Synthesis E. Yamaguchi et al. Special Topic

Photooxidative Keto-Trifluoromethylation of Styrenes by Means of an Anthraquinone-Based Organocatalyst

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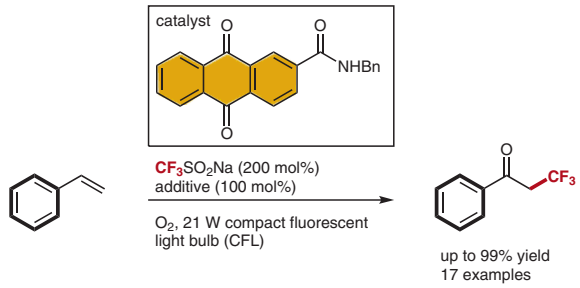

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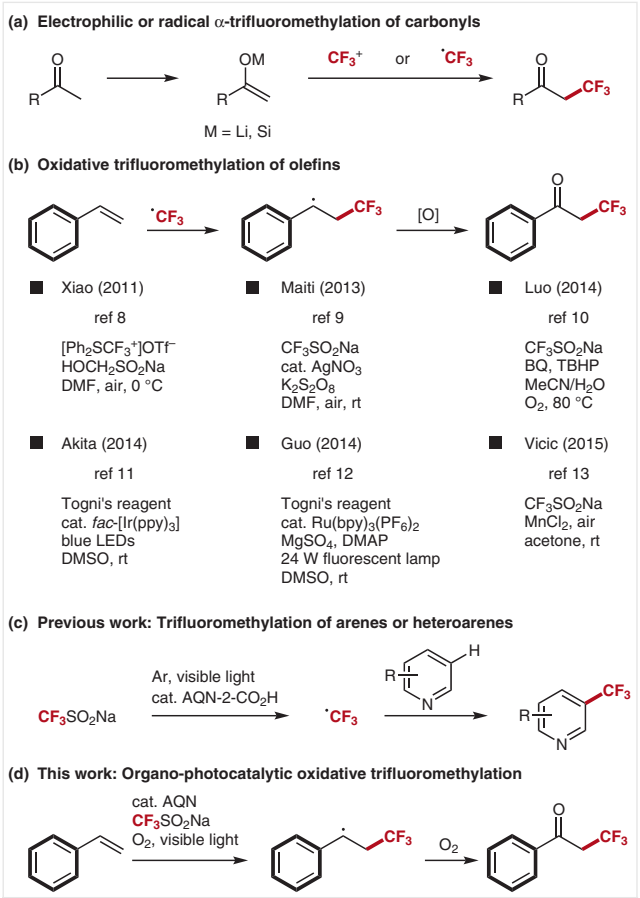
Abstract α-Trifluoromethyl ketones are versatile building blocks for the synthesis of various trifluoromethyl-functionalized molecules. Although there are significant advantages in the development of methods toward direct transformations of styrenes into α-trifluoromethyl ketones, most procedures leading to α-trifluoromethyl ketones require heavy- or transition-metal-based complexes. Herein, a novel method is developed for the synthesis of α-trifluoromethyl ketones via anthraquinone-catalyzed photooxidative keto-trifluoromethylation of styrenes with the readily available Langlois reagent (CF_3SO_2Na) under an oxygen atmosphere. The reactions proceed smoothly to give the products in moderate to excellent yield with good selectivity.

Key words anthraquinone, trifluoromethylation, trifluoromethyl radical, radical reaction, photoreaction

Trifluoromethyl groups are privileged structural motifs in pharmaceuticals, agrochemicals, and organofunctional materials.[1] In particular, from a medicinal point of view, the unique properties associated with the introduction of a fluorine group into target molecules allows significant enhancement of metabolic stability and lipophilicity.[2]

Thus, over the past decade, numerous efficient methods for carbon–CF_3 bond formation have been reported.[3] In particular, methodology leading to α-trifluoromethyl carbonyls has attracted a great deal of attention as these compounds are suitable building blocks for the synthesis of different fluorinated compounds.[4] In general, trifluoromethylated ketones are prepared by the electrophilic or radical trifluoromethylation of silyl or lithium enolates, which are derived from the corresponding carbonyl compounds (Scheme 1, a).[5–7]

However, only a few examples of 'direct' oxidative trifluoromethylation (keto-trifluoromethylation) of olefins have been reported (Scheme 1, b).[8–12] In 2011, Xiao et al. first re-



Scheme 1 (a) Synthesis of α-trifluoromethyl carbonyls from carbonyls. (b) Keto-trifluoromethylation of olefins. (c) Organocatalytic trifluoromethylation of heteroarenes. (d) Organo-photocatalytic oxidative trifluoromethylation.

