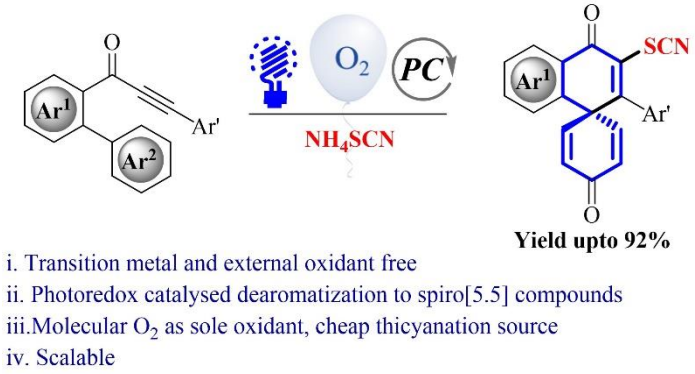
Transition Metal and external oxidant free visible light assisted dearomatization of biaryl yones: Synthesis of thiocyanated spiro [5.5] trienones

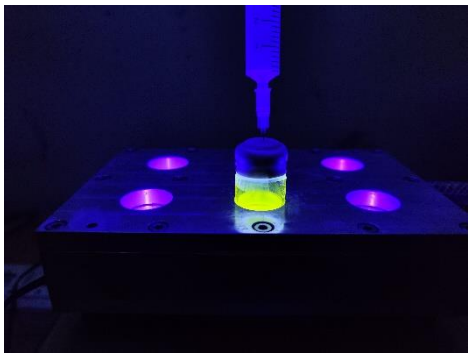
Shantanu Samanta[1] and Dr. Debayan Sarkar[2]

[1]Email: shantanuinemail@gmail.com, National Institute of Technology, Rourkela, India

[2]Email: debayan81orgchem@gmail.com Indian Institute of Technology, Indore, India

A photoredox catalyzed efficient protocol for the direct insertion of -SCN group onto spiro[5.5]trienone *via* dearomative cascade cyclization of biaryl ynone with inexpensive NH_4SCN has been developed employing 4CzIPN as a potent photocatalyst under blue light irradiation without external oxidant. This scalable 6-*exo*-trig cyclization led to the cascade formation of C-C and C-S bonds and incorporate diverse thiocyanated spiro compounds with excellent yield (up to 92%). Additionally, mechanistic investigation elaborated with fluorescence quenching, cyclic voltammetry, and radical scavenging study. Gram scale synthesis and further functionalization of thiocyanated compound highlighted the potential utility of this methodology.





Keywords: Photoredox Catalysis; Dearomatization; Thiocyanation; Biaryl Ynones.

1. N. Bera, S. Samanta, D. Sarkar *J. Org. Chem.* 2021, 86, 23, 16369–16395

2. N. Bera. BS. Lenka, S. Bishi, S. Samanta, D, Sarkar, *J. Org. Chem.* 2022, 87, 15, 9729–9754

Transition-Metal and External Oxidant Free Photo-redox Catalysed Dearomatization of Biaryl Yones: Synthesis of Thiocyanated spiro[5.5]trienones

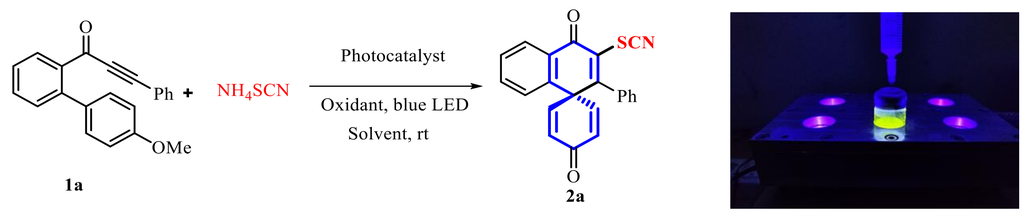
Shantanu Samanta and Dr. Debayan Sarkar, Department of Chemistry, NIT Rourkela*
**Department of Chemistry, IIT Indore*

Introduction

A photoredox catalyzed efficient protocol for the direct insertion of -SCN group onto spiro[5.5]trienone *via* dearomative cascade cyclization of biaryl ynone with inexpensive NH_4SCN has been developed employing 4CzIPN as a potent photocatalyst under blue light irradiation without external oxidant. This scalable 6-*exo*-trig cyclization led to the cascade formation of C-C and C-S bonds and incorporate diverse thiocyanated spiro compounds with excellent yield (up to 92%). Additionally, mechanistic investigation elaborated with fluorescence quenching, cyclic voltammetry, and radical scavenging study. Gram scale synthesis and further functionalization of thiocyanated compound highlighted the potential utility of this methodology.

