



HAL
open science

3-Sulfonyl Indoles via Gold-or Silver-Catalyzed Cyclization -1,3-Sulfonyl Migration Sequences under Visible Light Irradiation

Fen Zhao, Wided Hagui, María Ballarín-Marión, Cyril Ollivier, Virginie Mouriès-Mansuy, Louis Fensterbank

► **To cite this version:**

Fen Zhao, Wided Hagui, María Ballarín-Marión, Cyril Ollivier, Virginie Mouriès-Mansuy, et al.. 3-Sulfonyl Indoles via Gold-or Silver-Catalyzed Cyclization -1,3-Sulfonyl Migration Sequences under Visible Light Irradiation. ACS Organic & Inorganic Au, 2022, 3 (1), pp.19-26. 10.1021/acsorginorgau.2c00034 . hal-04293443

HAL Id: hal-04293443

<https://hal.science/hal-04293443>

Submitted on 18 Nov 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

3-Sulfonyl Indoles *via* Gold- or Silver-Catalyzed Cyclization – 1,3-Sulfonyl Migration Sequences under Visible Light Irradiation

Fen Zhao, Wided Hagui, Maria Ballarin-Marion, Cyril Ollivier*, Virginie Mouriès-Mansuy*, Louis Fensterbank*

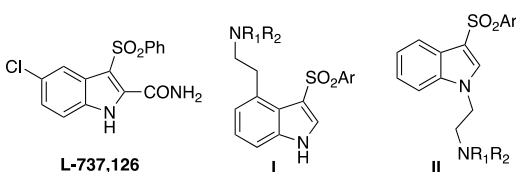
Sorbonne Université, CNRS, Institut Parisien de Chimie Moléculaire, IPCM, 4 place Jussieu, 75005 Paris, France

ABSTRACT: A pathway for the synthesis of 3-sulfonyl indoles has been devised. Upon blue LED irradiation, in the presence of a gold(I) or a silver(I) salt, *ortho*-alkynyl *N*-sulfonyl precursors readily undergo a 5-*endo-dig* cyclization concomitant with a 1,3-sulfonyl migration. While the gold-catalyzed reaction takes place in photocatalyst-free conditions, an iridium photocatalyst ($\text{Ir}[\text{dF}(\text{CF}_3)\text{ppy}]_2(\text{dtbbpy})\text{PF}_6$) is necessary with silver catalysis. Mechanistic studies featuring the generation of a sulfonyl radical support this dichotomy.

INTRODUCTION

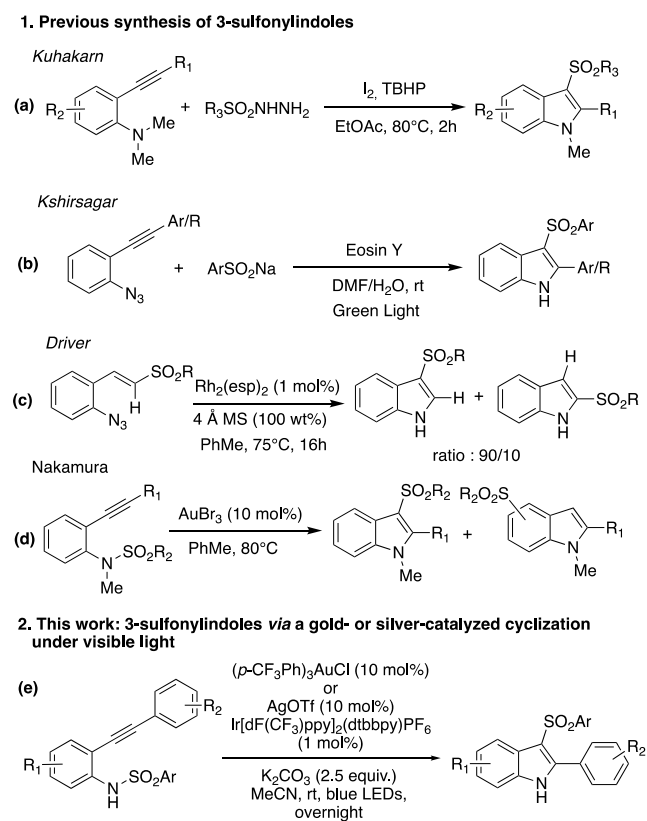
Indole structures are one of the most abundant skeletons in a wide variety of natural products and they are also useful targets in drug discovery.^{1,2,3} Among them, 3-sulfonyl indoles have raised a continuous interest in the synthetic community, notably because of their biological activities and therapeutic values such as L-737,126 and congeners that are non-nucleoside inhibitors of HIV-1 reverse transcriptase.^{4,5,6} Other examples include 4-dialkylaminoethyl-3-sulfonyl-1*H*-indoles **I**, which are dual action norepinephrine reuptake inhibitors (NRIs) and 5-HT_{2A} receptor antagonists⁷ and 1-aminoalkyl-3-aryl-sulfonyl-1*H*-indoles **II** that act as human 5-HT₆ receptor ligands^{8,9} (Figure 1).

