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Cu-Catalyzed Stereoconvergent and Enantioselective C–S Cross-Coupling of Alkenyl Halides with Sulfenamides via Alkenyl Radicals

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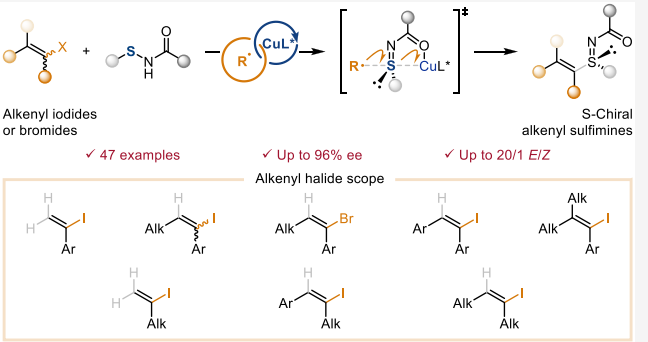
ABSTRACT: Transition-metal-catalyzed cross-coupling is a central strategy for installing alkenyl groups. Conventional two-electron oxidative addition of alkenyl halides is typically stereoretentive and, therefore, often requires geometrically highly enriched (*E*)- or (*Z*)-alkenyl halides, making stereoconvergent asymmetric cross-coupling of (*E*/*Z*)-mixed feedstocks challenging. Here we report a stereoconvergent and enantioselective Cu-catalyzed C–S cross-coupling of alkenyl iodides and bromides with sulfenamides to afford S-chiral alkenyl sulfilimines via alkenyl-radical intermediates that erase the initial alkene geometric information. The reaction proceeds under visible-light-driven Cu/photoredox conditions or Cu-catalyzed aryl radical-mediated halogen-atom transfer (XAT) conditions, delivering enantioenriched products with high alkene stereoselectivity and enantioselectivity across a broad substrate scope. The method is scalable, and the resulting chiral alkenyl sulfilimines can be readily diversified into a range of S-chiral sulfur(VI)-containing motifs, providing modular access to otherwise difficult-to-access enantioenriched sulfur-stereogenic alkenyl scaffolds.



INTRODUCTION

Alkenyl-containing compounds are prevalent in natural products and synthetic molecules and are widely used in organic synthesis, medicinal chemistry, and materials science.[1] Transition-metal-catalyzed cross-coupling reactions represent a key strategy for installing alkenyl functional groups.[2] Two-electron, oxidative-addition-based cross-couplings of alkenyl halides are well established. A defining feature of these reactions is that oxidative addition often proceeds with retention of alkene geometry, enabling subsequent coupling with nucleophiles to deliver products that generally preserve the alkene geometry of the starting alkenyl halides (Figure 1A).[3] These stereoretentive processes typically require alkenyl halide starting materials with high geometric (*E*/*Z*) purity. However, the synthesis and separation of geometrically pure alkenyl halides can be challenging, which limits the applicability of these methods when alkenyl halides are obtained with low *E*/*Z* ratios.[4] Therefore, developing a stereoconvergent method that can utilize readily available *E*/*Z* mixtures of alkenyl halide feedstock chemicals remains a key challenge.

In recent years, transition-metal-catalyzed reactions involving alkenyl radicals have advanced rapidly.[5] However, asymmetric catalytic reactions engaging alkenyl radicals remain scarce.[6] In contrast to two-electron, stereoretentive cross-couplings, radical activation of alkenyl halides can, in principle, depending on substitution, erase the stereochemical information on the starting alkene through rapid stereomutation of bent σ-type alkenyl radicals or through formation of approximately linear π-type alkenyl radicals,[7] thereby enabling stereoconvergent reactivity (Figure 1B, top). Despite this prospect, transition-metal-catalyzed asymmetric radical cross-coupling reactions between alkenyl halides and nucleophiles remain underdeveloped.[6g] Alkenyl radicals typically exhibit exceptionally high reactivity, often leading to chemoselectivity challenges. More importantly, the higher bond dissociation energy (BDE) of alkenyl C–X bonds[8] renders direct transition-metal-catalyzed single-electron activation of alkenyl halides generally more difficult than that of their alkyl counterparts. In this context, photoinduced single-electron transfer (SET)[9] and aryl radical-mediated halogen-atom transfer (XAT)[10] have emerged as viable approaches to access alkenyl radicals from alkenyl halides (Cl, Br, I) (Figure 1B, bottom left).

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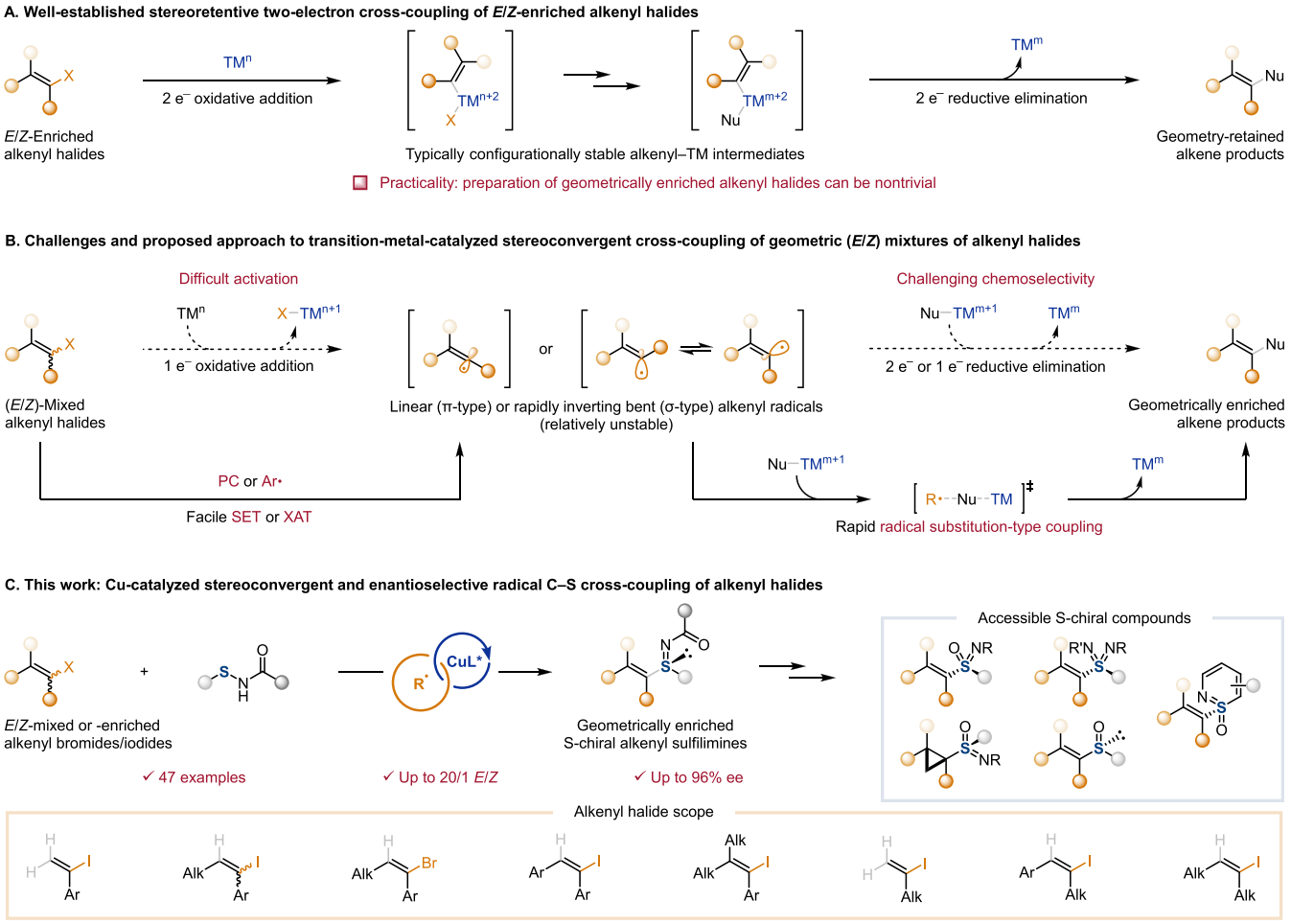