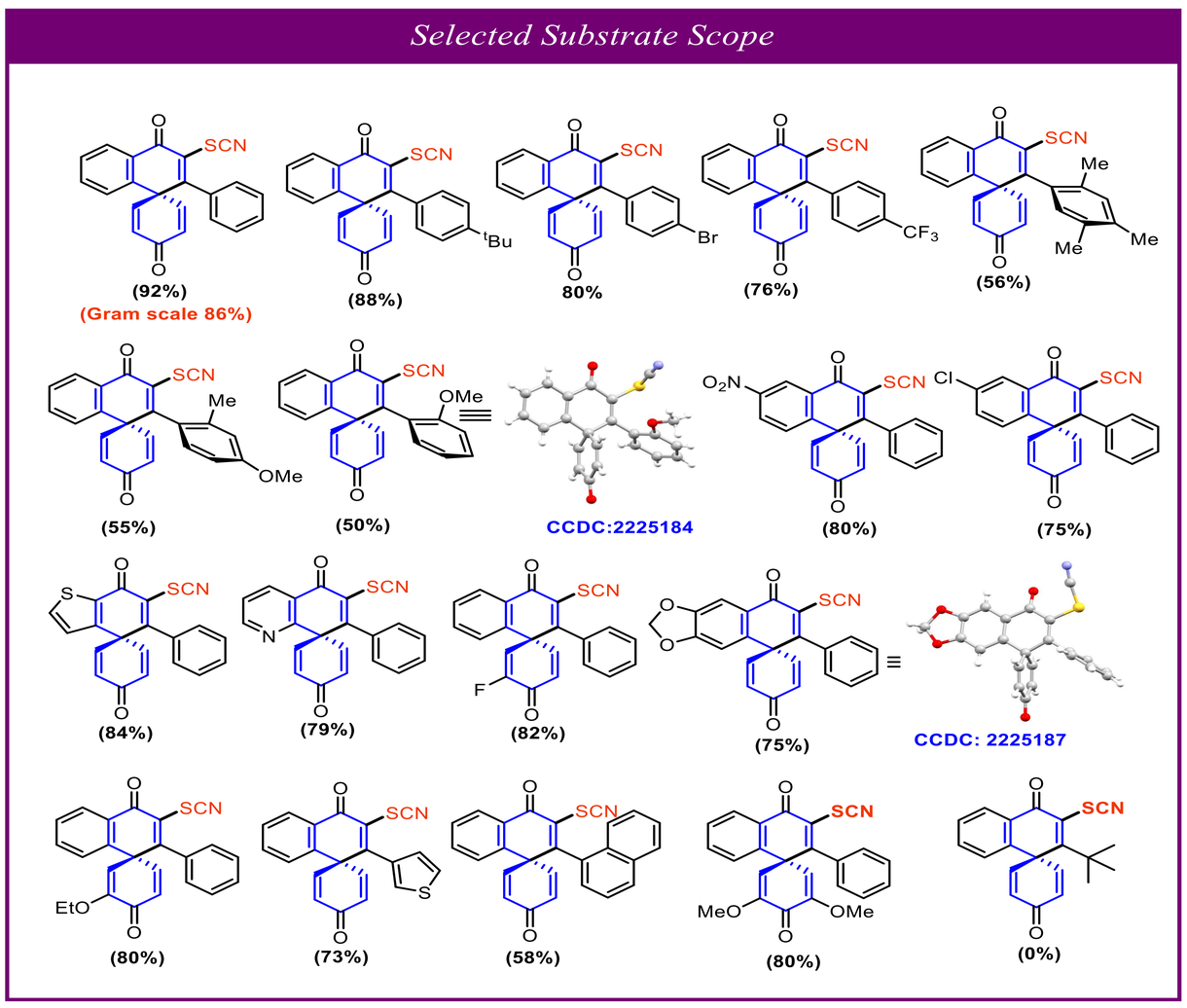
Objectives

- **Transition-Metal and external oxidant free**
- **Photoredox catalyzed dearomatization to spiro[5.5] compounds**
- **Molecular O_2 as sole oxidant, cheap thiocyanation source**
- **Scalable**



Entry	Deviation From Standard Condition	Yield of 2a (%)
1.	None	92
2.	Only MeCN	40
3.	DCE, DCM, 1,4-Dioxane	35,40,75
4.	DMF, DMSO	N.R
5.	Open Air instead of O_2 balloon	20
6.	$K_2S_2O_8$,TBHP, BPO instead of O_2 balloon	70, N.R, N.R
7.	Eosin Y, Eosin B, RFTA instead of 4CzIPN	20,50,65
8.	427 nm blue LED instead of 456 nm blue LED	37
9.	In dark or sunlight	N.R
10.	Without 4CzIPN	Traces

Table 1, Standard Condition: **1a** (0.2 mmol), NH_4SCN (0.6 mmol, 3 equiv), 4CzIPN (5 mol%), O_2 as oxidant, MeCN:H_2O (2.6 ml, 25:1) as a solvent, at room temperature under the irradiation of 10 W blue LED (λ_{max} = 456 nm).



