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Article

Selective Synthesis of Bis-Heterocycles via Mono- and Di-Selenylation of Pyrazoles and Other Heteroarenes

Jaspreet Kour, Pratiksha Khajuria, Praveen Kumar Verma, Neharika Kapoor, Amit Kumar, and Sanghapal D. Sawant*

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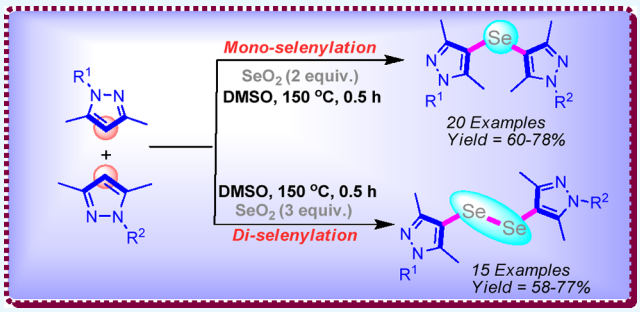
ABSTRACT: The insertion of selenium was achieved in the form of mono-selenides and di-selenides for the preparation of novel bis-heterocyclic compounds. This method is more general and provides scaffold diversity with high yields of products. The concentration-dependent mono- and di-selenylation reaction selectivity was achieved using SeO_2 as an efficient selenylating reagent.



INTRODUCTION

Organoselenium chemistry is a well-established field due to the applicability of selenium compounds as versatile tools in organic synthesis,[1] catalysis,[2] as well as privileged scaffolds in medicinal chemistry for bioactive molecules (Figure 1)[3] such as ebselen used for ischemic stroke,[4] hearing loss,[5] and recently used for bipolar disorder.[6] Elemental selenium has an important role in physiological functions and several dangerous viral infections (H1N1 influenza, SARS, HIV/AIDS, Ebola, etc.) are associated with selenium deficiency and outbreaks of them have originated either in bio-geo-chemically selenium-poor regions of China or selenium nutrient-depleted sub-Saharan Africa.[7]

Organoselenium compounds are effective precursors in organic chemistry avoiding the protection/deprotection protocols.[8] The construction of C−Se−C or C−Se−Se−C is mostly achieved by cross coupling of aryl boronic acids/aryl halides using selenium sources with transition metal catalysts, however, mostly limited to aryl substrates.[9] The literature review about the selenylating reagents revealed the drawbacks of specified reaction protocols due to the instability in air and moisture, multiple preparation steps, various reactive side products, toxic waste in equivalent amount and many others. To overcome some of these serious drawbacks of earlier used selenylating reagents, SeO_2 has been emerged as effective and stable alternative for various selenylation reactions.[10] The installation of selenium[11] in the heterocyclic scaffolds is an interesting and challenging task and further provides the opportunity for constructing bis-type of heterocyclic mono-selenide and di-selenide motifs.

Di-selenides resemble with the organic peroxides, although slightly more stable than peroxides, however, reactive enough to participate in electrophilic, nucleophilic, and radical processes. Pyrazoles[12] are the privileged biorelevant scaffolds in organic synthesis due to their potential in the drug discovery process. Bis-pyrazoles[13] incorporated with selenium offer more advantageous features to the molecules in terms of their biological applicability. Hence, developments of sustainable approaches for the construction of selenylated heterocyclic scaffolds are of high interest for chemists. In our recent work for the construction of bis-pyrazoles, the methylene ($-CH_2-$) moiety was incorporated between two pyrazoles using the oxone/dimethyl sulfoxide (DMSO) system.[14] Now, in continuation to this work on pyrazole scaffolds[14,15] and understanding the biological importance of selenium,[3−7] we directed our thought to incorporate the selenium between two pyrazole molecules in order to construct the selenylated bis-heterocycles (pyrazoles). Herein, we disclose a very simple protocol for the mono-selenylation and di-selenylation of pyrazoles for the construction of selenylated bis-pyrazoles using SeO_2 as the selenylating reagent (Scheme 1).

RESULTS AND DISCUSSION

The optimization studies were initiated for the activation of pyrazoles for the synthesis of bis-pyrazole compounds using 3,5-dimethyl-1-phenyl-1*H*-pyrazole as the model substrate and

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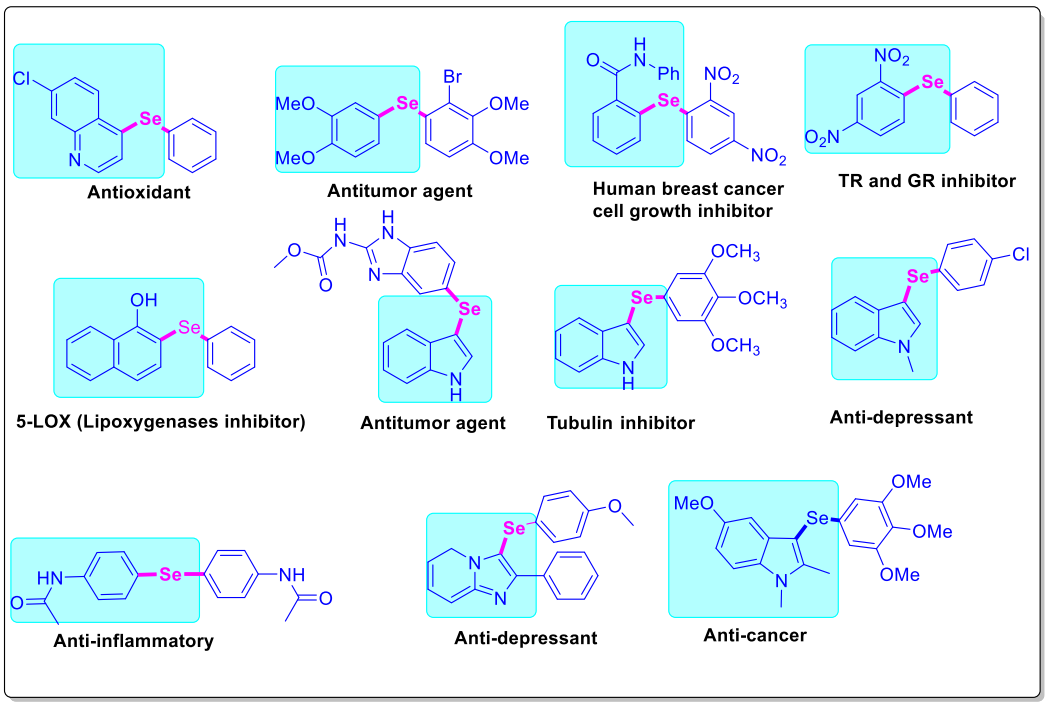

Figure 1. Biologically important aryl/heteroaryl selenide-based compounds with a wide range of activities.

