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# Visible-light-induced bifunctionalisation of (homo)propargylic amines with $CO_2$ and arylsulfinates†

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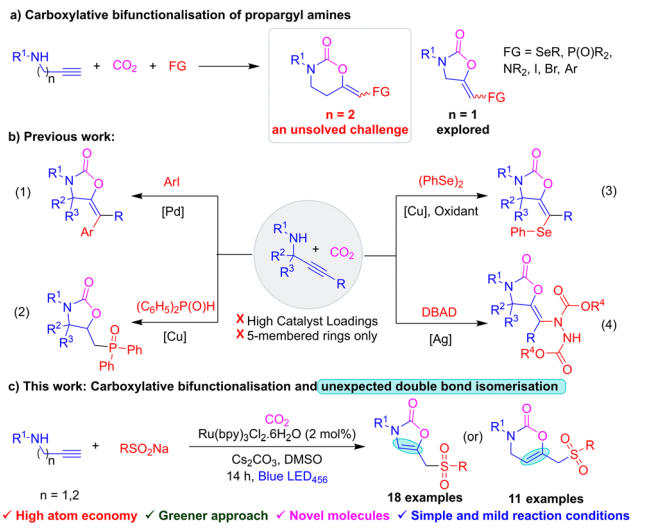
**An unprecedented carboxylative sulfonylation of (homo)propargyl amines with $CO_2$ and sodium arylsulfinates under visible light irradiation has been developed with high efficiency. This ruthenium-catalysed photochemical protocol offers broad substrate scope giving 2-oxazolidinones and 2-oxazinones bearing alkyl sulfones in good yields under ambient reaction conditions. An *in situ* double bond isomerisation occurs in tandem. A mechanistic rationale for these radical-initiated carboxylative cyclisations involving sulfinyl radicals is presented, supported by control and quenching experiments.**

Over the past century atmospheric $CO_2$ concentration has increased dramatically causing severe climate changes.[1] In this context, utilisation of $CO_2$ for the functionalisation of organic molecules has gained much attention.[2] The conversion of $CO_2$ typically requires high energy due to its thermodynamic stability and kinetic inertness.[3] Nonetheless, various synthetic methods have been developed to transform $CO_2$ into valuable organic compounds.[4] Among hem, multicomponent carboxylative bifunctionalisation of propargyl amines with $CO_2$ and other functional groups represents a promising strategy for synthesising valuable functionalised heterocycles like 2-oxazolidines.[5] 2-Oxazolidine and 2-oxazinone motifs are frequently found in various bio-active molecules and chiral auxiliaries.[6]

Generally, carboxylative bifunctionalisation of propargyl amines affords functionalized vinyloxazolidinones, but the analogous conversion of homopropargyl amines to synthesise larger ring vinyloxazinones is still an unsolved challenge (Scheme 1a).[7] Literature reported carboxylative bifunctionalisations of propargyl amines are depicted in Scheme 1b(1–4), including the synthesis of aryl, phosphono, selenyl and amino oxazolidinones.[8–11] While all have potential advantages, the previous methods use high loadings of metal catalysts, oxidants and/or elevated temperatures and are limited to propargyl amines. Therefore, carboxylative bifunctionalisations of (homo)propargyl amines with other functional groups under mild conditions are highly sought after. Recently, visible light-promoted fixation of $CO_2$ has played a promising role in organic synthesis because of the demonstrated complex bond constructions under mild reaction conditions and the environmentally benign nature of visible light.[12] On the other hand sulfones are versatile building blocks in organic chemistry as they can be readily transformed into various useful functional groups.[13] Furthermore, sulfones are frequently found in pharmaceuticals, agrochemicals and functional materials.[14] Sulfur is found more often than fluorine in drug molecules and recently alkyl/vinyl sulfones have been found to act as radical precursors in synthetic organic chemistry.[15] To the best of our knowledge, carboxylative sulfonylation of alkynyl amines to obtain sulfonylated oxazolidinones/oxazinones is unknown in the literature.




Scheme 1 Background and context of this work.

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† Electronic supplementary information (ESI) available: Detailed experimental procedures, characterisation, X-ray data for **3a** and **4a** and copies of NMR spectra. CCDC 2287477 and 2287478. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d3cc04160c

Continuing our interest in photocatalysis and sulfonylation,[16] herein we report an unprecedented double bond isomerised carboxylative sulfonylation of (homo)propargylamines with $CO_2$ for the synthesis of oxazolidinones and oxazinones under mild photochemical conditions (Scheme 1c).

