

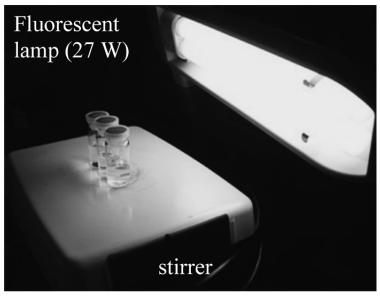
ysis of 8-QS derivatives were estimated by following changes in their UV absorption spectra (Table 1). The Φ values of **1c** (2.7×10^{-4}) and **1d** (3.2×10^{-4}) were greater than that of **1a** (1.5×10^{-4}), suggesting that bromine and iodine at the 7-position assist ISC, from the excited singlet state to the triplet state due to the heavy atom effect alluded to above. The improvement in photoreactivity and the red shift of **1f** and **g** can be attributed to the electron withdrawing effects of sulfonamide or nitro groups. The smaller Φ value of **1g** (7.6×10^{-5} at 366 nm) than those of other 8-QS derivatives allows us to handle the solutions of **1g** even in the daytime without strict dark conditions.

Photoreaction of 7-Nitro-8-quinolinyl Sulfonate under a Fluorescent Lamp During experiments, we noticed that the photolysis of **1g** proceeds under a fluorescent lamp in aqueous solution, while **1g** is relatively stable against light in the solid state. To date, 2-nitroveratrole group,[37,38] phenacyl group,[39] substituted nitrophenyl group,[14] and substituted coumarins[13,40] have been reported as caging groups that can be removed by visible light. In our experiments, it was found that the S–O bond of **1g** was cleaved under a fluorescent lamp (27 W) more effectively than **1e**, as displayed in Fig. 8. Unexpectedly **1e** and **f** undergo photolysis under the same conditions, because emissions at shorter wavelength (<350 nm) from the fluorescent lamp used in these experiments promote the photolysis of **1e** and **f**.

Photolysis of 1g on Silicon Wafer Surface Our next object is to develop photoreactive Si wafer devices modified with photoclevable linkers for trap and isolation of target biomolecules or cells with minimum damages. Si wafer is known to be one of the most versatile materials for detection or isolation of proteins, peptides and cells,[41—43] because it can be easily fabricated to desired shapes and modified by various silane-coupling reagents. Thus, we investigated chemical modification of Si wafer with **1g** and their photoreaction in order to evaluate photoreactivity of **1g** on Si surface for application of photoreactive Si devices. As depicted in Chart 5, Si wafers (150 mm×150 mm) were first reacted with 10% 3-aminopropyltriethoxysilane (APTES)/anhydrous toluene at room temperature for 24 h and then at 100 °C for

Table 1. Quantum Yields for Photolysis of 8-QS Derivatives **1a**—**g** ([**1a**—**g**]=10 μM in 90/10 CH_3CN/20 mM HEPES (pH 7.4 with I=0.1 ($NaNO_3$)) at 25 °C)

Substrate	Irradiation wavelength (mm)	Quantum yield for photolysis (Φ)
1a	313	1.5×10^{-4}
1b	313	0.9×10^{-4}
1c	313	2.7×10^{-4}
1d	313	3.2×10^{-4}
1e	328	2.5×10^{-4}
1f	330	6.9×10^{-4}
1g	366	7.6×10^{-4}



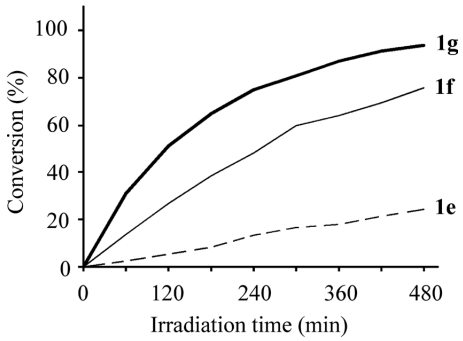


Fig. 8. Conversion of the Photoreaction of 10 μM of **1e** (Dashed Curve), **1f** (Plain Curve), and **1g** (Bold Curve) in 90/10 CH_3CN/10 mM HEPES (pD 7.4 with I=0.1 ($NaNO_3$)) against Irradiation Time under a Fluorescent Lamp (27 W)

