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Aqueous-Medium Carbon−Carbon Bond-Forming Radical Reactions Catalyzed by Excited Rhodamine B as a Metal-Free Organic Dye under Visible Light Irradiation

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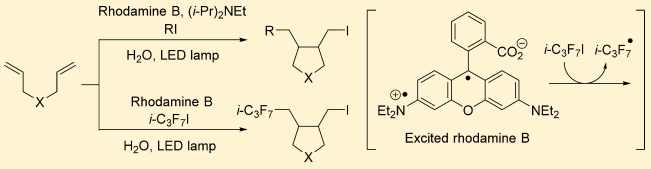
Supporting Information

ABSTRACT: The utility of rhodamine B as a water-soluble organic photocatalyst was studied in the cascade radical addition−cyclization−trapping reactions under visible light irradiation. In the presence of $(i\text{-Pr})_2$NEt, the electron transfer from the excited rhodamine B to perfluoroalkyl iodides proceeded smoothly to promote the carbon−carbon bond-forming radical reactions in aqueous media. When $i\text{-}C_3F_7I$ was employed as a radical precursor, the aqueous-medium radical reactions proceeded even in the absence of $(i\text{-Pr})_2$NEt. In these reactions, the direct electron transfer from the excited singlet state of rhodamine B would take place. Furthermore, the cleavage of the C−I bond in less reactive *i*-PrI could be achieved by the reductive electron transfer from the excited rhodamine B, which was confirmed by the fluorescence quenching of rhodamine B with the addition of *i*-PrI.



INTRODUCTION

In recent years, dyes have received much attention as visible light-activated photocatalysts in organic chemistry.[1] Although the use of dyes in organic synthesis has continued to increase, these studies have mainly concentrated on the redox transformations using transition-metal dyes such as ruthenium[2] or iridium[3] photocatalysts. In contrast, the use of metal-free organic dyes is still limited.[4] Eosin Y is the typical organic dye used to induce photoredox catalysis.[5] Recently, rose bengal, fluorenone, fluorescein, methylene blue, and other organic compounds have been studied as photocatalysts to promote single-electron transfer processes.[6] Fukuzumi's group has developed 3-cyano-1-methylquinolinium and 9-mesityl-10-methylacridinium ions as photocatalysts.[7] More recently, the Nicewicz group has studied photocatalysis using acridinium salts.[8] Indeed, metal-free photocatalysis has rapidly progressed in the past few years. However, less is known about organic dye-catalyzed carbon−carbon bond-forming reactions in aqueous media. Therefore, we have been interested in the aqueous-medium construction of carbon−carbon bonds based on radical reactions promoted by water-soluble organic dyes, such as eosin Y disodium salt and rhodamine B (Figure 1).

Organic dye absorbed visible light populate in a lowest excited singlet state (S_1) and induce both photophysical and photochemical processes. The photophysical process involves a spin-allowed fluorescence, a nonradiative internal conversion, and a spin-forbidden singlet−triplet intersystem crossing (ISC) to afford a lowest excited triplet state (T_1).[9,10] A photochemical process, such as photoinduced electron transfer (PIET), will be initiated by the molecules in both S_1 and T_1. In general, the photochemical process is feasible to occur from T_1 rather than S_1, as shown in Figure 2, because the molecule in T_1 usually possesses a long lifetime (microsecond to several seconds) compared to that in S_1 (nanosecond time scale).[9,10] Actually, most photoredox transformations are induced by PIET from T_1.[11] Eosin Y is the representative organic dye to induce the

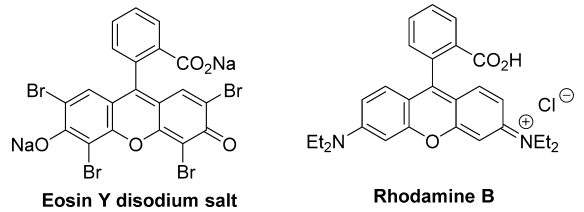


Figure 1. Water-soluble organic dyes.

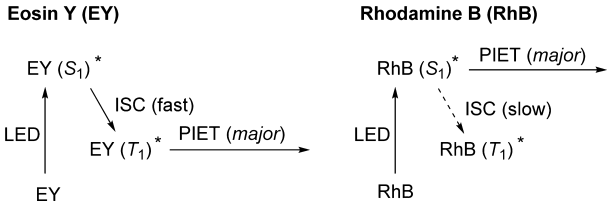


Figure 2. Photochemical process.

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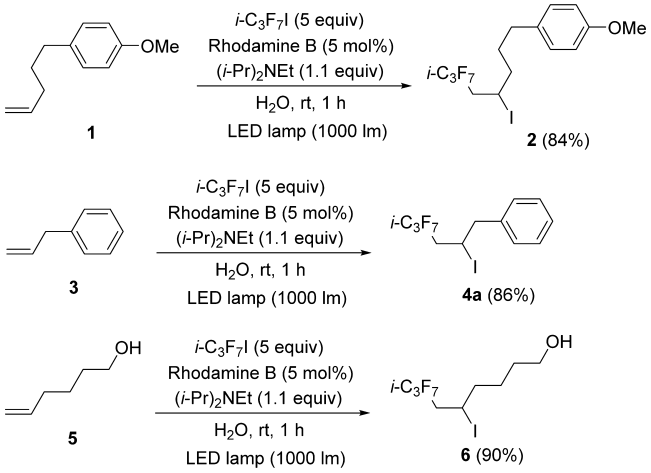
electron transfer from T_1, because the value of the quantum yield of ISC (Φ_{ST} = 0.33)[12] is high enough to populate in T_1 after the visible light excitation. This can be explained in terms of the so-called "internal heavy atom effect" by the substitution of four Br atoms in eosin Y. In marked contrast, Φ_{ST} of rhodamine B is reported to be very low (Φ_{ST} = 0.0024).[12] Therefore, it can be postulated that its ISC is slow and PIET occurs from S_1. We expect that the direct PIET from S_1 of rhodamine B will be an attractive process because catalysis can be performed without the loss of energy by the conversion from S_1 to T_1. The PIET associated with S_1 of 3-cyano-1-methylquinolinium ion was studied by Fukuzumi's group.[7a−c] The direct PIET is also proposed when BODIPY derivatives or methylene blue are employed as a photocatalyst.[13] Despite these significant advances, the full potential of rhodamine B as a photocatalyst remains unrealized.[14] In this paper, we report detailed experiments to prove the utility of rhodamine B as a water-soluble photocatalyst in aqueous-medium carbon−carbon bond-forming radical reactions. As a full article following up our initial communication,[15] we now report (1) the effect of several organic dyes and amines on the cyclization reaction of **7**; (2) the distribution of rhodamine B or eosin Y disodium salt in both water and *i*-C_3F_7I phases; (3) the utility of rhodamine B in the absence of amine as a reductive quencher; (4) the difference between rhodamine B and eosin Y disodium salt in the amine-free method; (5) the application into the cleavage of the C−I bond of the less reactive alkyl iodides such as ICH_2CF_3, ICH_2CN, ICF_2CO_2Et, and *i*-PrI; (6) the Stern−Volmer analysis of rhodamine B with *i*-PrI; and (7) the viability of the rhodamine B-catalyzed method by employing several new substrates.

RESULTS AND DISCUSSION

Aqueous-Medium Reactions with Perfluoroalkyl Radicals. Perfluoroalkyl radicals exhibit extraordinary reactivity, relative to their hydrocarbon counterparts,[16,17] mainly due to fluorine's potent σ inductive electron-withdrawing effect stabilizing polarization of the transition state.[18] Therefore, the use of perfluoroalkyl radicals in organic synthesis has continued to increase.[19] Recently, the development of the perfluoroalkyl radical reactions using ruthenium or iridium photocatalysts has become the most exciting research area[20] because these transition-metal dyes effectively cleave the C−I bond of perfluoroalkyl iodides under visible light irradiation.

In principle, the reactions using strictly neutral species are not affected by water. Therefore, the employment of uncharged radical species facilitates the construction of carbon−carbon bonds in aqueous media.[21,22] Recently, we studied the viability of ruthenium photocatalyst, $Ru(bpy)_3Cl_2·6H_2O$, in the aqueous-medium perfluoroalkyl radical reactions.[23] As a part of our studies on the radical reactions,[24] we started to study the rhodamine B-catalyzed radical reactions in aqueous media. At first, we studied the reaction of alkenes **1**, **3**, and **5** with *i*-C_3F_7I in the presence of rhodamine B (5 mol %) under white light-emitting diode (LED) light irradiation. (Scheme 1). To generate the rhodamine B species having the reduction property, *N*,*N*-diisopropylethyl amine ((*i*-Pr)$_2$NEt) was employed as a reductive quencher. Under the biphasic conditions using *i*-C_3F_7I and water, the reaction of substrate **1** proceeded smoothly to give the product **2** in 84% yield. In the absence of rhodamine B and amine, the reaction of **1** with *i*-C_3F_7I did not occur. Thus, the direct homolytic cleavage of C−I bond by LED irradiation would not take place effectively under the

Scheme 1. Rhodamine B-Induced Atom-Transfer Radical Reactions



reaction conditions. The addition of water as a solvent was important for the chemical efficiency.[15] In the absence of water, the monophasic reaction of **1** in *i*-C_3F_7I gave the product **2** in 51% yield, accompanied by the recovered alkene **1** in 32% yield after 1 h of irradiation. Under the biphasic conditions, the reactions of alkenes **3** and **5** also proceeded with excellent chemical efficiencies.

Rhodamine B in water is known to exist the photoactive zwitterionic form (RhB) (Figure 3).[25] To learn about the form

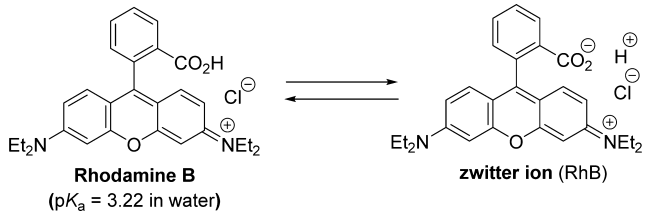


Figure 3. Zwitterionic form of rhodamine B.

of rhodamine B in the *i*-C_3F_7I phase, we compared the absorption spectra of rhodamine B in water and in *i*-C_3F_7I in our previous communication.[15] The shape of both measured spectra is quite similar, indicating that rhodamine B in *i*-C_3F_7I phase mainly exists in the zwitterionic form.[25,26] Furthermore, the zwitterionic form would be predominantly obtained under the reaction conditions using basic (*i*-Pr)$_2$NEt to remove HCl. Although the full effects of water are not clear, water suppresses the formation of a photoinactive lactone form of rhodamine B and promotes the formation of a photoactive zwitterionic form (RhB) by removing HCl from rhodamine B with the assistance of basic (*i*-Pr)$_2$NEt.

