Tetrahedron 67 (2011) 9565–9575

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Copper catalyzed/mediated synthetic methodology for ebselen and related isoselenazolones

Shah Jaimin Balkrishna, Bhagat Singh Bhakuni, Sangit Kumar *

Department of Chemistry, Indian Institute of Science Education and Research Bhopal (IISER), Bhopal, MP 462 023, India

ARTICLE INFO

Article history:
Received 29 August 2011
Received in revised form 29 September 2011
Accepted 30 September 2011
Available online 6 October 2011

ABSTRACT

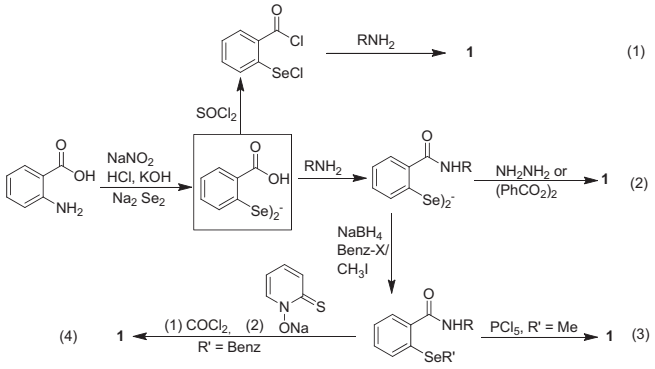
Scope of the copper catalyzed/mediated selenium-nitrogen coupling reaction has been studied for the synthesis of isoselenazolones. It is noticed that the 2-chloro, 2-bromo-, and 2-iodo-aryl amides substrates can be exploited in the selenium–nitrogen coupling reaction by employing 25–100 mol % of CuI/1,10-phenanthroline (L) and potassium carbonate as a base in DMF. Furthermore, electron rich 2-chloroarylamides also underwent selenium–nitrogen coupling reaction to give biologically important selenium–nitrogen heterocycles. Also, copper-catalyzed selenium–nitrogen coupling reaction has been meticulously applied for the synthesis of diaryl diselenides having methoxy, amine, and amide functionality from respective aryl iodides in the presence of stoichiometric amount of succinimide as an external Se–N coupling partner.

© 2011 Elsevier Ltd. All rights reserved.

1. Introduction

Ebselen (PZ 51, 2-phenyl-1,2-benzoisoselenazol-3-(2*H*)-one, **1**) having Se–N bond exhibits significant antioxidant activity and therefore is a promising mimic of glutathione peroxidase antioxidant selenoenzyme.[1,2] As a result, ebselen is a benchmark compound in many hydroperoxides and organic peroxides decomposing assays and exhibits a broad spectrum of biological activities, namely anti-inflammatory, anti-atherosclerotic, and cytoprotective.[3] Hydroperoxides and organic peroxides decomposing activity of ebselen and related isoselenazolones has also been studied as oxygen transfer reagent in many organic reactions.[4] In view of its biological applications, particularly hydroperoxides and organic peroxides decomposing antioxidant activity and minimal toxicity, synthesis of several related aryl/alkyl isoselenazolones comprising Se–N bond, have been reported.[1a,5] Ebselen was first synthesized by Lesser and Weiss in 1924.[6] After that several synthetic routes have been developed to prepare organoselenium–nitrogen heterocycles.[7–16] Literature survey on the synthetic methods for ebselen and related isoselenazolones, is depicted in Schemes 1 and 2 (Eqs. 1–8).

Synthesis of ebselen and related isoselenazolones mainly depends on two routes; bis(*ortho*-benzoic acid) diselenide and *ortho*-lithiation of benzanilide. Bis(*ortho*-benzoic acid) diselenide route is a conventional method, in which anthranilic acid is converted into Se–N heterocycle by a series of reactions (Eq. 1, Scheme 1).[7] Despite the lengthy nature, this method is commonly used for the construction of ebselen analogues due to its broad substrate scope, particularly, for the synthesis of ebselen analogues containing various N—*R* (R=alkyl, aryl) substituents.[1g,l,8,9] A broad range of ebselen analogues has been synthesized by this method in which treatment of *ortho*-benzoyl chloride selenenyl chloride occurs with various amines (ammonia, alkyl amines, substituted aryl amines).

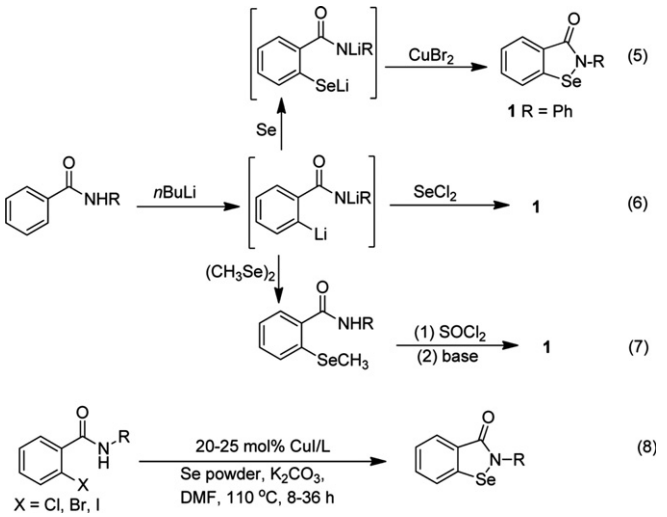


Scheme 1. Synthetic methods for ebselen and related isoselenazolones.

Lithiation route, which was developed by Engman et al., is an expeditious and also widely used method for the construction of Se–N heterocycles.[11–13] In this method, lithiation of benzanilide is occurred by the use of *n*-butyllithium, subsequent reaction with selenium powder, and finally ring closure by copper dibromide gave ebselen in one pot (Eq. 5). The obtained yield was 63%. Further

* Corresponding author. E-mail address: sangitkumar@iiserbhopal.ac.in (S. Kumar).

0040-4020/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2011.09.141



Scheme 2. Reported *ortho*-lithiation routes for the synthesis of ebselen and related isoselenazolones.

improvement in the yield was made by employing lithium diisopropylamide and *n*-butyllithium as lithiating reagent and subsequently ebselen was isolated in better yield (76%).[12]

Although, other methods for the synthesis of aryl isoselenazolones have been reported, these methods depend on either the bis(*ortho*-benzoic acid)diselenide route (Eqs. 2–4) or the Engman method (Eqs. 6 and 7).[10,14b,15] Despite the several reports on the construction of ebselen and related analogues, synthesis of Se–N heterocycles remains challenging. In this regard, of particular interest is the synthesis of substituted ebselen analogues and heteroaromatic isoselenazolones. Moreover, catalytic route to synthesize aryl isoselenazolones has not been described in the literature.

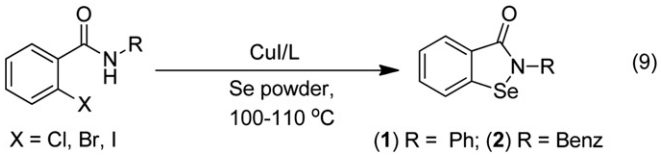
Transition metal catalyzed synthesis of organochalcogens (S, Se, and Te) are benign methods, which offer several advantages over the conventional methods, such as broad substrate scope, mild reaction conditions, and need catalytic amount of reagents to accomplish the transformations. As a result of this, in recent time several groups have explored transition metal catalyzed synthesis of organochalcogens.[17,18] Our research group has described a copper catalyzed synthesis of ebselen analogues from 2-iodo-, 2-bromo-, and activated 2-chloro-arylamide substrates in a preliminary communication (Eq. 9).[19] In this paper, we present the detail study on copper-catalyzed Se–N coupling reaction which includes the compatibility of non-activated 2-chloro-arylamides and synthesis of electron rich isoselenazolones. Also Cu-catalyzed Se–N coupling reaction is applied to the synthesis of diaryl diselenides.

2. Results and discussion

To achieve the compatibility of 2-chloro-arylamides in the copper-catalyzed Se–N coupling reaction and also as suggested by one of the reviewers of our preliminary communication, it was of the interest to study the effect of CuI/1,10-phenanthroline (L) complex loading versus Se–N product formation in the coupling reaction.

We have hereby chosen two substrates; 2-chloro-*N*-phenyl- and 2-chloro-*N*-benzylbenzamide for this purpose. It is evident from the Table 1 that high CuI/L catalyst loading (20–50 mol %) gave good yield of Se–N coupled products from chloro substrates. High CuI/L loading from 50 to 75 mol % produced nearly same yield of isoselenazolones. Other parameters, such as increase in temperature from 110 to 150 °C and change in base potassium *tert*-butoxide and sodium hydroxide were ineffective for chloro substrates in the Se–N coupling reaction and mainly lead to side products, despite the complete consumption of substrates.

Table 1
Optimization of selenium–nitrogen coupling reaction on 2-halo-aryl amide substrates



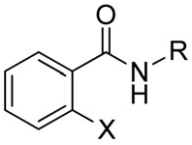
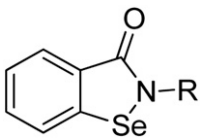
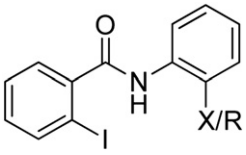
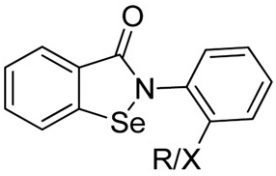
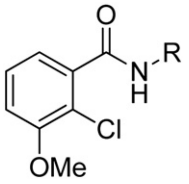
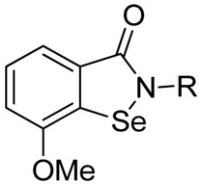
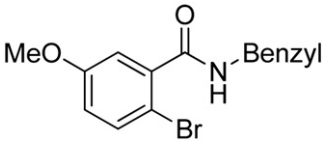
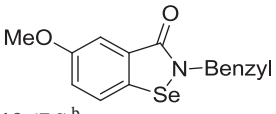
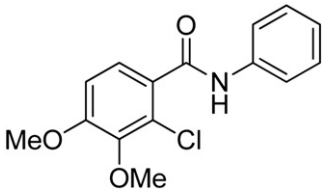
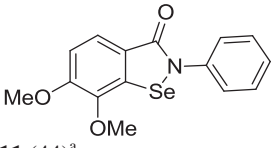
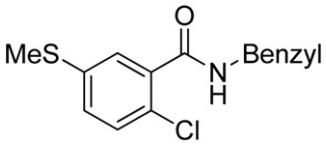
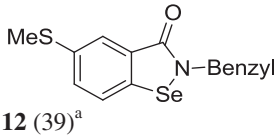
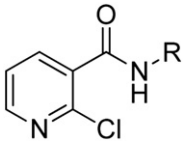
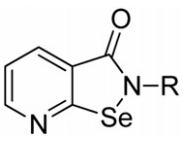
Entry	Substrates	CuI/L[a]	Base	Solvent	Time (h)	**1**[b] (%)	**2**[b] (%)
1	Ar–Cl	CuI/L, 20 mol %	K_2CO_3	DMF	24[c,d]	47	53
2	Ar–Cl	CuI/L, 50 mol %	K_2CO_3	DMF	24[c,d]	54	83
3	Ar–Cl	CuI/L, 75 mol %	K_2CO_3	DMF	24[c,d]	55	83
4	Ar–Cl	None	K_2CO_3	DMF	36[c,d]	None	None
5[e]	Ar–I	CuI/L	K_2CO_3	DMF	8,[c] 12[d]	84	94
6[e]	Ar–Br	CuI/L	K_2CO_3	DMF	16,[c] 26[d]	78	91

[a] CuI/1,10-phenanthroline (L) (20 mol %) was used otherwise noticed.
[b] Isolated yield otherwise mentioned.
[c] Reaction time for *N*-phenyl substrates.
[d] Reaction time for *N*-benzyl substrates.
[e] Reaction conditions included for comparison purpose (see Ref. 19).