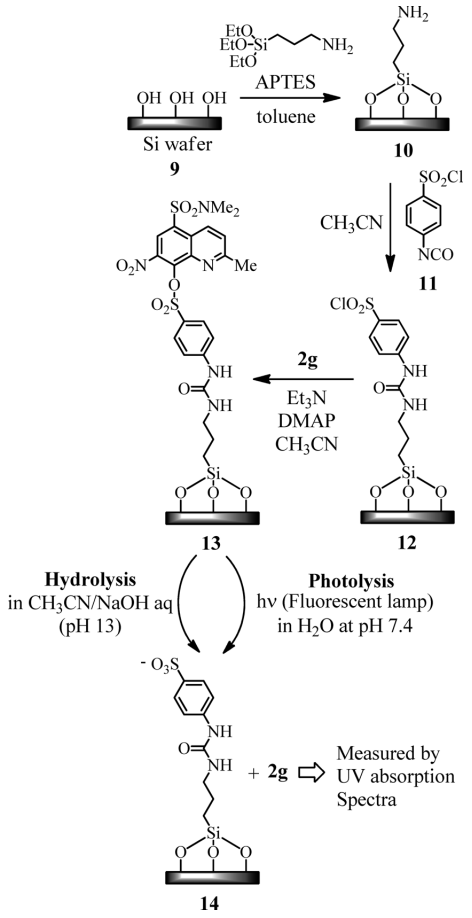


Chart 5. Modification of Si Wafer with **2g**

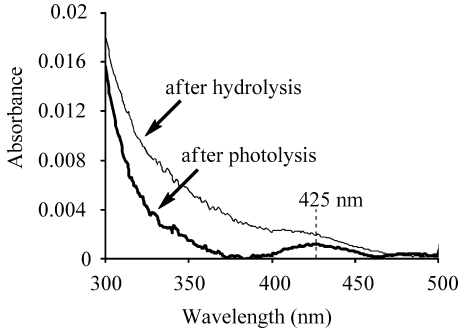


Fig. 9. UV Absorption Spectra of the Aqueous Phase after Hydrolysis of **13** (Plain Curve) under Dark Condition in 50/50 CH_3CN/NaOH aq. Solution (pH 13) at 25 °C for 6 h and Photolysis of **13** (Bold Curve) under Fluorescent Lamp (27 W) in 50/50 CH_3CN/10 mM HEPES (pH 7.4) at 25 °C for 6 h

The chemical yield of the photolysis was calculated based on the ε value (8.5×10^3 M^{-1} cm^{-1}) at 425 nm of the photoproduct **2g**.

24 h to obtain **10**. The amino group was reacted with 4-(chlorosulfonyl)phenylisocyanate (**11**) to give **12**, whose sulfonylchloride groups was reacted with **2g** to afford the **1g**-modified Si wafer **13**.

The photoreaction of **13** was performed under a fluorescent lamp. The modified Si wafer plate **13** was placed on the bottom of a vial containing a 50/50 mixture of CH_3CN and H_2O (10 mM HEPES at pH 7.4) and photoirradiated with a fluorescent lamp (27 W) from nearly vertical direction against Si wafer, so that all Si surface is exposed almost equally to the light (25—30 μW/cm^2 at Si surface). The reaction was followed by UV absorption spectra of the solution phase, to which the photoproduct **2g** is released (Fig. 9). In order to determine the total amount of **2g** on **13**, **13** was subjected to hydrolysis using a 50/50 mixture of CH_3CN and NaOH aq. (pH 13) and the UV absorption spectra of the aqueous phase was obtained. As shown by the plain curve in Fig. 9, the concentration of **2g** released by alkaline hydrolysis (**13**→**2g**+**14**) was determined to be 0.23 μM based on the increase in the absorption at 425 nm. Based on these values, the photorelease yields of **2g** from **13** (bold curve in Fig. 9) was calculated to be 56±3% (0.13 μM) after photoirradiation using the 27 W fluorescent lamp for 6 h at 25 °C. These results imply that the photoreaction of **1g** proceeds on the Si surface, as well, under a fluorescence lamp.

