Laser-Initiated Synthesis: 2,4,5,7-Tetraiodo-6-hydroxy-3-fluorone as a Visible Photoinitiator

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The photophysical properties of a 2,4,5,7-tetraiodo-6-hydroxy-3-fluorone (TIHF) and its application as a visible-light photoinitiator to induce the reduction of organic halides by tri-*n*-butyltin hydride were investigated. Photobleaching quantum yields of TIHF by tri-*n*-butyltin hydride were determined in DMF–toluene (1:1) solution, and the absorption spectra provided evidence of ground-state complex formation. TIHF-initiated reduction of organic halides afforded clean products for alkyl, alkenyl, and aryl halides at ambient temperature and −30 °C. The mechanisms of the initiation and the reaction are discussed.

Introduction

Xanthene dyes, such as rose bengal, are outstanding photosensitizers.[2] Though the most familiar applications are in the formation of singlet oxygen, other important applications are based on redox reactions, both oxidation and reduction. In the presence of appropriate electron donors[3] xanthenes function as electron-transfer acceptors. They are reduced by a partner molecule such as an amine, first to the radical anion and then to a neutral radical. An amine radical is produced from the amine radical cation derived in the reduction process. In commerce this amine radical is employed to initiate acrylate polymerization.

We anticipated that replacing the crowded aromatic subunit at the C-9 position of commercial xanthenes by a smaller hydrogen atom would increase the rate of electron transfer between the dye and an electron donor.[4] This, in fact, has proven to be the case, and the unsubstituted xanthenes form the basis of a new series of visible-light photoinitiators for vinyl polymerization, the H–Nu series.[5] Generated originally to form the basis of argon (+) laser direct write systems for applications such as stereolithography, these compounds have shown other important applications particularly in the formation of thick photopolymer films. Although the radicals generated from TIHF and electron donors are widely employed in visible-light induced photopolymerization, radicals are also important intermediates in small molecule synthesis. Since there were no reports on the applications of radicals generated by electron transfer to or from dyes in synthetic reactions, and since these new dyes can be phototuned to the wavelengths of most lasers, we undertook basic synthetic studies aimed at applying these new systems to this end. Our goal was to develop modalities for wavelength-specific laser-initiated photochemical processes. As part of this work, we present herein some photophysical properties on 2,4,5,7-tetraiodo-6-hydroxy-3-fluorone and apply this in synthetic radical reactions initiated at 514 nm with the green line of an Ar (+) laser.

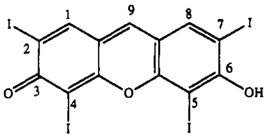
Experimental Section

TIHF obtained from Spectra Group, Ltd. was purified by column chromatography using 1:1 acetone–dichloromethane as the eluent. HPLC-grade solvents from Aldrich were used as received. Absorption spectra were recorded on a Hewlett-Packard 8452A diode array spectrophotometer. Emission spectra were obtained on a Spex-Fluorolog fluorimeter–phosphorimeter.

Photobleaching of TIHF by tri-*n*-butyltin hydride was studied spectrometrically in a solution of DMF and toluene (1:1). The photoreduction of organic halides was carried out in DMF and toluene (1:4). All the experiments were carried out under argon atmosphere by bubbling the samples with argon for about 10 min before irradiation. The 514-nm wavelength line obtained from a Spectra Physics 2016 argon ion laser was employed to irradiate the samples. The light beam was expanded to form a circle of 0.6-cm diameter, and output power was measured with a Scientech 365 power and energy meter.

Results and Discussion

The absorption spectra of 2,4,5,7-tetraiodo-6-hydroxy-3-fluorone (TIHF; H-Nu 535) in ethanol and in DMF are shown in Figure 1. As with the xanthenes,[6] the maximum absorption changes with solvent. Polar aprotic solvents cause the largest red shift; polar protic solvents cause the largest blue shift in the λ_{max} because of hydrogen bonding.



