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Divergent Functionalization of Styrenes via Radical/Polar Crossover with CO_2 and Sodium Sulfinates

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Abstract: Sulfones and carboxylic acids are prominent motifs widely present in the chemical structure of agrochemicals, pharmaceuticals and many other highly valuable compounds. Herein, we describe a conjunctive strategy for the precise installation of these functionalities onto styrenes using sodium sulfinates and CO_2 as coupling partners. The protocol allowed the preparation of carboxy-sulfonylated compounds in good yields and broad functional group tolerance. Additionally, taking advantage of the leaving group ability of the sulfone moiety, a one-pot photocatalytic carboxy-sulfonylation-elimination strategy was developed for the synthesis of α-aryl-acrylates.

Introduction

Alkenes are versatile synthetic building blocks.[1] Among their several applications, the conjunctive catalytic vicinal incorporation of two functional groups into the alkene's π system is a straightforward approach for the construction of highly functionalized molecules.[2–5] Over the last decades, the synthetic community has been witnessing great advances in the site-selective difunctionalization of alkenes. Among the different protocols already developed,[6–12] multicomponent strategies promoted by visible-light photoredox catalysis emerge as very promising alternatives, owing to high synthetic efficiency and functional group tolerance, mildness, and operational simplicity.[13–18]

In this context, the photocatalytic multicomponent sulfonylation of alkenes has attracted the attention of many research groups. The interest is related to the prominent biological properties that the presence of such functional group confer to the target molecules,[15] and also for its electronic and structural properties. Once present in a given molecular framework the sulfone group can behave as a modulator of chemical reactivity of an adjacent site or as a leaving group. In other words, sulfones are recognized as versatile precursors to a range of important functionalities which are otherwise difficult to obtain.[19–23] A considerable number of works describing the photocatalytic sulfonylation with concomitantly incorporation of a second moiety through C–C couplings have been already reported.[24–29] However, to the best of our knowledge, an efficient approach for the carboxy-sulfonylation of alkenes remains unprecedented.

Over the last decades, carbon dioxide (CO_2) has emerged as a potentially sustainable resource due to its abundance, availability, non-toxicity, and low cost.[30–33] In the field of organic chemistry, CO_2 is considered an ideal C1 feedstock to furnish valuable carbonates, carbamates, and carboxylic acids and their derivatives.[34–37] Despite its thermodynamic stability and/or kinetic inertness in certain transformations, different strategies to incorporate CO_2 into organic molecules have been reported, such as transition-metal-catalyzed protocols,[38–45] reduction strategies,[46–50] and more recently the nucleophilic attack by anionic intermediates generated via photocatalytic reductive radical–polar crossover processes. The latter approach has especially been applied to alkene difunctionalizations, providing structurally relevant β-functionalized carboxylic acids.[51–56] These protocols involves the generation of a radical **I** which adds to the olefin, forming a covalent bond that is kinetically stable, thereby generating a radical adduct intermediate **II** – the transient radical species will subsequently be converted via a reductive radical–polar crossover process into an anionic adduct **III** through single electron transfer (SET). However, in most of the previous reports the functional groups incorporated at the β-position can hardly be used for further modifications (Scheme 1A). In this regard, the development of a tunable alkene carboxy-functionalization process that inserts a functional group with inherent electron-withdrawing and leaving group properties would be of great utility.

With this rationale in mind, we hypothesized that the use of sulfonyl radicals would be a viable alternative to access β-sulfonylated carboxylic acids. Given the wide versatility of both

