Green
Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: V. Rathore and S. KUMAR, *Green Chem.*, 2019, DOI: 10.1039/C9GC00007K.

ROYAL SOCIETY
OF CHEMISTRY

rsc.li/green-chem

View Article Online
DOI: 10.1039/C9GC00007K

Journal Name

ARTICLE

Visible-Light-Induced Metal and Reagent-Free Oxidative Coupling of sp^2 C–H Bond with Organo-Dichalcogenides: Synthesis of 3-Organochalcogenyl Indoles

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Vandana Rathore,[a] and Sangit Kumar*[a]

Here, a unique visible-light-induced method for the organochalcogention of sp^2 C–H bond of indoles and aniline has been presented using diaryl dichalcogenides (S, Se, and Te) and oxygen as an oxidant avoiding photocatalyst, base, catalyst, and reagent in acetone at room temperature. This benign protocol allows to access a wide range of 3-arylselenylindoles, 3-arylthioindoles and even 3-aryltelluroindoles with good to excellent yields. Various functionalities namely, methoxy, and halo either on indoles or aryl dichalcogenide showed amenability to the developed reaction. Further, thiocynation of sp^2 C–H bond of indoles has been accomplished under the visible light induced method. Mechanistic understanding by UV-Visible, EPR spectroscopy, and cyclic voltametry suggest that the light induces electron transfer from electron rich arene to oxygen provide arene radical cation and superoxide radical anion. Subsequently, reaction of radical cation with aryl dichalcogenides provide diaryl chalcogenyl cation which upon removal of proton gave unsymmetrical 3-indolyl aryl chalcogenides.

Introduction

Organochalcogen compounds having C–E (E = S, Se, and Te and collectively referred as chalcogen) bond have great significance in biological, pharmaceutical industry,[1] structural chemistry,[2] material sciences,[3] and in synthetic chemistry acting as versatile reagents in advanced synthesis and catalysis.[4] The biological and medicinal properties of organochalcogens have achieved much interest as molecules consisting of these frameworks show antioxidant, antitumor, antimicrobial, anticancer, and antiviral properties,[1] for example, 3-arylselenylindoles **I** act as an antitumor agent, **II** shows activity to interfere with the tubulin system by acting as a prevailing inhibitor of its polymerization (Figure 1).[5]

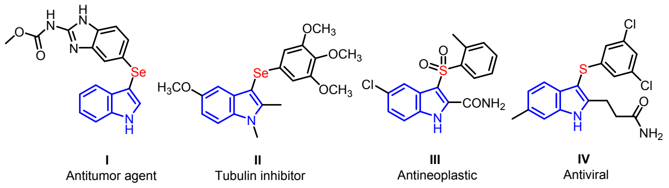


Figure 1. . Chalcogenyl heterocyclic drugs

3-Arylsulfonyl indole **III** exhibits antineoplastic activity, sulfide **IV** displays powerful antiviral activity and used in the treatment of smallpox.[5] Similarly, electron rich aniline containing chalcogenides such as ethoxyquin chalcogenides acts as promising radical chain breaking antioxidants.[6] Due to the significance in various bioactive molecules of organochalcogen moiety and because of the extensive value of biologically active indoles, several protocols have been accomplished for the synthesis of carbon-chalcogen bond.[7-9] The transition metal-free or metal catalyzed construction of C–Se and C–S bonds are well known, however, approaches for the synthesis of unsymmetrical diorgano tellurides are uncommon. Carbon-tellurium bond is weak, labile and tellurium oxidizes easily, consequently, few synthons are available to construct diorgano tellurides. Further, C_3 organotellurenylation of indole has not been presented till date. Earlier synthetic protocols involved coupling of pre-functionalized aryl substrates: aryllithiums, aryl boronic acids, aryl grignard reagents, triarylbismuthanes, aryl diazonium salts and aryl halides with aryl dichalcogenides (ArE–EAr, E = S, Se, Te) for the preparation of various unsymmetrical sulfides, selenides, and tellurides under transition-metal catalyzed or metal-free conditions.[10-11]

Light induced synthesis of diorgano chalocgenides have also been presented by Liu *and* Co-Workers.[12a,b] and Braga Co-Workers.[12c] recently. Nonetheless, success is limited to unsymmetrical diaryl selenides. Synthesis of diaryl sulfides and tellurides could not be established under light irradiation presumably due to strong S–S bond of disulfide and labile Te–Te bond of ditelluride. During our investigation, one example of 3-phenyl indolyl telluride has been synthesized under base promoted reaction.[13]

Earlier our group have developed chalcogenation (S, Se, Te) of indole, activated/electron rich arenes and ligand directed arenes by using stoichiometric amount of oxidant and transition

---

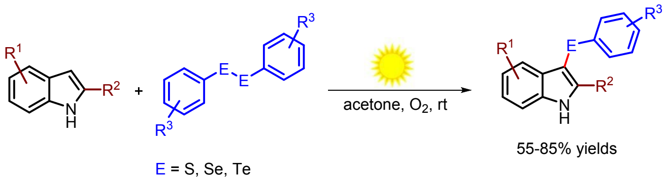
[a] *Department of Chemistry, Indian Institute of Science Education and Research.(IISER) Bhopal, Bhopal By-pass Road, Bhauri, Bhopal Madhya Pradesh India-462066, Email: sangitkumar@iiserb.ac.in*

† Electronic supplementary information (ESI) available: Experimental details, spectroscopic data, NMR (^{1}H, ^{13}C, ^{77}Se), mass spectra, single crystal structure of **2h** (CCDC: 1887962) and UV visible study. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/C9GC00007K

metal catalyzed methodology, respectively.[14] Although different methodologies have been developed for unsymmetrical diphenyl chalcogenides, however, approaches require long reaction time, use of toxic oxidants such as persulfate,[14a] halogen,[14b,15] high boiling solvents namely DMSO[16] and DMF,[17] and stoichiometric amount of additives,[17a,18] harsh reaction conditions,[19] sensitizer and expensive metal photocatalyst.[12] The use of heavy transition metal catalysts is undesirable in the synthesis of bio-relevant molecules and removal of them produces harmful waste which affect the environment and also lower the economy of the reaction. Consequently, mild and sustainable synthetic methods that avoid external oxidants, heavy transition metal catalysts, high boiling solvents, and harsh reaction conditions are highly desirable.

