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Sustainability Spotlight statement

This study presents a sustainable, metal-free, and oxidant-free photochemical strategy for synthesizing iodo-vinyl-thiocyanates and iodo-vinyl-selenocyanates under mild, visible-light irradiation condition. The dual role of iodine as both a reactant and a photocatalyst enables the in-situ generation of iodine radicals and singlet oxygen ($^1O_2$) without the need for external catalysts or hazardous oxidants. This approach minimizes chemical waste, reduces energy consumption, and aligns with the principles of green chemistry by promoting safer reaction conditions and resource efficiency. Evaluation through Green Chemistry Metrics (E-factor) and Eco-Scale further validates the environmental compatibility of this method. The resulting iodo-thiocyanates/-selenocyanates also offer valuable synthetic versatility, serving as useful intermediates for diverse organic transformations and functional group elaborations.

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Singlet Oxygen Driven Stereoselective Iodothiocyanation and Iodoselenocyanation of Alkynes

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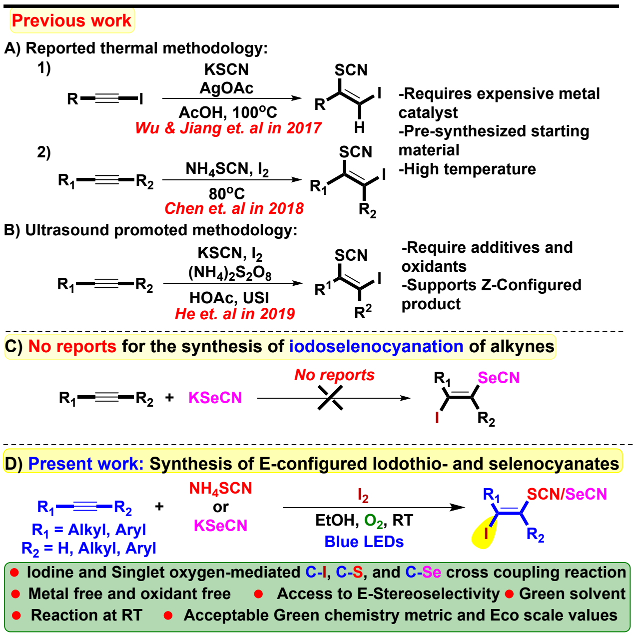
We present here a low-energy visible light-induced metal-free C-I, C-S, and C-Se cross coupling reactions for the formation of iodo-vinyl-thiocyanates (IVTs) and iodo-vinyl-selenocyanates (IVSs) using alkynes, iodine and ammonium thiocyanate (NH_4SCN)/ potassium selenocyanate (KSeCN) in the presence of oxygen at room temperature. Herein, iodine, molecular oxygen, and NH_4SCN on photo-irradiation synergistically generate iodine radical, singlet oxygen ($^1O_2$), and $^{\bullet}SCN$ /$^{\bullet}SeCN$ radicals and selectively react with alkyne to form stereoselective E-configured IVTs and IVSs. Significantly, iodine plays an important role as I_2 acts as a photoactive reactant, and upon photo-irradiation, generate iodine radicals via homolytic cleavage of I_2, singlet oxygen via energy transfer (ET), and thiocyanate/selenocyanate radicals via single electron transfer (SET) process. Moreover, Green chemistry metrics and Eco-scale evaluations highlight that the current stereoselective oxidative C-I, C-S, and C-Se coupling protocol aligns well with sustainable principles, establishing it as a viable and environmentally benign approach to organic synthesis.

1. Introduction

Adopting visible light to drive environmentally benign and cost-effective transformations while unlocking unique synthetic potential poses a substantial challenge in current synthetic strategies. In general, photoredox catalysis depends on the propensity of metal complexes and organic dyes to generate reactive radicals via single electron processes under photoirradiation[1-4]. Nevertheless, in certain instances, reactants simultaneously function as photocatalysts, and this dual role holds profound implications in green chemistry, serving as a cornerstone of sustainable chemistry and advanced organic synthesis[5-7]. Thus, a low-energy visible-light-induced metal-free and photocatalyst-free process for cross-coupling reactions involving heteroatoms or halogens would be an exceptional discovery in synthetic organic chemistry.



Scheme 1. Comparison of literature processes and the current photochemical process.

Organic thiocyanates and selenocyanates are highly significant due to their diverse applications in organic synthetic transformations, pharmaceuticals, and environmental chemistry[8-12]. Thiocyanates are widely used in catalysis[13], anti-inflammatory, antimicrobial treatments[14], and drug synthesis[15], while selenocyanates are currently gaining interest for their strong antioxidant[16], antileishmanial[17], anticancer[18], and electronic properties[19]. Their unique reactivity and biological roles[20,21] make them valuable compounds for ongoing research and practical use.

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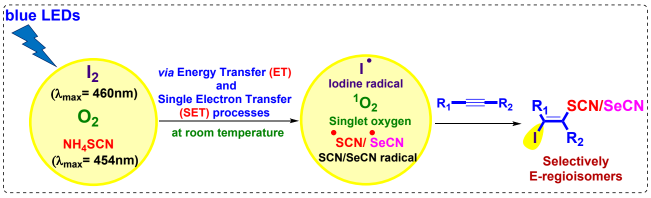
Sulfur- and selenium-containing organic compounds are indispensable across diverse fields, from biochemistry and medicine to materials and environmental science[22,23]. In particular, iodothiocyanates and iodoselenocyanates are important scaffolds in organic synthesis, incorporating more than one versatile functionality. Their structural significance establishes them as structural intermediates or precursors for synthesizing a wide range of multi-substituted alkenes, valuable heterocycles[24,25], and other complex molecules. [26] Importantly, E-configured iodo-vinyl-thiocyanates or iodo-vinyl-selenocyanates exhibit enhanced reactivity due to the presence of vinylic proton-coupled with an electrophilic iodine center, facilitating diverse organic transformation including cross-coupling reactions and cyclizations[27,28]. Considering their usefulness, there is a necessity to develop a simple and green synthetic protocol (metal-free, oxidant-free, and photocatalyst-free) for the synthesis of iodo-vinyl-thiocyanates (IVTs) and iodo-vinyl-selenocyanates (IVSs).