Figure 1. Motivation and development of the Cu-catalyzed stereoconvergent and enantioselective radical C−S cross-coupling of alkenyl halides. TM, transition metal; Nu, nucleophile; PC, photocatalyst; Ar, aryl; SET, single-electron transfer; XAT, halogen-atom transfer.

Sulfilimines,[11] the aza-analogues of sulfoxides, have attracted considerable attention owing to their presence in bioactive molecules,[12] including those in medicinal chemistry and crop protection (see Figure S1 for examples), and their utility as versatile synthetic intermediates.[13] Moreover, the Lewis basic sulfur(IV) center has enabled sulfur-stereogenic (S-chiral) sulfilimines to serve as ligands in enantioselective transition-metal catalysis.[14] Over the past decades, numerous approaches have been developed for the synthesis of S-chiral sulfilimines,[15] and several groups have reported the preparation of racemic alkenyl sulfilimines.[16] Despite these advances, convenient, broadly applicable, and efficient catalytic methods to access S-chiral alkenyl sulfilimines remain lacking, particularly for derivatives bearing tri- and tetrasubstituted sulfur-bound alkenyl groups.[17] Although cross-coupling could offer a modular and efficient entry to these otherwise difficult-to-access compounds and is therefore highly desirable, straightforward cross-coupling strategies for S-chiral alkenyl sulfilimines remain underdeveloped. Building on our recent studies on the efficient Cu-mediated, chirality-transferring radical substitution,[15q] as well as our copper/chiral anionic ligand-based single-electron catalysis platform that enables diverse modes of stereocontrol,[18] we envisioned that copper catalysts equipped with well-designed chiral ligands could enable stereoselective alkenyl-radical cross-couplings with sulfenamides (as sulfilimine precursors) to access S-chiral alkenyl sulfilimines (Figure 1B, bottom right). Critically, both the alkene geometry (E/Z) and the enantioselectivity must be controlled in the synthesis of S-chiral alkenyl sulfilimines.

Herein, we report a stereoconvergent and enantioselective Cu-catalyzed C−S cross-coupling of alkenyl halides with sulfenamides via alkenyl-radical intermediates (Figure 1C). This reaction proceeds under mild conditions and exhibits high E/Z-selectivity and enantioselectivity, a broad scope of alkenyl halides, and excellent functional-group tolerance. In addition, the synthesis of S-chiral alkenyl sulfilimines can be extended to an enantioselective radical 1,2-carbosulfilimination of alkynes. The reaction is scalable, and the resulting S-chiral alkenyl sulfilimines can be readily transformed into a range of S-chiral sulfur(VI)-containing motifs, enabling further diversification and utility.

RESULTS AND DISCUSSION

Reaction Development

Based on the activation strategy for alkenyl halides outlined above (Figure 1C), we initiated our studies by evaluating the coupling of sulfenamide **S1** with alkenyl iodide **A1** under visible-light-driven Cu/photoredox catalysis (Table 1).[19] After extensive optimization, we identified a set of conditions under which **S1** coupled efficiently with **A1** to furnish the desired alkenyl sulfilimine **1** in 80% yield with 94% enantiomeric excess (ee) (Table 1, entry 1). The optimal conditions employed $Cu(MeCN)_4PF_6$ (10 mol %), the chiral N,N,N-

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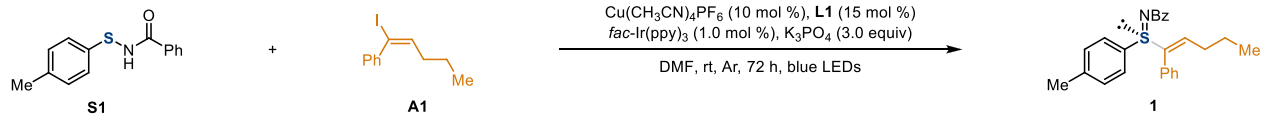
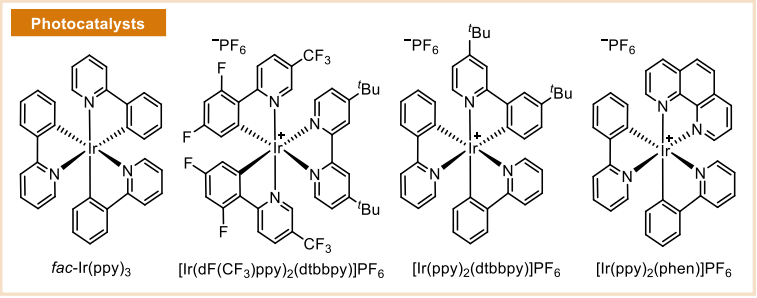
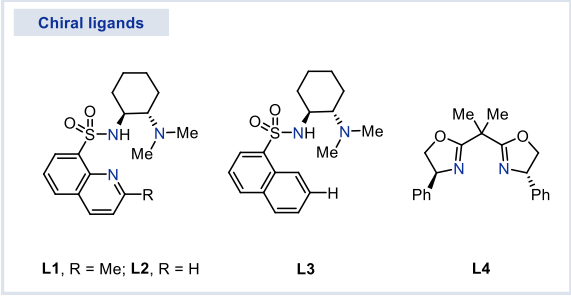
Table 1. Optimization of the Reaction Conditions[a]