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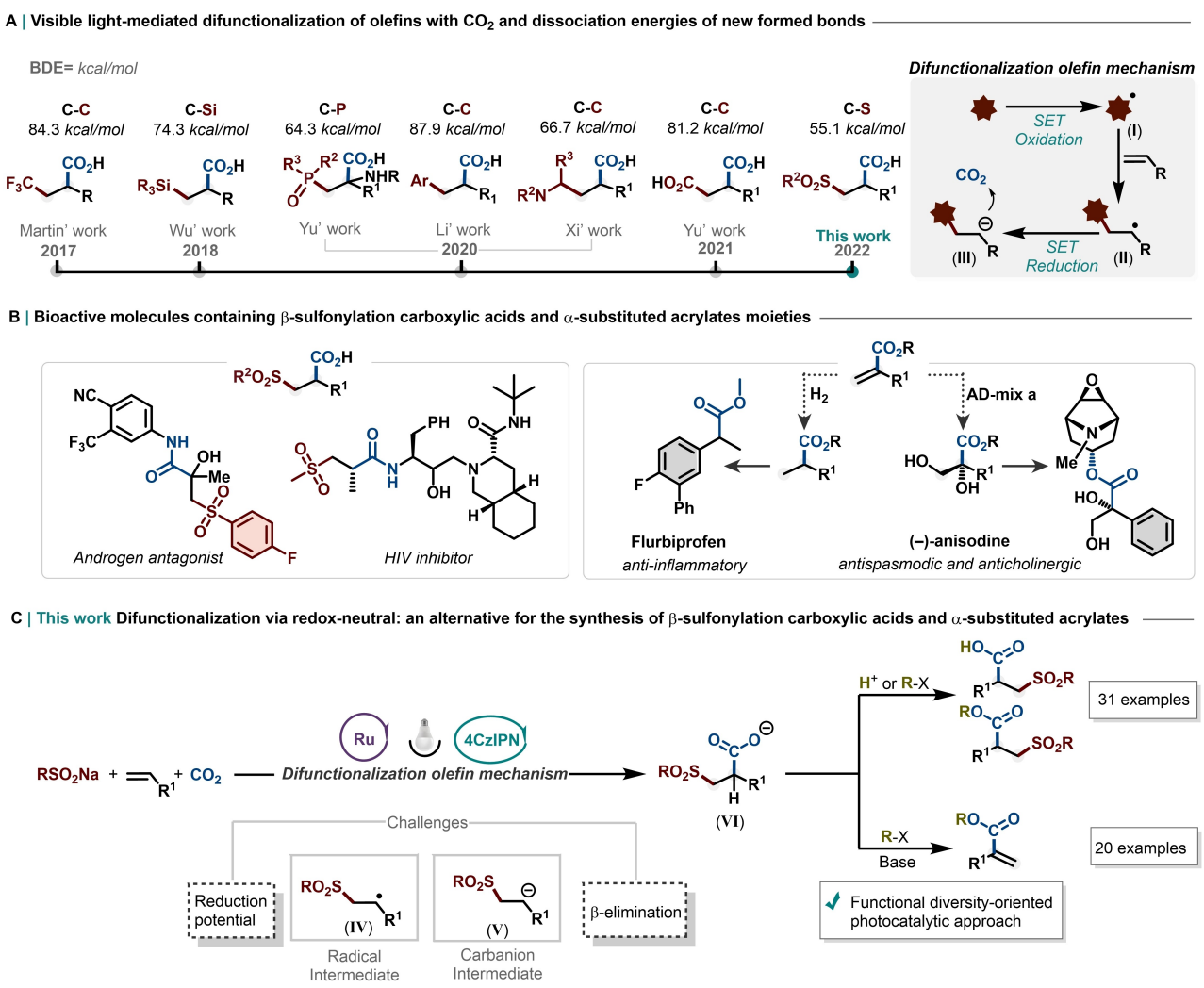


Scheme 1. Strategies for the visible-light-driven carboxylation of alkenes with CO_2. *The BDEs were predicted in the ALFABET (A machine-Learning derived, Fast, Accurate Bond dissociation Enthalpy Tool at https://bde.ml.nrel.gov/).

functionalities incorporated around the single bond, chain homologations would be possible in both directions. Additionally, we also assumed that taking advantage of the ability of sulfones to behave as leaving groups, a sequential radical–polar addition/elimination approach could be developed to afford α-substituted acrylates. These electron-poor alkenes are versatile building blocks, being not only good Michael acceptors but also able to be directly converted into polymers[57–61] or pharmacologically important compounds, such as metalloproteases[62] and ATP-dependent ligases inhibitors,[63,64] and antispasmodic[65] and anti-inflammatory agents[66] (Scheme 1B).

The development of our divergent strategy presents several challenges: First, the intermediate β-sulfonyl radical (**IV**) must have a reduction potential compatible with the redox potentials of the employed photocatalyst in order to guarantee its fast reduction. Second, the β-sulfonyl carbanion (**V**) must be stable enough to prevent a premature β-elimination of the sulfonyl group and nucleophilic enough to perform the attack to CO_2. Third, the strategy must allow the control of those events by few adjustments on the reaction conditions, in order to afford the selective access to both the β-sulfonylated carboxylatic acid/ester (**VI**) and the α-substituted acrylates in high yields (Scheme 1C).

Results and Discussion

Optimization study

We initiated our investigation by choosing methyl 4-vinylbenzoate (**1a**) and sodium *p*-toluenesulfinate (**2a**) as model substrates for the carboxylsulfonylation protocol. A screening of the reaction parameters led us to a condition in which the desired product (**4**) was obtained in 75% NMR yield, employing $Ru(bpy)_3(PF_6)_2$ (**3a**) as the photocatalyst, and DMA (0.2 M) as the solvent, under 1.5 atm of CO_2 atmosphere at 0 °C. The use of LiCl as an additive led to significant lower chemical yields