SeO_2 as the source of selenium, DMSO as the reaction solvent at 150 °C temperature, and systematically tested the required quantity of SeO_2, reaction temperature, and solvents (Table 1). Initially, the quantity of SeO_2 was optimized with the model reaction. While optimizing the quantities, 0.5 and 1.0 equiv of SeO_2 afforded the mono-selenylated bis-pyrazole product **2a** in 62 and 41 % yields, respectively (entries 1 and 2). On increasing the quantity of SeO_2 to 1.5 equiv gave mono-selenylated bis-pyrazole (**2a**) as well as di-selenylated bis-pyrazole (**3a**) products with almost equal yields (entry 3). Furthermore, increasing the quantity of SeO_2 to 2.0 equiv afforded the product **2a** with major yield (71%) as compared to the **3a** (9%) as minor (entry 4). On further increasing the quantity of SeO_2 to 2.5 and 3.0 equiv provided di-selenylated product **3a** as the major product and mono-selenylated product **2a** as the minor product (entries 5 and 6). Hence, 2.0 equiv quantity of SeO_2 for mono-selenylated product **2a** and 3.0 equiv for di-selenylated product **3a** were taken for the further optimization studies. The screening of different solvents was also carried out with model substrate 1. dimethylformamide (DMF), MeOH, 1,4-dioxane, and HCHO were found to be ineffective for the current reaction and afforded the desired products (**2a** or **3a**) with low yields (entries 7−10). However, moderate yields of **2a** were observed with ACN and DCM (entries 11 and 12). We also optimized the reaction temperature for the current model reaction. The reaction did not give the desired product at room temperature and at 50 °C (entries 13−16) as well. On increasing the temperature to 80 and 100 °C gave mono-selenylated product **2a** only in low yields (entries 17−20). Raising the reaction temperature to 120 °C gave the mono-selenylated product **2a** as the major (66%) product and di-selenylated product **3a** as the minor (28%) product with 2 equiv of SeO_2; however, with 3.0 equiv of SeO_2, **2a** was observed as the minor (37%) product and **3a** as the major (57%) product (entries 21 and 22).

Hence, 2 equiv SeO_2 with DMSO solvent at 150 °C for desired product **2a** and 3.0 equiv SeO_2 with DMSO solvent at 150 °C for product **3a** were taken as optimized conditions for further study.

With the optimized reaction conditions in hand, we explored the generality of the developed method using various pyrazole substrates. In order to synthesize mono-selenylated bis-pyrazoles, various phenyl ring-substituted pyrazole compounds were investigated with SeO_2 under the optimized conditions (Table 2). Simple phenyl ring derivative of pyrazole along with mono- and di-halogen atom bearing pyrazoles were tolerated under the developed method without affecting the different positions (*o*-, *m*-, and *p*-) of halogens on the phenyl ring to provide the corresponding mono-selenylated bis-pyrazoles in good yields (**2a−2h**).

The reaction of methyl-, ethyl-, and dimethyl-substituted pyrazoles provides the corresponding mono-selenylated bis-pyrazole products in high yields (**2i−2k**). The reaction of pyrazoles bearing pharmaceutically important[16] trifluoromethyl and trifluoromethoxy groups also underwent the formation of corresponding mono-selenylated bis-pyrazoles in good yields (**2l** and **2m**). The reaction of *o*- and *p*-methoxy-substituted pyrazoles proceeded in good yields (**2n** and **2o**). The reaction of *m*-nitro- and *p*-cyano-substituted compounds afforded the corresponding selenylated products in good yields (**2p** and **2q**). The reaction of pyrazole containing 2-pyridinyl ring also provided the targeted product in high yield (**2r**). The reaction of the 5-methyl-1,3-diphenyl-1*H*-pyrazole substrate also provided the corresponding mono-selenylated bis-pyrazole in high yield (**2s**). The reaction of the 1,3,5-trimethyl-1*H*-pyrazole moiety also proceeded well and provide the desired product in good yield (**2t**).

In order to further expand the scope of the developed method for the synthesis of di-selenylated bis-pyrazoles, reactions were performed with 3.0 equiv of SeO_2 (Table 3). The reactions of the unsubstituted phenyl ring bearing

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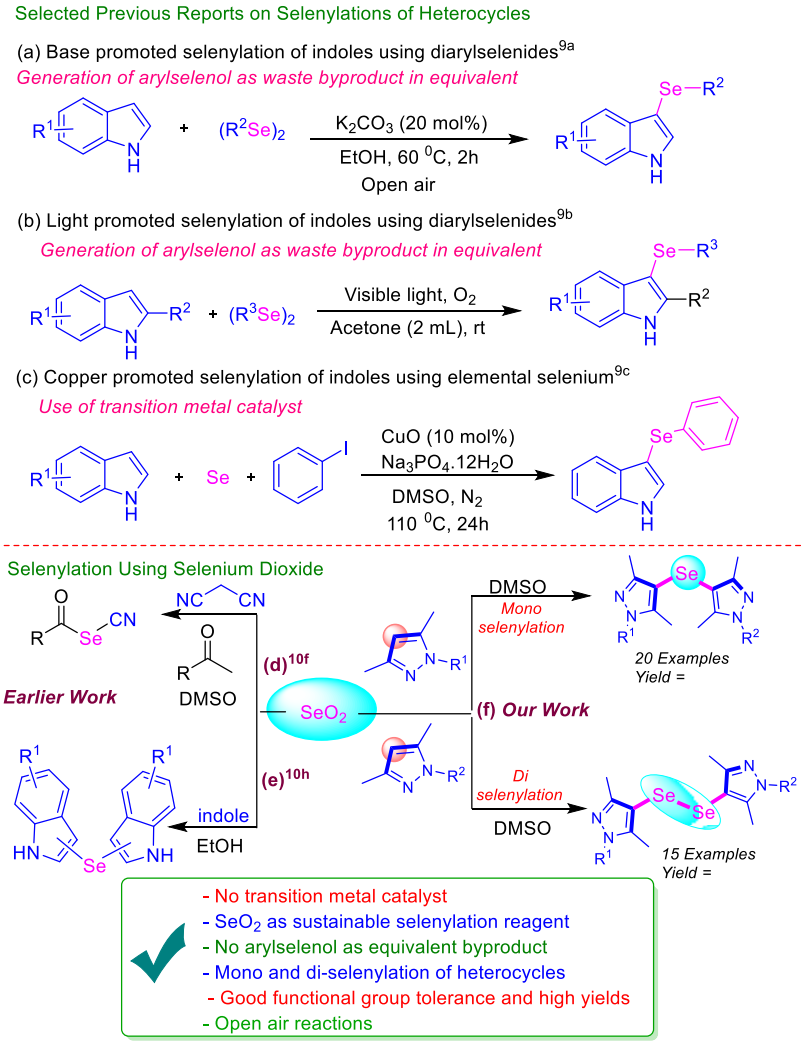
Scheme 1. State of the Art on Selenylation Reactions



