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Photochemistry of 2-Nitroarenes: 2-Nitrophenyl-α-trifluoromethyl Carbinols as Synthons for Fluoroorganics

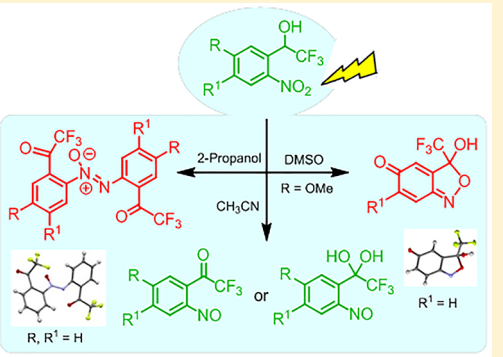
Kavita Belligund,[†,‡] Thomas Mathew,*[,†,‡] Jonathan R. Hunt,[‡] Archith Nirmalchandar,[†,‡] Ralf Haiges,[†,‡] Jahan Dawlaty,[‡] and G. K. Surya Prakash*[,†,‡]

[†]Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90089-1661, United States

[‡]Department of Chemistry, University of Southern California, Los Angeles, California 90089-1661, United States

Supporting Information

ABSTRACT: Facile synthesis of a new series of 2,2′-bis(trifluoroacetyl) azoxybenzene derivatives and trifluoromethylated benzo[*c*]isoxazoline systems, along with trifluoroacetyl nitrosobenzene derivatives was achieved by solvent controlled photolysis of appropriate 2-nitrobenzyl alcohols. Corresponding photoactive 2-nitrobenzyl chromophore plays a distinct role in this photosynthetic process, while, quite unprecedented, pertinent fluoromethyl substitution leads to high value fluoromethylated products, whose direct access is not feasible by common synthetic protocols. The significance of fluorine and fluoroalkyl substitution and its prominent biological effects makes this new photochemical approach an important discovery in synthetic methodology. Plausible mechanistic pathways involved in the formation of the products during steady-state photolysis are further established by picosecond laser flash photolysis experiments.

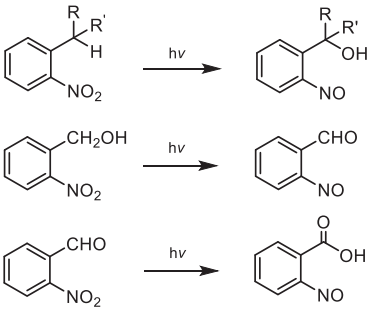


INTRODUCTION

The rich photochemistry of *o*-nitrobenzylic systems has been extensively explored and utilized in the past few decades for convenient application as effective photoremovable protecting groups,[1−7] which make these systems a vital tool in chemical biology[8] such as DNA polymerase technology and in the synthesis of photolabile caged compounds.[9−11] *o*-Nitrobenzylic group has been effectively used for the safe photochemical release of acids, alcohols, amines, phosphates, and ketones. In solid state peptide synthesis, it has been used as a very efficient photocleavable protecting group. In 1901, Ciamician and Silber[12] reported the intramolecular photoredox transformation of *o*-nitrobenzaldehyde to *o*-nitroso benzoic acid. Further studies were carried out by Spiteller,[13] Morrison and Migadolf[14] on similar systems. Time-resolved experiments by George and Sciano,[15] Yip and Sharma,[16] Gilch and coworkers[17] have suggested that the primary process among several elementary processes involved in the phototransformation of *o*-nitrobenzylic systems is the hydrogen transfer from the substituent with C−H functionality in the *ortho* position to the nitro group during irradiation (Scheme 1).

There is a huge drive toward the synthesis of fluoroorganic molecules as many of them are very valuable in medicinal and material chemistry. In pharmaceutical chemistry, introduction of fluorine and perfluoro groups in drug molecules generates significant changes in conformation, lipophilicity, metabolic stability, and pharmacokinetic properties that are highly desirable in medicinal chemistry.[18,19] These changes are attributed to the high electronegativity of fluorine and its small size, which is comparable to hydrogen.[20] So far, over 20% of approved pharmaceutical drugs contain one or more fluorine atoms, while in the case of newly registered agrochemicals, it is even higher (∼30%).[21,22] Some well-known fluorine containing drugs include the targeted chemotherapy drug sorafenib (Nexavar) **A**, selective Bcr-Abl kinase inhibitor nilotinib (Tasigna) **B**, nonsteroidal anti-inflammatory drug celecoxib (Celebrex) **C**, the cholesterol-lowering compound atorvastatin (Lipitor) **D**, the antidepressant fluoxetine (Prozac) **E**, and the antibiotic ciprofloxacin (Ciprobay) **F** (Figure 1). Strong dipoles introduced by partial

Scheme 1. Intramolecular Photoredox Processes in *o*-Nitrobenzylic Systems



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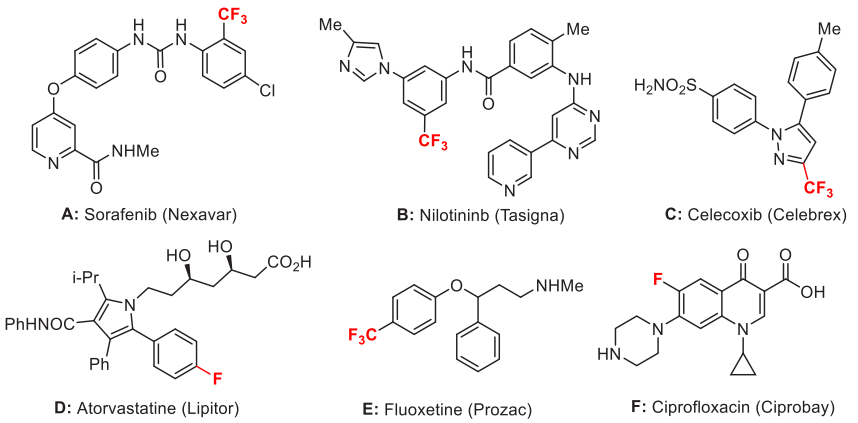
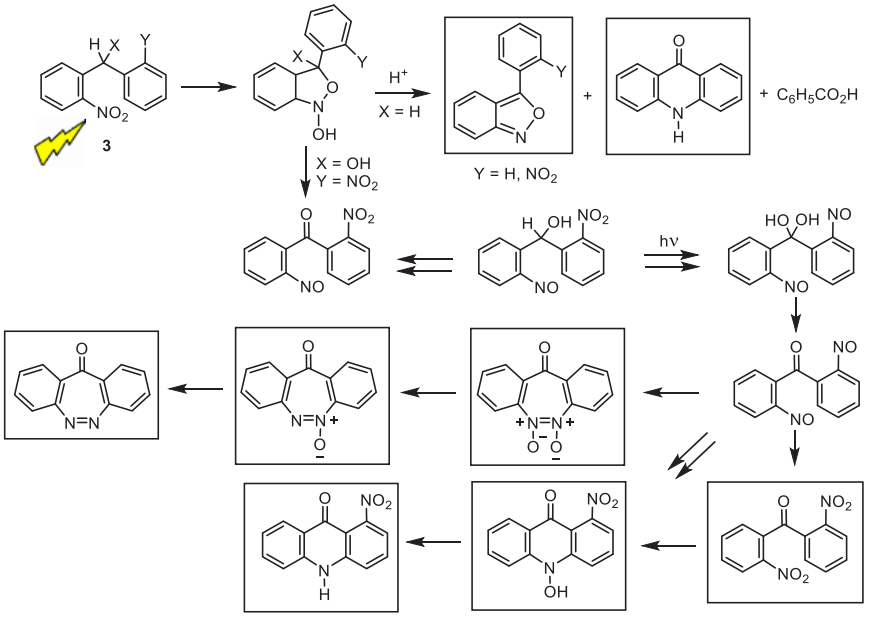