Results/Findings

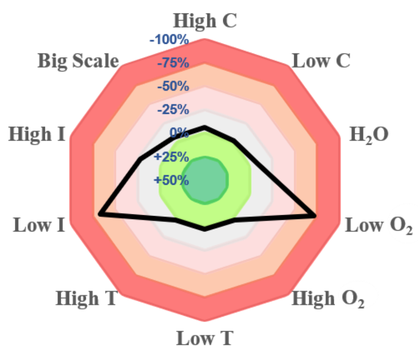


Fig 1: Sensitivity assessment of the reaction presented in radar diagram.

Parameter	Variation		Description	Yield	Deviation
Concentration (*C*)	High *C*	c+ 10%c	2.25 ml Solvent	86%	-6%
	Low *C*	c- 10%c	2.75 ml Solvent	90%	-2%
H_2O level	High H_2O	+ H_2O; VH_2O = 1%Vrxn	26 µL H_2O in 2.6 ml MeCN:H_2O (25:1)	82%	-8%
O_2 level	Low O_2	Open Air	Open Air instead of O_2 balloon	20%	-72%
Temperature (*T*)	High *T*	T+10°*C*	35 °*C*	89%	-3%
	Low *T*	T-10°*C*	25 °*C*	90%	-2%
Light Intensity(*W*)	Low I		0.9*W*	25%	-67%
	High I		32W	70%	-22%
Scale	Big Scale	n.20	4 mmol of **1a**	86%	-6%

Table 2 : Sensitivity assessment of this reaction.

