

Silver-mediated Room Temperature Reactions for the Synthesis of *N*- α -Ketoacyl Sulfoximines and *N*- α,β -Unsaturated Acyl Sulfoximines

Ria Gupta, Riyaz Ahmed, Zaheen Akhter, Mukesh Kumar, and Parvinder Pal Singh*

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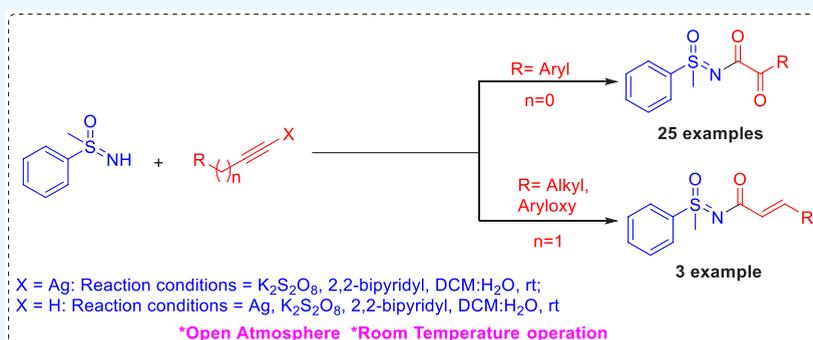
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ABSTRACT: Here, we report a silver-mediated coupling of acetylenes with sulfoximines to synthesize *N*- α -ketoacyl sulfoximines and *N*- α,β -unsaturated acyl sulfoximines. The reactions are performed under an open atmosphere using the oxidant $K_2S_2O_8$ and the ligand 2,2-bipyridyl. However, the fate of the product formation is controlled by the type of substrate used. The coupling between aryl acetylenes and sulfoximines afforded the *N*- α -ketoacylsulfoximines, while the alkyl acetylenes provided the *N*- α,β -unsaturated acyl sulfoximines. Controlled experiments reveal the differential reactivity patterns of substrates. The labeling ^{18}O experiments showed that water is the source of the incoming oxygen atom for the keto group of *N*- α -ketoacyl sulfoximines and *N*- α,β -unsaturated acyl sulfoximines.

INTRODUCTION

Sulfoximines constitute a significant group in organic chemistry because of their remarkable properties, such as chiral auxiliaries,^{1–3} ligands,^{4–6} and building blocks.^{7–12} Sulfoximines have played a pivotal role in drug discovery¹³ for improving specificity¹⁴ and oral bioavailability.¹⁵ They have also been employed for reducing undesired toxicity.^{16–18} Sulfoximines are also used as biososteres for different functional moieties (heterocyclic amidine,^{15,19} sulfones,²⁰ and secondary hydroxyl groups)^{21,22} as well as stable transition-state analogue inhibitors.²³ Therefore, developing new and efficient methods for their preparation and derivatization is highly needed. Our group has a persistent interest in the functionalization of the sulfoximine moiety and has developed new methods for the *N*-arylation and *N*-heteroarylation of sulfoximine.^{24,25} In the next curiosity, attempts were made for the *N*-alkynylation of sulfoximine using the combination of silver, oxidants, and additive, but tried conditions provided the *N*- α -ketoacyl sulfoximines instead of *N*-alkynyl sulfoximines (Figure 1). On the other hand, one report regarding the synthesis of *N*-alkynyl sulfoximines employed sensitive bromoacetylenes and copper catalysts.^{26,27} In the one decade, α -ketoamides have been highlighted due to their remarkable properties as precursors and pharmaceutical agents.²⁸ However, there are

many reports related to the synthesis of *N*-acyl sulfoximines.^{29,30} However, limited reports are available on the synthesis of *N*- α -ketoacyl sulfoximines. Zou et al.³¹ and Cheng and Bolm³² reported the synthesis of *N*- α -ketoacyl sulfoximines by coupling methyl ketones and *NH*-sulfoximines in the presence of copper catalysts and oxidants under heating conditions. Later, Cheng and Bolm developed another method for synthesizing *N*- α -ketoacyl sulfoximines using sulfoximidoyl-containing hypervalent iodine reagents in the presence of light.³³ In 2021, Baranwal et al. reported the synthesis of *N*- α -ketoacyl sulfoximines using selenium dioxide under heating conditions.³⁴ In the recent decade, silver catalysis has also made its impact beyond its use as cocatalysts or bond activators and has been exploited in many organic transformations, and the same has been nicely reviewed also.^{35a–c} Here, we have exploited the silver catalysis's use in synthesizing *N*- α -ketoacyl sulfoximines and *N*- α,β -unsaturated acyl sulfox-