entry	change from the standard conditions	yield (%)	Ee (%)
1	None	80	94
2	No $Cu(CH_3CN)_4PF_6$ or no K_3PO_4 or no *hν*	0	–
3	No *fac*-Ir(ppy)$_3$	0	–
4	[Ir(dFCF$_3$ppy)$_2$(dtbbpy)]PF$_6$ instead of *fac*-Ir(ppy)$_3$	5	90
5	[Ir(ppy)$_2$(dtbbpy)]PF$_6$ instead of *fac*-Ir(ppy)$_3$	16	82
6	[Ir(ppy)$_2$(phen)]PF$_6$ instead of *fac*-Ir(ppy)$_3$	11	77
7	**L2** instead of **L1**	68	86
8	**L3** instead of **L1**	32	74
9	**L4** instead of **L1**	11	11
10	MTBE instead of DMF	trace	–

[a]Standard reaction conditions: **S1** (0.20 mmol), **A1** (1.5 equiv), $Cu(CH_3CN)_4PF_6$ (10 mol %), **L1** (15 mol %), *fac*-Ir(ppy)$_3$ (1.0 mol %), and K_3PO_4 (3.0 equiv) in DMF (2.0 mL) at rt under argon and irradiation with blue LEDs for 72 h. Yields are ^{1}H NMR yields determined from the crude mixture using 1,3,5-trimethoxybenzene as an internal standard. Enantiomeric excesses (ee) were determined by chiral HPLC analysis. DMF, *N*,*N*-dimethylformamide; LEDs, light-emitting diodes; MTBE, methyl *tert*-butyl ether.

tridentate ligand **L1** (15 mol %), K_3PO_4 as the base, and *N*,*N*-dimethylformamide (DMF) as the solvent at room temperature, together with *fac*-Ir(ppy)$_3$ (1.0 mol %) as the photocatalyst under irradiation with blue light-emitting diodes (LEDs). Control experiments established that the reaction is strongly diminished in the absence of the copper salt, ligand, base, *fac*-Ir(ppy)$_3$, or blue LED irradiation (Table 1, entries 2−3; also see Table S2). The choice of photocatalyst proved to be particularly important. Replacing *fac*-Ir(ppy)$_3$ with other Ir(III) photosensitizers led to a pronounced decrease in efficiency (Table 1, entries 4−6). Consistent with this trend, *fac*-Ir(ppy)$_3$ is a substantially stronger photoreductant (E^*_{ox} = −1.73 V vs saturated calomel electrode (SCE)) than [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ (E^*_{ox} = −0.89 V vs SCE), [Ir(ppy)$_2$(dtbbpy)]PF$_6$ (E^*_{ox} = −0.96 V vs SCE), and [Ir(ppy)$_2$(phen)]PF$_6$ (E^*_{ox} = −0.88 V vs SCE).[20] The reduced photoreducing power is expected to compromise the single-electron reduction of alkenyl iodide **A1**, thereby lowering the efficiency of alkenyl-radical generation and overall product formation. The chiral ligand also had a marked impact on both reactivity and enantioselectivity. Using **L2**, which lacks the *ortho*-methyl substituent on one coordinating quinoline unit,[21] decreased the yield to 68% and the ee to 86% (Table 1, entry 7). Switching to the N,N-bidentate ligand **L3** further diminished both the yield and enantiocontrol (Table 1, entry 8). We speculate that the tridentate ligands (**L1**/**L2**) may create a more well-defined and sterically confined chiral environment around copper than the bidentate ligand **L3**, which may facilitate productive C−S bond formation. Consistent with this notion, neutral bidentate ligands such as the bisoxazoline ligand **L4** provided substantially lower reactivity and enantioselectivity, affording **1** in 11% yield and 11% ee (Table 1, entry 9), potentially due to a less reactive Cu complex and increased competitive pathways. Solvent effects were also significant: the reaction was completely suppressed in methyl *tert*-butyl ether (MTBE) (Table 1, entry 10), and screening additional solvents did not improve the yield (Table S1, entries 1−3). Finally, variations of copper salts (Table S1, entries 4−7) and bases (Table S1, entries 8−9) generally led to reduced reactivity with minimal impact on enantioselectivity (Table S2).

Substrate Scope

With the optimal conditions established, we first investigated the sulfenamide scope (Table 2). A range of *S*-aryl *N*-benzoyl sulfenamides bearing electron-donating substituents (4-Me, 4-^{t}Bu, and 4-OMe) as well as electron-withdrawing groups (4-Br and 3-F) were all well tolerated, delivering the corresponding *S*-chiral sulfilimines **1**−**5** in good yields with excellent enantioselectivity. In contrast, the *o*-bromo-substituted sulfenamide failed to deliver the desired sulfilimine **6** under the photoinduced conditions. We reasoned that the increased steric hindrance could retard the formation of the key *S*-chiral copper complex, thereby mismatching the rate of alkenyl-radical generation under the photoredox conditions and eroding the chemoselectivity of the desired radical coupling. Meanwhile, competitive side reactions of the sulfenamide under the basic photoinduced conditions became predominant (see Scheme S2 and Figure S3 for details), further diverting the reaction from the desired pathway. To address both issues, we turned to the aryl radical-mediated