TIHF (H-Nu 535)

Figure 2 shows the excitation and the emission spectra of TIHF in DMF–toluene (1:1) solution. The fluorescence excitation spectrum coincides exactly with the absorption spectrum, indicating that the fluorescence arises from the excitation solely of TIHF.

Electron transfer between the triplet state of TIHF and the ground state of amine donors produces radical ions.[7] Amines with as few as one hydrogen atom on the α carbon subsequently produce radicals by deprotonation, and these radicals are responsible for applications in photopolymerization. Bleaching of the dye usually accompanies this reductive electron-transfer process.

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[1] Contribution no. 154 from the Center for Photochemical Sciences.

[2] Neckers, D. C. *J. Photochem. Photobiol. A: Chem.* **1989**, *47*, 1; *J. Chem. Educ.* **1987**, *64*, 649.

[3] Eaton, D. *Advances in Photochemistry*; Wiley: New York, 1987; Vol. 14.

[4] Shi, J.; Zhang, X. P.; Neckers, D. C. *J. Org. Chem.* **1992**, *57*, 4418.

[5] Neckers, D. C.; Shi, J. U. S. Patent Applied for US 702886; Eur. P. Appl. no. 92304501.7, Japanese Patent Application.

[6] Neckers, D. C.; Valdes-Aguilera, O. *Acc. Chem. Res.* **1989**, *22*, 181.

[7] Klimtchuk, E.; Rodgers, M. A. J.; Neckers, D. C. *J. Phys. Chem.* **1992**, *96*, 9817.

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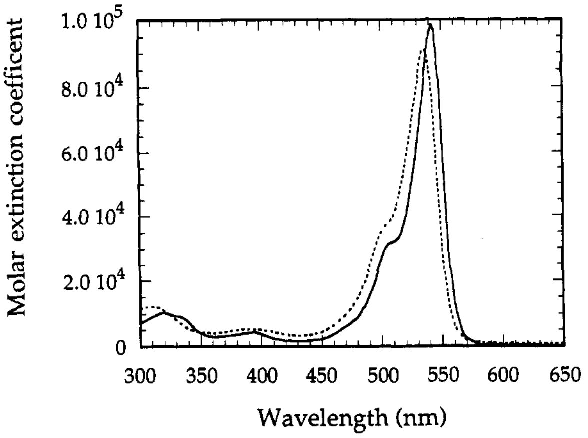

Figure 1. Absorption spectra of TIHF in DMF (solid line) and ethanol (dotted line).

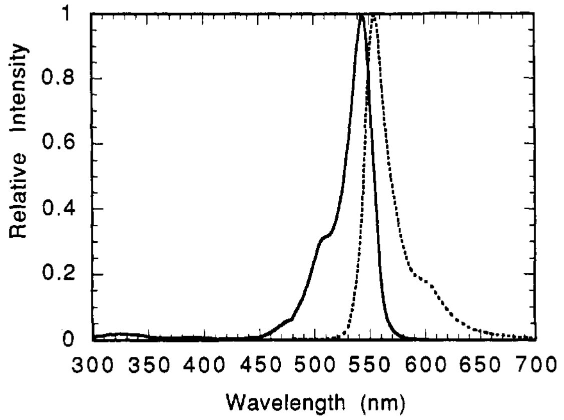

Figure 2. Excitation and emission spectra of TIHF in DMF-toluene (1:1): λ_{ex} 544 nm; λ_{em} 555 nm.

$$\text{dye}^* + \text{RCH}_2(\text{R}_2)\text{N:} \rightarrow \text{dye}^{\bullet -} + \text{RCH}_2(\text{R}_2)\text{N}^{\bullet +}$$

$$\text{RCH}_2(\text{R}_2)\text{N}^{\bullet +} + \text{dye}^{\bullet -} \rightarrow \text{dyeH}^{\bullet} + \text{RC}^{\bullet}\text{H}(\text{R}_2)\text{N:}$$

Reactions involving radical intermediates have found wide application in organic synthesis.[8] Radicals used for small molecule synthesis must be regenerated from a given chain process, as well as be of sufficient lifetime to react in the chain process. A reaction that meets these requirements, and which has been extensively applied in synthesis, is the trialkyltin hydride-mediated reduction of various organic functional groups, most notably halides. If the organotin hydride can serve as an electron donor as well as the chain mediator, an electron acceptor dye should be able to initiate the reduction of organic halides by the irradiation of visible light.