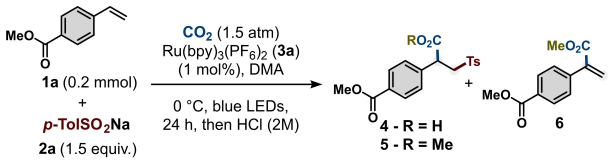
(entry 2). Surprisingly, a strong temperature influence on the reaction outcome was observed in the optimization studies. At higher temperatures, 10 °C and room temperature, the NMR yields decreased to 57% and 22% respectively (entries 3 and 4). The organic photocatalyst 4CzIPN (**3b**) was tested, but the yield dropped significantly (entry 5, 30% NMR yield). Further, by increasing the amount of photocatalyst the desired product **4** could be obtained in 91% NMR yield (entry 6). Given to the high polarity of product **4**, its isolation was initially performed through a basic extraction-acidification sequential protocol, which afforded the isolated **4** in 87% chemical yield (Table 1, entry 6– see section 4.2 in the Supporting Information for details). Although this procedure worked well for **4**, it didn't show to be reliable and reproducible during the scope investigation. Thus, we decided to isolate most of products as their respective esters, which ensured reliable and facile isolation (see section 4.2 in the Supporting Information for details). Using such one-pot esterification protocol, product **4** could be isolated as its respective methyl-ester in 79% chemical yield (Table 1, entry 7).

Due to the aforementioned wide applicability of α-aryl-acrylates in synthetic organic chemistry and polymer science, and the lack of synthetic methodologies employing styrenes and CO_2 as building blocks,[67–73] we envisioned adapting the reaction conditions of entry 6, in order to explore the leaving group ability of the sulfone moiety for the easy generation of α-aryl-acrylates. Therefore, carrying out the photocatalytic protocol in the presence of 1 equiv. of K_2CO_3, and performing the esterification step at room temperature using 3 equiv. of iodomethane, we obtained the β-sulfonylated carboxylate **4** in 53% chemical yield, along with the α-aryl-acrylate **6** in 44% yield (entry 8). This preliminary result suggested that the esterification of **4** was not complete, and therefore, an excess of CH_3I under basic conditions would possibly afford **6** in a higher chemical yield. To our delight, performing the esterification step using 5 equiv. of CH_3I, and increasing the reaction time to 12 h led to almost exclusive formation of **6** in 88% NMR yield (entry 9). Lastly, control experiments confirmed the crucial importance of light irradiation and the presence of the catalyst to the reaction outcome (entries 10 and 11).

With the optimized conditions in hand, we started the reaction scope evaluating a set of sodium sulfinates (Table 2). Arylsulfinates bearing both electron-withdrawing and electron-donating substituents reacted smoothly delivering their respective carboxy-arylsulfonylated products (**4**, **7**–**10**) in good to excellent yields. These results demonstrate the functional group tolerance and suggest that electron-rich arylsulfonyl-radicals (**4**, **8**, **9**, **12**) are better coupling partners in our transformation. It is worth mentioning that the incorporation of halogenated arylsulfones opens the possibility of further modifications by means of transition-metal-catalyzed cross-coupling strategies.[74,75] In contrast to other radical sulfonylation protocols, our method is not limited to arylsulfinates.[27,76,77] Aliphatic sulfonyl radicals could also successfully be incorporated into the styrene framework, affording products **13**–**15** in good to excellent yields. The possibility of the incorporation of aliphatic sulfonyl groups expands dramatically the applicability of our protocol, once such substrates can be easily accessed from alkyl-halides.[78,79]

Next, we turned our attention to the scope of styrenes (Table 3). We used alkyl-sulfinates in this scope. The only exception is product **16**, which was prepared by the coupling of 2-trifluoromethyl-styrene (**1b**) with **2a** and CO_2 in 62% chemical yield. Our optimized protocol worked also well with the 4-trifluormethyl-styrene (**1c**) and with 4-vinyl-benzoates bearing different types as side chains. The excellent chemoselectivity was evident when 4-vinyl-benzoates bearing unconjugated alkenes and alkynes were exclusively converted to their corresponding carboxy-sulfonylated products **18** and **19** in 78% and 67% yields, respectively. Next, vinyl-benzoates bearing

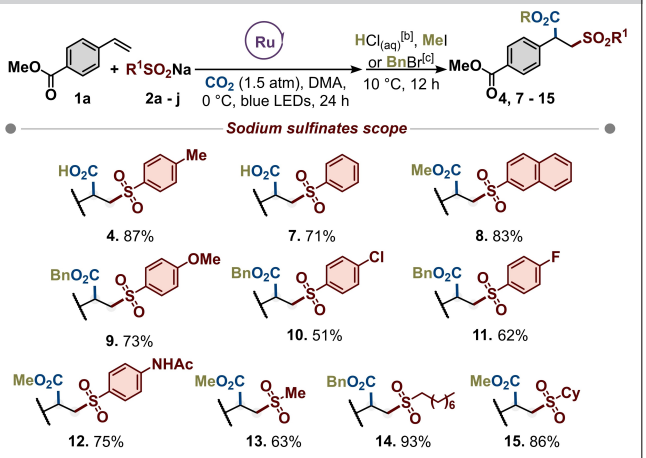
Table 1. Optimizations of the reaction conditions.