In continuation of our work on organochalcogen chemistry[14] and visible light induced synthesis of heterocycles,[20] herein, we disclose an attractive mild visible light induced strategy for the organo chalcogenylation (S, Se, Te) of indole in oxygen atmosphere by using commercially available substrates in acetone. Further, cyclic voltammetry, UV-visible and electron paramagnetic resonance (EPR) spectroscopic studies have been carried out to establish the mechanism of light induced reaction (Scheme 1).

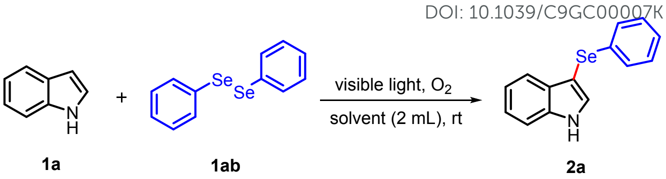


Scheme 1. 3-Chalcogenylation of indoles

Results and Discussion

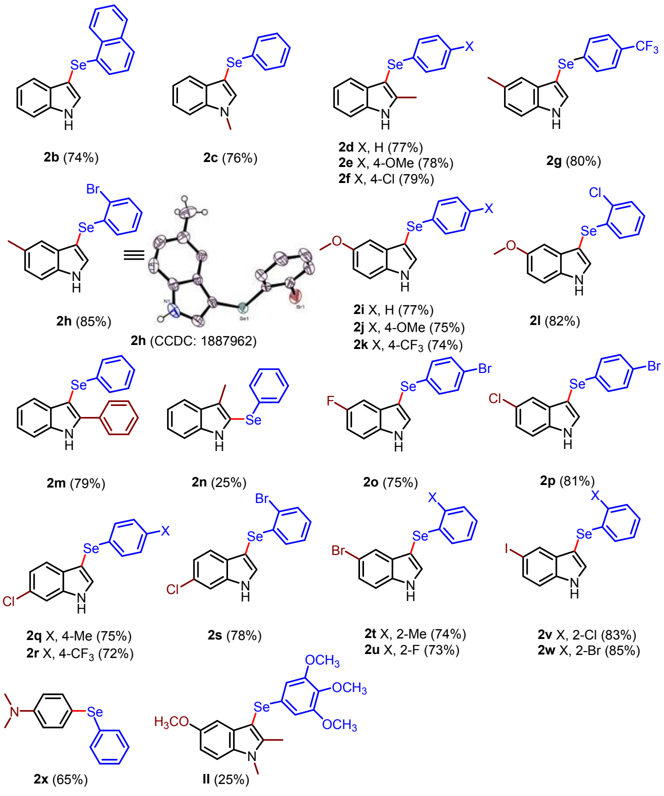
The optimization of the reaction was carried out using indole **1a** substrate and diphenyl diselenide **1ab** as organochalcogenating reagent under visible-light irradiation (5 mL RB). Various solvents were screened in the reaction mixture (entries 1–9) at room temperature. The formation of desired indolyl selenide **2a** in THF and benzene was observed in trace amount (Table 1, entries 1 and 2). When CH_2Cl_2, DMF, and DMSO solvents were tested, the desired selenide **2a** was obtained in 10, 26, and 28% yields, respectively (Table 1, entries 3, 4 and 5). Similarly, $CHCl_3$ and EtOH were also tried, however, led poor improvement in the yield of **2a** (Table 1, entries 6 and 7). Surprisingly, when reaction was performed in CH_3CN and acetone an observable increase in the yield of the selenide **2a** was perceived (Table 1, entries 8 and 9). Acetone found to be superior and 66% yield was observed under oxygen atmosphere (Table 1, entry 9). Reaction was also performed in a dark condition but only trace amount of desired selenide **2a** was realized (Table 1, entry 11). Moreover, the presented reaction was also tolerated under sunlight which provided nearly the same yield of **2a** (78% vs. 66% in CFL) although a shorter time (6 h for sunlight vs. 16 h for one 26 W CFL bulb) is required (Table 1, entry 11, see SI, page S3 for reaction setup under light irradiation). The reaction provided trace amount of desired product under N_2 atmosphere in degassed acetone (Table 1, entry 12).

Table 1. Optimization of the reaction conditions [a]



entry	solvent	yield[b] (%)
1	THF	trace
2	Benzene	trace
3	CH_2Cl_2	10
4	DMF	26
5	DMSO	28
6	$CHCl_3$	32
7	EtOH	35
8	CH_3CN	60
9	acetone	66
10[c]	acetone	trace
11[d]	acetone	78
12[e]	acetone (degassed under N_2)	trace

[a] The reactions were carried out using 0.2 mmol of indole and 0.1 mmol of diphenyl diselenide in 2 mL of solvent at room temperature under O_2 or N_2 atmosphere for indicated time under a household CFL bulb (26 W) for 16 h. [b] Percentage isolated yield. [c] Reaction was carried out in dark. [d] Reaction was carried out in sunlight for 6 h. [e] Reaction was carried out under strict N_2 atm.



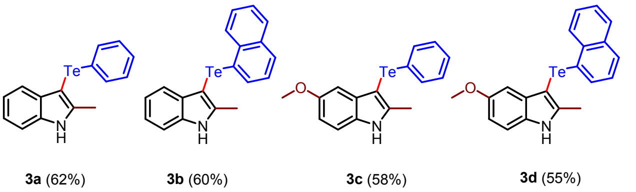
Scheme 2. Substrate scope with regard to 3-organoselenylindoles **2b-2w**.