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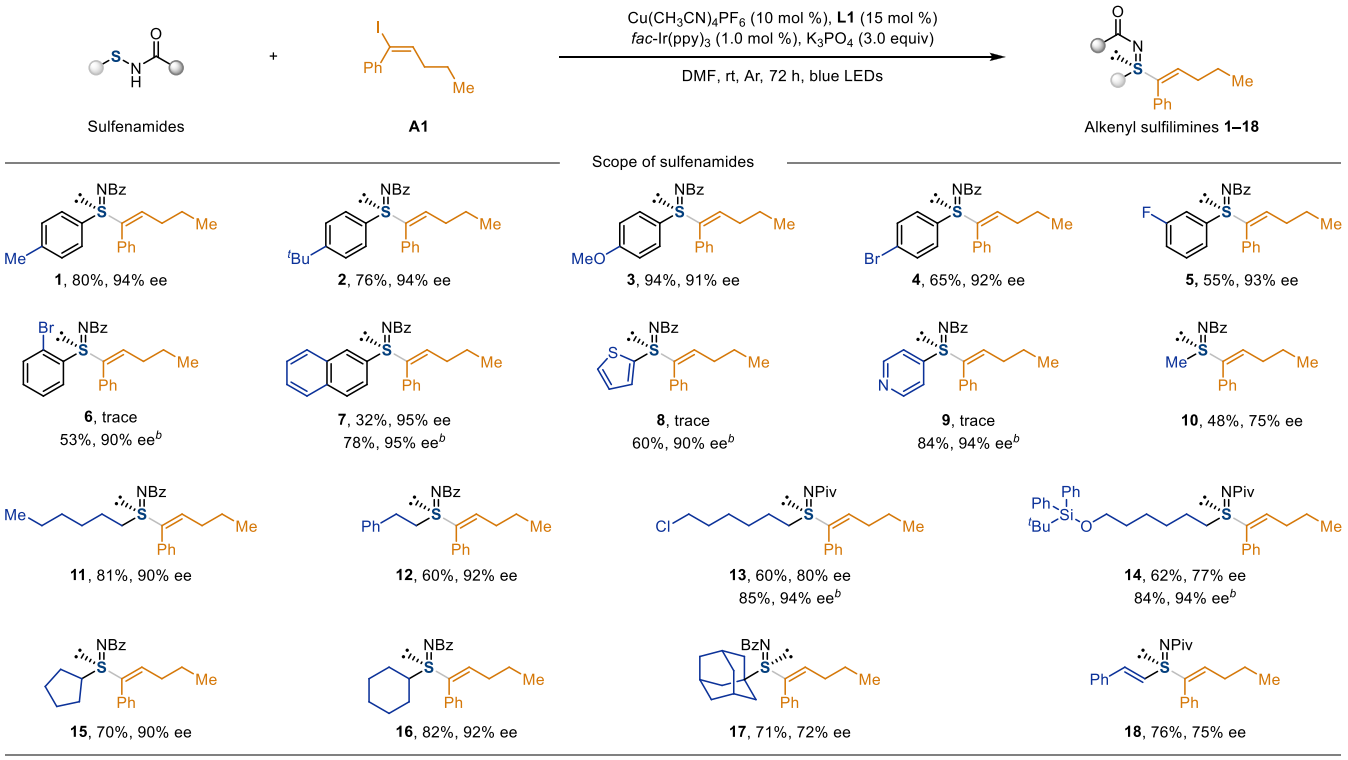
Table 2. Substrate Scope of Sulfenamides[a]



[a]Standard reaction conditions: sulfenamide **S** (0.20 mmol), alkenyl iodide **A1** (1.5 equiv), $Cu(CH_3CN)_4PF_6$ (10 mol %), **L1** (15 mol %), *fac*-$Ir(ppy)_3$ (1.0 mol %), and K_3PO_4 (3.0 equiv) in DMF (2.0 mL) at rt under an argon atmosphere and irradiation with blue LEDs for 72 h. [b]With sulfenamide **S** (0.20 mmol), alkenyl iodide **A1** (1.5 equiv), CuI (10 mol %), **L1** (15 mol %), $MesN_2BF_4$ (2.0 equiv), and K_3PO_4 (3.0 equiv) in MTBE (4.0 mL) at rt for 4 days under argon. Yields are isolated and ee values are determined by chiral HPLC analysis. Mes, mesityl.

XAT manifold,[10a−c] which operates under light-free conditions and could potentially modulate the rate of alkenyl-radical generation. Under copper-catalyzed, indirect aryl radical-mediated XAT conditions, sulfilimine **6** could be obtained in low yields with high enantioselectivity (Table S3, entries 3−5). Further optimization (Table S3, entries 6−10) of the copper salt, base additive, and solvent increased the yield of **6** to 53% while maintaining high enantioselectivity (90% ee; Table S3, entry 8; see Table S4 for control-experiment results under the optimized conditions). Similarly, sulfenamides bearing *S*-(hetero)aryl substituents, namely, 2-naphthyl, 2-thienyl, and 4-pyridyl groups, showed diminished performance under the photoinduced conditions but furnished the corresponding sulfilimines **7**−**9**, respectively, in moderate yields with 90−95% ee under the XAT conditions, presumably owing to competitive side reactions of these sulfenamides under the basic, photoinduced conditions (see Scheme S2 and Figure S3 for details).

We next evaluated *S*-alkyl sulfenamides. Despite complete consumption of the starting material, *S*-methyl sulfilimine **10** was obtained in only 48% yield with 75% ee. Increasing the *S*-alkyl chain length or steric bulk generally improved the enantioselectivity (**11**−**16**). However, an *S*-adamantyl sulfenamide afforded sulfilimine **17** with diminished enantioselectivity (72% ee). The nonconjugating nature of the adamantyl substituent presumably renders this sulfenamide less susceptible to competitive side reactions under the basic, photoinduced conditions (see Scheme S2 and Figure S3 for details), thus affording the desired product **17** in good yield despite its considerable steric bulk. Notably, functionalized *S*-alkyl sulfenamides bearing a chloro substituent or a *tert*-butyldiphenylsilyl (TBDPS)-protected hydroxyl group performed substantially better under the XAT conditions, furnishing products **13** and **14** in 84% and 85% yield, respectively, both with 94% ee. An alkenyl-substituted sulfenamide was also compatible, affording *S*,*S*-dialkenyl sulfilimine **18** in 76% yield with 75% ee.