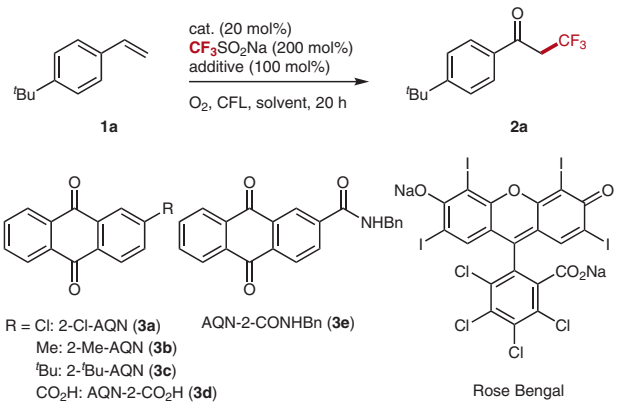
ported the stoichiometric oxidative trifluoromethylation of styrenes using *S*-(trifluoromethyl)diphenylsulfonium salt ($Ph_2SCF_3^+OTf^-$) with the reducing agent $HOCH_2SO_2Na$ under air, affording the corresponding products in only 20–40% yields.[8] Later, Maiti et al. discovered the first catalytic keto-trifluoromethylation of olefins using catalytic amounts of silver nitrate with $K_2S_2O_8$ and employing the Langlois reagent (CF_3SO_2Na).[9] However, oxidative metal-free trifluoromethylation of olefins using the Langlois reagent with *tert*-butyl hydroperoxide (TBHP) was described by Luo in 2014, which produced the corresponding oxy-trifluoromethylation products in a concerted manner with the desired ketones (ca. alcohol/ketone = 1:1).[10] Moreover, Akita et al. described that combining the photoredox-catalyzed trifluoromethylation and Kornblum oxidation methodologies enabled the synthesis of α-trifluoromethylated ketones in good to high yields.[11] At the same time, Guo reported that the reactions of non-terminal styrenes with Togni's reagent under photoredox conditions gave α-trifluoromethyl ketones in low yields.[12] Despite the excellent photophysical properties of transition-metal-based complexes (e.g., Ir and Ru) in visible light photocatalysis,[13] these complexes are generally expensive and potentially toxic, causing disadvantages when used on a larger scale. Recently, aerobic oxidative trifluoromethylations of olefins using the Langlois reagent catalyzed by manganese chloride were reported by Vicic, which mainly produced the corresponding α-trifluoromethyl alcohols in a concerted manner with the desired ketones (ca. alcohol/ketone = 2–10:1).[14] In these transformations, a key intermediate was the β-trifluoromethyl-substituted carbon radical, which was generated by the reaction of the trifluoromethyl radical with the alkene and subsequently reacted with the oxidant to produce the α-trifluoromethyl carbonyl compound.

We recently reported the visible-light-induced, metal-free trifluoromethylation of arenes and heteroarenes using the Langlois reagent catalyzed by anthraquinone-2-carboxylic acid (AQN-2-CO_2H) (Scheme 1, c).[14] According to the experimental and theoretical results, the photoinduced single electron transfer from $CF_3SO_2^-$ to photoexcited anthraquinone (AQN*) was expected to generate the trifluoromethylsulfinic radical ($CF_3SO_2^{\bullet}$) and $AQN^{\bullet-}$, with the radical being subsequently decomposed to produce the active trifluoromethyl radical ($CF_3^{\bullet}$) with liberation of SO_2.

During this study, we envisioned that combining the photoredox radical trifluoromethylation of olefins and the oxidation of the β-trifluoromethyl-substituted carbon radicals could provide the corresponding α-trifluoromethyl ketones. Herein, we disclose an efficient methodology for the transformation of styrenes into α-trifluoromethyl carbonyls catalyzed by anthraquinone as an organic photoredox catalyst (Scheme 1, d). This is the first example of metal-free, direct keto-trifluoromethylation of styrene through photoredox catalysis.

We began our study with the reaction of 4-*tert*-butyl styrene (**1a**) and the benchtop-stable Langlois reagent in the presence of a catalytic amount of 2-chloroanthraquinone (**3a**) (2-Cl-AQN) under an oxygen atmosphere and irradiation with a fluorescent light bulb (Table 1). Notably, the desired keto-trifluoromethylation was realized in 18% yield (entry 1). Evaluation of various solvents identified that aprotic polar solvents tended to accelerate this reac-

Table 1 Optimization of the Reaction Conditions[a]