View Article Online
DOI: 10.1039/C9GC00007K

Next, the substrate scope was studied under the optimized reaction for a variety of commercially available indoles and diaryl diselenides under sunlight irradiation (Scheme 2). In the beginning, indole with naphthyl diselenide successfully reacted to give respective 3-selenyl indole **2b** in 74% yield (Scheme 2). Moreover, *N*-methyl indole also react effectively with diphenyl diselenide to afford **2c** in 76% isolated yield. Indole with electron donating methyl and methoxy groups were well tolerated under the light induced reaction condition and provided methyl and methoxy-substituted indolyl selenides **2d**-**2l**. Similarly, halo fluoro, chloro, bromo and even iodo substituent on the phenyl ring of indole showed compatibility with the light induced reaction conditions and afforded respective 3-indolyl selenides **2o**-**2w** in 73-85% yields. 2-Bromophenyl selenide **2h** is also studied by single X-ray crystal structure analysis (see SI, page S184-S189). Furthermore, coupling of 2-phenyl indole with phenyl diselenide resulted formation of 2-phenyl-3-(phenylselanyl) indole **2m** with good (79%) yield. Interestingly, 3-methyl indole also coupled with phenyl diselenide and resulted 2-selenyl indole **2n** in 25% yield. The poor yield of **2n** could be due to low stability of C_2-centered radical cation which is the possible intermediate in the formation of **2n** (*vide infra*, mechanistic part). It seems that both electron-donating and withdrawing groups also with free N–H as well as *N*-protected indole substrates showed the compatibility to the reaction conditions and afforded respective structurally diverse 3-selenyl indoles.

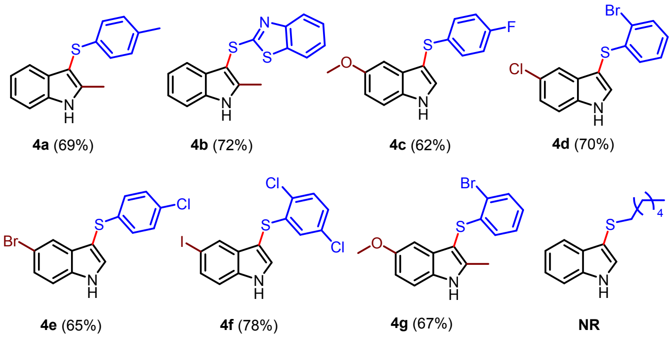
After variation of substitution in indole, functional group tolerance in diaryl diselenides was investigated under the light induced carbon-selenium bond forming reaction. Diphenyl diselenides with *ortho*-methyl, *para*-methyl and *para*-methoxy substituents coupled with variously substituted indoles to furnish desired unsymmetrical selenides **2e**, **2j**, **2q** and **2t** in 74-78% yields. Functional groups such as *ortho*-and *para*-halo (F, Cl, Br) and *para*-CF_3 containing diselenides were also amenable to the reaction and gave variously substituted C_3 selenyl indoles **2f**, **2g**, **2h**, **2k**, **2l**, **2o-p**, **2r-s** and **2u-w** smoothly. Next, *N,N*-dimethylaniline as the coupling partner was studied under light induced the carbon-selenium bond forming reaction. *N,N*-dimethylaniline smoothly reacted with diphenyl diselenide under light induced condition to afford unsymmetrical diaryl selenide **2x** in 65% yield. We also explored the synthesis of trimethoxy-substituted phenyl indolyl selenide **II** which has been studied as tubulin inhibitor.[5d] For this purpose, 5-methoxy-2-methyl indole was protected by using NaH base and subsequently reacted with methyl iodide to afford *N*-methyl-5-methoxy-2-methyl indole.[21] Reaction of 3,4,5-trimethoxyphenyl diselenide with *N*-methyl-5-methoxy-2-methyl indole under light induced reaction condition afforded trimethoxy-susbtituted phenyl indolyl selenide **II** in 25% yield.

Next, we explored another class of 3-chalcogenyl indole under the similar optimized reaction conditions. The formation of carbon-tellurium bond is difficult presumably due to its weak bond strength and metallic nature. Consequently, tellurium undergoes metal-tellurium exchange reaction in TM-catalyzed and electropositive alkali metal mediated reactions. Also, tellurides are easily oxidized due to low electropositive potential, as a result diorgano tellurides are difficult to access under oxidative reaction conditions used for the synthesis of unsymmetrical diorgano chalcogenides. Here, various aromatic phenyl and naphthyl ditellurides were compatible with substituted indole and furnished 3-telluroindoles **3a-3d** in 55-62% yields (Scheme 3).



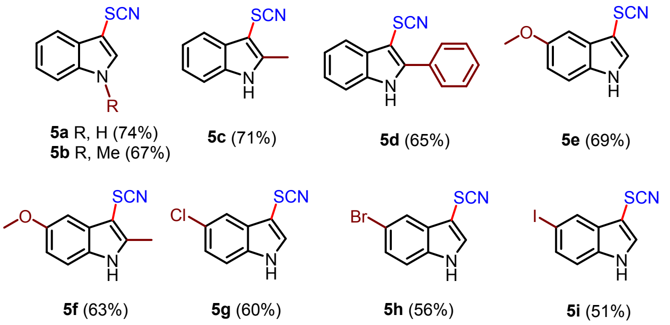
Scheme 3. Synthesis of 3-tellanylindoles

Similarly, diaryl disulfide reacted well under the light induced reaction condition (Scheme 4). 2-Methyl, 5-methoxy, 5-halo (Cl, Br, I) groups on indole substrates were tested with various aromatic disulfides. The studied diaryl disulfides afforded 3-sulfenyl indole **4a**-**4g** in 62-78 % yields (Scheme 4). Alkyl *n*-hexyl disulfide substrate was also reacted with indole **1a** under the reaction conditions, however, *n*-hexyl disulfide failed to afford any sulfide under light induced reaction conditions.



Scheme 4. Synthesis of 3-sulfenylindoles

After the success of organochalcogenation of indoles, motivated us to promote the thiocyanation under the optimized conditions.