We then explored the scope of alkenyl halides with varied substitution patterns (Figure 2A). Trisubstituted alkenyl iodides with C2 primary alkyl substituents, ranging from a simple aliphatic chain to functionalized chains containing a phenyl ring, ester, ether, silyl ether, amide, or cyano group, were readily incorporated to furnish the corresponding products **19**−**23** and **26**−**29** in moderate to good yields with excellent enantioselectivity. In contrast, analogous alkenyl iodides featuring a terminal *O*-acyl group (−OAc or −OBz) on the C2 primary alkyl substituent failed under the photoinduced conditions but, under the XAT conditions, delivered products **24** and **25** in good yields with 93% and 90% ee, respectively. Notably, an alkenyl iodide containing a potentially reactive chloro group was tolerated under the photoinduced conditions, affording product **30**. More sterically demanding alkenyl iodides bearing C2 secondary or tertiary alkyl substituents proved to be competent substrates, affording products **31** and **32** in good yields with excellent enantioselectivity. However, a related alkenyl chloride proved incompatible with the current photoinduced protocol, presumably due to the insufficient reducing power of the photocatalyst toward the C−Cl bond (see Scheme S1 and Figure S2). A 1,2-diphenyl-substituted alkenyl iodide coupled

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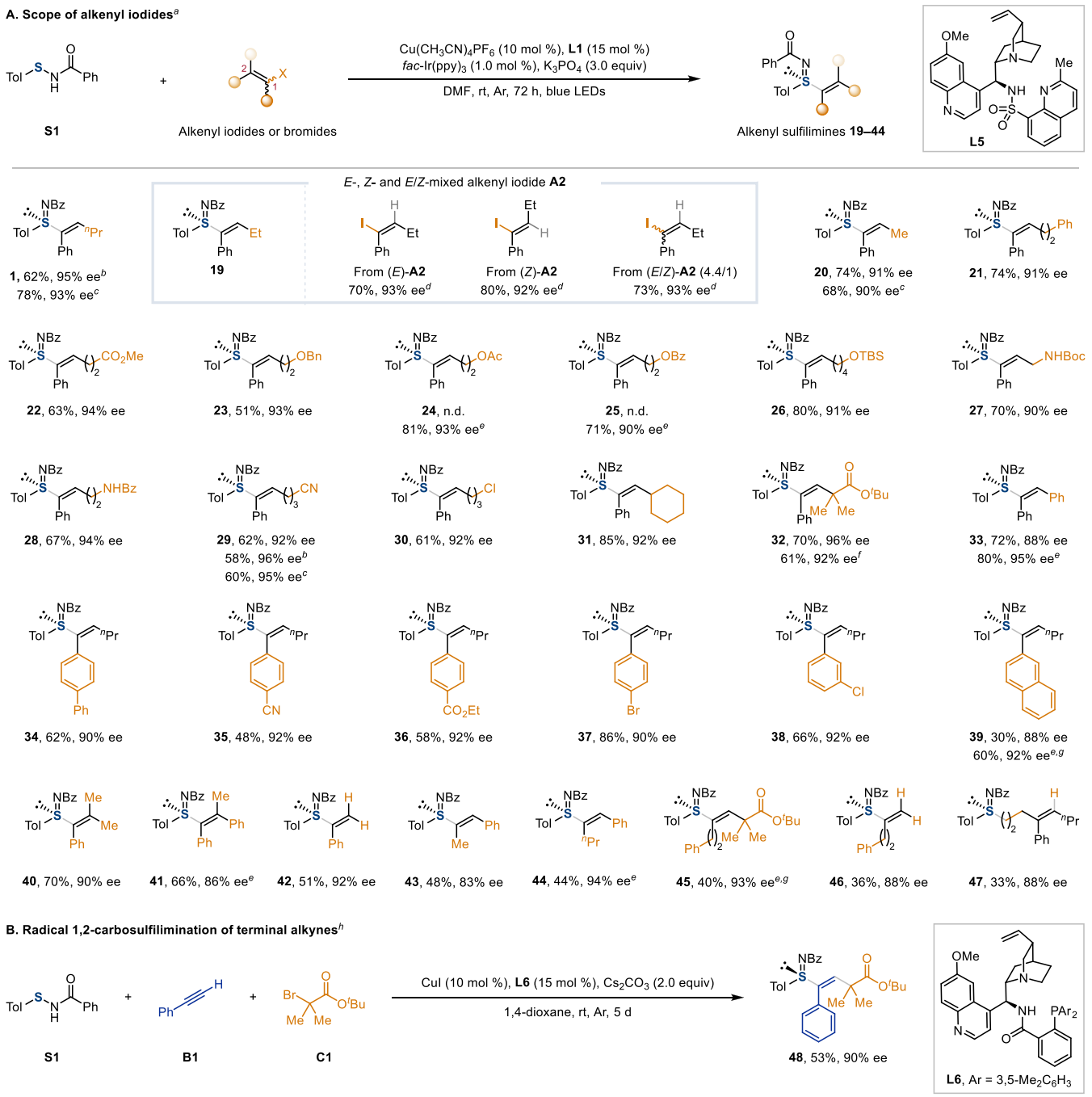

Figure 2. Substrate scope of alkenyl iodides and extension to a radical 1,2-carbosulfilimination of an alkyne. [a]Standard reaction conditions: sulfenamide **S1** (0.20 mmol), alkenyl iodide **A** (1.5 equiv), $Cu(CH_3CN)_4PF_6$ (10 mol %), **L1** (15 mol %), *fac*-Ir(ppy)$_3$ (1.0 mol %), and K_3PO_4 (3.0 equiv) in DMF (2.0 mL) at rt under argon and irradiation with blue LEDs for 72 h. [b]The (*Z*)-alkenyl iodide, (*Z*)-**A1**, or (*Z*)-**A12**, was used. [c]The (*E*/*Z*)-mixed alkenyl iodide was used ((*E*/*Z*)-**A1**: 6.5/1; (*E*/*Z*)-**A3**: 2.8/1; (*E*/*Z*)-**A12**: 1/1.3). [d]The *E*/*Z* ratio (>20:1) of **19** was determined by the ^{1}H NMR analysis of the crude reaction mixture. [e]With sulfenamide **S** (0.20 mmol), alkenyl iodide **A** (1.5 equiv), CuI (10 mol %), **L1** (15 mol %), $MesN_2BF_4$ (2.0 equiv), and K_3PO_4 (3.0 equiv) in MTBE (4.0 mL) at rt for 4 days under argon. [f]**A5-Br** was used instead of **A15-I**. [g]**L5** (15 mol %) was used instead of **L1**. [h]Sulfenamide **S1** (0.10 mmol), alkyne **B1** (2.0 equiv), *tert*-butyl α-bromoisobutyrate **C1** (3.0 equiv), CuI (10 mol %), **L6** (15 mol %), and Cs_2CO_3 (2.0 equiv) in 1,4-dioxane (1.0 mL) at rt for 5 days under argon. Yields are isolated, and ee values are determined by chiral HPLC analysis. Tol, *p*-tolyl; N.d., not detected.

