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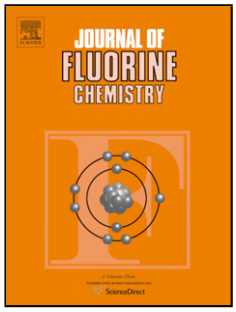

Title: A Green and Transition-Metal-Free Light-mediated Trifluoromethylation Reaction of Coumarins

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A Green and Transition-Metal-Free Light-mediated Trifluoromethylation Reaction of Coumarins

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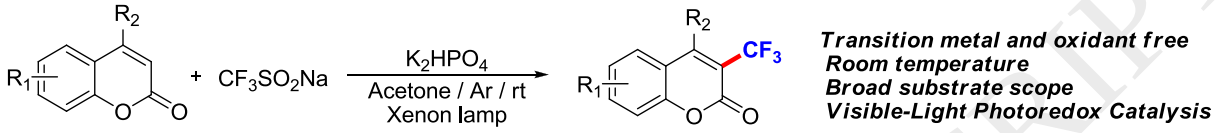
Grapgical abstract



An efficient and practical approach to the photoinduced trifluoromethylation of coumarins in the absence of additional metal photocatalyst was developed with easily handled CF_3SO_2Na. Significantly, this photochemical strategy employed acetone, one of the most widely used and cheapest organic solvents, instead of expensive metal catalyst or dangerous peroxides to generate CF_3 radical, which provides a green route to cost-effective large-scale synthesis of trifluoromethylated chemicals.

Highlights

- Coumarin is a common motif in a variety of natural products and/or synthetic molecules with interesting biological activities and technological applications and the trifluoromethyl coumarins are great attractive in the pharmaceutical and agrochemical fields.
- Visible light photoredox synthesis, employing photosensitizers have unrivaled advantages in terms the potential green chemistry.
- The combination of green visible light photocatalysis and cost-effective CF_3SO_2Na (Langlois reagent) has considerable interest in both academic and industry.

Abstract

A simple, metal- and oxidant-free photo catalysis strategy for the direct trifluoromethylation of coumarins with inexpensive sodium triflinate (Langlois reagent, CF_3SO_2Na) as the CF_3 source under xenon lamp irradiation is described. The reaction proceeds under ambient conditions and affords the corresponding products in moderate yields. The acetone can be used as low-cost radical initiator to generate CF_3 radicals from sodium triflinate efficiently.

Key words: Trifluoromethylation; Coumarins; Photo-Catalyzed; Transition-Metal-Free; Acetone; Langlois reagent

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1. Introduction

Coumarin is a common motif in a variety of natural products and/or synthetic molecules with interesting biological activities and technological applications [1]. In addition, owing to their remarkable fluorescent properties, coumarins also have been widely utilized in photosensitive polymeric materials [2], Lasers [3], and fluorescent probes for metal ions [4].

The trifluoromethyl compounds are great interest in the pharmaceutical and agrochemical fields due to their excellent performance in regulating the physical, chemical, and biological properties of potential drug candidates [5]. It is therefore greatly desirable to develop new practical and efficient methods for incorporating the CF_3 substituent into organic substrates [6]. During the past decade, a wide range of trifluoromethylation approaches of arenes and heteroarenes have been disclosed based on transition-metal catalyzed coupling strategies [7] and photoredox induced radical trifluoromethylation protocols [8]. α,β-Unsaturated carbonyls that contain an electron-deficient carbon–carbon double bond are not only versatile synthetic intermediates but also a structural motif in biologically active molecules [9]. Coumarin compounds contain the α,β-unsaturated carbonyl subunit. However, 3-trifluoromethyl coumarins were not easily accessible since 4-trifluoromethyl coumarins [10]. Recently Piasecka-Maciejewska [11] reported the preparation of 3-trifluoromethylcoumarins using 3-carboxylic acid coumarins and sulfur tetrafluoride. Wang [12] developed a copper-catalyzed trifluoromethylation of quinone with expensive Togni`s reagent. Nadia O. Ilchenko [13] found that quinones undergo copper-mediated C–H trifluoromethylation reactions using a hypervalent iodine reagent. In 2014, Zou [14] reported a general straightforward method for trifluoromethylation of coumarins with CF_3SO_2Na mediated by $Mn(OAc)_3$. Also, in 2015, Our group [15] reported a mild and fast method for Cu(I)-catalyzed trifluoromethylation of coumarins by using CF_3SO_2Na–TBHP partners in a continuous-flow system. Also, some reactions on the trifluoromethylation of coumarin derivatives were reported [16][17].