(a) Base promotes selenylation of indoles using diarylselenides. (b) Light promoted selenylation of indoles using diarylselenides.(c) Copper promoted selenylation of indoles using elemental selenium. (d) Selenylation of melononitriles using selenium dioxide. (e) Selenylation of indoles using selenium dioxide. (f) Mono- and Di-selenylation of pyrazoles using selenium dioxide.

pyrazole and other mono- and di-halogen-substituted (-F, -Cl, and -Br) pyrazoles provided the corresponding di-selenylated bis-pyrazoles in high yields (**3a**−**3g**). Methyl and dimethyl group substitution in the phenyl ring of pyrazole compounds did not affect the reaction yield and also provide the corresponding di-selenylated bis-pyrazoles products in a major quantity (**3h** and **3i**). Reaction of the trifluoromethoxy-substituted pyrazole substrate also gave the desired products in high yields (**3j**). Reaction of *o*-methoxy-, *m*-nitro-, and *p*-cyano-substituted pyrazoles also afforded the corresponding di-selenylated bis-pyrazoles as the major products in high yields (**3k**−**3m**). The reaction of pyrazole having the 2-pyridinyl group instead of the phenyl ring also afforded the corresponding di-selenylated product in high yield (**3n**). The reaction of 5-methyl-1,3-diphenyl-1*H*-pyrazole substrate provides the corresponding di-selenylated product in high yield (**3o**).

To further expand the scope and applicability of these products, mono- and di-selenylated bis-pyrazoles, we carried out some extension reactions using products **2a** and **3a** (Scheme 2). The oxidation of **2a** afforded the corresponding dioxide product **2aa** with oxone (2.2 equiv) in EtOH at 80 °C [Scheme 2, eq (i)]. As di-selenides are the important precursors in organic transformation, herein, we carried out the reaction of di-selenide bis-pyrazole (**3a**) with indole as the cross coupling substrate in the presence of a base in EtOH and successfully afforded the unsymmetric di-selenylated bis-pyrazole (**3aa**) in good yield [Scheme 2, eq (ii)]. Furthermore, the incorporation of tellurium (on reacting with TeO_2) was not possible under the current developed method [Scheme 2, eq (iii)]. The current methods were not applicable for the direct synthesis of unsymmetrical heterocycles as very low conversions were observed for the reaction of the equimolar mixture of two different heterocycles (Schemes S1 and S2).

The mechanism of the reaction is still unclear in the literature. Wilshire's assumption[17] suggested the possibilities for the formation of triselenide intermediate A during the formation of diaryl selenides **2a**. Based on the existing reports for selenium incorporation,[10,17] we proposed a hypothesis (Scheme 3) that SeO_2 on reaction with pyrazole 1 forms the mono-selenylated bis-pyrazole product **2a** via the triselenide intermediate A. We also proposed the possibility for the

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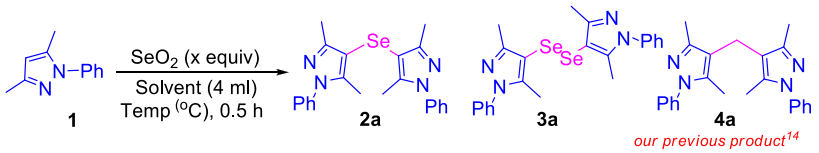
Table 1. Optimization Studies[a]



entry	equiv SeO_2	solvent	temp. (°C)	yield 2a[b] (%)	yield 3a[b] (%)	yield 4a[b] (%)
1	0.5	DMSO	150	62	8	0
2	1.0	DMSO	150	41	15	0
3	1.5	DMSO	150	51	48	0
4	2.0	DMSO	150	85 (71)[c]	9	5
5	2.5	DMSO	150	15	35	12
6	3.0	DMSO	150	30	65	5
7	2.0	DMF	150	3	0	0
8	2.0	MeOH	reflux	1	0	0
9	2.0	1,4-dioxane	100	19	1	0
10	2.0	formalin	150	0	0	40
11	2.0	ACN	reflux	67	0	0
12	2.0	DCM	reflux	50	0	0
13	2.0	DMSO	rt	0	0	0
14	3.0	DMSO	rt	0	0	0
15	2.0	DMSO	50	0	0	0
16	3.0	DMSO	50	0	0	0
17	2.0	DMSO	80	26	0	0
18	3.0	DMSO	80	26	0	0
19	2.0	DMSO	100	28	<1	<1
20	3.0	DMSO	100	33	<1	<1
21	2.0	DMSO	120	67	28	4
22	3.0	DMSO	120	37	57	5

[a]Reaction conditions: 1 (1 mmol) and SeO_2 (*x* equiv) in solvent (4 mL) were stirred upto 0.5 h. [b]LC−MS-based concentrations. [c]Isolated yield.

formation of intermediate B from the reaction of pyrazole 1 with SeO_2 in the presence of DMSO. The intermediate B on further reaction with either mono-selenylated pyrazole **2a** or with self-reacting provided the desired di-selenylated bis-pyrazole product **3a**. However, further study is continuing in our laboratory for the confirmation of the proposed pathway.

CONCLUSIONS

The current developed method is more general and successfully inserts the selenium in the form of mono-selenides and di-selenides using SeO_2 as the selenylating reagent in DMSO as the solvent for the construction of mono- and di-selenylated bis-pyrazoles. Reaction conditions tolerated the various functionalities at the aromatic ring of the arylated pyrazole substrates and afforded the desired products in high yields. We also extended the current method for further adding the applicability to the obtained mono- and di-selenylated bis-pyrazole products.

EXPERIMENTAL SECTION

General. All reaction solvents were purified using the standard laboratory protocols. All reagents used in the synthesis were purchased from commercially available sources and used without further purification. Brucker AVANCE DPX FT-NMR 400 and 500 MHz instruments were used to record the ^1H and ^{13}C NMR spectra. ^1H and ^{13}C positive chemical shifts (δ, given in ppm) are downfield from the standard tetramethylsilane signal. Multiplicity [s = singlet, d = doublet, t = triplet, m = multiplet, br = broad singlet, coupling constant(s) are given in Hz, integration]. Agilent 6540 ultra-high-definition accurate-mass quadrupole time-of-flight liquid chromatography/mass spectrometry (LC/MS) system was used in order to record the high-resolution mass spectrometry (HRMS) spectra.