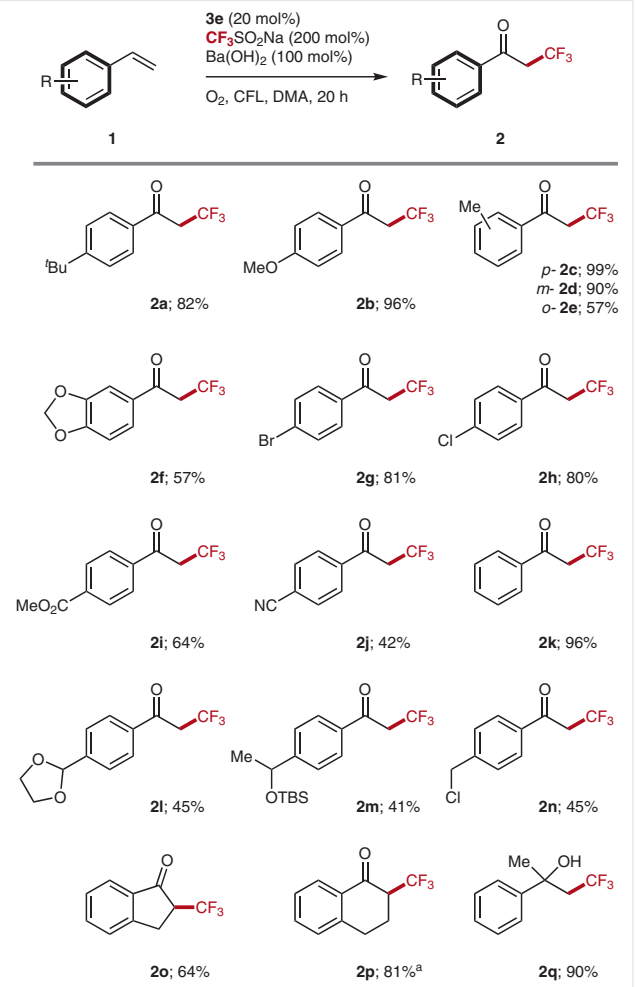
Entry	Solvent	Catalyst	Additive	Yield (%)[b,c]
1	EtOAc	**3a**	–	18
2	acetone	**3a**	–	16
3	MeCN	**3a**	–	5
4	MeOH	**3a**	–	6
5	DMF	**3a**	–	35
6	DMSO	**3a**	–	33
7	DMA	**3a**	–	52
8	DMA	anthracene	–	37
9	DMA	Rose Bengal	–	0
10	DMA	**3b**	–	51
11	DMA	**3c**	–	52
12	DMA	**3d**	–	58
13	DMA	**3d**	LiOH	16
14	DMA	**3d**	NaOH	10
15	DMA	**3d**	$Ca(OH)_2$	62
16	DMA	**3d**	$Ba(OH)_2$	64
17[d]	DMA	**3d**	$Ba(OH)_2$	74 (64)
18[d]	DMA	**3e**	$Ba(OH)_2$	(82)

[a] Unless otherwise noted, the reaction was conducted with 0.3 mmol of **1a**, 0.6 mmol of CF_3SO_2Na (200 mol%), 0.3 mmol of additive (100 mol%), and 0.06 mmol of catalyst in 4.0 mL of solvent under an oxygen atmosphere and irradiation with a 21 W compact fluorescence light bulb (CFL).
[b] Yield was determined by ^1H NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as the internal standard.
[c] The number in parentheses represents the isolated yield.
[d] Reaction performed for 30 h.

tion, with dimethylacetamide (DMA) found to be the optimum solvent (entries 2–7). Screening of various photocatalysts showed that anthracene promoted the reaction (entry 8), but that Rose Bengal was completely ineffective for keto-trifluoromethylation (entry 9). This indicated that the keto-trifluoromethylation did not involve a singlet oxygen generated by photoexcited Rose Bengal. In the subsequent evaluation of the substituents on anthraquinone, all AQNs efficiently catalyzed the desired reaction in a similar manner to that of 2-Cl-AQN (entries 7 vs 10–12), with anthraquinone-2-carboxylic acid (**3d**) (AQN-2-COOH) affording the desired product **2a** in a slightly better yield. Consequently, various additives were examined (entries 13–16) and it was found that alkaline earth metal hydroxides, such as $Ca(OH)_2$ (62%) and $Ba(OH)_2$ (64%), enhanced the reaction slightly, whereas alkaline hydroxides (e.g., LiOH and NaOH) did not. Prolonging the reaction time to 30 hours resulted in a 74% NMR yield and a 64% isolated yield (entry 17). Finally, modification of the catalyst from carboxylic acid **3d** to benzylamide **3e** was appropriate since **2a** could be isolated in 82% yield (entry 18). Unfortunately, the product yield dropped to 50–60% when the catalyst loading was decreased to 5–10 mol%.