Having optimization condition on 2-chloro substrates and earlier optimized condition on bromo and iodo substrates (entries 2, 5, and 6, Table 1) in hand, a series of isoselenazolones **1**–**15** have been synthesized from 2-chloro-, 2-bromo-, 2-iodo-arylamide substrates (entries 1–10, Table 2). Readers are suggested to follow our earlier communication for the synthesis of a diverse series of isoselenazolones from respective 2-iodo- and 2-bromo-arylamides.[19] Isoselenazolones **1** and **2** were obtained in 54 and 83% yield from respective chloro substrates (entries 1–3, Table 2). A small amount of byproduct presumably respective monoselenide was also formed along with the formation of **1**. However, respective monoselenides were not observed in the case of isoselenazolones **2**–**15**. In our preliminary study, difficulty was encountered in the purification of 2-bromo-substituted isoselenazolone **6**. In this study, isoselenazolones substituted with fluoro, chloro, bromo, and methoxy groups were isolated in pure form by using copper catalyzed coupling reaction at 90 °C (entries 4–6, Table 2). The next set of substrates was electron rich and readily accessible 2-chloro/bromo-arylamides, which we explored for the Se–N coupling reaction (entries 8–12, Table 2). It is worth mentioning that despite the theoretical investigation on the antioxidant activity of methoxy substituted ebselen analogues and promising hydroperoxides and organic peroxides decomposing activity of methoxy substituted diaryl diselenides, synthesis of methoxy substituted isoselenazolones has not been well documented.[15,20] Moreover, scarce availability of electron rich 2-bromo- and 2-iodo-aryloic acids made the synthesis even difficult. 2-Chloro/bromo-3-methoxy-arylamide substrates gave desired isoselenazolones in 57–76% yield in the copper-catalyzed Se–N coupling reaction. It follows that Se–N coupling reaction could not be observed for the electron rich chloro-aryl substrate in the presence of 20–25 mol % of CuI/L under standard conditions and substrate was recovered in 87% yield (entry 8, Table 2). Interestingly, Se–N coupling took place in the electron rich chloro substrates by employing 50 mol % of CuI/L catalyst. Under the same conditions, the chloro substrate with two methoxy groups reacted to give the corresponding isoselenazolone **11**. Similarly, chloro substrate with methylthio functionality was transformed into isoselenazolone **12**. Although isolated yield is moderate to good for electron rich aryl isoselenazolones **8**–**12**, this could possibly be the best method to construct electron rich isoselenazolones from readily available chloro-arylamide substrates.

For the synthesis of pyridyl isoselenazolones, readily accessible chloro nicotinamide substrates were under taken for Se–N coupling (entries 13–15, Table 2).

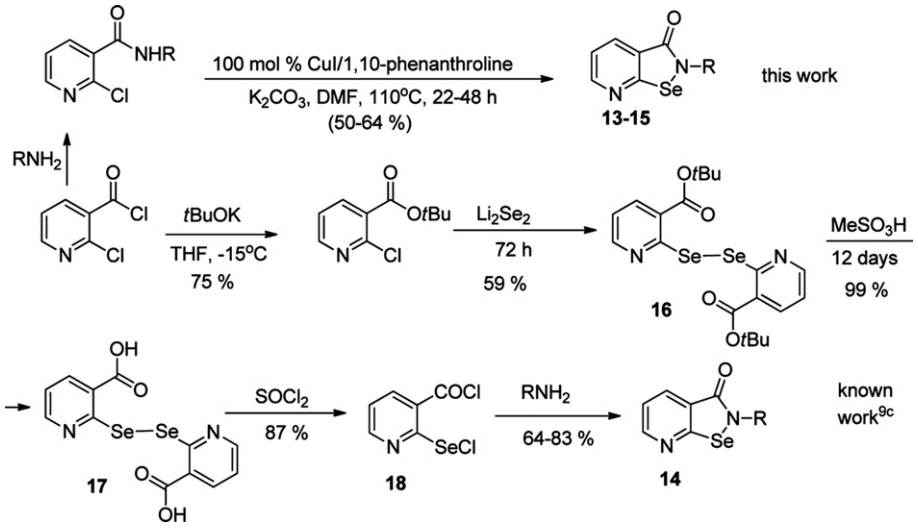
Table 2
Construction of isoselenazolones from 2-halo-arylamides by copper iodide catalyzed/mediated Se–N coupling reaction

Entry	Substrate	Product yield in %
		
1	R=Phenyl, X=Cl	**1** R=Phenyl (54)[a]
1	R=Benzyl, X=Cl	**2** R=Benzyl (83)[a]
3	R=*n*-Butyl, X=I	**3** R=*n*-Butyl (72)[b]
		
4	X/R=F	**4** X/R=F (71)[b]
5	X/R=Cl	**5** X/R=Cl (82)[b]
6	X/R=Br	**6** X/R=Br (93)[b]
7	X/R=OMe	**7** X/R=OMe (86)[b]
		
8	R=Ph (57)	**8** R=Ph (57)[a]
9	R=Benzyl (67)	**9** R=Benzyl (67)[a]
10		 **10** (76)[b]
11		 **11** (44)[a]
12		 **12** (39)[a]
		
13	R=Benzyl	**13** R=Benzyl (50)[c]
14	R=Cyclohexyl	**14** R=Cyclohexyl (64)[c]
15	R=*n*-Butyl	**15** R=*n*-Butyl (55)[c]

[a] Isolated yield by employing 50 mol % of CuI/1,10-phenanthroline (L) from chloro substrate, otherwise noted.
[b] Yield obtained from 2-bromo-arylamide, and 25 mol % of CuI/L was used.
[c] CuI/L (100 mol %) was used.

It is worth mentioning here that construction of pyridyl isoselenazolones has proven to be difficult by an earlier reported method (Scheme 3, see products **16**–**18**).[9c] Reported synthesis for pyridyl isoselenazolones, involves 2-chloronicotinoyl chloride as the precursor, which undergoes multi-step reactions: protection, selenation, deprotection, chlorination, and amination. Among these multi-steps, two of them: selenation in which reaction of dilithium diselenide occurs with *tert*-butyl 2-chloronicotinate; and deprotection of bis 2-(*tert*-butyl nicotinate) diselenide **16** into bis(nicotinic acid) diselenide **17** require 72 h and 12 days, respectively.

Preparation of thiophenyl and alkyl isoselenazolones was unsuccessful under optimized conditions developed for electron rich isoselenazolones and also by using 100 mol % CuI/L. Chloroalkylamides gave respective four-membered lactams **19** and **20** quantitatively under optimized reaction conditions instead of alkyl Se–N heterocycles (Scheme 4). It seems that the formation of copper–substrate complex (RN–CuLn) is not feasible in chloroalkylamides as we have proposed for the 2-iodo-arylamide substrates. Since formation of lactam **19** was observed without the addition of CuI/L complex in the presence of K_2CO_3, it is reasonable to assume that intramolecular coupling of alkyl carbon and nitrogen is faster than the formation of RN–CuLn complex and thus may not facilitate the formation of alkyl isoselenazolones.



Scheme 3. Synthetic methods for the construction of pyridyl isoselenazolones.

Chloro-nicotinamide substrates were subjected for Se–N coupling reaction by using 50 mol % of catalyst as established for the synthesis of **1**–**4** from corresponding chloro substrates. However, Se–N product formation was not observed even after 72 h. By exploiting stoichiometric amount of copper iodide/1,10-phenanthroline, pyridyl Se–N heterocycles were obtained in 50–64% yield from readily accessible 2-chloro-nicotinamide substrates. The obtained yield from pyridyl substrates are moderate and also high loading of CuI/L (100 mol %) complex is required. Nonetheless, the pyridyl isoselenazolones are obtained from easily accessible 2-chloro-nicotinamide in one pot and in 22–48 h. The structure of pyridyl isoselenazolone **13** was established by single crystal X-ray crystallography in addition to NMR and IR spectral characterization (Fig. 1).

Next, we were able to study that the copper-catalyzed Se–N coupling reaction could be used for the synthesis of diaryl diselenides, which are the key precursors in organoselenium chemistry, from aryl iodides. For this purpose, we set to use stoichiometric amount of *sec*-amide [RC(O)NHR] as an external Se–N coupling partner in the copper catalyzed reaction (Table 3).