A variety of trifluoromethylations in the presence of a suitable photosensitizer, including the precious Ru and Ir complexes [18] under visible-light irradiation have been disclosed. There are particular advantages for the combination of green visible light photocatalysis and cost-effective CF_3SO_2Na (Langlois reagent) [19] as trifluoromethylating reagents, offering a mild route to construct a C-CF_3 bond. In order to preserve expensive Ru- and Ir- photocatalysts, organic transformations under visible light irradiation without additional photocatalysts have received considerable attention. Recently, Li`s group reported a simple, metal and oxidant-free

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photochemical strategy for the direct trifluoromethylation of arenes from CF_3SO_2Na, in which photoexcited aliphatic ketones act as promising radical initiators under light irradiation [20]. And in 2018, they just applied their method to the synthesis of 6-trifluoromethylphenanthridines from isocyanides [21].

The trifluoromethylation of coumarins under visible light irradiation in the absence of additional metal photocatalyst is a more challenging access to coumarin scaffolds in an efficient and atom-economical manner. Herein, we report a simple, transition-metal and oxidant free photochemical strategy for the direct trifluoromethylation of coumarins under xenon lamp irradiation using the inexpensive CF_3SO_2Na as the CF_3 source.

2. Results and discussion

Our investigation commenced with the trifluoromethylation of coumarin using CF_3SO_2Na (4.0 equiv) as a CF_3 source, and acetone (2.0 mL) as a solvent at the room temperature under an argon atmosphere (Table 1). After 24 h reaction, the desired trifluoromethylation product was obtained in 65% yield (Table 1, entry 1). Encouraged by this result, we then reduced the reaction time to 12h and found that the yield remains without change. When further cutting down the reaction time to 6 h, the yield of trifluoromethylation product was significant decreased to 41% (Table 1, entries 2-3). It should be noted that replacing K_2HPO_4 with other bases including K_3PO_4, K_2CO_3, Cs_2CO_3 and KOH leads to lower yields (Table 1, entry 2, entries 4-7). By slightly reducing the amount of the CF_3SO_2Na also resulted in a lower yield of 41% (Table 1, entry 8). Various solvents were then screened, acetone was the most suitable one (Table 1, entry 2, entries 9-12). Especially, No further increment of the yield was found with dried acetone as solvent (water free, Table 1, entry 9). Finally, when the reaction was carried out without irradiation, no desired product was obtained (Table 1, entry 13). The optimized conditions for this process were defined as the use of **1a** (0.2 mmol) with CF_3SO_2Na (4 equiv), and K_2HPO_4 (2 equiv) in acetone (2 mL) at the room temperature under argon atmosphere with the irradiation of a Xenon lamp for 12 h.

With optimized condition in hand, the scope of substrates was explored and the results are summarized in Scheme 2. A wide variety of coumarins bearing either electron-withdrawing or electron-donating groups at the aryl ring could be transformed into the corresponding trifluoromethylation products in moderate to good yields. The halogens (Cl, Br), nitro, methyl, methoxy and ester groups were tolerated in this system owing to the mildness of the reaction

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conditions. The trifluoromethylation of coumarins bearing methyl and t-butyl at the 6-position were effective and resulted in moderate to good yields (**2b, 2c, 2d**). Good yields could also be obtained with a 7-methoxyl substituted derivative, giving 67% yield (**2e**). In the case of a weak electron-withdrawing group, such as acetoxyl, chlorine and bromo at the 6-position, moderate yields of 62%, 54% and 56% were obtained respectively (**2f**, **2g**, **2h**). However, the strong electron-withdrawing group nitro at the 6-position afforded a poor yield of 41% (**2i**). For 4-phenyl-coumarins, the family members of coumarin derivatives, their corresponding trifluoromethyl products were obtained in moderate yields (**2k**-**2o,** 55-67%). Notably, the trifluoromethylation product of quinolinone afforded a good yield of 65% (**2p**).

Based on our experiment and previous work[15][20], a reaction mechanism was proposed (Scheme 3), which included a radical initial, followed by a radical addition, and the loss of hydrogen atom to aromatization. First, under the irradiation of the xenon lamp, acetone, acted as a photosensitizer, absorbs resonant photons, a lone pair electron transits from oxygen to the carbonyl carbon. Next the resulting electron-deficient oxygen atom of the carbonyl may abstract one electron from CF_3SO_2Na to generate a CF_3 radical, which is called the photoreduction of ketone. Then the CF_3 radical attacked the α-position of coumarin (**1**), the more stable free radical intermediate (**A**) was formed. Afterwards the radical intermediate (**A**) interacted with the reduction product of acetone, the reduction product of acetone captured the hydrogen radical and absorbed SO_2 to the salt. At last the radical intermediate lost the hydrogen radical and formed a double bond to obtain 3-trifluoromethyl coumarin (**2**).