The absorption spectra taken during a typical photobleaching of TIHF in the presence of tri-*n*-butyltin hydride were studied in an argon-saturated DMF-toluene (1:1) solution and are shown in Figure 3. The rate of photobleaching was determined by the decrease of the absorption of TIHF at 562 nm. The concentration of TIHF used was determined so that the absorption at 514 nm, the incident laser irradiation wavelength, was kept approximately constant. The bleaching of TIHF was negligible in the absence of tri-*n*-butyltin hydride. The quantum yields, which were calculated from the rate of photobleaching, concentration of the dye, and the absorbed light, are listed in Table I.

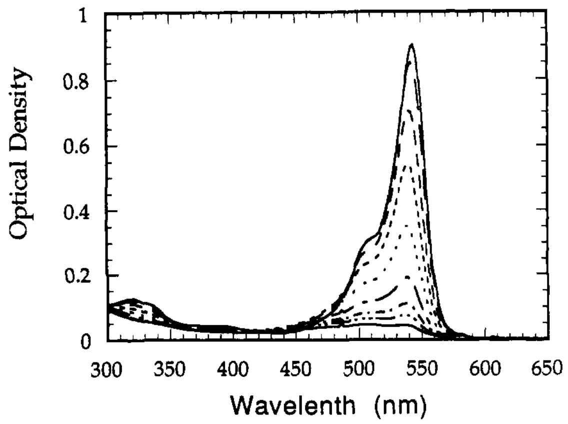

Figure 3. Photobleaching of TIHF by tributyltin hydride in DMF-toluene (1:1).

Table I. Photobleaching Quantum Yields of TIHF at Different Concentrations of Tri-*n*-butyltin Hydride[a]

[nBu$_3$SnH]	quantum yield	[nBu$_3$SnH]	quantum yield
0.0014	0.0024	0.041	0.031
0.0034	0.0035	0.060	0.079
0.0054	0.0086	0.067	0.077
0.0067	0.0042	0.096	0.19
0.014	0.011	0.12	0.27
0.027	0.021		

[a] The quantum yields were measured in DMF-toluene (1:1) solution under argon atmosphere at [TIHF] = 6×10^{-5} M, incident laser light intensity, $I_0 = 2.01 \times 10^{-5}$ einstein·L^{-1}·s^{-1}.

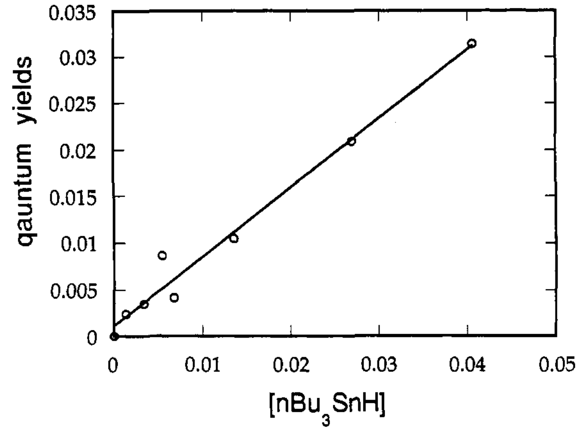

Figure 4. Plot of quantum yields of bleaching of TIHF versus concentration of tributyltin hydride.

At the lower concentrations of tri-*n*-butyltin hydride ([nBu$_3$SnH] < 0.04 M), the quantum yields of photobleaching of TIHF increase linearly with the increasing concentration of the tin hydride (Figure 4). However, at higher concentrations of tri-*n*-butyltin hydride the quantum yields increase more rapidly.