The literature records include only a limited number of reports on the synthesis of iodo-vinyl-thiocyanates, specifically three, as illustrated in **Scheme 1**. In 2017, Wu and Jiang co-authors[29] proposed a synthetic approach for the preparation of (Z)-iodo vinyl thiocyanates via silver-catalyzed thiocyanation of (iodoethynyl)benzene (**Scheme 1, A. 1**). However, a notable limitation lies in the necessity of pre-synthesizing 1-iodoalkynes from corresponding terminal alkynes through a cumbersome two-step procedure. [30] Later, Chen et al.[31] attempted to promote the synthesis of β-iodo vinylthiocyanates from alkynes at 80 ℃ (**Scheme 1, A. 2**). Subsequently, He et al.[32] reported a novel ultrasound-assisted β-iodo vinylthiocyanation reaction from alkynes, iodine, potassium thiocyanate and ammonium persulfate $(NH_4)_2S_2O_8$) (a strong oxidant) (**Scheme 1, B**). Moreover, it is important to note that no report has been reported in the literature on the synthesis of iodo-vinyl-selenocyanates (**Scheme 1, C**). Despite all these excellent advances, these protocols still have some limitations, such as: a) use of expensive metal catalyst; b) harsh reaction conditions; c) requiring pre-synthesized starting material (iodoalkynes); d) use of non-disposable and excess amounts of strong oxidants; d) require specialized equipment; and e) generation of huge amounts of chemical wastes (leading to higher E-factors), lowers the reaction mass efficiency (RME) and atom efficiency. Thus, these methods are economically infeasible and add deleterious effects on the environment. To overcome the limitations associated with thermal reactions; visible light is a green and sustainable mode of activation for various chemical transformations[33,34].

In this regard, no study has ever documented the visible-light-driven stereoselective synthesis of iodothiocyanation of alkynes. Also, to mitigate chemical waste generation and environmental pollution, there is a need to develop a green photochemical and sustainable process that minimizes the formation of side products and chemical wastes. To this context, our group has reported various green methods for a variety of C-C, C-N, C-S, C-O oxidative cross-coupling, and C-H annulation reactions[35,53] by using visible light and a simple, inexpensive, earth-abundant CuCl as a catalyst. Herein, we report metal-free and photocatalyst-free oxidative C-I, C-S, and C-Se cross-coupling reactions for the formation of iodo-vinyl-thiocyanates (IVTs) and iodo-vinyl-selenocyanates (IVSs) using alkynes, iodine and ammonium thiocyanate (NH_4SCN)/ potassium selenocyanate (KSeCN) in presence of oxygen under low energy visible light irradiation at room temperature (**Scheme 1, D**). Here, iodine plays an important role as it acts as a photochemical reagent as well as a reactant. Iodine on photoirradiation generates iodine radicals via homolytic cleavage of I_2, singlet oxygen via energy transfer (ET), and thiocyanate/selenocyanate radicals via single electron transfer (SET) process (**Scheme 2**).

Besides, molecular oxygen on photoirradiation generates singlet oxygen which ultimately generates SCN/SeCN radicals in the SET process and NH_4SCN generates $^1O_2$ via the ET process. Further, these generated radicals selectively react with alkyne and form stereoselectively E-configured iodo-vinyl-thiocyanates (IVTs) and iodo-vinyl-selenocyanates (IVSs) (**Scheme 2**).



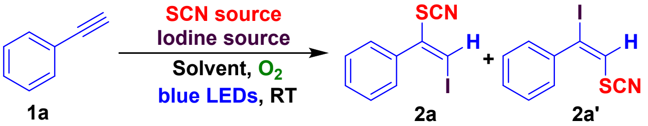
Scheme 2. Iodine (I_2) and singlet oxygen $(^1O_2)$-mediated C-I, C-S, and C-Se cross-coupling reaction.

The overall significance of this green protocol includes a) a green and simple protocol for the oxidative C-I, C-S, and C-Se cross-coupling reaction for the formation of E-configured IVTs and IVSs at RT; b) the versatile role of iodine as a photochemical reagent and a reactant; c) first to report the synthetic protocol for iodo-vinyl-selenocyanates; d) green chemistry metrics and Eco scale evaluations indicate product formation is accompanied with a minimal amount of wastes (low E-factor) and with high reaction mass efficiency (RME).

2. Results and Discussion

The optimization of reaction parameters for the photooxidative iodothiocyanation reaction of alkynes is outlined in **Table 1**. Herein, phenylacetylene, ammonium thiocyanate (SCN source), and molecular iodine (I source) were selected as the model substrates. First, the reaction of phenylacetylene with ammonium thiocyanate (SCN source) and molecular iodine (I source) in presence of oxygen (O_2) in acetonitrile (ACN) solvent under visible light irradiation for 11 h formed inseparable regioisomers, (E)-(2-iodo-1-thiocyanatovinyl)benzene (**2a**) and (E)-(1-iodo-2-thiocyanatovinyl)benzene (**2a'**) in 73% yield with a ratio of 5.3:1 (entry 1, Table 1). To investigate the iodine source, potassium iodide (KI) and sodium iodide (NaI) were used in the reaction (instead of I_2) (entries 2 and 3) and obtained the desired products in trace yields. Next, using alternative SCN sources, such as NaSCN (sodium thiocyanate) and KSCN (potassium thiocyanate) formed the desired products **2a/2a'** in low yields of 47% and 52%, respectively (entries 4 and 5). Subsequently, employing NH_4SCN as the thiocyanate source and iodine as an iodine source, a comprehensive solvent screening was conducted with solvents such as dichloromethane (DCM), ethanol (EtOH), dimethylformamide (DMF), tetrahydrofuran (THF) and water (H_2O) (entries 6-10), among which ethanol formed the desired products (**2a/2a'**) in 81% yield and with good selectivity ratio of **2a:2a'**=5.3:1.

Table 1. Optimization of reaction conditions[a]