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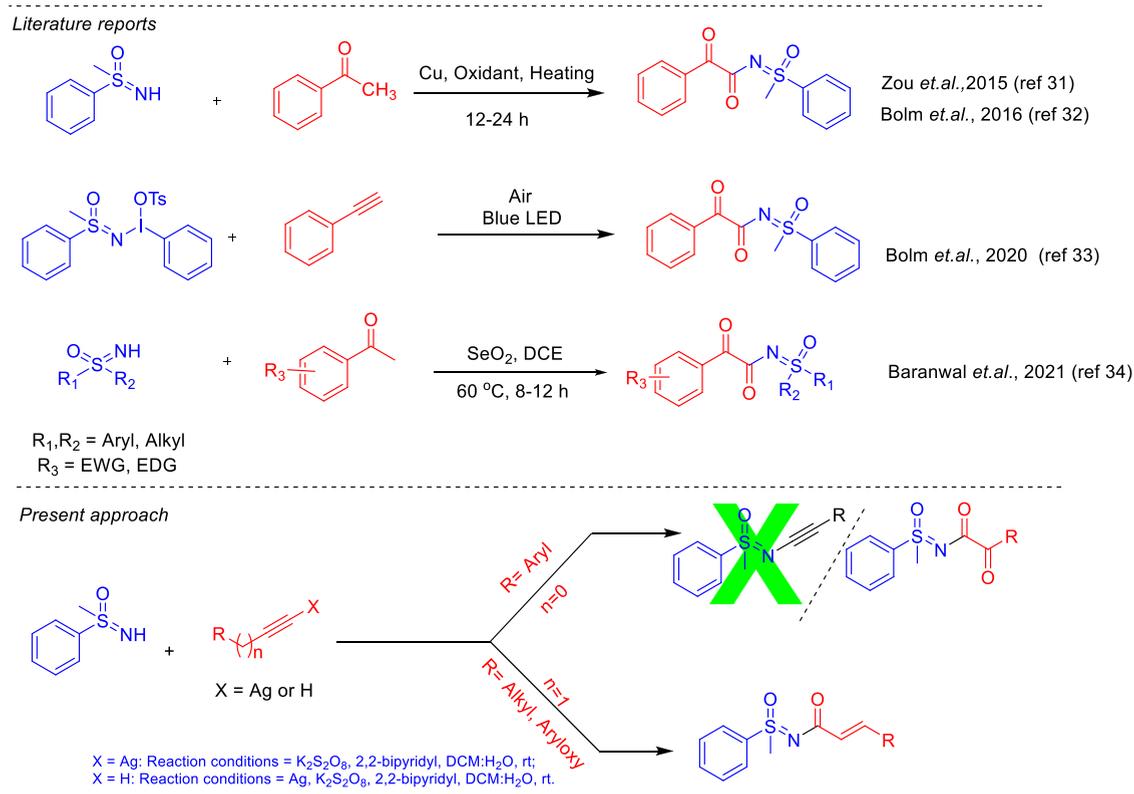


Figure 1. Previous and present approaches for the synthesis of *N*- α -ketoacyl sulfoximines and *N*- α,β -unsaturated acyl sulfoximines.

imines. The coupling of *NH*-sulfoximines with aryl acetylenes leads to *N*- α -ketoacyl sulfoximines. However, aliphatic alkynes provided the *N*- α,β -unsaturated acyl sulfoximines.

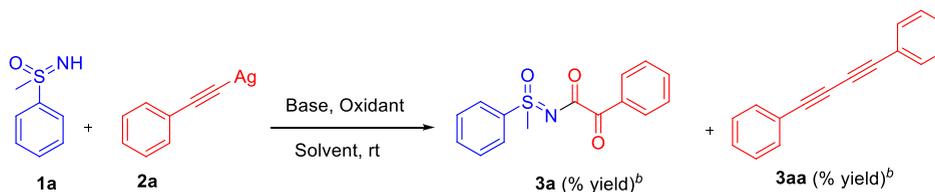
RESULTS AND DISCUSSION

The reaction optimization started with the reaction of sulfoximine **1a** (0.645 mmol) and silver acetylide **2a** (0.967 mmol, 1.5 equiv) as the coupling partners (Table 1). The study was initiated with the reaction of the selected substrates with potassium persulfate (1.935 mmol, 3 equiv) as an oxidant and 2,2-bipyridyl (1.29 mmol, 2 equiv) as an additive under different solvents such as tetrahydrofuran (THF), dimethylformamide (DMF), acetonitrile (CH₃CN), toluene, dichloromethane (DCM), and dichloroethane (DCE). All the tried conditions did not provide the required coupled product, but the formation of 1,4-diphenylbuta-1,3-diyne, **3aa**, as a sole product is observed (entries 1–6). In the subsequent attempts, a combination of solvents such as toluene/water, DCE/H₂O, and DCM/H₂O systems was explored; among all the tried conditions, DCE/H₂O and DCM/H₂O systems provided the corresponding *N*- α -ketoacyl sulfoximines **3a** in a yield of 56 and 63%, respectively, along with 1,4-diphenylbuta-1,3-diyne, **3aa**, (entries 7–9). When the reaction was performed in water, no *N*- α -ketoacyl sulfoximines **3a** was observed, but the formation of 1,4-diphenylbuta-1,3-diyne, **3aa**, was observed in a yield of 46% (entry 10). When the amount of 2,2'-bipyridyl was decreased to 1.5 and 1 equiv, the yield of *N*- α -ketoacyl sulfoximine, **3a**, was reduced to 32 and 17%, respectively, while no *N*- α -ketoacyl sulfoximine, **3a**, was observed when the concentration of 2,2'-bipyridyl was decreased less than one equivalent (entries 11–13). On the other hand, increasing the concentration of 2,2'-bipyridyl to 3 equiv also drastically affect yields (entry 14). When the

potassium persulfate was changed with other oxidants such as ammonium persulfate, sodium persulfate, selectfluor, *tert*-butyl hydroperoxide, hydrogen peroxide, and oxone, **3a** was observed with sodium persulfate only (entries 15–20). To suppress the formation of homo-coupled 4-diphenylbuta-1,3-diyne, the reactions were carried out in presence of bases such as cesium carbonate (Cs₂CO₃), potassium carbonate (K₂CO₃), and *N,N*-diisopropyl ethyl amine (DIPEA), but no improvement was observed in the yield of *N*- α -ketoacyl sulfoximines **3a** (entries 21–23). In other attempts, changes in the molar concentration of reactants and additives also did not provide any advantage (results not shown here). When the reaction was performed without additives, no product formation was observed (entry 24). Considering all the attempts, entry no. 9 is considered the best condition (entry 9), and all the next diversity generations were attempted with the same conditions.