The absorption spectra of TIHF with varying concentrations of tri-*n*-butyltin hydride in DMF-toluene solution exhibit the features illustrated in Figure 5. In argon-saturated solution and [TIHF] = 5×10^{-5} M the absorption spectra superposed on each other in the absence or presence of up to 500-fold excess of tri-*n*-butyltin hydride. At higher concentrations of tri-*n*-butyltin hydride the λ_{max} blue-shifts with an increase in [tri-*n*-butyltin hydride]. No such spectral change was observed in an aerated solution of TIHF in DMF-toluene proving that the polarity change

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(8) (a) Neumann, W. P. *Synthesis* **1987**, 665. (b) Curran, D. P. *Synthesis* **1988**, 417.

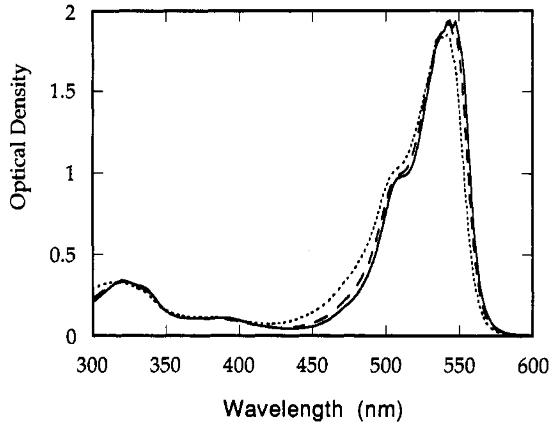


Figure 5. Absorption spectra of 5 × 10^{-5} M TIHF in DMF–toluene (1:1) solution (0.4-cm light pass): —, in the absence of tributyltin hydride (TBTH); – – , in the presence of 4.2 × 10^{-2} M TBTH; ···, in the presence of 5.3 × 10^{-2} M TBTH.

Scheme I

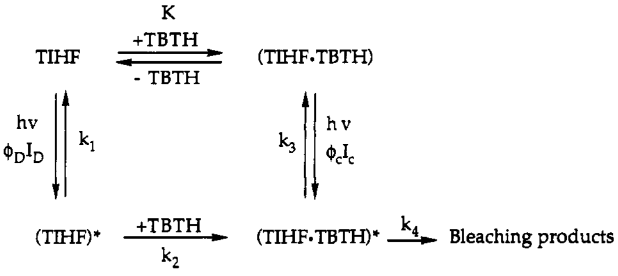


Table II. Photoreaction of Organic Halides with Tri-*n*-butyltin Hydride[a]

entry	halides	[halides]	[Bu_3SnH]	prod % (red:cy)	SM, %
1	$Br(CH_2)_4CH{=}CH_2$	0.063	0.078	80 (25:55)	19
2	$I(CH_2)_4CH{=}CH_2$	0.062	0.078	92 (30:62)	9[b]
3	$Br(CH_2)_6CH{=}CH_2$	0.059	0.068	51 (51:0)	47[c]
4	$Br(CH_2)_9CH{=}CH_2$	0.062	0.078	42 (42:0)	60
5	$BrCH_2Si(Me)_2OCH_2$-$CH{=}CH_2$	0.072	0.096	82 (82:0)	15[b,c]
6	$Br(CH_2)_5CH_3$	0.062	0.078	71	28
7	$BrCH(CH_3)(CH_2)_3CH_3$	0.062	0.078	95	7
8	Br-cy-C_6H_{11}	0.062	0.078	9	3
9	$I(CH_2)_5CH_3$	0.063	0.078	90	10[b]
10	$Br(CH_2)_2C_6H_5$	0.065	0.078	54	41[d]
11	$Br(CH_2)_3C_6H_5$	0.062	0.078	53	41
12	BrC_6H_5	0.073	0.092	18	80
13	IC_6H_5	0.062	0.078	51	46

[a] The reactions were generally performed in a solution of DMF–toluene (1:3 volumetric) at ambient temperature under argon atmosphere: [TIHF] = 1.25 × 10^{-3} M; laser power at 30 mw; reaction time was 4 h. [b] Reaction time was 2.5 h. [c] In *o*-xylene. [d] In benzene.

