Electrochemical Regioselective C(sp^2)-H Bond Chalcogenation of Pyrazolo[1,5-*a*]pyrimidines via Radical Cross Coupling at Room Temperature

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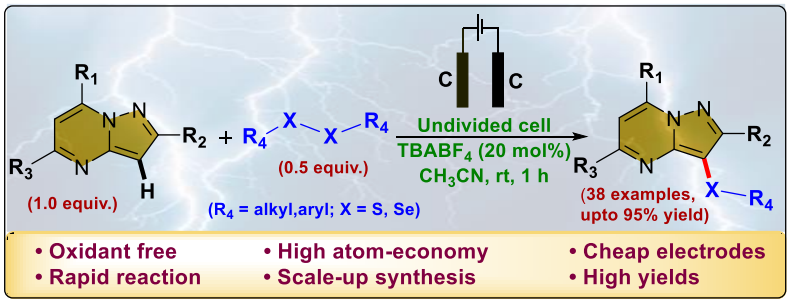
Graphical abstract:



Abstract

In this report, we disclose an electrochemical approach for the C(sp^2)-H chalcogenation of pyrazolo[1,5-*a*]pyrimidines at room temperature via radical cross-coupling reaction. The reaction takes place within an undivided cell employing graphite electrodes, with $TBABF_4$ acting as the supporting electrolyte. This technique offers a rapid, oxidant-free, and environmentally conscious protocol for achieving regioselective chalcogenation specifically at the C3 position of pyrazolo[1,5-*a*]pyrimidines. Furthermore, the procedure uses only 0.5 equivalents of diaryl chalcogenides which underscores the atom economy of the protocol. Key attributes of this methodology include mild reaction conditions, short reaction time, utilization of cost-effective electrode materials, and reliable achievement of yields ranging from good to excellent and environmentally friendly reaction conditions. Cyclic voltammetry studies and radical quenching experiments suggest a radical pathway for the reaction mechanism.

Introduction

Organoselenides and organosulfides are prevalent in pharmaceutically and therapeutically significant molecules, showcasing their widespread presence and importance in medicinal chemistry.[1] In addition to their roles in medicinal and synthetic chemistry, organochalcogen compounds also find applications in diverse fields such as material sciences, agrochemicals, and catalysis.[2] The construction of C-Se, as well as C-S bond formation, stands as a critical

juncture in synthetic chemistry, underscored by the profound significance of chalcogen-containing compounds. For the formation of C-X (X = S, Se) bonds, organic chemists have adopted various strategies such as metal catalysis, the utilization of iodine-based reagents, oxidant facilitated transformations, and photocatalysis.[3]

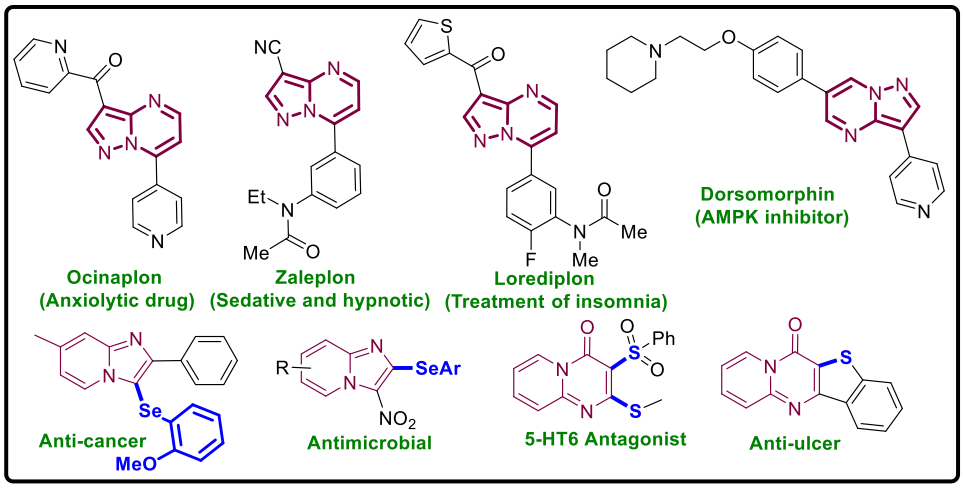
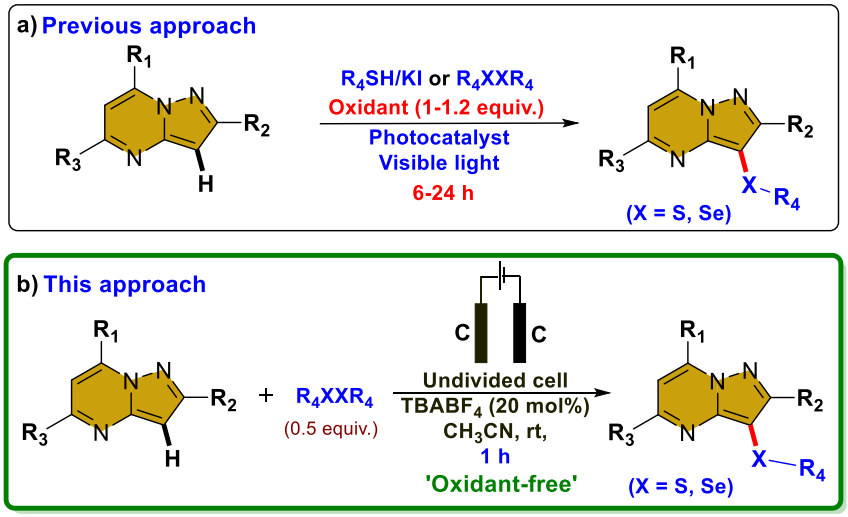


Figure 1. Important compounds containing pyrazolo[1,5-*a*]pyrimidine scaffold and bioactive chalcogen containing N-heterocycles

Pyrazolo[1,5-*a*]pyrimidines constitute a significant class of N-fused heterocyclic scaffolds with versatile biological activities, encompassing antiviral,[4] anticancer,[5] anti-malarial,[6] and anxiolytic properties.[7] This structural motif serves as the core foundation for pharmaceutical agents such as zaleplon, loredipion, ocinaplon, and dorsomorphin. These compounds play pivotal roles in the treatment of insomnia and anxiety disorders, exemplifying the diverse therapeutic applications of pyrazolo[1,5-*a*]pyrimidines in modern medicine.[8] Pyrazolo[1,5-*a*]pyrimidine derivatives are crucial in material sciences, offering intriguing optical properties and applications in chemo-sensing.[9] Their unique structure makes them valuable for developing materials with distinct optical attributes, showcasing versatility beyond medicinal uses. Thus, the synthesis of functionalized pyrazolo[1,5-a]pyrimidines holds great significance.

In past few years, electrochemical synthesis of organic molecules has emerged as a powerful and environmentally friendly approach for the synthesis of organic compounds.[10] The advantages of electrochemical synthesis, such as oxidant free and gentle reaction conditions, short reaction durations, and the utilization of electrons as reagents, distinguish it from conventional synthesis methods. This approach not only proves to be environmentally friendly by minimizing waste through the avoidance of stoichiometric amounts of oxidants but also embraces an eco-conscious strategy by directly harnessing electrical energy for organic synthesis.[11] Furthermore, electrochemical synthesis demonstrates scalability for industrial applications, as it can be seamlessly conducted in continuous flow, facilitating the efficient scaling up of organic synthesis processes.[12]

Previously, visible light-promoted, KI-catalyzed chalcogenation of pyrazolo[1,5-*a*]pyrimidines in the presence of potassium peroxodisulfate ($K_2S_2O_8$) as an oxidant is known (**Scheme 1a**).[13]



Scheme 1. Chalcogenation approaches for pyrazolo[1,5-*a*]pyrimidines.