With the best coupling condition, we then explored its diversity using various substituted phenyl acetylides and phenyl sulfoximines, and all the results are presented in Scheme 1. The scope of the approach was found to be very broad and provided the corresponding *N*- α -ketoacyl sulfoximines with good yields. Phenyl sulfoximine underwent smooth coupling reactions with an electron-donating group containing silver phenylacetylides, such as *p*-tolylethynylsilver, {(4-propylphenyl)ethynyl}silver, {(4-*tert*-butylphenyl)ethynyl}-silver, and {(3-methoxyphenyl)ethynyl}silver, and gave the corresponding coupled products **3b**, **3c**, **3d**, and **3e**, respectively, in yields of 53, 54, 56, and 62%, respectively.

Similarly, electron-withdrawing groups containing silver phenylacetylides such as {(4-trifluoromethylphenyl)ethynyl}silver and {(4-bromophenyl)ethynyl}silver also underwent coupling reactions with sulfoximine **1a** and furnished the corresponding coupled products **3f** and **3g** in yields of 61 and

Table 1. Optimization study^a

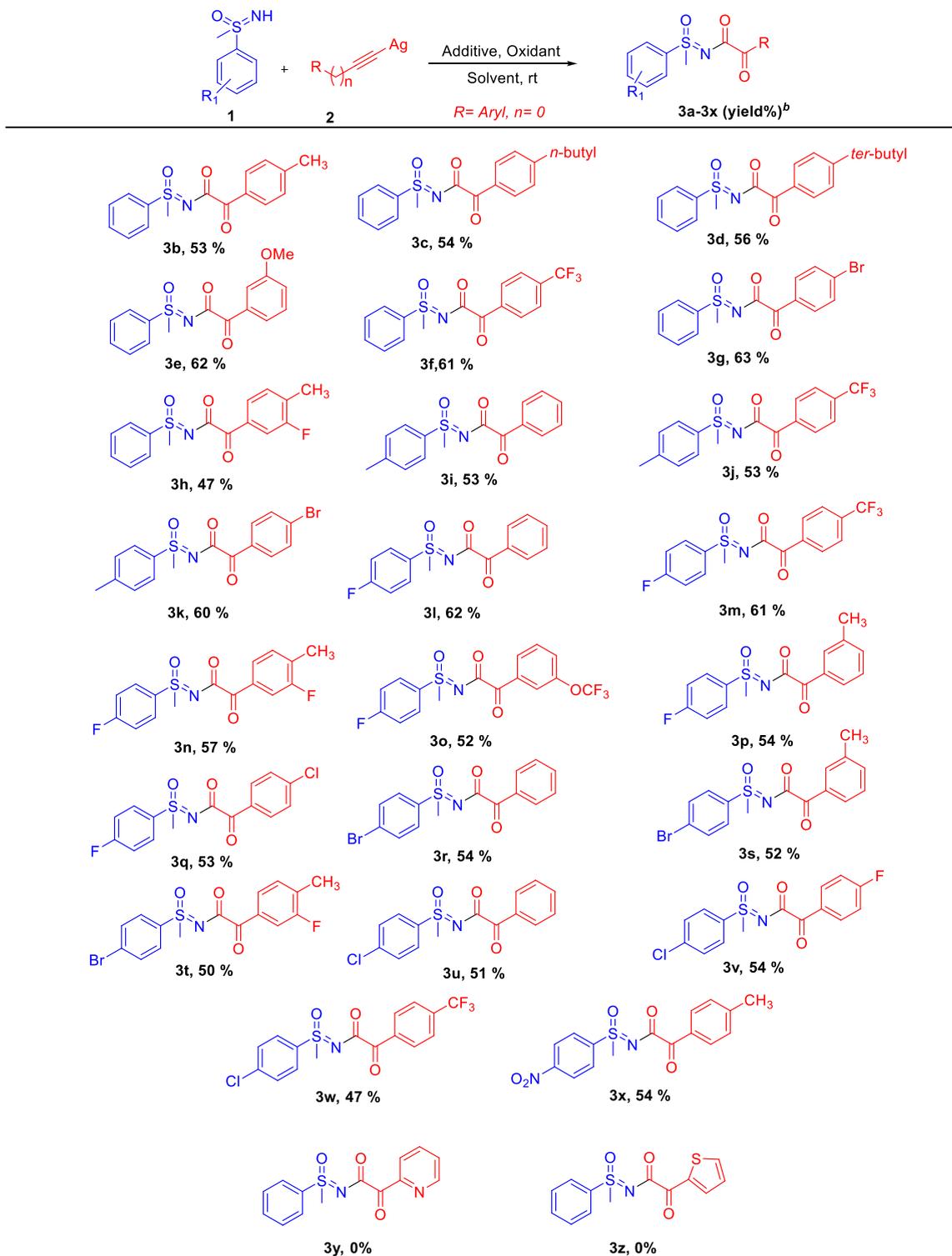
entry	oxidant (equiv)	additive (equiv)	solvent	% yield ^b	
				3a (%)	3aa
1	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	THF	0	67
2	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	DMF	0	64
3	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	CH ₃ CN	0	62
4	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	toluene	0	57
5	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	DCM	0	61
6	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	DCE	traces	67
7	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	toluene/H ₂ O	0	58
8	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	DCE/H ₂ O	56	43
9	K₂S₂O₈ (3)	2,2-bipyridyl (2)	DCM/H₂O	63	26
10	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	H ₂ O	0	46
11	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (1.5)	DCM/H ₂ O	32	59
12	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (1)	DCM/H ₂ O	17	56
13	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (0.8)	DCM/H ₂ O	0	49
14	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (3)	DCM/H ₂ O	0	46
15	(NH ₄) ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	DCM/H ₂ O	traces	34
16	Na ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2)	DCM/H ₂ O	52	51
17	select fluor	2,2-bipyridyl (2)	DCM/H ₂ O	0	59
18	TBHP (3)	2,2-bipyridyl (2)	DCM/H ₂ O	0	0
19	H ₂ O ₂ (3)	2,2-bipyridyl (2)	DCM/H ₂ O	0	0
20	Oxone	2,2-bipyridyl (2)	DCM/H ₂ O	0	0
21	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2) + Cs ₂ CO ₃ (1.2)	DCM/H ₂ O	12	49
22	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2) + K ₂ CO ₃ (1.2)	DCM/H ₂ O	56	37
23	K ₂ S ₂ O ₈ (3)	2,2-bipyridyl (2) + DIPEA (2)	DCM/H ₂ O	0	0
24	K ₂ S ₂ O ₈ (3)		DCM/H ₂ O	0	0

