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Au@ZnO Core-Shell: Scalable Photocatalytic Trifluoromethylation using CFCONa as an Inexpensive Reagent under Visible Light Irradiation.

Zahra Bazyar, and Mona Hosseini-Sarvari

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Au@ZnO Core-Shell: Scalable Photocatalytic Trifluoromethylation using CF$_3$CO$_2$Na as an Inexpensive Reagent under Visible Light Irradiation.

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37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table of Contents

Photocatalyst

Blue LED

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
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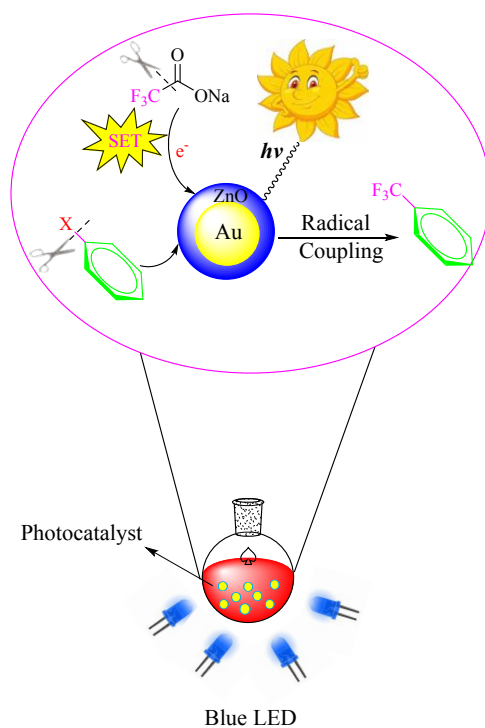
ABSTRACT: Trifluoromethylation is of significant importance in the synthesis of many small molecules vital for medicinal and agrochemical research. The importance of the CF_3 group as well as the related synthetic challenges are so evident that many reagents have been reported for the synthesis of trifluoromethylated compounds, but these typical reagents are expensive and the methods for preparing them are difficult. Here we report a new scalable and operationally simple trifluoromethylation reaction using sodium trifluoroacetate as a reagent and Au-modified ZnO as a photocatalyst under visible light irradiation. The reaction succeeds to trifluoromethylate a broad range of aryl halides, arylboronic acids, arene and heteroarene substrates. Some pharmaceutical and agrochemical compounds have been trifluoromethylated directly to demonstrate the applicability of the method.

1. INTRODUCTION

The incorporation of trifluoromethyl groups into molecules can considerably change their biological, physical and chemical properties, mostly due to the fluorine atom's high electronegativity, its small size fluorine and the less polarizable nature of C-F bonds compared to C-H bonds.[1-3] The unparalleled benefits that the trifluoromethyl moiety confers on bioavailability, metabolic stability, lipophilicity, and electronic properties have led to its wide utilization in the synthesis of pharmaceuticals (**Scheme 1A**), agrochemicals and special materials.[4, 5] Approximately 20% of pharmaceuticals, and 30% of all agrochemicals contain fluorine atoms.[6] In a multi-step synthesis of compounds bearing CF_3 group, a substitution or incorporation of the CF_3 moiety is required. As a result, scalability, broad substrate applicability and inexpensive methods for trifluromethylation are challenging. A number of efficient methodologies utilizing nucleophilic (CF_3^-) and electrophilic (CF_3^+) trifluoromethylation reagents have been reported.[7-11] Although these are very important methods they suffer from one or more disadvantages such as limited substrate scope and generality, expensive catalyst or reagent, use of harsh reaction conditions (temperature above 100 °C or use of strong acid or base).[12-14] Initally thermally metal-catalyzed trifluoromethylation reactions generating trifluoromethyl radical ($CF_3^•$) by means of a strong oxidant or photoredox catalysts were developed and were highly regarded by organic chemists.[15-21] Compared to these traditional methods visible light photo redox catalytic reactions can improve on a wide range of important reactions with advantages such as environmental adaptability, versatilility and practical reaction conditions (ambient temperature and pressure) and in many cases with high selectivity and scalability.[5,12-24] Visible light trifluoromethylation reactions, commonly involving Ru, Ir and Pt complexes as photocatalysts, allow accomplishment of the reactions under efficient conditions (room temperature, good selectivity, operationally simple). [1,5,22,23] However, these transition metal complexes also have drawbacks such as high cost, potential toxicity, and low sustainability and homogeneity (**Scheme 1B-D**) (see SI for price comparison page S4). Moreover, the other reagents used for trifluoromethylation are also expensive due to their laborious multistep syntheses and unavailability in quantities required for scale up (see SI for price comparison page S4). Among the different trifluoromethylating reagents, trifluoroacetate salts are the cheapest and most stable, and therefore the most attractive CF_3 sources for many applications.
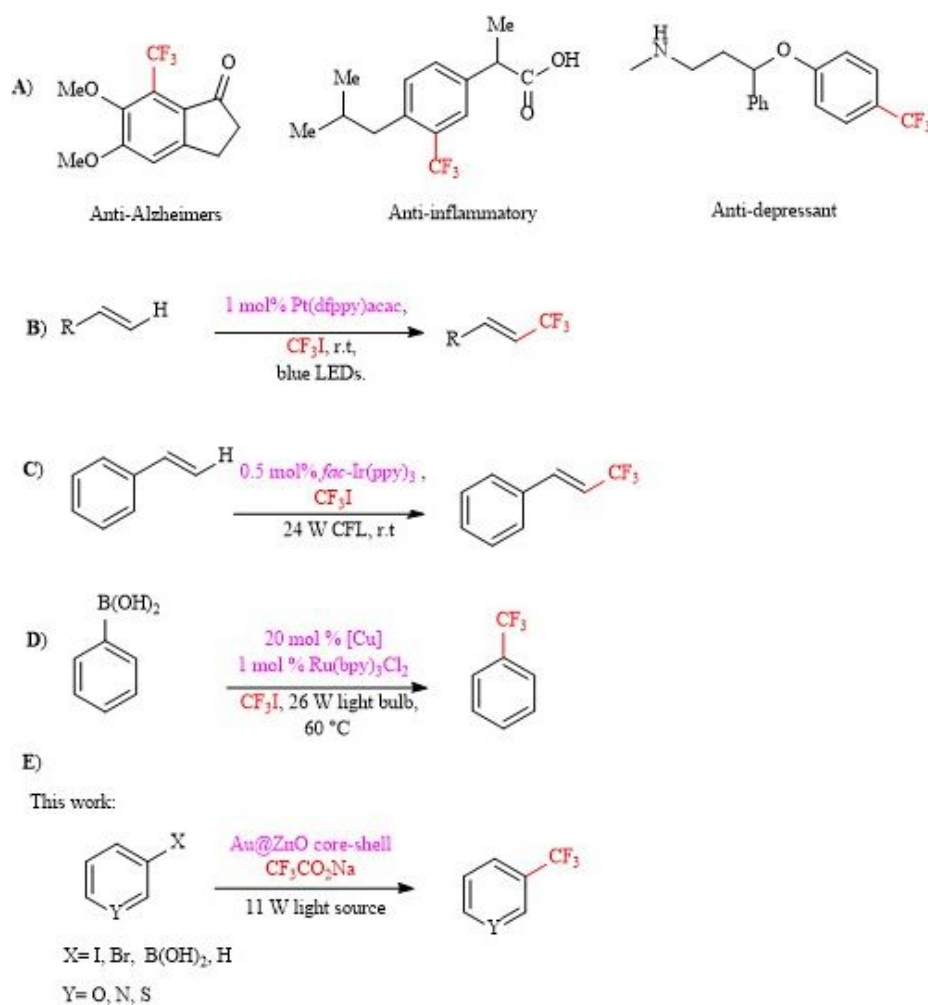
Scheme1. A) Selective bioactive molecules bearing trifluoromethyl group. **B-D**) Reported methods suffer from disadvantages. **E**) Our strategy for the photocatalytic radical trifluoromethylation.

