Research article Open Access

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Lewis acid / Base-free Strategy for the Synthesis of 2-Arylthio and Selenyl Benzothiazole / Thiazole and Imidazole

https://doi.org/10.1515/hc-2020-0119
Received January 27, 2020; accepted January 27, 2021.

Abstract: A Cu(II)-catalyzed Csp^2-Se and Csp2-Sulfur bond formation was achieved with moderate to good yields without the aid of Lewis acid and base. The reaction is compatible with a wide range of heterocycles such as benzothiazole, thiazole, and imidazole. Also, this typical protocol is found to be active in thio-selenation via S-H activation. Additionally, we proposed a plausible mechanistic pathway involving Cu(III) putative intermediate.

Keywords: Selenation, thiolation, diphenyl diselenide, thioaryl and selenoaryl derivatives, chalcogenide

Introduction

Organoselenium scaffolds engrossed much attention from chemists owing to their varied pharmaceutical activity such as antioxidants [1-5], anti-inflammatory [6-8], and antimicrobial agents [9]. Additionally, the organoselenium molecular entities were assessed for anticancer [10-11], neuroprotective [12], and antiviral properties [13-14]. Recently, selenium-containing molecules have gained a great deal of significance due to the optical activities of organic materials [15-16].

The functionalization of C–H bonds adjacent to a hetero-atom utilizing cross-coupling is a conceptually ideal process. Also, this strategy represents an extremely attractive and competent route for the substitution of C–H bond. Moreover, the strategy is considered to be straightforward and has a step-economic advantage than traditional reactions [17-18]. Primarily, this process was induced by a sub-stoichiometric transition metal in combination with additives and bases. This regioselective oxidative coupling strategy enabled the synthesis of various pharmaceutically active heterocyclic molecular motifs [19-21]. Various groups have reported the cross-coupling of C–H bonds adjacent to a nitrogen atom to give new C–C, C-X (X = S, Se, and Te) bond containing molecules. In particular, the construction of new C–S and C-Se bonds via oxidative functionalization of a C(sp2)-H bond of benzothiazoles, thiazoles, benzoxazoles, azoles, benzimidazole, imidazole, and oxadiazole has been reported elegantly [22-29]. Amongst such strategies, a Lewis acid-catalyzed, stoichiometric Cu(II)-mediated thiolation reaction between heteroarenes and thiols strategy offers an appealing alternative to the conventional methods [30] (Scheme 1).

However, all these methods require stoichiometric amounts of external oxidants and bases. Hence, there is still a great need for the development of sole oxidant as air and base free protocol to produce various thioaryl and selenoaryl derivatives of benzothiazoles, thiazoles, azoles, benzimidazole, and imidazole.

Results and discussion

In our continuous interest in developing base-free Cu catalyzed reactions [31-34], we assessed the direct selenation and thiolation of benzothiazole. Initially, conducting the reaction between benzothiazole **1a** (1 equiv.) and diphenyl diselenide **2a** (1.2 equiv.) in the presence of $Cu(OAc)_2$ (100 mol%) and heating 100 °C in 1,4-dioxane resulted in the desired product **3a** at a 54% yield (Table 1, Entry 1). When the catalyst loading reduced to 50 mol%, the same