3. Conclusion

In summary, an efficient and practical approach to the photoinduced trifluoromethylation of coumarins in the absence of additional metal photocatalyst was developed with easily handled CF_3SO_2Na. Significantly, this photochemical strategy employed acetone, one of the most widely used and cheapest organic solvents, instead of expensive metal catalyst or dangerous peroxides to generate CF_3 radical, which provides a green route to cost-effective large-scale synthesis of trifluoromethylated chemicals.

4. Experimental

4.1 General

All reagents unless otherwise noted were obtained from commercial sources and used without further purification. Sodium Trifluoromethanesulfinate (>95.0%) was used without any

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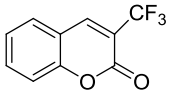
purification. Reactions were monitored by thin-layer chromatography (TLC) on silica gel plates and visualization of the plates was performed under UV light (254 nm and 365nm). Further flash column chromatography was performed on silica gel (200-300 mesh). ^{1}H NMR and ^{19}F NMR spectra were recorded on a Bruker-500 or 400 NMR spectrometer using TMS as an internal standard and the external standard of ^{19}F NMR uses trifluoroacetic acid. ^{13}C NMR spectra were recorded on a Bruker NMR(126M). Chemical shifts for ^{1}H NMR were reported in ppm relative to TMS. All ^{13}C NMR spectra were reported in ppm relative to deuterated chloroform (77.00 ppm). The following abbreviations are used to set multiplicities: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, q = quartet, tq = triplet of quartets, qt = quartet of triplets, and m = multiplet. Coupling constants (J) were reported in Hertz (Hz). GC-MS data were also recorded. High-resolution mass spectrometry data were recorded on a high-resolution mass spectrometer in the ESI mode.

To a tube were added **1a** (1.0 equiv), CF_3SO_2Na(4.0 equiv), K_2HPO_4, Acetone (2 mL) . Then the tube was evacuated and backfilled with argon for three times. The tube around condensate water was stirred at room temperature in argon with the irradiation of Xenon lamp for 12 h. After the reaction was finished, the mixture was washed with saturated sodium chloride solution and then extracted with ethyl acetate for three times. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure, then purified by chromatography on silica gel.

4.2 Characterization of compounds

3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2a).



White powder, 27.4 mg, 64%; mp 130-131^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 6.7 Hz, 1H), 7.44 – 7.34 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.85 (s), 154.62 (s), 143.32 (q, *J* = 4.8 Hz), 134.42 (s), 129.47 (s), 125.26 (s), 121.33 (q, *J* = 272.0 Hz), 117.68 (q, *J* = 33.4 Hz), 116.96 (s), 116.76 (s).^{19}F NMR (470 MHz, $CDCl_3$): δ -66.18 (s). GC-MS (EI, m/z): 214(M^+, 100), 186(57), 136(52), 63(34). IR (KBr), ν 3120 (C=C-H), 1755 (C=O), 1628 (C=C) cm^{-1}.

6-Methyl-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2b).

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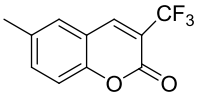
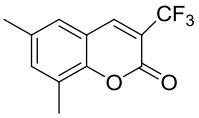


White powder, 26 mg, 57%; mp 141-142^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10 (s, 1H), 7.48 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.40 (s, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.12 (s), 152.83 (s), 143.26 (q, *J* = 4.9 Hz), 135.53 (s), 135.19 (s), 129.11 (s), 121.44 (q, *J* = 272.0 Hz), 117.58 (q, *J* = 33.1 Hz), 116.73 (s), 116.55 (s), 20.70 (s). ^{19}F NMR (470 MHz, $CDCl_3$) δ: -66.14 (s). GC–MS (EI, m/z): 228(M^+, 100), 200(48), 199(43), 131(43). IR (KBr), ν 3125 (C=C-H), 1750 (C=O), 1623 (C=C) cm^{-1}.

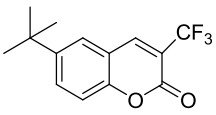
6, 8-Dimethyl-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2c).