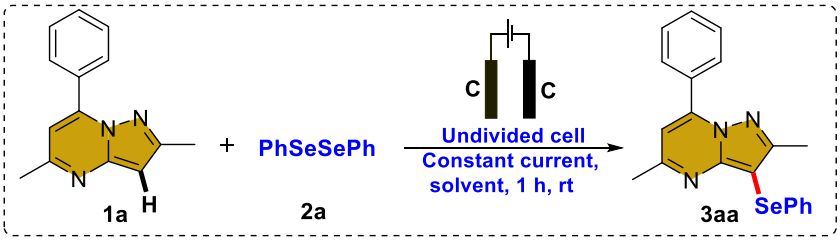
Continuing our exploration of environmentally friendly approaches for the direct C-H functionalization of heterocycles,[14] here we report rapid, high yielding, oxidant-free, direct and regioselective C3 selenylation and sulfenylation of pyrazolo[1,5-*a*]pyrimidines under electrochemical conditions (**Scheme 1b**). This technique utilizes tetrabutylammonium tetrafluoroborate ($TBABF_4$) as an efficient and economical electrolyte (20 mol%), only 0.5 equivalent of diphenyl dichalcogenides as chalcogen source with graphite serving as a cost-effective and readily available electrode material.

Result and discussion

The electrochemical selenylation of 2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine (**1a**) was carried out in an undivided cell for the duration of 1 hour under a constant current of 10 mA, utilizing 0.5 equivalents of diphenyl diselenide (**2a**), 20 mol% of $TBABF_4$ as an electrolyte, DMSO as the solvent, and graphite electrodes as cathode and anode. This reaction yielded the desired selenylated product **3aa** in a 41% yield (**Table 1**, Entry 1). Maintaining all other parameters constant, we opted to investigate the influence of different solvents on the reaction conditions. When ethanol was employed as the solvent (entry 2), product **3aa** was obtained with a yield of 31%. Shifting to methanol as the solvent (entry 3) resulted in a substantial enhancement, yielding a noteworthy 62% of **3aa**. The use of dimethyl carbonate (DMC) as a solvent proved ineffective in generating product **3aa** (entry 4). Interestingly, when acetonitrile was utilized as the solvent, the yield of product **3aa** significantly increased to 89% (entry 5), indicating that acetonitrile is the optimal solvent for the selenylation process. Further, we evaluated the influence of different electrolytes such as potassium iodide and tetrabutylammonium bromide (TBAB) on the reaction outcome. When potassium iodide was employed, the desired selenylated product **3aa** was not formed (entry 6). However, in contrast, when TBAB was utilized, product **3aa** was obtained in 56% yield (entry 7), this suggested that $TBABF_4$ was the optimal electrolyte for the reaction. Subsequently, we opted to conduct the reaction under reduced currents of 8 mA and 6 mA. However, as the current decreased, so did the yield of the reaction (entries 8 and 9). In the absence of electric current,

no product formation was observed, underscoring the essential role of electricity in driving the reaction forward (entry 10).

Table 1. Optimization of reaction conditions[a]

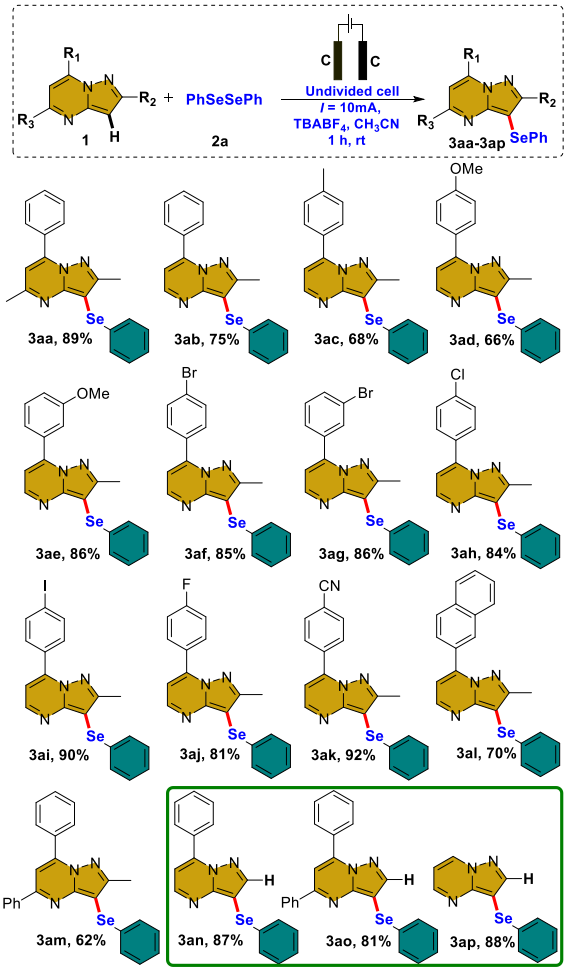


Entry	Electrolyte (20 mol%)	Solvent	Current	Yield[b]
1.	$TBABF_4$	DMSO	10 mA	41%
2.	$TBABF_4$	EtOH	10 mA	31%
3.	$TBABF_4$	MeOH	10 mA	62%
4.	$TBABF_4$	DMC	10 mA	NR
5.	**$TBABF_4$**	**CH_3CN**	**10 mA**	**89%**
6.	KI	CH_3CN	10 mA	NR
7.	TBAB	CH_3CN	10 mA	56%
8.	$TBABF_4$	CH_3CN	8 mA	70%
9.	$TBABF_4$	CH_3CN	6 mA	58%
10.[c]	$TBABF_4$	CH_3CN	0 mA	NR
11.[d]	$TBABF_4$	CH_3CN	10 mA	78%
12.[e]	$TBABF_4$	CH_3CN	10 mA	67%
13.[f]	$TBABF_4$	CH_3CN	10 mA	57%
14.[g]	$TBABF_4$	CH_3CN	10 mA	87%

[a]**Reaction conditions**: **1a** (0.2 mmol), **2a** (0.1 mmol), electrolyte (20 mol%), solvent 4.0 mL, constant current, rt, reaction mixture was electrolyzed in Electrasyn 2.0 instrument for 1 h. [b]Isolated yields, [c]no electric current, [d] C(+)|Pt(-), [e] Pt(+)|C(-),[f] 10 mol% $TBABF_4$,[g] 30 mol% $TBABF_4$.

For further optimisation of the reaction conditions, we conducted test reactions in different undivided cells, specifically C || Pt and Pt || C, maintaining a constant current of 10 mA, acetonitrile served as the solvent, and $TBABF_4$ was utilized as the electrolyte, with reaction duration of 1 hour. Despite these adjustments, no enhancement in the reaction yield was observed in either case (entries 11 and 12). Reaction was also conducted using varying concentrations of the supporting electrolyte $TBABF_4$. At 10 mol% concentration of $TBABF_4$ reaction yield decreased to 57% (entry 13) while at 30 mol% concentration of $TBABF_4$ reaction yield was 87% (entry 14). As the concentration of the electrolyte was reduced, the reaction yield decreased. However, when the electrolyte concentration was increased, a yield nearly comparable to that achieved with a 20 mol% concentration was observed. Thus, we opted to maintain the electrolyte concentration at 20 mol%. The highest yield of product **3aa** was achieved by employing 1 equivalent of **1a**, 0.5 equivalent of diphenyl diselenide (**2a**), 20 mol% of $TBABF_4$, and conducting the reaction in an undivided cell with graphite anode and cathode under galvanostatic conditions (I = 10 mA), utilizing acetonitrile as the solvent for a duration of 1 hour. With this encouraging result, we decided to check the substrate scope for the electrochemical selenylation of pyrazolo[1,5-*a*]pyrimidines using the optimized condition