Figure 1. Examples of biologically active 3-sulfonylindole derivatives



Several approaches have been devised toward these derivatives. While sulfonylation of preformed indole frameworks has been developed,^{10,11,12} a series of more convergent indole-forming processes have been investigated, notably the cascade annulation of acyclic precursors to build the indole core and install the sulfonyl group. For instance, a general metal-free reaction of 2-alkynyl-*N,N*-dialkylanilines with sulfonyl hydrazines as sulfonylating reagents in the presence of iodine and *tert*-butylhydroperoxide allowed the formation of 3-sulfonylindoles *via* a radical sulfonylation cascade process (Scheme 1a).¹³ A photoredox-catalyzed radical process starting from 2-alkynyl-azidoarenes and based on the oxidation of arylsulfinate anions by eosin Y as photocatalyst under green light irradiation leads to the formation of alkyl-3-sulfonyl-indoles (Scheme 1b).^{14,15,16}

Scheme 1. Synthetic approaches to 3-sulfonyl indoles



Readily accessible styryl azides β -substituted by sulfones gave 3-sulfonylindoles by catalysis with a rhodium(II) carboxylate complex. The reaction transits through a rhodium nitrene obtained by N_2 loss enabling the C-N bond formation (Scheme 1c).¹⁷ The gold-catalyzed cyclization of 2-alkynyl *N*-alkyl, *N*-tosyl anilines represents an interesting approach. Transiting via a quaternary ammonium intermediate, the cyclization process is followed by a 1,3-migration of the sulfonyl group on the vinylgold intermediate and allows the formation of the desired skeleton when the aromatic moiety is unsubstituted.^{18,19}

In the course of our studies on gold(I) catalysis under visible light irradiation,^{20,21,22,23,24} we now report the reactivity of 2-alkynyl-*N*-tosyl anilines in the presence of gold(I) and silver(I) salts to provide an expedient access to 2-aryl,3-sulfonyl-NH-indoles (Scheme 1e). This study stems from the observation of an intriguing faint fluorescent blue spot on the crude products TLCs

of some of the recently reported gold(I)-catalyzed alkylation reactions of 2-alkynyl-*N*-tosyl anilines under visible-light irradiation.²² These spots significantly gained in intensity when the reactions were conducted without alkyne partner and aroused our interest. Structural identification concluded to 3-sulfonylindole derivatives **2**. These compounds, to the best of our knowledge, have never been obtained from *N*-tosyl anilines through a 1,3-migration of the sulfonyl²⁵ group and this is what we wish to develop in this study.

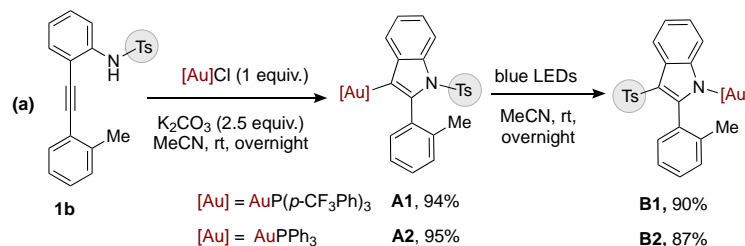
RESULTS AND DISCUSSIONS

Our investigation for the synthesis of 3-sulfonylindole derivatives **2** began by using the *N*-tosylalkynylaniline **1a** as model substrate in the presence of a photocatalyst and a gold(I) catalyst. Thus, we submitted **1a** to 10 mol% of (*p*-CF₃Ph)₃PAuCl in the presence of 1 mol% of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆, 2.5 equivalents of K₂CO₃ under blue LEDs irradiation. These conditions delivered 3-sulfonylindole **2a** in a moderate 43% yield (Table 1, entry 1) accompanied by recovered starting material **1a** (around 30%). A lower catalytic amount of Au(I) catalysts resulted in a lower yield in **2a** (entry 2). Importantly, photocatalyst-free conditions could also afford **2a** in better yield (entry 3). The loading and the nature of Au(I) bear some impact on the reaction outcomes, as using 5 mol% of (*p*-CF₃Ph)₃PAuCl or 10 mol% of Ph₃PAuCl gave **2a** in 41% or 37% yield respectively (entries 4 and 5). A final control experiment revealed that the reaction is not operative using only of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ without Au(I) catalyst (entry 6). The structure of **2a** was secured by X-ray diffraction.²⁶

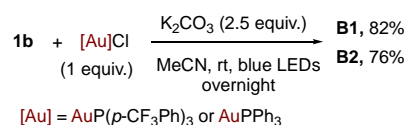
In order to gain some insight into this reaction, we prepared indolyl-gold complexes **A1** and **A2** through a stoichiometric reaction between the related Ts-aniline substrate **1b** and (*p*-CF₃Ph)₃PAuCl or PPh₃AuCl in the presence of 2.5 equiv K₂CO₃. Both complexes **A1** and **A2** proved to be highly stable and could be isolated in more than 90%. They were then dissolved in MeCN and submitted to blue LED irradiation. The evolution of **A1** in these conditions was confirmed by ³¹P NMR (δ_{A1} = 44.7 ppm). Interestingly, a new peak appeared at the chemical shift of 33 ppm (Scheme 2a). This new NMR peak corresponded to the formation of the indolyl (*p*-CF₃Ph)₃P-Au-*N* complex **B1** that was isolated in 90% yield and fully characterized by X-ray diffraction analysis.²⁷ Similarly, complex **A2** was obtained from PPh₃AuCl and further isomerized to Au-indolyl complex **B2** (Scheme 2a).²⁸

Scheme 2. Formation and reactivity of gold-indolyl complexes

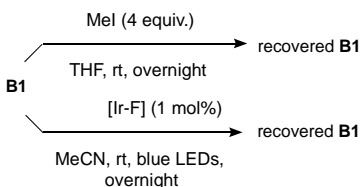
Stoichiometric with gold(I), formation of vinylgold complexes **A** and indolyl complexes **B**



(b) One pot synthesis of complexes **B1** and **B2**



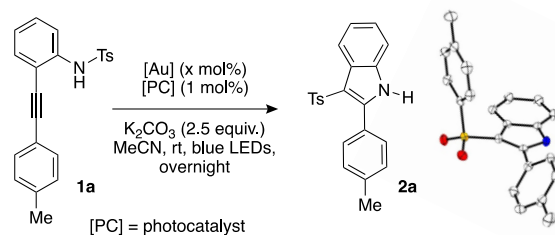
(c) Reactivity of complex **B1**



(d) Filtration of **B1** through silica gel



Table 1. Optimization of reaction conditions using photoinduced Au(I) dual catalysis