Entry	Deviations	4 (%)[a]	5 (%)[a]	6 (%)[a]
1	None	75	-	-
2	LiCl as additive	trace	-	-
3	10 °C	57	-	-
4	r.t.	22	-	-
5	4CzIPN instead **3a**	30	-	-
6	2 mol % of **3a**	91 (87)[b]	-	-
7	then CH_3I (3 equiv.),10°C, 5h	N.D.	84 (79)[c]	N.D.
8[d]	K_2CO_3 (1 equiv.), then CH_3I (3 equiv.)	53	N.D	44
9[e]	K_2CO_3 (3 equiv.), then CH_3I (5 equiv.)	N.D.	7	88
10	Without light	N.D.	N.D.	N.D.
11	Without $Ru(bpy)_3(PF_6)_2$	N.D.	N.D.	N.D.

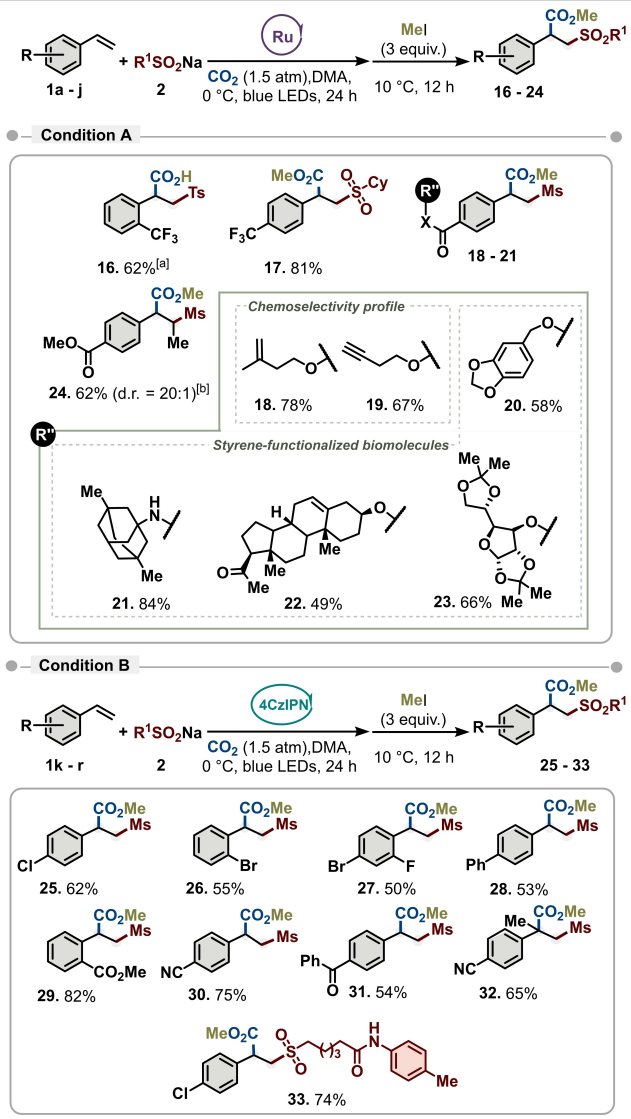
N.D. = not detected, 4CzIPN = 2,4,5,6-tetrakis(carbazol-9-yl)-1,3-dicyanobenzene. [a] Yields determined by ^1H NMR using 1,3,5 trimethoxybenzene as an internal standard and yields of isolated products in parentheses. [b] Isolated yield using the basic extraction-acidification protocol. [c] Isolated yield using the esterification protocol. [d] r.t., 5 h. [e] r.t., 12 h.

Table 2. Scope of sodium sulfinates.[a]



[a] Reaction conditions: standard conditions (Table 1, entries 6 or 7). [b] Isolated yield using the basic extraction-acidification protocol. [c] Isolated as the corresponding ester upon treatment with MeI or BnBr (3 equiv.), 10 °C, 12 h; see Supporting Information for details.

Table 3. Scope of styrenes.



Reaction conditions A: standard conditions (Table 1, entry 7). [a] Isolated yield using the basic extraction-acidification protocol. [b] d.r. ratio based on the analysis of ^{1}H NMR spectra of crude product. Reaction conditions B: 2 mol% of 4CzIPN (**3b**) in lieu of Ru(bpy)$_3$(PF$_6$)$_2$ (**3a**) see Supporting Information for details.

active pharmaceutical ingredients, namely piperonyl alcohol (anti-oxidant activity) and memantine (used in the treatment of Alzheimer's disease), and natural products frameworks, such as pregnenolone and a carbohydrate-derived moiety, could also be successfully employed under our optimized conditions, affording the corresponding products (**20**–**23**) in good yields. Our method also showed to be applicable to methyl 4-propenyl-benzoate (**1j**), affording the carboxyl-sulfonylated **24** in 62% yield and high diastereoselectivity. Furthermore, we observed that halogenated styrenes, which are less electron-poor substrates than the 4-vinyl-benzoates, were not compatible with our initial optimized conditions. In order to access the reactivity of these compounds, we performed a reoptimization of the reaction parameters using sodium methanesulfinate (**2h**) and 4-chlorostyrene (**1k**) as reaction partners and observed that the simple exchange of Ru(bpy)$_3$(PF$_6$)$_2$ (**3a**) to 4CzIPN afforded the desired product **25** in 62% yield (see Supporting Information for more details). Surprisingly, the correspondent carboxy-arysulfonylated product was not obtained when *p*-toluenesulfinate (**2a**) was employed under the same conditions. The data suggests that alkylsulfonyl radicals are more reactive towards less electron-poor styrenes than arylsulfonyl radicals, and indicates that their reactivity is higher when the reaction is catalyzed by 4CzIPN.