Scheme 5. Scope of thiocyanation of indoles

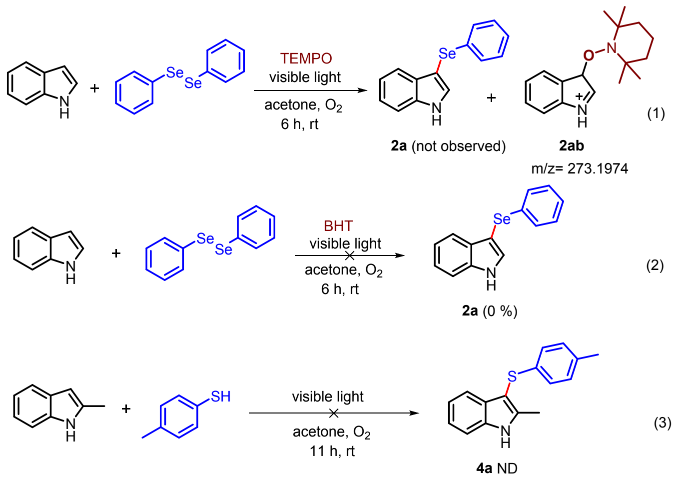
Organothiocyanates are valuable synthetic intermediates which can be easily transformed into an array of organosulfur molecules.[22] Thiocyanide group has been introduced in to arenes by electrophilic thiocyanation using thiocyanate salt in the presence of oxidizing agents namely hypervalent iodine reagents,[23] and related oxidants[24] or photocatalyzed reaction conditions.[25] We sustained our studies by treating substituted indoles with NH_4SCN (2 equiv) in acetone under sunlight, the corresponding thiocyanated product **5a**-**5i** were obtained with 51-74% yields (Scheme 5).

Worth comparing the reactivity of diaryl disulfides, diselenides, and ditellurides under the light induced reaction conditions. Reaction hours for disulfide, diselenide and ditelluride substrates are 9-11 h, 6-7 h, and 5-6 h, respectively. Also, yield of tellurides **3a**-**3d** noticed to be less than the respective selenides, for example 77% for selenium in **2d** vs 62% for tellurium in **3a**. It seems that diselenide substrates are reacted well under the light induced conditions and provided better yields of unsymmetrical selenides whereas disulfides substrates noticed to less reactive and require longer irradiation of the reaction mixture. Ditellurides seem to be sensitive to the light and noticed to be more reactive, however, provided poor yields of unsymmetrical tellurides presumably because of weak carbon-tellurium bond.

Mechanistic Study

Insight into the mechanism involved was made by control experiments, UV-visible spectroscopy and cyclic voltammetry study on the substrates, and EPR study on the reaction mixture (see SI, page S22).

When reaction was performed in the presence of a radical scavenger (TEMPO) the reaction was inhibited, suggesting the participation of radical species in the transformation (Scheme 6, eq. 1). The mass analysis of the reaction mixture indicates the formation of TEMPO-indole adduct **2ab** (m/z = 273.1974, calcd 273.1961, Figure S1, SI page S20) and the mass peak due to selenide **2a** was not observed.



Scheme 6. Control experiments for mechanistic study

View Article Online
DOI: 10.1039/C9GC00097K

Next, reaction was performed in the presence of another radical scavenger 2,6-di-*tert*-butyl-4-methylphenol (BHT). Expectedly, the formation of desired selenide **2a** was also not observed (Scheme 6, eq. 2). We also studied the reaction of *para*-toluenethiol with 2-methyl indole under the reaction conditions (eq 3). Desired sulfide **4a** was not realized, although, trace of oxidized *para*-tolyl disulfide was observed.

Absorption Spectra. The UV-visible study was carried out for Indole and diphenyl diselenide. Absorption spectra of Indole **1a** (5×10^{-3} M) in acetonitrile shows an absorption in visible range 380-420 nm while diphenyl diselenide **1ab** absorb in UV range at 331 nm in acetonitrile (Figure 2).

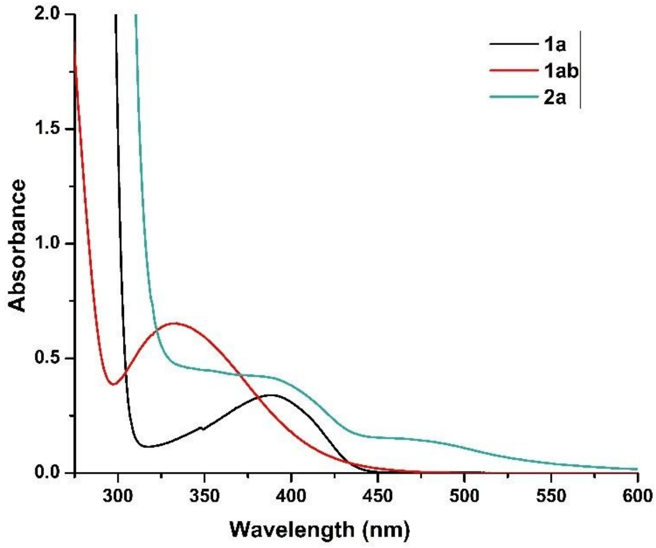


Figure 2. Absorption spectra of indole **1a**, diphenyl diselenide **1ab** and **2a** in acetonitrile

Cyclic Voltammetric Study

To have insight into redox behaviour of indole **1a**, cyclic

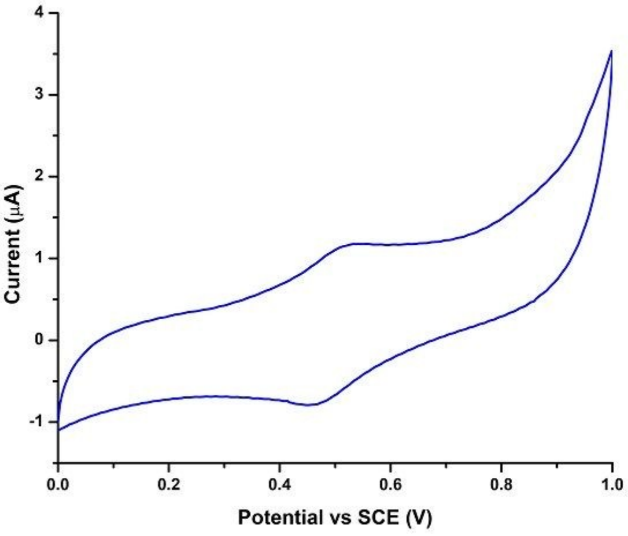


Figure 3. Cyclic voltammogram of **1a** (2 mM) in CH_3CN using SCE, scan rate 5 mV s^{-1} in $TBAPF_6$.

View Article Online
DOI: 10.1039/C9GC00097K

voltammetry study was carried out (Figure 3). The Cyclic voltammogram (CV) of **1a** shows a redox potential of +0.497 V (Figure 3). The observed oxidation potential of **1a** is +0.455 V. Indole **1a** has a triplet exited state energy of +3.0355 V.[26] Thus, excited state oxidation potential $E_{1/2}^{\mathrm{ox}*}$ **1a**$^{\bullet+}$/ ^{3}**1a*** is –2.59 V [27,28] and the reduction potential of oxygen into hydrogen peroxide is +0.65 V (*vs*. SCE) which suggests that the oxygen could oxidize indole.