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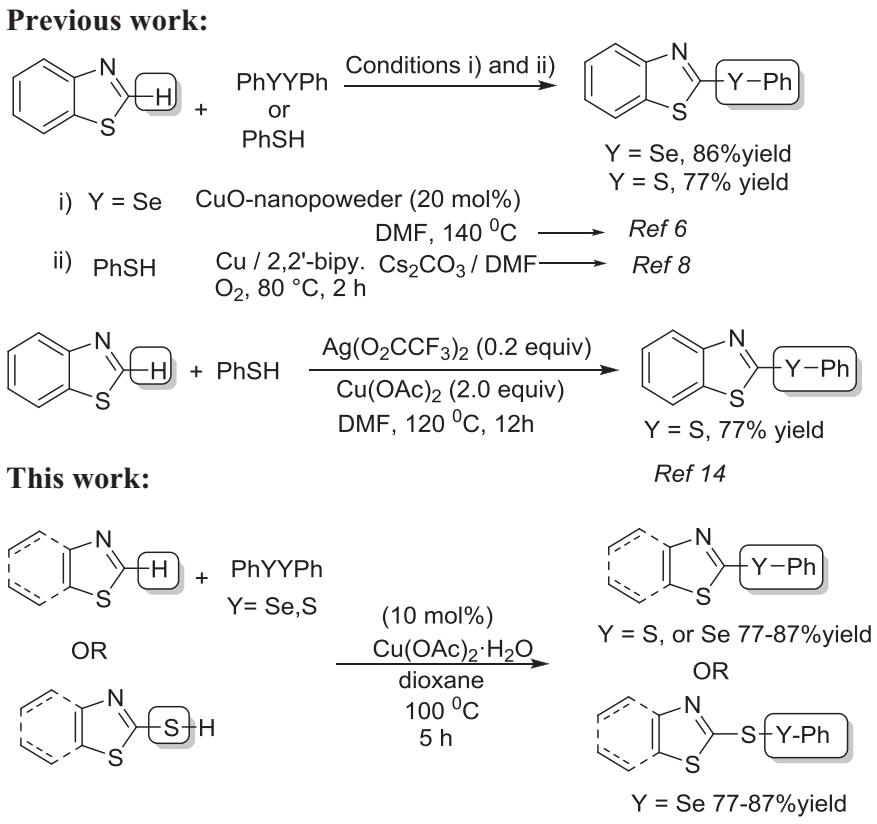


Scheme 1 Previous routs for selenation and thiolation of C–H bonds adjacent to a hetero-atom

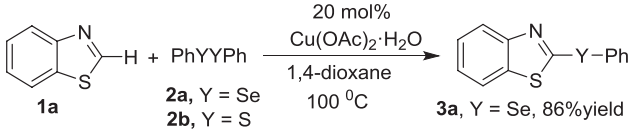
reaction under otherwise identical condition gave the product **3a in** 70% yield (Table 1, Entry 2).

In another reaction, the increased yield of **3a** was observed with 20 mol% of Cu(OAc)2 under the same set of conditions (Table 1, Entry 3). A reaction with 10% Cu(OAc)2 loading under typical conditions afforded **3a** in a decreased yield (Table 1, Entry 4). Interestingly, it was observed that the diphenyl diselenide **2a** was not completely consumed (*vide-supra*) and the unreacted **2a** was recovered at a yield of 40%. When **2a** molar ratio was reduced from 1.0 mmol to 0.6 mmol and carried out under identical conditions as above, this resulted in **3a** with similar yields (Table 1, Entry 5). This result indicates that the by-product PhSeH re-oxidized to PhSeSePh under the atmosphere of air. Hence, it needs in an only half-molar equivalent. After considerable experimentation, we established that benzothiazole **1a** (1 equiv.), diphenyl diselenide **2a** (0.6 equiv.) and 20 mol% of Cu(OAc)2 in 1,4-dioxane at 100 °C for 5 h was most effective set of conditions, yielding the **3a** at yield of 86% (Table 1, Entry 5).

Among the solvents tested, only 1,4-dioxane gave a better yield of the desired compound **3a** while other solvents, such as $ClCH_2CH_2Cl$, CH_3CN, DMF, DMSO, and H_2O gave a lower yield of **3a** (Table 1, Entries 6 to 10). Interestingly, the reaction proceeded without solvent but with albeit inferior yield (Table 1, Entry 11). A screening of copper salts indicated that $Cu(OAc)_2.H_2O$ performed with good efficiency for this transformation, while CuI and CuOTf, $CuCl_2$, and $Cu(CH_3CN)_4PF_6$ led to inferior yields of **3a** (Table 1, Entries 11 to 15). The $Co(OAc)_2$ and $Pd(OAc)_2$ as catalyst failed to initiate the reaction (Table 1, Entries 16-17). The reaction performed under an air balloon and oxygen balloon gave **3a** in trace amount. To demonstrate the viability of this protocol, a scale-up reaction at 10 mmol levels had also been conducted and the desired product **3a** was obtained with a similar yield.