Synthesis of Aryl-Substituted Pyrazole Starting Compounds. The phenyl group (bearing various substitutions) containing pyrazole compounds, used as starting materials, were prepared using our earlier developed report.[14,15]

Typical Procedure for the Synthesis of Mono-Selenylated Bis-Pyrazoles. Pyrazole (1 mmol) and SeO_2 (2 mmol) in DMSO (4 mL) at 150 °C were added in a dry round-bottom flask (25 mL) and heated at oil-bath for 0.5 h. The reaction was monitored by thin-layer chromatography (TLC), and after completion, the reaction mixture was transferred in ethyl acetate (20 mL) and washed with H_2O (50 mL × three times). The combined organic phases were concentrated on a rotary evaporator and the crude obtained was purified over silica gel (ethyl acetate: *n*-hexane) to give mono-selenylated bis-pyrazole products.

Bis(3,5-Dimethyl-1-phenyl-1*H*-pyrazol-4-yl)selane (2a). Pale yellow solid, mp 139−140 °C, yield = 71% (173 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.38−7.27 (m, 10H), 2.36 (s, 6H), 2.29 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 151.9, 142.3, 139.9, 129.0, 127.6, 124.8, 104.5, 13.2, 12.6 ppm. HRMS (ESI) calcd for $C_{22}H_{23}N_4Se$ $[M + H]^+$, 423.1082; found, 423.1088.

Bis[1-(3-fluorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]-selane (2b). Dark brown semisolid, yield = 70% (168 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9).^1H NMR (400 MHz, $CDCl_3$): δ 7.42 (dd, *J* = 14.5, 7.5 Hz, 2H), 7.24−7.15 (m, 4H), 7.08 (t, *J*

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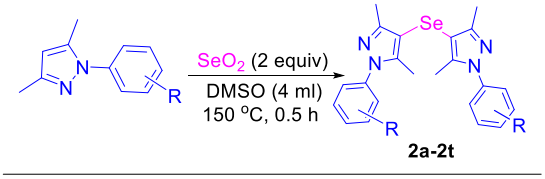
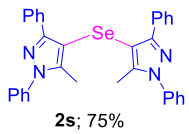
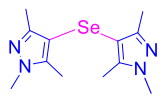
Table 2. Synthesis of Mono-Selenylated Bis-Pyrazoles[a,b]



2a, R = H; 71%
2b, R = *m*-F; 70%
2c, R = *m*-Cl; 66%
2d, R = *p*-Cl; 70%
2e, R = *m*-Br; 63%
2f, R = *p*-Br; 66%
2g, R = *o*-F, *p*-F; 64%
2h, R = *o*-Cl, *p*-Cl; 60%
2i, R = *p*-CH_3; 68%
2j, R = *o*-C_2H_5; 73%
2k, R = *m*-CH_3, *p*-CH_3; 74%
2l, R = *o*-CF_3; 76%
2m, R = *p*-OCF_3; 73%
2n, R = *o*-OCH_3; 72%
2o, R = *p*-OCH_3; 74%
2p, R = *m*-NO_2; 78%
2q, R = *p*-CN; 77%

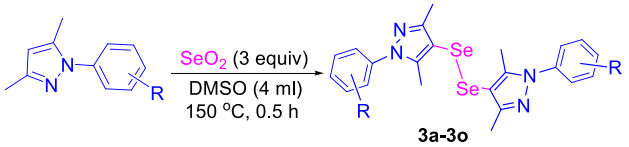

2r; 70%

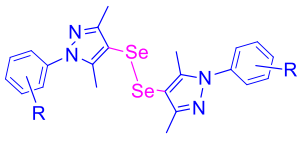

2s; 75%


2t; 78%

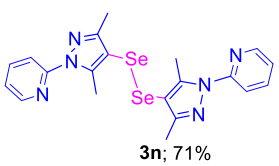
[a]Reaction conditions: 1 (1 mmol), SeO_2 (2 equiv) were stirred in DMSO (4 mL) at 150 °C for 0.5 h. [b]Isolated yields.

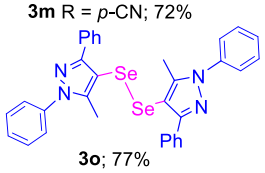
Table 3. Synthesis of Di-Selenylated Bis-Pyrazoles[a,b]





3a, R = H; 65%
3b, R = *m*-F; 66%
3c, R = *m*-Cl; 61%
3d, R = *p*-Cl; 60%
3e, R= m-Br 64%
3f, R = *p*-Br; 63%
3g, R = *o*-Cl, *p*-Cl; 58%
3h R = *p*-CH_3; 68%
3i R = *m*-CH_3, *p*-CH_3; 70%
3j, R = *p*-OCF_3; 76%
3k R = *o*-OCH_3; 64%
3l R = *m*-NO_2; 72%
3m R = *p*-CN; 72%


3n; 71%


3o; 77%

[a]Reaction conditions: 1 (1 mmol) and SeO_2 (3 equiv) were stirred in DMSO (4 mL) at 150 °C for 0.5 h. [b]Isolated yields.

= 8.0 Hz, 2H), 2.48 (s, 6H), 2.36 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 162.7 (d, J = 202.0 Hz), 152.41 (s), 141.8 (d, J = 131.3 Hz), 130.2 (d, J = 10.0 Hz), 120.0 (d, J = 3.0 Hz), 114.5 (d, J = 20.2 Hz), 112.1 (d, J = 20.2 Hz), 105.0, 13.3, 12.8 ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ −111.08 (dd, J = 15.2, 8.8 Hz). HRMS (ESI) calcd for $C_{22}H_{21}F_2N_4Se$ $[M + H]^+$, 459.0987; found, 459.0900.

Bis[1-(3-chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]-selane (2c). Light yellow viscous, yield = 66% (157 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.38 (s, 2H), 7.32−7.22 (m, 6H), 2.38 (s, 6H), 2.28 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.4, 142.3, 140.9, 134.8, 130.0, 127.7, 124.9, 122.6, 105.0, 13.2, 12.7 ppm. HRMS (ESI) calcd for $C_{22}H_{21}Cl_2N_4Se$ $[M + H]^+$, 491.0303; found, 491.0308.

Bis[1-(4-chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]-selane (2d). White solid, mp 160 °C, yield = 70% (166 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, J = 8.7 Hz, 4H), 7.27 (d, J = 8.7 Hz, 4H), 2.35 (s, 6H), 2.27 (s, 6H) ppm. $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.2, 142.3, 138.4, 133.4, 129.2, 125.8, 104.8, 13.2, 12.6 ppm. HRMS (ESI) calcd for $C_{22}H_{21}C_{l2}N_4Se$ $[M + H]^+$, 491.0303; found, 491.0308.