Emission quenching experiment (Stern Volmer study)

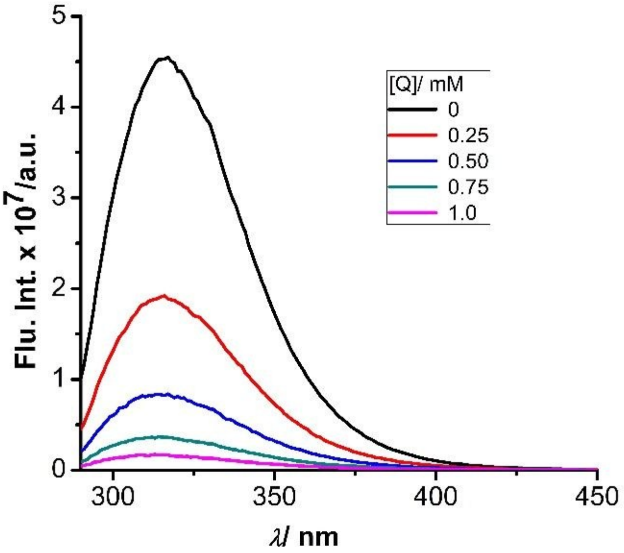


Figure 4 The emission quenching of indole **1a** by diphenyl diselenide **1ab**

Emission intensities were recorded using a HORIBA Jobin Yvon Fluorolog3 Spectrofluorimeter. Initially, emission spectra of 10 μM indole in CH_3CN was collected. Then, appropriate amount of quencher was added with increasing concentration and subsequent emission spectrum were recorded (Figure 4).

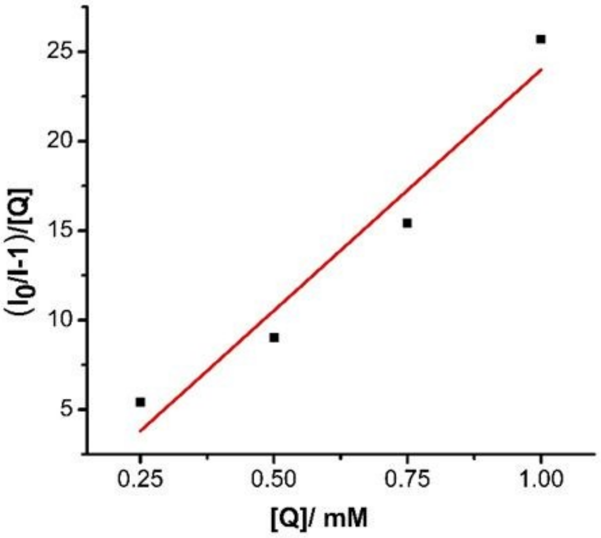
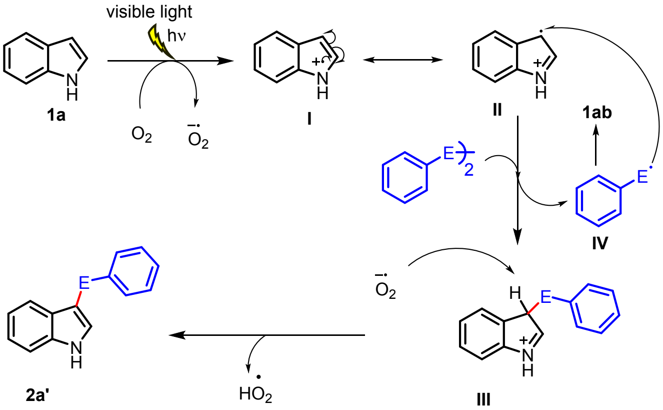


Figure 5 The modified Stern Volmer plot for quenching indole **1a** fluorescence by the quencher diphenyl diselenide **1ab** yields a linear plot

Here I_0 and I denote the intensities of the emission in the absence and presence of the quencher. The quenching curve was plotted using the modified Stern Volmer equation, and the Stern Volmer constant (K_{sv}) was calculated to be 13.34 mM^{-1} (Figure 5).

Mechanism

Based on the control experiments, it is equitable to assume that indole, excited by visible light, resulted in radical cation **I** upon reaction with oxygen (Scheme 7). Oxidation potential of indole is +0.455 V where reduction potential of oxygen into hydrogen peroxide is +0.65 V, which suggests that oxidation of indole by oxygen is feasible by –1.94 V. Indolyl radical cation **I** could be stabilized resonance to form **II**. Indolyl radical **II** would add to diaryl dichalcogenide, forming an arylchalcogenylated indole cation **III** and a radical PhE$^{\bullet}$ **IV**. The anion radical of $O_2^{\bullet-}$ generated by visible light irradiation, would abstract a proton from cation **III**, thus, would facilitate the formation of desired unsymmetrical selenide **2a'** and perhydroxyl radical $H_2O^{\bullet}$ (Scheme 7). In the second cycle, perhydroxyl radical $H_2O^{\bullet}$ would abstract the electron from **1a** and subsequent abstraction of proton from **III** gave hydrogen peroxide. The formation of hydrogen peroxide in the reaction mixture of indole **1a** and diphenyl diselenide **1ab** was also confirmed by ^{1}H NMR experiment (please see SI, page S24) which shows a peak at 10.14 ppm. Intermediate aryl chalcogenyl radical **IV** could dimerize to provide diaryl dichalcogenides. Also aryl chalcogenyl radical **IV** could couple with indolyl radical **II** to afford indolyl aryl chalcogenide cation **III**. Formation of aryl thiols and selenols under optimized reaction conditions seem unlikely as our control experiment suggest that the reaction of *para*-toluenethiol with indole does not provide any indolyl tolyl sulfide **4a**.



Scheme 7. Proposed mechanism for C_3-chalcogenylation of indoles

Conclusions

In summary, we have developed a benign oxidant, photocatalyst and transition-metal-free visible light induced methodology for the construction of carbon-chalcogen (S, Se, Te) bond that enables 3-chalcogenyl indole. The mild reaction conditions tolerate various diaryl selenides/tellurides/sulfides

View Article Online
DOI: 10.1039/C9GC00007K

and ammonium thiocyanate with substituted indole for this transformation and accessed heterocyclic unsymmetrical chalcogenides in excellent yields. We believe that the developed methodology is sustainable and easy to their potentially operational procedures.