We began our investigation with amine **1aa** and sulfinate **2a** as model substrates to optimise photochemical carboxylative bifunctionalisation, and the results are shown in Table 1. Initially, the visible light irradiation of **1aa** (0.14 mmol), **2a** (0.21 mmol) and iodine (0.14 mmol) with MTBD as a base (0.28 mmol) under a $CO_2$ balloon in DMF (2 mL) afforded **3a** in 50% isolated yield (entry 1). We examined different organic and inorganic bases ($Cs_2CO_3$, DBU and DABCO) and photocatalysts (Eosin Y, 4-CzIPN and $Ru(bpy)_3^{2+}$) (entries 2–8). After screening it was found that 2 mol% $Ru(bpy)_3^{2+}$ and 2 equiv. of $Cs_2CO_3$ in DMSO under a $CO_2$ atmosphere for 14 h were the best reaction conditions, yielding **3a** in 84% yield (entry 8). Decreasing the loading of the catalyst and reaction time was found to lower the yield (entries 9 and 10). We screened different solvents: DMA was found to be less efficient than DMSO (entry 11) and other solvents such as MeCN, EtOH and $H_2O$ failed to afford **3a** (entries 12–14). No product was observed in the absence of $CO_2$ (entry 15) or blue light irradiation (entry 16).

Having found suitable reaction conditions, we examined the generality of this photochemical carboxylative bifunctionalisation reaction and the results are shown in Table 2. Various propargyl amines with different *N*-substituents **1** and sulfinate **2a** smoothly underwent photochemical carboxylative sulfonylation and afforded the corresponding oxazolidinones (**3a–3t**) in moderate to good yields. We established the structures of these novel double bond isomerized sulfonylative oxazolidinones from an X-ray crystal structure of **3a** (see ESI† for details). α-Methyl and ethyl-substituted bulky propargyl amines **1ab** and **1ac** were well tolerated in this photochemical protocol giving the corresponding compounds **3b** and **3c** in 68% and 65% yields, respectively. *N*-Phenethyl-tethered propargyl amine **1ad** afforded oxazolidone **3d** in 82% yield. Furthermore, *N*-benzyl motifs bearing methoxyl groups at *o*/*m*/*p*-positions underwent photochemical carboxylative bifunctionalisation with sulfinate **2a** smoothly, affording the corresponding sulfonylated oxazolidinones **3e–3g** in 66–79% yield. Propargyl amines with halogen-substituents on the benzyl ring such as 2-Cl, 4-Cl, 3-Br and 4-Br were also suitable for this bifunctionalisation reaction giving the corresponding compounds **3g–3k** in 69–75% yields. *N*-Benzyl motifs bearing electron-withdrawing groups such as 4-CN, 4-COOMe and 3-$CF_3$ were well tolerated in this photochemical method giving compounds **3l–3o** in good yields. Aromatic heterocyclic furan-3-ylmethyl and aliphatic cyclohexyl and propyl-substituted propargyl amines were also well tolerated in this protocol and afforded the corresponding oxalidones **3o–3q** in 62–82% yield. In contrast, *N*-phenyl and *N*-tosyl substituted

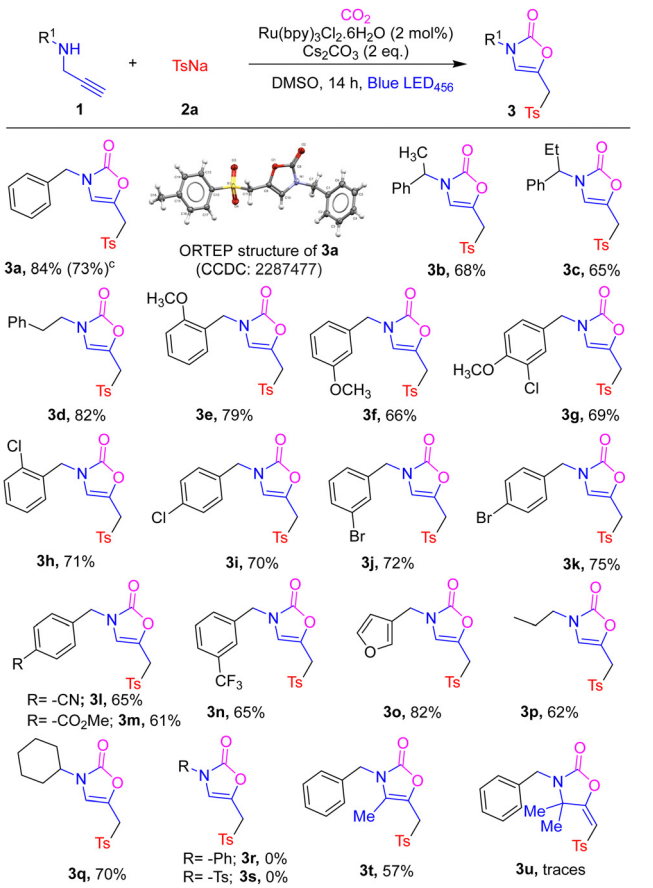
Table 1 Optimisation of reaction conditions[a]