As a model reaction investigated by our group,[27] we next selected the cascade radical addition−cyclization−trapping reaction of substrate **7** (Scheme 2). At first, the effect of organic dyes on this cascade transformation was explored in the presence of (*i*-Pr)$_2$NEt as a reductive quencher (Table 1). The biphasic solution of **7** and *i*-C_3F_7I (5 equiv) in H_2O−CH_3CN (9:1, v/v) was stirred with LED light irradiation under Ar atmosphere. The use of rhodamine B (5 mol %) promoted the reaction to give the cyclic products **8a** and **9a** in 87% combined yield (entry 1). Under similar conditions, eosin Y disodium salt (eosin Y Na_2) acted as an efficient catalyst (entry 2). In

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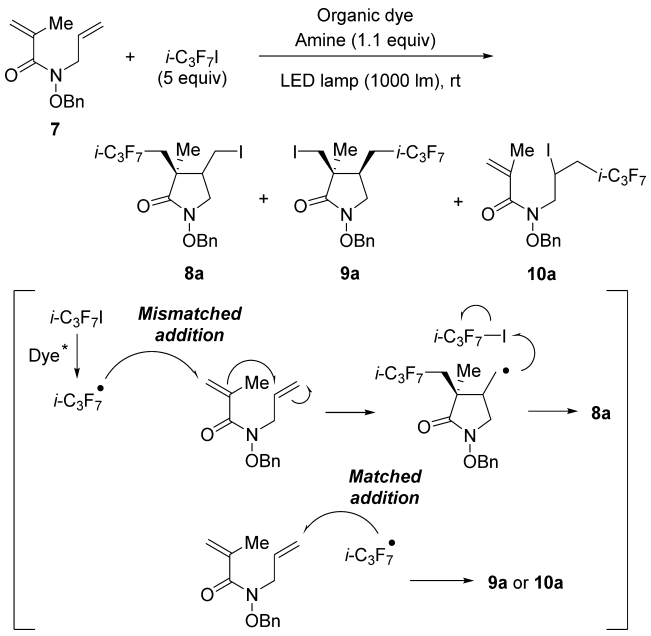
Scheme 2. Radical Addition−Cyclization−Trapping Reaction



contrast, the electron transfer from the excited fluorescein, alizarin red S, or basic blue 12 was less effective (entries 3, 4, and 5, respectively). Although 20 mol % of organic dyes were employed, chemical yields decreased and the starting material **7** was recovered. Additionally, the reactions using alizarin or nile red did not take place (entries 6 and 7, respectively). The catalytic efficiency of rhodamine B was confirmed by comparing with the reaction induced by a radical initiator Et_3B (entry 8).[27] In the case of a radical initiator, excess amounts of Et_3B were required for sufficient conversion. In the reaction of **7**, decreasing the amount of Et_3B to 20 mol % led to a low conversion.

Next, several amines having different oxidation potentials[12,28] were tested (Table 2). The replacement of $(i\text{-Pr})_2NEt$ having less positive oxidation potential (+0.68 V) with Et_3N having positive oxidation potential (+0.96 V) also led to an effective reaction (entry 1). In contrast, the addition of 1,2,2,6,6-pentamethylpiperidine (+0.73 V) led to a slight decrease in chemical yield (entry 2). However, the enhancement in chemical yield was not observed by using $PhNMe_2$ having more positive oxidation potential (+0.81 V) (entry 3). In this case, the starting material **7** was recovered in 64% yield. Consequently, the oxidation potential of amines is not important for chemical efficiencies. The use of simple tertiary amines such as $(i\text{-Pr})_2NEt$ or Et_3N effectively promoted this reaction, irrespective of these oxidation potentials. Next, the effect of H_2O as solvent was studied. In the absence of CH_3CN as organic cosolvent, the biphasic reactions using H_2O also proceeded without any problems (entries 4 and 5). Interestingly, the reaction did not proceed under monophasic conditions in the absence of H_2O (entry 6). These results indicate that the use of H_2O is essential for this transformation.

We studied the distribution of rhodamine B or eosin Y disodium salt in both water and $i\text{-}C_3F_7I$ phases by the partition experiment between water and $i\text{-}C_3F_7I$ (Figure 4). Rhodamine B or eosin Y disodium salt dissolved in water (1×10^{-5} mol L^{-1} in 10 mL) was initially placed in a separatory funnel, then 5.00 mmol of $i\text{-}C_3F_7I$ (0.7 mL) was added in accordance with the experimental conditions using H_2O and $i\text{-}C_3F_7I$. Both rhodamine B (zwitterionic form) and eosin Y disodium salt (dianionic form) were first distributed in the upper water phase. While the mixture was slowly stirred, rhodamine B gradually transferred into the lower $i\text{-}C_3F_7I$ phase, whereas most of eosin Y disodium salt remained in water phase (see Figure S1 in the Supporting Information). This observation was traced by measuring the change in absorption spectra of rhodamine B dissolved in water (Figure 4a). After 10 min, the apparent transfer of rhodamine B from water to $i\text{-}C_3F_7I$ was stopped and the equilibrium was attained. As a consequence, ca. 80% of rhodamine B was distributed in $i\text{-}C_3F_7I$ phase under the distribution equilibrium (Figure 4a). Thus, rhodamine B is moderately distributed in both phases. Because the water-soluble rhodamine B was sufficiently distributed in the $i\text{-}C_3F_7I$ phase, the electron transfer from the exited rhodamine B to $i\text{-}C_3F_7I$ will proceed effectively. Moreover, the substrates dissolve well in the $i\text{-}C_3F_7I$ phase; thus, the radical reactions are proposed to mainly occur in the $i\text{-}C_3F_7I$ phase. In contrast, eosin Y disodium salt was not distributed in the $i\text{-}C_3F_7I$ phase because of the stable dianionic form in water (Figure 4b). However, it is important to note that eosin Y disodium salt promoted the reaction of **7** with an excellent efficiency in spite of the low solubility of eosin Y disodium salt toward $i\text{-}C_3F_7I$ phase (entry 2 in Table 1).

The photoredox cycle is initiated by the visible light irradiation of the photoactive zwitterionic rhodamine B in the ground state to produce S_1. The possible two PIET processes by rhodamine B in S_1 are the reductive PIET to $i\text{-}C_3F_7I$ and the oxidative PIET from amine (Figure 5a). As reported in our communication,[15] we studied the possibility of two PIET

Table 1. Reaction of 7 Using Organic Dyes

entry	organic dye	solvent	conversion yield (%)[a]	ratio[b] (**8a**:**9a**:**10a**)	dr of **8a**[b] (*cis*:*trans*)
1[c]	rhodamine B (5 mol %)	H_2O−CH_3CN (9:1, v/v)	87	60:40:−	73:27
2[c]	eosin Y Na_2 (5 mol %)	H_2O−CH_3CN (9:1, v/v)	82	65:28:7	74:26
3[c]	fluorescein (20 mol %)	H_2O−CH_3CN (9:1, v/v)	42 (50)	57:29:14	72:28
4[c]	alizarin red S (20 mol %)	H_2O−CH_3CN (9:1, v/v)	31 (54)	58:26:16	75:25
5[c]	basic blue 12 (20 mol %)	H_2O−CH_3CN (9:1, v/v)	28 (56)	57:25:18	71:29
6[c]	alizarin (20 mol %)	H_2O−CH_3CN (9:1, v/v)	NR		
7[c]	nile red (20 mol %)	H_2O−CH_3CN (9:1, v/v)	NR		
8[d]	none [Et_3B (5 equiv)]	CH_2Cl_2	77	62:38:−	79:21

[a]Based on isolated yields. The yield in parentheses is for the recovered substrate **7**. [b]Determined by ^1H NMR analysis. [c]Reactions were carried out with dye and $i\text{-}C_3F_7I$ (5 equiv) in the presence of $(i\text{-Pr})_2NEt$ (1.1 equiv) at rt for 2 h under white LED light irradiation. [d]In the absence of organic dye, the reaction was carried out with radical initiator Et_3B (5 equiv) and $i\text{-}C_3F_7I$ (5 equiv) in the presence of $Zn(OTf)_2$ (1 equiv) at rt for 30 min.[27]

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Table 2. Reaction of 7 Using Rhodamine B[a]

entry	amine[b]	solvent	conversion yield (%)[c]	ratio[d] (**8a**:**9a**:**10a**)	dr of **8a**[d] (*cis*:*trans*)
1	Et_3N	H_2O-CH_3CN (9:1, v/v)	83	70:22:8	76:24
2	1,2,2,6,6-pentamethylpiperidine	H_2O-CH_3CN (9:1, v/v)	75	67:28:5	73:27
3	$PhNMe_2$	H_2O-CH_3CN (9:1, v/v)	29 (64)	64:21:15	76:24
4	$(i\text{-}Pr)_2NEt$	H_2O	84	64:29:7	74:26
5	Et_3N	H_2O	78	71:19:10	77:23
6	$(i\text{-}Pr)_2NEt$	none[e]	trace		

[a]Reactions were carried out with rhodamine B (5 mol %) and $i\text{-}C_3F_7I$ (5 equiv) at rt for 2 h under white LED light irradiation. [b]Amine (1.1 equiv) was added as the reductive quencher. [c]Based on isolated yields. The yield in parentheses is for the recovered substrate **7**. [d]Determined by ^1H NMR analysis. [e]Reaction was carried out without solvent.

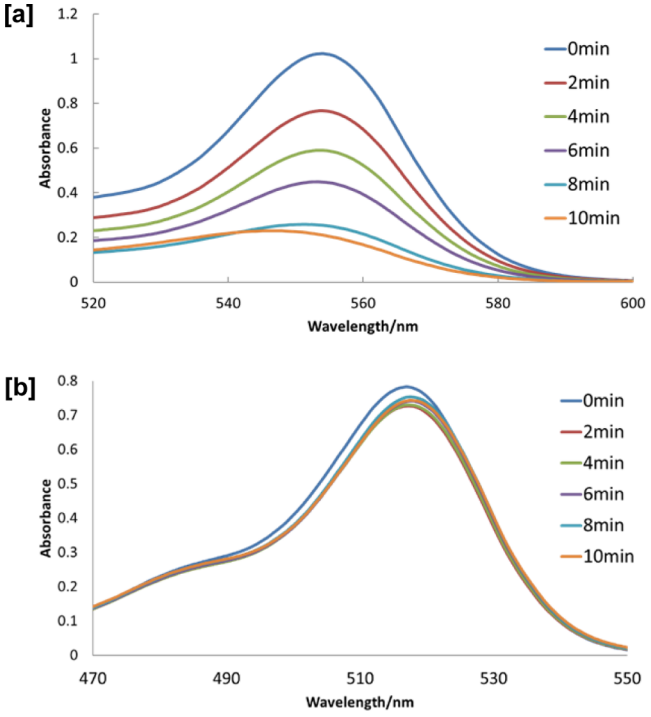

Figure 4. Change in absorption spectra of (a) rhodamine B and (b) eosin Y disodium salt dissolved in water phase during the partition experiment. While the mixture of water (10 mL) and $i\text{-}C_3F_7I$ (0.7 mL) containing rhodamine B or eosin Y disodium salt was slowly stirred in a separatory funnel, (a) rhodamine B gradually transferred into $i\text{-}C_3F_7I$ phase, whereas (b) most of the eosin Y disodium salt remained in the water phase.