As a result there is a need for scalable trifluoromethylation reactions using inexpensive catalysts and reagents, applicable on a wide range of substrates, and operationally simple. Here we report a photocatalytically-induced reaction to address most of the described challenges in direct trifluoromethylation: Nano Au@ZnO core-shell nanoparticles is used as a new photocatalyst without the need for external oxidant to generate the trifluoromethyl radical (CF$_3$·) from an inexpensive reagent (CF$_3$CO$_2$Na) in a trifluoromethylation reaction applicable to a wide range of substrates and that is also gram scalable (**Scheme 1E**).

2. RESULTS AND DISCUSSION

2.1 Proposed Mechanism

We came to the conclusion that a radical pathway could be applied, specifically that the efficient and mild conditions (under visible light at room temperature) of photoredox catalysis required more attention. In the initial part of our project, we focused on finding a practical trifluoromethylating reagent. As described above, among all the trifluoromethylation reagents, CF$_3$CO$_2$Na is an attractive source of CF$_3$ due to its low cost, commercial availablility and ease of use, but it was rarely used as a CF$_3$ source. Generation of CF$_3$· radical by means of CF$_3$CO$_2$Na and thus avoiding high temperature and/or strongly oxidizing conditions had not been reported. In addition, most of the photoredox catalysts used for trifluoromethylation were not capable of generating CF$_3$· radical from CF$_3$CO$_2$Na because of its high oxidation potential (E$_{1/2}^{ox}$= 1.6-2.46)[25] (**Figure S1**), which results in loss of performance. So we focused on the search for a photocatalyst that would have the ability to oxidize CF$_3$CO$_2$Na to generate the CF$_3$· radical and absorb visible light. Recently Li and co-workers reported a method for

trifluoromethylation of (hetero)arenes with TFA by using Rh/TiO$_2$ as a photocatalyst using 10-40 mol % K$_2$S$_2$O$_8$ as an oxidant under UV (365 nm) irradiation.[26] Taking into account all these aspects gave us a good idea of how to design a new catalyst with high performance for trifluoromethylation reactions.

TiO$_2$ and ZnO nanoparticles have been widely studied as photocatalysts in various applications.[27, 28] Especially ZnO was interesting for this study due to its low cost and, according to some reports, better photocatalytic activity than TiO$_2$.[28] However photocatalytic processes by ZnO using visible light are difficult to achieve due to its wide band gap and large excitation binding energy.[29] Therefore, research efforts have been focused on improving the photocatalytic performance of ZnO. One approach is to load gold nanoparticles on the surface of ZnO nanostructures. Owing to localized surface plasmon resonance (LSPR), gold (Au) placed on semiconductor-based photocatalysts shows strong visible-light absorption characteristics.[30, 31] Among noble metals (Ag, Pd, etc.) gold nanocrystals have generated more interest for use as plasmonic photocatalysts due to their great stability and LSPR effect.[30, 36] The wavelength (frequency) and intensity of the LSPR absorption band of gold nanoparticles is strongly dependent on their size, shape, and morphology, as well as the surface and the local environments surrounding them.[30-33] In comparison with pure ZnO, when ZnO is modified with Au nanoparticles, LSPR absorption can lead to improved use of UV-visible light.[34, 35] The work functions of ZnO and gold were reported 5.2-5.3 and 4.7-5.12 eV, respectively.[30-33, 37]

Due to the larger work function of ZnO, its Fermi energy level is lower than gold (**Figure 1A**). Thus, when Au and ZnO combine, due to the LSPR effect (the LSPR energy for noble metal nanoparticles is between 1 and 4 eV) gold absorbs visible light and an electron cloud and oscillate were formed. Electrons can then transfer to the conduction bond (CB) of ZnO, which prevents the electron/hole (e$^-$/h$^+$) recombination and the holes (h$^+$) were generated on gold (**Figure 1B**).
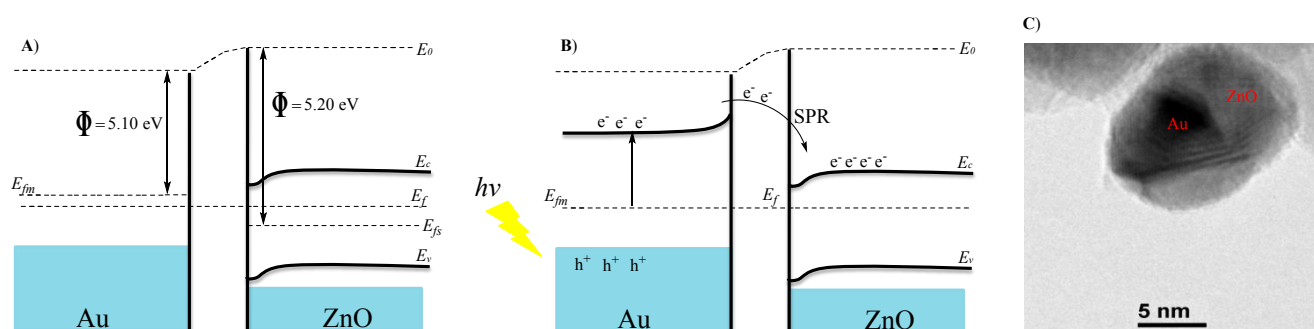

Figure 1. (**A**) The band structure of Au and ZnO. (**B**) Localized surface plasmon resonance (LSPR) of gold. (**C**) High-resolution transmission electron microscopy image of the Au@ZnO core-shell nanoparticles (1.89 wt % Au) core-shell photocatalyst, the dark area is Au and the lighter surrounding area is ZnO.