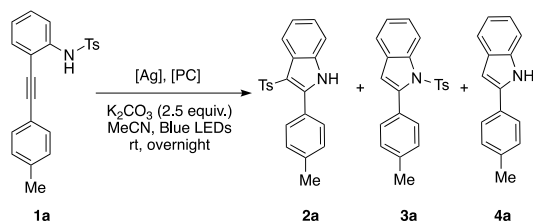
Entry	Catalyst (mol%)	[PC] (1 mol%)	Yield of 2a (%) ^[a]
1	(<i>p</i> -CF ₃ Ph) ₃ PAuCl (10)	[Ir-F]	43
2	(<i>p</i> -CF ₃ Ph) ₃ PAuCl (5)	[Ir-F]	40
3	(<i>p</i> -CF ₃ Ph) ₃ PAuCl (10)	None	57
4	(<i>p</i> -CF ₃ Ph) ₃ PAuCl (5)	None	41
5	Ph ₃ PAuCl (10)	None	37
6	None	[Ir-F]	NR

1 (0.2 mmol), gold catalyst [Au], photocatalyst [PC], K₂CO₃ (2.5 equiv), degassed solvent (3 mL) and overnight stirring. [Ir-F] = Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆.^[a] Isolated yield; 20 – 30% of **1a** was recovered.

While it has been reported in the literature that indolyl-gold complexes could be obtained by reacting *N*-H indole derivatives with (*p*-CF₃Ph)₃P-Au-Cl in the presence of an excess of CsCO₃ in CH₂Cl₂,²⁹ we could consolidate a *one-pot* reaction starting from **1b** under blue LEDs irradiation delivering gold complexes **B1** in 82% yield and **B2** in 76% yield (Scheme 2b). The reactivity of **B1** has been examined under different conditions. It was found that this gold complex is stable toward an electrophilic species such as iodomethane and also to the exposure to 1 mol% of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (Scheme 2c). However, the stability of **B1** was slightly affected by an acidic medium since the formation of 3-tosylindole **2b** was observed after filtration through a short pad of silica gel, a **B1/2b** mixture in a 66/34 ratio being formed (Scheme 2d).

We next examined the possibility of running this type of transformations with more economical noble metal salts and we focused on Ag(I) catalysis.^{30,31} Silver salts are indeed also known to efficiently catalyze the cyclization of 2-alkynyl-*N*-sulfonyl derivatives.^{32,33}

Table 2. Optimization of reaction conditions using photoinduced-Ag(I) dual catalysis



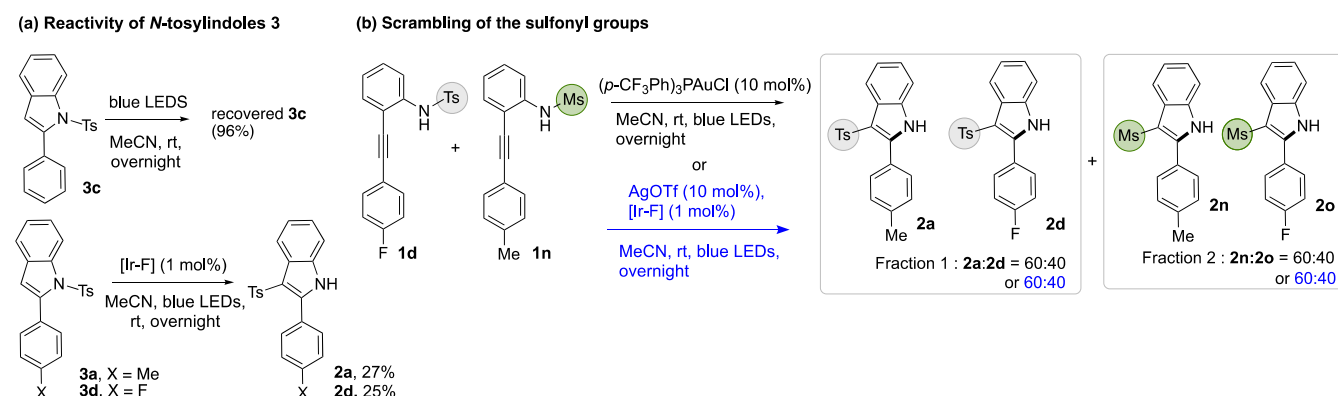
Entry	[Ag] (mol%)	[PC] (mol%)	Solvent	Yield of 2a (%) ^[a]
1 ^[b]	AgOTf (10)	[Ir-F] (1)	MeCN	65 (4a , 17)
2 ^[b]	AgOTf (10)	[Ir-F] (5)	MeCN	47 (4a , 17)
3	AgOTf (5)	[Ir-F] (1)	MeCN	35 (4a , 15)
4	AgBF ₄ (10)	[Ir-F] (1)	MeCN	35 (4a , 14)
5	Ag ₂ CO ₃ (10)	[Ir-F] (1)	MeCN	50 (4a , 20)
6 ^[b]	AgOTf (10)	Ru(bpy) ₃ (PF ₆) ₂ (5)	MeCN	8 (3a , 58)
7 ^[b]	AgOTf (10)	<i>fac</i> -Ir(ppy) ₃ (1)	MeCN	56 (4a , 19)
8 ^[b]	AgOTf (10)	Eosine Y (1)	MeCN	18 (3a , 62)
9 ^[b]	AgOTf (10)	4CzIPN (1)	MeCN	24 (3a , 76)
10 ^[b]	AgOTf (10)	Benzophenone (1)	MeCN	16 (3a , 24; 4a , 20)
11	AgOTf (10)	[Ir-F] (1)	MeOH	- ^[c]
12	AgOTf (10)	[Ir-F] (1)	DCE	35 (4a , 20)
13	AgOTf (10)	None	MeCN	0 (3a , 82)
14	None	[Ir-F] (1)	MeCN	NR
15 ^[d]	AgOTf (10)	[Ir-F] (1)	MeCN	NR
16 ^[e]	AgOTf (10)	[Ir-F] (1)	MeCN	0 (3a , 78)

1 (0.2 mmol), silver catalyst [Ag], photocatalyst [PC], K₂CO₃ (2.5 equiv), degassed solvent (3 mL) and stirring for overnight, [Ir-F] = Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆. ^[a] Isolated yields. ^[b] Determined by ¹H NMR by using 1,3,5-trimethoxybenzene as an internal standard. ^[c] Complex mixture, ^[d] Without K₂CO₃, ^[e] No light.