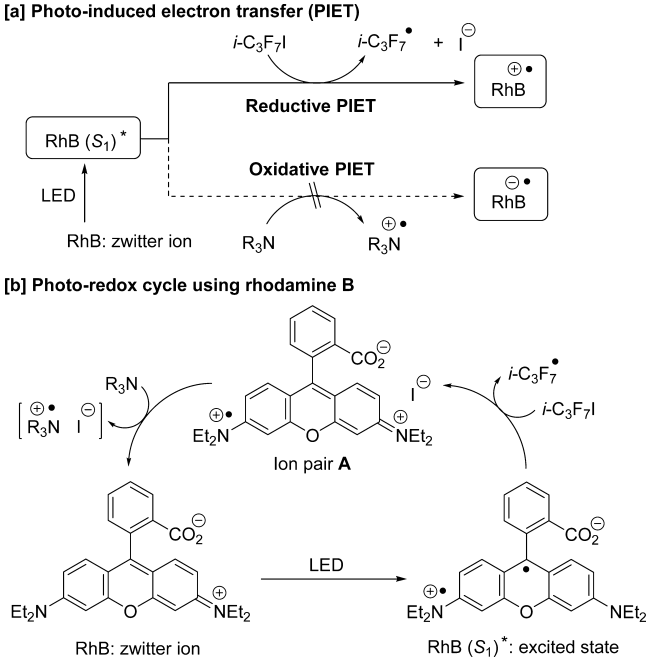

Figure 5. Photoinduced electron transfer and photoredox cycle.

processes by the fluorescence quenching of rhodamine B with the addition of $i\text{-}C_3F_7I$ or amine. In this study, we observed the decrease in fluorescence intensity of rhodamine B with increasing concentration of $i\text{-}C_3F_7I$, whereas the fluorescence was not quenched by amine. Therefore, the oxidative PIET from amine is excluded. The pathway starting from the reductive PIET to $i\text{-}C_3F_7I$ is a reasonable photoredox cycle (Figure 5b). The reductive PIET process is also supported by sufficient negative potential of E_{ox}* ($RhB^{+\bullet}/RhB$*: −1.3 V)[29] compared to reduction potential of $i\text{-}C_3F_7I$ ($i\text{-}C_3F_7I/i\text{-}C_3F_7^{\bullet}+I^-$: −0.66 V).[30]

On the basis of the above results, we think that the photoredox cycle mainly proceeds in the $i\text{-}C_3F_7I$ phase. Therefore, $(i\text{-}Pr)_2NEt$, having the good solubility toward $i\text{-}C_3F_7I$, was used for further study. We next studied the rhodamine B-catalyzed reaction of **7** with primary perfluoroalkyl radicals (Table 3). At first, *n*-heptafluoropropyl iodide ($n\text{-}C_3F_7I$) was used as a primary perfluoroalkyl radical source in H_2O-CH_3CN (9:1, v/v) (entry 1). The cyclic products *cis*-**8b**, *trans*-**8b**, and **9b** were obtained in 74% combined yield. The primary perfluoroalkyl radicals are known to exhibit electrophilicities lower than those of the branched secondary perfluoroalkyl radical generated from $i\text{-}C_3F_7I$.[31] Indeed, the use of primary perfluoroalkyl iodide led to an enhancement of the ratio of **8b** and **9b** into 81:19, as compared with the 60:40 ratio of **8a** and **9a** obtained from $i\text{-}C_3F_7I$ (see entry 1 in Table 1). A similar trend was observed in our previous study on the Et_3B-induced reactions.[27] The cyclic products **8c** and **9c** were obtained in 77% combined yield and 82:18 ratio when primary $n\text{-}C_4F_9I$ was employed in H_2O-CH_3CN (9:1, v/v) (entry 2). The biphasic reactions using H_2O also proceeded with good chemical efficiencies (entries 3 and 4).

To learn about the substituent effect on regioselectivity and chemical efficiency, we studied the reaction of the other substrates **11** and **13** having substituents at the allyl moiety (Scheme 3). In the presence of rhodamine B and $(i\text{-}Pr)_2NEt$, the reaction of **11** with $i\text{-}C_3F_7I$ was carried out in H_2O. The introduction of a methyl group at the allyl moiety had an impact on the regiochemical course of the cascade reaction. Owing to the steric effect of the substituent, the perfluoroalkyl radical selectively added to the methacryloyl moiety of **11** to give the cyclized product **12** without the formation of regioisomer such as **9a**–**c**. The cyclized product **12** involves

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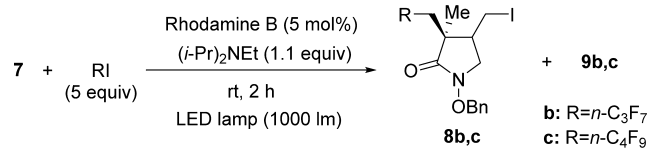
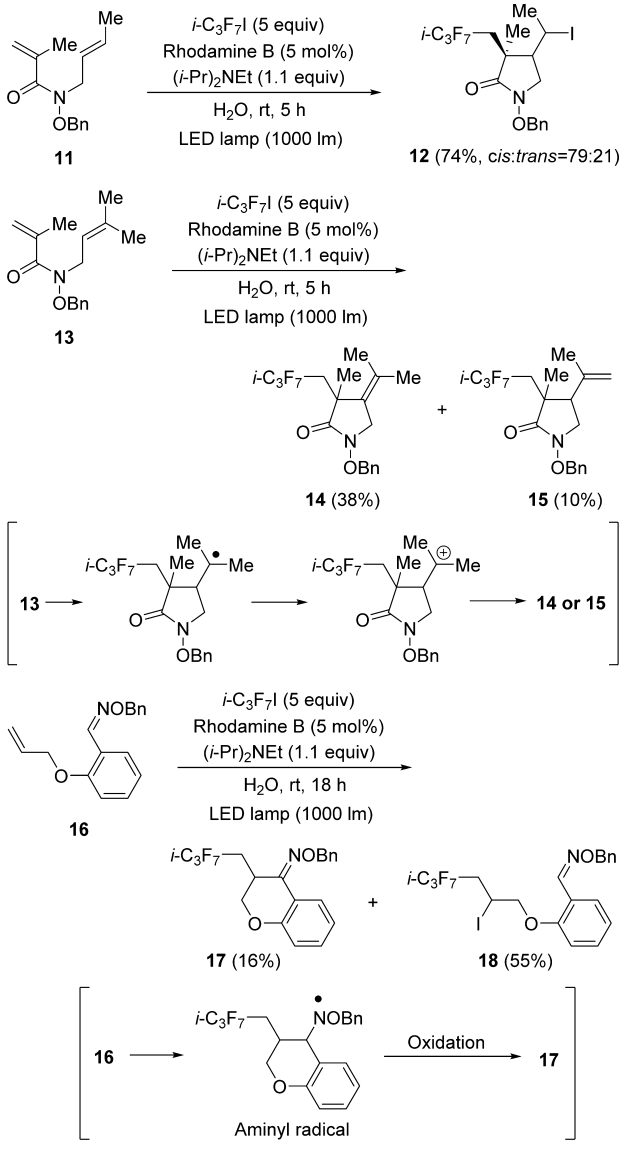
Table 3. Rhodamine B-Catalyzed Reaction with Primary Perfluoroalkyl Iodides[a]



entry	RI	solvent	conversion yield (%)[b]	ratio[c] (8b,c:9b,c)	dr of 8b,c[c] (*cis*:*trans*)
1	n-C_3F_7I	H_2O–CH_3CN (9:1, v/v)	74	81:19	57:43
2	n-C_4F_9I	H_2O–CH_3CN (9:1, v/v)	77	82:18	60:40
3	n-C_3F_7I	H_2O	75	81:19	56:44
4	n-C_4F_9I	H_2O	72	83:17	58:42

[a]Reactions were carried out with rhodamine B (5 mol %) and RI (5 equiv) in the presence of $(i\text{-Pr})_2$NEt (1.1 equiv) at rt for 2 h under white LED light irradiation. [b]Based on isolated yields. [c]Determined by ^{1}H NMR analysis.

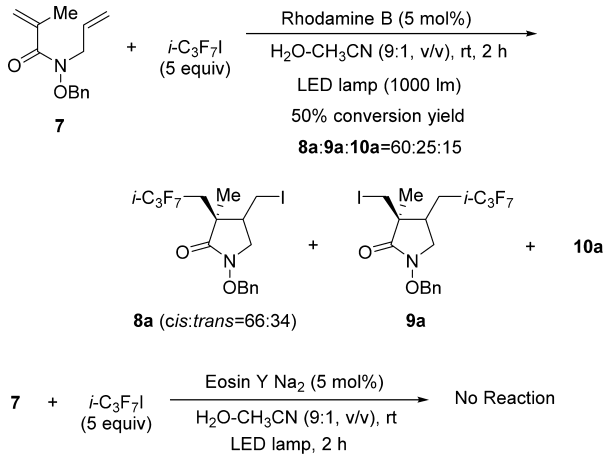
Scheme 3. Reaction of Substrates 11, 13, and 16



the four stereoisomeric products *cis*-**12** (major), *cis*-**12** (minor), *trans*-**12** (major), and *trans*-**12** (minor).[32] Under the similar conditions, the reaction of substrate **13** having two methyl groups at the allyl moiety proceeded effectively. The isomeric products **14** and **15** having a carbon–carbon double bond were obtained in 38% and 10% yields, respectively. The iodine atom transfer from i-C_3F_7I to stable tertiary alkyl radical intermediate would be a less effective process. Therefore, we assume that the alkene products **14** and **15** were generated from cation intermediate via the oxidation of radical intermediate by rhodamine B species. It is important to note that the Et_3B-induced reaction of **13** with perfluoroalkyl iodides did not take place.[27b] At this point, we think that the method using rhodamine B as a photocatalyst will gain some advantages over the method using Et_3B as a radical initiator. Next, substrate **16** having an oxime ether moiety as an additional radical acceptor was employed. The perfluoroalkyl radical did not add to the oxime ether moiety to give the cyclized product **17** and the simple adduct **18**. The cyclized oxime ether **17** would be generated by the oxidation of intermediate aminyl radical.

Rhodamine B-Catalyzed Reaction in the Absence of Amine. In our proposed photoredox cycle (Figure 5b), an ion pair **A** with iodine ion (I^-) is formed. Therefore, we assumed that iodine ion (I^-) may play the role of electron donor toward the cation radical of rhodamine B in an ion pair **A** to give free iodine I_2 and the zwitterionic rhodamine B (RhB) in the ground state. Thus, the reaction of **7** with i-C_3F_7I was next studied in the absence of amine acting as an electron donor (Scheme 4). Interestingly, the clear difference between rhodamine B and eosin Y disodium salt (eosin Y Na_2) was observed in the absence of amine. When rhodamine B was employed, the reaction proceeded even in the absence of $(i\text{-Pr})_2$NEt. The desired products **8a–10a** were obtained in 50% conversion yield, although chemical yield decreased (see entry

Scheme 4. Rhodamine B-Catalyzed Reaction in the Absence of Amine



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1 in Table 1). In marked contrast, eosin Y disodium salt did not work as a photocatalyst in the absence of $(i\text{-Pr})_2$NEt (see entry 2 in Table 1).

Figure 6 shows the possible photoredox cycle. The oxidation potential of rhodamine B ($RhB^{\bullet+}$/RhB: +0.92 V vs SCE)[25] is

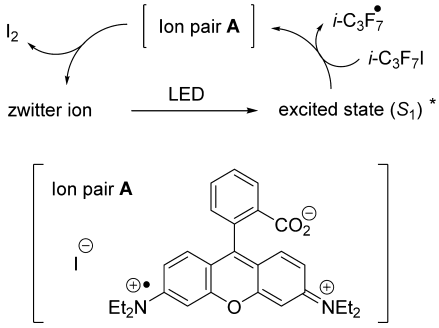


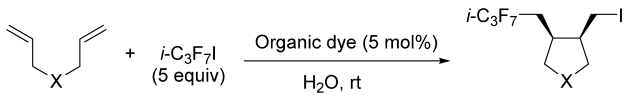
Figure 6. Photoredox cycle in the absence of amine.

positive enough to oxidize I^- into I_2 ($I_2/2I^-$: +0.30 V vs SCE).[33] Therefore, the electron transfer from iodine ion (I^-) to the cation radical of rhodamine B in ion pair **A** proceeds to give I_2 and zwitterionic rhodamine B (RhB) in the ground state. Furthermore, the formation of ion pair **A** in the less polar organic $i\text{-}C_3F_7I$ phase would promote the reductive electron transfer toward the cation radical.