^aReaction and conditions: compound **1a** (100 mg, 0.645 mmol), compound **2a** (0.967 mmol), solvent, rt, 4–10 h. ^bIsolated yields.

63%, respectively. Sulfoximine **1a** also reacted well with bisubstituted phenylacetylides such as {(3-fluoro-4-methylphenyl)ethynyl}silver to afford the product **3h** in a yield of 47%. Substituted phenyl sulfoximines were also used to explore the further possible extension of the optimized method. 4-Tolyl sulfoximine on reaction with (phenylethynyl)silver, {(4-(trifluoromethylphenyl)ethynyl}silver, and {(4-(bromophenyl)ethynyl}silver under optimized conditions provided the corresponding *N*- α -ketoacyl sulfoximines **3i** (53%), **3j** (53%), and **3k** (60%), respectively. 4-Fluorophenyl containing sulfoximine also reacted well with (phenylethynyl)silver, {(4-(trifluoromethylphenyl)ethynyl}silver, {(3-fluoro-4-methylphenyl)ethynyl}silver, {(3-trifluoromethoxyphenyl)ethynyl} silver, {(3-methylphenyl)ethynyl} silver, {(4-chlorophenyl)ethynyl}silver, and provided the corresponding coupled products **3l** (62%), **3m** (61%), **3n** (57%), **3o** (52%), **3p** (54%), and **3q** (53%), respectively. 4-Bromophenyl-containing sulfoximine reacted with (phenylethynyl)silver, {(3-(methylphenyl)ethynyl} silver, and {(3-fluoro-4-methylphenyl)ethynyl}silver and provided coupled products **3r** (54%), **3s** (52%), and **3t** (50%), respectively. Likewise, 4-chlorophenyl containing sulfoximine also reacted well with (phenylethynyl)silver, {(4-fluoromethylphenyl)ethynyl}silver, and {(4-trifluoromethylphenyl)ethynyl}silver and provided sulfoximines **3u** (51%), **3v** (54%), and **3w** (47%), respectively. Interestingly, 4-nitro containing sulfoximine was also compat-

ible under optimized conditions and coupled with {(4-methylphenyl)ethynyl} silver and provided corresponding *N*- α -ketoacyl sulfoximine **3x** in a yield of 54%. Under optimized conditions, when heteroaromatic acetylides, such as pyridine and thiophene-based silver acetylides, were tried, no coupled products (**3y** and **3z**) were observed. In all the reactions, the formation of corresponding buta-1,3-diyne was observed with yields ranging from 20 to 30%. In further diversification, sulfoximine was replaced with other nucleophiles such as benzamide, sulfonamide, and isatin, but no coupling was observed, suggesting the specificity of the reactions with respect to sulfoximine.

We further explored the reaction conditions for the coupling of sulfoximine with various silver salts of aliphatic acetylides (Scheme 2); however, the coupled product was identified as *N*- α,β -unsaturated acyl sulfoximines. The formation of *N*- α,β -unsaturated acyl sulfoximines has been explained in the latter part of the manuscript. When the sulfoximine **1a** was reacted with (hexynyl)silver under the abovementioned optimized conditions, the reactions proceeded smoothly and yielded corresponding *N*- α,β -unsaturated acyl sulfoximines **4a** in a yield of 43%. Similarly, when (heptynyl)silver was used, the corresponding product **4b** was formed in a yield of 47%. Interestingly, (3-phenoxyprop-1-yn-1-yl)silver also reacted well with sulfoximine and provided the corresponding coupled product **5** in a yield of 51% (Scheme 3). On the other hand,