smoothly to give **33** in 72% yield with 88% ee; switching to the XAT conditions improved both the yield and enantioselectivity. Aryl-substituted alkenyl iodides were broadly tolerated: para- and meta-substituted 1-phenyl derivatives, as well as π-extended 1-aryl analogues (4-biphenyl and 2-naphthyl), delivered products **34**−**39** in moderate to good yields with consistently high enantioselectivity. Alternative substitution patterns were viable, with tetrasubstituted and 1,1-disubstituted 1-phenyl alkenyl iodides furnishing **40**, **41**, and **42** in moderate yields with excellent enantioselectivity. In contrast, 1-alkyl-substituted alkenyl iodides that were either 1,1,2-trisubstituted or 1,1-disubstituted gave the corresponding products **43**−**46** in low to modest yields, albeit with good to excellent enantioselectivity. We speculate that the diminished

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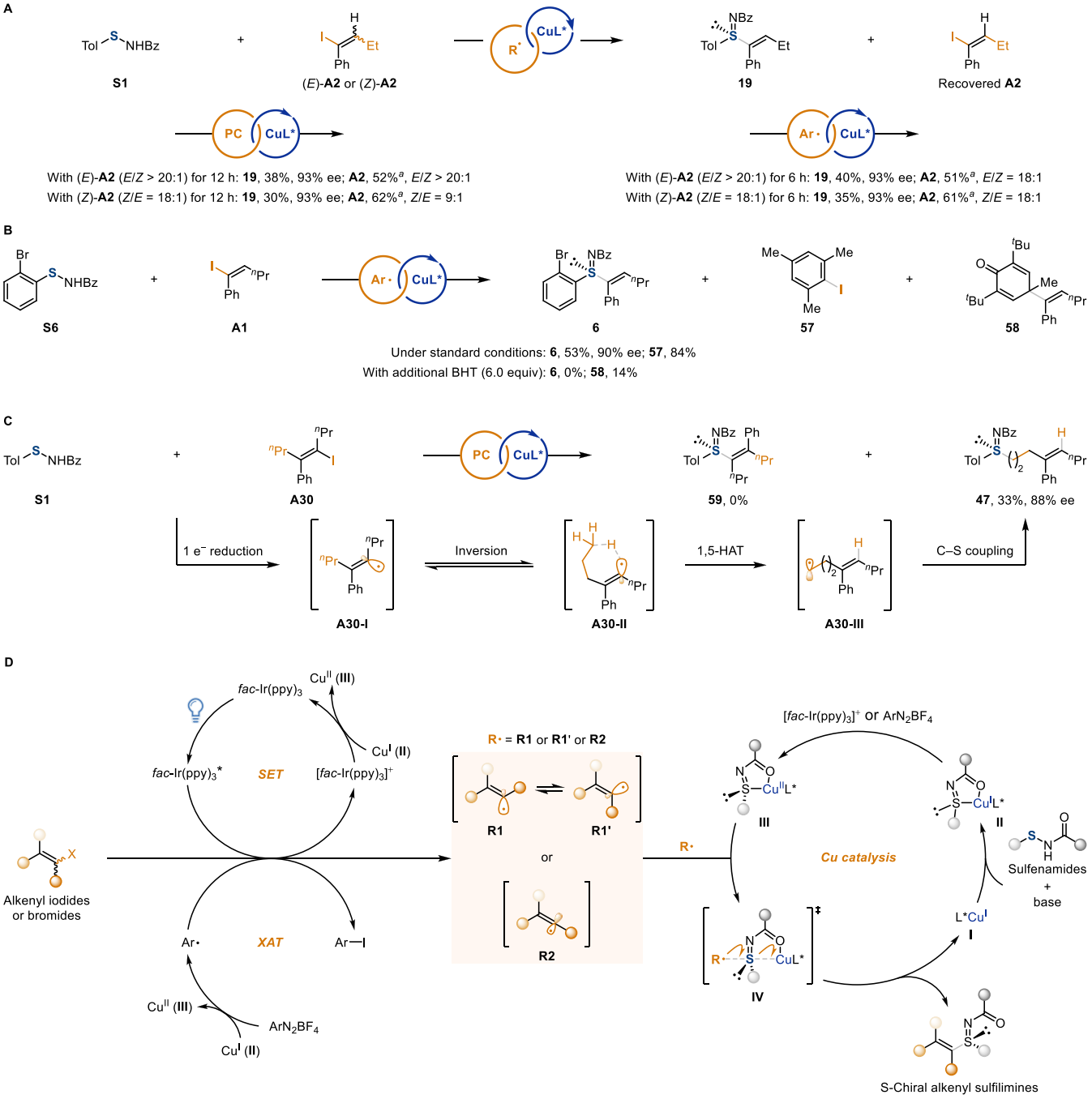

Figure 3. Mechanistic studies and proposed catalytic cycle. [a]Recovered yield was calculated based on the initial amount of **A2**.

yields for these substrates arise from the higher reactivity of σ-type alkenyl radicals, which may promote competitive side pathways.[5,8,9] Consistent with this rationale, the 1,2-di-*n*-propyl-substituted alkenyl iodide preferentially underwent intramolecular 1,5-hydrogen atom transfer (HAT;[22] bond dissociation energy (BDE) of the 1-alkyl-substituted alkenyl C−H bond: ∼106 kcal/mol[23] cf. and unactivated primary C−H bond: ≥100 kcal/mol[24]) followed by C−S coupling to afford the remotely C−H-functionalized sulfilimine **47** (see Figure 3C for details; see Figure S4 for two-dimensional nuclear Overhauser effect spectroscopy analysis supporting the structural assignment of **47**). Interestingly, no analogous HAT/C−S coupling products were observed with other tested 1-alkyl-substituted iodides or with 1-aryl-2-*n*-propyl alkenyl iodides; in the former case, the corresponding 1,*n*-HAT ($n \neq 5$) processes are presumably kinetically disfavored,[25] while in the latter, the enhanced stability (BDE of the 1-phneyl-substituted C−H bond: ∼100 kcal/mol[26]) and unfavorable geometry[27] of the corresponding π-type alkenyl radicals likely impede 1,5-HAT.[28] Notably, the use of several *Z*-enriched or *E*/*Z*-mixed iodides all afforded the same products with yields and stereoselectivities comparable to those obtained from *E*-enriched iodides (**1**, **19**, **20**, and **29**), highlighting the excellent tolerance of this protocol toward different alkenyl iodide configurations. The *E* alkene geometry of **19** was confirmed by X-ray crystallographic analysis (Figure S5), which also established the *R* absolute configuration at sulfur. The