Firstly, we investigated the effect of ratio of silver (AgOTf) and photocatalyst Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ under basic conditions (Table 2, entries 1-3). When the reaction was carried out in the presence of AgOTf (10 mol%)/ Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (1 mol%), the di-substituted indole **2a** was obtained in 65% isolated yield (entry 1) along with desulfonylated indole **4a**. Lower yields of the product **2a** were obtained when a larger amount of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (5 mol%, entry 2) or AgOTf (5 mol%, entry 3) were used. As the silver catalyst plays a crucial role in this transformation of 3-alkynyl-*N*-tosylaniline **1a**, the catalytic activity of other silver salts such as AgBF₄ and Ag₂CO₃ was evaluated (entries 4 & 5). Both exhibited a low reactivity, giving the desired C3-tosylindole **2a** in 35% and 50% yield respectively accompanied by **4a**. Other photocatalysts (e.g. Ru(bpy)₃(PF₆)₂, *fac*-Ir(ppy)₃, Eosine Y, 4CzIPN and benzophenone) were also tested (entries 6–10). However, none of them have outperformed Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆. In addition, the nature of solvent was also examined. MeOH gave an intractable mixture and DCE was not effective for this reaction (entries 11 & 12). Some control experiments were carried out. When the reaction was performed without photocatalyst, 1,3-sulfonyl migration did not occur and *N*-tosylalkynylaniline **1a** was converted into *N*-tosylindole **3a** in 82% yield (entry 13). No reaction took place in the absence of silver salt or without base (entries 14 & 15). In addition, when the reaction was carried out without blue LEDs irradiation, only 78% of *N*-tosylindole **3a** was obtained (entry 16). These results indicate that the silver salt, the base and the photocatalyst are necessary for this transformation. Thus, the use of 10 mol% of AgOTf in combination with 3 mol% of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ and excess of K₂CO₃ in MeCN for overnight appeared as the optimal reaction conditions (entry 2). But in economic terms, we used 1 mol% of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ for our investigation and scope reaction.

This difference of reactivity between the photosensitizer-free gold catalysis and the dual Ag/Ir dual catalysis was puzzling. To be consistent with the gold related study, we tried to isolate vinylsilver intermediates presumably resulting from stoichiometric reactions with AgOTf. Unfortunately, as mentioned in literature, these putative intermediates proved to be reluctant to isolation.³⁴ Mechanistic investigations were therefore based on several control experiments. First, the stability of *N*-tosylindole derivatives **3** under blue LEDs irradiation was probed. No reaction occurred when *N*-tosylindole **3c** was irradiated overnight (Scheme 3a). In contrast, among complex mixtures, marginal 1,3-sulfonyl migration was observed from **3a** or **3d** in the presence of 1 mol% [Ir-F] (27% of indole **2a**, 25% of indole **2d**).