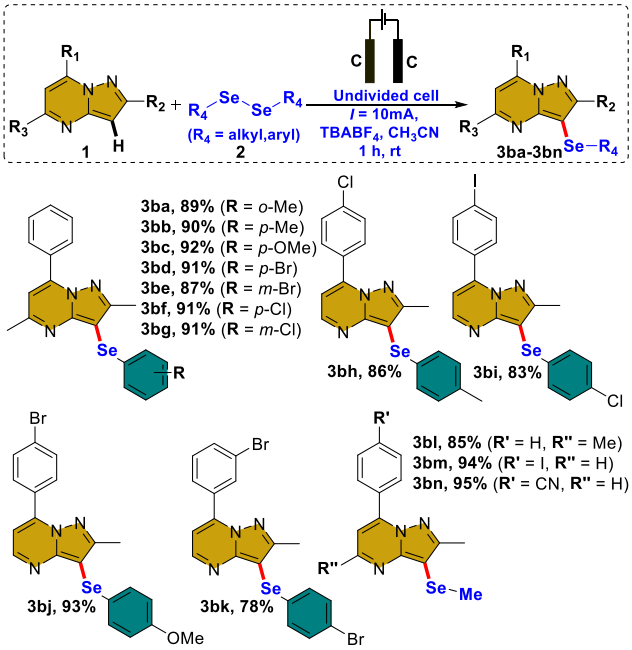
(**Scheme 2**). The selenylation of 2-methyl-7-phenylpyrazolo[1,5-*a*]pyrimidine was conducted under optimized conditions, resulting in the formation of the desired C-3 selenylated compound **3ab** with a good yield of 75%. Subsequently, pyrazolo[1,5-*a*]pyrimidine derivatives containing electron-donating moieties (*p*-Me, *p*-OMe, *m*-OMe) on the phenyl ring exhibited good reactivity towards diorganyl diselenides, affording the selenylated products **3ac-3ae** in yields ranging from 66% to 86%, respectively. Pyrazolo[1,5-*a*]pyrimidine derivatives bearing halogen substituents (*p*-F, *p*-Cl, *p*-Br, *m*-Br, *p*-I) on the phenyl ring exhibited excellent reactivity in the electrochemical selenylation process, yielding products **3af-3aj** with outstanding yields ranging from 84% to 90% respectively. Under the optimized conditions, the pyrazolo[1,5-*a*]pyrimidine derivative featuring a strong electron-withdrawing cyano substituent demonstrated exceptional tolerance, affording the selenylated product **3ak** in an impressive yield of 92%. Additionally, both 2-methyl-7-(naphthalen-2-yl)pyrazolo[1,5-*a*]pyrimidine and 2-methyl-5,7-diphenylpyrazolo[1,5-*a*]pyrimidine exhibited robust reactivity with diphenyl diselenides under optimized conditions, giving the selenylated products **3al** and **3am** in yields of 70% and 62%, respectively.



Scheme 2. Substrate scope for electrochemical selenylation of pyrazolo[1,5-*a*]pyrimidines.[a]Reaction conditions: **1** (0.2 mmol), **2a** (0.1 mmol), $TBABF_4$ (20 mol%), CH_3CN 4.0 mL, constant current (*I* = 10 mA), rt, reaction mixture was electrolyzed in Electrasyn 2.0 instrument for 1 h. Yields are isolated yields.

When subjected to electrochemical selenylation, pyrazolo[1,5-*a*]pyrimidine lacking substituents on the C2 position exclusively yielded the corresponding C3 selenylated products **3an-3ap** in good yields (81%-88%), emphasising the excellent regioselectivity

inherent to the developed methodology. Subsequently, the range of various aryl and alkyl diorganyl diselenides was explored for the electrochemical selenylation of pyrazolo[1,5-*a*]pyrimidine derivatives (**Scheme 3**). Diaryl diselenides possessing various electron donating (*o*-Me, *p*-Me, *p*-OMe) as well as electron withdrawing groups (*p*-Br, *m*-Br, *p*-Cl, *m*-Cl) reacted with 2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine exclusively giving respective C3 selenylated derivatives **3ba-3bg** with remarkable yields (87-92%). Upon subjecting diverse halogen-substituted pyrazolo[1,5-*a*]pyrimidine derivatives to reaction with an array of substituted diaryl diselenides, the resultant selenylated products **3bh-3bk** were obtained in good to excellent yields ranging from 78% to 93%. Furthermore, dimethyl diselenide underwent reactions with diverse substituted pyrazolo[1,5-*a*]pyrimidine derivatives under optimized reaction parameters, yielding products **3bl-3bn** with yields ranging from 85% to 95%, respectively.



Scheme 3. Substrate scope of various diorganyl diselenides. [a]Reaction conditions: **1** (0.2 mmol), **2** (0.1 mmol), $TBABF_4$ (20 mol%), CH_3CN 4.0 mL, constant current (I = 10 mA), rt, reaction mixture was electrolysed in Electrasyn 2.0 instrument for 1 h. Yields are isolated yields.

After developing a mild and straightforward protocol for the regioselecive selenylation of pyrazolo[1,5-*a*]pyrimidines we decided to extend the methodology to carry out C3 sulfenylation of the pyrazolo[1,5-a]pyrimidine scaffold under electrochemical conditions. At first, optimised condition for selenylation was tried for achieving sulfenylation but only 10% of the desired sulfenylated product **3ca** was obtained. To understand the reaction parameters and requirements, cyclic voltammetry studies for both, selenylation and sulfenylation reaction were done. Cyclic voltammetry (CV) studies were meticulously conducted for the selenylation reaction (**Figure 2**, **graph A**) and as expected, the CV of $TBABF_4$ (0.1 M) revealed an absence of any oxidation peak. However, CV of compound **1a** (20 mM) in $TBABF_4$ (0.1 M) showed distinct oxidation peak at +1.80 V. Similarly, the CV analysis of diphenyl diselenide **2a** (20 mM) in 0.1 M $TBABF_4$ showed oxidation peak at +1.65 V. CV of the mixture of **1a** (20 mM), **2a** (20 mM) along with $TBABF_4$ (0.1 M) showed the oxidation peaks at +1.70 V, +2.10 V. The oxidation peaks at +1.70 V and +2.10 V were possibly due to

the chemical interaction between the diphenyl diselenide and **1a**. The close proximity of the oxidation potentials of substrate **1a** and diphenyl diselenide **2b** makes situation more favourable for the plausible radical cross coupling between them.

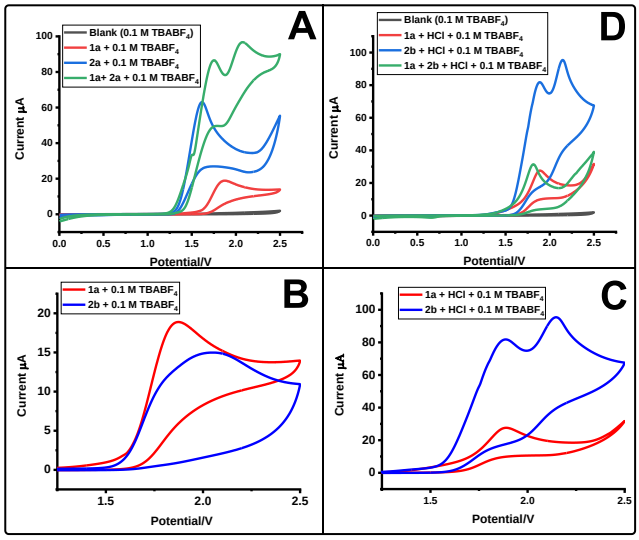
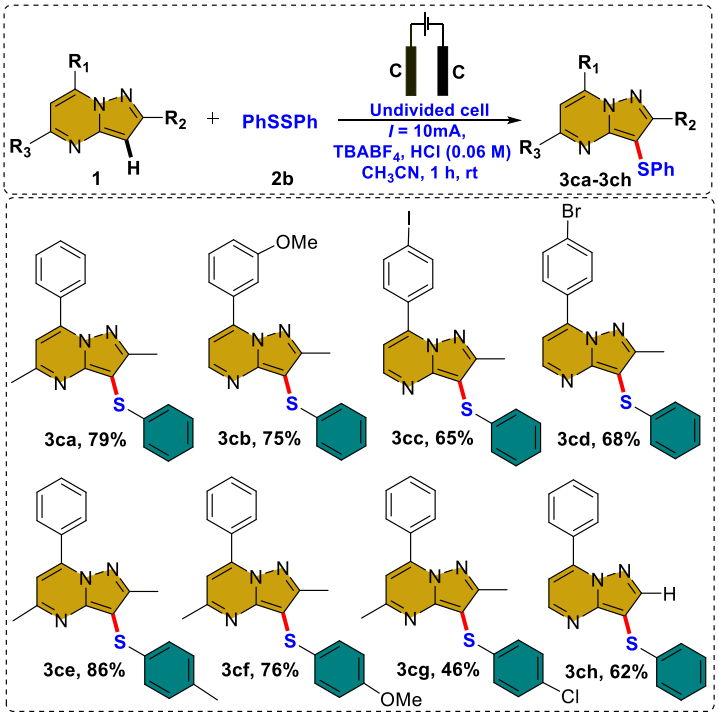