Figure 1. A few widely used fluorine-containing drugs.

Scheme 2. Photochemical Transformation of 2,2′-Dinitrodiphenylmethanes to *N*-Heterocycles



fluorination cause changes in electrical effects which are useful in the development of ferroelectric, antiferroelectric, and liquid crystal materials.[23]

Our continued interest in the development of efficient synthetic approaches for fluorination and fluoromethylation of a wide range of organic substrates prompted us to search for simple and convenient protocols. As earlier studies on the photochemical transformation of 2-nitrobenzyl derivatives, especially 2,2′-dintrodiphenylmethane derivatives **3**,[24−28] showed that direct access to heterocycles such as diazepines, diazepine-*N*-oxides, acridines, and their derivatives could be achieved (Scheme 2), we became curious to examine the photochemistry of α-trifluoromethylated 2-nitrobenzyl alcohols to see if we could exploit their rich photochemistry to generate novel trifluoromethylated substituted arenes. While there have been several approaches, where the trifluoromethylated 2-nitrobenzyl systems have been used as photoremovable groups, very few studies on their application as useful photosynthons exist. Studies published recently on the use of 2-nitrophenyl-α-trifluoromethyl carbinol as an efficient photoremovable group[11] caught our attention and the effective photocleavage/deprotection steps further sparked our interest to investigate the transformation occurring to 2-nitrophenyl-α-trifluoromethylcarbinyl part and its synthetic utility.

RESULTS AND DISCUSSION

Steady-State Photolysis of 2-Nitrophenyl-α-trifluoromethyl Carbinols in 2-Propanol: Synthesis of 2,2′-Bis(trifluoroacetyl)azoxyarenes. As trifluoromethylated *o*-nitrobenzyl alcohols can be easily synthesized by trifluoromethylation of the corresponding aldehydes using Ruppert−Prakash reagent, we decided to examine initially the photoreaction of the simple trifluoromethylated alcohol, 2-nitrophenyl-α-trifluoromethyl carbinol **4a**, synthesized by the trifluoromethylation of 2-nitrobenzaldehyde.[29−31] As this trifluoromethylated carbinol absorbs in the UV-B region, in our initial studies, we irradiated **4a** and its derivatives using a medium pressure Hg lamp with a Pyrex glass filter. However, Rayonet reactor with monochromatic lamps, being more convenient for irradiation, was chosen for further studies. Irradiation using 300 nm phosphorus lamps provided products with similar or better yields depending on the nature of the solvent. We carried out the photolysis in three solvents, 2-propanol, dimethyl sulfoxide (DMSO), and acetonitrile.

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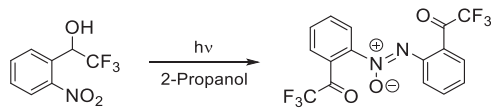
We started our photolytic studies using 2-nitrophenyl-α-trifluoromethyl carbinol **4a** by irradiating it in 2-propanol using 100 W medium pressure Hg lamp with a Pyrex glass filter. After irradiation for 1 h, aliquots of the reaction mixture were analyzed by ^{19}F NMR which showed the formation of a mixture of products, though with low selectivity. Irradiation for 5 h could afford 20% of a major product, which was later identified as 2,2-bis(trifluoroacetyl)azoxybenzene **5a**. Since the reaction was not very clean, we switched over to a Rayonet reactor fitted with 300 nm monochromatic lamps. Irradiation of a solution of 2-nitrophenyl-α-trifluoromethyl carbinol in 2-propanol in the Rayonet photoreactor for 5 h resulted in the formation of a red solution, which on ^{19}F NMR analysis showed the formation of a major product. After separation and identification, we were very intrigued to know that it is the corresponding 2,2′-bis(trifluoroacetyl)azoxybenzene **5a**, same as the one obtained during irradiation using Hg lamp but with double the yield. To the best of our knowledge, this is the first report on the synthesis of trifluoroacetylated azobenzene-*N*-oxide by a simple one-step method as shown (Scheme 3).

Scheme 3. Photolysis of 2-Nitrophenyl-α-trifluoromethyl Carbinol 4a: Direct Access to 2,2′-Bis(trifluoroacetyl)azoxybenzene 5a



4a **5a**

While the general route to oxidation of the trifluoromethyl carbinol functions to trifluoroacetyl groups involves the use of harsh reaction conditions,[32−36] even mild reaction conditions involve addition of oxidants in more than stoichiometric amounts.[30,37] However, this intramolecular photoredox process readily oxidizes the trifluoromethylated alcoholic group to the corresponding trifluoroacetyl group, eliminating the need for an external oxidant. Azoxy compounds exhibit photochromic properties, find applications in nonlinear optics and as dopants materials used in liquid crystals,[38−43] as substrates for synthesis of heterocyclic compounds,[44,45] while some derivatives display retinoid and antiandrogenic activity.[46,47] Therefore, direct synthesis of trifluoroacetyl derivatives drew our keen attention.