Bis[1-(3-bromophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]selane (2e). Yellow semisolid, yield = 63% (145 mg). R_f 0.3 (EtOAc/*n*-Hexane = 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (s, 2H), 7.42 (dd, J = 7.4, 1.5 Hz, 2H), 7.34−7.19 (m, 4H), 2.39 (s, 6H), 2.28 (s, 6H) ppm. $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.4, 142.4, 140.9, 130.6, 130.3, 127.7, 123.0, 122.6, 105.0, 13.3, 12.8 ppm. HRMS (ESI) calcd for $C_{22}H_{21}Br_2N_4Se$ $[M + H]^+$, 578.9293; found, 578.9298.

Bis[1-(4-bromophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]selane (2f). Light yellow solid, mp 153−154 °C, yield = 66% (152 mg). R_f 0.3(EtOAc/*n*-hexane = 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, J = 8.3 Hz, 4H), 7.21 (d, J = 8.3 Hz, 4H), 2.37 (s, 6H), 2.28 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.3, 142.3, 138.8, 132.2, 126.1, 121.3, 105.0, 13.3, 12.8 ppm. HRMS (ESI) calcd for $C_{22}H_{21}Br_2N_4Se$ $[M + H]^+$, 578.9293; found, 578.9298.

Bis[1-(2,4-difluorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]selane (2g). White solid, mp 101 °C, yield = 64% (152 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9).^1H NMR (400 MHz, $CDCl_3$): δ 7.35−7.29 (m, 2H), 6.92−6.86 (m, 4H), 2.23 (s, 6H), 2.19 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ162.6 (dd, J = 252.5, 11.1 Hz), 157.0 (dd, J = 255.5, 13.3 Hz), 152.8, 144.3, 130.0 (dd, J = 10.1, 1.0 Hz), 124.1 (dd, J = 13.1, 4.0 Hz), 111.9 (dd, J = 22.2, 3.0 Hz), 105.1, 104.9 (d, J = 2.0 Hz), 104.6, 103.6, 13.1, 11.3 (d, J = 4.0 Hz) ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ −107.65 (dd, J = 14.1, 7.8 Hz), −116.71 (t, J = 8.6 Hz). HRMS (ESI) calcd for $C_{22}H_{19}F_4N_4Se$ $[M + H]^+$, 495.0706; found, 495.0711.

Bis[1-(2,4-dichlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]selane (2h). Light yellow solid, mp 173 °C, yield = 60% (139 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 1.3 Hz, 2H), 7.28 (dd, J = 8.7, 1.7 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 2.22 (s, 6H), 2.13 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.5, 144.0, 136.1, 135.8, 133.3, 130.5, 130.1, 127.9, 103.2, 13.1, 11.3 ppm. HRMS (ESI) calcd for $C_{22}H_{19}C_{l4}N_4Se$ $[M + H]^+$, 558.9524; found, 558.9529.

Bis[3,5-dimethyl-1-(*p*-tolyl)-1*H*-pyrazol-4-yl]selane (2i). White solid, mp 141−142 °C, yield = 68% (164 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^1H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, J = 8.5 Hz, 4H), 7.20 (d, J = 8.5 Hz, 4H), 2.38 (s,6H), 2.36 (s, 6H), 2.33 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz,

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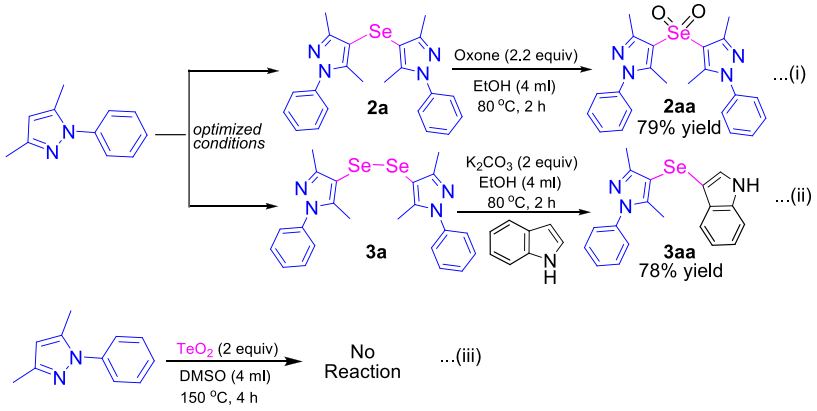
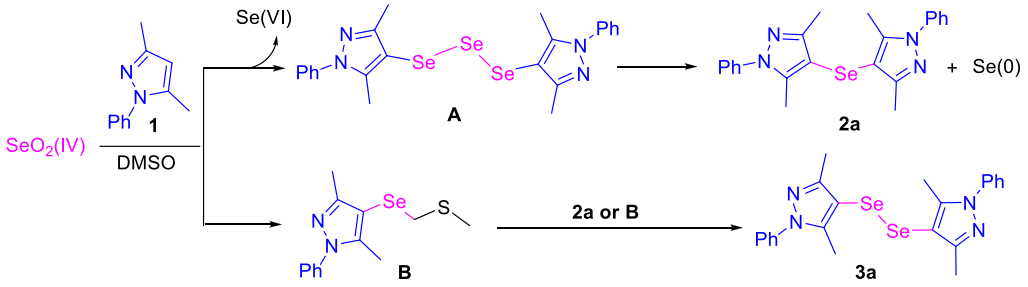
Scheme 2. Further Exploration of Products 2a and 3a



Scheme 3. Plausible Reaction Pathway



$CDCl_3$): δ 151.6, 142.3, 137.6, 137.5, 129.6, 124.7, 104.2, 21.0, 13.2, 12.5 ppm. HRMS (ESI) calcd for $C_{24}H_{27}N_4Se$ $[M + H]^+$, 451.1395; found, 451.1401.

Bis[1-(2-ethylphenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]-selane (2j). Light yellow semisolid, yield = 73% (173 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.34 (m, 4H), 7.30−7.24 (m, 2H), 7.16 (dd, *J* = 7.8, 1.2 Hz, 2H), 2.37−2.30 (m, 10H), 2.17 (s, 6H), 1.04 (t, *J* = 7.6 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 151.2, 143.1, 141.9, 138.2, 129.4, 129.3, 127.9, 126.5, 102.4, 23.8, 14.3, 13.1, 11.5 ppm. HRMS (ESI) calcd for $C_{26}H_{31}N_4Se$ $[M + H]^+$, 479.1708; found, 479.1714.

Bis[1-(3,4-dimethylphenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]selane (2k). White solid, mp 111−112 °C, yield = 74% (177 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (d, *J* = 7.0 Hz, 4H), 7.00 (d, *J* = 8.1 Hz, 2H), 2.32 (s, 6H), 2.28 (s, 6H), 2.21 (s, 12H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 151.5, 142.2, 137.7, 137.5, 136.2, 129.9, 126.1, 122.1, 104.1, 19.7, 19.3, 13.2, 12.5 ppm. HRMS (ESI) calcd for $C_{26}H_{31}N_4Se$ $[M + H]^+$, 479.1708; found, 479.1714.