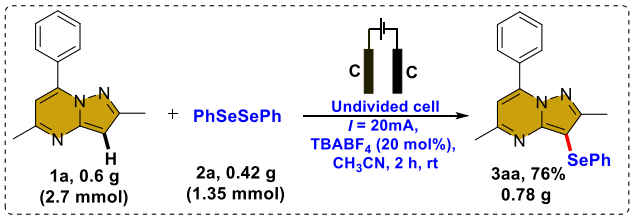
Figure 2. Cyclic voltammetry

Whereas cyclic voltammetry of diphenyl disulfide (**Figure 2**, **graph B**) showed oxidation peak at somewhat higher side (+2.10 V) as compared to that of substrate **1a** (+1.80 V). This prompted us to perform the CV study in the presence of acid additives.[15] Interestingly, the cyclic voltammetry experiment conducted in the presence of HCl as additive, substrate **1a** and diphenyl disulfide (**2b**) displayed oxidation peaks at 1.88 V and +1.87 V, respectively, showing a remarkably close match favourable for the radical cross coupling reaction (**Figure 2, graph C**, **D**). After diminutive optimisation (see supporting information table S1), C3 sulfenylation of 2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine (**1a**) was achieved using 0.5 equivalents of diphenyl disulfide (**2b**), $TBABF_4$ (20 mol%) as an electrolyte in the presence of 0.06 M HCl as an additive, CH_3CN as solvent and carrying out reaction for the duration of 1 hour under galvanostatic conditions (I = 10mA, C(+)|C(-)). Corresponding sulfenylated product **3ca** was obtained in 79% yield. After determining the optimized condition, we decided to investigate the substrate scope for the sulfenylation reaction (**Scheme 4**). Pyrazolo[1,5-*a*]pyrimidine derivatives having electron-rich (-OMe), as well as electron-withdrawing substituents (-I, -Br) on the phenyl ring, underwent sulfenylation furnishing corresponding products **3cb-3cd** with yields ranging from 65-75% respectively. Substituted diphenyl disulfide derivatives having -Me, -OMe, and -Cl substituents were also tested under optimized conditions for the sulfenylation of compound **1a**, yielding corresponding products **3ce-3cg** (yields ranging from 46-86%, respectively). Sulfenylation of 7-phenylpyrazolo[1,5-*a*]pyrimidine was also carried out, giving the product **3ch** in 62% yield, highlighting the developed protocol's regio-selectivity.



Scheme 4. Substrate scope for electrochemical sulfenylation of pyrazolo[1,5-*a*]pyrimidines. [a]Reaction conditions: **1** (0.2 mmol), **2b** (0.1 mmol), $TBABF_4$ (20 mol%), HCl (0.06 M), CH_3CN 4.0 mL, constant current (*I* = 10 mA), rt, reaction mixture was electrolysed in Electrasyn 2.0 instrument for 1 h. Yields are isolated yields.

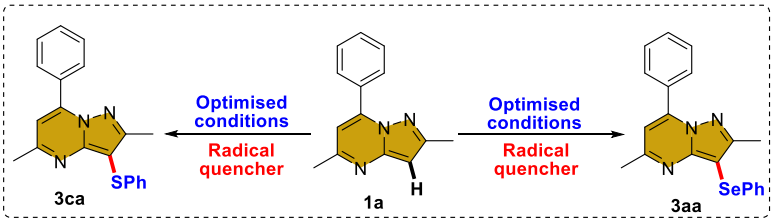
To demonstrate the practical applicability of the developed methodology, a scale-up reaction was conducted. Specifically, 0.6 g (2.7 mmol) of compound **1a** was reacted with 0.42 g (1.35 mmol) of diphenyl diselenide (**2a**), employing 20 mol% of $TBABF_4$ as a supporting electrolyte in the presence of 25 mL of acetonitrile under galvanostatic conditions (*I* = 20 mA) for a duration of 2 hours, as outlined in **Scheme 5**. The desired selenylated product **3aa** was obtained in a yield of 76%, thus affirming the scalability of the reaction.



Scheme 5. Scale-up synthesis

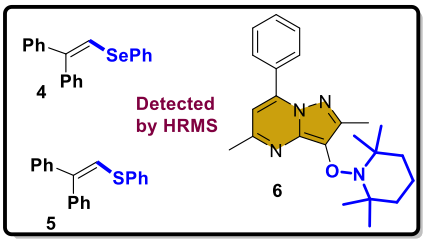
Next to this a series of control experiments were carried out to gain further insight into the reaction mechanism. The reactions were systematically carried out under optimized conditions, in presence of radical scavengers (5.0 equiv.), namely 2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) and 2,6-di-tert-butyl-4-methylphenol (BHT), 1,1-diphenyl ethylene (DPE) to evaluate the potential engagement of radical intermediates (**Scheme 6**). In presence of TEMPO as radical scavenger, the yield of selenylated product **3aa** reduced to 73%. Whereas the yield of product **3aa** significantly declined to 43%, and 25% in the case of BHT, and DPE, respectively. However, in the case of the sulfenylation reaction, radical scavengers completely inhibited the formation of the sulfenylated product **3ca**. Along with this, the TEMPO trapped adduct **6** was also detected and confirmed by HRMS analysis. When diphenyl diselenide **2a** and diphenyl

disulfide **2b** were reacted with DPE (5.0 equiv.) under optimized conditions without **1a**, radical intermediates **4** and **5** were trapped and detected by HRMS analysis. The radical adducts **4**, **5**, and **6** strongly support the involvement of the radical pathway in the reaction mechanism.



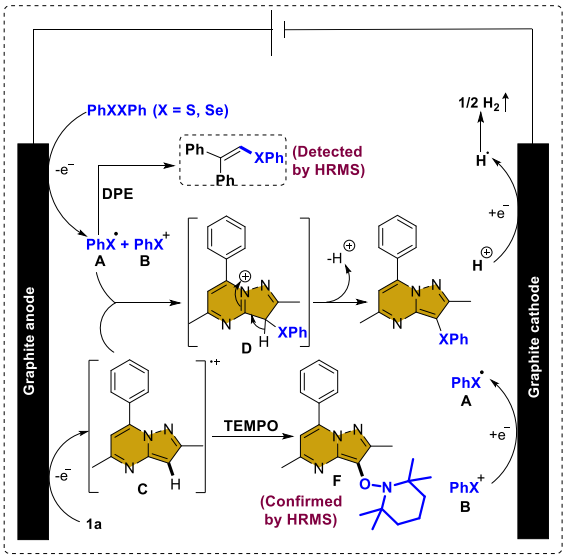
Radical Quencher	3aa	3ca
TEMPO	73%	N.D.
BHT	43%	N.D.
DPE	25%	N.D.