Scheme 3. Control and crossover experiments

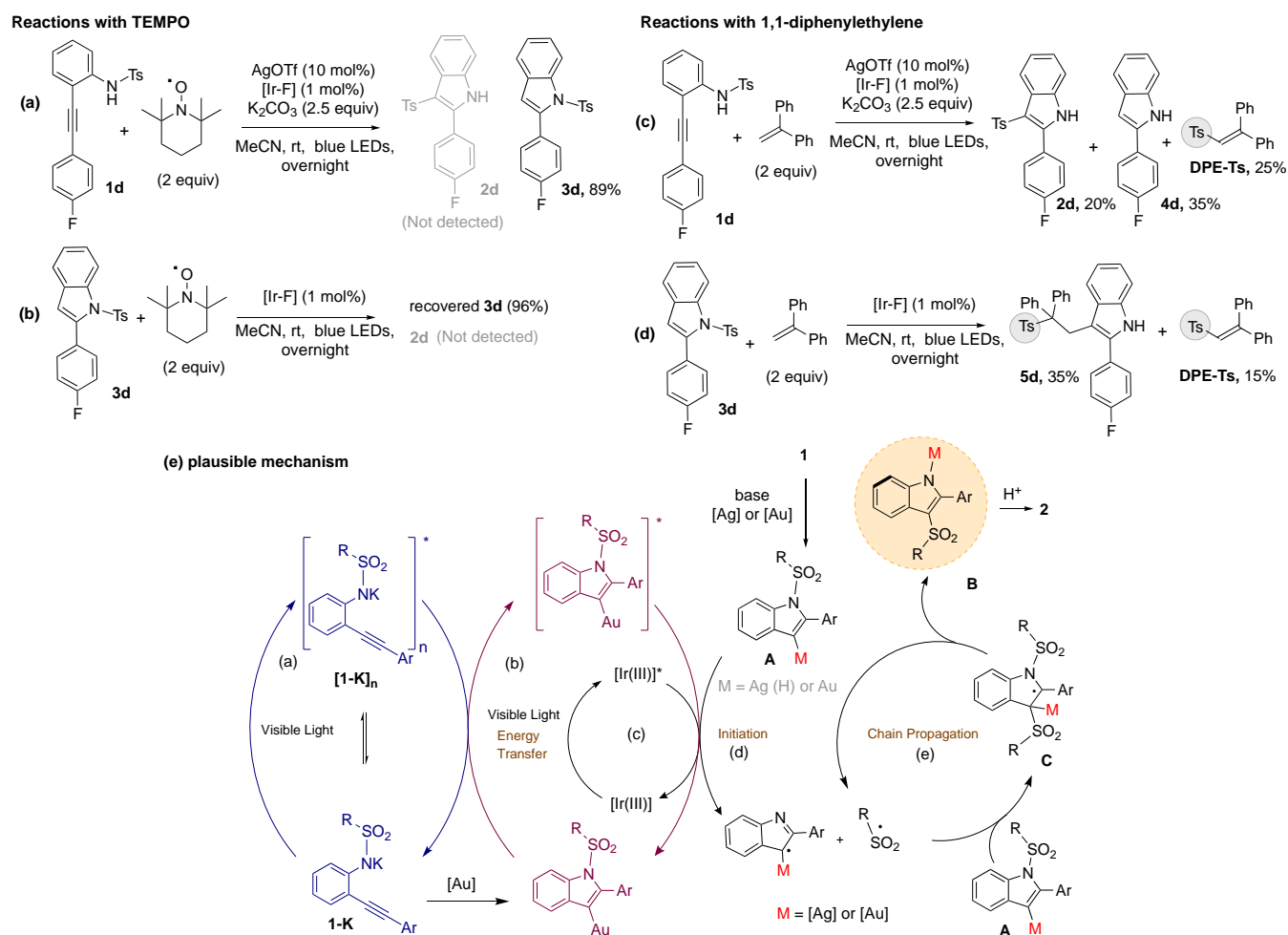


In addition, to find out if the migration of the sulfonyl group occurs in an intramolecular or intermolecular fashion, crossover experiments were run with *N*-tosyl aniline **1d** and *N*-mesylaniline **1n** in the presence of (*p*-CF₃Ph)PAuCl (10 mol%) (black pathway, Scheme 3b). We observed the formation of a mixture of the four products **2a**, **2d**, **2n** and **2o**. We isolated two fractions containing a mixture of unseparated sulfonylindole products in 60:40 and 60:40 ratio for **2a:2d** and **2n:2o**. Similarly, the silver-catalyzed reaction (blue pathway of Scheme 3b) provided comparable outcomes. Overall, these findings clearly evidenced the scrambling of the sulfonyl groups in these reactions and were suggestive of the intervention of sulfonyl radicals.

To probe the radical character of the sulfonyl migration,³⁵ a reaction was performed from **1d** under standard dual catalysis conditions in the presence of 2 equivalents of TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl) as radical scavenger, the desired

product **2d** was not observed only *N*-tosylindole **3d** (89%) and the starting product were obtained (Scheme 4a). Moreover, when *N*-tosylindole **3d** was irradiated in the presence of 1 mol% of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ and of 2 equivalents of TEMPO only **3d** was recovered (Scheme 4b). Similar experiments were performed using 1,1-diphenylethylene owing to it is a more versatile radical scavenger, which does not affect the catalytic activities of transition metals.³⁶ Thus, precursor **1d** was engaged in the silver-catalysis reaction conditions in the presence of 2 equiv of 1,1-diphenylethylene. In addition to **2d** (20%) and **4d** (35%), **DPE-Ts** adduct resulting from the addition of the tosyl radical³⁷ to 1,1-diphenylethylene was isolated in 25% (Scheme 4c). Starting from *N*-tosylindole **3d** in the presence of 1 mol% of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆, **DPE-Ts** was isolated in 15% yield, as well as the unexpected product **5d** in 35% yield (Scheme 4d).

Scheme 4. Probing the intervention of sulfonyl radicals and mechanism proposal



Based on these mechanistic investigations and our precedent studies,²² it seems reasonable to assume a preliminary formation of a vinylmetal (gold or silver) intermediate **A** resulting from the cyclization of the TsN amide anion on the π -activated alkyne by the metal salt (gold/silver). In the case of gold activation, the stable vinylgold intermediate **A** would reach an excited state by direct irradiation as in Scheme 2a or by energy transfer (EnT) from the excited state of potassium amide aggregate [**1a-K**] (cycles (a) and (b) of Scheme 4e) as in the alkynylative reaction²² and undergo homolytic cleavage of the N-SO₂Tol bond to gener-

ate *in-situ* an indolyl and a sulfonyl radicals (initiation (d)).³⁸ Such EnT-driven homolytic cleavage has been for instance reported for the photoinduced rearrangement of vinyl tosylates to β -ketosulfones.³⁹ In our case, the sulfonyl radical would add in position 3 of another vinylgold species (intermediate **C**) and triggers the β -elimination of another sulfonyl radical, which propagates a radical chain process (cycle (e)). This also generates an imine intermediate⁴⁰ that would tautomerize and give the previously isolated indolyl N-Au species **B** (Scheme 2). Protonation

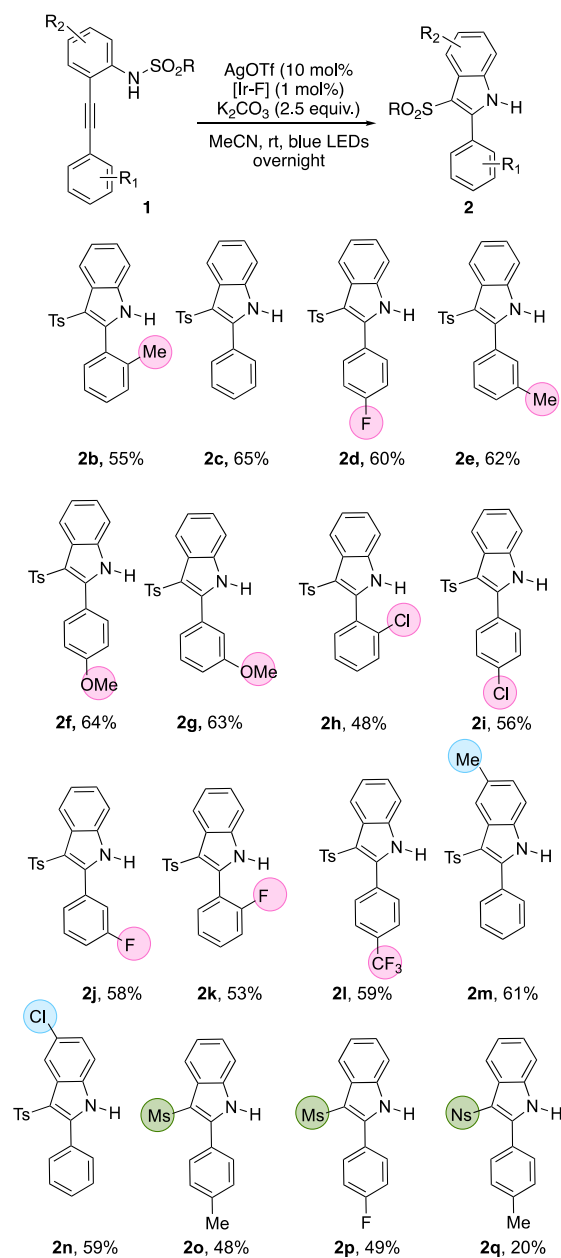
liberates the final 3-sulfonylindole **2** and regenerates the gold catalyst.