N-Benzyl-, *N*-butyl-, and *N*-phenyl-benzamides were studied as the external Se–N coupling partner for the synthesis of diaryl diselenides. None of the *sec*-amides gave satisfactory results under optimized condition for CuI/L catalyzed Se–N coupling reaction. The use of succinimide as a Se–N coupling partner provided diaryl diselenides in moderate to good yield. A small amount of

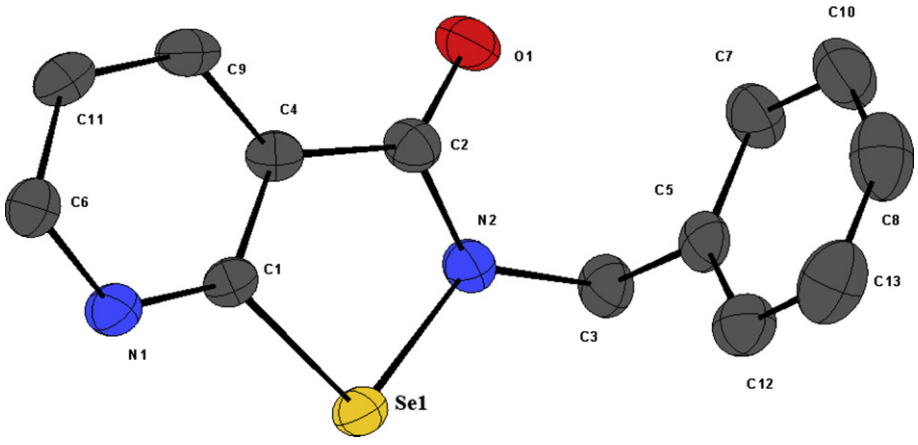
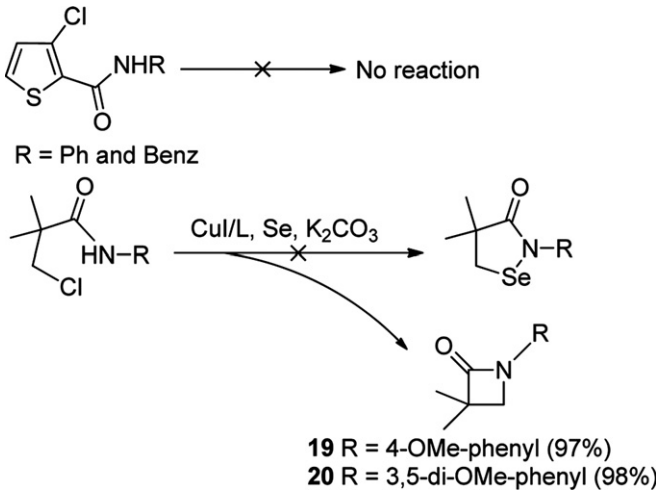


Fig. 1. ORTEP view of **13** with 50% ellipsoidal probability.



Scheme 4. Attempted synthesis of thiophenyl and alkyl isoselenazolones.

byproducts presumably respective triselenides was also observed in the case of diselenides **21**–**28**. It turns out that the succinimide offers many advantages, such as easy availability, facile hydrolysis of Se–N bond (vide infra), which in turns facilitate diaryl diselenide formation, and easy removal of succinimide from reaction mixture. These features make succinimide a better Se–N external coupling partner for the synthesis of diaryl diselenides. Copper-catalyzed Se–N coupling occurred smoothly with aryl iodides, succinimide, and selenium powder under the optimized conditions as described for the synthesis of isoselenazolones. Aqueous hydrolysis of the reaction mixture afforded diaryl diselenides **21**–**28** from respective aryl iodides (Table 3). Diaryl diselenides **23**–**25** having $-NH_2$, $-NHCOR$, and $-CONR_2$ functional groups are difficult to access by conventional methods and either involves protection and deprotection strategy and/or require excess of reagents. Diaryl diselenides **23**–**25** were obtained in 45–84% by this Se–N coupling reaction using easily available CuI/1,10-phenanthroline catalyst in the presence of potassium carbonate base under mild reaction conditions. Also hetero-aryl; thiophenyl and pyridyl diselenides (**26** and **27**) were accessible by copper catalyzed reaction.

3. Mechanistic consideration

In the mechanistic considerations, plausible reaction pathway is depicted in Scheme 5 based on the control experiments, related reported copper catalyzed amidation of aryl halides, and copper amide complexes.[21] We believe that this is a base promoted reaction which proceeds by Cu–N bond formation intermediate. As the formation of selenazolones was not observed in the absence of base and in the presence of 100 mol % of catalyst, the base may facilitates the formation of LnCu–N complex intermediate. Insertion of selenium in to Cu–N bond might lead to the N–Se–CuLn intermediate and this intermediate could react intramolecularly to *ortho* halogen and then followed by reductive elimination lead to form desired Se–N heterocycle and concomitant regeneration CuLnX catalyst. Although the isolation of proposed N–Se–CuLn intermediate was unsuccessful, the formation of diaryl diselenides from aryl iodide in the presence of stoichiometric amount of succinimide in this copper catalyzed reaction supports the proposed mechanism.

4. Conclusion

In summary, scope of copper-catalyzed Se–N coupling reaction has been studied with respect 2-halo-aryl/alkylamides. We have shown that copper-catalyzed selenium–nitrogen coupling reaction can be applied not only for 2-iodo- and 2-bromo-arylamides but also 2-chloro-arylamides substrates. This has been established by the synthesis of methoxy and methylthio substituted electron rich phenyl isoselenazolones and pyridyl isoselenazolones from respective 2-chloro-arylamides. It is indeed noteworthy that the copper-catalyzed Se–N coupling reaction has been constructively utilized for the synthesis of diaryl diselenides from the respective aryl iodides.

5. Experimental section

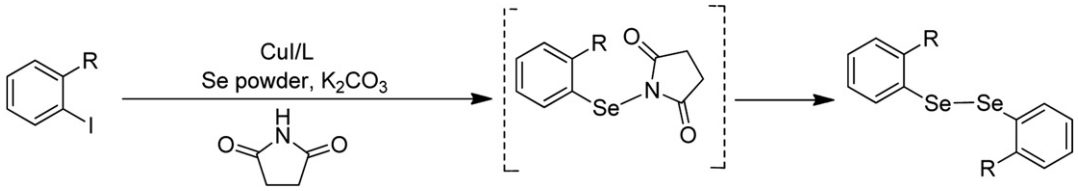
5.1. General experimental details

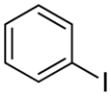
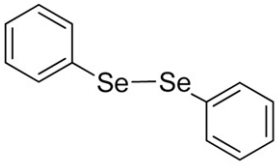
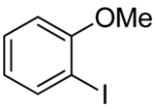
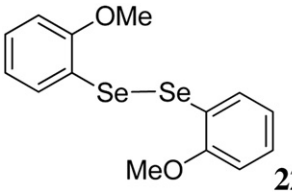
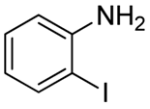
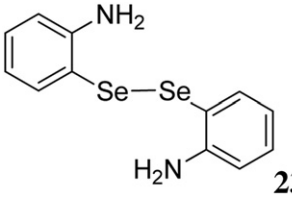
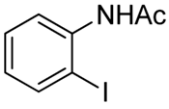
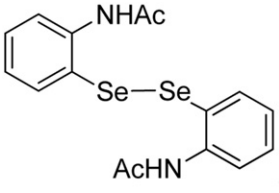
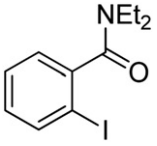
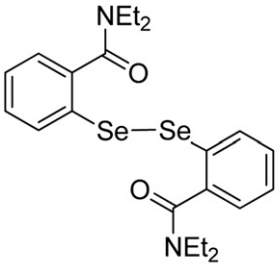
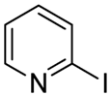
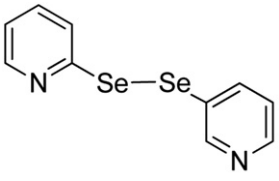
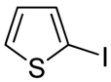
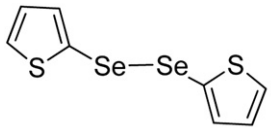
All NMR experiments were carried out on 400 or 500 MHz spectrometers in DMSO-d_6 or $CDCl_3$ and NMR chemical shifts are reported in parts per million referenced to the solvent peaks of $CDCl_3$ (7.26 ppm for ^1H and 77.0 ($\pm$0.1) ppm for ^{13}C, respectively) or DMSO-d_6 (2.50 ppm for ^1H and 39.50 ppm for ^{13}C, respectively). High resolution mass spectra (HRMS) are reported for ions of ^{80}Se. Mass analysis is performed on quadruple-time of flight (Q-TOF) mass spectrometer equipped with an ESI source (+ve). Infrared (IR) spectra were recorded as a pellet in KBr with an FTIR machine. Melting points are uncorrected. DMF with sure seal septa, selenium powder (60 mesh size), copper iodide, and 1,10-phenanthroline were used as received from Aldrich. Grinded anhydrous K_2CO_3 powder was used which was grinded using mortar, dried in oven at 160 °C for 6 h and stored in a desiccator. Selenium–nitrogen coupling reactions were carried out under nitrogen atmosphere. Substituted benzoyl chlorides were prepared from respective benzoic acids by refluxing with excess of thionyl chloride otherwise prepared according to reported procedure. Excess of thionyl chloride was removed under vacuo and resulted residue was used for amide preparation without further purification. Silica gel (60–120 mesh size) was used for column chromatography. TLC analysis of reaction mixtures was performed using silica gel plates.

*5.1.1. Representative copper-catalyzed Se–N coupling procedure for the preparation of isoselenazolones; synthesis of ebselen (**1**).* Copper iodide (82 mg, 0.4 mmol) and 1,10-phenanthroline (78 mg, 0.4 mmol) were added into DMF (3 mL) in a single neck flask. Resulted brownish solution was stirred for 15 min and then 2-chloro-*N*-phenylbenzamide[22] (0.20 g, 0.86 mmol), selenium powder (81 mg, 1.0 mmol), and potassium carbonate powder (178 mg, 1.3 mmol) were added sequentially to same reaction flask. Brown colored reaction mixture was refluxed at 110 °C using refluxing condenser under nitrogen atmosphere. Progress of reaction was monitored by TLC. Reaction mixture was refluxed for 24 h. After this, reaction mixture was poured into brine solution (50 mL) and stirred for 3 h. Product was precipitated as white solid, which was collected by filtration over Buchner funnel, washed with water (15 mL×3), dried in air, dissolved in ethyl acetate, and concentrated over rotary evaporator. The resulted brown solid was purified by column chromatography using hexane/ethyl acetate (8:2) over silica gel. Yield 128 mg (54%). Characterization data (mp, ^1H NMR, Mass, and IR) is in accordance with reported one.[19]