To gain further insight into the amine-free method,[34] we next explored the reaction of substrates **19**–**22** by employing several organic dyes (Table 4). In the presence of $(i\text{-Pr})_2$NEt, the utility of several organic dyes as a photocatalyst was initially investigated in the reaction of substrate **19** with $i\text{-}C_3F_7I$ (entries 1–4). As expected, rhodamine B worked well (entry 1). The rhodamine B-catalyzed reaction was completed within 30 min to give product **23a** in 93% yields. Eosin Y disodium salt (eosin Y Na_2) also acted as an effective catalyst (entry 2). Additionally, we newly found that tetrabromofluorescein promoted the reaction with an excellent chemical efficiency (entry 3), although the chemical yield of **23a** decreased by using fluorescein (entry 4). The four Br atoms in tetrabromofluorescein would enhance the probability of ISC from S_1 to T_1 as internal heavy atom effect. We again observed the clear difference between rhodamine B and eosin Y disodium salt (eosin Y Na_2) in the absence of $(i\text{-Pr})_2$NEt (entries 5 and 6). The amine-free reaction using rhodamine B was carried out with $i\text{-}C_3F_7I$ in H_2O for 180 min to give the product **23a** in 84% yield (entry 5). In contrast, the amine-free reaction using eosin Y disodium salt did not take place (entry 6). The rhodamine B-catalyzed reaction of substrate **20** also proceeded effectively to give the product **24** in 95% yield (entry 7). The chemical yield of **24** decreased to 56% in the absence of $(i\text{-Pr})_2$NEt even after being stirred for 180 min (entry 8). A similar trend was observed in the reactions of **21** (entries 9 and 10). The product **25** was obtained in 70% yield even when rhodamine B was employed in the absence of $(i\text{-Pr})_2$NEt (entry 10). Interestingly, both methods were highly effective for the reaction of diethyl malonate derivative **22** (entries 11 and 12). The product *cis*-**26** was isolated in 98% yield even by the amine-free method (entry 12). It is also important to note that the cyclization of **22** proceeded with excellent *cis*/*trans* diastereoselectivities.[20a] The cyclization of **22** leading to *cis*-diastereomer occurs via the conformer having two olefin units adopting a *cis* configuration, probably due to the effect of orbital symmetry reported by Beckwith and Houk.[35]

Reaction Using Other Radical Precursors. To understand the generality and practicality of the rhodamine B-catalyzed aqueous-medium reactions, we finally studied the reactions using less reactive radical precursors. The C–I bond

Table 4. Radical Reactions of Substrates 19–22



19: X=NAc
20: X=NBz
21: X=NBoc
22: X=C(CO_2Et)$_2$

23a: X=NAc
24: X=NBz
25: X=NBoc
26: X=C(CO_2Et)$_2$

entry	substrate	organic dye	$(i\text{-Pr})_2$NEt (equiv)	time (min)	product (% yield)[a]	dr[b] (*cis*:*trans*)
1[c]	**19**	rhodamine B	1.1	30	**23a** (93)	69:31
2[c]	**19**	eosin Y Na_2	1.1	30	**23a** (72)	68:32
3[c]	**19**	tetrabromofluorescein	1.1	30	**23a** (84)	64:36
4[c]	**19**	fluorescein	1.1	30	**23a** (23)	66:34
5[d]	**19**	rhodamine B	none	180	**23a** (84)	68:32
6[d]	**19**	eosin Y Na_2	none	180	NR	
7[c]	**20**	rhodamine B	1.1	30	**24** (95)	73:27
8[d]	**20**	rhodamine B	none	180	**24** (56)	80:20
9[c]	**21**	rhodamine B	1.1	30	**25** (85)	63:37
10[d]	**21**	rhodamine B	none	180	**25** (70)	65:35
11[c]	**22**	rhodamine B	1.1	30	**26** (94)	>99:1
12[d]	**22**	rhodamine B	none	180	**26** (98)	>99:1
13[c]	**22**	eosin Y Na_2	1.1	30	**26** (95)	>99:1
14[d]	**22**	eosin Y Na_2	none	180	NR	

[a]Isolated yield. [b]Determined by ^{1}H NMR analysis. [c]Reactions were carried out with organic dye (5 mol %) and $i\text{-}C_3F_7I$ (5 equiv) in the presence of $(i\text{-Pr})_2$NEt (1.1 equiv) at rt for 30 min under white LED light irradiation. [d]Reactions were carried out with organic dye (5 mol %) and $i\text{-}C_3F_7I$ (5 equiv) at rt for 180 min under white LED light irradiation.

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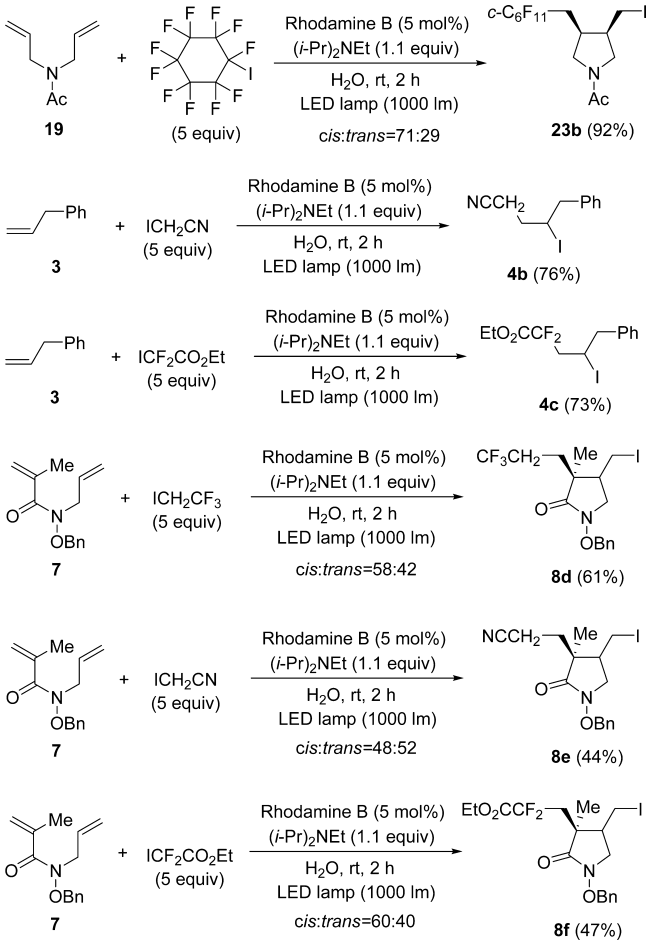
of i-C_3F_7I is activated by fluorine atoms; thus, the reductive PIET from S_1 of rhodamine B to i-C_3F_7I easily leads to the cleavage of the C−I bond. Therefore, the cleavage of the C−X bond in less reactive radical precursors is a challenging issue as a radical generation method.

First, we used the heavy fluorous reagent such as cyclo-$C_6F_{11}I$. The reaction of substrate **19** with cyclo-$C_6F_{11}I$ proceeded effectively to give the product **23b** in 92% yield (Scheme 5). In our previous communication,[15] we reported

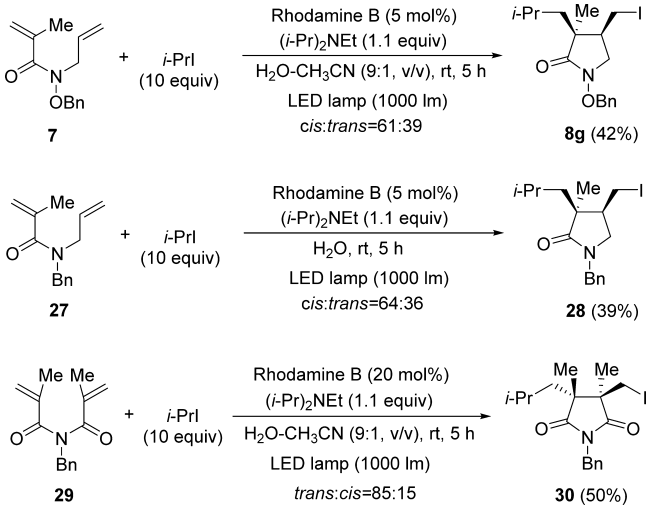
Scheme 5. Reactions with Other Radical Precursors



that the cleavage of the C−Br bond of Cl_3CBr took place under the rhodamine B-catalyzed reaction conditions. Therefore, several alkyl iodides were employed as less reactive carbon radical precursors. Next, alkyl iodides, ICH_2CN and ICF_2CO_2Et, having an electron-withdrawing group were employed in the reaction of substrate **3**. Both alkyl iodides worked well to give the adducts **4b** and **4c** in good yields. The utility of ICH_2CF_3, ICH_2CN, and ICF_2CO_2Et was also examined in the cyclization reaction of **7**. The reaction of **7** with ICH_2CF_3 gave the product **8d** in 61% yield. Under the analogous conditions, ICH_2CN and ICF_2CO_2Et worked as a radical precursor. These reactions were carried out in the presence of $(i\text{-Pr})_2NEt$ because the amine-free method was less effective for theses reactions.

Next, the inactivated alkyl iodide i-PrI was employed in the cyclization reaction of **7** (Scheme 6). As expected, the generation of i-Pr radical from i-PrI was observed. After the reaction mixture was stirred for 5 h, the product **8g** was

Scheme 6. Rhodamine B-Catalyzed Reactions with i-PrI



obtained in 42% yield. In our previous study on the aqueous-medium radical reactions induced by ruthenium-photocatalyst,[23a] we reported that the ruthenium-photocatalyst could not cleave the C−I bond of i-PrI. Thus, it is noteworthy that the reductive PIET from S_1 of rhodamine B could cleave the C−I bond of inactivated i-PrI. Similarly, the cyclization reaction of substrate **27** having N-benzyl group with i-PrI proceeded with moderate chemical efficiency. The method using i-PrI was successfully extended to the cascade radical reaction of another substrate, **29**. Under the reaction conditions using rhodamine B and $(i\text{-Pr})_2NEt$, the reaction of the bulky substrate **29** with i-PrI proceeded with reasonable chemical efficiency, although 20 mol % of rhodamine B was required. The bulky product **30** having two quaternary carbons was isolated in 50% yield. We also studied the distribution of rhodamine B in both water and i-PrI phases by the partition experiment between water and i-PrI (see Figures S2 and S3 in the Supporting Information). This result indicates that the water-soluble rhodamine B can be distributed in the i-PrI phase.

To confirm the reductive PIET process from a photoactivated rhodamine B, we finally examined the fluorescence quenching of rhodamine B with increasing i-PrI concentration (Figure 7). The decrease in fluorescence intensity of rhodamine B was observed with increasing the concentration of i-PrI (Figure 7a).[36] The plots of a ratio of fluorescence quantum yields in the absence (Φ_f^0) and presence (Φ_f) of additive versus the concentration of additive is shown in Figure 7b, which is called the Stern−Volmer plot.[9,37] The value of k_q (2.7×10^9 L mol^{-1}s^{-1}) obtained from the Stern−Volmer analysis indicates that the encounter between rhodamine B in S_1 and i-PrI occurs in the diffusion-limited manner and PIET from rhodamine B in S_1 into i-PrI can proceed in the order of 10^{-2} mol L^{-1} additive. This PIET process is associated with the formation of i-Pr radical and the cation radical of rhodamine B. The rough estimation of E_{ox}* of rhodamine B also explains the photoreduction of i-PrI followed by initiating the cascade radical reactions because the E_{ox}* is roughly comparable to the reduction potential for i-PrI (i-PrI/i-Pr$^{\bullet}$+I$^-$: −1.67 V vs Ag wire in CH_3CN).[38]

■ CONCLUSION

We have demonstrated that a water-soluble organic dye, rhodamine B, has the potential to induce the carbon−carbon

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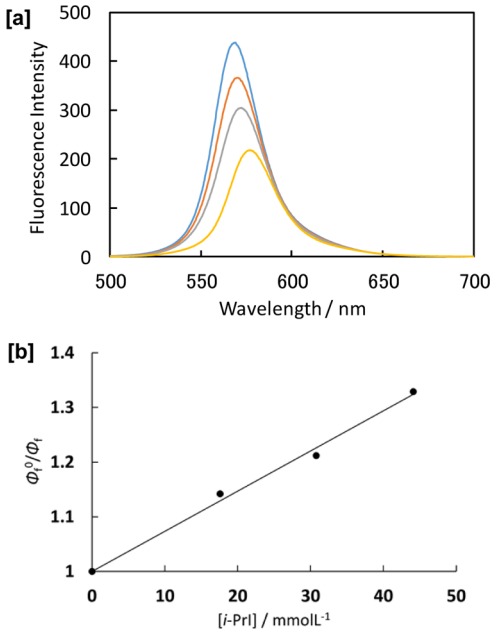

Figure 7. (a) Fluorescence quenching of rhodamine B and (b) its Stern–Vormer plot. Fluorescence quenching of rhodamine B in ethanol was recorded with increasing *i*-PrI concentration (0, 20, 50, 100 mM). The excitation wavelength was set to be at 480 nm (absorbance: 0.071 for the four solutions).

bond-forming radical reactions in aqueous media. The radical addition–cyclization–trapping reactions using perfluoroalkyl iodides proceeded in the presence of rhodamine B and amine as a reductive quencher. When *i*-C_3F_7I was employed, the rhodamine B-catalyzed reactions proceeded in the absence of amine. The utility of rhodamine B as a photocatalyst was also shown in the cleavage reaction of the C–I bond of the less reactive alkyl iodides such as ICH_2CF_3, ICH_2CN, and *i*-PrI.