Acknowledgements

We are grateful for the financial support from DST-SERB New Delhi (EMR/2015/000061). VR acknowledges UGC for fellowship [23/12/2012(ii)EU-V] and also thankful to Miss Cavya Jose for the column chromatography of the reaction mixture of tellurides **3a-3d**. SK thanks to Dr. Apurba Lal Koner and Mr. Tanoy Dutta for emission quenching experiment and Dr. Sadhan Jana for cyclic voltammetry study.

Notes and references

1 Application in biology: C. W. Nogueira, G. Zeni, J. B. T. Rocha, *Chem. Rev.* 2004, **104**, 6255.

2 K. Selvakumar and H. B. Singh, *Chem. Sci.*, 2018, **9**, 7027

3 a) S. Patai, Z. Rappoport, Wiley, C. In *The Chemistry of Organic Selenium and Tellurium Compounds*; John Wiley and Sons: New York, NY, 1987; Vol. 2; b) J. Hellberg, T. Remonen, M. Johansson, O. Inganas, M. Theander, L. Engman, P. Eriksson, *Synth. Met.* 1997, **84**, 251; c) G. Evano, N. Blanchard, M. Toumi, *Chem. Rev.* 2008, **108**, 3054; d) S. Kumar, H. Johansson, T. Kanda, L. Engman, T. Müller, H. Bergenudd, M. Jonsson, G. F. Pedulli, R. Amorati, L. Valgimigli, *J. Org. Chem.* 2010, **75**, 716; e) T. Wirth, *Organoselenium Chemistry: Synthesis and Reactions*; Wiley-VCH: Weinheim, Germany, 2012; pp 1-65.

4 For application in the synthesis of organic compounds: a) M. Besev, L. Engman, *Org. Lett.* 2002, **4**, 3023; b) B. Berlin, C. Ericsson, L. Engman, *J. Org. Chem.* 2003, **68**, 8386; c) D. M. Freudendahl, S. Santoro, S. A. Shahzad, C. Santi, T. Wirth *Angew. Chem. Int. Ed*. 2009, **48**, 8409; d) P. Srivastava, L. Engman, *Tetrahedron Lett.* 2010, **51**, 1149; e) Y. Okada, M. Oba, A. Arai, K. Tanaka, K. Nishiyama, W. Ando, *Inorg. Chem.* 2010, **49**, 383.

5 a) G. L. Regina, R. Bai, W. M. Rensen, E. D. Cesare, A. Coluccia, F. Piscitelli, V. Famiglini, A. Reggio, M. Nalli, S. Pelliccia, E. D. Pozzo, B. Costa, I. Granata, A. Porta, B. Maresca, A. Soriani, M. L. Iannitto, A. Santoni, J. Li, M. M. Cona, F. Chen, Y. Ni, A. Brancale, G. Dondio, S. Vultaggio, M. Varasi, C. Mercurio, C. Martini, E. Hamel, P. Lavia, E. Novellino, R. Silvestri, *J. Med. Chem.* 2013, **56**, 123; b) M. Nuth, H. C. Guan, N. Zhukovskaya, Y. L. Saw, R. P. Ricciardi, *J. Med. Chem.* 2013, **56**, 3235; c) Q. Guan, C. M. Han, D. Y. Zuo, M. A. Zhai, Z. Q. Li, Q. Zhang, Y. P. Zhai, X. W. Jiang, K. Bao, Y. L. Wu, W. G. Zhang, *Eur. J. Med. Chem.* 2014, **87**, 306; d) Z. Y. Wen, J. W. Xu, Z. W. Wang, H. Qi, Q. L. Xu, Z. S. Bai, Q. Zhang, K. Bao, Y. L. Wu, W. G. Zhang, *Eur. J. Med. Chem.* 2015, **90**, 184.

6 S. Kumar, L. Engman, L. Valgimigli, R. Amorati, M. G. Fumo, G. F. Pedulli, *J. Org. Chem*. 2007, **72**, 6046.

7 a) S. Ranjit, R. Lee, D. Heryadi, C. Shen, J. Wu, P. Zhang, *J. Org. Chem*. 2011, **76**, 8999; b) Q. Wu, D. Zhao, X. Qin, J. Lan, J. You, *Chem. Commun*. 2011, **47**, 9188; c) P. Anbarasan, H. Neumann, M. Beller, *Chem. Commun*. 2011, **47**, 3233; d) M. Chen, Z-T. Huang, Q-Y. Zheng, *Chem. Commun*. 2012, **48**, 11686; e) F. L. Yang, S. K. Tian, *Angew. Chem. Int. Ed.* 2013, **52**, 4929; f) T. Hostier, V. Ferey, G. Ricci D. G. Pardo, J. Cossy, *Org. Lett.* 2015, **17**, 3898; g) T. Hostier, V. Ferey, G. Ricci, D. G. Pardo, J. Cossy, *Chem. Commun.* 2015, **51**, 13898. h) L.Bering, L. D'Ottavio, G. Sirvinskaitea, A. P. Antonchick, *Chem. Commun.* 2018, **54**, 13022.

8 a) X. L. Fang, R. Y. Tang, P. Zhong, J. H. Li, *Synthesis* 2009, 4183; b) W. Ge, Y. Wei, *Green Chem.* 2012, **14**, 2066; c) J. B. Azeredo, M. Godoi, G. M. Martins, C. C. Silveira, A. L. Braga, *J. Org. Chem.* 2014, **79**, 4125; d) N. L. Ferreira, J. B. Azeredo, B. L. Fiorentin, A. L. Braga, *Eur. J. Org. Chem.* 2015, 5070; e) B. M. Vieira, S. Thurow, J. S. Brito, G. Perin, D. Alves, R. G. Jacob, C. Santi, E. J. Lenardão, *Ultrasonics Sonochemistry* 2015, **27**, 192; f) X. Zhang, C. Wang, H. Jiang, L. Sun, *Chem. Commun*. 2018, **54**, 8781.