According to these data, we questioned whether Au@ZnO core-shell nanoparticles might be a good photocatalyst candidate for visible light trifluoromethylation. We hoped to render a mechanism whereby the visible light excitation (*hv*) of Au@ZnO core-shell nanoparticles incurs e$^-$ injection from the LSPR of Au NPs to the underlying CB of ZnO resulting in holes (h$^+$) at the Au NP side. The photo-generated hole (h$^+$) (E$_f$ = 0.45 Vvs NHE)[30-33, 37, 38] has the ability to oxidize CF$_3$CO$_2$Na (E$_{1/2}$^{ox}= 1.6-2.46 Vvs NHE)[25] generating the CF$_3$ radical through decarboxylation.[39, 40] After generating the CF$_3$ radical two pathways are possible: A) the light-excited electron transfers from the CB of ZnO to the aryl halide or boronic acid molecule. In these cases when one electron enters the unoccupied orbital, the C-X bond extends making cleavage easier for yielding a transient radical anion **I**. With the loss of the –X anion, aryl radical **II** was generated which then coupled with CF$_3$ radical to generate the desired product (**Figure 2A**); B) under oxygen atmosphere the light-excited electron reacted with O$_2$ to generate the O$_2$ radical anion, while the CF$_3$ radical reacts with Ar-H to generate the aryl radical species **III** which by loss of a hydrogen rearomatizes[26, 41] to generate the desired product (**Figure 2B**).
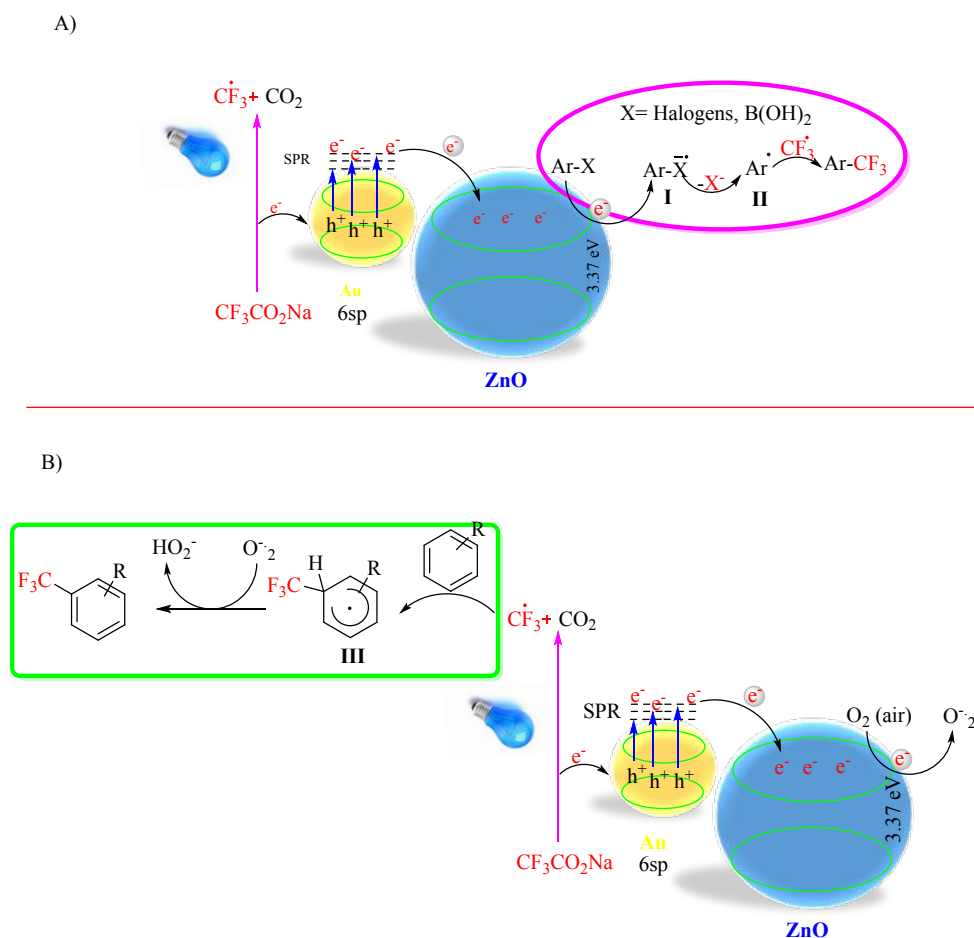
Figure 2. Propose mechanism for the photocatalytic trifluoromethylation coupling reaction.

During the implementation part of this project, we were initially prepared the Au@ZnO core-shell nanoparticles photocatalyst by modifying previous reported methods.[27, 42-44] Our method is simple, low-cost and efficient, with no need for heat or temperature and will have many potential applications for large scale and industrial purposes. The Au@ZnO core-shell nanoparticles was fully analyzed by XRD, ICP, SEM, TEM, HR-TEM, XPS, BET, and UV-Vis absorption which are shown in SI (**Figures S2-S8 and Tables. S1, S2**).

The induced coupled plasma (ICP) analysis confirmed that the Au@ZnO core-shell nanoparticles photocatalyst contains only 1.89 wt % Au. The transmission electron microscopy (TEM) (**Figure S4a**) and high-resolution TEM images (**Figure 1C**) indicated that Au is covered by ZnO with nearly spherical shape. XPS analysis indicated the signals of Au $4f_{5/2}$ and Au $4f_{7/2}$ with binding energies of 91.78 and 89.18 eV of the metallic Au, respectively, (**Figure S5**).

2.2 Trifluoromethylation using Au@ZnO Core-Shell Nanoparticles Photocatalyst

Using our strategy outlined in **Figures 1** and **2**, we began to optimize conditions for the synthesis of 4-nitrobenzotrifluoride (**2a**). Primary studies showed that irradiation of 4-nitroiodobenzene by blue 11 W LED in the presence of CF_3CO_2Na, Au@ZnO core-shell nanoparticles as photocatalyst, Cs_2CO_3 as base, KF as additive, in DMF, produced (**2a**) in 29% yield. These encouraging results inspired us to improve the reaction conditions. So, other factors such as solvent, photocatalyst loading, additive, base, light source, atmosphere and reaction time were investigated. The selected optimized results are shown in **Table 1** and details are given in **Tables S3-S9**. The most remarkable result found about this trifluoromethylation

reaction is that it does not require high temperature or external strong oxidant for the decarboxylation of CF_3CO_2Na and is not sensitive to moisture, so set-up of the reaction is practical (no need for drying or degassing solvent or reagents).

Table 1. Selected optimization data[a]

1a						**2a**
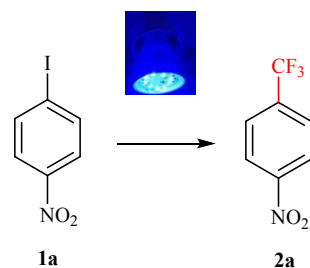
Entry	Au@ZnO (g)	Additive (mmol)	Base (mmol)	Solvent (mL)	Atmosphere	Yield[b] (%)
1	0.003	KF (1)	Cs_2CO_3 (1)	NMP (2)	Argon	29
2	0.003	KF (1)	Cs_2CO_3 (1)	NMP (2)	Air	10
3	0.003	KF (1)	Pyridine (1)	NMP (2)	Argon	Trace
4[c]	-	KF (1)	Pyridine (1)	NMP (2)	Argon	0
5	0.003	KF (1)	K_3PO_4 (1)	DMF (2)	Argon	39
6[d]	-	KF (1)	K_3PO_4 (1)	DMF (2)	Argon	0
7	0.003	KF (1)	K_3PO_4 (1)	DMF (2)	O_2	0
8[e]	0.003	KF (1)	K_3PO_4 (1)	DMF (2)	Argon	0
9[f]	0.003	KF (1)	K_3PO_4 (1)	DMF (2)	Argon	0
10	0.003	KF (1)	K_3PO_4 (1)	DMF/H_2O (5:1 v/v)	Argon	46
11	0.003	KF (3)	K_3PO_4 (2)	DMF/H_2O (5:1 v/v)	Argon	71
12	**0.01**	**KF (3)**	**K_3PO_4 (2)**	**DMF/H_2O (5:1 v/v)**	**Argon**	**80**