N.D. = not detected



Scheme 6. Control experiments

Based on the control experiments, cyclic voltammetry studies and previous literature reports[16] a plausible mechanism is depicted in **Scheme 7**. Initially, diphenyl dichalcogenide molecule (**2a**/**2b**) is subjected to anodic oxidation, leading to the formation of radical species **A** and cationic species **B**. Simultaneously, Substrate **1a** undergoes one-electron oxidation at the anode to form radical cation C, which was trapped with TEMPO (adduct **F**) and confirmed by HRMS analysis. Radical **A** combines with radical cation **C** to form intermediate **D** which on deprotonation and aromatization transforms into the product **3aa** in case of selenylation and **3ca** in case of sulfenylation respectively. At cathode radical **A** is regenerated by reduction of **B**, this step facilitates the full utilization of the diorganyl dichalcogenide reagent, enhancing the atom economy of the overall transformation by minimizing wastage. The electrochemical reaction cycle is completed by the cathodic reduction of protons into hydrogen.



Scheme 7. Proposed reaction mechanism

Conclusion

In summary, we have designed a protocol for direct, regioselective C-H chalcogenation of pyrazolo[1,5-*a*]pyrimidines using electro-catalysis via generation of reactive chalcogen species. The developed method uses mild reaction conditions, a minimum amount of reagents as well as cheap electrode materials for the selenylation of pyrazolo[1,5-*a*]pyrimidine scaffold. Mechanistic studies (control experiments and CV experiments) were also carried out to understand the nature of reactive species and overall reaction mechanism. This method is rapid, high-yielding, and scalable, which proves its synthetic utility.

Acknowledgements

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General Information

All chemicals and reagents were procured from commercial suppliers (BLD pharma, TCI, Spectrochem) and used without further purification. All elecrtocatalytic reactions were performed using IKA electrasyn 2.0 instrument. Graphite anode and cathode (0.8 cm × 0.2 cm × 5.2 cm) were used in the electrolysis. Scale-up experiment was carried out using VarTech® single output linear DC power supply (Model 1802B) using graphite electrodes (diameter 0.5 cm). Thin layer chromatography was carried out on aluminum sheets pre-coated with Merck silica gel $60F_{254}$, followed by visualization under UV light (254 nm). Product isolation was accomplished through column chromatography on silica gel with a mesh size of 100-200 using hexanes and ethyl acetate as eluent. Nuclear magnetic resonance spectra (^{1}H, ^{13}C, ^{19}F) were obtained using a Fourier transform nuclear magnetic resonance spectrometer, including the Bruker Avance 500MHz model. $CDCl_3$ served as the solvent for spectroscopic acquisition, with chemical shifts indicated in δ values (parts per million) relative to tetramethylsilane. High-resolution mass spectrometric analyses (HRMS) were performed using an electrospray ionization time-of-flight mass spectrometer (ESI-TOF-MS), comprising Dionex Ultimate 3000 and YL9100 components. Melting points were determined utilizing an electrothermal melting point apparatus, without any rectification applied. Cyclic voltammetry experiments were recorded on CH instruments electrochemical workstation (model CHI1103C) with the three-electrode cell (beaker type cell) at room temperature. All the starting materials and substrates were synthesized according to literature reports.

General experimental procedure for the preparation of C3 selenylated pyrazolo[1,5-*a*]pyrimidine derivatives: Substituted pyrazolo[1,5-*a*]pyrimidines **1** (0.2 mmol), diorganyl diselenides **2** (0.1 mmol), and $TBABF_4$ (20 mol%) were combined in a 10 mL undivided cell vial along with 4 mL of CH_3CN. Graphite cathode (0.8 cm × 0.2 cm × 5.2 cm) and Graphite anode (0.8 cm × 0.2 cm × 5.2 cm) were placed in the setup. The reaction mixture was stirred

at 620 rpm and subjected to electrolysis at a constant current of 10 mA using an IKA Electrasyn 2.0 instrument at room temperature for 1 hour. TLC analysis was used to monitor the progression of the reaction. Upon completion, the solvent was removed under vacuum, and the resulting products **3aa-3ap** and **3ba-3bn** were purified through silica gel column chromatography using 5-15% ethyl acetate in petroleum ether as the eluting solvent.

General experimental procedure for the preparation of C3 sulfenylated pyrazolo[1,5-*a*]pyrimidine derivatives:Substituted pyrazolo[1,5-*a*]pyrimidines **1** (0.2 mmol), diorganyl disulfides **2'** (0.1 mmol), and $TBABF_4$ (20 mol%) were combined in a 10 mL undivided cell vial along with 4 mL of CH_3CN and 20µL HCl was added to the reaction mixture. Graphite cathode (0.8 cm × 0.2 cm × 5.2 cm) and Graphite anode (0.8 cm × 0.2 cm × 5.2 cm) were placed in the setup. The reaction mixture was stirred at 620 rpm and subjected to electrolysis at a constant current of 10 mA using an IKA Electrasyn 2.0 instrument at room temperature for 1 hour. TLC analysis was used to check the progress of the reaction. Upon completion, the solvent was evaporated in vacuo, and the resulting products **3ca-3ch** were purified through silica gel column chromatography using 5-15% ethyl acetate in petroleum ether as the eluting solvent.

Characterisation data of compounds (3aa-3ap, 3ba-3bn, 3ca-3ch)

2,5-Dimethyl-7-phenyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3aa): Yellow solid; 89% (67.6 mg); m.p. 102-104 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.2 Hz, 2H), 7.59 – 7.53 (m, 3H), 7.23 (d, *J* = 8.2 Hz, 2H), 7.18 – 7.08 (m, 3H), 6.80 (s, 1H), 2.68 (s, 3H), 2.50 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.7, 159.4, 151.8, 146.3, 133.4, 131.2, 130.9, 129.5, 129.1, 128.9, 128.8, 125.9, 109.1, 90.8, 25.1, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{18}N_3Se$ $[M+H]^+$: 380.0661, found 380.0670.

2-Methyl-7-phenyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ab): Yellow solid; 75% (54.9 mg); m.p. 122-124 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.4 Hz, 1H), 8.08 (d, *J* = 4.0 Hz, 2H), 7.58 (s, 3H), 7.25 (s, 2H), 7.17 – 7.08 (m, 3H), 6.93 (d, *J* = 4.3 Hz, 1H), 2.56 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.6, 151.9, 150.6, 147.1, 133.0, 131.4, 130.7, 129.5, 129.1, 129.0, 128.8, 126.1, 108.0, 92.3, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{16}N_3Se$ $[M+H]^+$: 366.0505, found 366.0492.

2-Methyl-3-(phenylselanyl)-7-(p-tolyl)pyrazolo[1,5-*a*]pyrimidine(3ac): Yellow solid; 68% (51.7 mg); m.p. 102-104 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.4 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 7.9 Hz, 2H), 7.25 (d, *J* = 7.3 Hz, 2H), 7.18 – 7.10 (m, 3H), 6.91 (d, *J* = 4.6 Hz, 1H), 2.55 (s, 3H), 2.47 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.5, 152.0, 150.5, 147.2, 141.9, 133.0, 129.5, 129.4, 129.1, 129.0, 127.8, 126.0, 107.6, 92.0, 21.7, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{18}N_3Se$ $[M+H]^+$: 380.0661, found 380.0670.

7-(4-Methoxyphenyl)-2-methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ad):[2] Off white solid; 66% (52.2 mg); m.p. 96-98 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 4.4 Hz, 1H), 8.13 (d, *J* = 8.9 Hz, 2H), 7.24 (s, 2H), 7.20 – 7.04 (m, 5H), 6.92 (d, *J* = 4.4 Hz, 1H), 3.91 (s, 3H), 2.56 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 162.2, 159.6, 152.0, 150.4, 147.0, 133.1, 131.4, 129.2, 129.1, 126.1, 122.9, 114.3, 107.2, 91.9, 55.7, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{18}N_3OSe$ $[M+H]^+$: 396.0611, found 396.0613.