EXPERIMENTAL SECTION

General. Melting points are uncorrected. ^{1}H NMR spectra were measured at 400 or 600 MHz. ^{13}C NMR spectra were measured at 101 or 126 MHz. ^{19}F-NMR spectra were measured at 376 MHz with C_6F_6 as an internal standard (−162.2 ppm). The commercially available reagents were used without further purification. HRMS measurements using electrospray ionization (ESI) were performed with a time-of-flight (TOF) mass analyzer. White LED (400–700 nm, 1000 lm) was used. Substrates **1**,[39] **19**,[40] **20**,[41] **21**,[42] **22**,[43] **27**,[44] and **29**[45] are known compounds. Substrates **3** and **5** are commercially available compounds. The preparation of substrates **7**, **11**, and **13** was reported in our previous article.[27b]

Procedure for the Reaction of 1 with *i*-C_3F_7I. A suspension of substrate **1** (176 mg, 1.00 mmol) in H_2O (10 mL) was degassed using three pump–thaw cycles under argon atmosphere at 0 °C. To this suspension were added diisopropylethylamine (192 μL, 1.10 mmol), rhodamine B (24 mg, 0.050 mmol), and *i*-C_3F_7I (705 μL, 5.00 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 1 h, the reaction mixture was concentrated under reduced pressure. The purification of the residue by flash silica gel column chromatography (AcOEt:hexane = 1:20) afforded the product **2** (396 mg, 84%).

1-Methoxy-4-[6,7,7,7-tetrafluoro-4-iodo-6-(trifluoromethyl)-hepat-1-yl]benzene (2). Colorless oil. IR (KBr): 2937, 2837, 1612, 1513, 1462 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.09 (2H, br dt, *J* = 8.7, 2.5 Hz), 6.84 (2H, br dt, *J* = 8.7, 2.5 Hz), 4.36–4.30 (1H, m), 3.79 (3H, s), 2.96–2.75 (2H, m), 2.67–2.51 (2H, m), 1.87–1.66 (4H, m). ^{13}C NMR ($CDCl_3$) δ: 157.9, 133.4, 129.2, 120.7 (qd, *J* = 288, 28 Hz), 120.4 (qd, *J* = 288, 29 Hz), 113.8, 91.9 (dsep, *J* = 210, 32 Hz), 55.2, 40.3 (d, *J* = 2 Hz), 39.6 (d, *J* = 18 Hz), 33.7, 31.6, 22.3. ^{19}F NMR ($CDCl_3$) δ: −76.5 (3F, quin, *J* = 9 Hz), −7.8 (3F, br quin, *J* = 9 Hz), −186.1 (1F, m). HRMS (ESI$^+$): calcd for $C_{15}H_{16}F_7IONa$ (M+Na$^+$), 495.0026; found, 495.0042.

Procedure for the Reaction of 3 or 5 with *i*-C_3F_7I. A suspension of substrate **3** or **5** (1.00 mmol) in H_2O (10 mL) was degassed using three pump–thaw cycles under argon atmosphere at 0 °C. To this suspension were added diisopropylethylamine (192 μL, 1.10 mmol), rhodamine B (24 mg, 0.050 mmol), and *i*-C_3F_7I (705 μL, 5.00 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 1 h, the reaction mixture was diluted with diethyl ether, washed with H_2O and saturated NaCl, and dried over $MgSO_4$. The organic layer was concentrated under reduced pressure. The purification of the residue from **3** by flash silica gel column chromatography (hexane) afforded the product **4a** (356 mg, 86%). The purification of the residue from **5** by flash silica gel column chromatography (acetone:hexane = 1:4) afforded the product **6** (334 mg, 90%).

1-(4,5,5,5-Tetrafluoro-4-trifluoromethyl-2-iodopentyl)-benzene (4a). Colorless oil. IR (KBr): 3032, 2927, 1604, 1497, 1433 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.36–7.17 (5H, m), 4.45 (1H, br qn, *J* = 7.8 Hz), 3.28 (1H, dd, *J* = 14.7, 5.5 Hz), 3.15 (1H, dd, *J* = 14.7, 9.2 Hz), 3.02–2.95 (2H, m). ^{13}C NMR δ: 138.6, 128.9, 128.6, 127.3, 120.7 (qd, *J* = 288, 27 Hz), 120.5 (qd, *J* = 288, 27 Hz), 91.9 (dsep, *J* = 209, 32 Hz), 47.4 (d, *J* = 3 Hz), 38.9 (d, *J* = 18 Hz), 21.7. ^{19}F NMR δ: −76.6 (3F, quin, *J* = 9 Hz), −77.7 (3F, quin, *J* = 8 Hz), −185.8 (1F. m). HRMS (ESI$^+$): calcd for $C_{12}H_{10}F_7INa$ (M+Na$^+$), 436.9608; found, 436.9602.

7,8,8,8-Tetrafluoro-7-trifluoromethyl-5-iodooctanol (6). Colorless oil. IR (KBr): 3307 (br), 2940, 2866, 1656, 1434 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 4.31 (1H, sep, 4.6 Hz), 3.65 (2H, t, *J* = 6.4 Hz), 2.91 (1H, m), 2.82 (1H, td, *J* = 16.0, 8.7 Hz), 1.88–1.72 (2H, m), 1.67–1.38 (4H, m). ^{13}C NMR δ: 120.7 (qd, *J* = 288, 28 Hz), 120.4 (qd, *J* = 288, 28 Hz), 92.0 (dsep, *J* = 209, 32 Hz), 62.4, 40.5 (d, *J* = 3 Hz), 39.6 (d, *J* = 18 Hz), 31.4, 26.1, 22.4. ^{19}F NMR δ: −76.4 (3F, quin, J = 9 Hz), −77.8 (3F, m), −185.9 (1F, m). HRMS (ESI$^-$) calcd for $C_9H_{11}F_7IO$ (M−H$^-$), 394.9748; found, 394.9761.

Procedure for the Reaction of 7 in H_2O in the Presence of (*i*-Pr)$_2$NEt. A suspension of substrate **7** (231 mg, 1.00 mmol) in H_2O (10 mL) was degassed using three pump–thaw cycles under argon atmosphere at 0 °C. To this suspension were added diisopropylethylamine (192 μL, 1.10 mmol), rhodamine B (24 mg, 0.050 mmol), and perfluoroalkyl iodide (5.00 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 2–5 h, the reaction mixture was concentrated under reduced pressure. Rough purification of the residue by flash silica gel column chromatography (AcOEt:hexane = 1:3) afforded the products as a mixture of isomers. The ratio of products was determined by ^{1}H NMR analysis of the mixture. Second purification of the mixture by preparative TLC (AcOEt:hexane = 1:6, 2-fold development) afforded the isolated products *cis*-**8a** (215 mg, 40%), *trans*-**8a** (75 mg, 14%), **9a** (131 mg, 24%), and **10a** (32 mg, 6%) (entry 4 in Table 2); *cis*-**8b** (179 mg, 34%), *trans*-**8b** (141 mg, 27%), and **9b** (75 mg, 14%) (entry 3 in Table 3); and *cis*-**8c** (200 mg, 35%), *trans*-**8c** (145 mg, 25%), and **9c** (71 mg, 12%) (entry 4 in Table 3). The characterization data of *cis*-**8a–c**,[27b] *trans*-**8a–c**,[27b] **9a–c**,[27b] and **10a**[23b] were reported in our previous articles. Regarding the ratio of products, slight differences between ^{1}H NMR analysis of the mixture after the first purification and the isolated yields after the second purification were observed.

Preparation of Oxime Ether 16. To a solution of 2-allyloxybenzaldehyde (3.24 g, 20.0 mmol) in acetonitrile-H_2O (1:1 v/v, 40 mL) was added *O*-benzylhydroxylamine hydrochloride (3.18 g, 20.0 mmol) at room temperature. After being stirred at same temperature for 4 h, the reaction mixture was diluted with water and then extracted with AcOEt. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the residue by flash silica gel column chromatography (AcOEt:hexane = 1:30) afforded the product **16** (5.07 g, 95%).

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2-(2-Propen-1-yloxy)-benzaldehyde, *O*-(phenylmethyl)-oxime (16). A colorless oil. IR (KBr): 3032, 2925, 1604, 1486, 1452 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.59 (1H, s), 7.81 (1H, dd, J = 7.8, 1.4 Hz), 7.44 (2H, br d, J = 6.9 Hz), 7.39−7.29 (4H, m), 6.95 (1H, br t, J = 7.6 Hz), 6.88 (1H, br d, J = 8.2 Hz), 6.08−5.98 (1H, m), 5.40 (1H, br dd, J = 17.4, 1.4 Hz), 5.28 (1H, br dd, J = 10.5, 1.4 Hz), 5.22 (2H, s), 4.55 (2H, d, J = 5.0 Hz). ^{13}C NMR ($CDCl_3$) δ: 156.5, 145.2, 137.6, 132.9, 131.0, 128.4, 127.9, 126.5, 121.1, 120.9, 117.7, 112.4, 76.3, 69.1. One carbon peak was missing because of overlapping. HRMS (ESI$^+$): calcd for $C_{17}H_{17}NO_2Na$ (M+Na$^+$), 290.1152; found, 290.1176.

Procedure for the Reaction of 11, 13, or 16 with *i*-C_3F_7I in the Presence of (*i*-Pr)$_2$NEt. A suspension of substrate **11**, **13**, or **16** (1.00 mmol) in H_2O (10 mL) was degassed using three pump−thaw cycles under argon atmosphere at 0 °C. To this suspension were added diisopropylethylamine (192 μL, 1.10 mmol), rhodamine B (24 mg, 0.050 mmol), and *i*-C_3F_7I (705 μL, 5.00 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 2−5 h, the reaction mixture was concentrated under reduced pressure. Rough purification of the residue from **11** by flash silica gel column chromatography (AcOEt:hexane = 1:3) afforded the products as a mixture of isomers. The ratio of isomers of **12** was determined by ^1H NMR analysis of the mixture. Second purification of the mixture by preparative TLC (AcOEt:hexane = 1:6, 2-fold development) afforded the four stereoisomeric products *cis*-**12** (major) (191 mg, 35%), *cis*-**12** (minor) (127 mg, 23%), *trans*-**12** (major) (56 mg, 10%), and *trans*-**12** (minor) (28 mg, 5%) (reaction of **11** in Scheme 3). Regarding the ratio of products, slight differences between ^1H NMR analysis of the mixture after the first purification and the isolated yields after the second purification were observed. The characterization data of these four stereoisomeric products were reported in our previous articles.[27b] Rough purification of the residue from **13** by flash silica gel column chromatography (AcOEt:hexane = 1:3) afforded the products as a mixture of **14** and **15**. Second purification of the mixture by preparative TLC (AcOEt:hexane = 1:6, 2-fold development) afforded the isolated products **14** (162 mg, 38%) and **15** (43 mg, 10%) (reaction of **13** in Scheme 3. The characterization data of **14** and **15** were reported in our previous articles.[23b] Rough purification of the residue by flash silica gel column chromatography (AcOEt:hexane = 1:3) afforded the products as a mixture of **17** and **18**. Second purification of flash silica gel column chromatography (AcOEt:hexane = 1:10) afforded the isolated products **17** (68 mg, 16%) and **18** (309 mg, 55%) (reaction of **16** in Scheme 3).