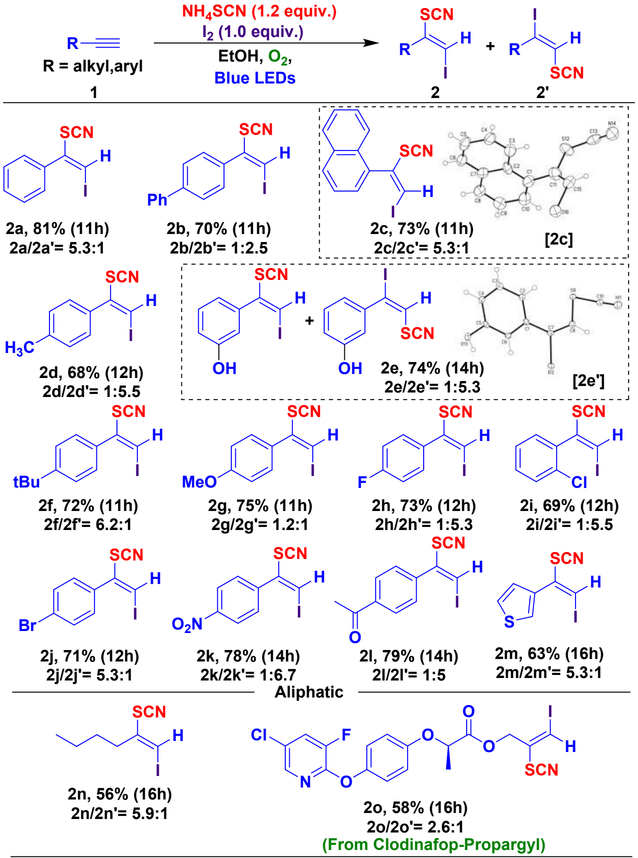


Entry	SCN Source	Iodine Source	Solvent	Yield (%)[b]	(2a:2a')[c]
1	NH_4SCN	I_2	CH_3CN	73	5.3:1
2	NH_4SCN	KI	CH_3CN	trace	-
3	NH_4SCN	NaI	CH_3CN	trace	-
4	NaSCN	I_2	CH_3CN	47	5:1
5	KSCN	I_2	CH_3CN	52	2:1
6	NH_4SCN	I_2	DCM	26	5.3:1
7	**NH_4SCN**	**I_2**	**EtOH**	**81**	**5.3:1**
8	NH_4SCN	I_2	DMF	27	5.3:1
9	NH_4SCN	I_2	THF	39	5:3
10	NH_4SCN	I_2	H_2O	22	5.3:1
11[d]	NH_4SCN	I_2	EtOH	trace	-
12[e]	NH_4SCN	I_2	EtOH	46	3.4:1
13[f]	NH_4SCN	I_2	EtOH	68	5.3:1
14[g]	NH_4SCN	I_2	EtOH	66	5.3:1
15[h]	NH_4SCN	I_2	EtOH	52	5.3:1

[a] Unless otherwise mentioned, the reaction condition is as follows; 1a (0.5 mmol), 1.2 equiv of SCN source, 1.0 equiv. of Iodine source, solvent (3 mL). The mixture was irradiated with Blue LEDs (power density: 150 mW/cm² at 460 nm) for 11 h in an oxygen atmosphere (1 atm). [b] Yield of the isolated product. [c] Ratio of **2a/2a'** was estimated by the integral area of vinyl hydrogen atom of the product. [d] Reaction was conducted in the dark at RT. [e] In N_2 atmosphere. [f] In Air. [g] used 0.6 equiv of Iodine source. [h] used 0.5 equiv of Iodine source. n.r= No reaction.

Besides, ethanol solvent is recognized as a green and sustainable solvent. Further, the reaction in the dark (entry 11) formed the products in only a trace amount, and to our surprise, the reaction in the nitrogen atmosphere (entry 12) also obtained the products **2a/2a'** in 46% of yield. Thus, it indicates that the reaction proceeds through two different pathways (or mechanisms). Later, when the reaction was conducted in an air atmosphere, products **2a/2a'** were obtained in a moderate yield of 68% (entry 13). Moreover, products **2a/2a'** were obtained with a moderate yield of 66% and 52% when the reaction was conducted with 0.6 and 0.5 equivalent of iodine (instead of 1.0 equiv.), respectively. Thus, these optimization reactions show that NH_4SCN, I_2, and visible light are vital components for the formation of E-configured iodo-vinyl-thiocyanate (IVTs) products in a good yield.

Having the optimal reaction conditions in hand, we directed our efforts toward examining the substrate scope of terminal alkynes for this oxidative difunctionalization (iodo and thiocyanate) reaction (**Scheme 3**). First, electron-neutral terminal alkynes and those bearing more than one aromatic ring (such as 4-ethynyl-1,1'-biphenyl and 2-ethynylnaphthalene) formed the respective E-configured iodothiocyanates in good yields (**2a**-**2c**). In the case of the substrate 1b, 4-ethynyl-1,1'-biphenyl (**2b'**) (thiocyanate at terminal position) formed as a major product. Next, the terminal alkynes with electron-donating substituents (such as –Me, –OH, and –OMe) worked efficiently and formed the terminal substituted thiocyanate products **2d'**, **2e'**, **2g'** as the major products in good to moderate yields, while distinctly 1-(tert-butyl)-4-ethynylbenzene selectively formed (E)-1-(tert-butyl)-4-(2-iodo-1-thiocyanatovinyl)benzene (**2f**) as the major product. Further, the halogen (-Br, -Cl, and -F) substituted aromatic terminal alkynes regardless of their positions on the phenyl rings (-ortho, -meta, -para) all were well tolerated by this green oxidative iodothiocyanation reaction and formed E-configured iodo thiocyanatovinyl benzene **2h**-**2j** in an average yield of 69-73%. Additionally, the terminal alkynes bearing electron-withdrawing groups, such as $-NO_2$, and $-COCH_3$ formed the vinyl-thiocyanates as the major products (**2k'**, **2l'**) in the good yields.



Scheme 3. Substrate scope of terminal alkynes for iodothiocyanation.

Later, heteroaryl terminal acetylene, 3-ethynylthiophene (**1m**) formed (E)-3-(2-iodo-1-thiocyanatovinyl)thiophene (**2m**) in a moderate yield of 63%. Whereas, ethynylpyridine did not undergo an oxidative iodothiocyanation reaction. This observation is consistent with our previous findings that the ethynylpyridines are inert for the photo-oxidation reaction. We practically observed that the pyridine-containing alkynes or internal alkynes could not undergo photo-oxidation reaction[44,52,54-57]. Besides, aliphatic terminal alkyne, such as 1-hexyne formed the desired E-configured iodothiocyanate products **2n/2n'** in an average yield of 56%. Importantly, clodinafop-propargyl, a widely used herbicide was well tolerated by this green photo oxidative difunctionalization reaction and formed (E)-3-iodo-2-thiocyanatoallyl (R)-2-(4-((5-chloro-3-

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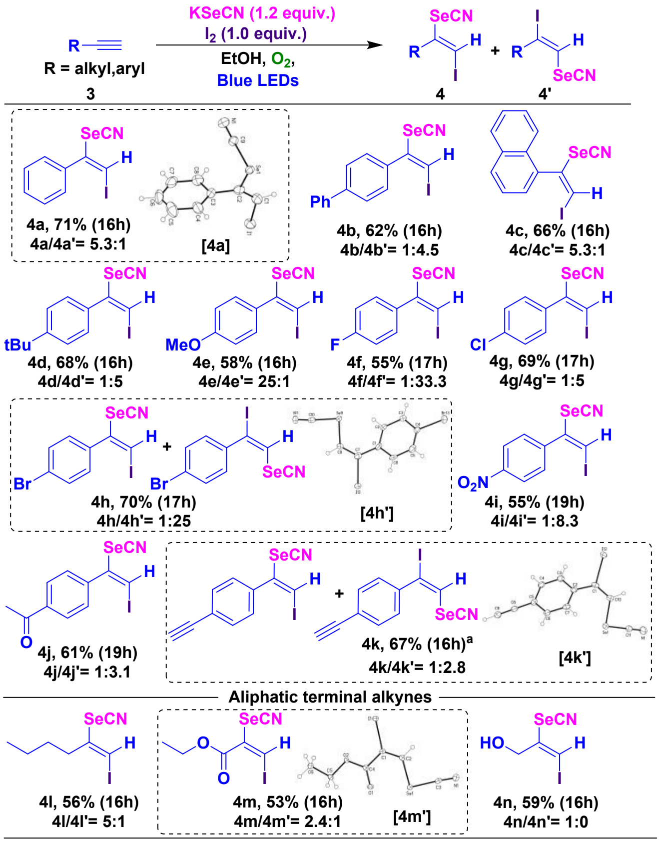
fluoropyridin-2-yl)oxy)phenoxy)propanoate (**2o**) as major product. The structures of products **2c** (CCDC 2426651) and **2e'** (CCDC 2415478) were confirmed by single-crystal X-ray diffraction[58].