[a] Reaction conditions: Sodium trifluoroacetate (3 mmol), 4-nitroiodobenzene (1 mmol), additive, base, Au@ZnO core-shell nanoparticles (1.89 wt % Au), solvent, at room temperature, 11 W blue LED (wavelength in the range 400-495 nm), 48 h.
[b] Yield of isolated product.
[c] CuI (0.1 g).
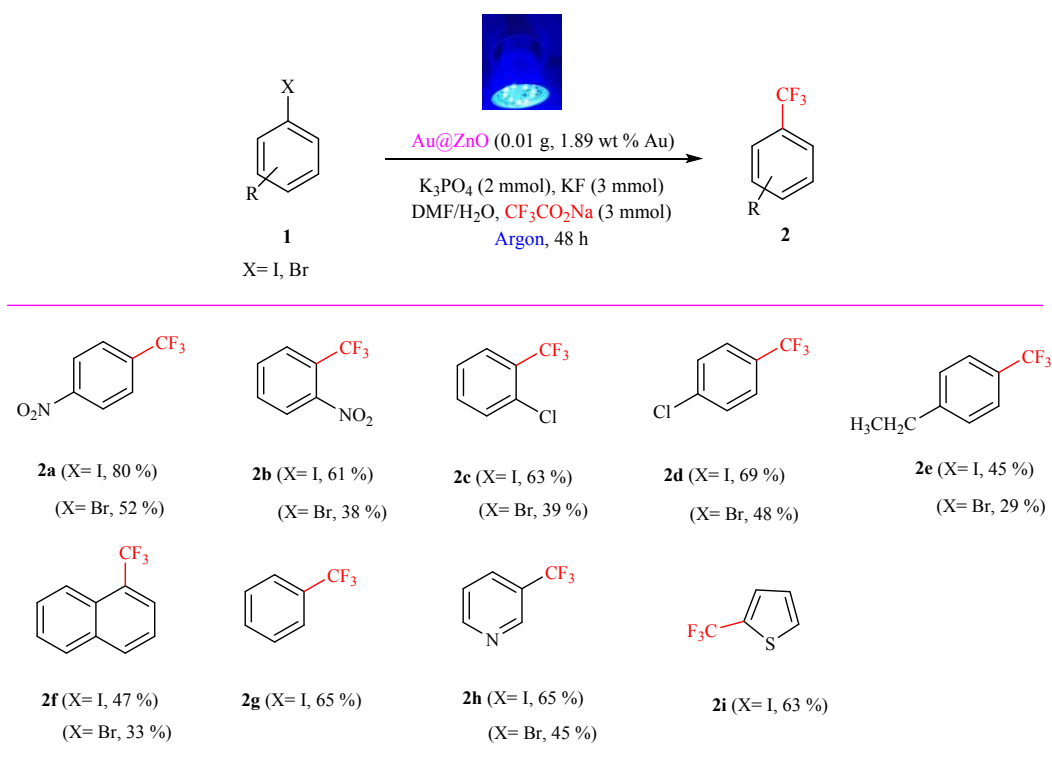[d] Pd/ZnO (0.002g).
[e] Dark.
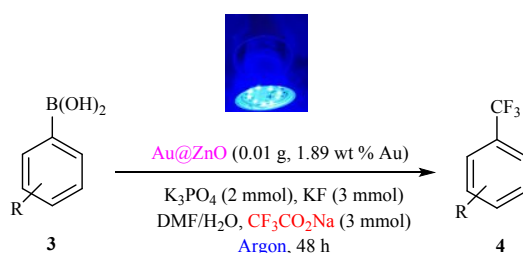[f] Without catalyst.

2.3 Substrate Scope

We found that this new photocatalytic protocol allows the incorporation of CF_3 into a wide range of substrates. We first focused on halogen-bearing substrates which are very important in pharmaceutical syntheses. As can be seen from **Table 2**, ortho and para positioned electron-withdrawing and electron-donating groups of aryl halides, successfully underwent trifluoromethylation. As expected, aryl iodides were found to be more reactive in comparison with aryl bromides. So it is interesting to see that trifluoromethylation of chloro-bromo or chloro-iodo substitutions took place selectively (entries **2c-2d**). Heteroaryl iodides (entries **2h**, **2i**) could also be trifluoromethylated in synthetically useful yields.
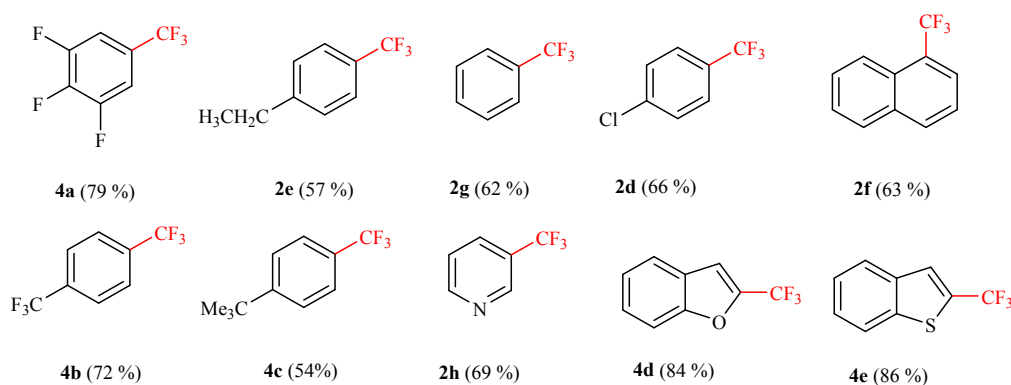
We next turned our attention to the trifluoromethylation of arylboronic acids. According to the literature, trifluoromethylation of boronic acides involving Cu-catalysts generally proceed by electrophilic or nucleophilic shift of CF_3

to Cu. To the best of our knowledge, there is only one report for Cu-catalyzed trifluoromethylation of boronic acids using visible light in which used gaseous CF$_3$I (a very expensive and toxic substance) was used as the trifluoromethylation reagent.[17] As shown in **Table 3**, we found that this new trifluoromethylation method was also applicable on aryl and heteroaryl boronic acids (54-86% yield). In the case of 1-naphthyl boronic acid the main challenge is cross-coupling reactions, competing protodeboronation was a problem and naphthalene was obtained as the major side product. Interestingly, product (**2f**) was obtained in good yield (63%) and no side product was observed.

Table 2. Substrate scope[a]

2a (X= I, 80 %)	**2b** (X= I, 61 %)	**2c** (X= I, 63 %)	**2d** (X= I, 69 %)	**2e** (X= I, 45 %)
(X= Br, 52 %)	(X= Br, 38 %)	(X= Br, 39 %)	(X= Br, 48 %)	(X= Br, 29 %)
2f (X= I, 47 %)	**2g** (X= I, 65 %)	**2h** (X= I, 65 %)	**2i** (X= I, 63 %)	
(X= Br, 33 %)		(X= Br, 45 %)		

[a] Reaction conditions: Sodium trifluoroacetate (3 mmol), aryl halide (1 mmol), KF (3 mmol), K$_3$PO$_4$ (2 mmol), Au@ZnO core-shell nanoparticles (0.01 g, 1.89 wt % Au), DMF:H$_2$O (5 mL, 5:1), room temperature, 11 W blue LED (wavelength in the range 400-495 nm), under argon atmosphere, 48 h, yield of isolated product.