Scheme 1. Coupling of Sulfoximines with Phenyl Acetylene Silver^a

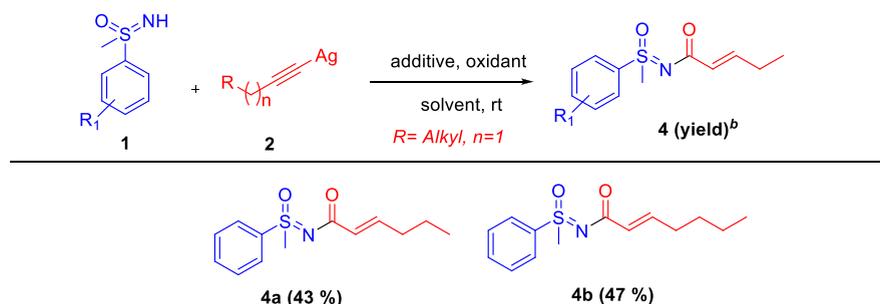
^aReaction conditions: compound 1 (100 mg, 0.429–0.645 mmol), compound 2 (1.5 equiv), K₂S₂O₈ (3 equiv), and 2,2-bipyridyl (2 equiv) in DCM/H₂O (3:1, 12 mL solvent), rt, 4–8 h. ^bIsolated yields.

when aliphatic sulfoximines, such as dibutyl(imino)- λ^6 -sulfanone, were used, no desired product was obtained.

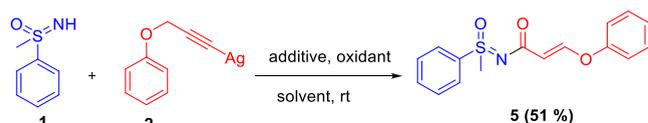
In the next efforts toward extending the scope of the reaction, the coupling was tried with in-situ-generated (phenylethynyl)silver by using the phenyl acetylene and sulfoximine in the presence of silver nitrate, persulfate, and

2,2-bipyridyl, the corresponding product 3a was formed in a yield of 47% (Scheme 4).

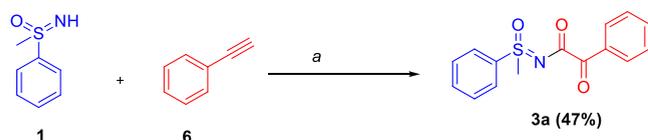
To understand the reaction mechanism, we performed a series of controlled experiments (Scheme 5). When the reactions were performed in the presence of free radical scavengers such as TEMPO the formation of the product 3a

Scheme 2. Coupling of Sulfoximines with Alkynylsilver^a

^aReaction conditions: compound **1** (100 mg, 0.429–0.645 mmol), **2** (1.5 equiv), $\text{K}_2\text{S}_2\text{O}_8$ (3 equiv), and 2,2-bipyridyl (2 equiv) in DCM/ H_2O (3:1, 12 mL of solvent), rt, 4–8 h. ^bIsolated yields.

Scheme 3. Coupling of Sulfoximines with Phenoxypropynyl Silver^a

^aReaction conditions: compound **1** (100 mg, 0.645 mmol), compound **2** (1.5 equiv 0.967 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (3 equiv 1.935 mmol), and 2,2-bipyridyl (2 equiv 1.290 mmol), DCM/ H_2O (3:1, 12 mL), rt, 5 h. ^bIsolated yields.

Scheme 4. Coupling of Sulfoximines with In-Situ-Generated Phenyl Acetylene Silver^a

^aReaction condition: compound **1** (100 mg, 0.645 mmol), AgNO_3 (0.5 equiv, 0.322 mmol), $\text{K}_2\text{S}_2\text{O}_8$ (3 equiv, 1.935 mmol), and 2,2-bipyridyl (2 equiv, 1.290 mmol), DCM/ H_2O (3:1, 12 mL), rt, 7 h.

was significantly suppressed (eq i), which suggested that there might be involvement of a free radical pathway. When the reaction was conducted under a nitrogen atmosphere after performing freeze–thaw cycles of the solvent system, the reaction worked and provided product **3a**, suggesting that the reaction does not have any role with the atmospheric oxygen (eq ii). In the literature, there are reports where phenylacetylenes get converted into glyoxal,^{36–39} glyoxylic acid,^{40–43} and acetophenone^{44–46} under oxidative conditions; therefore, there must be a likely chance of their formation as intermediates and are likely responsible for the formation of coupled product **3a**. To rule out the possibility, the reactions were performed with glyoxal/glyoxylic acid/acetophenone (eqs iii–v), but no coupling was observed, suggesting their noninvolvement in the present optimized reaction. In the further reaction, (phenylethynyl)silver was treated with persulfate and additive without sulfoximine and looked for the formation of glyoxal, glyoxylic acid, and acetophenone; however, none of these were observed, which further suggests their noninvolvement in the present optimized conditions (eq vi). When *N*-alkynyl sulfoximine (**10**, prepared following known procedure²⁷) was treated under optimized conditions, the corresponding required compound **3a** was formed in a yield of 58% (eq vii). The experiment suggested that *N*-alkynyl

sulfoximines could be possible key intermediates during the reaction.

Next, we performed the reaction in the presence of ^{18}O -labeled water to check the source of oxygen in the product. The LC–MS experiment confirmed that ^{18}O is present in the product in 30% (Figure 2), which indicated oxygen atom is coming from water in the acylated product.