Furthermore, the reaction scope was extended by employing typical conditions and the results are shown in Table 2. To this end, *N*-methyl benzimidazole **1b** and *N*-ethyl benzimidazole **1c** reacted in the presence of **2a** using similar conditions. The expected products **3b** and **3c** were isolated in 87% and 82% yields, respectively (Table 2, Entry 1). Likewise, *N*-methyl imidazole **1d** and *N*-phenyl imidazole **1e** reacted smoothly in the presence of **2a** under standard protocol and the corresponding products **3d** and **3e** were isolated in 86% and 85% yields, correspondingly (Table 2, Entry 2). Remarkably, under optimized conditions, the substrates 4-methyl thiazole **1f** and 5-methyl-4-vinylthiazole **1g** showed good reactivity with **2a** in the presence of $Cu(AcO)_2$ and provided the seleno derivatives

Table 1 Optimization of reaction conditions for direct selenation[a]



Entry	Catalyst	Solvent	3a (% yield)[c]
1	$Cu(OAc)_2$ (100 mol%)	dioxane	54
2	$Cu(OAc)_2$ (50 mol%)	dioxane	70
3	$Cu(OAc)_2$ (20 mol%)	dioxane	86
4	$Cu(OAc)_2$ (10 mol%)	dioxane	56
5	$Cu(OAc)_2$ (20 mol%)	dioxane	86[b,d]
6	$Cu(OAc)_2$ (20 mol%)	$(CH_2Cl_2)_2$	40
7	$Cu(OAc)_2$ (20 mol%)	CH_3CN	60
8	$Cu(OAc)_2$ (20 mol%)	DMF	35
9	$Cu(OAc)_2$ (20 mol%)	DMSO	40
10	$Cu(OAc)_2$ (20 mol%)	H_2O	20
11	$Cu(OAc)_2$ (20 mol%)	neat	40
12	CuI(20 mol%)	dioxane	20
13	CuOTf(20 mol%)	dioxane	25
14	$CuCl_2$ (20 mol%)	dioxane	20
15	$Cu(CH_3CN)_4PF_6$ (20 mol%)	dioxane	30
16	$Co(OAc)_2$ (20 mol%)	dioxane	NR[e]
17	$Pd(OAc)_2$ (20 mol%)	dioxane	NR[e]

a) All reactions were carried out unless otherwise stated on the 1 mmol scale with 1.0 equiv. **1a** and 1.1 equiv. of **2a** in 2 mL of dioxane heating at 100 °C for 5 h in the open air.
b) The reaction was carried out with 1.0 equiv. **1a** and 0.6 equiv. of **2a**.
c) Isolated yield but not optimized. Yields based on the disappearance of **2a**.
d) This reaction was also carried out at 10 mmol scale.
e) NR = No reaction.

3f and **3g**, in the same way (Table 2, Entries 3 and 4). The significant aspect of the reaction under this oxidative condition is that it sustains a vinyl functionality (Table 2, Entry 4). Furthermore, the direct thiolation protocol was also achieved using typical selenation conditions. Then, benzothiazole **1a**, *N*-methyl benzimidazole **1b**, 4-methyl thiazole **1h** and 2-phenyl-1, 3, 4-oxadiazole were subjected to direct thiolation protocol using **2b**. As expected, the thiolation products **3h-k** were furnished in good to high yields demonstrating the generality of this reaction (Table 2, Entries 5-8).