7-(3-Methoxyphenyl)-2-methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ae): Yellow solid; 86% (68.1 mg); m.p. 106-108 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.66 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.26 (d, *J* = 6.7 Hz, 2H), 7.14 (dd, *J* = 13.1, 8.1 Hz, 4H), 6.94 (d, *J* = 3.8 Hz, 1H), 3.90 (s, 3H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.7, 159.6, 151.9, 150.6, 147.0, 133.0, 131.9, 130.0, 129.2, 129.1, 126.1, 121.9, 117.1, 115.2, 108.0, 92.3, 55.7, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{18}N_3OSe$ $[M+H]^+$: 396.0611, found 396.0606.

7-(4-Bromophenyl)-2-methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3af): Yellow solid; 85% (75.3 mg); m.p. 96-98 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.60 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.24 (s, 2H), 7.19 – 7.06 (m, 3H), 6.91 (s, 1H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.8, 152.0, 150.6, 145.9, 132.9, 132.2, 131.1, 129.6, 129.3, 129.2, 126.2, 126.1, 107.8, 92.7, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{15}BrN_3Se$ $[M+H]^+$: 443.9607, found 443.9593.

7-(3-Bromophenyl)-2-methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ag): Brown solid; 86% (76.2 mg); m.p. 128-130 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.4 Hz, 1H), 8.21 (s, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.24 (s, 2H), 7.21 – 7.07 (m, 3H), 6.91 (d, *J* = 4.3 Hz, 1H), 2.56 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.8, 151.9, 150.5, 145.4, 134.3, 132.8, 132.6, 132.4, 130.4, 129.3, 129.2, 128.2, 126.2, 122.9, 108.1, 92.8, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{15}BrN_3Se$ $[M+H]^+$: 443.9607, found 443.9611.

7-(4-Chlorophenyl)-2-methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ah): Yellow solid; 84% (67.2 mg); m.p. 100-102 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.4 Hz, 1H), 8.05 (d, *J* = 8.7 Hz, 2H), 7.56 (d, *J* = 8.7 Hz, 2H), 7.25 (s, 2H), 7.21 – 7.07 (m, 3H), 6.92 (d, *J* = 4.3 Hz, 1H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.7, 151.9, 150.5, 145.9, 137.6, 132.8, 130.9, 129.3, 129.2, 129.1, 129.0, 126.2, 107.8, 92.6, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{15}ClN_3Se$ $[M+H]^+$: 400.0112, found 400.0113.

7-(4-Iodophenyl)-2-methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ai): Yellow solid; 90% (88.3 mg); m.p. 106-108 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.93 (d, *J* = 7.8 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 2H), 7.15 (d, *J* = 7.6 Hz, 3H), 6.91 (s, 1H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.7, 151.9, 150.8, 146.1, 138.1, 132.8, 131.1, 130.1, 129.3, 129.2, 126.2, 107.9, 98.3, 92.6, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{15}IN_3Se$ $[M+H]^+$: 491.9471, found 491.9480.

7-(4-Fluorophenyl)-2-methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3aj): Off white solid; 81% (62.2 mg); m.p. 100-102 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.12 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.30 – 7.24 (m, 4H), 7.19 – 7.11 (m, 3H), 6.91 (s, 1H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 165.5, 163.5, 159.7, 152.0, 150.6, 146.0, 132.9, 131.9, 131.8, 129.2, 126.8, 126.7, 126.1, 116.2, 116.0, 107.8, 92.5, 14.2; **^{19}F NMR** (471 MHz, $CDCl_3$) δ -107.68; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{15}FN_3Se$ $[M+H]^+$: 384.0411, found 384.0410.

4-(2-Methyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidin-7-yl)benzonitrile(3ak): Orange solid; 92% (72.0 mg), m.p. 136-138 °C; **^{1}H NMR** (500 MHz,) δ 8.63 (d, *J* = 4.3 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.19 – 7.10 (m, 3H), 6.95 (d, *J* = 4.3 Hz, 1H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.0,

151.8, 150.5, 144.7, 135.0, 132.6, 132.5, 130.2, 129.4, 129.2, 126.3, 118.2, 114.9, 108.3, 93.3, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{14}N_4SeNa$ $[M+Na]^+$: 413.0277, found 413.0264.

2-Methyl-7-(naphthalen-2-yl)-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3al): Off white solid; 70% (58.2 mg); m.p. 124-126 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.63 (s, 2H), 8.10 (d, *J* = 8.7 Hz, 1H), 8.00 (dd, *J* = 17.5, 8.3 Hz, 2H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.59 (p, *J* = 6.8 Hz, 2H), 7.26 (d, *J* = 12.4 Hz, 2H), 7.21 – 7.08 (m, 3H), 7.04 (s, 1H), 2.57 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.7, 152.0, 150.7, 147.1, 134.6, 133.0 (2C), 130.3, 129.2, 129.1, 129.0, 128.5, 128.1, 128.0, 127.9, 127.0, 126.1, 125.8, 108.3, 92.3, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{23}H_{18}N_3Se$ $[M+H]^+$: 416.0662, found 416.0655.

2-Methyl-5,7-diphenyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3am): Yellow solid; 62% (54.8 mg); m.p. 158-160 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.24 – 8.17 (m, 2H), 8.11 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.64 – 7.56 (m, 3H), 7.50 (d, *J* = 6.9 Hz, 3H), 7.38 (s, 1H), 7.36 (d, *J* = 7.5 Hz, 2H), 7.21 – 7.09 (m, 3H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.8, 157.3, 151.9, 147.0, 137.4, 133.4, 131.3, 131.2, 130.6, 129.6, 129.5, 129.1, 129.0, 128.9, 127.6, 126.1, 105.5, 92.6, 14.3; **HRMS** (ESI, *m/z*): Calculated for $C_{25}H_{20}N_3Se$ $[M+H]^+$: 442.0818, found 442.0811.

7-Phenyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3an): Off white solid; 87% (61.2 mg); m.p. 140-144 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.3 Hz, 1H), 8.33 (s, 1H), 8.04 (dd, *J* = 6.7, 3.2 Hz, 2H), 7.66 – 7.52 (m, 3H), 7.36 (d, *J* = 7.5 Hz, 2H), 7.23 – 7.07 (m, 3H), 7.00 (d, *J* = 4.3 Hz, 1H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 151.1, 150.9, 150.8, 147.8, 133.0, 131.5, 130.6, 129.8, 129.5, 129.2, 128.9, 126.4, 108.4, 92.8; **HRMS** (ESI, *m/z*): Calculated for $C_{18}H_{14}N_3Se$ $[M+H]^+$: 352.0348, found 352.0335.

5,7-Diphenyl-3-(phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ao): Yellow solid; 81% (69.3 mg); m.p. 128-132 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.19 (d, *J* = 5.8 Hz, 2H), 8.06 (d, *J* = 3.5 Hz, 2H), 7.61 (s, 3H), 7.51 (d, *J* = 6.7 Hz, 3H), 7.49 – 7.42 (m, 3H), 7.19 (dt, *J* = 11.7, 6.7 Hz, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 157.6, 151.0, 150.9, 147.7, 137.2, 133.3, 131.3, 131.2, 130.8, 130.3, 129.5, 129.2, 129.1, 128.9, 127.7, 126.4, 106.0, 93.2; **HRMS** (ESI, *m/z*): Calculated for $C_{24}H_{18}N_3Se$ $[M+H]^+$: 428.0662, found 428.0677.

3-(Phenylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ap): White solid; 88% (48.6 mg); m.p. 102-104 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 7.5 Hz, 1H), 8.62 (s, 1H), 8.29 (s, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.19 – 7.11 (m, 3H), 6.97 – 6.85 (m, 1H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 151.3, 151.0, 149.9, 135.9, 132.8, 129.8, 129.2, 126.5, 108.9, 92.8; **HRMS** (ESI, *m/z*): Calculated for $C_{12}H_9N_3SeNa$ $[M+Na]^+$: 297.9854, found 297.9842.