To get insight into the involvement of reaction intermediates, the reaction was also performed and examined through the LC–MS study. The aliquots were taken at different time intervals and analyzed under LC–MS. The LC–MS revealed one intermediate **I**₄ ($m/z = 290.25$) (experimental details are given on Page nos. 16 and 17, Supporting Information).

Based on the controlled and labeling experiments as well as LC–MS study and literature reports,^{47–49} we proposed the plausible pathways for the synthesis of *N*- α -ketoacyl sulfoximines and *N*- α,β -unsaturated acyl sulfoximines, as shown in Figure 3. Initially, (phenylethynyl)silver reacted with sulfoximines, leading to the formation of intermediate **I**₁ (confirmed by a controlled experiment, eq vii). The intermediate **I**₁ gets attacked by water molecules and generates the intermediate **I**₂. In the case of aryl acetylenes, the intermediate **I**₂ undergoes rearrangement and provides the intermediate **I**₃. The intermediate **I**₃ underwent oxidation in the presence of silver, and the oxidant generates the *N*- α -hydroxyacyl sulfoximines **I**₄, and subsequent oxidation affords *N*- α -ketoacyl sulfoximines **3**. However, in the case of alkyl acetylenes, the intermediate **I**₂ underwent deprotonation at the β -position and generated the allenyl intermediate **I**₅ followed by the rearrangement afford the *N*- α,β -unsaturated acyl sulfoximines **4**.

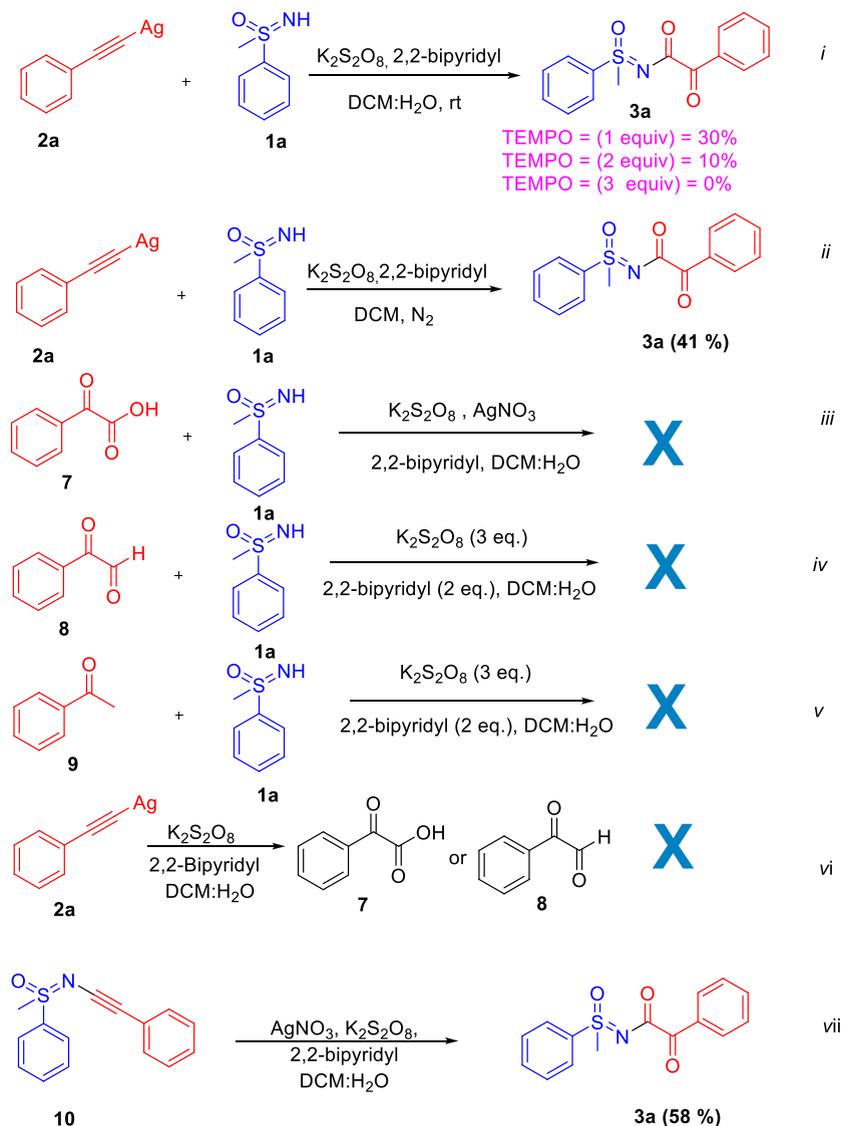
CONCLUSIONS

In conclusion, a novel synthetic methodology has been developed for C–N bond formation and for the synthesis of *N*- α -ketoacyl sulfoximines and *N*- α,β -unsaturated acyl sulfoximines. The reaction worked well at room temperature with the use of mild reaction conditions and inexpensive silver catalysts. Further, the labeling experiment suggested that water plays a major role as a source of oxygen in the acylated product.