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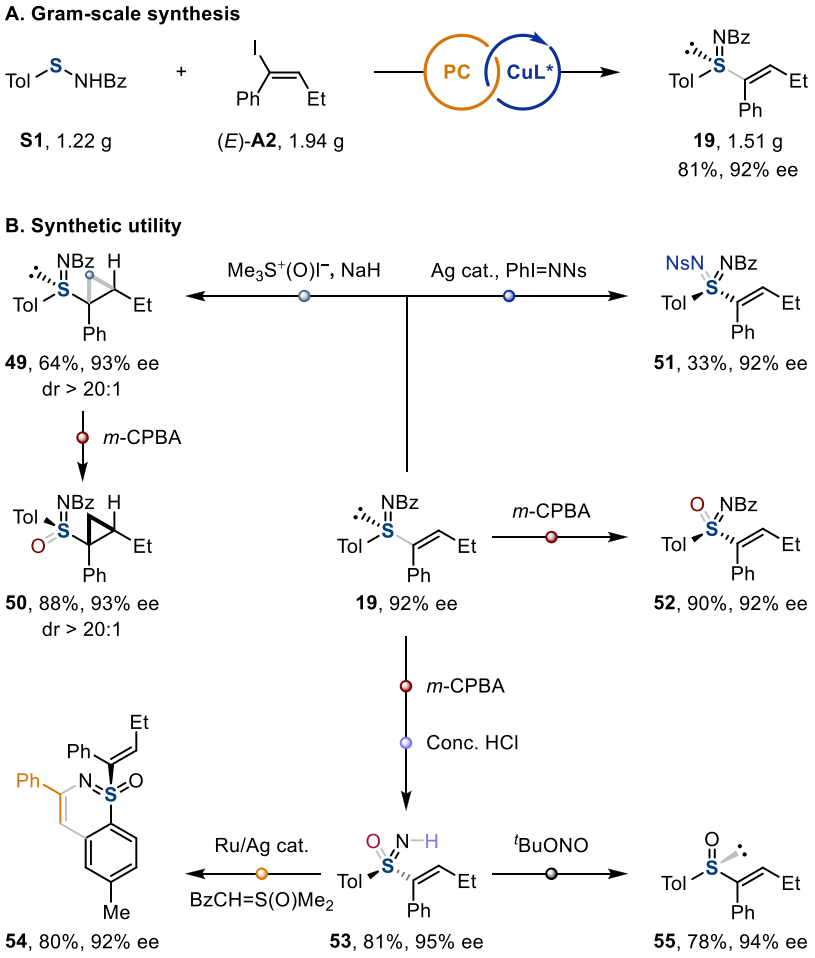
Scheme 1. Scale-Up and Derivatization of *S*-Chiral Sulfilimines[a]



[a]Ag cat., $AgNTf_2$, and 4,4′,4″-tri*tert*-butyl-2,2′:6′,2″-terpyridine; *m*-CPBA, 3-chloroperoxybenzoic acid; and Ru/Ag cat., $[(p\text{-cymene})RuCl_2]_2$/$AgSbF_6$.

corresponding alkene geometries and sulfur configurations of the remaining products were assigned by analogy.

Finally, inspired by the Cu-catalyzed three-component asymmetric radical difunctionalization of terminal alkynes and the ready availability of these feedstocks,[6d−f] we investigated whether an asymmetric radical 1,2-carbosulfilimination of alkynes could be achieved with high chemo- and stereoselectivity (Figure 2B). After optimization of the copper salt, ligand, base, and solvent (Table S5), we found that the reaction of sulfenamide **S1**, ethynylbenzene **B1**, and *tert*-butyl α-bromoisobutyrate **C1** in the presence of CuI/**L6** and Cs_2CO_3 afforded **48** in 53% yield and 90% ee in 1,4-dioxane (Table S5, entry 3). Unfortunately, internal alkynes proved to be incompatible with the current reaction conditions (Scheme S4), presumably due to their relatively low reactivity toward the addition of sterically bulky tertiary alkyl radicals. Notably, during the preparation of this manuscript, a related enantioselective radical 1,2-trifluoromethyl-sulfilimination reaction of terminal alkynes was reported.[29]

Synthetic Utility

To demonstrate the synthetic potential of these S-chiral sulfilimines, we performed the reaction on a gram scale using (*E*)-**A2** (Scheme 1A), affording **19** in 81% yield and 92% ee (1.51 g) with no loss in enantioselectivity upon scale-up. The enantioenriched sulfilimine **19** was readily diversified with minimal impact on enantiopurity (Scheme 1B). For example, cyclopropanation with dimethyl sulfoxonium methylide furnished **49** in 64% yield with excellent diastereoselectivity (diastereomeric ratio (dr) >20:1).[30] Oxidation of **49** with *m*-chloroperoxybenzoic acid (*m*-CPBA)[31] then provided sulfoximine **50** in 88% yield without loss of diastereoselectivity (dr >20:1). Ag-catalyzed imination of **19** with *N*-tosyl iminoiodinane (PhI=NTs) gave sulfondiimine **51** in 92% ee.[15q] In a complementary oxidation, *m*-CPBA converted **19** to sulfoximine **52** in 90% yield with 92% ee. Subsequent *N*-debenzoylation with concentrated HCl delivered the free-NH sulfoximine **53** in 81% yield with no detectable racemization.[15q] Finally, Ru-catalyzed C−H activation/annulation of **53** with a sulfonium ylide enabled selective ortho C−H functionalization to furnish **54** in 80% yield and 92% ee.[32] In addition, sulfoximine **52** could be converted straightforwardly into sulfoxide **55** in 78% yield and 94% ee.[15q] Interestingly, similar S-oxidation of sulfilimine **43** delivered sulfoximine **56** in 81% yield with 84% ee, where both the starting sulfilimine and the resulting sulfoximine bear the same essential *S*-aryl-*S*-(1-alkyl-2-arylalkenyl) skeleton as a reported bioactive alkenyl sulfone compound,[33] thus constituting the S-stereogenic analogues of the latter (Figure S6).