Encouraged by these results, we further explored the applicability of this alternative protocol with other halogenated styrenes (Table 3). Both ortho- and para-halogenated styrenes performed well, being converted to their respective difunctionalized products (**26** and **27**) in good yields. This alternative condition was also amenable to other styrenes that didn't show good or any reactivity when Ru(bpy)$_3$(PF$_6$)$_2$ (**3a**) was employed. In this regard, 4-vinyl-1,1′-biphenyl (**1n**) could smoothly be converted into its respective carboxyl-sulfonylated product **28** in 53% yield. Surprisingly, other electron-poor styrenes – methyl 2-vinyl-benzoate, 4-cyano-styrene and 4-vinyl-benzophenone – also performed well, affording the respective products (**29**–**31**) in good yields. The reaction also showed to be an effective method to accessing difunctionalized products containing quaternary centers, which was showcased by the preparation of product **32** from α-methyl-4-cyanostyrene (**1r**), in 65% yield. Of note, tertiary carboxylic acids could be effectively utilized for the preparation of quaternary carbon centers.[80–82] Still exploring the good performance of alkylsufinates in our study, an alkylsulfinate bearing a *p*-toluil-amide moiety in the side-chain could also be incorporated, affording the respective product **33** in 74% chemical yield.

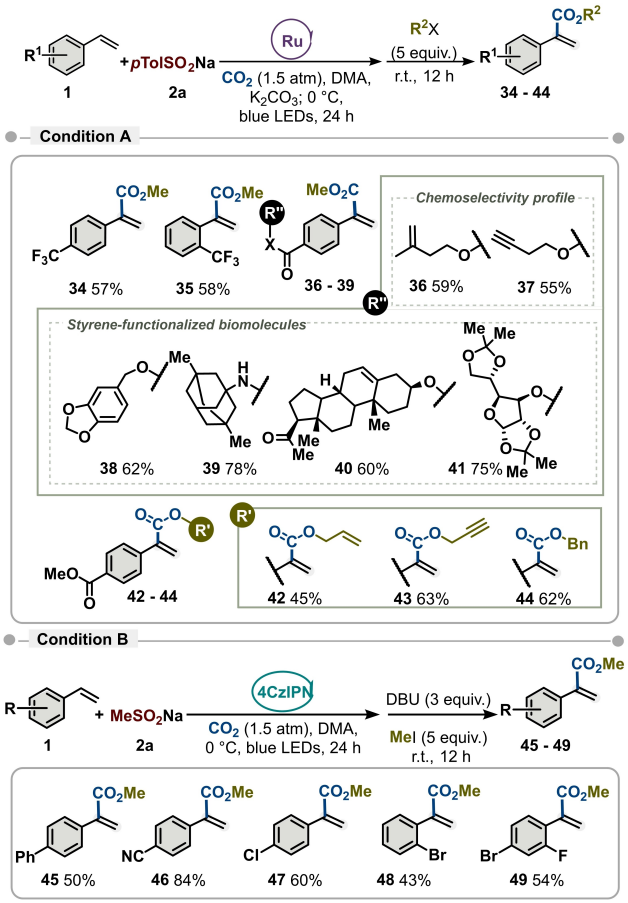
One-pot photocatalytic synthesis of α-aryl-acrylates

With the optimized conditions described in Table 1, entry 9 in hand, we next evaluated the scope and limitations of our unprecedent one-pot synthesis of α-aryl acrylates (Table 4). Gratifyingly, *ortho*- and *para*-trifluoromethyl-styrenes, as well as the previously tested set of 4-vinyl-benzoate containing biologically relevant scaffolds were smoothly converted to the corresponding acrylates (**34**–**41**) with yields ranging from 57% to 78%.

Furthermore, we explored the incorporation of different functionalities on the ester moiety. Allyl-bromide, propargyl-bromide and benzyl-bromide could successfully be employed as alkylating agents, affording the respective acrylates (**42**–**44**) in good yields. It is worth mentioning that pericyclic reactions[83] and Ireland–Claisen rearrangement[84] are among the most relevant synthetic applications of such derivatives (Table 4, condition A).

In order to access α-aryl-acrylates derived from halogenated styrenes, we had to adapt the reaction condition developed for the difunctionalization of those substrates in the previous section. Therefore, new reaction conditions using 4CzIPN as

Table 4. One-pot photocatalytic synthesis of α-aryl-acrylates.