2,5-Dimethyl-7-phenyl-3-(o-tolylselanyl)pyrazolo[1,5-*a*]pyrimidine(3ba): Yellow solid; 89% (70.1 mg); m.p. 120-122°C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.62 – 7.52 (m, 3H), 7.12 (d, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.90 (t, *J* = 7.6 Hz, 1H), 6.80 (s, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 2.67 (s, 3H), 2.50 (s, 3H), 2.48 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.7, 159.7, 152.0, 146.3, 136.4, 133.9, 131.2, 130.9, 130.1, 129.5, 128.8, 127.3, 126.5, 125.5, 109.1, 89.6, 25.2, 21.4, 14.1; **HRMS** (ESI, *m/z*): Calculated for $C_{21}H_{20}N_3Se$ $[M+H]^+$: 394.0818, found 394.0814.

2,5-Dimethyl-7-phenyl-3-(p-tolylselanyl)pyrazolo[1,5-*a*]pyrimidine(3bb): Yellow solid; 90% (70.9 mg); m.p. 108-110 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.62 – 7.51 (m, 3H), 7.17 (d, *J* = 8.2 Hz, 2H), 6.98 (d, *J* = 8.2 Hz, 2H), 6.78 (s, 1H),

2.67 (s, 3H), 2.50 (s, 3H), 2.25 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.6, 159.3, 151.8, 146.2, 135.8, 131.2, 131.0, 129.9, 129.5, 129.4, 128.8, 109.0, 91.3, 25.2, 21.1, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{21}H_{20}N_3Se$ $[M+H]^+$: 394.0818, found 394.0817.

3-((4-Methoxyphenyl)selanyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(3bc): Yellow solid; 92% (75.4 mg); m.p. 100-102 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.60 – 7.50 (m, 3H), 7.29 (d, *J* = 8.9 Hz, 2H), 6.77 (s, 1H), 6.73 (d, *J* = 8.9 Hz, 2H), 3.73 (s, 3H), 2.68 (s, 3H), 2.50 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.5, 159.0, 158.6, 151.6, 146.2, 131.8, 131.1, 131.0, 129.5, 128.8, 123.2, 114.9, 108.9, 92.2, 55.4, 25.2, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{21}H_{20}N_3OSe$ $[M+H]^+$: 410.0767, found 410.0760.

3-((4-Bromophenyl)selanyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(3bd): Brown solid; 91% (83.2 mg); m.p. 120-122 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 6.0, 2.1 Hz, 2H), 7.57 (s, 3H), 7.31 – 7.22 (m, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 6.80 (s, 1H), 2.67 (s, 3H), 2.48 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.9, 159.2, 151.8, 146.4, 132.5, 132.1, 131.3, 130.8, 130.4, 129.5, 128.8, 119.8, 109.2, 90.3, 25.2, 14.1; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{17}BrN_3Se$ $[M+H]^+$: 457.9763, found 457.9767.

3-((3-Bromophenyl)selanyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(3be): Yellow gummy mass; 87% (79.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 6.4, 3.2 Hz, 2H), 7.68 (s, 3H), 7.44 (s, 1H), 7.37 – 7.33 (m, 1H), 7.24 (s, 1H), 7.12 (t, *J* = 7.9 Hz, 1H), 6.93 (s, 1H), 2.79 (s, 3H), 2.60 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 161.0, 159.3, 151.8, 146.4, 135.8, 131.3, 131.1, 130.8, 130.4, 129.6, 129.0, 128.8, 127.2, 123.3, 109.3, 90.0, 25.2, 14.1; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{17}BrN_3Se$ $[M+H]^+$: 457.9763, found 457.9772.

3-((4-Chlorophenyl)selanyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(3bf): Off white solid; 91% (80.3 mg); m.p. 110-112 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 6.7, 2.9 Hz, 2H), 7.62 – 7.48 (m, 3H), 7.13 (q, *J* = 8.5 Hz, 4H), 6.81 (s, 1H), 2.68 (s, 3H), 2.49 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.9, 159.2, 151.8, 146.4, 131.9, 131.7, 131.3, 130.8, 130.2, 129.5, 129.2, 128.8, 109.2, 90.5, 25.2, 14.1; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{17}ClN_3Se$ $[M+H]^+$: 414.0269, found 414.0259.

3-((3-Chlorophenyl)selanyl)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(3bg): Yellow solid; 91% (75.3 mg); m.p. 86-88 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 5.6, 2.1 Hz, 2H), 7.57 (s, 3H), 7.16 (d, *J* = 2.0 Hz, 1H), 7.09 (d, *J* = 11.3 Hz, 3H), 6.82 (s, 1H), 2.67 (s, 3H), 2.50 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 161.0, 159.3, 151.8, 146.4, 135.4, 135.0, 131.3, 130.8, 130.0, 129.5, 128.8, 128.2, 126.7, 126.0, 109.2, 90.0, 25.1, 14.1; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{17}ClN_3Se$ $[M+H]^+$: 414.0269, found 414.0269.

7-(4-Chlorophenyl)-2-methyl-3-(p-tolylselanyl)pyrazolo[1,5-*a*]pyrimidine(3bh): Yellow solid; 86% (71.0 mg); m.p. 108-110 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.58 (d, *J* = 4.4 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 2H), 7.55 (d, *J* = 8.5 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.90 (d, *J* = 4.4 Hz, 1H), 2.55 (s, 3H), 2.25 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.6, 151.8, 150.4, 145.8, 137.6, 136.2, 130.9, 130.0, 129.8, 129.2, 129.1, 128.9, 107.7, 93.2, 21.1, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{17}ClN_3Se$ $[M+H]^+$: 414.0269, found 414.0257.

3-((4-Chlorophenyl)selanyl)-7-(4-iodophenyl)-2-methylpyrazolo[1,5-*a*]pyrimidine(3bi): Off white solid; 83% (87.2 mg); m.p. 130-132 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* =

4.4 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 4.4 Hz, 1H), 2.53 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.6, 151.9, 150.7, 146.2, 138.2, 132.2, 131.1, 131.0, 130.6, 130.0, 129.3, 107.9, 98.4, 92.3, 14.1; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{14}ClIN_3Se$ $[M+H]^+$: 525.9079, found 525.9071.

7-(4-Bromophenyl)-3-((4-methoxyphenyl)selanyl)-2-methylpyrazolo[1,5-*a*]pyrimidine(3bj): Yellow solid; 93% (87.8 mg); m.p. 122-124 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.4 Hz, 1H), 7.95 (d, *J* = 8.7 Hz, 2H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.9 Hz, 2H), 6.88 (d, *J* = 4.3 Hz, 1H), 6.73 (d, *J* = 8.9 Hz, 2H), 3.73 (s, 3H), 2.55 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.3, 158.9, 151.7, 150.3, 145.8, 132.3, 132.2, 131.0, 129.6, 126.0, 122.7, 114.9, 107.6, 94.1, 55.4, 14.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{17}BrN_3OSe$ $[M+H]^+$: 473.9713, found 473.9717.

7-(3-Bromophenyl)-3-((4-bromophenyl)selanyl)-2-methylpyrazolo[1,5-*a*]pyrimidine(3bk): Yellow solid; 78% (81.3 mg); m.p. 140-142 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 4.4 Hz, 1H), 8.21 (s, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 10.1 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.28 (s, 2H), 7.11 (d, *J* = 8.4 Hz, 2H), 6.93 (d, *J* = 4.4 Hz, 1H), 2.54 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.6, 151.7, 150.6, 145.4, 134.3, 132.4, 132.3, 132.1, 131.8, 130.7, 130.3, 128.1, 122.8, 120.1, 108.1, 92.2, 14.0; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{13}Br_2N_3SeK$ $[M+K]^+$: 559.8268, found 559.8265.