It is evident that its formation occurs by an intramolecular photoredox reaction in which the photooxidation of trifluoromethylcarbinol to trifluoroacetyl group by the excited nitro group with its simultaneous photoreduction to nitroso group. Nitrosoarenes, being significantly photoactive, undergoes subsequent photoreductive coupling to form the corresponding azoxyarene product.[48] Another product was also observed in noticeable amount, but could not be separated due to decomposition. These azoxy arenes are characterized by two sharp ^{19}F singlets with equal integration in the region −77 to −71 ppm. The structures were completely characterized by NMR (^{1}H, ^{13}C, ^{19}F NMR) and were further established by X-ray crystallographic analysis (Figure 2).

Table 1 shows the results of irradiation of the trifluoromethylated carbinols **4a−h** in 2-propanol. As shown, the solutions of various substituted phenyl analogues **4a−d** and **4f** in 2-propanol on irradiation with 300 nm gave the corresponding azoxy products **5a−d** and **5f** in moderate yields. In the case of **4e** with methoxy substitution at the *para* position to the nitro group, the yield of the azoxy product was reduced to 2−4%, giving the trifluoromethylated benzo[*c*]-isoxazolone **6e** as the major product. However, for **4f** with two methoxy substituents, *para* to both nitro and carbinol functionalities, azoxy product **5f** was obtained as the sole product (Figure 3).

As seen in Table 1, apart from unsubstituted and halogen substituted 2,2′-bis(trifluoracetyl)azoxybenzenes, direct synthesis of 2,2′-bis(trifluoracetyl)azoxynaphthalene **5h** was also made possible by this very convenient photochemical method, albeit in lower yield (Figure 3).

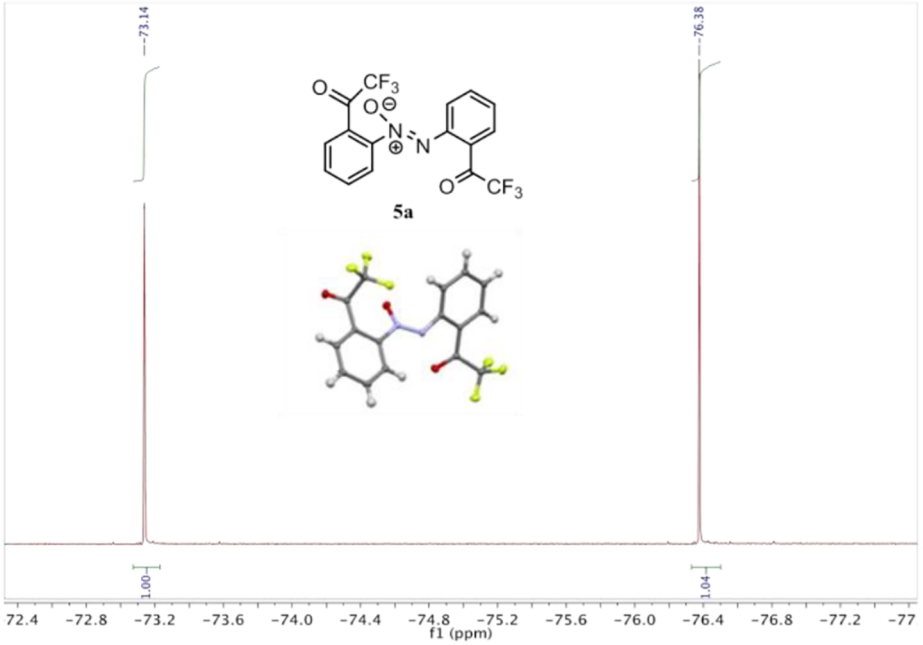


Figure 2. ^{19}F NMR spectrum and X-ray crystal structure of **5a**.

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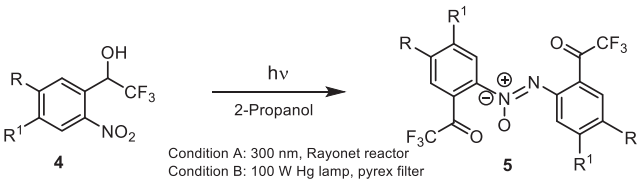
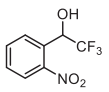
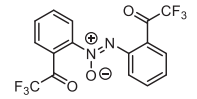
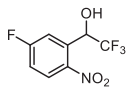
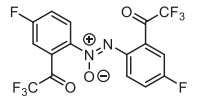
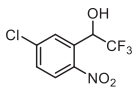
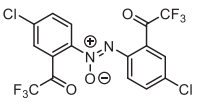
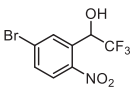
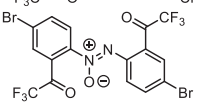
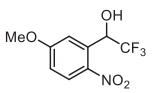
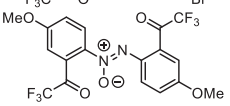
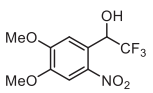
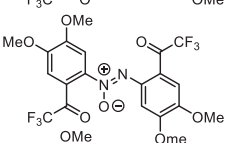
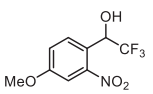
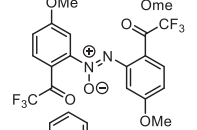
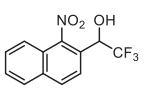
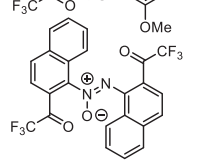
Table 1. Synthesis of 2,2-Bis(trifluoroacetyl)azoxyarenes by the Photolysis of 2-Nitrophenyl-α-trifluoromethyl Carbinols in 2-Propanol



Entry	Substrate (4a-h)	Condition: Time [h]	*N,N*-Oxide (5a-h)	Yield (%)
a		A: 5 B: 5		A: 40 B: 20
b		A: 5 B: 7		A: 25 B: 16
c		A: 4 B: 4		A: 35 B: 18
d		A: 5 B: 5		A: 37 B: 37
e		A: 4 B: 4		A: 4 B: 2
f		A: 3.5		A: 50
g		A: 4		A: 16
h		A: 2 B: 7		A: 23 B: 4

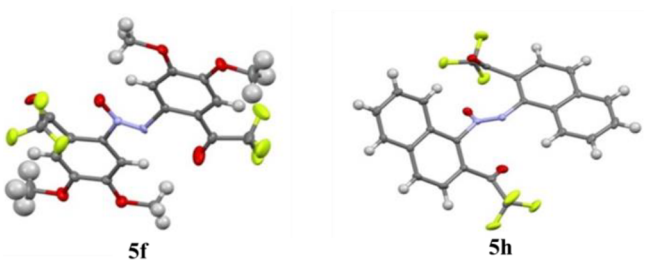
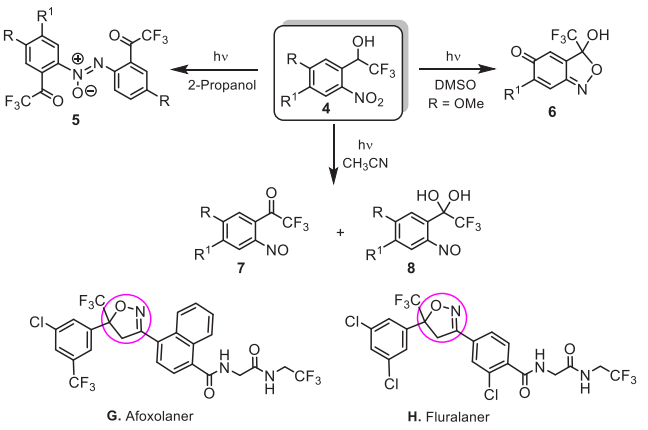


Figure 3. X-ray crystal structures of **5f** and **5h**.