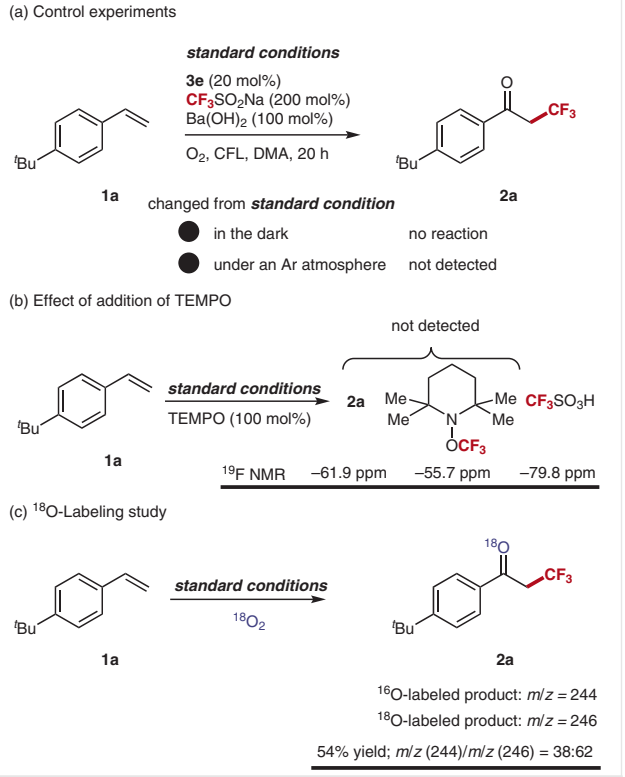
Using the optimized conditions, we investigated the keto-trifluoromethylation of various styrenes (**1**) (Scheme 2). The reaction was not significantly affected by the electronic nature of the substituents and worked well with styrenes bearing electron-donating substituents (**1a–f**) and electron-withdrawing substituents (**1g–j**). In contrast, a styrene with an *o*-Me group (**1e**) significantly suppressed the formation of the desired C–CF_3 bond, whereas *m*-Me (**1d**) and *p*-Me (**1c**) substituents did not. In the cases of styrenes bearing protecting groups such as acetal (**1l**) and TBS (**1m**), keto-trifluoromethylation occurred only at the styrene moiety. Remarkably, a styrene bearing a chloromethyl group (**1n**), which can be oxidized to the aldehyde, could be keto-trifluoromethylated in moderate yield. Furthermore, the products derived from α,β-substituted olefins are ubiquitous in synthetic and medicinal chemistry; thus, we applied our keto-trifluoromethylation conditions to the reactions of these olefins. Notably, indene (**1o**) and 1,2-dihydronaphthalene (**1p**) were successfully converted into cyclic ketones containing CF_3 groups. Gratifyingly, α-methylstyrene (**1q**) also reacted as efficiently as the unsubstituted styrene, affording the corresponding β-trifluoromethyl alcohol in 90% yield. The attempted keto-trifluoromethylation of 1-octene resulted in no reaction.

Numerous control experiments were conducted to gain insight into the mechanistic pathway (Scheme 3). Visible light irradiation and an oxygen environment were found to be essential for this transformation. Complete suppression of this process was observed when the reaction was conducted under the optimized conditions with the addition of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO). Furthermore, TEMPO–CF_3, a commonly observed CF_3 radical adduct, was not detected in the reaction mixture by ^{19}F NMR (–55.7 ppm) spectroscopy, while another compound, identified as CF_3SO_3H, was observed (–79.8 ppm). This indicated that the single-electron oxidation of CF_3SO_2Na could be accelerated by excited AQN*, suggesting that AQN plays important roles in the reaction process.[13]



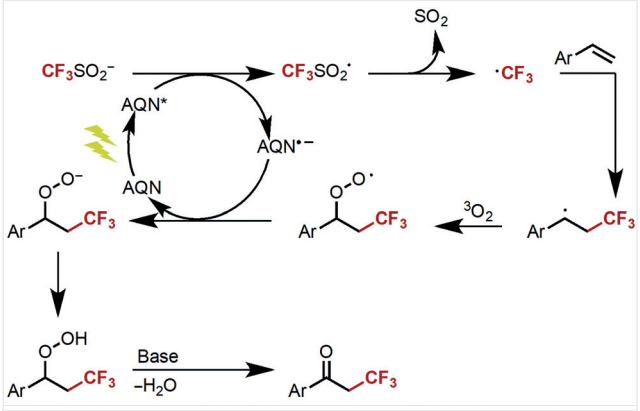
Scheme 2 Substrate scope of the organocatalytic keto-trifluoromethylation of styrenes. Unless otherwise noted, the reaction was conducted with 0.3 mmol of **1**, 0.6 mmol of CF_3SO_2Na (200 mol%), 0.3 mmol of $Ba(OH)_2$ (100 mol%), and 0.06 mmol of AQN-2-CONHBn (**3e**) in 4.0 mL of DMA under an oxygen atmosphere and irradiation with a 21 W CFL. Yields are those of isolated products. [a] Reaction performed with 4.0 equivalents of CF_3SO_2Na.

An $^{18}O_2$-labeling study was also conducted under an $^{18}O_2$ atmosphere. The reaction afforded the corresponding product in 55% yield and formation of the ^{18}O-labeled keto-trifluoromethylation product was confirmed by GC–MS analysis; the ^{16}O-labeled product was also observed, probably due to remaining $^{16}O_2$ in the solvent. This indicated that the oxygen atom in the target molecule originated from molecular oxygen.



Scheme 3 Mechanistic investigation of AQN-catalyzed keto-trifluoromethylation

Based on these results, a plausible reaction mechanism for the keto-trifluoromethylation of styrene catalyzed by AQN can be proposed (Scheme 4). First, irradiation with visible light causes excitation of AQN to AQN*, which undergoes SET oxidation of trifluoromethylsulfinate ($CF_3SO_2^-$) to generate the trifluoromethylsulfinic radical ($CF_3SO_2^{\bullet}$), accompanied by formation of $AQN^{\bullet-}$.[13] The active trifluoromethyl radical ($CF_3^{\bullet}$) is then generated through decomposition of the unstable trifluoromethylsulfinic radical to liberate SO_2. Subsequently, the trifluoromethyl radical attacks styrene to provide an α-benzyl radical intermediate, which reacts with triplet oxygen to generate a peroxy radical intermediate. SET oxidation of the peroxy radical should then occur through reduction of $AQN^{\bullet-}$ to AQN (ground state), leading to the peroxy anion. Finally, protonation of the peroxy anion and base-mediated decomposition of peroxide leads to the formation of the α-trifluoromethylated ketone.[15]