Next, we intended to explore Cu-catalyzed S-H activation and trap the resulting organo-copper intermediate with diphenyl diselenide **2a** under established protocol as above. Under the typical procedure, the substrates **4a-c** were submitted for S-H activation. To our delight, all the substrates underwent reaction and the expected 2-phenylselenothio derivatives **5a-c** were isolated at a yield of 80%, 70%, and 80%, respectively (Table 3, Entries 1-3). Interestingly, this method represents a novel and mild method for the preparation of organo-sulfur-selenium containing heterocycles.

In light of this work, we now propose the following mechanism (Scheme 2). At first, copper insertion leads to the active intermediate **A** which activates benzothiazole resulting in a Cu-thiolate complex and concomitant abstraction of a C-H by releasing AcOH and the copper (II) complex **B**. The copper (II) complex of **B** undergoes oxidation via disproportion to form Cu(III)-complex **C** [35]. Then, reductive elimination of Cu(I)OAc liberates the desired product. The Cu(I)OAc undergoes further oxidation in the presence of air and AcOH to form copper(II) acetate. A similar mechanistic pathway can be expected to perform in the synthesis of sulfur-selenium heterocycles of **5a-c**. This hypothesis needs further study.

Conclusion

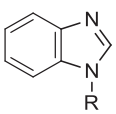
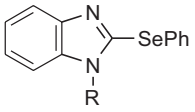
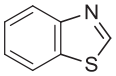
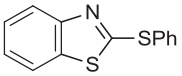
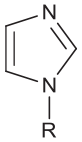
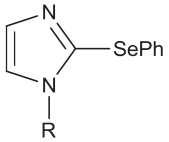
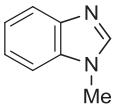
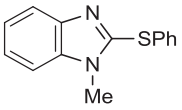
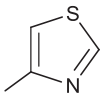
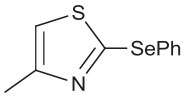
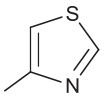
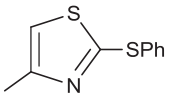
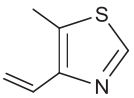
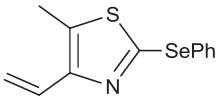
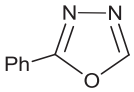
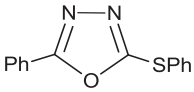
In conclusion, this study may contribute to a refinement of the cross-coupling of C–H bonds, in particular, adjacent to a nitrogen atom to give new C-X (X = S and Se) bond containing molecules. Furthermore, the significant practical advantage is circumventing the stoichiometric use of base and oxidant. This protocol provides an alternative expedient synthesis of chalcogenide containing heterocyclic bioactive molecules. In particular, the synthesis of sulfur-selenium heterocycles via oxidative copper catalysis is the first of its kind to the best of our knowledge. Further work is under progress towards this end in our laboratory.

Experimental Section

All reactions were conducted under an open-air atmosphere. Apparatus used for reactions are oven-dried. 1,4-dioxane and other solvents were used as received. ^{1}H-NMR spectra were recorded at 300, 400 and 500 MHz and ^{13}C-NMR at 75 and 125 MHz in $CDCl_3$. *J* values were recorded in hertz and abbreviations used were s = singlet, d = doublet, m = multiplet, br = broad, dd = doublet of doublet. Chemical shifts (δ) are reported relative to TMS (δ = 0.0) as an internal standard. IR (FT-IR) spectra were measured as KBr pellets or as films. Mass spectral data were compiled using MS (ESI), HR-MS mass spectrometers. Column chromatography was carried out using Silica gel 100–200 mesh (commercial suppliers).

A typical procedure for the Synthesis of 2-phenylseleno benzothiozole (3a): Benzothizole **1a** (1.0 mmol), diphenyl diselinide (0.6 mmol), and $Cu(OAc)_2.H_2O$ (0.2 mmol,

Table 2 Copper catalyzed synthesis of selenium and sulphur containing heterocycles