Bis{3,5-dimethyl-1-[2-(trifluoromethyl)phenyl]-1*H*-pyrazol-4-yl}selane (2l). Light brown solid, mp 132 °C, yield = 76% (181 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 7.7 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 2H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.23 (d, *J* = 7.7 Hz, 2H), 2.20 (s, 6H), 2.03 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 151.7, 144.0, 137.5, 132.7, 130.4, 129.7, 128.5 (q, *J* = 30.3 Hz), 127.3 (q, *J* = 5.0 Hz), 124.1, 121.4, 102.8, 12.9, 11.2 ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ −60.53 (s). HRMS (ESI) calcd for $C_{24}H_{21}F_6N_4Se$ $[M + H]^+$, 559.0830; found, 559.0836.

Bis{3,5-dimethyl-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazol-4-yl}selane (2m). White solid, mp 110−112 °C, yield = 73% (167 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (d, *J* = 8.9 Hz, 4H), 7.22 (d, *J* = 8.6 Hz, 4H), 2.37 (s, 6H), 2.27 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.4, 148.2, 142.4, 138.3, 126.0, 121.6 (d, *J* = 8.0 Hz), 119.1, 104.9, 13.2, 12.6 ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ −58.01 (s). HRMS (ESI) calcd for $C_{24}H_{21}F_6N_4O_2Se$ $[M + H]^+$, 591.0728; found, 591.0734.

Bis[1-(2-methoxyphenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]selane (2n). Light brown solid, mp 130 °C, yield = 72% (172 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 (dd, *J* = 11.3, 4.5 Hz, 2H), 7.21 (t, *J* = 9.3 Hz, 2H), 6.95 (dd, *J* = 15.9, 8.0 Hz, 4H), 3.69 (s, 6H), 2.24 (s, 6H), 2.15 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 154.6, 151.8, 144.4, 130.1, 129.0, 128.8, 120.9, 112.0, 102.6, 55.7, 13.2, 11.4 ppm. HRMS (ESI) calcd for $C_{24}H_{27}N_4O_2Se$ $[M + H]^+$, 483.1294; found, 483.1299.

Bis[1-(4-methoxyphenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]selane (2o). Dark brown solid, mp 143 °C, yield = 74% (176 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, *J* = 8.8 Hz, 4H), 6.87 (d, *J* = 8.8 Hz, 4H), 3.76 (s, 6H), 2.30 (s, 6H), 2.28 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 159.1, 151.5, 142.5, 133.1, 126.4, 114.2, 103.9, 55.5, 13.2, 12.4 ppm. HRMS (ESI) calcd for $C_{24}H_{27}N_4O_2Se$ $[M + H]^+$, 483.1294; found, 483.1299.

Bis[3,5-dimethyl-1-(3-nitrophenyl)-1*H*-pyrazol-4-yl]-selane (2p). Light yellow solid, mp 164 °C, yield = 78% (184 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (t, *J* = 2.1 Hz, 2H), 8.16−8.13 (m, 2H), 7.77−7.74 (m, 2H), 7.59 (t, *J* = 8.1 Hz, 2H), 2.48 (s, 6H), 2.31 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.1, 148.5, 142.5, 140.7, 130.1, 129.9, 122.0, 119.1, 105.9, 13.3,13.0 ppm. HRMS (ESI) calcd for $C_{22}H_{21}N_6O_4Se$ $[M + H]^+$, 513.0784; found, 513.0790.

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4,4′-[Selenobis(3,5-dimethyl-1*H*-pyrazole-4,1-diyl)]-dibenzonitrile (2q). White solid, mp 202 °C, yield = 77% (184 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.5 Hz, 4H), 7.51 (d, J = 8.5 Hz, 4H), 2.45 (s, 6H), 2.26 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.3, 143.2, 142.4, 133.1, 124.2, 118.0, 110.9, 106.2, 13.2 (2C) ppm. HRMS (ESI) calcd for $C_{24}H_{21}N_6Se$ $[M + H]^+$, 473.0987; found, 473.0993.

Bis[3,5-dimethyl-1-(pyridin-2-yl)-1*H*-pyrazol-4-yl]-selane (2r). White solid, mp 151 °C, yield = 70% (172 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (d, J = 4.7 Hz, 2H), 7.73−7.68 (m, 4H), 7.11−7.07 (m, 2H), 2.72 (s, 6H), 2.27 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ153.3, 152.7, 147.5, 143.9, 138.2, 121.1, 116.2, 106.5, 14.4, 13.4 ppm. HRMS (ESI) calcd for $C_{20}H_{21}N_6Se$ $[M + H]^+$, 425.0987; found, 425.0993.

Bis(5-methyl-1,3-diphenyl-1*H*-pyrazol-4-yl)selane (2s). Dark yellow semisolid, yield = 75% (174 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80−7.78 (m, 4H), 7.44−7.39 (m, 4H), 7.38−7.31 (m, 12H), 2.00 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.6, 143.7, 139.7, 133.4, 129.0, 128.8, 127.9, 127.9, 125.0, 103.8, 12.3 ppm. HRMS (ESI) calcd for $C_{32}H_{27}N_4Se$ $[M + H]^+$, 547.1395; found, 547.1401.

Bis(1-methyl-1*H*-pyrazol-3-yl)selane (2t). Dark yellow semisolid, yield = 78% (231 mg). R_f 0.3 (EtOAc/*n*-hexane = 4:6). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J = 9.0 Hz, 2H), 7.39 (d, J = 19.3 Hz, 2H), 3.84 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 144.5, 143.4, 135.1, 133.7, 104.2, 39.0 (d, J = 10.1 Hz) ppm. HRMS (ESI) calcd for $C_8H_{11}N_4Se$ $[M + H]^+$, 243.0143; found, 243.0149.

Typical Procedure for the Synthesis of Di-Selenylated Bis-Pyrazoles. Pyrazole (1 mmol) and SeO_2 (3 mmol) in DMSO (4 mL) were added to the dry round-bottom flask (25 mL) at 150 °C and heated on an oil-bath for 0.5 h. The reaction was monitored by TLC, and after completion, the reaction mixture was transferred in ethyl acetate (20 mL) and washed with H_2O (50 mL × three times). The combined organic phases were concentrated on a rotary evaporator and crude was purified over silica gel (ethyl acetate: *n*-hexane) to give di-selenylated bis-pyrazole products.