In the case of photo/Ag(I) dual catalysis, we assumed that an energy transfer would occur from the photoexcited-[Ir(III)*] to the vinylsilver intermediate **A** (cycle (c)) leading to the homolytic cleavage of the N-SO₂ bond and chain radical isomerization. As before, protonation would deliver final product **2**. Alternatively, the unstabilized vinylsilver intermediate undergoes protodesilveration giving an indole intermediate of type **3** which could also undergo the 1,3-sulfonyl migration to give product **2** in the presence of 1 mol% of Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ as in see Scheme 3b. However, the 1,3-sulfonyl migration on these intermediates would be less efficient giving rise to products like **4a** as in Table 2.

Based on the optimization of the reaction conditions and the mechanistic investigations, we examined the scope of this transformation. Several 2,3-disubstituted indoles have been synthesized **2b-2p**, from 3-alkynyl-*N*-tosyl, -mesyl or -nosyl anilines, in 20%-65% yields (Table 3). The tosyl substrates provided better yields compared to mesyl (**2n**, **2o**) and nosyl (**2p**) precursors. Precursors featuring either a *para* electron-donating group (-Me, -OMe) or electron-withdrawing group (-F, -Cl, -CF₃) on the 2-alkynylaryl moiety were found to be compatible, affording the corresponding cyclization-migration products **2b-2k** in 48%-65% yields. Of note, -Me or -Cl group on the aniline aryl moiety did not affect the yield of the reaction (**2l**, **2m**).

In conclusion, an expedient access to valuable 3-sulfonyl indoles has been devised. Starting from *ortho*-alkynyl-*N*-sulfonylanilines **1**, gold(I)- or silver(I)-triggered cyclization concomitant with a light-induced 1,3-sulfonyl migration leads to the desired scaffolds. Mechanistic studies are consistent with the generation *via* photoexcitation of a sulfonyl radical which propagates the 1,3-migration. These findings confirm the vast opportunities of the practice of organometallic catalysis under visible-light irradiation.

Table 3. Scope of the reaction



ASSOCIATED CONTENT

Supporting Information

General procedures, experimental details, characterization, and spectral data for all new compounds and crystal data and structural refinement for compounds **B1**, **B2** and **2a**.

AUTHOR INFORMATION

Corresponding Author:

ACKNOWLEDGMENT

The authors thank Sorbonne Université, CNRS, IUF for financial support as well as CSC for a PhD grant to FZ and ANR-20-CE07-0038 LuxOr for a post-doctoral funding to WH. They are also grateful to Mr. Jérémy Forte for the XRD analyses.

Author Contributions

FZ, WH and MBM ran all the experiments and provided all analytical data for the newly synthesized compounds. CO, VMM and LF supervised the work and wrote the manuscript.

Notes

The authors declare no competing financial interests.