Table 3. Substrate scope[a]

4a (79 %)   **2e** (57 %)   **2g** (62 %)   **2d** (66 %)   **2f** (63 %)

4b (72 %)   **4c** (54%)   **2h** (69 %)   **4d** (84 %)   **4e** (86 %)

[a] Reaction conditions: Sodium trifluoroacetate (3 mmol), boronic acid (1 mmol), KF (3 mmol), K_3PO_4 (2 mmol), Au@ZnO core-shell nanoparticles (0.01 g, 1.89 wt % Au), DMF:H_2O (5 mL, 5:1) at room temperature, 11 W blue LED (wavelength in the range 400-495 nm), under argon atmosphere, 48 h, yield of isolated product.
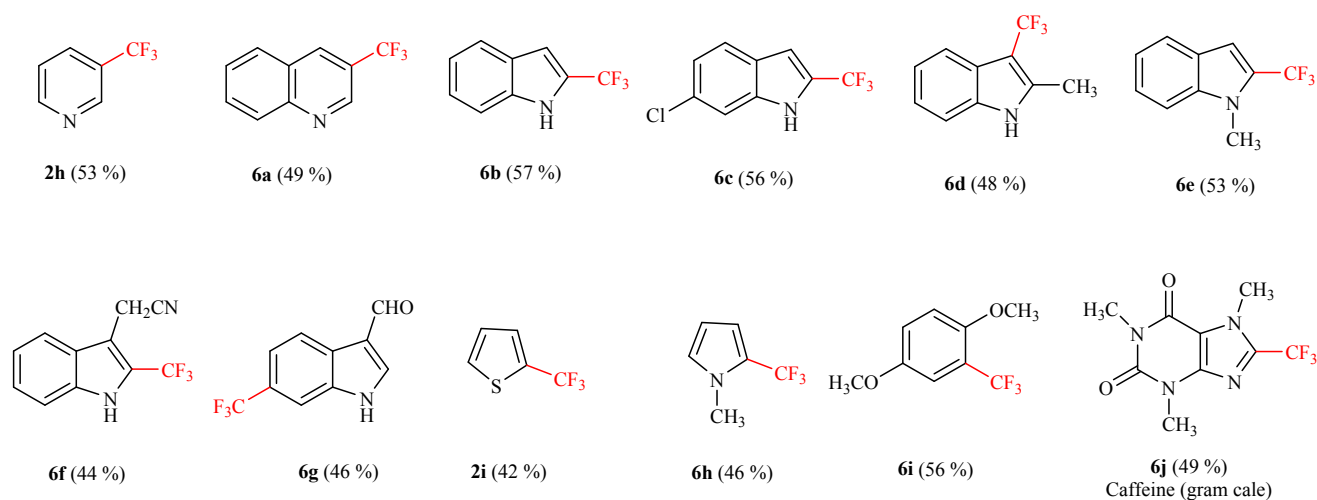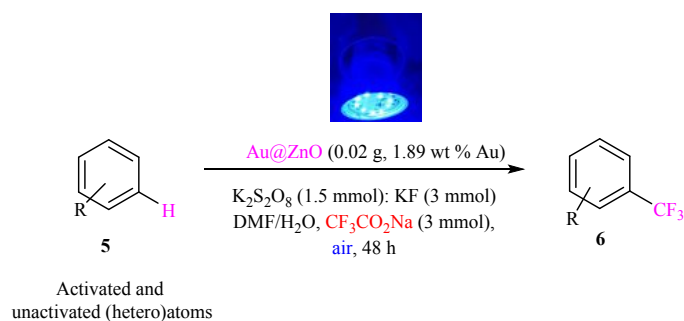
Because of simplicity, efficient synthetic routes, readily available starting materials, and potentially step- and atom-economy, we next put our attention to direct C-H functionalization of activated and nonactivated (hetero)arenes with Au@ZnO core-shell nanoparticles as photocatalyst and CF_3CO_2Na as trifluoromethylation reagent. The results are shown in **Table 4**. In the case of nonactivated (hetero)arenes as substrate, some modification of the photocatalyst and base were needed to achieve the optimal yield (see SI for more details).

Table 4. Substrate scope[a]

2h (53 %)   **6a** (49 %)   **6b** (57 %)   **6c** (56 %)   **6d** (48 %)   **6e** (53 %)

6f (44 %)   **6g** (46 %)   **2i** (42 %)   **6h** (46 %)   **6i** (56 %)   **6j** (49 %) Caffeine (gram cale)

[a] Reaction conditions: Sodium trifluoroacetate (3 mmol), (hetero)arenes (1 mmol), KF(3 mmol), $K_2S_2O_8$ (1.5 mmol), Au@ZnO core-shell nanoparticles (0.02 g, 1.89 wt % Au), DMF:H_2O (5 mL, 5:1) at room temperature, 11 W blue LED (wavelength in the range 400-495 nm), under Air atmosphere 48 h, yield of isolated product.

Using this new photoredox method all selected substrates in **Table 4** underwent direct trifluoromethylation in good to excellent yields. *N*-methylpyrrole and 2-methylthiophene were trifluoromethylated with excellent selectivity and good yields (**2i and 6h**). For these 5-membered heteroaromatic rings, selectivity was observed at the C-2 position, due to the formation of the conjugated radical. Due to potential pharmaceutical activity of 2-trifluoromethylated indole derivatives, development of methods accessing these compounds is still a challenge. However, direct C-H trifluoromethylation, by controlling the regioselectivity (2-CF_3 vs 3-CF_3) was generally difficult and limited the previous reported methods. As can be seen from **Table 4** (entries **6b-6g**) different derivatives of indoles with electron donating and withdrawing groups, were trifluoromethylated at C2-position in good yields and, in the case of compound (**6c**), when the C2-position was blocked the CF_3 group was located at the C-3 position. Trifluoromethylated derivatives of six-membered heterocycles are valuable pharmacophores and these could also be trifluoromethylated under our conditions in good yields. In the case of C-H activation for activated and un-activated (hetero)arenes the electron deficient $CF_3^{\bullet}$ has been selectively suitable to add to the most electron-rich positions.

Another potential benefit of our method is its potential use for biologically active molecules. To demonstrate this, some active molecules such as an anti-inflammatory drug,[45] a flavorant, and a DNA base analogue were chosen to obtain their CF_3 analogues. High regioselectivity was observed and in all cases the trifluoromethylation occurred at a single position. The last example showed the synthesis of CF_3-azauracil from unprotected NH groups which have anti-viral and anticancer treating properties (**Scheme 2**).[46]
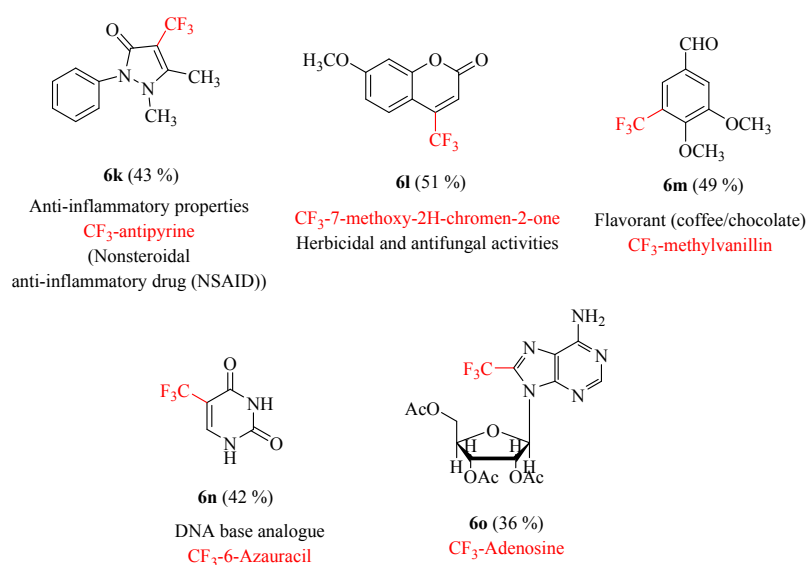
Scheme2. **Direct trifluoromethylation of biologically active molecules.** C–H functionalization of more metabolically stable medicines occurs none selectively, allowing for rapid access to drug analogues.