Conclusion

In this paper, we report on the design and synthesis of photocleavable 8-QS derivatives having halogen atoms or a nitro group at the 7-position of 8-quinolinols, in an attempt to improve their photoreactive properties. The findings show that the photoreaction of **1c** (7-bromo-8-QS) and **1d** (7-iodo-8-QS) are accelerated in comparison to that of **1a** (8-QS), possibly due to the heavy atom effect of bromine or iodine, which facilitates ISC. On the other hand, the introduction of a nitro group contributed to a red shift in the absorbance of **1g**, so that it undergoes selective photoclevage reaction of its S–O bond in aqueous solution upon photoirradiation at 360 nm. Moreover, it is demonstrated that the photolysis of **1g** undergoes in aqueous solution and on a Si wafer upon photoirradiation by a fluorescent lamp. For the synthesis of photoclevable linker (Chart 2), it is considered that the introduction of nitro group at the 7-position of 5-aminosulfonyl-

8-QS would be easier than the discrimination of two aminosulfonyl groups of 5,7-bis(aminosulfonyl)-8-QS. These photochemical properties of **1g** may be useful for the isolation of UV-sensitive biological materials such as proteins, oligo nucleotides and cells.

Experimental

General Information Reagents and solvents were purchased at the highest commercial quality and used without further purification. All aqueous solutions were prepared using deionized and distilled water. Buffer solutions (HEPES, pH 7.4) were used and the ionic strengths were adjusted with $NaNO_3$. The Good's buffer reagents (Dojindo) were commercially available: HEPES (*N*-(2-hydroxyethyl)piperazine-*N*′-2-ethanesulfonic acid, pK_a=7.5). Melting points were obtained on a Büchi 510 Melting Point Apparatus and are uncorrected. UV absorption spectra were recorded on a Hitachi U-3500 spectrophotometer and JASCO UV–VIS spectrophotometer V-550, and fluorescence (excitation and emission) spectra were recorded on a JASCO FP-6200 and FP-6500 spectrofluorometers at 25±0.1 °C. IR spectra were recorded on Perkin-Elmer Fourier transform (FT)-IR spectrophotometer at room temperature. ^{1}H- (300 MHz) and ^{13}C- (75 MHz) NMR spectra were recorded on a JEOL Always 300 spectrometer. Tetramethylsilane was used as an internal reference for ^{1}H- and ^{13}C-NMR measurements in $CDCl_3$. 3-(Trimethylsilyl)propionic-2,2,3,3-d_4 acid (TSP) sodium salt was used as an external reference for ^{1}H- and ^{13}C-NMR measurements in D_2O. The pD values in D_2O were corrected for a deuterium isotope effect using pD=(pH-meter reading)+0.40. MS measurements were performed on a JEOL JMS-SX-102A and Agilent (Varian) 910-MS. Elemental analyses were performed on a Perkin-Elmer CHN 2400 analyzer. Thin-layer (TLC) and silica gel column chromatographies were performed using a Merck Silica gel 60 F_{254} TLC plate and Fuji Silysia Chemical FL-100D, respectively.

5-*N*-Boc-*N*,*N*′-dimethylethylenediaminosulfonyl-8-hydroxyquinaldine (2a) Triethylamine (Et_3N) (0.8 ml, 5.7 mmol) was added to a solution of *N*-Boc-*N*,*N*′-dimethyl-ethylenediamine **7**[44] in CH_2Cl_2 (14 ml) at 0 °C under an argon (Ar) atmosphere, to which sulfonyl chloride **5**[27,29,45,46] (490 mg, 1.90 mmol) was added in small portion over 1 h. The reaction mixture was stirred for 30 min at 0 °C and overnight at room temperature. The solvent was removed under reduced pressure and the remaining residue was purified by silica gel column chromatography (hexane/ethyl acetate (AcOEt)) to yield **2a** as a yellow amorphous solid (610.2 mg, 78% yield). IR (neat) cm^{-1}: 3008, 2977, 2931, 1686, 1600, 1567, 1503, 1394, 1366, 1324, 1140, 1117, 960, 879, 835, 749, 713, 666, 559, 532. ^{1}H-NMR ($CDCl_3$) δ: 1.42 (9H, s), 2.76 (3H, s), 2.83 (6H, br), 3.25 (2H, t), 3.37 (2H, t), 7.13 (1H, d, *J*=8.3 Hz), 7.47 (1H, d, *J*=8.8 Hz), 8.06 (1H, br), 8.87 (1H, br). ^{13}C-NMR ($CDCl_3$) δ: 24.61, 28.25, 28.32, 34.61, 46.39, 46.91, 47.04, 107.89, 123.17, 124.28, 131.23, 131.42, 134.12, 137.48, 155.67, 156.19, 157.87. HR-FAB-MS *m*/*z*: 410.1750 (Calcd for $C_{19}H_{28}N_3O_5S$ $[M+H]^+$: 410.1750).