1,2-Bis(3,5-dimethyl-1-phenyl-1*H*-pyrazol-4-yl)-diselane (3a). Light yellow semisolid, yield = 65% (190 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37−7.33 (m, 5H), 7.30−7.26 (m, 5H), 2.17 (s, 6H), 2.02 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.2, 144.4, 139.7, 129.1, 127.8, 124.7, 104.7, 12.6, 11.8 ppm. HRMS (ESI) calcd for $C_{22}H_{23}N_4Se_2$ $[M + H]^+$, 503.0248; found, 503.0253.

1,2-Bis[1-(3-fluorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3b). Dark brown viscous, yield = 66% (187 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.28 (m, 2H), 7.06 (t, J = 7.7 Hz, 4H), 6.99 (t, J = 8.2 Hz, 2H), 2.15 (s, 6H), 2.05 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 162.8 (d, J = 248.4 Hz), 153.6 (s), 142.7 (d, J = 348.4 Hz), 130.3 (d, J = 9.0 Hz), 119.9 (d, J = 3.0 Hz), 114.7 (d, J = 20.2 Hz), 112.0 (d, J = 30.3 Hz), 105.4, 12.6, 12.0 ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ −110.72 (dd, J = 15.4, 8.3 Hz). HRMS (ESI) calcd for $C_{22}H_{21}F_2N_4Se_2$ $[M + H]^+$, 539.0059; found, 539.0065.

1,2-Bis[1-(3-chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3c). Dark yellow semisolid, yield = 61% (169 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 2H), 7.28 (d, J = 6.5 Hz, 4H), 7.19−7.15 (m, 2H), 2.15 (s, 6H), 2.05 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.7, 144.5, 140.6, 135.0, 130.1, 127.9, 124.7, 122.4, 105.4, 12.6, 12.0 ppm. HRMS (ESI) calcd for $C_{22}H_{21}Cl_2N_4Se_2$ $[M + H]^+$, 570.9468; found, 570.9474.

1,2-Bis[1-(4-chlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3d). Dark yellow semisolid, yield = 60% (166 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (d, J = 8.7 Hz, 4H), 7.22 (d, J = 8.7 Hz, 4H), 2.14 (s, 6H), 2.03 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.5, 144.4, 138.2, 133.7, 129.3, 125.7, 105.2, 12.5, 11.9 ppm. HRMS (ESI) calcd for $C_{22}H_{21}Cl_2N_4Se_2$ $[M + H]^+$, 570.9468; found, 570.9474.

1,2-Bis[1-(3-bromophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3e). White viscous, yield = 64% (168 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 1.9 Hz, 2H), 7.45−7.39 (m, 2H), 7.26−7.16 (m, 4H), 2.15 (s, 6H), 2.05 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.7, 144.5, 140.6, 130.9, 130.4, 127.6, 122.8, 122.8, 105.4, 12.6, 12.0 ppm. HRMS (ESI) calcd for $C_{22}H_{21}Br_2N_4Se_2$ $[M + H]^+$, 658.8458; found, 658.8463.

1,2-Bis[1-(4-bromophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3f). Dark yellow semisolid, yield = 63% (165 mg). R_f 0.3(EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, J = 8.3 Hz, 4H), 7.16 (d, J = 8.3 Hz, 4H), 2.13 (s, 6H), 2.02 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.5, 143.3, 137.4, 131.2, 125.0, 124.8, 120.4, 104.2, 11.5, 10.8 ppm. HRMS (ESI) calcd for $C_{22}H_{21}Br_2N_4Se_2$ $[M + H]^+$, 657.8458; found, 658.8463.

1,2-Bis[1-(2,4-dichlorophenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3g). Dark yellow semisolid, yield = 58% (154 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (s, 2H), 7.29 (s, 1H), 7.20−7.16 (m, 3H), 2.16 (s, 6H), 2.00 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.2, 145.7, 138.9, 133.4, 130.7, 129.8, 128.2, 122.1, 104.0, 12.8, 11.4 ppm. HRMS (ESI) calcd for $C_{22}H_{18}Cl_4N_4Se_2$ $[M + Na]^+$, 660.8514; found, 660.8514.

1,2-Bis[3,5-dimethyl-1-(*p*-tolyl)-1*H*-pyrazol-4-yl]-diselane (3h). Dark yellow liquid, yield = 68% (194 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (s, 8H), 2.32 (s, 6H), 2.16 (s, 6H), 1.99 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.0, 144.4, 137.8, 137.2, 129.6, 124.6, 104.4, 21.0, 12.6, 11.7 ppm. HRMS (ESI) calcd for $C_{24}H_{27}N_4Se_2$ $[M + H]^+$, 531.0561; found, 531.0566.

1,2-Bis[1-(3,4-dimethylphenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3i). Dark yellow semisolid, yield = 70% (190 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (d, J = 8.1 Hz, 4H), 7.21 (t, J = 9.3 Hz, 2H), 6.95−6.93 (m, 2H), 2.21 (s, 6H), 2.18 (s, 6H), 2.16 (s, 6H), 1.98 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.8, 144.4, 137.6, 137.5, 136.4, 130.0, 125.9, 122.0, 104.2, 19.7, 19.3, 12.6, 11.8 ppm. HRMS (ESI) calcd for $C_{26}H_{31}N_4Se_2$ $[M + H]^+$, 559.0874; found, 559.0879.

1,2-Bis{3,5-dimethyl-1-[4-(trifluoromethoxy)phenyl]-1*H*-pyrazol-4-yl}diselane (3j). Dark yellow semisolid, yield = 76% (199 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, J = 8.8 Hz, 4H), 7.20 (d, J = 8.6 Hz, 4H), 2.13 (s, 6H), 2.05 (s, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 153.6, 148.3, 144.4, 138.1, 126.0 (d, J = 21.2 Hz), 121.7, 105.3, 12.5, 11.9 ppm. ^{19}F NMR (400 MHz, $CDCl_3$): δ −58.04 (s). HRMS (ESI) calcd for $C_{24}H_{21}F_6N_4O_2Se_2$ $[M + H]^+$, 670.9894; found, 670.9899.

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1,2-Bis[1-(2-methoxyphenyl)-3,5-dimethyl-1*H*-pyrazol-4-yl]diselane (3k). Dark yellow semisolid, yield = 64% (178 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (t, J = 7.7 Hz, 2H), 7.18−7.13 (m, 2H), 6.93 (t, J = 7.8 Hz, 4H), 3.65 (s, 6H), 2.18 (s, 6H), 1.92 (s, 6H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 154.5, 152.8, 146.4, 130.3, 129.0, 128.4, 120.8, 112.0, 103.2, 55.7, 12.6, 10.8 ppm. HRMS (ESI) calcd for $C_{24}H_{27}N_4O_2Se_2$ [M + H]$^+$, 563.0459; found, 563.0464.