Synthesis of Trifluoromethylated Isoxazolines. To explore the synthetic utility of this photoprocess, we continued the study with a series of 2-nitrophenyl-α-trifluoromethyl carbinols using different solvents. Therefore, as our next approach, we chose the highly polar, aprotic solvent DMSO as the solvent for irradiation. We observed an interesting phenomenon when there was a methoxy group located para to the nitro group. When the *para*-methoxy substituted (para to nitro group) substrates were irradiated in DMSO as solvent, intramolecular cyclization with the elimination of a molecule of methanol occurred, leading to the formation of a trifluoromethylated benzo[*c*]isoxazol-5(3*H*)-one **6** (Scheme 4). More

Scheme 4. 2-Nitrophenyl-α-trifluoromethyl Carbinol, an Efficient Photosynthon for Solvent-Controlled Synthesis of 2,2′-Bis(trifluoroacetyl)azoxyarenes, 2-Trifluoroacetyl Nitrosoarenes, and Trifluoromethylated Isoxazolines



intriguingly, changing the solvent to acetonitrile led to the formation of 2-trifluoroacetyl nitrosoarenes and their hydrates as the major products. Molecules containing the isoxazoline core are found to exhibit significant antiplatelet activity.[49,50] These types of molecules also exhibit insecticidal properties; Afoxolaner and Fluralaner are commercial drugs used to treat fleas in mammals (Scheme 4).[51,52] Nitroso compounds serve as reactants for various synthetic transformations such as those involving nitroso aldol reactions,[53−55] ene reactions,[56] cycloaddition, etc.[54] They are also used as effective metal coordinating ligands[57] and antiviral compounds.[58]

While irradiation of **4a** in DMSO formed the corresponding 2-trifluoroacetyl nitrosobenzene **7a** through its hydrate **8a** as intermediate, **4e** (with a methoxy group present *para* to the nitro group) eventually formed the corresponding isoxazoline derivative, 3-hydroxy-3-(trifluoromethyl)-benzo[*c*]isoxazol-5(3*H*)-one **6e** by the elimination of a molecule of methanol. The 4,5-dimethoxy substituted carbinol **4f**, which formed 2,2′-bis(trifluoroacetyl)-4,4′,5,5′-tetramethoxy azoxybenzene **5f** previously in 2-propanol, is now transformed to 3-hydroxy-6-methoxy-3-(trifluoromethyl)benzo[*c*]isoxazol-5(3*H*)-one **6f**. We were very delighted to see that the methoxy substituted substrate **5i** with an adjacent difluoromethoxy substituent also formed the corresponding difluoromethoxy substituted isoxazoline **6i** (Table 2). Formation of the isoxazolines were identified by the formation of a distinct singlet in the ^{19}F NMR spectra between −85 to −83 ppm depending on the substrate and solvent (Figure 4). Formation of the isoxazoline derivatives, noticed during the irradiation in 2-propanol in minute concentration, reached maximum concentration when the solvent was switched to DMSO.

To obtain these compounds in substantial yields, after irradiating the solution at a proper wavelength (300 nm) for a specific period of time with monitoring the fading of substrate concentration, the solution had to be kept undisturbed under dark for a period of 48−168 h to avoid any secondary photoprocesses. This allows the formation and rearrangement of the cyclic intermediate with the elimination of a molecule of

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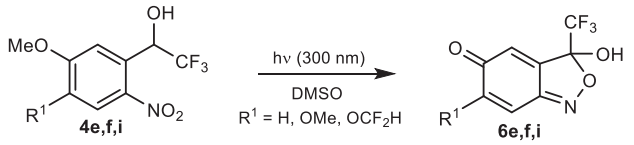
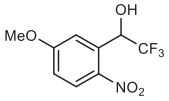
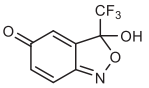
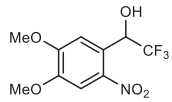
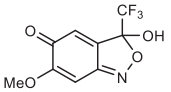
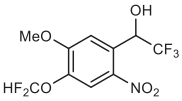
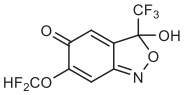
Table 2. Synthesis of Trifluoromethylated Benzo[*c*]isoxazol-5(3*H*)-ones by the Photolysis of 2-Nitrophenyl-*α*-trifluoromethyl carbinols in DMSO[a]



Entry	Substrate (**4e,f,i**)	Time [h] t_i	Time [h] t_s	Benzo[c]isoxazolone (**6e,f,i**)	Yield (%)
e		4.5	72		37
f		4	48		12
i		5.25	168		22

[a] t_i = time of irradiation, t_s = time kept undisturbed in the dark.

methanol to form the 3-hydroxy-3-(trifluoromethyl)benzo[*c*]-isoxazol-5(3*H*)-ones **6e**,**f**,**i** (Table 2).

Fascinated by the reactions in DMSO as solvent, we decided to change the solvent to CH_3CN, an aprotic solvent with lower polarity. Irradiation of carbinol **4a**−**4e** showed the formation of one of the two major products, which were identified as 2-trifluoroacetyl nitrosoarene **7** and its hydrate **8**. Irradiation of **4a**, **4b**, **4e** formed the corresponding 2-trifluorocetyl nitrosoarene **7a**, **7b**, **7e**, while **4c** and **4d** formed the respective hydrates **8c** and **8d** as shown (Scheme 5, Table 3).