9 a) H. Cao, J. Yuan, C. Liu, X. Hu, A. Lei, *RSC Adv*. 2015, **5**, 41493; b) Q. Lu, H. Wang, P. Peng, C. Liu, Z. Huang, Y. Luoa, A. Lei, *Org. Chem. Front*. 2015, **2**,908; c) G. Zhang, C. Liu, H. Yi, Q. Meng, C. Bian, H. Chen, J-X. Jian, L-Z Wu, A. Lei, *J. Am. Chem. Soc*. 2015, **137**, 9273; d) H. Wang, Q. Lu, C. Qian, C. Liu, W. Liu, K. Chen, A. Lei, *Angew. Chem. Int. Ed*. 2016, **55**, 1094; e) H. Wang, Q. Lu, C-W Chiang, Y. Luo, J. Zhou, G. Wang, A. Lei *Angew. Chem. Int. Ed*. 2017, **56**, 595.

10 S. Kumar, L. Engman, *J. Org. Chem.* 2006, **71**, 5400; b) V. G. Ricordi, C. S. Freitas, G. Perin, E. J. Lenardão, R. G. Jacob, L. Savegnago, D. Alves, *Green Chem.* 2012, **14**, 1030; c) D. Kundu, S. Ahammed, B. C. Ranu, *Green Chem.* 2012, **14**, 2024; d) N. Mukherjee, T. Chatterjee, B. C. Ranu, *J. Org. Chem.* 2013, **78**, 11110; e) A. Kumar, S. Kumar *Tetrahedron* 2014, **70**, 1763; h) D. Kundu, S. Ahammed, B. C. Ranu, *Org. Lett.* 2014, **16**, 1814.

11 a) N. Taniguchi, *J. Org. Chem.* 2007, **72**, 1241; b) M. S. Silva, J. V. Comasseto, *Tetrahedron* 2011, **67**, 8763; c) B. Mohan, S. Hwang, S. Jang, K. H. Park, *Synlett* 2014, **25**, 2078; d) M. Matsumura, H. Kumagai, Y. Murata, N. Kakusawa, S. Yasuike, *J. Organomet. Chem.* 2016, **807**, 11; e) N. Taniguchi, *Tetrahedron* 2016, **72**, 5818; f) P. Maity, S. Ahammed, R. N. Manna, B. C. Ranu, *Org Chem Front.* 2017, **4**, 69; g) J. Rafique, S. S. Saba, M. S. Franco, L. Bettanin, A. R. Schneider, L. T. Silva, A. L. Braga, *Chem. Eur. J.* 2018, **24**, 4173.

12 a) Q-B. Zhang, Y-L. Ban, P-F. Yuan, S-J. Peng, J-G. Fang, L-Z. Wu, Q. Liu, *Green Chem*. 2017, **19**, 5559; b) P-F. Yuan, Q-B. Zhang, X-L. Jin, W-L. Lei, L-Z. Wu, Q. Liu, *Green Chem*. 2018, **20**, 5464; c) S. Saba, J. Rafique, M. S. Franco, A. R. Schneider, L. Espíndola, D. O. Silva, A. L. Braga *Org. Biomol. Chem*. 2018, **16**, 880.

13 S. K. Bhunia, P. Das, R. Jana, *Org. Biomol. Chem.* 2018, **16**, 9243.

14 a) C. D. Prasad, S. J. Balkrishna, A. Kumar, B. S. Bhakuni, K. Shrimali, S. Biswas, S. Kumar, *J. Org. Chem*. 2013, **78**, 1434; b) A. Kumar, B. S. Bhakuni, C. D. Prasad, S. Kumar, S. Kumar, *Tetrahedron* 2013, **69**, 5383. (c) C. D. Prasad, S. Kumar, M. Sattar, A. Adhikary, S. Kumar, *Org. Bio. Chem.* 2013, **11**, 8036. (d) C. D. Prasad, M. Sattar, R. Kumar, S. Kumar, *Org. Lett.* 2017, **19**, 774. (e) M. Sattar, M. Shareef, K. Patidar, S. Kumar, *J. Org. Chem*. 2018, **83**, 8241.

15 E. G. Zimmermann, S. Thurow C. S. Freitas, S. R. Mendes, G. Perin, D. Alves, R. G. Jacob, E. J. Lenardão, *Molecules* 2013, **18**, 4081; b) C. C. Silveira, S. R. Mendes, L. Wolf, G. M. Martins, L. V. Mühlen, *Tetrahedron* 2012, **68**, 10464.

16 a) W. Ge, Y. Wei, *Green Chem.* 2012, **14**, 2066; b) J. B. Azeredo, M. Godoi, G. M. Martins, C. C. Silveira, A. L. Braga, *J. Org. Chem*. 2014, **79**, 4125; c) F. H. Xiao, H. Xie, S. W. Liu, G. J. Deng, *Adv. Synth. Catal.* 2014, **356**, 364.

17 a) N. Taniguchi, *J. Org. Chem*., 2015, **80**, 7797; b) V. Rathore, A. Upadhyay, *Org. Lett*., 2018, **20**, 6274.

18 N. Taniguchi, and T. Onami, *J. Org. Chem*. 2004, **69,** 915.

19 a) Z. Li, J. Q. Hong, X. J. Zhou, *Tetrahedron* 2011, **67**, 3690; b) W. Ge, Y. Wei, *Synthesis* 2012, **44**, 934; c)) X. L. Fang, R. Y. Tang, P. Zhong, J. H. Li, *Synthesis* 2009, 4183; d) J. S. Yadav, B. V. S. Reddy, Y. J. Reddy, K. Praneeth, *Synthesis* 2009, 1520; d) Y. Maeda, M. Koyabu, T. Nishimuraand, S. Uemura, *J. Org. Chem*. 2004, **69**, 7688.

View Article Online
DOI: 10.1039/C9GC00007K

20 S. Jana, A. Verma, R. Kadu, S. Kumar, *Chem. Sci.* 2017,**8***,* 6633.

21 X. Chen, G. Zheng, Y. Li, G. Song, X. Li, *Org. Lett.* 2017, **19**, 6184.

22 a) T. Nguyen, M. Rubinstein, C. Wakselman, *J. Org. Chem*. 1981, **46**, 1938; b) Z. H. Zhang, L. S. Liebeskind, *Org. Lett*. 2006, **8**, 4331; c) R. Riemschneider, *J. Am. Chem. Soc*. 1956, **78**, 844; d) Y. T. Lee, S. Y. Choi, Y. K. Chung, *Tetrahedron Lett*. 2007, **48**, 5673 and references cited therein.