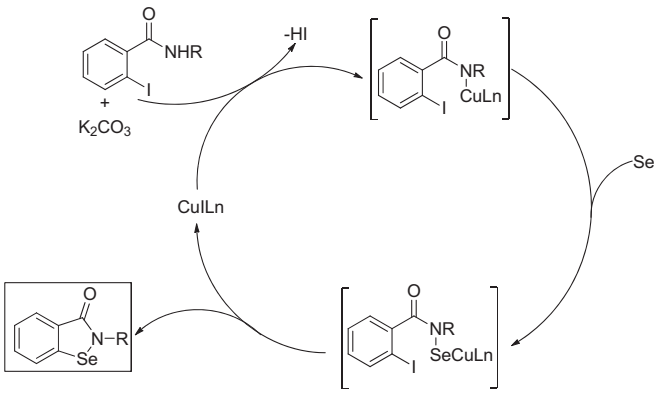
*5.1.2. 2-Benzylbenzo[d][1,2]selenazol-3(2H)-one (**2**).* Synthesis of **2** from 2-chloro-*N*-benzylbenzamide[23] (0.4 g, 1.6 mmol) was carried out at 1.6 mmol scale using CuI (154 mg, 0.8 mmol), 1,10-phenanthroline (146 mg, 0.8 mmol), selenium powder (0.15 g, 1.9 mmol), and K_2CO_3 (0.34 g, 2.46 mmol) in DMF (4 mL). Reaction mixture was refluxed for 24 h at 110 °C. After this reaction mixture was poured into brine solution, stirred for 3 h, reaction mixture together with brine solution (30 mL) extracted with ethyl acetate (15 mL×4). Ethyl acetate layer washed with water (15 mL), dried

Table 3
Synthesis of diaryl diselenide from aryl iodide by using CuI/L catalyst and succinimide



Entry	Substrate	Product (% yield)[a]
1		 **21** 65 %)
2		 **22** (84 %)
3		 **23** (45 %)
4		 **24** (60 %)
5		 **25** (50%)
6		 **26** (54%)
7		 **27** (65%)

[a] Isolated yield by employing 15–25 mol % of CuI/1,10-phenanthroline (L), 1.2 equiv of Se powder, and 1.5 equiv of K_2CO_3.



Scheme 5. Proposed reaction pathway for the copper-catalyzed Se–N coupling.

over Na_2SO_4, evaporated on rotary evaporator. The resulted yellowish liquid product was chromatographed over silica gel using CH_2Cl_2 and yielded crystalline solid (0.39 g, 83%). Characterization data (mp, ^{1}H NMR, Mass, and IR) is in accordance with reported one.[19]

*5.1.3. 2-Butylbenzo[d][1,2]selenazol-3(2H)-one (**3**).* Compound **3** was prepared from 2-iodo-*N*-butylbenzamide[24] (700 mg, 2.4 mmol) and selenium powder (220 mg, 2.8 mmol) using CuI (110 mg, 0.58 mmol), 1,10-phenanthroline (104 mg, 0.58 mmol), and K_2CO_3 (0.48 g, 3.5 mmol) in 5.0 mL of DMF. Resulted reaction mixture was refluxed at 110 °C for 10 h. Standard workup and column chromatography as mentioned for isoselenazolone **2** yielded white liquid, which solidified on standing. Yield 423 mg (72%), mp 92 °C (92 °C).[10] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J=7.7 Hz, 1H), 7.63 (d, J=7.9, 1.0 Hz, 1H), 7.57 (dt, J=7.8, 1.0 Hz, 1H), 7.42 (t, J=7.7 Hz, 1H), 3.86 (t, J=7.2 Hz, 2H), 1.71 (p, J=7.3 Hz, 2H), 1.42 (sextet, J=7.3 Hz, 2H), 0.96 (t, J=7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.2, 138.1, 131.7, 128.5, 127.7, 126.0, 124.3, 44.4, 32.5, 19.8, 13.6. HRMS (ESI) m/z 256.0249 (calcd for $C_{11}H_{13}N_1O_1$ $^{80}Se_1$ + H^+: 256.0235).

*5.1.4. 2-(2-Fluorophenyl)benzo[d][1,2]selenazol-3(2H)-one (**4**).* Compound **4** was prepared at 1.2 mmol scale from 2-iodo-*N*-(2-fluorophenyl)benzamide[25] (0.30 g, 0.9 mmol), CuI (41 mg, 0.22 mmol), 1,10-phenanthroline (40 mg, 0.22 mmol), selenium powder (83 mg, 1.05 mmol), and K_2CO_3 (0.18 g, 1.3 mmol) in 5 mL of DMF. Resulted reaction mixture was refluxed at 90 °C for 16 h and then poured into brine solution (100 mL) and stirred for 2 h. Resulted aqueous layer together with brown precipitate was extracted with ethyl acetate (25 mL×4), organic layer washed with water (100 mL), dried over Na_2SO_4, concentrated under vacuo to obtain brown solid, which was purified by column chromatography on silica gel using hexane/ethyl acetate (7:3). R_f (30% hexanes/EtOAc) 0.5. Yield 182 mg (71%), mp 160–161 °C (165–167 °C).[7] ^{1}H NMR (400 MHz, $CDCl_3$) δ ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (d, J=8.0 Hz, 1H), 7.92 (dd, J=7.8, 1.0 Hz, 1H), 7.71 (m, 1H), 7.54–7.29(m, 5H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.0, 159.4, 156.9, 140.8, 132.8, 130.7, 130.00, 129.92, 128.4, 127.3, 126.90, 126.77, 126.69, 126.52, 125.41, 125.38, 117.1, 116.9. HRMS (ESI) m/z 315.9649 (calcd for $C_{13}H_8F_1N_1O_2^{80}Se_1$+Na: 315.9648).

*5.1.5. 2-Iodo-N-(2-chlorophenyl)benzamide (substrate for isoselenazolone **5**).* 2-Chloroaniline (1.15 g, 9.0 mmol) and triethyl amine (3.1 mL, 22.0 mmol) in DCM (30 mL) was added drop wise to a cold solution of 2-iodo-benzoyl chloride (2.00 g, 7.5 mmol) in DCM (40 mL). The resulted reaction mixture was stirred at 0 °C for 1 h and 3 h at room temperature. After this reaction mixture was poured into water (200 mL) and 50 mL of DCM was added. Organic layer was separated, washed with 10% (v/v) aqueous HCl solution. Dried over Na_2SO_4 (5 g), concentrated under vacuo, purification by column chromatography using DCM as an eluent yielded white crystalline product. R_f (2% DCM/MeOH) 0.5. Yield 2.47 g, 92%, mp 139–141 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J=8.2 Hz, 1H), 7.99–7.96 (m, 2H), 7.58 (d, J=7.6 Hz, 1H), 7.48 (t, J=7.5 Hz, 1H), 7.44 (dd, J=8.1, 1.4 Hz, 1H), 7.37 (t, J=8.0 Hz, 1H), 7.20 (td, J=7.6, 1.6 Hz, 1H), 7.14 (td, J=7.6 Hz, 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 141.8, 140.4, 134.3, 131.8, 129.2, 128.45, 128.41, 127.4, 125.3, 123.3, 121.9, 92.4. IR (plate): 3263, 2920, 2852, 1654, 1581, 1523, 1478, 1438, 1307, 1057, 750 cm^{-1}. HRMS (ESI) m/z 379.9327 (calcd for $C_{13}H_9Cl_1I_1N_1O_1$+Na: 379.9310).

*5.1.6. 2-(2-Chlorophenyl)benzo[d][1,2]selenazol-3(2H)-one (**5**).* Compound **5** was prepared at 1.2 mmol scale from 2-iodo-*N*-(2-chlorophenyl)benzamide (0.50 g, 1.4 mmol), CuI (66 mg, 0.35 mmol), 1,10-phenanthroline (63 mg, 0.35 mmol), selenium powder (0.13 g, 1.7 mmol), and K_2CO_3 (0.29 g, 2.1 mmol) in 5 mL of DMF. Resulted reaction mixture was refluxed at 90 °C for 14 h and then poured into brine solution (100 mL) and stirred for 2 h. Resulted aqueous layer together with brown precipitate was extracted with ethyl acetate (30 mL×4), organic layer washed with water (120 mL), dried over Na_2SO_4, concentrated under vacuo to obtain brown solid, which was purified by column chromatography on silica gel using hexane/ethyl acetate (8:2). R_f (20% hexanes/EtOAc) 0.3. Yield 354 mg (82%), mp 194 °C (decomposed). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (d, J=8.0 Hz, 1H), 7.91 (dd, J=7.8, 1.5 Hz, 1H), 7.71 (m, 1H), 7.63 (m, 1H), 7.53–7.50 (m, 2H), 7.48–7.44 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.1, 140.9, 136.7, 133.1, 132.7, 131.6, 130.65, 130.25, 128.56, 128.47, 127.3, 126.6, 126.5. IR (plate): 2920, 1666, 1585, 1510, 1480, 1431, 1303, 1242, 1026, 748 cm^{-1}. HRMS (ESI) m/z 331.9350 (calcd for $C_{13}H_8Cl_1N_1O_1^{80}Se_1$+Na: 331.9355).

*5.1.7. 2-(2-Bromophenyl)benzo[d][1,2]selenazol-3(2H)-one (**6**)[19].* Compound **6** was prepared at 1.0 mmol scale from 2-iodo-*N*-(2-bromophenyl)benzamide[19] (0.40 g, 1.0 mmol), CuI (47 mg, 0.25 mmol), 1,10-phenanthroline (45 mg, 0.25 mmol), selenium powder (94 mg, 1.2 mmol), and K_2CO_3 (0.20 g, 1.5 mmol) in 5 mL of DMF. Resulted reaction mixture was refluxed at 90 °C for 20 h and then poured into brine solution (100 mL) and stirred for 2 h. Resulted aqueous layer together with brown precipitate was extracted with ethyl acetate (25 mL×4), organic layer washed with water (100 mL), dried over Na_2SO_4, concentrated under vacuo to obtain brown solid, which was purified by column chromatography on silica gel using hexane/ethyl acetate (8:2). Yield 327 mg (93%), ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J=8.0 Hz, 1H), 7.71–765 (m, 3H), 7.49–7.47 (m, 2H), 7.40 (t, J=7.8 Hz, 1H), 7.28 (d, J=7.8 Hz, 1H). HRMS (ESI) m/z: 353.9032($C_{13}H_8Br_1N1O_1$ $^{80}Se_1$+H^+: 353.9033)

*5.1.8. 2-(2-Methoxyphenyl)benzo[d][1,2]selenazol-3(2H)-one (**7**).* Compound **7** was prepared at 0.9 mmol scale from 2-iodo-*N*-(2-methoxyphenyl)benzamide[26] (0.30 g, 0.85 mmol), CuI (40 mg, 0.20 mmol), 1,10-phenanthroline (38 mg, 0.21 mmol), selenium powder (80 mg, 1.0 mmol), and K_2CO_3 (0.18 g, 1.3 mmol) in 4 mL of DMF. Resulted reaction mixture was refluxed at 90 °C for 18 h and then poured into brine solution (100 mL) and stirred for 2 h. Resulted aqueous layer together with brown precipitate was extracted with ethyl acetate (25 mL×4), organic layer washed with water (100 mL), dried over Na_2SO_4, concentrated under vacuo to obtain brown solid, which was purified by column chromatography on silica gel using hexane/ethyl acetate (5:5). R_f (50% hexanes/EtOAc) 0.6. Yield 220 mg (86%), mp 172–174 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, J=8.0 Hz, 1H), 7.88 (dd, J=7.8, 1.0 Hz, 1H), 7.67 (m, 1H), 7.47 (t, J=7.6 Hz, 1H), 7.40–7.35 (m, 2H), 7.16 (d, J=8.0 Hz, 1H), 7.03 (dt, J=7.8, 1.0 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.2, 155.7, 140.8, 132.4, 130.2, 129.6, 128.3, 127.79,

127.67, 126.35, 126.28, 121.0, 113.1, 56.2. IR (plate): 2920, 1670, 1634, 1496, 1442, 1342, 1269, 1246, 1107, 1045, 1022, 741 cm^{-1}. ESMS (ESI) *m/z*: 306 ($M+H^+$). HRMS (ESI) *m/z* 306.0040 (calcd for $C_{14}H_{11}N_1O_2{}^{80}Se_1+H^+$: 306.0033).