Evaporation of acetonitrile from the photolysates of **4c** and **4d** yielded solids, which were found to be the dimers **8c′** and **8d′** of the respective monomers **8c** (hydrate of **7c**) and **8d** (hydrate of **7d**). Solvent evaporation leads to increase in the concentration of monomer hydrate **8c** and **8d** and promoted dimerization to the corresponding *N*,*N*-dioxides **8c′** and **8d′**. The NMR spectra recorded for the solid **8d′** were found to be similar to the intermediate observed during photolysis of **4e** in DMSO. The structure of the solid **8d′** was determined by X-ray single crystal analysis (Scheme 5). However, when the hydrate was left in $CDCl_3$ or excess $CHCl_3$, it gradually dissolved and formed the nonhydrated monomer, 2-triffluoroacteyl nitrosoarene **7d**. This could be attributed to dehydration due to the residual acidity of these solvents.

Transient Absorption Spectroscopy. To better understand the mechanism of the photoreaction, femtosecond UV-pump/vis-probe transient absorption spectroscopy was used to study the transient intermediates involved in the reaction. The details of the transient absorption apparatus are described elsewhere.[59] Study was conducted using **4a** in 2-propanol and a mixture of water and 2-propanol (Figure 5). At 300 fs, the shortest delay resolved by our instrument, a broad spectrum is seen that is assigned to the S1 state of the molecule. In the first ten picoseconds, this spectrum evolves. The evolved spectrum, consisting of a narrow short wavelength feature (∼430 nm) and a broad long wavelength feature, is assigned as a mixed population of the *o*-quinonoid singlet and the T1 triplet states. These assignments are made based on previous works by Yip and Sharma,[16,60,61] who illustrated that the short wavelength feature is associated with the *o*-quinonoid species and the long wavelength feature is associated with the triplet state. Overlapping absorption of these two states was similarly observed by Yip and Sharma.

To probe the identities of these features experimentally, water was gradually added to the 2-propanol solution to observe its effects on the spectral evolution. Addition of water

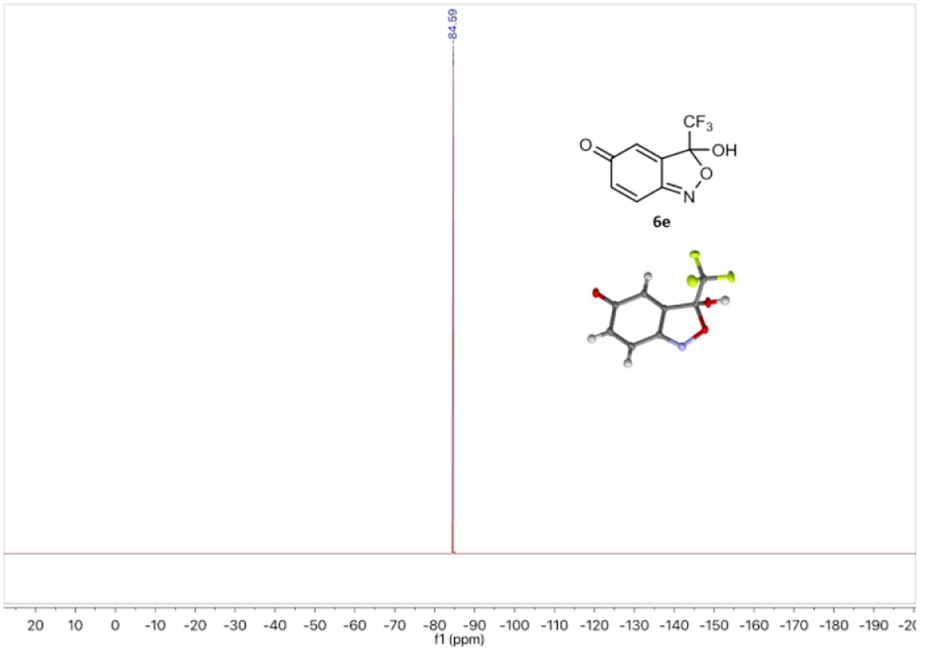


Figure 4. ^{19}F NMR spectrum and X-ray crystal structure of **6e**.

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Scheme 5. Photolysis of 4a−e in CH_3CN; Formation of 2-Trifluorocetyl Nitrosoarenes 7a, 7b, 7e and the Hydrates 8c, 8d; X-ray Crystal Structure of 8d′ (the Dimer of the Hydrate 8d)

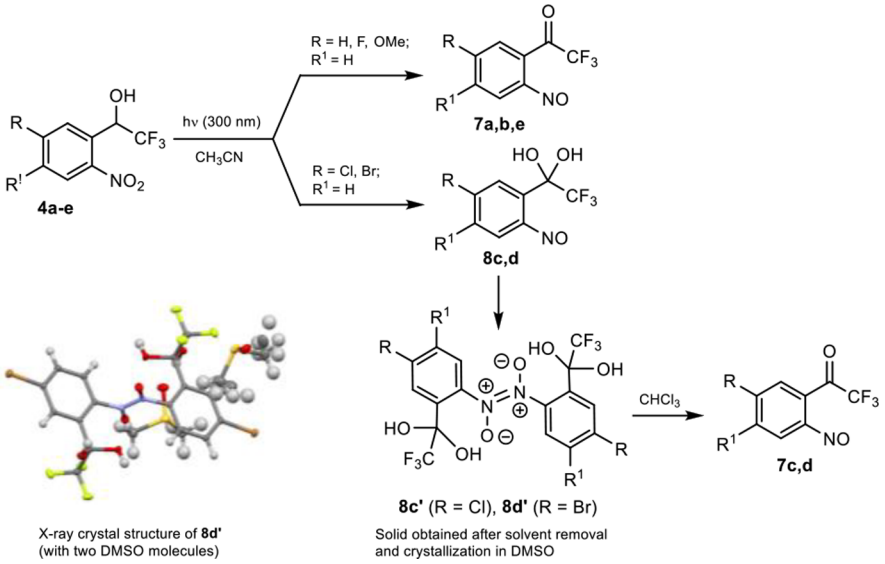
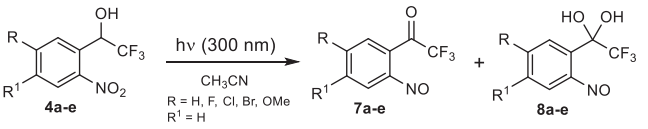
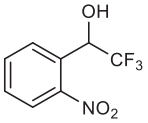
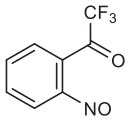
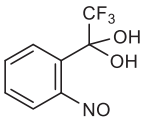
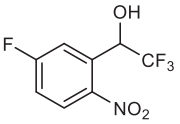
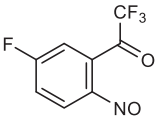
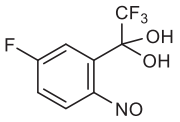
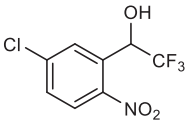
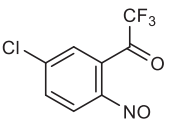
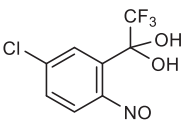
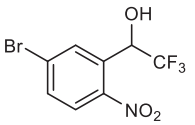
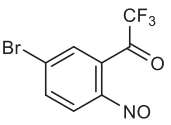
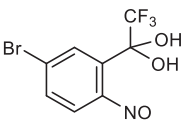
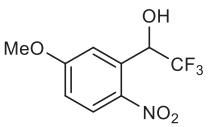
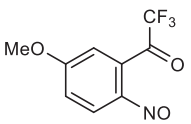
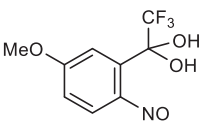