Scheme 4 A plausible mechanism for keto-trifluoromethylation of styrene

In conclusion, we have developed the first organocatalytic system using AQN-2-CONHBn for keto-trifluoromethylation under an oxygen atmosphere. Various styrenes as well as cyclic olefins and 1,1-disubstituted alkenes easily afforded the corresponding α-trifluoromethyl ketones in high selectivity and moderate to high yields. The anthraquinone-based organophotoredox catalyst is readily available, inexpensive, and environmentally friendly. Thus, we expect that the present study will expand the potential of (transition)-metal-free transformations of C–C unsaturated bonds.

All dry solvents were obtained from Kanto Kagaku Co., Ltd., Wako Pure Chemical Industries, Ltd. Other chemicals used were of reagent grade and were obtained from Tokyo Kasei Kogyo Co., Ltd., Wako Pure Chemical Industries, Ltd., Nacalai Tesque and Sigma Aldrich Co., Ltd. Thin-layer chromatography (TLC) was carried out on precoated silica gel plates (MERCK, silica gel F-254, 0.5 mm). After elution, the plates were visualized under UV radiation (254 nm) using a Handy UV lamp SLUV-4 254 nm (AS ONE Co.). Preparative thin-layer chromatography (PTLC) was carried out on precoated silica gel plates (MERCK, silica gel F-254, 0.5 mm). Flash column chromatography was performed with Kanto silica gel 60N (spherical, neutral, 40–50 mm) and on a Biotage Isolera® automated chromatography system using normal phase cartridges with YMC*GEL SIL (YMC Co., Ltd., 25 μm). Irradiation of reactions with visible light was achieved with a 21 W fluorescent lamp (TOSHIBA Co., Ltd., EFD21EN). Melting points were obtained using a Yanagimoto micro melting point apparatus. Infrared spectra were recorded on a Perkin Elmer Spectrum 100 FTIR and are reported in reciprocal centimeters (cm^{-1}). ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were obtained with JEOL ECA 500 and JEOL AL 400 spectrometers at room temperature in $CDCl_3$ as the solvent (500 MHz and 400 MHz for ^1H NMR, 125 MHz and 100 MHz for ^{13}C NMR, and 470 MHz for ^{19}F NMR). Chemical shifts (δ) are expressed in parts per million and are internally referenced [0.00 ppm (tetramethylsilane) for ^1H NMR and 77.0 ppm ($CDCl_3$) for ^{13}C NMR]. High-resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100TD spectrometer. GC -MS was performed using a JEOL JMS-T100GC instrument.

1-[4-(*tert*-Butyl)phenyl]-3,3,3-trifluoropropan-1-one (2a);[16] Typical Procedure

A Pyrex test tube (16.5 cm × 1.5 cm) containing a solution of 4-*tert*-butylstyrene (**1a**) (48.1 mg, 0.3 mmol, 1.0 equiv), sodium trifluoromethanesulfinate (93.6 mg, 0.6 mmol, 2.0 equiv), AQN-2-CONHBn (**3e**) (20.6 mg, 0.06 mmol, 0.2 equiv), $Ba(OH)_2$ (51.4 mg, 0.3 mmol, 1.0 equiv) and dry DMA (4 mL) was equipped with an O_2 balloon. The stirred reaction mixture was irradiated for 30 h at room temperature by a 21 W fluorescent lamp placed at a distance of 5 mm. The mixture was diluted with Et_2O (10 mL) and H_2O (10 mL) and the aqueous layer extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel (hexane/EtOAc, 94:6) provided 1-[4-(*tert*-butyl)phenyl]-3,3,3-trifluoropropan-1-one (**2a**) (60.0 mg, 0.25 mmol, 82%) as a white solid.

Mp 35–37 °C; R_f = 0.4 (*n*-hexane/EtOAc, 16:1).

IR (neat): 2963, 1692, 1232 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.6 Hz, 2 H), 7.53 (d, *J* = 8.6 Hz, 2 H), 3.79 (q, *J* = 10.1 Hz, 2 H), 1.36 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.3, 158.2, 133.2, 128.4, 125.8, 124.0 (q, *J* = 275.4 Hz), 41.9 (q, *J* = 28.6 Hz), 35.2, 31.0.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.87 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 244.11 $[M]^+$.

3,3,3-Trifluoro-1-(4-methoxyphenyl)propan-1-one (2b)[9]

Prepared according to the typical procedure. The product (62.7 mg, 0.29 mmol, 96%) was obtained as a colorless oil.

Mp 51–52 °C; R_f = 0.3 (*n*-hexane/EtOAc, 16:1).

IR (neat): 2943, 1686, 1230 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.9 Hz, 2 H), 6.98 (d, *J* = 8.9 Hz, 2 H), 3.90 (s, 3 H) 3.75 (q, *J* = 10.3 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.1, 164.3, 130.8, 128.9, 124.1 (q, *J* = 274.2 Hz), 114.1, 55.6, 41.8 (q, *J* = 27.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.83 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 218.06 $[M]^+$.