Entry	Substrate	Product[a,b,c](%Yield)	Entry	Substrate	Product[a,b,c](%Yield)
1	 **1b,** R = Me **1c,** R = Et	 **3b,** R = Me (87%) **3c,** R = Et (82%)	5	 **1a**	 **3h** (77%)
2	 **1d,** R = Me **1e,** R = Ph	 **3d,** R = Me (86%) **3e,** R = Ph (85%)	6	 **1b**	 **3i** (77%)
3	 **1f**	 **3f** (85%)	7	 **1h**	 **3j** (78%)
4	 **1g**	 **3g** (80%)	8	 **1i**	 **3k** (80%)

a) All reactions were carried out unless otherwise stated on the 1 mmol scale with 1.0 equiv. **1a-i** and 0.6 equiv. of **2a** and **2b** in 2 mL of dioxane heating at 100 °C for 5 h in the open air.

b) Isolated yield but not optimized. Yields based on the disappearance of **2a** and **2b**.

c) All products fully characterized by ^{1}H-NMR, ^{13}C-NMR, IR, and Mass.

20 mol%) were charged sequentially into a 10 mL round-bottomed flask. To this, 1,4-dioxane (5 mL) was added and the resulting reaction mixture was stirred at 100 °C for 5 h. Then, cooled to ambient temperature and the solvent was evaporated to give a residue that was purified over silica gel column chromatography eluting with hexane / EtOAc (9:1) to give the desired product **3a** (185 mg, 86%) as a yellow solid, mp. 38-40 °C, lit. [22] 35-36 °C. ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.90 (d, 1H, *J* = 8.2 Hz), 7.80 (d, 2H, *J* = 8.0 Hz), 7.70 (d, 1H, *J* = 7.6 Hz), 7.40-7.50 (m, 4H), 7.26-7.29 (m, 1H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 162.7, 154.5, 136.6, 130.0, 129.9, 126.5, 125.9, 124.3, 121.9, 120.7. IR (KBr): 3056, 2969, 2923, 2851, 1739, 1453, 1418, 1368, 1307, 1067, 1018, 968, 851, 737, 686 cm^{-1}. MS (ESI): 291 (M+H). HR-MS (*m/z*): Calculated for $C_{19}H_{19}NSSe$ (M+H) = 291.9684. Found (M+H) = 291.9693.

All other compounds including the sulfur-selenium heterocycles were synthesized 1mmol scale employing above typical procedure.

1-Methyl-2-(phenylselenyl)-1H-benzo(d)imidazole (3b) (Table 2, Entry 1): Yellow solid, yield 190 mg (87%), mp. 58-62 °C. ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.80 (d, 1H, *J* = 8.2 Hz), 7.50-7.52 (m, 2H), 7.20-7.30 (m, 6H), 3.70 (s, 3H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 143.6, 142.7, 136.0, 132.4, 129.6, 128.0, 123.4, 124.3, 122.5, 119.4, 109.5, 31.8. IR (KBr): 3019, 1710, 1661, 1628, 1549, 1515, 1214, 742, 667, 627 cm^{-1}. MS (ESI): 291 (M+H). HR-MS: Calculated for $C_{14}H_{12}N_2Se$ (M+H) = 289.0238. Found (M+H) = 289.0231.

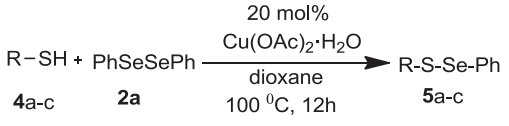
Ethyl-2-(phenylselenyl)-1H-benzo(d)imidazole (3c) (Table 2, Entry 1)**:** Dense liquid, yield 170 mg (82%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.80-7.84 (m, 1H), 7.50-7.56 (m, 2H), 7.20-7.31 (m, 6H), 4.32 (q, *J* = 7.3 Hz, 2H*)*, 1.24 (t, *J* = 7.3 Hz, 3H*)*. ^{13}C-NMR (75MHz, $CDCl_3$): δ 143.6, 142.9, 135.1, 132.4, 129.6, 128.0, 123.2, 118.9.109.6, 40.6, 14.8. IR (neat): 3055, 2977, 2927, 2852, 1609, 1576, 1414, 1343, 1251, 1152, 1102, 1067, 1020, 772, 737, 688, 668 cm^{-1}. MS (ESI): 303 (M+H). HR-MS: Calculated for $C_{15}H_{14}N_2Se$ (M+H) = 303.0395. Found = 303.0387.