White powder, 29 mg, 60%; mp 126-127^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.34 (s, 1H), 7.22 (s, 1H), 2.43 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.30 (s), 151.22 (s), 143.60 (q, *J* = 4.8 Hz), 136.92 (s), 134.62 (s), 126.78 (s), 126.29 (s), 121.56 (q, *J* = 271.9 Hz), 117.14 (q, *J* = 33.0 Hz), 116.36 (s), 20.61 (s), 15.26 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -66.05 (s). HRMS (ESI) m/z: $[M + Na]^+$ Calcd For $C_{12}H_9F_3O_2Na$ 265.0452; found 265.0446. IR (KBr), ν 3118 (C=C-H), 1753 (C=O), 1626 (C=C) cm^{-1}.

6-*t*-Butyl-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2d).



White powder, 37.8 mg, 70%; mp 162-163^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.73 (d, *J* = 8.8 Hz, 1H), 7.58 (s, 1H), 7.33 (d, *J* = 8.8 Hz, 1H), 1.37 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.24 (s), 152.72 (s), 148.61 (s), 143.81 (q, *J* = 4.9 Hz), 132.26 (s), 125.68 (s), 121.49 (q, *J* = 271.9 Hz), 117.38 (q, *J* = 33.3 Hz), 116.27 (s), 113.80 (s), 34.65 (s), 31.22 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -66.11 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd. For $C_{14}H_{13}F_3O_2Na$ 293.0765; found 293.0733. IR (KBr), ν 3116 (C=C-H), 1752 (C=O), 1625 (C=C) cm^{-1}.

7-Methoxyl-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2e).

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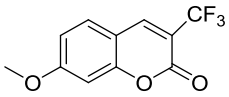
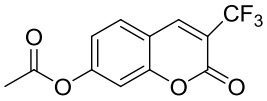


White powder, 32.7 mg, 67%; mp 124-125^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 6.93 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.84 (d, *J* = 2.3 Hz, 1H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 165.01 (s), 156.84 (s), 156.38 (s), 143.26 (q, *J* = 4.8 Hz), 130.59 (s), 121.77 (q, *J* = 271.5 Hz), 113.77 (q, *J* = 33.3 Hz), 113.76 (s), 110.38 (s), 100.74 (s), 56.04 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -65.68 (s). GC-MS (EI, m/z): 244(M^+, 78), 216(73), 201 (100), 69(40). IR (KBr), ν 3118 (C=C-H), 1750 (C=O), 1630 (C=C) cm^{-1}.

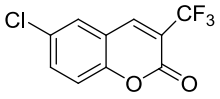
7-Acetyloxy-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2f).



White powder, 33.6 mg, 62%; mp 146-147^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (s, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.20 (d, *J* = 2.2 Hz, 1H), 7.16 (dd, *J* = 8.5, 2.2 Hz, 1H), 2.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 168.30 (s), 155.51 (s), 155.39 (s), 155.22 (s), 142.72 (q, *J* = 4.9 Hz), 130.31 (s), 121.32 (q, *J* = 272.0 Hz), 119.36 (s), 117.04 (q, *J* = 33.4 Hz), 114.47 (s), 110.52 (s), 21.11 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -66.14 (s). GC-MS (EI, m/z): 230(M^+, 26), 202(27), 43(100), 32(38). IR (KBr), ν 3123 (C=C-H), 1769, 1762 (C=O), 1621 (C=C) cm^{-1}.

6-Chloro-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2g).



White powder, 26.7 mg, 54%; mp 161-162^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.63 (d, *J* = 11.8 Hz, 2H), 7.36 (d, *J* = 8.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.18 (s), 153.04 (s), 142.07 (q, *J* = 4.9 Hz), 134.36 (s), 130.68 (s), 128.54 (s), 121.06 (q, *J* = 272.4 Hz), 118.98 (q, *J* = 33.5 Hz), 118.53 (s), 117.75 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -66.35 (s). HRMS (ESI) m/z: $[M+Na]^+$ Calcd. For $C_{10}H_4ClF_3O_2Na$ 270.9758; found 270.9750. IR (KBr), ν 3113 (C=C-H), 1743 (C=O), 1625 (C=C) cm^{-1}.

6-Bromo-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2h).