3,3,3-Trifluoro-1-(*p*-tolyl)propan-1-one (2c)[9]

Prepared according to the typical procedure. The product (60.0 mg, 0.3 mmol, 99%) was obtained as a white solid.

Mp 61–61.5 °C; R_f = 0.4 (*n*-hexane/EtOAc, 16:1).

IR (neat): 2952, 1685, 1226 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.3 Hz, 2 H), 7.31 (d, *J* = 8.3 Hz, 2 H), 3.78 (q, *J* = 9.9 Hz, 2 H), 2.44 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.3, 145.3, 133.4, 129.6, 128.5, 124.0 (q, *J* = 274.2 Hz), 41.9 (q, *J* = 28.2 Hz), 21.7.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.90 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 202.06 $[M]^+$.

3,3,3-Trifluoro-1-(*m*-tolyl)propan-1-one (2d)[9]

Prepared according to the typical procedure. The product (54.3 mg, 0.27 mmol, 90%) was obtained as a colorless oil

R_f = 0.3 (*n*-hexane/EtOAc, 16:1).

IR (neat): 2941, 1694, 1249 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.76 (s, 1 H), 7.74 (d, *J* = 7.5 Hz, 1 H), 7.46 (d, *J* = 7.5 Hz, 1 H), 7.39 (t, *J* = 7.5 Hz, 1 H), 3.80 (q, *J* = 9.9 Hz, 2 H), 2.44 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.9, 138.9, 135.8, 135.0, 128.79, 128.77, 125.6, 124.0 (q, *J* = 275.4 Hz), 42.1 (q, *J* = 28.6 Hz), 21.3.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.94 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 202.06 $[M]^+$.

3,3,3-Trifluoro-1-(*o*-tolyl)propan-1-one (2e)[9]

Prepared according to the typical procedure. The product (34.2 mg, 0.17 mmol, 57%) was obtained as a colorless oil.

R_f = 0.3 (*n*-hexane/EtOAc, 16:1).

IR (neat): 2970, 1696, 1226 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 7.8 Hz, 1 H), 7.46 (t, *J* = 7.8 Hz, 1 H), 7.33–7.30 (m, 2 H), 3.76 (q, *J* = 9.9 Hz, 2 H), 2.55 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.7, 139.6, 135.8, 132.6, 132.5, 128.9, 125.9, 124.0 (q, *J* = 275.4 Hz), 44.3 (q, *J* = 27.4 Hz), 21.6.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.96 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 202.06 $[M]^+$.

1-(Benzo[*d*][1,3]dioxol-5-yl)-3,3,3-trifluoropropan-1-one (2f)[17]

Prepared according to the typical procedure. The product (39.7 mg, 0.17 mmol, 57%) was obtained as a white solid.

Mp 91–93 °C; R_f = 0.4 (*n*-hexane/EtOAc, 4:1).

IR (neat): 2924, 1675, 1283 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.51 (dd, *J* = 8.0, 1.7 Hz, 1 H), 7.43 (d, *J* = 1.7 Hz, 1 H), 6.89 (d, *J* = 8.0 Hz, 1 H), 6.09 (s, 2H), 3.72 (q, *J* = 9.9 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 187.7, 152.8, 148.6, 130.7, 125.1, 124.0 (q, *J* = 277.1 Hz), 108.0, 107.9, 102.2, 41.9 (q, *J* = 28.8 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.90 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 232.02 $[M]^+$.

1-(4-Bromophenyl)-3,3,3-trifluoropropan-1-one (2g)[9]

Prepared according to the typical procedure. The product (64.8 mg, 0.24 mmol, 81%) was obtained as a white solid.

Mp 73–75 °C; R_f = 0.5 (*n*-hexane/EtOAc, 9:1).

IR (neat): 2956, 1699, 1223 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.9 Hz, 2 H), 7.67 (d, *J* = 8.9 Hz, 2 H), 3.78 (q, *J* = 9.9 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.8, 134.4, 132.3, 129.8, 129.7, 123.8 (q, *J* = 275.4 Hz), 42.1 (q, *J* = 27.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.88 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 265.96 $[M]^+$.

1-(4-Chlorophenyl)-3,3,3-trifluoropropan-1-one (2h)[9]

Prepared according to the typical procedure. The product (53.6 mg, 0.24 mmol, 80%) was obtained as a white solid.

Mp 55–57 °C; R_f = 0.3 (*n*-hexane/EtOAc, 16:1).

IR (neat): 2925, 1699, 1224 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.6 Hz, 2 H), 7.50 (d, *J* = 8.6 Hz, 2 H), 3.78 (q, *J* = 9.9 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.5, 140.9, 134.0, 129.8, 129.3, 123.8 (q, *J* = 275.4 Hz), 42.1 (q, *J* = 27.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.88 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 222.01 $[M]^+$.

Methyl 4-(3,3,3-Trifluoropropanoyl)benzoate (2i)[9]

Prepared according to the typical procedure. The product (47.2 mg, 0.19 mmol, 64%) was obtained as a white solid.