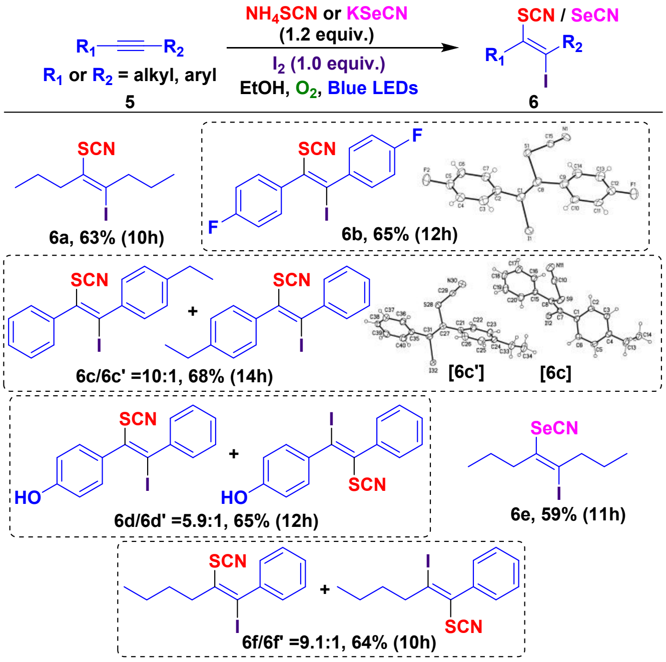
To our delight, we discovered that the current metal-free, oxidative iodothiocyanation reaction conditions are effectively applicable to iodoselenocyanation of alkynes. Wherein, only potassium selenocyanate (KSeCN) was used as a SeCN source as other SeCN salts, such as sodium selenocyanate (NaSeCN) and ammonium selenocyanate (NH_4SeCN) were not commercially available. The reaction conditions for the iodoselenocyanation of alkynes are as follows: 0.5 mmol alkyne (1), Iodine (1.0 equiv.), and KSeCN (1.2 equiv.) in 3 mL of ethanol solvent. The reaction mixture was irradiated with Blue LEDs (power density: 150 mW/cm² at 460 nm) for 11 h in an oxygen atmosphere (1 atm). Using standard reaction conditions, we have explored the substrate scope of terminal alkynes presented in **Scheme 4**. Terminal alkynes bearing electron-neutral, electron-donating, halogen, and electron-withdrawing functional groups obtained iodoselenocyanate products **4/4'** as an inseparable mixture of regio-isomers in good yield (**4a-4m**). The 4-ethynyl-1,1'-biphenyl and 1-(tert-butyl)-4-ethynylbenzene formed **4b'** and **4d'**, respectively (SeCN at terminal position) as a major product, whereas, -OMe substituted terminal alkyne **3e** produced (E)-1-(2-iodo-1-selenocyanatovinyl)-4-methoxybenzene (**4e**) as the major product.



Scheme 4. Substrate scope of terminal alkynes for iodoselenocyanation. [a]Used 2.0 equivalent of iodine and 2.4 equivalent of KSeCN.

Subsequently, alkynes bearing halogen substituents and electron-withdrawing functional groups predominantly formed the iodoselenocyanate-functionalized products **4f', 4g', 4h', 4i'**, and **4j'** as the major product. Besides, when the reaction of the diethynyl benzene substrate (**3k**) was performed with 2.0 equivalent of iodine and 2.4 equivalent of KSeCN, only mono-ethynyl iodoselenocyanate-functionalized products **4k/4k'** were obtained in 67% yield with (E)-1-ethynyl-4-(1-iodo-2-selenocyanatovinyl)benzene (**4k'**) as a major product and we did not observe di-ethynyl iodoselenocyanate-functionalized products. Moreover, the present oxidative photochemical protocol also worked well with aliphatic terminal alkynes, such as 1-hexyne, ethyl propiolate, prop-2-yn-1-ol, and formed the corresponding iodoselenocyanate products **4l–4n** with high stereoselectivity. The structures of products **4a** (CCDC 2415348), **4h'** (CCDC 2415349), **4k'** (CCDC 2415484), and **4m'** (CCDC 2415490) were confirmed by single-crystal X-ray diffraction[58].

Next, we investigated the substrate scope of symmetrical and unsymmetrical internal alkynes for iodothiocyanation and Iodoselenocyanation reactions (**Scheme 5**). The symmetrical internal alkynes such as oct-4-yne, 1,2-bis(4-fluorophenyl)ethyne) worked well under standard reaction conditions and obtained (E)-4-iodo-5-thiocyanatooct-4-ene (**6a**) and (E)-4,4'-(1-iodo-2-thiocyanatoethene-1,2-diyl)bis (fluorobenzene) (**6b**) in good yield, respectively. The unsymmetrical internal alkynes 1-ethyl-4-(phenylethynyl) benzene **5c** and 4-(phenylethynyl)phenol 5d formed products **6c/6c'** and **6d/6d'** as inseparable regisomers in good yield, respectively.



Scheme 5. Substrate scope of terminal alkynes for internal alkynes.