Table III. Low-Temperature Photoreaction of Organic Halides with Tri-*n*-butyltin Hydride[a]

entry	halides	*t* (min)	[halides]	prod % (red:cy)	SM, %
1	$Br(CH_2)_4CH{=}CH_2$	240	0.063	7.5 (5.5:2)	96
2	$BrCH(CH_3)(CH_2)_3CH_3$	240	0.064	10	93
3	$I(CH_2)_4CH{=}CH_2$	150	0.062	41 (28:13)	54
4	$I(CH_2)_5CH_3$	150	0.065	48	55

[a] The reactions were performed in a solution of DMF–toluene (1:3) under argon atmosphere in a long-neck cuvette immersed in a bromobenzene/dry ice bath contained in a nonmirrored Dewar. The temperature was maintained at −30 ± 3 °C: [TIHF] = 1.25 × 10^{-3} M; [*n*-Bu_3SnH] = 0.078 M; laser power = 30 mw.

in the solvent due to the addition of large excesses of tri-*n*-butyltin hydride is not responsible for the shift. Instead, we propose a new species is to be formed when a large excess of tri-*n*-butyltin hydride is added to TIHF. We propose this new species to be a ground-state complex formed from TIHF and tri-*n*-butyltin hydride.

A bleaching mechanism consistent with these observations is presented in Scheme I.

Under the assumption that the molar absorption coefficients of TIHF and the complex are approximately same, the quantum yields of bleaching are given by:

$$\Phi = \phi_c k_4 K[\mathrm{TBTH}]/\{(1 + K[\mathrm{TBTH}])(k_3 + k_4)\} + \phi_D k_2 k_4/\{(1 + K[\mathrm{TBTH}])(k_3 + k_4)(k_1 + k_2[\mathrm{TBTH}])\} \quad (1)$$

Fluorescence quenching of TIHF by tri-*n*-butyltin hydride in DMF–toluene (1:1) was not observed, and laser flash photolysis indicates that under our experimental conditions the triplet state of TIHF is not quenched by tri-*n*-butyltin hydride. We conclude from these experiments that k_2 is close to zero. Equation 1 thus reduces to

$$\Phi = \phi_c k_4 K[\mathrm{TBTH}]/(1 + K[\mathrm{TBTH}])(k_3 + k_4) \quad (2)$$

At low concentrations of tri-*n*-butyltin hydride, $K[\mathrm{TBTH}] \ll 1$ such that

$$\Phi = \phi_c k_4 K[\mathrm{TBTH}]/(k_3 + k_4) \quad (3)$$

The plot of quantum yields at low concentrations of tri-*n*-butyltin hydride is linear with a slope of 0.74 (Figure 4).

We suggest that the significant deviation of the quantum yields from that predicted by eq 3 at higher concentrations of tri-*n*-butyltin hydride can be explained by the formation of a ground-state complex between TIHF and tin hydride. The optical density changes as measured at 562 nm reflect a mixture of the two absorbing species, dye and complex, and the optical density determined is likely the sum of the optical density of TIHF and of the complex. The quantum yield derived from the determined optical density changes includes both the bleaching of as well as the formation of the ground-state complex from TIHF and tin hydride. This is observed in the absorption spectra as a blue shift of λ_{max} at high concentration of tri-*n*-butyltin hydride.

Irradiation of a solution containing TIHF, tri-*n*-butyltin hydride, and various alkyl and aryl halides caused both bleaching of the dye and formation of reduction products of the halides, confirming the formation of an initiating radical from the electron-transfer processes of dye and tri-*n*-butyltin hydride. Table II gives the results of the photoreaction of various organic halides. Under the experimental conditions these reactions are clean with high yields of reduction products formed from alkyl, alkenyl, and aryl bromides and iodides.