Mp 78–80 °C; R_f = 0.2 (*n*-hexane/EtOAc, 8:1).

IR (neat): 2961, 1694, 1224 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.6 Hz, 2 H), 7.99 (d, *J* = 8.6 Hz, 2 H), 3.95 (s, 3 H), 3.83 (q, *J* = 9.7 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.3, 165.9, 138.7, 134.8, 130.0, 128.2, 123.7 (q, *J* = 275.4 Hz), 52.6, 42.3 (q, *J* = 27.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.98 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 246.05 $[M]^+$.

1-(4-Cyanophenyl)-3,3,3-trifluoropropan-1-one (2j)[9]

Prepared according to the typical procedure. The product (26.2 mg, 0.12 mmol, 42%) was obtained as a white solid.

Mp 129–131 °C; R_f = 0.3 (*n*-hexane/EtOAc, 8:1).

IR (neat): 2955, 1661, 1225 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.6 Hz, 2 H), 7.84 (d, *J* = 8.6 Hz, 2 H), 3.83 (q, *J* = 9.7 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.5, 138.5, 132.8, 128.8, 123.5 (q, *J* = 277.8 Hz), 117.53, 117.49, 42.5 (q, *J* = 28.8 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.83 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 213.04 $[M]^+$.

3,3,3-Trifluoro-1-phenylpropan-1-one (2k)[9]

Prepared according to the typical procedure. The product (50.6 mg, 0.29 mmol, 96%) was obtained as a white solid.

Mp 38–40 °C; R_f = 0.3 (*n*-hexane/EtOAc, 16:1).

IR (neat): 2948, 1683, 1226 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 7.7 Hz, 2 H), 7.66 (t, *J* = 7.7 Hz, 1 H), 7.52 (t, *J* = 7.7 Hz, 2 H), 3.81 (q, *J* = 9.9 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.7, 135.8, 134.2, 128.9, 128.3, 124.0 (q, *J* = 275.4 Hz), 42.1 (q, *J* = 28.6 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.92 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 188.04 $[M]^+$.

3,3,3-Trifluoro-1-[4-(1,3-dioxolan-2-yl)phenyl]propanone (2l)

Prepared according to the typical procedure. The product (34.8 mg, 0.14 mmol, 45%) was obtained as a white solid.

Mp 104.0–105.0 °C; R_f = 0.2 (*n*-hexane/EtOAc, 8:1).

IR (neat): 2952, 1724, 1663, 1226 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.6 Hz, 2 H), 7.63 (d, *J* = 8.6 Hz, 2 H), 5.88 (s, 1 H), 4.16–4.06 (m, 4 H), 3.81 (q, *J* = 9.7 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.4, 144.1, 136.2, 128.4, 127.0, 123.9 (q, *J* = 277.1 Hz), 102.6, 65.4, 42.2 (q, *J* = 27.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.90 (t, *J* = 10.8 Hz, 3 F).

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{12}F_3O_3$: 261.0733; found: 261.0731.

1-[4-(1-{[(1,1-Dimethylethyl)dimethylsilyl]oxy}ethyl)phenyl]-3,3,3-trifluoropropan-1-one (2m)

Prepared according to the typical procedure. The product (43.0 mg, 0.12 mmol, 41%) was obtained as a pale yellow oil.

R_f = 0.3 (*n*-hexane/EtOAc, 20:1).

IR (neat): 2951, 1660, 1287 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 4.93 (q, *J* = 8.0 Hz, 1H), 3.89 (q, *J* = 9.7 Hz, 2H), 1.42 (d, *J* = 8.0 Hz, 3H), 0.91 (s, 9H), 0.07 (s, 3H), –0.01 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.3, 153.7, 134.4, 128.5, 125.6, 124.0 (q, *J* = 276.6 Hz), 70.3, 42.0 (q, *J* = 27.4 Hz), 27.0, 25.8, 18.2, –4.86, –4.92.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.90 (t, *J* = 10.8 Hz, 3 F).

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{26}F_3O_2Si$: 347.1649; found: 347.1642.

3,3,3-Trifluoro-1-(4-chloromethylphenyl)propan-1-one (2n)

Prepared according to the typical procedure. The product (31.9 mg, 0.14 mmol, 45%) was obtained as a yellow solid.

Mp 78–80 °C; R_f = 0.3 (*n*-hexane/EtOAc, 20:1).

IR (neat): 2943, 1663, 1224 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 8.0 Hz, 2 H), 7.54 (d, *J* = 8.0 Hz, 2 H), 4.63 (s, 2 H), 3.81 (q, *J* = 9.7 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 189.1, 143.6, 135.5, 129.0, 128.8, 124.9 (q, *J* = 277.1 Hz), 45.0, 42.1 (q, *J* = 28.8 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –61.86 (t, *J* = 9.7 Hz, 3 F).

HRMS (DART): *m*/*z* $[M + H]^+$ calcd for $C_{10}H_9ClF_3O$: 237.0289; found: 237.0280.

2-(Trifluoromethyl)-2,3-dihydro-1*H*-inden-1-one (2o)[9]

Prepared according to the typical procedure. The product (38.3 mg, 0.19 mmol, 64%) was obtained as a white solid.