2,3-Dihydro-3-[2-(trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-4H-1-benzopyran-4-one, *O*-(phenylmethyl)oxime (17). A colorless oil. IR (KBr): 2930, 2881, 1614, 1485, 1455 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.90 (1H, dd, J = 7.8, 1.8 Hz), 7.39−7.25 (6H, m), 6.98−6.91 (2H, m), 5.28 (1H, d, J = 11.9 Hz), 5.21 (1H, d, J = 11.9 Hz), 4.40 (1H, br d, J = 11.9 Hz), 4.01 (1H, dd, J = 11.9, 2.3 Hz), 3.82 (1H, m), 2.48 (1H, m), 2.16−2.01 (1H, m). ^{13}C NMR ($CDCl_3$) δ: 156.0, 150.1, 137.3, 131.3, 128.5, 128.4, 128.1, 124.6, 121.8, 120.9 (qd, J = 288, 28 Hz), 120.8 (qd, J = 288, 28 Hz), 117.7, 116.9, 91.7 (dsep, J = 207, 33 Hz), 76.9, 67.3 (d, J = 5 Hz), 28.5, 24.8 (d, J = 18 Hz). ^{19}F NMR ($CDCl_3$) δ: −75.8 (3F, dq, J = 15, 6 Hz), −78.4 (3F, dq, J = 16, 6 Hz), −186.8 (1F, m). HRMS (ESI$^+$): calcd for $C_{20}H_{16}F_7NO_2Na$ (M+Na$^+$), 458.0961; found, 458.0977.

2-((4,5,5,5-Tetrafluoro-2-iodo-4-(trifluoromethyl)pentyl)-oxy)benzaldehyde *O*-(phenylmethyl)oxime (18). A colorless oil. IR (KBr): 3033, 2930, 1604, 1489, 1453 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.57 (1H, d, J = 2.3 Hz), 7.83 (1H, br d, J = 7.8 Hz), 7.45−7.30 (6H, m), 7.01 (1H, br t, J = 7.6 Hz), 6.82 (1H, br d, J = 8.2 Hz), 5.23 (2H, s), 4.55 (1H, br quin, J = 6.0 Hz), 4.25 (1H, dd, J = 10.6, 5.5 Hz), 4.18 (1H, dd, J = 10.6, 6.0 Hz), 3.19 (1H, m), 2.84 (1H, m). ^{13}C NMR ($CDCl_3$) δ: 155.4, 144.6, 137.7, 131.1, 128.4, 128.3, 127.9, 127.0, 121.9, 121.4, 120.6 (qd, J = 288, 28 Hz), 120.5 (qd, J = 288, 28 Hz), 112.3, 91.4 (dsep, J = 207, 33 Hz), 76.3, 73.0, 35.8 (d, J = 19 Hz), 14.3. ^{19}F NMR ($CDCl_3$) δ: −76.8 (3F, br quin, J = 9 Hz), −77.5 (3F, br quin, J = 9 Hz), −186.8 (1F, m). HRMS (ESI$^+$): calcd for $C_{20}H_{17}F_7INO_2Na$ (M+Na$^+$), 586.0084; found, 586.0070.

Procedure for the Reaction of 19−22 with *i*-C_3F_7I in the Presence of (*i*-Pr)$_2$NEt. A suspension of substrate **19**−**22** (1.00 mmol) in H_2O (10 mL) was degassed using three pump−thaw cycles under argon atmosphere at 0 °C. To this suspension were added diisopropylethylamine (192 μL, 1.10 mmol), rhodamine B (24 mg, 0.050 mmol), and *i*-C_3F_7I (705 μL, 5.00 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 30 min, the reaction mixture was concentrated under reduced pressure. Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:1) afforded *cis*-**23a** and *trans*-**23a** as a mixture. Second purification of the mixture by flash silica gel column chromatography (AcOEt:hexane = 2:3−3:1) afforded the isolated products *cis*-**23a** (279 mg, 64%) and *trans*-**23a** (125 mg, 29%) (entry 1 in Table 4). Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:1) afforded *cis*-**24** and *trans*-**24** as a mixture. Second purification of the mixture by preparative TLC (AcOEt:benzene = 3:2) afforded the isolated isomers *cis*-**24** (345 mg, 69%) and *trans*-**24** (127 mg, 26%) (entry 7 in Table 4). Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:1) afforded *cis*-**25** and *trans*-**25** as a mixture. Second purification of the mixture by flash silica gel column chromatography (AcOEt:hexane = 1:10−1:2) afforded the isolated isomers *cis*-**25** (264 mg, 54%) and *trans*-**25** (155 mg, 31%) (entry 9 in Table 4). The purification of the residue by flash silica gel column chromatography (AcOEt:hexane = 1:20) afforded *cis*-**26** (504 mg, 94%) as a single isomer (entry 11 in Table 4). The ratio of products was determined by ^1H NMR analysis of the mixture after rough purification. Regarding the ratio of products, slight differences between ^1H NMR analysis of the mixture after the first purification and the isolated yields after the second purification were observed.

***cis*-1-Acetyl-4-[2-(trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-3-(iodomethyl)pyrrolidine (*cis*-23a).** Colorless oil. IR (KBr): 2955, 2877, 1649, 1442, 1423 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.74−3.56 (5/2H, m), 3.50 (1/2H, dd, J = 12.4, 5.0 Hz), 3.44 (1/2H, dd, J = 10.6, 6.0 Hz), 3.32−3.26 (2/2H, m), 3.15 (1/2H, dd, J = 10.1, 6.0 Hz), 3.07 (1/2H, dd, J = 10.1, 8.7 Hz), 2.99 (1/2H, br t, J = 10.8 Hz), 2.80−2.63 (4/2H, m), 2.32−2.21 (2/2H, m), 2.14−2.02 (2/2H, m), 2.08 (3/2H, s), 2.04 (3/2H, s). ^1H NMR (DMSO-d6 at 120 °C) δ: 3.66−3.08 (6H, br m), 2.75−2.37 (3H, br m), 2.25−2.17 (1H, br m), 1.91 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 169.6, 169.5, 120.8 (qd, J = 287, 28 Hz), 120.7 (qd, J = 286, 28 Hz), 91.8 (dsep, J = 209, 33 Hz), 52.8, 51.0 (d, J = 4 Hz), 50.3, 49.1 (d, J = 2 Hz), 45.1, 43.6, 36.5, 35.0, 26.7 (d, J = 20 Hz), 25.9 (d, J = 20 Hz), 22.1 (2C), 2.2, 1.3. The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −76.2 (3/2F, quin, J = 9 Hz), −76.8 (3/2F, quin, J = 9 Hz), −77.2 (3/2F, dq, J = 9, 7 Hz), −77.9 (3/2F, dq, J = 9, 7 Hz), −185.7 (1F, m). HRMS (ESI$^+$): calcd for $C_{11}H_{13}F_7INONa$ (M+Na$^+$), 457.9822; found, 457.9828.

***trans*-1-Acetyl-4-[2-(trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-3-(iodomethyl)pyrrolidine (*trans*-23a).** Colorless crystals. mp 73−74 °C (hexane). IR (KBr): 2952, 2873, 1647, 1446, 1423 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 4.11 (1/2H, ddd, J = 12.4, 7.8, 2.7 Hz), 3.92−3.86 (2/2H, m), 3.76 (1/2H, dd, J = 10.5, 7.8 Hz), 3.36 (1/2H, dd, J = 10.5, 3.2 Hz), 3.35 (1/2H, dd, J = 10.5, 3.6 Hz), 3.27−3.21 (2/2H, m), 3.18−3.08 (4/2H, m), 2.43−2.20 (4/2H, m), 2.14−2.01 (3/2H, m), 2.06 (3/2H, s), 2.04 (3/2H, s), 1.98−1.89 (1/2H, m). ^{13}C NMR ($CDCl_3$) δ: 169.1, 120.8 (qm, J = 282 Hz), 91.6 (dm, J = 224 Hz), 53.1 (d, J = 5 Hz), 53.0, 51.9 (d, J = 4 Hz), 51.0, 46.5, 44.8, 39.2, 37.6, 30.8 (d, J = 20 Hz), 30.7 (d, J = 20 Hz), 22.1, 21.9, 4.2, 3.9. The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −75.7 (3/2F, quin, J = 9 Hz), −76.0 (3/2F, quin, J = 9 Hz), −78.0 (3/2F, quin, J = 9 Hz), −78.2 (3/2F, br quin, J = 9 Hz), −184.6 (1F, br m). HRMS (ESI$^+$): calcd for $C_{11}H_{13}F_7INONa$ (M+Na$^+$), 457.9822; found, 457.9836.

***cis*-1-Benzoyl-4-[2-(trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-3-(iodomethyl)pyrrolidine (*cis*-24).** Colorless oil. IR (KBr): 3028, 2979, 1631, 1422 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.52−7.38 (10/2H, m), 3.84 (2/2H, br d, J = 12.4, 7.3 Hz), 3.68−3.46 (6/2H, m), 3.24−3.14 (3/2H, m), 2.96 (1/2H, t, J = 10.5 Hz), 2.84 (1/2H, br q, J

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= 6.9 Hz), 2.77 (1/2H, br q, J = 6.9 Hz), 2.70−2.64 (2/2H, m), 2.37−2.11 (3/2H, m), 1.99 (1/2H, br td, J = 15.8, 9.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 170.2, 135.9, 135.8, 130.3 (2C), 128.4, 127.1, 127.0, 120.7 (qd, J = 288, 28 Hz), 91.6 (dsep, J = 239, 33 Hz), 54.7, 53.0 (d, J = 4 Hz), 50.9, 49.6, 45.1, 43.3, 36.7, 35.0, 26.9 (d, J = 20 Hz), 25.3 (d, J = 20 Hz), 1.7 (2C). The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −76.4 (3/2F, quin, J = 8 Hz), −76.8 (3/2F, quin, J = 8 Hz), −77.3 (3/2F, quin, J = 8 Hz), −77.9 (3/2F, quin, J = 8 Hz), −185.8 (1/2F, m), −186.2 (1/2F, m). HRMS (ESI$^+$): calcd for $C_{16}H_{15}F_7INONa$ (M+Na$^+$), 519.9979; found, 519.9999.

***trans*-1-Benzoyl-4-[2-(trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-3-(iodomethyl)pyrrolidine (*trans*-24).** Colorless oil. IR (KBr): 3027, 2979, 2630, 1423 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.52−7.44 (10/2H, m), 4.20−4.14 (1/2H, m), 3.98 (1/2H, dd, J = 12.4, 7.8 Hz), 3.89−3.84 (1/2H, m), 3.69 (1/2H, dd, J = 10.5, 7.3 Hz), 3.49−3.29 (6/2H, m), 3.17 (1/2H, dd, J = 10.5, 7.8 Hz), 3.09 (1/2H, dd, J = 10.5, 7.8 Hz), 2.40−2.26 (4/2H, m), 2.15−1.95 (4/2H, m). ^{13}C NMR ($CDCl_3$) δ: 169.6, 135.9, 135.7, 130.4, 128.4, 127.2, 120.7 (qm, J = 287 Hz), 91.5 (dsep, J = 206, 33 Hz), 55.0, 54.8, 52.4, 51.7, 46.3, 44.9, 39.3, 37.5, 30.9 (d, J = 20 Hz), 30.3 (d, J = 20 Hz), 4.3, 3.9. The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −75.8 (3/2F, quin, J = 8 Hz), −76.0 (3/2F, quin, J = 8 Hz), −78.2 (3/2F, quin, J = 8 Hz), −78.3 (3/2F, quin, J = 8 Hz), −184.8 (1F, br m). HRMS (ESI$^+$): calcd for $C_{16}H_{15}F_7INONa$ (M+Na$^+$), 519.9979; found, 519.9988.