Similarly, the aliphatic internal alkyne such as oct-4-yne readily undergoes photochemical oxidative iodoselenocyanation reaction and forms (E)-4-iodo-5-selenocyanatooct-4-ene (**6e**) in 59% yield. Unfortunately, diaryl alkynes did not undergo the

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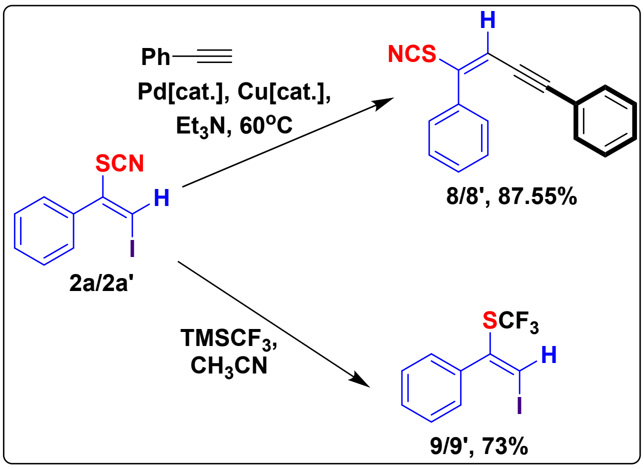
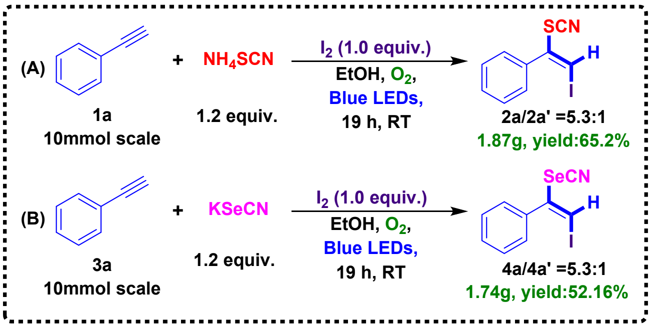
current photochemical oxidative iodoselenocyanation reaction. The reason for these unsuccessful substrates is not clear. Moreover, alky aryl internal alkyne such as hex-1-yn-1-ylbenzene (**5f**) readily formed products **6f/6f'** in 64% yield. The structures of **6b** (CCDC 2415489), and **6c**, **6c'** (CCDC 2415491) were confirmed by single-crystal X-ray diffraction[58].

To demonstrate the utility of these E-configured organic iodo-vinyl-thiocyanates (IVTs) products, we have performed some synthetic modifications reactions of products **2a/2a'**. The synthetic modifications reactions of products **2a/2a'** are presented in **Scheme 6**. Given that iodine substituents serve as highly effective handles for palladium-catalyzed cross-coupling reactions, we carried out the Sonogashira cross-coupling reaction of (E)-(2-iodo-1-thiocyanatovinyl)benzene (**2a/2a'**) with phenylacetylene and afforded the product(E)-(1-thiocyanatobut-1-en-3-yne-1,4-diyl)dibenzene (**7/7'**) in 87% yield. Next, the thiocyanate functionality of (E)-(2-iodo-1-thiocyanatovinyl)benzene (**2a/2a'**) readily undergoes trifluoromethylation, leading to the formation of (E)-(2-iodo-1-phenylvinyl)(trifluoromethyl)sulfane (**8/8'**). Thus, these facile transformations of iodo-vinyl-thiocyanate products (bearing two versatile functionalities, thiocyanate, and iodine) exhibit the significance of current photochemical oxidative C-I and C-S cross-coupling reactions in organic synthetic chemistry.

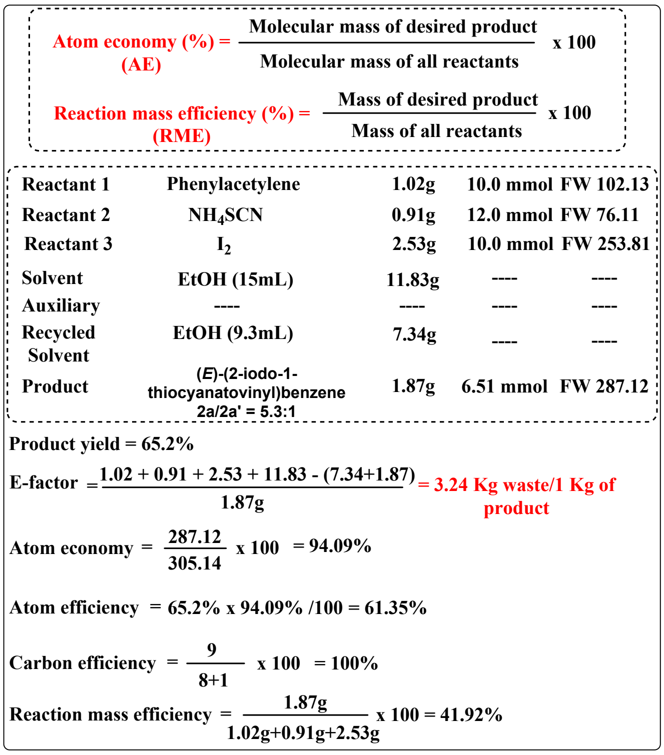


Scheme 6. Late-stage functionalization of **2a/2a'**.



Scheme 7. Gram Scale synthesis of (E)-(2-iodo-1-thiocyanatovinyl) benzene (**2a**), and (E)-(2-iodo-1-selenocyanatovinyl)benzene (**4a**).

Table 2. Evaluation of green chemistry metrics for synthesis of **2a**



$$\text{Atom economy (\%) (AE)} = \frac{\text{Molecular mass of desired product}}{\text{Molecular mass of all reactants}} \text{ x } 100$$

$$\text{Reaction mass efficiency (\%) (RME)} = \frac{\text{Mass of desired product}}{\text{Mass of all reactants}} \text{ x } 100$$

Reactant 1	Phenylacetylene	1.02g	10.0 mmol	FW 102.13
Reactant 2	NH_4SCN	0.91g	12.0 mmol	FW 76.11
Reactant 3	I_2	2.53g	10.0 mmol	FW 253.81
Solvent	EtOH (15mL)	11.83g	----	----
Auxiliary	----	----	----	----
Recycled Solvent	EtOH (9.3mL)	7.34g	----	----
Product	(*E*)-(2-iodo-1-thiocyanatovinyl)benzene 2a/2a' = 5.3:1	1.87g	6.51 mmol	FW 287.12

Product yield = 65.2%

$$\text{E-factor} = \frac{1.02 + 0.91 + 2.53 + 11.83 - (7.34+1.87)}{1.87\text{g}} = 3.24 \text{ Kg waste/1 Kg of product}$$

$$\text{Atom economy} = \frac{287.12}{305.14} \text{ x } 100 = 94.09\%$$

$$\text{Atom efficiency} = 65.2\% \text{ x } 94.09\% /100 = 61.35\%$$

$$\text{Carbon efficiency} = \frac{9}{8+1} \text{ x } 100 = 100\%$$

$$\text{Reaction mass efficiency} = \frac{1.87\text{g}}{1.02\text{g}+0.91\text{g}+2.53\text{g}} \text{ x } 100 = 41.92\%$$