2.4 Reactions at Large Scale and in Flow

The low-cost and availability of CF_3CO_2Na and the simplicity of the reaction allowed us to investigate scaling up the process (**Figure 3 A-B**). A reaction using 10.5 g of caffeine furnished a comparable yield to that obtained on small scale (6.32 g 43%). These primary results showed that the method is potentially appropriate for large-scale production; although, another potential option for scale up involves the use of continuous processing. We tried the reaction in continuous flow in a simple and recyclable continuous-flow photo-reactor built by using a column filled with glass beads, silica gel and the Au@ZnO core-shell nanoparticles as catalyst (**Figure 3C**, for details see the Supporting Information). In comparison to the batch

reaction, the continuous flow photo-reactor shortened the reaction time showing that the method has high practical application potential.
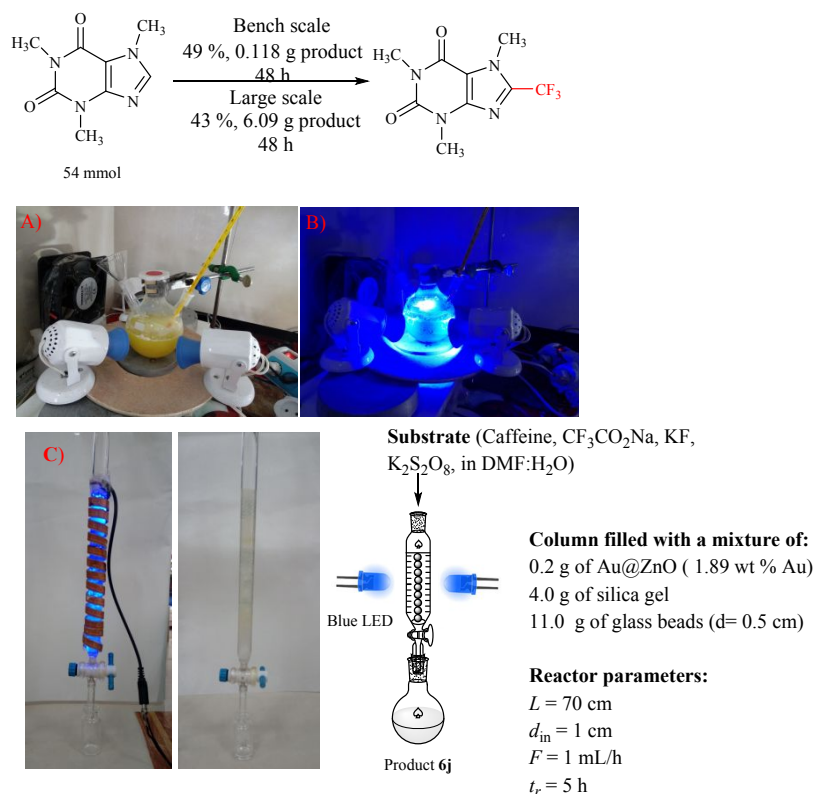

**Figure 3.** (**A-B**) 10.5 g batch reaction set up. (**C**) Flow reactor[a]

[a] L = column length, d_{in} = column internal diameter, F = flow rate, t_r = residence time. 10 mmol-scale, 43 % yield (1.101 g) of **6j**.

2.5 Reusability Study

The benefit of a heterogeneous catalyst is its removal and reusability after isolation. The recycling capability of the catalyst is important for both cost and environmental reasons and was studied by running the trifluoromethylation reaction for 4-nitroiodobenzene and sodium trifluoroacetate under optimized conditions ten times. After each run the catalyst was retrieved by centrifugation and washed with water followed by ethanol and finally dried at 80˚C. Au@ZnO core-shell nanoparticles exhibits excellent reusability (**Figure S12**) and its catalytic capability was not remarkably decreased even after ten runs. The amount of leached gold was determined by induced coupled plasma (ICP) analysis (0.021 wt%).

2.6 Control Experiments

In order to understand the reaction mechanism better, some control experiments were performed as shown in **Scheme3**. Addition of triethanolamine and ammonium oxalate (hole (h^+) scavengers) gave only trace and 0% of product (**2a**), respectively, denoting the participation of holes. When TEMPO, a radical scavenger, was added to the reaction mixture, the it trapped the trifluoromethyl radicals generated from the decarboxylation of sodium trifluoroacetate to form a TEMPO-CF_3 adduct that was confirmed by ^{19}F NMR spectroscopy (**Figure S14**).[47] The lack of any reaction in the dark verified that the trifluoromethylation formation is activated and deactivated by visible light. To find this "On-Off" switch, a visible light irradiation experiment was performed and the preparative results show that radical-chain propagation is not a key step in this transformation (**Figure S16b**).
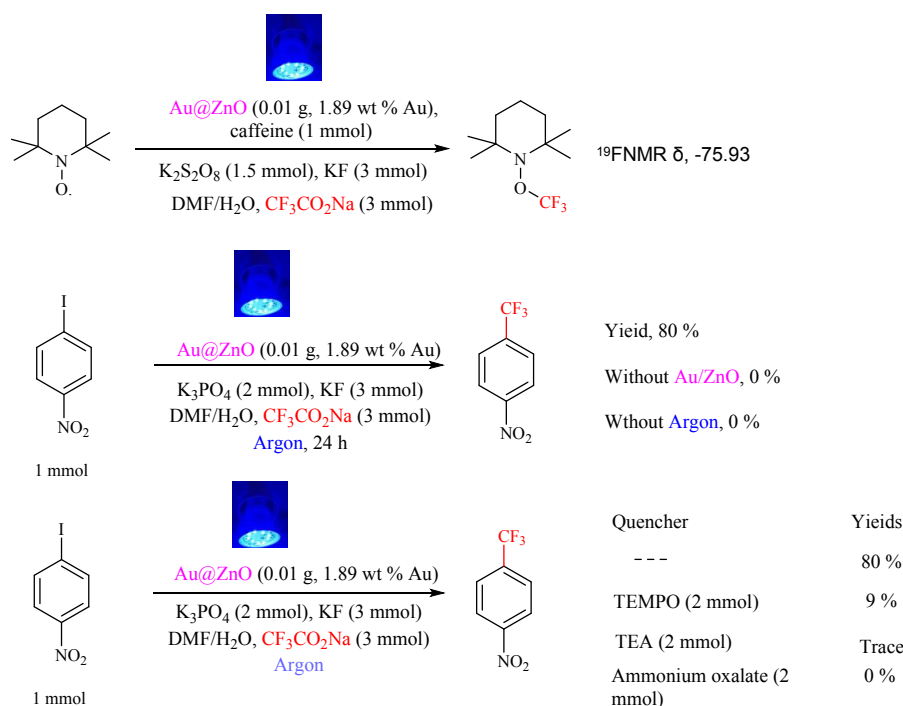
Scheme 3. Mechanistic experiments.

3. CONCLUSIONS

In this work we have shown Au@ZnO core-shell nanoparticles to be a viable as a photoredox catalyst for the facile trifluoromethylation of a wide range of substrates using sodium trifluoroacetate as an inexpensive reagent. Trifluoromethylation of biologically active molecules and scalability enhance the value of this method. We believe this catalytic system is the key to accessing visible light photocatalysis for the insertion of CF_3 groups into organic molecules in order to gain the full range of reaction pathways.