*5.1.9. 2-Chloro-3-methoxy-N-phenylbenzamide (substrate for Isoselenazolone **8**).* 2-Chloro-3-methoxybenzoyl chloride (0.95 g, 5.0 mmol) was dissolved in dry CH_2Cl_2 (15 mL) in a single neck flask and cooled to 0 °C. Aniline (0.95 g, 10.1 mmol) in 10 mL of CH_2Cl_2 was slowly added to this solution by dropping funnel. Resulted reaction mixture was stirred for 1 h at 0 °C and 12 h at room temperature. After this, water (50 mL) was added to the reaction flask and stirred for 30 min. Organic layer was extracted with CH_2Cl_2 (50 mL×3) and water layer separated by separating funnel. Organic layer was washed with 10% aqueous HCl (25 mL), with water (25 mL), dried over Na_2SO_4, and evaporated on rotary evaporator under vacuo. The resulted white solid was passed through silica gel using CH_2Cl_2 to obtain pure amide. R_f (3% DCM/MeOH) 0.6. Yield 1.26 g (95%), mp 140–142 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (br s, 1H), 7.63 (d, *J*=8.0 Hz, 2H), 7.37 (t, *J*=7.5 Hz, 2H), 7.31 (t, *J*=8.0 Hz, 1H), 7.27–7.25 (m, 1H), 7.16 (t, 7.5 Hz, 1H), 7.02 (dd, *J*=8.0, 1.2 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.7, 155.3, 137.6, 137.1, 129.0, 127.8, 124.7, 121.2, 120.1, 119.4, 113.6, 56.4. IR (plate): 3282, 3071, 3011, 2929, 1655, 1599, 1495, 1440, 1326, 1273, 1054, 754 cm^{-1}.

*5.1.10. 7-Methoxy-2-phenylbenzo[d][1,2]selenazol-3(2H)-one (**8**).* Isoselenazolone **8** was synthesized using CuI (76 mg, 0.4 mmol), 1,10-phenanthroline (72 mg, 0.4 mmol), 2-chloro-3-methoxy-*N*-phenylbenzamide (0.21 g, 0.8 mmol), selenium powder (0.07 g, 0.9 mmol), and K_2CO_3 (0.42 g, 3.0 mmol) in DMF (3 mL). Reaction mixture was heated at 110 °C for 24 h. Workup and purification for this compound is similar to the isoselenazolone **2**. R_f (100% DCM) 0.4. Yield 137 mg, 57%, mp 138–141 °C (139–140 °C).[15] ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J*=3.0 Hz, 1H), 7.63 (d, *J*=8.5 Hz, 2H), 7.44 (q, *J*=7.5 Hz, 3H), 7.28 (t, *J*=7.5 Hz, 1H), 7.07 (d, *J*=8.0 Hz, 1H), 3.97 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 154.1, 139.4, 129.3, 128.87, 128.26, 126.84, 126.62, 125.3, 121.1, 112.2, 56.0. IR (plate): 2922, 1640, 1590, 1454, 1299, 1270, 1135, 733 cm^{-1}. HRMS (ESI) *m/z* 306.0055 ($C_{14}H_{11}N_1O_2$ $^{80}Se_1+H^+$: 306.0027).

*5.1.11. 2-Benzyl-7-methoxybenzo[d][1,2]selenazol-3(2H)-one (**9**).* Isoselenazolone **9** was prepared by following similar method as described for **3** from 2-chloro-3-methoxy-*N*-benzylbenzamide[23] (0.30 g, 1.1 mmol), CuI (104 mg, 0.5 mmol), 1,10-phenanthroline (98 mg, 0.5 mmol), selenium powder (0.10 g, 1.3 mmol), and K_2CO_3 (0.61 g, 4.4 mmol) in DMF (5 mL). The resulted reaction mixture was stirred for 24 h at 110 °C. Workup procedure is similar to **2**. Compound **9** was purified by column chromatography using silica gel and eluent hexane/ethyl acetate (8:2). R_f (20% Hexane/EtOAc) 0.2. Yield 232 mg, 67%, mp 66–68 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J*=8.0 Hz, 1H), 7.41 (t, *J*=8.0 Hz, 1H), 7.62–7.32 (m, 5H), 6.99 (t, *J*=8.0 Hz, 1H), 5.00 (s, 2H), 3.91 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.4, 154.3, 137.3, 128.78, 128.51, 128.23, 127.92, 127.80, 127.33, 120.6, 111.7, 55.9, 48.7. IR (plate): 3030, 2926, 1644, 1578, 1479, 1270, 1071, 740 cm^{-1}. HRMS (ESI) *m/z* 320.0196 ($C_{15}H_{13}N_1O_2$ $^{80}Se_1$+H+: 320.0184).

*5.1.12. 2-Benzyl-5-methoxybenzo[d][1,2]selenazol-3(2H)-one (**10**).* 5-Methoxybenzyl isoselenazolone **10** was prepared from 2-bromo-5-methoxy-*N*-benzylbenzamide[27] (0.50 g, 1.6 mmol), copper iodide (74 mg, 0.4 mmol), 1,10-phenanthroline (71 mg, 0.4 mmol), selenium powder (0.15 g, 1.9 mmol), and potassium carbonate (0.32 g, 2.3 mmol). The reaction mixture was refluxed for 22 h. Workup and purification procedures are similar as described for compound **2**. Yield 380 mg, 76%, mp 124–126 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J*=3.0 Hz, 1H), 7.43 (d, *J*=8.5 Hz, 1H), 7.36–7.32 (m, 5H), 7.19 (dd, *J*=8.5, 3.0 Hz, 1H), 5.00 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.9, 158.7, 137.1, 129.1, 128.6, 128.29, 128.26, 128.01, 124.9, 121.6, 110.5, 55.5, 48.6. IR (plate): 2925, 1603, 1470, 1342, 1274, 1230, 1126, 1150, 1022, 700 cm^{-1}. HRMS (ESI) *m/z* 320.0194 ($C_{15}H_{13}N_1O_2$ $^{80}Se_1+H^+$: 320.0184).

*5.1.13. 6,7-Dimethoxy-2-phenylbenzo[d][1,2]selenazol-3(2H)-one (**11**).* 6,7-Dimethoxy isoselenazolone **11** was prepared from 2-chloro-3,4-dimethoxy-*N*-phenylbenzamide[23] (0.5 g, 1.7 mmol), copper iodide (164 mg, 0.9 mmol), 1,10-phenanthroline (154 mg, 0.9 mmol), selenium powder (0.16 g, 2.0 mmol), and potassium carbonate (0.94 g, 6.8 mmol). The reaction mixture was refluxed for 24 h. Workup and purification procedures are similar as described for compound **2**. Yield 252 mg, 44%, mp 139–141 °C (139–141 °C).[15] ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J*=8.5 Hz, 1H), 7.61 (d, *J*=8.5 Hz, 2H), 7.42 (t, *J*=8.5 Hz, 2H), 7.26 (m, 1H), 7.09 (d, *J*=8.5 Hz, 1H), 4.003 (s, 3H), 3.997 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 154.7, 142.2, 139.5, 131.3, 129.3, 126.5, 125.3, 125.2, 121.3, 112.7, 60.5, 56.3. IR (plate): 2925, 2853, 1664, 1599, 1492, 1441, 1281, 1040, 744 cm^{-1}. HRMS (ESI) *m/z* 336.0134 ($C_{15}H_{13}N_1O_3$ $^{80}Se_1+H^+$: 336.0133).

*5.1.14. 2-Benzyl-5-(methylthio)benzo[d][1,2]selenazol-3(2H)-one (**12**).* Heterocycle **7** was prepared from copper iodide (82 mg, 0.4 mmol), 1,10-phenanthroline (77 mg, 0.4 mmol), 2-chloro-5-(methylthio)-*N*-benzylbenzamide[28] (0.50 g, 1.7 mmol), selenium powder (0.16 g, 2.1 mmol), and potassium carbonate (0.94 g, 6.8 mmol) in DMF (8 mL). Resulted reaction mixture was heated for 36 h at 110 °C. Reaction workup procedure is similar to **2**. Purification was carried out by using hexane/ethyl acetate (8:2) on silica gel. R_f (20% Hexane/EtOAc) 0.6. Yield (223 mg, 39%), mp 139–141 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.47 (d, *J*=8.5 Hz, 1H), 7.44 (d, *J*=8.5 Hz, 1H), 7.38–7.34 (m, 5H), 5.00 (s, 2H), 2.56 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 137.7, 137.1, 134.4, 130.9, 128.9, 128.5, 128.3, 128.1, 125.4, 124.2, 48.7, 15.9. IR (plate): 2918, 1590, 1543, 1449, 1337, 1079, 816, 761, 695 cm^{-1}. HRMS (ESI) *m/z* 335.9968 ($C_{15}H_{13}N_1O_1S_1$ $^{80}Se_1+H^+$: 335.9956).