REFERENCES

- ¹ (a) Kochanowska-Karamyan, A. J.; Hamann, M. T. Marine Indole Alkaloids: Potential New Drug Leads for the Control of Depression and Anxiety. *Chem. Rev.* **2010**, *110*, 4489–4497. (b) Dhuguru, J.; Skouta, R. Role of Indole Scaffolds as Pharmacophores in the Development of Anti-Lung Cancer Agents. *Molecules* **2020**, *25*, 1615–1639.
- ² (a) Fu, L. Advances in the Total Syntheses of Complex Indole Natural Products. In *Heterocyclic Scaffolds II: Reactions and Applications of Indoles*; Gribble, G. W., Ed.; Topics in Heterocyclic Chemistry; Springer: Berlin, Heidelberg, 2010; pp 433–480.
- ³ (c) Dhuguru, J.; Skouta, R. Role of Indole Scaffolds as Pharmacophores in the Development of Anti-lung Cancer agents. *Molecules* **2020**, *25*, 1615–1639.
- ⁴ (a) Williams T. M.; Ciccarone, T. M.; MacTough, S. C.; Rooney, C. S.; Balani, S. K.; Condra, J. H.; Emini, E. A.; Goldman, M. E.; Greenlee, W. J.; Kauffman, L. R.; O' Brien, J. A.; Sardana, V. V.; Schleif, W. A.; Theoharides A. D.; Anderson, P. S. 5-Chloro-3-(phenylsulfonyl)indole-2-carboxamide: a Novel, Non-nucleoside Inhibitor of HIV-1 Reverse Transcriptase. *J. Med. Chem.* **1993**, *36*, 1291-1294.. (b) Famigliini, V.; Silvestri, R. Indolylarylsulfones, a Fascinating Story of Highly Potent Human Immunodeficiency Virus Type 1 Non-nucleoside Reverse Transcriptase Inhibitors. *Antivir. Chem. Chemother.* **2018**, *26*, 1-19.
- ⁵ (b) Gao, D.; Back, T. G. Synthesis of the Reverse Transcriptase Inhibitor L-737,126 and the CB2 Cannabinoid Receptor Agonist Pravadoline by a Copper-Catalyzed Intramolecular Cross-Coupling. *Synlett* **2013**, 389-393..
- ⁶ (c) Famigliini, V.; Silvestri, R. Indolylarylsulfones, a Fascinating Story of Highly Potent Human Immunodeficiency Virus type 1 Non-nucleoside Reverse Transcriptase Inhibitors *Antivir. Chem. Chemother.* **2018**, *26*, 1-19.
- ⁷Heffernan, G.; Coghlan, R.; Manas, E.; McDevitt, R.; Li, Y.; Mahaney, P.; Robichaud, A.; Huselton, C.; Alfinito, P.; Bray, J.; Cosmi, S.; Johnston, G.; Kenney, T.; Koury, E.; Winneker, R.; Deecheer, D.; Trybulski, E. Dual Acting Norepinephrine Reuptake Inhibitors and 5-HT_{2A} Receptor Antagonists: Identification, Synthesis and Activity of Novel 4-Aminoethyl-3-(phenylsulfonyl)-1H-indoles. *Bioorg. Med. Chem.* **2009**, *17*, 7802-7815..
- ⁸ Bernotas, R.; Lenicek, S.; Antane, S.; Zhang, G. M.; Smith, D.; Coupet, J.; Harrison, B.; Schechter, L. E. 1-(2-Aminoethyl)-3-(arylsulfonyl)-1H-indoles as Novel 5-HT₆ Receptor Ligands. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5499-5502.
- ⁹ Bernotas, R. C.; Antane, S.; Shenoy, R.; Le, V.-D.; Chen, P.; Boyd L. Harrison, B. L.; Robichaud, A. J.; Zhang, G. M.; Smith, D.; Schechter, L. E. 3-(Arylsulfonyl)-1-(azacyclyl)-1H-indoles are 5-HT₆ receptor modulators. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1657-1660.
- ¹⁰ Yadav, J. S.; Reddy, B. V. S.; Krishna, A. D.; Swamy, T. InBr₃-Catalyzed Sulfonation of Indoles: A Facile Synthesis of 3-Sulfonyl Indoles. *Tetrahedron Lett.* **2003**, *44*, 6055–6058.
- ¹¹ Du, Y.; Liu, Y. Copper-Catalysed Selective 3-Sulfonylation of Indoles: A Mild Synthesis of Indolyl Sulfones. *J. Chem. Res.* **2016**, *40*, 579–582.
- ¹² Zhang, Z.W.; Xue, H.; Li, H.; Kang, H.; Feng, J.; Lin, A.; Liu, S. Collective Synthesis of 3-Acylindoles, Indole-3-carboxylic Esters, Indole-3-sulfinic Acids, and 3-(Methylsulfonyl)indoles from Free (N–H) Indoles via Common N–Indolyl Triethylborate. *Org. Lett.* **2016**, *18*, 3918–3921.
- ¹³ Meesin, J.; Pohmakotr, M.; Reutrakul, V.; Soorukram, D.; Leowanawat, P.; Kuhakarn, C. Synthesis of N-alkyl-3-sulfonylindoles and N-alkyl-3-sulfanylindoles by Cascade Annulation of 2-Alkynyl-N,N-dialkylanilines. *Org. Biomol. Chem.* **2017**, *15*, 3662–3669.
- ¹⁴ Rohokale, R. S.; Shrikant, D.; Tambe, S. d.; Kshirsagar, U. A. Eosin Y Photoredox Catalyzed Net Redox Neutral Reaction for Regiospecific Annulation to 3-Sulfonylindoles via Anion Oxidation of Sodium Sulfinat Salts. *Org. Biomol. Chem.* **2018**, *16*, 536–540.
- ¹⁵ Chen, F.; Meng, Q.; Han, S.-Q.; Han, B. Tert-Butyl Hydroperoxide (TBHP)-Initiated Vicinal Sulfonation of Alkynes: A Radical Annulation toward 3-Sulfonylindoles. *Org. Lett.* **2016**, *18*, 3330–3333.