The dye initiator system is also useful at low temperatures as the reactions at −30 °C and the results listed in Table III indicate. The reactions of bromides were much slower at −30 °C than at ambient temperature, while the iodides reacted at an appreciable rate at both temperatures. The clean reactions of both bromides and iodides indicate that quantitative yields of reduction products could be obtained from either bromides or iodides after a longer period of irradiation. The ratio of the hexene and methylcyclopentane formed depends not only on the concentration of reactants but also on the reaction temperatures. The rate of cyclization of hex-5-enyl radical dropped dramatically as the reaction temperature decreases, (entry 1, 2 in Table II and entry 1, 3 in Table III).

The widely accepted mechanism for the propagation steps of the reduction of organic halides by tri-*n*-butyltin hydride is as follows:

$$n\text{-Bu}_3\text{Sn}^{\bullet} + \text{RX} \rightarrow \text{R}^{\bullet} + n\text{-Bu}_3\text{SnX} \qquad (4)$$

$$\text{R}^{\bullet} + n\text{-Bu}_3\text{SnH} \rightarrow \text{RH} + n\text{-Bu}_3\text{Sn}^{\bullet} \qquad (5)$$

Cyclization of the hex-5-enyl radical to give mainly the cyclopentylmethyl radical is one of the best known of the radical rearrangements,[9] and this process has been used as a probe which confirms the intervention of radical intermediates.[10] Reduction of 6-bromohex-1-ene by tri-*n*-butyltin hydride was examined at the outset to ensure the formation of the hex-5-enyl radical in our photoreactions initiated with visible radiation. The clean reduction of 6-bromohex-1-ene at ambient temperature produced methylcyclopentane as the major product along with hexane, confirming the radical mechanism of the reaction.

Further confirmation of our proposal that a ground-state complex is involved in the process is given by the fact that the rate of bleaching of the dye does not parallel the rate of the reduction of the halides. For example, irradiation of a solution of TIHF, tri-*n*-butyltin hydride, and 1-bromohexane with 514-nm light for about 2 min caused almost complete bleaching of the dye. However, only ~3% of *n*-hexane, the reduction product, was detected by GC analysis. When the above mixture was kept in the dark for 2 h no additional *n*-hexane was produced.[11] When the mixture, which appeared colorless, was subsequently irradiated again for 4 h 80% yield of *n*-hexane was obtained. This experiment indicates that light was critical to a second reaction of an initially formed intermediate, although the absorption of the light by the compounds which existed in the system was much lessened after the first few minutes of irradiation. The same result was obtained after a mixture of TIHF and tri-*n*-butyltin hydride was irradiated to appear colorless, and then halide was added to the system. In other words, formation of the reaction intermediate responsible for formation of the reduced product involved the dye and tin hydride, but not the alkyl halide. Another interesting feature of the reaction was that the apparently colorless bleached mixture of TIHF/tin hydride underwent no further change when stored under argon in the dark for 12 h. However, when air was bubbled into the solution, the color of TIHF appeared almost simultaneously.

All these facts clearly indicate that a long-lived intermediate is generated during bleaching of the dye. This intermediate, which has absorption in the visible region of the spectrum but whose extinction coefficient is much less than the original dye, undergoes a second photochemical reaction when irradiated at 514 nm, and this causes the reduction of the halides.