Mp 56–58 °C; R_f = 0.3 (*n*-hexane/EtOAc, 8:1).

IR (neat): 2948, 1721, 1225 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.0 Hz, 1 H), 7.67 (dd, *J* = 7.5, 7.4 Hz, 1 H), 7.53 (d, *J* = 7.4 Hz, 1 H), 7.44 (dd, *J* = 8.0, 7.5 Hz, 1 H), 3.49–3.39 (m, 2 H), 3.34–3.29 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 196.9, 152.1, 135.8, 128.2, 126.5, 124.9 (q, *J* = 276.6 Hz), 124.7, 124.4, 49.7 (q, *J* = 27.4 Hz), 27.6 (q, *J* = 2.8 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –67.63 (d, *J* = 8.1 Hz, 3 F).

MS (EI+): *m*/*z* = 200.04 $[M]^+$.

2-(Trifluoromethyl)-3,4-dihydronaphthalen-1(2*H*)-one (2p)[9]

Prepared according to the typical procedure. The product (51.8 mg, 0.24 mmol, 81%) was obtained as a colorless oil

R_f = 0.5 (*n*-hexane/EtOAc, 9:1).

IR (neat): 2950, 1663, 1287 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, *J* = 8.0 Hz, 1 H), 7.54 (dd, *J* = 8.0, 7.5 Hz, 1 H), 7.36 (t, *J* = 7.5 Hz, 1 H), 7.28 (d, *J* = 7.5 Hz, 1 H), 3.29 (ddq, *J* = 12.0, 8.6, 4.6 Hz, 1 H), 3.15–3.04 (m, 2 H), 2.51 (dq, *J* = 13.8, 4.6 Hz, 1 H), 2.28 (dddd, *J* = 13.2, 12.0, 10.3, 5.7 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 190.2, 143.1, 134.2, 131.9, 128.8, 127.8, 127.1, 125.0 (q, *J* = 279.0 Hz), 50.8 (q, *J* = 25.0 Hz), 27.5, 23.4 (q, *J* = 2.8 Hz).

^{19}F NMR (470 MHz, $CDCl_3$): δ = –67.43 (d, *J* = 8.1 Hz, 3 F).

MS (EI+): *m*/*z* = 214.06 $[M]^+$.

4,4,4-Trifluoro-2-phenylbutan-2-ol (2q)[18]

Prepared according to the typical procedure. The product (54.8 mg, 0.27 mmol, 90%) was obtained as a colorless oil.

R_f = 0.3 (*n*-hexane/EtOAc, 10:1).

IR (neat): 2927, 1261 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 (dd, *J* = 8.0, 1.2 Hz, 2 H), 7.37 (t, *J* = 8.0 Hz, 2 H), 7.29 (td, *J* = 8.0, 1.2 Hz, 1 H), 2.70–2.60 (m, 2 H), 2.21 (s, 1 H), 1.71 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 146.1, 128.4, 127.4, 125.8 (q, *J* = 276.6 Hz), 124.3, 71.9, 46.5 (q, *J* = 25.0 Hz), 29.6.

^{19}F NMR (470 MHz, $CDCl_3$): δ = –59.96 (t, *J* = 10.8 Hz, 3 F).

MS (EI+): *m*/*z* = 204.06 $[M]^+$.

Synthesis of the Anthraquinone-Based Photocatalyst: *N*-Benzyl-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (3e)[19]

To a solution of AQN-2-CO_2H (1.0 g, 4.0 mmol) in toluene (20 mL) was added $SOCl_2$ (0.43 mL, 6.0 mmol, 1.5 equiv) and one drop of DMF at room temperature. The resulting solution was heated at reflux for 2 h. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was diluted with CH_2Cl_2 (10 mL) and added to a solution of benzylamine (0.66 mL, 6.0 mmol, 1.5 equiv) and Et_3N (0.83 mL, 6.0 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL) at room temperature. After being stirred for 17 hours, the reaction mixture was diluted with CH_2Cl_2 (20 mL) and H_2O (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography on silica gel ($CHCl_3$/MeOH, 95:5) provided *N*-benzyl-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide (1.11 g, 3.3 mmol, 82%) as an off-white solid.

Mp >200 °C; R_f = 0.2 ($CHCl_3$/MeOH, 95:5).

IR (neat): 2925, 1674, 1329, 1284, 1134, 1003, 706 cm^{-1}.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.55 (t, *J* = 5.7 Hz, 1 H), 8.69 (s, 1 H), 8.37 (d, *J* = 8.0 Hz, 1 H), 8.29 (d, *J* = 8.6 Hz, 1 H), 8.25–8.21 (m, 2 H), 7.96–7.94 (m, 2 H), 7.37–7.25 (m, 4 H), 4.54 (d, *J* = 5.7 Hz, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 182.2, 164.7, 139.3, 139.1, 134.69, 134.67, 133.15, 133.12, 133.08, 132.9, 128.4, 127.4, 127.2, 126.90, 126.87, 126.84, 125.6, 42.9; (two carbon atoms were overlapped).

MS (DART): *m*/*z* = 342.1 $[M + H]^+$.

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Supporting Information

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