***cis*-1-(*tert*-Butoxycarbonyl)-4-[2-(trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-3-(iodomethyl)pyrrolidine (*cis*-25).** Colorless oil. IR (KBr): 2978, 2936, 2877, 1691, 1479, 1409 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.61−3.36 (6/2H, m), 3.30−2.99 (6/2H, m), 2.71−2.63 (4/2H, m), 2.22−1.99 (4/2H, m), 1.47 (9/2H, s), 1.46 (9/2 H, s). ^{1}H NMR ($CDCl_3$ at 40 °C) δ: 3.52−3.03 (6H, br m), 2.72−2.60 (2H, m), 2.29−2.01 (2H, br m), 1.47 (9H, s). ^{13}C NMR ($CDCl_3$) δ: 154.4, 120.9 (qd, J = 288, 28 Hz), 120.8 (qd, J = 287, 28 Hz), 91.8 (dsep, J = 206, 34 Hz), 79.9, 51.4, 50.5, 49.9, 49.4, 44.9, 44.2, 36.1, 35.4, 28.4, 26.5 (d, J = 20 Hz), 26.0 (d, J = 20 Hz), 2.5, 1.9. The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −76.5 (3/2F, quin, J = 9 Hz), −76.7 (3/2F, quin, J = 9 Hz), −77.3 (3/2F, quin, J = 9 Hz), −77.3 (3/2F, quin, J = 9 Hz), −185.9 (1F, m). HRMS (ESI$^+$): calcd for $C_{14}H_{20}F_7INO_2$ (M+H$^+$), 494.0421; found, 494.0415.

***trans*-1-(*tert*-Butoxycarbonyl)-4-[2-(trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-3-(iodomethyl)pyrrolidine (*trans*-25).** Colorless crystals. mp 98−100 °C (hexane). IR (KBr): 2971, 2942, 2873, 1671, 1479, 1415 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.91−3.64 (2H, br m), 3.32 (1H, dd, J = 10.6, 4.1 Hz), 3.09 (3H, br dd, J = 10.0, 8.2 Hz), 2.35−2.23 (2H, br m), 2.07−1.98 (2H, br m), 1.45 (9H, s). ^{13}C NMR ($CDCl_3$) δ: 154.0, 120.8 (qd, J = 288, 28 Hz), 120.7 (qd, J = 228, 28 Hz), 91.6 (dsep, J = 210, 33 Hz), 79.8, 52.0 (br s), 51.6, 51.3, 46.3, 45.5, 38.7, 38.0, 30.9 (d, J = 20 Hz), 28.4, 4.5. The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −75.9 (3/2F, br m), −76.0 (3/2F, br m), −78.1 (3/2F, br m), −78.2 (3/2F, br m), −184.8 (1F, br m). HRMS (ESI$^+$): calcd for $C_{14}H_{20}F_7INO_2$ (M+H$^+$), 494.0421; found, 494.0442.

***cis*-3-[2-(Trifluoromethyl)-2,3,3,3-tetrafluoropropyl]-4-(iodomethyl)-1,1-cyclopentandicarboxylic acid, diethyl ester (*cis*-26).** Colorless oil. IR (KBr): 2983, 1729, 1446, 1367 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 4.23−4.16 (4H, m), 3.17 (1H, dd, J = 9.6, 5.5 Hz), 3.04 (1H, t, J = 9.6 Hz), 2.60−2.45 (4H, m), 2.31 (1H, dd, J = 13.8, 5.5 Hz), 2.25−2.00 (3H, m), 1.27−1.22 (6H, m). ^{13}C NMR ($CDCl_3$) δ: 172.2, 171.9, 120.9 (qd, J = 288, 29 Hz), 120.8 (qd, J = 288, 28 Hz), 92.0 (dsep, J = 206, 32 Hz), 61.9, 61.8, 58.1, 45.7, 39.5, 38.5 (d, J = 3 Hz), 36.6, 27.5 (d, J = 19 Hz), 13.9 (2C), 5.2. ^{19}F NMR ($CDCl_3$) δ: −76.4 (3F, quin, J = 8 Hz), −77.5 (3F, quin, J = 8 Hz), −185.7 (1F, m). HRMS (ESI$^+$): calcd for $C_{16}H_{20}F_7IO_4Na$ (M+Na$^+$), 559.0187; found, 559.0178.

Procedure for the Reaction of 19−22 with *i*-C_3F_7I in the Absence of Amine. A suspension of substrate **19**−**22** (1.00 mmol) in H_2O (10 mL) was degassed using three pump−thaw cycles under argon atmosphere at 0 °C. To this suspension were added rhodamine B (24 mg, 0.050 mmol) and *i*-C_3F_7I (705 μL, 5.00 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 180 min, the reaction mixture was concentrated under reduced pressure. Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:1) afforded *cis*-**23a** and *trans*-**23a** as a mixture. Second purification of the mixture by flash silica gel column chromatography (AcOEt:hexane = 2:3−3:1) afforded the isolated products *cis*-**23a** (248 mg, 57%) and *trans*-**23a** (117 mg, 27%) (entry 5 in Table 4). Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:1) afforded *cis*-**24** and *trans*-**24** as a mixture. Second purification of the mixture by preparative TLC (AcOEt:benzene = 3:2) afforded the isolated isomers *cis*-**24** (223 mg, 45%) and *trans*-**24** (56 mg, 11%) (entry 8 in Table 4). Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:1) afforded *cis*-**25** and *trans*-**25** as a mixture. Second purification of the mixture by flash silica gel column chromatography (AcOEt:hexane = 1:10−1:2) afforded the isolated isomers *cis*-**25** (224 mg, 46%) and *trans*-**25** (121 mg, 24%) (entry 10 in Table 4). The purification of the residue by flash silica gel column chromatography (AcOEt:hexane = 1:20) afforded *cis*-**26** (525 mg, 94%) as a single isomer (entry 12 in Table 4). The ratio of products was determined by ^{1}H NMR analysis of the mixture after rough purification. Regarding the ratio of products, slight differences between ^{1}H NMR analysis of the mixture after the first purification and the isolated yields after the second purification were observed.

Procedure for the Reaction of 19, 3, or 7 with alkyl iodides. A suspension of substrate **19**, **3**, or **7** (1.00 mmol) in H_2O (10 mL) was degassed using three pump−thaw cycles under argon atmosphere at 0 °C. To this suspension were added diisopropylethylamine (192 μL, 1.10 mmol), rhodamine B (24 mg, 0.050 mmol), and alkyl iodides (5.00 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 2−5 h, the reaction mixture was concentrated under reduced pressure. Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:3) afforded *cis*-**23b** and *trans*-**23b** as a mixture. Second purification of the mixture by preparative TLC (AcOEt:hexane = 1:7, 2-fold development) afforded the isolated isomers *cis*-**23b** (355 mg, 65%) and *trans*-**23b** (147 mg, 27%) (reaction of **19** with cyclo-$C_6F_{11}I$ in Scheme 5). Purification by flash silica gel column chromatography (AcOEt:hexane = 1:10) afforded the product **4b** (217 mg, 76%) (reaction of **3** with ICH_2CN in Scheme 5). Purification by flash silica gel column chromatography (AcOEt:hexane = 1:8) afforded the product **4c** (269 mg, 73%) (reaction of **3** with ICF_2CO_2Et in Scheme 5). Rough purification of the residue by flash silica gel column chromatography (AcOEt:hexane = 1:3) afforded the products as a mixture of isomers. Second purification of the mixture by preparative TLC (AcOEt:hexane = 1:6, 2-fold development) afforded the isolated products *cis*-**8d** (156 mg, 35%) and *trans*-**8d** (113 mg, 26%) (reaction of **7** with ICH_2CF_3 in Scheme 5), *cis*-**8e** (84 mg, 21%) and *trans*-**8e** (91 mg, 23%) (reaction of **7** with ICH_2CN in Scheme 5), and *cis*-**8f** (136 mg, 28%) and *trans*-**8f** (91 mg, 19%) (reaction of **7** with ICF_2CO_2Et in Scheme 5). The characterization data of *cis*-**8d,e** and *trans*-**8d,e** were reported in our previous articles.[23b] The ratio of products was determined by ^{1}H NMR analysis of the mixture. Regarding the ratio of products, slight differences between ^{1}H NMR analysis of the mixture after the first purification and the isolated yields after the second purification were observed.

***cis*-1-Acetyl-3-(iodomethyl)-4-[(perfluorocyclohexyal)-methyl]pyrrolidine (*cis*-23b).** Colorless oil. IR (KBr): 2956, 2876, 1649, 1423 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 3.74 (1/2H, dd, J = 12.4, 7.2 Hz), 3.68−3.58 (2H, m), 3.51 (1/2H, m), 3.45 (1/2H, m), 3.34−3.27 (1H, m), 3.19−3.00 (3/2H. m), 2.87−2.74 (2H, m), 2.46−2.35 (1H, m), 2.25−2.07 (1H, m), 2.09 (3/2H, s), 2.05 (3/2H, s). ^{13}C NMR ($CDCl_3$) δ: 169.6, 169.5, 113.3−104.6 (5C, m), 91.6 (dm, J = 209 Hz), 52.8, 51.2, 50.2, 49.2, 45.2, 43.7, 36.5, 35.1, 23.8, 23.6, 23.1, 23.0, 22.2, 22.1, 2.1, 1.2. The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −118.1 (2F, br m), −122.9 (2F, br d, J = 288 Hz), −124.5 (1F, br d, J = 284 Hz), −133.2 (2F, m), −139.5 (2F, br d, J =

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288 Hz), −142.5 (1F, br d, J = 289 Hz), −185.5 (1F, br m). HRMS (ESI$^+$): calcd for $C_{14}H_{13}F_{11}INONa$ (M+Na$^+$), 569.9758; found, 569.9770.

***trans*-1-Acetyl-3-(iodomethyl)-4-[(perfluorocyclohexyal)-methyl]pyrrolidine (*trans*-23b).** Colorless oil. IR (KBr): 2931, 2871, 1648, 1423 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 4.12 (1/2H, ddd, J = 11.9, 7.6, 3.8 Hz), 3.93−3.86 (1H, m), 3.76 (1/2H, dd, J = 10.5, 7.6 Hz), 3.38 (1H, m), 3.24 (1H, m), 3.20−3.12 (2H, m), 2.57−2.32 (2H, m), 2.18−2.09 (3/2H, m), 2.07 (3/2H, s), 2.05 (3/2H, s), 1.96−1.91 (1/2H, m). ^{13}C NMR ($CDCl_3$) δ: 169.0, 113.4−104.8 (5C, m), 91.8 (dm, J = 208 Hz), 53.2, 53.0, 51.9, 50.9, 46.7, 45.0, 39.3, 37.7, 27.7 (d, J = 21 Hz), 22.1, 22.0, 4.3, 4.0. The presence of rotamers precluded a comprehensive assignment of all proton and carbon resonances. ^{19}F NMR ($CDCl_3$) δ: −118.0 (1F, br m), −118.5 (1F, br m), −122.9 (2F, br m), −124.5 (1F, br m), −132.0 (1F, br m), −134.6 (1F, br m), −139.5 (2F, br d, J = 289 Hz), −142.4 (1F, br d, J = 281 Hz), −184.4 (1F, br m). HRMS (ESI$^+$): calcd for $C_{14}H_{13}F_{11}INONa$ (M+Na$^+$), 569.9758; found, 569.9760.