5-*N*-Boc-*N*,*N*′-dimethylethylenediaminosulfonyl-8-benzenesulfonyloxyquinaldine (1a) Benzenesulfonyl chloride (0.1 ml, 0.78 mmol) was added dropwise to a solution of **2a** (131.0 mg, 0.32 mmol) and Et_3N (0.2 ml, 1.44 mmol), 4-dimethylaminopyridine (DMAP) (*ca.* 1—2 mg) in CH_2Cl_2 (4 ml) at 0 °C under an argon atmosphere. The reaction mixture was stirred for 30 min at 0 °C and then 30 min at room temperature. The reaction mixture was evaporated and was extracted with AcOEt. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/AcOEt), to give **1a** (130.3 mg, 74% yield) as a colorless amorphous solid.

IR (neat) cm^{-1}: 2977, 2931, 1690, 1601, 1498, 1451, 1367, 1332, 1188, 1146, 1060, 951, 854, 797, 755, 717, 686, 648, 623, 590. ^{1}H-NMR ($CDCl_3$) δ: 1.44 (9H, s), 2.54 (3H, s), 2.85—2.91 (6H, br), 3.33 (2H, br), 3.41 (2H, br), 7.37 (1H, d, *J*=9.0 Hz), 7.49 (2H, t, *J*=9.0 Hz), 7.62 (1H, t, *J*=7.3 Hz), 7.72 (1H, d, *J*=8.0 Hz), 8.01 (3H, m), 8.84 (1H, br). ^{13}C-NMR ($CDCl_3$) δ: 24.33, 28.23, 34.51, 34.83, 46.34, 46.97, 47.19, 121.16, 124.13, 124.22, 127.74, 127.94, 128.66, 133.11, 134.07, 135.96, 141.24, 148.43, 155.08, 155.63, 160.38. HR-FAB-MS *m*/*z*: 550.1684 (Calcd for $C_{25}H_{32}N_3O_7S_2$ $[M+H]^+$: 550.1682).

5-*N*-Boc-*N*,*N*′-dimethylethylenediaminosulfonyl-8-benzenesulfonyloxy-7-chloroquinaldine (1b) To a stirred solution of **2a** (119.8 mg, 0.29 mmol) in CH_3CN (1.5 ml) at 0 °C, a solution of NCS (41.4 mg, 0.30 mmol) in CH_3CN (5 ml) was added dropwise. The reaction mixture was allowed to warm to room temperature. After 3 h, the solution was dissolved in AcOEt, and then washed with water, and brine. After drying the organic layer over Na_2SO_4 and filtration, the solution was concentrated under reduced pressure to give the crude product as a yellow amorphous solid **2b** (91.4 mg, 71.4% yield), which was used without further purification in the synthesis of **1b**.

^{1}H-NMR ($CDCl_3$) δ: 1.43 (9H, s), 2.73 (3H, s), 2.83 (6H, br), 3.26 (2H, br), 3.38 (2H, t), 7.47 (1H, d, *J*=8.6 Hz), 8.08 (1H, br), 8.83 (1H, br).

Benzenesulfonyl chloride (0.05 ml, 0.39 mmol) was added dropwise to a solution of **2b** (73.1 mg, 0.16 mmol) and Et_3N (0.1 ml, 0.72 mmol), DMAP (*ca.* 1—2 mg) in CH_2Cl_2 (2 ml) at 0 °C under an argon atmosphere. The reaction mixture was stirred for 30 min at 0 °C and then overnight at room temperature. The reaction mixture was poured into water and the solution was extracted with $CHCl_3$. The organic layer was washed with saturated K_2CO_3 aq., and brine. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/AcOEt), to give **1b** (87.3 mg, 65% yield for 2 steps) as a colorless solid.