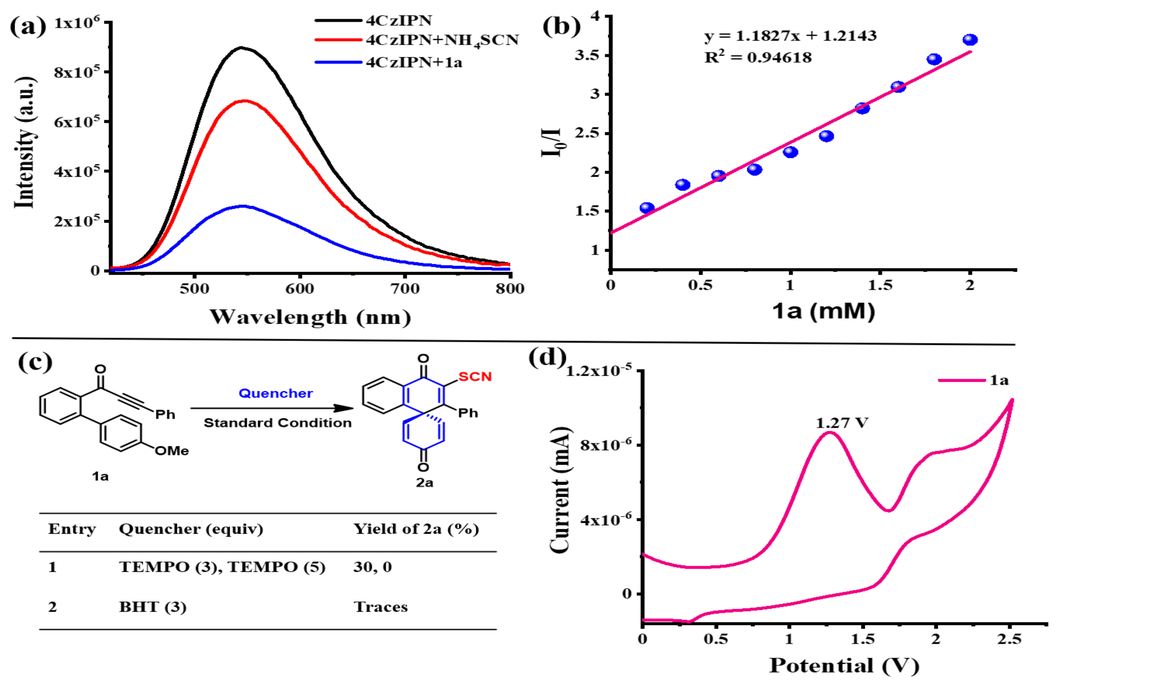
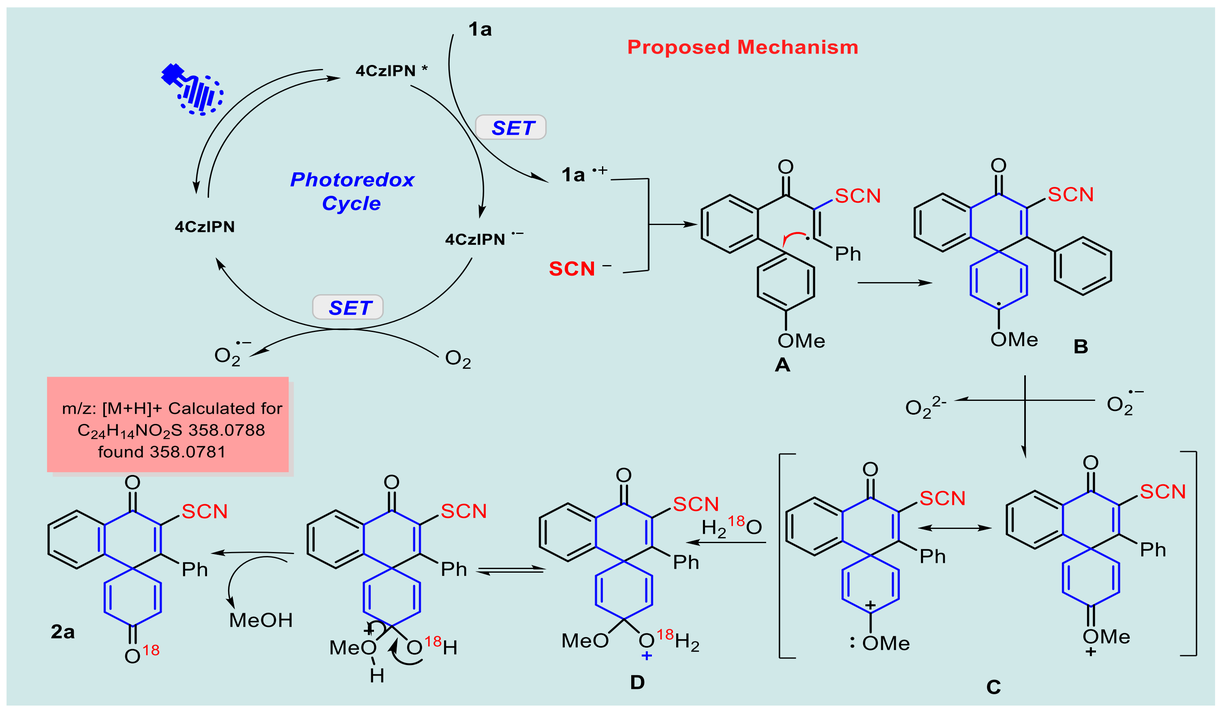
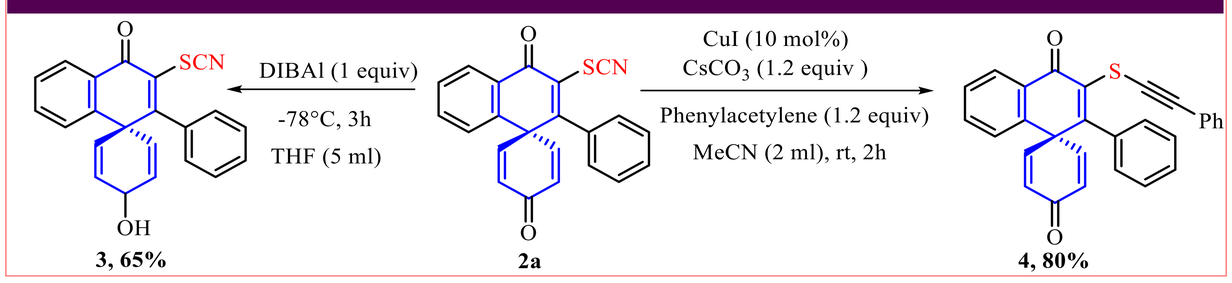


Fig 2: (a) Luminescence quenching: 4×10^{-4} M solution of 4CzIPN is excited at 378 nm in anhydrous MeCN (b) Stern-Volmer plot (c) Radical quenching experiment (d) Cyclic-voltamogram of 1a





Conclusion

Herein, using 4CzIPN as a visible light photocatalyst via radical-initiated 6-*exo*-trig cyclization, we created a practical technique for the synthesis of thiocyanated spiro[5.5]trienones from **1** and NH_4SCN using molecular oxygen as green oxidant. Great advantage of this methodology includes diverse substrate scope, one-pot easy scalability and high efficiency. Importantly, we were able to demonstrate that the formation of the C–C and C–S bonds occurred in a cascade fashion. The spirocyclic motifs generated would be functionalised further to accomplish the synthesis of biologically important motifs.

Bibliography

1. N. Bera, S. Samanta, D. Sarkar *J. Org. Chem.* 2021, 86, 23, 16369–16395
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