Additionally, to check the efficiency of the current stereoselective oxidative difunctionalization reaction, a 10 mmol scale (a gram scale) reaction was performed (**Scheme 7**). The reaction of Phenylacetylene (**1a**) (1.02 g, 10.0 mmol) with ammonium thiocyanate (0.91 g, 12.0 mmol) and molecular iodine (2.53 g, 10 mmol) in the presence of 15 mL ethanol solvent and O_2 (1 atm) under blue LEDs irradiation at room temperature for 19 h formed (E)-(2-iodo-1-thiocyanatovinyl) benzene products (**2a**) in 1.87 g (65.2% yield) along with the regio-isomer (E)-(1-iodo-2-thiocyanatovinyl)benzene (**2a'**). Following similar reaction conditions and using potassium selenocyanate (1.74 g, 12.0 mmol) as the selenocyanate source, we obtained (E)-(2-iodo-1-selenocyanatovinyl) benzene product (**4a**) in 1.74 g (52.16 % yield) together with the regio-isomer **4a'**. Further, we evaluated the green chemistry metrics[50-53] for the current visible-light-driven difunctionalization reaction on a preparative scale for the synthesis of 2a (Table 2) and 4a (detailed evaluations shown in Table S1 in the ESI). Among the various parameters of green chemistry metrics, the E-factor (Environmental Impact Factor) is a crucial parameter of the green chemistry metrics as it denotes the total amount of waste generated in a reaction. The E-factor values for the synthesis of (E)-(2-iodo-1-thiocyanatovinyl) benzene (**2a**) and (E)-(2-iodo-1-selenocyanatovinyl)benzene (**4a**) are 3.24 and 4.61, respectively. Moreover, the literature lacks any reported photochemical approach for synthesizing **2a**, while the literature reported thermal methodologies exclusively form the Z-configured iodo-vinyl-thiocyantes.

Next, we evaluated the Eco-Scale[50-53] value for the synthesis of (E)-(2-iodo-1-thiocyanatovinyl) benzene (**2a**) (Table 3), and (E)-(2-iodo-1-selenocyanatovinyl)benzene (**4a**) (see ESI, Table S2). The EcoScale values for the current green photochemical method for synthesis of 2a and 4a are 64.6 and 58.08 on a scale of 100, respectively. These values indicate that the current oxidative green photochemical method is an acceptable green protocol for the formation of stereoselective iodo-thiocyanation and iodo-selenocyanation products from a safety, economic, and ecological features point of view. In addition, to these numeric evaluations of green chemistry metrics, the current photochemical oxidative C-I, C-S, and C-Se coupling method does not require harsh reaction conditions, metal catalysts, exogenous ligands, external photosensitizers, and additives.

Table 3. Eco-Scale calculation for the synthesis of **2a**.

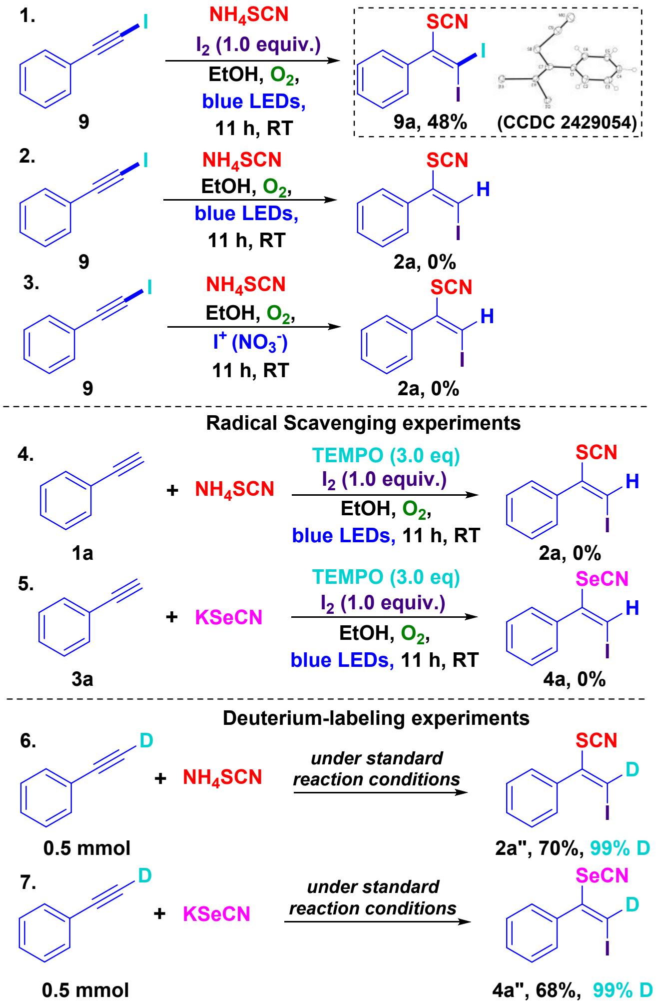
EcoScale = 100 - Sum of individual penalties
Score on EcoScale: >75, Excellent; >50, Acceptable; <50, Inadequate

A) Calculation of penalty points:

Parameters	Penalty points
1. Yield (100-%yield)/2 = (100-65.2)/2 = 17.4	17.4
2. Price of reaction components (To obtain 10 mmol of end product)	
a. Phenylacetylene = 1.02g = \$0.82	
b. NH_4SCN = 0.91g = \$0.07	
c. Iodine = 2.53g = \$0.17	
d. Ethanol = 15mL = \$0.01	
Total price (USD) = \$1.07 Thus, expensive (> \$10 and < \$50)	0
3. Safety Solvent : Ethanol Highly flammable (F)	5
4. Technical Setup Inconventional activation technique (Photochemical activation)	2
5. Temperature and time Room temperature and <24h	1
6. Workup and purification	
Removal of solvent with bp <150°C	0
Classical Chromatography	10
Total Penalty Points	**35.4**

B) EcoScale calculation:
EcoScale = 100- 35.4 = 64.6 (an acceptable synthesis)

Mechanistic studies: A series of control experiments were conducted to help elucidate the mechanistic pathway of the current green photochemical stereoselective oxidative difunctionalization reaction (Scheme 8). First, when the reaction of (iodoethynyl)benzene with ammonium thiocyanate and molecular iodine was conducted under standard reaction conditions for 11 h, the 2,2-diiodo-1-thiocyanatovinyl)benzene product (9a) obtained in 48% yield (Eq.1, Scheme 8). Whereas when the reaction was performed in the absence of molecular iodine, the desired product 2a was not obtained (Eq 2, Scheme 8). This observation indicates that molecular iodine plays a crucial role in the reaction. To examine whether iodonium cation was involved in the formation of 2a, iodonium nitrate was added to the reaction mixture at RT in dark for 11h. However, no formation of **2a** was observed (Eq. 3, Scheme 8), suggesting that iodonium cation was not involved in the formation of **2a**. Next, the products (E)-(2-iodo-1-thiocyanatovinyl) benzene (**2a/2a'**) and (E)-(2-iodo-1-selenocyanatovinyl)benzene (**4a/4a'**) were not obtained when the current oxidative cross-coupling reactions were performed in the presence of a radical scavenger TEMPO ((2,2,6,6-tetramethylpiperidin-1yl)oxyl) under standard reaction conditions, confirming that the current oxidative coupling reactions are likely to proceed via a radical pathway (Eq. 4 and 5, Scheme 8). Moreover, the EPR measurements of the reaction mixture show EPR signals corresponding to iodine radical ($I^•$) and singlet oxygen ($^1O_2$) in the reaction mixture (See Figure S1 in the ESI).