IR (neat) cm^{-1}: 3009, 2978, 2932, 1687, 1606, 1492, 1451, 1367, 1337, 1156, 1143, 1073, 955, 894, 809, 750, 725, 713, 684, 654, 600, 583. ^{1}H-NMR ($CDCl_3$) δ: 1.46 (9H, s), 2.45 (3H, s), 2.88—2.95 (6H, br), 3.36 (2H, br), 3.43 (2H, br), 7.41 (1H, d, *J*=8.9 Hz), 7.60 (2H, t, *J*=7.9 Hz), 7.74 (1H, t, *J*=7.5 Hz), 8.11 (3H, m), 8.86 (1H, br). ^{13}C-NMR ($CDCl_3$) δ: 24.89, 28.34, 29.52, 34.88, 46.37, 47.05, 47.34, 122.65, 124.03, 127.88, 128.58, 128.77, 129.64, 131.34, 133.19, 134.04, 137.82, 142.69, 146.09, 155.19, 161.26. HR-ESI-MS *m*/*z*: 584.12865 (Calcd for $C_{25}H_{31}ClN_3O_7S_2$ $[M+H]^+$: 584.12860).

5-*N*-Boc-*N*,*N*′-dimethylethylenediaminosulfonyl-8-benzenesulfonyloxy-7-bromoquinaldine (1c) 5-*N*-Boc-*N*,*N*′-dimethylethylenediaminosulfonyl-7-bromo-8-hydroxyquinaldine (**2c**) was prepared as a yellow amorphous solid (139.2 mg, 95% yield) from **2a** (123.9 mg, 0.30 mmol) and NBS (53.4 mg, 0.30 mmol) in a manner similar to that described for **2b**.

^{1}H-NMR ($CDCl_3$) δ: 1.43 (9H, s), 2.77 (3H, s), 2.84 (6H, br), 3.29 (2H, t), 3.40 (2H, t), 7.97 (1H, d, *J*=9.2 Hz), 8.23 (1H, br), 8.86 (1H, br).

Sulfonate **1c** was prepared as a colorless solid (160.3 mg, 85% yield for 2 steps) from **2c** and benzenesulfonyl chloride in a manner similar to that described for **1b**.

IR (neat) cm^{-1}: 3008, 2977, 2931, 1690, 1606, 1586, 1491, 1451, 1367, 1337, 1146, 1141, 1073, 955, 895, 796, 746, 726, 714, 686, 650, 608, 584. ^{1}H-NMR ($CDCl_3$) δ: 1.45 (9H, s), 2.42 (3H, s), 2.87—2.94 (6H, br), 3.35 (2H, br), 3.43 (2H, br), 7.39 (1H, d, *J*=8.8 Hz), 7.60 (2H, t, *J*=7.7 Hz), 7.73 (1H, t, *J*=7.4 Hz), 8.08 (2H, d, *J*=7.3 Hz), 8.22 (1H, br), 8.81 (1H, br). ^{13}C-NMR ($CDCl_3$) δ: 24.89, 28.31, 29.63, 34.86, 46.41, 47.09, 47.30, 123.12, 124.16, 126.90, 128.58, 128.80, 129.65, 133.38, 134.00, 135.20, 138.15, 142.66, 148.11, 155.76, 161.20. HR-FAB-MS *m*/*z*: 628.0790 (Calcd for $C_{25}H_{31}BrN_3O_7S_2$ $[M+H]^+$: 628.0787).

5-*N*-Boc-*N*,*N*′-dimethylethylenediaminosulfonyl-8-benzenesulfonyloxy-7-iodequinaldine (1d) 5-*N*-Boc-*N*,*N*′-dimethylethylenediaminosulfonyl-7-iode-8-hydroxyquinaldine (**2d**) was prepared as a yellow amorphous solid (152.6 mg, 95% yield) from **2a** (123.9 mg, 0.30 mmol) and NIS (67.5 mg, 0.30 mmol) in a manner similar to that described for **2b**.

^{1}H-NMR ($CDCl_3$) δ: 1.43 (9H, s), 2.77 (3H, s), 2.85 (6H, br), 3.28 (2H, t), 3.40 (2H, t), 7.50 (1H, d, *J*=9.2 Hz), 8.37 (1H, br), 8.85 (1H, br).

Sulfonate **1d** was prepared as a colorless solid (172.3 mg, 84% yield for 2 steps) from **2d** and benzenesulfonyl chloride in a manner similar to that described for **1b**.