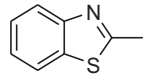
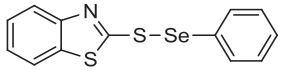
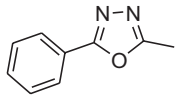
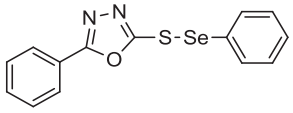
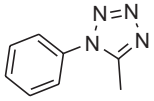
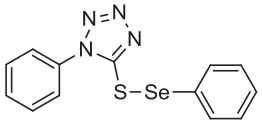
1-Methyl-2-(Phenylselenyl)-1*H*-imidazole (3d) (Table 2, Entry 2): Yellow liquid, yield 250 mg (86%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.31-7.00 (m, 7H), 3.60 (s, 3H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 133.9, 130.5, 130.1, 129.3, 126.9, 123.7, 34.7. IR (neat): 2922, 2851, 1576, 1476, 1451, 1441, 1408,

1277, 1219, 1113, 1067, 1021, 913, 772, 687 cm^{-1}. MS (ESI): 239 (M+H). HR-MS: Calculated for $C_{10}H_{10}N_2Se$ (M+H) = 239.0082. Found = 239.0077.

1-Phenyl-2-(phenylselenyl)-1H-imidazole (3e) (Table 2, Entry 2): Yellow liquid, yield 180 mg (86%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.40-7.10 (m, 12H). ^{13}C-NMR(75MHz, $CDCl_3$): δ 132.2, 130.9, 129.2, 128.1, 128.5, 127.4, 126.2. IR (neat): 2921, 2852, 1730, 1597, 1498, 1458, 1422, 1300, 1219, 1078, 968, 772, 690 cm^{-1}. MS (ESI): 301 (M+H). HR-MS: Calculated for $C_{15}H_{12}N_2Se$ (M+H) = 301.9684. Found = 301.9693.

Table 3 Synthesis of sulphur-selenium heterocycles via oxidative copper catalysis



Entry	R	R-S-Se-Ph[a,b,c] (Yield)
1	 **4a**	 **5a** (80%)
2	 **4b**	 **5b** (70%)
3	 **4c**	 **5c** (80%)

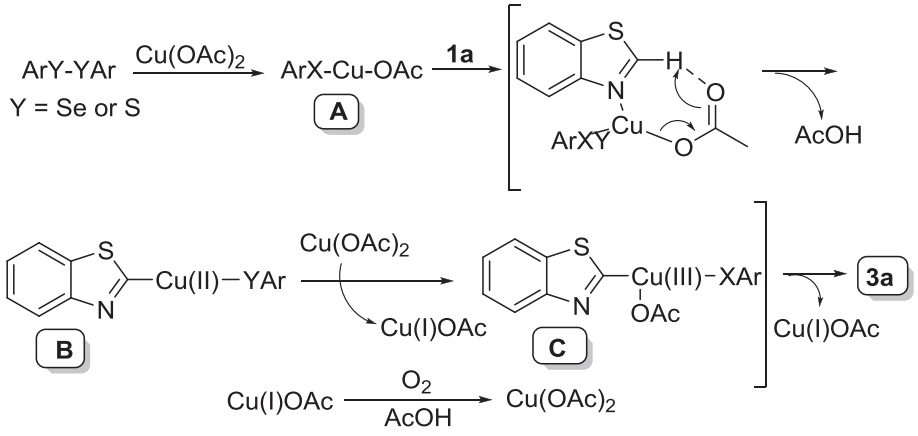
a) All reactions were carried out unless otherwise stated on the 1 mmol scale with 1.0 equiv. **4a-c** and 0.6 equiv. of **2a** in 2 mL of dioxane heating at 100 °C for 5 h in the open air.
b) Isolated yield but not optimized. Yields based on the disappearance of **2a**.
c) All products fully characterized by ^{1}H-NMR, ^{13}C-NMR, IR, and Mass.