1aa 2a 3a

| Entry | Solvent | Catalyst | Additive | Base | Time (h) | Yield **3a**[b] (%) |
|---|---|---|---|---|---|---|
| 1 | DMF | — | $I_2$ | MTBD | 14 | 50 |
| 2 | DMF | — | $I_2$ | $Cs_2CO_3$ | 14 | 48 |
| 3 | DMF | Eosin Y | $I_2$ | $Cs_2CO_3$ | 14 | 55 |
| 4 | DMF | — | $I_2$ | DABCO | 14 | 0 |
| 5 | DMF | — | $I_2$ | DBU | 14 | 0 |
| 6 | DMF | 4-CzIPN | — | $Cs_2CO_3$ | 14 | 15 |
| 7 | DMF | Ru(II) | — | $Cs_2CO_3$ | 14 | 81 |
| 8 | DMSO | Ru(II) | — | $Cs_2CO_3$ | 14 | 84 |
| 9[c] | DMSO | Ru(II) | — | $Cs_2CO_3$ | 14 | 68 |
| 10 | DMSO | Ru(II) | — | $Cs_2CO_3$ | 10 | 71 |
| 11 | DMA | Ru(II) | — | $Cs_2CO_3$ | 14 | 51 |
| 12 | MeCN | Ru(II) | — | $Cs_2CO_3$ | 14 | 0 |
| 13 | EtOH | Ru(II) | — | $Cs_2CO_3$ | 14 | 0 |
| 14 | $H_2O$ | Ru(II) | — | $Cs_2CO_3$ | 14 | 0 |
| 15[d] | DMSO | Ru(II) | — | $Cs_2CO_3$ | 14 | 0 |
| 16[e] | DMSO | Ru(II) | — | $Cs_2CO_3$ | 14 | 0 |

[a] Standard reaction conditions: **1aa** (0.14 mmol), **2a** (0.21 mmol), base (0.28 mmol), catalyst (2 mol%) and additive (0.14 mmol) in solvent (2 mL) was irradiated with a blue LED (456 nm, 40 W) under a $CO_2$ atmosphere. Ru(II) = $Ru(bpy)_3Cl_2{\cdot}6H_2O$. [b] Isolated yields. [c] 1 mol% Ru(II). [d] Reaction mixture was irradiated under $N_2$. [e] Without light.

Table 2 Scope of the synthesis of sulfonylative vinyloxazolidinones[ab]




[a] Reaction conditions: **1** (0.14 mmol), **2a** (0.21 mmol) and $Ru(bpy)_3Cl_2{\cdot}6H_2O$ (2 mol%) in DMSO (2 mL) was irradiated with a blue LED (456 nm, 40 W) under a $CO_2$ atmosphere. [b] Isolated yields. [c] 1.4 mmol scale, 346 mg.