IR(neat) cm^{-1}: 3008, 2976, 2928, 1687, 1606, 1580, 1488, 1450, 1367, 1336, 1153, 1139, 1069, 954, 896, 794, 751, 734, 685, 646, 628, 603, 583. ^{1}H-NMR ($CDCl_3$) δ: 1.45 (9H, s), 2.39 (3H, s), 2.87—2.94 (6H, br), 3.34 (2H, br), 3.43 (2H, br), 7.41 (1H, d, *J*=8.8 Hz), 7.60 (2H, t, *J*=7.7 Hz), 7.73 (1H, t, *J*=7.4 Hz), 8.09 (2H, d, *J*=7.1 Hz), 8.40 (1H, br), 8.81 (1H, br). ^{13}C-NMR ($CDCl_3$) δ: 24.90, 28.37, 29.68, 35.01, 46.47, 47.18, 47.34, 123.85, 124.36, 128.61, 128.86, 128.92, 133.39, 133.97, 137.21, 137.53, 138.72, 141.99, 152.09, 155.78, 160.92. HR-FAB-MS *m*/*z*: 676.06426 (Calcd for $C_{25}H_{31}BrN_3O_7S_2$ $[M+H]^+$: 676.06382).

5-*N*,*N*-Dimethylaminosulfonyl-8-hydroxy-7-nitroquinaldine (2g) To a cooled (0 °C) mixture of 5-*N*,*N*-dimethylaminosulfonyl-8-hydroxy-quinaldine (**2e**)[26,32] (131.8 mg, 0.50 mmol) in 1 ml of conc. HCl was added $NaNO_2$ (114 mg, 1.65 mmol) in 5 ml of water over a 10 min period. The reaction mixture was stirred overnight at room temperature. The reaction mixture was filtered and washed with excess cold water to give a yellow solid, the product which was dried under vacuum to give a yellow solid. The solid was suspended in an aqueous solution of 30% (w/v) H_2O_2 for 12 h. The reaction mixture was then extracted with $CHCl_3$. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give **2g** (122.4 mg, 84%) as a yellow solid: mp >250 °C.

IR (neat) cm^{-1}: 2938, 1596, 1585, 1521, 1356, 1313, 1272, 1213, 1173,

1136, 1113, 1048, 963, 940, 870, 854, 769, 727, 719, 665, 576, 554, 516. ^{1}H-NMR ($CDCl_3$) δ: 2.82 (3H, s), 2.86 (6H, s), 7.66 (1H, d, J=8.8 Hz), 8.76 (1H, s), 8.99 (1H, d, J=8.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 23.75, 37.02, 126.98, 127.18, 127.90, 130.76, 131.21, 135.50, 139.21, 140.33, 155.41. HR-FAB-MS m/z: 296.0704 (Calcd for $C_{12}H_{13}N_3O_4S$ $[M+H]^+$: 296.0705).

8-Benzenesulfonyloxy-5-*N*,*N*-dimethylaminosulfonyl-7-nitroquinaldine (1g) A solution of benzenesulfonyl chloride (0.1 ml, 0.78 mmol) was added dropwise to a solution of **2g** (120.0 mg, 0.41 mmol) and Et_3N (0.1 ml, 0.72 mmol), DMAP (*ca.* 1—2 mg) in CH_2Cl_2 (2 ml) at 0 °C under an argon atmosphere. The reaction mixture was stirred for 30 min at 0 °C and then overnight at room temperature. The reaction mixture was poured into water and the solution was extracted with $CHCl_3$. The organic layer was washed with saturated K_2CO_3 aq., and brine. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The remaining residue was purified by silica gel column chromatography (hexane/AcOEt), to give **1g** (50.2 mg, 23% yield) as a colorless solid: mp 172.0—174.5 °C.

IR (neat) cm^{-1}: 3097, 2975, 1595, 1569, 1537, 1452, 1383, 1347, 1213, 1186, 1148, 1078, 955, 856, 834, 790, 757, 727, 702, 685, 640, 598, 583. ^{1}H-NMR ($CDCl_3$) δ: 2.51 (3H, s), 2.92 (6H, s), 7.51 (1H, d, J=8.8 Hz), 7.57 (2H, t, J=7.7 Hz), 7.73 (1H, t, J=7.3 Hz), 7.99 (2H, d, J=7.3 Hz), 8.52 (1H, s), 8.97 (1H, d, J=8.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 25.09, 37.53, 122.89, 126.16, 126.44, 128.63, 129.03, 133.29, 133.46, 134.50, 136.78, 140.99, 142.20, 142.39, 162.57. HR-FAB-MS m/z: 451.0512 (Calcd for $C_{18}H_{17}N_3O_7S_2$ $[M+H]^+$: 451.0508).