1,2-Bis[3,5-dimethyl-1-(3-nitrophenyl)-1*H*-pyrazol-4-yl]diselane (3l). Light yellow semisolid, yield = 72% (196 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (t, J = 2.0 Hz, 2H), 8.15 (d, J = 8.2 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.58 (t, J = 8.1 Hz, 2H), 2.18 (s, 6H), 2.16 (s, 6H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 154.3, 148.6, 144.5, 140.5, 130.2, 129.6, 122.2, 118.9, 106.5, 12.6, 12.3 ppm. HRMS (ESI) calcd for $C_{22}H_{21}N_6O_4Se_2$ [M + H]$^+$, 592.9949; found, 592.9955.

4,4′-[Diselanediylbis(3,5-dimethyl-1*H*-pyrazole-4,1-diyl)]dibenzonitrile (3m). Light yellow semisolid, yield = 72% (202 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, J = 8.4 Hz, 4H), 7.48 (d, J = 8.4 Hz, 4H), 2.18 (s, 6H), 2.11 (s, 6H)ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 154.4, 144.4, 142.9, 133.2, 124.2, 117.9, 111.2, 106.9, 12.6, 12.5 ppm. HRMS (ESI) calcd for $C_{24}H_{21}N_6Se_2$ [M + H]$^+$, 553.0153; found, 553.0158.

1,2-Bis[3,5-dimethyl-1-(pyridin-2-yl)-1*H*-pyrazol-4-yl]diselane (3n). Dark yellow semisolid, yield = 71% (207 mg). R_f 0.4 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 4.6 Hz, 2H), 7.73−7.65 (m, 4H), 7.07 (t, J = 5.4 Hz, 2H), 2.33 (s, 6H), 2.18 (s, 6H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 153.7, 153.1, 147.6, 146.0, 138.2, 121.3, 116.3, 106.9, 13.6, 12.9 ppm. HRMS (ESI) calcd for $C_{20}H_{21}N_6Se_2$ [M + H]$^+$, 505.0153; found, 505.0158.

1,2-Bis(5-methyl-1,3-diphenyl-1*H*-pyrazol-4-yl)-diselane (3o). Dark yellow viscous, yield = 77% (205 mg). R_f 0.3 (EtOAc/*n*-hexane = 1:9). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J = 1.7 Hz, 2H), 7.85 (t, J = 1.5 Hz, 2H), 7.37−7.31 (m, 7H), 7.30−7.26 (m, 7H), 7.24 (dd, J = 3.6, 1.9 Hz, 2H), 2.09 (s, 6H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 152.2, 144.3, 137.9, 131.2, 127.5, 126.7, 126.5, 126.4, 123.3, 100.7, 10.5 ppm. HRMS (ESI) calcd for $C_{32}H_{27}N_4Se_2$ [M + H]$^+$, 627.0561; found, 627.0566.

Typical Procedure for the Oxidation of Mono-Selenylated Bis-Pyrazole (2a). Pyrazole, **2a** (1 mmol) and oxone (2.2 mmol) in EtOH (4 mL) were added to a dry round-bottom flask (25 mL) and heated at 80 °C in an oil-bath for 2 h. The reaction was monitored by TLC, and after completion, the reaction mixture was transferred in ethyl acetate (20 mL) and washed with H_2O (50 mL × three times). The combined organic phases were concentrated on a rotary evaporator and crude was purified over silica gel (ethyl acetate/*n*-hexane) to give dioxide mono-selenylated bis-pyrazole product (**2aa**).

4,4′-Selenonylbis(3,5-dimethyl-1-phenyl-1*H*-pyrazole) (2aa). White solid, mp 201−202 °C, yield = 79% (84 mg). R_f 0.3 (EtOAc/*n*-hexane = 4:6). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (t, J = 8.8 Hz, 6H), 7.32 (d, J = 7.3 Hz, 4H), 2.57 (s, 6H), 2.42 (s, 6H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 148.3, 142.9, 138.0, 129.5, 129.2, 125.6, 118.4, 12.8, 11.7 ppm. HRMS (ESI) calcd for $C_{22}H_{23}N_4O_2Se$ [M + H]$^+$, 455.0981; found, 455.0986.

Typical Procedure for the Coupling of Di-Selenylated Bis-Pyrazole (3a) with Indole. Pyrazole, **3a** (1 mmol), indole (1 mmol), and K_2CO_3 (2.2 mmol) in EtOH (4 mL) were added to a dry round-bottom flask (25 mL) and heated at 80 °C in an oil-bath for 2 h. The reaction was monitored by TLC, and after completion, the reaction mixture was transferred in ethyl acetate (20 mL) and washed with H_2O (50 mL × three times). The combined organic phases were concentrated on a rotary evaporator and crude was purified over silica gel (ethyl acetate: *n*-hexane) to give unsymmetric di-selenylated bis-pyrazole product (**3aa**).

3-[(3,5-Dimethyl-1-phenyl-1*H*-pyrazol-4-yl)selanyl]-1*H*-indole (3aa). Dark brown semisolid, yield = 78% (57 mg). R_f 0.3 (EtOAc/*n*-hexane = 3:7).^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 1H), 7.74 (d, J = 7.4 Hz, 1H), 7.45−7.39 (m, 2H), 7.36 (d, J = 7.4 Hz, 5H), 7.24−7.16 (m, 2H), 2.50 (s, 3H), 2.45 (s, 3H) ppm. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 152.2, 142.6, 139.9, 136.1, 129.5, 129.1,129.0, 127.5, 124.8, 122.6, 120.4, 120.1, 111.2, 105.1, 101.1, 13.2, 12.6 ppm. HRMS (ESI) calcd for $C_{19}H_{18}N_3Se$ [M + H]$^+$, 368.0660; found, 368.0666.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.2c00323.

Characterization data of all compounds and ^{1}H and ^{13}C NMR and HRMS spectra for all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Sanghapal D. Sawant − *Natural Products and Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, Uttar Pradesh 201002, India;* orcid.org/0000-0002-6224-3214; Email: sdsawant@iiim.res.in

Authors

Jaspreet Kour − *Natural Products and Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, Uttar Pradesh 201002, India*

Pratiksha Khajuria − *Natural Products and Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; Academy of Scientific and Innovative Research (AcSIR), Ghaziabad, Uttar Pradesh 201002, India*

Praveen Kumar Verma − *Natural Products and Medicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India; School of Advanced Chemical Sciences, Shoolini University, Solan, Himachal Pradesh 173229, India;* orcid.org/0000-0002-0505-3502

Neharika Kapoor − *Quality Management and Instrumentation Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India*

Amit Kumar − *Quality Management and Instrumentation Division, CSIR-Indian Institute of Integrative Medicine, Jammu 180001, India*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.2c00323

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Notes

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