Scheme 8: Mechanistic investigations.

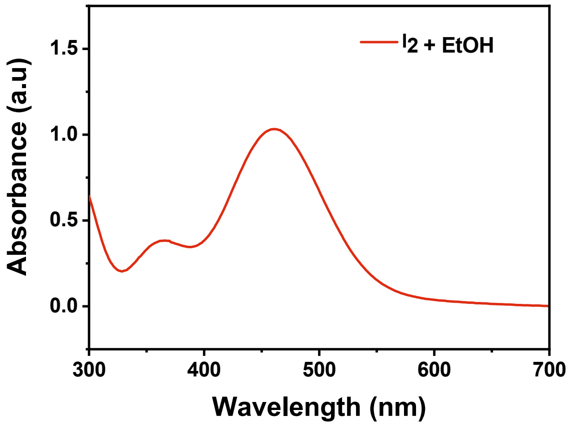


Figure 1. UV-visible absorption spectra of I_2 in Ethanol (EtOH).

Furthermore, we have performed deuterium-labeling experiments for iodothiocyanation and iodoselenocyanation reactions under standard reaction conditions by using phenylacetylene-D1 as a substrate and obtained oxidative difunctionalized compounds **2a"**

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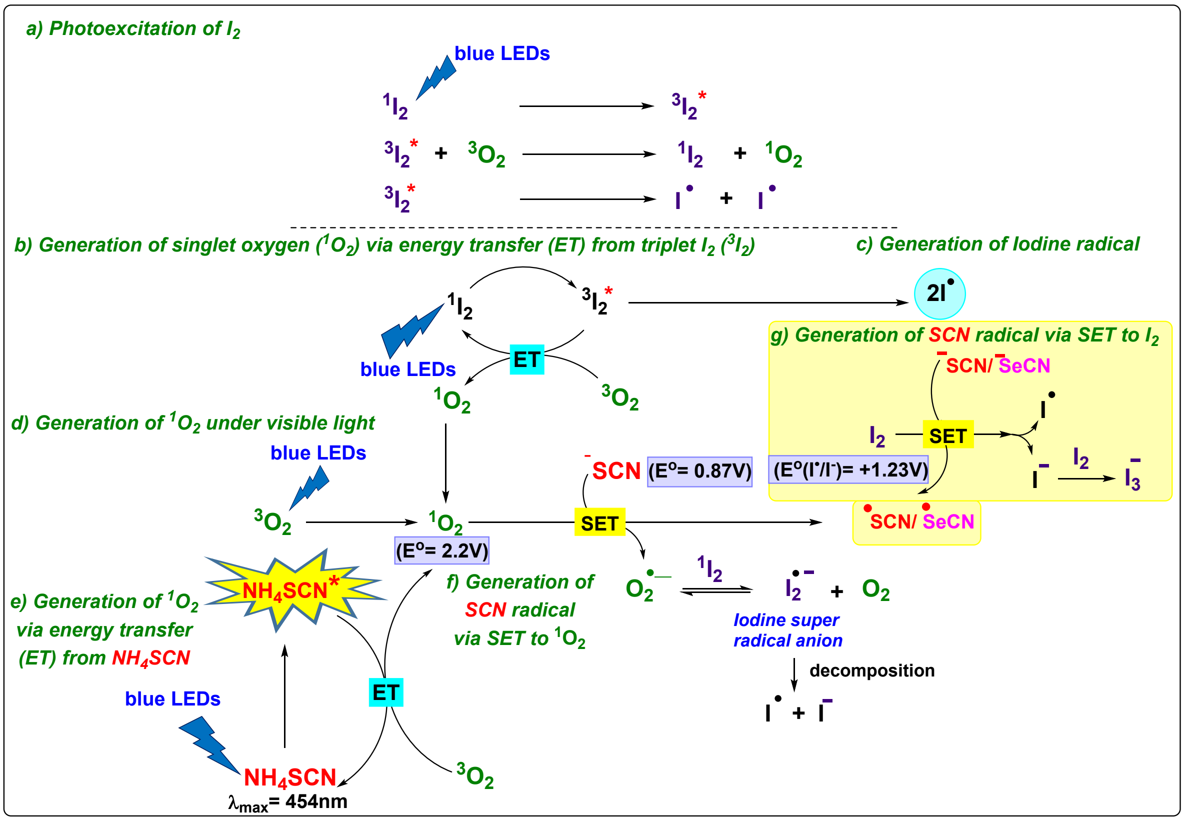
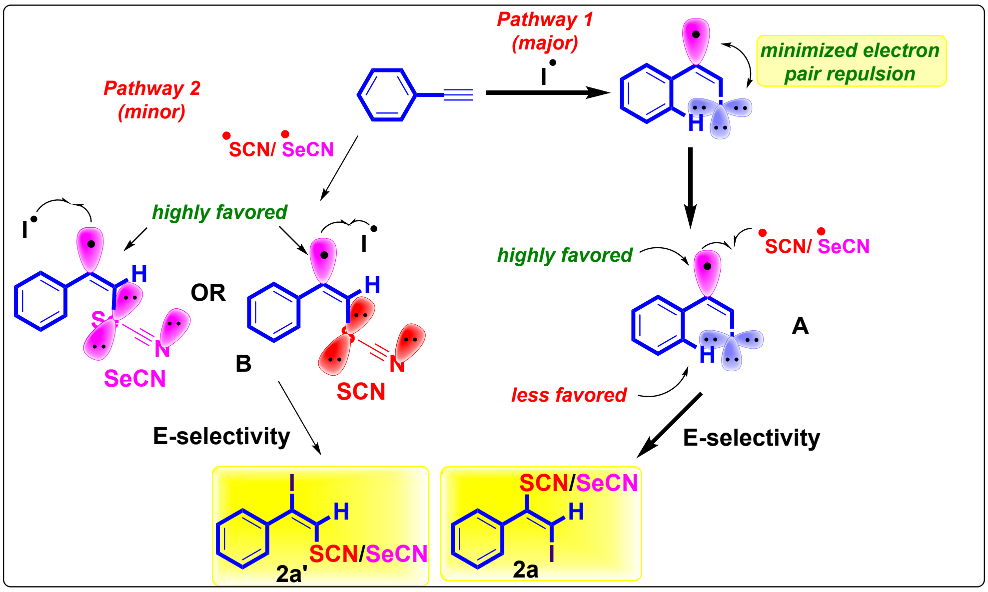
and **4a”** in 70% and 68% yields, respectively, with 99% of deuteration in both the cases. (Eq. 6 and 7, Scheme 8) (see details in the ESI). In addition, we have presented the UV-visible absorption spectra of I_2 in ethanol (EtOH) in Figure 1 and it shows that I_2 has an absorbance at 460 nm.