EXPERIMENTAL SECTION

General Information. The reactions were carried out at room temperature under an open atmosphere and detected with the help of thin-layer chromatography (60 F254, 20 × 20 cm). Rotavapor was used for the concentration of the solvents

Scheme 5. Controlled Experiments



as well as for drying the compounds. The column chromatography was done using 230–400 mesh silica gel to purify the compounds. The 400 and 101 MHz spectrometers were used to record the ^1H NMR and ^{13}C NMR spectra of all the compounds. The units for chemical data for protons are given in parts per million (ppm, scale) relative to TMS. The coupling constant (J) is in Hz. Also, the LC–MS study and mass spectra were obtained by using a Q-TOF-LC/MS spectrometer using electron spray ionization.

General Procedure for the Synthesis of *N*- α -Ketoacyl Sulfoximines (Table 1 and Scheme 1). The reactants phenylethynyl silver **2** (1.5 equiv) and 2,2-bipyridyl (2 equiv) were dissolved in 12 mL of DCM/ H_2O in a 50 mL round bottom flask and stirred for about 5 min at room temperature. Then potassium persulfate and sulfoximine **1** were added to the above-resulting mixture. This solution was then kept at room temperature for 4–8 h with thorough stirring. The development of the reaction was examined with the help of thin-layer chromatography. As soon as the reaction was completed, the workup was done by transferring the whole reaction mixture to a separating funnel and then extracting it with a dilute solution of hydrochloric acid and dichloro-

methane. Sodium sulfate was added to the organic layer so as to absorb water molecules if present. The organic layer was then dried using a rotavapor. The crude material obtained was then purified with the help of column chromatography to give the purified compounds, *N*- α -ketoacyl sulfoximines **3a–3x** in a yield of 47–63%. The elution system was 30% ethyl acetate/hexane. All the synthesized compounds were then characterized with the help of ^1H NMR, ^{13}C NMR, and HR MS spectra.

General Procedure for the Coupling of Sulfoximines with Alkynylsilver (Schemes 2 and 3). Here, alkynyl silver **2** (1.5 equiv) and 2,2-bipyridyl (2 equiv) were mixed in a 100 mL round bottom flask, and both were dissolved in DCM/ H_2O in a 3:1 ratio. The resulting solution was allowed to stir continuously for about 5–10 min. After 10 min, potassium persulfate (3 equiv) and sulfoximine **1** (100 mg) were added to the abovementioned reaction mixture. This solution was then kept at room temperature for 4–8 h with thorough stirring. The development of the reaction was examined with the help of thin-layer chromatography. As soon as the reaction was completed, the workup was done in the separating funnel. To the reaction mixture was added a dilute solution of