*5.1.15. 2-Benzyl[1,2]selenazolo[5,4-b]pyridin-3(2H)-one (**13**).* Isoselenazolone **13** containing pyridine moiety was constructed from *N*-benzyl-2-chloronicotinamide[29] (0.4 g, 1.6 mmol), CuI (310 mg, 1.6 mmol), 1,10-phenanthroline (292 mg, 1.6 mmol), selenium powder (0.19 g, 2.4 mmol), and K_2CO_3 (0.45 g, 3.2 mmol) in DMF (5 mL). Resulted reaction mixture was refluxed for 22 h at 110 °C. Workup was carried out by pouring reaction mixture into saturated $NaHCO_3$ aqueous solution followed by extraction with EtOAc (25 mL×5). Crude product obtained after evaporating EtOAc layer and purified by column chromatography on silica gel using CH_2Cl_2 and EtOAc (8:2). R_f (20% DCM/EtOAc) 0.5 afforded a white crystalline solid. X-ray quality crystals were obtained by using CH_2Cl_2 and hexane (9:1) solvent mixture. 0.234 g (50%), mp: 162–164 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J*=5.0 Hz, 1H), 8.28 (d, *J*=8.0 Hz, 1H), 7.39 (d, *J*=5.0 Hz, 1H), 7.38–7.36(m, 5H), 5.03(s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): 165.3, 162.1, 152.9, 151.1, 136.9, 136.6, 128.9, 128.6, 128.5, 121.5, 48.5 IR (plate): 2921, 2853, 1648, 1579, 1388, 1324, 1228, 1081, 749, 698 cm^{-1}. HRMS (ESI) *m/z* 291.0037 ($C_{13}H_{10}N_2O_1{}^{80}Se_1+H^+$: 291.0031).

*5.1.16. 2-Cyclohexyl[1,2]selenazolo[5,4-b]pyridin-3(2H)-one (**14**).* For the preparation of cyclohexyl containing Se–N heterocycle **14**, reaction was carried in a similar manner as described for **13** by using *N*-cyclohexyl-2-chloronicotinamide[30] (0.7 g, 2.9 mmol), CuI (560 mg, 2.9 mmol), 1,10-phenanthroline (530 mg, 2.9 mmol), selenium powder (0.34 g, 4.3 mmol), and K_2CO_3 (3.0 g, 21.7 mmol) in DMF (7 mL) and resulted reaction mixture was refluxed for 48 h at 110 °C. Standard workup as described for **13**, and purification by column chromatography on silica gel using CH_2Cl_2 and EtOAc (8:2)

afforded a white crystalline solid. Yield 0.528 g (64%), mp: 181–183 °C (183–187 °C).[9c] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, J=4.5 Hz, 1H), 8.24 (d, J=8.0 Hz, 1H), 7.37 (dd, J=4.5, 8.0 Hz, 1H), 4.51 (m, 1H), 2.12 (m, 2H), 1.87 (m, 2H), 1.73 (m, 1H), 1.53–1.38 (m, 4H), 1.29–1.16 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.3, 161.9, 151.9, 136.4, 124.8, 121.3, 53.5, 34.1, 25.5, 25.2. IR (plate): 2953, 2844, 1638, 1586, 1390, 1364, 1069, 892, 743 cm^{-1}. HRMS (ESI) m/z 283.0354 ($C_{12}H_{14}N_2O_1{}^{80}Se_1$+$H^+$: 283.0344).

*5.1.17. 2-Butyl[1,2]selenazolo[5,4-b]pyridin-3(2H)-one (**15**).* For the preparation of heterocycle **15**, reaction was carried in a similar manner as described for **13** by using *N*-*n*-butyl-2-chloronicotinamide[31] (0.55 g, 2.6 mmol), CuI (493 mg, 2.6 mmol), 1,10-phenanthroline (466 mg, 2.6 mmol), selenium powder (0.31 g, 3.9 mmol), and K_2CO_3 (1.7 g, 12.3 mmol) in DMF (6 mL) and refluxed for 48 h at 110 °C. Standard workup as described for **13** and purification by column chromatography on silica gel using CH_2Cl_2 and EtOAc (8:2) afforded a white crystalline solid. R_f (20% DCM/EtOAc) 0.5. Yield 0.363 g (55%), mp 120–122 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (dd, J=1.5, 4.5 Hz, 1H), 8.24 (dd, J=1.5, 8.0 Hz, 1H), 7.39 (dd, J=4.5, 8.0 Hz, 1H), 3.89 (t, J=7.5 Hz, 2H), 1.73 (p, J=7.5 Hz, 2H), 1.44 (sextet, J=7.5 Hz, 2H), 0.97 (t, J=7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 161.7, 152.1, 136.6, 123.9, 121.4, 44.2, 32.5, 19.9, 13.7. IR (plate): 2960, 2925, 2857, 1633, 1582, 1463, 1392, 1190, 753 cm^{-1}. HRMS (ESI) m/z 257.0193 ($C_{10}H_{12}N_2O_1{}^{80}Se_1$+$H^+$: 257.0188).

*5.1.18. 3-Chloro-N-(4-methoxyphenyl)-2,2-dimethylpropanamide (substrate for azetidine **19**).* 3-Chloro-2,2-dimethylpropanoyl chloride (0.6 g, 3.7 mmol) was dissolved in dry CH_2Cl_2 (15 mL) in a single neck flask and cooled to 0 °C. 4-Methoxyaniline (0.7 g, 5.5 mmol) in 10 mL of CH_2Cl_2 was slowly added to 3-chloro-2,2-dimethylpropanoyl chloride solution by dropping funnel. Resulted reaction mixture stirred for 1 h at 0 °C and 12 h at room temperature. After this, water (50 mL) was added to the reaction flask and stirred for 30 min. Dichloromethane (50 mL) was added to the reaction mixture and water layer separated by separating funnel. Dichloromethane layer was washed with 10% aqueous HCl (25 mL), and then with water (25 mL). Dichloromethane layer dried over Na_2SO_4, evaporated on rotary evaporator under vacuo. Resulted white solid was passed through silica gel using CH_2Cl_2 to obtain pure 3-chloro-*N*-(4-methoxyphenyl)-2,2-dimethylpropanamide. R_f (2% DCM/MeOH) 0.6. Yield 0.8 g (90%), mp 94–96 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, J=8.5 Hz, 2H), 6.86 (d, J=8.5 Hz, 2H) 3.79 (s, 3H), 3.69 (s, 2H), 1.40 (s, 6H), signal due to NH proton is not visible in the spectrum. ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 156.7, 130.5, 122.5, 114.0, 55.4, 52.8, 44.7, 23.6. IR (plate): 3320, 2962, 1654, 1512, 1239, 1180, 1034, 830 cm^{-1}.

*5.1.19. 1-(4-Methoxyphenyl)-3,3-dimethylazetidin-2-one (**19**).* Lactam **19** was obtained from 3-chloro-*N*-(4-methoxyphenyl)-2,2-dimethylpropanamide (0.3 g, 1.2 mmol), CuI (60 mg, 0.3 mmol), 1,10-phenanthroline (56 mg, 0.3 mmol), selenium powder (0.12 g, 1.5 mmol), and K_2CO_3 (0.26 g, 1.9 mmol) in DMF (4 mL) and refluxing for 8 h at 110 °C. Standard workup is similar to isoselenazolone **2** and crude product was purified by column chromatography on silica gel using hexane and ethyl acetate (8:2) afforded a brown crystalline solid. R_f (20% Hexane/EtOAc) 0.5. Yield 0.238 g (97%), mp 63–65 °C (69–70 °C).[32] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J=8.5 Hz, 2H), 6.87 (d, J=8.5 Hz, 2H) 3.78 (s, 3H), 3.39 (s, 2H), 1.39 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 161.2, 132.3, 117.5, 114.3, 55.5, 53.3, 49.8, 21.4. IR (plate): 2962, 139, 1514, 1397, 1295, 1246, 1154, 1033, 830 cm^{-1}. HRMS (ESI) m/z 206.1059 and 228.1007 (calcd for $C_{12}H_{15}N_1O_2$+H^+: 206.1176 and for $C_{12}H_{15}N_1O_2$+Na: 228.0995).

*5.1.20. 3-Chloro-N-(3,5-dimethoxyphenyl)-2,2-dimethylpropanamide (substrate for azetidine **20**).* 3-Chloro-2,2-dimethylpropanoyl chloride (0.42 g, 2.7 mmol) was dissolved in dry CH_2Cl_2 (15 mL) in a single neck flask and cooled to 0 °C. 3,5-Dimethoxyaniline (0.63 g, 4.1 mmol) in 10 mL of CH_2Cl_2, was slowly added to 3-chloro-2,2-dimethylpropanoyl chloride solution by dropping funnel. Resulted reaction mixture stirred for 1 h at 0 °C and 12 h at room temperature. After this water (50 mL) was added to reaction flask and stirred for 30 min. Dichloromethane (50 mL) was added to reaction mixture and water layer separated by separating funnel. Dichloromethane layer was washed with 10% HCl (25 mL), and then with water (25 mL). Dichloromethane layer dried over Na_2SO_4, evaporated on rotary evaporator under vacuo. Resulted white solid was passed through silica gel using CH_2Cl_2 to obtain pure amide. R_f (2% DCM/MeOH) 0.6. Yield 0.34 g (46%), mp 116–118 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (br s, 1H), 6.78 (d, J=2.5 Hz, 2H), 6.26 (t, J=2.5 Hz, 1H), 3.78 (s, 6H), 3.69 (s, 2H), 1.40 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 161.0, 139.2, 98.4, 97.2, 55.3, 52.6, 45.0, 23.6. IR (plate): 3337, 2935, 2838, 1664, 1618, 1559, 1453, 1418, 1197, 1153, 1068, 828 cm^{-1}.

*5.1.21. 1-(3,5-Dimethoxyphenyl)-3,3-dimethylazetidin-2-one (**20**).* Lactam **20** was obtained by following similar procedure as described for **19** by using 3-chloro-*N*-(3,5-dimethoxyphenyl)-2,2-dimethylpropanamide (0.23 g, 0.85 mmol), CuI (40 mg, 0.2 mmol), 1,10-phenanthroline (38 mg, 0.2 mmol), selenium powder (78 mg, 1.0 mmol), and K_2CO_3 (0.17 g, 1.2 mmol) in DMF (5 mL) and refluxing for 8 h at 110 °C. Standard workup and purification as described for **19** afforded a brown crystalline solid. R_f (20% Hexane/EtOAc) 0.5. Yield 0.198 g (98%), mp 58–60 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.54 (d, J=2.5 Hz, 2H), 6.20 (t, J=2.5 Hz, 1H), 3.78 (s, 6H), 3.40 (s, 2H), 1.39 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 161.2, 140.3, 96.1, 94.8, 55.3, 53.5, 49.6, 21.3. IR (plate): 2962, 1598, 1482, 1334, 1272, 1207, 115, 1091, 830 cm^{-1}. HRMS (ESI) m/z 236.1115 and 258.1098 (calcd for $C_{12}H_{15}N_1O_2$+H^+: 236.1281 and for $C_{13}H_{17}N_1O_3$+Na: 258.1100).