Table 3. 2-Trifluorocetyl Nitrosoarenes 7a−e and Their Hydrates 8a−e from the Irradiation of 4a−e in CH_3CN[a]



Entry	Substrate (**4a-e**)	Time (h)	Nitrosoarene (**7a-e**)	Hydrate (**8a-e**)	Yield (%)
a		4			7a: 60* 8a: 0
b		4			7b: 27* 8b: 0
c		4			7c: 0 8c: 36
d		4			7d: 0 8d: 50
e		3			7e: 94 8e: 0

[a]An asterisk (*) indicates ^{19}F NMR yield.

led to an increased prevalence of the short wavelength feature in the transient absorption spectrum. This is consistent with the short wavelength feature being assigned the *o*-quinonoid species, since addition of water could aid in the proton transfer process necessary for *o*-quinonoid generation. Oxygen was also added to the solution to observe its effects on the spectral evolution. Over the temporal range of our instrument (600 ps), there were no spectral changes observed by the addition of

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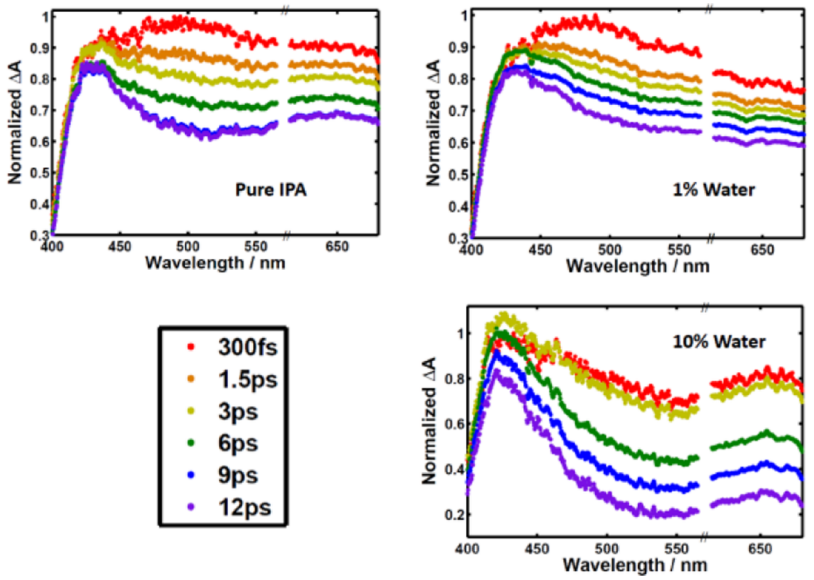

Figure 5. Transient absorption spectra of 2,2,2-trifluoro-1-(2-nitrophenyl)ethanol **4a** in 2-propanol, 2-propanol with 1% water, and 2-propanol with 10% water

oxygen. While we expect the contributing T1 state to be quenched by the presence of oxygen, it is possible that such effects take place on longer time scales.

Steady-State Photolysis in DMSO and Analysis of the Photolysate. On irradiation of **4a** in DMSO-d_6, an intermediate, which was characterized by the formation of a peak (quartet) at −84.35 ppm in the ^{19}F NMR was detected. As the reaction progressed, the peak corresponding to Cα (to CF_3) in the ^{13}C spectrum moved from 65.21 ppm (J = 31.4 Hz) to 93.98 (J = 32.4 Hz) ppm on irradiation. This intermediate finally gives rise to the 2-trifluoroacetyl nitrosobenzene **7a**.

On irradiation of 2,2,2-trifluoro-1-(5-methoxy-2-nitrophenyl)ethanol **4e** in DMSO, a similar transition was observed. The compound on irradiation formed an intermediate (evidenced by the appearance of a signal at −84.44 ppm in the ^{19}F NMR spectrum), which on being left undisturbed transforms into **6e** (Figure 6). As the reaction progressed, monitoring the reaction with ^{13}C NMR showed the transformation of quartet corresponding Cα (to CF_3) in the alcohol **4e** (65.24 ppm) to the one corresponding to Cα in the intermediate (94.21 ppm) and finally to the one in isoxazoline **6e** (103.29 ppm) (Scheme 6, for detailed procedure, see Supporting Information). This intermediate was eventually characterized as the hydrated 2-trifluoroacetyl nitrosoarene **8e**.

Plausible Mechanism. On the basis of the laser flash photolysis studies, steady state analysis conducted (vide supra) and comparing the results with previous observations,[16,60−62] we suggest that the following plausible mechanism for the transformations and the rearrangements involved in these photoprocesses. On irradiation, the nitrochromophore in the trifluoromethylated *o*-nitrobenzyl alcohol **4** undergoes $n-\pi^*$ excitation to form both the excited singlet and triplet states. Following intramolecular hydrogen abstraction, subsequent formation of the primary intermediates consisting of the triplet diradical **10** and the *o*-quinonoid singlet **11** occurs. Both **10** and **11** can advance to the cyclic intermediate **12**, the former by intersystem crossing to **11** (Scheme 7).

In 2-propanol, the cyclic intermediate **12** very likely opens to give the corresponding trifluoroacetyl nitroso product **7**, which itself being highly photoactive undergoes photoreductive coupling to form the trifluoroacetyl azoxy products. It is also possible that in 2-propanol, part of **7** might get reduced to the corresponding hydroxylamine followed by condensation with nitroso product **7** to form trifluoroacetyl azoxy products. In **4e**, the presence of methoxy group in the para position enhances the rate of formation of cyclic intermediate **12e** during the photoreaction and incites the elimination of a molecule of CH_3OH resulting in **6e**. This process is highly favored in DMSO.