2,5-Dimethyl-3-(methylselanyl)-7-phenylpyrazolo[1,5-*a*]pyrimidine(3bl): Yellow solid; 85% (54.1 mg); m.p. 118-120 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.99 (dt, *J* = 5.5, 3.1 Hz, 2H), 7.59 – 7.49 (m, 3H), 6.72 (s, 1H), 2.67 (s, 3H), 2.57 (s, 3H), 2.18 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.8, 158.2, 151.0, 146.0, 131.1, 131.0, 129.4, 128.7, 108.6, 92.1, 25.1, 14.2, 9.1; **HRMS** (ESI, *m/z*): Calculated for $C_{15}H_{15}N_3SeNa$ $[M+Na]^+$: 340.0324, found 340.0321.

7-(4-Iodophenyl)-2-methyl-3-(methylselanyl)pyrazolo[1,5-*a*]pyrimidine(3bm): Yellow solid; 94% (80.7 mg); m.p. 142-144 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.55 (d, *J* = 4.3 Hz, 1H), 7.90 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 4.3 Hz, 1H), 2.59 (s, 3H), 2.20 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 158.6, 151.2, 149.7, 145.8, 138.1, 130.9, 130.3, 107.3, 98.1, 93.8, 14.2, 9.1; **HRMS** (ESI, *m/z*): Calculated for $C_{14}H_{13}IN_3Se$ $[M+H]^+$: 429.9314, found 429.9309.

4-(2-Methyl-3-(methylselanyl)pyrazolo[1,5-*a*]pyrimidin-7-yl)benzonitrile(3bn): Orange solid; 95% (62.3 mg); m.p. 146-148 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.4 Hz, 1H), 8.17 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 4.4 Hz, 1H), 2.59 (s, 3H), 2.20 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 158.8, 151.1, 149.6, 144.5, 135.1, 132.5, 130.1, 118.2, 114.7, 107.8, 94.3, 14.1, 9.0; **HRMS** (ESI, *m/z*): Calculated for $C_{15}H_{13}N_4Se$ $[M+H]^+$: 329.0300, found 329.0285.

2,5-Dimethyl-7-phenyl-3-(phenylthio)pyrazolo[1,5-*a*]pyrimidine(3ca): Yellow gummy solid; 79% (52.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.09 – 7.98 (m, 2H), 7.57 (d, *J* = 3.5 Hz, 3H), 7.18 (t, *J* = 7.7 Hz, 2H), 7.15 – 7.00 (m, 3H), 6.81 (s, 1H), 2.67 (s, 3H), 2.47 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.9, 159.4, 151.5, 146.4, 138.6, 131.3, 130.8, 129.5, 128.9, 128.8, 126.0, 125.0, 109.2, 94.4, 25.1, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{18}N_3S$ $[M+H]^+$: 322.1216, found 322.1221.

7-(3-Methoxyphenyl)-2-methyl-3-(phenylthio)pyrazolo[1,5-*a*]pyrimidine(3cb): Brown gummy solid, 75% (52.0 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 4.4, 1.5 Hz, 1H), 7.66 (s, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 2H), 7.16 – 6.99 (m, 4H), 6.95 (d, *J* = 4.6 Hz, 1H), 3.90 (s, 3H), 2.52 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.7, 159.6, 151.6, 150.6, 147.1, 138.2, 131.8, 130.0, 128.9, 126.2, 125.3, 121.9, 117.1, 115.2, 108.2, 96.0, 55.6, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{17}N_3OSNa$ $[M+Na]^+$: 370.0985, found 370.0976.

7-(4-Iodophenyl)-2-methyl-3-(phenylthio)pyrazolo[1,5-*a*]pyrimidine(3cc): Brown gummy mass; 65% (57.7 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.4 Hz, 1H), 7.94 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.18 (t, *J* = 7.7 Hz, 2H), 7.14 – 7.03 (m, 3H), 6.93 (d, *J* = 4.3 Hz, 1H), 2.51 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.8, 151.5, 150.6, 146.2, 138.2, 138.0, 131.0, 130.9, 130.0, 129.0, 126.2, 125.3, 107.9, 98.4, 96.4, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{15}IN_3S$ $[M+H]^+$: 444.0026, found 444.0016.

7-(4-Bromophenyl)-2-methyl-3-(phenylthio)pyrazolo[1,5-*a*]pyrimidine(3cd): Off white solid; 68% (53.9 mg); m.p. 116-118 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.6 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.2 Hz, 2H), 7.19 (t, *J* = 7.8 Hz, 2H), 7.10 (d, *J* = 7.6 Hz, 3H), 6.94 (d, *J* = 4.6 Hz, 1H), 2.52 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 159.8, 151.5, 150.6, 146.1, 138.0, 132.2, 131.1, 129.5, 129.0, 126.2, 126.1, 125.4, 107.9, 96.5, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{19}H_{14}BrN_3SNa$ $[M+Na]^+$:417.9988, found 417.9984.

2,5-Dimethyl-7-phenyl-3-(p-tolylthio)pyrazolo[1,5-*a*]pyrimidine(3ce): Brown oil, 86% (59.5 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.62 – 7.50 (m, 3H), 7.11 – 6.90 (m, 4H), 6.80 (s, 1H), 2.67 (s, 3H), 2.47 (s, 3H), 2.26 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.8, 159.3, 151.4, 146.4, 135.0, 134.9, 131.2, 130.9, 129.6, 129.5, 128.8, 126.4, 109.1, 95.1, 25.1, 21.0, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{21}H_{20}N_3S$ $[M+H]^+$:346.1372, found 346.1381.

3-((4-Methoxyphenyl)thio)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(3cf): Yellow gummy mass; 76% (55.1 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 6.8, 3.0 Hz, 2H), 7.60 – 7.53 (m, 3H), 7.15 (d, *J* = 8.9 Hz, 2H), 6.76 (d, *J* = 11.9 Hz, 3H), 3.75 (s, 3H), 2.69 (s, 3H), 2.49 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 160.7, 159.0, 158.1, 151.3, 146.3, 138.5, 131.2, 130.9, 129.5, 128.9, 128.8, 114.6, 109.1, 96.3, 55.4, 25.1, 13.3; **HRMS** (ESI, *m/z*): Calculated for $C_{21}H_{20}N_3OS$ $[M+H]^+$:362.1322, found 362.1330.

3-((4-Chlorophenyl)thio)-2,5-dimethyl-7-phenylpyrazolo[1,5-*a*]pyrimidine(3cg): White solid; 46% (33.6 mg); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 6.4, 2.6 Hz, 2H), 7.62 – 7.54 (m, 3H), 7.14 (d, *J* = 6.9 Hz, 2H), 7.01 (d, *J* = 8.5 Hz, 2H), 6.83 (s, 1H), 2.67 (s, 3H), 2.45 (s, 3H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 161.1, 159.3, 151.4, 146.5, 137.3, 131.3, 130.9, 130.7, 129.5, 128.9, 128.9, 127.2, 109.3, 94.0, 25.1, 13.2; **HRMS** (ESI, *m/z*): Calculated for $C_{20}H_{16}ClN_3SK$ $[M+K]^+$: 404.0385, found 404.0383.

7-Phenyl-3-(phenylthio)pyrazolo[1,5-*a*]pyrimidine(3ch): Yellow solid; 62% (37.7 mg); m.p. 135-137 °C; **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.4 Hz, 1H), 8.33 (s, 1H), 8.05 (dd, *J* = 6.7, 3.1 Hz, 2H), 7.62 – 7.58 (m, 3H), 7.20 (d, *J* = 4.4 Hz, 4H), 7.10 (q, *J* = 4.7 Hz, 1H), 7.02 (d, *J* = 4.4 Hz, 1H); **^{13}C {^{1}H} NMR** (126 MHz, $CDCl_3$) δ 151.0, 150.7, 150.3, 148.0, 138.3, 131.6, 130.5, 129.5, 129.0, 128.9, 126.7, 125.6, 108.6, 97.9; **HRMS** (ESI, *m/z*): Calculated for $C_{18}H_{14}N_3S$ $[M+H]^+$:304.0903, found 304.0903.

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