4. EXPERIMENTAL METHODS

4.1 Preparation of Au@ZnO Core-Shell Nanoparticles

Au@ZnO core-shell nanoparticles were prepared with the modified procedure reported by Sun et.al.[27] In a round bottom flask, 20 mL aqueous solution of 2.6×10^{-4} M tri-sodium citrate and 2.6×10^{-4} M $HAuCl_4.3H_2O$ were prepared. Afterwards, 1 mL 0.1 M fresh aqueous sodium borohydride ($NaBH_4$) was added before stirring for 5 h at room temperature. The solution turned red after addition of $NaBH_4$. Next, 20 mL of 60 mM cetyltrimethylammonium bromide (CTAB) and 0.2 M $Zn(NO_3)_2$ in ethanol was mixed with the previous solutionbefore adding 20 mL 0.5 M NaOH ethanolic solution and stirring for 30 min. The resulting light pink suspension was centrifuged, washed with ethanol and then distilled water to get the Au@ZnO core-shell nanoparticles (1.89 wt % Au).

4.2 General Procedure for the Trifluoromethylation of Aryl halids and Boronic acids

A mixture of arylhalide or boronic acids (1 mmol) or one of its derivatives, sodium trifluoroacetate (3 mmol), KF (3 mmol), K_3PO_4 (2 mmol), Au@ZnO core-shell nanoparticles (0.01g, 1.89 wt % Au) and DMF:H$_2$O (4 mL, 5:1) was put into a pyrex glass tube in which an 11 W blue LED was used as a light source and the reaction was carried out under argon atmosphere at

room temperature for 48 h. After the reaction was complete, the mixture was centrifuged to remove the catalyst and the supernatant was purified by column chromatography (see SI for details).

4.3 General Procedure for the Trifluoromethylation of Nonactivated (hetero)arens

A mixture of (hetero)arene (1 mmol), sodium trifluoroacetate (3 mmol), KF (3 mmol), $K_2S_2O_8$ (1.5 mmol), Au@ZnO core-shell nanoparticles (0.02g, 1.89 wt % Au) and DMF:H_2O (4 mL, 5:1) was put into a pyrex glass tube in which an 11 W blue LED was used as a light source and the reaction was carried out under air atmosphere at room temperature for 48 h. After the reaction was complete, he mixture was centrifuged to remove the catalyst and the supernatant was purified by column chromatography (see SI for details).

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SUPPORTING INFORMATION

Experimental procedures, compounds and catalyst characterization data. Additional investigations on reaction conditions, and mechanistic studies.

REFERENCES

(1)   Chatterjee, T.; Iqbal, N.; You, Y.; Cho, E. J. Controlled fluoroalkylation reactions by visible-light photoredox catalysis. *Acc. Chem. Res*. **2016**, *49*, 2284-2294.

(2)   Furuya, T.; Kamlet, A. S.; Ritter, T. Catalysis for fluorination and trifluoromethylation. *Nature* **2011**, *473*, 470-477.

(3)   Tomashenko, O. A.; Grushin, V. V. Aromatic trifluoromethylation with metal complexes. *Chem. Rev.* **2011**, *111*, 4475-4521.

(4)   Shen, H.; Liu, Z.; Zhang, P.; Tan, X.; Zhang, Z.; Li, C. Trifluoromethylation of alkyl radicals in aqueous solution. *J. Am. Chem. Soc.* **2017**, *139*, 9843-9846.

(5)   Nagib, D. A.; MacMillan, D. W. C. Trifluoromethylation of arenes and heteroarenes by means of photoredox catalysis. *Nature* **2011**, *480*, 224-228.

(6)   Ilardi, E. A.; Vitaku, E.; Njardarson, J. T. Data-mining for sulfur and fluorine: an evaluation of pharmaceuticals to reveal opportunities for drug design and discovery: miniperspective. *J. Med. Chem.* **2013**, *57*, 2832-2842.

(7)   Barata-Vallejo, S.; Lantano, B.; Postigo, A. Recent advances in trifluoromethylation reactions with electrophilic trifluoromethylating reagents. *Chem. Eur. J.* **2014**, *20*, 16806-16829.

(8)   Liu, X.; Xu, C.; Wang, M.; Liu, Q. Trifluoromethyltrimethylsilane: Nucleophilic trifluoromethylation and beyond. *Chem. Rev.* **2014**, *115*, 683-730.

(9)   Zhang, C. Recent advances in trifluoromethylation of organic compounds using Umemoto's reagents. *Org. Biomol. Chem.* **2014**, *12*, 6580-6589.

(10) Senecal, T. D.; Parsons, A. T.; Buchwald, S. L. Room temperature aryl trifluoromethylation via copper-mediated oxidative cross-coupling. *J. Org. Chem*. **2011**, *76*, 1174-1176.

(11) Chu, L.; Qing, F. L. Copper-mediated oxidative trifluoromethylation of boronic acids. *Org. Lett*. **2010**, *12*, 5060-5063.

(12) Chen, M.; Buchwald, S. L. Rapid and efficient trifluoromethylation of aromatic and heteroaromatic compounds using potassium trifluoroacetate enabled by a flow system. *Angew. Chem. Int. Ed.* **2013**, *52*, 11628-11631.

(13) Lefebvre, Q. Toward sustainable trifluoromethylation reactions: sodium triflinate under the spotlight. *Synlett* **2017**, *28*, 19-23.

(14) Zhang, H.; Wang, H.; Luo, Y.; Chen, C.; Cao, Y.; Chen, P.; Guo, Y. L.; Lan, Y.; Liu, G. Regioselective palladium-catalyzed CH bond trifluoroethylation of indoles: exploration and mechanistic insight. *ACS Catal.* **2018**, *8*, 2173-2180.

(15) Abdiaj, I.; Bottecchia, C.; Alcazar, J.; Noël, T. Visible-light-induced trifluoromethylation of highly functionalized arenes and heteroarenes in continuous flow. *Synthesis* **2017**, *49*, 4978-4985.

(16) Sosa, V.; Melkie, M.; Sulca, C.; Li, J.; Tang, L.; Li, J.; Faris, J.; Foley, B.; Banh, T.; Kato, M.; Cheruzel, L. E. Selective light-driven chemoenzymatic trifluoromethylation/hydroxylation of substituted arenes. *ACS Catal.* **2018**, *8*, 2225-2229.

(17) Ye, Y.; Sanford, M. S. Merging visible-light photocatalysis and transition-metal catalysis in the copper-catalyzed trifluoromethylation of boronic acids with CF$_3$I. *J. Am. Chem. Soc.* **2012**, *134*, 9034-9037.

(18) Das, Somnath.; Hashmi, A. S. K.; Schaub, T. Direct photoassisted α-trifluoromethylation of aromatic ketones with trifluoroacetic anhydride (TFAA). *Adv. Synth. Catal.* **2019**, *361*, 720-724.

(19) Beatty, J. W.; Douglas, J. J.; Cole, K. P.; Stephenson, C. R. J. A scalable and operationally simple radical trifluoromethylation. *Nat. Commun.* **2015**, *6*, 7919-7924.

(20) Yang, B.; Yu, D.; Xu, X. H.; Qing, F. L. Visible-light photoredox decarboxylation of perfluoroarene iodine (III) trifluoroacetates for C-H trifluoromethylation of (hetero)arenes. *ACS. Catal.* **2018**, *8*, 2839-2846.

(21) Beatty, J. W.; Douglas, J. J.; Miller, R.; Mc Atee, R. C.; Cole, K. P.; Stephenson, C. R.J. Photochemical perfluoroalkylation with pyridine *N*-oxides: mechanistic insights and performance on a kilogram scale. *Chem.* **2016**, *1*, 456-472.