4-Methyl-2-(phenylselenyl)thiazole (3f) (Table 2, Entry 3): Yellow liquid, yield 220 mg (85%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.58-7.60 (m, 2H), 7.38-7.40 (m, 2H), 7.21 (s, 1H), 6.70 (s,1H), 2.41 (s, 3H). **^{13}C-**NMR (75MHz, $CDCl_3$): δ 156.3, 154.4 134.9, 132.0, 129.6, 129.0, 128.2, 116.6, 17.0. IR (neat): 3019, 1710, 1661, 1628, 1549, 1515, 1214, 742, 667, 627 cm^{-1}. MS (ESI): 256 (M+H). HR-MS: Calculated for $C_{10}H_9NS$ Se (M+H) = 256.0249. Found = 256.0250.

5-Methyl-2-(phenylselenyl)-4-vinylthiazole (3g) (Table 2, Entry 4): Yellow liquid, yield 180 mg (80%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.69-7.70 (m, 2H), 7.31-7.40 (m, 2H), 7.2 (s, 1H), 6.6 (q, 1H, *J* = 11.3 Hz), 5.1 (q, 1H, *J* = 17.3 Hz), 2.38 (s, 3H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 180.0, 136.0, 135.0, 135.0, 130.6, 130.3, 129.7, 129.2, 15.2. IR(neat): 2922, 2852, 1657, 1576, 1475, 1438, 1401, 1375, 1301, 1219, 1018, 999, 772,689 cm^{-1}. MS (ESI): 282 (M+H). HR-MS: Calculated for $C_{12}H_{11}NSSe$ (M+H) = 282.1021. Found = 282.1017.

2-(Phenylthio)benzo(d)thiazole (3h) (Table 2, Entry 5): Yellow liquid, Yield 140 mg (77%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.28 (t, 1H, *J* = 7.2 Hz), 7.55-7.40 (m, 4H), 7.66 (d, 1H, *J* = 8.3 Hz), 7.76 (d, 2H, *J* = 8.3 H), 7.90 (d, 1H, *J* = 8.2 Hz). ^{13}C-NMR (75MHz, $CDCl_3$): δ 169.4, 153.6, 135.1, 130.2, 129.7, 125.9, 124.1, 121.7, 120.6. IR(neat): 3019, 1710, 1661, 1628, 1549, 1515, 1214, 742, 667, 627 cm^{-1}. MS (ESI): 244 (M+H). HR-MS: Calculated for $C_{13}H_9NS_2$ (M+H) = 244.0249. Found = 244.0244.

1-Methyl-2-(phenylthio)-1H-benzo(d)imidazole (3i) (Table 2, Entry 6): Yellow liquid, yield 150 mg (82%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.70 (d, 1H, *J* = 7.6 Hz), 7.20-7.30 (m, 8H), 3.70 (s, 3H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 142.0, 132.0, 130, 129.4, 129.0, 127.6, 23.2, 122.4, 119.8, 109.0, 30.7. IR (neat): 3056, 2923, 2852, 1741, 1645, 1611, 1581, 1441, 1365, 1277, 1219, 1153, 1110, 1023, 1003, 818, 772, 688, 567 cm^{-1}. MS



Scheme 2 Plausible catalytic cycle for the direct selenation

(ESI): 241 (M+H). HR-MS: Calculated for $C_{14}H_{12}N_2S$ (M+H) = 241.0794. Found = 241.0793.