5.2. Preparation of bisphenyl diselenide (21); representative copper catalyzed procedure for the synthesis of diaryl diselenides

To a DMF solution (5 mL), CuI (233 mg, 1.2 mmol) and 1,10-phenanthroline (221 mg, 1.2 mmol) was added sequentially under N_2 atmosphere and stirred for 15 min. To this red colored solution of CuI/L, succinimide (0.48 g, 5.9 mmol), benzene iodide (0.55 mL, 4.9 mmol), selenium powder (0.46 g, 5.9 mmol), and potassium carbonate (2.03 g, 14.7 mmol) were added in same order and the resulted reaction mixture was heated at 110 °C for 8 h (progress of reaction was monitored by TLC continuously. For TLC, an aliquot of reaction mixture was poured into brine solution (2.0 mL) and mixed well with brine. After this, ethyl acetate was added, shaken well, and organic layer was used for TLC). After this, reaction mixture was poured into a beaker containing brine solution (80 mL) and resulted solution stirred for 2 h in air. Reaction mixture was extracted with ethyl acetate (25 mL×3). Combined organic layer was washed with water (50 mL), dried over Na_2SO_4 and evaporated under vacuo to provide resulted yellowish residue. Column chromatography of crude product using hexane gave yellowish oil. Crystallization by *n*-hexane at 0 °C gave yellow colored bisphenyl diselenide. Yield 0.497 g (65%), mp 58–60 °C (60–62 °C).[33] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (dd, J=7.5, 1.5 Hz, 4H), 7.29–7.25 (m, 6H). IR (plate): 3070, 2929, 1571, 1473, 1435, 1067, 733, 686 cm^{-1}.

*5.2.1. Bis-(2-methoxyphenyl)diselenide (**22**).* Diselenide **22** was synthesized from 2-iodo anisole (0.9 g, 3.8 mmol), *N*-succinimide (0.38 g, 3.8 mmol), CuI (190 mg, 1.0 mmol), 1,10-phenanthroline (180 mg, 1.0 mmol), selenium powder (0.36 g, 4.6 mmol), and K_2CO_3 (1.6 g, 11.6 mmol) in DMF (7 mL) by following similar

procedure as described for **21**. Reaction mixture was refluxed for 24 h at 110 °C. Standard workup as described for **21** and purification by column chromatography on silica gel using hexane as mobile phase afforded a yellow thick oil, which converted into crystalline orange solid upon cooling. Yield 0.601 g (84%), mp 83–85 °C (85–87 °C).[34] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (dd, J=8.0, 1.0 Hz, 1H), 7.29–7.25 (m, 1H), 7.23–7.17 (m, 2H), 6.92–6.81 (m, 4H), 3.91 (s, 6H). IR (plate): 3060, 3003, 2933, 2834, 1576, 1472, 1270, 1054, 1022, 748 cm^{-1}.

*5.2.2. Bis-2-(aniline) diselenide (**23**).* Diselenide **23** was prepared by following similar procedure as described for **21** using 2-iodo aniline (1.0 g, 4.6 mmol), *N*-succinimide (0.45 g, 4.5 mmol), CuI (217 mg, 1.1 mmol), 1,10-phenanthroline (205 mg, 1.1 mmol), selenium powder (0.43 g, 5.5 mmol), and K_2CO_3 (1.9 g, 13.7 mmol) in DMF (7 mL). Resulted reaction mixture was refluxed for 12 h at 110 °C. Standard workup followed as mentioned for **21**. Crude product obtained after evaporating ethyl acetate layer was purified by column chromatography on silica gel using hexane and ethyl acetate as mobile phase (8:2) afforded a yellow thick oil, which converted into crystalline orange solid on standing. Yield 0.351 g (45%), mp 80–83 °C (83 °C).[35] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (dd, J=8.0 Hz, 2H), 7.18–7.12 (m, 2H), 6.72 (d, J=8.5 Hz, 2H), 6.56 (t, J=7.5 Hz, 2H), 4.27 (br s, 4H). IR (plate): 3435, 3353, 2924, 2859, 1603, 1467, 1440, 1304, 1257, 1158, 1013, 742 cm^{-1}. HRMS (ESI) m/z 344.9416 (calcd for $C_{12}H_{12}N_2^{80}Se_2$+H$^+$: 344.9403).

*5.2.3. Bis[2-(N-acetylaniline)] diselenide (**24**).* Preparation of diselenide **24** carried out at 2.9 mmol from 2-iodoacetanilide (0.75 g, 2.9 mmol), *N*-succinimide (0.28 g, 2.8 mmol), CuI (137 mg, 0.7 mmol), 1,10-phenanthroline (130 mg, 0.7 mmol), selenium powder (0.27 g, 3.4 mmol), and K_2CO_3 (1.2 g, 8.6 mmol) in DMF (6 mL) by following similar procedure as described for **21** and refluxed for 12 h at 110 °C. Standard workup similar to **21** and crude product was purified by flash column chromatography on silica gel using hexane and ethyl acetate (7:3) afforded a brown colored solid. Yield 0.367 g (60%), mp 160–162 °C (164 °C).[36] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J=8.0 Hz, 1H), 7.83 (s, 2H), 7.57 (d, J=7.5 Hz, 2H), 7.38 (t, J=7.5 Hz, 2H), 6.99 (t, J=7.5 Hz, 2H), 1.94 (s, 6H). IR (plate): 3263, 2926, 1667, 1579, 1519, 1470, 1296, 1028, 754 cm^{-1}. HRMS (ESI) m/z 428.9624 ($C_{16}H_{16}N_2O_2{}^{80}Se_2$+H$^+$: 428.9615).

*5.2.4. Bis[2-(N,N-diethylbenzamide)] diselenide[37] (**25**).* Preparation of diselenide **25** was carried out from 2-iodo *N*,*N*-diethylbenzamide (0.5 g, 1.6 mmol), *N*-succinimide (0.16 g, 1.6 mmol), CuI (79 mg, 0.4 mmol), 1,10-phenanthroline (74 mg, 0.4 mmol), selenium powder (0.16 g, 2.0 mmol), and K_2CO_3 (0.7 g, 5.0 mmol) in DMF (8 mL). Reaction mixture was refluxed for 9 h at 110 °C. Standard workup and purification by column chromatography on silica gel using hexane and ethyl acetate (6:4) afforded brown colored thick oil. Yield 0.212 g (50%), ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, J=1.5, 8.0 Hz, 2H), 7.26–7.16 (m, 6H), 3.55 (br, 4H), 3.16 (d, 4H), 1.24 (b, 6H), 1.06 (b, 6H). IR (plate): 2972, 2931, 1626, 1584, 1428, 1364, 1291, 1099, 772, 743 cm^{-1}. HRMS (ESI) m/z 513.0557 ($C_{22}H_{28}N_2O_2{}^{80}Se_2$+H+: 513.0554).

*5.2.5. Bis-2-pyridinyl diselenide (**26**)[38].* Diselenide **26** was obtained from 2-iodo-pyridine (200 mg, 0.98 mmol), succinimide (97 mg, 0.98 mmol), CuI (37 mg, 0.19 mmol), 1,10-phenanthroline (35 mg, 0.19 mmol), selenium powder (85 mg, 1.1 mmol), K_2CO_3 (270 mg, 1.95 mmol) in DMF (5 mL) by following procedure as described for diselenide **21**. Reaction mixture was refluxed for 5 h. After this reaction mixture poured in saturated sodium bicarbonate solution (100 mL), extracted with ethyl acetate (25 mL×3), dried over Na_2SO_4 (6 g), concentrated under vacuo, column chromatography using silica gel and hexane as an eluent yielded yellowish semi solid. Yield 82 mg, 54%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (dm, J=4.8 Hz, 2H), 7.82 (dt, J=8.1, 1.0 Hz, 2H), 7.56 (td, J=8.0, 2.0 Hz, 2H), 7.10 (ddd, J=7.50, 4.8, 1.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 149.6, 137.5, 123.6, 121.3. ESMS m/z 338.9 ($C_{10}H_8N_2Se_2$+Na). IR (plate): 3060, 2960, 2920, 1565, 1555, 1444, 1408, 1105, 1076, 1041, 987, 741, 689 cm^{-1}.

*5.2.6. Bis-2-thiophenyl diselenide (**27**).* Synthesis of diselenide **27** was carried out at 2.4 mmol using 2–iodo-thiophene (500 mg, 2.38 mmol), succinimide (236 mg, 2.38 mmol), CuI (113 mg, 0.6 mmo1), 1,10-phenanthroline (107 mg, 0.6 mmol), selenium powder (207 mg, 2.6 mmol), and K_2CO_3 (0.493 mg, 3.57 mmol) in DMF (6 mL). Reaction mixture was refluxed at 110 °C for 3 h. Workup and column chromatography on silica gel using hexane as an eluent yielded a white solid. Yield 251 mg (65%), mp 55–57 °C (57–59 °C).[39] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, J=5.3, 1.2 Hz, 2H), 7.26 (dd, J=3.5, 1.2 Hz, 2H), 7.03 (dd, J=5.3, 3.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.9, 132.9, 128.1, 125.6.

Acknowledgements

S.K. thanks Department of Science and Technology (DST) New Delhi for financial support. S.J.B. and B.S.B. thank IISER Bhopal for research fellowship. S.K. thanks Professor Vinod K. Singh, Dr. Pradeep K. Singh, and Mr. Suresh Allu (Department of Chemistry, IIT Kanpur) for HRMS data. We heartedly thank Professor T.N. Guru Row and Dr. Susanta Kumar Nayak for data collection on the CCD facility at IISc, Bangalore.