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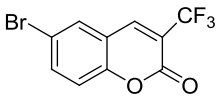
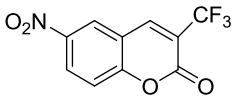


White powder, 32.6 mg, 56%; mp 162-163^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.76 (dd, *J* = 7.0, 2.2 Hz, 2H), 7.30 (d, *J* = 9.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 155.11 (s), 153.49 (s), 142.01 (q, *J* = 4.9 Hz), 137.16 (s), 131.63 (s), 121.04 (q, *J* = 272.4 Hz), 118.90 (q, *J* = 33.4 Hz), 118.75 (s), 118.25 (s), 117.84 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -66.34 (s). GC-MS (EI, m/z): 292(M^+, 71), 294(70), 157(89), 87(100). IR (KBr), ν 3115 (C=C-H), 1740 (C=O), 1627 (C=C) cm^{-1}.

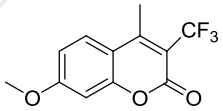
6-Nitro-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2i).



White powder, 21.2 mg, 41%; mp 188-189^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.58 (d, *J* = 2.0 Hz, 1H), 8.54 (dd, *J* = 9.1, 2.3 Hz, 1H), 8.25 (s, 1H), 7.56 (d, *J* = 9.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 157.85 (s), 154.11 (s), 144.50 (s), 142.02 (q, *J* = 5.0 Hz), 128.86 (s), 125.24 (s), δ 120.70 (q, *J* = 272.7 Hz), 120.14 (q, *J* = 34.1 Hz), 118.41 (s), 116.81 (s). ^{19}F NMR (470 MHz, $CDCl_3$): δ -66.51 (s). GC-MS (EI, m/z): 256(M^+, 59), 157(100), 87(83), 62(55). IR (KBr), ν 3135 (C=C-H), 1734 (C=O), 1646 (C=C) cm^{-1}.

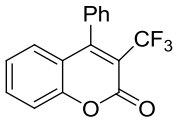
7-Methoxy-4-Methyl-3-(trifluoromethyl)-2*H*-1-Benzopyran-2-one (2j).



White powder, 35.6 mg, 69%; mp 140-141^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J* = 9.1 Hz, 1H), 6.92 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.78 (d, *J* = 2.5 Hz, 1H), 3.91 (s, 3H), 2.63 (dd, *J* = 4.2, 2.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.40 (s), 156.32 (s), 155.13 (s), 155.10 (d, *J* = 1.2 Hz), 127.16 (s), 123.15 (q, *J* = 274.7 Hz), 113.37 (s), 112.47 (s), 112.00 (q, *J* = 30.3 Hz), 100.43 (s), 55.96 (s), 15.65 (q, *J* = 4.1 Hz).^{19}F NMR (470 MHz, $CDCl_3$) δ -56.33 (q, *J* = 1.9 Hz). GC-MS (EI, m/z): 258(M^+, 68), 230(99), 215(100), 32(17). IR (KBr), ν 3105 (C=C-H), 1755 (C=O), 1621 (C=C) cm^{-1}.

4-Phenyl-3-(trifluoromethyl)-2*H*-1-benzopyran-2-one (2k).



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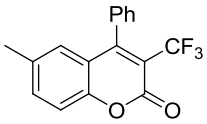
White powder, 34.8 mg, 60%; mp 132-133^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (t, J = 7.7 Hz, 1H), 7.53 (s, 3H), 7.41 (d, J = 8.3 Hz, 1H), 7.26 (s, 2H), 7.20 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 8.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.86 (d J = 2.0 Hz), 156.32 (s), 153.46 (s), 134.09 (s), 132.86 (s), 129.31 (s), 129.26 (s), 128.49 (s), 127.30 (d, J = 1.5 Hz), 124.77 (s), 121.87 (q, J = 275.4 Hz), 119.49 (s), 116.84 (s), 114.98 (q, J = 30.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.90 (s). GC–MS (EI, m/z): 290.06. IR (KBr), ν 1753 (C=O), 1620 (C=C) cm^{-1}.

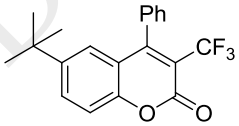
6-Methyl-4-Phenyl-3-(trifluoromethyl)-2*H*-1-benzopyran-2-one (2l).



White powder, 34 mg, 56%; mp 121-122^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 – 7.49 (m, 3H), 7.43 (dd, J = 8.4, 1.7 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.25 (dd, J = 6.5, 2.9 Hz, 2H), 6.75 (s, 1H), 2.27 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.84 (d, J = 2.0 Hz), 156.55 (s), 151.64 (s), 135.19 (s), 134.63 (s), 132.98 (s), 129.24 (s), 128.78 (s), 128.46 (s), 127.29 (d, J = 1.6 Hz), 121.95 (q, J = 275.1 Hz), 119.15 (s), 116.61 (s), 114.92 (q, J = 29.9 Hz), 20.91 (s). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.82 (s). GC–MS (EI, m/z): 304.07. IR (KBr), ν 1752 (C=O), 1623 (C=C) cm^{-1}.