4-Methyl-2-(phenylthio)thiazole (**3j**) (Table 2, Entry 7): Yellow liquid, yield 175 mg (78%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.58-7.60 (m, 2H), 7.38-7.40 (m, 2H), 7.21 (s, 1H), 6.70 (s,1H), 2.41 (s, 3H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 164.7, 153.5 133.5, 132.0, 129.6, 129.3, 115.0, 17.1. IR (neat): 3019.7, 1710, 1661.4, 1628, 1549, 1515.3, 1214.8, 742, 667, 627 cm^{-1}. MS (ESI): 208 (M+H). HR-MS: Calculated for $C_{10}H_9NS_2$ (M+H) = 208.0249. Found = 208.0250.

2-Phenyl-5-(phenylthio)-1, 3, 4-oxadiazole (**3k**) (Table 2, Entry 8): Yellow liquid, yield 140 mg (80%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.97-7.90 (m, 2H), 7.69-7.60 (m, 2H), 7.50-7.40 (m, 6H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 166.3, 162.8, 133.6, 131.7, 129.7, 128.9, 126.7, 123.4. IR (neat): 3019, 1710, 1661, 1628, 1549, 1515, 1214, 742, 667, 627 cm^{-1}. MS (ESI): 255 (M+H). HR-MS: Calculated for $C_{14}H_{10}N_2OS$ (M+H) = 255.9684. Found = 255.9693.

2-((Phenylselanyl)thio)benzo(d)thiazole (5a) (Table 3, Entry 1): Yellow liquid, yield 155 mg (77%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.90 (d, 1H, *J* = 8.2 Hz), 7.70 (d, 1H, *J* = 7.6 Hz), 7.50-7.61 (m, 2H), 7.24-7.28 (m,5H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 131.4, 129.8, 129.5, 129.1, 128.9, 127.6, 126.5, 125.2, 122.5, 121.2. IR (neat): 2956, 2918, 2850, 1727, 1462, 1426.3, 1377.8, 1265, 1123, 1077, 1003, 972, 909, 727, 687 cm^{-1}. MS (ESI): 323 (M+H). HR-MS: Calculated for $C_{13}H_9NSeS_2$ (M+H) = 323.9414. Found = 323.9409.

2-Phenyl-5-((phenylselanyl)thio)-1,3,4-oxadiazole (5b) (Table 3, Entry 2): Yellow liquid, Yield 160 mg (70%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.90 (d, 1H, *J* = 7.5 Hz), 7.20-7.61 (m, 9H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 133.2, 132.0, 131.4, 129.5, 129.1, 127.6, 126.8. IR(neat): 2919, 2851, 1781, 1726, 1609, 1578, 1576, 1549, 1465, 1349, 1286, 1219, 1170, 1066, 1023, 956, 772, 689 cm^{-1}. MS (ESI): 335 (M+H). HR-MS: Calculated for $C_{14}H_{10}N_2OSSe$ (M+H) = 335.1021. Found = 335.1017.

1-Phenyl-5-((phenylselanyl)thio)-1H-tetrazole (5c) (Table 3, Entry 3): Yellow liquid, yield 150 mg (80%). ^{1}H-NMR (500MHz, $CDCl_3$): δ 7.70 (d, 1H, *J* = 7.5 Hz), 7.60-7.20 (m, 9H). ^{13}C-NMR (75MHz, $CDCl_3$): δ 153.2, 150.9, 149.9, 149.2, 149.1, 149.0, 148.6 147.1, 144.0. IR (neat): 3019, 1710, 1661, 1628, 1549, 1515, 1214, 742, 667, 627 cm^{-1}. MS (ESI): 334 (M+H). HR-MS: Calculated for $C_{13}H_{10}N_4SSe$ (M+H) = 334.9864; Found (M+H) = 334.9860.

Supporting Information: Copies of ^{1}H and ^{13}C NMR spectra are available.

Acknowledgements: ORGIN program (CSIR) and CSIR (New Delhi) is gratefully acknowledged for awarding the fellowship to G. B and VN.

Research funding: Financial support was provided by the DST, New Delhi, India (Grant No: SR/S1/OC-08/2011).

Conflict of interest: Authors state no conflict of interest.

Data availability statement: All data generated or analyzed during this study are included in this published article and its supplementary information files.

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