Mechanism: Based on our previous works[35-54], above presented mechanistic investigations and the UV-visible spectrum, a possible reaction mechanism for the current stereoselective oxidative difunctionalization reaction is proposed in **Scheme 9** and **Scheme 10**. Scheme **9** shows various schematic representations for the



Scheme 9. Proposed mechanism for the generation of singlet oxygen ($^1O_2$), I radical (•I), and SCN/SeCN radical (•SCN/•SeCN) under visible light irradiation at room temperature.



Scheme 10. Proposed mechanism for the formation of selectively E-regioisomer of iodo-vinyl-thiocyanates (IVTs) and iodo-vinyl-selenocyanates (IVSs).

generation of iodine radicals, singlet oxygen ($^1O_2$), and thiocyanate/selenocyanate ($^{\bullet}$SCN/$^{\bullet}$SeCN) radicals through multiple pathways, and scheme **10** presents the reaction mechanism for the reaction of $^{\bullet}$SCN/$^{\bullet}$SeCN and $^{\bullet}$I radicals with phenylacetylene (**1a**) to form selectively E-configured iodothiocyanate/ iodo-selenocyanate products. First, upon photo-irradiation, (I_2, λmax = 460 nm) molecular iodine generates photoexcited triplet state iodine, which on energy transfer (ET) with O_2 forms singlet oxygen ($^1O_2$) and molecular I_2[59,60] (**Scheme 9a and 9b)**. Besides, photoexcited triplet state iodine ($^3I_2^*$) undergoes homolytic cleavage and generates two iodine radicals (**Scheme 9c)**. Next, singlet oxygen ($^1O_2$) is also generated through the direct visible light photo irradiation of molecular oxygen[61] and via the energy transfer (ET) process from NH_4SCN to O_2[54] (**Scheme 9d and 9e)**. Further, this generated singlet oxygen ($^1O_2$) ($E° = +2.2\ V_{NHE}$)[54-57] undergoes a single electron transfer process (SET) by accepting an electron from thiocyanate anion (-SCN) ($E° = +0.87\ V_{NHE}$)[54-57] and forms $^{\bullet}$SCN radical and superoxide ($O_2^{\bullet-}$) simultaneously. This highly reactive superoxide further reacts with I_2 and forms molecular oxygen and iodine super radical anion ($I_2^{\bullet-}$), which further decomposes and forms iodine radical and iodide ion (**Scheme 9f)**. Moreover, thiocyanate (-SCN)/ selenocyanate (-SeCN) ($E° = +0.87\ V_{NHE}$) anion undergoes single electron transfer (SET) process by transferring an electron to I_2 ($E° = +1.23\ V_{NHE}$)[62], which leads to the formation of thiocyanate ($^{\bullet}$SCN)/ selenocyanate ($^{\bullet}$SeCN) radicals, iodine radical and iodide ion. This iodide ion further reacts with I_2 to form I_3^-, which further reacts with singlet oxygen ($^1O_2$) and generates I_2 and iodine radicals (**Scheme 9g)**. These $^{\bullet}$I and $^{\bullet}$SCN readily add to the alkyne and form a carbon-centered radical intermediate **A** (Pathway **1**) and **B** (Pathway **2**), respectively **(Scheme 10)**. The intermediate **A** formation pathway appears to dominate over the reaction intermediate **B** pathway under our standard reaction condition, presumably due to generating a larger quantity of $^{\bullet}$I radical than the $^{\bullet}$SCN/$^{\bullet}$SeCN radicals. The free radical on the intermediate **A** located at the trans-position relative to the terminal iodine substituent due to the minimization of electron pair repulsion energy between the free radical electron and the three lone pair electrons on the terminal iodine substituent, which is similar to the valence shell electron pair repulsion (VSEPR) model for explanation of molecular geometry commonly described in General Chemistry textbooks. Subsequent coupling of the thiocyanate ($^{\bullet}$SCN) or selenocyanate ($^{\bullet}$SeCN) radicals to the free radical site at the trans-position leads to the formation of the desired stereoselective oxidative difunctionalized products. The current photochemical free radical pathway for the formation of stereoselective (E)-configured iodo-thiocyanation/ iodo-selenocyanation of alkynes is different from the literature-reported thermal-driven iodonium cation-mediated formation of (Z)-configured iodovinylthiocyanates.[29,31,32] In this mechanism, molecular iodine serves as a singlet oxygen photosensitizer/ photochemical reagent and one of the reactants of the iodo-thiocyanation and -selenocyanation reaction, displaying its dynamic capability and unveiling extensive synthetic opportunities for advanced organic synthesis.

3. Conclusions

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We report a highly efficient, novel, practical yet simple photo-oxidative metal-free and photocatalyst-free C-I, C-S, and C-Se cross-coupling reactions for the stereoselective synthesis of (E)-configured iodo-vinyl-thiocyanates (IVTs) and iodo-vinyl-selenocyanates (IVSs). Iodine acts as a photoactive reactant and generates iodine radicals via homo-lytic cleavage of I_2, singlet oxygen via energy transfer (ET), and thiocyanate/selenocyanate radicals via single electron transfer (SET) process. Moreover, the stereoselectivity occurs through a unique photochemical driven iodine substituent-mediated trans-position (E)-configured radical-radical coupling process, which is in contrast to the literature reported thermal driven iodonium-cation mediated cis-position (Z)-configured nucleophilic addition process. Overall, 35 examples are presented. Besides, the IVTs and IVSs are also applicable for the synthesis of valuable heterocycles and pharmaceutically active compounds. Besides, green chemistry metric evaluations show that the current photochemical process generates minimum amounts of wastes with an E-factor of 3.24 and 4.61 for the synthesis of IVTs and IVSs, respectively. Further, the Eco Scale value signifies that this protocol is an acceptable green process from the safety, cost-efficient, and eco-conscious points of view.

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Conflicts of interest

There are no conflicts to declare.

Data Availability

Experimental details and characterization data can be found in the ESI.

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Data Availability Statement

Experimental details and characterization data can be found in the ESI.