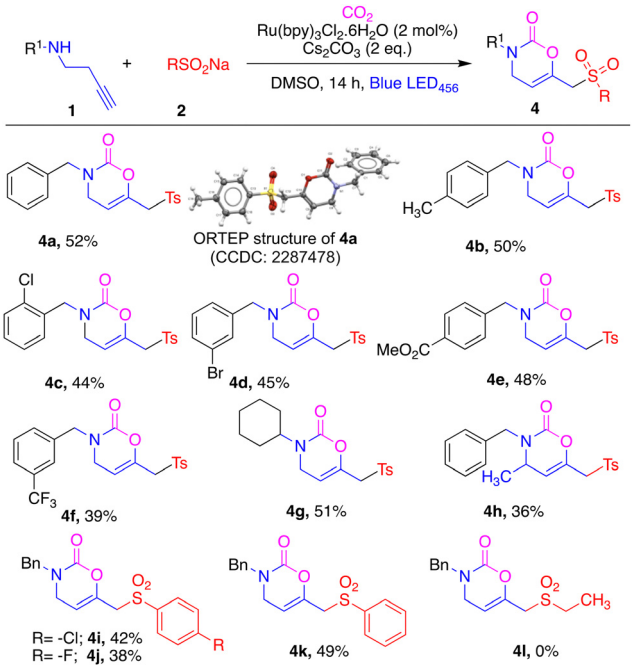
propargyl amines failed to produce the corresponding sulfonylated oxazolidinones **3r** and **3s**, presumably due to the poorer nucleophilicity of the amines. Notably, *N*-benzylbut-3-yn-2-amine **1at** and *N*-benzyl-2-methylbut-3-yn-2-amine **1au** afforded the corresponding products **3t** and **3u** in 57% yield and in trace amounts, respectively.

Then we addressed the unsolved challenge of the synthesis of vinyloxazinones using *N*-substituted homopropargyl amines under our optimised conditions and the results are depicted in Table 3. To our delight, *N*-benzylbut-3-yn-1-amine **1ba** smoothly reacted with sulfinate **2a** under this protocol and gave the corresponding oxazinone compound **4a** in 52% yield. We established the structure of the novel sulfonylated oxazinone from an X-ray crystal structure of **4a** (see ESI† for details). To the best of our knowledge, this is the first report of carboxylative functionalization of homopropargyl amines for the synthesis of 6-membered rings. Homopropargyl amines with electron-donating groups (4-Me), halogen-substituents (2-Cl and 3-Br) and electron-withdrawing groups (4-$CO_2$Me and 3-$CF_3$) on the benzyl ring smoothly reacted in this photochemical carboxylative sulfonylation reaction and afforded the corresponding compounds **4b–4f** in 39–50% yield. *N*-Cyclohexyl homopropargyl amine **1bg** and *N*-benzylpent-4-yn-2-amine **1bh** were also well tolerated, giving the corresponding products **4g** and **4h** in moderate yields. Finally, we screened the scope of sulfinates in this photochemical bifunctionalisation. Halogen (4-Cl and 4-F) bearing sulfinates and simple benzenesulfinate **1bi–1bj** reacted smoothly under this protocol affording the corresponding compounds **4i–4j** in 38–49% yield. In contrast, alkyl sulfinate **1bl** failed to produce compound **4l** under these photochemical conditions.

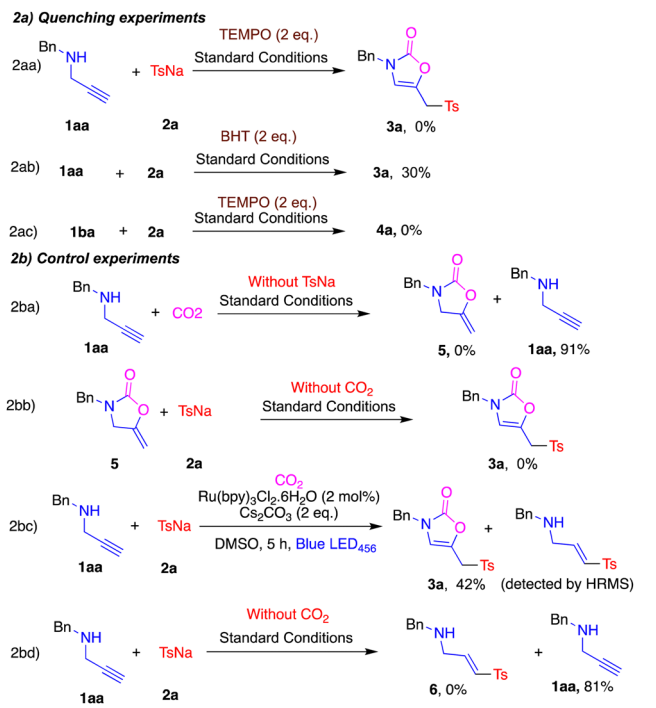
To gain insights into the reaction mechanism we performed quenching and control experiments (Scheme 2a and b). Addition of the radical scavenger TEMPO under standard reaction conditions stopped the production of **3a** and **4a** (Scheme 2aa and ab). Addition of BHT also lowered the yield of **3a** (Scheme 2ac). Thus, both reactions are proposed to proceed *via* a radical pathway. When **1aa** was subjected to the standard conditions without **2a** the reaction failed to produce the carboxylative cyclization product **5** and the starting material **1aa** was recovered in 91% yield (Scheme 2ba). The cyclized product **5** was synthesized[17] and subjected to the standard conditions without $CO_2$ but this failed to produce the product **3a** (Scheme 2bb). Both these reaction outcomes suggest that the reaction is not proceeding *via* carboxylative cyclization intermediate **5**. When the reaction mixture was quenched after 5 h and analysed by HRMS, target product **3a** and intermediate **6** were observed (Scheme 2bc). When **1aa** was subjected to the standard conditions without $CO_2$ the reaction failed to produce intermediate **6**, implying that in the case of free amine sulfinate **2a** failed to react with propargyl amine (Scheme 2bd).