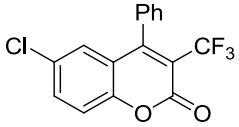
6-*t*-Butyl-4-Phenyl-3-(trifluoromethyl)-2*H*-1-benzopyran-2-one (2m).



White powder, 46.4 mg, 67%; mp 98-99^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 – 7.47 (m, 3H), 7.40 (d, J = 1.3 Hz, 1H), 7.26 – 7.21 (m, 3H), 6.93 (d, J = 8.5 Hz, 1H), 1.34 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.11 (s), 156.74 (s), 153.53 (s), 133.12 (s), 129.17 (s), 128.79 (s), 128.40 (s), 127.27 (s), 122.40 (s), 122.04 (q, J = 274.9 Hz), 116.99 (s), 114.02 (q, J = 29.9 Hz), 113.59 (s), 35.43 (s), 30.87 (s).^{19}F NMR (377 MHz, $CDCl_3$) δ -57.77 (s). GC–MS (EI, m/z): 346.12. IR (KBr), ν 1750 (C=O), 1618 (C=C) cm^{-1}.

6-Chloro-4-Phenyl-3-(trifluoromethyl)-2*H*-1-benzopyran-2-one (2n).



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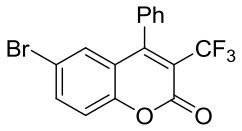
White powder, 35.6 mg, 55%; mp 137-138^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 1H), 7.41 (d, J = 1.9 Hz, 1H), 7.24 (dd, J = 6.5, 2.9 Hz, 1H), 7.17 (dd, J = 8.7, 1.9 Hz, 1H), 6.95 (d, J = 8.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.27 (d, J = 2.0 Hz), 155.71 (s), 153.61 (s), 140.38 (s), 132.44 (s), 130.22 (s), 129.56 (s), 128.66 (s), 127.21 (d, J = 1.5 Hz), 125.47 (s), 121.71 (q, J = 275.3 Hz), 118.14 (s), 117.06 (s), 114.93 (q, J = 30.4 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.95 (s). GC–MS (EI, m/z): 324.02. IR (KBr), ν 1749 (C=O), 1625 (C=C) cm^{-1}.

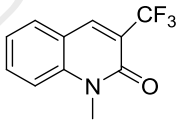
6- Bromo-4-Phenyl-3-(trifluoromethyl)-2*H*-1-benzopyran-2-one (2o).



White powder, 39.7 mg, 54%; mp 131-132^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, J = 8.8, 2.3 Hz, 1H), 7.56 (dd, J = 4.9, 1.8 Hz, 3H), 7.30 (d, J = 8.8 Hz, 1H), 7.25 (dd, J = 6.4, 3.1 Hz, 2H), 7.10 (d, J = 2.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.75 (d, J = 2.2 Hz), 155.61 (s), 152.30 (s), 136.91 (s), 132.04 (s), 131.40 (s), 129.72 (s), 128.76 (s), 127.22 (s), 121.57 (q, J = 276.1 Hz), 121.08 (s), 118.63 (s), 117.65 (s), 116.04 (q, J = 30.8 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -58.08 (s). GC–MS (EI, m/z): 367.96, 369.96. IR (KBr), ν 1755 (C=O), 1624 (C=C) cm^{-1}.

1-Methyl-3-(trifluoromethyl)-2(1*H*)-Quinolinone (2p).



White powder, 29.5 mg, 65%; mp 63-64^{0}C;

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.77 – 7.60 (m, 2H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 3.75 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.00 (s), 141.00 (s), 138.86 (q, *J* = 5.2 Hz), 133.15 (s), 130.44 (s), 122.92 (s), 122.40 (q, *J* = 271.7 Hz), 121.13 (q, *J* = 30.3 Hz), 118.06 (s), 114.40 (s), 29.52 (s). ^{19}F NMR (470 MHz, $CDCl_3$) δ -66.16 (s). GC-MS (EI, m/z): 227(M^+, 69), 179(78), 176(100), 121(68). IR (KBr), ν 3119 (C=C-H), 1720 (C=O), 1627 (C=C) cm^{-1}.