A close examination of the absorption spectrum of the irradiated TIHF solution in DMF–toluene (1:1) reveals that a small absorption band between 420 and 560 nm appears during the irradiation (Figure 6) and that this absorption band slowly decreases upon prolonged irradiation of the solution. Similar spectral observations were obtained by Kimura[12] in the irradiation of solutions of eosin (tetrabromofluorescein) and uranin (fluorescein, disodium salt), C-9 aromatic substituted xanthene dyes. They concluded that the new peaks were from the semireduced dye. In our case that would be:

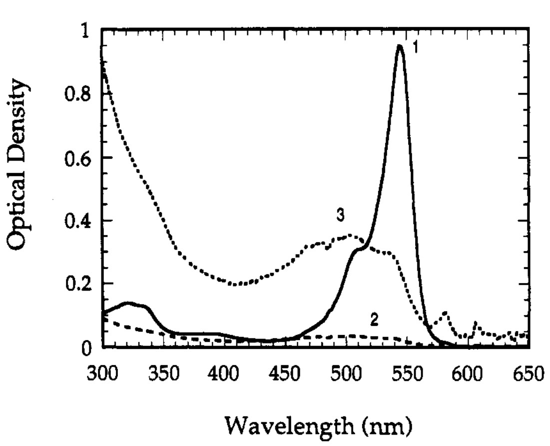
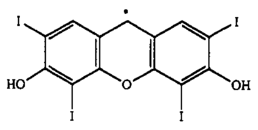


Figure 6. Absorption spectra of TIHF in DMF–toluene (1:1): (1) before irradiation; (2) after 7-min irradiation; (3) enlargement (10×) of (2).



TIHFH•

The photobleaching of TIHF in the presence of tri-*n*-butyltin hydride in DMF–toluene (1:1) indicates that the radicals required to initiate the chain reduction of partner organic compounds must be generated from processes involving the formed ground-state complex. We assume that it is the semireduced TIHF, TIHFH•, which absorbs the light at 514 nm[13] and which would be susceptible to reoxidation in the presence of oxygen, and it is this that is involved in the chain process of the reaction of organic halides with tri-*n*-butyltin hydride.

$$(\text{TIHF}\cdot\text{TBTH})^* \rightarrow \text{TIHF}^{\bullet-} + \text{TBTH}^{\bullet+}$$

$$\text{TBTH}^{\bullet+} \rightarrow n\text{-Bu}_3\text{Sn}^{\bullet} + \text{H}^+$$

$$\text{TIHF}^{\bullet-} + \text{H}^+ \rightarrow \text{TIHFH}^{\bullet}$$

$$\text{RX} + n\text{-Bu}_3\text{Sn}^{\bullet} \rightarrow \text{R}^{\bullet} + n\text{-Bu}_3\text{SnX}$$

$$\text{TIHFH}^{\bullet} \xrightarrow{hn} (\text{TIHFH}^{\bullet})^*$$

$$\text{R}^{\bullet} + (\text{TIHFH}^{\bullet})^* \rightarrow \text{RH} + \text{TIHF}$$

$$\text{R}^{\bullet} + n\text{-Bu}_3\text{SnH} \rightarrow \text{RH} + n\text{-Bu}_3\text{Sn}^{\bullet}$$

$$\text{TIHFH}^{\bullet} + n\text{-Bu}_3\text{SnH} \rightarrow \text{TIHFH}_2 + n\text{-Bu}_3\text{Sn}^{\bullet}$$

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[9] Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*: de Mayo, P., Ed.; Academic Press: New York, 1980, p 161.

[10] Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317. Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073.

[11] There is no continued reaction of $\text{Bu}_3\text{Sn}^{\bullet}$ with RX in the dark because of the known short lifetime of tin radicals even in the absence of alkyl halides.

[12] Kimura, K.; Miwa, T.; Imamura, M. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 1329.

[13] The absorption spectrum of the reaction intermediates formed in transient time domains from TIHF are being reported: see ref 7.

Conclusions

The photophysical properties and application to organic reactions of a new xanthene dye, TIHF, have been investigated. The absorption spectra indicate that a ground-state complex is formed from a photochemical reaction between TIHF and tri-*n*-butyltin hydride. The semireduced dye is postulated as the likely intermediate, and this is likely involved in the reduction of organic halides by tri-*n*-butyltin hydride initiated at 514 nm by the green line of an argon (+) laser.

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