It is quite intriguing to note that a mixture of the nitrosoketone product **7** and its hydrate **8** are formed when the reaction is carried out in acetonitrile. As the formation of stable hydrates in the case of aldehydes, ketones and imines containing several electronegative substituents such as CCl_3/CF_3 group due to their strong electron withdrawing effect is well-known,[63−68] formation of the hydrates **8** is quite reasonable. In fact, the hydration ability of trifluoromethylated ketones has been exploited in the development of many organic synthetic methodologies, recently for the development of histone deacetylase (HDAC) inhibitors.[69] However, as expected, on workup and drying the product, conversion to the nitroso product occurs gradually. Addition of chloroform/$CDCl_3$ pushes the equilibrium toward the nonhydrated trifluoroacetyl nitrosoarene due the residual acidity of chloroform/$CDCl_3$.[70−72] Thus, the formation of the photoproducts could be rationalized based on these observations. The photoreaction mixture would become more colored as the reaction proceeds; hence, the low reaction yield could also be attributed to the competitive absorption of the photoproducts.

CONCLUSION

Through the described approach, the synthetic utility of α-trifluoromethylated *o*-nitrobenzyl alcohols as efficient photosynthons toward the synthesis of new series of fluoroorganics with versatile functional motifs such as trifluoromethylated azoxy arenes, trifluoromethylated benzo[*c*]isoxazol-5(3*H*)-

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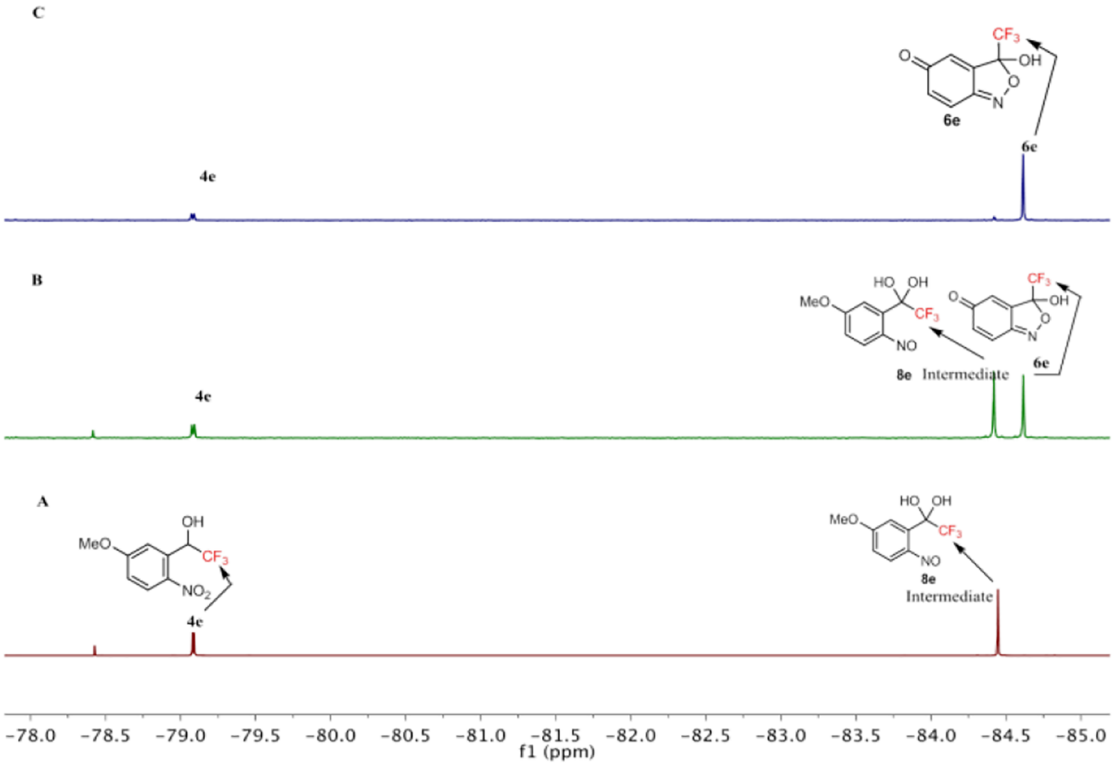