- ¹⁶ See also: Zhang, J.; Chen, J.; Zhai, Y.; Yu, J.-T.; Pan, C. Three-Component Vicinal Sulfonamination of Alkynes toward 3-Sulfonylindoles via the Insertion of Sulfur Dioxide. *Asian J. Org. Chem.* **2022**, *11*, e2021100671.
- ¹⁷ Stokes, B. J.; Liu, S.; Driver, T. G. Rh₂(II)-Catalyzed Nitro-Group Migration Reactions: Selective Synthesis of 3-Nitroindoles from β-Nitro Styryl Azides. *J. Am. Chem. Soc.* **2011**, *133*, 4702–4705.
- ¹⁸ Nakamura, I.; Yamagishi, U.; Song, D.; Konta, S.; Yamamoto, Y. Gold- and Indium-Catalyzed Synthesis of 3- and 6-Sulfonylindoles from ortho-Alkynyl-N-sulfonylanilines. *Angew. Chem. Int. Ed.* **2007**, *46*, 2284–2287.
- ¹⁹ Nakamura, I.; Uichiro Yamagishi, U.; Dschun Song, D.; Konta, S.; Yamamoto, Y. Synthesis of 3- and 6-Sulfonylindoles from ortho-Alkynyl-N-sulfonylanilines by the Use of Lewis Acidic Transition-Metal Catalysts. *Chem. Asian J.* **2008**, *3*, 285–295.
- ²⁰ Xia, Z.; Khaled, O.; Mouriès-Mansuy, V.; Ollivier, C.; Fensterbank, L. Dual Photoredox/Gold Catalysis Arylative Cyclization of *o*-Alkynylphenols with Aryldiazonium Salts: A Flexible Synthesis of Benzofurans. *J. Org. Chem.* **2016**, *81*, 7182–7190.
- ²¹ Xia, Z.; Corcé, V.; Zhao, F.; Przybylski, C.; Espagne, A.; Jullien, L.; Le Saux, T.; Gimbert, Y.; Dossman, H.; Mouriès-Mansuy, V.; Ollivier, C.; Fensterbank, L. Photosensitized Oxidative Addition to Gold(I) Enables Alkynylative Cyclization of *o*-Alkynylphenols with Iodoalkynes. *Nat. Chem.* **2019**, *11*, 797–805.
- ²² Zhao, F.; Abdellaoui, M.; Hagui, W.; Ballarin Marion, M.; Berthet, J. Corcé, V.; Delbaere, S.; Dossman, H.; Espagne, A.; Forté, J.; Jullien, L.; Le Saux, T.; Mouriès-Mansuy, V.; Ollivier, C.; Fensterbank, L. Reactant-Induced Photoactivation of In Situ Generated Organogold Intermediates Leading to Alkynylated Indoles via *Csp*²-*Csp* Cross-Coupling. *Nature Comm.* **2022**, *13*, 2295.
- ²³ For a review, Sadek, O.; Abdellaoui, M.; Millanvois, A.; Ollivier, C.; Fensterbank, L. Organometallic Catalysis under Visible Light Activation: Benefits and Preliminary Rationales. *Photochem. Photobiol. Sci.* **2022**, *21*, 585–606.
- ²⁴ Cheung, K. P. S.; Sarkar, S.; Gevorgyan, V. Visible Light-Induced Transition Metal Catalysis. *Chem. Rev.* **2022**, *122*, 1543–1625.
- ²⁵ For a review, see: Flynn, A. J.; Ford, A.; Maguire, A. R. Synthetic and Mechanistic Aspects of Sulfonyl Migrations. *Org. Biomol. Chem.* **2020**, *18*, 2549–2610.
- ²⁶ CCDC deposition number for **2a**: 2176568
- ²⁷ CCDC deposition number for **B1**: 2176567.
- ²⁸ CCDC deposition number for **B2**: 2176539.
- ²⁹ Fernandez-Moreira, V.; Val-Campillo, C.; Ospino, I.; Herrera, R. P.; Marzo, I.; Laguna, A.; Gimeno, M. C. Bioactive and Luminescent Indole and Isatin Based Gold(I) Derivatives. *Dalton Trans* **2019**, *48*, 3098–3108.
- ³⁰ Belmont, P.; Parker, E. Silver and Gold Catalysis for Cycloisomerization Reactions. *Eur. J. Org. Chem.* **2009**, 6075–6089.
- ³¹ Chen, X.; Fontaine-Vive, F.; Poulain-Martini, S.; Michelet, V. Silver-catalyzed Intramolecular [4 + 2] Cycloaddition Reaction of Amide-1,6-enynes. *Catal. Commun.* **2020**, *147*, 106–117 and references therein.
- ³² Liu, J.; Xie, X.; Liu, Y. Silver-Catalyzed Cascade Cyclization–Stannylation of *o*-Alkynylaniline Derivatives with 2-Tributylstannylfuran: an Efficient Synthesis of (3-Indolyl)stannanes. *Chem. Commun.* **2013**, *49*, 11794–11796.
- ³³ Zhang, T.-S.; Wang, R.; Cai, P.-J.; Hao, W.-J.; Tu, S.-J.; Jiang, B. Silver-Catalyzed Nitration/Annulation of 2-Alkynylanilines for a Tunable Synthesis of Nitrated Indoles and Indazole-2-oxides. *Org. Chem. Front.* **2019**, *6*, 2968–2973.
- ³⁴ Sadamitsu, Y.; Saito, K.; Yamada, T. Stereoselective Amination via Vinyl-Silver Intermediates Derived from Silver-Catalyzed Carboxylative Cyclization of Propargylamine. *Chem. Commun.* **2020**, *56*, 9517–9520 and references therein.
- ³⁵ Yeh, P.-P.; Taylor, J. E.; Stark, D. G.; Daniels, D. S. B.; Fallan, C.; Walton, J. C.; Smith, A. D. N- to C-Sulfonyl Photoisomerisation of Dihydropyridinones: a Synthetic and Mechanistic Study. *Org. Biomol. Chem.* **2017**, *15*, 8914–8922.
- ³⁶ Mao, S.; Gao, Y.; Zhu, X. Q.; Guo, D. D.; Wang, Y. Q. Copper-Catalyzed Radical Reaction of N-Tosylhydrazones: Stereoselective Synthesis of (E)-Vinyl Sulfones. *Org. Lett.* **2015**, *17*, 1692–1695.
- ³⁷ Gancarz, R. A.; Kice, J. L. Se-Phenyl Areneselenosulfonates: Their Facile Formation and Striking Chemistry. *J. Org. Chem.* **1981**, *46*, 4899–4906
- ³⁸ For a recent report, see: Yu, X.; Zhang, Z.; Dong, G. Catalytic Enantioselective Synthesis of γ-Lactams with β-Quaternary Centers via Merging of C-C Activation and Sulfonyl Radical. *J. Am. Chem. Soc.* **2022**, *144*, 21, 9222–9228.
- ³⁹ Xie, L.; Zhen, X.; Huang, S.; Su, X.; Lin, M.; Li, Y. Photoinduced Rearrangement of Vinyl Tosylates to β-Ketosulfones. *Green Chem.* **2017**, *19*, 3530–3534.
- ⁴⁰ Serafino, A.; Balestri, D.; Marchio, L.; Malacria, M.; Derat, E.; Maestri, G. Orthogonal Syntheses of 3.2.0 Bicycles from Enallenes Promoted by Visible Light. *Org. Lett.* **2020**, *22*, 6354–6359.