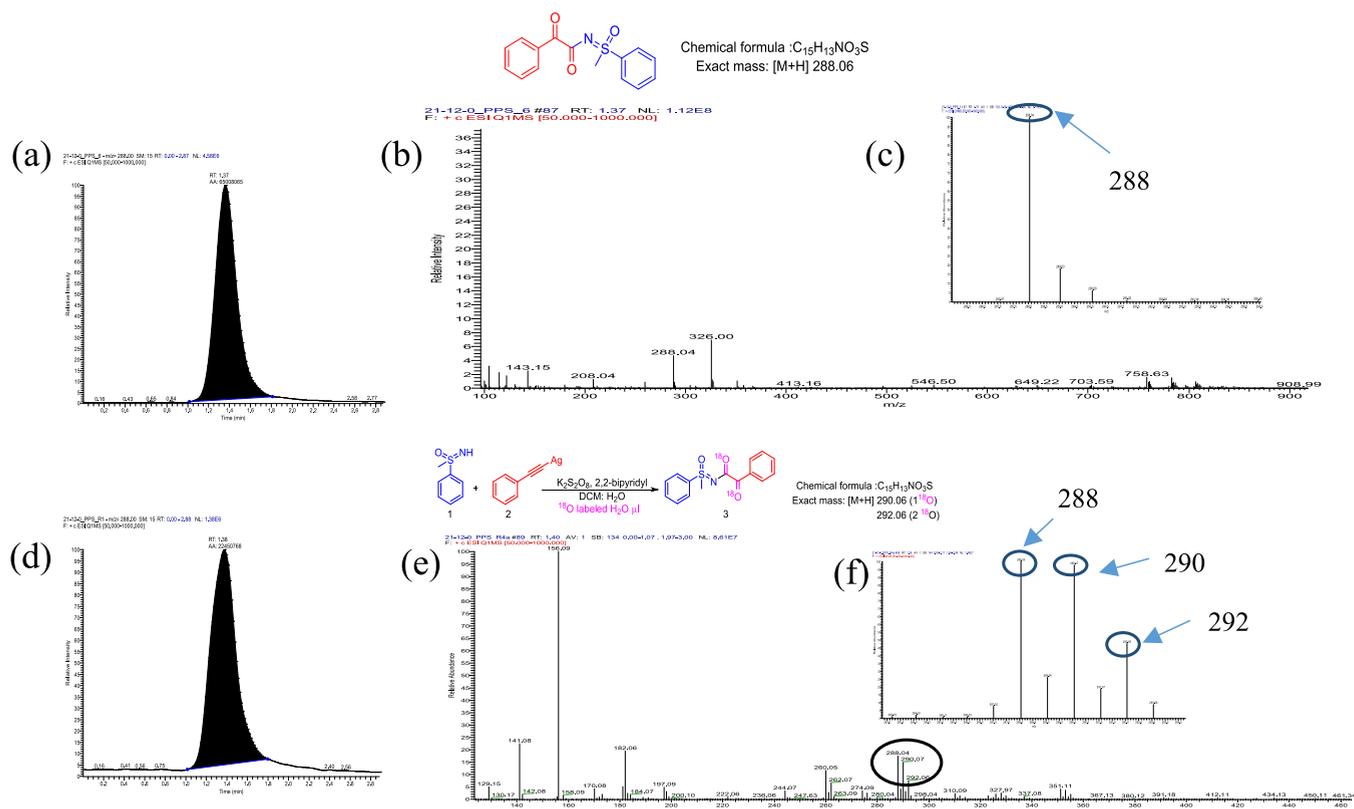


Figure 2. Labeling experiment (a) LC–MS chromatogram of the reaction mixture with DCM and normal water; (b) MS of the reaction mixture for **3a**; (c) expanded MS of **3a**; (d) LC–MS chromatogram of the reaction mixture with DCM and ^{18}O labeled H_2O ; (e) MS of ^{18}O labeled **3a**; (f) expanded MS of ^{18}O labeled **3a**.

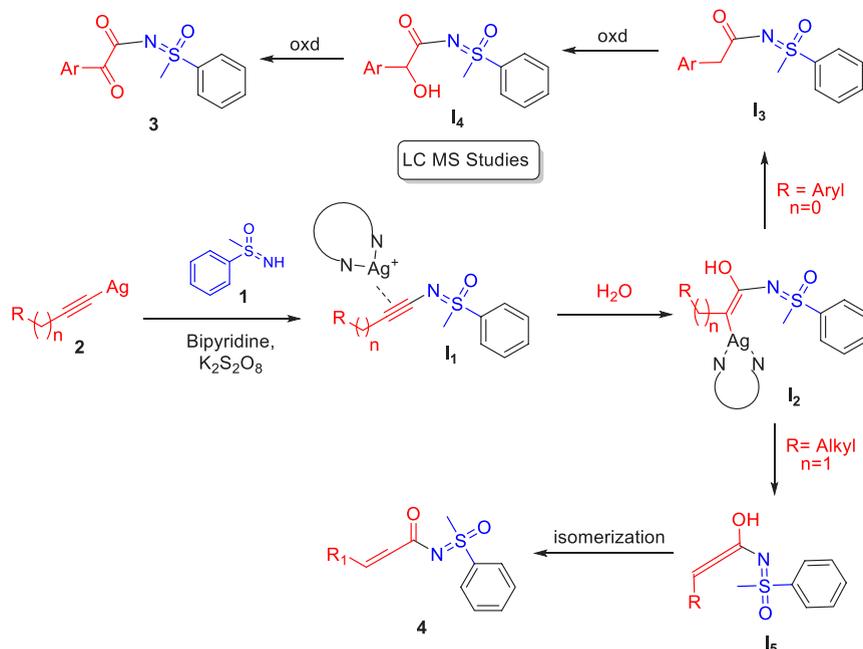


Figure 3. Plausible reaction mechanism for the formation of *N*- α -ketoacyl sulfoximines and *N*- α,β -unsaturated acyl sulfoximines.

hydrochloric acid and extracted with dichloromethane. Sodium sulfate was added to the organic layer so as to absorb water molecules if present. The organic layer was then dried using a rotavapor. The crude material obtained was then purified with the help of column chromatography using ethyl acetate/hexane as eluent to give the purified compounds, **4a–4b** and **5** in good

yields (43–51%). The synthesized compounds were then characterized with the help of 1H NMR, ^{13}C NMR, and HR MS spectra.

General Procedure for the Coupling of Sulfoximines with In-Situ-Generated Phenyl Acetylene Silver (Scheme 4). In this case, phenylacetylene **6** (1.5 equiv),

silver nitrate (0.8 equiv), and 2,2-bipyridyl (2 equiv) were taken in a 50 mL round bottom flask and dissolved in DCM/H₂O in a 3:1 ratio. The resulting solution was kept at room temperature and stirred continuously for 4 h. After this, potassium persulfate (3 equiv) was added to the above-mentioned mixture, and the reaction mixture was allowed to stir thoroughly at room temperature for about 1 h. Finally, sulfoximine **1** (100 mg) was added to the above-mentioned mixture. This final solution was then kept at room temperature for 4–8 h with thorough stirring. The development of the reaction was examined with the help of thin-layer chromatography. As soon as the reaction was completed, the workup was done in the separating funnel. To the reaction mixture was added a dilute solution of hydrochloric acid and extracted with dichloromethane. Sodium sulfate was added to the organic layer so as to absorb water molecules if present. The organic layer was then dried using a rotavapor. The crude material obtained was then purified with the help of column chromatography by using ethyl acetate/hexane as eluent to give the purified compound *N*- α -ketoacetyl sulfoximine **3a** in a yield of 47%. The synthesized compound was then characterized with the help of ¹H NMR, ¹³C NMR, and HR MS spectra.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acsomega.2c05894>.

General procedures, details of controlled experiments, isotope labeling experiments, LC–MS experiments, and spectral data (NMR and mass spectra) of all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Parvinder Pal Singh – Natural Product & Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; orcid.org/0000-0001-8824-7945; Email: ppsingh@iiim.res.in

Authors

Ria Gupta – Natural Product & Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

Riyaz Ahmed – Natural Product & Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

Zaheen Akhter – Natural Product & Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

Mukesh Kumar – Natural Product & Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; Academy of Scientific and Innovative Research (AcSIR), Ghaziabad 201002, India

Complete contact information is available at:

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Notes

The authors declare no competing financial interest.

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