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Mechanistic Investigation

In the coupling studies of alkenyl iodide **A2** (Figure 2A), the same enantiomer of product **19** was obtained regardless of whether (*E*)-**A2**, (*Z*)-**A2**, or an *E*/*Z* mixture was employed, indicating a stereoconvergent process with respect to the alkene geometry. This observation prompted us to examine whether direct *E*/*Z* interconversion of the alkenyl iodide occurs under the reaction conditions (Figure 3A). A 12 h time-course experiment starting from (*E*)-**A2** (*E*/*Z* > 20:1) or (*Z*)-**A2** (*Z*/*E* = 18:1) under the standard photoinduced conditions afforded **19** in comparable isolated yields and high enantioselectivity, while the recovered alkenyl iodides remained highly geometrically enriched (isomeric ratios ≥9:1; Figure 3A, left; Figures S7 and S8). Importantly, the corresponding experiments conducted under the XAT conditions for 6 h led to the same qualitative outcome (Figure 3A, right; Figures S9 and S10). Although a slight erosion of the isomeric ratios was observed in two of the four experiments, it could reflect minor secondary processes (e.g., slow *E*/*Z* isomerization) and/or modest kinetic differences between the *E* and *Z* isomers under the two sets of conditions. Collectively, these results argue against a mechanism involving rapid substrate-level *Z*/*E* interconversion under either set of conditions. Instead, they are consistent with formation of a common alkenyl intermediate (e.g., an alkenyl radical) that does not retain the geometric information on the starting alkenyl iodide, thereby enabling stereoconvergence.

To probe the involvement of radical intermediates, radical-inhibition experiments were performed using TEMPO ((2,2,6,6-tetramethylpiperidin-1-yl)oxyl) and BHT (2,6-di-*tert*-butyl-4-methylphenol) under XAT conditions (Figure 3B) and photoinduced conditions (Figure S11B). In both cases, product formation was strongly suppressed, consistent with a radical pathway. Moreover, BHT-trapped adduct **58** was isolated under both conditions, providing direct evidence for the participation of radical species in each manifold. Under the XAT conditions, the near-stoichiometric formation of mesityl iodide (**57**) was observed, supporting the generation of mesityl radicals and their efficient iodine-atom abstraction from alkenyl iodides to initiate the XAT pathway (Figure 3B). Additional support for an alkenyl-radical intermediate was obtained using the aforementioned 1,2-di-*n*-propyl-substituted alkenyl iodide **A30** as a radical probe substrate. Under the standard photoinduced conditions, the desired direct cross-coupling product was not detected (Figure 3C). Instead, the initially formed alkenyl radical **A30-I** is proposed to undergo rapid *E*/*Z* interconversion to give **A30-II**, followed by intramolecular 1,5-HAT[22] to generate the alkyl radical **A30-III**. Subsequent coupling of **A30-III** with **S1** afforded the product **47**. A Stern–Volmer study further showed that the excited state of *fac*-Ir(ppy)$_3$ is readily quenched by (*E*)-**A2** (Figure S12), consistent with a photoredox pathway in which the alkenyl iodide participates in an oxidative quenching event.[34]

On the basis of the above experiments and previous studies,[15q] a plausible unified mechanism is proposed (Figure 3D). Under the photoinduced conditions, irradiation with blue LEDs generates the excited photocatalyst *fac*-Ir(ppy)$_3$*, which engages in SET with alkenyl iodides or bromides to form an alkenyl radical (**R•**) together with the oxidized photocatalyst. In parallel, coordination of the sulfenamide to the chiral Cu^{I} catalyst **I** under basic conditions furnishes a Cu-bound sulfenamide intermediate **II**, which can reduce the oxidized photocatalyst to regenerate the ground-state photocatalyst while generating a higher-valent Cu species **III**. Interception of the alkenyl radical by **III** and subsequent radical-substitution-type C–S bond formation furnish enantioenriched S-chiral alkenyl sulfilimines, concomitantly regenerating the chiral Cu^{I} catalyst **I**. Under the XAT conditions, SET between Cu^{I} complex **II** and diazonium salt generates an aryl radical and the corresponding higher-valent Cu species **III**. The aryl radical then abstracts iodine from the alkenyl iodide to form the same alkenyl radical **R•**, which undergoes the same Cu-mediated C–S bond-forming process. In both manifolds, generation of the alkenyl radical—either approximately linear (thus lacking *E*/*Z* geometric information) or rapidly interconverting between bent *E*/*Z*-related forms—accounts for efficient erasure of the initial alkene geometry and, consequently, the observed stereoconvergent coupling.

CONCLUSIONS

In summary, we have developed a stereoconvergent and enantioselective Cu-catalyzed C–S cross-coupling of alkenyl iodides and bromides with sulfenamides. By exploiting the loss of alkene geometric information at the alkenyl-radical stage—via rapidly interconverting bent σ-type radicals and/or approximately linear π-type radicals—the initial *E*/*Z* stereochemistry of the starting alkenyl halides can be effectively erased, enabling enantioenriched S-chiral alkenyl sulfilimines to be obtained irrespective of the initial alkene geometry. These reactions proceed efficiently, accommodate a broad range of alkenyl halides, and deliver high levels of stereoselectivity and enantioselectivity. The protocol is scalable to the gram scale, and the resulting S-chiral alkenyl sulfilimines can be readily derivatized into a range of *S*-chiral sulfur(VI)-containing motifs, highlighting their synthetic versatility. Collectively, these results underscore a general and efficient Cu-catalyzed platform for the synthesis of enantioenriched alkenyl S-chiral scaffolds.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.6c02132.

Additional experimental and theoretical results, experimental procedures, characterization of compounds, computational details, NMR spectra, and HPLC traces (PDF)

Accession Codes

Deposition Number 2504953 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via the joint Cambridge Crystallographic Data Centre (CCDC) and Fachinformationszentrum Karlsruhe Access Structures service.

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Notes

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