Reaction conditions A: standard conditions (Table 1, entry 9); Reaction conditions B: 2 mol% of 4CzIPN (**3b**) instead of $Ru(bpy)_3(PF_6)_2$ (**3a**) were used and 3 equiv. of DBU as base were added after the photocatalytic reaction; see Supporting Information for details.

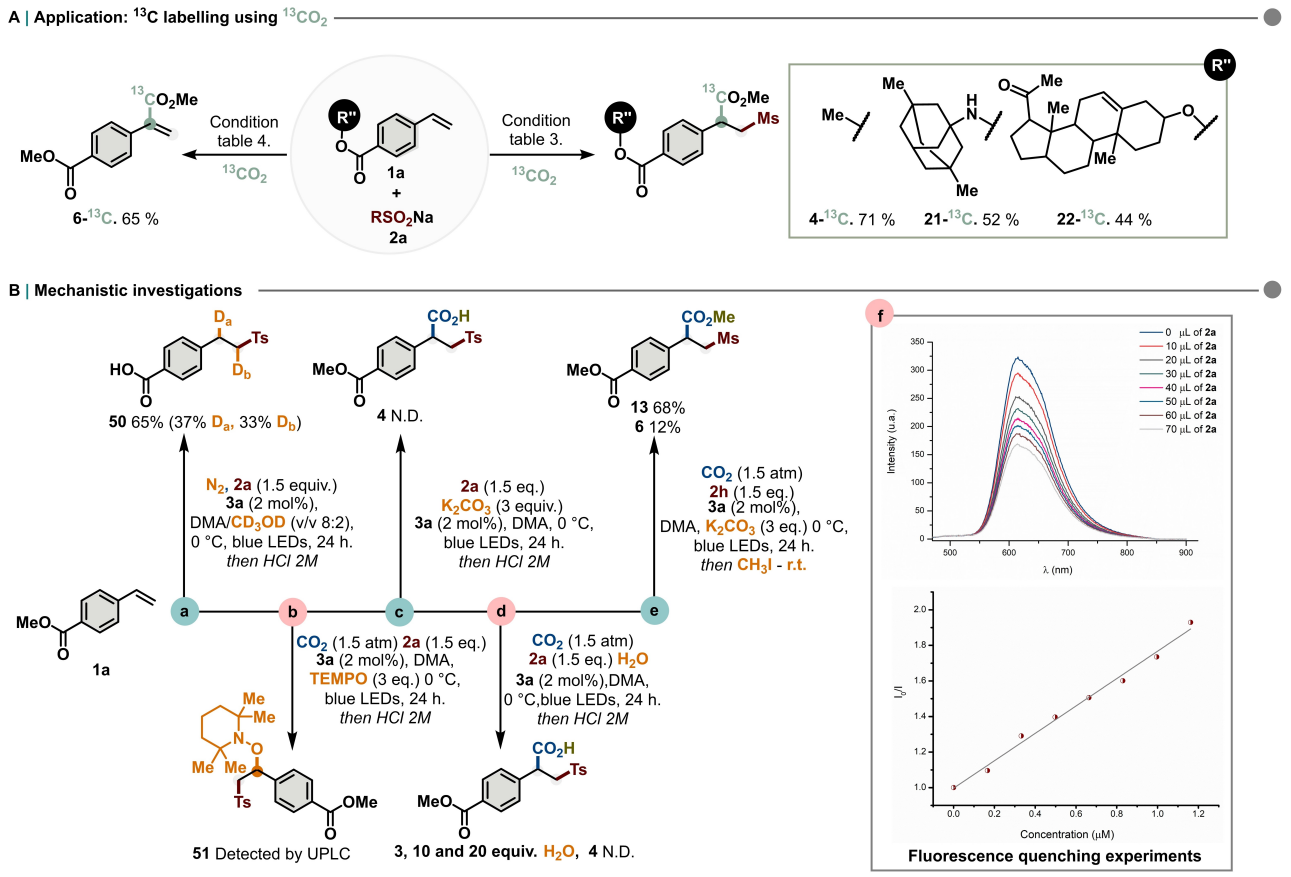
photocatalyst and DBU as base were found, and allowed not only the synthesis of the targeted halogenated α-aryl-acrylates (**47**-**49**), but also of other *p*-substituted-aryl-acrylates (**45** and **46**) with yields ranging from 43% to 84% yield (Table 4, condition B, see mechanistic studies section for more details). It is important to be mentioned that DBU was added only after the photocatalytic event, along with CH_3I. The addition of such strong base before irradiation led to low yields and many side products.

The synthesis of molecularly diversified carboxylic acids using CO_2 as C1 building block represents a great opportunity for the selective isotopic labeling of organic molecules.[85,86] Recognizing the relevance of this topic, both protocols developed herein were performed using $^{13}CO_2$ in lieu of $^{12}CO_2$ (Scheme 2A). To our delight, the respective ^{13}C-labelled β-sulfonylated esters **4**-^{13}C, **21**-^{13}C and **22**-^{13}C were smoothly accessed with yields ranging from 44% to 71% yield. The incorporation of $^{13}CO_2$ also worked well in the synthesis of acrylate **6**-^{13}C.