Based on the above experiments and earlier literature,[18] we propose the reaction pathway of carboxylative sulfonylation (Scheme 3). Initially, a $Ru^{II}$ complex is excited by the absorption of blue light, which then oxidises sulfinate **2** to form sulfinyl radical **A** and $Ru^{I}$ species. Propargyl amine **1** reacts with $CO_2$ and a base to form carbamate intermediate **B**.[19] The addition of sulfinyl radical **A** to carbamate **B** produces vinyl radical intermediate **C**. Intermediate **C** then undergoes single electron transfer (SET) with Ru, followed by cyclization to afford cyclic intermediate **D**.

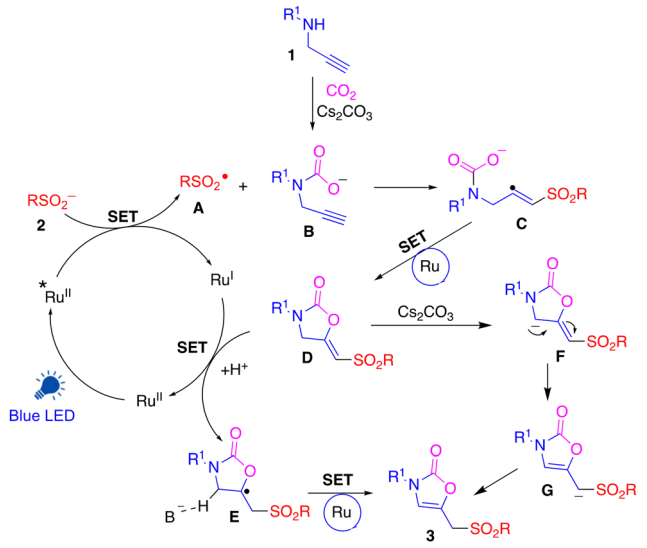
Table 3 Scope of the synthesis of sulfonylative vinyloxazinones[ab]




[a] Reaction conditions: **1** (0.14 mmol), **2** (0.21 mmol) and $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (2 mol%) in DMSO (2 mL) was irradiated with a blue LED (456 nm, 40 W) under a $CO_2$ atmosphere. [b] Isolated yields.




Scheme 2 Mechanistic investigations.




Scheme 3 Plausible mechanism.

Intermediate **D** might undergo SET with $Ru^{I}$ followed by $H^{+}$ addition to produce radical intermediate **E** and regenerate the $Ru^{II}$ complex. The reaction of intermediate **E** in the presence of a base and photocatalyst can result in the loss of $H^{+}$ affording the final product **3**. Alternatively, intermediate **D** in the presence of a base could form anion **F/G** and the addition of $H^{+}$ to the intermediate **F/G** affords the final product **3**.[20]

In conclusion, we have demonstrated a sustainable carboxylative sulfonylation of propargylamines with $CO_2$ and sodium arylsulfinates under photochemical conditions. This photochemical bifunctionalisation afforded a broad substrate scope of sulfonylated 5- and 6-membered heterocycles, 2-oxazolidinones (18 examples) and 2-oxazinones (11 examples), with good to moderate yields. A plausible mechanism was supported by control and quenching experiments. We anticipate that this methodology will enable further applications of carboxylative bifunctionalisation, especially with respect to homopropargyl amine bifunctionalisation with $CO_2$, which was previously unknown in the literature.

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## Conflicts of interest

There are no conflicts to declare.

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