Supplementary data

Additional experimental details, copies of spectra for compounds and crystallographic data, CIF file for **13** (CCDC No. 808789) are available. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.09.141. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. For antioxidant activities of isoselenazolones see: (a) Mugesh, G.; du Mont, W.-W.; Sies, H. *Chem. Rev.* **2001**, *101*, 2125 and references therein; (b) Nogueira, C. W.; Zeni, G.; Rocha, J. B. T. *Chem. Rev.* **2004**, *104*, 6255; (c) Mishra, B.; Priyadarsini, K. I.; Mohan, H.; Mugesh, G. *Free Radical Biol. Med.* **2005**, *39*, S14; (d) Kalai, T.; Mugesh, G.; Roy, G.; Sies, H.; Berente, Z.; Hideg, K. *Org. Biomol. Chem.* **2005**, *3*, 3564; (e) Sarma, B. K.; Mugesh, G. *J. Am. Chem. Soc.* **2005**, *127*, 11477; (f) Mishra, B.; Priyadarsini, K. I.; Mohan, H.; Mugesh, G. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5334; (g) Bhabak, K. P.; Mugesh, G. *Chem.—Eur. J.* **2007**, *13*, 4594; (h) Sarma, B. K.; Mugesh, G. *Chem.—Eur. J.* **2008**, *14*, 10603; (i) Sarma, B. K.; Manna, D.; Minoura, M.; Mugesh, G. *J. Am. Chem. Soc.* **2010**, *132*, 5364; (j) Seminario-Vidal, L.; van Heusden, C.; Mugesh, G.; Lazarowski, E. R. *Purinergic Signalling* **2010**, *6*, 383; (k) Bhabak, K. P.; Mugesh, G. *Acc. Chem. Res.* **2010**, *43*, 1408 see recent references on Se–N heterocycles; (l) Satheeshkumar, K.; Mugesh, G. *Chem.—Eur. J.* **2011**, *17*, 4849; (m) Bhabak, K. P.; Vernekar, A. A.; Jakka, S. R.; Roy, G.; Mugesh, G. *Org. Biomol. Chem.* **2011**, *9*, 5193.
2. Terentis, A. C.; Freewan, M.; Plaza, T. S. S.; Raftery, M. J.; Stocker, R.; Thomas, S. R. *Biochemistry* **2010**, *49*, 591.
3. Parnham, M.; Sies, H. *Expert Opin. Invest. Drugs* **2000**, *9*, 607.
4. Freudendahl, D. M.; Santoro, S.; Shahzad, S. A.; Santi, C.; Wirth, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 8409.
5. Reich, H. J.; Jasperse, C. P. *J. Am. Chem. Soc.* **1987**, *109*, 5549.
6. Lesser, R.; Weiss, R. *Ber. Dtsch. Chem. Ges.* **1924**, *57*, 1077.
7. Welter, A.; Christiaens, L.; W.-P., Ferdinand, Eur. Pat. Appl. EP 44453, 1982; *Chem. Abstr.* **1982**, *96*, 199699v.
8. Cantineau, R.; Tihange, G.; Plenevaux, A.; Christiaens, L.; Guillaume, M. *J. Labelled Compd. Radiopharm.* **1985**, *28*, 59.
9. (a) Pietka-Ottlik, M.; Wójtowicz-Młochowska, H.; Kołoddziejczyk, K.; Piasecki, E.; Młochowski, J. *Chem. Pharm. Bull.* **2008**, *56*, 1423; (b) Osajda, M.; Młochowski, J. *Tetrahedron* **2002**, *58*, 7531; (c) Kloc, K.; Maliszewska, I.; Młochowski, J. *Synth. Commun.* **2003**, *33*, 3805.
10. Fong, M. C.; Schiesser, C. H. *J. Org. Chem.* **1997**, *62*, 3103.
11. Engman, L.; Hallberg, A. *J. Org. Chem.* **1989**, *54*, 2964.
12. Oppenheimer, J.; Silks, L. A. *J. Labelled Compd. Radiopharm.* **1996**, *38*, 281.

13. Chang, T.-C.; Huang, M.-L.; Hsu, W.-L.; Hwang, J.-M.; Hsu, L.-Y. *Chem. Pharm. Bull.* **2003**, *51*, 1413.
14. (a) Zade, S. S.; Panda, S.; Tripathi, S. K.; Singh, H. B.; Wolmershäuser, G. *Eur. J. Org. Chem.* **2004**, 3857; (b) Zade, S. S.; Panda, S.; Singh, H. B.; Wolmershäuser, G. *Tetrahedron Lett.* **2005**, *46*, 665; (c) Singh, V. P.; Singh, H. B.; Butcher, R. J. *Eur. J. Inorg. Chem.* **2010**, 637; (d) Singh, V. P.; Singh, H. B.; Butcher, R. J. *Eur. J. Org. Chem.* **2011**, *28*, 5485–5497; (e) Singh, V. P.; Singh, H. B.; Butcher, R. J. *Chem. Commun.* **2011**, 7221.
15. Lambert, C.; Hilbert, M.; Christiaens, L.; Dereu, N. *Synth. Commun.* **1991**, *21*, 85.
16. Erdelmeier, I.; Tailhan-Lomont, C.; Yadan, J.-C. *J. Org. Chem.* **2000**, *65*, 8152.
17. Zeni, G.; Braga, A. L.; Stefani, H. A. *Acc. Chem. Res.* **2003**, *36*, 731; Silveira, C. C.; Braga, A. L.; Vieira, A. S.; Zeni, G. *J. Org. Chem.* **2003**, *68*, 662; Braga, A. L.; Barcellos, T.; Paixão, M. W.; Deobald, A. M.; Godoi, M.; Stefani, H. A.; Cella, R.; Sharma, A. *Organometallics* **2008**, *27*, 4009; Godoi, B.; Sperança, A.; Back, D. F.; Brandão, R.; Nogueira, C. W.; Zeni, G. *J. Org. Chem.* **2009**, *74*, 3469; Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev.* **2011**, *111*, 1596; Narayanaperumal, S.; Alberto, E. E.; Gul, K.; Rodrigues, O. E. D.; Braga, A. L. *J. Org. Chem.* **2010**, *75*, 3886.
18. Selenium/Sulfur Coupling Reactions: (a) Taniguchi, N. *J. Org. Chem.* **2004**, *69*, 6904; (b) Taniguchi, N.; Onami, T. *J. Org. Chem.* **2004**, *69*, 915; (c) Taniguchi, N. *Synlett* **2005**, 1185; (d) Taniguchi, N. *J. Org. Chem.* **2006**, *71*, 7874; (e) Kumar, S.; Engman, L. *J. Org. Chem.* **2006**, *71*, 5400; (f) Taniguchi, N. *J. Org. Chem.* **2007**, *72*, 1241; (g) Taniguchi, N. *Eur. J. Org. Chem.* **2010**, 2670; (h) Singh, D.; Deobald, A. M.; Camargo, L. R. S.; Tabarelli, G.; Rodrigues, O. E. D.; Braga, A. L. *Org. Lett.* **2010**, *12*, 3288; (i) Gay, R. M.; Manarin, F.; Schneider, C. C.; Barancelli, D. A.; Costa, M. D.; Zeni, G. *J. Org. Chem.* **2010**, *75*, 5701.
19. Balkrishna, S. J.; Bhakuni, B. S.; Chopra, D.; Kumar, S. *Org. Lett.* **2010**, *12*, 5394.
20. (a) For theoretical study on methoxy substituted ebselen, see: Pearson, J. K.; Boyd, R. J. *J. Phys. Chem. A* **2008**, *112*, 1013; (b) For methoxy substituted GPx mimics, see: Bhabak, K. P.; Mugesh, G. *Chem.—Eur. J.* **2008**, *14*, 8640.
21. Tye, J. W.; Weng, Z.; Johns, A. M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 9971; Barros, O. S. d. R.; Nogueira, C. W.; Stangherlin, E. C.; Menezes, P. H.; Zeni, G. *J. Org. Chem.* **2006**, *71*, 1552.
22. Suezawa, H.; Yuzuri, T.; Hirota, M.; Ito, Y.; Hamada, Y. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 328.
23. Thansandote, P.; Hulcoop, D. G.; Langer, M.; Lautens, M. *J. Org. Chem.* **2009**, *74*, 1673.
24. Wang, L.; Zhong, C.; Xue, P.; Fu, E. *J. Org. Chem.* **2011**, *76*, 4874.
25. Nayak, S. K.; Reddy, M. K.; Guru Row, T. N.; Chopra, D. *Crystal Growth Des.* **2011**, *11*, 1578.
26. Zhou, J.; Fu, L.; Lv, M.; Liu, J.; Pei, D.; Ding, K. *Synthesis* **2008**, 3974.
27. Grigg, R.; Kordes, M. *Eur. J. Org. Chem.* **2001**, 707.
28. Vágó, E.; Greiner, I. *Tetrahedron Lett.* **2002**, *43*, 6039.
29. Ferraccioli, R.; Carenzi, D.; Rombolá, O.; Catellani, M. *Org Lett.* **2004**, *6*, 4759.
30. McCoull, W.; Packer, M.; Scott, J. S.; Whittamore, P. R. O. PCT Int. Appl. WO 2008012532 A2, 2008.
31. Mikhalev, A. I.; Kudryashova, V. K.; Konshin, M. E.; Zalesov, V. S. *Khim.—Farm. Zh.* **1975**, *9*, 15.
32. (a) Merger, F. Ger. Offen. Patent: DE2012216, 1971; *Chem. Abstr.* **1972**, *76*, 3683e; (b) Merger, F. Patent: CH546759 DE2048080, 1971; *Chem. Abstr. 77*, p 61977.
33. Reich, H. J.; Cohen, M. L.; Clark, P. D. *Org. Synth*; 1988; Collect. Vol. VI, 533. Organic Syntheses, Inc. (http://www.orgsyn.org/orgsyn/prep.asp?prep=cv6p0533).
34. Nakanishi, W.; Ikeda, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1661.
35. Kloc, K.; Młochowski, J.; Osajda, K.; Syper, L.; Wójtowicz, H. *Tetrahedron Lett.* **2002**, *43*, 4071.
36. Matti, J. *Bull. Soc. Chim. Fr.* **1940**, *7*, 617.
37. Watanabe, M.; Date, M.; Tsukazaki, M.; Furukawa, S. *Chem. Pharm. Bull. Jpn.* **1989**, *37*, 36.
38. Bhasin, K. K.; Singh, J. *J. Organomet. Chem.* **2002**, *658*, 71.
39. Jen, K.-Y.; Cava, M. P. *J. Org. Chem.* **1983**, *48*, 1449; Taboury, F. J. *Bull. Soc. Chim. Fr.* **1903**, *29*, 763.