23 Hypervalent iodine reagents a) A. De Mico, R. Margarita, A. Mariani, G. Piancatelli, *Tetrahedron Lett*. 1996, **37**, 1889; b) A. De Mico, R. Margarita, A. Mariani, G. Piancatelli, *Chem. Commun*. 1997, 1237; c) J. S. Yadav, Reddy, B. V. S.; B. B. Murali Krishna, Synthesis 2008, 3779.

24 a) V. K. Jadhav, R. R. Pal, P. P. Wadgaonkar, M. M. Salunkhe, *Synth. Commun*. 2001, **31**, 3041; b) J. S. Yadav, B. V. S. Reddy, M. K. Gupta, *Synthesis* 2004, 1983; c) J. S. Yadav, B. V. S. Reddy, A. D. Krishna, C. S. Reddy, A. V. Narsaiah, *Synthesis* 2005, 961; d) D. S. Bhalerao, K. G. Akamanchi, *Synlett* 2007, 2952; e) J. S.; Yadav, B. V. S.; Reddy, B. B. M. Krishna, *Synthesis* 2008, 3779; f) A. Dey, A. Hajra, *Adv. Synth. Catal.* 2018, **360**, 1.

25 Photocatalyzed reaction conditions S. Mitra, M. Ghosh, S. Mishra, A. Hajra *J. Org. Chem*. 2015, **80**, 8275; b) W. Zhang, J. Tang, W. Yu, Q. Huang, Y. Fu, G. Kuang, C. Pan, G. Yu, *ACS Catal.* 2018, **8**, 8084.

26 E. M. Evleth, O. Chalvet, P. Bamiere, *J. Phys. Chem*. 1977, **81**, 1913.

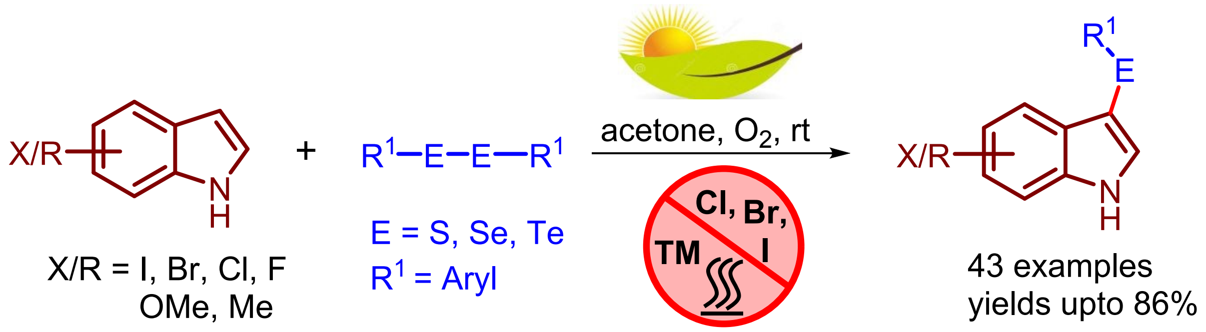
27 For calculation of oxidation potential ($E_{1/2}^{\mathrm{ox}\,*}$) in excited state from ground state ($E_{1/2}^{\mathrm{ox}}$): N. A. Romero, D. A. Nicewicz, *Chem. Rev.*, 2016, **11***,* 10075.

28 Oxidation potential ($E_{1/2}^{\mathrm{ox}\,*}$) Indole **1a** in excited state was calculated by using formulae: ($E_{1/2}^{\mathrm{ox}\,*}$ $\mathbf{1a}^{\bullet+}/{}^{3}\mathbf{1a}^{*}$) = ground state oxidation potential ($E_{1/2}^{\mathrm{ox}}$ $\mathbf{1a}^{\bullet+}/\,{}^{3}\mathbf{1a}^{*}$) – triplet excited state energy ($E_{0,0}^{\mathrm{T}}$) of **1a**. Indole **1a** has a triplet energy ($E_{0,0}^{\mathrm{T}}$) 70 kcal mol^{-1} or 3.0355 V. Oxidation potential ($E_{1/2}^{\mathrm{ox}\,*}$) = ($E_{1/2}^{\mathrm{ox}}$ $\mathbf{1a}^{\bullet+/3}\mathbf{1a}^{*}$) – $E_{0,0;}^{\mathrm{T}}$ +0.45 – 3.0355 = –2.5855 V ≈ –2.59 V.

View Article Online
DOI: 10.1039/C9GC00007K

Visible-Light-Induced Metal and Reagent-Free Oxidative Coupling of sp^2 C─H Bond with Organo-Dichalcogenides: Synthesis of 3-Organochalcogenyl Indoles

Vandana Rathore and Sangit Kumar*



- Light induced organochalcogenation of C-H bond
- Intruction of organosulfur, selenium, tellurium, SCN
- Metal, base, additive, organic dye, photocatalyst free
- O_2 as an oxidant

Here, a unique visible-light-induced method for the organochalcogention of sp^2 C─H bond of indoles and aniline has been presented using diaryl dichalcogenides (S, Se, and Te) and oxygen as an oxidant avoiding photocatalyst, base, catalyst, and reagent in acetone at room temperature. This benign protocol allows to access a wide range of 3-arylselenylindoles, 3-arylthioindoles and even 3-aryltelluroindoles with good to excellent yields. Various functionalities namely, methoxy, and halo either on indoles or aryl dichalcogenide showed amenability to the developed reaction. Further, thiocynation of of sp^2 C─H bond of indoles has been accomplished under the visible light induced method. Mechanistic understanding by UV-Visible, EPR spectroscopy, and cyclic voltametry suggest that the light induces electron transfer from electron rich arene to oxygen provide arene radical cation and superoxide radical anion. Subsequently, reaction of radical cation with aryl dichalcogenides provide diaryl chalcogenyl cation which upon removal of proton gave unsymmetrical 3-indolyl aryl chalcogenides.