(22) Iqbal, N.; Jung, J.; Park, S.; Cho, E. J. Controlled trifluoromethylation reactions of alkynes through visible-light photoredox catalysis. *Angew. Chem. Int. Ed.* **2014**, *53*, 539-542.

(23) Straathof, N. J. W.; Cramer, S. E.; Hessel, V.; Noel, T. Practical photocatalytic trifluoromethylation and hydrotrifluoromethylation of styrenes in batch and flow. *Angew. Chem.* **2016**, *55*, 15549-15553.

(24) Le, C.; Chen, T. Q.; Liang, T.; Zhang, P.; MacMillan, D. W. C. Radical approach to the copper oxidative addition problem: trifluoromethylation of bromoarenes. *Science* **2018**, *360*, 1010-1014.

(25) Grinberg, V.; Vassiliev, Y. B. Investigation of the processes of electrochemical perfluoroalkylation and fluorosulphation: part 1. electrode processes and the electrochemical perfluoroalkylation mechanism. *J. Electroanal. Chem.* **1992**, *325*, 167-184.

(26) Lin, J.; Li, Z.; Kan, J.; Huang, S.; Su, W.; Li, Y. Photo-driven redox-neutral decarboxylative carbon-hydrogen trifluoromethylation of (hetero) arenes with trifluoroacetic acid. *Nat. Commun.* **2017**, *8*, 14353-14359.

(27) Sun, L.; Wei, G.; Song, Y.; Liu, Z.; Wang, L.; Li, Z. Soulotion-phase synthesis of Au@ZnO core-shell composites. *Mater Lett.* **2006,** *60*, 1291-1295.

(28) Silva, C. G.; Silva, C. G.; M. J.; Carabineiro, S. A.; Oliveira, J. W. L.; Baptista, D. L.; Bacsa, R.; Machado, B. F.; Serp, P.; Figueiredo, J. L.; Silva, A. M. T.; Faria. J. L. Developing highly active photocatalysts: gold-loaded ZnO for solar phenol oxidation. *J. Catal.* **2014**, *316*, 182-190.

(29) Kim, K. J.; Kreider, P. B.; Chang, C. H.; Park, C. M.; Ahn, H. G. Visible light sensitive nanoscale Au–ZnO photocatalysts. *J. Nanopart. Res.* **2013**, *15*, 1606-1616.

(30) Sarina, S.; Waclawik, E. R.; Zhu, H. Photocatalysis on supported gold and silver nanoparticles under ultraviolet and visible light irradiation. *Green Chem.* **2013**, *15*, 1814-1833.

(31) Ye, W.; Long, R; Huang, H.; Xiong, Y. Plasmonic nanostructures in solar energy conversion. *J. Mater. Chem. C.* **2017**, *5*, 1008-1021.

(32) Linic, S.; Christopher, P.; Ingram, D. B. Plasmonic-metal nanostructures for efficient conversion of solar to chemical energy. *Nat. Mater.* **2011**, *10*, 911-921.

(33) Al-Azri, Z. H.; Chen,W.-T.; Chan, A.; Jovic, V.; Ina, T.; Idriss, H.; Waterhouse, G. I. N. The roles of metal co-catalysts and reaction media in photocatalytic hydrogen production: performance evaluation of M/TiO2 photocatalysts (M= Pd, Pt, Au) in different alcohol–water mixtures. *J. Catal.* **2015**, *329*, 355-367.

(34) Georgiev, P.; Kaneva, N.; Bojinova, A.; Papazova, K.; Mircheva, K.; Balashev, K. Effect of gold nanoparticles on the photocatalytic efficiency of ZnO films. *Colloids Surf. A.* **2014**, *460*, 240-247.

(35) Mishra, Y.; Mohapatra, S.; Singhal, R.; Avasthi, D. K. Au-ZnO: A tunable localized surface plasmonic nanocomposite. *Appl. Phys. Lett.* **2008**, *92*, 043107-043109.

(36) Leong, K. H.; Chu, H. Y.; Ibrahim, S.; Saravanan, P. Palladium nanoparticles anchored to anatase TiO_2 for enhanced surface plasmon resonance-stimulated, visible-light-driven photocatalytic activity. *Beilstein J Nanotech.* **2015**, *6*, 428-437.

(37) Chang, Y.; Xu, J.; Zhang, Y.; Ma, S.; Xin, L.; Zhu, L.; Xu, C. Optical properties and photocatalytic performances of Pd modified ZnO samples. *J. Phys. Chem. C.* **2009**, *113*, 18761-18767.

(38) Subramanian, V.; Wolf, E. E.; Kamat, P. V. Green emission to probe photoinduced charging events in ZnO−Au nanoparticles. Charge distribution and Fermi-level equilibration. *J. Phys. Chem. B.* **107**, 7479-7485 (2003).

(39) Man, L.; Huiying, K.; Xiao-Song, X.; Jin-Pei, C. Computational study of the trifluoromethyl radical donor abilities of CF_3 sources. *Acta. Chim. Sinica.* **2018**, *76*, 988-996.

(40) Shi, G.; Shao, C.; Pan, S.; Yu, J.; Zhang, Y. Silver-catalyzed C-H trifluoromethylation of arenes using trifluoroacetic acid as the trifluoromethylating reagent. *Org. Lett.* **2015**, *17*, 38-41.

(41) Cheng, Y.; Yang, J.; Q. Yue.; Li, P. Aerobic visible-light photoredox radical C-H functionalization: catalytic synthesis of 2-substituted benzothiazoles. *Org. Lett.* **2012**, *14*, 102-105.

(42) Zeng, D.; Gong, P.; Chen, Y.; Wang, C.; Peng, D. L. Preparation of multi-branched Au–ZnO hybrid nanocrystals on graphene for enhanced photocatalytic performance. *Mater. Lett.* **2015**, *161*, 379-383.

(43) Liu, X.; Li, Z.; Zhao, W.; Zhao, C.; Yang, J.; Wang, Y. Zinc Oxide nanorod/Au composite arrays and their enhanced photocatalytic properties. *J. Colloid Interface Sci.* **2014**, *432*, 170-175.

(44) Sun, L.; Zhao, D.; Song, Z.; Shan, C.; Zhang, Z.; Li, B.; Shen, D. Gold nanoparticles modified ZnO nanorods with improved photocatalytic activity. *J. Colloid Interface Sci.* **2011**, *363*, 175-181.

(45) Agafonova, N.; Shchegolkov, E.; Burgart, Y.; Saloutin, V.; Trefilova, A.; Triandafilova, G.; Solodnikov, S.; Maslova, V.; Borisevich, S.; Krasnykh, O.; Khursan, S. Synthesis and biological evaluation of polyfluoroalkylated antipyrines and their isomeric O-methylpyrazoles. *J. Med. Chem.* **2018**.

(46) Dexter, D. L.; Wolberg, W. H.; Ansfield, F. J.; Helson, L.; Heidelberger, C. The clinical pharmacology of 5-trifluoromethyl-2′-deoxyuridine. *Cancer Res.* **1972**, *32*, 247-253.

(47) Maji, A.; Hazra, A.; Maiti, D. Direct synthesis of α-trifluoromethyl ketone from (hetero) arylacetylene: design, intermediate trapping, and mechanistic investigations. *Org. Lett.* **2014**, *16*, 4524-4527.