Mechanistic investigations

In order to get insights into the reaction mechanism, some control experiments were conducted. As illustrated in Scheme 2Ba, the isotopic labeling study with CD_3OD suggests the formation of a benzylic anionic intermediate – wherever compound **50** was formed after the concomitant deuteration of the α-sulfone carbon. We also observed that the addition of 2,2,6,6-tetramethyl-piperidinyloxyl (TEMPO) inhibited the reaction, which was corroborated by the detection of the adduct between TEMPO and the sulfonylated intermediate by MS analysis of the reaction crude, indicating that radical species are involved in the process (Scheme 2Bb). When the reaction was performed using K_2CO_3 as CO_2 source (N_2 atmosphere), the difunctionalized product could not be detected after the acidic quenching (Scheme 2Bc). Intriguingly, the addition of water to the optimized conditions inhibited the formation of the carboxyl-sulfonylation product but didn't afford the respective alkylsulfone derived from the protonation of the anionic intermediate (Scheme 2Bd). Finally, a tentative α-aryl-acrylate synthesis experiment using methyl sulfinate instead of phenyl-sodium sulfinate and carbonate as base afforded the respective carboxysulfonylated compound as the major product (Scheme 2Be). This experiment, which is in consonance with the results described in Table 4 demonstrates that aliphatic sulfinates are less efficient leaving groups than arylsulfinates, requiring the use of a stronger base such as DBU to be eliminated. Additionally, Stern–Volmer experiments demonstrated that the excited $Ru(bpy)_3(PF_6)_2$ (**3a**) was quenched by **2a**. Moreover, the analysis of the redox potentials – obtained by cyclic voltammetry of the involved species – indicates that the reaction could be initiated by a reductive quenching process (Scheme 2Bf).

Based on the mechanistic investigation and precedents in literature,[51–56] a plausible reaction mechanism is proposed as shown in Scheme 2C. The photoexcited catalyst $[Ru(bpy)_3(PF_6)_2$ (**3a**) ($E = +0{,}77$ V vs. SCE in MeCN),[87] 4CzIPN (**3b**) ($E = +1.35$ V vs. SCE in MeCN)][88] – or either an excited photocatalyst, which is in situ generated from the 4CzIPN photosubstitution under the reaction conditions[89] – is reductively quenched by the sodium sulfinate leading to the sulfonyl radical **A**. Subsequently, this species adds to styrene **1** to selectively generate the benzylic radical **B**. At this point, a single electron transfer (SET) process between **B** and the reduced photocatalyst affords the benzylic carbanion **C**, which finally traps the CO_2 to generate carboxylate **D**. From this stage, two divergent pathways can be followed according to the final performed treatment: I) The first one leads to the formation of the β-sulfonylated acid/ester **E** by the treatment of the reaction with an acid or an alkylating agent. II) The second leads to the formation of α-substituted acrylate **F** when a base and the alkylating agent are added to the system.



Scheme 2. A. Application: Synthesis of carboxy-sulfonylated compounds and α-aryl-acrylates using $^{13}CO_2$. **B.** Mechanistic investigations. **C.** plausible reaction mechanism to the divergent functionalization of styrenes via radical/polar crossover with CO_2 and sodium sulfinate.

Conclusions

In summary, we have described the development of an unprecedented divergent photocatalytic approach for the incorporation of CO_2 into styrenes. Firstly, we developed a multicomponent carbosulfonylation protocol that enable the access to β-sulfonylated carboxylic acids. This reaction was shown to perform better at lower temperatures, and two different catalysts were employed to access a wider structural diversity. In a general overview, while $Ru(bpy)_3$ was the best catalyst for more electron-poor substrates, 4CzIPN showed a better performance when less electron-poor styrenes were employed. The reaction showed a good functional group tolerance, allowing the difunctionalization of styrenes bearing pharmaceutical ingredients and natural products, and the incorporation of both aromatic and aliphatic sulfone moieties. Later, taking advantage of the inherent leaving group ability of the sulfone group, we adapted our conditions to promote its elimination. In this new protocol, which is unique since it has as overall outcome the selective incorporation of CO_2 at α-position of the styrene, a family of α-aryl-acrylates could easily be accessed with good functional group tolerance and yields.

Lastly, we also demonstrated that our protocol can be employed as a simple and straightforward strategy for the preparation of ^{13}C labeled molecules. The synthetic potential of the obtained products may open new opportunities to access an even broader chemical space. We do believe that our contribution will serve as inspiration to further studies in this arena.