Modification of Si Wafer with 1g The modification of a Si wafer with **1g** was carried out as shown in Chart 5. The Si wafer (150 mm×150 mm) cleaned by pretreatment with a piranha solution was reacted with 10% APTES in anhydrous toluene at room temperature for 24 h to give **10**. After modification, **10** was sonicated with toluene and dried by a stream of Ar gas. Then the **10** was incubated at 100 °C for 24 h to cure the APTES and the **10** was then sonicated with distilled water and dried under a stream of Ar gas.[47] Next, **10** was reacted with 5 mg/ml anhydrous CH_3CN solutions containing 4-(chlorosulfonyl)phenylisocyanate (**11**) at room temperature for 6 h to give **12**. After the modification step, **12** was sonicated with anhydrous CH_3CN solution and dried under a stream of Ar gas. Finally, **12** was treated with 10 mg/ml anhydrous CH_3CN solution of **2g** containing 5% Et_3N and one portion of DMAP to give **13**. **13** was sonicated with anhydrous CH_3CN and dried under a stream of Ar gas.

Photoreactions of 1 in Aqueous Solution Followed by UV Absorption Spectrometry In a typical experiment, a 10 μM or 50 μM solution of substrate in a 9 : 1 mixture of CH_3CN and H_2O (10 mM HEPES at pH 7.4) was irradiated with a 150 W Xe lamp equipped in a spectrofluorometer (JASCO FP-6500 with band-width 20 nm) or 27 W fluorescent lamp. The reaction mixtures were analyzed by a UV absorption spectrometry.

Photoreaction of 13 (on the Silicon Surface) Followed by UV Absorption Spectrometry The modified Si wafer plate (**13**) was placed on the bottom of a vial containing a 50/50 mixture of CH_3CN and H_2O (10 mM HEPES at pH 7.4) and photoirradiated with a fluorescent lamp (27 W) from nearly vertical direction against Si wafer, so that all Si surface is nearly equally exposed to the light (25—30 μW/cm^2 at Si surface measured with UV light meter (UV-340 (CUSTOM Ltd.))). The reaction was followed by UV absorption spectra of the solution phase, to which the photoproduct **2g** is released.

Photoreactions of 1 Followed by ^{1}H-NMR In a typical experiment, a 1 mM solution of substrate in a 9 : 1 mixture of CD_3CN and D_2O (100 mM HEPES at pD 7.4) was irradiated with a 150 W Xe lamp equipped in a spectrofluorometer (JASCO FP-6500 with band-width 20 nm). The photoreaction was follwed by ^{1}H-NMR .

Determination of Quantum Yields of Photolysis Quantum yields for the photocleavage of **1c** were determined as follows: 10 μM solution of a given substrate in CH_3CN and HEPES buffered water (20 mM, pH 7.4) (9 : 1) was placed into a 1×1 cm quartz cell, and irradiated with a 150 W Xe lamp in a spectrofluorometer (JASCO FP-6500 with a band-width of 5 nm). The initial rate of the photolysis (v_i) was determined by UV absorption spectrometry. The quantum yield was calculated using the equation $\Phi = v_i \times V / \{I_0 \times (1-10^{-abs})\}$, where V is the volume of the reaction solution, I_0 is the number of photon per second (2.83×10^{-6} mol/s at 313 nm, 3.59×10^{-6} mol/s at 328 nm, 3.67×10^{-6} mol/s at 330 nm, 6.48×10^{-6} mol/s at 366 nm), and *abs* is the initial absorbance (cell length=1 cm) of **2c** (0.06043 at 313 nm [**2c**]=10 μM). The I_0 value was determined by means of ferroxalate actinometry.[48]

Acknowledgements This study was supported by Grant-in-Aid from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japan (No. 23790023 for S. Ariyasu and No. 18390009, 19659026, and 22659005 for S. Aoki) and the "Academic Frontier" project for Private Universities: matching fund subsidy from MEXT 2009—2013.

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35) DFT calculations (B3LYP/6-31+G(d)) (ref. 28) of **1a**—**d** implied that their shape and energy levels of their lowest unoccupied molecular

orbitals (LUMOs) are almost identical.
36) The pK_a values of 8-OH group of **2e**—**g**, which are photoproducts from **1e**—**g**, respectively, are 7.8, 6.1 (ref. 27) and 4.2 (determined in this work). It is likely that the photolysis of **1g** by irradiation at 360 nm depends on its absorption at this wavelength rather than pK_a values of these products.
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