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Acknowledgements

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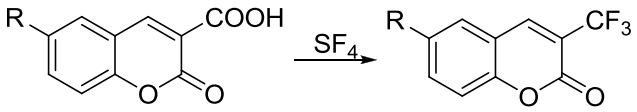
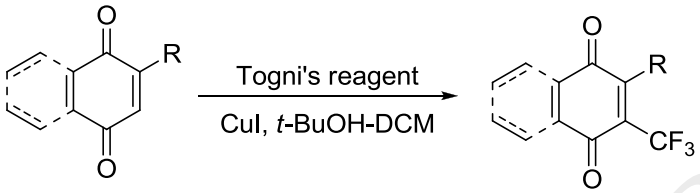
Scheme captions

Piasecka-Maciejewska, 2002



Wang, 2013



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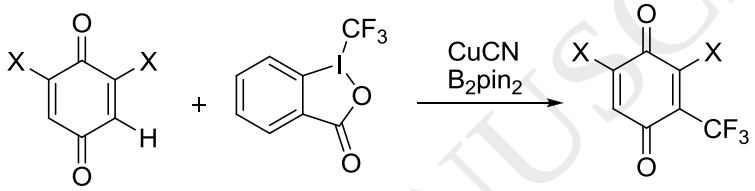
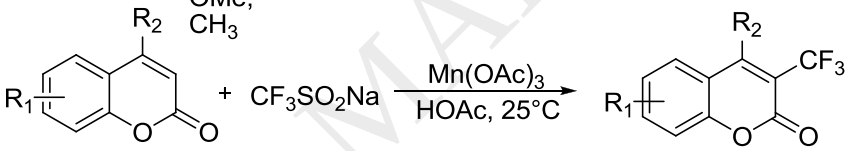
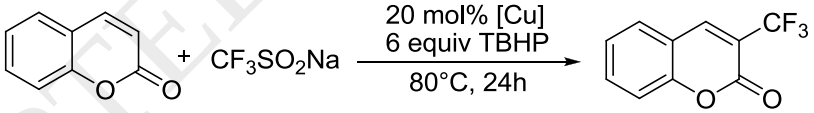


X = H, Cl, OMe, CH_3

Zou, 2014



Our group, 2015



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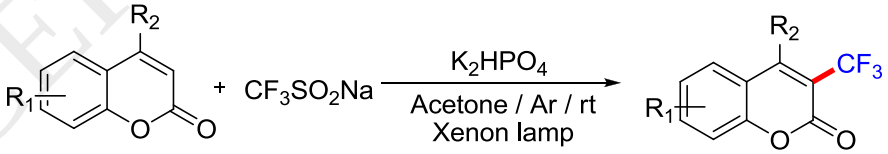

Scheme 1. Methods for the trifluoromethylation of *α,β*-unsaturated carbonyl subunit and our strategy

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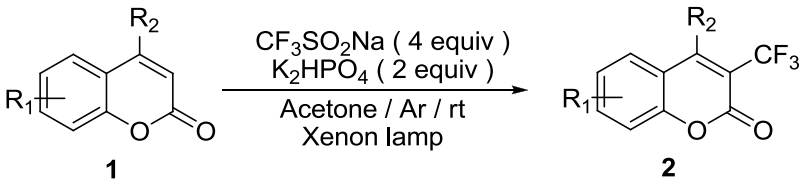
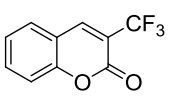
Scheme 2. Scope of Coumarins[a]





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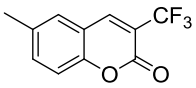

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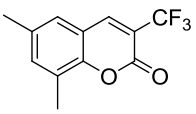

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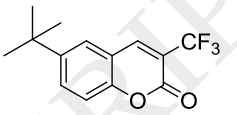

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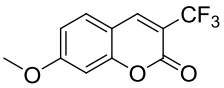

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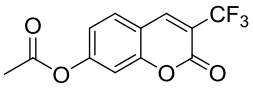

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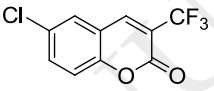

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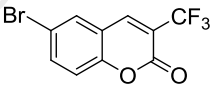

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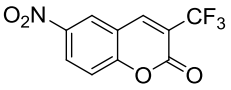

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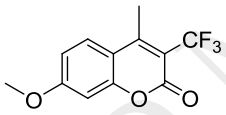

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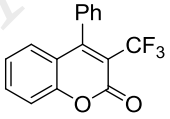

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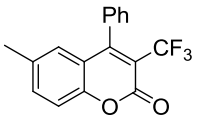