Experimental Section

General procedures for synthesis of β-functionalized carboxylic acids

Esterification protocol: Protocol for isolation of products as esters. To an oven dried Schlenk tube (10 mL) equipped with a stirring bar were added the styrene **1** (0.2 mmol), sodium sulfinate **2** (1.5 equiv.) and the photocatalyst (**3a**/**3b**) (2 mol%). Subsequently, the flask was connected to a Schlenk line, and the atmosphere was exchanged through three cycles of evacuation followed by re-filling with CO_2. Next, maintaining the CO_2 flow opened, DMA (1 mL) was added, the Schlenck was closed again and the internal pressure of the system was adjusted to 1.5 atm. The tube was properly sealed and the mixture was placed in the reactor at a pre-set temperature of 0 °C and irradiated under stirring for 24 h (prior starting the irradiation, the reaction was left stirring for about 5 minutes to allow the temperature stabilization). After this period, the system was transferred from the reactor to the Schlenk line, and the atmosphere was changed to N_2 (again via the careful evacuation and re-filling protocol). Keeping the N_2 flow, the mixture was treated with CH_3I or BnBr, and kept under stirring at 10 °C for 12 h. At the end of this period, the system was opened and diluted with about 2–3 mL of distilled water, and extracted with EtOAc at least 3 times. The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexanes:EtOAc, 90–80:10–20) to give the pure desired product.

Acid-base extraction protocol of 4: After completion, the reaction was carefully quenched with 3 mL of saturated $NaHCO_{3(aq)}$ and the mixture was extracted with ethyl acetate (3×5 mL). The combined organic layers were washed again with 10 mL of saturated $NaHCO_3$ solution. The combined aqueous layers were brought to pH 4 with 10% HCl solution. After, the mixture was extracted with ethyl acetate and dried over anhydrous Na_2SO_4 and concentrated under reduced pressure.

General procedures for synthesis of α-substituted acrylates

Condition A: An oven dried Schlenk tube (10 mL) equipped with a stirring bar were added styrene **1** (0.2 mmol), sodium sulfinate **2** (1.5 equiv.), K_2CO_3 (3.0 equiv.) and $Ru(bpy)_3(PF_6)_2$ **3a** (1 mol%). Subsequently, the flask was connected to a Schlenk line, and the atmosphere was exchanged through three cycles of evacuation followed by re-filling with CO_2. Next, maintaining the CO_2 flow opened, DMA (1 mL) was added, the Schlenck was closed again and the internal pressure of the system was adjusted to 1.5 atm. The tube was properly sealed and the mixture was placed in the reactor at a pre-set temperature of 0 °C and irradiated under stirring for 24 h (prior starting the irradiation, the reaction was left stirring for about 5 minutes to allow the temperature stabilization). After this period, the system was transferred from the reactor to the Schlenck line, and the atmosphere was changed to N_2 (again via evacuation and refilling with N_2). Keeping the N_2 flow, the mixture was treated with CH_3I, and kept under stirring at room temperature for 12 h. At the end of this period, the system was opened and diluted with about 2–3 mL of distilled water, and extracted with EtOAc at least 3 times. The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexanes:EtOAc, 90–80:10–20) to give the pure desired product.

Condition B: An oven-dried Schlenk tube (10 mL) containing a stirring bar were added styrene **1** (0.2 mmol), sodium sulfinate **2** (1.5 equiv.) and 4CzIPN (**3b**) (2 mol%). Subsequently, the flask was connected to a Schlenk line, and the atmosphere was exchanged through three cycles of evacuation followed by re-filling with CO_2. Next, maintaining the CO_2 flow opened, DMA (1 mL) was added, the Schlenck was closed again and the internal pressure of the system was adjusted to 1.5 atm. The tube was properly sealed and the mixture was placed in the reactor at a pre-set temperature of 0 °C and irradiated under stirring for 24 h (prior starting the irradiation, the reaction was left stirring for about 5 minutes to allow the temperature stabilization). After this period, the system was transferred from the reactor to the Schlenck line, and the atmosphere was changed to N_2 (again via evacuation and refilling with N_2). Keeping the N_2 flow, the mixture was treated with CH_3I and DBU, and kept under stirring at room temperature for 12 h. At the end of this period, the system was opened and diluted with about 2–3 mL of distilled water, and extracted with EtOAc at least 3 times. The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (Hexanes:EtOAc, 90–80:10–20) to give the pure desired product.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: α-substituted acrylates · carbon dioxide · carboxylic acids · photocatalysis · sustainability

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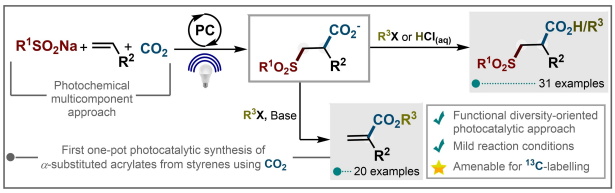

Not so radical: The amalgamation of radical chemistry with polar chemistry is used to develop a tunable multi-component reaction which involves CO_2, sodium sulfinates and styrenes to access both β-sulfonylateds carboxylic acids through radical–polar crossover process and to α-substituted acrylates through sequential sulfonyl radical addition/coupling/elimination process. This setup exhibits excellent tolerance to different functional groups and its application towards biologically relevant molecules and product diversification contributes to the synthetic utility of this method.

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1 – 10

Divergent Functionalization of Styrenes via Radical/Polar Crossover with CO_2 and Sodium Sulfinates