4-Iodo-5-phenypentanenitrile (4b). Colorless oil. IR (KBr): 3028, 2924, 2247, 1676, 1602, 1495, 1452 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.36−7.27 (3H, m), 7.19 (2H, br d, J = 6.4 Hz), 4.33−4.26 (1H, m), 3.38 (1H, dd, J = 14.2, 7.3 Hz), 3.20 (1H, dd, J = 14.2, 7.8 Hz), 2.68−2.50 (2H, m), 2.09−2.00 (2H, m). ^{13}C NMR ($CDCl_3$) δ: 138.6, 128.9, 128.7, 127.3, 118.4, 47.3, 34.7, 33.6, 18.4. HRMS (ESI$^+$): calcd for $C_{11}H_{12}INNa$ (M+Na$^+$):, 307.9907; found, 307.9879.

2,2-Difluoro-4-iodo-5-phenylvalericacid, ethylester (4c). Colorless oil. IR (KBr): 2984, 2933, 1767, 1496, 1452 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.36−7.27 (3H, m), 7.19 (2H, br d, J = 6.4 Hz), 4.39−4.30 (3H, m), 3.26 (1H, dd, J = 14.7, 6.4 Hz), 3.20 (1H, dd, J = 14.7, 8.2 Hz), 2.99−2.72 (2H, m), 1.37 (3H, t, J = 7.3 Hz). ^{13}C NMR ($CDCl_3$) δ: 163.4 (t, J = 32 Hz), 138.8, 129.0, 128.6, 127.2, 115.2 (dd, J = 255, 253 Hz), 63.3, 47.1, 44.3 (t, J = 24 Hz), 21.9 (t, J = 4 Hz), 13.9. ^{19}F NMR ($CDCl_3$) δ: −102.3 (1F, br d, J = 263 Hz), −107.1 (1F, br d, J = 263 Hz). HRMS (ESI$^+$): calcd for $C_{13}H_{15}F_2IO_2Na$ (M+Na$^+$), 390.9977; found, 390.9981.

***cis*-3-(Ethoxycarbonyl-2,2-difluoroethyl)-4-(iodomethyl)-3-methyl-1-(phenylmethoxy)-2-pyrrolidinone (*cis*-8f).** Colorless crystals. Mp 89−90 °C (hexane). IR (KBr): 2979, 2941, 1767, 1714, 1456 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.44−7.37 (5H, m), 5.01 (1H, d, J = 11.2 Hz), 4.98 (1H, d, J = 11.2 Hz), 4.32 (2H, q, J = 7.1 Hz), 3.46 (1H, dd, J = 9.4, 6.7 Hz), 3.33 (1H, dd, J = 9.7, 3.5 Hz), 3.21 (1H, dd, J = 9.4, 4.1 Hz), 2.82 (1H, dd, J = 11.5, 9.7 Hz), 2.54−2.45 (1H, m), 2.42−2.38 (1H, m), 2.22−2.14 (1H, m), 1.35 (3H, t, J = 7.1 Hz), 1.28 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 171.1, 163.6 (t, J = 32 Hz), 134.8, 129.5, 129.1, 128.6, 115.7 (dd, J = 254, 251 Hz), 76.7, 63.3, 51.0, 44.9, 44.5, 35.0 (t, J = 23 Hz), 22.4, 13.8, 4.0. ^{19}F NMR ($CDCl_3$) δ: −101.4 (br dt, J = 265 Hz), −101.8 (br d, J = 265 Hz). HRMS (ESI$^+$): calcd for $C_{18}H_{22}F_2INO_4Na$ (M+Na$^+$), 504.0454; found, 504.0475.

***trans*-3-(Ethoxycarbonyl-2,2-difluoroethyl)-4-(iodomethyl)-3-methyl-1-(phenylmethoxy)-2-pyrrolidinone (*trans*-8f).** A colorless oil. IR (KBr): 2979, 1765, 1716, 1456, 1374 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.45−7.36 (5H, m), 5.01 (1H, d, J = 10.5 Hz), 4.94 (1H, d, J = 10.5 Hz), 4.33 (2H, q, J = 7.2 Hz), 3.47 (1H, dd, J = 8.7, 7.3 Hz), 3.31 (1H, dd, J = 9.6, 4.1 Hz), 2.94−2.89 (2H, m), 2.81−2.73 (1H, m), 2.53−2.33 (2H, m), 1.37 (3H, t, J = 7.2 Hz), 1.02 (3H, s). ^{13}C NMR ($CDCl_3$) δ: 172.3, 163.6 (t, J = 32 Hz), 134.8, 129.6, 129.1, 128.6, 115.5 (t, J = 252 Hz), 77.0, 63.3, 51.5, 43.8, 40.7, 39.3 (t, J = 22 Hz), 17.4, 13.9, 1.2. ^{19}F NMR ($CDCl_3$) δ: −101.5 (br d, J = 263 Hz), −103.5 (br d, J = 263 Hz). HRMS (ESI$^+$): calcd for $C_{18}H_{22}F_2INO_4Na$ (M+Na$^+$), 504.0454; found, 504.0444.

Procedure for the Reaction of 7, 27, or 29 with *i*-PrI. A suspension of substrate **7**, **27**, or **29** (1.00 mmol) in H_2O (10 mL) was degassed using three pump−thaw cycles under argon atmosphere at 0 °C. To this suspension were added diisopropylethylamine (192 μL, 1.10 mmol), rhodamine B (96 mg, 0.20 mmol), and *i*-PrI (998 μL, 10.0 mmol) at room temperature. The stirring reaction mixture was irradiated with a white LED lamp (1000 lm) at room temperature. After 5 h, the reaction mixture was concentrated under reduced pressure. Rough purification by flash silica gel column chromatography (AcOEt:hexane = 3:1) afforded *cis*-**8g** and *trans*-**8g** as a mixture. Second purification of the mixture by preparative TLC (AcOEt:hexane = 1:6, 2-fold development) afforded the isolated isomers *cis*-**8g** (103 mg, 26%) and *trans*-**8g** (66 mg, 16%) (reaction of **7** in Scheme 6). Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:3) afforded *cis*-**28** and *trans*-**28** as a mixture. Second purification of the mixture by preparative TLC (AcOEt:hexane = 1:6, 2-fold development) afforded the isolated isomers *cis*-**28** (96 mg, 25%) and *trans*-**28** (54 mg, 14%) (reaction of **27** in Scheme 6). Rough purification by flash silica gel column chromatography (AcOEt:hexane = 1:6) afforded *trans*-**30** and *cis*-**30** as a mixture. Second purification of the mixture by preparative TLC (AcOEt:benzene = 1:10, 2-fold development) afforded the isolated isomers *trans*-**30** (176 mg, 43%) and *cis*-**30** (31 mg, 7%) (reaction of **29** in Scheme 6). The ratio of products was determined by ^{1}H NMR analysis of the mixture after rough purification. Regarding the ratio of products, a slight difference between ^{1}H NMR analysis of the mixture after the first purification and the isolated yields after the second purification was observed. The characterization data of *cis*-**8g** and *trans*-**8g** were reported in our previous articles.[46]

***cis*-4-(Iodomethyl)-3-methyl-3-(2-methylpropyl)-1-(phenylmethyl)-2-pyrrolidinone (*cis*-28).** Colorless crystals. Mp 56−58 °C (hexane). IR (KBr): 2955, 1689, 1793, 1425 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.36−7.22 (5H, m), 4.58 (1H, d, J = 14.7 Hz), 4.36 (1H, d, J = 14.7 Hz), 3.34 (1H, dd, J = 10.1, 7.3 Hz), 3.30 (1H, dd, J = 9.6, 4.1 Hz), 3.04 (1H, dd, J = 11.9, 9.6 Hz), 2.92 (1H, dd, J = 10.1, 9.2 Hz), 2.44−2.36 (1H, m), 1.92−1.83 (1H, m), 1.37 (1H, dd, J = 14.2, 4.6 Hz), 1.25 (3H, s), 1.15 (1H, dd, J = 14.2, 6.4 Hz), 0.93 (3H, d, J = 6.9 Hz), 0.87 (3H, d, J = 6.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 177.6, 136.2, 128.7, 128.1, 127.6, 50.6, 48.6, 47.7, 46.7, 40.7, 25.1, 24.5, 23.8, 22.4, 3.4. HRMS (ESI$^+$): calcd for $C_{17}H_{24}INONa$ (M+Na$^+$), 408.0795; found, 408.0807.

***trans*-4-(Iodomethyl)-3-methyl-3-(2-methylpropyl)-1-(phenylmethyl)-2-pyrrolidinone (*trans*-28).** A colorless oil. IR (KBr): 2957, 1692, 1492, 1441 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.36−7.21 (5H, m), 4.50 (1H, d, J = 14.7 Hz), 4.41 (1H, d, J = 14.7 Hz), 3.41 (1H, dd, J = 9.6, 7.8 Hz), 3.22 (1H, dd, J = 9.6, 4.1 Hz), 3.00 (1H, dd, J = 11.5, 9.6 Hz), 2.80 (1H, dd, J = 9.6, 9.2 Hz), 2.69−2.61 (1H, m), 1.71−1.65 (2H, m), 1.45−1.39 (1H, m), 0.95 (3H, d, J = 6.4 Hz), 0.94 (3H, s), 0.88 (3H, d, J = 6.4 Hz). ^{13}C NMR ($CDCl_3$) δ: 178.5, 136.4, 128.7, 128.2, 127.6, 50.6, 48.1, 46.7, 43.9, 41.6, 24.9, 24.8, 22.8, 18.5, 3.5. HRMS (ESI$^+$): calcd for $C_{17}H_{24}INONa$ (M+Na$^+$), 408.0795; found, 408.0781.

***trans*-4-(Iodomethyl)-3,4-dimethyl-3-(2-methylpropyl)-1-(phenylmethyl)-2-pyrrolidin-2,5-dione (*trans*-30).** Colorless oil. IR (KBr): 2956, 1773, 1711, 1466 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.37−7.20 (5H, m), 4.60 (2H, s), 3.28 (1H, d, J = 10.5 Hz), 3.12 (1H, d, J = 10.5 Hz), 1.72−1.64 (1H, m), 1.40 (1H, dd, J = 14.2, 5.5 Hz), 1.28−1.22 (7H, m), 0.78 (3H, d, J = 6.4 Hz), 0.62 (3H, d, J = 6.9 Hz). ^{13}C NMR ($CDCl_3$) δ: 180.5, 178.8, 135.5, 129.0, 128.6, 127.9, 50.3, 49.8, 46.9, 42.4, 24.8, 24.6, 23.9, 17.7, 15.7, 10.8. HRMS (ESI$^+$): calcd for $C_{18}H_{24}INO_2Na$ (M+Na$^+$), 436.0744; found, 436. 0739.

***cis*-4-(Iodomethyl)-3,4-dimethyl-3-(2-methylpropyl)-1-(phenylmethyl)-2-pyrrolidin-2,5-dione (*cis*-30).** Colorless oil. IR (KBr): 2956, 1772, 1703, 1458 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.36−7.24 (5H, m), 4.64 (1H, d, J = 14.2 Hz), 4.59 (1H, d, J = 14.2 Hz), 3.53 (1H, d, J = 11.0 Hz), 3.33 (1H, dd, J = 11.0, 1.0 Hz), 1.68−1.60 (2H, m), 1.44−1.39 (1H, m), 1.29 (3H, s), 1.26 (3H, s), 0.83 (3H, d, J = 6.0 Hz), 0.66 (3H, d, J = 6.4 Hz). ^{13}C NMR ($CDCl_3$) δ: 180.7, 178.9, 135.5, 128.8, 128.6, 128.0, 50.6, 49.5, 45.6, 42.4, 25.1, 24.7, 24.0, 16.2 (2C), 7.1. HRMS (ESI$^+$): calcd for $C_{18}H_{24}INO_2Na$ (M+Na$^+$), 436.0744; found, 436.0753.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01102.

Photophysical properties of rhodamine B and eosin Y; distribution experiment of rhodamine B; and ^{1}H, ^{13}C, and ^{19}F NMR spectra of obtained products (PDF)

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Notes

The authors declare no competing financial interest.

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