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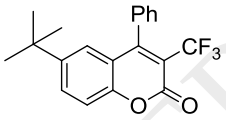
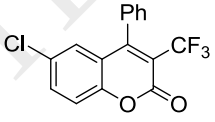
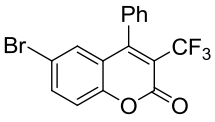


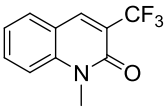
2m, 67%



2n, 55%



2o, 56%



2p, 65%

[a]Unless stated otherwise all reactions were performed in a tube around condensate water with **1** (1.0 equiv, 0.2 mmol), CF_3SO_2Na(4 equiv), K_2HPO_4(2 equiv) in acetone(2 mL) at room temperature under argon atmosphere with the irradiation of a Xenon lamp for 12 h. All listed yields are isolated yields.

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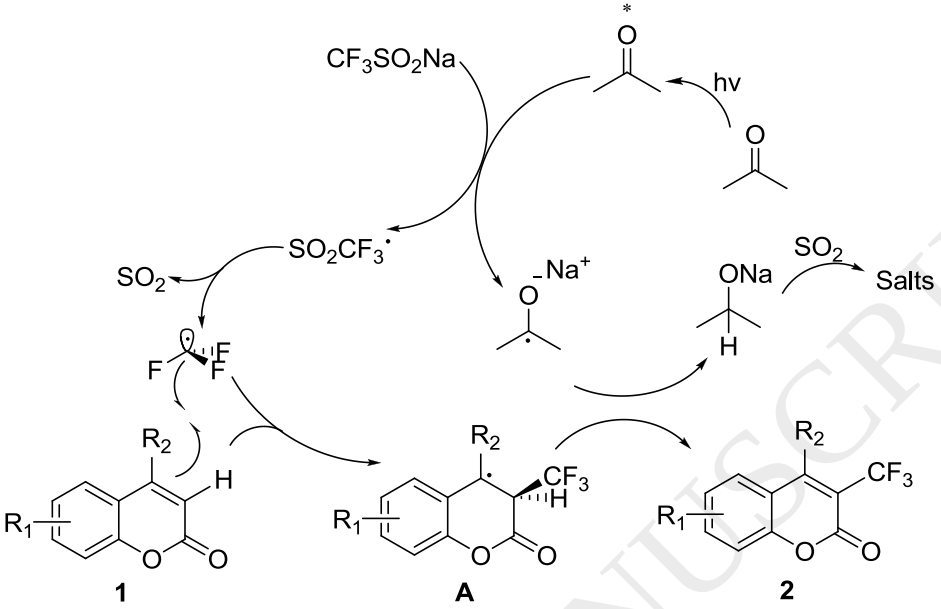
Scheme 3. Proposed Mechanism



Proposed mechanism for trifluoromethylation of Coumarins

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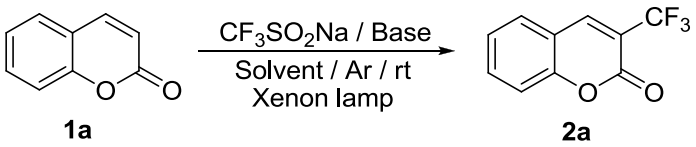
Table

Table 1. Optimization of the Reaction Conditions[a]



1a **2a**

Entry	Solvent	Reagent (equiv)	Base (equiv)	Time (h)	Yield(%)[b]
1	Acetone	4	K_2HPO_4	24	65
2	Acetone	4	K_2HPO_4	12	64
3	Acetone	4	K_2HPO_4	6	41
4	Acetone	4	K_3PO_4	12	32
5	Acetone	4	K_2CO_3	12	27
6	Acetone	4	Cs_2CO_3	12	34
7	Acetone	4	KOH	12	19
8	Acetone	3	K_2HPO_4	12	41
9	Acetone(dry)	4	K_2HPO_4	12	60
10	CH_3CN	4	K_2HPO_4	12	27
11	CH_2Cl_2	4	K_2HPO_4	12	trace
12	DMA	4	K_2HPO_4	12	N.R
13[c]	Acetone	4	K_2HPO_4	12	N.R

[a]Unless stated otherwise all reactions were performed in a tube around condensate water with **1a** (1.0 equiv, 0.2 mmol), base(2 equiv) in solvent (2 mL) at room temperature under argon atmosphere with the irradiation of a Xenon lamp for 12 h. [b]Isolated yields. [c]Without irradiation.

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