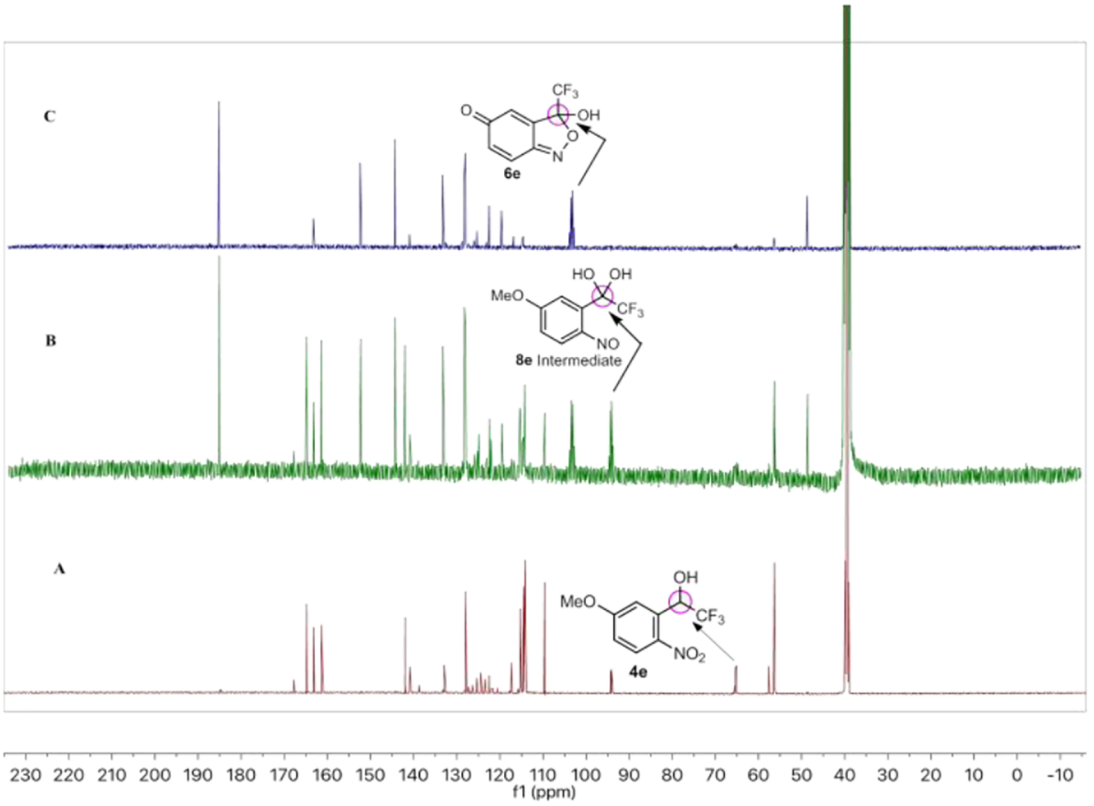

Figure 6. ^{19}F and ^{13}C NMR taken at different intervals: (A) Solution of **4e** in DMSO-d_6 after irradiation for 2.5 h, showing the formation of intermediate, **8e**. (B) Irradiated mixture left undisturbed for 24 h showing transition of the intermediate **8e** to product **6e**. (C) After 72 h, showing almost complete conversion of the intermediate, **8e** to the product **6e**.

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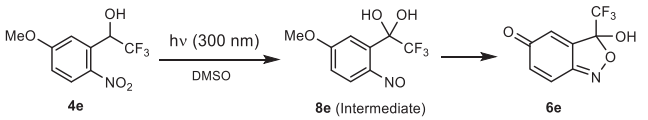
Scheme 6. Synthesis of Isoxazoline 6e by the Photolysis of 2,2,2-Trifluoro-1-(5-methoxy-2-nitrophenyl)-ethanol 4e in DMSO



ones and trifluoroacetyl nitroso arenes is revealed. Mechanistic studies by picosecond laser flash photolysis and monitoring of the steady state photolysate by NMR spectroscopic analysis shed light on the transient species and intermediates involved in the reaction. This work is the first report underscoring the importance of re-evaluating the potential of perfluorinated *o*-nitrobenzyl alcohols as photosynthons in addition to their protecting and photodeprotecting ability. The authors also anticipate that further studies in the area will provide key synthetic pathways for direct access to many biologically active small fluoroorganic molecules of great importance in the pharmaceutical arena in the future.

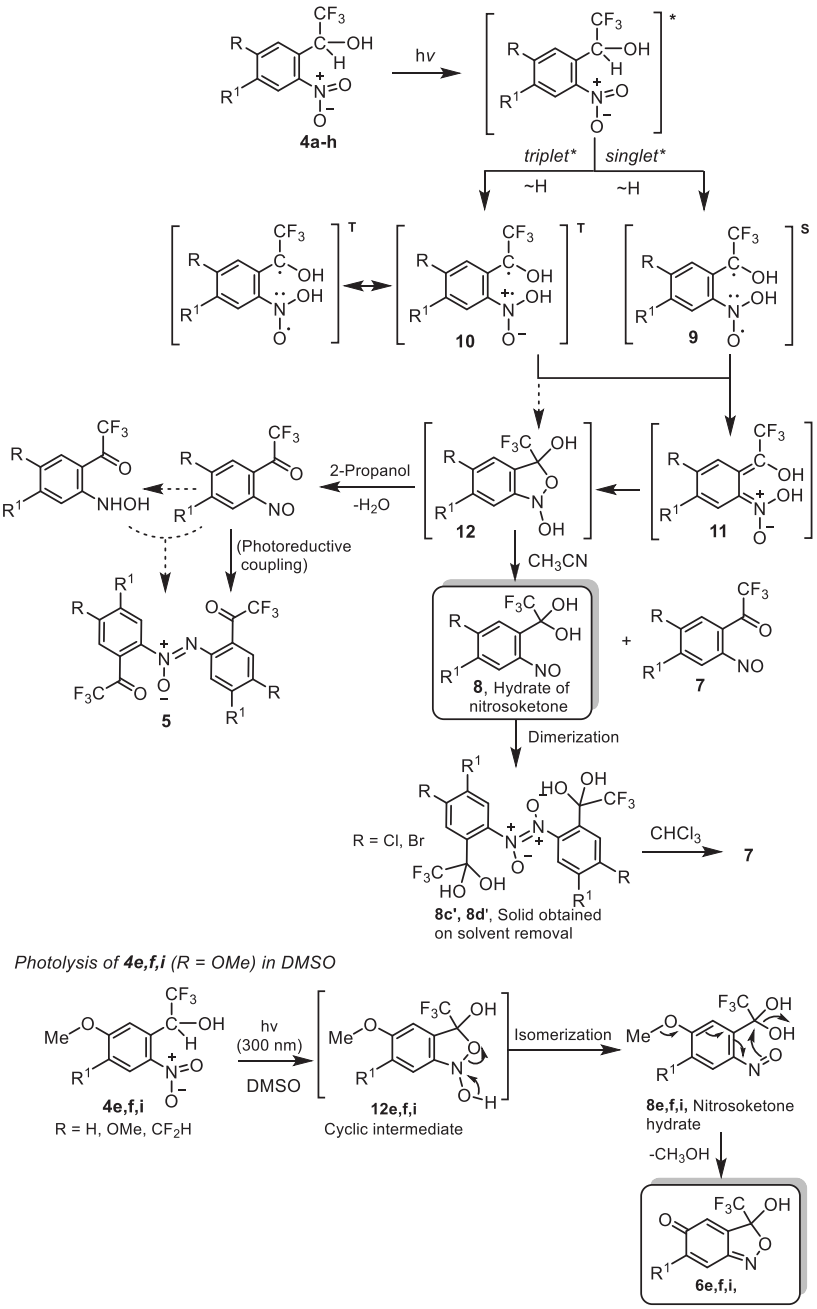
■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.9b07241.

Experimental Procedures and Spectral Data (PDF)
Summary of Data CCDC Numbers (PDF)
Crystal data for **5a** (CIF)
Crystal data for **5f** (CIF)

Scheme 7. Plausible Mechanism Leading to Photoproducts Observed during the Irradiation of 4a−i in Various Solvents



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Crystal data for **5h** (CIF)
Crystal data for **6e** (CIF)
Crystal data for **8d′** (CIF)

AUTHOR INFORMATION

Corresponding Authors

*tmathew@usc.edu
*gprakash@usc.edu

ORCID

Thomas Mathew: 0000-0002-2896-1917
Ralf Haiges: 0000-0003-4151-3593
Jahan Dawlaty: 0000-0001-5218-847X
G. K. Surya Prakash: 0000-0002-6350-8325

Notes

The authors declare no competing financial interest.

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